Supporting Information

Alkyl Nitrite-Enabled Palladium-Catalyzed Terminal Selective Oxidative Cyclization of 4-Penten-1-ols

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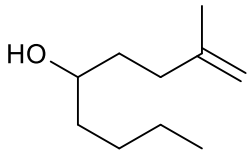
General Information

Unless otherwise indicated, all reactions were performed under an oxygen atmosphere (1 atm). $PdCl_2(MeCN)_2$[1] was prepared as described in the literature. Deionized water was used as a solvent. *t*-BuOH was distilled over CaH_2 before use. BQ was purified by sublimation. Other chemicals were also commercially available and were used without further purification. Flash column chromatography was performed using silica gel SILICYCLE SiliaFlash F60 (40–63 μm, 230–400 mesh). NMR spectra were recorded on either a Bruker AV-300N (300 MHz (^{1}H), 75 MHz (^{13}C)) spectrometer or a JEOL JNM-AL400 (400 MHz (^{1}H), 100 MHz (^{13}C)) spectrometer. Chemical shift values (σ) were expressed relative to $SiMe_4$. High-resolution mass spectra were recorded on a JEOL JMS-T100LC spectrometer (ESI-TOF MS) with positive ionization mode.

Preparation of Substrates 1

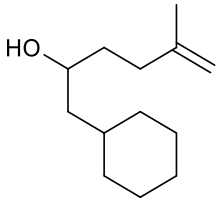
Substrates **1a**,[2] **1j**,[3] **1r**,[4] and **1u**[5] were prepared as described in the literature. Substrates **1b−1i**, **1k−1q**, **1s**, and **1t** were prepared as described below.

Synthesis of 2-methyl-1-nonen-5-ol (1b)



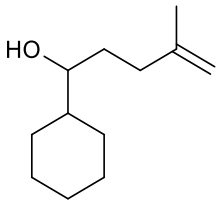
A two-neck flask equipped with a dropping funnel and a three-way cock was dried and filled with Ar. To the flask, *n*-BuLi (20.8 mL, 33.4 mmol, 1.2 eq., 1.6 M in hexanes) and THF (12.6 mL) were added to prepare a 1.0 M *n*-BuLi solution. 4-Methyl-4-pentenal[6] (3.21 mL, 27.8 mmol) and THF (5.4 mL) were added dropwise to the solution by the dropping funnel at -78 °C over 3 min. The dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was warmed to room temperature and stirred at room temperature for 2.5 h. Saturated NH_4Cl aq. (20 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (40 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (40 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 10:1) afforded **1b** as a pale yellow oil (1.45 g, 9.27 mmol, 33% yield). The NMR spectral data were in accordance with those reported in the literature.[7]

Synthesis of α-(3-methyl-3-buten-1-yl)cyclohexaneethanol (1c)



CyclohexylmethylMgBr was prepared as described in the literature.[8] Mg (1.15 g, 47.2 mmol, 2.7 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (3.9 mL) were added, and the mixture was stirred until the yellow iodine color had faded. THF (11.7 mL) was then added. (Bromomethyl)cyclohexane (2.9 mL, 20.7 mmol, 1.2 eq.) and THF (3.9 mL) were added in the dropping funnel. The THF solution of (bromomethyl)cyclohexane was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was heated at 50 °C for 5 h. 4-Methyl-4-pentenal[5] (1.9 mL, 17.3 mmol, 1.0 eq.) and THF (21 mL) were added to the dropping funnel, and THF (52 mL) was added to the reaction mixture. The solution of 4-methyl-4-pentenal was added dropwise to the reaction mixture at room temperature over 2 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 16 h. HCl aq. (1.0 M, 30 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 10:1) afforded **1c** as a pale yellow oil (1.71 g, 8.71 mmol, 50% yield).
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.71 (s, 2H, C=CH_2), 3.76–3.69 (m, 1H), 2.22–2.02 (m, 2H), 1.81–1.08 (m, 14H, CH_2, OH, cyclohexyl), 1.74 (s, 3H, Me), 1.01–0.79 (m, 2H, –CH_2–cyclohexyl). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.3, 110.3, 69.4, 45.8, 36.2, 34.6, 34.45, 34.37, 33.2, 26.9, 26.7, 26.5, 22.8.

Synthesis of α-(3-methyl-3-buten-1-yl)cyclohexanemethanol (1d)

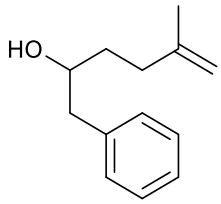


CyclohexylMgBr was prepared as described in the literature.[9] Mg (1.17 g, 48.0 mmol, 2.4 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (25.5 mL) were added. Bromocyclohexane (2.9 mL, 24.0 mmol, 1.2 eq.) and THF (9.1 mL) were added in the dropping funnel. The THF solution of bromocyclohexane was added dropwise to the flask, keeping

the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was stirred until the reaction mixture reaches room temperature. 4-Methyl-4-pentenal[5] (2.3 mL, 20.0 mmol, 1.0 eq.) and THF (20 mL) were added to the dropping funnel, and THF (50 mL) was added to the reaction mixture. The solution of 4-methyl-4-pentenal was added dropwise to the reaction mixture at room temperature over 3 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 18 h. HCl aq. (1.0 M, 40 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 9:1) afforded **1d** as a pale yellow oil (1.44 g, 7.93 mmol, 40% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.72 (s, 2H, C=CH_2), 3.38–3.34 (m, 1H), 2.25–2.01 (m, 2H), 1.83–0.95 (m, 14H, CH_2, OH, cyclohexyl), 1.74 (s, 3H, Me). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.4, 110.3, 76.3, 44.0, 34.6, 32.3, 29.6, 28.1, 26.9, 26.7, 26.5, 22.8.

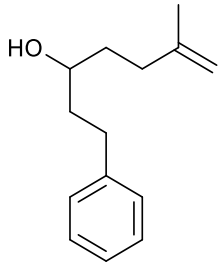
Synthesis of α-(3-Methyl-3-buten-1-yl)benzeneethanol (1e)



BnMgBr was prepared as described in the literature.[10] Mg (0.72 g, 29.7 mmol, 1.4 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (130 mL) were added, and the mixture was stirred until the yellow iodine color had faded. Benzyl bromide (2.9 mL, 24.7 mmol, 1.2 eq.) and THF (5.0 mL) were added in the dropping funnel. The THF solution of benzyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 3 h. 4-Methyl-4-pentenal[5] (2.4 mL, 20.6 mmol, 1.0 eq.) and THF (5.0 mL) were added to the dropping funnel. The solution of 4-methyl-4-pentenal was added dropwise at room temperature over 6 min to the reaction mixture. The dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 16 h. HCl aq. (1.0 M, 40 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 8:1) afforded **1e** as a pale yellow oil (2.16 g, 11.4 mmol, 55% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.23 (m, 5H, Arom), 4.751 (s, 1H, C=C*H*H), 4.747 (s, 1H, C=CH*H*), 3.89–3.80 (m, 1H), 2.87 (dd, *J* = 13.5 Hz, 4.4 Hz, 1H), 2.70 (dd, *J* = 13.5 Hz, 8.4 Hz, 1H), 2.36–2.10 (m, 2H), 1.76 (s, 3H, Me), 1.74–1.65 (m, 2H), 1.61 (s, 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.0, 138.8, 129.8 (2C), 128.9 (2C), 126.8, 110.5, 72.8, 44.4, 34.9, 34.4, 22.8.

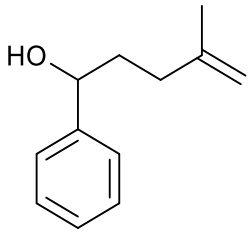
Synthesis of α-(3-Methyl-3-buten-1-yl)benzenepropanol (1f)



PhenethylMgBr was prepared as described in the literature.[11] Mg (1.66 g, 68.2 mmol, 2.4 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (10.0 mL) were added, and the mixture was stirred until the yellow iodine color had faded. Phenethyl bromide (4.6 mL, 34.1 mmol, 1.2 eq.) was added in the dropping funnel. Phenethyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (4.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 3 h. 4-Methyl-4-pentenal[5] (3.28 mL, 28.4 mmol, 1.0 eq.) and THF (5.0 mL) were added to the dropping funnel, and THF (15.5 mL) was added to the reaction mixture. The solution of 4-methyl-4-pentenal was added dropwise at room temperature over 1 min to the reaction mixture. The dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 17 h. Saturated NH_4Cl aq. (50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 7:1) afforded **1f** as a pale yellow oil (1.10 g, 5.36 mmol, 19% yield).

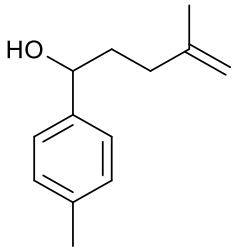
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17–7.01 (m, 5H, arom), 4.57–4.56 (m, 2H, C=CH_2), 3.52–3.48 (m, 1H), 2.70–2.47 (m, 2H), 2.05–1.88 (m, 2H), 1.58 (s, 3H, Me), 1.68–1.35 (m, 5H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.2, 142.5, 128.7, 126.2, 110.5, 71.6, 39.4, 35.7, 34.4, 32.4, 22.8.

Synthesis of 4-methyl-1-phenyl-4-penten-1-ol (1g)



Mg (0.642 g, 26.4 mmol, 1.2 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (140 mL) were added. Bromobenzene (2.80 mL, 26.4 mmol, 1.2 eq.) and THF (10 mL) were added in the dropping funnel. The THF solution of bromobenzene was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was refluxed for 1.5 h (bath temp. 70 °C). 4-Methyl-4-pentenal[5] (2.54 mL, 22.0 mmol, 1.0 eq.) and THF (10 mL) were added to the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 8 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was refluxed for 6 h (bath temp. 70 °C). After cooling to room temperature, HCl aq. (1.0 M, 50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 9:1) afforded **1g** as a pale yellow oil (1.76 g, 9.95 mmol, 65% yield). The NMR spectral data were in accordance with those reported in the literature.[12]

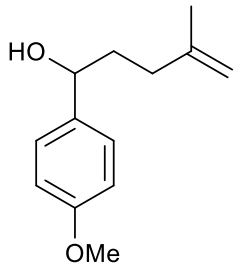
Synthesis of 4-methyl-1-(*p*-tolyl)pent-4-en-1-ol (1h)



4-MethylphenylMgBr was prepared as described in the literature.[13] Mg (0.78 g, 32.2 mmol, 1.3 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (13 mL) were added. *p*-Bromotoluene (3.60 mL, 29.3 mmol, 1.2 eq.) and THF (5.0 mL) were added in the dropping funnel. The THF solution of *p*-bromotoluene was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 30 min. 4-Methyl-4-pentenal[5] (2.82 mL, 24.4 mmol, 1.0 eq.) and THF (40 mL) were added to the dropping funnel, and THF (95 mL) was added to the reaction mixture. The solution of 4-methyl-4-

pentenal was added dropwise to the reaction mixture at room temperature over 5 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 17 h. HCl aq. (1.0 M, 30 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 9:1) afforded **1h** as a pale yellow oil (2.17 g, 11.4 mmol, 47% yield).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18–7.10 (m, 4H, arom), 4.65 (s, 1H, C=C*H*H), 4.63 (s, 1H, C=CH*H*), 4.70–4.56 (m, 1H), 2.28 (s, 3H, $C_6H_4CH_3$), 2.06–1.74 (m, 5H, CH_2, OH), 1.65 (s, 3H, Me). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 145.8, 142.0, 137.6, 129.5 (2C), 126.2 (2C), 110.4, 74.5, 37.1, 34.4, 22.9, 21.4.

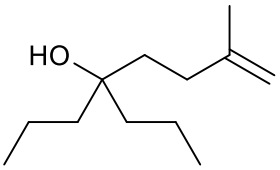
Synthesis of 1-(*p*-methoxyphenyl)-4-methylpent-4-en-1-ol (1i)



4-MethoxyphenylMgBr was prepared as described in the literature.[14] A three-neck flask equipped with a three-way cock was dried and filled with Ar. To the flask, LiCl (1.12 g, 26.5 mmol, 1.5 eq.) was added, and the flask was equipped with a dropping funnel and a reflux condenser. The flask was heated with a heat gun under vacuum for 20 min. To the flask, Mg (1.28 g, 52.5 mmol, 2.0 eq.), THF (50.5 mL), and DIBAL-H (0.17 mL, 0.17 mmol, 0.01 eq., 1.0 M in hexanes) were added. The reaction mixture was stirred at room temperature for 5 min. *p*-Bromoanisole (2.60 mL, 21.0 mmol, 1.2 eq.) was placed in the dropping funnel, and was added dropwise to the flask at 0 °C. After the addition, the dropping funnel was washed with THF (2.5 mL) that was also added to the reaction mixture. The mixture was stirred at 0 °C for 20 min. 4-Methyl-4-pentenal[5] (2.0 mL, 17.5 mmol, 1.0 eq.) and THF (15.4 mL) were placed in the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 2 min. The dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 13 h. HCl aq. (1.0 M, 50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 4:1) afforded **1i** as a pale yellow oil (1.92 g, 9.31 mmol, 53% yield).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 8.6 Hz, 2H, arom), 6.88 (d, J = 8.6 Hz, 2H, arom), 4.73–4.72 (m, 1H, C=C*H*H), 4.70 (m, 1H, C=CH*H*), 4.64–4.62 (m, 1H), 3.81 (s, 3H, OMe), 2.17–1.76 (m,

5H, CH_2, OH), 1.73 (s, 3H, Me). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.4, 145.8, 137.2, 127.5 (2C), 114.2 (2C), 110.4, 74.2, 55.6, 37.1, 34.4, 22.8.

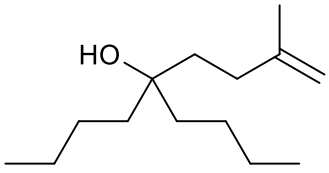
Synthesis of 7-methyl-4-*n*-propyl-7-octen-4-ol (1k)



Compound **1k** was prepared similarly as described in the literature.[3] Mg (3.08 g, 126.8 mmol, 3.6 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (76 mL) were added. *n*-Propyl bromide (9.55 mL, 105.7 mmol, 3.0 eq.) and THF (25 mL) were added in the dropping funnel. The THF solution of *n*-propyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was stirred for 30 min at room temperature. Ethyl 4-methyl-4-pentenoate[2] (5.60 mL, 35.22 mmol, 1.0 eq.) and THF (5.0 mL) were added to the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 7 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The reaction mixture was stirred at room temperature. After 15 h, saturated NH_4Cl aq. (50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with THF (25 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 10:1) afforded **1k** as a colorless oil (3.66 g, 19.83 mmol, 56% yield).

^1H NMR (300 MHz, $CDCl_3$) δ 4.70 (s, 1H, C=C*H*H), 4.69 (s, 1H, C=CH*H*), 2.04–1.99 (m, 2H, CH_2), 1.74 (s, 3H, Me), 1.59–1.53 (m, 2H, CH_2), 1.45–1.27 (m, 8H, CH_2), 1.19 (s, 1H, OH), 0.94–0.90 (t, J = 7.1 Hz, 6H, CH_3). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 146.7, 109.9, 74.7, 41.9, 37.5, 32.0, 23.0, 17.1, 15.0.

Synthesis of 5-*n*-butyl-2-methyl-1-nonen-5-ol (1l)

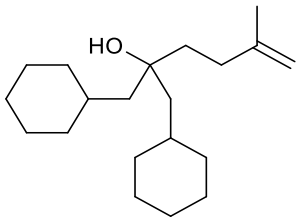


Compound **1l** was prepared similarly as described in the literature.[3] A two-neck flask equipped with a dropping funnel and a three-way cock was dried and filled with Ar. To the flask, *n*-BuLi (67.5 mL, 108 mmol, 3.0 eq., 1.6 M in hexanes) and THF (40.5 mL) were added to prepare a 1.0 M *n*-BuLi solution. Ethyl 4-methyl-4-pentenoate[2] (5.81 mL, 36.0 mmol) and THF (5.0 mL) were added dropwise

to the solution by the dropping funnel at -78 °C over 4 min. The dropping funnel was washed with THF (5.0 mL) that was also added to the reaction mixture. The mixture was warmed to room temperature and stirred at room temperature for 2.5 h. Saturated NH_4Cl aq. (20 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (40 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (40 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 10:1) afforded **1l** as a pale yellow oil (4.11 g, 19.3 mmol, 54% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.703 (s, 1H, C=CH*H*), 4.700 (s, 1H, C=C*H*H), 2.05–1.99 (m, 2H, CH_2), 1.75 (s, 3H, Me), 1.60–1.53 (m, 2H, CH_2), 1.64–1.23 (m, 12H, CH_2), 1.83 (s, 1H, OH), 0.93–0.89 (t, J = 6.8 Hz, 6H, CH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.8, 109.9, 74.7, 39.2 (2C), 37.5, 32.0, 26.0 (2C), 23.7 (2C), 23.0, 14.5 (2C).

Synthesis of 1-cyclohexyl-2-(cyclohexylmethyl)-5-methylhex-5-en-2-ol (1m)

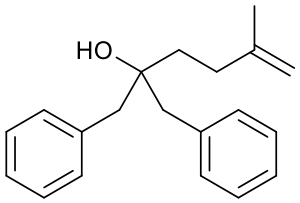


CyclohexylmethylMgBr was prepared as described in the literature.[8] Mg (4.40 g, 180.4 mmol, 7.9 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and THF (14 mL) were added, and the mixture was stirred until the yellow iodine color had faded. THF (42 mL) was then added. (Bromomethyl)cyclohexane (8.5 mL, 61.4 mmol, 2.7 eq.) and THF (10 mL) were placed in the dropping funnel. The THF solution of (bromomethyl)cyclohexane was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with THF (4.0 mL) that was also added to the reaction mixture. The mixture was heated at 50 °C for 5 h. Ethyl 4-methyl-4-pentenoate[2] (3.6 mL, 22.8 mmol, 1.0 eq.) was placed in the dropping funnel, and was added dropwise to the reaction mixture at 0 °C over 2 min. The dropping funnel was washed with THF (2.0 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 16 h. Saturated NH_4Cl aq. (30 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ethyl acetate (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 13:1) afforded **1m** as a pale yellow oil (0.45 g, 1.46 mmol, 6% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.702 (s, 1H, C=CH*H*), 4.700 (s, 1H, C=C*H*H), 2.03–1.98 (m, 2H, CH_2), 1.75 (s, 3H, Me), 1.80–0.91 (m, 29H, CH_2, cyclohexylmethyl, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.7, 109.9, 76.3, 47.7, 38.3, 35.75 (2C), 35.73 (2C), 33.7 (2C), 32.5, 31.6, 26.87 (2C), 26.86 (2C),

26.6 (2C), 23.1.

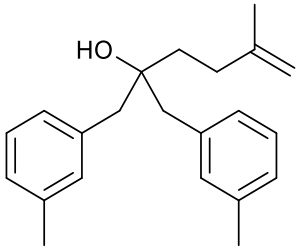
Synthesis of 2-benzyl-5-methyl-1-phenyl-5-hexen-2-ol (1n)



Compound **1n** was prepared similarly as described in the literature.[15] Mg (3.43 g, 141 mmol, 3.6 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and diethyl ether (80 mL) were added. Benzyl bromide (14.0 mL, 117 mmol, 3.0 eq.) and diethyl ether (20 mL) were added in the dropping funnel. The diethyl ether solution of benzyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with diethyl ether (4 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 3 h. Ethyl 4-methyl-4-pentenoate[2] (6.24 mL, 39.2 mmol, 1.0 eq.) and diethyl ether (80 mL) were placed in the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 15 min. The dropping funnel was washed with diethyl ether (10 mL) that was also added to the reaction mixture. The mixture was refluxed for 20 min (bath temp. 40 °C). After cooling to room temperature, the reaction mixture was stirred at room temperature. After 15 h, saturated NH_4Cl aq. (100 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with diethyl ether (100 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (150 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 15:1) afforded **1n** as a colorless oil (5.71 g, 20.4 mmol, 52% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.23 (m, 10H, arom), 4.68 (s, 1H, C=CH*H*), 4.65 (s, 1H, C=C*H*H), 2.83 (s, 4H, CH_2), 2.24–2.18 (m, 2H, CH_2), 1.68 (s, 3H, CH_3), 1.55–1.47 (m, 2H, CH_2), 1.40 (s, 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.0, 137.5, 131.0, 128.5, 126.8, 110.1, 74.4, 45.7, 36.5, 32.3, 23.0.

Synthesis of 5-methyl-2-(3-methylbenzyl)-1-(3-methylphenyl)-5-hexen-2-ol (1o)

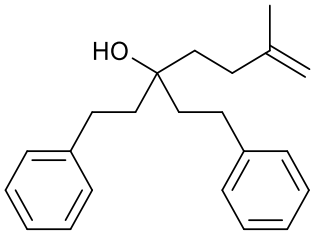


Compound **1o** was prepared similarly as described in the literature.[15] Mg (1.38 g, 56.9 mmol, 3.15 eq.)

was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and diethyl ether (3.3 mL) were added. α-Bromo-*m*-xylene (7.3 mL, 54.2 mmol, 3.0 eq.) and diethyl ether (3.8 mL) were added in the dropping funnel. The diethyl ether solution of α-bromo-*m*-xylene was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with diethyl ether (1 mL) that was also added to the reaction mixture. The mixture was refluxed for 1 h (bath temp. 40 °C). After cooling to room temperature, the reaction mixture was diluted with diethyl ether (36 mL). Ethyl 4-methyl-4-pentenoate[2] (2.9 mL, 18.1 mmol, 1.0 eq) and diethyl ether (51.6 mL) were placed in the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 30 min. The dropping funnel was washed with diethyl ether (2 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature. After 13 h, saturated NH_4Cl aq. (50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with diethyl ether (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 15:1) afforded **1o** as a colorless oil (1.11 g, 3.59 mmol, 20% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–6.99 (m, 8H, arom), 4.64 (s, 1H, C=CH*H*), 4.61 (s, 1H, C=C*H*H), 2.75 (s, 4H, CH_2), 2.30 (s, 6H, CH_3), 2.20–2.14 (m, 2H, CH_2), 1.64 (s, 3H, CH_3), 1.48–1.42 (m, 2H, CH_2), 1.38 (s, 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.2, 138.1, 137.4, 131.9, 128.4, 128.0, 127.6, 110.1, 74.4, 45.7, 36.6, 32.5, 23.0, 21.8.

Synthesis of 6-methyl-3-phenethyl-1-phenylhept-6-en-3-ol (1p)

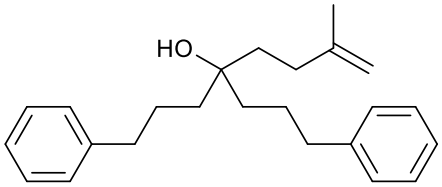


Compound **1p** was prepared similarly as described in the literature.[15] Mg (4.52 g, 186.0 mmol, 6.2 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 and diethyl ether (35 mL) were added. Phenethyl bromide (12.2 mL, 90.1 mmol, 3.0 eq.) and diethyl ether (10 mL) were placed in the dropping funnel. The diethyl ether solution of phenethyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with diethyl ether (2 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 3 h. To the flask, diethyl ether (40 mL) was added. Ethyl 4-methyl-4-pentenoate[2] (4.8 mL, 30.1 mmol, 1.0 eq.) and diethyl ether (86 mL) were placed in the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 15 min. The

dropping funnel was washed with diethyl ether (2 mL) that was also added to the reaction mixture. The reaction mixture was stirred at room temperature. After 14 h, saturated NH_4Cl aq. (100 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with diethyl ether (100 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (150 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 7:1) afforded **1p** as a pale yellow oil (6.31 g, 20.5 mmol, 68% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.19 (m, 10H, arom), 4.77 (s, 2H, C=CH_2), 2.74–2.68 (m, 4H, CH_2), 2.16–2.10 (m, 2H, CH_2), 1.90–1.84 (m, 4H, CH_2), 1.80 (s, 3H, CH_3), 1.79–1.73 (m, 2H, CH_2), 1.37 (s, 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.3, 142.7, 128.8, 128.7, 126.2, 110.4, 74.6, 41.5, 37.4, 32.2, 30.4, 23.0.

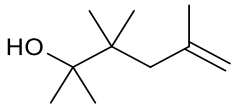
Synthesis of 7-methyl-1-phenyl-4-(3-phenylpropyl)oct-7-en-4-ol (1q)



Compound **1q** was prepared similarly as described in the literature.[15] Mg (2.39 g, 98.3 mmol, 4.5 eq.) was placed in a three-neck flask. The flask equipped with a dropping funnel, a reflux condenser, and a three-way cock was dried and filled with Ar. To the flask, a small amount of I_2 was added. 3-Phenylpropyl bromide (9.9 mL, 65.5 mmol, 3.0 eq.) and diethyl ether (45 mL) were placed in the dropping funnel. The diethyl ether solution of 3-phenylpropyl bromide was added dropwise to the flask, keeping the reaction mixture refluxing moderately. After the addition, the dropping funnel was washed with diethyl ether (2 mL) that was also added to the reaction mixture. The mixture was stirred at room temperature for 3 h. Ethyl 4-methyl-4-pentenoate[2] (3.47 mL, 21.8 mmol, 1.0 eq.) and diethyl ether (60 mL) were placed in the dropping funnel, and the solution was added dropwise to the reaction mixture at room temperature over 15 min. The dropping funnel was washed with diethyl ether (2 mL) that was also added to the reaction mixture. The reaction mixture was stirred at room temperature. After 12 h, saturated NH_4Cl aq. (50 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with diethyl ether (50 mL × 3), and the combined organic layer was washed with saturated NaCl aq. (80 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 7:1) afforded **1q** as a colorless oil (5.71 g, 17.0 mmol, 78% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.18 (m, 10H, arom), 4.70 (s, 1H, C=CH*H*), 4.67 (s, 1H, C=C*H*H), 2.64–2.59 (m, 4H, CH_2), 1.97–1.92 (m, 2H, CH_2), 1.73 (s, 3H, CH_3), 1.65–1.46 (m, 10H, CH_2), 1.17 (s, 1H, OH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 146.5, 142.6, 128.7, 128.6, 126.1, 110.1, 74.5, 38.8, 37.3, 36.6, 31.9, 25.6, 22.9.

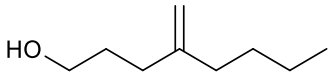
Synthesis of 2,3,3,5-tetramethylhex-5-en-2-ol (1s)



Compound **1s** was prepared similarly as described in the literature.[3] A two-neck flask equipped with a dropping funnel and a three-way cock was dried and filled with Ar. To the flask, MeLi (19.4 mL, 60.0 mmol, 3.0 eq., 3.1 M in dimethoxyethane) and diethyl ether (30.6 mL) were added to prepare a 1.0 M MeLi solution. A diethyl ether solution of methyl 2,2,4-trimethyl-4-pentenoate[4] (3.5 mL, 20.1 mmol in 5 mL diethyl ether) was added dropwise to the solution by the dropping funnel at -78 °C over 4 min. The dropping funnel was washed with diethyl ether (5.0 mL) that was also added to the reaction mixture. The mixture was warmed to room temperature and stirred at room temperature for 2 h. Saturated NH_4Cl aq. (20 mL) was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with diethyl ether (40 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (40 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 6:1) afforded **1s** as a pale yellow oil (1.80 g, 11.5 mmol, 57% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90–4.88 (m, 1H, C=C*H*H), 4.71–4.70 (m, 1H, C=CH*H*), 2.12 (s, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.44 (s, 1H, OH), 1.21 (s, 6H, CH_3), 0.95 (s, 6H, CH_3). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 145.1, 115.2, 76.1, 45.0, 41.4, 25.9, 25.6 (2C), 22.8 (2C).

Synthesis of 4-methylene-1-octanol (1t)



A two-neck flask equipped with a three-way cock and a reflux condenser was dried and filled with Ar. To the flask, ethyl 4-methyleneoctanoate[16] (2.43 g, 13.2 mmol) and THF (30 mL) were added. To the suspension of $LiAlH_4$ (1.00 g, 26.4 mmol, 2.0 eq.) in THF (20 mL), was added the ethyl 4-methyleneoctanoate solution at 0 °C. The reaction mixture was stirred at room temperature for 1.5 h. H_2O (0.95 mL, 52.8 mmol, 4.0 eq.) and 15% NaOH sol. (0.95 mL) were added to the reaction mixture at 0 °C. The reaction mixture was stirred at room temperature for 5 min, and H_2O (1.57 mL, 87.1 mmol, 6.6 eq.) was added to the reaction mixture and stirred for 15 min. The reaction mixture was filtered through celite. The filtrated aqueous layer was extracted with ethyl acetate (10 mL × 2), and the combined organic layer was washed with saturated NaCl aq. (30 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. Purification by silica gel column chromatography (hexane/ethyl acetate = 6:1) afforded **1t** as a pale yellow oil (1.80 g, 6.24 mmol, 47% yield).

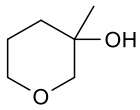
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.73 (s, 2H, C=CH_2), 3.65 (t, J = 6.5 Hz, 2H, –C*H*$_2$OH), 2.09 (t, J = 7.7 Hz, 2H), 2.02 (t, J = 7.5 Hz, 2H), 1.75–1.66 (m, 2H), 1.47–1.24 (m, 5H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 149.9, 109.3, 63.2, 36.0, 32.6, 31.0, 30.3, 22.8, 14.3.

Optimization of Reaction Conditions for the Oxidative Cyclization

The following procedure is representative. To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added, and O_2 was purged. *n*-BuONO (11.3 μL, 0.10 mmol), *t*-BuOH (0.3 mL) and H_2O (1.7 mL) were added to the reaction mixture, which was stirred at 40 °C for 1 h. Then, **1a** (60 μL, 50 mg, 0.50 mmol) was added over 5 h by a syringe pump. During the addition, the reaction mixture was stirred at 40 °C. After the addition, the reaction mixture was stirred at 40 °C for an additional 1 h (6 h in total). After cooling to room temperature, 1,1,2,2-tetrachloroethane was added as an internal standard. The reaction mixture was extracted with $CDCl_3$ five times, and the combined organic layer was dried over $MgSO_4$. After filtration, the sample was analyzed by ^1H NMR (300 MHz, $CDCl_3$).

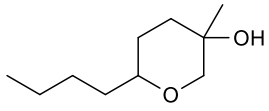
Synthesis of 3-Hydroxytetrahydropyrans 2

3-Hydroxy-3-methyltetrahydropyran (2a)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added, and O_2 was purged. *t*-BuOH (0.3 mL) and H_2O (1.7 mL) were added to the reaction mixture, which was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the mixture. Then, **1a** (60 μL, 50 mg, 0.50 mmol) was added over 5 h by a syringe pump. During the addition, the reaction mixture was stirred at 40 °C. After the addition, the reaction mixture was stirred at 40 °C for an additional 1 h (6 h in total). After cooling to room temperature, the reaction mixture was extracted with diethyl ether (2.0 mL × 5), and the combined organic layer was washed with NaOH aq. (1 M, 4.0 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under reduced pressure to afford **2a** as a pale yellow oil (57.9 mg, 0.498 mmol, 99% yield). The ^1H and ^{13}C NMR data were in accordance with those reported previously.[17]

6-*n*-Butyl-3-hydroxy-3-methyltetrahydropyran (2b)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1b** (93 μL, 78 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-

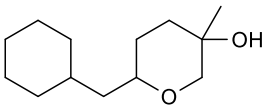
BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4:1). Compound **2b** was obtained as a pale yellow oil (45.6 mg, 0.26 mmol, 53% yield, major:minor = 57:43).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (dd, J = 10.8, 2.5 Hz, 1H), 3.30–3.19 (m, 1H), 3.22 (d, J = 10.8 Hz, 1H), 1.82–1.25 (m, 11H), 1.31 (s, 3H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 77.9, 76.8, 68.2, 37.9, 35.3, 30.0, 28.3, 25.1, 23.1, 14.4.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.59 (dd, J = 11.5, 2.8 Hz, 1H), 3.31 (d, J = 11.5 Hz, 1H), 3.24–3.14 (m, 1H), 2.52 (s, 1H), 1.77–1.18 (m, 10H), 1.11 (s, 3H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 78.2, 77.3, 67.2, 36.2, 36.1, 28.1, 28.0, 24.9, 23.1, 14.4.

HRMS (ESI): m/z calcd for $C_{10}H_{20}NaO_2$ $[M+Na]^+$ 195.1361, found 195.1355.

6-Cyclohexylmethyl-3-hydroxy-3-methyltetrahydropyran (2c)



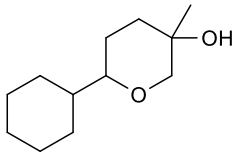
To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1c** (98 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4:1). Compound **2c** was obtained as a pale yellow oil (59.3 mg, 0.28 mmol, 56% yield, major:minor = 50:50).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.58 (dd, J = 11.5, 2.9 Hz, 1H), 3.33–3.25 (m, 1H), 3.29 (d, J = 11.5 Hz, 1H), 2.55 (s, 1H), 1.77–0.79 (m, 17H), 1.10 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 77.3, 75.6, 67.2, 44.2, 36.2, 34.3, 34.1, 33.5, 28.5, 26.9, 26.6, 26.5, 24.9.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (dd, J = 10.8, 2.5 Hz, 1H), 3.40–3.32 (m, 1H), 3.21 (dd, J = 10.8, 0.5 Hz, 1H), 1.82–0.82 (m, 18H), 1.30 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 76.8, 75.3, 68.2, 43.4, 37.9, 34.4, 34.3, 33.4, 30.6, 26.9, 26.7, 26.6, 25.1.

HRMS (ESI): m/z calcd for $C_{13}H_{24}NaO_2$ $[M+Na]^+$ 235.1668, found 235.1671.

6-Cyclohexyl-3-hydroxy-3-methyltetrahydropyran (2d)



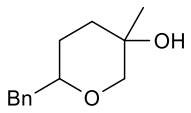
To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1d** (91 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 4:1). Compound **2d** was obtained as a pale yellow oil (43.7 mg, 0.21 mmol, 42% yield, major:minor = 69:31).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.59 (dd, J = 11.5, 3.0 Hz, 1H), 3.29 (d, J = 11.5 Hz, 1H), 2.98–2.92 (m, 1H), 2.52 (s, 1H), 1.93–0.89 (m, 15H), 1.10 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 82.5, 77.5, 67.3, 43.1, 36.3, 29.4, 29.0, 26.9, 26.6, 26.5, 24.8, 24.6.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.58 (dd, J = 10.7, 2.6 Hz, 1H), 3.19 (d, J = 10.7 Hz, 1H), 3.02–2.96 (m, 1H), 1.91–0.90 (m, 16H), 1.30 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 82.4, 77.1, 68.3, 42.5, 38.0, 29.6, 29.2, 26.9, 26.7, 26.6, 26.5, 25.0.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{22}NaO_2$ $[M+Na]^+$ 221.1512, found 221.1513.

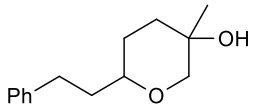
6-Benzyl-3-hydroxy-3-methyltetrahydropyran (2e)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1e** (95.1 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 11.5:1). Compound **2e** was obtained as a pale yellow oil (48.4 mg, 0.23 mmol,

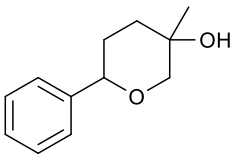
46% yield, major:minor = 51:49).
Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 3.61 (dd, J = 11.6, 2.9 Hz, 1H), 3.50–3.42 (m, 1H), 3.31 (d, J = 11.6 Hz, 1H), 2.93 (dd, J = 13.7, 6.6 Hz, 1H), 2.71 (dd, J = 13.7, 6.4 Hz, 1H), 2.62–2.06 (br s, 1H), 1.77–1.14 (m, 4H), 1.10 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 138.7, 129.7 (2C), 128.6 (2C), 126.6, 78.9, 77.6, 67.1, 42.9, 36.1, 27.5, 24.9.
Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.20 (m, 5H), 3.60 (dd, J = 10.8, 2.5 Hz, 1H), 3.57–3.48 (m, 1H), 3.23 (d, J = 10.5 Hz, 1H), 2.92 (dd, J = 13.7, 6.5 Hz, 1H), 2.70 (dd, J = 13.6, 6.6 Hz, 1H), 1.84–1.10 (m, 5H), 1.33 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 138.9, 129.6 (2C), 128.6 (2C), 126.6, 78.7, 77.6, 68.1, 42.2, 37.8, 29.5, 25.1.
HRMS (ESI): m/z calcd for $C_{13}H_{18}NaO_2$ $[M+Na]^+$ 229.1199, found 229.1201.

3-Hydroxy-3-methyl-6-phenethyltetrahydropyran (2f)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1f** (102 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3:1). Compound **2f** was obtained as a pale yellow oil (68.0 mg, 0.31 mmol, 62% yield, major:minor = 50:50).
Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 3.63 (dd, J = 10.5, 2.9 Hz, 1H), 3.30 (d, J = 11.5 Hz, 1H), 3.23–3.14 (m, 1H), 2.84–2.63 (m, 2H), 2.50 (s, 1H), 1.93–1.52 (m, 6H), 1.11 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.4, 128.8 (2C), 128.7 (2C), 126.1, 77.2, 77.0, 67.3, 38.0, 36.1, 32.1, 28.0, 24.9.
Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 3.62 (dd, J = 10.8, 2.5 Hz, 1H), 3.31–3.23 (m, 1H), 3.23 (d, J = 10.8 Hz, 1H), 2.82–2.60 (m, 2H), 1.93–1.40 (m, 7H), 1.32 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.4, 128.8 (2C), 128.7 (2C), 126.1, 76.8, 76.7, 68.2, 37.8, 37.2, 32.3, 30.0, 25.1.
HRMS (ESI): m/z calcd for $C_{14}H_{20}NaO_2$ $[M+Na]^+$ 243.1355, found 243.1366.

3-Hydroxy-3-methyl-6-phenyltetrahydropyran (2g)



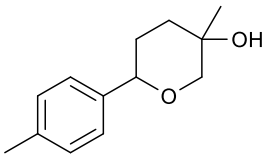
To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1g** (88 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 2:1). Compound **2g** was obtained as a pale yellow oil (35.9 mg, 0.22 mmol, 44% yield, major:minor = 54:46).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.26 (m, 5H), 4.31 (dd, J = 10.7, 2.8 Hz, 1H), 3.79 (dd, J = 11.6, 2.8 Hz, 1H), 3.54 (d, J = 11.6 Hz, 1H), 2.63 (s, 1H), 1.98–1.65 (m, 4H), 1.19 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.4, 128.7, 128.0, 126.1, 80.1, 67.0, 36.6, 29.9, 25.0.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29–7.19 (m, 5H), 4.32–4.28 (m, 1H), 3.66 (dd, J = 10.8, 2.3 Hz, 1H), 3.35 (d, J = 10.4 Hz, 1H), 1.91–1.68 (m, 4H), 1.49 (s, 1H), 1.35 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.2, 128.7, 127.9, 126.2, 79.8, 67.9, 38.2, 31.9, 25.2.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}NaO_2$ $[M+Na]^+$ 215.1050, found 215.1051.

3-Hydroxy-3-methyl-6-(*p*-tolyl)tetrahydropyran (2h)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1h** (95 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3.5:1). Compound **2h** was obtained as a pale yellow oil (53.4 mg, 0.26 mmol,

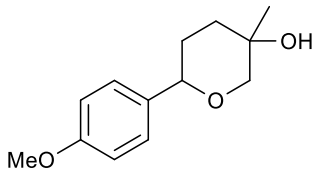
52% yield, major:minor = 59:41).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19–7.06 (m, 4H), 4.28–4.24 (m, 1H), 3.63 (dd, J = 10.8, 2.3 Hz, 1H), 3.33 (dd, J = 10.8, 2.3 Hz, 1H), 2.26 (s, 3H), 1.85–1.66 (m, 4H), 1.54 (br s, 1H), 1.33 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 139.2, 137.5, 129.4, 126.2, 79.6, 77.1, 67.9, 38.2, 31.8, 25.1, 21.5.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27–7.17 (m, 4H), 4.27 (dd, J = 11.2, 2.9 Hz, 1H), 3.78 (dd, J = 11.6, 2.7 Hz, 1H), 3.54 (d, J = 11.6 Hz, 1H), 2.83–2.01 (br s, 1H), 2.35 (s, 3H), 1.94–1.69 (m, 4H), 1.19 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 139.4, 137.6, 129.4, 126.0, 80.0, 77.7, 67.0, 36.6, 29.8, 25.0, 21.5.

HRMS (ESI): m/z calcd for $C_{13}H_{18}NaO_2$ $[M+Na]^+$ 229.1205, found 229.1211.

3-Hydroxy-6-(*p*-methoxyphenyl)-3-methyltetrahydropyran (2i)



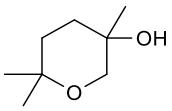
To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1i** (103 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 2:1). Compound **2i** was obtained as a pale yellow oil (65.7 mg, 0.30 mmol, 59% yield, major:minor = 53:47).

Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–6.86 (m, 4H), 4.34–4.31 (m, 1H), 3.80 (s, 3H), 3.69 (dd, J = 10.8, 2.2 Hz, 1H), 3.40 (d, J = 10.8 Hz, 1H), 1.92–1.73 (m, 4H), 1.56 (br s, 1H), 1.41 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.3, 134.4, 127.6 (2C), 114.1 (2C), 79.4, 77.1, 67.9, 55.6, 38.2, 31.7, 25.1.

Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–6.87 (m, 4H), 4.25 (dd, J = 10.9, 2.4 Hz, 1H), 3.80 (s, 3H), 3.76 (dd, J = 11.7, 2.7 Hz, 1H), 3.52 (d, J = 11.6 Hz, 1H), 2.68 (br s, 1H), 1.95–1.63 (m, 4H), 1.17 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 159.4, 134.5, 127.4 (2C), 114.1 (2C), 79.7, 77.8, 67.0, 55.6, 36.6, 29.6, 25.0.

HRMS (ESI): m/z calcd for $C_{13}H_{18}NaO_3$ $[M+Na]^+$ 245.1154, found 245.1155.

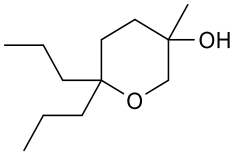
3-Hydroxy-3,6,6-trimethyltetrahydropyran (2j)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (0.050 mmol) were added and O_2 was introduced. *t*-BuOH (0.3 mL) and H_2O (1.7 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (56.5 μL, 0.50 mmol) was added to the solution. Then, **1j** (97 μL, 64 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C. The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with diethyl ether (2.0 mL × 5), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (4.0 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by alumina column chromatography (pentane/diethyl ether = 1:1). Compound **2j** was obtained as a pale yellow oil (45.8 mg, 0.38 mmol, 77% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.51 (d, J = 11.9 Hz, 1H), 3.35 (d, J = 12.0 Hz, 1H), 2.46 (s, 1H), 1.77–1.38 (m, 4H), 1.24 (s, 3H), 1.19 (s, 3H), 1.13 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 71.6, 70.9, 67.1, 33.1, 32.8, 30.1, 25.1, 22.3. HRMS (ESI): *m*/*z* calcd for $C_8H_{16}KO_2$ $[M+K]^+$ 183.0782, found 183.0788.

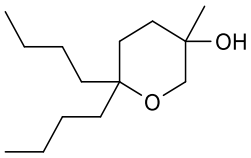
6,6-Di-*n*-propyl-3-hydroxy-3-methyltetrahydropyran (2k)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1k** (92 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 6:1). Compound **2k** was obtained as a pale yellow oil (83.8 mg, 0.42 mmol, 84% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44 (d, J = 11.8 Hz, 1H), 3.30 (d, J = 11.8 Hz, 1H), 2.58 (br s, 1H), 1.72–1.58 (m, 4H), 1.54–1.14 (m, 8H), 1.13 (s, 3H), 0.94–0.88 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 75.2, 70.2, 67.2, 41.3, 33.8, 32.5, 29.5, 25.0, 16.8, 16.7, 15.0 (2C). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{24}NaO_2$ $[M+Na]^+$ 223.1676, found 223.1679.

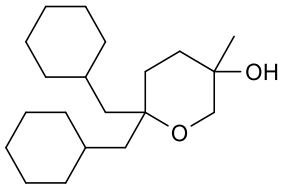
6,6-Di-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (2l)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1l** (106 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7:1). Compound **2l** was obtained as a pale yellow oil (97.7 mg, 0.43 mmol, 86% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 3.43 (d, J = 11.8 Hz, 1H), 3.30 (d, J = 11.9 Hz, 1H), 2.49 (br s, 1H), 1.71–1.57 (m, 4H), 1.56–1.20 (m, 12H), 1.12 (s, 3H), 0.93–0.88 (m, 6H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 75.2, 70.2, 67.2, 38.7, 32.5, 31.0, 29.6, 25.7, 25.6, 25.0, 23.7, 14.51, 14.46. HRMS (ESI): *m*/*z* calcd for $C_{14}H_{28}NaO_2$ $[M+Na]^+$ 251.1987, found 251.1982.

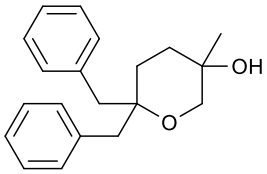
6,6-Di(cyclohexylmethyl)-3-hydroxy-3-methyltetrahydropyran (2m)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1m** (154 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 6:1). Compound **2m** was obtained as a pale yellow oil (79.2 mg, 0.26 mmol, 51% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.47 (d, J = 11.9 Hz, 1H), 3.27 (d, J = 12.0 Hz, 1H), 2.37 (s, 1H), 1.88–0.89 (m, 30H), 1.12 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 76.7, 70.4, 67.2, 46.8, 39.4, 35.9, 35.7, 34.9, 33.8, 33.7, 32.8, 30.7, 27.0 (2C), 26.9 (2C), 26.70, 26.67, 25.1. HRMS (ESI): *m*/*z* calcd for $C_{20}H_{36}NaO_2$ $[M+Na]^+$ 331.2607, found 331.2610.

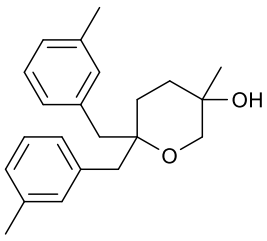
6,6-Dibenzyl-3-hydroxy-3-methyltetrahydropyran (2n)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1n** (140 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5:1). Compound **2n** was obtained as a pale yellow oil (62.8 mg, 0.21 mmol, 42% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.20 (m, 10H), 3.75 (d, J = 11.6 Hz, 1H), 3.51 (dd, J = 11.6, 2.0 Hz, 1H), 3.10 (d, J = 14.0 Hz, 1H), 2.85 (d, J = 13.2 Hz, 1H), 2.82 (d, J = 14.0 Hz, 1H), 2.64 (d, J = 13.6 Hz, 1H), 2.10 (s, 1H), 1.72–1.20 (m, 4H), 1.09 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 137.9, 137.8, 131.2, 130.9, 128.4, 128.3, 126.70, 126.68, 75.7, 70.7, 66.7, 44.8, 39.7, 32.7, 26.4, 24.6. HRMS (ESI): *m*/*z* calcd for $C_{20}H_{24}NaO_2$ $[M+Na]^+$ 319.1674, found 319.1687.

6,6-Di-*m*-methylbenzyl-3-hydroxy-3-methyltetrahydropyran (2o)

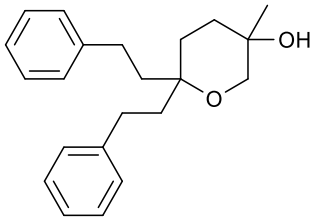


To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1o** (154 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was

stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5:1). Compound **2o** was obtained as a pale yellow oil (52.4 mg, 0.16 mmol, 32% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.01 (m, 8H), 3.76 (d, J = 11.7 Hz, 1H), 3.50 (dd, J = 11.7, 2.2 Hz, 1H), 3.05 (d, J = 13.9 Hz, 1H), 2.82 (d, J = 13.5 Hz, 1H), 2.79 (d, J = 13.8 Hz, 1H), 2.69 (d, J = 13.7 Hz, 1H), 2.37 (s, 3H), 2.31 (s, 3H), 2.17 (s, 1H), 1.64–1.28 (m, 4H), 1.10 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 137.93, 137.85, 137.8, 137.7, 132.0, 131.7, 128.3, 128.19, 128.16, 127.9, 127.4, 75.8, 70.7, 66.8, 45.0, 39.7, 32.7, 26.4, 24.6, 21.8, 21.7. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{28}NaO_2$ $[M+Na]^+$ 347.1987, found 347.1988.

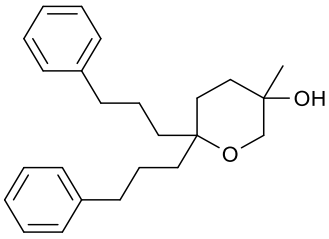
6,6-Diphenethyl-3-hydroxy-3-methyltetrahydropyran (2p)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1p** (154 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3:1). Compound **2p** was obtained as a pale yellow oil (90.0 mg, 0.27 mmol, 54% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26–7.11 (m, 10H), 3.46 (d, J = 11.9 Hz, 1H), 3.34 (d, J = 11.9 Hz, 1H), 2.64 (d, J = 8.8 Hz, 1H), 2.61 (d, J = 8.6 Hz, 1H), 2.56 (d, J = 8.2 Hz, 1H), 2.53 (d, J = 9.1 Hz, 1H), 2.35 (br s, 1H), 2.05–1.58 (m, 8H), 1.09 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 142.7, 142.6, 128.84, 128.79, 128.7, 128.6, 126.3, 126.2, 74.8, 70.3, 67.1, 40.6, 33.9, 32.5, 30.04, 30.01, 29.3, 25.1. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{28}NaO_2$ $[M+Na]^+$ 347.1989, found 347.1990.

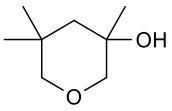
6,6-Di(3-phenylpropyl)-3-hydroxy-3-methyltetrahydropyran (2q)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1q** (168 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3:1). Compound **2q** was obtained as a pale yellow oil (88.8 mg, 0.25 mmol, 50% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20–7.07 (m, 10H), 3.22 (d, J = 11.9 Hz, 1H), 3.16 (d, J = 12.0 Hz, 1H), 2.54–2.49 (m, 4H), 2.29 (br s, 1H), 1.68–1.19 (m, 12H), 1.00 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.6, 142.5, 128.7, 128.6, 126.14, 126.09, 75.0, 70.1, 67.1, 38.5, 36.7, 36.50, 36.45, 32.4, 30.5, 29.6, 25.5, 25.1. HRMS (ESI): *m*/*z* calcd for $C_{24}H_{32}NaO_2$ $[M+Na]^+$ 375.2302, found 375.2318.

3-Hydroxy-3,5,5-trimethyltetrahydropyran (2r)

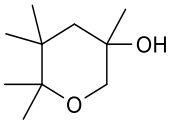


To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1r** (77 μL, 64 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 0.50 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with diethyl ether (2.0 mL × 5), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (4.0 mL) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (pentane/diethyl ether = 1:1). Compound **2r** was obtained as a pale yellow oil (41.0 mg, 0.28 mmol, 57% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (dd, J = 11.6, 1.6 Hz, 1H), 3.50 (d, J = 11.1 Hz 1H), 3.21 (d, J =

11.7 Hz, 1H), 3.07 (d, J = 11.1 Hz, 1H), 2.02 (s, 1H), 1.61 (d, J = 14.0 Hz, 1H), 1.35 (d, J = 14.1 Hz, 1H), 1.17 (s, 3H), 1.11 (s, 3H), 0.83 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 78.8, 68.9, 48.8, 30.9, 28.7, 26.9, 26.7. HRMS (ESI): m/z calcd for $C_8H_{16}KO_2$ $[M+K]^+$ 183.0782, found 183.0787.

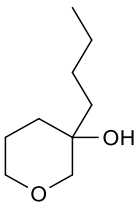
3-Hydroxy-3,5,5,6,6-pentamethyltetrahydropyran (2s)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1s** (90 μL, 78 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL×2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 2:1). Compound **2s** was obtained as a pale yellow oil (36.6 mg, 0.21 mmol, 42% yield).

^1H NMR (300 MHz, $CDCl_3$) δ 3.56 (d, J = 12.4 Hz, 1H), 3.43 (dd, J = 12.4, 2.4 Hz, 2H), 2.03 (br s, 1H), 1.62 (d, J = 14.5 Hz, 1H), 1.46 (dd, J = 14.4, 2.3 Hz, 1H), 1.18 (s, 3H), 1.15 (s, 6H), 1.10 (s, 3H), 0.81 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 77.2, 71.0, 69.3, 47.4, 35.4, 27.7, 26.9, 26.1, 24.4, 21.2. HRMS (ESI): m/z calcd for $C_{10}H_{20}NaO_2$ $[M+Na]^+$ 195.1361, found 195.1356.

3-*n*-Butyl-3-hydroxytetrahydropyran (2t)

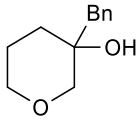


To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1t** (71.5 μL, 71 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL×2) and dried over $MgSO_4$. After filtration, the filtrate

was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3:1). Compound **2t** was obtained as a pale yellow oil (30.7 mg, 0.19 mmol, 38% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88–3.83 (m, 1H), 3.51 (dd, J = 11.4, 2.2 Hz, 1H), 3.37 (dt, J = 11.3, 2.6 Hz, 1H), 3.30 (d, J = 11.4 Hz, 1H), 2.39 (s, 1H), 1.93–1.30 (m, 10H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 76.5, 69.3, 68.6, 38.4, 34.2, 24.9, 23.7, 22.6, 14.4. HRMS (ESI): m/z calcd for $C_9H_{18}NaO_2$ $[M+Na]^+$ 181.1199, found 181.1204.

3-Benzyl-3-hydroxytetrahydropyran (2u)

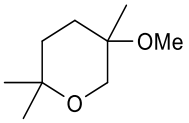


To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and H_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (22.7 μL, 0.20 mmol) was added to the solution. Then, **1u** (90 μL, 88 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.20 mmol × 4, total amount: 113.3 μL, 1.0 mmol). The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 3), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (3.0 mL×2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 3:1). Compound **2u** was obtained as a colorless oil (26.9 mg, 0.19 mmol, 38% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.20 (m, 5H), 3.82–3.77 (m, 1H), 3.49–3.38 (m, 3H), 2.80 (d, J = 13.5 Hz, 1H), 2.72 (d, J = 13.5 Hz, 1H), 2.15 (s, 1H), 1.88–1.54 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 136.5, 130.8 (2C), 128.6 (2C), 127.0, 76.0, 69.3, 68.5, 44.7, 34.4, 22.8. HRMS (ESI): m/z calcd for $C_{12}H_{16}NaO_2$ $[M+Na]^+$ 215.1043, found 215.1054.

Synthesis of 3-Methoxytetrahydropyrans 3

3-Methoxy-3,6,6-trimethyltetrahydropyran (3j)

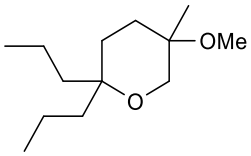


To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added and O_2 was introduced. MeOH (2.0 mL) was added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (56.5 μL, 0.50 mmol) was added to the solution. Then, **1j** (97 μL, 64 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was

stirred at 40 °C. The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was washed with saturated $NaHCO_3$ aq. (2.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (pentane/diethyl ether = 7:1). Compound **3j** was obtained as a pale yellow oil (22.9 mg, 0.12 mmol, 25% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (dd, *J* = 12.1, 1.8 Hz, 1H), 3.39 (d, *J* = 12.2 Hz, 1H), 3.23 (s, 3H), 1.81–1.31 (m, 4H), 1.23 (s, 3H), 1.20 (s, 3 H), 1.10 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 71.4, 71.2, 68.3, 49.3, 32.9, 29.8, 28.1, 24.5, 20.5. HRMS (ESI): *m*/*z* calcd for $C_9H_{20}NaO_2$ $[M+Na]^+$ 243.1355, found 243.1366.

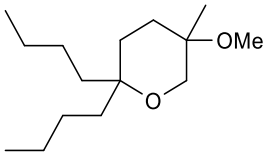
6,6-Di-*n*-propyl-3-methoxy-3-methyltetrahydropyran (3k)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added and O_2 was introduced. MeOH (2.0 mL) was added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (28.3 μL, 0.25 mmol) was added to the solution. Then, **1k** (92.2 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 10 h. During the addition, the reaction mixture was stirred at 40 °C. *n*-BuONO was added again 5 hours after the previous addition (0.25 mmol, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 8 h (reaction time: 18 h in total). After cooling to room temperature, the reaction mixture was washed with saturated $NaHCO_3$ aq. (2.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 12:1). Compound **3k** was obtained as a pale yellow oil (71.3 mg, 0.33 mmol, 66% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.51 (dd, *J* = 12.0, 1.4 Hz, 1H), 3.31 (d, *J* = 12.1 Hz, 1H), 3.22 (s, 3H), 1.75–1.22 (m, 12H), 1.10 (s, 3H), 0.93–0.87 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 75.0, 71.4, 67.3, 49.3, 38.8, 36.6, 29.8, 29.7, 20.5, 16.9, 16.7, 15.12, 15.05. HRMS (ESI): *m*/*z* calcd for $C_{13}H_{26}NaO_2$ $[M+Na]^+$ 237.1825, found 237.1833.

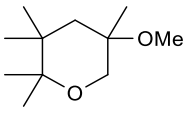
6,6-Di-*n*-butyl-3-methoxy-3-methyltetrahydropyran (3l)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added and O_2 was introduced. MeOH (2.0 mL) was added. The solution was stirred at 40 °C for 1 h. *n*-

BuONO (28.3 μL, 0.25 mmol) was added to the solution. Then, **1l** (106 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 10 h. During the addition, the reaction mixture was stirred at 40 °C. *n*-BuONO was added again 5 hours after the previous addition (0.25 mmol, total amount: 56.5 μL, 0.50 mmol). The mixture was kept at 40 °C for additional 8 h (reaction time: 18 h in total). After cooling to room temperature, the reaction mixture was washed with saturated $NaHCO_3$ aq. (2.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 11:1). Compound **3l** was obtained as a pale yellow oil (56.8 mg, 0.23 mmol, 47% yield).
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.51 (dd, *J* = 12.0, 1.2 Hz, 1H), 3.30 (d, *J* = 12.0 Hz, 1H), 3.22 (s, 3H), 1.75–1.56 (m, 4H), 1.41–1.20 (m, 12H), 1.10 (s, 3H), 0.94–0.87 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 75.0, 71.4, 67.3, 49.3, 36.1, 33.8, 29.80, 29.76, 25.8, 25.6, 23.72, 23.67, 20.5, 14.49, 14.48. HRMS (ESI): *m*/*z* calcd for $C_{15}H_{30}NaO_2$ $[M+Na]^+$ 265.2146, found 265.2150.

3-Methoxy-3,5,5,6,6-pentamethyltetrahydropyran (3s)



To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) and BQ (5.4 mg, 0.050 mmol) were added and O_2 was introduced. MeOH (2.0 mL) was added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (56.6 μL, 0.50 mmol) was added to the solution. Then, **1s** (90 μL, 78 mg, 0.50 mmol) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C. After the addition, the reaction mixture was stirred at 40 °C for an additional 1 h (6 h in total). After cooling to room temperature, the reaction mixture was washed with saturated $NaHCO_3$ aq. (2.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 11.5:1). Compound **3s** was obtained as a pale yellow oil (26.3 mg, 0.15 mmol, 30% yield).
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (dd, *J* = 12.6, 2.3 Hz, 1H), 3.40 (d, *J* = 12.6 Hz, 1H), 3.19 (s, 3H), 1.64 (dd, *J* = 14.6, 2.3 Hz, 1H), 1.42 (d, *J* = 14.6 Hz, 1H), 1.17 (s, 3H), 1.14 (s, 3H), 1.08 (s, 3H), 1.03 (s, 3 H), 0.80 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 77.0, 72.6, 68.1, 49.0, 42.9, 35.3, 27.5, 25.2, 24.1, 22.3, 21.5. HRMS (ESI): *m*/*z* calcd for $C_{11}H_{22}NaO_2$ $[M+Na]^+$ 209.1512, found 209.1514.

Control Experiment Using D_2O/*t*-BuOH instead of H_2O/*t*-BuOH

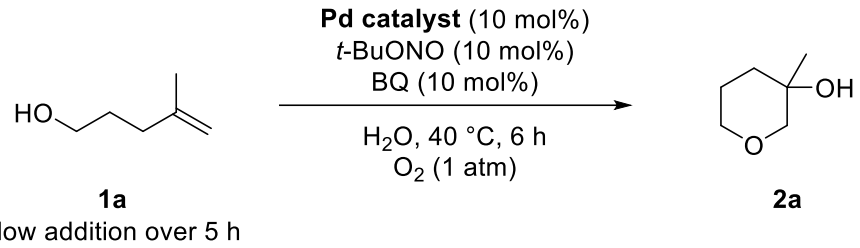
To a reaction vessel, $PdCl_2(MeCN)_2$ (13 mg, 0.050 mmol) was added and O_2 was introduced. *t*-BuOH (1.0 mL) and D_2O (1.0 mL) were added. The solution was stirred at 40 °C for 1 h. *n*-BuONO (11.3 μL, 0.10 mmol) was added to the solution. Then, **1l** (106 mg, 0.50 mmol, 2.5 M *t*-BuOH solution) was added to the solution using a syringe pump over 5 h. During the addition, the reaction mixture was stirred at 40 °C and *n*-BuONO was added every 1 h (0.10 mmol × 4, total amount: 56.5 μL, 0.50 mmol).

The mixture was kept at 40 °C for additional 1 h (reaction time: 6 h in total). After cooling to room temperature, the reaction mixture was extracted with chloroform (2.0 mL × 5), and the combined organic layer was washed with saturated $NaHCO_3$ aq. (2.0 mL × 2) and dried over $MgSO_4$. After filtration, the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7:1). Compound **2l** was obtained as a pale yellow oil (55.4 mg, 0.24 mmol, 48% yield). The isolated **2l** was analyzed by ^1H NMR (300 MHz, $CDCl_3$) and ^2H NMR (61 MHz, $CDCl_3$).

Stoichiometric Reactions Using Various Additives

To a reaction vessel, $PdCl_2(MeCN)_2$ (44.9 mg, 0.125 mmol) was added, and O_2 was purged. In the case of solid additives, they were added at this stage. *t*-BuOH (75 μL) and H_2O (425 μL) were added to the reaction mixture, which was stirred at 40 ℃ for 1 h. In the case of liquid and gaseous additives, they were added at this stage. Then, **1a** (15.0 μL, 0.125 mmol) was added and the reaction mixture was stirred at 40 ℃ for 6 h. After cooling to room temperature, 1,1,2,2-tetrachloroethane (13.1 μL, 0.125 mmol) was added as an internal standard. The reaction mixture was extracted with $CDCl_3$ (0.5 mL×5), and the organic layer was combined to prepare NMR samples. The samples were analyzed by ^1H NMR (300 MHz,$CDCl_3$).

Table S1. Effect of Pd catalysts.



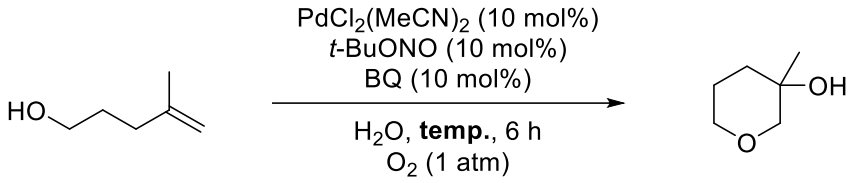
1a
slow addition over 5 h

2a

entry	Pd catalyst	conv. of **1a** (%)[a]	yield of **2a** (%)[a]
1	none	55	0
2	$PdCl_2(MeCN)_2$	90	27
3	$PdCl_2(PhCN)_2$	99	8
4	$PdCl_2$	71	3

Reaction conditions: **1a** (0.50 mmol), Pd catalyst (0.050 mmol), *t*-BuONO (0.050 mmol), BQ (0.050 mmol), H_2O (2.0 mL), O_2 (1 atm), 40 °C, 5 h. **1a** was added over 5 h by a syringe pump, and the reaction mixture was stirred for an additional 1 h. [a] Determined by ^1H NMR.

Table S2. Effect of reaction temperature.



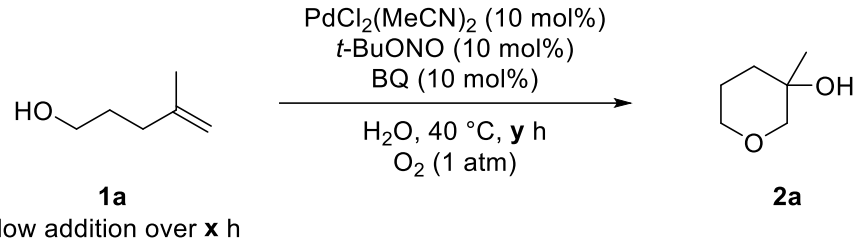
1a
slow addition over 5 h

2a

entry	temp. (°C)	conv. of **1a** (%)[a]	yield of **2a** (%)[a]
1	rt	63	0
2	40	90	27
3	60	96	13

Reaction conditions: **1a** (0.50 mmol), $PdCl_2(MeCN)_2$ (0.050 mmol), *t*-BuONO (0.050 mmol), BQ (0.050 mmol), H_2O (2.0 mL), O_2 (1 atm), 5 h. **1a** was added over 5 h by a syringe pump, and the reaction mixture was stirred for an additional 1 h. [a] Determined by ^1H NMR.

Table S3. Effect of slow addition of substrate and reaction time.



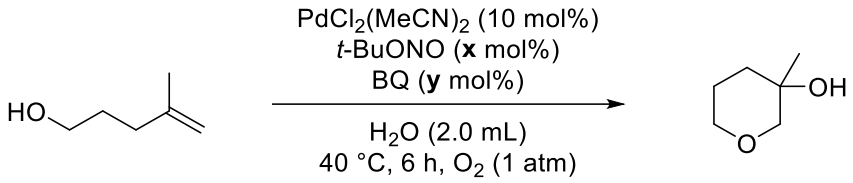
1a
slow addition over **x** h

2a

entry	x (h)	y (h)	conv. of **1a** (%)[a]	yield of **2a** (%)[a]
1	0	6	86	0
2	5	6	90	27
3	10	18	84	22

Reaction conditions: **1a** (0.50 mmol), $PdCl_2(MeCN)_2$ (0.050 mmol), *t*-BuONO (0.050 mmol), BQ (0.050 mmol), H_2O (2.0 mL), O_2 (1 atm), 40 °C, y h. **1a** was added over x h by a syringe pump, and the reaction mixture was stirred for an additional (y-x) h. [a] Determined by ^1H NMR.

Table S4. Effect of the amount of additives.



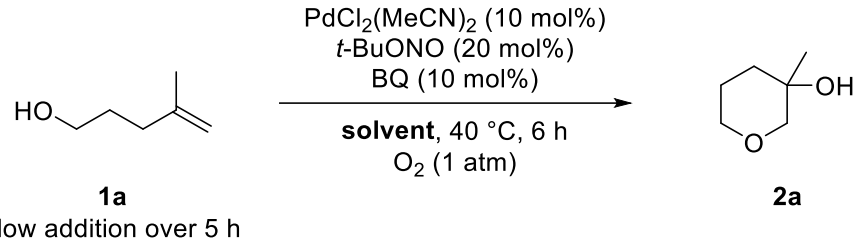
1a
slow addition over 5 h

2a

entry	**x**	**y**	conv. of **1a** (%)[a]	yield of **2a** (%)[a]
1	0	10	75	0
2	10	0	72	6
3	10	10	90	27
4	20	10	94	37
5	10	20	88	24

Reaction conditions: **1a** (0.50 mmol), $PdCl_2(MeCN)_2$ (0.050 mmol), *t*-BuONO, BQ, H_2O (2.0 mL), O_2 (1 atm), 40 °C, 6 h. **1a** was added over 5 h by a syringe pump, and the reaction mixture was stirred for an additional 1 h.
[a] Determined by ^1H NMR.

Table S5. Effect of solvents.



1a
slow addition over 5 h

2a

entry	solvent	conv. of **1a** (%)[a]	yield of **2a** (%)[a]
1	H_2O (2.0 mL)	94	37
2	H_2O (1.5 mL)/DMF (0.5 mL)	77	27
3	H_2O (1.5 mL)/1,4-dioxane (0.5 mL)	100	50
4	H_2O (1.5 mL)/MeCN (0.5 mL)	84	32
5	H_2O (1.5 mL)/acetone (0.5 mL)	100	49
6	H_2O (1.5 mL)/*t*-BuOH (0.5 mL)	100	52
7	H_2O (1.0 mL)/*t*-BuOH (1.0 mL)	97	44
8	H_2O (1.7 mL)/*t*-BuOH (0.3 mL)	99	56

Reaction conditions: **1a** (0.50 mmol), $PdCl_2(MeCN)_2$ (0.050 mmol), *t*-BuONO (0.10 mmol), BQ (0.050 mmol), solvent (2.0 mL), O_2 (1 atm), 40 °C, 6 h. **1a** was added over 5 h by a syringe pump, and the reaction mixture was stirred for an additional 1 h.
[a] Determined by ^1H NMR.

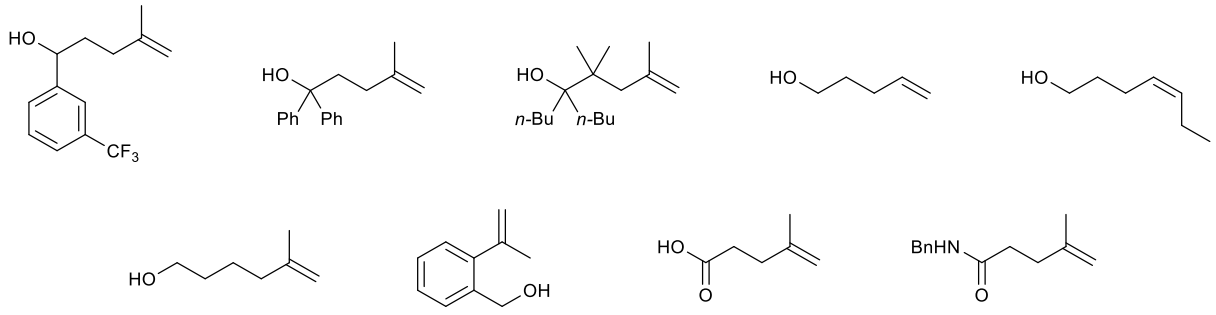


Figure S1. Substrates that afforded little or no corresponding products.

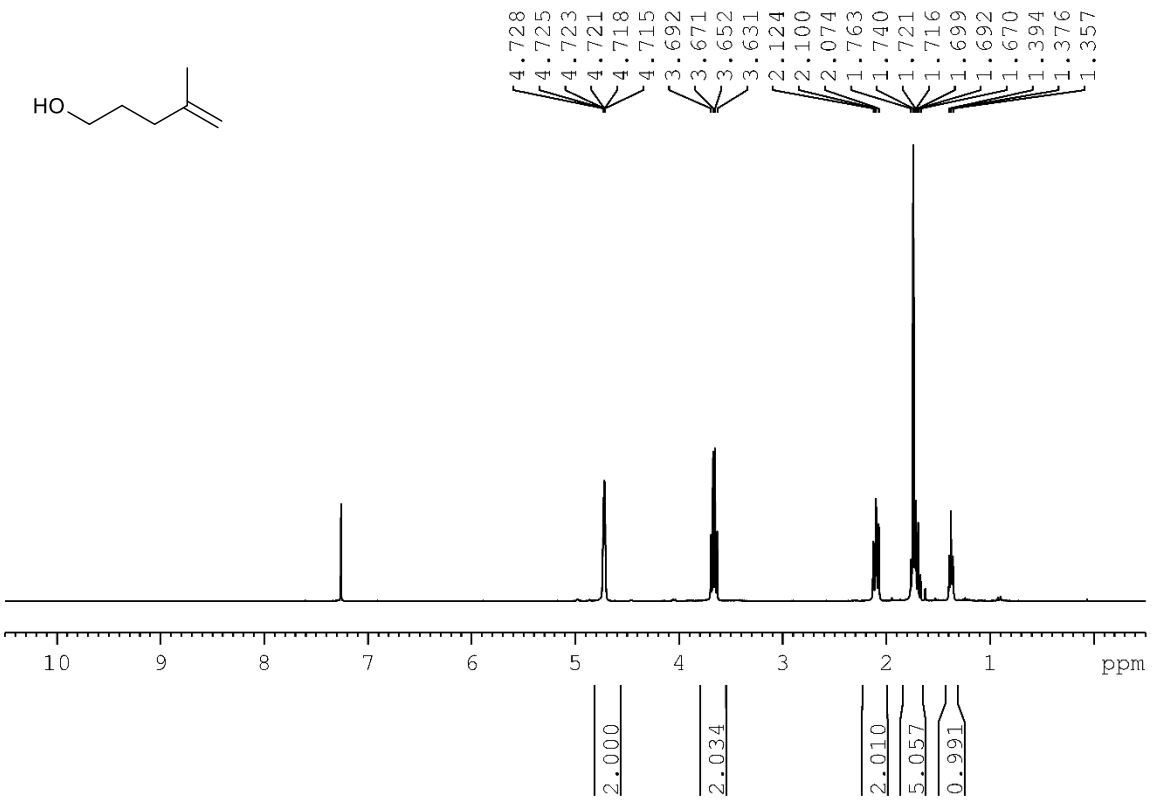


Figure S2. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 4-methyl-4-penten-1-ol (**1a**).

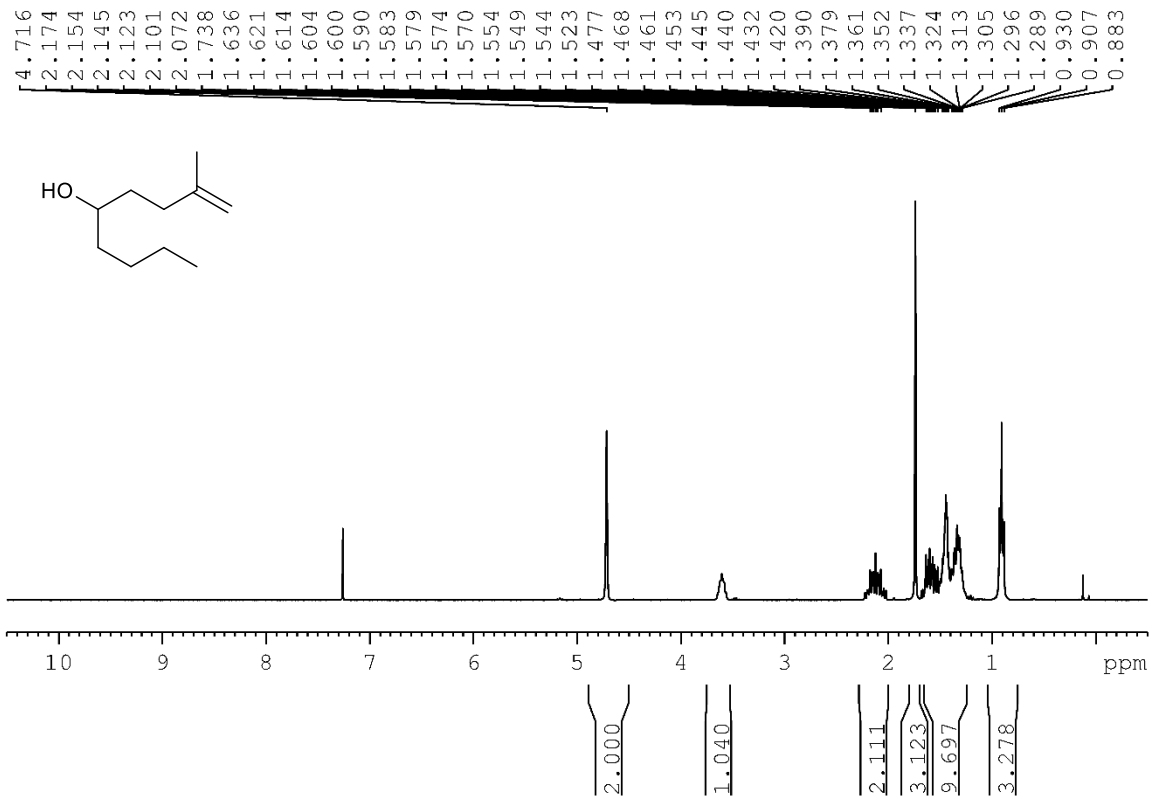


Figure S3. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2-methylnon-1-en-5-ol (**1b**).

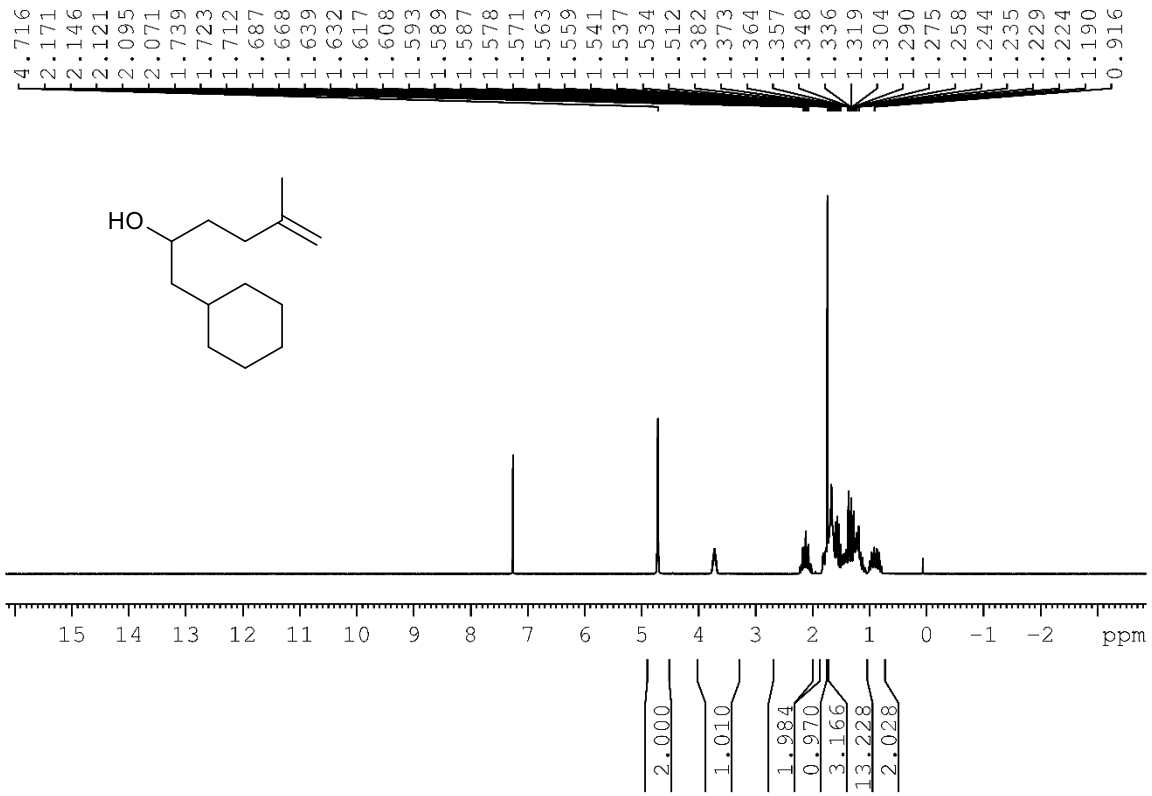


Figure S4. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of α-(3-methyl-3-buten-1-yl)cyclohexaneethanol (**1c**).

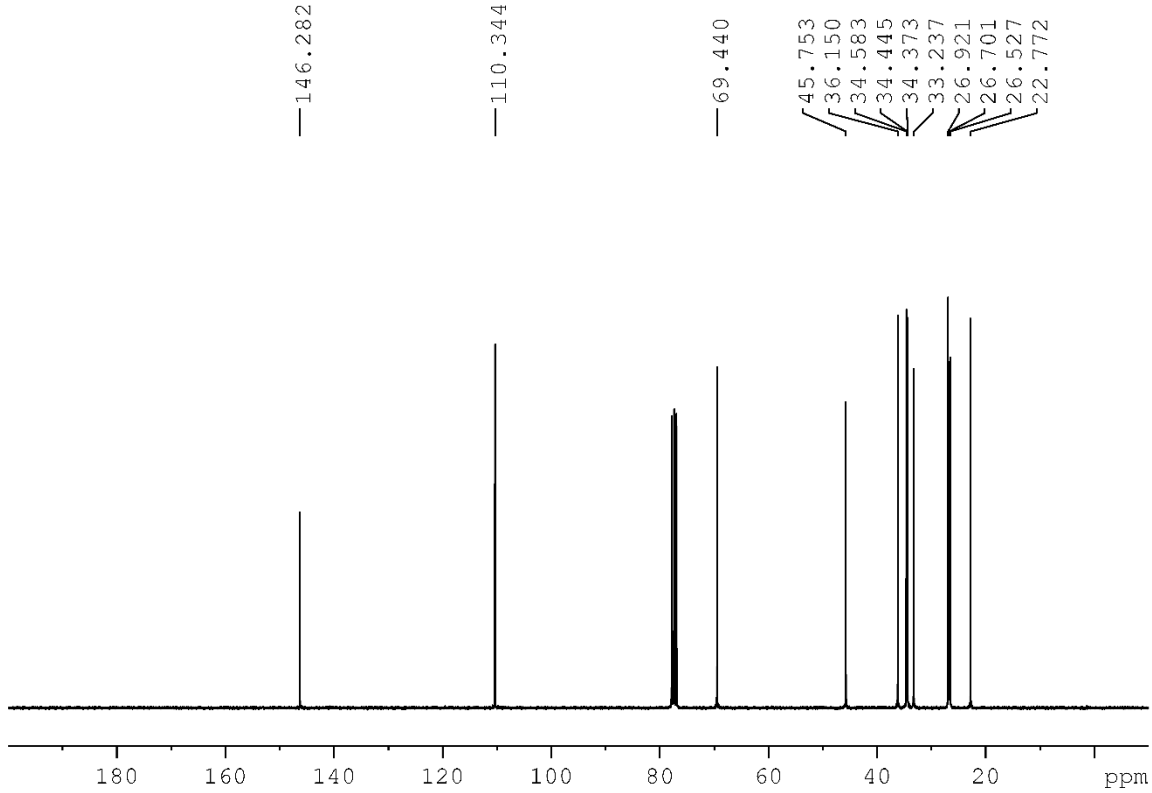


Figure S5. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of α-(3-methyl-3-buten-1-yl)cyclohexaneethanol (**1c**).

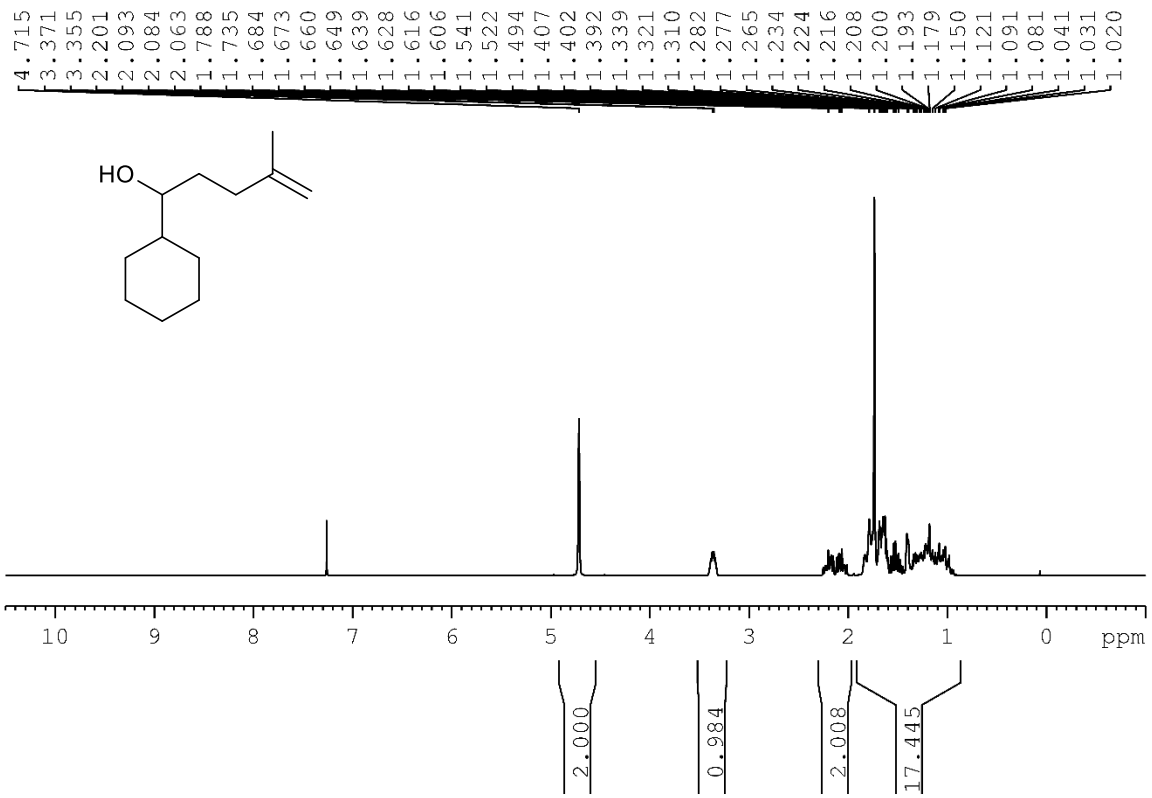


Figure S6. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of α-(3-methyl-3-buten-1-yl)cyclohexanemethanol (**1d**).

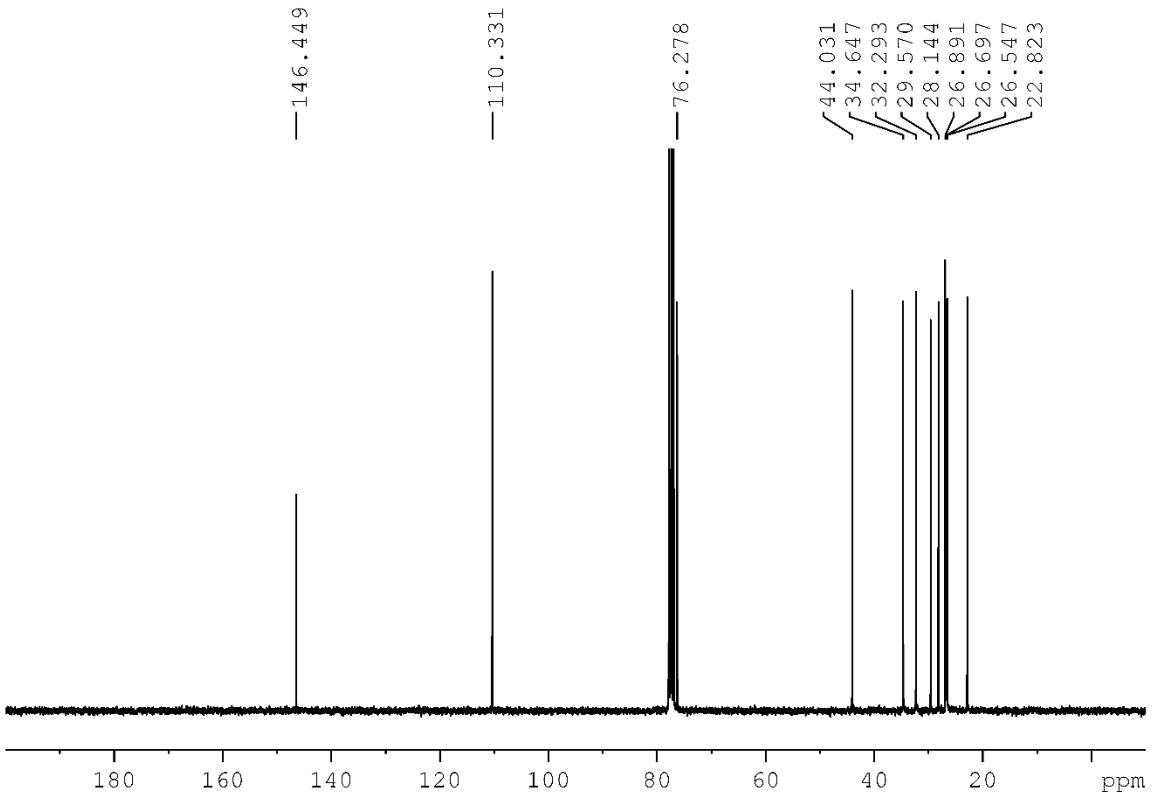


Figure S7. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of α-(3-methyl-3-buten-1-yl)cyclohexanemethanol (**1d**).

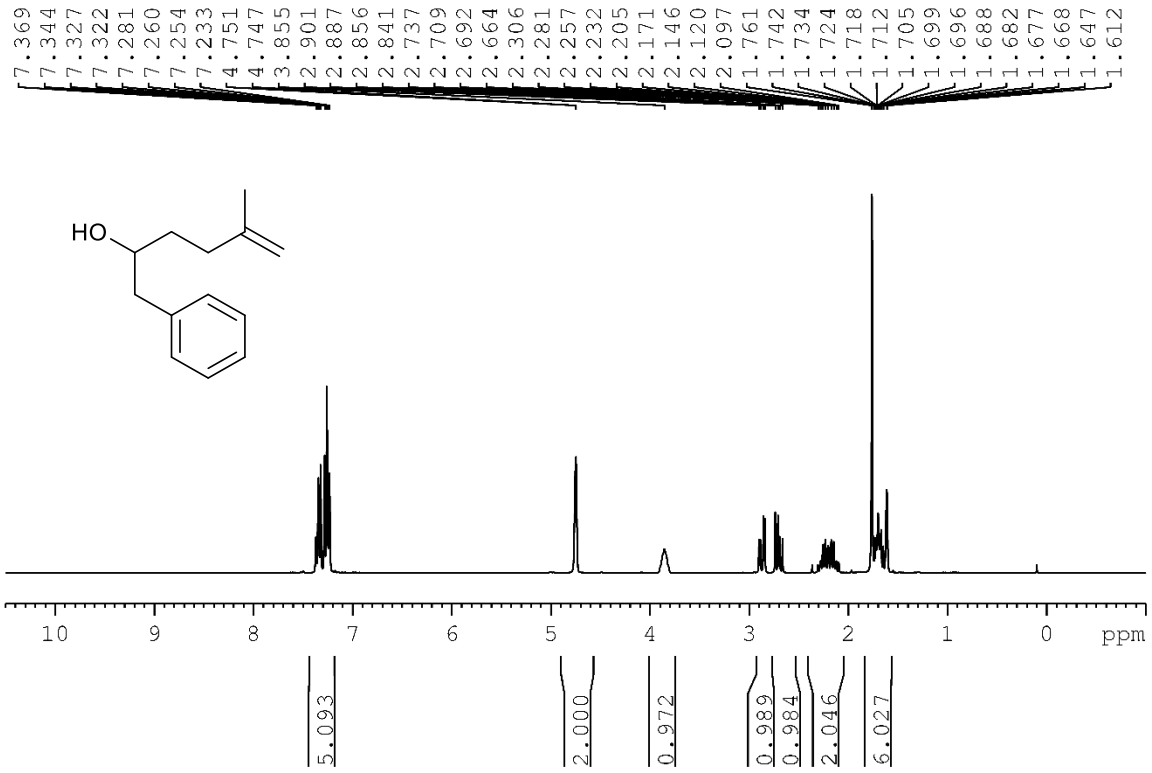


Figure S8. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of α-(3-Methyl-3-buten-1-yl)benzeneethanol (**1e**).

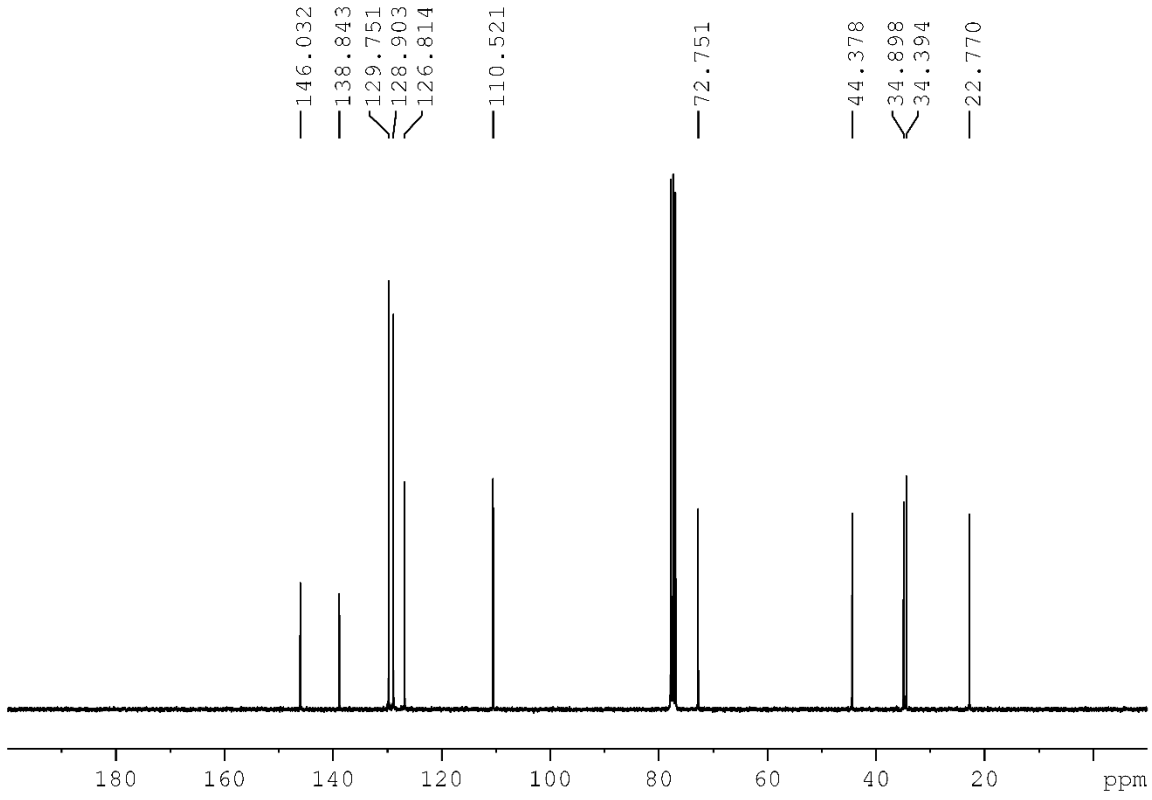


Figure S9. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of α-(3-Methyl-3-buten-1-yl)benzeneethanol (**1e**).

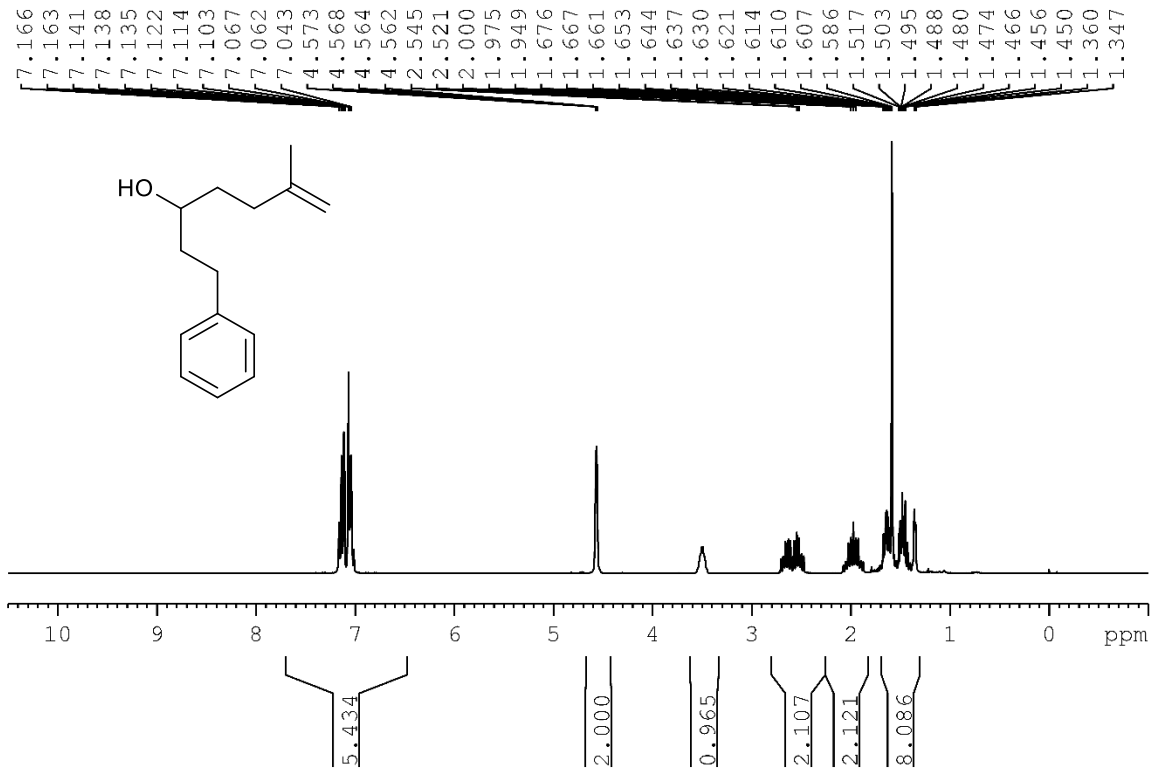


Figure S10. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of α-(3-Methyl-3-buten-1-yl)benzenepropanol (**1f**).

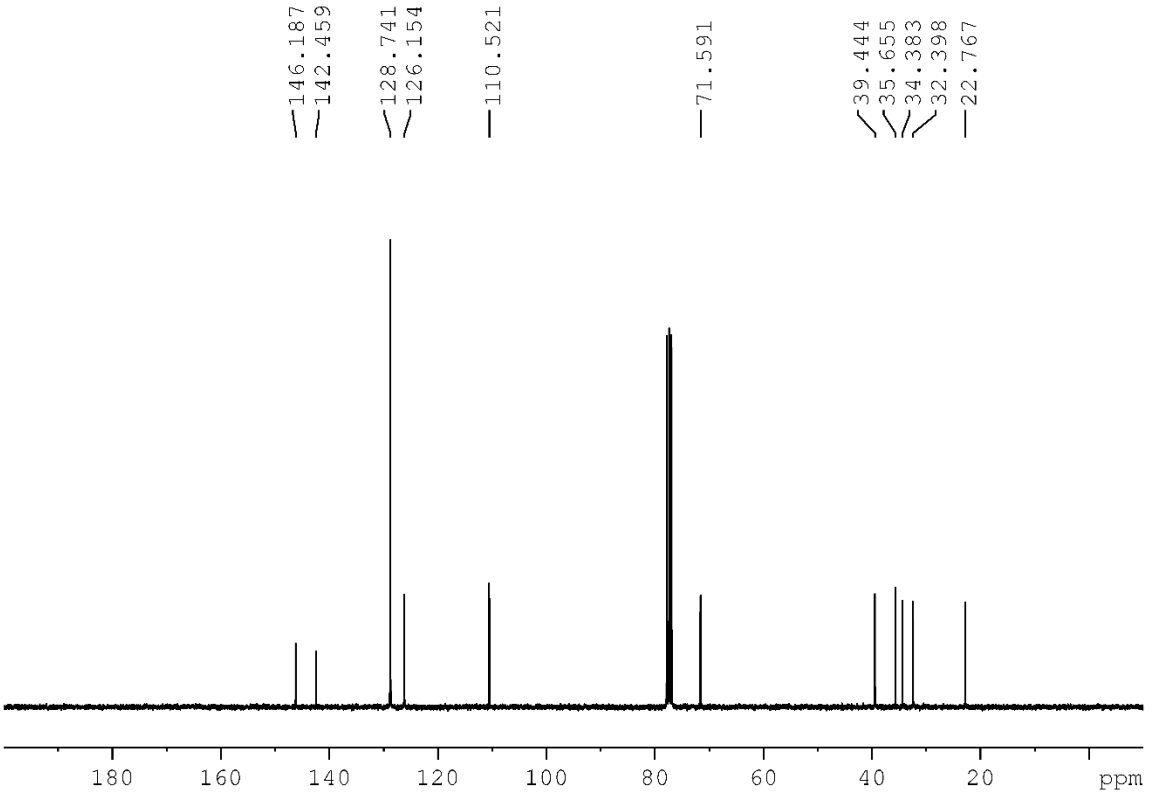


Figure S11. ^{13}C{^{1}H} NMR spectrum (75 MHz, $CDCl_3$) of α-(3-Methyl-3-buten-1-yl)benzenepropanol (**1f**).

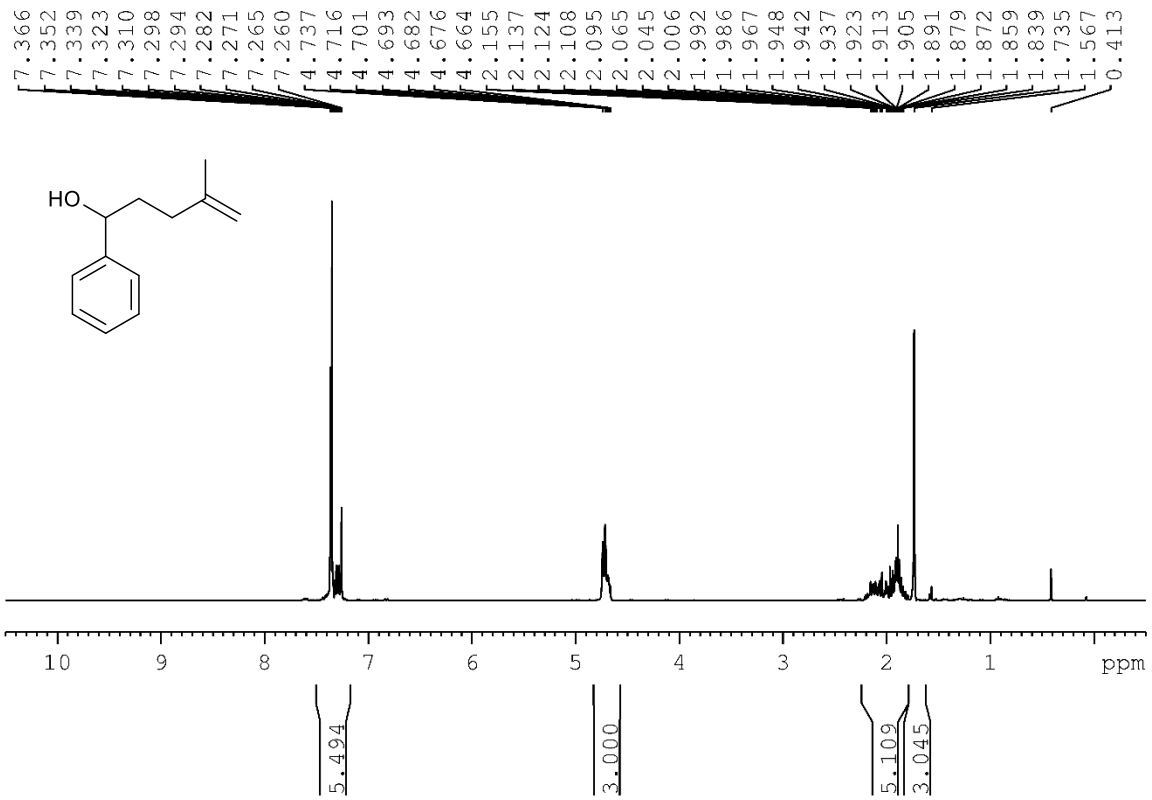


Figure S12. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 4-methyl-1-phenyl-4-penten-1-ol (**1g**).

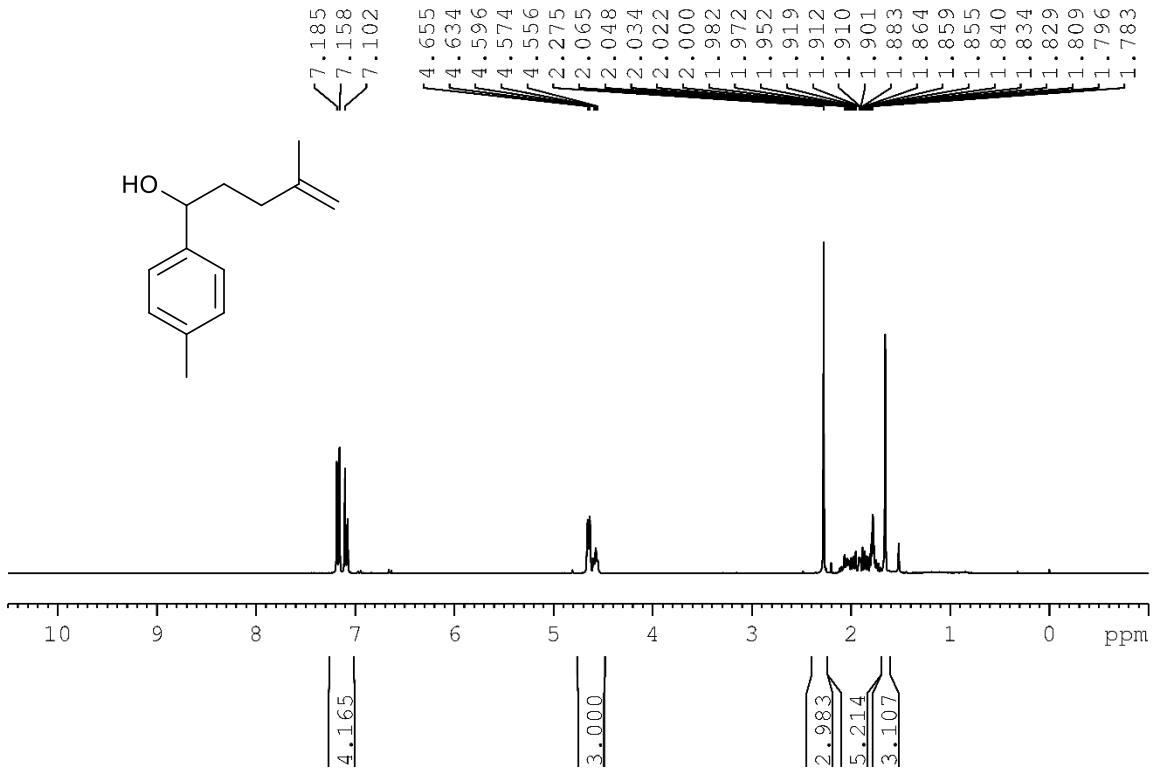


Figure S13. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 4-methyl-1-(*p*-tolyl)pent-4-en-1-ol (**1h**).

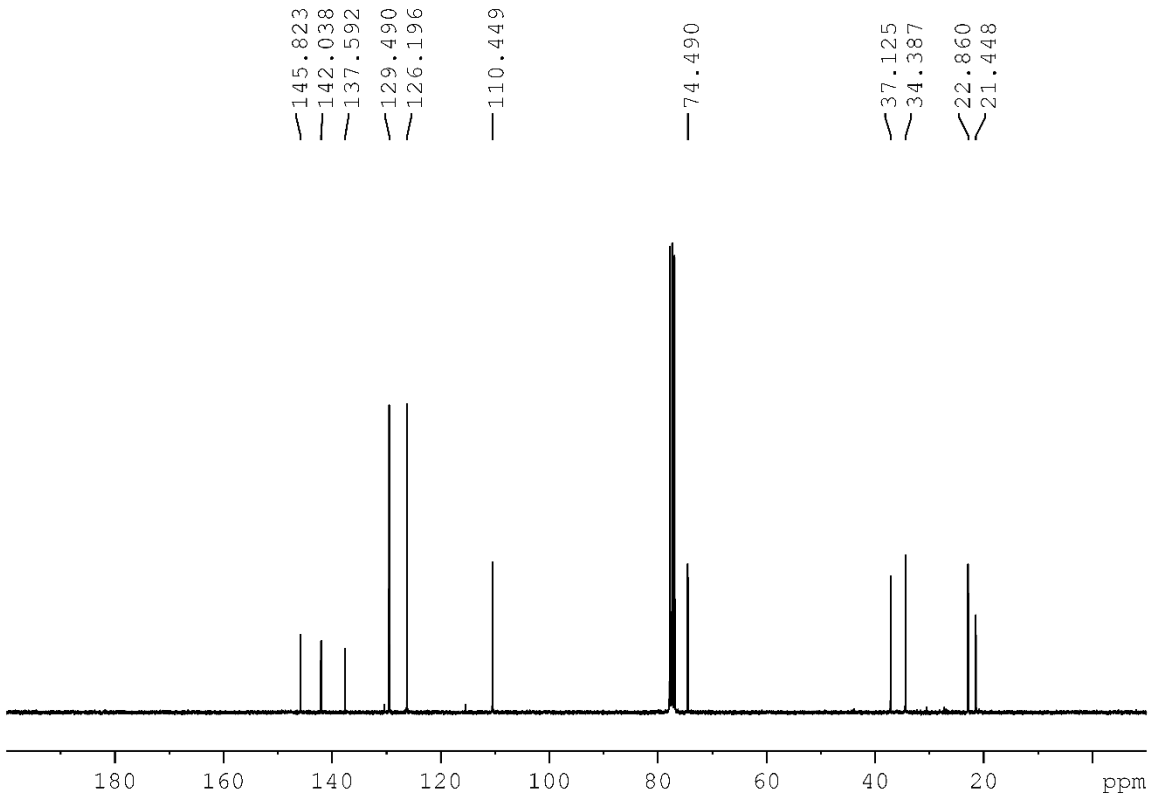


Figure S14. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 4-methyl-1-(*p*-tolyl)pent-4-en-1-ol (**1h**).

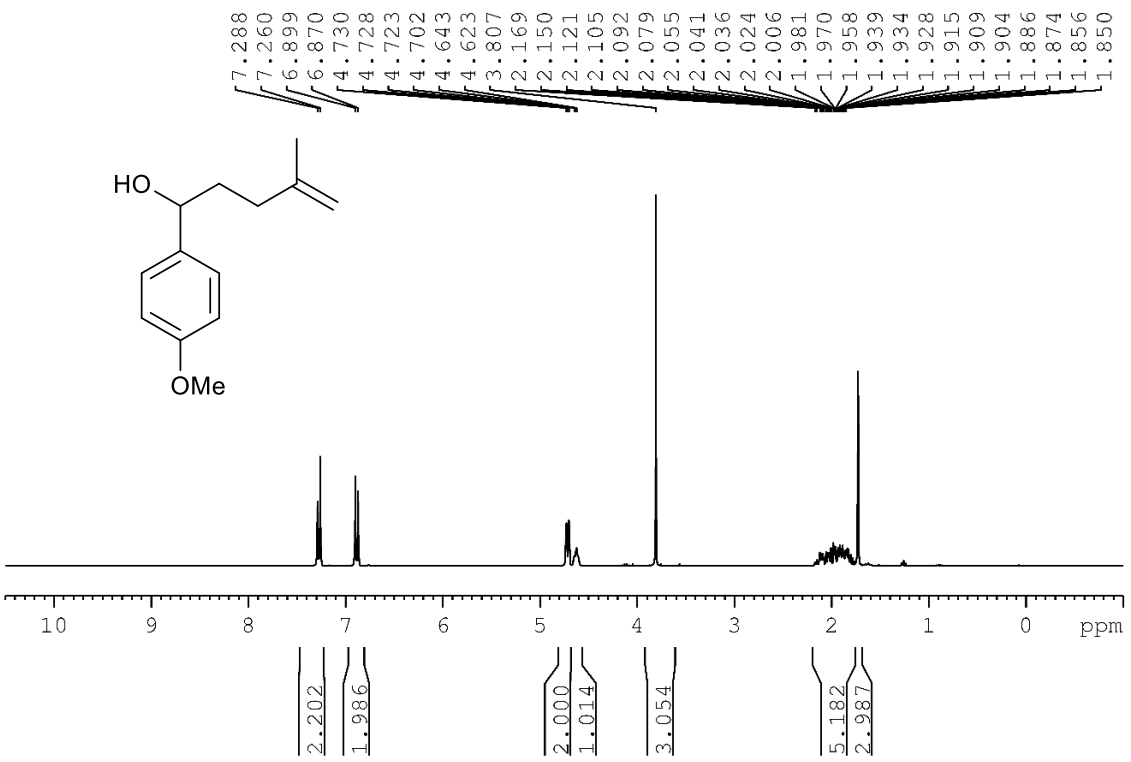


Figure S15. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 1-(*p*-methoxyphenyl)-4-methylpent-4-en-1-ol (**1i**).

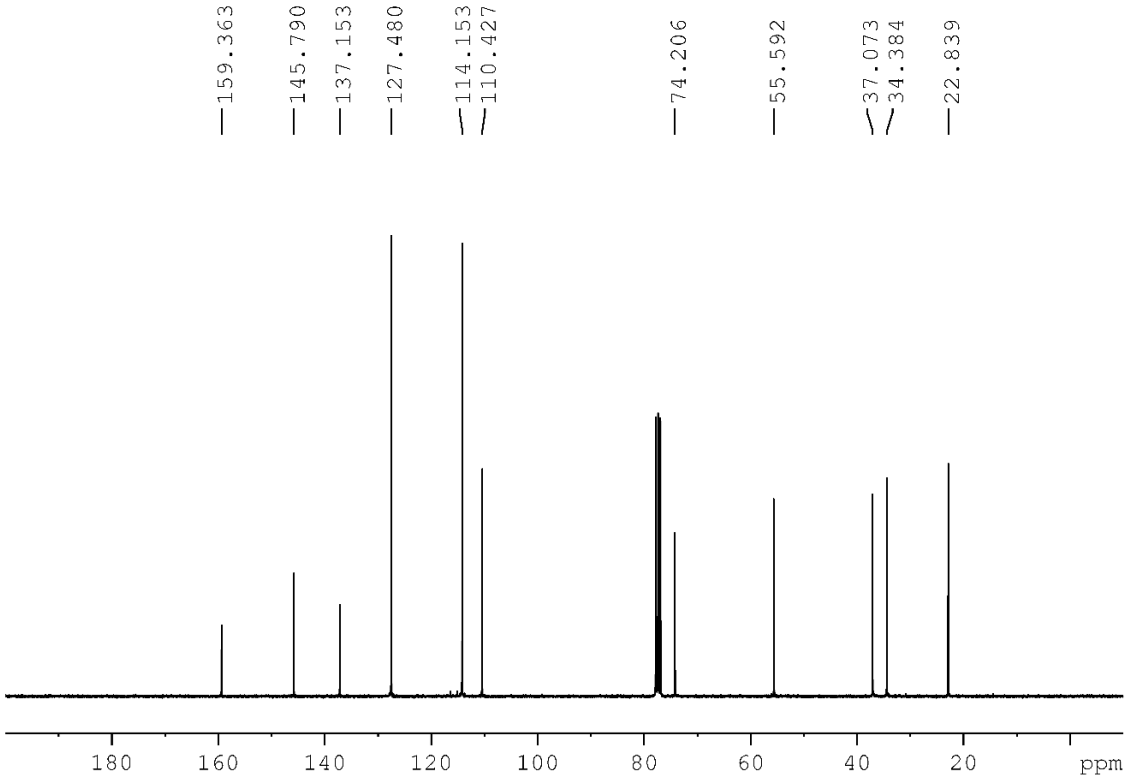


Figure S16. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 1-(*p*-methoxyphenyl)-4-methylpent-4-en-1-ol (**1i**).

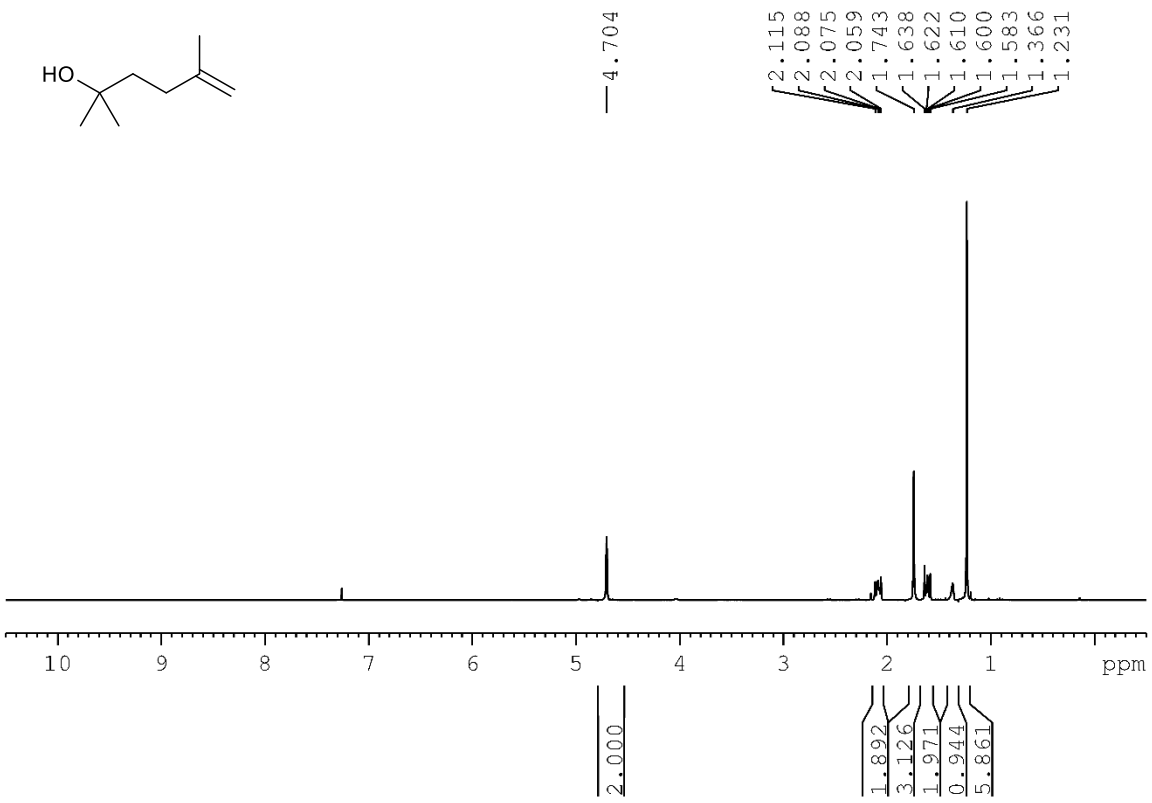


Figure S17. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2,5-dimethylhex-5-en-2-ol (**1j**).

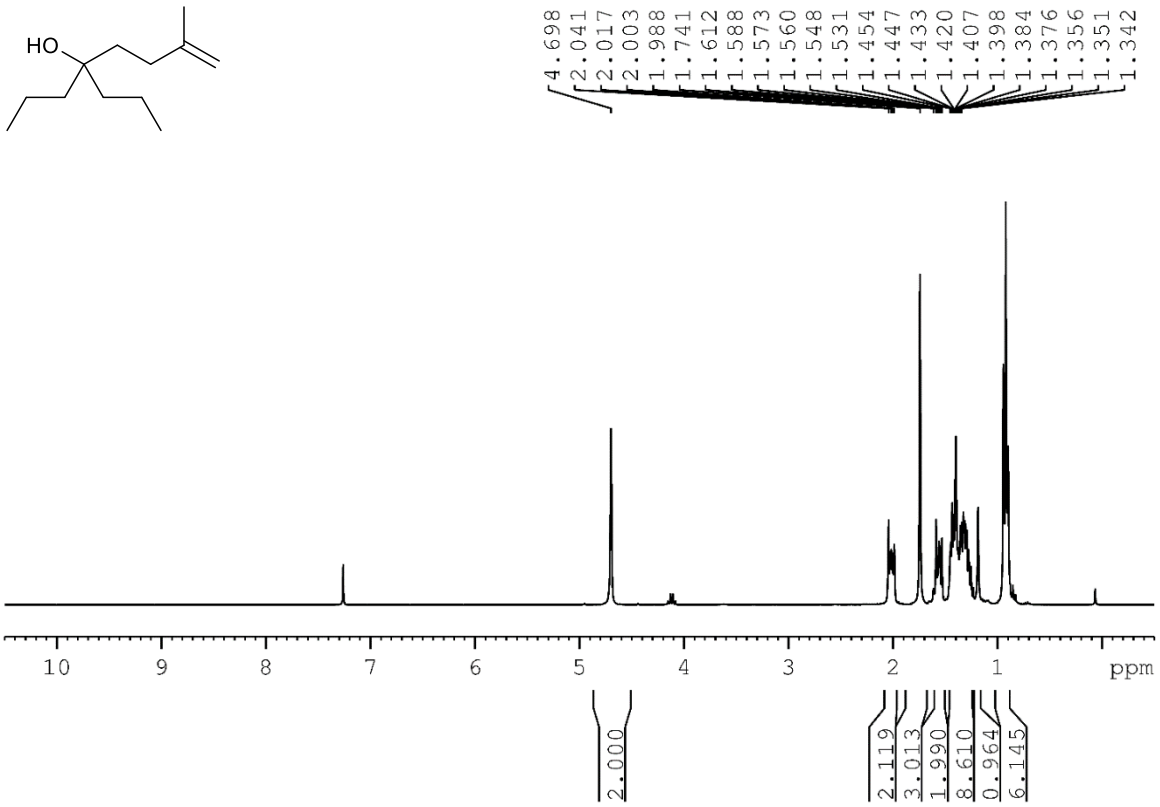


Figure S18. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 7-methyl-4-*n*-propyl-7-octen-4-ol (**1k**).

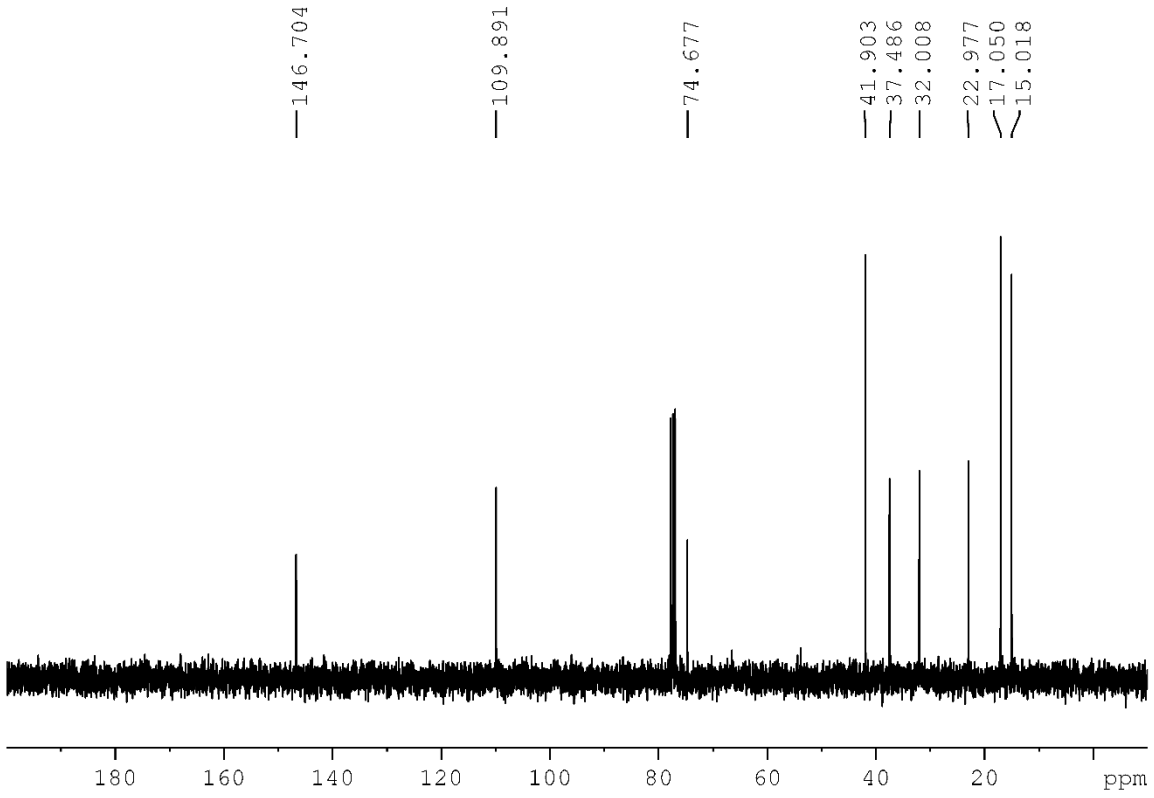


Figure S19. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 7-methyl-4-*n*-propyl-7-octen-4-ol (**1k**).

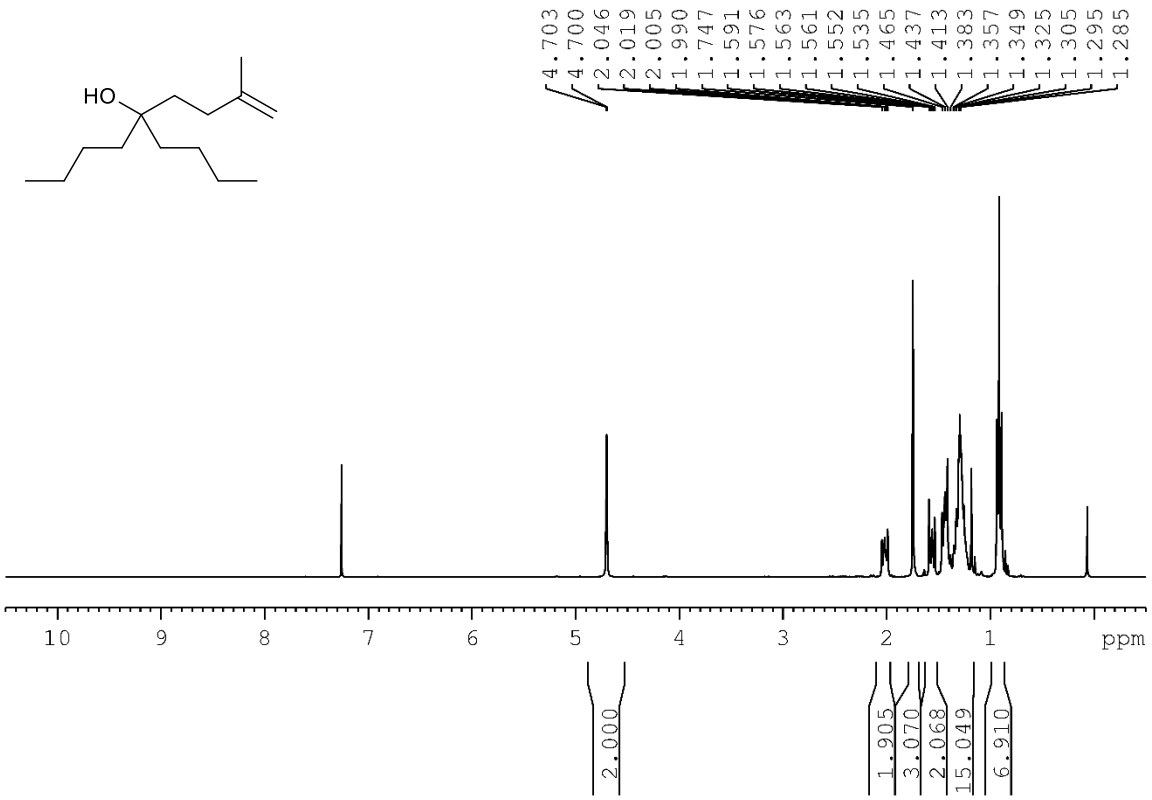


Figure S20. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 5-*n*-butyl-2-methyl-1-nonen-5-ol (**1l**).

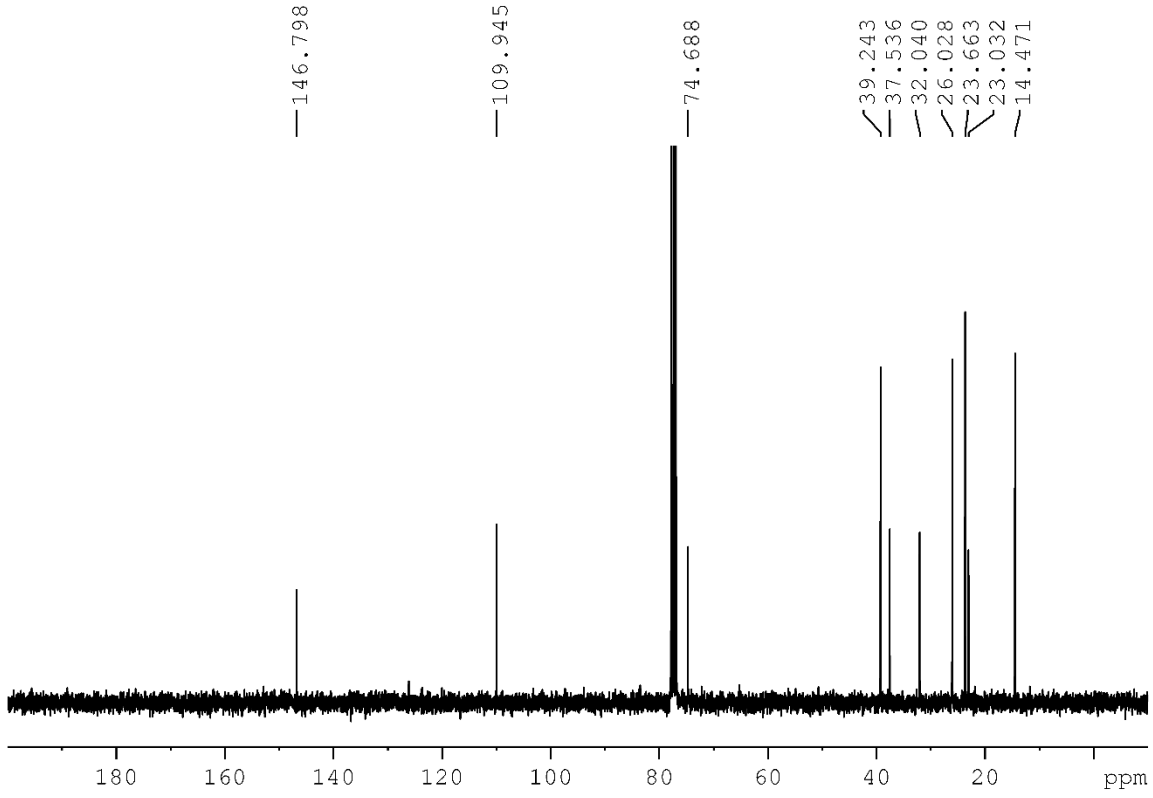


Figure S21. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 5-*n*-butyl-2-methyl-1-nonen-5-ol (**1l**).

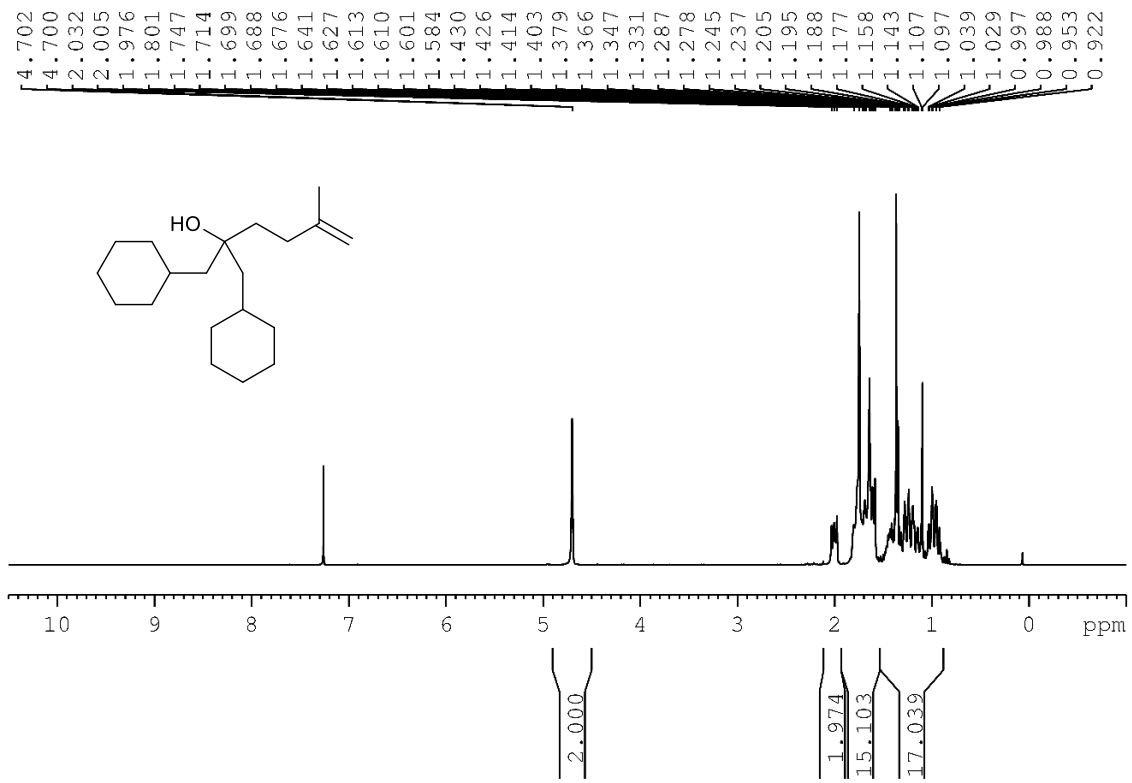


Figure S22. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 1-cyclohexyl-2-(cyclohexylmethyl)-5-methylhex-5-en-2-ol (**1m**).

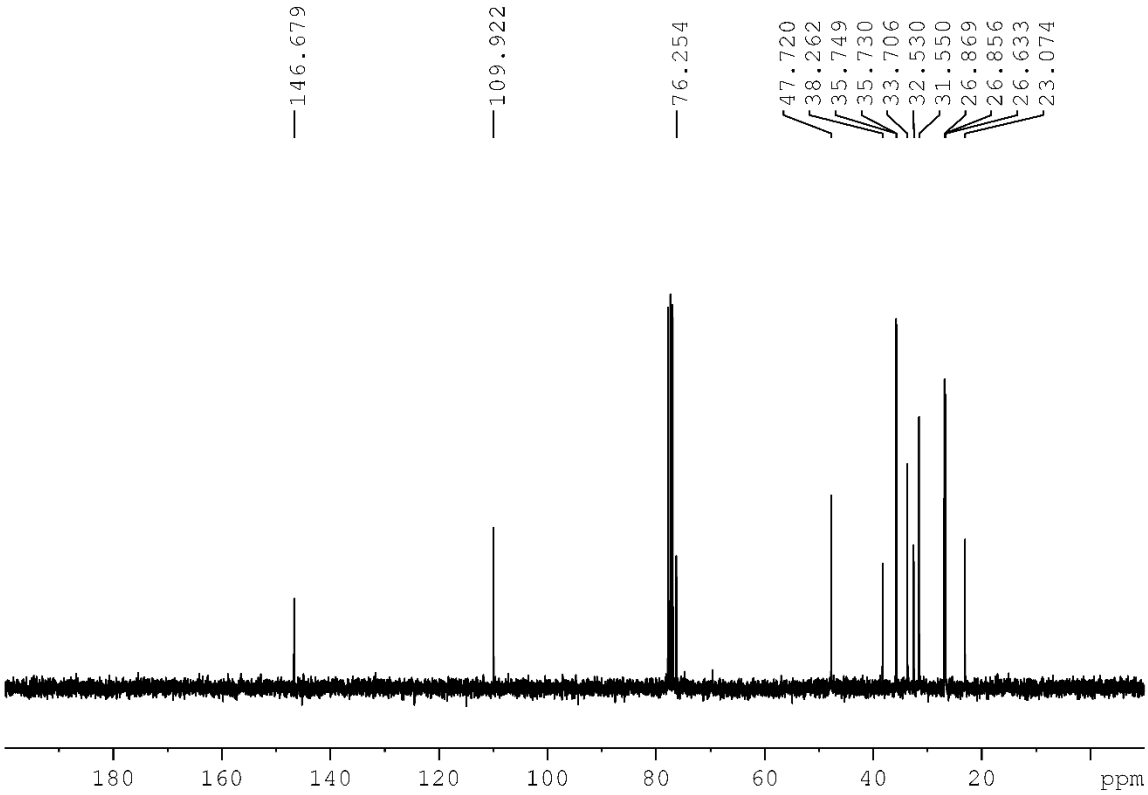


Figure S23. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 1-cyclohexyl-2-(cyclohexylmethyl)-5-methylhex-5-en-2-ol (**1m**).

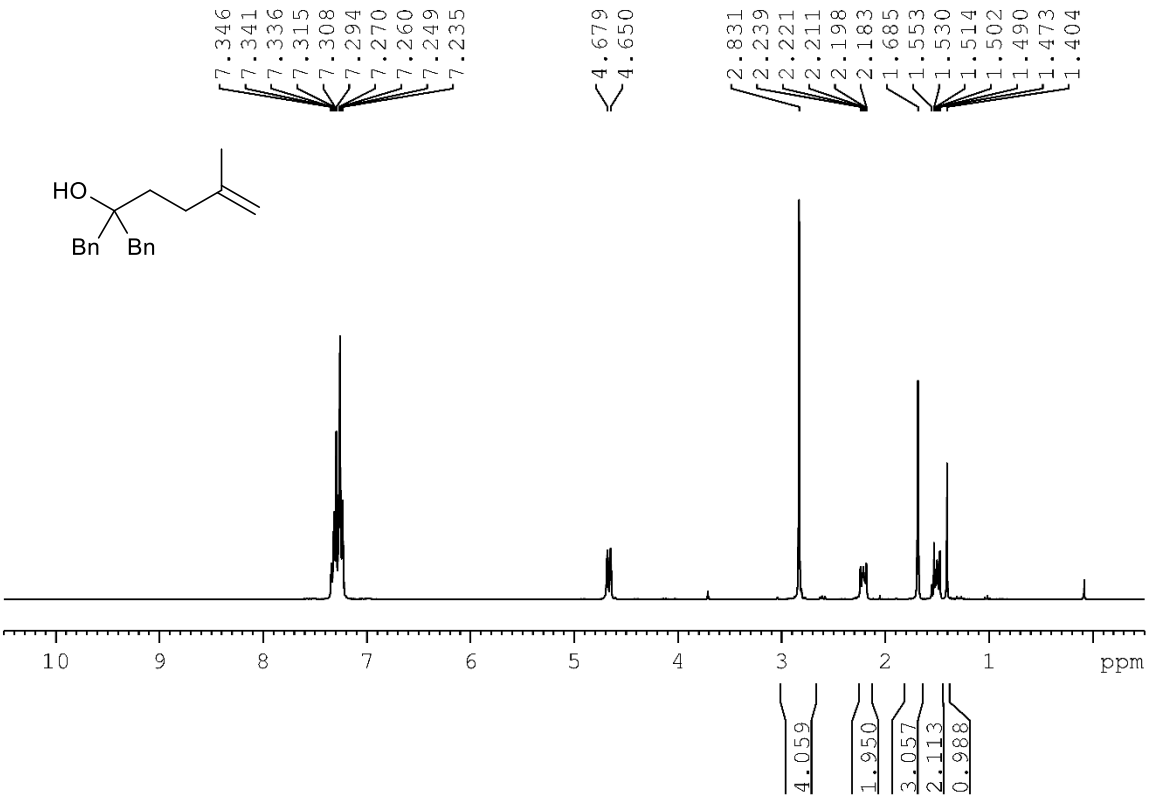


Figure S24. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2-benzyl-5-methyl-1-phenyl-5-hexen-2-ol (**1n**).

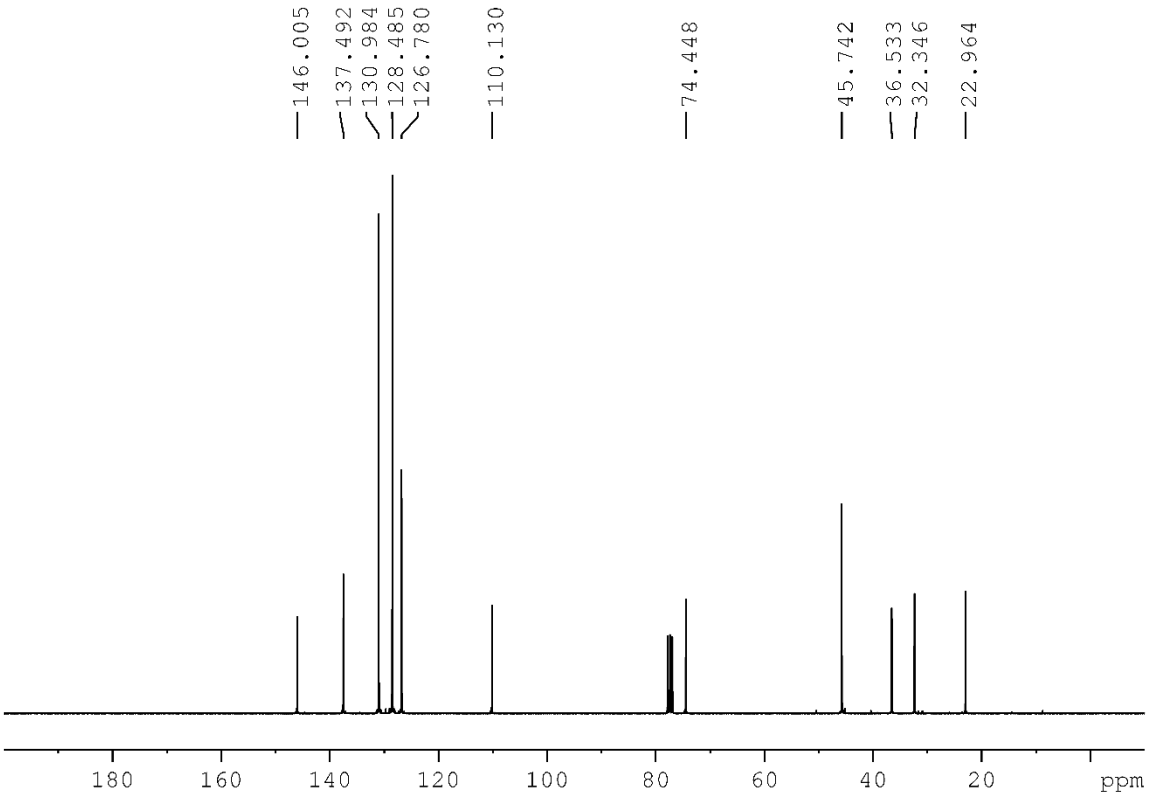


Figure S25. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 2-benzyl-5-methyl-1-phenyl-5-hexen-2-ol (**1n**).

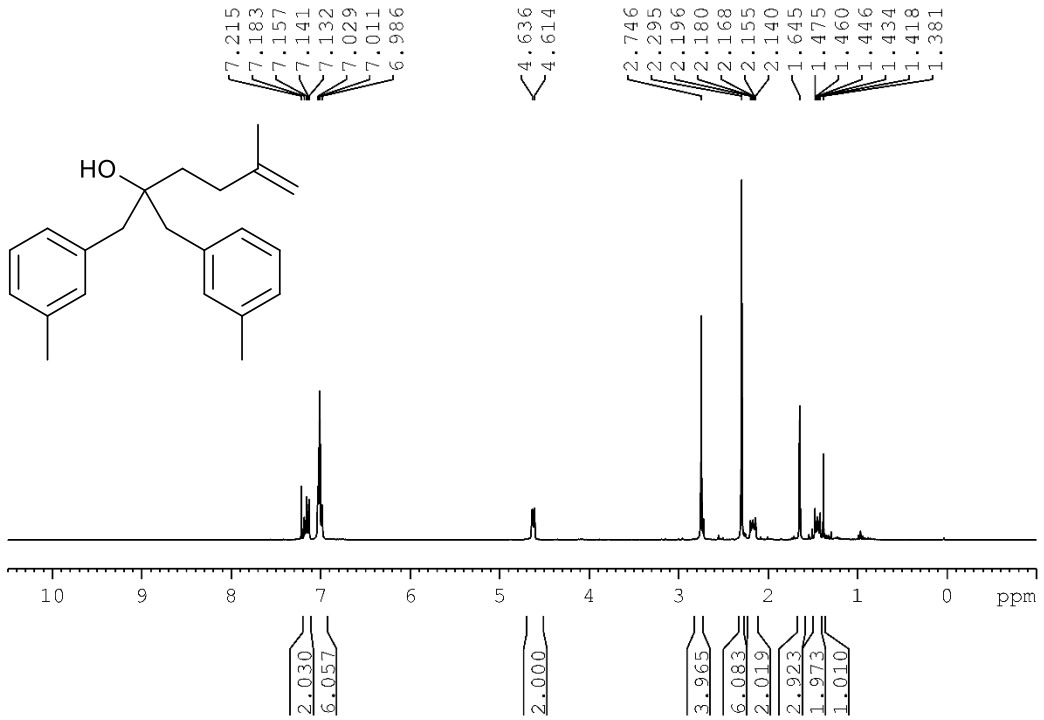


Figure S26. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 5-methyl-2-(3-methylbenzyl)-1-(3-methylphenyl)-5-hexen-2-ol (**1o**).

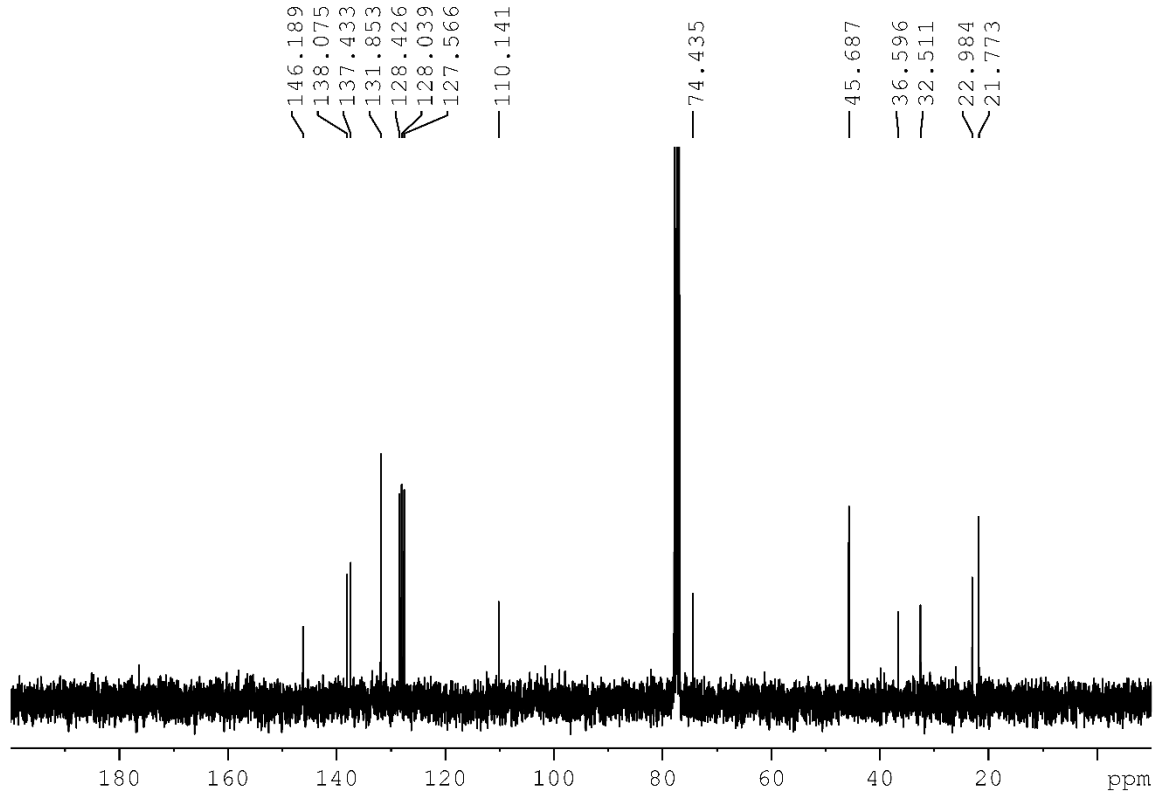


Figure S27. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 5-methyl-2-(3-methylbenzyl)-1-(3-methylphenyl)-5-hexen-2-ol (**1o**).

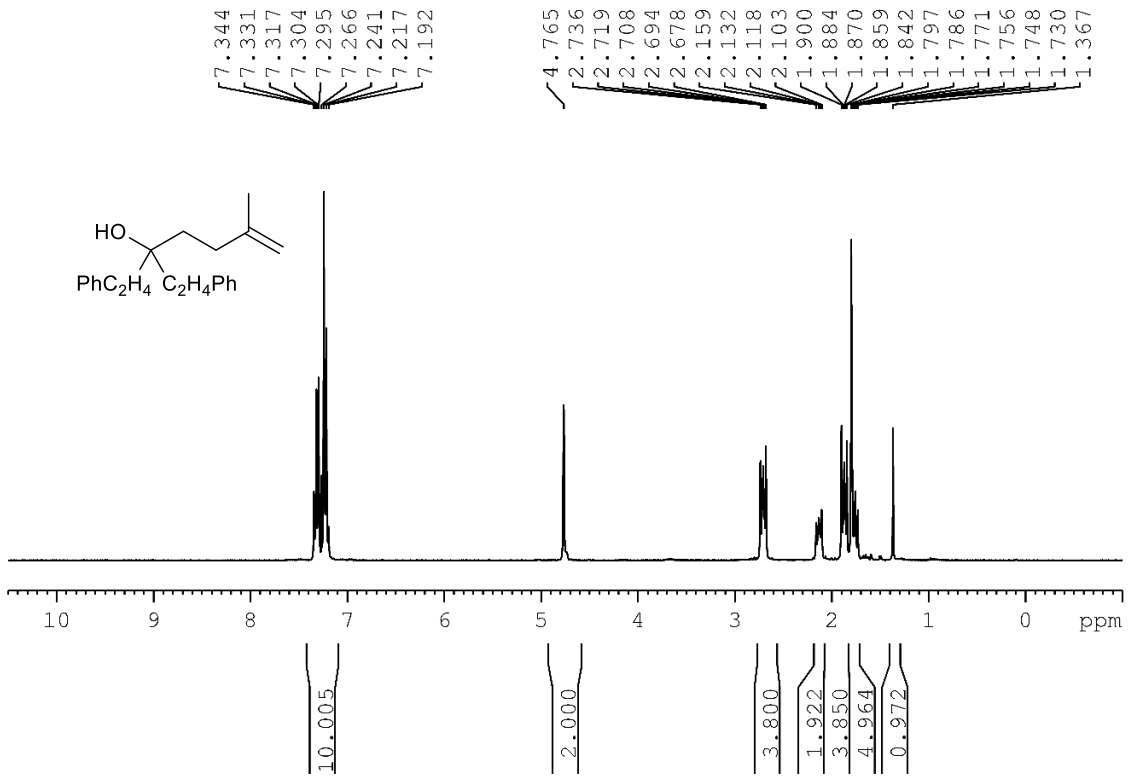


Figure S28. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-methyl-3-phenethyl-1-phenylhept-6-en-3-ol (**1p**).

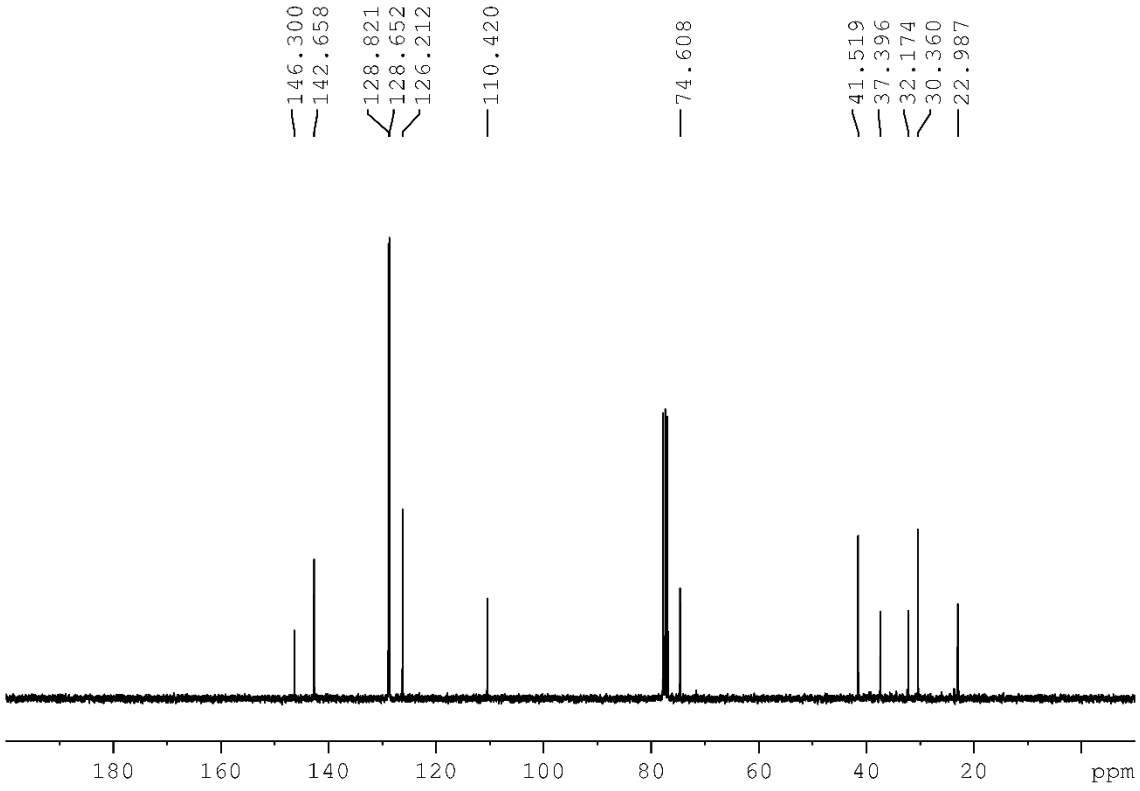


Figure S29. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-methyl-3-phenethyl-1-phenylhept-6-en-3-ol (**1p**).

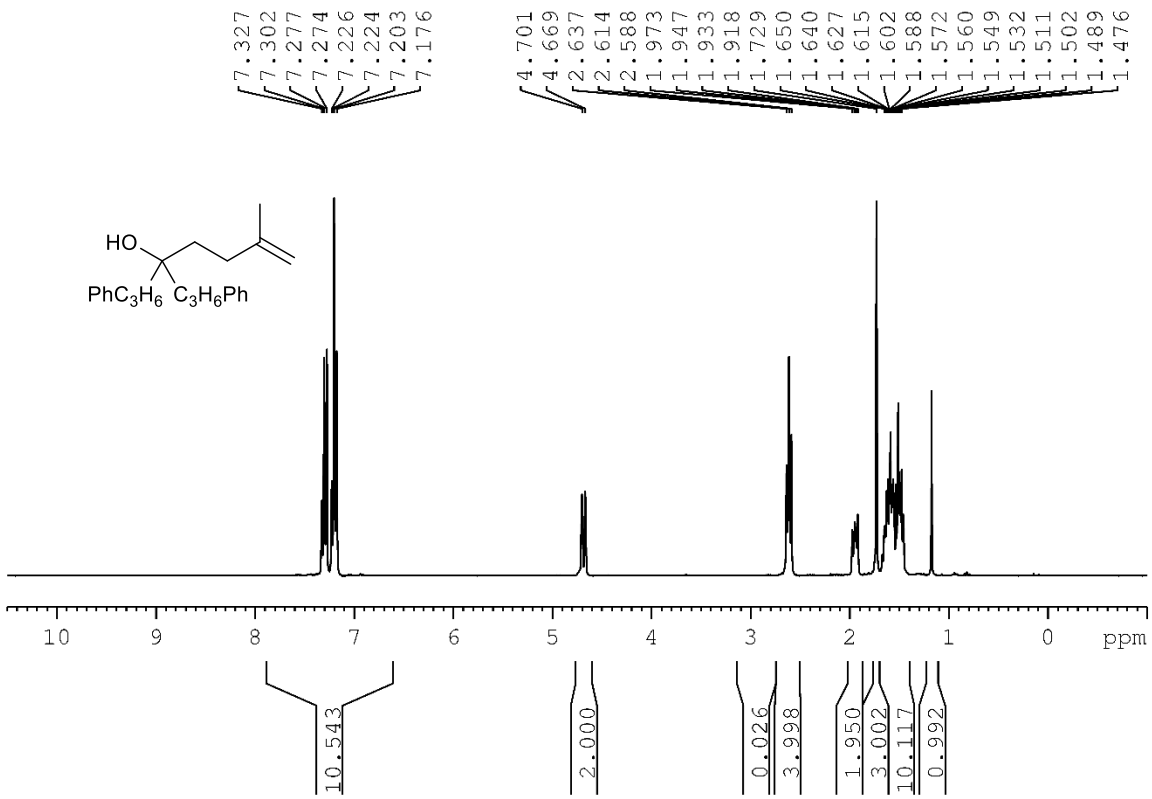


Figure S30. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 7-methyl-1-phenyl-4-(3-phenylpropyl)oct-7-en-4-ol (**1q**).

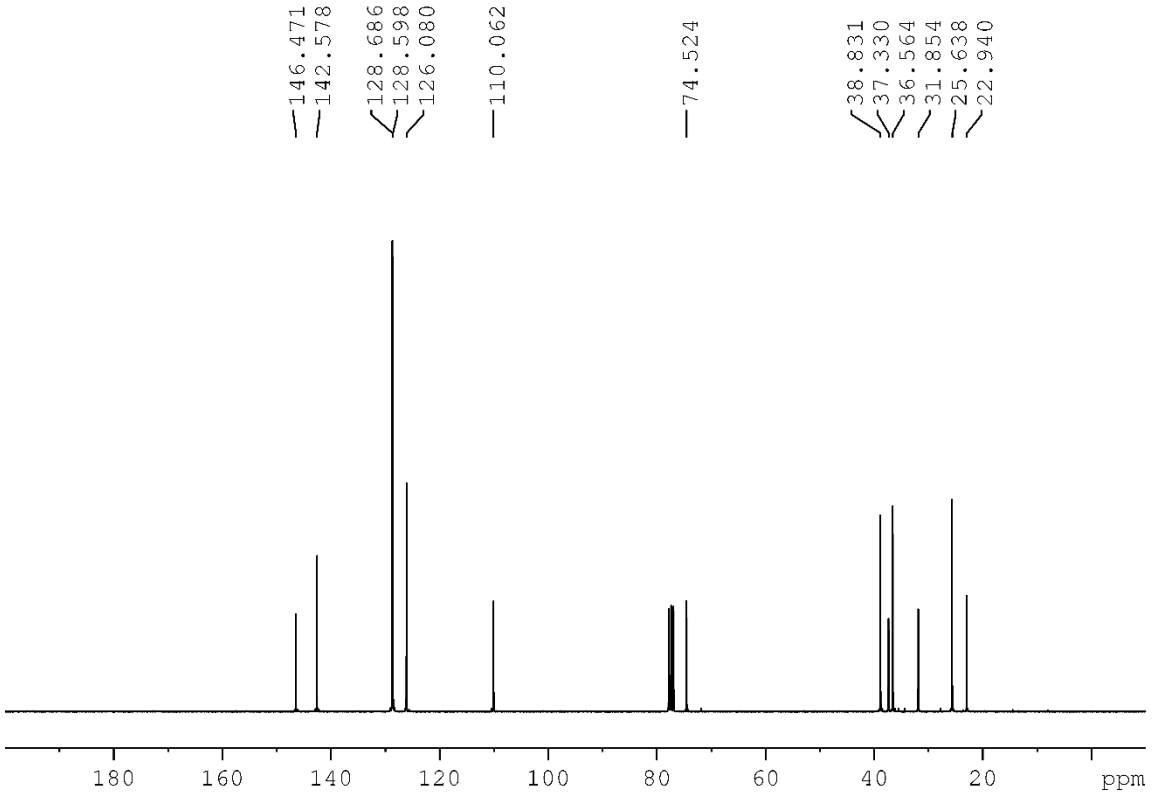


Figure S31. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 7-methyl-1-phenyl-4-(3-phenylpropyl)oct-7-en-4-ol (**1q**).

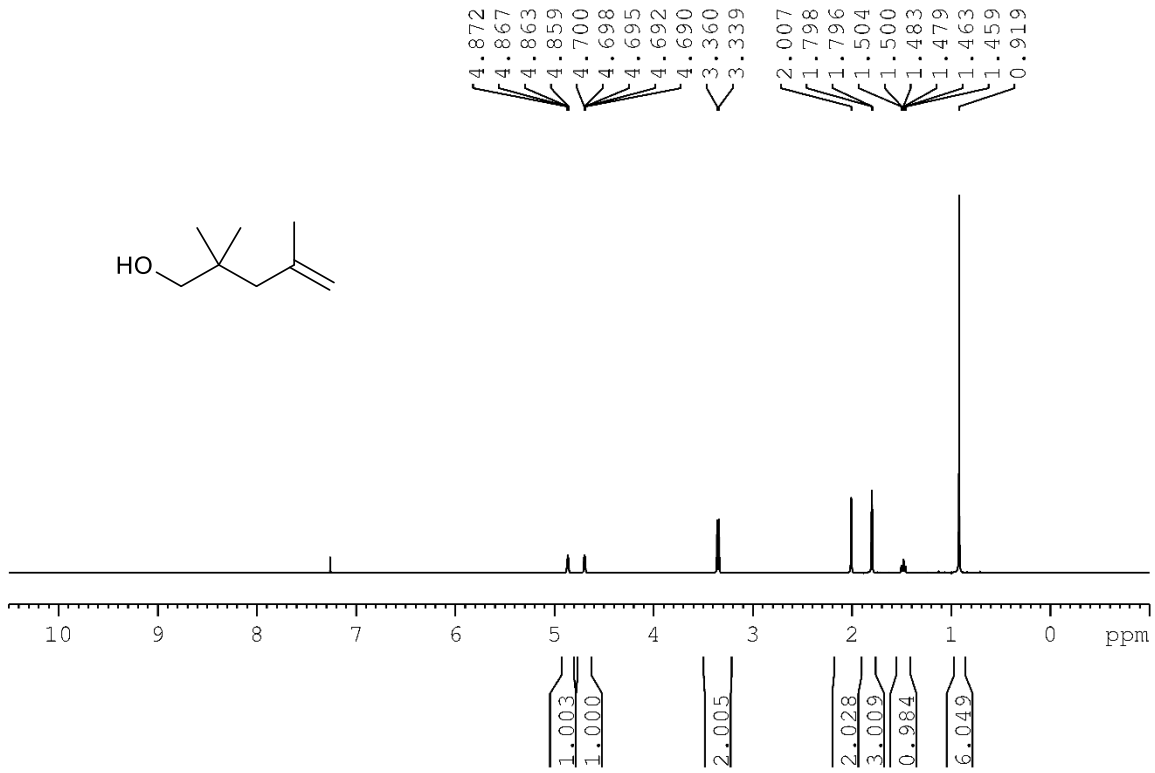


Figure S32. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2,2,4-trimethyl-4-penten-1-ol (**1r**).

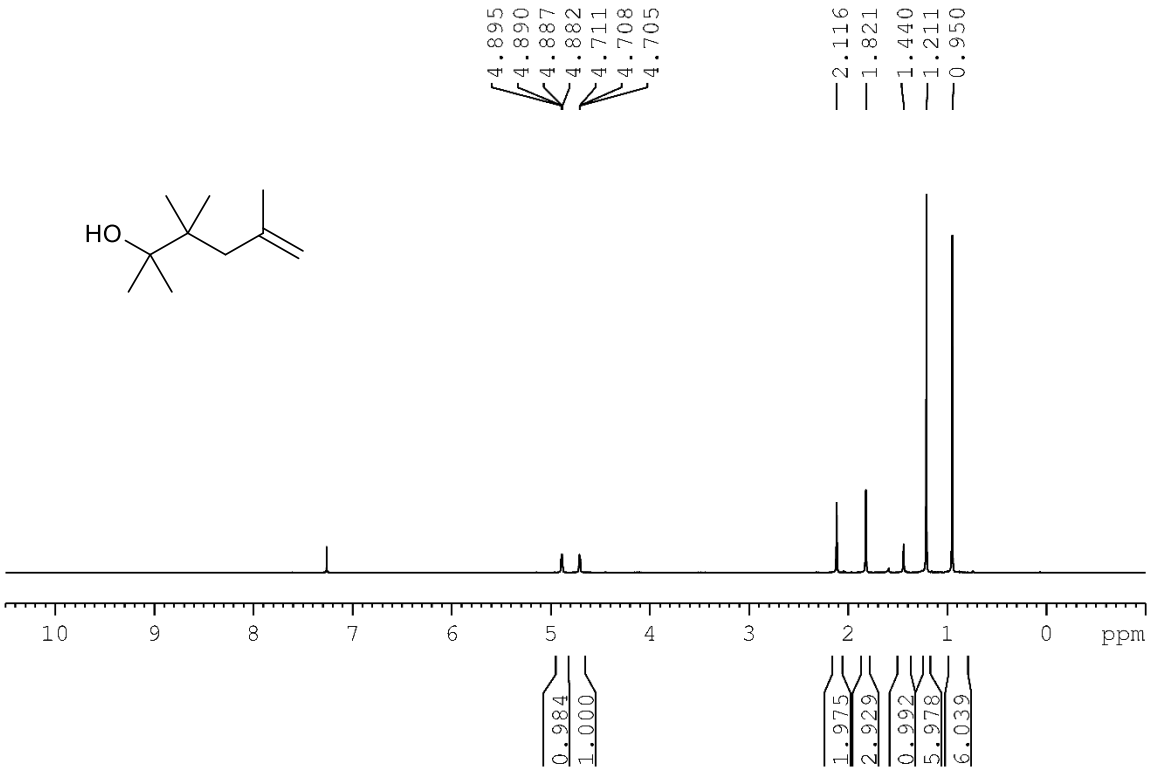


Figure S33. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 2,3,3,5-tetramethylhex-5-en-2-ol (**1s**).

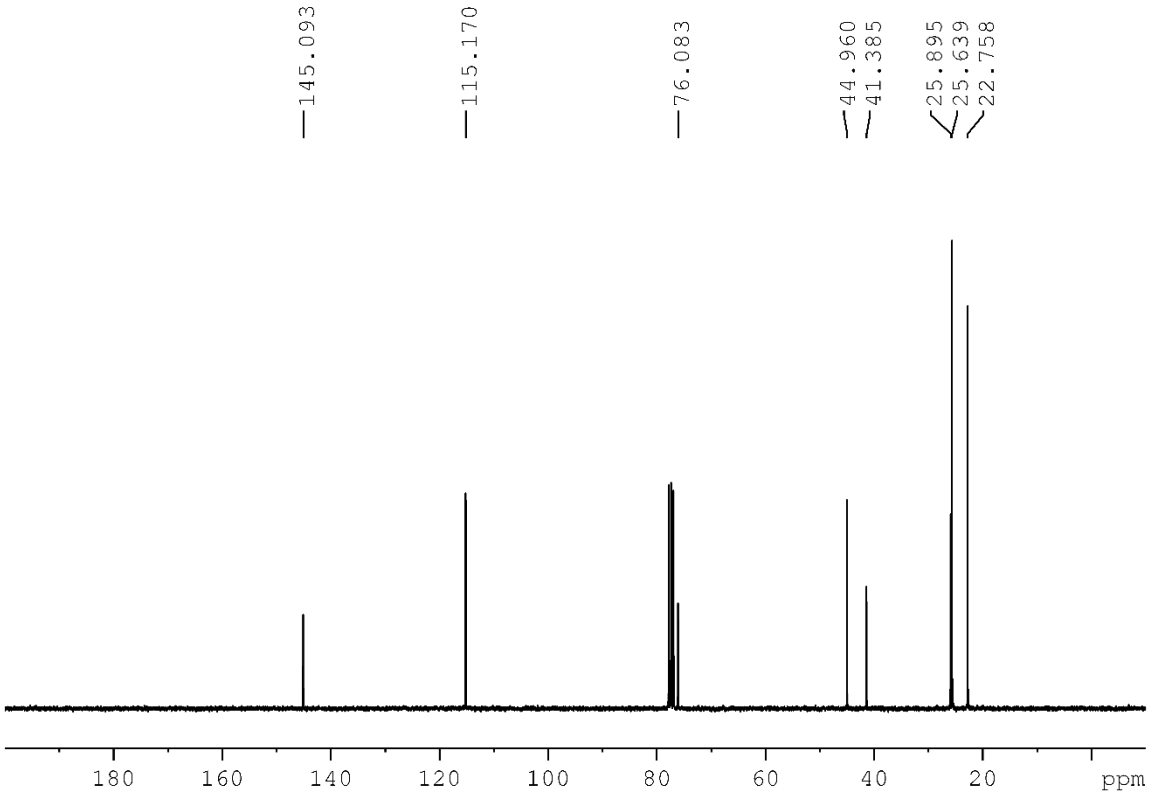


Figure S34. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 2,3,3,5-tetramethylhex-5-en-2-ol (**1s**).

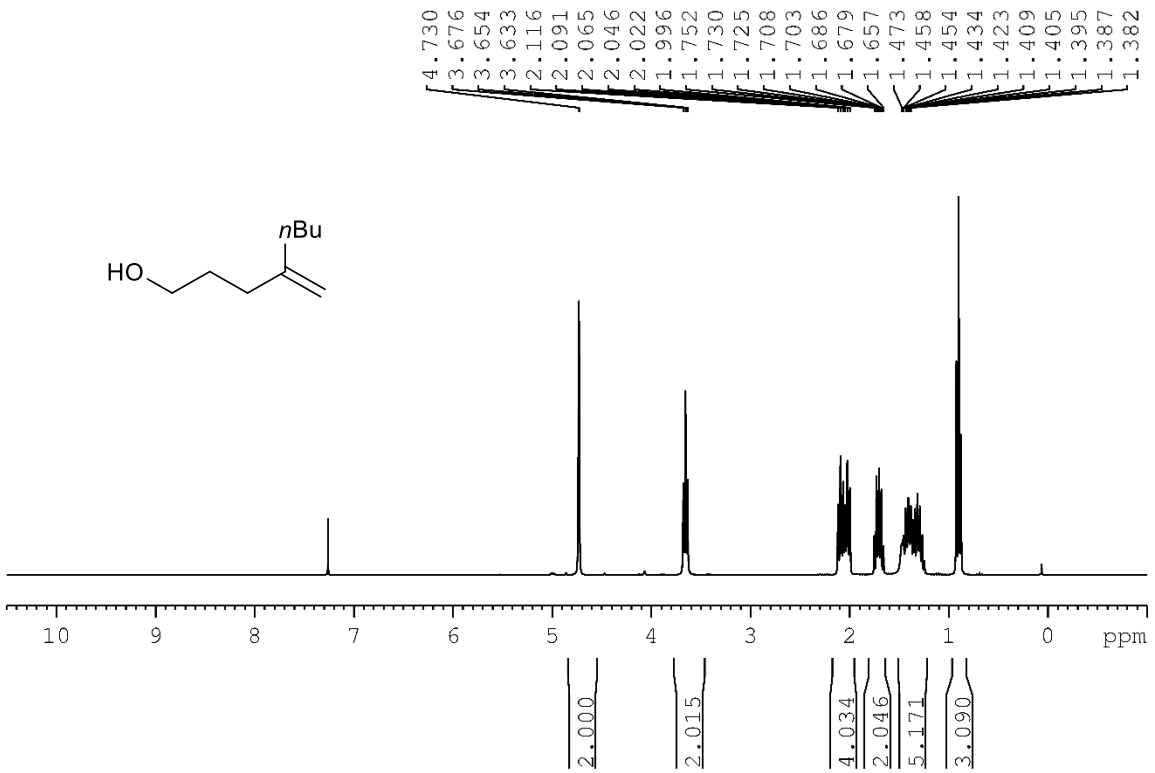


Figure S35. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 4-methylene-1-octanol (**1t**).

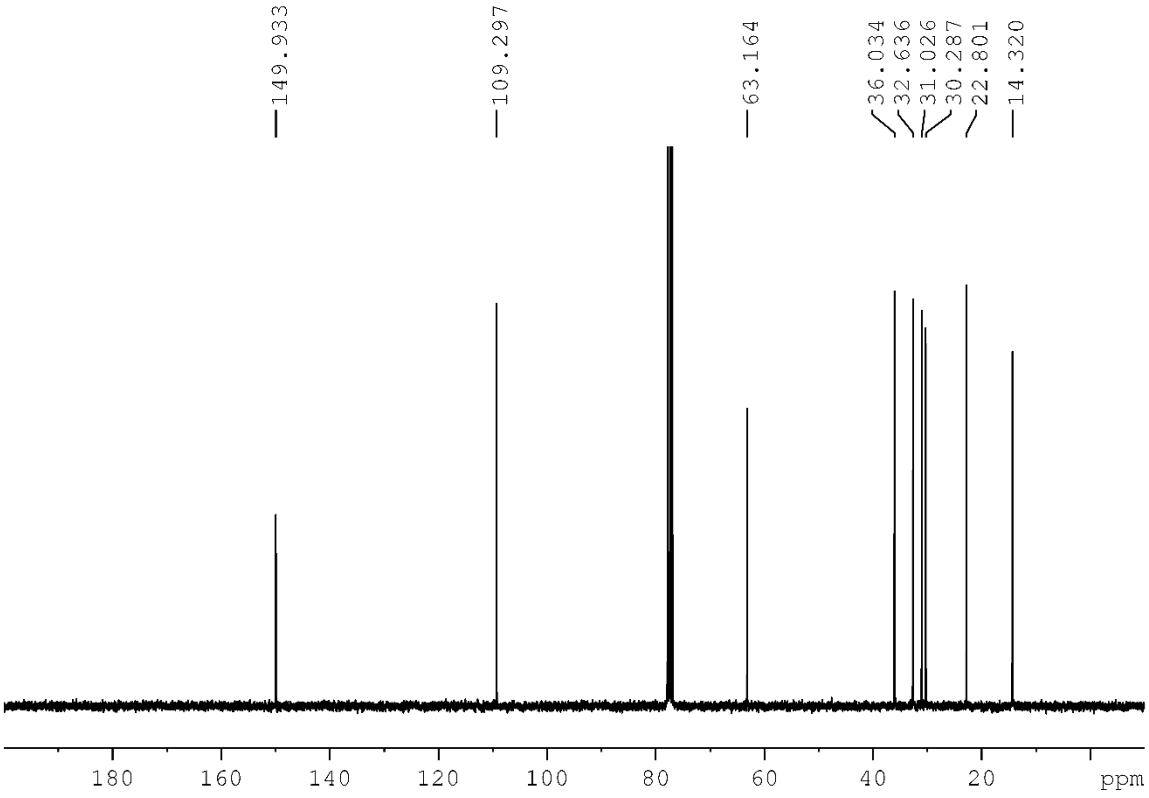


Figure S36. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 4-methylene-1-octanol (**1t**).

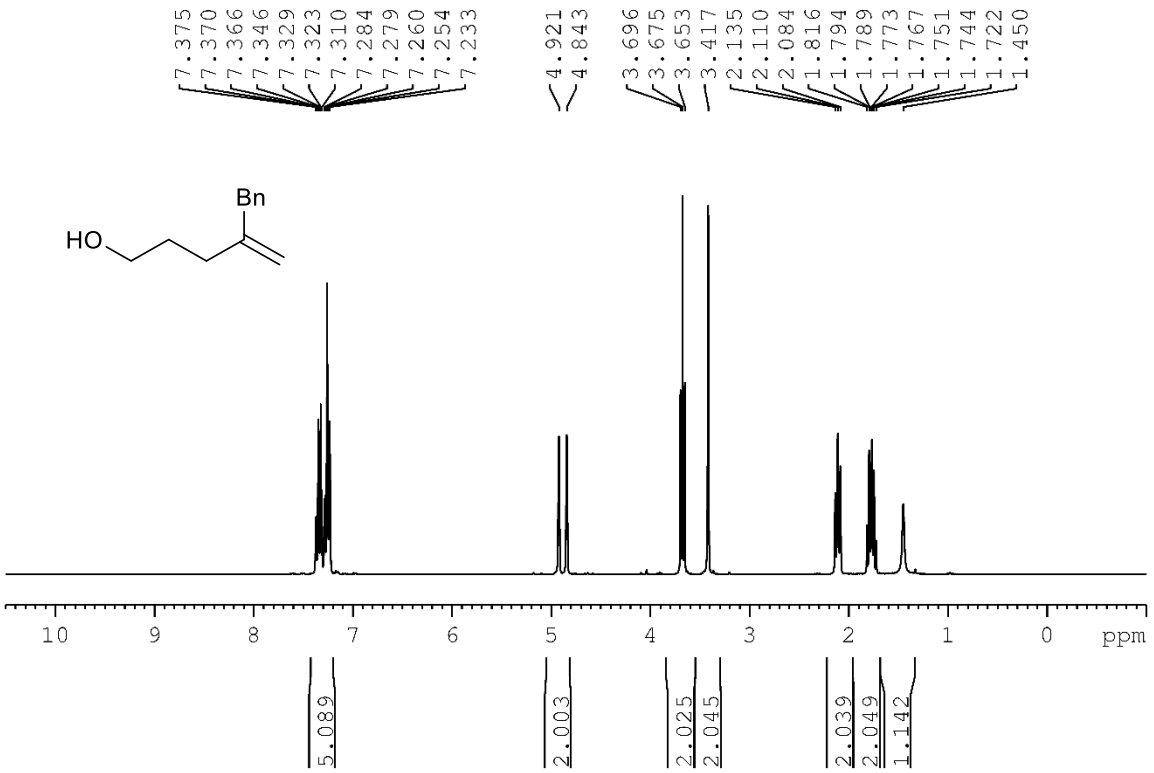


Figure S37. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 4-benzyl-4-penten-1-ol (**1u**).

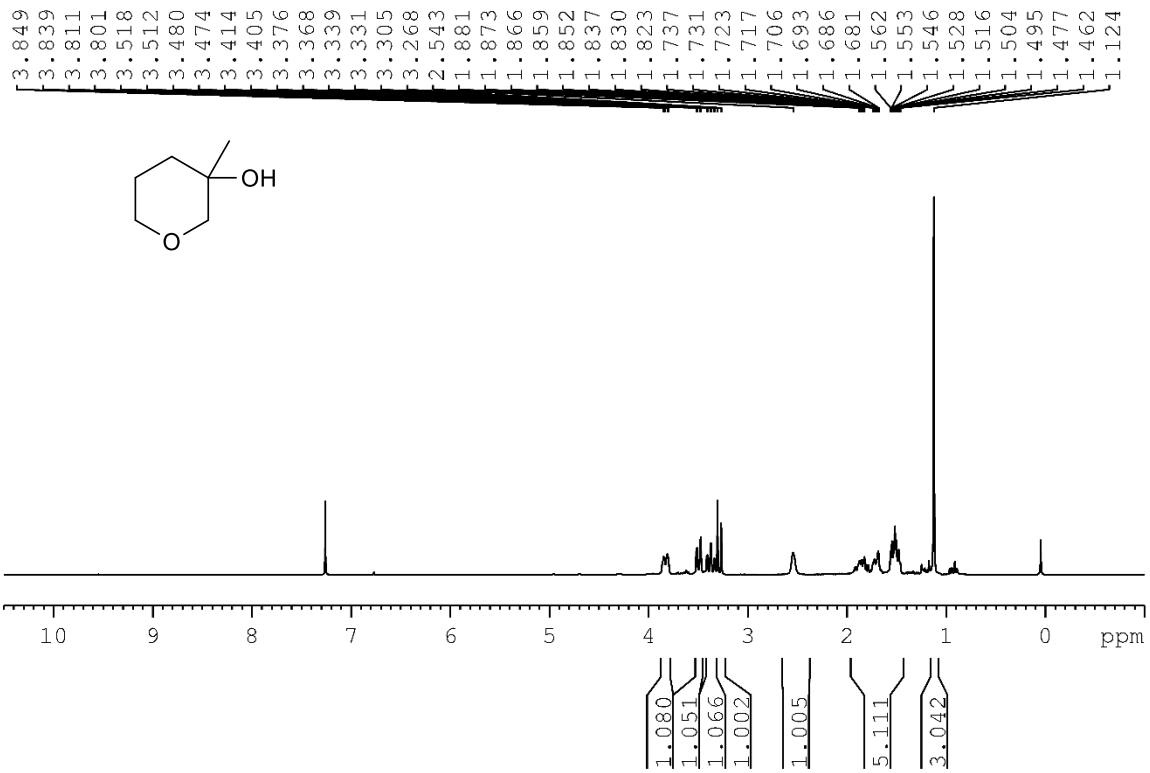


Figure S38. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3-methyltetrahydropyran (**2a**).

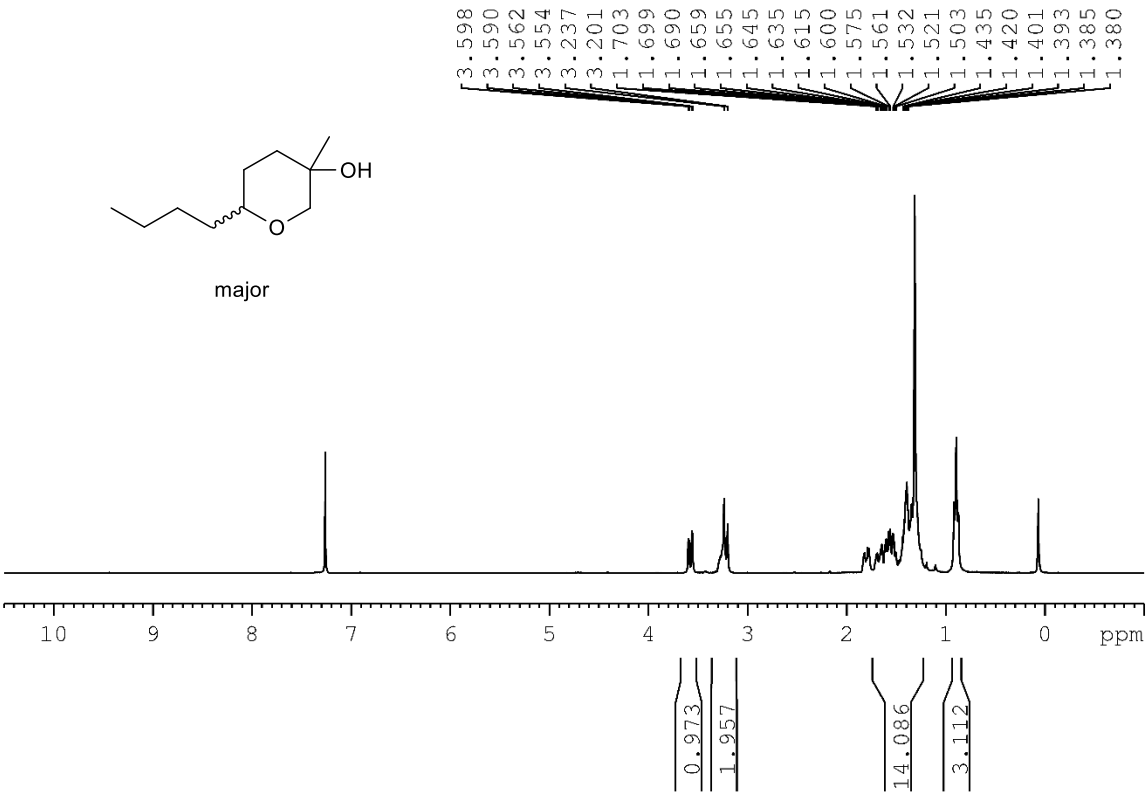


Figure S39. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2b**) major isomer.

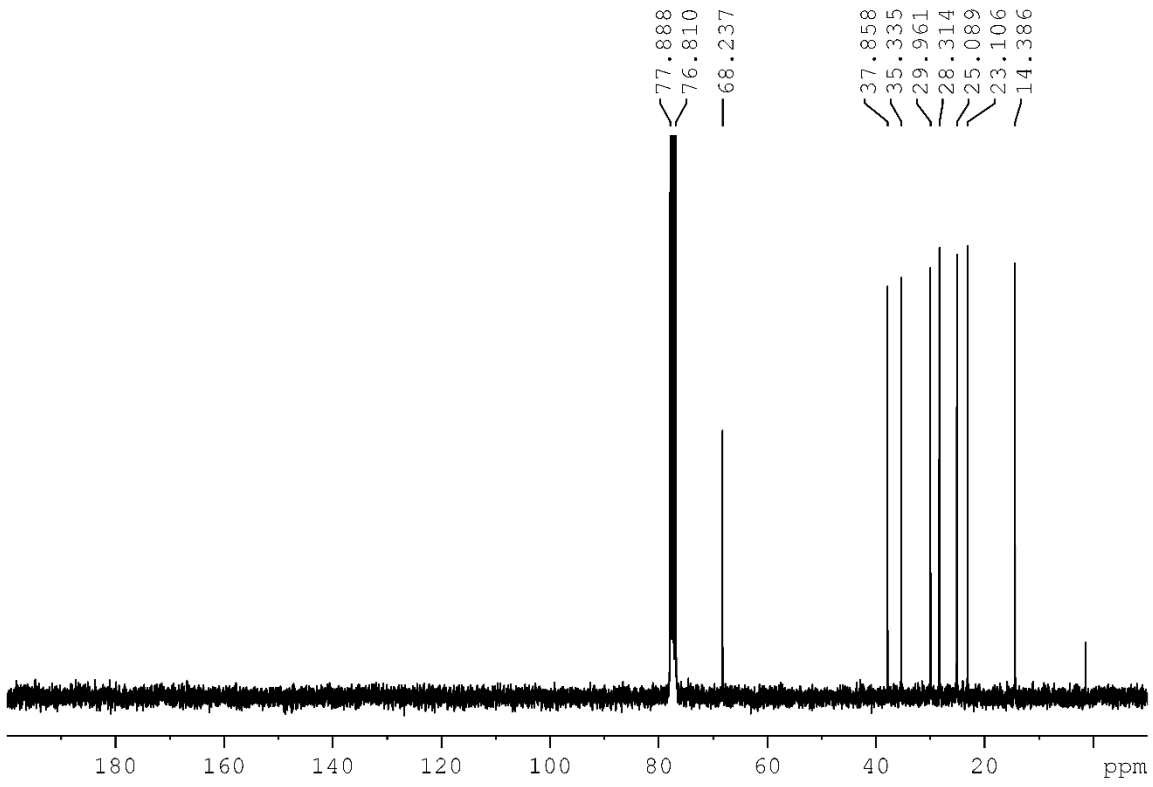


Figure S40. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2b**) major isomer.

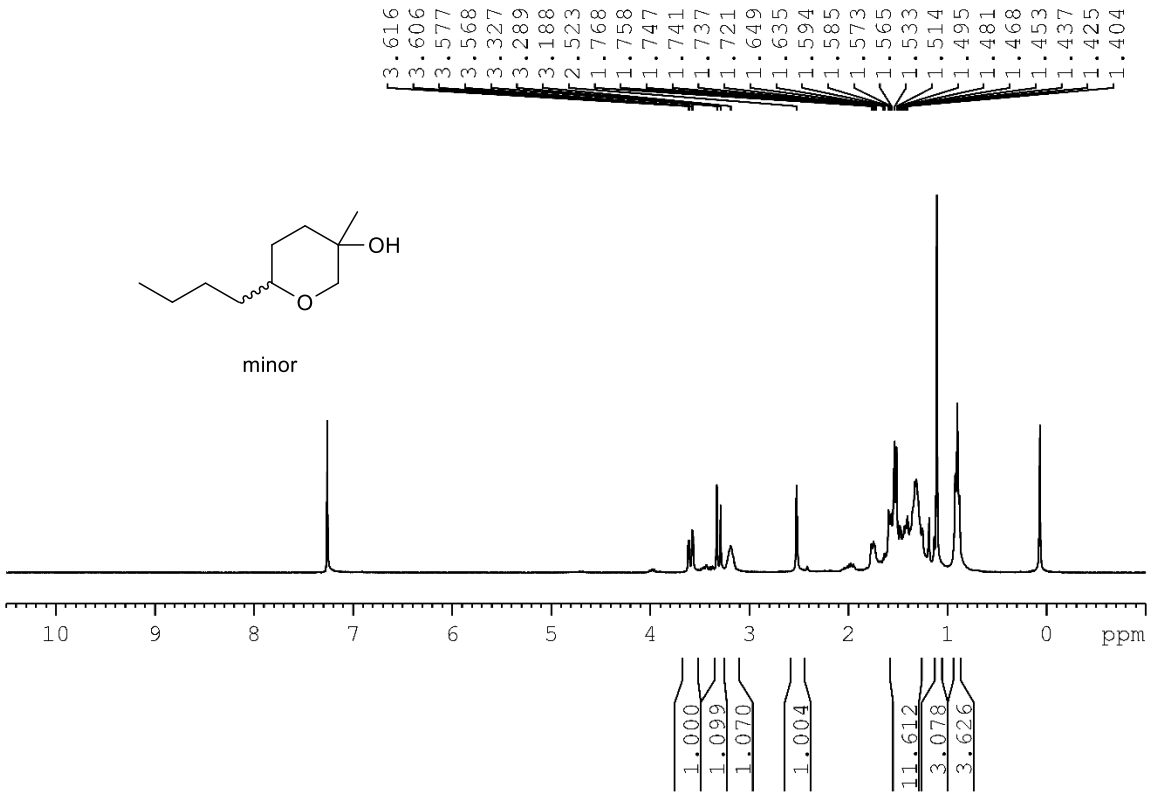


Figure S41. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2b**) minor isomer.

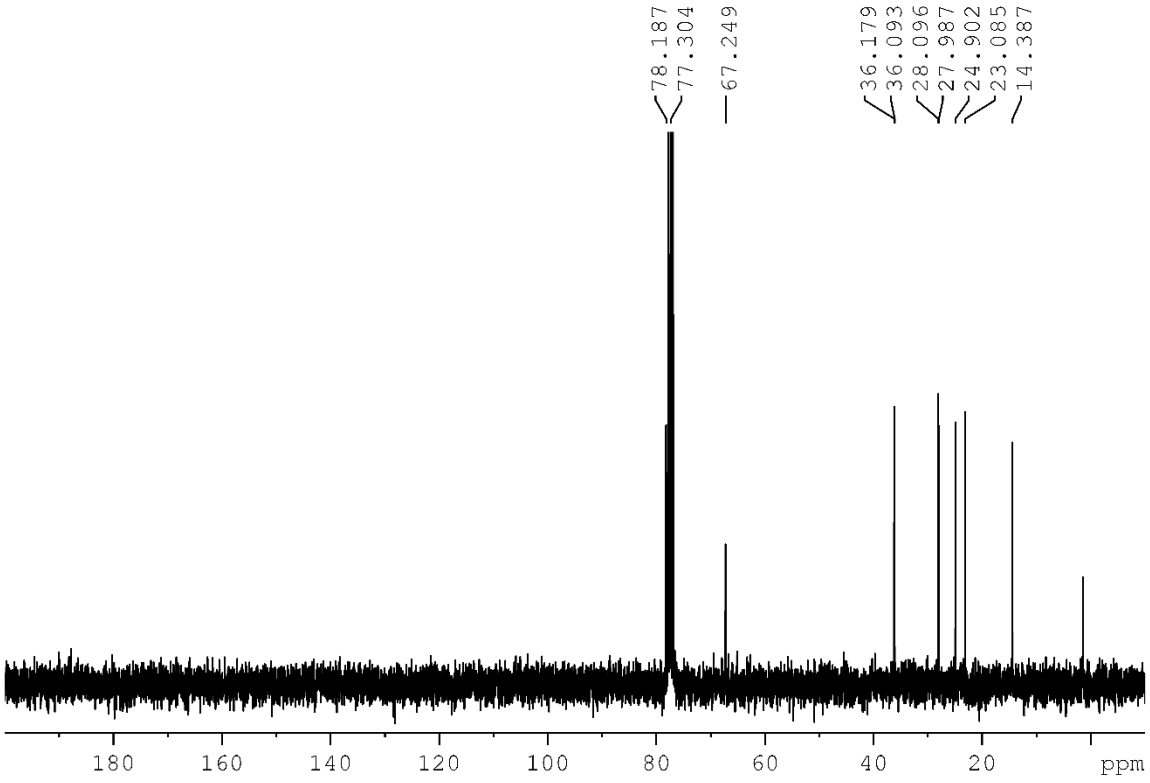


Figure S42. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2b**) minor isomer.

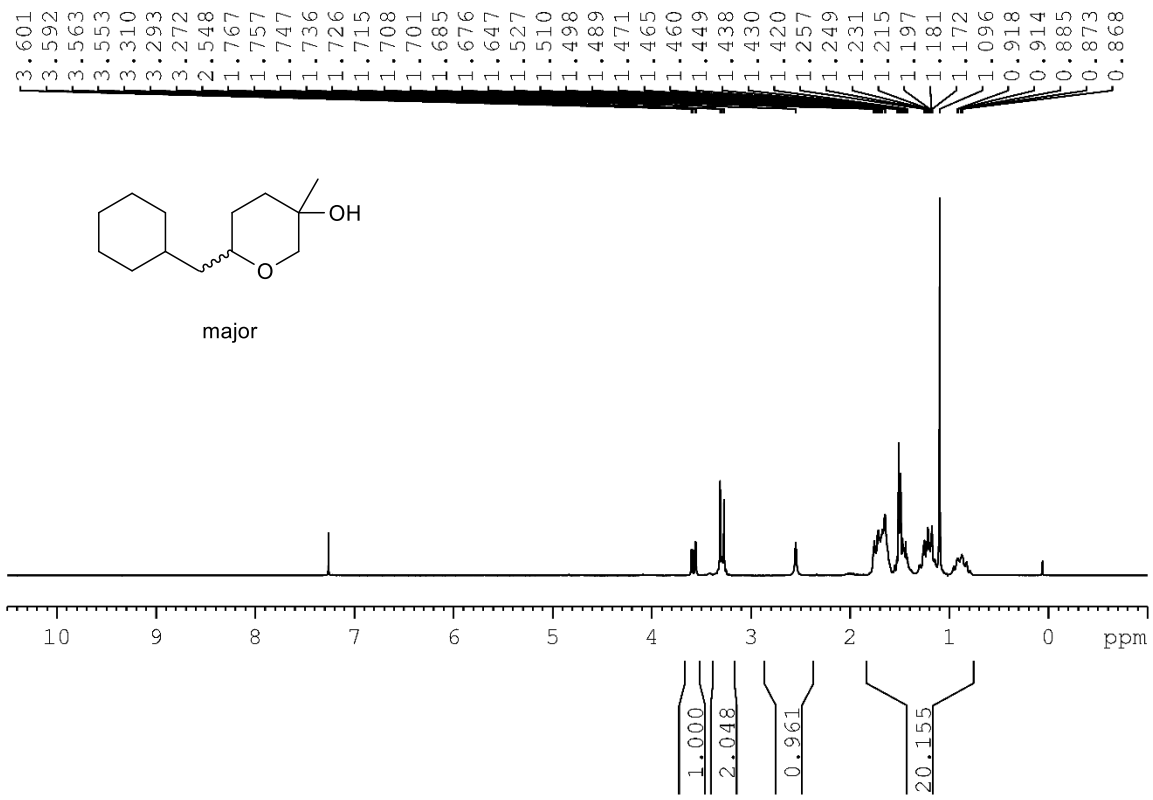


Figure S43. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-cyclohexylmethyl-3-hydroxy-3-methyltetrahydropyran (**2c**) major isomer.

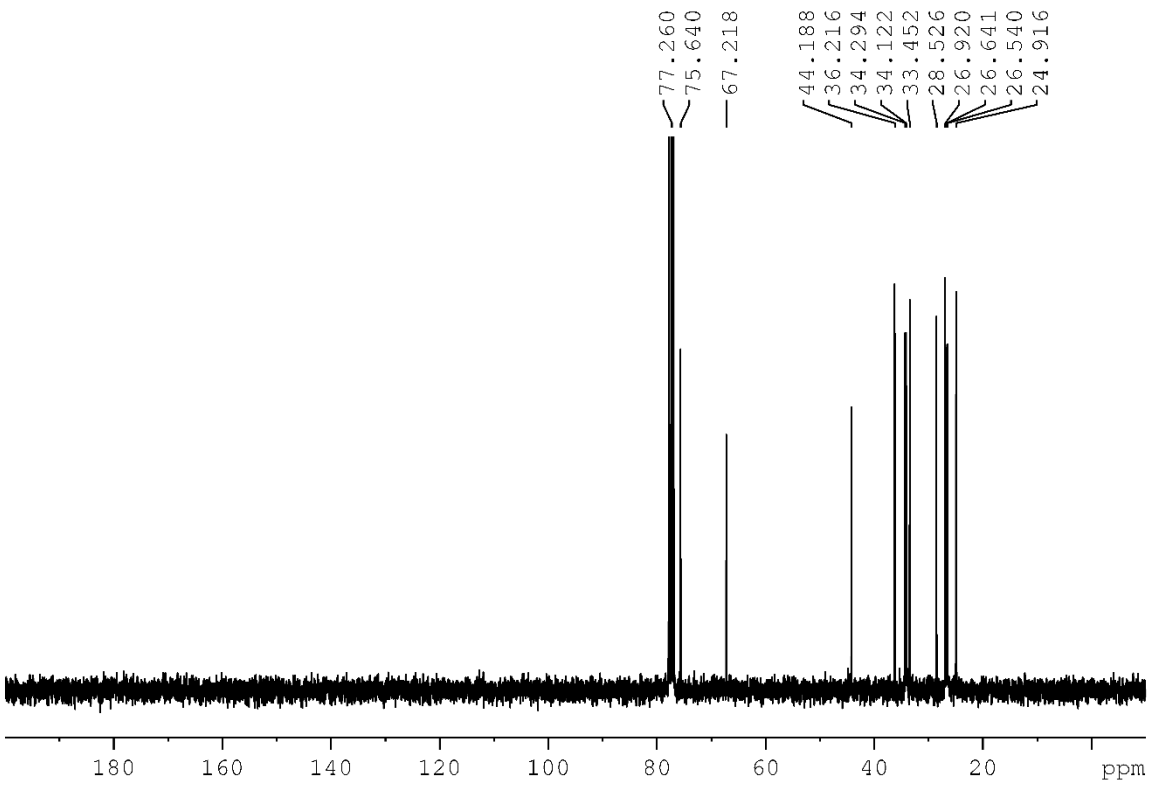


Figure S44. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-cyclohexylmethyl-3-hydroxy-3-methyltetrahydropyran (**2c**) major isomer.

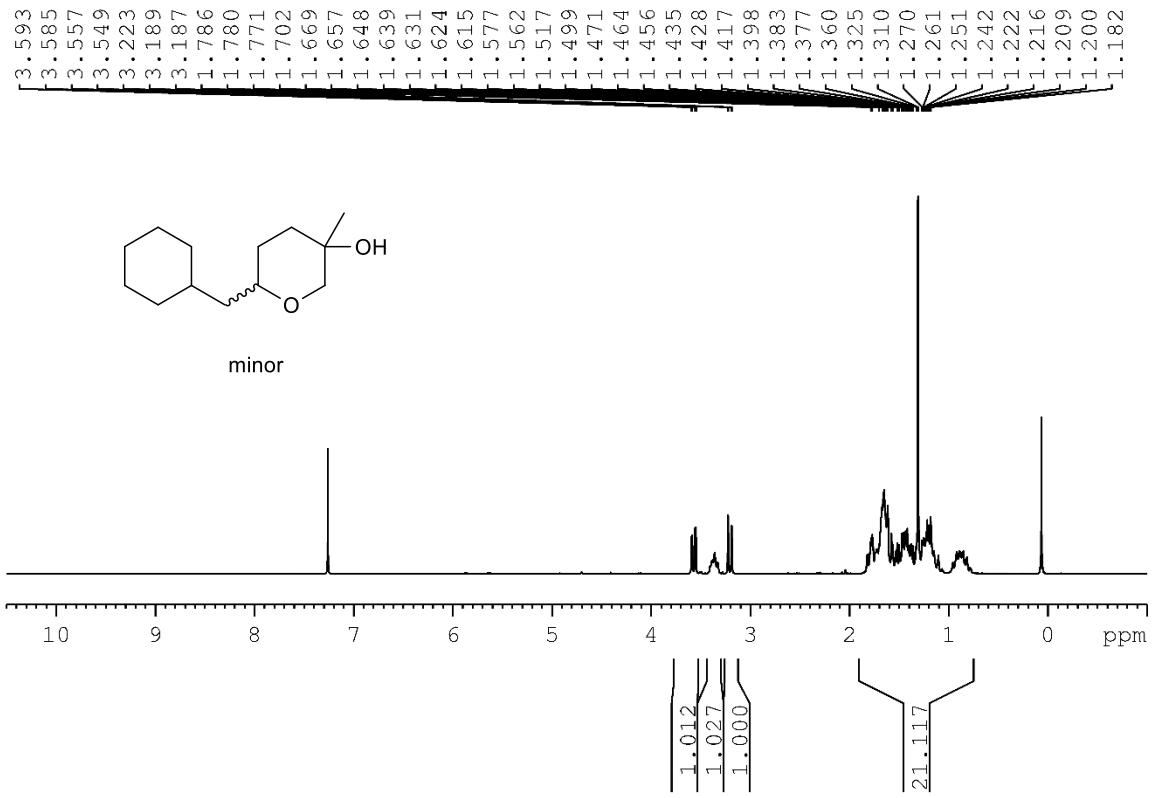


Figure S45. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-cyclohexylmethyl-3-hydroxy-3-methyltetrahydropyran (**2c**) minor isomer.

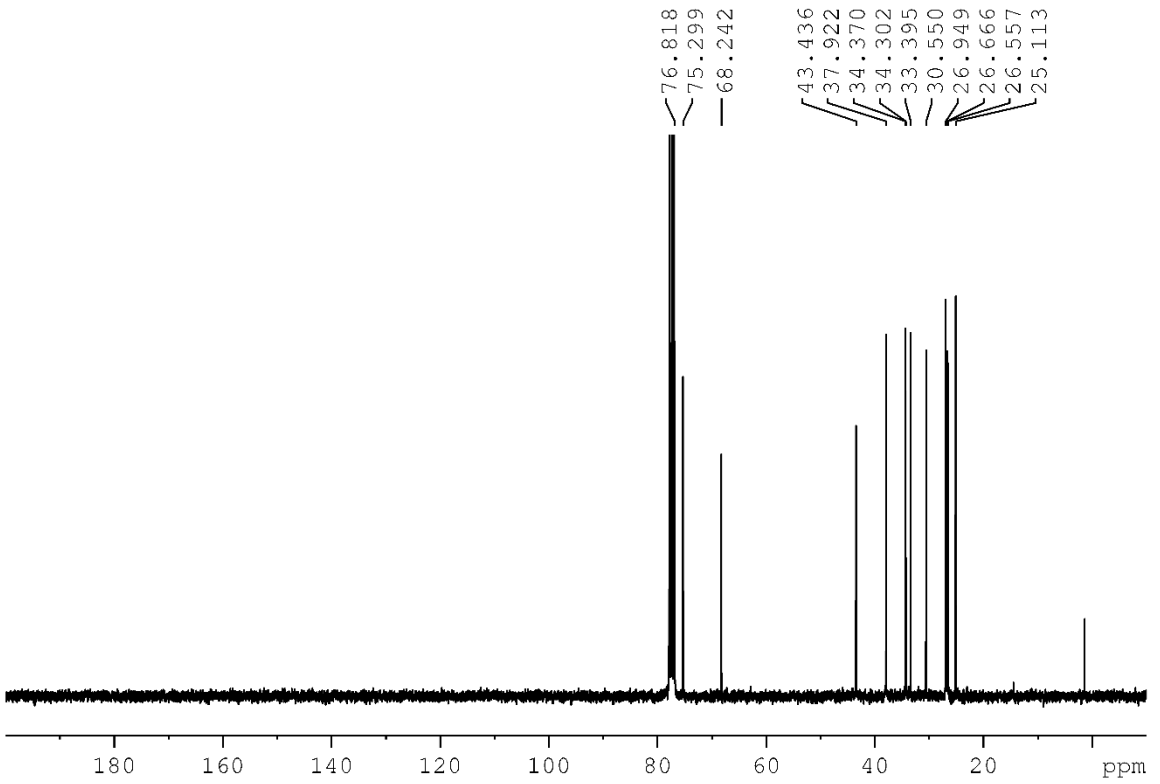


Figure S46. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-cyclohexylmethyl-3-hydroxy-3-methyltetrahydropyran (**2c**) minor isomer.

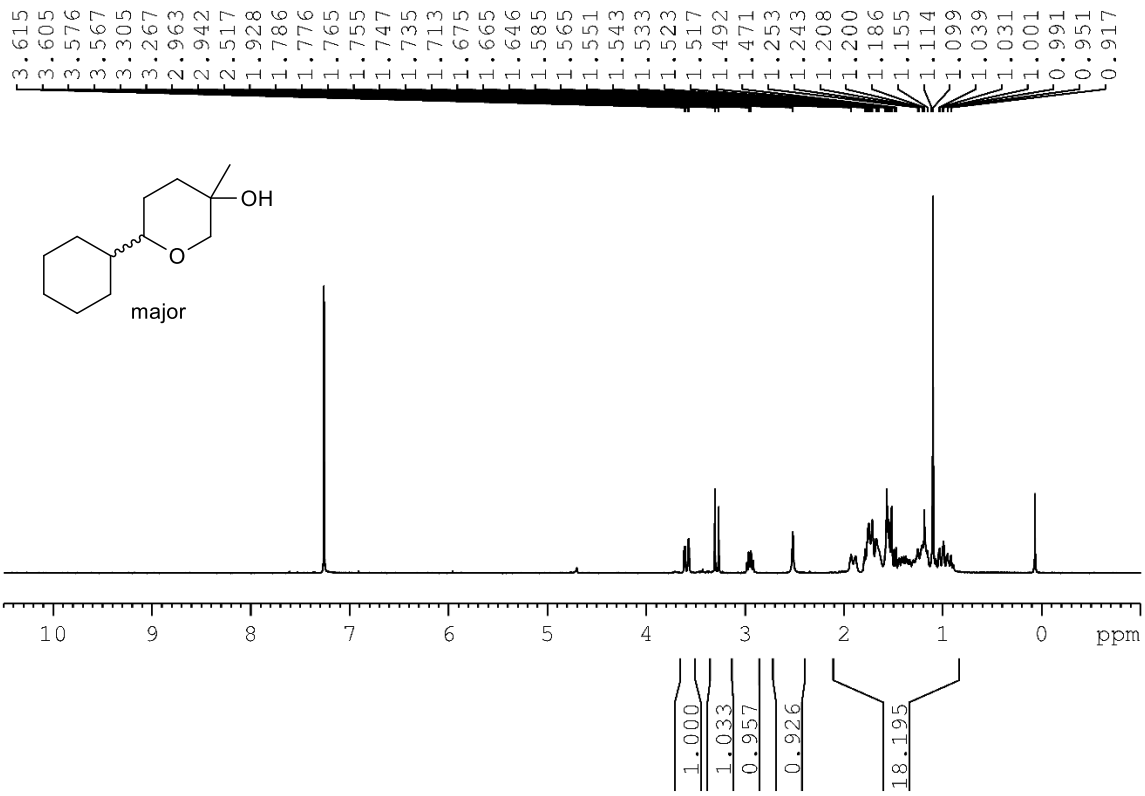


Figure S47. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-cyclohexyl-3-hydroxy-3-methyltetrahydropyran (**2d**) major isomer.

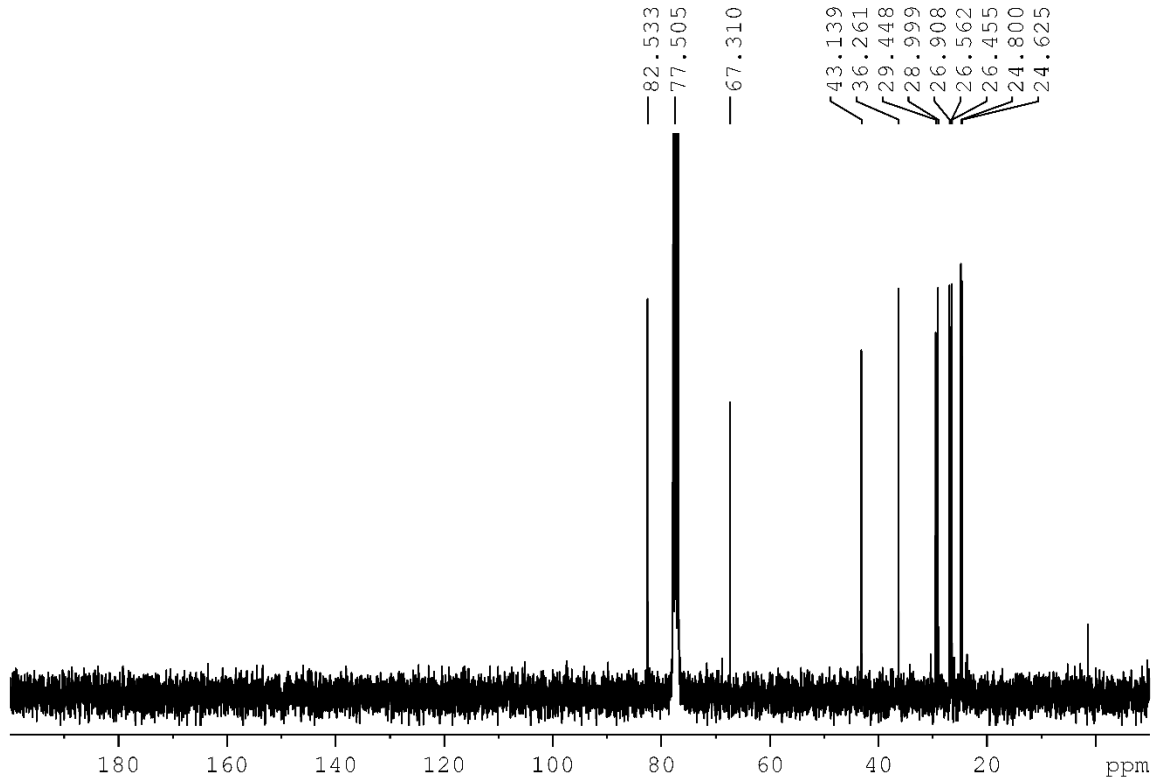


Figure S48. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-cyclohexyl-3-hydroxy-3-methyltetrahydropyran (**2d**) major isomer.

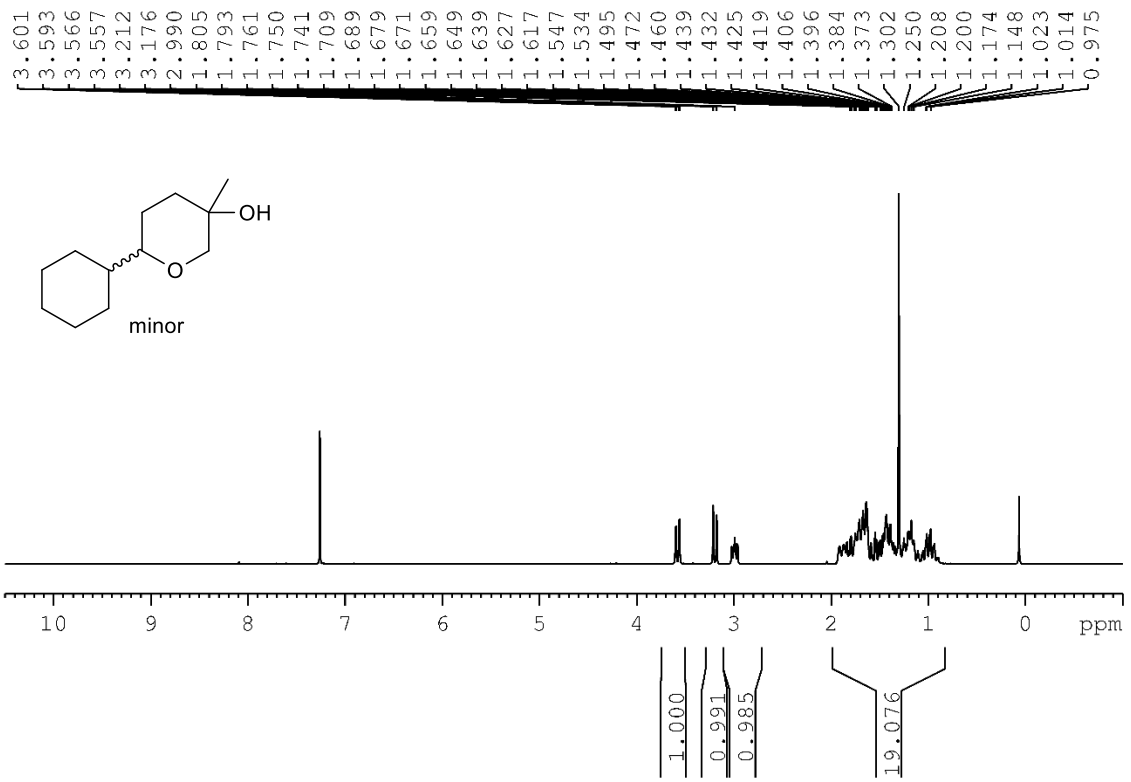


Figure S49. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-cyclohexyl-3-hydroxy-3-methyltetrahydropyran (**2d**) minor isomer.

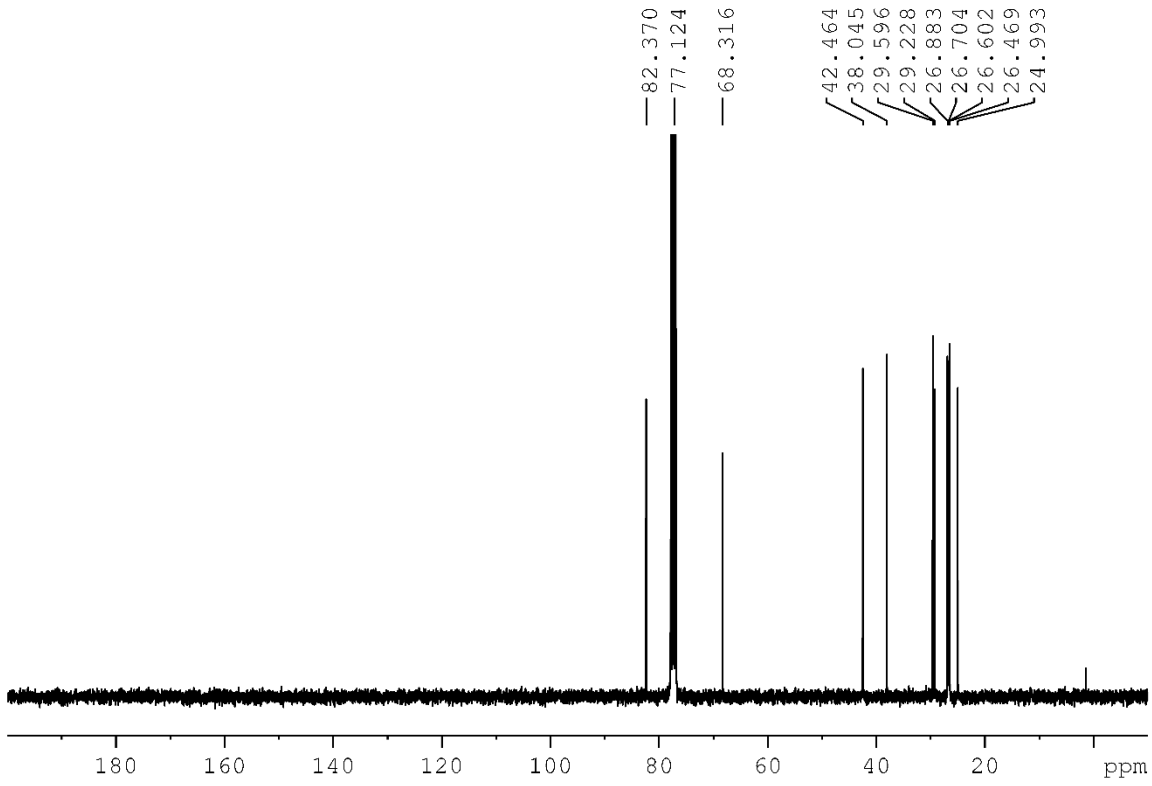


Figure S50. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-cyclohexyl-3-hydroxy-3-methyltetrahydropyran (**2d**) minor isomer.

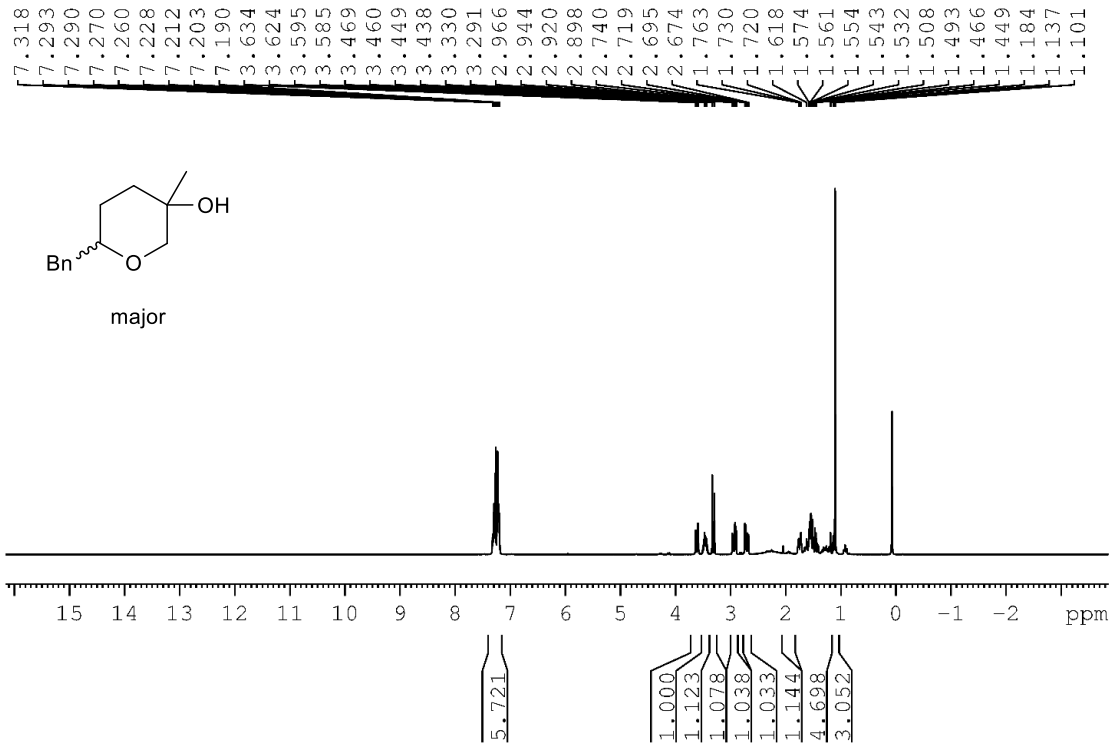


Figure S51. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-benzyl-3-hydroxy-3-methyltetrahydropyran (**2e**) major isomer.

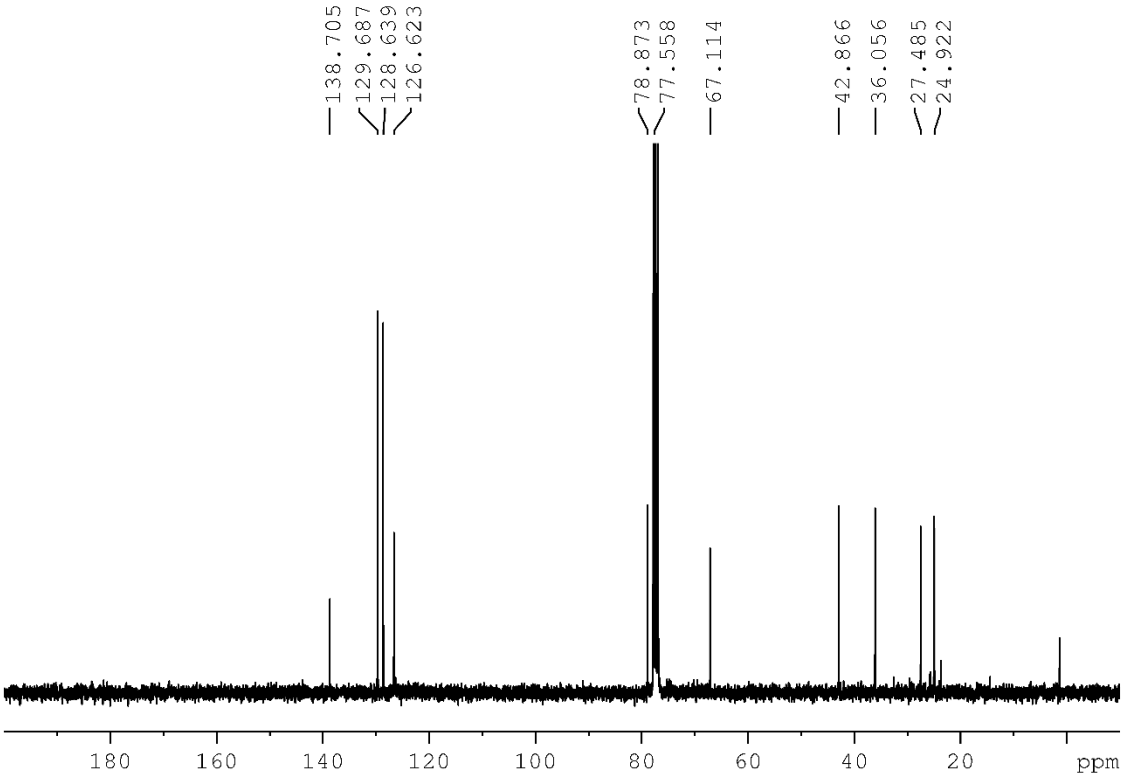


Figure S52. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-benzyl-3-hydroxy-3-methyltetrahydropyran (**2e**) major isomer.

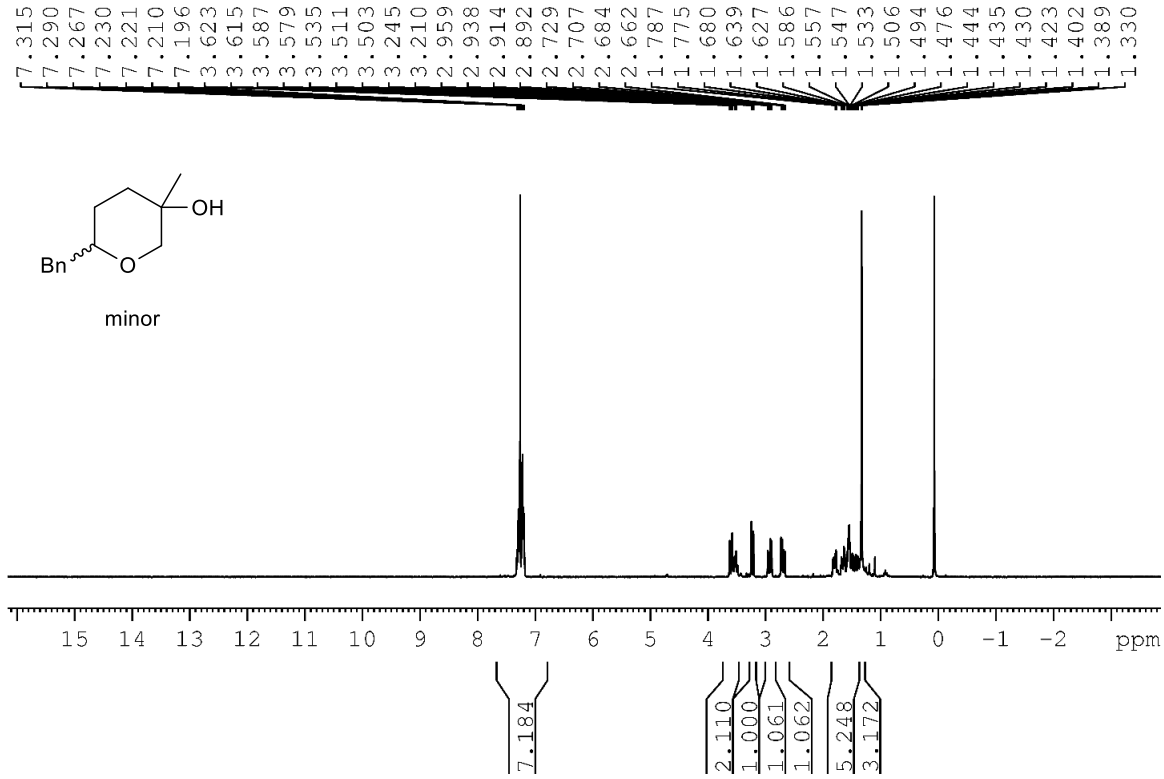


Figure S53. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6-benzyl-3-hydroxy-3-methyltetrahydropyran (**2e**) minor isomer.

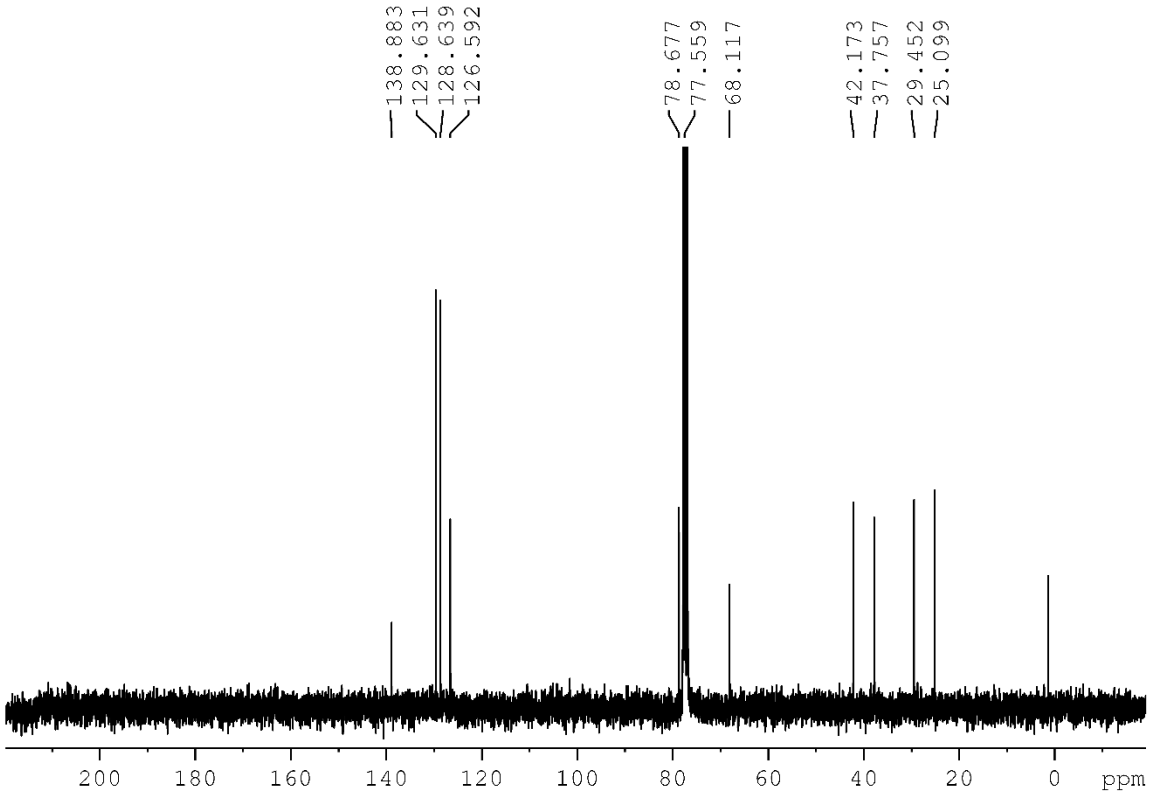


Figure S54. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6-benzyl-3-hydroxy-3-methyltetrahydropyran (**2e**) minor isomer.

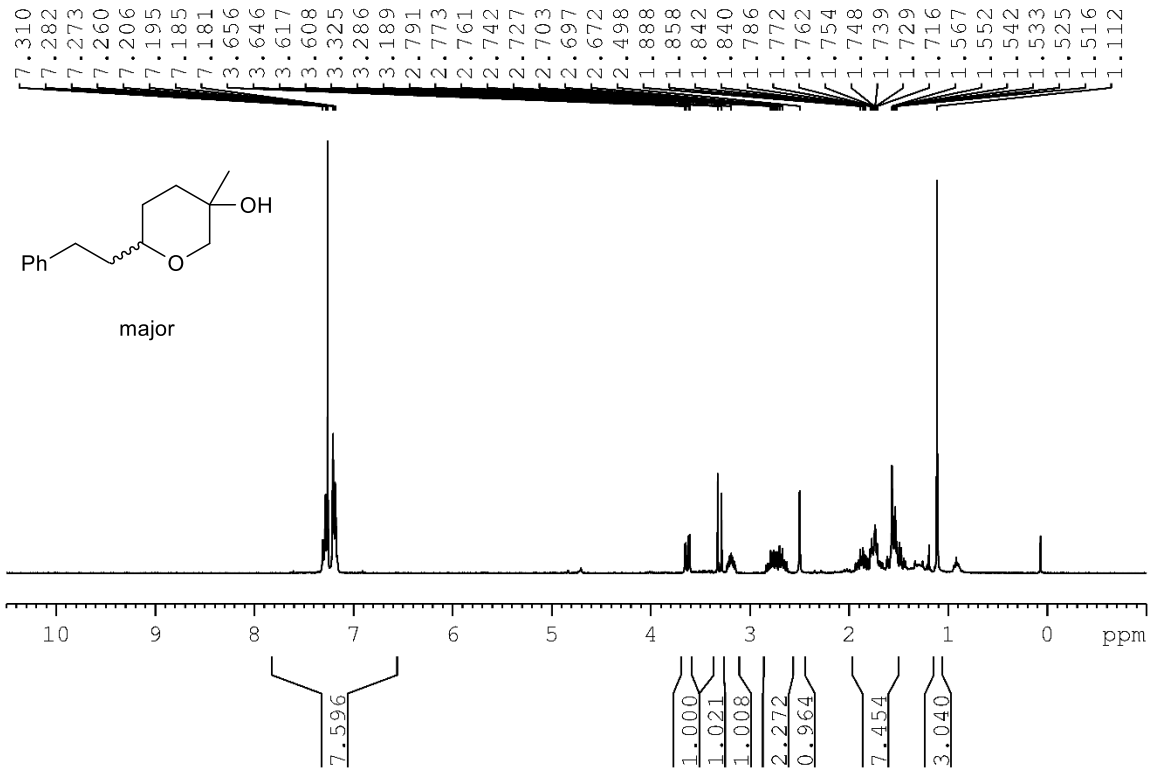


Figure S55. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-Hydroxy-3-methyl-6-phenethyltetrahydro pyran (**2f**) major isomer.

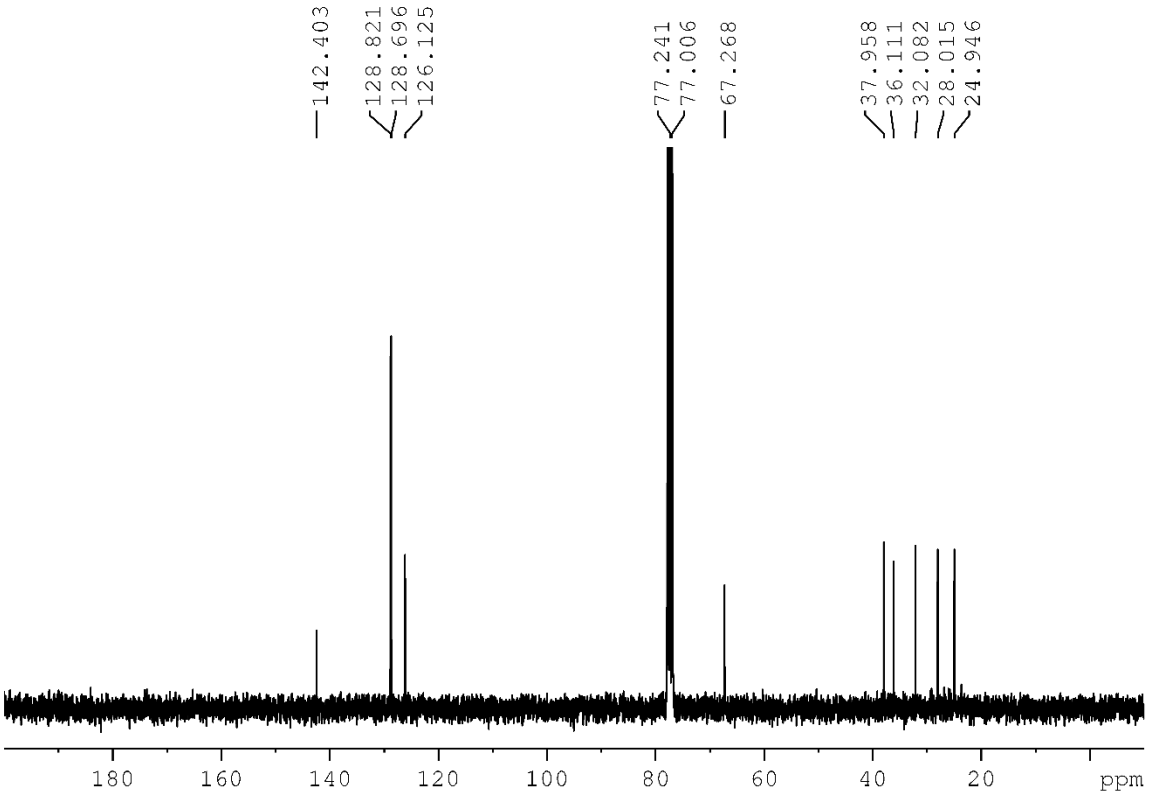


Figure S56. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-Hydroxy-3-methyl-6-phenethyltetrahydro pyran (**2f**) major isomer.

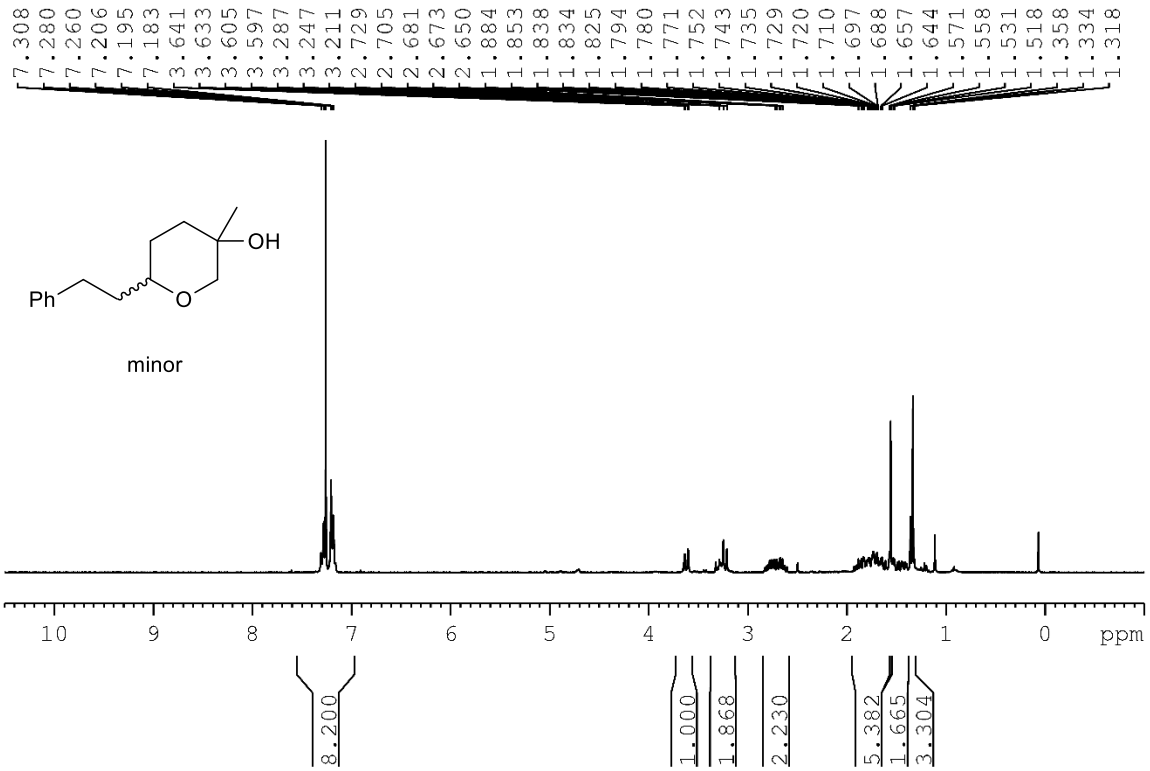


Figure S57. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-Hydroxy-3-methyl-6-phenethyltetrahydro pyran (**2f**) minor isomer.

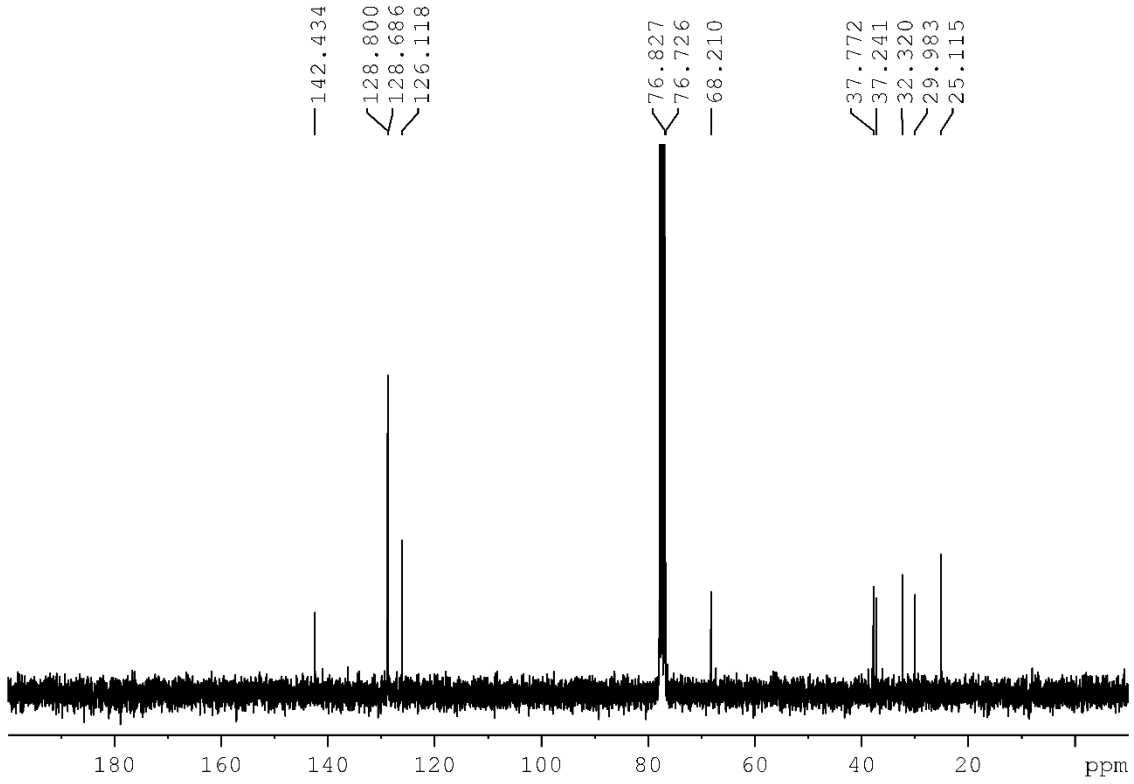


Figure S58. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-Hydroxy-3-methyl-6-phenethyltetrahydro pyran (**2f**) minor isomer.

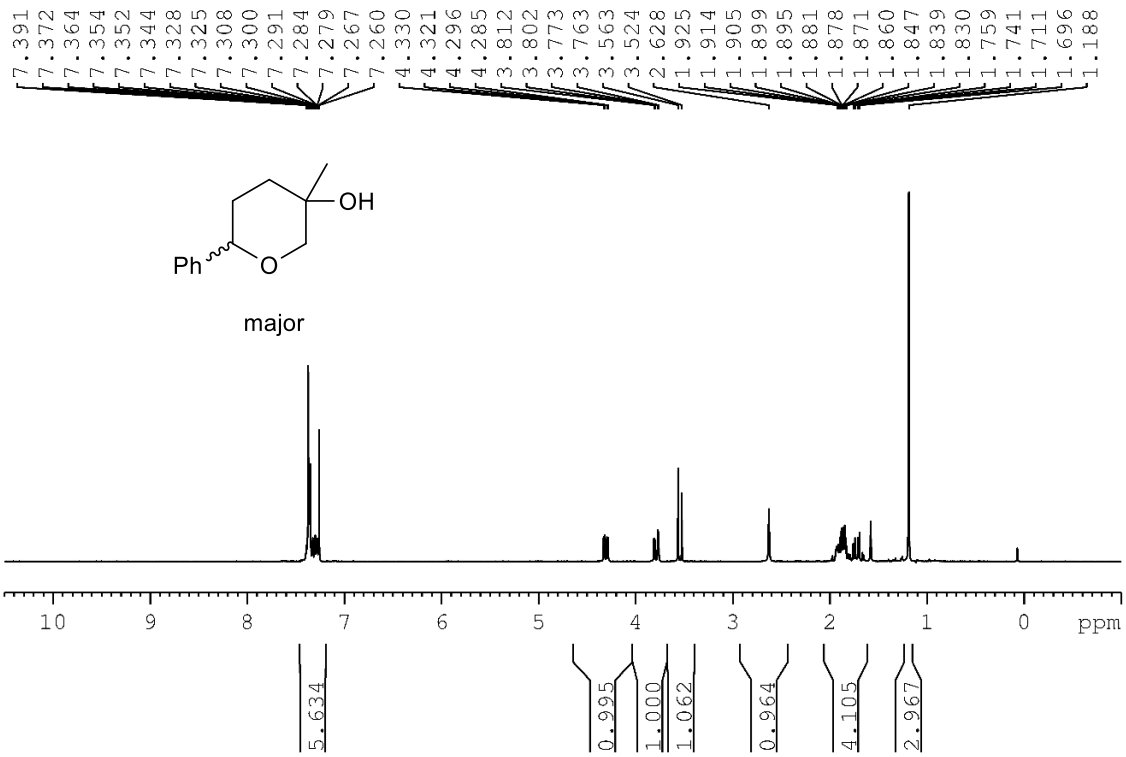


Figure S59. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-phenyltetrahydropyran (**2g**) major isomer.

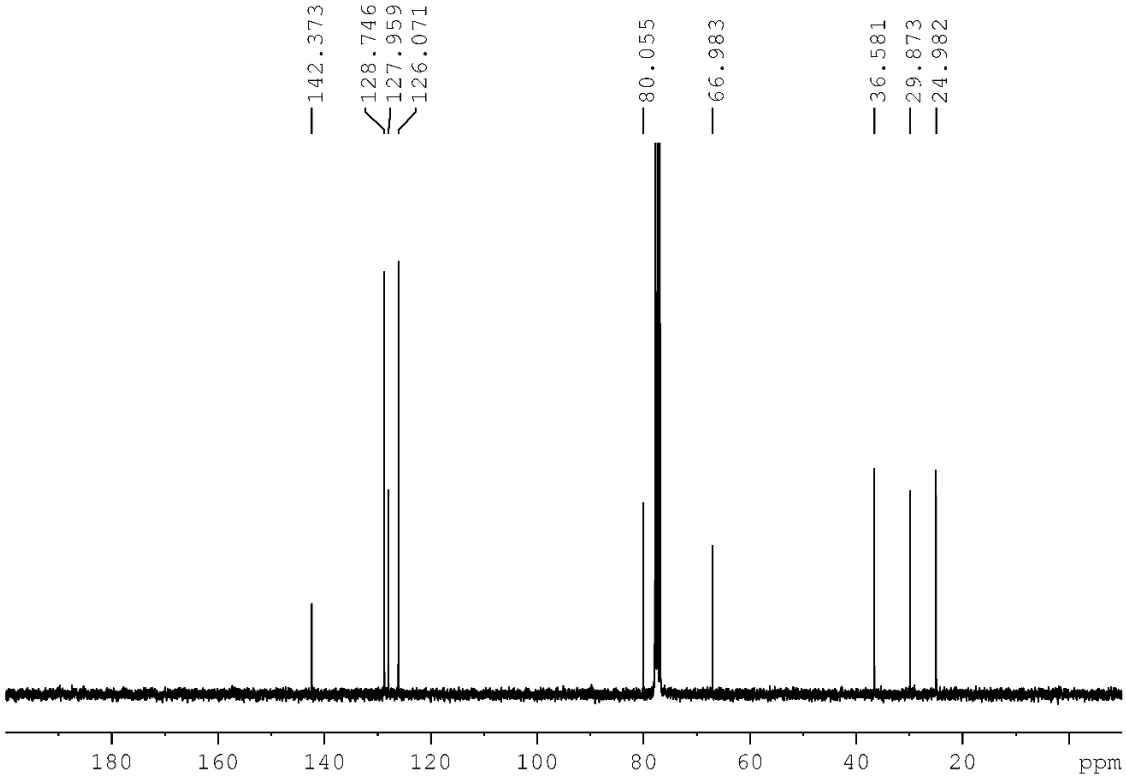


Figure S60. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-phenyltetrahydropyran (**2g**) major isomer.

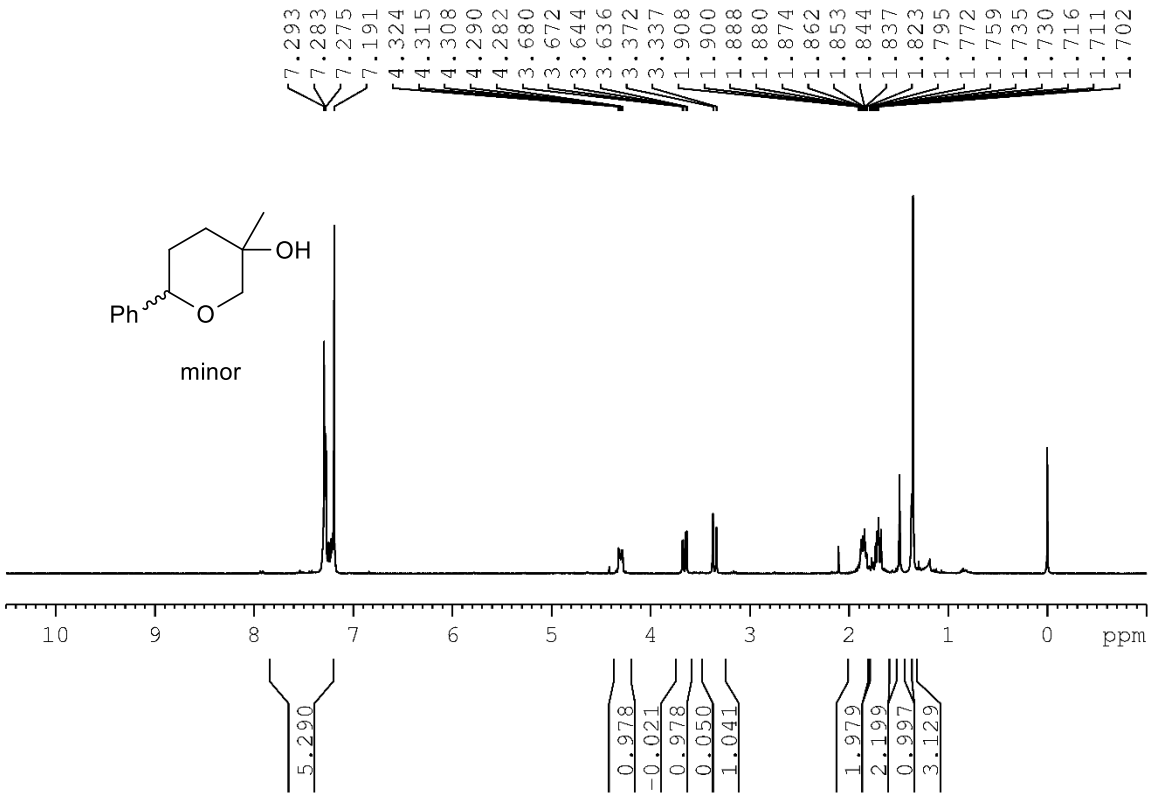


Figure S61. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-phenyltetrahydropyran (**2g**) minor isomer.

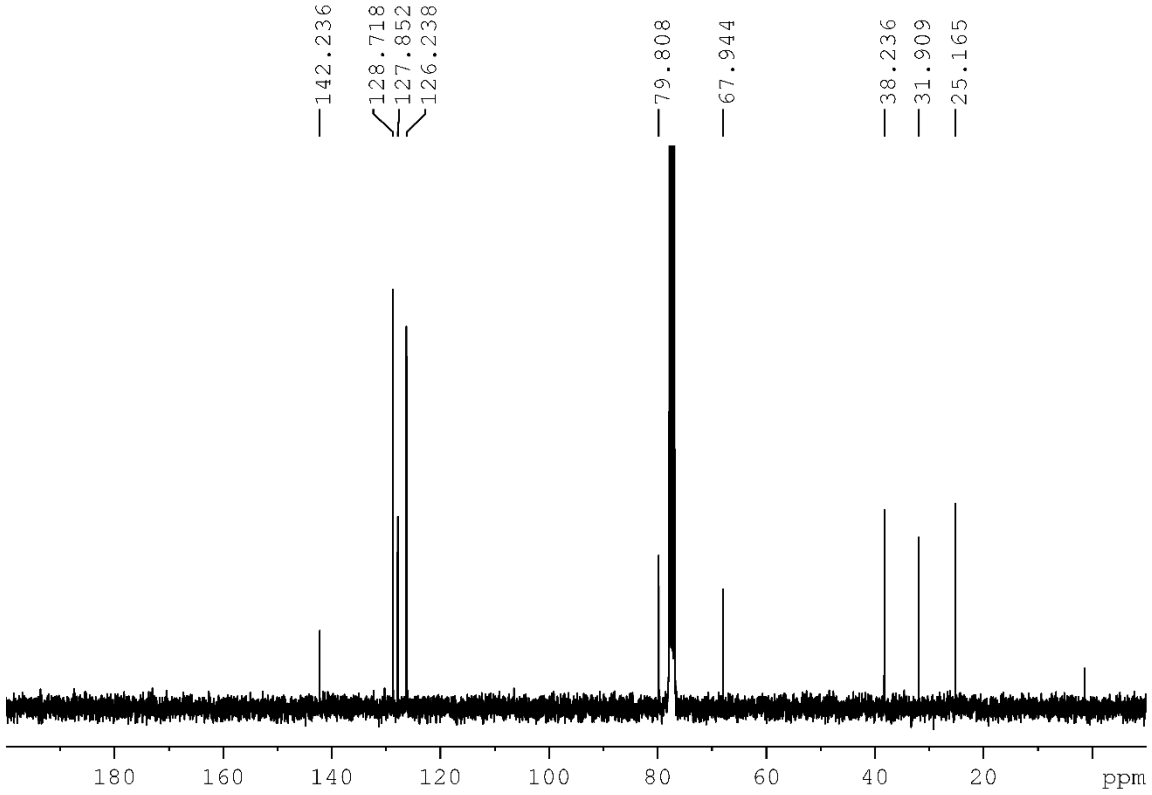


Figure S62. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-phenyltetrahydropyran (**2g**) minor isomer.

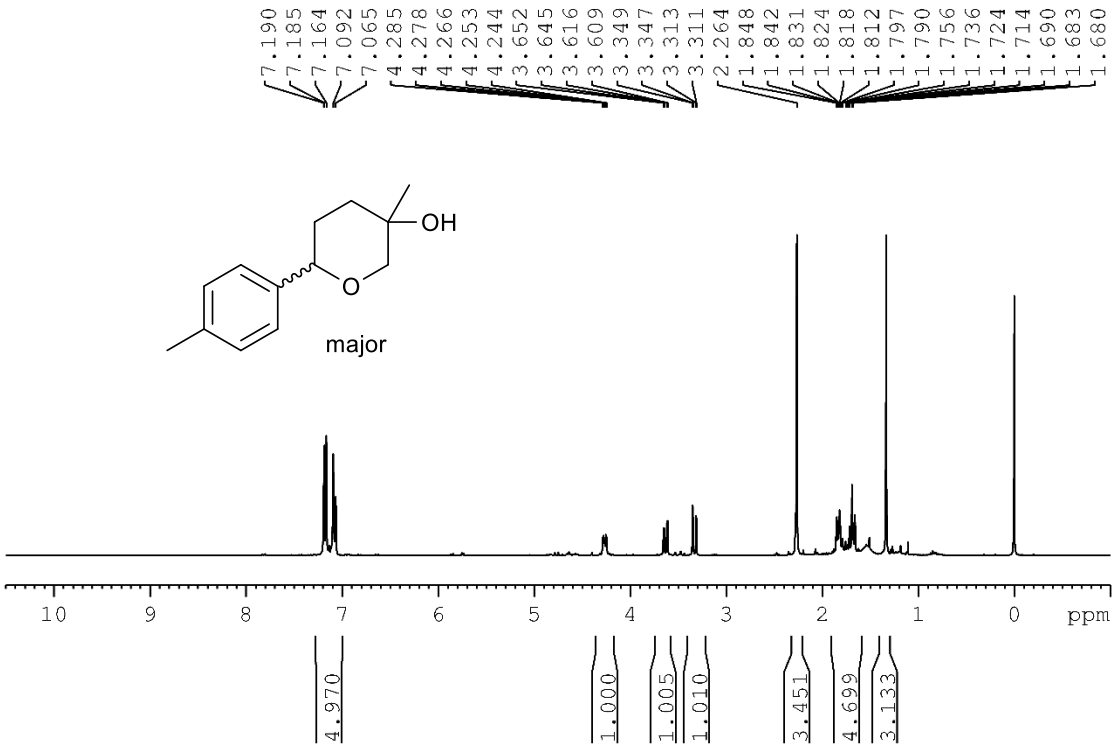


Figure S63. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-(*p*-tolyl)tetrahydropyran (**2h**) major isomer.

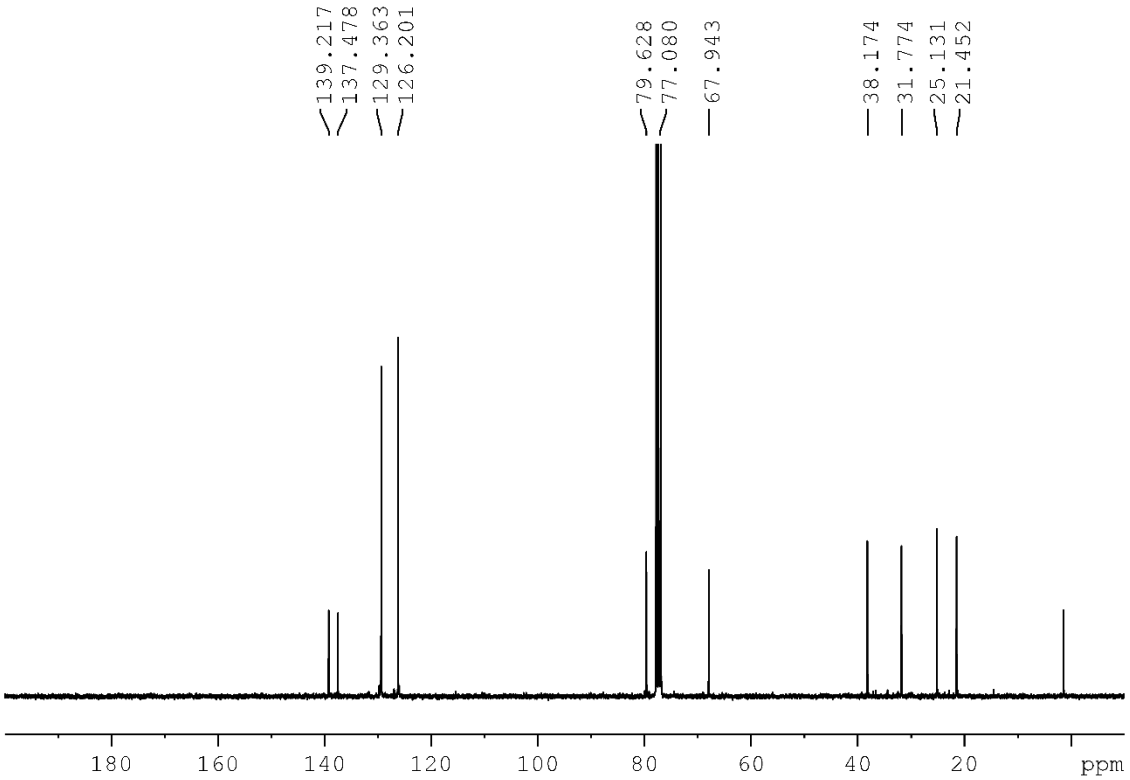


Figure S64. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-(*p*-tolyl)tetrahydropyran (**2h**) major isomer.

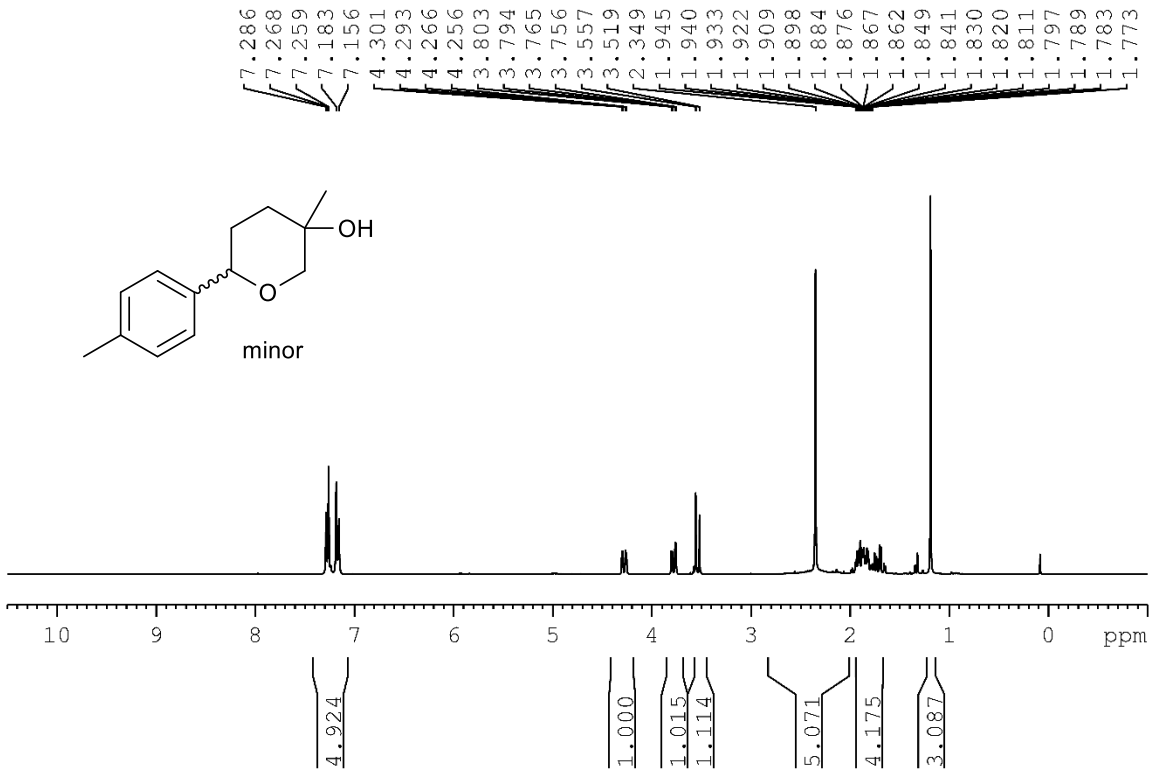


Figure S65. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-(*p*-tolyl)tetrahydropyran (**2h**) minor isomer.

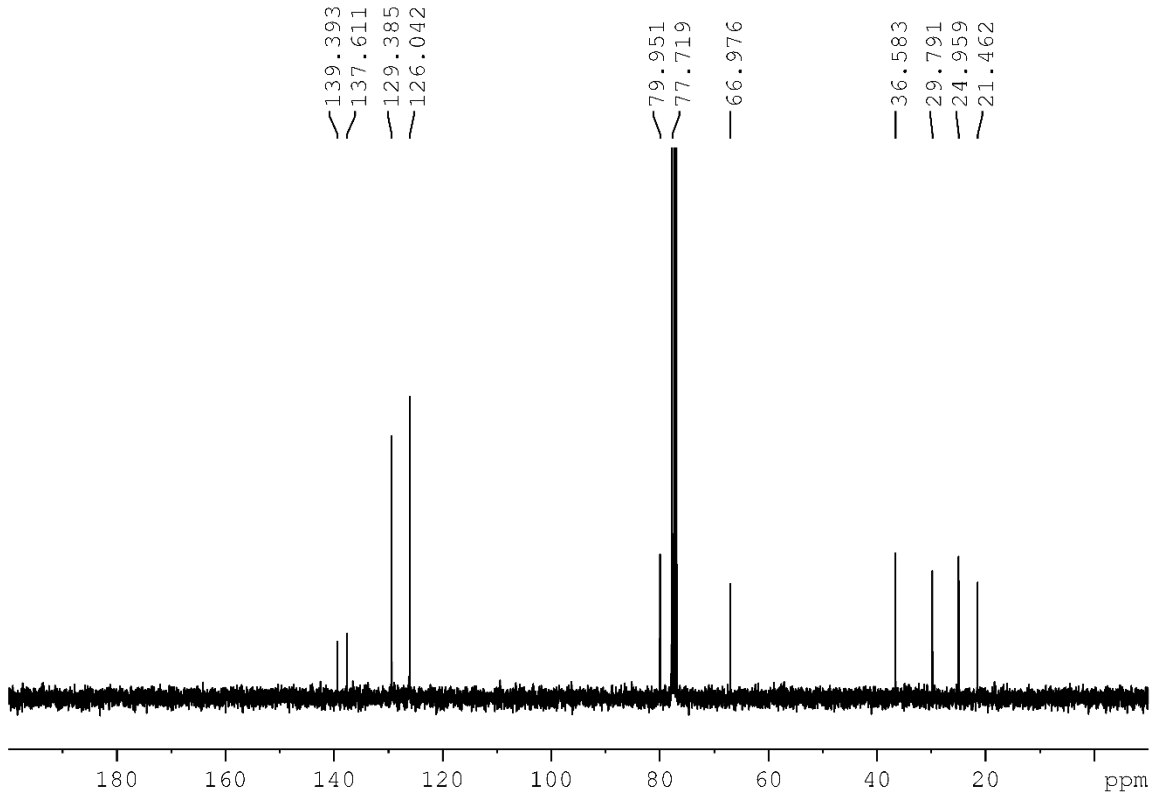


Figure S66. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3-methyl-6-(*p*-tolyl)tetrahydropyran (**2h**) minor isomer.

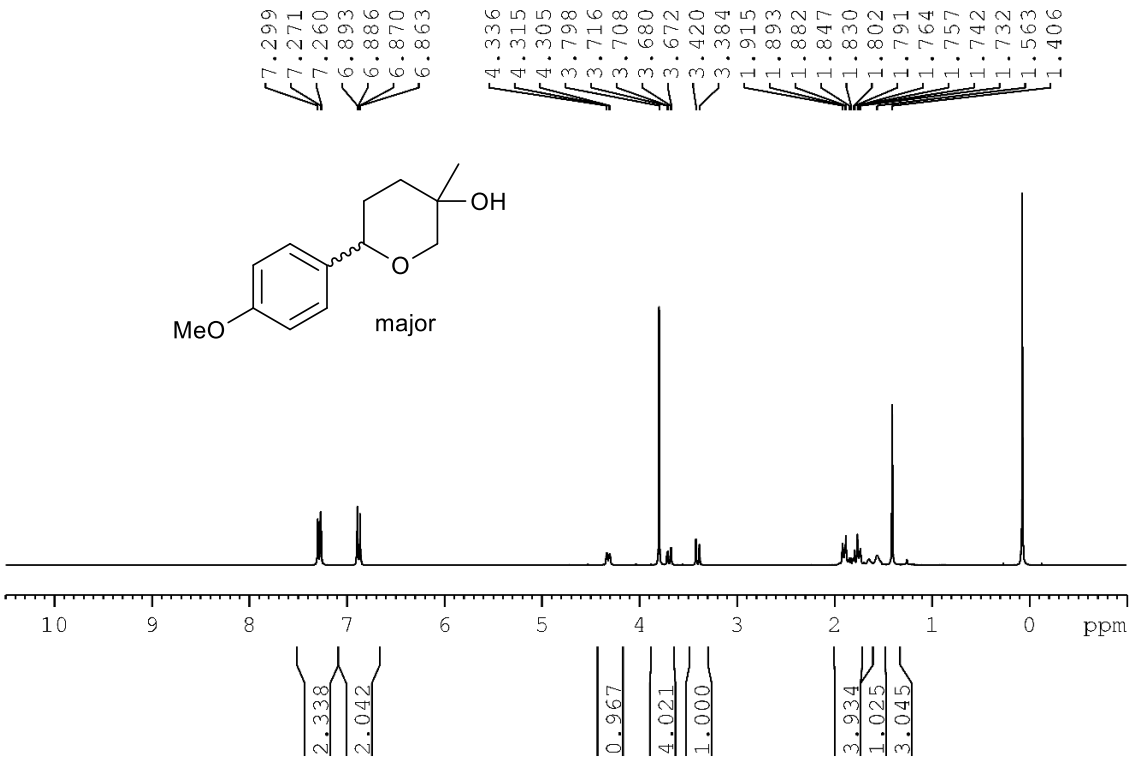


Figure S67. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-6-(*p*-methoxyphenyl)-3-methyltetrahydropyran (**2i**) major isomer.

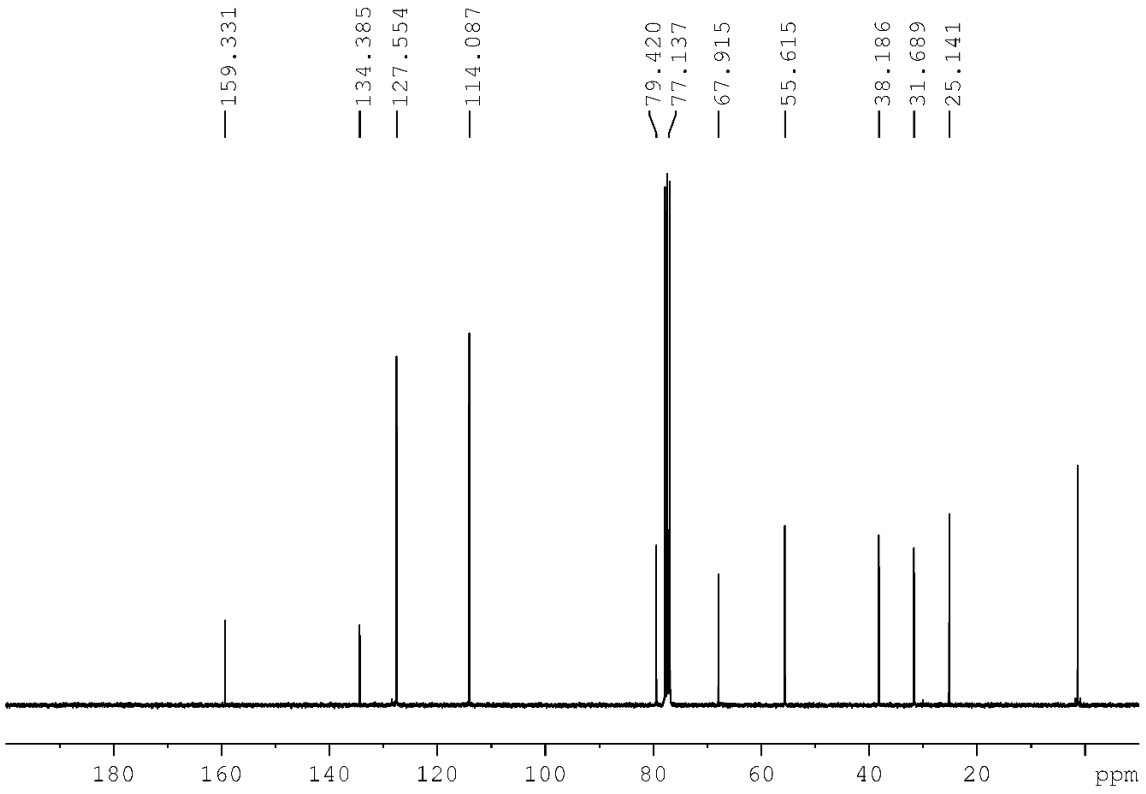


Figure S68. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-6-(*p*-methoxyphenyl)-3-methyltetrahydropyran (**2i**) major isomer.

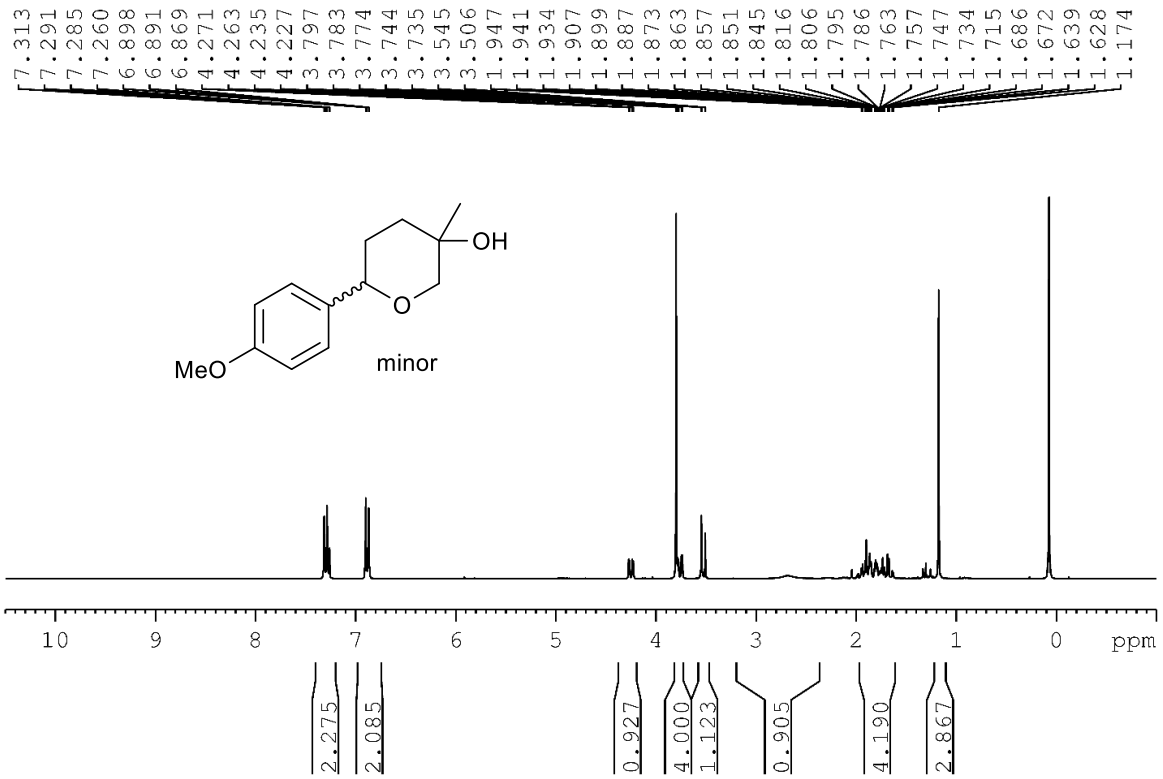


Figure S69. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-6-(*p*-methoxyphenyl)-3-methyltetrahydropyran (**2i**) minor isomer.

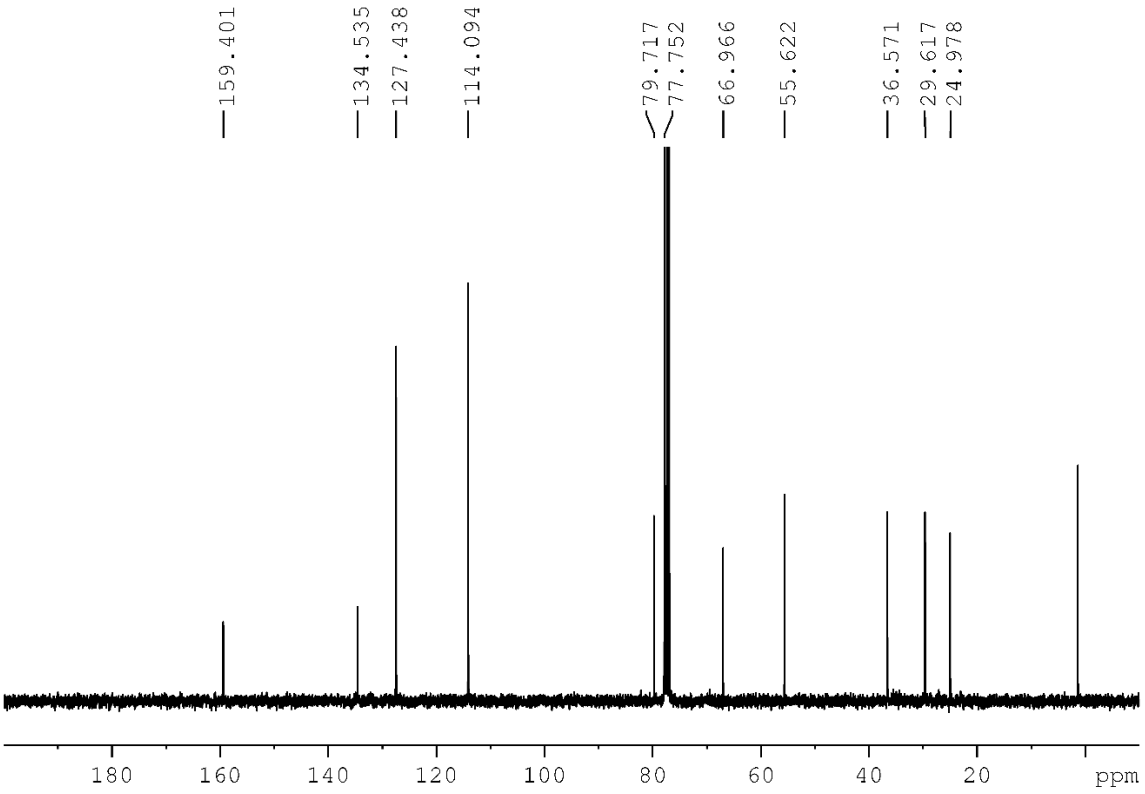


Figure S70. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-6-(*p*-methoxyphenyl)-3-methyltetrahydropyran (**2i**) minor isomer.

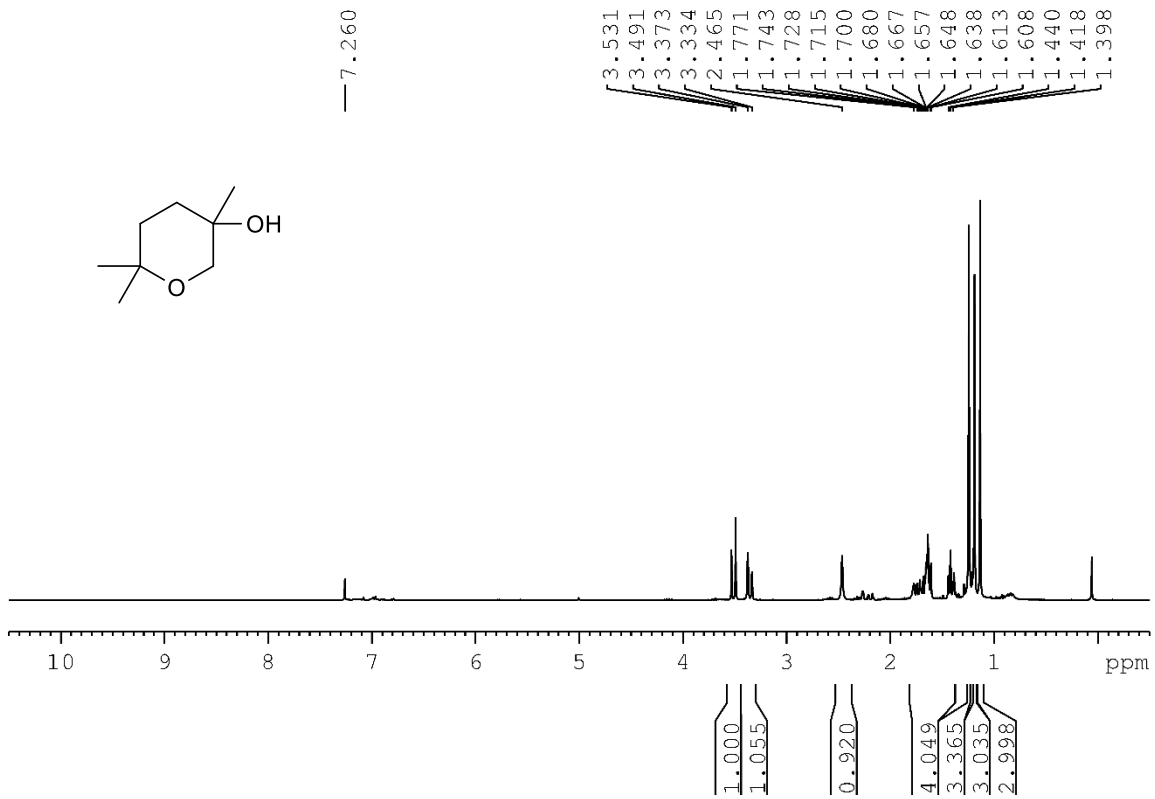


Figure S71. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3,6,6-trimethyltetrahydropyran (**2j**).

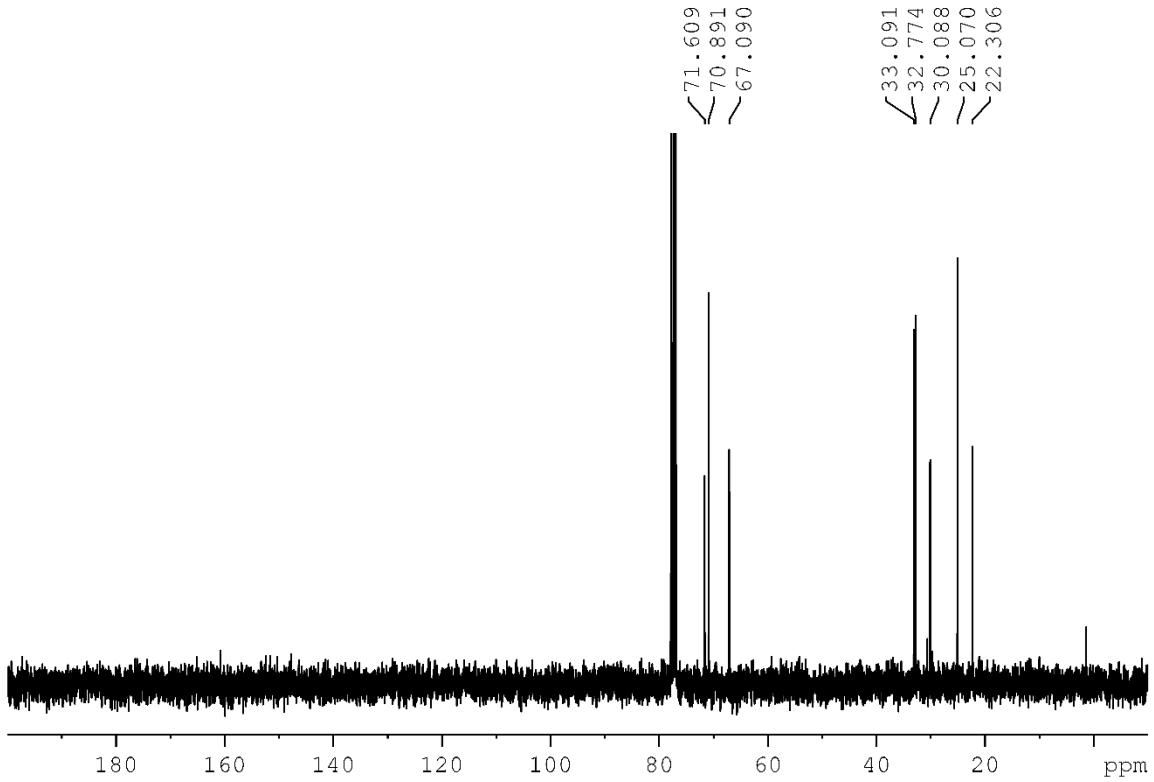


Figure S72. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3,6,6-trimethyltetrahydropyran (**2j**).

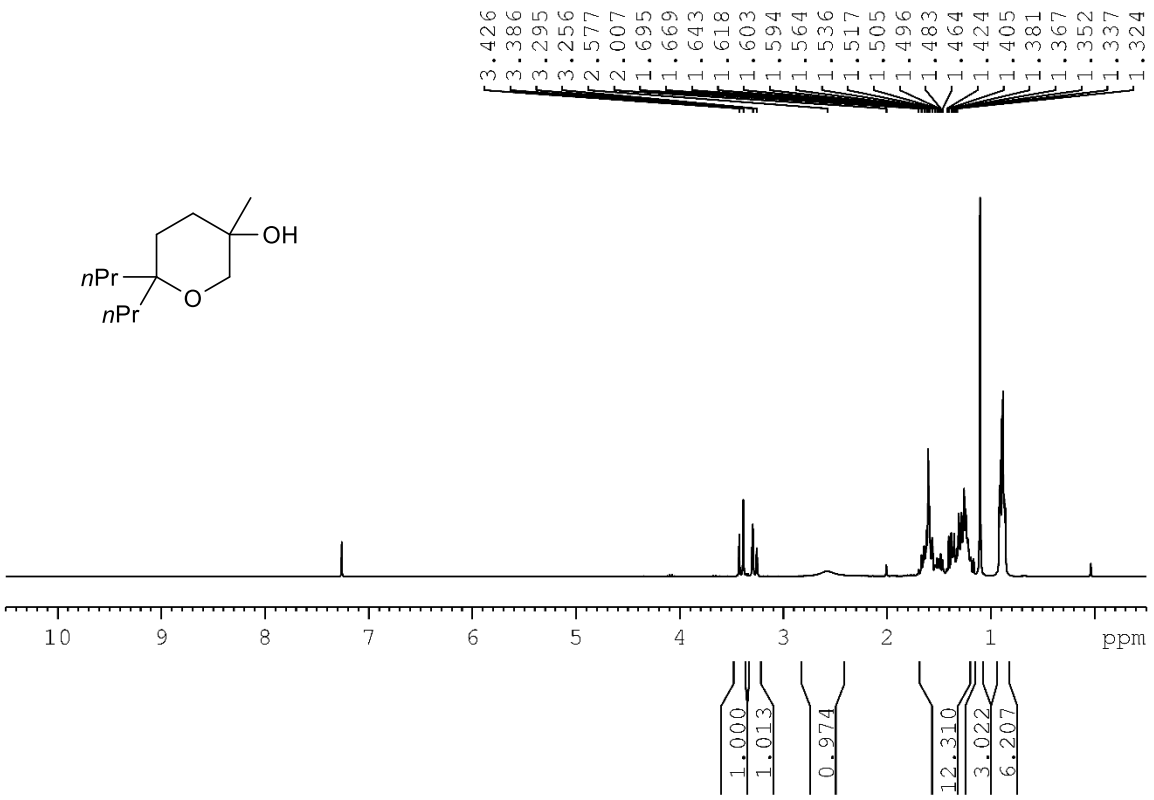


Figure S73. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-di-*n*-propyl-3-hydroxy-3-methyltetrahydropyran (**2k**).

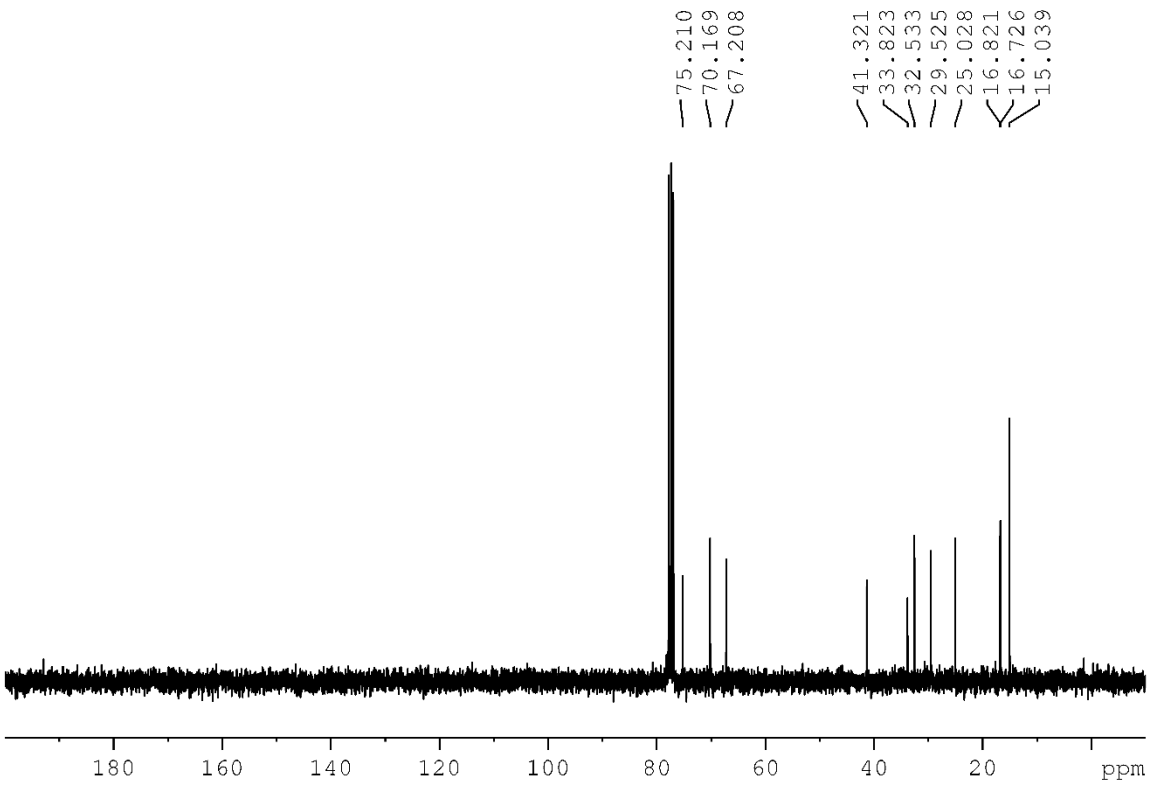


Figure S74. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di-*n*-propyl-3-hydroxy-3-methyltetrahydropyran (**2k**).

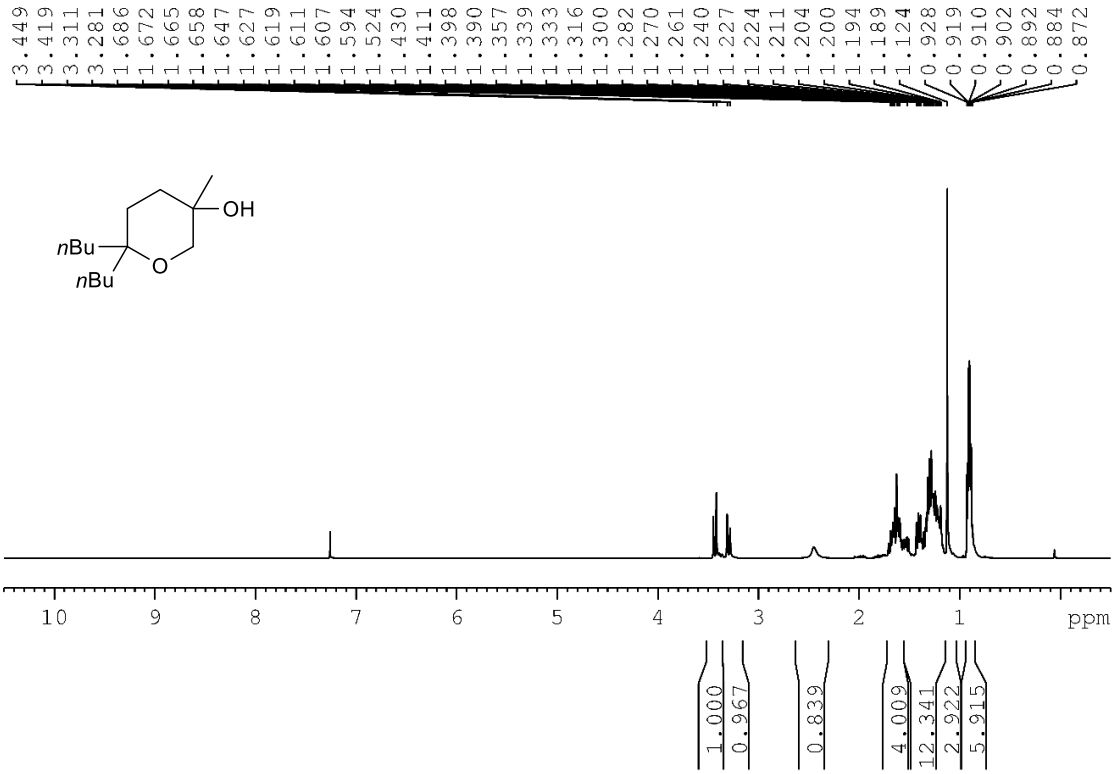


Figure S75. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 6,6-di-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2l**).

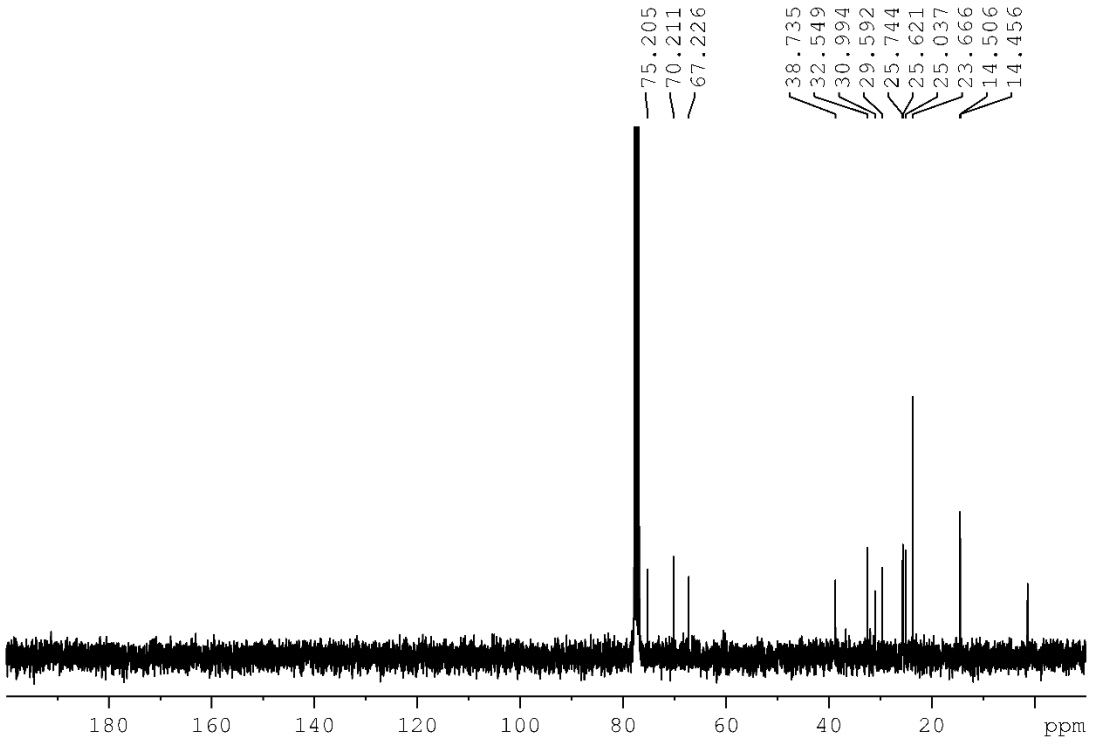


Figure S76. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di-*n*-butyl-3-hydroxy-3-methyltetrahydropyran (**2l**).

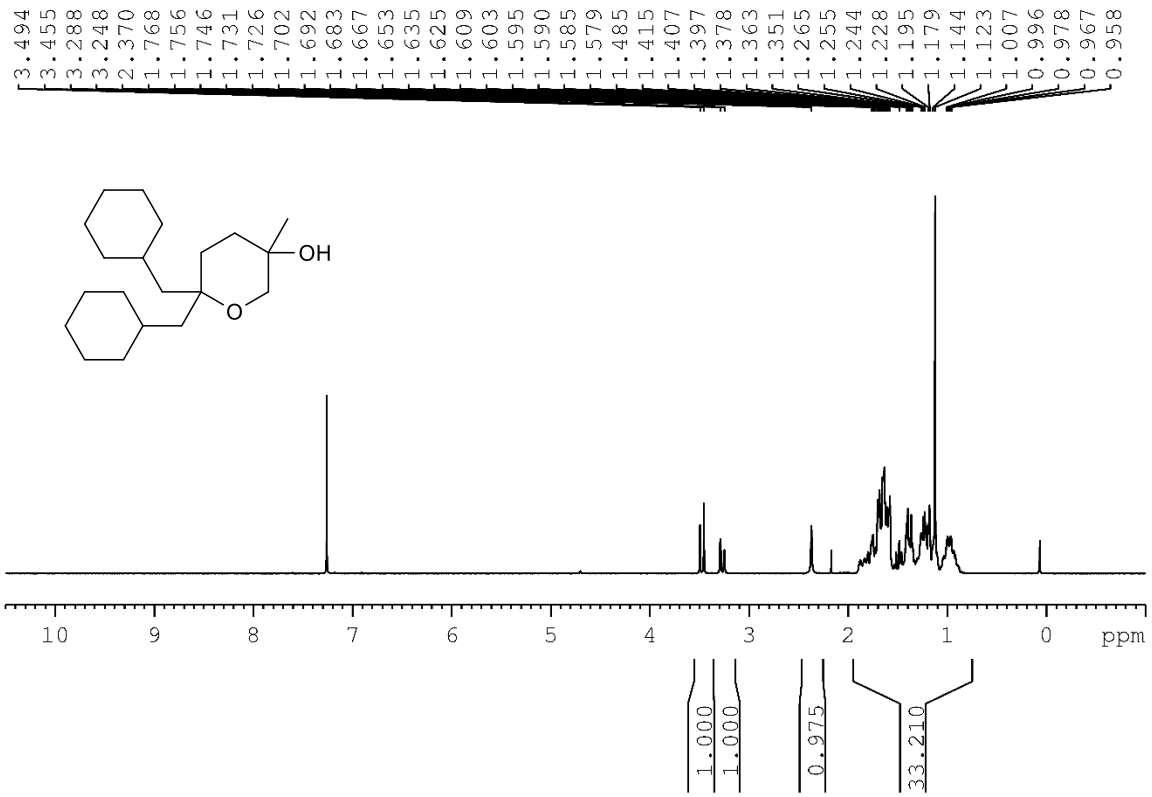


Figure S77. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-di(cyclohexylmethyl)-3-hydroxy-3-methyltetrahydropyran (**2m**).

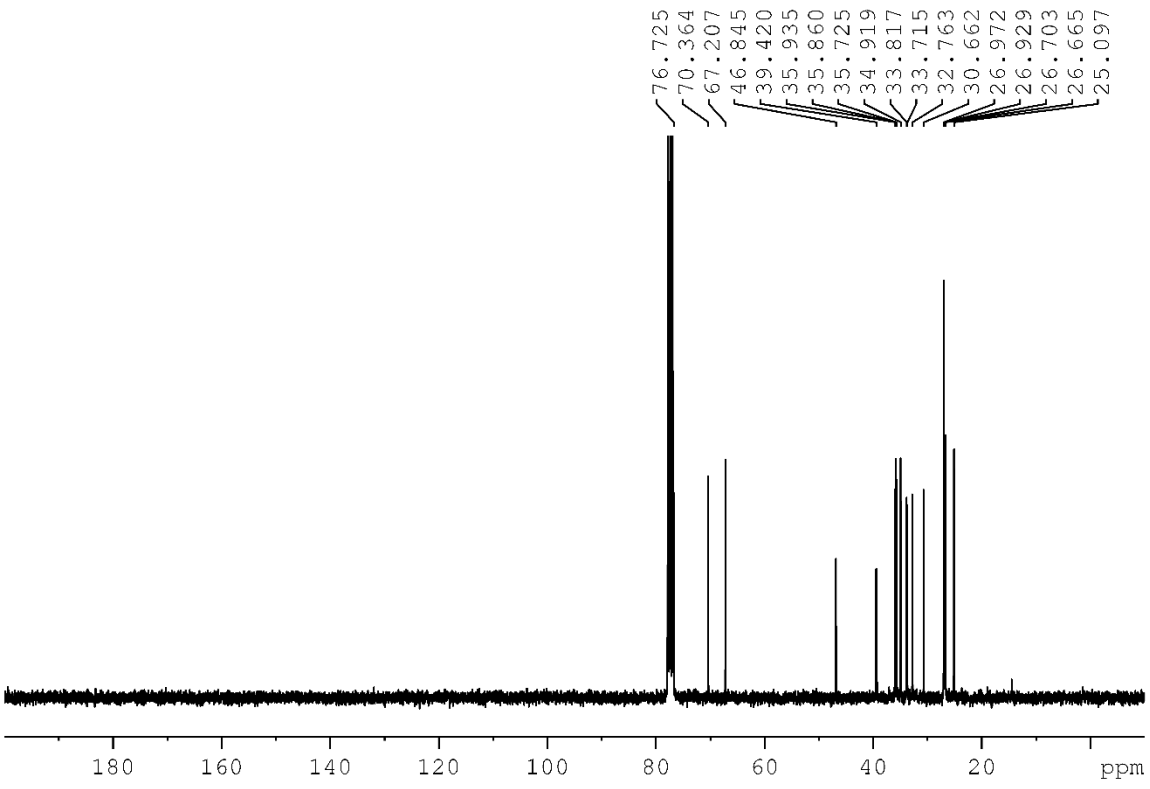


Figure S78. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di(cyclohexylmethyl)-3-hydroxy-3-methyltetrahydropyran (**2m**).

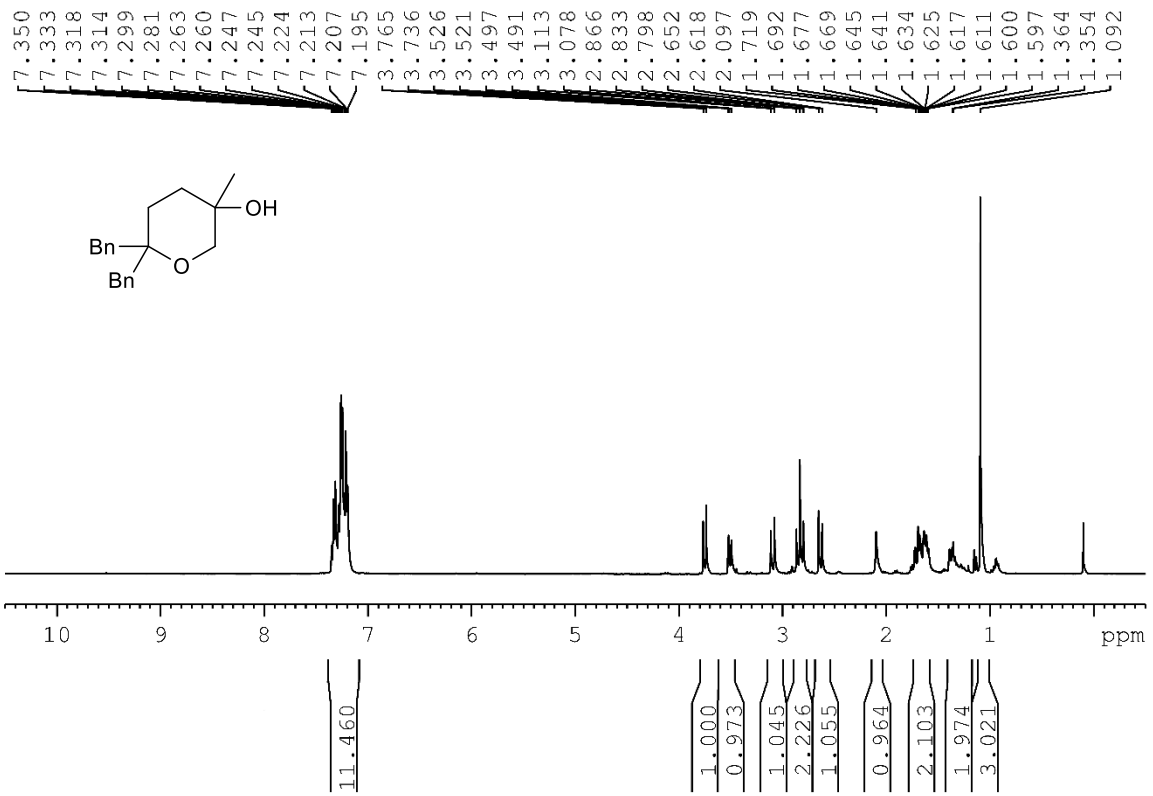


Figure S79. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 6,6-dibenzyl-3-hydroxy-3-methyltetrahydropyran (**2n**).

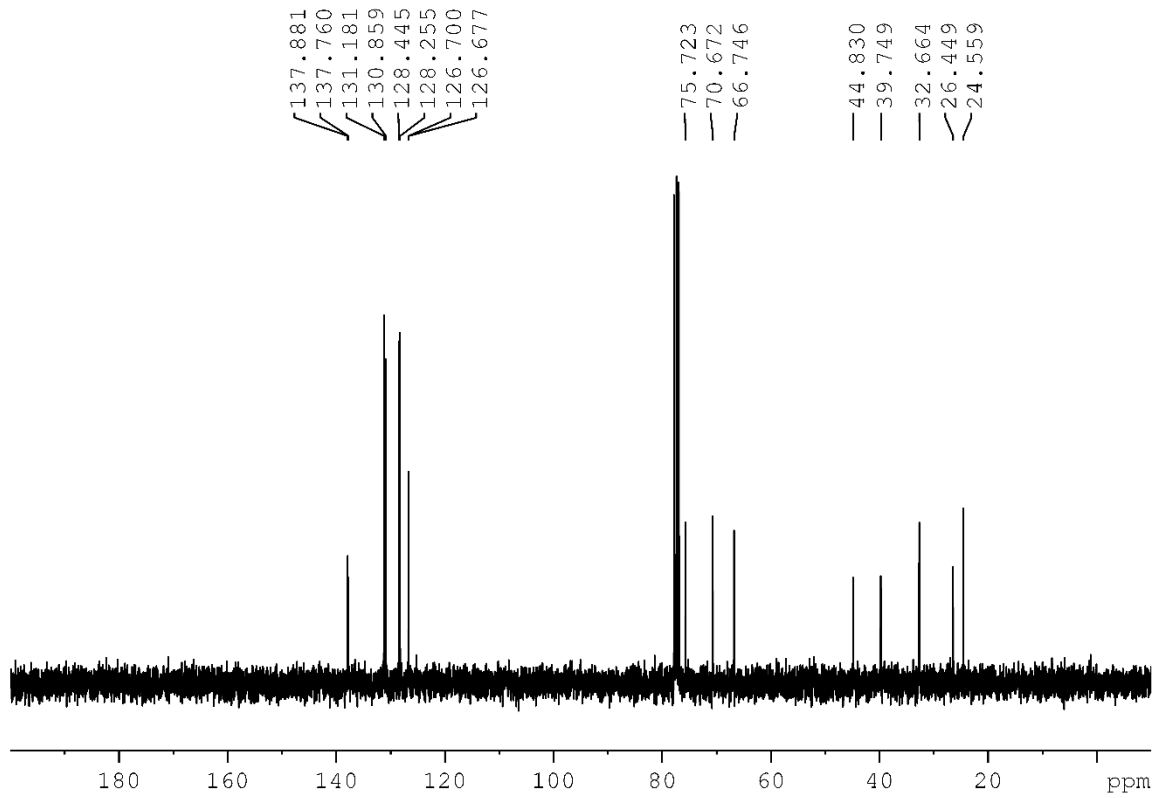


Figure S80. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-dibenzyl-3-hydroxy-3-methyltetrahydropyran (**2n**).

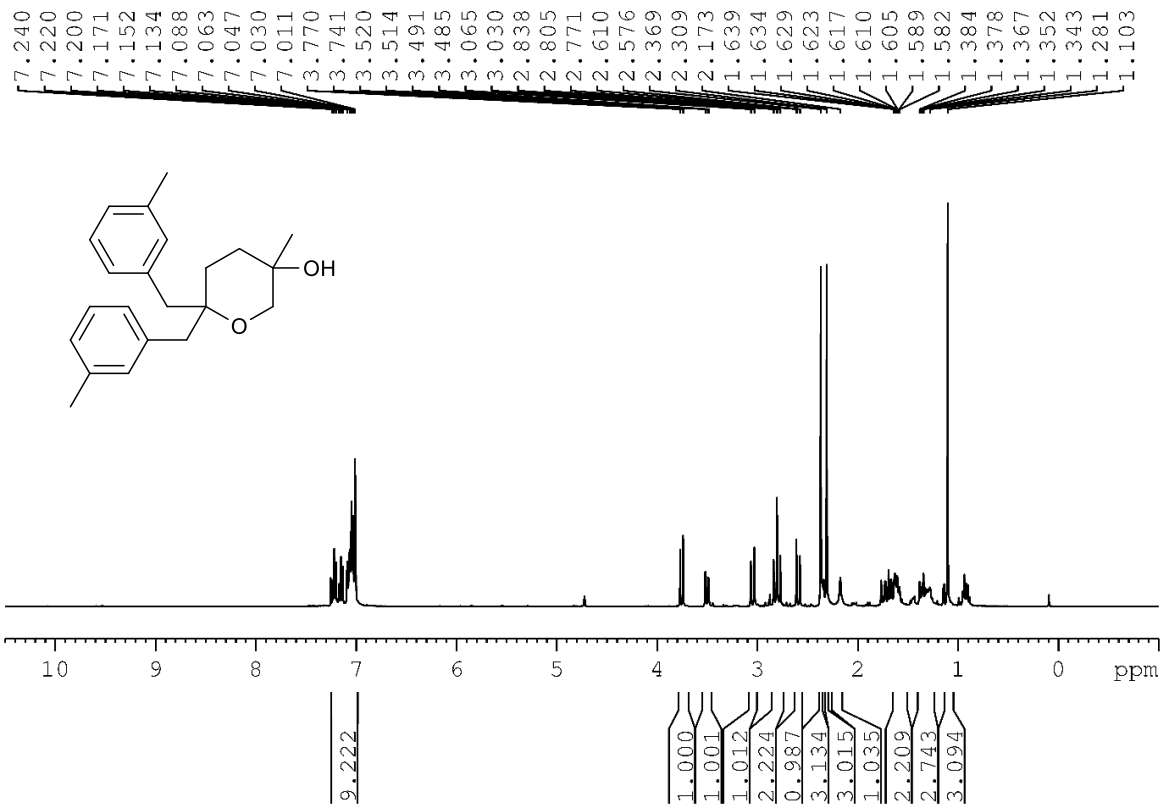


Figure S81. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 6,6-di-*m*-methylbenzyl-3-hydroxy-3-methyltetrahydropyran (**2o**).

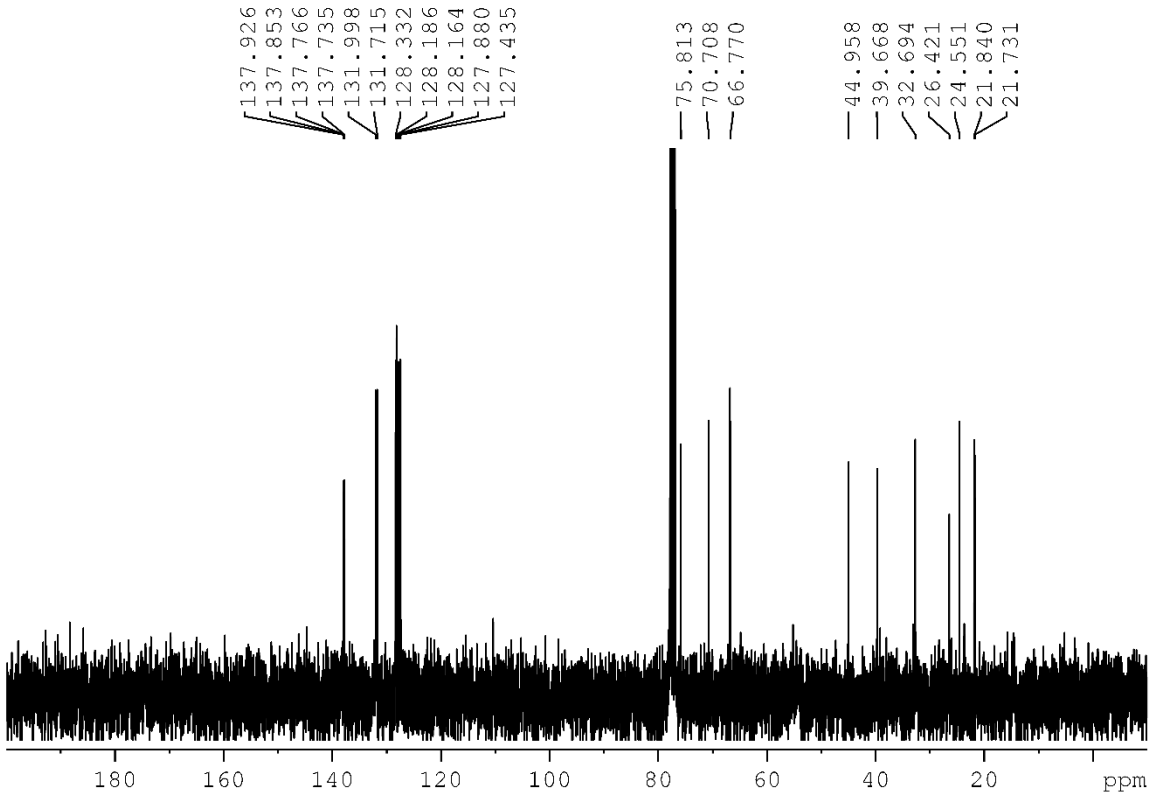


Figure S82. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di-*m*-methylbenzyl-3-hydroxy-3-methyltetrahydropyran (**2o**).

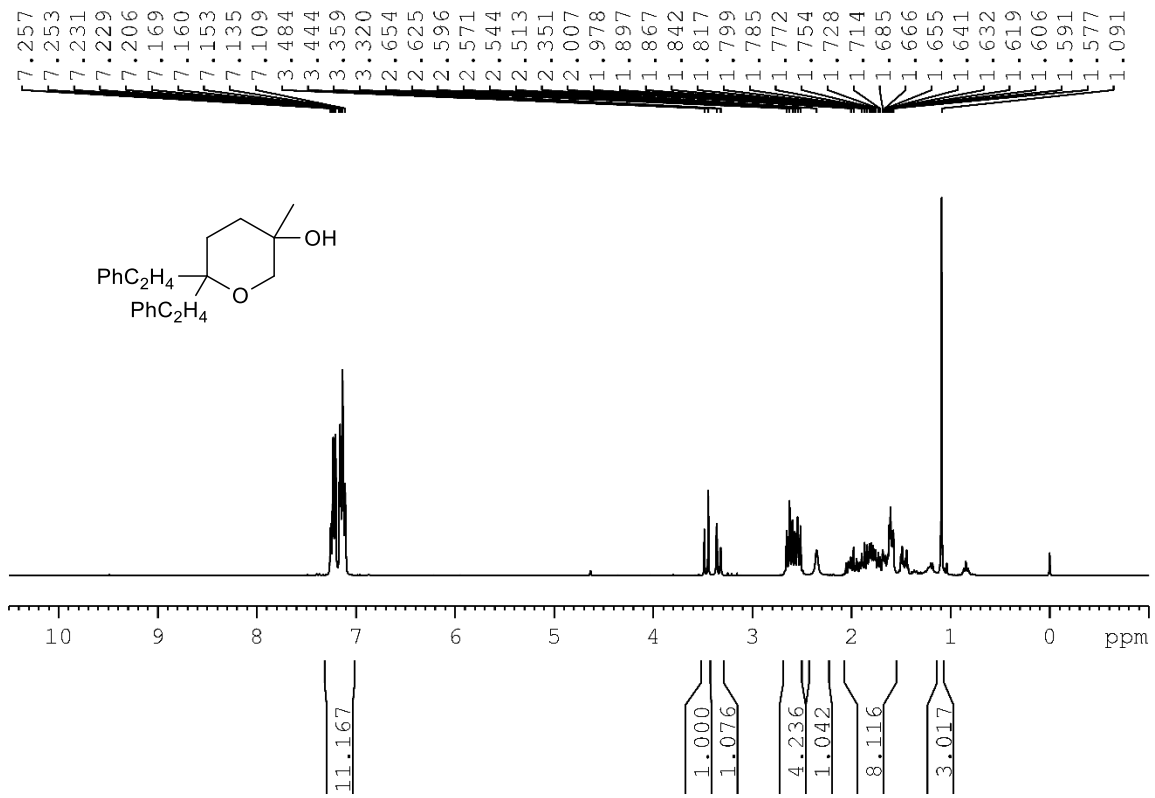


Figure S83. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-diphenethyl-3-hydroxy-3-methyltetrahydropyran (**2p**).

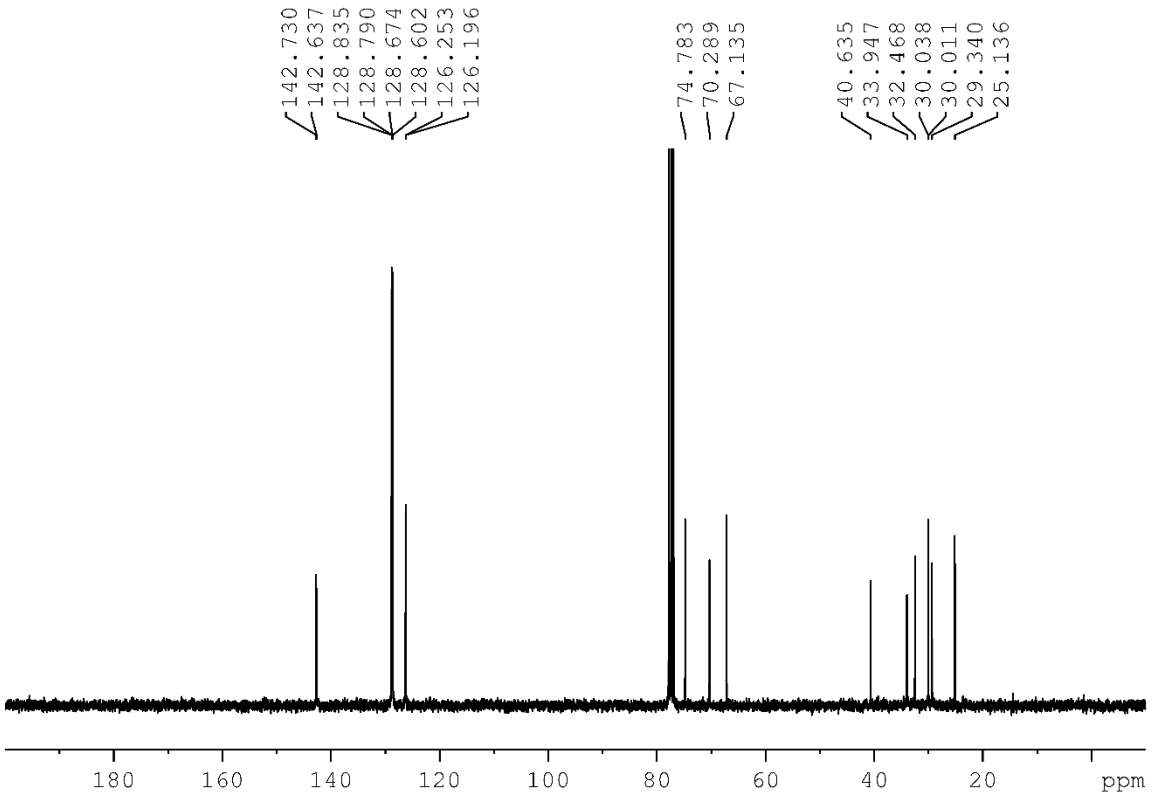


Figure S84. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-diphenethyl-3-hydroxy-3-methyltetrahydropyran (**2p**).

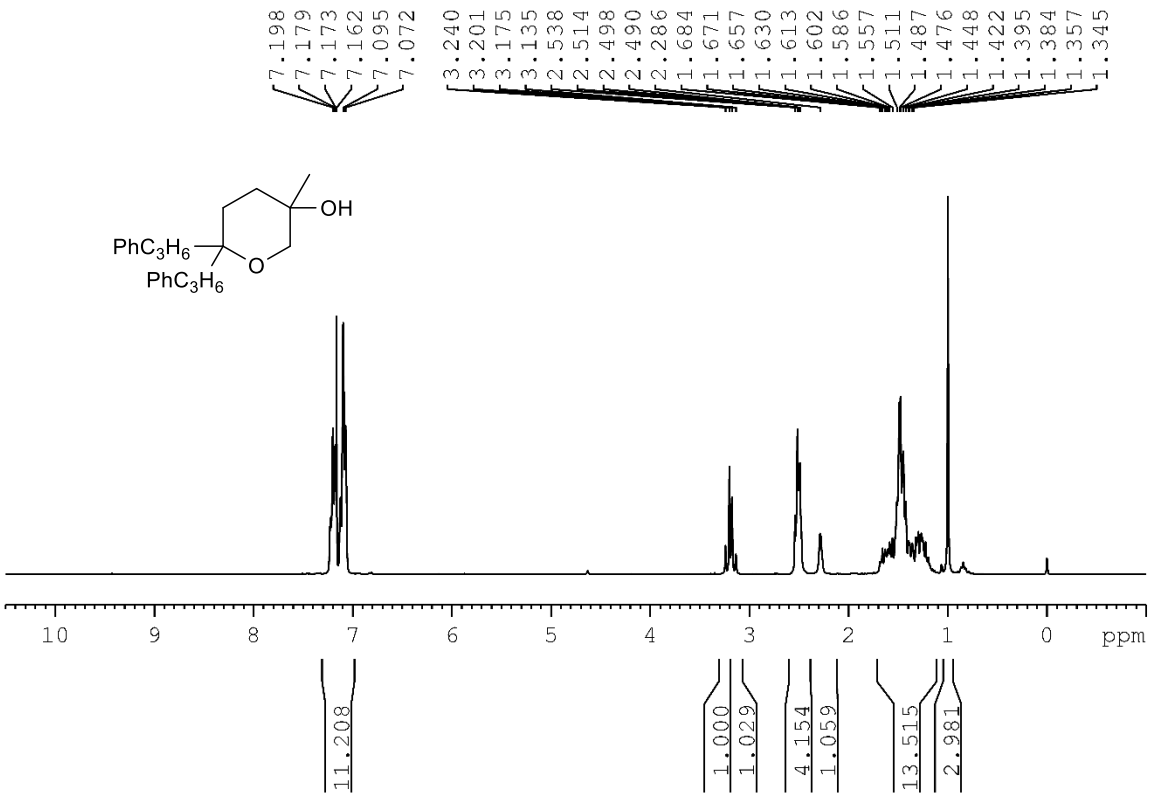


Figure S85. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-di(3-phenylpropyl)-3-hydroxy-3-methyltetrahydropyran (**2q**).

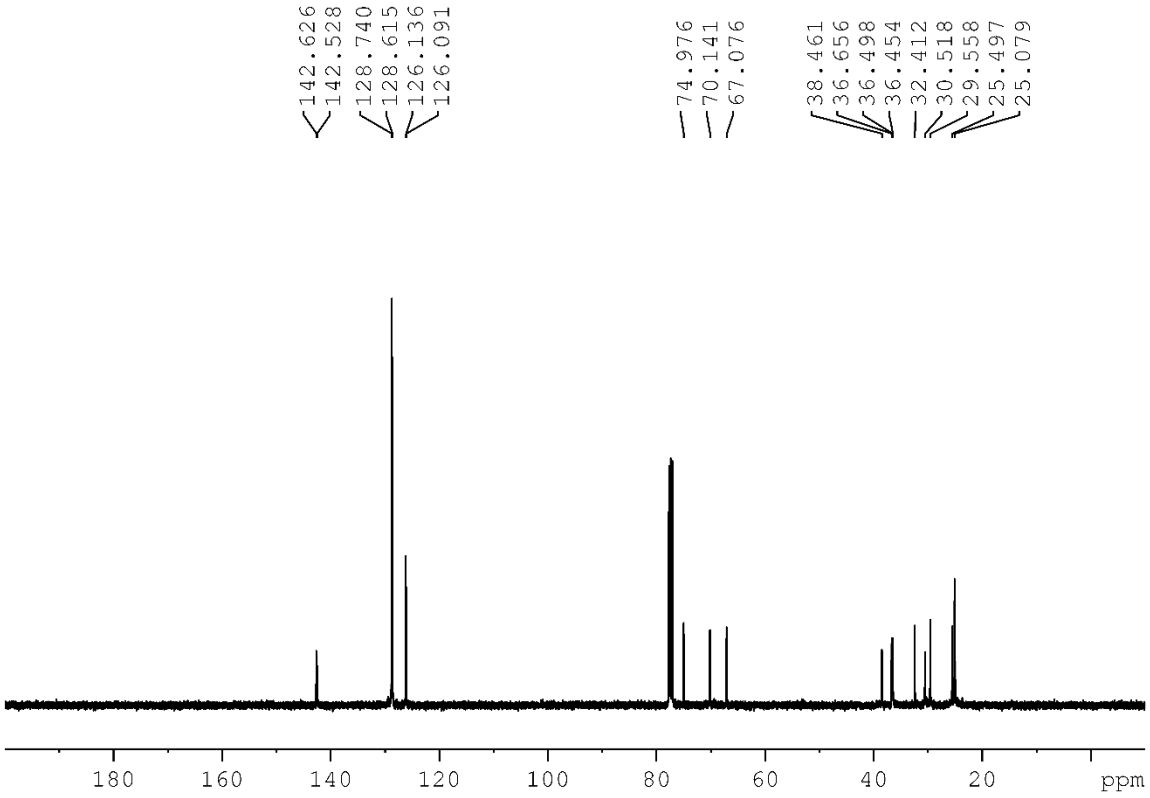


Figure S86. $^{13}C\{^{1}H\}$ NMR spectrum (100 MHz, $CDCl_3$) of 6,6-di(3-phenylpropyl)-3-hydroxy-3-methyltetrahydropyran (**2q**).

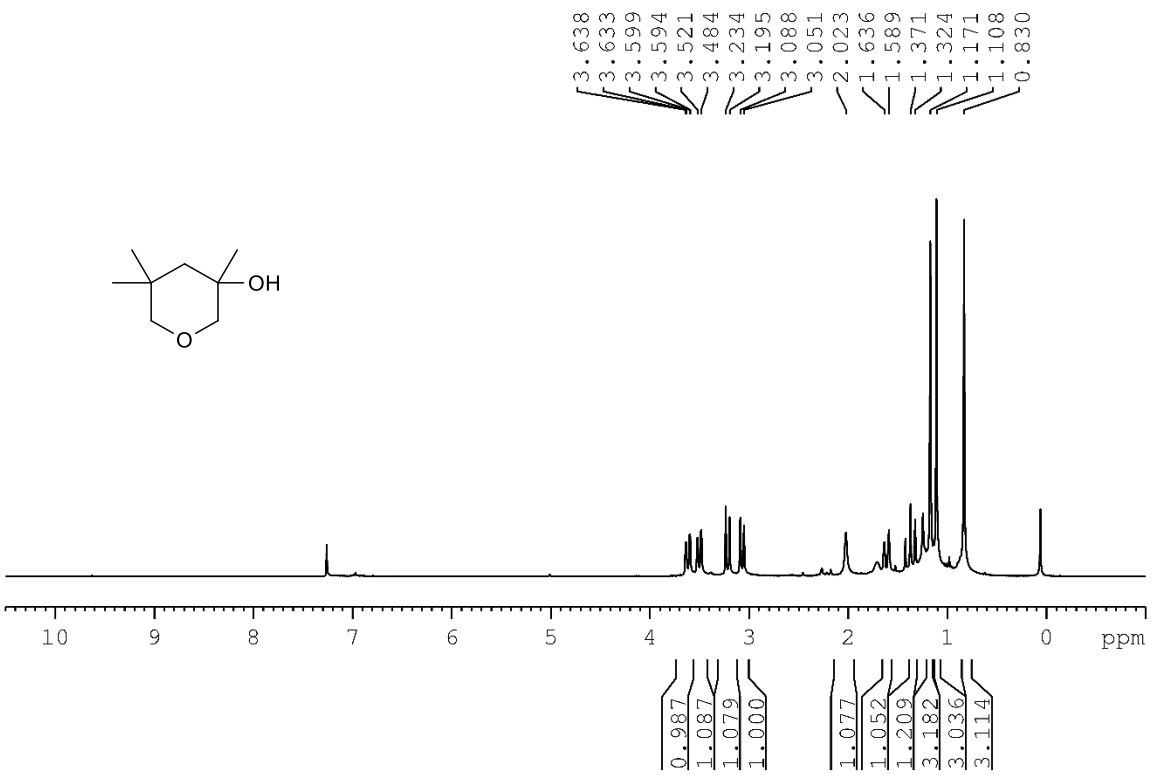


Figure S87. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3,5,5-trimethyltetrahydropyran (**2r**).

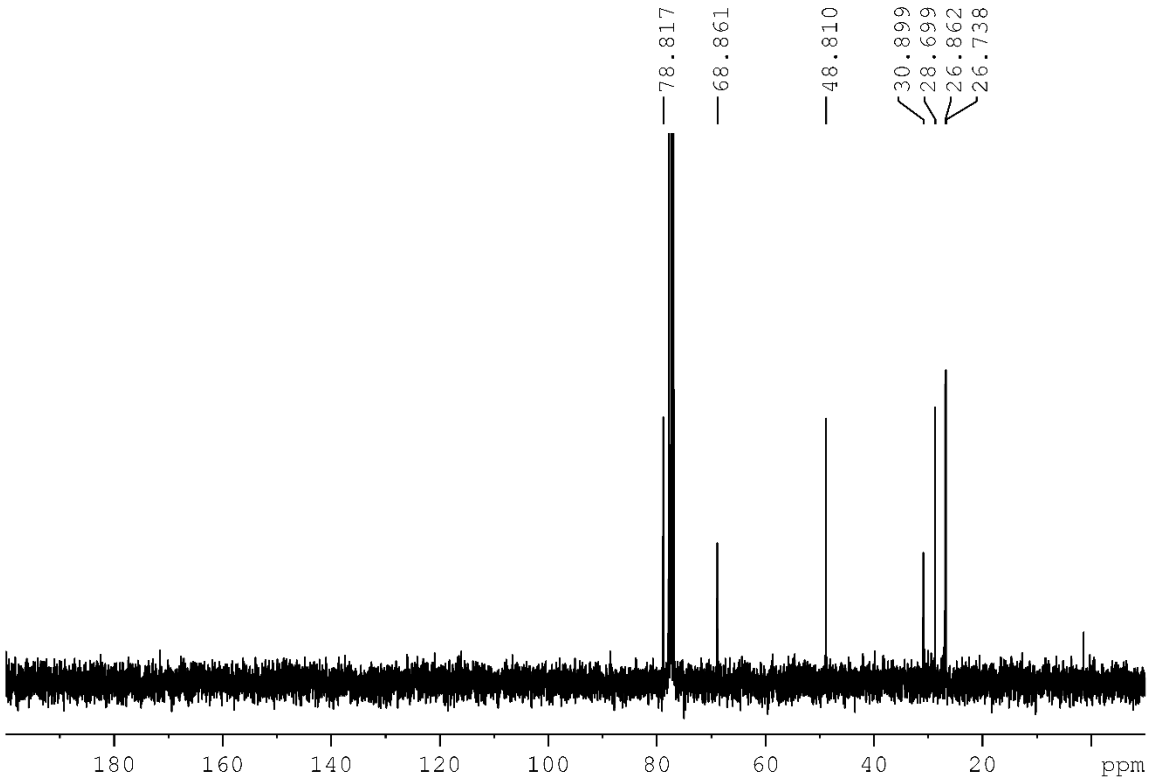


Figure S88. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3,5,5-trimethyltetrahydropyran (**2r**).

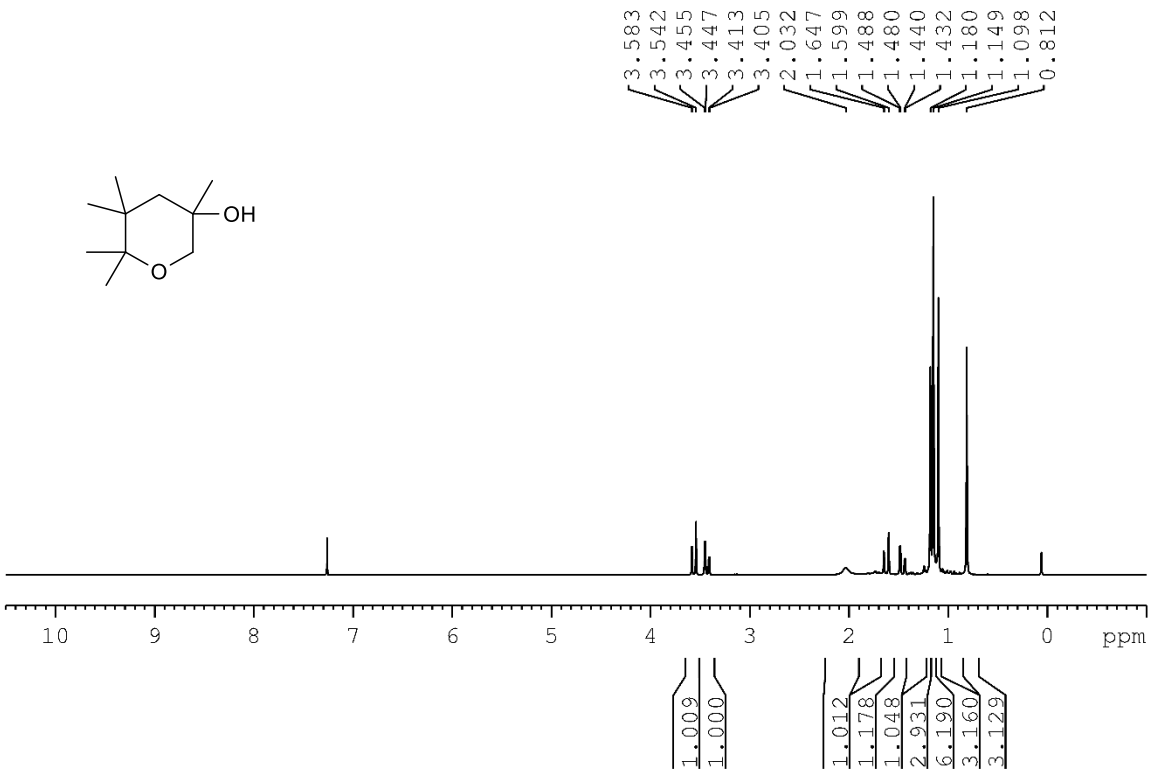


Figure S89. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-hydroxy-3,5,5,6,6-pentamethyltetrahydropyran (**2s**).

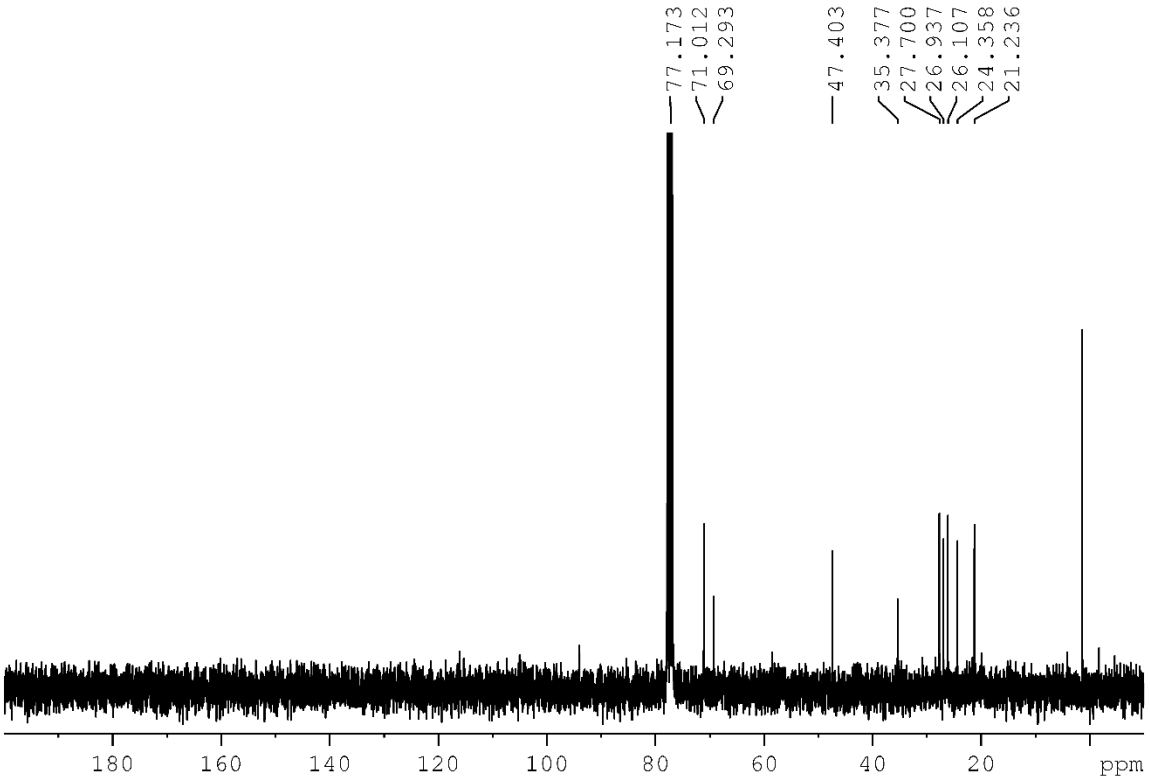


Figure S90. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-hydroxy-3,5,5,6,6-pentamethyltetrahydropyran (**2s**).

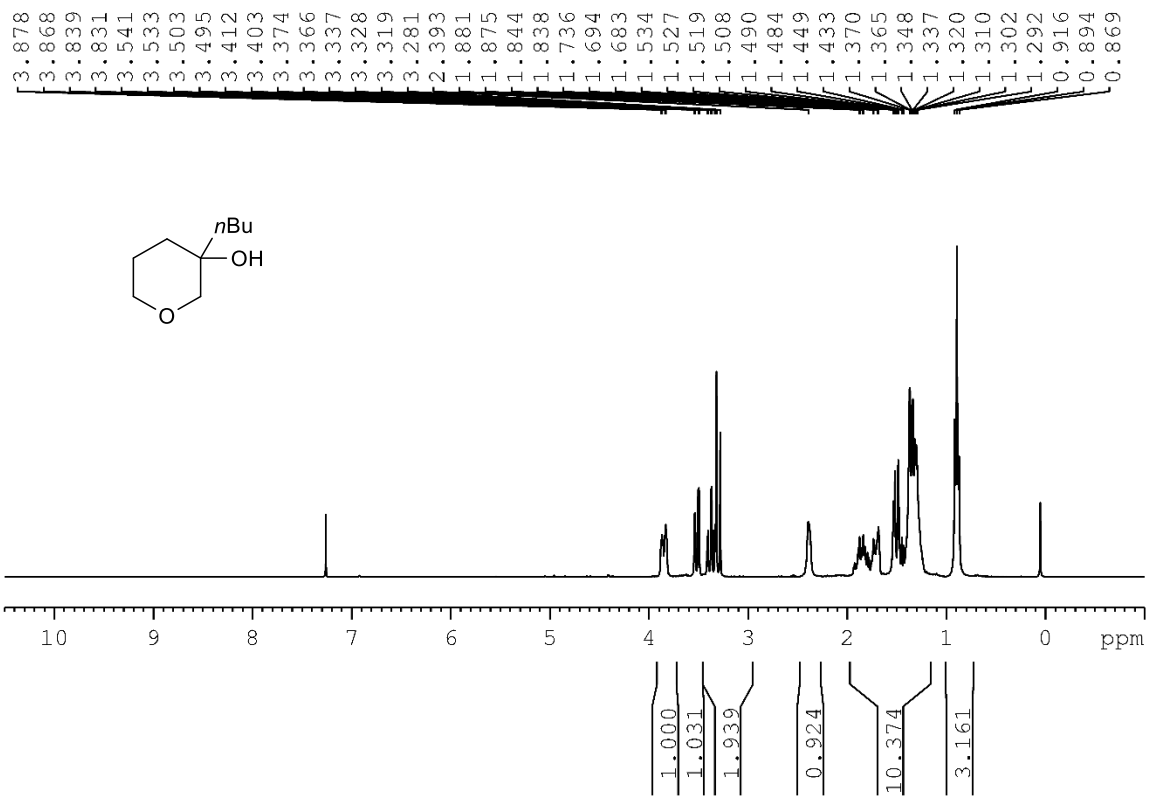


Figure S91. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-*n*-butyl-3-hydroxytetrahydropyran (**2t**).

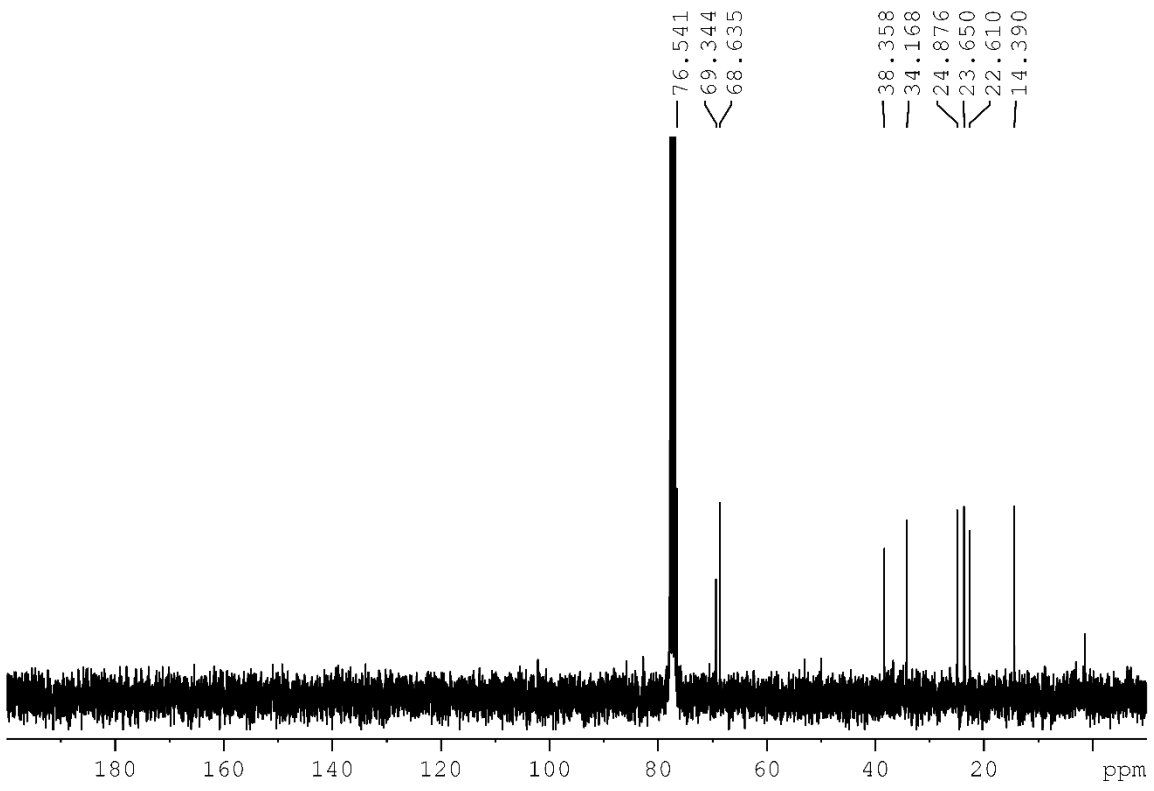


Figure S92. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-*n*-butyl-3-hydroxytetrahydropyran (**2t**).

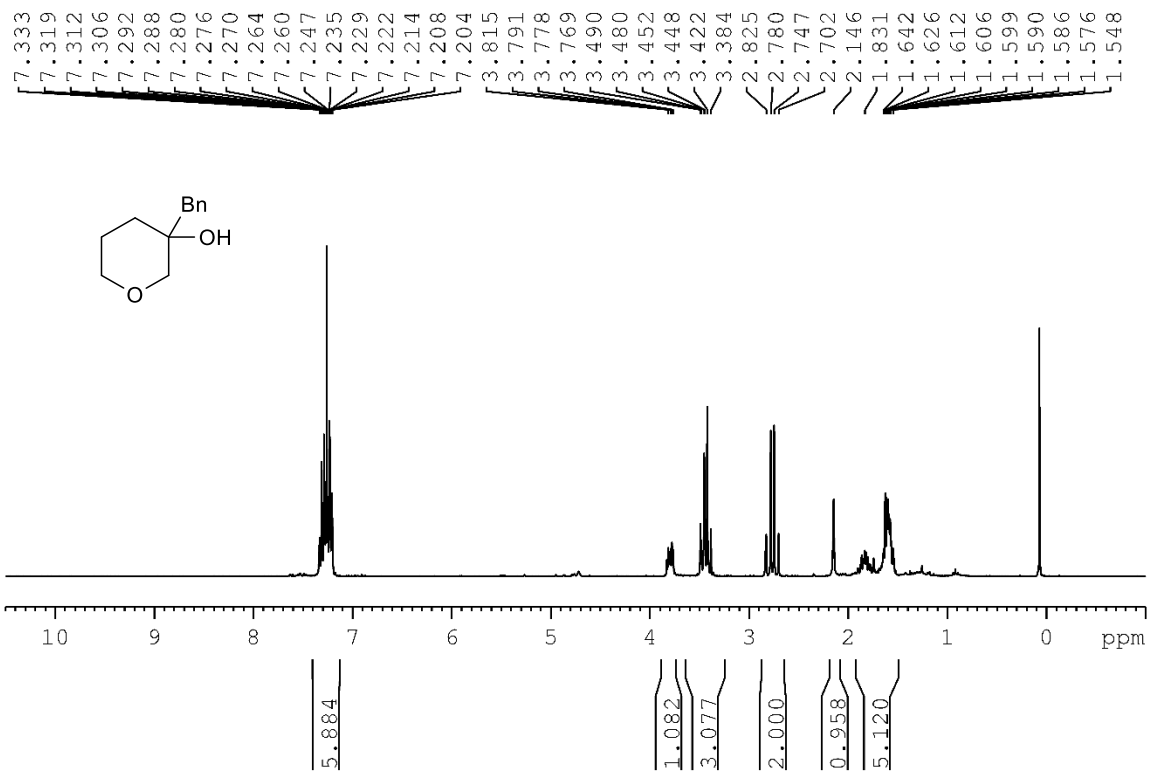


Figure S93. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-benzyl-3-hydroxytetrahydropyran (**2u**).

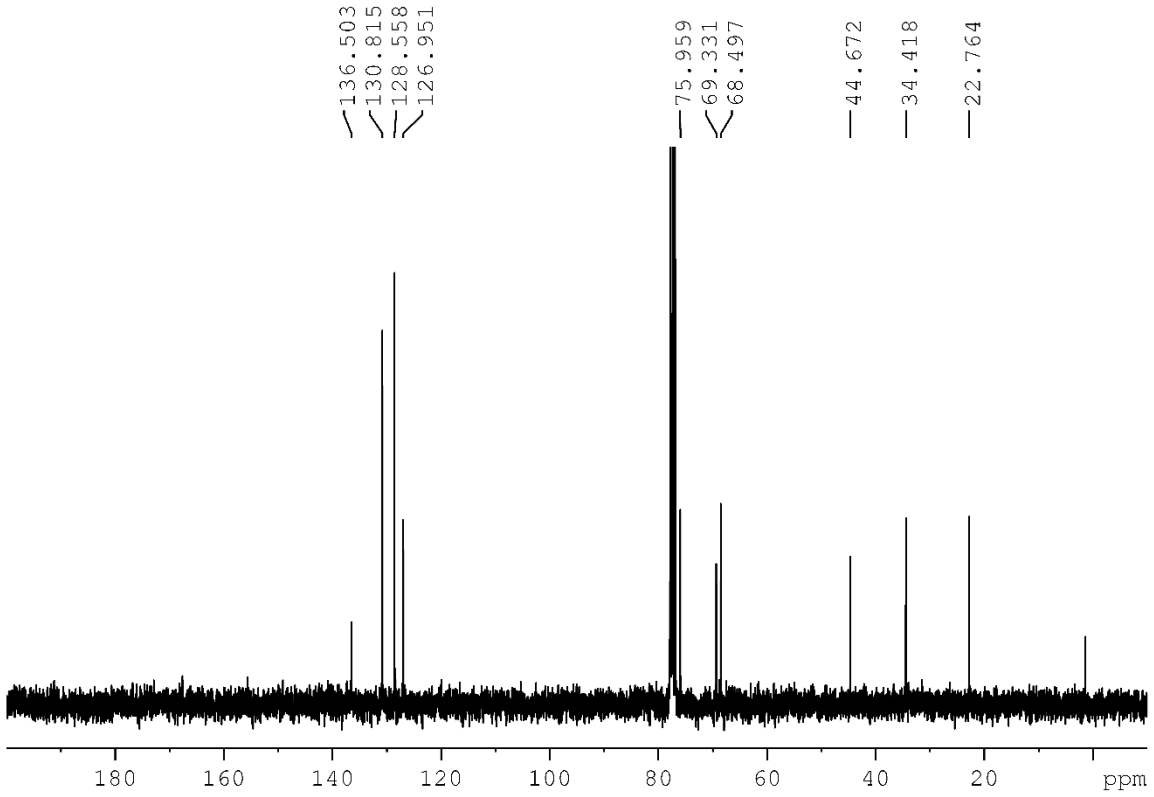


Figure S94. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-benzyl-3-hydroxytetrahydropyran (**2u**).

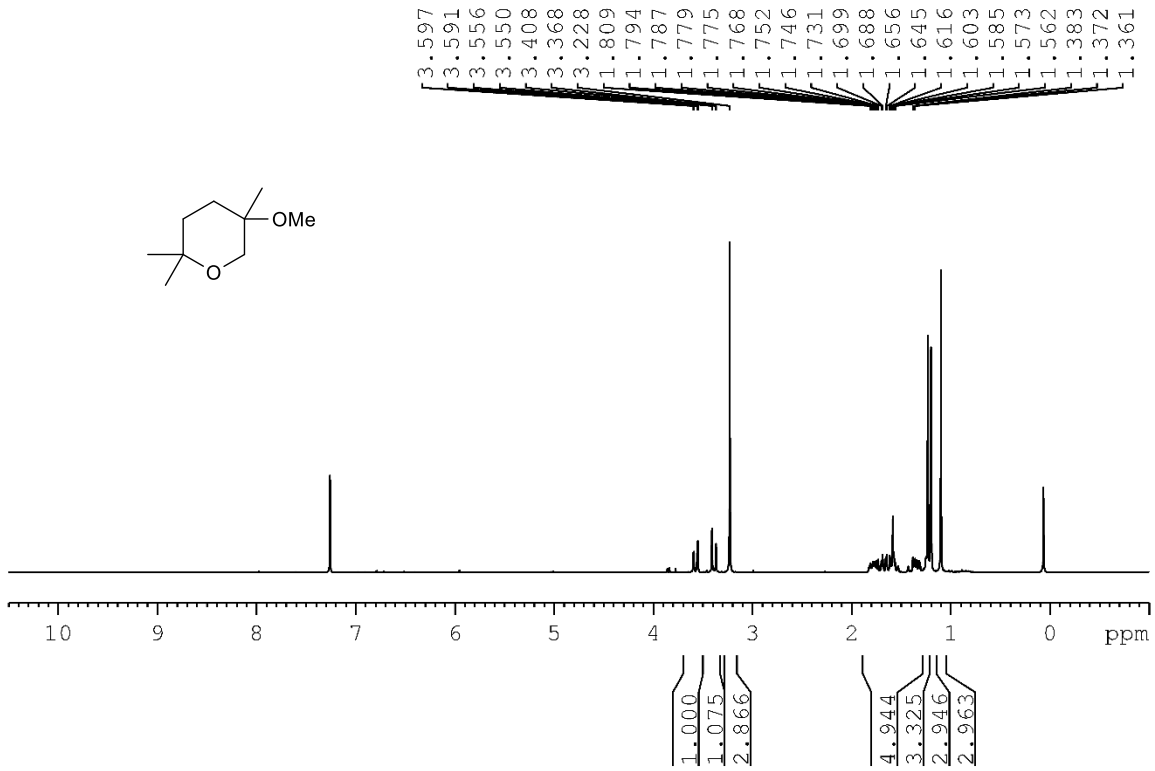


Figure S95. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-methoxy-3,6,6-trimethyltetrahydropyran (**3j**).

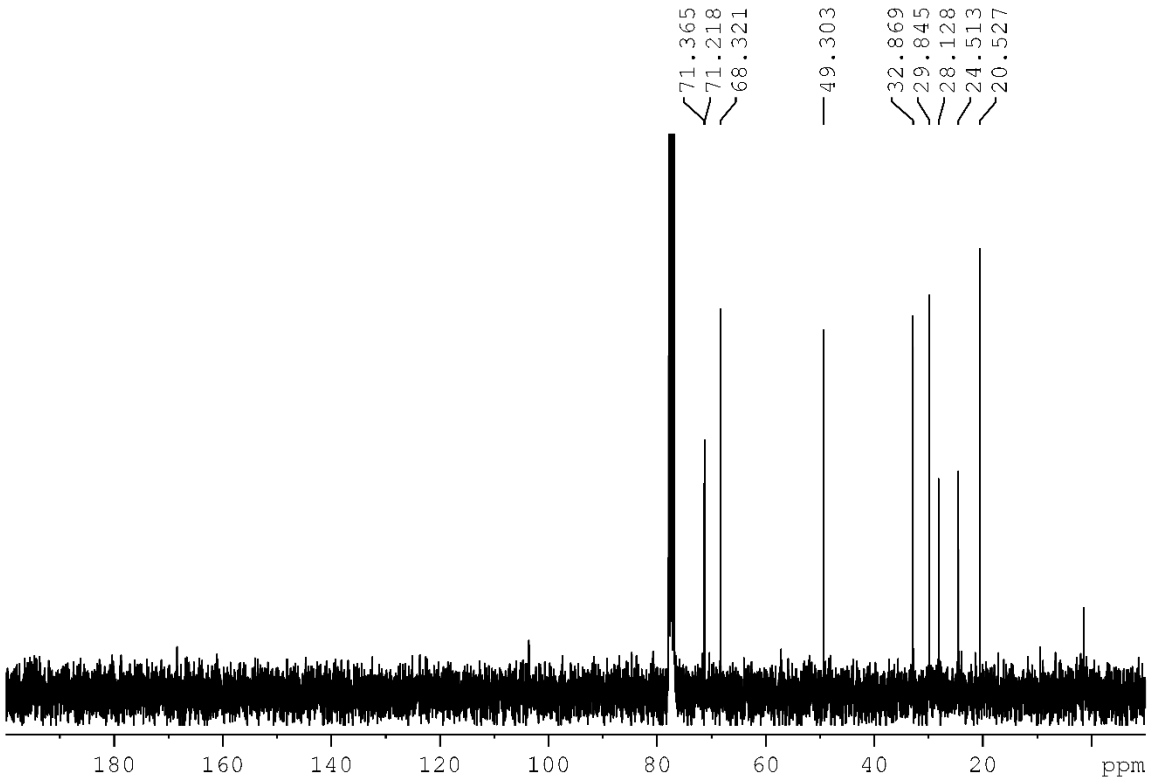


Figure S96. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-methoxy-3,6,6-trimethyltetrahydropyran (**3j**).

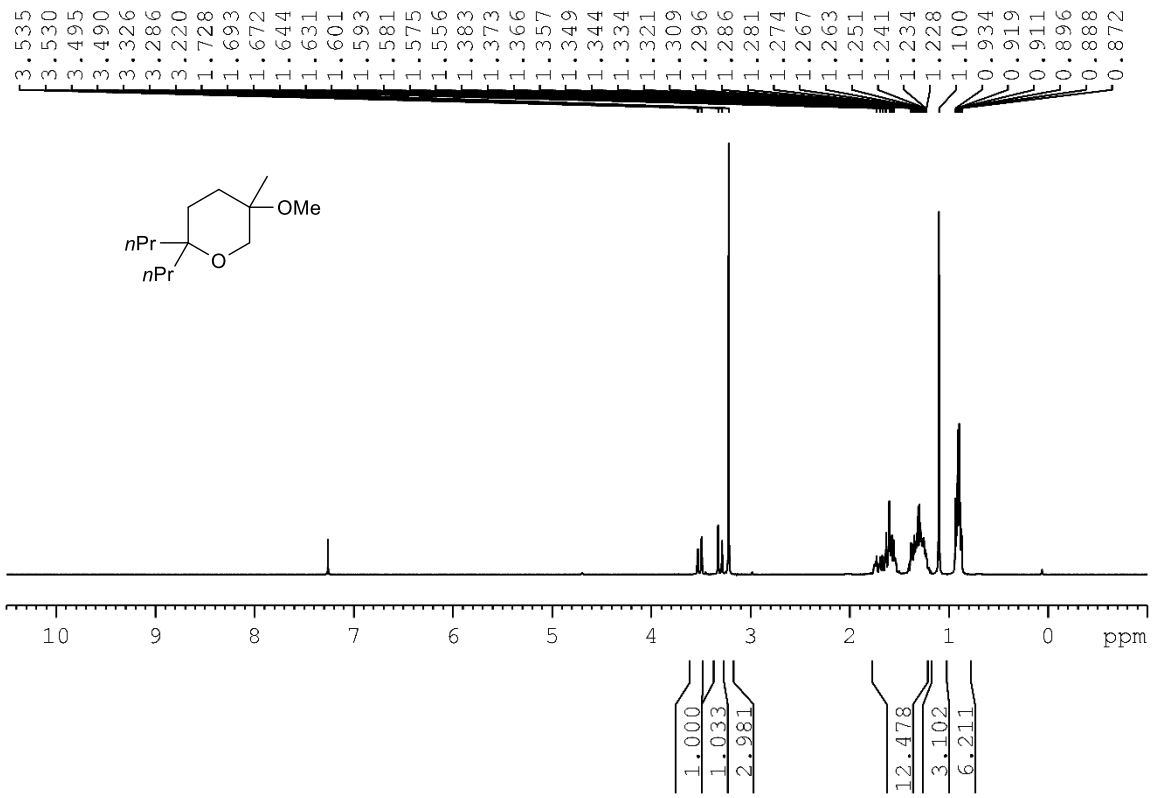


Figure S97. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-di-*n*-propyl-3-methoxy-3-methyltetrahydropyran (**3k**).

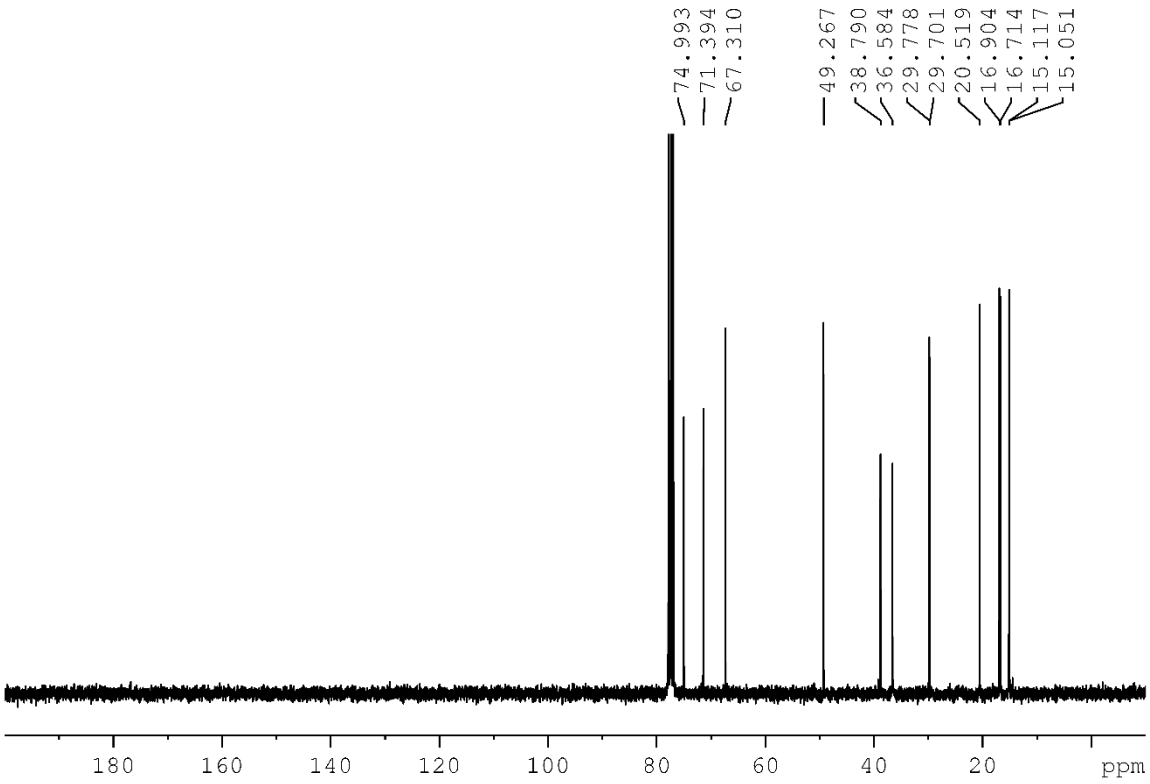


Figure S98. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di-*n*-propyl-3-methoxy-3-methyltetrahydropyran (**3k**).

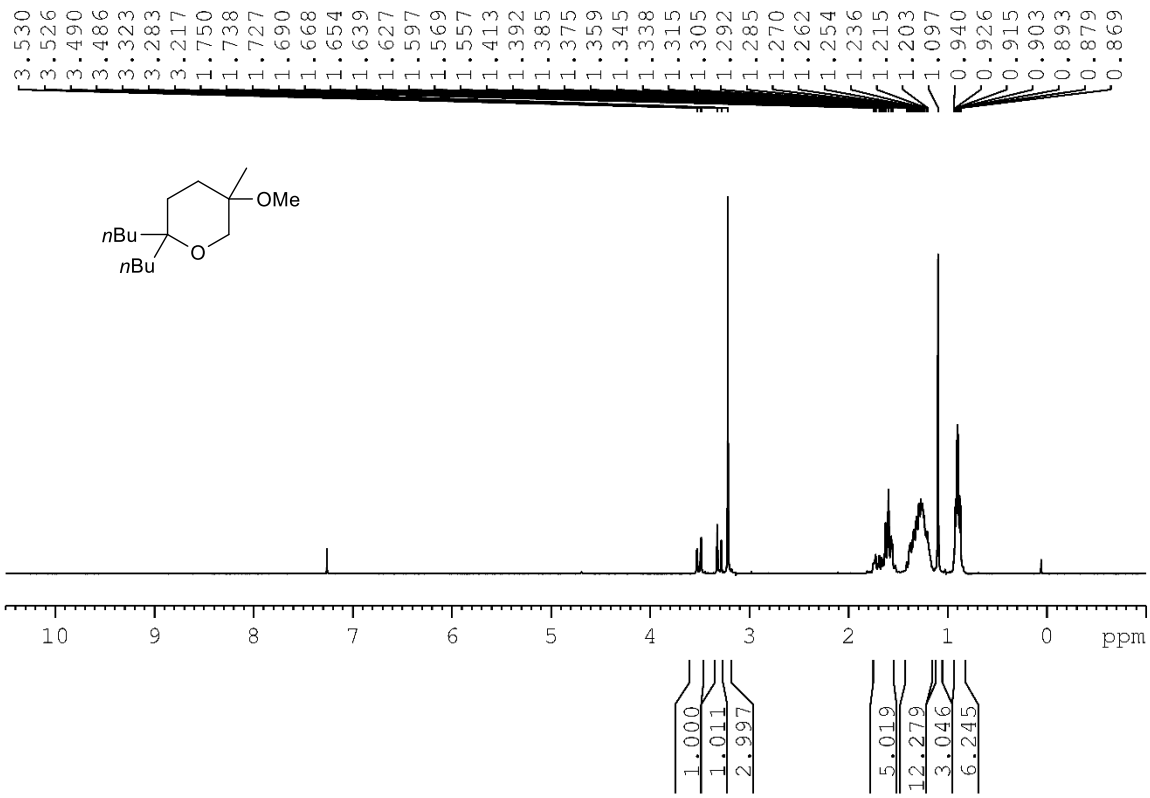


Figure S99. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 6,6-di-*n*-butyl-3-methoxy-3-methyltetrahydropyran (**3l**).

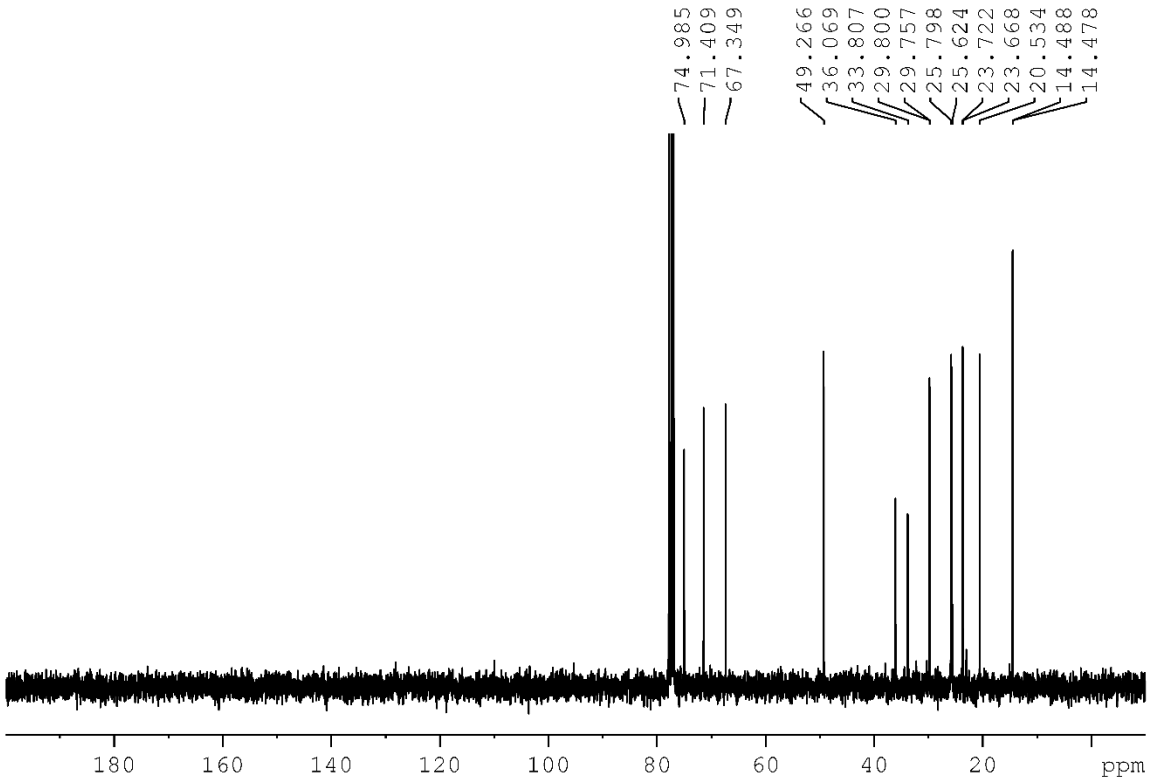


Figure S100. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 6,6-di-*n*-butyl-3-methoxy-3-methyltetrahydropyran (**3l**).

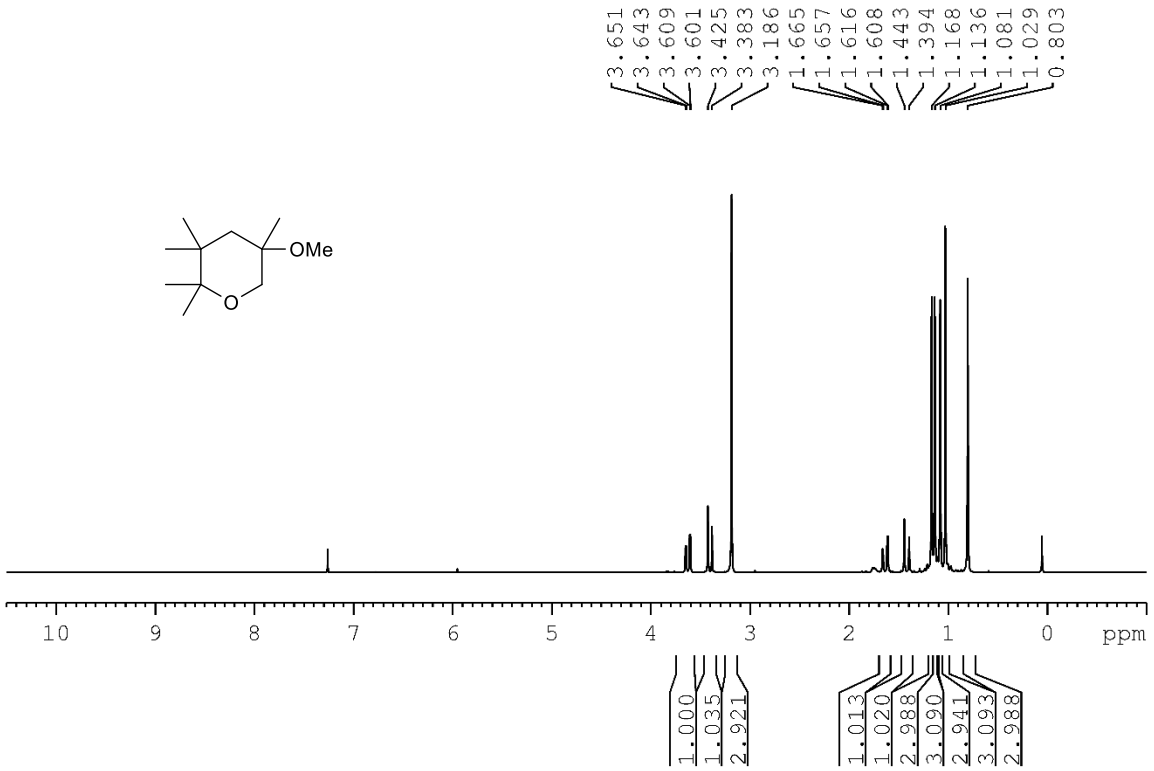


Figure S101. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of 3-methoxy-3,5,5,6,6-pentamethyltetrahydropyran (**3s**).

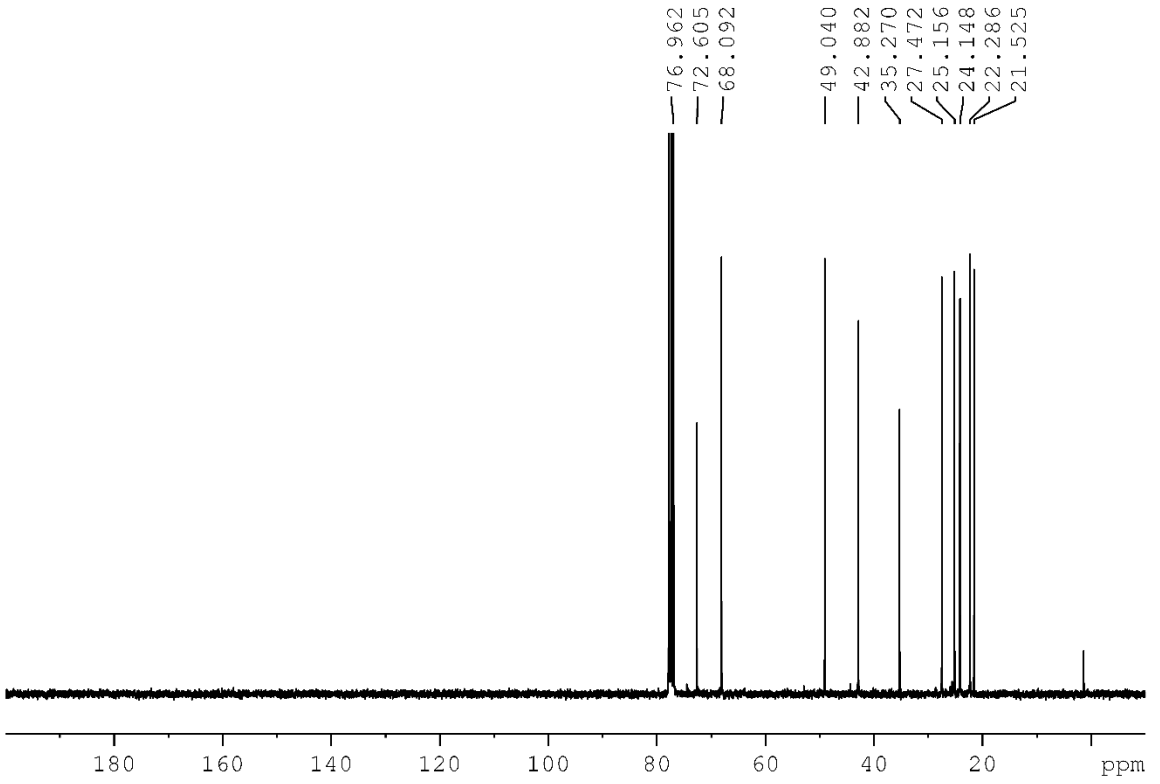


Figure S102. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of 3-methoxy-3,5,5,6,6-pentamethyltetrahydropyran (**3s**).

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