# SUPPORTING INFORMATION

## (1*R*)-(+)-Camphor and Acetone Derived α'–Hydroxy Enones in Asymmetric Diels-Alder Reaction: Catalytic Activation by Lewis and Brønsted Acids, Substrate Scope, Applications in Syntheses, and Mechanistic Studies

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## General

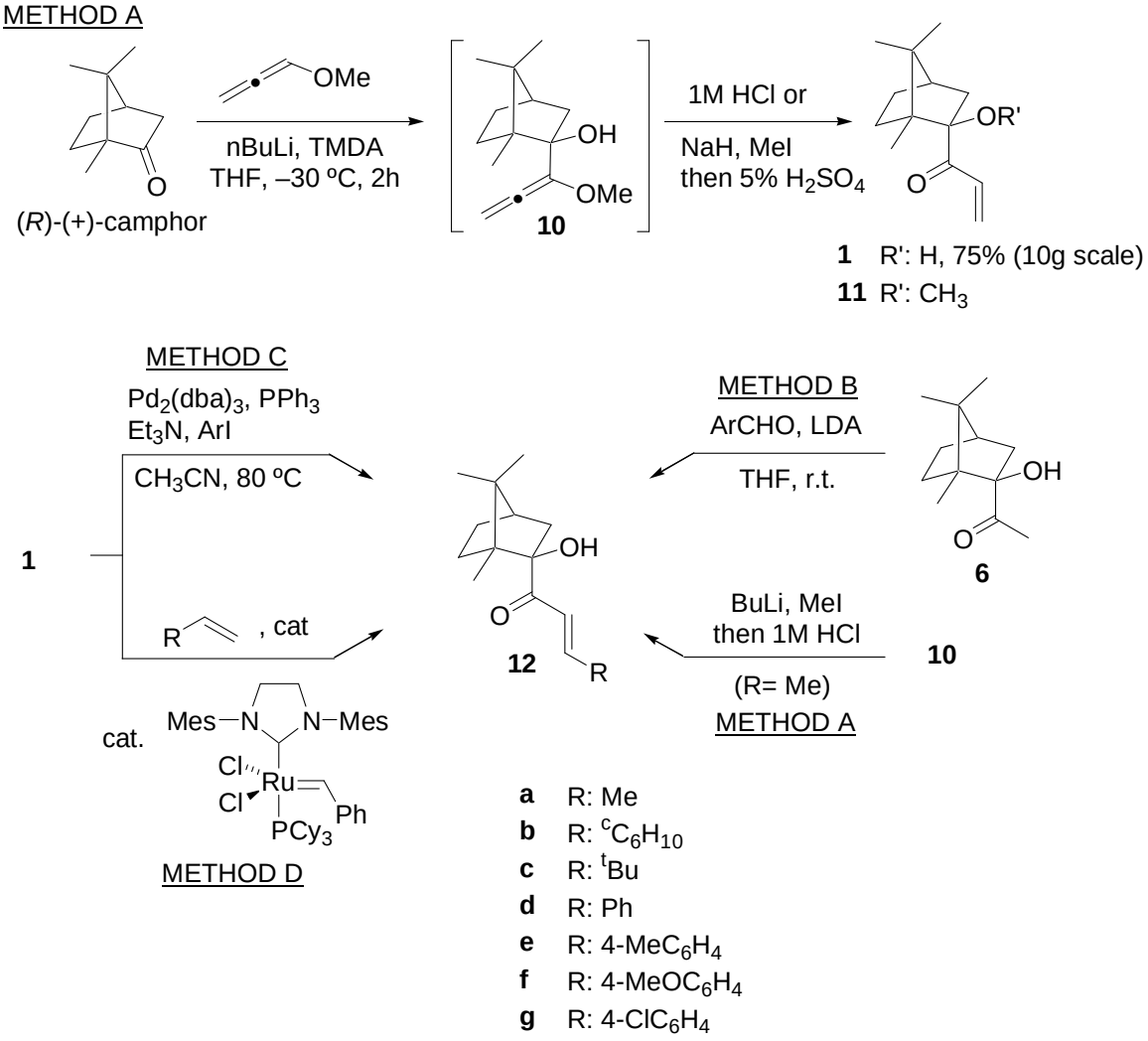
All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. Tetrahydrofuran (THF) was distilled from sodium metal/benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Anhydrous dimethylformamide (DMF) and trifluoromethanesulfonic acid (TfOH) were used from commercial sources without further purification. Cyclopentadiene was distilled by cracking dicyclopentadiene prior to use. Myrcene was distilled (167 ºC / 760 mm Hg) prior to use. The remaining dienes were used as acquired without further purification.

Purification of reaction products was carried out by flash chromatography using silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on 0,25 mm silica gel 60-F plates. Visualization was accomplished with UV light and p-anisaldehyde solution followed by heating. Melting points were measured with a melting point apparatus and are uncorrected. Infrared spectra were recorded on a FT-IR spectrometer. $^{1}$H NMR and $^{13}$C NMR spectra were recorded on a 200 MHz (50MHz) spectrometer and are reported in ppm from internal $CHCl_3$. Optical rotations were measured at 25 ±0.2 °C on a Polarimeter in dichloromethane unless otherwise stated. Combustion analyses were performed on a elemental analyzer. Electrospray ionization (ESI) mass spectrometry experiments were performed on an API ion trap spectrometer.

## Preparation of α'–hydroxy enones

### Preparation of camphor-derived α'–hydroxy enones

All camphor-derived α'–hydroxy enones were prepared according to either of the alternate, sometimes complementary, procedures described in Scheme S1, as follows:




**Scheme S1**. Routes employed for the preparation of camphor-derived α'–hydroxy enones

**METHOD A (via allene 10): Multigram preparation of 1.** Compound **1** was prepared at 10 g scale starting from (1*R*)-(+)-camphor according to the following procedure which is adapted from a previously described protocol.[1]

Methoxyallene (8.82 g, 126 mmol) was added to a solution of nBuLi (2.5 M in hexanes, 48 mL, 120 mmol) in THF (60 mL) cooled to -30 ºC under a nitrogen atmosphere. After stirring for 30 minutes at the same temperature, TMEDA (18.3 mL, 120 mmol) and a solution of (1*R*)-(+)-camphor (9.12 g, 60 mmol) in THF (10 mL) were added dropwise. The resulting mixture was allowed to stir for 2 hours at -30 ºC and then was quenched with a saturated aqueous solution of $NH_4Cl$ (60 mL). The aqueous layer was extracted with $CH_2Cl_2$ (2 x 60 mL), the combined organics were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The product was purified by distillation (about 10% of the starting camphor was separated) and collected as a colorless liquid. Yield of allene **10**: 10 g (75%); b.p. 70-72 ºC/0.1 torr; $[\alpha]_D^{25}$ + 38.0 (*c* 1.0, $CH_2Cl_2$); IR (neat, $cm^{-1}$) 3585, 2950, 2924, 2868, 1951, 1066, 876; $^1H$ NMR ($CDCl_3$) δ 5.55 (d, 1H, J= 7.7Hz), 5.47 (d, 1H, J= 7.7Hz), 3.44 (s, 3H), 2.80 (s, 1H), 2.06-1.95 (m, 1H), 1.80-1.73 (d, 1H, J= 13Hz), 1.69-1.57 (m, 1H), 1.48-1.29 (m, 2H),

[1] Palomo, C.; Oiarbide, M.; García, J.M.; González, A.; Lecumberri, A.; Linden, A.; *J. Am. Chem. Soc.* **2002**, *124*, 10288.

1.12 (s, 3H), 1.08-0.88 (m, 2H), 1.00 (s, 3H), 0.80 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 197.5, 138.9, 92.1, 82.0, 56.4, 52.9, 49.8, 44.8, 42.5, 31.5, 26.6, 21.1, 20.9, 11.3. The distillate product was dissolved in $CH_2Cl_2$ (90 mL) and washed twice with 1M HCl (50 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give **1** as a white solid. Purification was effected by flash silica gel column chromatography using a 1:30 ethyl acetate/hexane mixture as the eluant. Yield of (1*R*)-2-*endo*-propenoyl-1,7,7-trimethylbicyclo[2.2.1]-heptan-2-ol (**1**): 9.36 g (75% from (1R)-(+)-camphor); m.p. 72-73 ºC; $[\alpha]_D^{25}$ -34.5 (*c* 1.0, $CH_2Cl_2$); IR (neat, $cm^{-1}$) 3488 (OH), 1685 (C=O); $^1$H NMR ($CDCl_3$) δ 6.88 (dd, 1H, J= 10.6Hz, J'= 17.2Hz), 6.34 (dd, 1H, J= 2.2Hz, J'= 16.9Hz), 5.67 (dd, 1H, J= 2.2Hz, J'= 10.3Hz), 2.88 (s, 1H), 2.34-2.25 (m, 1H), 1.88-1.64 (m, 2H), 1.44-0.80 (m, 4H), 1.10 (s, 3H), 0.89 (s, 3H), 0.82 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 201.6, 131.8, 128.7, 86.9, 52.6, 50.6, 45.2, 41.3, 30.2, 26.5, 20.9, 20.4, 10.6; Anal. Calcd for $C_{13}H_{20}O_2$ (208.33) C, 74.94; H, 9.70. Found: C, 74.85; H, 10.01.

**Preparation of 11.** The method described in Reference 1 was employed: Methyl iodide (0.51 mL, 8 mmol) was added to a solution of NaH (0.20 g, 8 mmol) in dry DMF (12 mL) cooled to –50 ºC under a nitrogen atmosphere. Then a solution of allene **10** (0.889 g, 4 mmol, obtained as above) in DMF (4 mL) was added at the same temperature and the mixture was stirred at 0 ºC for 1 hour. The reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (10 mL) and then was extracted twice with $Et_2O$ (15 mL), and the combined organic layers were washed with water (2 x 10 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue thus obtained was dissolved in $Et_2O$ (8 mL) and a 5% aqueous solution of $H_2SO_4$ (8 mL) was added at 0 ºC and the mixture was stirred at the same temperature for 16 hours. The layers were separated, and the aqueous layer was extracted with $CH_2Cl_2$ (2 x 10 mL). The combined organics were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification of the product **11** was effected by flash silica gel column chromatography using a 1:30 ethyl acetate/hexane mixture as the eluant. Yield of (1R)-2-endo-propenoyl-2-exo-methoxy-1,7,7-trimethylbicyclo[2.2.1]heptane (**11**): 0.534 g (60% from **10**); oil; $[\alpha]_D^{25}$ +27.0 (*c* 1.0, $Cl_2CH_2$); IR (neat, $cm^{-1}$) 1691 (CO); $^1$H NMR ($CDCl_3$) δ 6.98 (dd, 1H, J=10.3Hz, J´=17.2Hz), 6.33 (dd, 1H, J=2.2Hz, J´=17.6Hz), 5.64 (dd, 1H, J=2.2Hz, J´=10.3Hz), 3.00 (s, 3H), 2.16 (d, 1H, J=12.8), 1.92-1.55 (m, 3H), 1.35-1.10 (m, 2H), 1.00 (s, 3H), 0.98 (s, 3H), 0.87-0.75 (m, 1H), 0.81 (s, 3H); $^{13}$C NMR ($CDCl_3$) δ 201.6, 132.5, 127.9, 93.5, 52.1, 51.1, 50.6, 45.2, 33.3, 30.6, 26.0, 20.6, 20.6, 11.3.

**Preparation of 12a.** Compound **12a** was prepared following a previously described procedure:[2] To a solution of allene **10** (0.222 g, 1 mmol, obtained as mentioned above) in THF (4 mL) at –78 ºC, nBuLi (2.5 M in hexanes, 1.2 mL, 3 mmol) was added and the reaction was stirred at –25 ºC for 4 h. Then, MeI (0.21 mL, 3.5 mmol) was added and the mixture was stirred for 2 h at the same temperature. The reaction was quenched with 1N HCl (5 mL) and extracted with $CH_2Cl_2$ (2 x 15 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (eluant: ethyl acetate/hexane 1:60) to afford the corresponding enone. 0.150 g (67%); m.p. 82 ºC; $[\alpha]_D^{25}$ -54.0 (*c* 1.0, $Cl_2CH_2$); IR (neat, $cm^{-1}$) 3427 (OH), 1680 (CO); $^1$H NMR ($CDCl_3$) δ 7.01-6.90 (dq, 1H, J=7.0Hz, J'=14.7Hz), 6.61 (dq, 1H, J=2.0Hz, J'=15.0Hz), 3.13 (s, 1H), 2.24 (d, 1H, J=12.8Hz), 1.87 (d, 3H, 7.0Hz), 1.80-1.61 (m, 2H), 1.40-1.14 (m, 3H), 1.08 (s, 3H), 1.06-0.72 (m, 1H), 0.85 (s, 3H), 0.80 (s, 3H); $^{13}$C NMR

[2] Palomo, C.; Oiarbide, M.; Arceo, E.; García, J. M.; González, A.; Linden, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 6187.

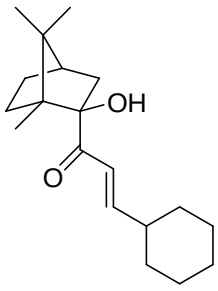
($CDCl_3$) δ 201.5, 143.5, 127.0, 86.6, 52.6, 50.5, 45.2, 41.1, 30.2, 26.6, 20.9, 20.4, 18.5, 10.6; Anal. calcd for $C_{14}H_{22}O_2$ (222.36) C, 75.62; H, 9.99. Found: C, 75.33; H, 10.07.

**METHOD B (aldol condensation).** n-Butyllithium (2.5M in hexanes, 4.8 mL, 12 mmol) was added to a solution of diisopropylamine (1.6 mL, 12 mmol) in THF (15 mL) cooled to -78ºC under a nitrogen atmosphere. The mixture was stirred at the same temperature for 30 min. Then, a solution of α-hydroxy methylketone **6** (0.98 g, 5 mmol) in THF (10 mL) was added dropwise and the reaction was stirred for 1 hour. Then a solution of the corresponding aldehyde (7.5 mmol) in THF (50 mL) was added and the mixture was allowed to warm to room temperature for 20 to 24 hours**.** After this time, the resulting mixture was quenched with a saturated aqueous solution of $NH_4Cl$ (75 mL), the layers were separated, and the aqueous layer was extracted with $CH_2Cl_2$ (2 x 75 mL). The combined organics were dried over $MgSO_4$, and evaporated under reduced pressure. Purification of the crude product was effected by flash silica gel column chromatography using a 1:50 ethyl acetate/hexane mixture as the eluant.

**METHOD C (Heck reaction).** A mixture of $Pd_2(dba)_3$ (0.0022 g, 2.4 μmol), $PPh_3$ (0.0052 g, 20 μmol) and $Et_3N$ (0.28 mL, 2 mmol) in $CH_3CN$ (4 mL) was stirred for 30 minutes at room temperature. Then a solution of α'–hydroxy enone **1** (0.208 g, 1 mmol) and the corresponding iodobenzene (3 mmol) was added and the mixture was stirred at 80 ºC for 1.5 h. After this time, the reaction was allowed to cool to room temperature and then 1N HCl (5 mL) was added and the mixture was extracted with $CH_2Cl_2$ (2 x 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and the solvent evaporated. The crude product was purified by column chromatography (eluant: ethyl acetate/hexane 1:60) to afford the corresponding enone.

**METHOD D (olefin metathesis).** A method adapted from the literature[3] was employed. α'-Hydroxy enone **1** (1.04 g, 5 mmol) and the corresponding alkene (7.5 mmol) were dissolved in $CH_2Cl_2$ (25 mL) and the solution was degassed by 3 freeze-pump-thaw cycles. Grubbs' 2nd generation catalyst (8.49 g, 1 mmol) in $CH_2Cl_2$ (10 mL) was added dropwise and the resulting mixture was allowed to stir at room temperature for 24 hours. Then, the solvent was removed *in vacuo* and purification of the crude product was effected by flash silica gel column chromatography using ethyl acetate/hexane 1:30 as the eluant.

**(1R)-2-*endo*-3'-cyclohexyl-2'-propenoyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (12b)**

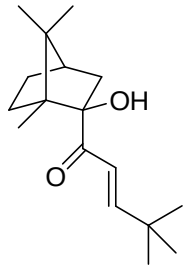



The title compound was prepared according to METHOD B starting from cyclohexanecarboxaldehyde (0.858 g, 7.5 mmol) in 24h. 0.825g (57%); white solid; m.p. 71-73ºC; $[\alpha]_D^{25}$= -34.0 (c 1.0, $CH_2Cl_2$); IR (neat, $cm^{-1}$) 3476 (OH), 1680 (CO); $^1H$ NMR ($CDCl_3$) δ 6.92 (dd, 1H, $J_1$=6.6Hz, $J_2$=15.4Hz), 6.57 (d, 1H, J=15.4Hz) 3.18 (s, 1H), 2.26 (d, 1H, J=12.8Hz), 2.13-0.84 (m, 17H), 1.12 (s, 3H), 0.87 (s, 3H), 0.84 (s, 3H); $^{13}C$ NMR ($CDCl_3$) δ 202.3, 153.3, 122.8, 86.8, 52.8, 50.5, 45.3, 41.3, 40.8, 31.7, 30.3, 26.7, 25.9, 25.7 20.9, 20.3, 10.5. Anal. calcd for $C_{19}H_{30}O_2$ (290.49) C, 78.55; H, 10.43. Found: C, 78.50; H, 10.41.

[3] Pfeiffer, M.W.B.; Phillips, A. *J. Am. Chem. Soc*. **2005**, *127*, 5334-5335.

Alternatively, the title compound could also be prepared according to the General Procedure METHOD D from vinylcyclohexane (1 mL, 7.5 mmol). Yield 0.724 g, 50%.

**(1R)-2-*endo*-4'4'-dimethyl-2'-pentenoyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (12c)**

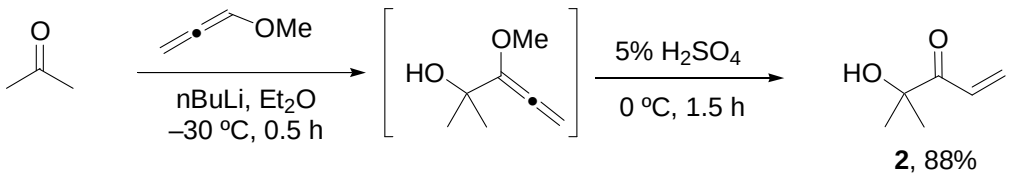



The title compound was prepared according to METHOD B starting from pivalaldehyde (0.646 g, 7.5 mmol) in 20 h. 0.977 g (73%); white solid; m.p. 74-76ºC; $[\alpha]_D^{25}$= -40.0 (c 1.0, $CH_2Cl_2$); IR (neat, $cm^{-1}$) 3477 (OH), 1685 (CO); $^1H$ NMR ($CDCl_3$) δ 6.97 (d, 1H, J=15.4Hz), 6.55 (d, 1H, J=15.8Hz), 3.15 (s, 1H), 2.28 (d, 1H, J=12.8Hz), 1.94-0.85 (m, 6H), 1.13 (s, 3H), 1.09 (s, 9H), 0.88 (s, 3H), 0.85 (s, 3H); $^{13}C$ NMR ($CDCl_3$) δ 202.4, 157.9, 120.5, 86.9, 52.8, 50.5, 45.3, 41.3, 33.9, 30.3, 28.7, 26.7, 20.9, 20.4, 10.5. Anal. calcd for $C_{17}H_{28}O_2$ (264.40) C, 77.22; H, 10.67. Found: C, 77.18; H, 10.65.

**Preparation of enones 12d-g**: The title enones were prepared according to the General Procedure METHOD C and their characterization data were fully coincident with those previously reported in the literature.[1] Copies of the $^1H$ and $^{13}C$ NMR spectra of thus obtained compounds are provided in the corresponding Section of this SI.

**Preparation of achiral α'–hydroxy enones**[4]

**METHOD E (preparation of 2 from acetone via allene intermediate)**[5]




**Scheme S2**

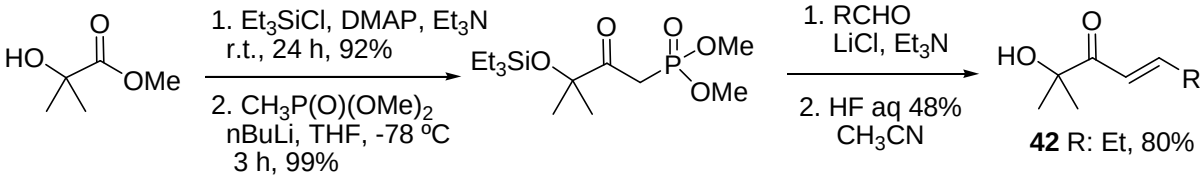
To a solution of methoxypropadiene (3.50 g, 50 mmol) in dry $Et_2O$ (100 mL) at -40°C, nBuLi (2.5 M in hexanes, 22 mL, 55 mmol) was added under nitrogen and the reaction was stirred at -40°C for 10 min. Then, acetone (4.04 mL, 55 mmol) in dry $Et_2O$ (55 mL) was added within 5 min. The reaction was stirred at the same temperature for 0.5 h and quenched with $H_2O$ (100 mL). The resulting mixture was allowed to warm to room temperature and extracted with $Et_2O$ (3 x 100 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure to afford 2-methyl-3-methoxy-3,4-pentadien-2-ol as a yellow liquid (5.65 g) (82%) that was employed in the next step without further purification.
The resulting methoxyallene (5.65 g, 44 mmol) was added dropwise to 5% aq $H_2SO_4$ (110 mL) at 0°C and the mixture was stirred for 1.5 h. After this time the reaction was allowed to

[4] These procedures have been previously described in the literature. See: Palomo, C.; Oiarbide, M.; García, J.M.; González, A.; Arceo, E.; *J. Am. Chem. Soc.* **2003**, *125*, 13942.

[5] Adapted from: a) Zimmer, R. *Synthesis* **1993**, 165-178. b) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 1179-1184

warm to room temperature and the solution was saturated with solid NaCl. The mixture was extracted with $Et_2O$ (5 x 60 mL) and the combined extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed to give a yellow oil which upon distillation afforded the enone as a colorless liquid (4.42 g) (88%) b.p. 45°C (13 mmHg); IR (neat, $cm^{-1}$) 3445 (OH), 1693 (C=O); $^1H$ NMR ($CDCl_3$) δ 6.73 (dd, 1H, J= 9.5Hz, J'= 16.8Hz), 6.50 (dd, 1H, J= 2.2 Hz, J'= 16.8Hz), 5.82 (dd, 1H, J= 2.2Hz, J'= 10.3Hz), 1.38 (s, 6H); $^{13}C$ NMR ($CDCl_3$) δ 202.3, 131.1, 128.8, 75.4, 26.1.

**METHOD F (via Horner-Wadsworth-Emmons olefination)**[6]



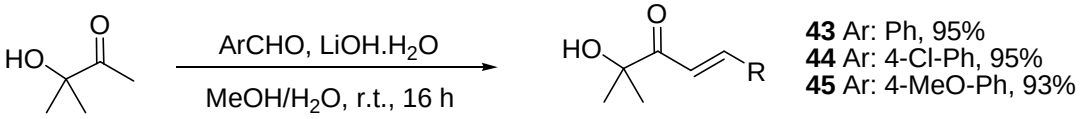

**Scheme S3**

Methyl 2-hydroxyisobutyrate (6.9 mL, 60 mmol) was added under a nitrogen atmosphere to a solution of dimethyl amino pyridine (1.22 g, 10 mmol), triethylamine (10 mL, 50 mmol) and triethylchlorosilane (8.5 mL, 50 mmol) in 50 mL of dichloromethane. The reaction mass was stirred at room temperature for 24 hours. After filtering over celite to remove the salt, the filtrate was diluted with diethyl ether (150 mL) and the resulting solution was washed with brine (1 x 50 mL) and water (1 x 50 mL). The solvent was removed under reduced pressure to give the triethylsilyl ether. Yield: 12.6 g (92%). No further purification is needed. Dimethyl methyl phosphonate (13.8 mL, 130 mmol, 2.5 eq) in dry THF (40 mL) was added drop-wise to a cold solution of n-BuLi (1.6 M in hexanes, 79 mL, 130 mmol) in dry THF (80 mL) at –78 °C under a nitrogen atmosphere. After stirring the resulting solution for 30 min, a solution of the crude triethylsilyl ether prepared above (12 g, 51 mmol) in dry THF (100 mL) was added dropwise at –78 °C. The mixture was stirred at the same temperature (-78ºC) for 3h and then quenched at this temperature with saturated ammonium chloride solution (200 mL). After allowing reaction mass to come to room temperature, it was extracted with diethyl ether (3 x 250 mL), dried over $MgSO_4$ and the solvent was evaporated under reduced pressure to get the title compound. Yield: 17g (99 %). It was used for the next step without further purification.

Dried LiCl (1.17 g, 27 mmol) and $Et_3N$ (3.8 mL, 27 mmol) were added successively to a solution of (3-methyl-2-oxo-3-triethylsilyloxybutyl)-phosphonic acid dimethyl ester (9.0 g, 27 mmol) in dry MeCN (67 mL). The resulting milky suspension was stirred for 15 min at room temperature and aldehyde (27 mmol) was added drop-wise. The mixture was stirred for 40 h, diluted with water and extracted with $Et_2O$. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The resulting oil was dissolved in $CH_3CN$ (120 mL) and HF (48% aqueous, 1.2 mL) was added dropwise. The mixture was stirred for 3 h, diluted with $CH_2Cl_2$, washed with brine, dried and concentrated *in vacuo*. Flash cromatography (hexanes-EtOAc, 10:1) of the residue gave pure α'-hydroxy enone **42** in 85% yield. Characterization data of thus obtained compound were fully coincident with those reported in the literature.[4]

[6] Adapted from: (a) P. Sampson, V. Roussis, G. J. Drtina, F. L. Koerwitz, D. F. Wiemer, *J. Org. Chem.* **1986**, *51*, 2525-2529. (b) D. G. McCarthy, C. C. Collins, J. P. O'Driscoll, S. E. Lawrence, *J. Chem. Soc., Perkin Trans. 1* **1999**, 3667-3675

**METHOD G (Aldol condensation)**

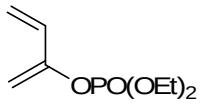



**Scheme S4**

3-Hydroxy-3-methyl-2-butanone (5.0 g, 49 mmol) was dissolved in a mixture of MeOH (120 mL) and $H_2O$ (40 mL). Freshly distilled aldehyde (87.5 mmol) was then added followed by $LiOH{\cdot}H_2O$ (10.28 g, 245 mmol). The reaction was stirred at reflux for 3 h, and after removal of MeOH under reduced pressure, the aqueous residue was diluted with $H_2O$ (40 mL) and extracted with $CH_2Cl_2$ (3 x 100 mL). The $CH_2Cl_2$ extracts were combined, dried over $MgSO_4$ and concentrated. The crude product was flash chromatographed ($SiO_2$) using a 10:1 hexane:ethyl acetate mixture as eluent to get the corresponding α-hydroxy enone.

Characterization data of thus obtained products **43-45** were fully coincident with those previously reported.[4]

**Preparation of 2-diethylphosphoryloxy-1,3-butadiene (33)**[7]




To a solution of 2,2,6,6-tetramethylpiperidine (5.69 g, 40.3 mmol) in THF (50mL) at –78ºC and under an atmosphere of nitrogen, was added a 2.5M solution of n-butyllithium in hexane (16.1 mL, 40.3 mmol) with stirring. After 10 min, a solution of methyl vinyl ketone (3.08 mL, 37 mmol) in THF (20 ml) was added dropwise over 10 min. After another 10 min, diethyl chlorophosphate (6.4 mL, 44.4 mmol) was added and the reaction mixture was allowed to warm up to room temperature. Then, ice-cold water (100 ml) was added and the resulting mixture was extracted with a solution of ether and n-hexane (1:1, 4 x 100 mL). The combined organics was washed two times with water, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the crude product was effected by flash silica gel column chromatography using a 1:5 ethyl acetate/hexane mixture as the eluant, to afford 4.11 g (54 %) of the title compound. Characterization data of thus obtained compound were in good agreement with those reported in the literature.[7] Yelow oil; IR (neat, $cm^{-1}$) 1643, 1593 (C=C), 1268, 1027, 999 (phosphate); $^1H$ NMR ($CDCl_3$) δ 6.10 (ddd, 1H, $J_1$=3.3Hz, $J_2$=10.5Hz, $J_3$=17.1Hz), 5.48 (d, 1H, J=17.2Hz), 5,12 (d, 1H, J=17.2Hz), 5.01 (dd, 1H, $J_1$=4.1Hz, $J_2$=2.2Hz), 4.66 (dd, 1H, $J_1$=4.1Hz, $J_2$=2.2Hz), 4.10 (dq, 4H, $J_1$= 7.3, $J_2$= 7Hz), 1,35 (dt, 6H, $J_1$=1.1Hz, $J_2$=6.9Hz); $^{13}C$ NMR ($CDCl_3$) δ 151.3 (d), 131.3 (d), 116.1, 101.4 (d), 64.6 (d), 16.2 (d).

[7] Procedure adapted from: (a) Hayasi, T.; Fujiwa, T.; Okamoto, Y.; Katsuro, X.; Kumada, M. *Synthesis* **1981**, 1001–1003. (b) Liu, H. J.; Feng, W. M.; Kim, J. B.; Browne, E. N. C. *Can. J. Chem.* **1994**, *72*, 2163–2175.

**Camphor-derived Diels-Alder adducts not included in the Experimental Section**

Diels-Alder adducts **13**–**20**, **27**, and **29–32**, were obtained by following the General Procedure C of the Experimental Section. Characterization data of thus obtained products were fully coincident with those previously reported in the literature.[1] Copies of their $^{1}H$ and $^{13}C$ NMR spectra are provided in the corresponding Section of this SI.

**$Cu(OTf)_2$-tBOX-catalyzed enantioselective Diels-Alder reaction of achiral α'-hydroxy enones**

**Preparation of catalyst [Cu ((*S, S*)-*tert*-Bu-box)] $(SbF_6)_2$**[8]

(*S,S*)-*tert*-butyl-bis-(oxazoline) (16.2 mg, 0.055 mmol), $CuCl_2$ (6.7 mg, 0.050 mmol) and $AgSbF_6$ (34.4 mg, 0.10 mmol) were combined in an inert atmosphere and $CH_2Cl_2$ (0.8 mL) was added. The flask was wrapped in alumina foil to protect the reaction mixture from light. The reaction was stirred for 14 h in the dark to produce a blue or green solution with a white-orange AgCl precipitate. At the end of this time the mixture was filtered in air through a short column of oven-dried Celite, and rinsed with 0.2 mL of $CH_2Cl_2$. The clear blue solution of [Cu ((*S, S*)-*tert*-Bu-box)] $(SbF_6)_2$ was employed as a catalyst solution (0.05 M ) for the Diels-Alder reactions.

To a solution of the corresponding α'-hydroxy enone (0.5 mmol) in $CH_2Cl_2$ (1 mL) was added the diene (5-10 equiv) at the temperature indicated in tables 5 and 6. Immediately after, the 0.05 M solution of catalyst prepared as indicated above (1mL) was added dropwise. The reaction mixture was stirred at the same temperature for the amount of time specified in the tables. The reaction mixture was then diluted with 5 mL of 1:1 ethyl acetate/hexane and directly applied to a short silica gel column (1.5 cm x 1.5 cm) to remove copper salts. It was eluted with approximately 50 mL of 1:1 ethyl acetate/hexane and concentration afforded the unpurified product which was then analyzed by $^{13}C$ NMR. Subsequent purification was accomplished by column chromatography (silica gel, 1:30 ethyl acetate/hexane).

**Cycloadducts from the Diels-Alder reaction with achiral α'-hydroxyenones**

Cu-catalyzed Diels-Alder adducts **36**, and **38–41**, were obtained following the above procedure. Their synthesis and characterization have been previously reported by us.[4]

**Oxidative removal of the auxiliary (I). Synthesis of carboxylic acids 50 and 51**

To a solution of the corresponding α'-hydroxy ketone **13** or **27** (1 mmol) in acetonitrile (12 mL) at 0 ºC was added dropwise a solution of ceric ammonium nitrate (CAN) (1.64 g, 3 mmol) in water (6 mL) and the mixture was stirred at the same temperature for 10 minutes.

[8] The procedure described by Evans was followed: Evans D.A.; Barnes D.M.; Johnson J.S.; Lectka T.; Von Matt P.; Miller S.J.; Murry J.A.; Norcross R.D.; Shaughnessy E.A.; Campos K.R. *J. Am. Chem. Soc.* **1999**, *121*, 7582-7594.

Then water (3 mL) was added and the mixture was extracted with $CH_2Cl_2$ (2 x 20 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (2 x 10 mL), dried over $MgSO_4$, filtered, and the solvent evaporated to afford the starting (R)-(+)-camphor in about 90% yield. The basic aqueous layer was acidified by adding concentrate HCl and then extracted with $CH_2Cl_2$ (2 x 20 mL). The combined extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude product was purified by column chromatography (eluant: ethyl acetate/hexane 1:30) to afford the corresponding carboxylic acid **50** or **51**.

For full characterization of compounds **50** and **51**, see Reference 1.

**Oxidative removal of the auxiliary (II). Synthesis of ketones 54 and 55**

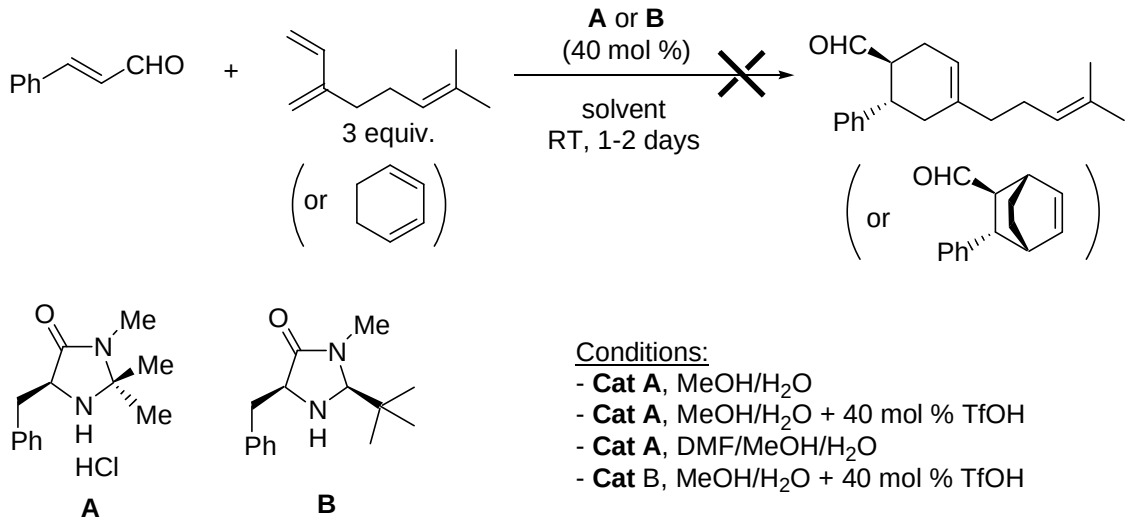
nBuLi (2.5 M in hexanes, 1.2 mL, 3 mmol) or MeLi (1.4 M in $Et_2O$, 2.14 mL, 3 mmol) was added to a solution of α'-hydroxy ketone **15** (1 mmol) in THF (3 mL) at –78 ºC and the solution was stirred at 0 ºC for 1.5 h. The reaction mixture was quenched with a saturated aqueous solution of $NH_4Cl$ (5 ml) and the resulting mixture was allowed to warm to room temperature, after which the layers were separated and the aqueous layer was extracted twice with $CH_2Cl_2$ (15 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed under reduced pressure. The residue thus obtained was subjected to oxidative scission by treatment with CAN, under the same conditions reported above. The resulting crude product **54** or **55** was purified by column chromatography (eluant: ethyl acetate/hexane 1:30).

For full characterization of compounds **54** and **55**, see Reference 1.

The synthesis and characterization of carboxylic acids **52/53** and ketones **56**/**57** by oxidative scission of the corresponding D-A cycloadducts have been described earlier. For pertinent information, see Reference 4.

**Attempted direct organocatalytic Diels-Alder reaction of cynnamaldehyde with myrcene and 1,3-cyclohexadiene**

The cycloaddition reaction of cinnamaldehyde with either myrcene or 1,3-cyclohexadiene was attempted unsuccessfully using MacMillan's catalytic methodology. Several conditions were employed (see Scheme S5), but no detectable amount of cycloadduct was observed by $^1H$ NMR in either case, being the unchanged starting materials obtained instead. See below for the detailed experimental procedure.




**Scheme S5**

**Procedure with catalyst A in MeOH/$H_2O$:**[9]
To a solution of (5S)-5-benzyl-2,2,3-trimethylimidazolidin-4-one hydrochloride (0.20 g, 0.8 mmol, catalyst **A**) in MeOH/$H_2O$ (95/5 v/v, 2 mL, 1.0 M) was added *trans*-cinnamaldehyde (0.25 mL, 2 mmol). The solution was stirred for 2 minutes before addition of the corresponding diene (6 mmol). After two days, the reaction mixture was diluted with $Et_2O$ and washed successively with $H_2O$ and brine. The organic layer was dried ($Na_2SO_4$), filtered and concentrated. After evaporation, the crude product was analyzed by $^1H$ NMR and the presence of the corresponding cycloadduct (as dimethyl acetal) was not observed.

**Procedure with catalyst A in DMF/MeOH/$H_2O$ as solvents:**[10]
To a solution of cinnamaldehyde (0.25 mL, 2 mmol) in DMF, MeOH, and water (1/1/0.1 mL respectively) was added (5S)-5-benzyl-2,2,3-trimethylimidazolidin-4-one hydrochloride (0.20 g, 0.8 mmol, catalyst **A**). After the solution was stirred for 2 min. at room temperature, myrcene (1.02 mL, 6 mmol) was added dropwise. The reaction was stirred 20 h, then diluted with water and $Et_2O$ and separated. The aqueous portion was extracted again with $Et_2O$, and the organics portions were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated. After evaporation, the crude product was analyzed by $^1H$ NMR and the presence of the corresponding cycloadduct (as dimethyl acetal) was not observed.

**Procedure in the presence of TfOH:**
To a solution of (5S)-5-benzyl-2,2,3-trimethylimidazolidin-4-one hydrochloride (0.20 g, 0.8 mmol, catalyst **A**) or (2S,5S)-5-benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one (0.20 g, 0.8 mmol, catalyst **B**) in MeOH/$H_2O$ (95/5 v/v, 2 mL, 1.0 M) at 0ºC, was added *trans*-cinnamaldehyde. Then TfOH (0.07 mL, 0.8 mmol) was added and the solution was stirred for 2 minutes at 0 ºC before addition of myrcene (1.02 mL, 6 mmol). After one day of stirring at room temperature, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL). The aqueous layer was extracted with $CH_2Cl_2$ (2 x 10 mL). The combined organics were dried over $MgSO_4$, and the solvent was removed under reduced pressure. After

[9] Adapted from Ahrendt K.A.; Borths J.; MacMillan D.W.C. *J. Am. Chem. Soc.* **2000**, *122*, 4243-4244.
[10] Adapted from Kinsman A.C.; Kerr M.A. *J. Am. Chem. Soc.* **2003**, *125*, 14120-14125.

evaporation, the crude product was analyzed by $^1$H NMR and the presence of the corresponding cycloadduct (as dimethyl acetal) was not observed.

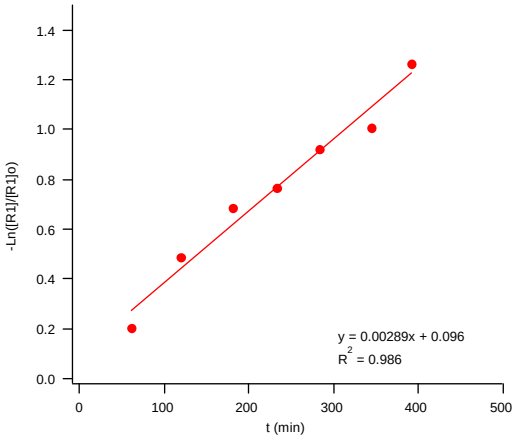
**Kinetic measurements for the Brønsted acid-catalyzed Diels-Alder reactions.**

The kinetic measurements were obtained from experiments performed in parallel using samples prepared from the same stock solutions of enone **1** and internal standard to avoid interexperimental errors. The reactions were performed in tightly stoppered NMR tubes using $CDCl_3$ as solvent and the temperature was controlled by a thermostatic bath where the tubes were kept at 293 K and periodically shacked. The measurements started after addition and fast mixing of the diene (2,3-dimethyl-1,3-butadiene) and the corresponding amount of catalyst (TFA) to the stock solutions containing the α'–hydroxy enone **1** and internal standard (2-methylnaphtalene). The evolution of the reaction was followed by the periodical quantification of enone disappearance by NMR spectroscopy measuring the decrease of the signal of its methylene groups (dd at δ 5.67 ppm) respect to the methyl signal (s at δ 2.53 ppm) of the internal standard, 2-methylnaphtalene.

For rate constants calculation, the experimental data points of $-\ln([\mathbf{1}]/[\mathbf{1}]_0)$ were plotted against time, with [**1**] and $[\mathbf{1}]_0$ being the actual and the initial concentration of species **1**, respectively. The points were adjusted to lines by linear regression and the rate constants calculated from the values of the slopes [[using Igor Pro software (Wavemetrics Inc.)]]. To determine the reaction order in acid TFA, four different concentrations (5, 10, 15, and 20 mol %) of TFA were tested and the calculated kinetic rate constants ($k_{obs}$) were plotted versus the catalyst loading. The straight line obtained ($R^2$ = 0.984) indicates the first order dependence in TFA acid (see graphics below).

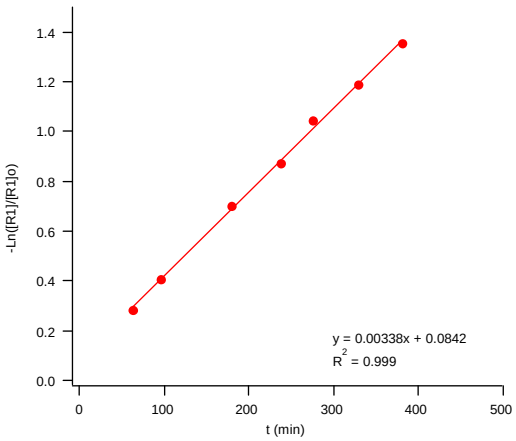
Experimental procedure. To a mixture of α'–hydroxy enone **1**, (156.2 mg, 0.75 mmol) and 2-methylnaphtalene (21.3 mg, 0.15 mmol) as internal standard in $CDCl_3$ (3 mL), were successively added 2,3-dimethyl-1,3-butadiene (308 mg, 3.75 mmol, 5 equiv.) and the corresponding increasing amounts of TFA (0.05, 0.1, 0.15 or 0.20 equivalents in four experiments). After fast mixing of the mixture, 600 µL aliquots were taken into NMR tubes and spectra were recorded at suitable intervals.

**Figure S1** (5 mol % TFA)



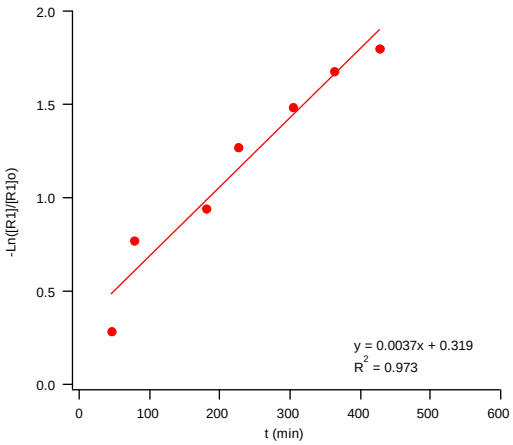

a = 0.096212 ± 0.056
b = 0.0028892 ± 0.000219
Pr= 0.985904
y = 0.00289x + 0.096
$R^2$ = 0.986

**Figure S2** (10 mol % TFA)



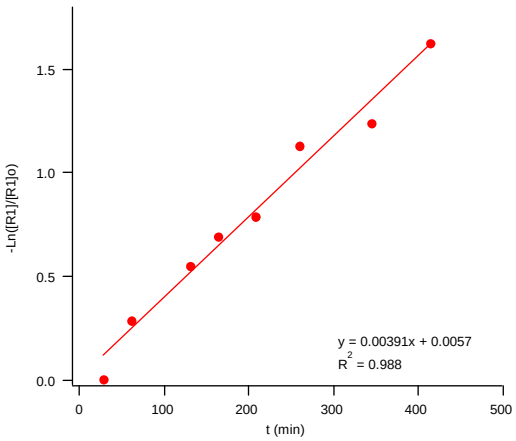

a = 0.084243 ± 0.0147
b = 0.0033771 ± 5.92e-05
Pr= 0.999233
y = 0.00338x + 0.0842
$R^2$ = 0.999

**Figure S3** (15 mol % TFA)



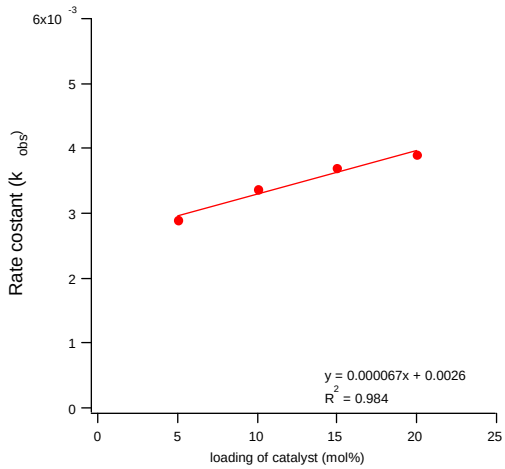

a = 0.31948 ± 0.105
b = 0.0036963 ± 0.000394
Pr= 0.972721
y = 0.0037x + 0.319
$R^2$ = 0.973

**Figure S4** (20 mol % TFA)




a = 0.0057038 ± 0.0583
b = 0.0039087 ± 0.000246
Pr= 0.988309
y = 0.00391x + 0.0057
$R^2$ = 0.988

**Figure S5**. Order in acid TFA.




a = 0.0026234 ± 0.00012
b = 6.7554e-05 ± 8.76e-06
Pr= 0.983612
y = 0.000067x + 0.0026
$R^2$ = 0.984

**Quantum calculations of Brønsted acid-catalyzed Diels-Alder reactions**

**General Information**.

All structures were optimized using the functional B3LYP[11] and the 6-31+G** basis sets as implemented in Gaussian 03.[12] Density Functional Theory has been shown to reliably predict the results of [4 + 2] Diels-Alder and other pericyclic reactions.[13] All energy minima and transition structures were characterized by frequency analysis. The stationary points were characterized by frequency calculations in order to verify that they have the right number of negative eigenvalues. The intrinsic reaction coordinates (IRC)[14] were followed to verify the energy profiles connecting each TS to the correct local minima. The gas-phase energies reported in this work include zero-point and thermal corrections and are not scaled. Solvent effects were included by means of single-point calculations with the self-consistent reaction field (SCRF) based on the IEF-PCM solvation model ($CH_2Cl_2$, as solvent, $\varepsilon = 8.93$, Pauling radii) on the previously gas-phase optimized structures.[15] The transition states shown in the Text correspond to the Diels-Alder reaction of α'-hydroxy enone **1** with cyclopentadiene, in the absence of any external acid and in the presence of one molecule of $CF_3CO_2H$ or $CF_3SO_3H$.

**Reaction of 1 and cyclopentadiene**

For the catalytic Diels-Alder reaction of **1** and cyclopentadiene a range of ternary TS geometries were evaluated. Among them those with the lowest energy values were further considered for more refined calculations and correspond to structures depicted in Figure 7 of the Article. Coordinates and geometries of such structures are shown below. In Figure S6, several other structures are depicted, which were subsequently discarded because of the considerably higher energy.

[11] (a) Lee, C.; Yang, W.; Parr, R.G. *Phys. Rev. B* **1988**, *37*, 785. (b) Becke, A.D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Kohn, W.; Becke, A.D.; Parr, R.G. *J. Phys. Chem.* **1996**, *100*, 12974.

[12] See Full Reference 22 in this page.

[13] (a) Goldstein, E.; Beno, B.; Houk, K.N. *J. Am. Chem. Soc.* **1996**, *118*, 6036. (b) Wiest, O.; Montiel, D.C.; Houk, K.N. *J. Phys. Chem. A* **1997**, *101*, 8378. (c) García, J.I.; Martínez-Merino, V.; Mayoral, J.A.; Salvatella, L. *J. Am. Chem. Soc.* **1998**, *120*, 2415. (d) Birney, D.M. *J. Am. Chem. Soc.* **2000**, *122*, 10917.

[14] Gonzalez, C.; Schlegel, H.B. *J. Phys. Chem.* **1990**, *94*, 5523.

[15] (a) Cancès, E.; Mennucci, B.; Tomasi, J. J. Chem. Phys. 1997, 107, 3032–3047. (b) Cossi, M.; Barone, V.; Mennuci, B.; Tomasi, J. Chem. Phys. Lett. 1998, 286, 253–260. (c) Tomasi, J.; Mennucci, B.; Cancès, E. J. Mol. Struct. (Theochem), 1999, 464, 211–226.

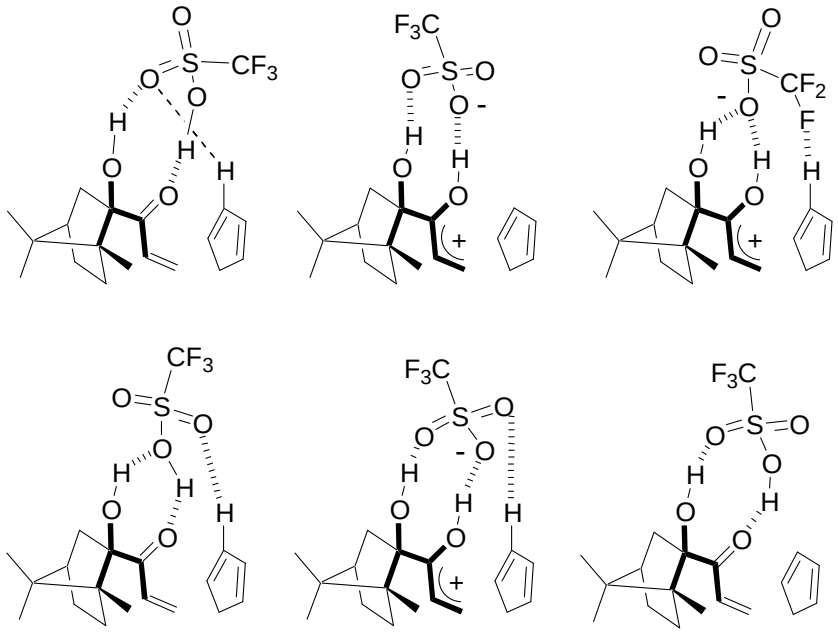
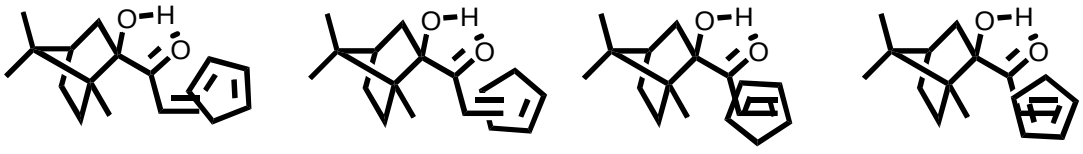


**Figure S6**. Pool of structures also computed at the outset. Their contribution was subsequently discarded because of the comparatively high energy.

**Coordinates of the most plausible TS structures for the Diels-Alder reaction between hydroxyenone 1 and cyclopentadiene in the presence of TfOH.**

For the non-catalyzed reaction between **1** and cyclopentadiene, the four possible diastereoisomers with an intramolecular hydrogen bond (Figure S7) were computed. The comparison of $\Delta G^{\ddagger}$ predicts an *endo*/*exo* selectivity of 4.4:1 and a diastereoselectivity greater than 100:1.



| endo-major | exo-major | endo-minor | exo-minor |
|---|---|---|---|
| 26.8 | 27.7 | 31.7 | 30.5 |

**Figure S7.** Diastereomeric transition structures for the non-catalyzed reaction between **1** and cyclopentadiene . Values of $\Delta G^{\ddagger}$ are given in kcal/mol.

After introduction of one molecule of $CF_3SO_3H$, different activation options arise for each diastereoisomer, whose main difference is based on the hydrogen bond network formed between acid activator, diene and dienophile. As an example, the overall lowest in energy for the *endo* approach are depicted in Figure S8.

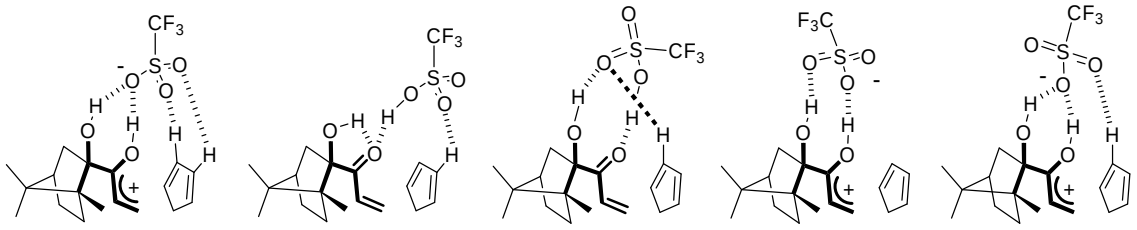
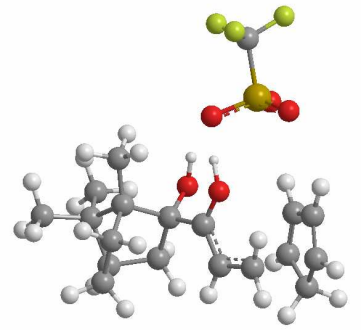


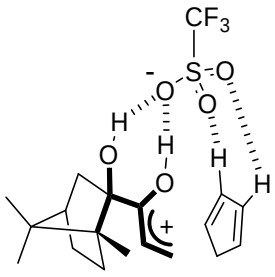

**Figure S8**

**TS hydroxyenone 1+CP (endo) (trifluoromethanesulfonic acid)**

Atomic Coordinates (Ångstroms)

| Type | X | Y | Z |
|---|---|---|---|
| C | -4.0390 | -1.3978 | 0.6065 |
| C | -3.2288 | -2.7126 | 0.4206 |
| C | -2.6126 | -3.2750 | 1.7174 |
| C | -3.2088 | -1.4915 | -1.6700 |
| C | -2.2184 | -2.0501 | -0.6037 |
| C | -1.1403 | -2.9546 | -1.1862 |
| C | -2.9576 | -0.3935 | 1.0502 |
| C | -4.0592 | -3.8653 | -0.1845 |
| C | -4.4452 | -1.0289 | -0.8402 |
| C | -1.7761 | 1.5382 | -1.0122 |
| C | -1.1435 | 0.3153 | -0.7082 |
| C | -1.6912 | -0.7849 | 0.2202 |
| C | -1.1365 | 2.4868 | -1.8032 |
| H | -0.4450 | -3.3182 | -0.4244 |
| H | -4.8805 | -1.4601 | 1.3045 |
| H | -3.4717 | -2.2840 | -2.3769 |
| H | -2.7723 | -0.6870 | -2.2691 |
| H | -4.6445 | 0.0440 | -0.9437 |
| H | -5.3568 | -1.5482 | -1.1509 |
| H | -3.2813 | 0.6411 | 0.9168 |
| H | -2.6946 | -0.5082 | 2.1038 |
| H | -1.6045 | -3.8272 | -1.6597 |
| H | -0.5488 | -2.4484 | -1.9565 |
| H | -1.9717 | -2.5721 | 2.2457 |
| H | -3.4144 | -3.5991 | 2.3932 |
| H | -4.8303 | -4.1743 | 0.5316 |
| H | -3.4259 | -4.7402 | -0.3703 |
| H | -2.0049 | -4.1600 | 1.4932 |
| H | -4.5652 | -3.6205 | -1.1208 |
| H | -2.7392 | 1.7597 | -0.5753 |
| H | -1.6816 | 3.3734 | -2.1119 |
| H | -0.3118 | 2.1909 | -2.4384 |
| H | 0.1247 | -1.4684 | 0.7522 |
| O | 0.0092 | 0.1404 | -1.2885 |
| O | -0.6707 | -1.0700 | 1.1682 |
| C | -0.7604 | 3.8261 | 0.7231 |
| C | -0.4087 | 2.6271 | 1.5535 |
| C | 0.1786 | 3.6810 | -0.4583 |
| C | 0.7435 | 2.0612 | 1.0874 |





**endo**

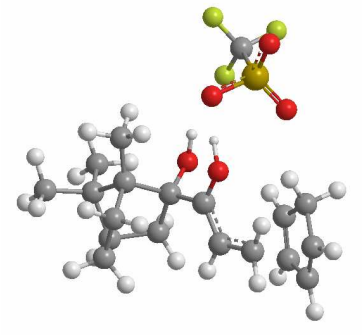
| | | | |
|---|---|---|---|
| C | 1.1310 | 2.7273 | -0.1212 |
| H | -0.4917 | 4.7402 | 1.2781 |
| H | -1.8234 | 3.9158 | 0.4798 |
| H | -0.9545 | 2.3201 | 2.4384 |
| H | 0.3436 | 4.4709 | -1.1834 |
| H | 1.2736 | 1.2241 | 1.5273 |
| H | 2.0147 | 2.4633 | -0.6916 |
| H | 0.6260 | -0.6212 | -0.9505 |
| O | 1.5977 | -1.5969 | -0.3512 |
| S | 2.8833 | -0.9051 | 0.1158 |
| O | 3.2380 | 0.2394 | -0.7396 |
| O | 2.9219 | -0.7081 | 1.5713 |
| C | 4.1464 | -2.2207 | -0.2529 |
| F | 4.1745 | -2.4841 | -1.5645 |
| F | 5.3568 | -1.7981 | 0.1285 |
| F | 3.8529 | -3.3467 | 0.4070 |

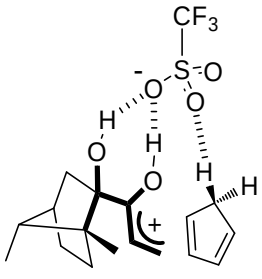
HF= -1813.559623 (including sum of electronic and thermal free energies)
Freq: -224.4

**TS hydroxyenone 1+CP (exo)(trifluoromethanesulfonic acid)**

Atomic Coordinates (Ångstroms)

| Type | X | Y | Z |
|---|---|---|---|
| C | -3.3770 | -1.6775 | 0.7567 |
| C | -2.6055 | -2.9328 | 0.2586 |
| C | -1.7351 | -3.6188 | 1.3308 |
| C | -3.0163 | -1.4765 | -1.6320 |
| C | -1.8273 | -2.1217 | -0.8570 |
| C | -0.8816 | -2.9188 | -1.7469 |
| C | -2.2405 | -0.6934 | 1.0947 |
| C | -3.5275 | -4.0363 | -0.3021 |
| C | -4.0695 | -1.1602 | -0.5267 |
| C | -1.4978 | 1.4985 | -0.8903 |
| C | -0.8087 | 0.2742 | -0.8954 |
| C | -1.1614 | -0.9409 | -0.0110 |
| C | -1.1095 | 2.6135 | -1.6390 |
| H | -0.0441 | -3.3462 | -1.1887 |
| H | -4.0602 | -1.8487 | 1.5951 |
| H | -3.4039 | -2.1878 | -2.3672 |
| H | -2.7167 | -0.5910 | -2.2002 |
| H | -4.3010 | -0.0909 | -0.4590 |
| H | -5.0172 | -1.6744 | -0.7130 |
| H | -2.5965 | 0.3367 | 1.1585 |
| H | -1.7702 | -0.9224 | 2.0531 |
| H | -1.4254 | -3.7448 | -2.2194 |
| H | -0.4615 | -2.3087 | -2.5531 |
| H | -1.0158 | -2.9566 | 1.8080 |
| H | -2.3806 | -4.0553 | 2.1038 |
| H | -4.1446 | -4.4412 | 0.5091 |
| H | -2.9350 | -4.8682 | -0.6992 |
| H | -1.1674 | -4.4435 | 0.8833 |
| H | -4.2058 | -3.7086 | -1.0933 |
| H | -2.3530 | 1.5935 | -0.2371 |
| H | -1.8225 | 3.4176 | -1.7846 |
| H | -0.3770 | 2.4910 | -2.4298 |
| H | 0.7286 | -1.6186 | 0.0685 |
| O | 0.1817 | 0.1668 | -1.7428 |
| O | 0.0309 | -1.2958 | 0.6808 |
| C | 1.2212 | 2.6522 | -0.0871 |
| C | 0.2720 | 3.7708 | -0.4489 |
| C | 0.6115 | 2.1007 | 1.1539 |
| C | -0.5017 | 4.0315 | 0.6850 |






**exo**

| | | | |
|---|---|---|---|
| C | -0.3372 | 2.9811 | 1.6270 |
| H | 2.1989 | 3.0890 | 0.1800 |
| H | 1.4512 | 1.9075 | -0.8492 |
| H | 0.4963 | 4.5169 | -1.2044 |
| H | 0.9407 | 1.1772 | 1.6155 |
| H | -1.1841 | 4.8682 | 0.7993 |
| H | -0.8922 | 2.8807 | 2.5531 |
| H | 0.8640 | -0.5932 | -1.5853 |
| O | 1.9514 | -1.6127 | -1.2861 |
| S | 3.3114 | -1.0107 | -0.9147 |
| O | 4.3016 | -1.1050 | -1.9862 |
| O | 3.1648 | 0.2768 | -0.2088 |
| C | 3.8587 | -2.2104 | 0.3988 |
| F | 4.0202 | -3.4352 | -0.1125 |
| F | 5.0172 | -1.8078 | 0.9321 |
| F | 2.9380 | -2.2737 | 1.3763 |

HF= -1813.555917 (including sum of electronic and thermal free energies)
Freq: -259.9

**Reaction of methyl vinyl ketone and cyclopentadiene**

From the calculations involving the Brønsted acid-promoted Diels-Alder reaction of camphor-derived α'–hydroxy enone **1** and cyclopentadiene (Figure 7, Main Text), the existence of a secondary CH···O hydrogen bond (between 2.3 and 2.5 Å) was observed, which involves a basic atom of the Brønsted acid and a hydrogen atom at the $sp^2$ hybridized carbons of the diene. In order to ascertain whether this particular interaction is specific to the mentioned system or more general, we conducted a computational study on a simple system, namely the Diels-Alder reaction of cyclopentadiene (CP) and methyl vinyl ketone (MVK) in the presence of HCN, $CF_3CO_2H$ and $CF_3SO_3H$. While MVK is monodentate and thus lacks an additional point for hydrogen bond interaction, the model would serve to establish whether or not Brønsted acids are able to build an efficient H-bonding network with these simple systems.

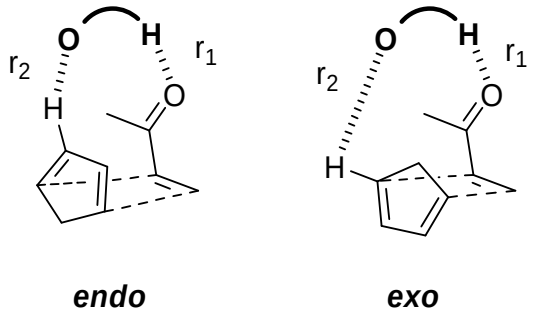
Among the Brønsted acids examined (Table S1) there is a good correlation between the pKa of the acid and the activation energy, in the gas-phase and in solvent. Triflic acid showed the largest activation effect (energy decreasing of $\Delta\Delta E^* = 9.0$ kcal/mol) resulting in $10^6$-fold faster reaction as compared with the non-catalyzed reaction. The activation barrier for the *endo* approach was lower than that of the *exo* approach, and the *endo*/*exo* gap for TFA (entry 3, Table S1) and TfOH (entry 4) is higher than for the weaker HCN (entry 2) or in the absence of added acid (entry 1). As expected, the activation values measured in $CH_2Cl_2$ as solvent are lower than those of the gas-phase due to the higher charge separation during the TS over the initial reactants. Nonetheless, the incorporation of the solvent effect does not alter the general reactivity-selectivity trends.

**Table S1.** Activation energies[a] for the DA reaction between MVK and CP in the presence of one molecule of the BA promoter, and calculated *endo*/*exo* selectivities.

| entry | BA | $pK_a$[b] | $\Delta E^{‡}$(endo) | $\Delta E^{‡}$(exo) | endo/exo[c] |
|---|---|---|---|---|---|
| 1 | No acid | --- | 18.6 (*17.0*) | 18.8 (*17.4*) | 1.3:1 |
| 2 | HCN | 9.1 | 16.5 (*11.6*) | 17.0 (*11.6*) | 2.3:1 |
| 3 | $F_3CCOOH$ | -0.2 | 13.1 (*12.9*) | 14.3 (*14.0*) | 7.7:1 |
| 4 | $F_3CSO_3H$ | -14.0 | 9.6 (*2.7*) | 10.7 (*3.7*) | 6.1:1 |

[a] $\Delta E^{‡}$ energies in kcal/mol, computed at B3LYP/6-31+G**. IEF-PCM ($CH_2Cl_2$) single-point values are shown in parenthesis. [b] Reported $pK_a$ values in water (from: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463, and http://www.chem.wisc.edu/areas/reich/pkatable/index.htm). [c] Based on the gas-phase activation energies.

An analysis of the calculated transition state geometries for the acid-promoted reaction is also noteworthy. The reduction in the activation barrier for the acid-promoted reaction as compared to the uncatalyzed process is accompanied by a shortening of the $r_1$ distance (Figure S9), and the magnitude of this shortening correlates well with the acid strength of the Brønsted acid involved. For instance, whereas HCN presents the larger $r_1$ distance (1.90 Å, entry 1, Table S2) and the lowest catalytic activity, the $r_1$ value for stronger acids (TFA, TfOH) falls below 1.5 Å. The very short $r_1$ distance for triflic acid (1.07 Å) corresponds to an essentially covalent O–H bond, reflecting the capacity of triflic acid for extensive proton transfer to the carbonyl group during the transition state.




***endo*** ***exo***

**Figure S9.** Hydrogen-bond interactions in the calculated *endo* and *exo* TS for the Brønsted acid-promoted Diels-Alder reaction between MVK and cyclopentadiene. O-H represents a Brønsted acid with a basic oxygen atom.

**Table S2.** Computed values (B3LYP/6-31+G** level) in Å for the $r_1$ and $r_2$ distances as defined in Figure S9 for selected Brønsted acids.

| Entry | Acid | r1 (endo) | r2 (endo) | r1 (exo) | r2 (exo) |
|---|---|---|---|---|---|
| 1 | HCN | 1.90 | --- | 1.92 | --- |
| 2 | $F_3CCOOH$ | 1.48 | 2.47 | 1.49 | 2.94 |
| 3 | $F_3CSO_3H$ | *1.07* | 2.31 | *1.05* | 2.38 |

Actually, for $CF_3COOH$ and $CF_3SO_3H$, a second electrostatic positive interaction $r_2$ was also observed, which involves a basic atom of the Brønsted acid and a hydrogen atom at the $sp^2$ hybridized carbon of the diene. In sharp contrast, HCN did not lead to any appreciable secondary interaction (Figure S9).[16] Although this secondary hydrogen-bond interaction is weak (2.3 Å < $r_2$ < 2.5 Å, Table S2), it contributes to both the diminishing of the activation barrier of the reaction and the increasing of the degree of order of the TS. Noteworthy, whilst TfOH presents similar interactions in the *endo* and *exo* trajectories, TFA shows a stronger interaction in the *endo* approach, which might contribute to the slightly higher *endo*/*exo* selectivity of the latter. Although solvent effects are expected to weaken hydrogen bonds, the transition state in the presence of formic acid was optimized in a $CH_2Cl_2$ model (PCM), leading to a structure that retains the $r_2$ secondary interaction in the *endo* approach (2.60 Å in $CH_2Cl_2$, 2.44 Å in gas-phase), whilst it is completely lost in the *exo* approach (>3.50 Å in $CH_2Cl_2$, 2.76 Å in gas-phase). The corresponding refined activation energies are 13.9 kcal/mol (*endo*) and 15.5 kcal/mol (*exo*), corresponding to 15:1 selectivity, slightly higher than in the gas-phase.

**Representative geometries of the computed transition states (MVK + Cyclopentadiene)**

Figure S10 shows the transition state geometry of two instructive examples which involve HCN and TFA-promoted Diels-Alder reactions. While the H-O-C=O angularity in TFA

[16] The unsuitability of HCN to engage in such secondary hydrogen-bond interaction was tentatively ascribed to the lack of highly hydrophilic basic sites (primarily oxygen atoms) and in part to geometrical restrictions imparted by the linearity of this Brønsted acid.

molecule can effectively accommodate the double H-bond interaction, the lack of oxygen atoms and the linearity of the H-C-N system in HCN seemingly prevent second interaction to be effective.

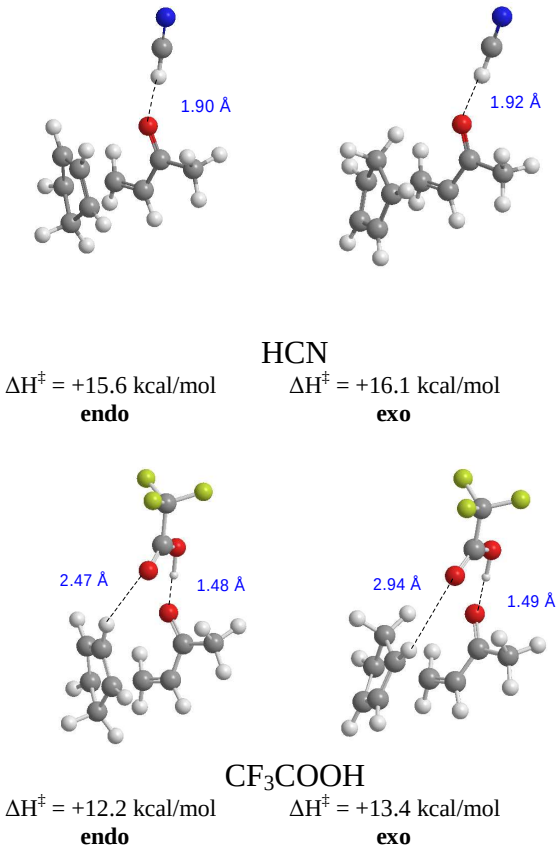



**Figure S10**

## 5. Coordinates and structures for the non-catalyzed Diels-Alder reaction between cyclopentadiene and 3-buten-2-one at B3LYP/6-311+G**

**$TS_{A1}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.1535 | 0.7750 | -1.2655 |
| C | 2.9855 | -0.2550 | -0.4475 |
| C | 3.3525 | -1.5280 | -1.2345 |
| C | 1.6955 | 1.0860 | 1.0935 |
| C | 1.8685 | -0.4000 | 0.6645 |
| C | 2.1455 | -1.3480 | 1.8215 |
| C | 0.8255 | 0.0220 | -1.5095 |
| C | 4.3195 | 0.3080 | 0.0835 |
| C | 1.8735 | 1.8880 | -0.2305 |
| H | 4.2235 | 1.2160 | 0.6775 |
| H | 2.2835 | -2.3730 | 1.4715 |

| | | | |
|---|---|---|---|
| H | 2.6245 | 1.1300 | -2.1855 |
| H | 2.4615 | 1.3490 | 1.8255 |
| H | 0.7355 | 1.2700 | 1.5765 |
| H | 0.9855 | 2.4710 | -0.4945 |
| H | 2.7025 | 2.5950 | -0.1645 |
| H | 0.0075 | 0.7060 | -1.7385 |
| H | 0.8995 | -0.6830 | -2.3385 |
| H | 3.0475 | -1.0460 | 2.3615 |
| H | 1.3175 | -1.3500 | 2.5375 |
| H | 2.5065 | -2.0250 | -1.6985 |
| H | 3.8305 | -2.2580 | -0.5745 |
| H | 4.0795 | -1.2710 | -2.0135 |
| H | 4.9825 | 0.5350 | -0.7575 |
| H | 4.8285 | -0.4380 | 0.7005 |
| C | 0.5915 | -0.7960 | -0.2025 |
| C | -0.7425 | -0.5580 | 0.5565 |
| C | -1.4805 | 0.6760 | 0.5035 |
| C | -2.6095 | 0.8320 | 1.3255 |
| H | -1.1375 | 1.4910 | -0.1175 |
| H | -2.9665 | 1.8430 | 1.4955 |
| H | -2.6685 | 0.1850 | 2.1935 |
| H | 0.0325 | -2.5950 | 0.1675 |
| O | -1.1755 | -1.5150 | 1.2215 |
| O | 0.5955 | -2.1890 | -0.5135 |
| C | -3.9465 | 0.8410 | -0.9775 |
| C | -3.0635 | -0.1860 | -1.6195 |
| C | -4.2005 | 0.1980 | 0.3785 |
| C | -3.2545 | -1.3940 | -0.9885 |
| C | -3.9905 | -1.1860 | 0.1935 |
| H | -4.9005 | 0.8740 | -1.5255 |
| H | -3.5485 | 1.8550 | -0.9565 |
| H | -2.5135 | -0.0300 | -2.5375 |
| H | -4.9825 | 0.5640 | 1.0355 |
| H | -2.8295 | -2.3390 | -1.2975 |
| H | -4.2475 | -1.9560 | 0.9075 |

Sum of electronic and thermal Free Energies = -851.798340
Freq: -384.9

**$TS_{A2}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 4.3140 | -0.6450 | -0.3845 |
| C | 1.6440 | -0.5510 | -1.5535 |
| C | 2.3870 | 1.8670 | -1.0495 |
| C | 0.7290 | 0.5930 | 0.5165 |
| C | 3.5320 | 0.4380 | 1.6785 |
| C | 1.9730 | 0.5210 | -0.4755 |
| C | 0.8390 | -0.7680 | 1.2705 |
| C | 2.0780 | -1.4540 | 0.6535 |
| C | -0.6080 | 0.9000 | -0.2185 |
| C | -2.5600 | 0.1430 | -1.5695 |
| C | -1.4740 | -0.1460 | -0.7265 |
| C | 3.0400 | -0.2590 | 0.3965 |
| C | 1.6980 | -1.9020 | -0.7765 |
| H | 4.2010 | -0.2380 | 2.2225 |
| H | 2.6260 | 2.5800 | -0.2585 |

| | | | |
|---|---|---|---|
| H | 1.5890 | 2.3020 | -1.6595 |
| H | -1.1780 | -1.1740 | -0.5835 |
| H | 4.9300 | -1.3120 | 0.2255 |
| H | -2.6230 | 1.1600 | -1.9445 |
| H | -2.8750 | -0.6160 | -2.2755 |
| H | 4.1310 | -1.1490 | -1.3335 |
| H | 4.9150 | 0.2440 | -0.5945 |
| H | 3.2690 | 1.7570 | -1.6875 |
| H | 2.4830 | -2.2550 | 1.2775 |
| H | -0.0560 | -1.3840 | 1.1775 |
| H | 0.9740 | -0.5530 | 2.3305 |
| H | 0.7450 | -2.4370 | -0.7925 |
| H | 2.4440 | -2.5800 | -1.1985 |
| H | 4.1120 | 1.3310 | 1.4275 |
| H | 2.7370 | 0.7540 | 2.3465 |
| O | -0.8980 | 2.0980 | -0.3405 |
| C | -4.3750 | -1.1150 | -0.0235 |
| C | -3.5470 | -1.3390 | 1.0865 |
| C | -4.2200 | 0.2220 | -0.4515 |
| C | -2.9360 | -0.1450 | 1.4445 |
| C | -3.6160 | 0.9710 | 0.7195 |
| H | -3.3570 | -2.3030 | 1.5415 |
| H | -4.9210 | 0.6960 | -1.1305 |
| H | -4.9300 | -1.8790 | -0.5535 |
| H | -2.2560 | -0.0040 | 2.2735 |
| H | -2.9830 | 1.8210 | 0.4705 |
| H | -4.4420 | 1.3370 | 1.3495 |
| H | 2.3940 | -0.5160 | -2.3465 |
| H | 0.6820 | -0.3760 | -2.0365 |
| O | 0.8810 | 1.6570 | 1.4565 |
| H | 0.4020 | 2.4070 | 1.0665 |

Sum of electronic and thermal Free Energies = -851.731987
Freq: -418.1

**$TS_{A3}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.2475 | 1.0290 | -1.1530 |
| C | 3.2075 | 0.1400 | -0.3130 |
| C | 4.3325 | 0.9310 | 0.3850 |
| C | 0.9725 | -0.8910 | -0.3280 |
| C | 2.0545 | -0.3300 | 0.6670 |
| C | 2.4625 | -1.2730 | 1.7920 |
| C | 1.6375 | 1.9720 | -0.0920 |
| C | 3.9135 | -0.9610 | -1.1280 |
| C | 1.1425 | 0.0350 | -1.5700 |
| C | -2.7895 | -1.7010 | -0.2930 |
| C | 1.5095 | 1.0460 | 1.1540 |
| C | -0.4725 | -1.0250 | 0.2350 |
| C | -1.5615 | -1.1720 | -0.7200 |
| H | 0.2205 | 0.5520 | -1.8370 |
| H | 1.4365 | -0.5770 | -2.4240 |
| H | 0.6745 | 2.3730 | -0.4190 |
| H | 2.2855 | 2.8300 | 0.1050 |
| H | 1.6065 | -1.5190 | 2.4240 |
| H | 3.9855 | 1.7460 | 1.0200 |
| H | 4.9405 | 0.2660 | 1.0040 |
| H | 4.9975 | 1.3650 | -0.3690 |
| H | 2.8875 | -2.2040 | 1.4030 |
| H | 4.4925 | -1.6140 | -0.4670 |

| | | | |
|---|---|---|---|
| H | 3.2395 | -1.5950 | -1.6960 |
| H | 3.2255 | -0.8090 | 2.4230 |
| H | 2.7075 | 1.5450 | -1.9990 |
| H | 4.6245 | -0.4970 | -1.8210 |
| H | -1.3515 | -1.0620 | -1.7750 |
| H | -3.4105 | -2.1840 | -1.0400 |
| H | -2.7985 | -2.1800 | 0.6790 |
| H | 0.4915 | 0.9620 | 1.5290 |
| O | -0.6675 | -1.1530 | 1.4460 |
| C | -3.6845 | 0.6450 | -1.1340 |
| C | -4.0505 | -0.2220 | 0.0600 |
| C | -2.5125 | 1.3280 | 0.7710 |
| C | -3.5085 | 0.4290 | 1.1890 |
| C | -2.4595 | 1.3340 | -0.6100 |
| H | -4.4775 | 1.3970 | -1.2660 |
| H | -1.7985 | 1.9390 | -1.2150 |
| H | -4.9975 | -0.7490 | 0.1070 |
| H | -1.8385 | 1.8560 | 1.4300 |
| H | -3.7235 | 0.1750 | 2.2180 |
| H | -3.5635 | 0.1230 | -2.0820 |
| H | 2.1155 | 1.4100 | 1.9870 |
| O | 1.2585 | -2.2430 | -0.7650 |
| H | 1.1645 | -2.8300 | -0.0060 |

Sum of electronic and thermal Free Energies = -851.724930
Freq: -420.5

**$TS_{A4}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | -4.1970 | 1.1005 | -0.5700 |
| C | -3.2100 | 1.7385 | 0.1950 |
| C | -4.1370 | -0.2935 | -0.3320 |
| C | -2.5920 | 0.7995 | 1.0070 |
| C | -3.3910 | -0.4605 | 0.9790 |
| H | -4.8030 | 1.5755 | -1.3310 |
| H | -2.9290 | 2.7805 | 0.1120 |
| H | -4.9520 | -0.9545 | -0.6060 |
| H | -1.8050 | 1.0015 | 1.7190 |
| H | -4.1290 | -0.4225 | 1.7970 |
| H | -2.8140 | -1.3785 | 1.0860 |
| C | 3.0590 | 0.2905 | -0.1640 |
| C | 1.5830 | -0.7135 | -1.8070 |
| C | 4.0210 | -0.9105 | -0.0870 |
| C | 1.0110 | -1.0525 | -0.3870 |
| C | 1.5600 | -0.1465 | 1.9880 |
| C | 0.9630 | 1.4625 | 0.0650 |
| C | 3.8520 | 1.4905 | 0.3950 |
| C | 1.6220 | 0.1215 | 0.4920 |
| C | 1.5280 | 1.7375 | -1.3610 |
| C | 2.4690 | 0.5325 | -1.5840 |
| H | 3.6280 | -1.8255 | -0.5180 |
| H | 4.2770 | -1.1305 | 0.9540 |
| H | 4.9520 | -0.6525 | -0.6020 |
| H | 3.2070 | 0.6845 | -2.3750 |
| H | 1.2520 | 2.2485 | 0.7650 |
| H | -0.1230 | 1.4175 | 0.0920 |
| H | 0.7480 | 1.7865 | -2.1260 |
| H | 2.0680 | 2.6865 | -1.4040 |
| H | 0.8010 | -0.5285 | -2.5470 |
| H | 2.1550 | -1.5765 | -2.1480 |

| | | | |
|---|---|---|---|
| H | 4.1940 | 1.2785 | 1.4130 |
| H | 3.3020 | 2.4305 | 0.4220 |
| H | 4.7470 | 1.6535 | -0.2140 |
| H | 0.7660 | -2.7805 | 0.4130 |
| H | 2.0480 | -1.0895 | 2.2390 |
| H | 2.0480 | 0.6575 | 2.5470 |
| H | 0.5240 | -0.2095 | 2.3380 |
| O | 1.5350 | -2.2965 | 0.0580 |
| C | -2.7070 | -0.8925 | -1.5320 |
| C | -1.4590 | -0.3965 | -1.0970 |
| C | -0.5450 | -1.2485 | -0.3600 |
| H | -1.0790 | 0.5115 | -1.5410 |
| H | -2.8690 | -1.9565 | -1.3930 |
| H | -3.0940 | -0.5085 | -2.4680 |
| O | -0.9560 | -2.2515 | 0.2400 |

Sum of electronic and thermal Free Energies = -851.727378
Freq: -411.0

**$TS_{B1}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.1535 | 0.7750 | -1.2655 |
| C | 2.9855 | -0.2550 | -0.4475 |
| C | 3.3525 | -1.5280 | -1.2345 |
| C | 1.6955 | 1.0860 | 1.0935 |
| C0.6775 | | | |
| H | 2.2835 | -2.3730 | 1.4715 |
| H | 2.6245 | 1.1300 | -2.1855 |
| H | 2.4615 | 1.3490 | 1.8255 |
| H | 0.7355 | 1.2700 | 1.5765 |
| H | 0.9855 | 2.4710 | -0.4945 |
| H | 2.7025 | 2.5950 | -0.1645 |
| H | 0.0075 | 0.7060 | -1.7385 |
| H | 0.8995 | -0.6830 | -2.3385 |
| H | 3.0475 | -1.0460 | 2.3615 |
| H | 1.3175 | -1.3500 | 2.5375 |
| H | 2.5065 | -2.0250 | -1.6985 |
| H | 3.8305 | -2.2580 | -0.5745 |
| H | 4.0795 | -1.2710 | -2.0135 |
| H | 4.9825 | 0.5350 | -0.7575 |
| H | 4.8285 | -0.4380 | 0.7005 |
| C | 0.5915 | -0.7960 | -0.2025 |
| C | -0.7425 | -0.5580 | 0.5565 |
| C | -1.4805 | 0.6760 | 0.5035 |
| C | -2.6095 | 0.8320 | 1.3255 |
| H | -1.1375 | 1.4910 | -0.1175 |
| H | -2.9665 | 1.8430 | 1.4955 |
| H | -2.6685 | 0.1850 | 2.1935 |
| H | 0.0325 | -2.5950 | 0.1675 |
| O | -1.1755 | -1.5150 | 1.2215 |
| O | 0.5955 | -2.1890 | -0.5135 |
| C | -3.9465 | 0.8410 | -0.9775 |
| C | -3.0635 | -0.1860 | -1.6195 |
| C | -4.2005 | 0.1980 | 0.3785 |
| C | -3.2545 | -1.3940 | -0.9885 |
| C | -3.9905 | -1.1860 | 0.1935 |
| H | -4.9005 | 0.8740 | -1.5255 |
| H | -3.5485 | 1.8550 | -0.9565 |

| | | | |
|---|---|---|---|
| H | -2.5135 | -0.0300 | -2.5375 |
| H | -4.9825 | 0.5640 | 1.0355 |
| H | -2.8295 | -2.3390 | -1.2975 |
| H | -4.2475 | -1.9560 | 0.9075 |

Sum of electronic and thermal Free Energies = -851.798340
Freq: -405.3

**$TS_{B2}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 4.3140 | -0.6450 | -0.3845 |
| C | 1.6440 | -0.5510 | -1.5535 |
| C | 2.3870 | 1.8670 | -1.0495 |
| C | 0.7290 | 0.5930 | 0.5165 |
| C | 3.5320 | 0.4380 | 1.6785 |
| C | 1.9730 | 0.5210 | -0.4755 |
| C | 0.8390 | -0.7680 | 1.2705 |
| C | 2.0780 | -1.4540 | 0.6535 |
| C | -0.6080 | 0.9000 | -0.2185 |
| C | -2.5600 | 0.1430 | -1.5695 |
| C | -1.4740 | -0.1460 | -0.7265 |
| C | 3.0400 | -0.2590 | 0.3965 |
| C | 1.6980 | -1.9020 | -0.7765 |
| H | 4.2010 | -0.2380 | 2.2225 |
| H | 2.6260 | 2.5800 | -0.2585 |
| H | 1.5890 | 2.3020 | -1.6595 |
| H | -1.1780 | -1.1740 | -0.5835 |
| H | 4.9300 | -1.3120 | 0.2255 |
| H | -2.6230 | 1.1600 | -1.9445 |
| H | -2.8750 | -0.6160 | -2.2755 |
| H | 4.1310 | -1.1490 | -1.3335 |
| H | 4.9150 | 0.2440 | -0.5945 |
| H | 3.2690 | 1.7570 | -1.6875 |
| H | 2.4830 | -2.2550 | 1.2775 |
| H | -0.0560 | -1.3840 | 1.1775 |
| H | 0.9740 | -0.5530 | 2.3305 |
| H | 0.7450 | -2.4370 | -0.7925 |
| H | 2.4440 | -2.5800 | -1.1985 |
| H | 4.1120 | 1.3310 | 1.4275 |
| H | 2.7370 | 0.7540 | 2.3465 |
| O | -0.8980 | 2.0980 | -0.3405 |
| C | -4.3750 | -1.1150 | -0.0235 |
| C | -3.5470 | -1.3390 | 1.0865 |
| C | -4.2200 | 0.2220 | -0.4515 |
| C | -2.9360 | -0.1450 | 1.4445 |
| C | -3.6160 | 0.9710 | 0.7195 |
| H | -3.3570 | -2.3030 | 1.5415 |
| H | -4.9210 | 0.6960 | -1.1305 |
| H | -4.9300 | -1.8790 | -0.5535 |
| H | -2.2560 | -0.0040 | 2.2735 |
| H | -2.9830 | 1.8210 | 0.4705 |
| H | -4.4420 | 1.3370 | 1.3495 |
| H | 2.3940 | -0.5160 | -2.3465 |
| H | 0.6820 | -0.3760 | -2.0365 |
| O | 0.8810 | 1.6570 | 1.4565 |
| H | 0.4020 | 2.4070 | 1.0665 |

Sum of electronic and thermal Free Energies = -851.731987
Freq: -405.3

**$TS_{B3}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.1535 | 0.7750 | -1.2655 |
| C | 2.9855 | -0.2550 | -0.4475 |
| C | 3.3525 | -1.5280 | -1.2345 |
| C | 1.6955 | 1.0860 | 1.0935 |
| C | 1.8685 | -0.4000 | 0.6645 |
| C | 2.1455 | -1.3480 | 1.8215 |
| C | 0.8255 | 0.0220 | -1.5095 |
| C | 4.3195 | 0.3080 | 0.0835 |
| C | 1.8735 | 1.8880 | -0.2305 |
| H | 4.2235 | 1.2160 | 0.6775 |
| H | 2.2835 | -2.3730 | 1.4715 |
| H | 2.6245 | 1.1300 | -2.1855 |
| H | 2.4615 | 1.3490 | 1.8255 |
| H | 0.7355 | 1.2700 | 1.5765 |
| H | 0.9855 | 2.4710 | -0.4945 |
| H | 2.7025 | 2.5950 | -0.1645 |
| H | 0.0075 | 0.7060 | -1.7385 |
| H | 0.8995 | -0.6830 | -2.3385 |
| H | 3.0475 | -1.0460 | 2.3615 |
| H | 1.3175 | -1.3500 | 2.5375 |
| H | 2.5065 | -2.0250 | -1.6985 |
| H | 3.8305 | -2.2580 | -0.5745 |
| H | 4.0795 | -1.2710 | -2.0135 |
| H | 4.9825 | 0.5350 | -0.7575 |
| H | 4.8285 | -0.4380 | 0.7005 |
| C | 0.5915 | -0.7960 | -0.2025 |
| C | -0.7425 | -0.5580 | 0.5565 |
| C | -1.4805 | 0.6760 | 0.5035 |
| C | -2.6095 | 0.8320 | 1.3255 |
| H | -1.1375 | 1.4910 | -0.1175 |
| H | -2.9665 | 1.8430 | 1.4955 |
| H | -2.6685 | 0.1850 | 2.1935 |
| H | 0.0325 | -2.5950 | 0.1675 |
| O | -1.1755 | -1.5150 | 1.2215 |
| O | 0.5955 | -2.1890 | -0.5135 |
| C | -3.9465 | 0.8410 | -0.9775 |
| C | -3.0635 | -0.1860 | -1.6195 |
| C | -4.2005 | 0.1980 | 0.3785 |
| C | -3.2545 | -1.3940 | -0.9885 |
| C | -3.9905 | -1.1860 | 0.1935 |
| H | -4.9005 | 0.8740 | -1.5255 |
| H | -3.5485 | 1.8550 | -0.9565 |
| H | -2.5135 | -0.0300 | -2.5375 |
| H | -4.9825 | 0.5640 | 1.0355 |
| H | -2.8295 | -2.3390 | -1.2975 |
| H | -4.2475 | -1.9560 | 0.9075 |

Sum of electronic and thermal Free Energies = -851.798340
Freq: -405.3

**$TS_{B4}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 4.3140 | -0.6450 | -0.3845 |
| C | 1.6440 | -0.5510 | -1.5535 |
| C | 2.3870 | 1.8670 | -1.0495 |
| C | 0.7290 | 0.5930 | 0.5165 |
| C | 3.5320 | 0.4380 | 1.6785 |
| C | 1.9730 | 0.5210 | -0.4755 |
| C | 0.8390 | -0.7680 | 1.2705 |
| C | 2.0780 | -1.4540 | 0.6535 |
| C | -0.6080 | 0.9000 | -0.2185 |
| C | -2.5600 | 0.1430 | -1.5695 |
| C | -1.4740 | -0.1460 | -0.7265 |
| C | 3.0400 | -0.2590 | 0.3965 |
| C | 1.6980 | -1.9020 | -0.7765 |
| H | 4.2010 | -0.2380 | 2.2225 |
| H | 2.6260 | 2.5800 | -0.2585 |
| H | 1.5890 | 2.3020 | -1.6595 |
| H | -1.1780 | -1.1740 | -0.5835 |
| H | 4.9300 | -1.3120 | 0.2255 |
| H | -2.6230 | 1.1600 | -1.9445 |
| H | -2.8750 | -0.6160 | -2.2755 |
| H | 4.1310 | -1.1490 | -1.3335 |
| H | 4.9150 | 0.2440 | -0.5945 |
| H | 3.2690 | 1.7570 | -1.6875 |
| H | 2.4830 | -2.2550 | 1.2775 |
| H | -0.0560 | -1.3840 | 1.1775 |
| H | 0.9740 | -0.5530 | 2.3305 |
| H | 0.7450 | -2.4370 | -0.7925 |
| H | 2.4440 | -2.5800 | -1.1985 |
| H | 4.1120 | 1.3310 | 1.4275 |
| H | 2.7370 | 0.7540 | 2.3465 |
| O | -0.8980 | 2.0980 | -0.3405 |
| C | -4.3750 | -1.1150 | -0.0235 |
| C | -3.5470 | -1.3390 | 1.0865 |
| C | -4.2200 | 0.2220 | -0.4515 |
| C | -2.9360 | -0.1450 | 1.4445 |
| C | -3.6160 | 0.9710 | 0.7195 |
| H | -3.3570 | -2.3030 | 1.5415 |
| H | -4.9210 | 0.6960 | -1.1305 |
| H | -4.9300 | -1.8790 | -0.5535 |
| H | -2.2560 | -0.0040 | 2.2735 |
| H | -2.9830 | 1.8210 | 0.4705 |
| H | -4.4420 | 1.3370 | 1.3495 |
| H | 2.3940 | -0.5160 | -2.3465 |
| H | 0.6820 | -0.3760 | -2.0365 |
| O | 0.8810 | 1.6570 | 1.4565 |
| H | 0.4020 | 2.4070 | 1.0665 |

Sum of electronic and thermal Free Energies = -851.731987
Freq: -405.3

**$TS_{C1}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.1535 | 0.7750 | -1.2655 |
| C | 2.9855 | -0.2550 | -0.4475 |
| C | 3.3525 | -1.5280 | -1.2345 |
| C | 1.6955 | 1.0860 | 1.0935 |

C0.6775

| | | | |
|---|---|---|---|
| H | 2.2835 | -2.3730 | 1.4715 |
| H | 2.6245 | 1.1300 | -2.1855 |
| H | 2.4615 | 1.3490 | 1.8255 |
| H | 0.7355 | 1.2700 | 1.5765 |
| H | 0.9855 | 2.4710 | -0.4945 |
| H | 2.7025 | 2.5950 | -0.1645 |
| H | 0.0075 | 0.7060 | -1.7385 |
| H | 0.8995 | -0.6830 | -2.3385 |
| H | 3.0475 | -1.0460 | 2.3615 |
| H | 1.3175 | -1.3500 | 2.5375 |
| H | 2.5065 | -2.0250 | -1.6985 |
| H | 3.8305 | -2.2580 | -0.5745 |
| H | 4.0795 | -1.2710 | -2.0135 |
| H | 4.9825 | 0.5350 | -0.7575 |
| H | 4.8285 | -0.4380 | 0.7005 |
| C | 0.5915 | -0.7960 | -0.2025 |
| C | -0.7425 | -0.5580 | 0.5565 |
| C | -1.4805 | 0.6760 | 0.5035 |
| C | -2.6095 | 0.8320 | 1.3255 |
| H | -1.1375 | 1.4910 | -0.1175 |
| H | -2.9665 | 1.8430 | 1.4955 |
| H | -2.6685 | 0.1850 | 2.1935 |
| H | 0.0325 | -2.5950 | 0.1675 |
| O | -1.1755 | -1.5150 | 1.2215 |
| O | 0.5955 | -2.1890 | -0.5135 |
| C | -3.9465 | 0.8410 | -0.9775 |
| C | -3.0635 | -0.1860 | -1.6195 |
| C | -4.2005 | 0.1980 | 0.3785 |
| C | -3.2545 | -1.3940 | -0.9885 |
| C | -3.9905 | -1.1860 | 0.1935 |
| H | -4.9005 | 0.8740 | -1.5255 |
| H | -3.5485 | 1.8550 | -0.9565 |
| H | -2.5135 | -0.0300 | -2.5375 |
| H | -4.9825 | 0.5640 | 1.0355 |
| H | -2.8295 | -2.3390 | -1.2975 |
| H | -4.2475 | -1.9560 | 0.9075 |

Sum of electronic and thermal Free Energies = -851.798340
Freq: -405.3

**$TS_{C2}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 4.3140 | -0.6450 | -0.3845 |
| C | 1.6440 | -0.5510 | -1.5535 |
| C | 2.3870 | 1.8670 | -1.0495 |
| C | 0.7290 | 0.5930 | 0.5165 |
| C | 3.5320 | 0.4380 | 1.6785 |
| C | 1.9730 | 0.5210 | -0.4755 |
| C | 0.8390 | -0.7680 | 1.2705 |
| C | 2.0780 | -1.4540 | 0.6535 |
| C | -0.6080 | 0.9000 | -0.2185 |
| C | -2.5600 | 0.1430 | -1.5695 |
| C | -1.4740 | -0.1460 | -0.7265 |
| C | 3.0400 | -0.2590 | 0.3965 |
| C | 1.6980 | -1.9020 | -0.7765 |

| | | | |
|---|---|---|---|
| H | 4.2010 | -0.2380 | 2.2225 |
| H | 2.6260 | 2.5800 | -0.2585 |
| H | 1.5890 | 2.3020 | -1.6595 |
| H | -1.1780 | -1.1740 | -0.5835 |
| H | 4.9300 | -1.3120 | 0.2255 |
| H | -2.6230 | 1.1600 | -1.9445 |
| H | -2.8750 | -0.6160 | -2.2755 |
| H | 4.1310 | -1.1490 | -1.3335 |
| H | 4.9150 | 0.2440 | -0.5945 |
| H | 3.2690 | 1.7570 | -1.6875 |
| H | 2.4830 | -2.2550 | 1.2775 |
| H | -0.0560 | -1.3840 | 1.1775 |
| H | 0.9740 | -0.5530 | 2.3305 |
| H | 0.7450 | -2.4370 | -0.7925 |
| H | 2.4440 | -2.5800 | -1.1985 |
| H | 4.1120 | 1.3310 | 1.4275 |
| H | 2.7370 | 0.7540 | 2.3465 |
| O | -0.8980 | 2.0980 | -0.3405 |
| C | -4.3750 | -1.1150 | -0.0235 |
| C | -3.5470 | -1.3390 | 1.0865 |
| C | -4.2200 | 0.2220 | -0.4515 |
| C | -2.9360 | -0.1450 | 1.4445 |
| C | -3.6160 | 0.9710 | 0.7195 |
| H | -3.3570 | -2.3030 | 1.5415 |
| H | -4.9210 | 0.6960 | -1.1305 |
| H | -4.9300 | -1.8790 | -0.5535 |
| H | -2.2560 | -0.0040 | 2.2735 |
| H | -2.9830 | 1.8210 | 0.4705 |
| H | -4.4420 | 1.3370 | 1.3495 |
| H | 2.3940 | -0.5160 | -2.3465 |
| H | 0.6820 | -0.3760 | -2.0365 |
| O | 0.8810 | 1.6570 | 1.4565 |
| H | 0.4020 | 2.4070 | 1.0665 |

Sum of electronic and thermal Free Energies = -851.731987
Freq: -405.3

**$TS_{C3}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 2.1535 | 0.7750 | -1.2655 |
| C | 2.9855 | -0.2550 | -0.4475 |
| C | 3.3525 | -1.5280 | -1.2345 |
| C | 1.6955 | 1.0860 | 1.0935 |
| C | 1.8685 | -0.4000 | 0.6645 |
| C | 2.1455 | -1.3480 | 1.8215 |
| C | 0.8255 | 0.0220 | -1.5095 |
| C | 4.3195 | 0.3080 | 0.0835 |
| C | 1.8735 | 1.8880 | -0.2305 |
| H | 4.2235 | 1.2160 | 0.6775 |
| H | 2.2835 | -2.3730 | 1.4715 |
| H | 2.6245 | 1.1300 | -2.1855 |
| H | 2.4615 | 1.3490 | 1.8255 |
| H | 0.7355 | 1.2700 | 1.5765 |
| H | 0.9855 | 2.4710 | -0.4945 |
| H | 2.7025 | 2.5950 | -0.1645 |
| H | 0.0075 | 0.7060 | -1.7385 |
| H | 0.8995 | -0.6830 | -2.3385 |
| H | 3.0475 | -1.0460 | 2.3615 |
| H | 1.3175 | -1.3500 | 2.5375 |
| H | 2.5065 | -2.0250 | -1.6985 |

| | | | |
|---|---|---|---|
| H | 3.8305 | -2.2580 | -0.5745 |
| H | 4.0795 | -1.2710 | -2.0135 |
| H | 4.9825 | 0.5350 | -0.7575 |
| H | 4.8285 | -0.4380 | 0.7005 |
| C | 0.5915 | -0.7960 | -0.2025 |
| C | -0.7425 | -0.5580 | 0.5565 |
| C | -1.4805 | 0.6760 | 0.5035 |
| C | -2.6095 | 0.8320 | 1.3255 |
| H | -1.1375 | 1.4910 | -0.1175 |
| H | -2.9665 | 1.8430 | 1.4955 |
| H | -2.6685 | 0.1850 | 2.1935 |
| H | 0.0325 | -2.5950 | 0.1675 |
| O | -1.1755 | -1.5150 | 1.2215 |
| O | 0.5955 | -2.1890 | -0.5135 |
| C | -3.9465 | 0.8410 | -0.9775 |
| C | -3.0635 | -0.1860 | -1.6195 |
| C | -4.2005 | 0.1980 | 0.3785 |
| C | -3.2545 | -1.3940 | -0.9885 |
| C | -3.9905 | -1.1860 | 0.1935 |
| H | -4.9005 | 0.8740 | -1.5255 |
| H | -3.5485 | 1.8550 | -0.9565 |
| H | -2.5135 | -0.0300 | -2.5375 |
| H | -4.9825 | 0.5640 | 1.0355 |
| H | -2.8295 | -2.3390 | -1.2975 |
| H | -4.2475 | -1.9560 | 0.9075 |

Sum of electronic and thermal Free Energies = -851.798340
Freq: -405.3

**$TS_{C4}$**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 4.3140 | -0.6450 | -0.3845 |
| C | 1.6440 | -0.5510 | -1.5535 |
| C | 2.3870 | 1.8670 | -1.0495 |
| C | 0.7290 | 0.5930 | 0.5165 |
| C | 3.5320 | 0.4380 | 1.6785 |
| C | 1.9730 | 0.5210 | -0.4755 |
| C | 0.8390 | -0.7680 | 1.2705 |
| C | 2.0780 | -1.4540 | 0.6535 |
| C | -0.6080 | 0.9000 | -0.2185 |
| C | -2.5600 | 0.1430 | -1.5695 |
| C | -1.4740 | -0.1460 | -0.7265 |
| C | 3.0400 | -0.2590 | 0.3965 |
| C | 1.6980 | -1.9020 | -0.7765 |
| H | 4.2010 | -0.2380 | 2.2225 |
| H | 2.6260 | 2.5800 | -0.2585 |
| H | 1.5890 | 2.3020 | -1.6595 |
| H | -1.1780 | -1.1740 | -0.5835 |
| H | 4.9300 | -1.3120 | 0.2255 |
| H | -2.6230 | 1.1600 | -1.9445 |
| H | -2.8750 | -0.6160 | -2.2755 |
| H | 4.1310 | -1.1490 | -1.3335 |
| H | 4.9150 | 0.2440 | -0.5945 |
| H | 3.2690 | 1.7570 | -1.6875 |
| H | 2.4830 | -2.2550 | 1.2775 |
| H | -0.0560 | -1.3840 | 1.1775 |
| H | 0.9740 | -0.5530 | 2.3305 |
| H | 0.7450 | -2.4370 | -0.7925 |
| H | 2.4440 | -2.5800 | -1.1985 |

| | | | |
|---|---|---|---|
| H | 4.1120 | 1.3310 | 1.4275 |
| H | 2.7370 | 0.7540 | 2.3465 |
| O | -0.8980 | 2.0980 | -0.3405 |
| C | -4.3750 | -1.1150 | -0.0235 |
| C | -3.5470 | -1.3390 | 1.0865 |
| C | -4.2200 | 0.2220 | -0.4515 |
| C | -2.9360 | -0.1450 | 1.4445 |
| C | -3.6160 | 0.9710 | 0.7195 |
| H | -3.3570 | -2.3030 | 1.5415 |
| H | -4.9210 | 0.6960 | -1.1305 |
| H | -4.9300 | -1.8790 | -0.5535 |
| H | -2.2560 | -0.0040 | 2.2735 |
| H | -2.9830 | 1.8210 | 0.4705 |
| H | -4.4420 | 1.3370 | 1.3495 |
| H | 2.3940 | -0.5160 | -2.3465 |
| H | 0.6820 | -0.3760 | -2.0365 |
| O | 0.8810 | 1.6570 | 1.4565 |
| H | 0.4020 | 2.4070 | 1.0665 |

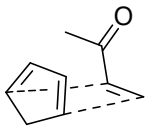
Sum of electronic and thermal Free Energies = -851.731987
Freq: -405.3

# MVK + CP

**TS endo (acid free)**
**Table S1, entry 1**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | -0.2331 | 1.6796 | 0.4817 |
| C | 0.8197 | 0.7522 | 0.4189 |
| C | 1.0413 | -0.1703 | 1.5233 |
| C | 2.2879 | -1.0434 | 1.5016 |
| O | 0.2508 | -0.2418 | 2.4743 |
| H | -0.1761 | 2.5565 | -0.1587 |
| H | -0.6605 | 1.8588 | 1.4632 |
| H | 1.5411 | 0.7793 | -0.3916 |
| H | 2.0602 | -2.0198 | 1.9372 |
| H | 3.0575 | -0.5756 | 2.1277 |
| H | 2.6993 | -1.1705 | 0.4959 |
| C | -0.5984 | -1.0056 | -1.0099 |
| C | -1.8213 | 0.8851 | -0.4160 |
| C | -1.3992 | -1.3236 | 0.0730 |
| C | -2.1830 | -0.2024 | 0.4112 |
| C | -1.0980 | 0.2776 | -1.6102 |
| H | 0.1109 | -1.6684 | -1.4918 |
| H | -2.4609 | 1.7570 | -0.5244 |
| H | -1.3598 | -2.2455 | 0.6406 |
| H | -2.8515 | -0.1454 | 1.2620 |
| H | -0.3399 | 0.9077 | -2.0787 |
| H | -1.8510 | 0.0356 | -2.3787 |

HF= -425.164652; Freq: -405.3

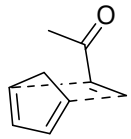



***s-cis-endo***

**TS exo (acid free)**
**s-cis enone**
**Table S1, entry 1**

| Atomic Type | X | Y | Z |
|---|---|---|---|
| C | -2.6211 | 0.0979 | -0.6551 |
| C | -1.9979 | 1.3030 | -0.2871 |
| C | -1.9545 | -0.9764 | -0.0210 |
| C | -1.0015 | 1.0303 | 0.6463 |
| C | -1.1876 | -0.3719 | 1.1402 |
| H | -3.3862 | -0.0042 | -1.4173 |
| H | -2.2036 | 2.2746 | -0.7229 |
| H | -2.3796 | -1.9747 | 0.0319 |
| H | -0.3746 | 1.7681 | 1.1335 |
| H | -1.8618 | -0.3444 | 2.0132 |
| H | -0.2741 | -0.8918 | 1.4341 |
| C | -0.3473 | -1.2701 | -1.2176 |
| C | 0.4921 | -0.1512 | -1.0875 |
| C | 1.6593 | -0.1569 | -0.2049 |
| O | 1.8629 | -1.0477 | 0.6286 |
| C | 2.6653 | 0.9735 | -0.3722 |
| H | -0.8685 | -1.4195 | -2.1571 |
| H | -0.0129 | -2.1843 | -0.7330 |
| H | 0.4096 | 0.6697 | -1.7921 |
| H | 3.2244 | 1.1087 | 0.5562 |
| H | 3.3786 | 0.7007 | -1.1603 |
| H | 2.1903 | 1.9143 | -0.6673 |

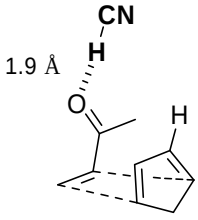
HF= -425.164401; Freq: -419.5



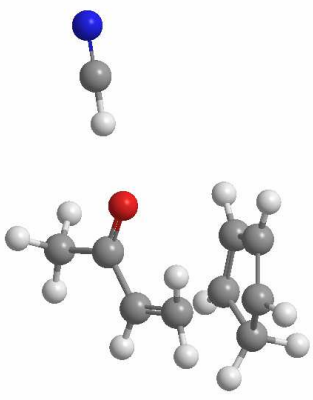

***s-cis-exo***

**TS endo (cyanhidric acid)**
**Table S2, entry 5**

| Atomic Type | X | Y | Z |
|---|---|---|---|
| C | 2.0041 | 0.1902 | -1.6677 |
| C | 1.5366 | 1.0975 | -0.7017 |
| C | 0.1808 | 1.0023 | -0.2154 |
| C | -0.3444 | 2.0623 | 0.7368 |
| H | 2.8875 | 0.4689 | -2.2368 |
| H | 1.2497 | -0.3458 | -2.2349 |
| H | 2.1568 | 1.9193 | -0.3602 |
| H | -0.8057 | 1.5838 | 1.6063 |
| H | -1.1280 | 2.6384 | 0.2315 |
| H | 0.4340 | 2.7520 | 1.0734 |
| O | -0.5650 | 0.0664 | -0.5718 |
| C | 2.5408 | -0.4132 | 1.3716 |
| C | -3.3359 | -0.9755 | -0.1627 |
| C | 2.8492 | -1.3509 | -0.7427 |
| N | -4.3882 | -1.4350 | -0.0030 |
| C | 1.5721 | -1.3776 | 1.1758 |
| H | -2.3461 | -0.5429 | -0.3023 |
| C | 1.7802 | -1.9921 | -0.0783 |
| C | 3.6088 | -0.5840 | 0.3313 |
| H | 2.6293 | 0.2335 | 2.2368 |
| H | 3.3659 | -1.8224 | -1.5741 |



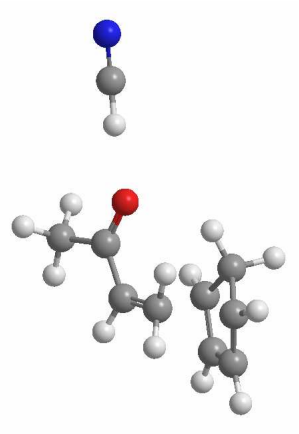

***endo***



| | | | |
|---|---|---|---|
| H | 0.7333 | -1.5761 | 1.8320 |
| H | 1.1406 | -2.7520 | -0.5115 |
| H | 4.1015 | 0.3339 | 0.0059 |
| H | 4.3882 | -1.2500 | 0.7377 |

HF= -518.590477; Freq: -379.6

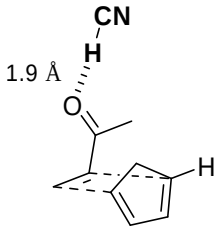
**TS exo (cyanhidric acid)**
**Table S2, entry 5**



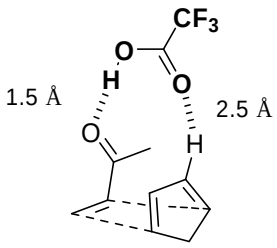
Atomic Coordinates (Ångstroms)

| Type | X | Y | Z |
|---|---|---|---|
| C | -3.8389 | -0.8475 | 0.0281 |
| C | -3.4396 | -0.1461 | -1.1247 |
| C | -2.7359 | -1.5750 | 0.5331 |
| C | -2.1293 | -0.4914 | -1.4312 |
| C | -1.7409 | -1.6787 | -0.6081 |
| H | -4.7945 | -0.7355 | 0.5291 |
| H | -4.0344 | 0.5960 | -1.6456 |
| H | -2.8548 | -2.3736 | 1.2599 |
| H | -1.5591 | -0.1223 | -2.2758 |
| H | -1.9793 | -2.5904 | -1.1818 |
| H | -0.6883 | -1.7296 | -0.3240 |
| C | -1.7507 | -0.2013 | 1.6138 |
| C | 3.7171 | -1.1192 | -0.0909 |
| C | -1.2192 | 0.7597 | 0.7346 |
| N | 4.7945 | -1.4777 | -0.3240 |
| C | 0.1502 | 0.7051 | 0.2622 |
| H | 2.7054 | -0.7767 | 0.1183 |
| C | 0.7011 | 1.9064 | -0.4880 |
| H | -2.5558 | 0.0996 | 2.2758 |
| H | -1.0401 | -0.8961 | 2.0555 |
| H | -1.7857 | 1.6562 | 0.5085 |
| H | 1.3770 | 2.4578 | 0.1766 |
| H | -0.0811 | 2.5904 | -0.8271 |
| H | 1.2923 | 1.5702 | -1.3447 |
| O | 0.8904 | -0.2760 | 0.4747 |

HF= -518.589693; Freq: -399.




***exo***

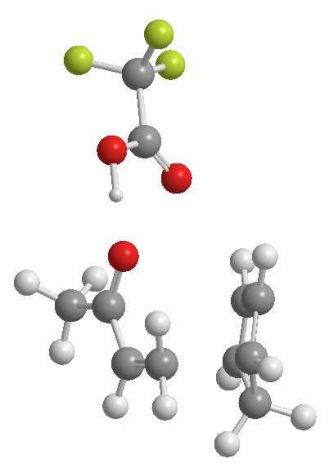



***endo***

**TS endo (trifluoroacetic acid)**
**Table S2, entry 10**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | 3.1842 | 0.0608 | -1.5378 |
| C | 2.6171 | 0.9022 | -0.5656 |
| C | 1.1962 | 1.0142 | -0.4514 |
| C | 0.5808 | 1.9492 | 0.5659 |
| O | 0.4475 | 0.3257 | -1.2004 |
| H | 4.2375 | 0.1944 | -1.7708 |
| H | 2.5605 | -0.1958 | -2.3878 |
| H | 3.2399 | 1.4875 | 0.1019 |
| H | -0.0726 | 1.3828 | 1.2377 |
| H | -0.0420 | 2.6880 | 0.0493 |
| H | 1.3355 | 2.4737 | 1.1566 |
| C | 2.6572 | -1.2034 | 1.3712 |
| C | 3.3867 | -1.7765 | -0.7746 |
| C | 1.6123 | -1.8066 | 0.7074 |
| C | 2.0616 | -2.2140 | -0.5726 |
| C | 3.9269 | -1.4211 | 0.6040 |
| H | 2.6107 | -0.7623 | 2.3602 |
| H | 4.0221 | -2.2183 | -1.5372 |
| H | 0.5897 | -1.8739 | 1.0597 |
| H | 1.4430 | -2.6947 | -1.3215 |
| H | 4.6424 | -0.5972 | 0.6417 |
| H | 4.4352 | -2.3112 | 1.0102 |
| O | -2.0419 | 0.0198 | -0.9440 |
| C | -2.3961 | -0.5665 | 0.1692 |
| O | -1.6901 | -0.9160 | 1.0959 |
| C | -3.9335 | -0.7953 | 0.2068 |
| F | -4.3113 | -1.3755 | 1.3557 |
| F | -4.3245 | -1.5944 | -0.8119 |
| F | -4.5993 | 0.3762 | 0.0935 |
| H | -1.0110 | 0.1704 | -1.0038 |

HF= -951.974944
Freq: -358.9

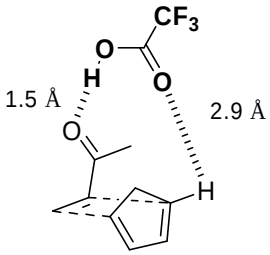


**TS exo (trifluoroacetic acid)**
**Table S2, entry 10**

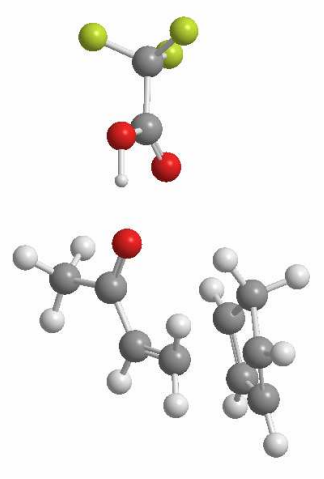
Atomic Coordinates (Ångstroms)

| Type | X | Y | Z |
|---|---|---|---|
| C | -2.2228 | -3.2849 | -1.4027 |
| C | -2.0930 | -3.0468 | -0.0195 |
| C | -1.8780 | -2.1120 | -2.1131 |
| C | -1.7857 | -1.7094 | 0.1807 |
| C | -1.9508 | -0.9757 | -1.1085 |
| H | -2.4259 | -4.2502 | -1.8543 |
| H | -2.1659 | -3.8004 | 0.7565 |
| H | -2.1515 | -1.9711 | -3.1550 |
| H | -1.6206 | -1.2189 | 1.1329 |
| H | -2.9717 | -0.5591 | -1.1383 |
| H | -1.2565 | -0.1480 | -1.2608 |
| C | 0.1115 | -2.2356 | -2.2690 |
| C | 0.6825 | -2.1375 | -0.9857 |
| C | 1.1416 | -0.8986 | -0.4280 |
| O | 0.9735 | 0.1991 | -1.0282 |
| C | 1.8514 | -0.9080 | 0.9087 |
| H | 0.1802 | -3.1878 | -2.7847 |
| H | 0.2206 | -1.3672 | -2.9141 |
| H | 0.8674 | -3.0367 | -0.4089 |
| H | 2.8206 | -0.4086 | 0.8070 |
| H | 2.0079 | -1.9187 | 1.2922 |
| H | 1.2613 | -0.3378 | 1.6343 |
| O | 0.8818 | 2.4518 | 0.1194 |
| C | 0.0399 | 2.4434 | 1.1211 |
| O | -0.5821 | 1.5009 | 1.5726 |
| H | 0.9632 | 1.5142 | -0.3212 |
| C | -0.1105 | 3.8662 | 1.7284 |
| F | -0.8885 | 3.8485 | 2.8211 |
| F | -0.6725 | 4.7076 | 0.8301 |
| F | 1.0901 | 4.3763 | 2.0798 |

HF= -951.973022
Freq: -372.7



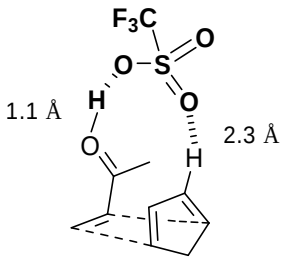

***exo***



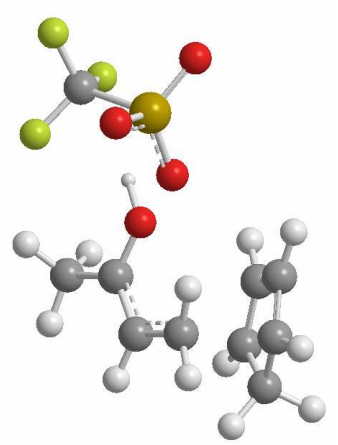
**TS endo (trifluoromethanesulfonic acid)**
**Table S2, entry 13**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| S | -2.2803 | -1.1375 | -0.6924 |
| O | -1.7314 | -0.0395 | -1.5886 |
| O | -1.4016 | -1.3801 | 0.4757 |
| O | -2.8002 | -2.3019 | -1.4097 |
| C | -3.7897 | -0.2868 | 0.0335 |
| F | -4.4136 | -1.1049 | 0.8954 |
| F | -4.6563 | 0.0632 | -0.9277 |
| F | -3.4268 | 0.8289 | 0.7013 |
| C | 3.4103 | 0.6405 | -1.2760 |
| C | 2.5358 | 1.1925 | -0.3319 |
| C | 1.1392 | 1.0697 | -0.4696 |
| C | 0.1758 | 1.6534 | 0.5167 |
| O | 0.6888 | 0.4263 | -1.5011 |
| H | 4.4580 | 0.9227 | -1.2369 |
| H | 3.0278 | 0.4188 | -2.2653 |
| H | 2.9133 | 1.7059 | 0.5446 |
| H | -0.4384 | 0.8546 | 0.9470 |
| H | -0.5081 | 2.3402 | 0.0062 |
| H | 0.6983 | 2.1878 | 1.3117 |
| H | -0.3636 | 0.2522 | -1.5145 |
| C | 2.5687 | -1.3965 | 1.2461 |
| C | 3.8116 | -1.3566 | -0.7405 |
| C | 1.7959 | -1.9275 | 0.2456 |
| C | 2.5684 | -1.9628 | -0.9524 |
| C | 3.9735 | -1.2047 | 0.7620 |
| H | 2.2467 | -1.2151 | 2.2653 |
| H | 4.6563 | -1.5007 | -1.4065 |
| H | 0.7500 | -2.2017 | 0.3287 |
| H | 2.2108 | -2.3402 | -1.9038 |
| H | 4.4560 | -0.2863 | 1.1053 |
| H | 4.5932 | -2.0404 | 1.1263 |

HF= -1387.201898
Freq: -289.6



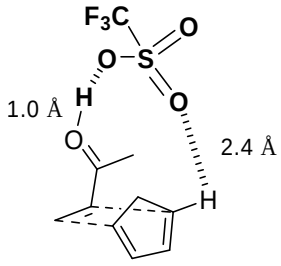

***endo***



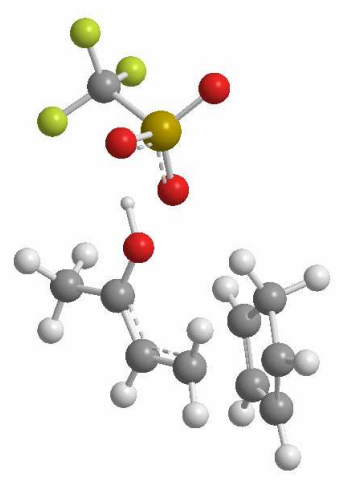
**TS exo (trifluoromethanesulfonic acid)**
**Table S2, entry 13**

| Atomic Type | Coordinates (Ångstroms) X | Y | Z |
|---|---|---|---|
| C | -2.8118 | -2.5930 | -1.4284 |
| C | -1.9462 | -1.7327 | -2.1552 |
| C | -3.0653 | -2.0509 | -0.1640 |
| C | -1.7298 | -0.5904 | -1.4185 |
| C | -2.5937 | -0.6124 | -0.2044 |
| H | -3.1565 | -3.5634 | -1.7725 |
| H | -1.5099 | -1.9586 | -3.1219 |
| H | -3.8822 | -2.3835 | 0.4689 |
| H | -1.1030 | 0.2567 | -1.6705 |
| H | -3.4676 | 0.0352 | -0.3901 |
| H | -2.1135 | -0.2221 | 0.6946 |
| C | -1.4947 | -2.8980 | 0.9619 |
| C | -0.2644 | -2.4471 | 0.4682 |
| C | 0.3793 | -1.2858 | 0.9295 |
| O | -0.1760 | -0.5881 | 1.8742 |
| C | 1.7024 | -0.8482 | 0.3780 |
| H | -1.7725 | -3.9341 | 0.8008 |
| H | -1.8661 | -2.4625 | 1.8846 |
| H | 0.2379 | -3.0058 | -0.3135 |
| H | 2.4017 | -0.6455 | 1.1960 |
| H | 2.1254 | -1.6029 | -0.2881 |
| H | 1.5714 | 0.0917 | -0.1691 |
| O | 0.7290 | 1.7288 | 2.0903 |
| O | -0.1268 | 1.8220 | -0.2374 |
| H | 0.2486 | 0.3758 | 1.9987 |
| S | 0.2809 | 2.6199 | 0.9453 |
| C | 1.8951 | 3.3875 | 0.4298 |
| O | -0.5801 | 3.7345 | 1.3384 |
| F | 1.7031 | 4.2058 | -0.6115 |
| F | 2.4361 | 4.0850 | 1.4327 |
| F | 2.7671 | 2.4301 | 0.0582 |

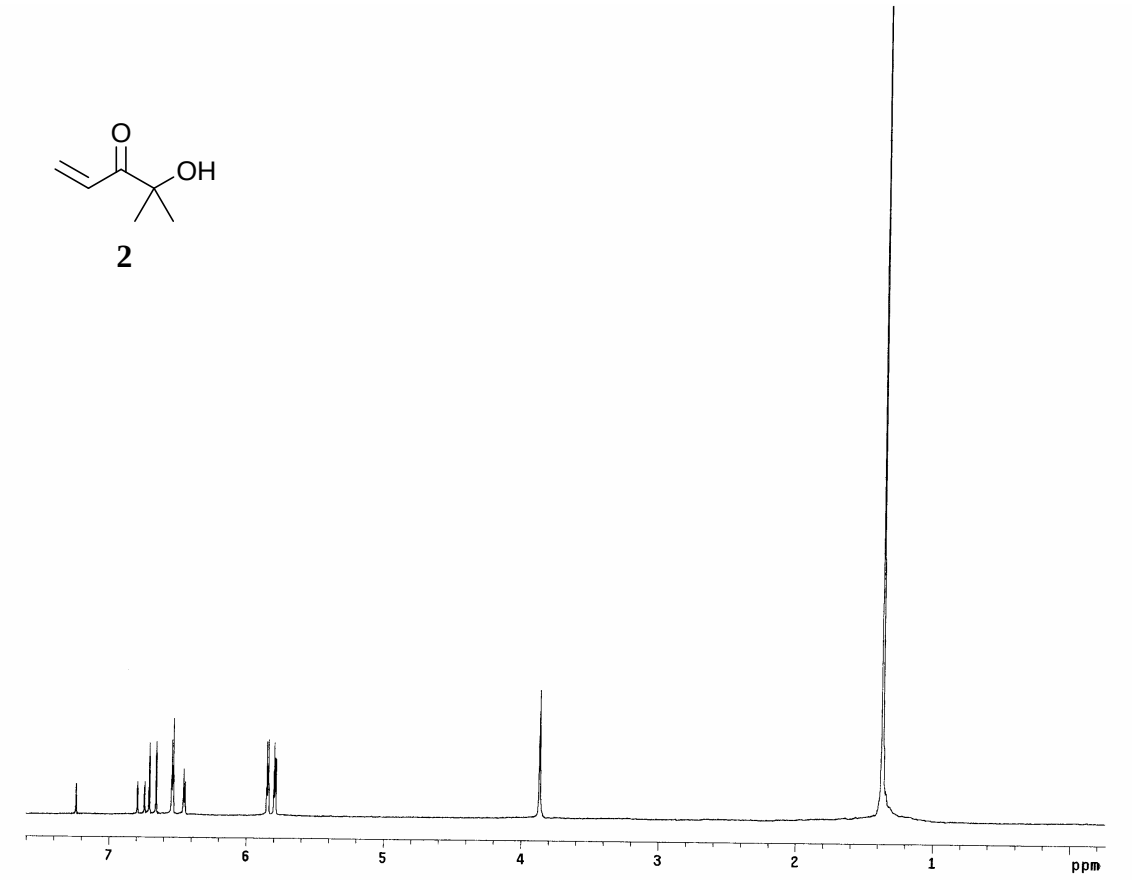
HF= -1387.200199
Freq: -290.3



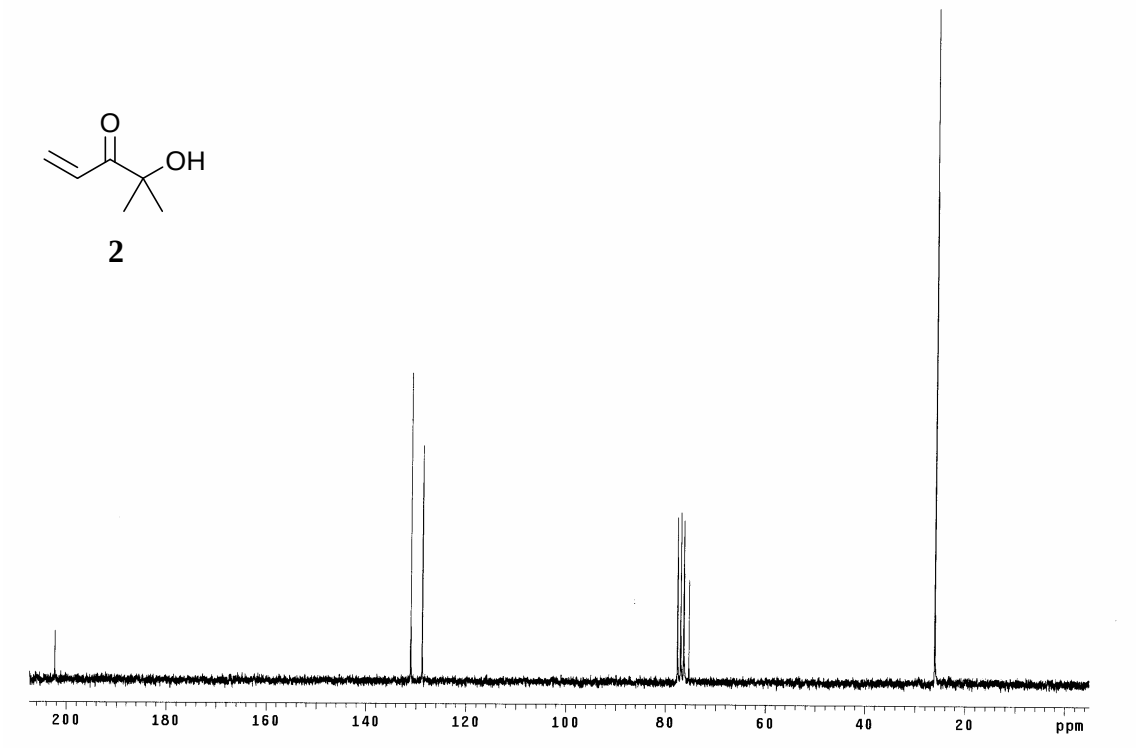

***exo***



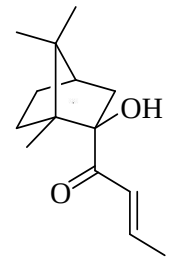
**NMR spectra of new compounds**




**2**

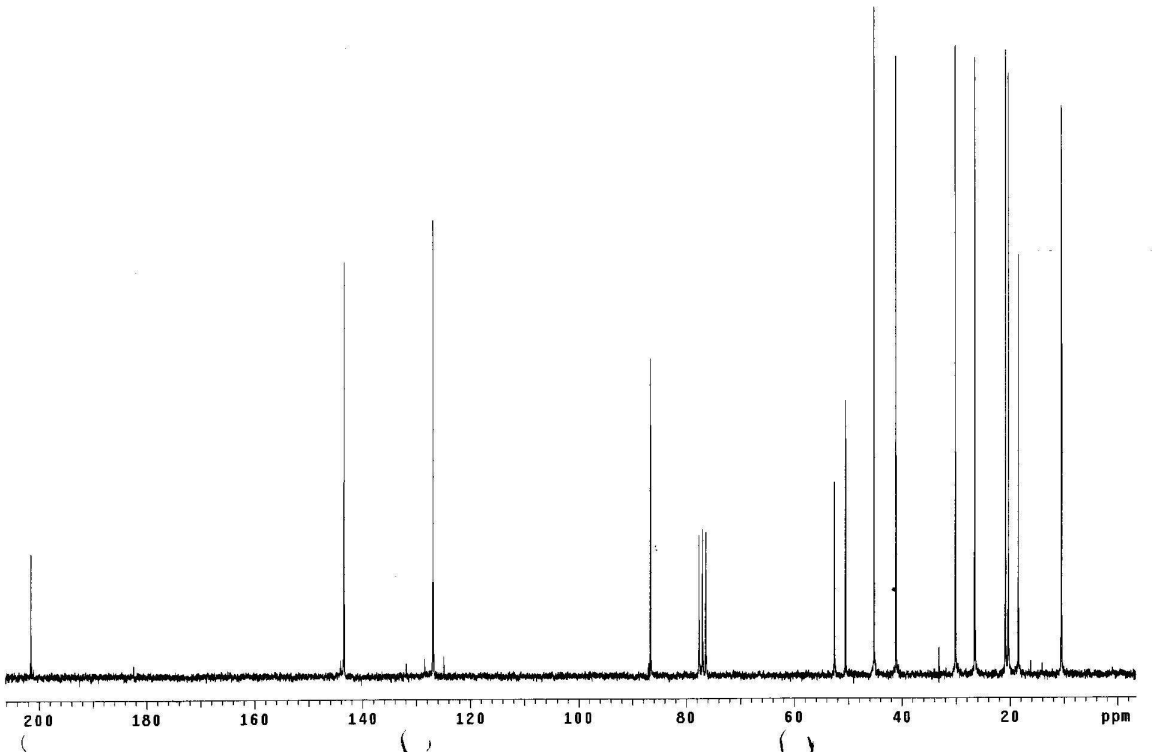


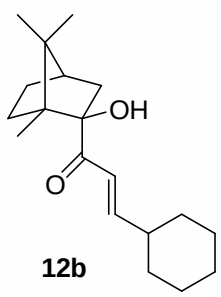

**2**




**12a**

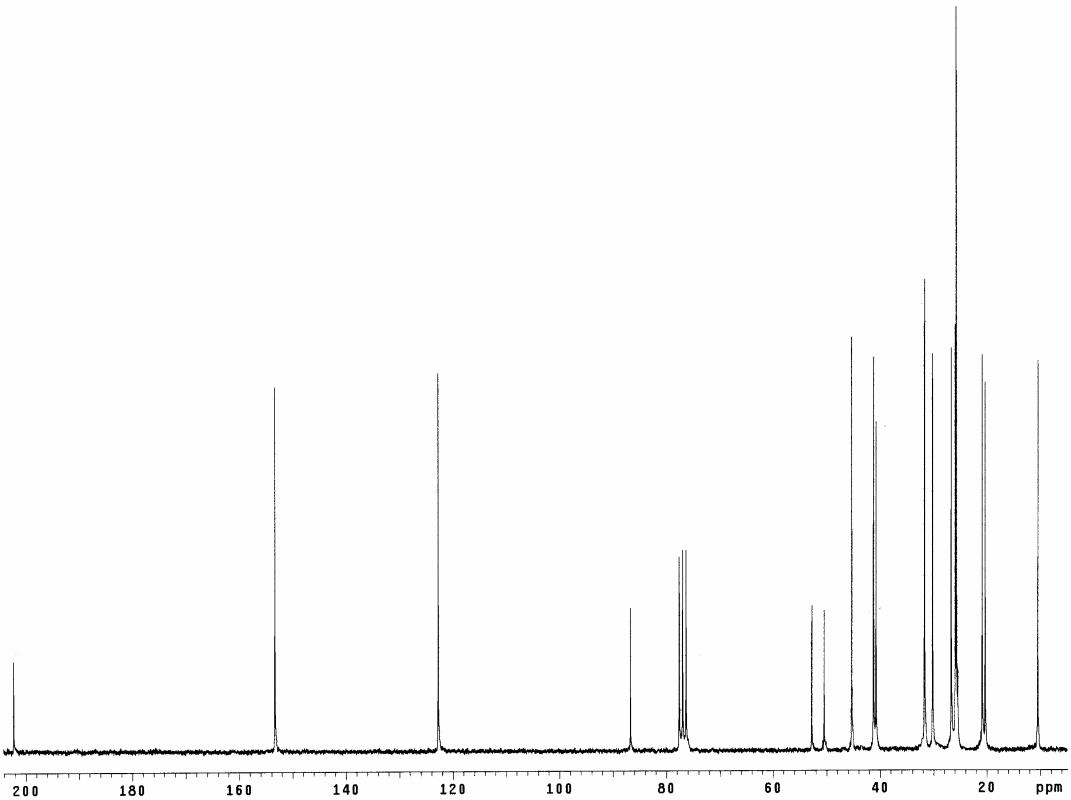


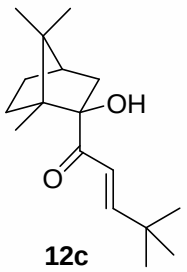






**12b**

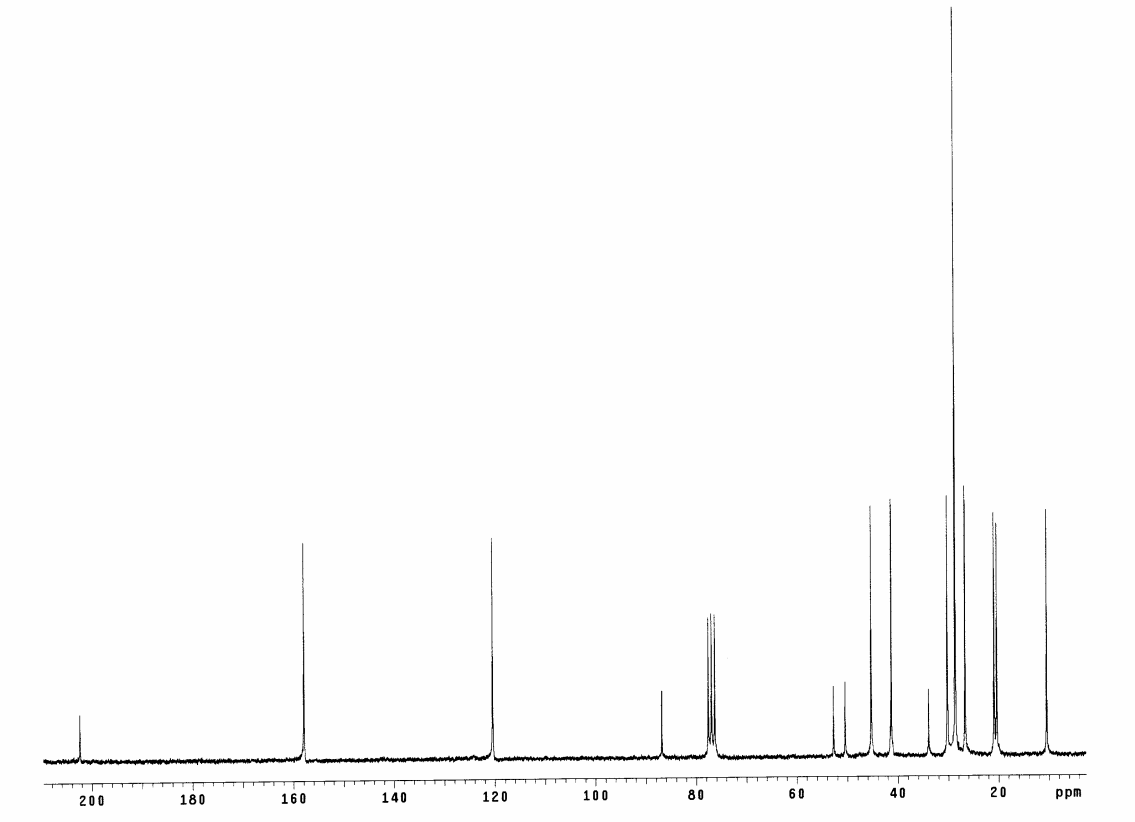


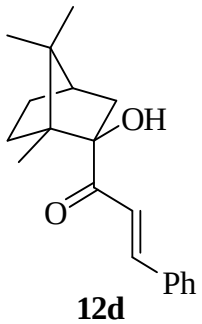






**12c**

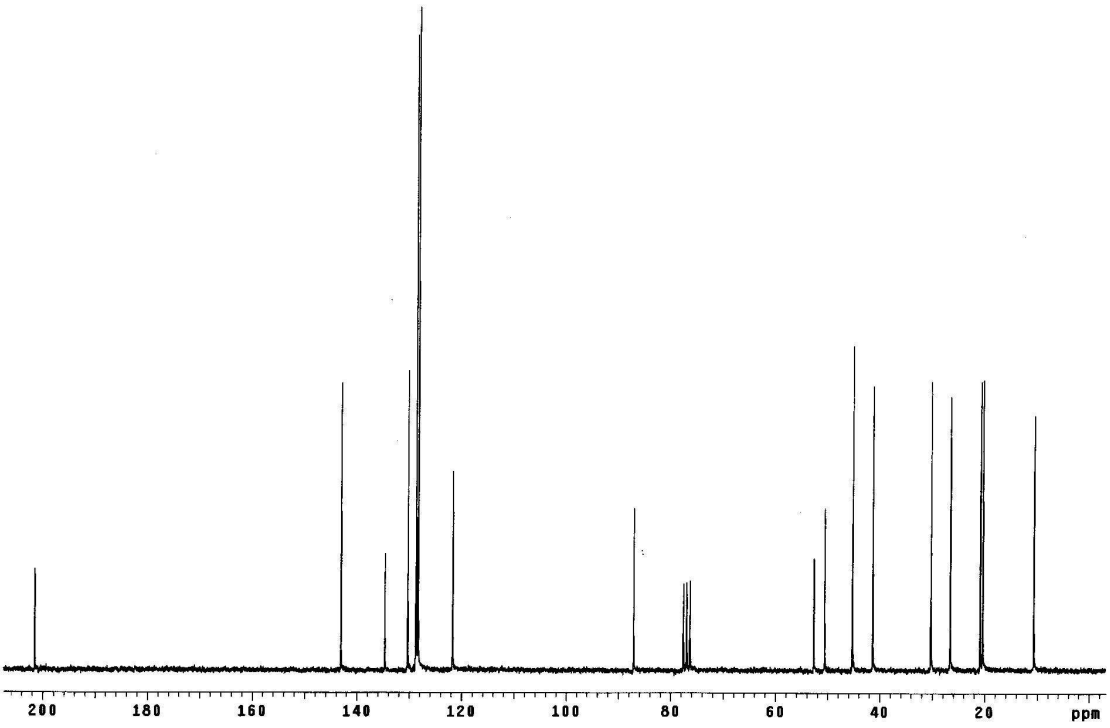


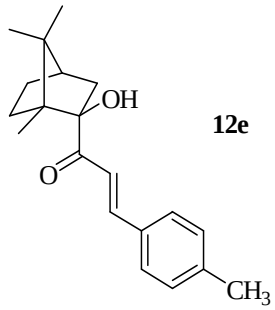






**12d**

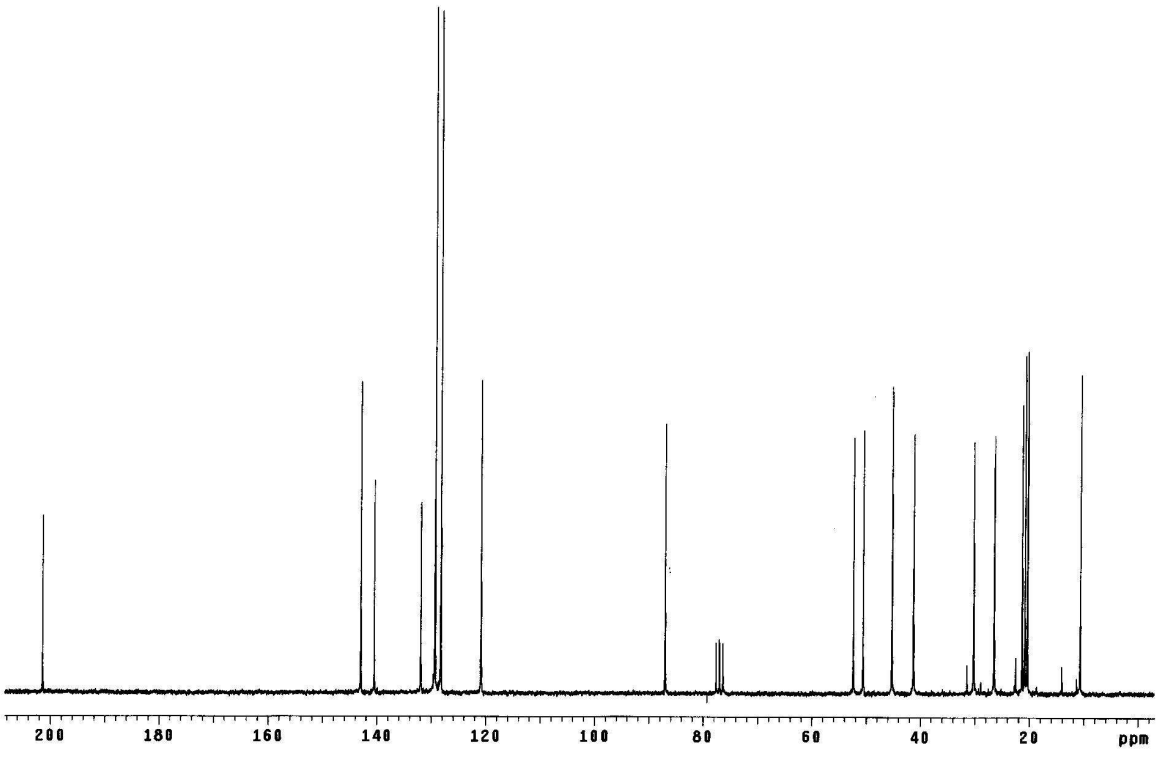


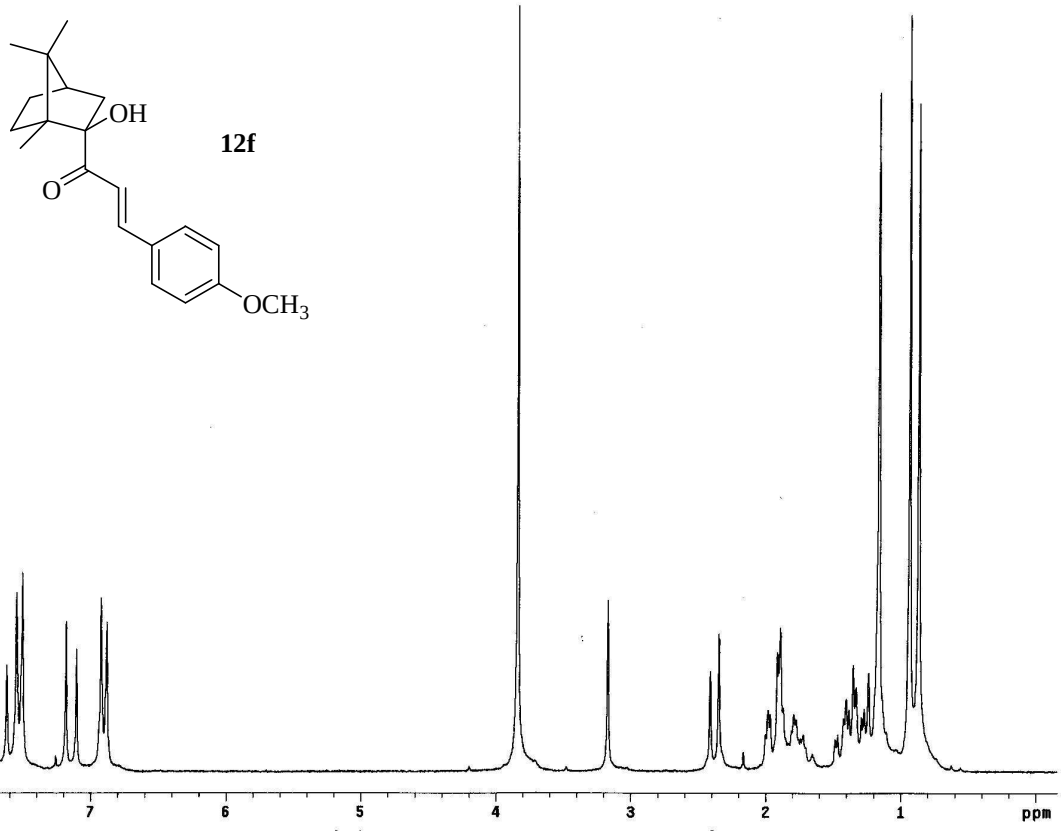



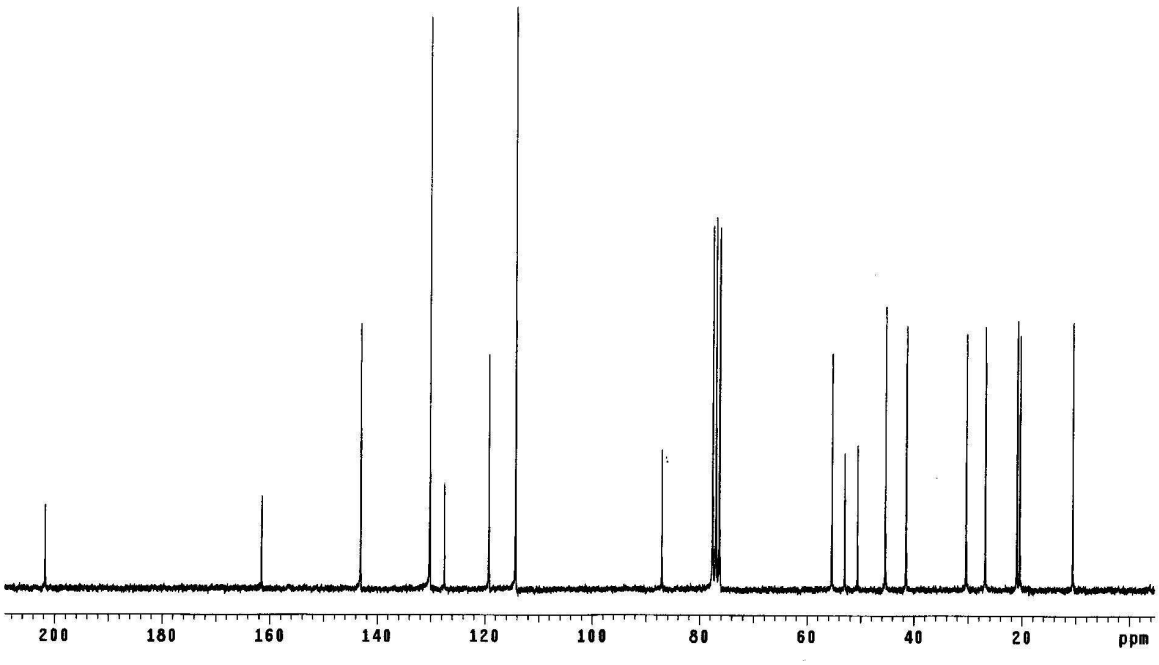


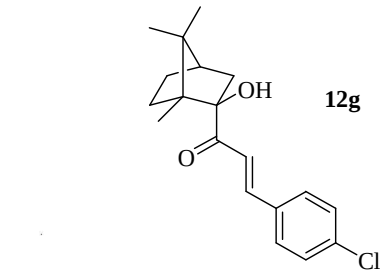

**12e**




OH
O
OCH3
12f
8
7
6
5
4
3
2
1
ppm


200
180
160
140
120
100
80
60
40
20
ppm

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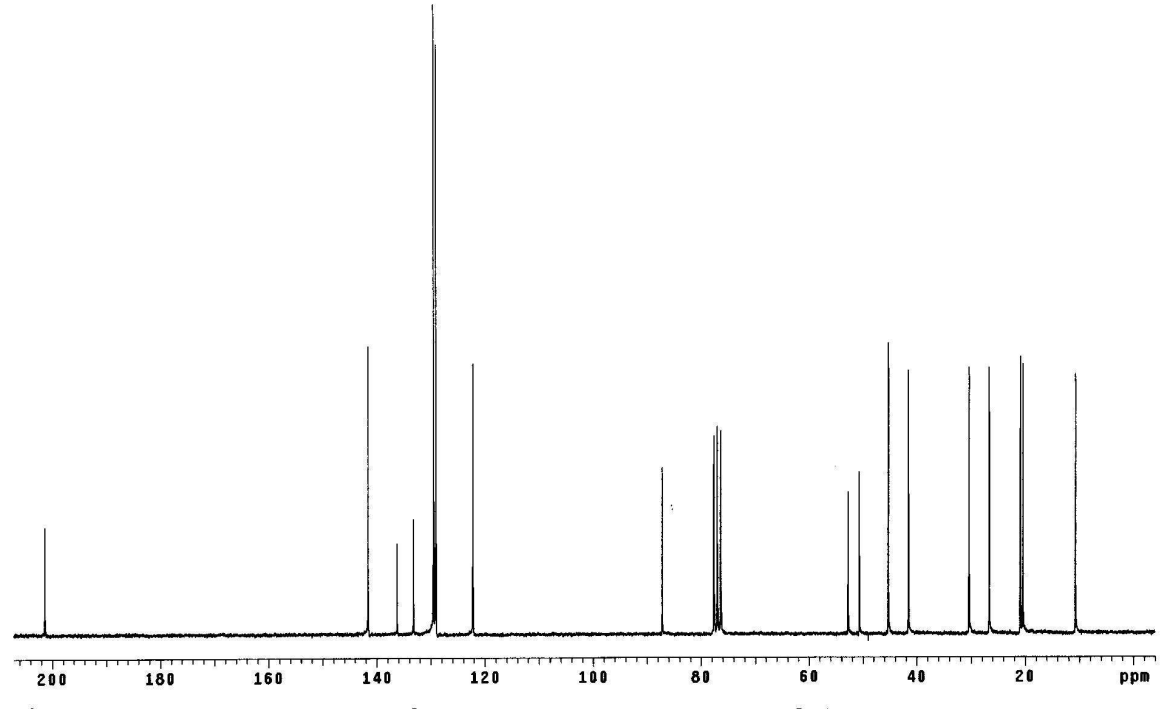

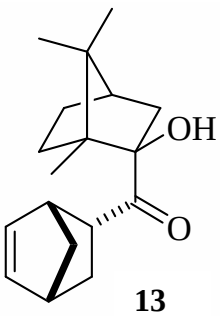


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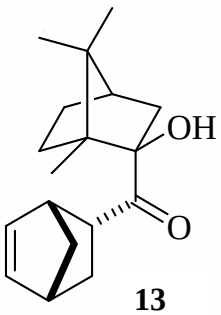


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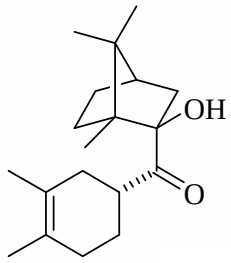


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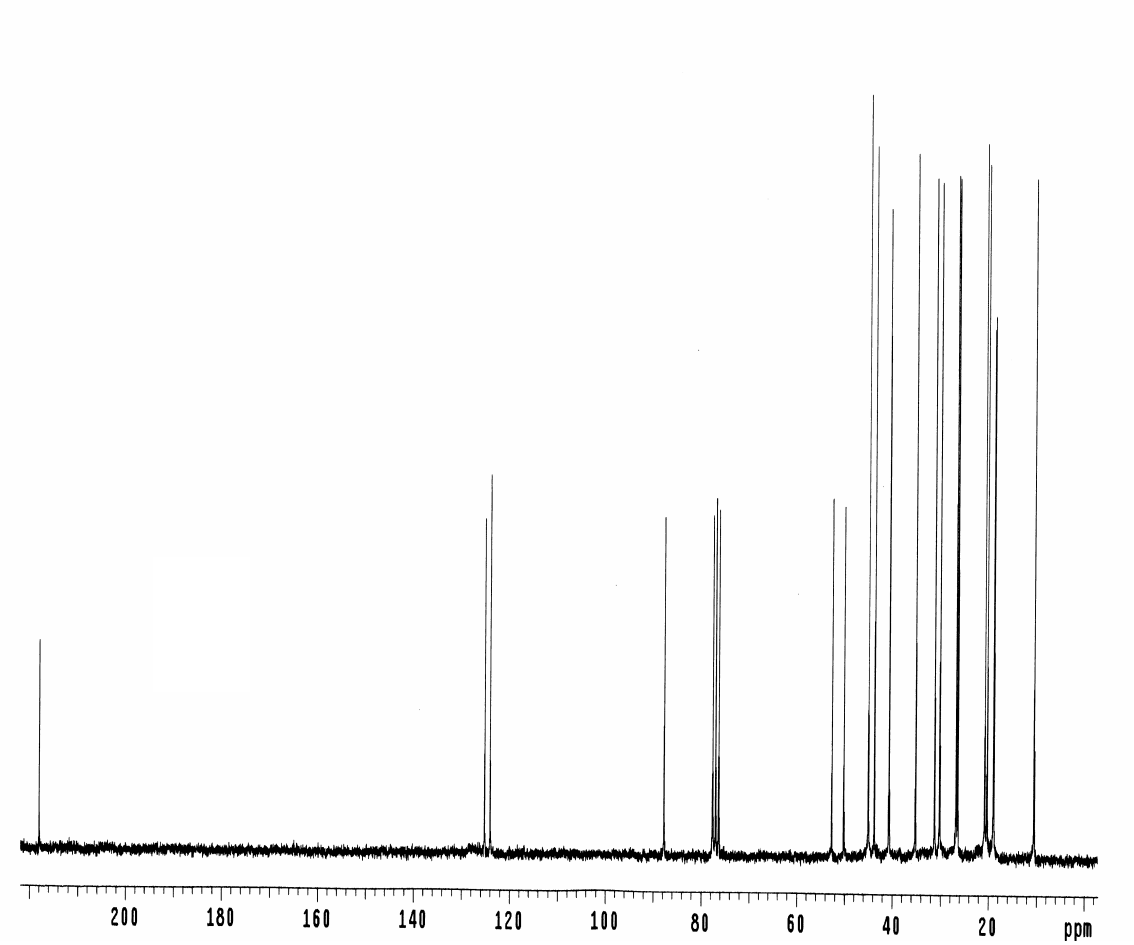

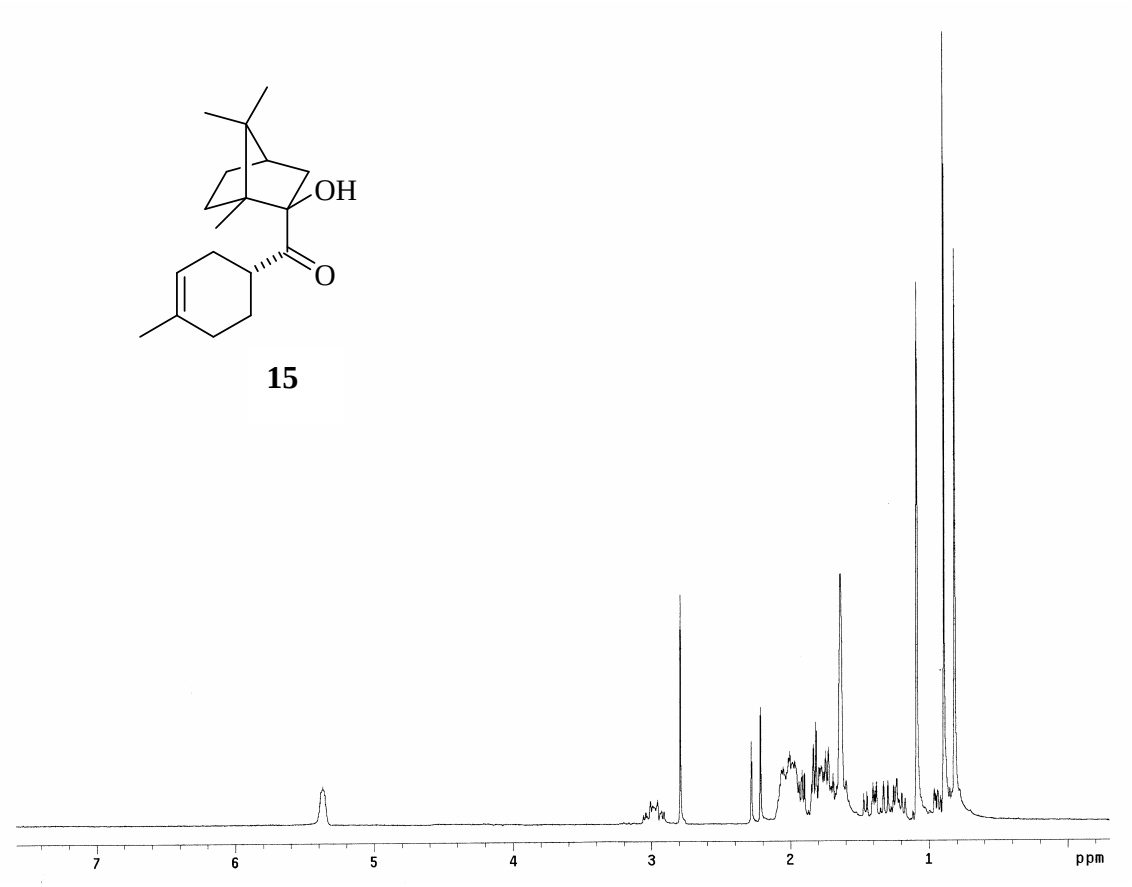


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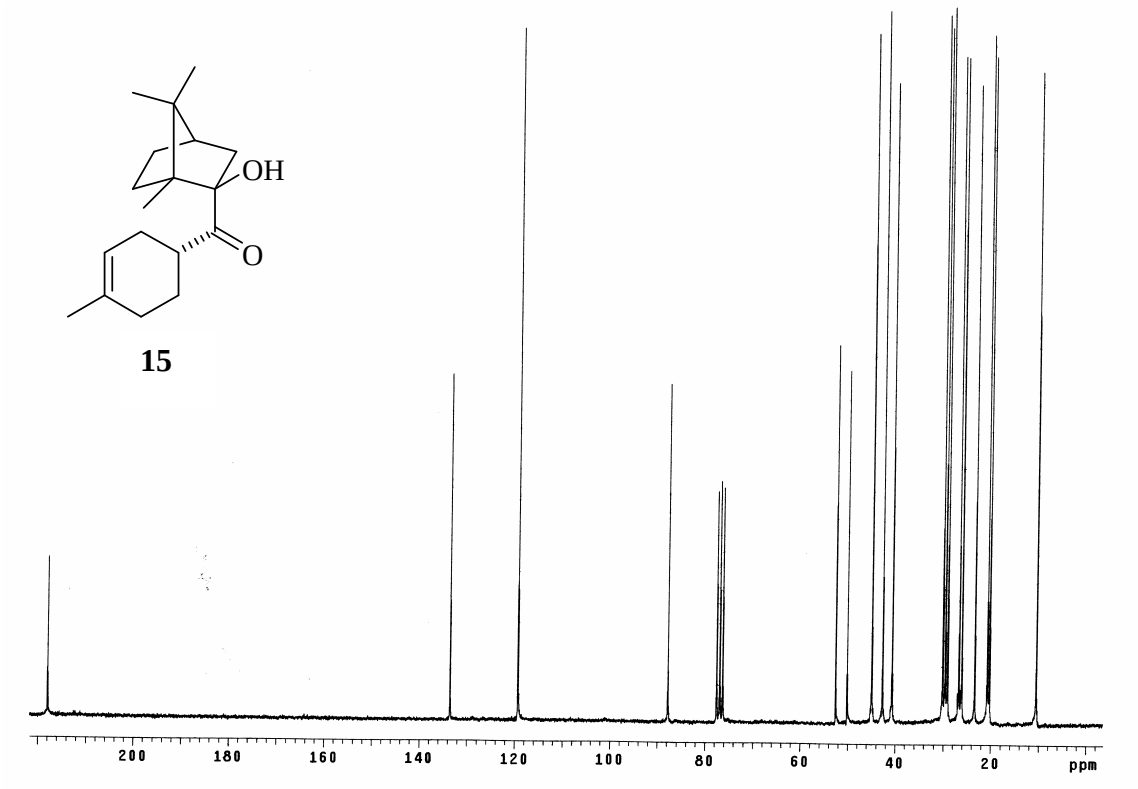


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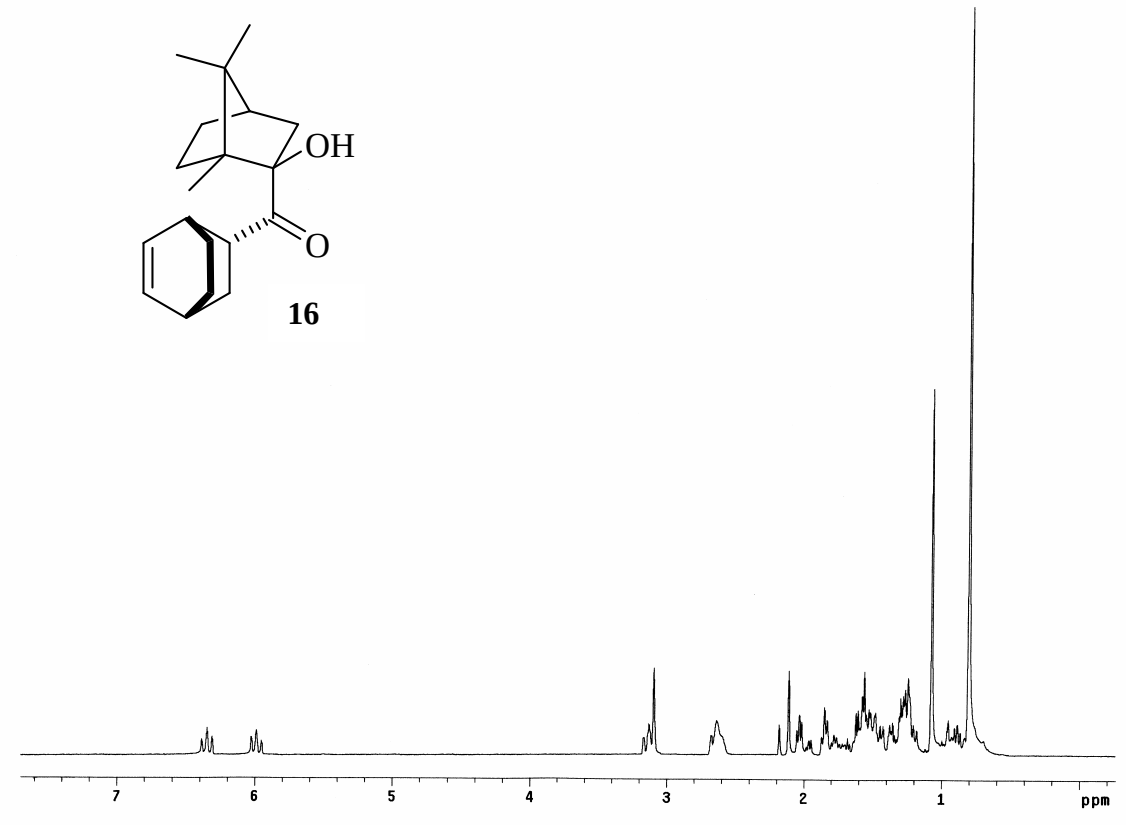
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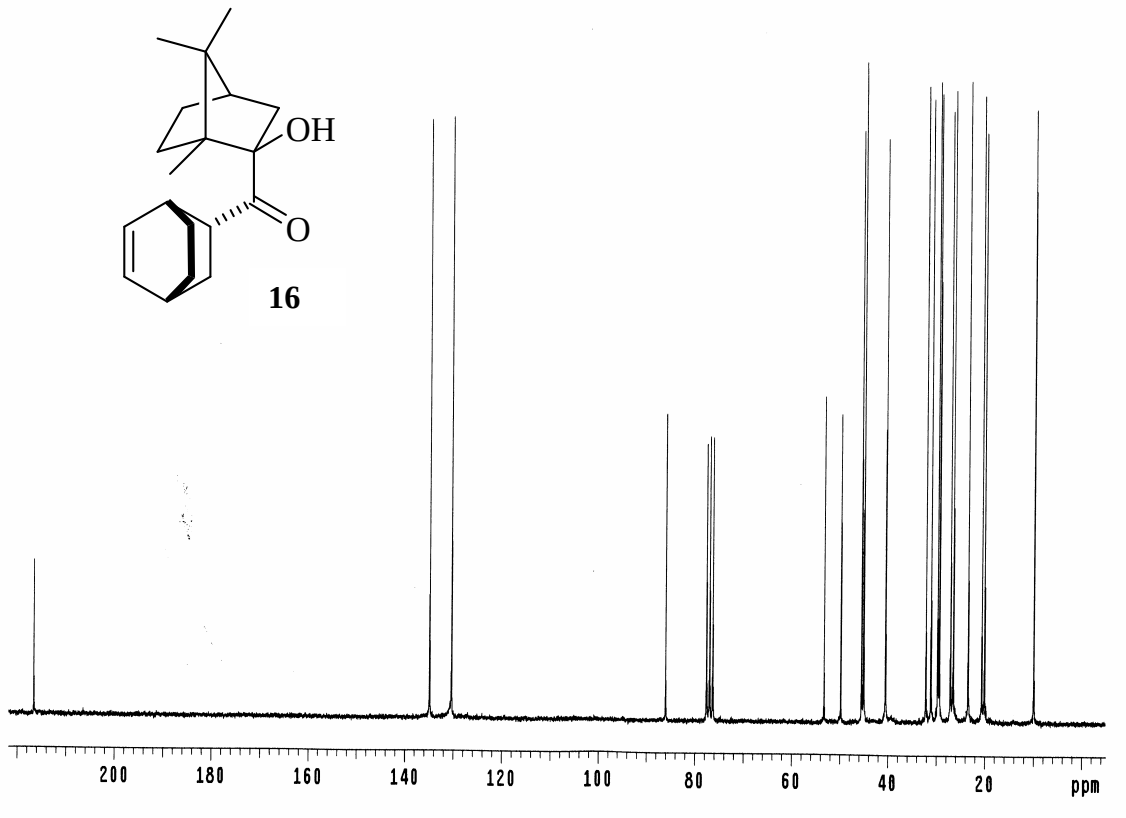
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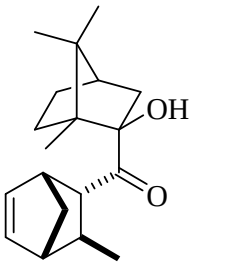


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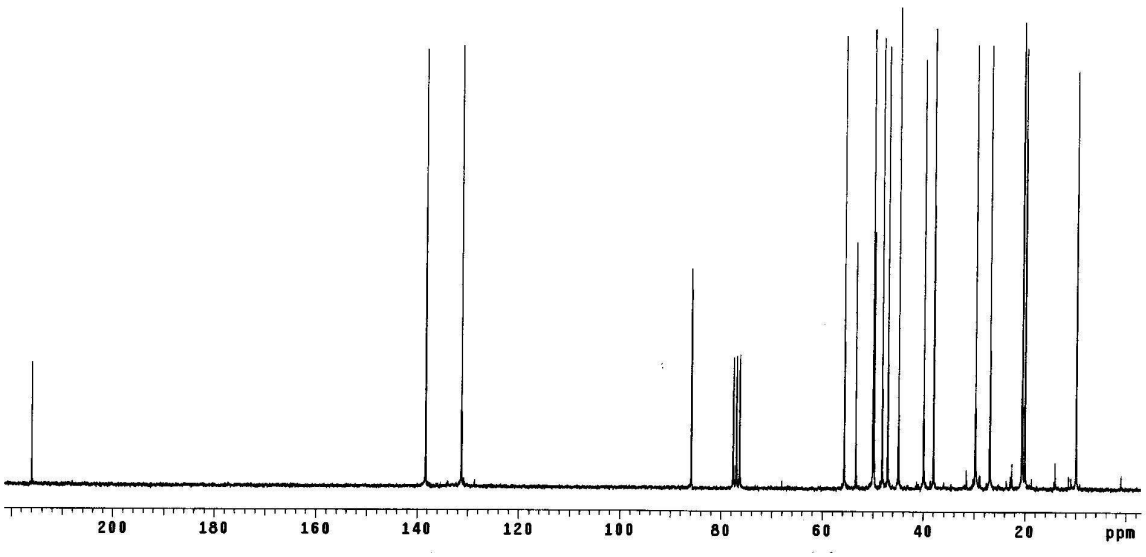

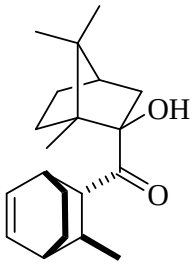


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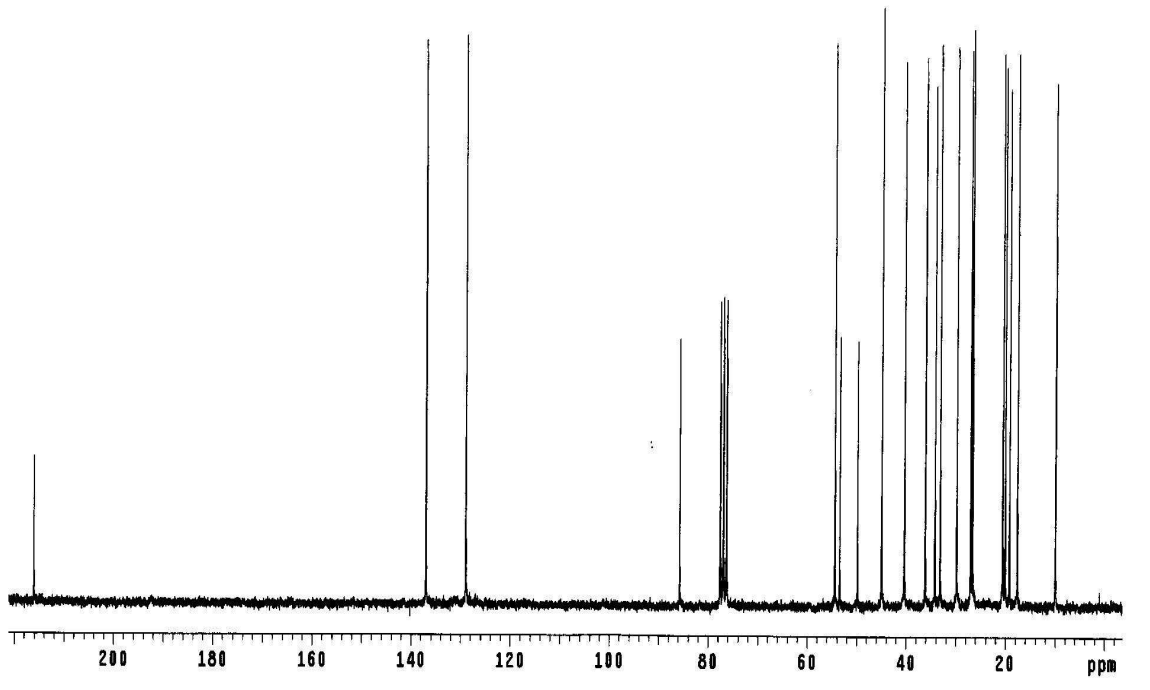

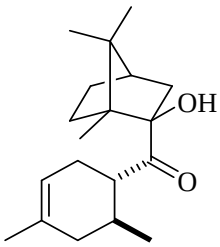


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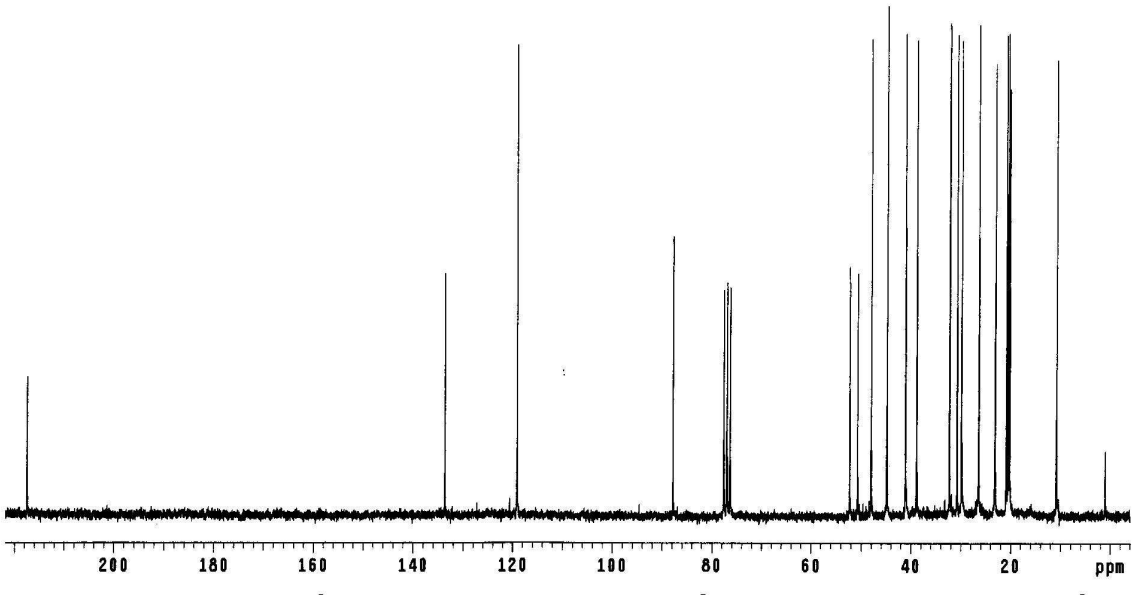

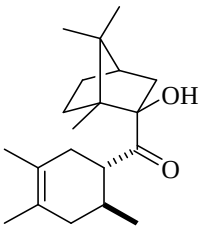


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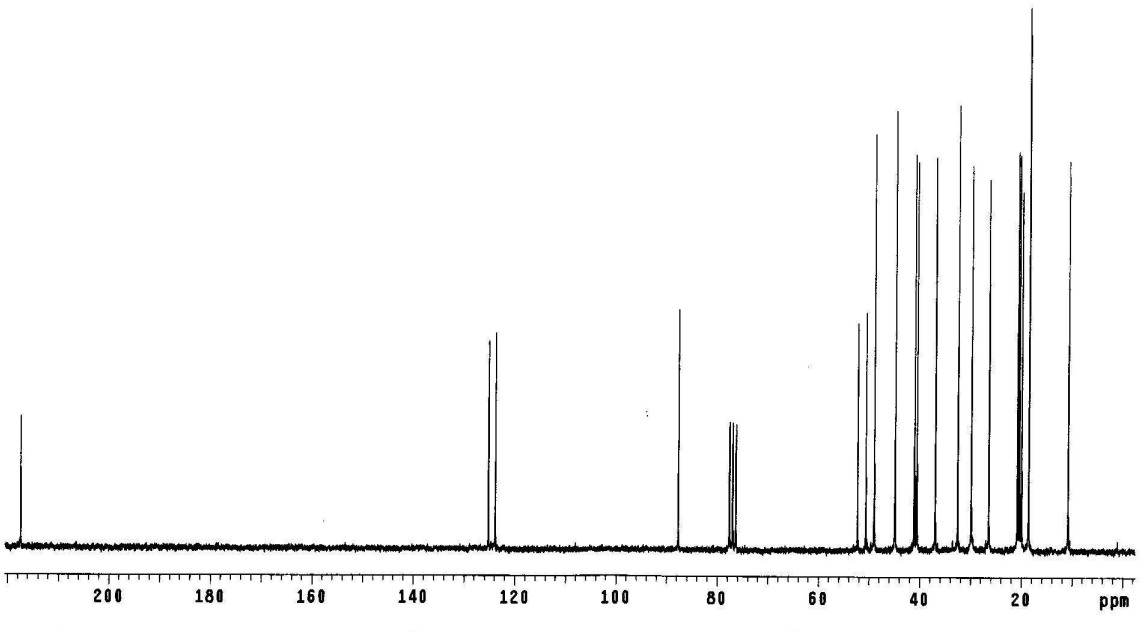

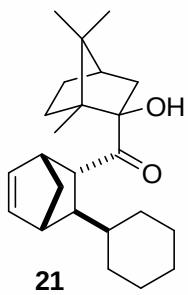


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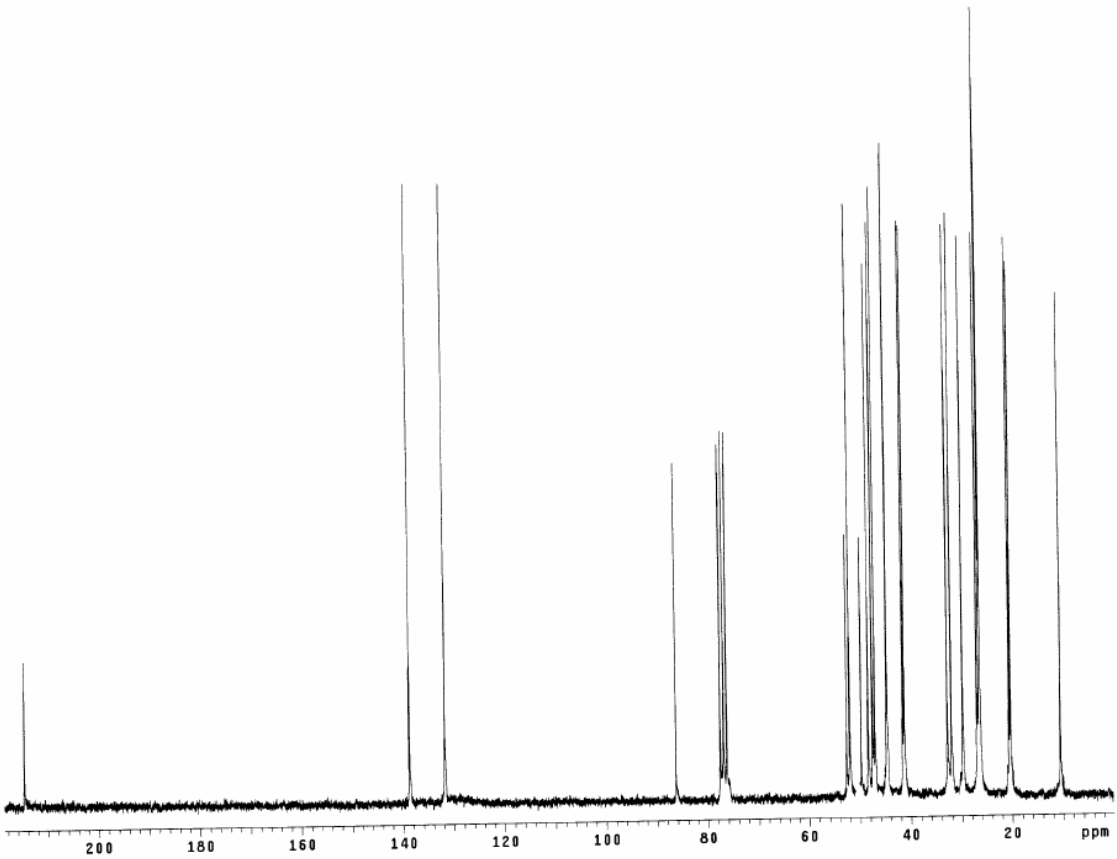

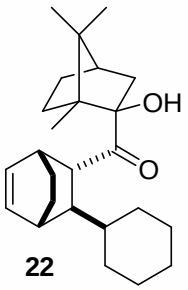


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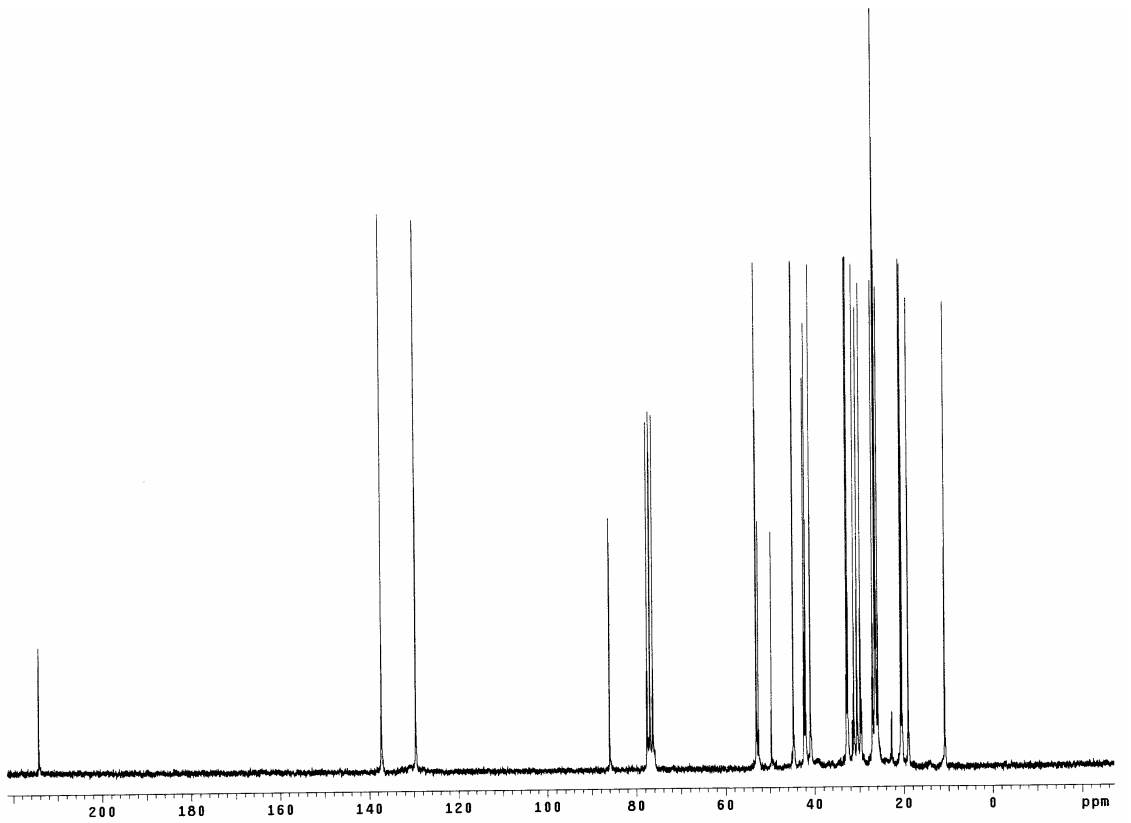

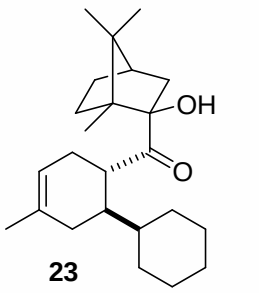


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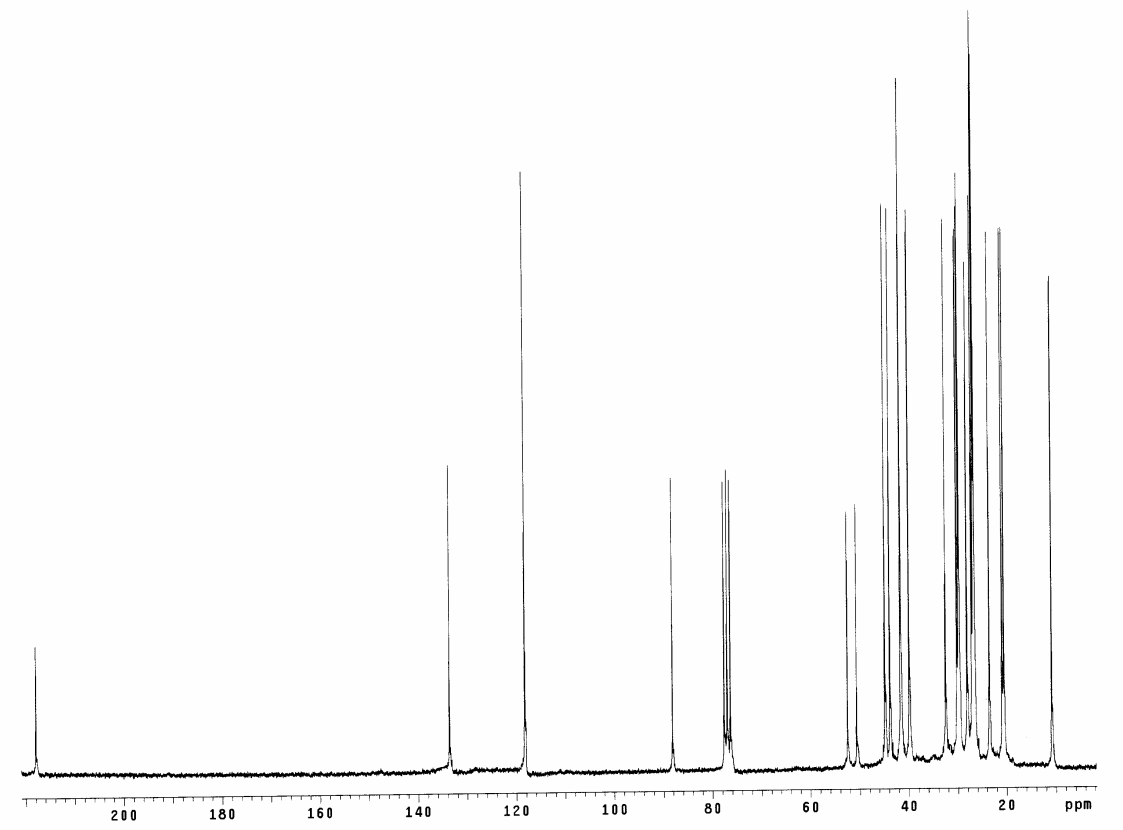

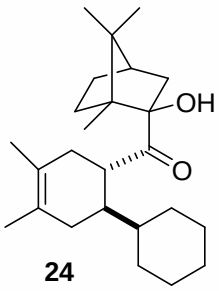


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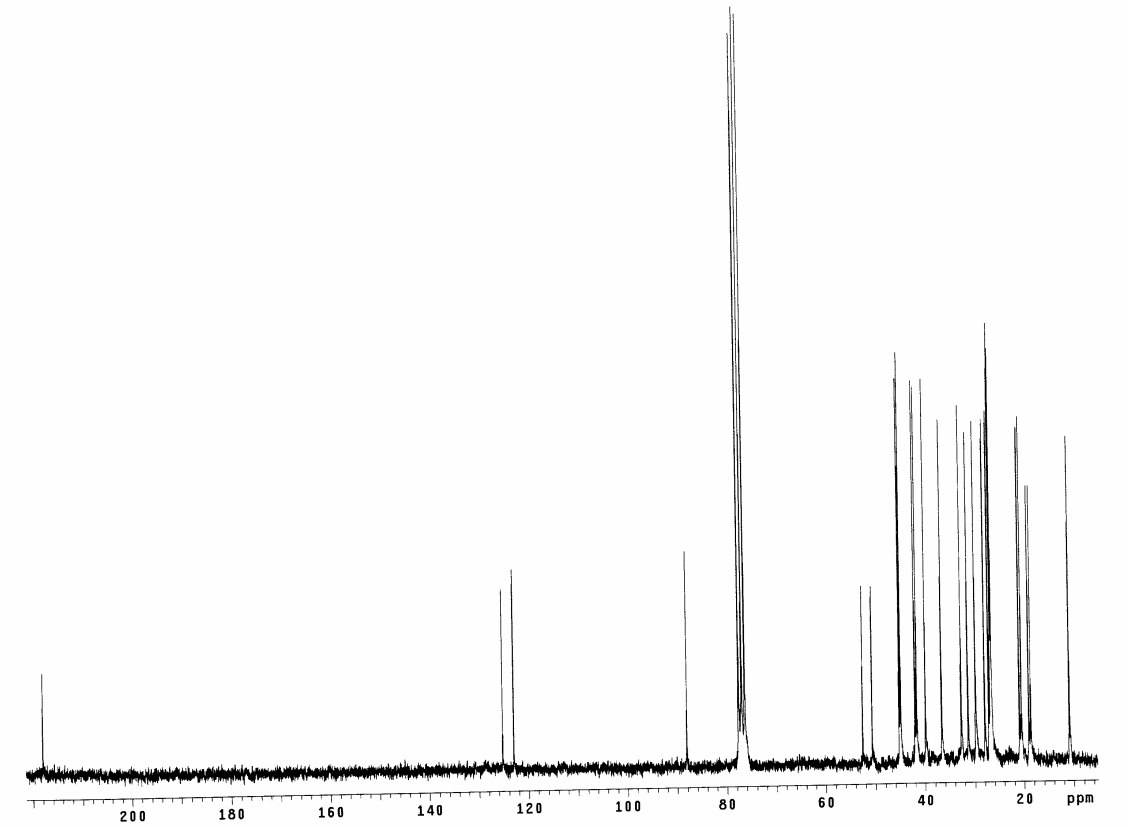

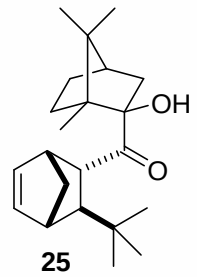


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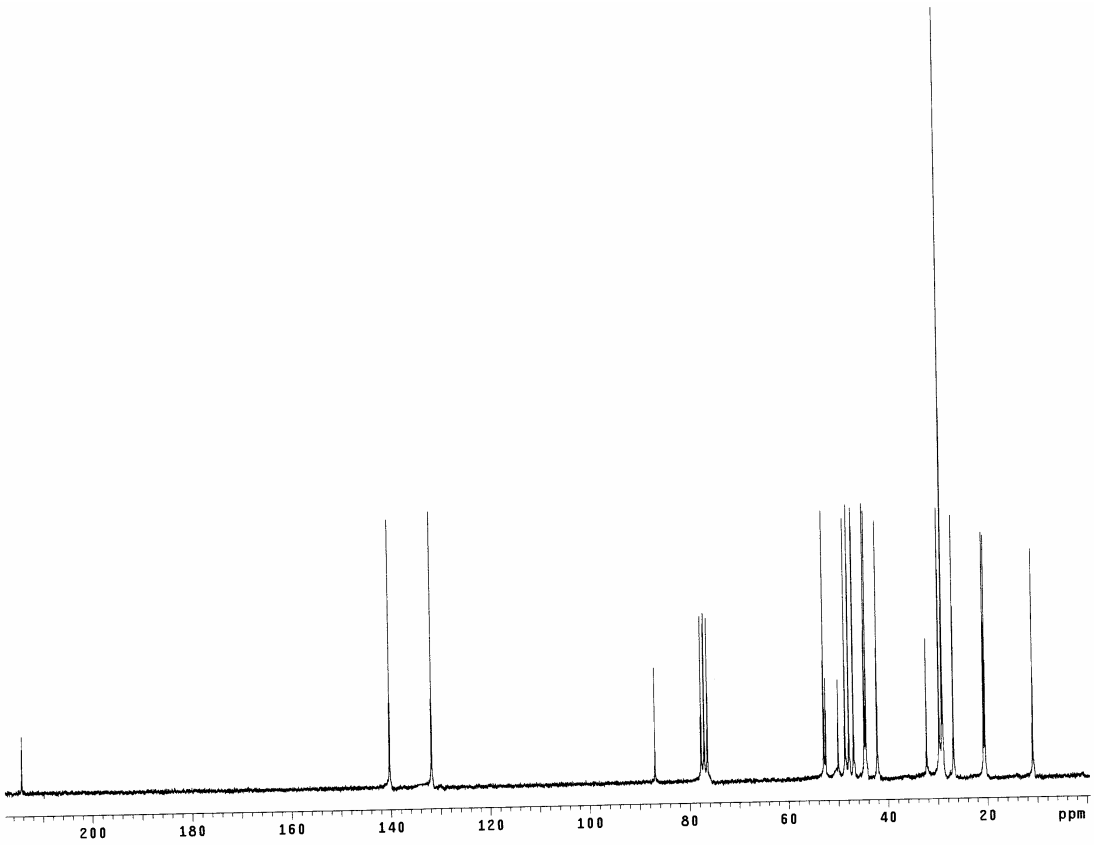

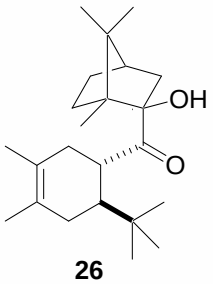


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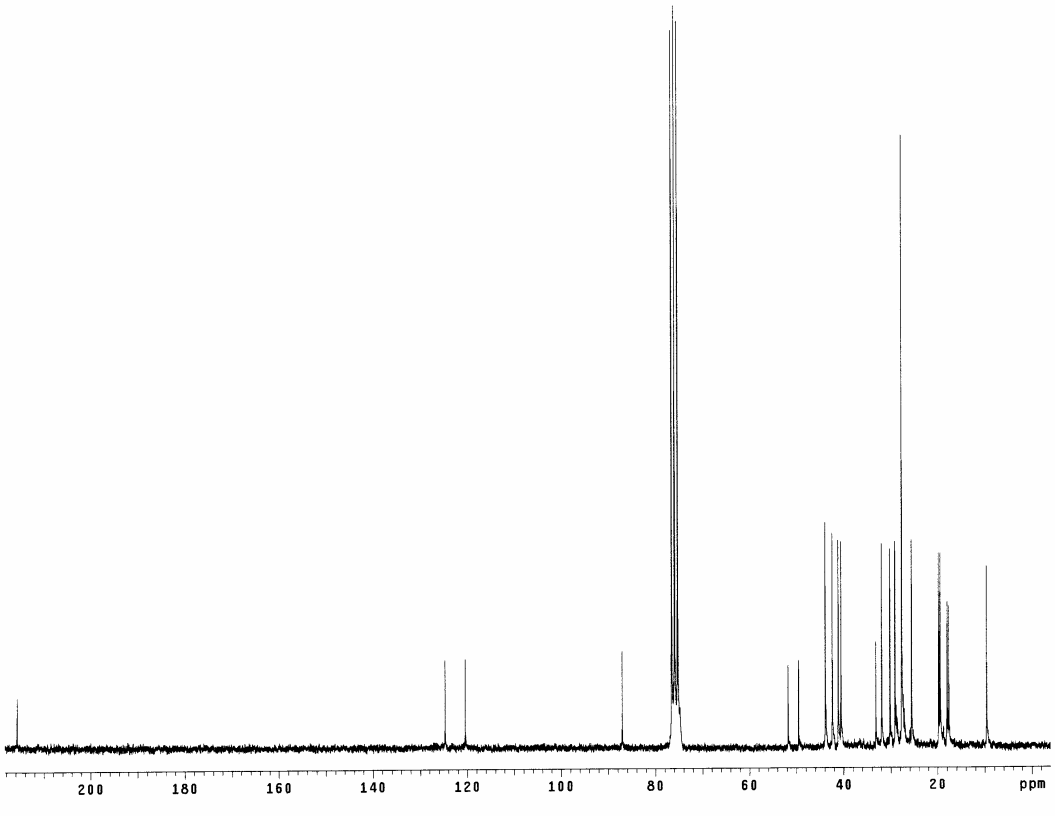

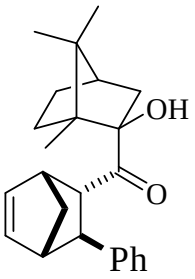


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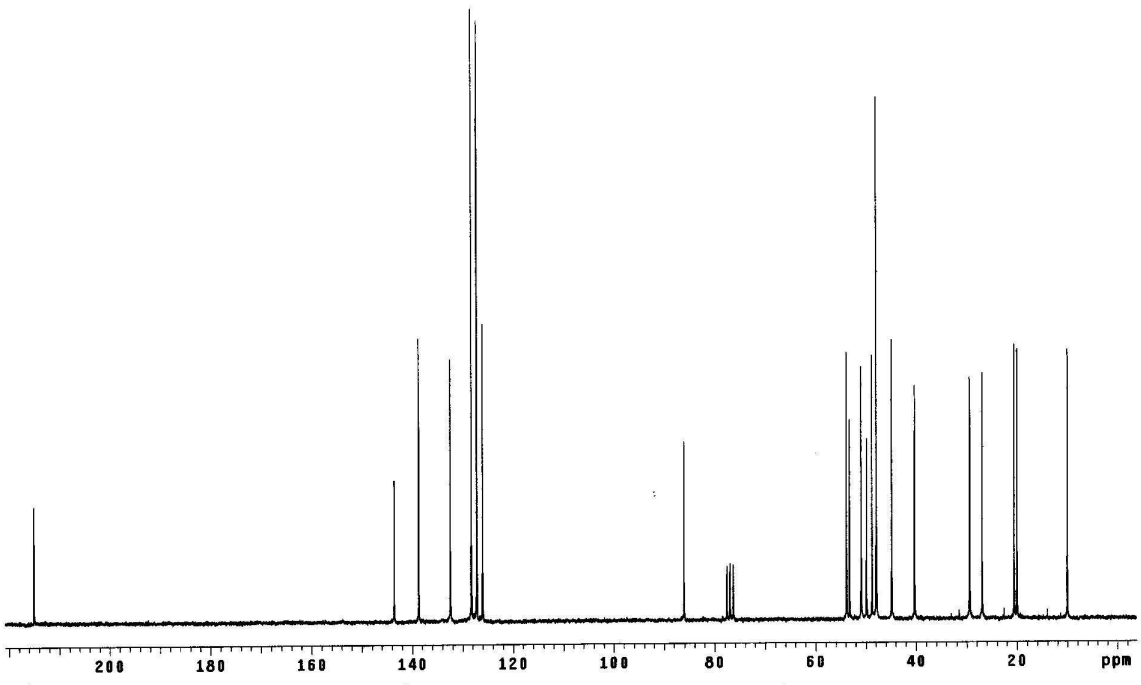

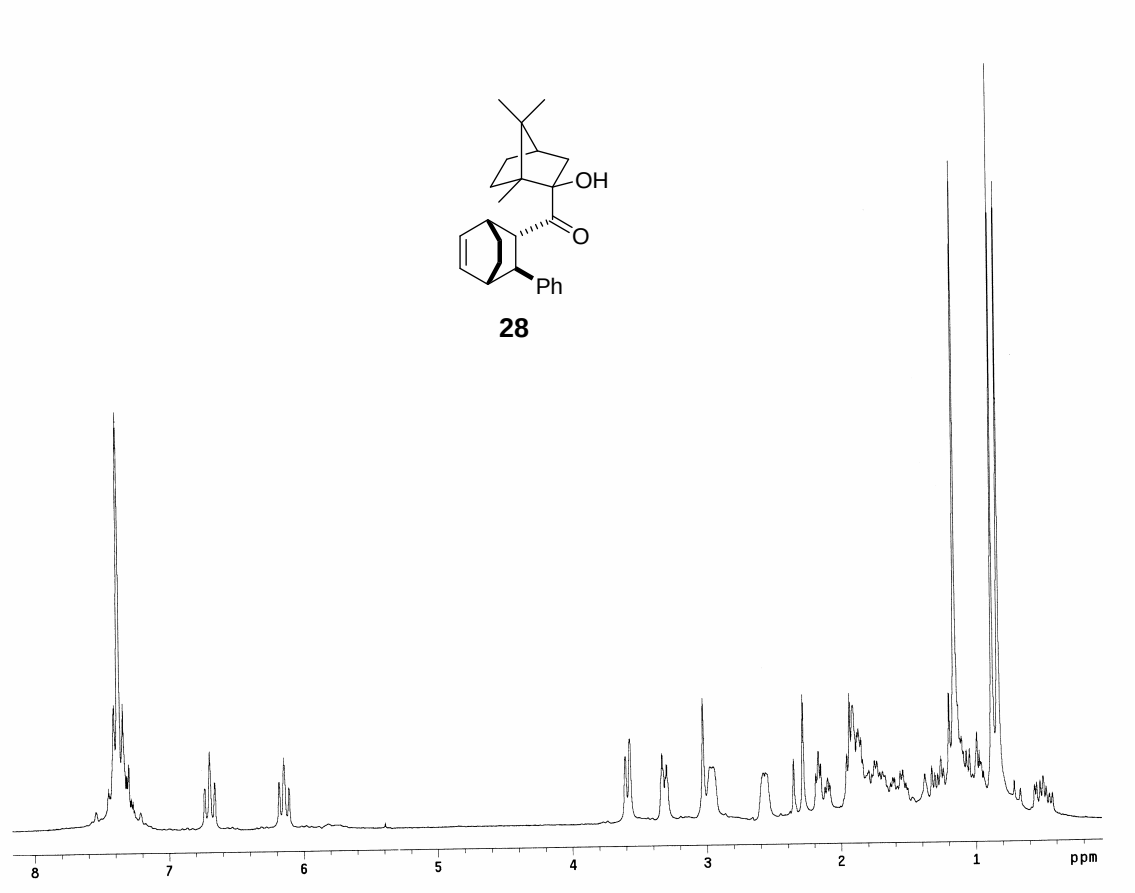


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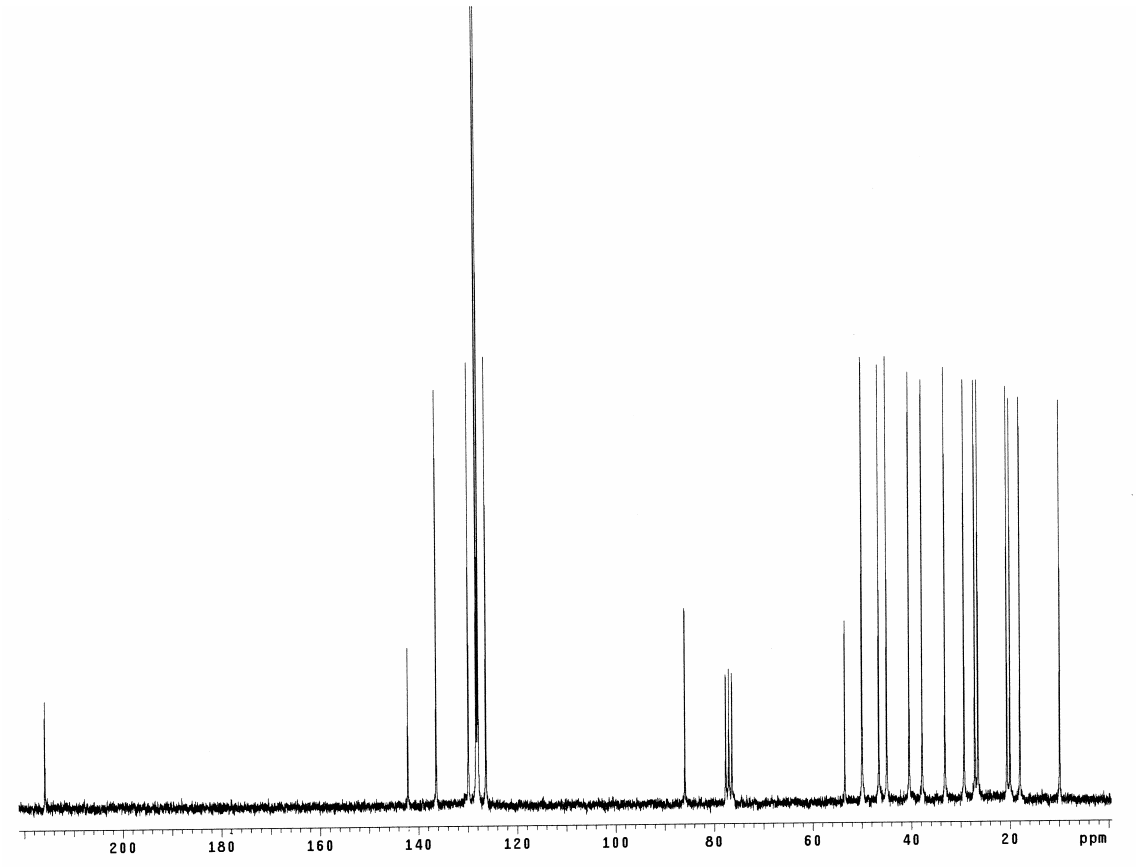

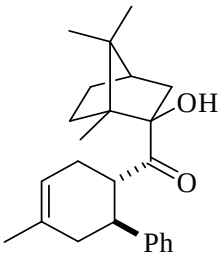


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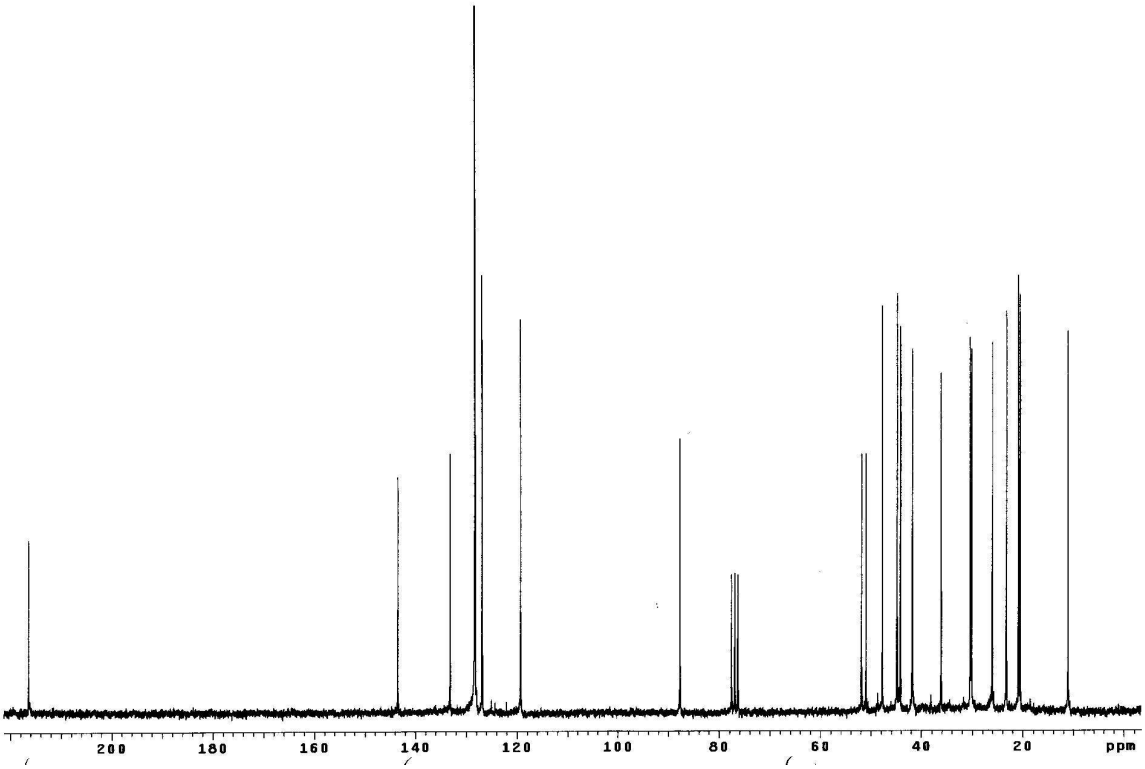

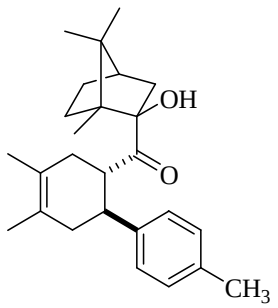


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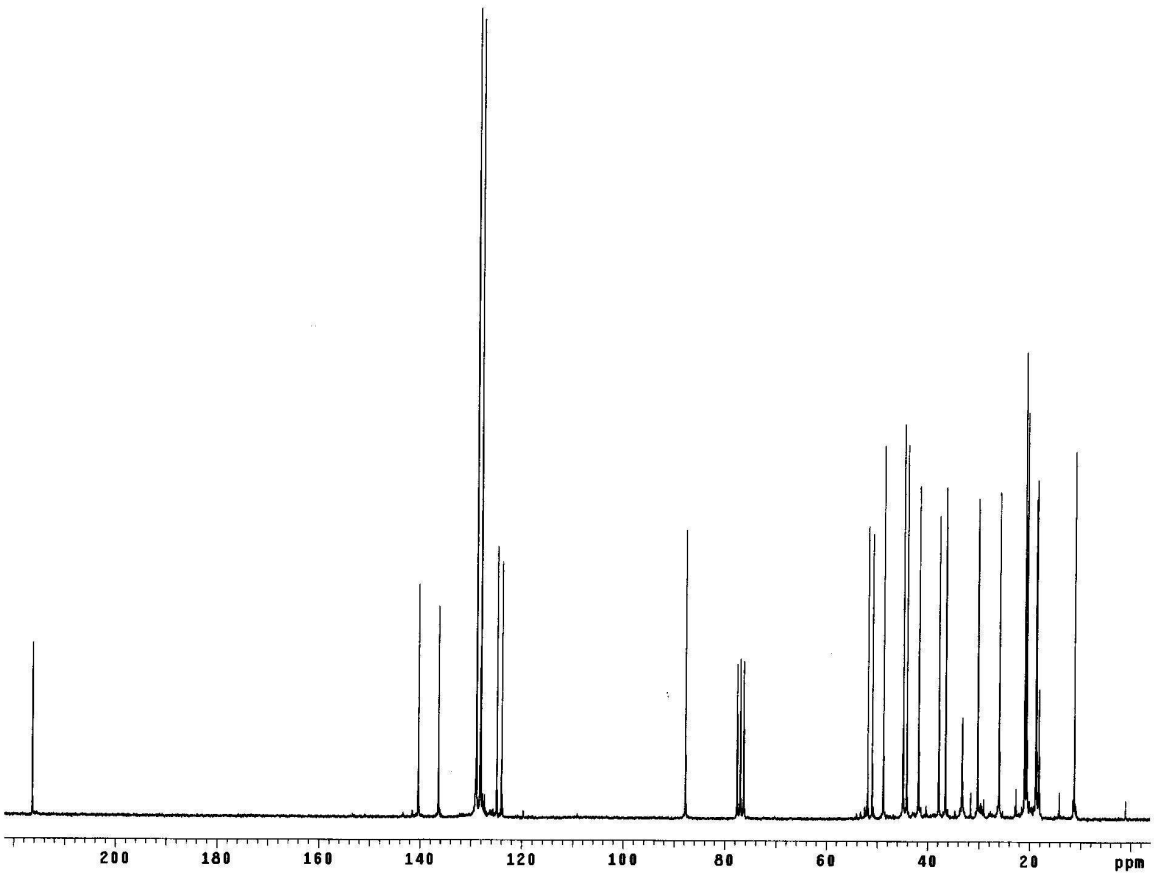

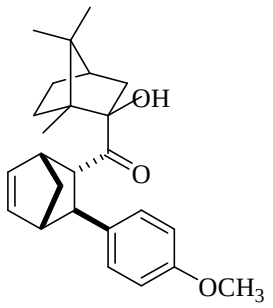


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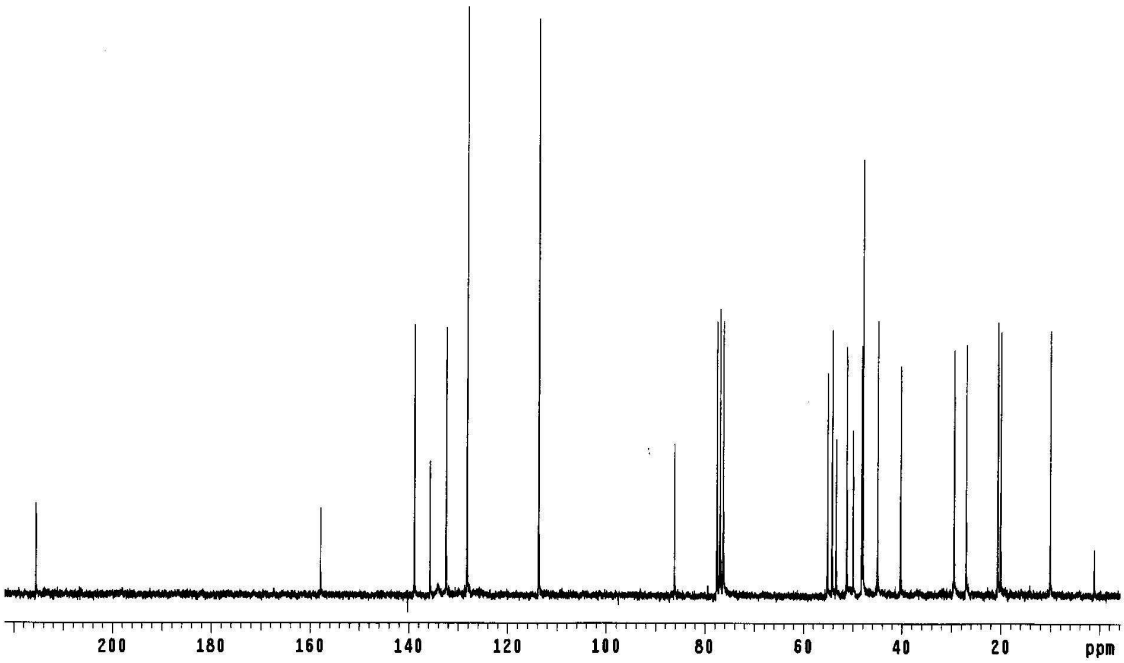

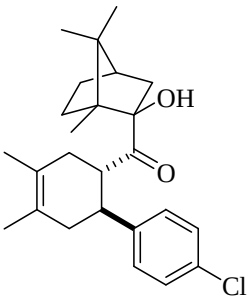


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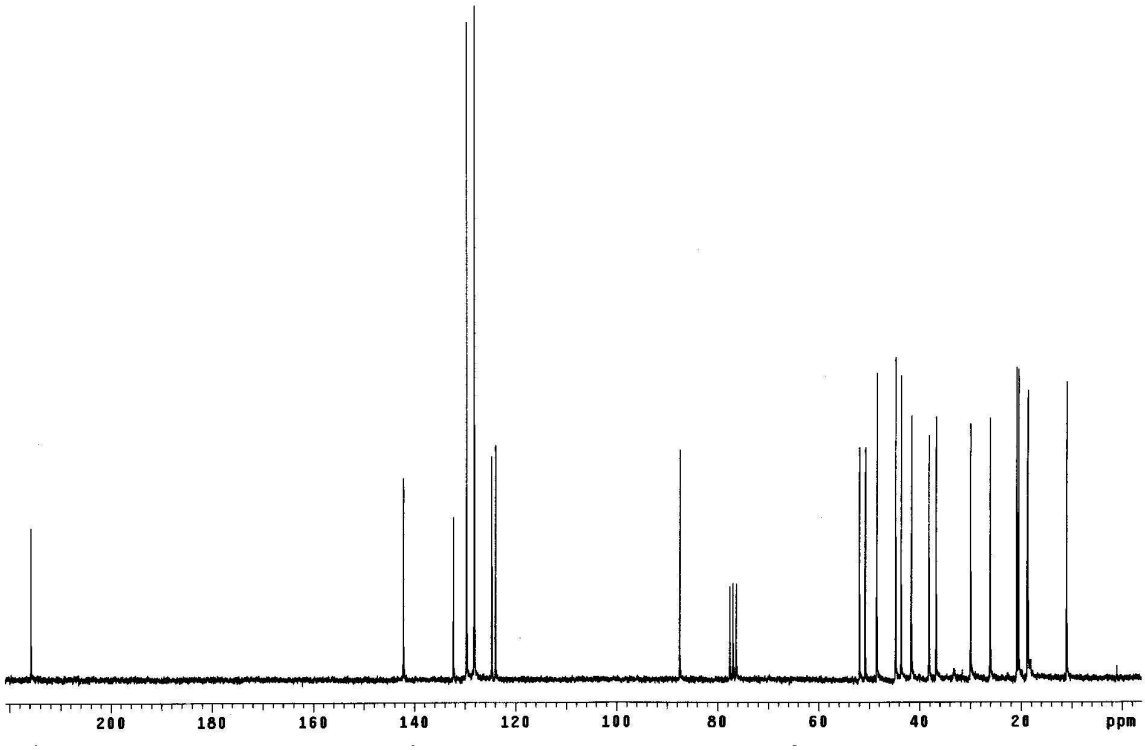

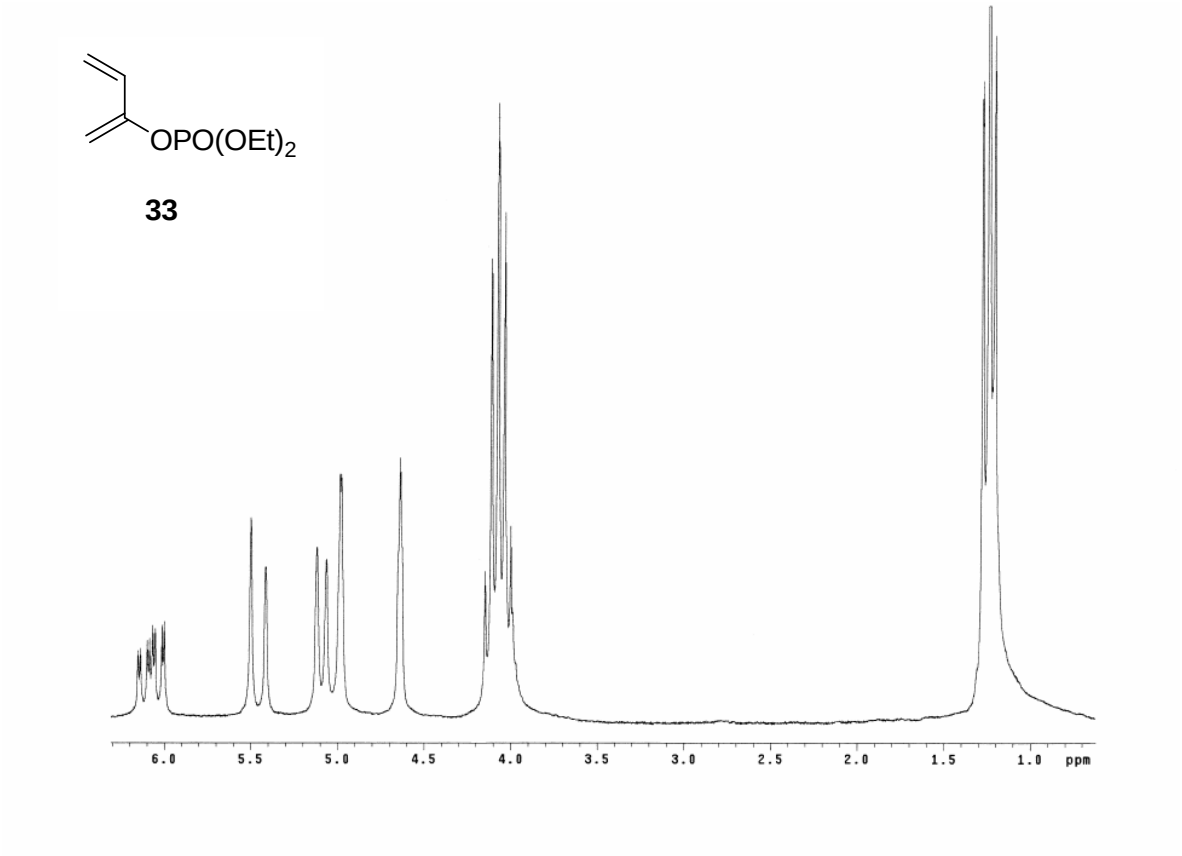
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1.0
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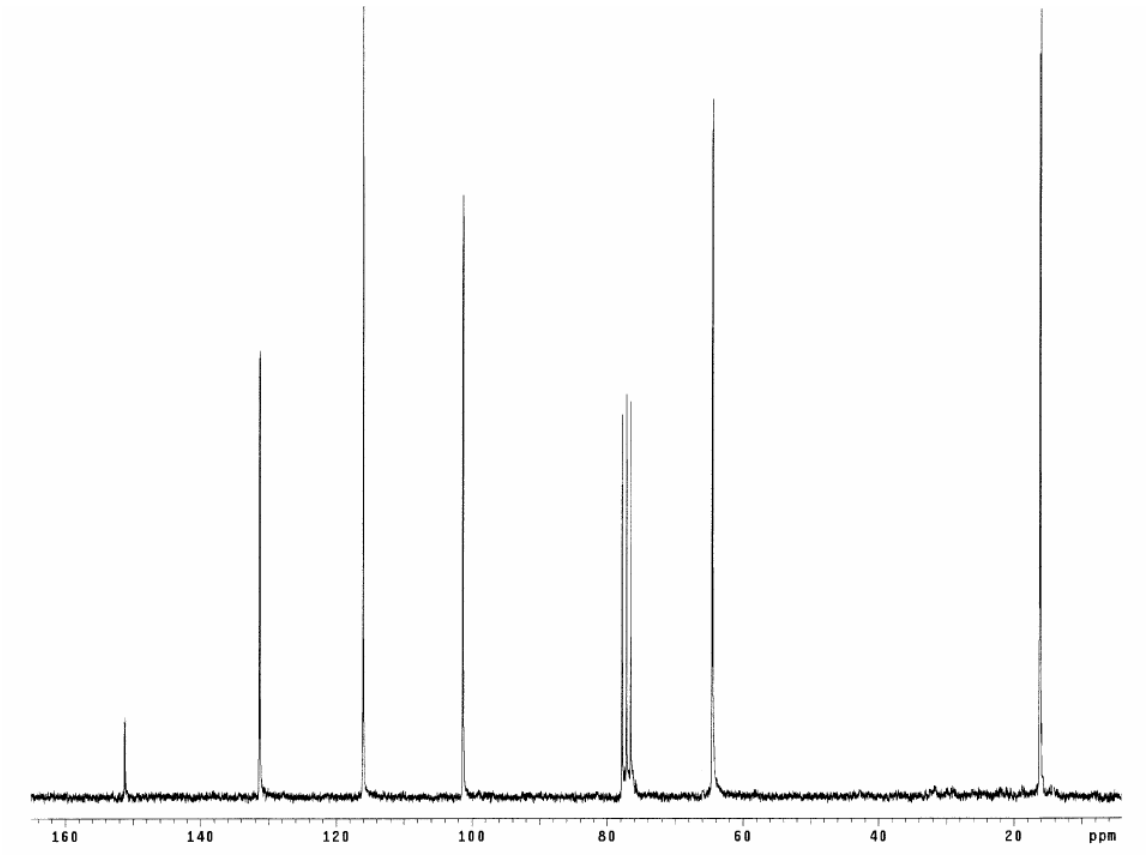
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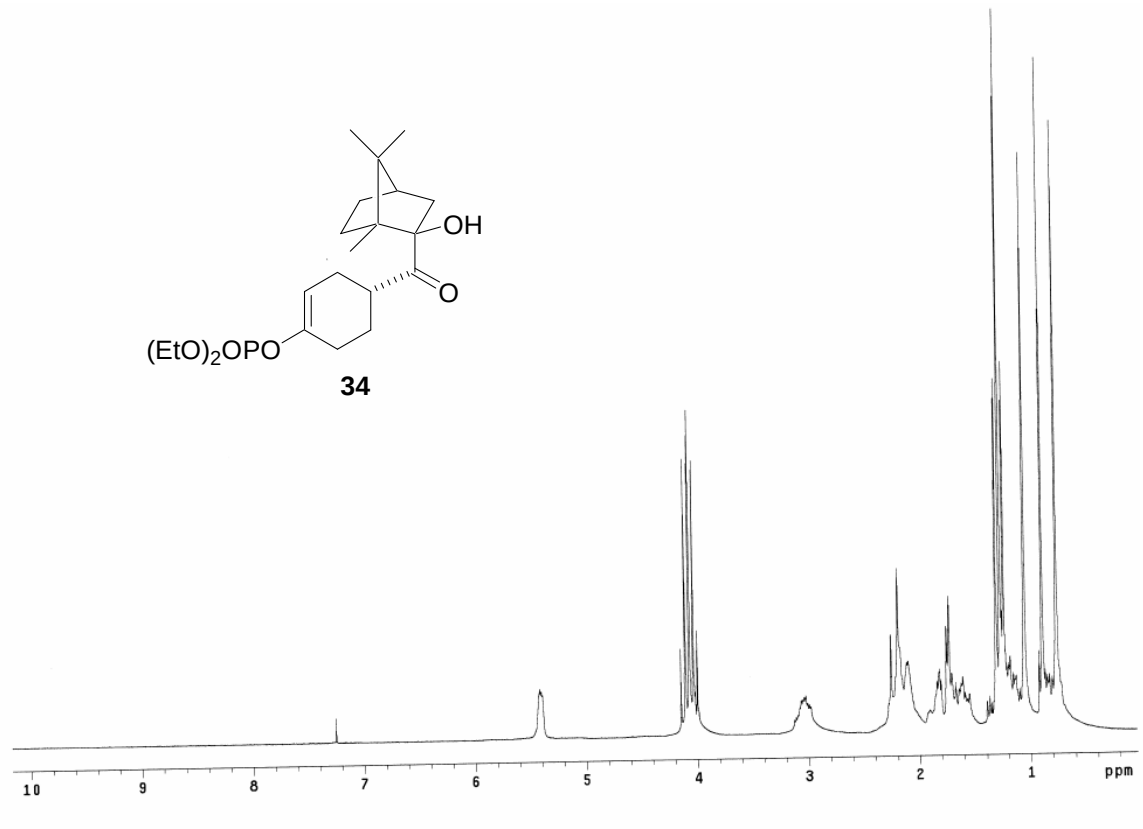
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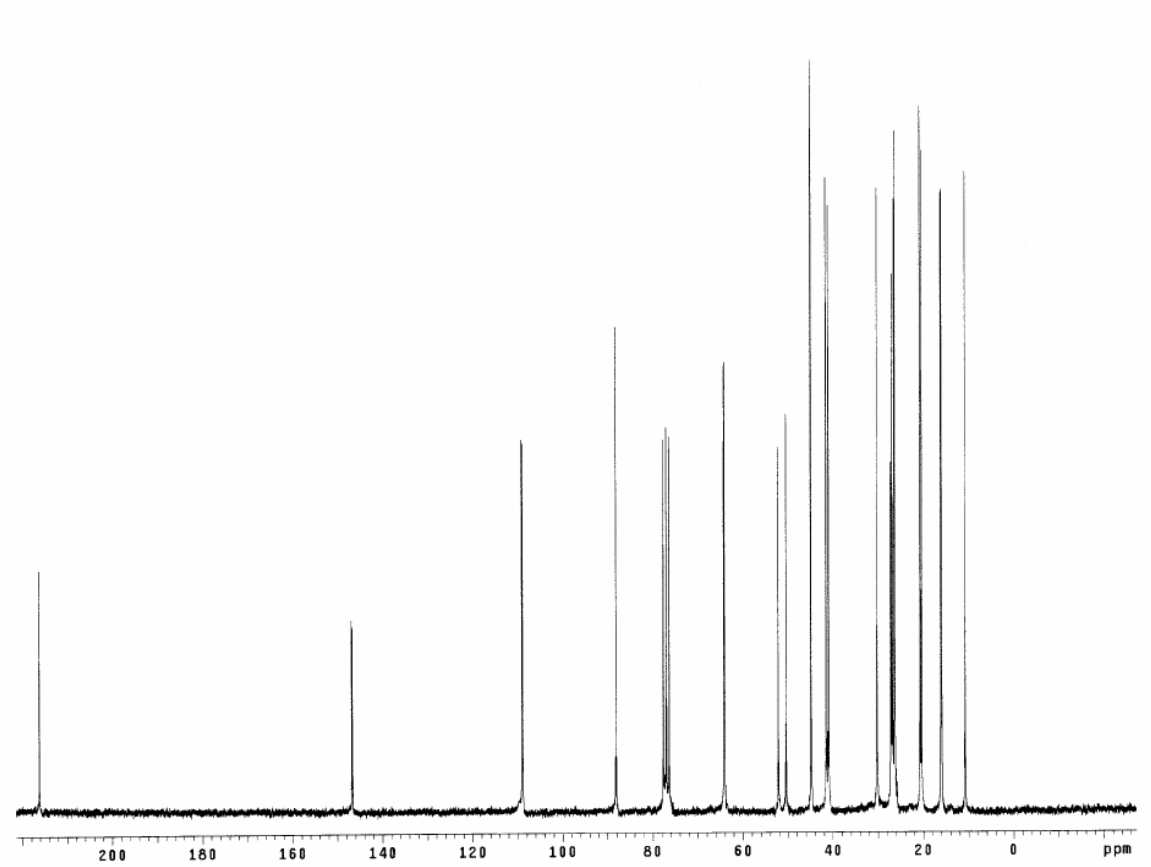
1
ppm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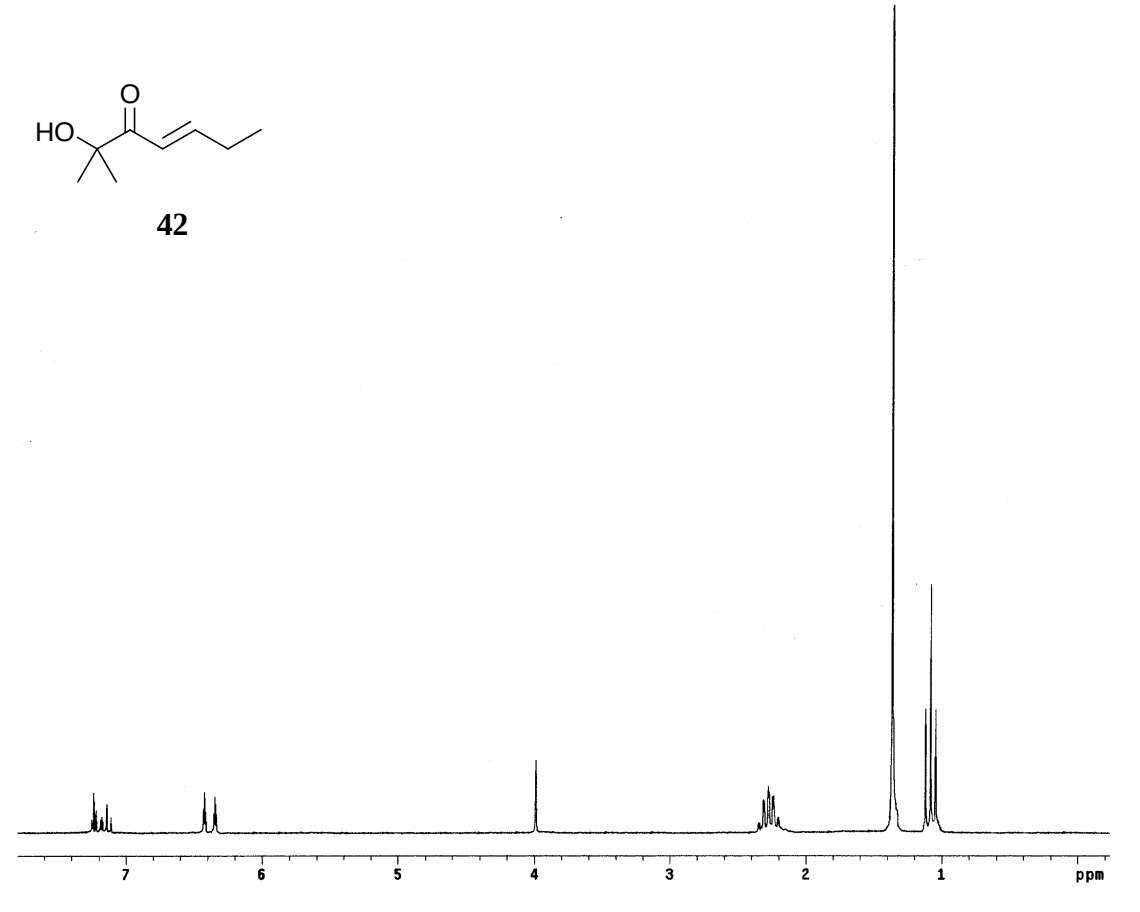
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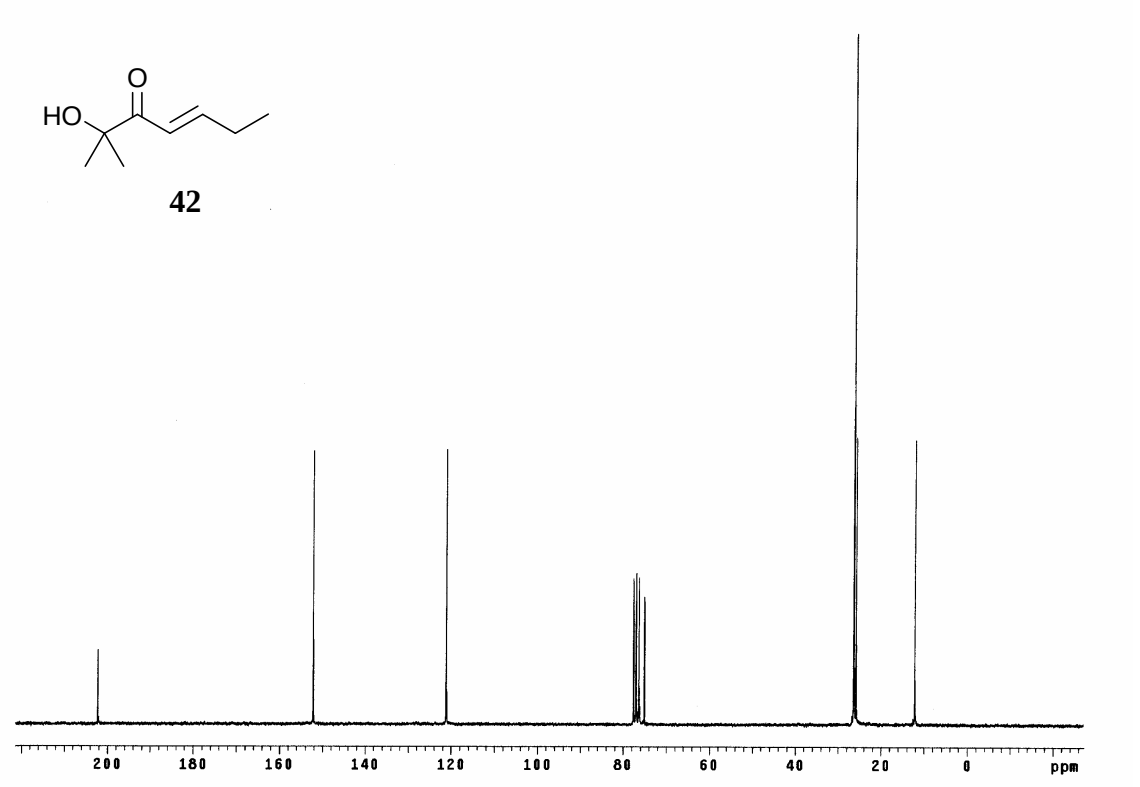
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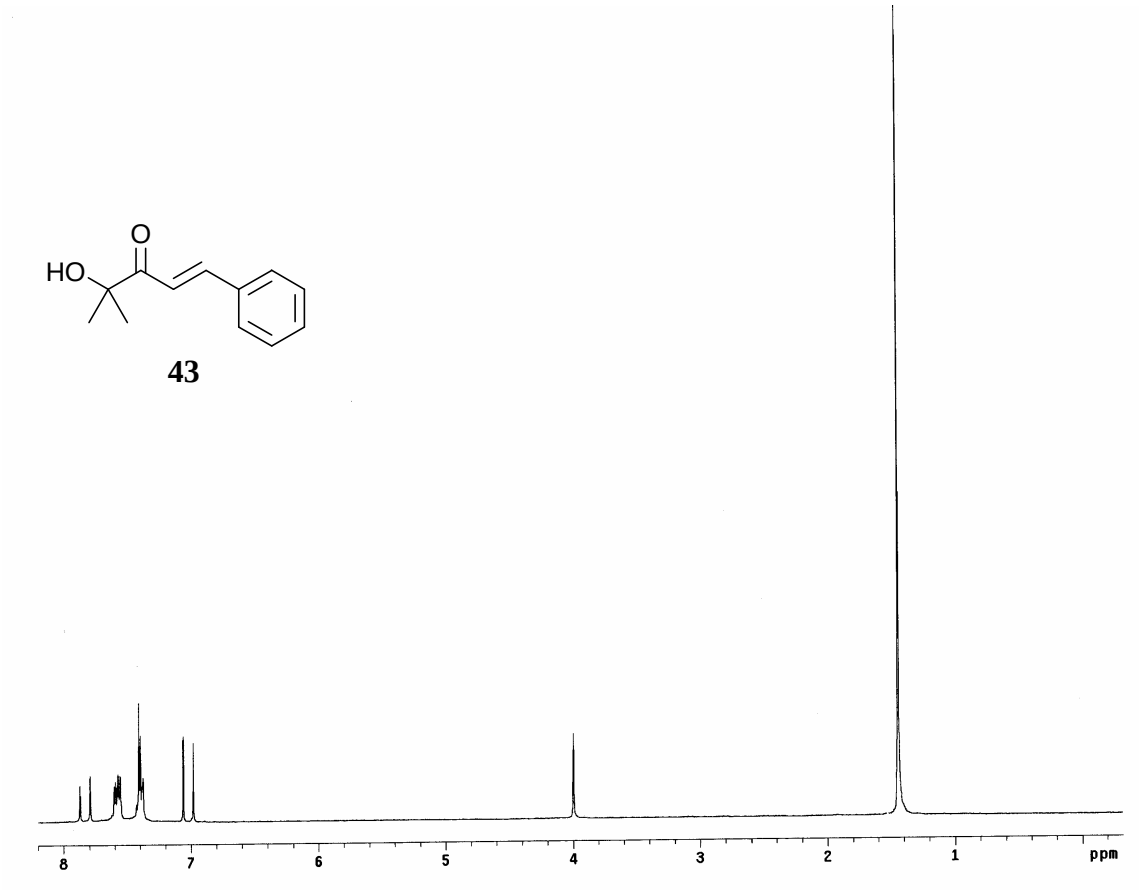


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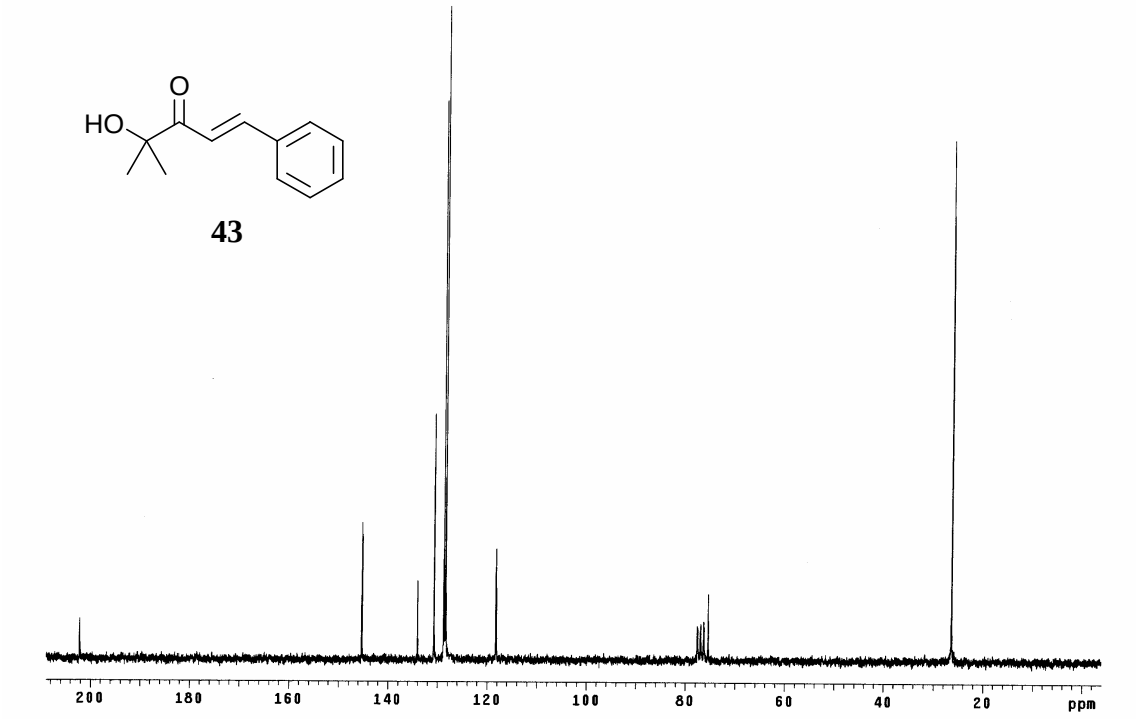


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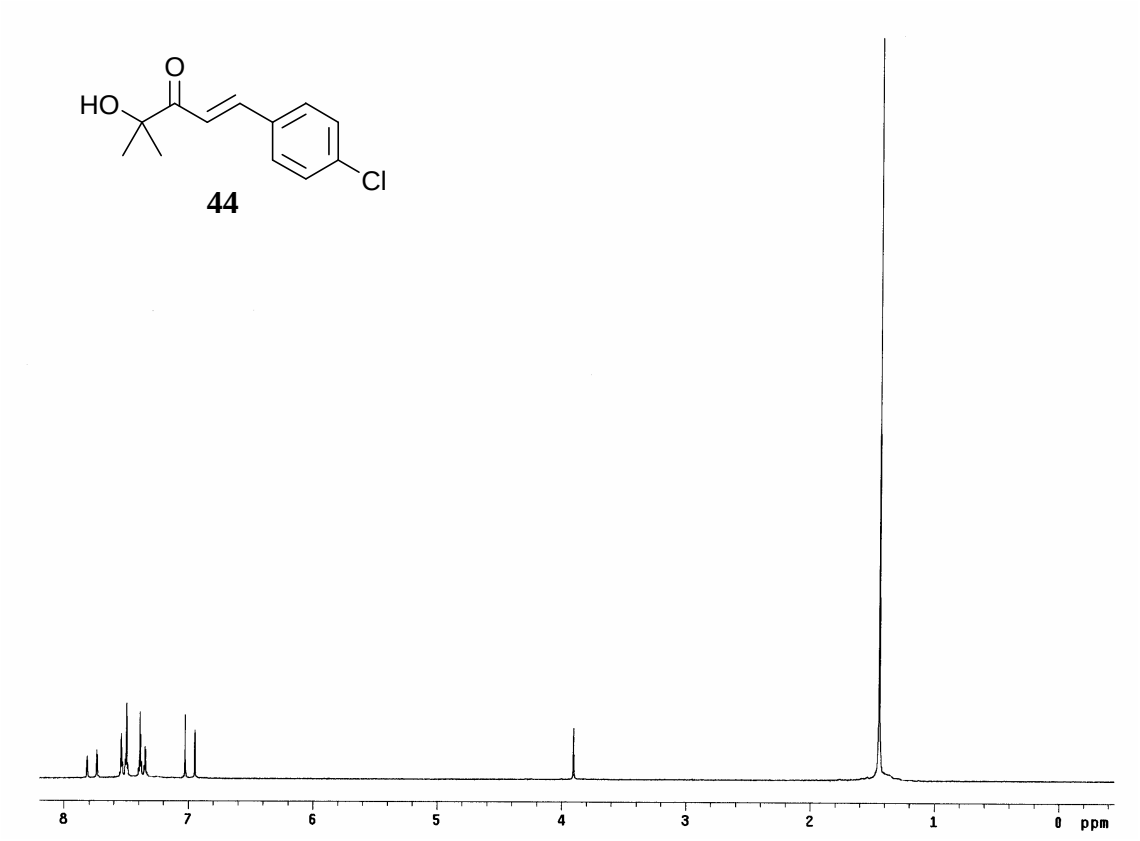
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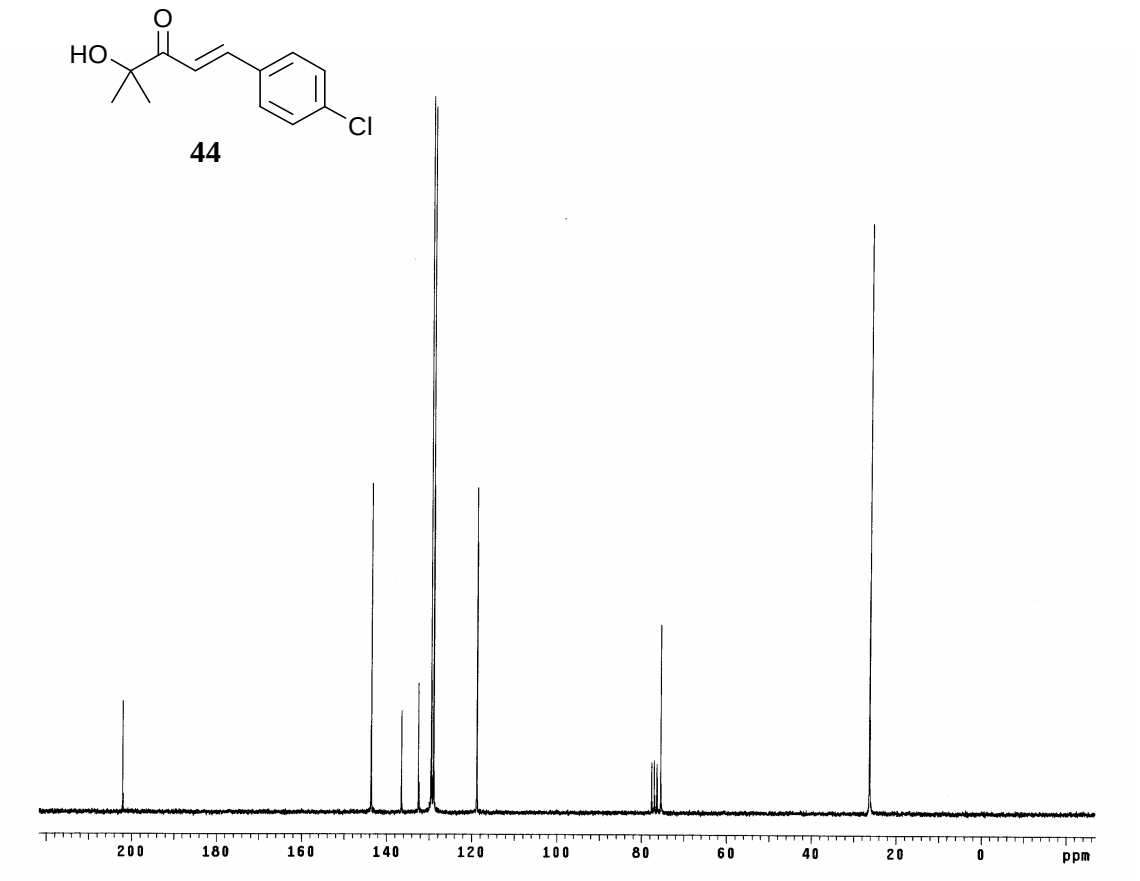
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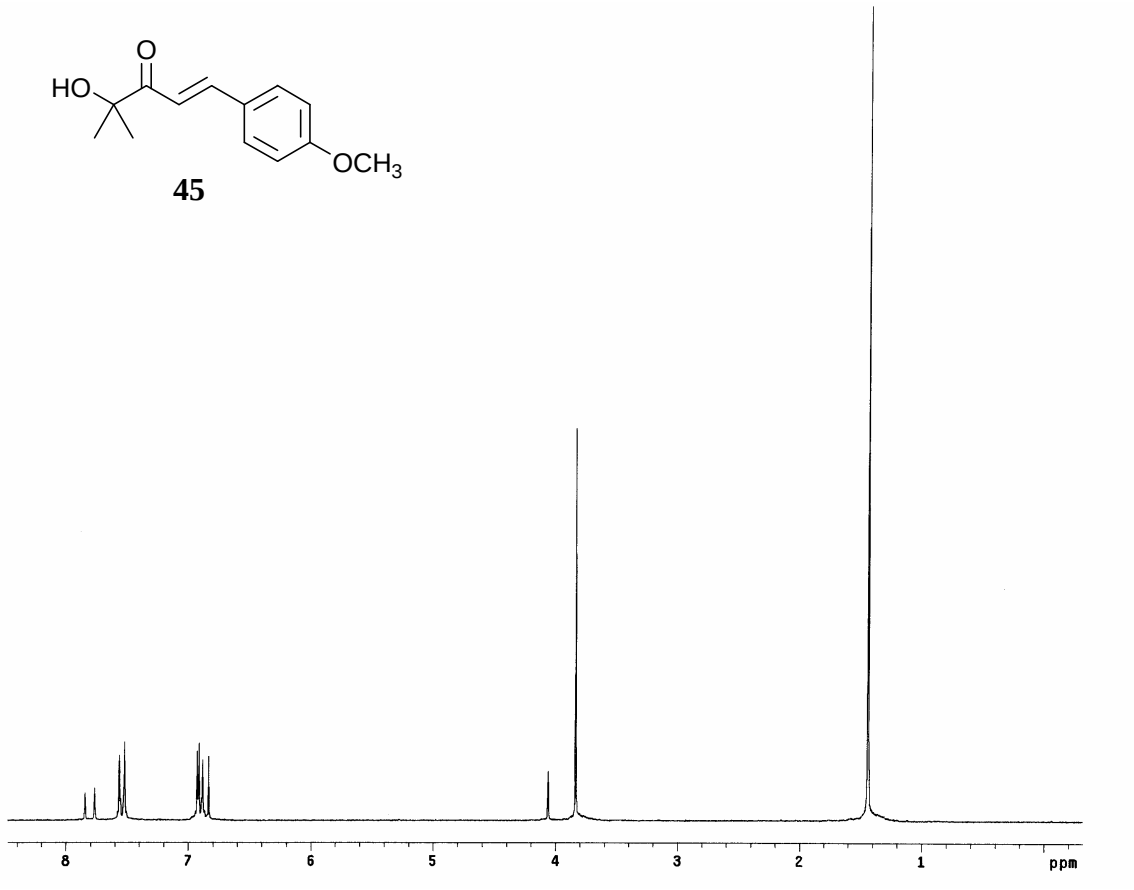
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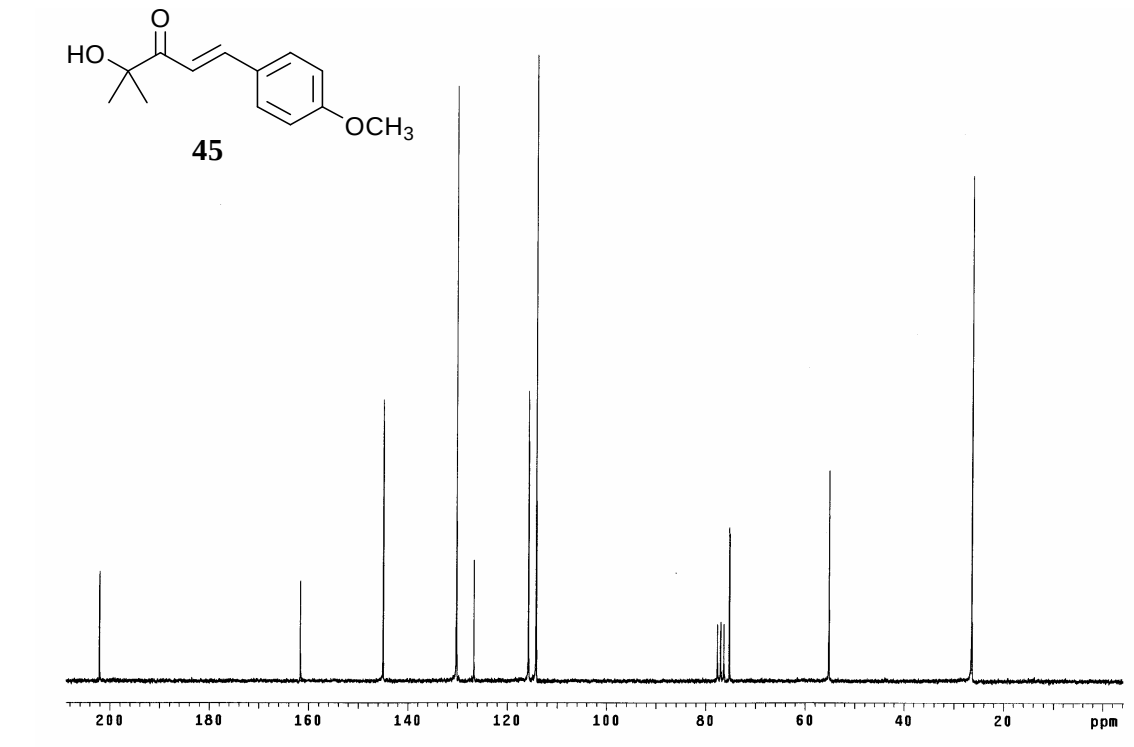
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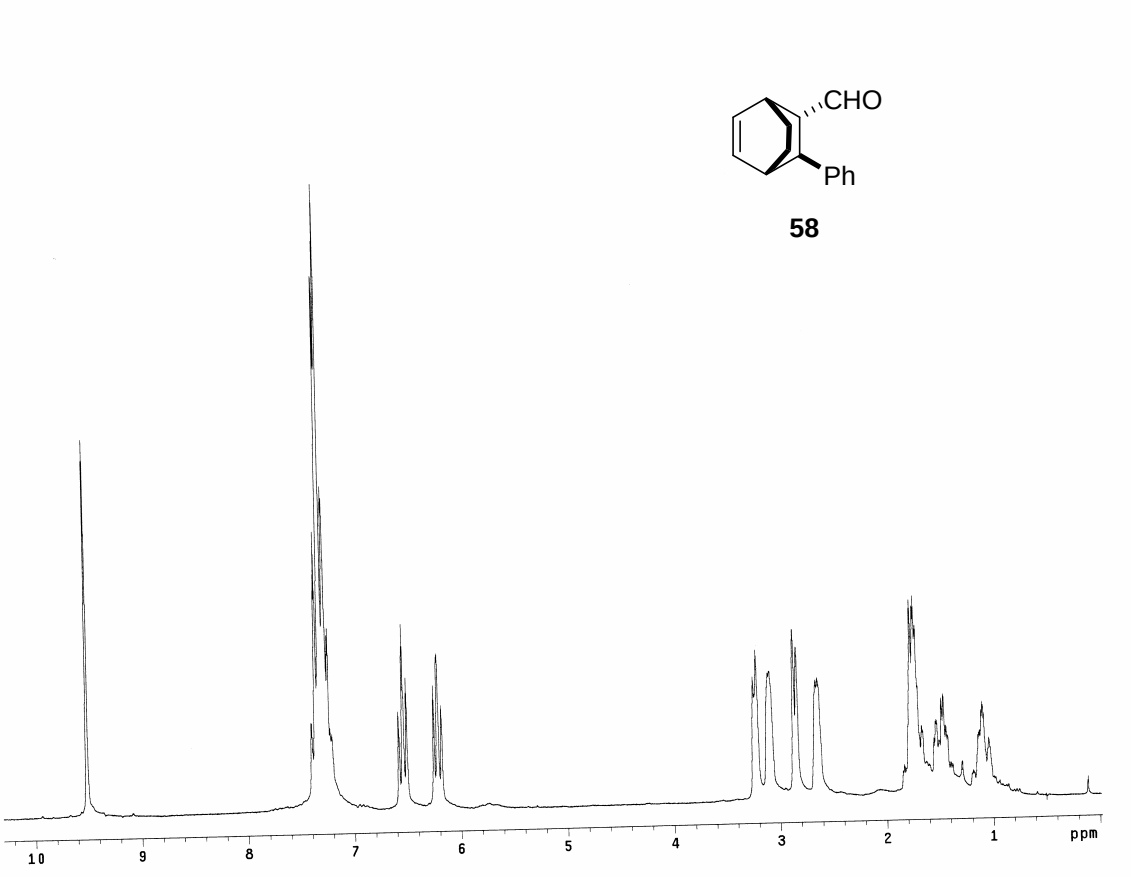
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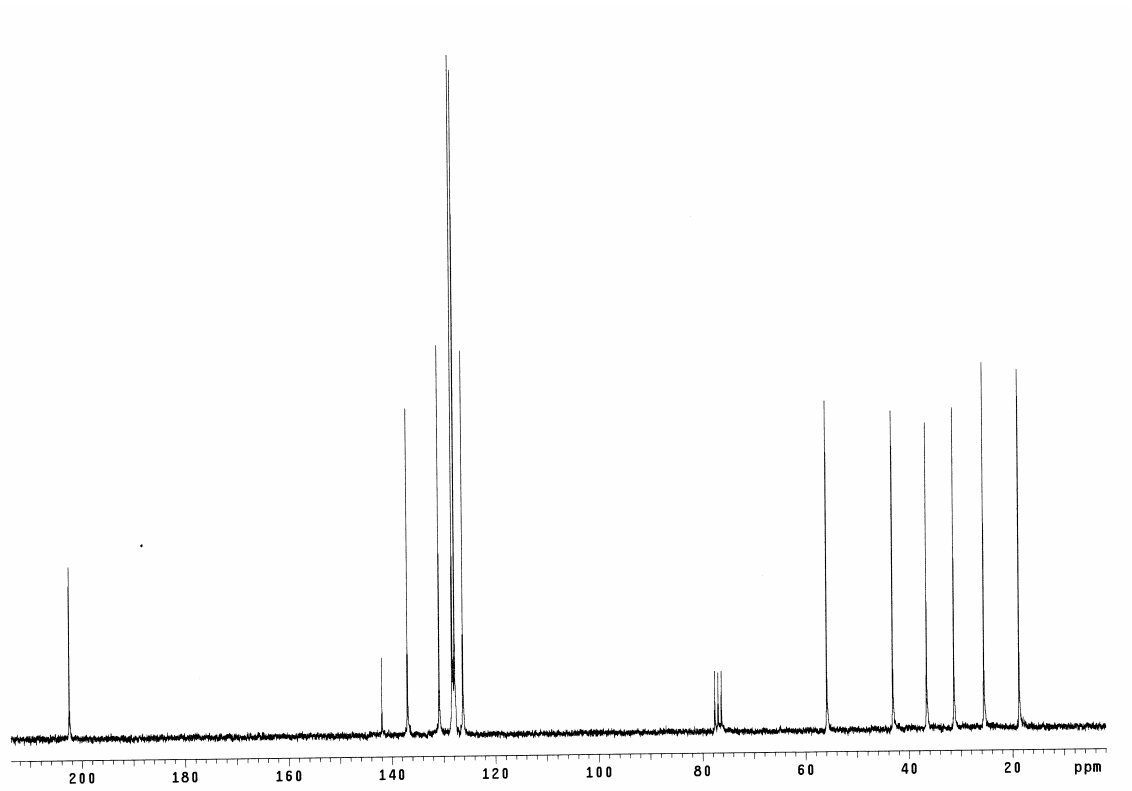
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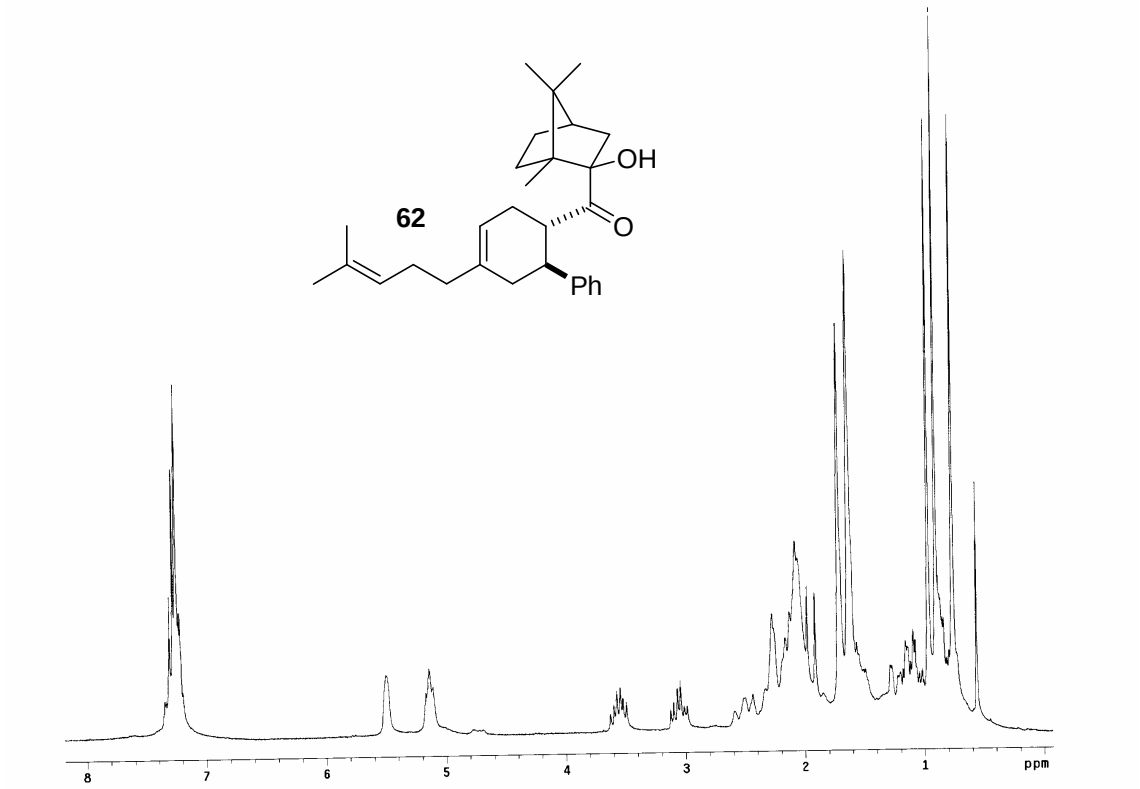
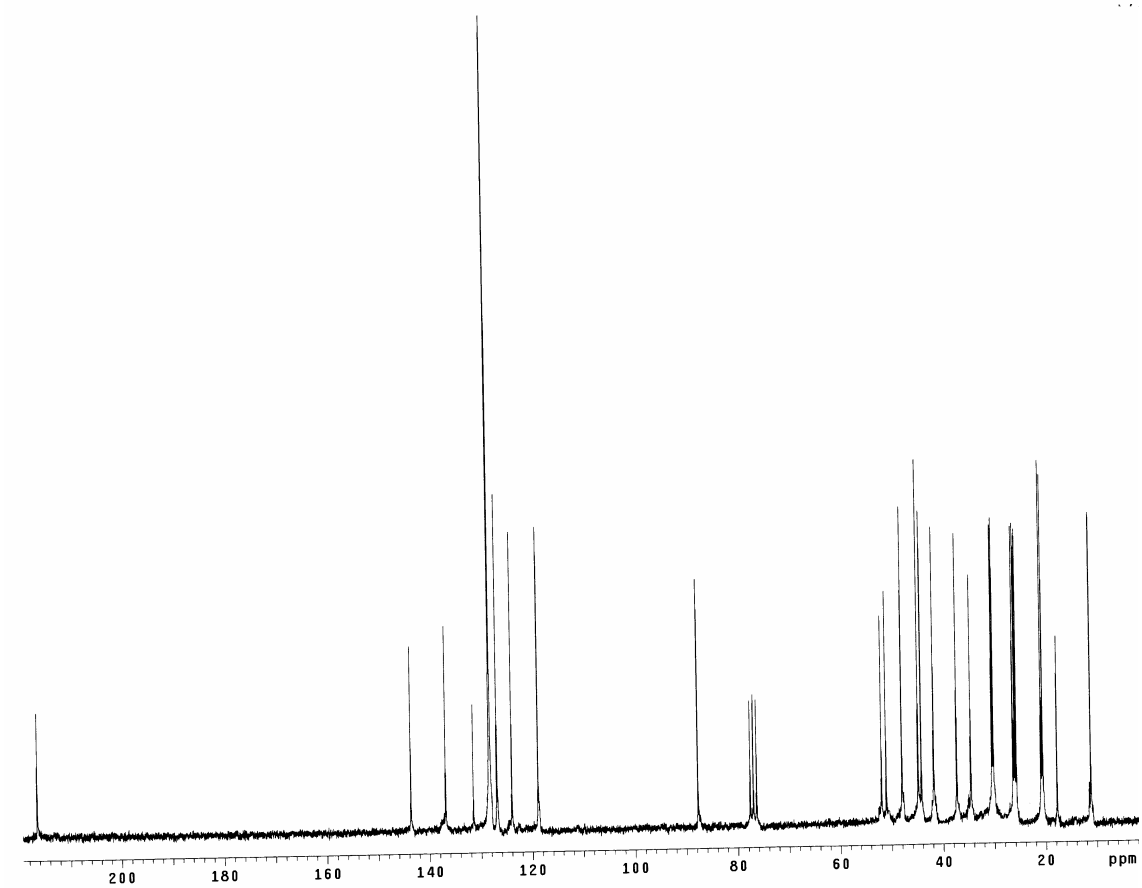
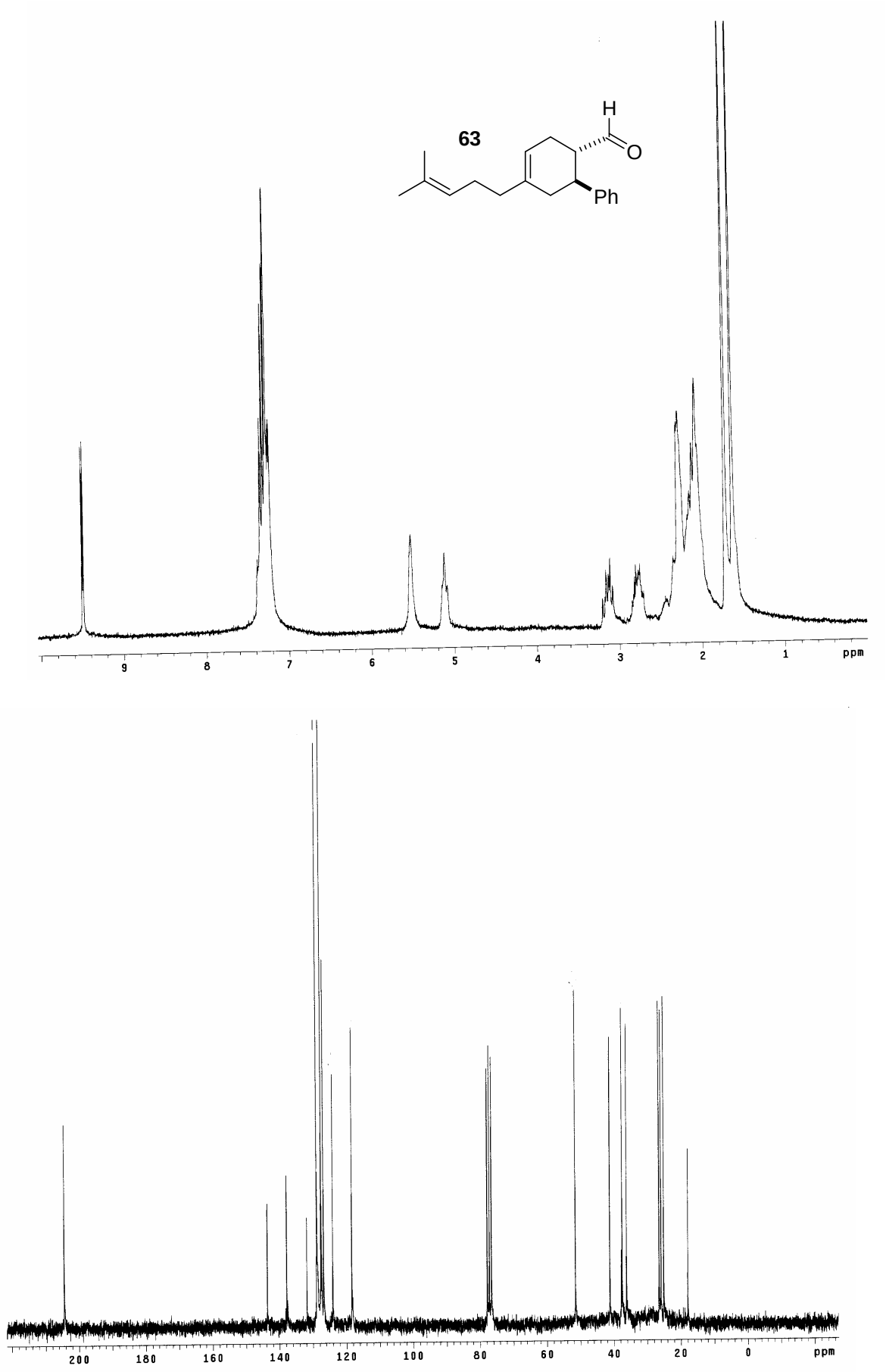



**62**


63
H
O
Ph
9
8
7
6
5
4
3
2
1
ppm
200
180
160
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120
100
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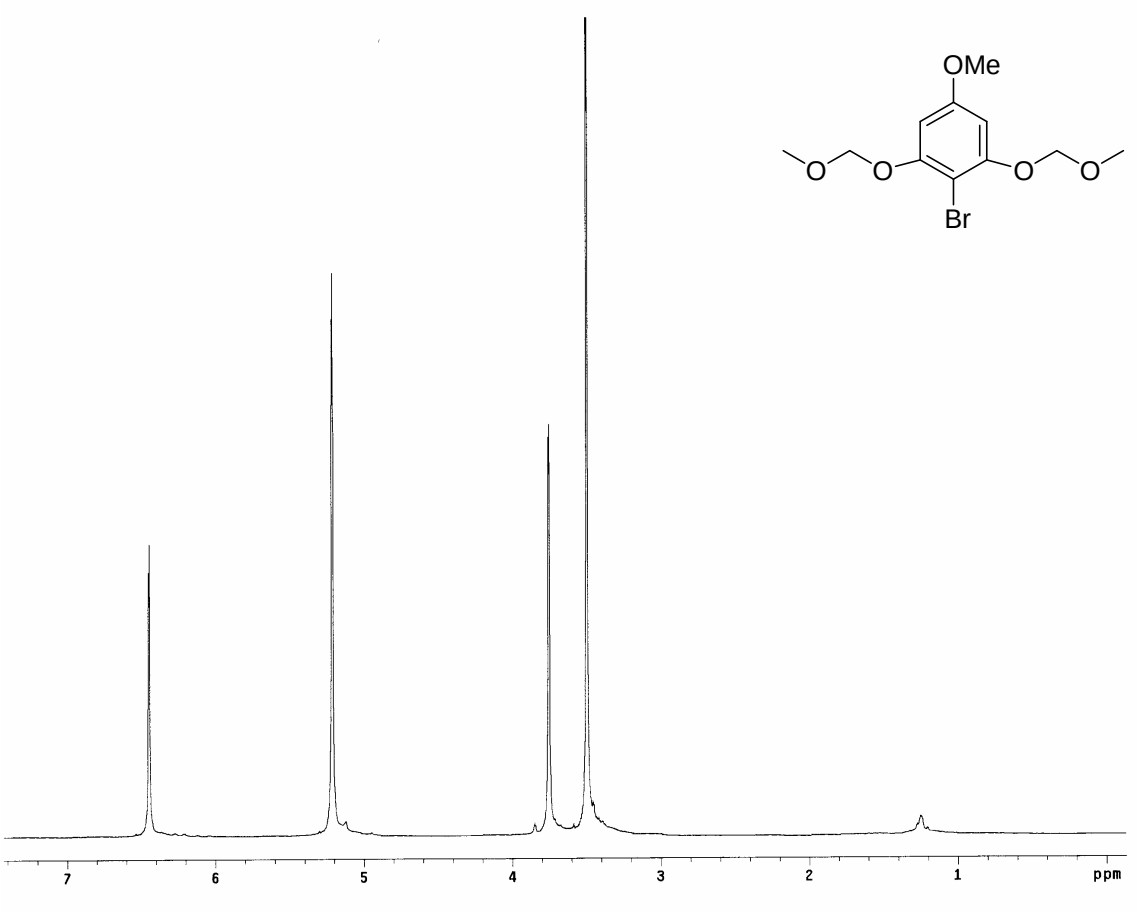
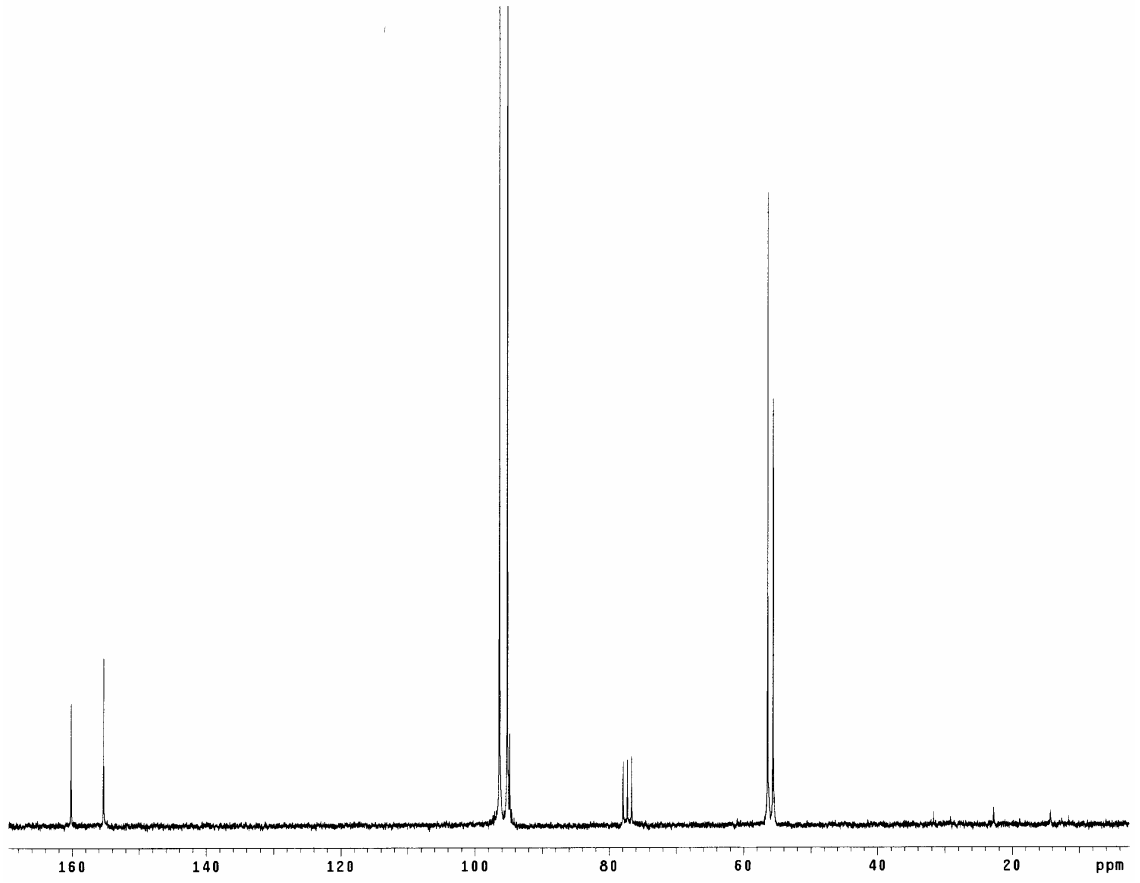
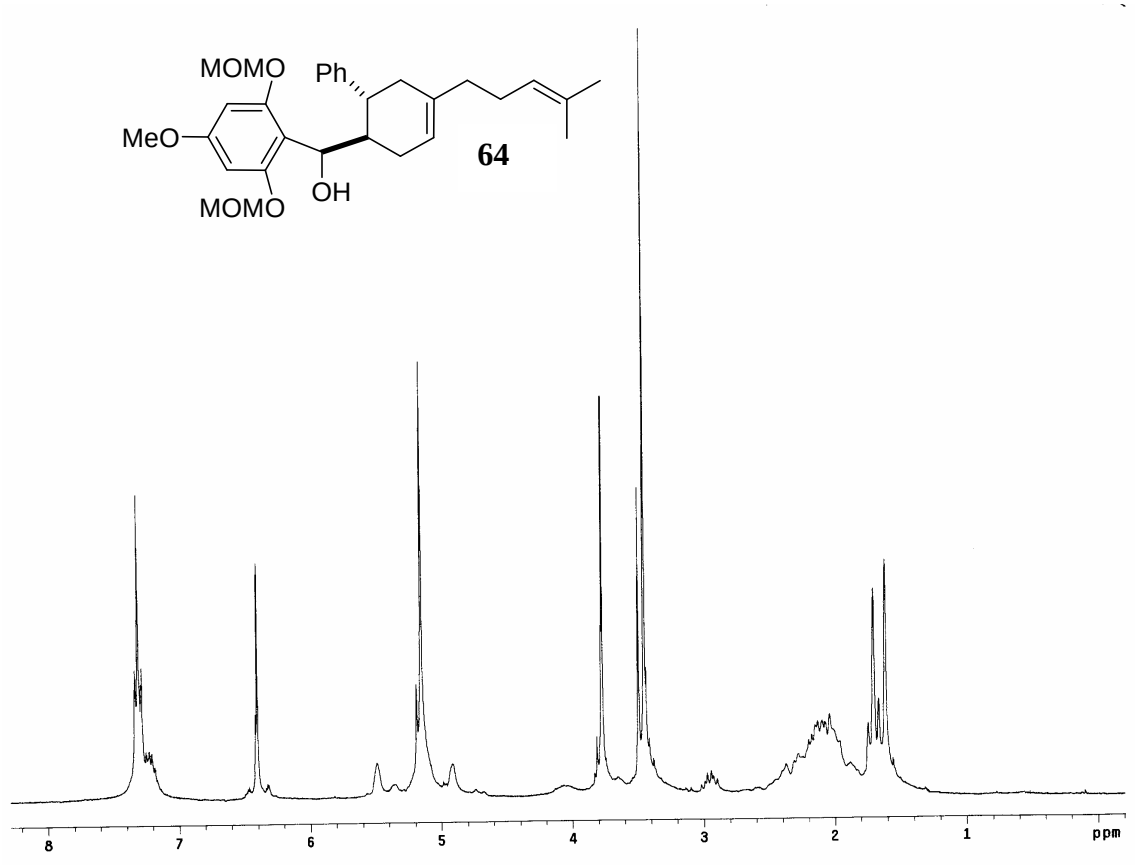
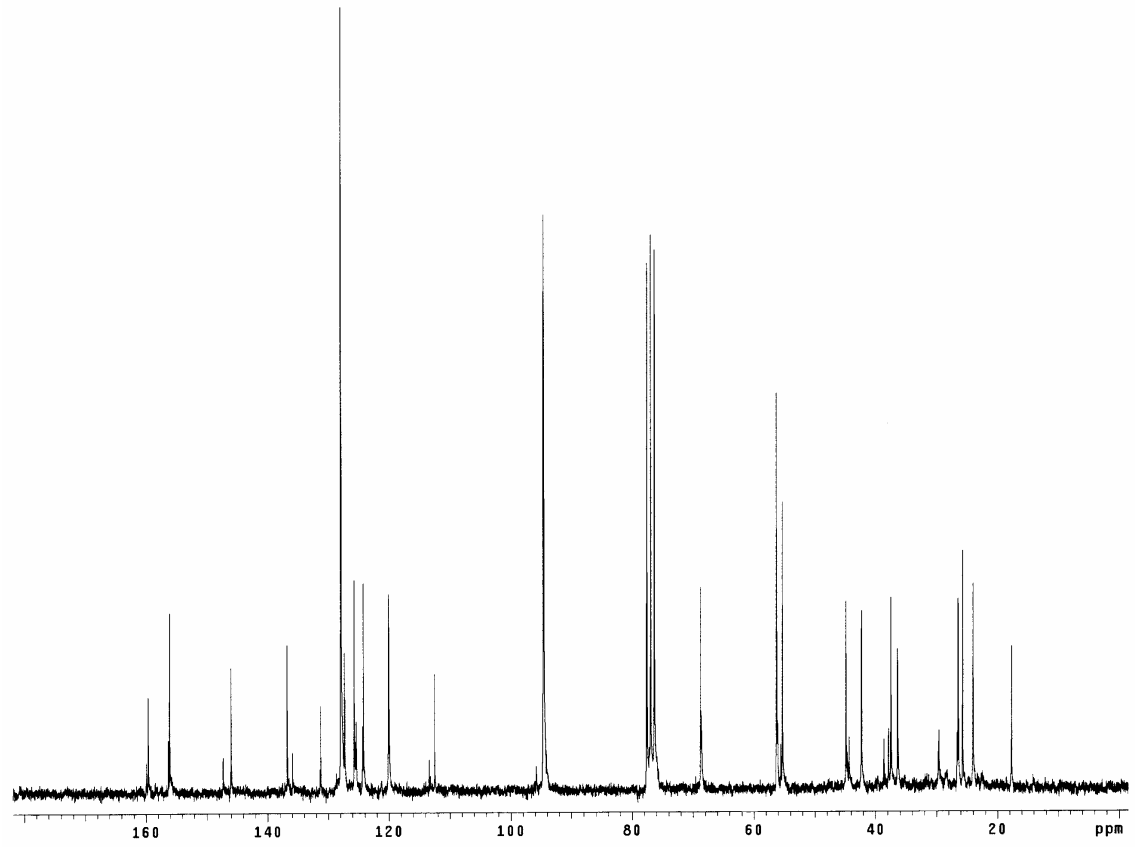
60
40
20
0
ppm


OMe
O
O
O
O
Br
7
6
5
4
3
2
1
ppm


160
140
120
100
80
60
40
20
ppm


MOMO
Ph
MeO
OH
MOMO
64
8
7
6
5
4
3
2
1
ppm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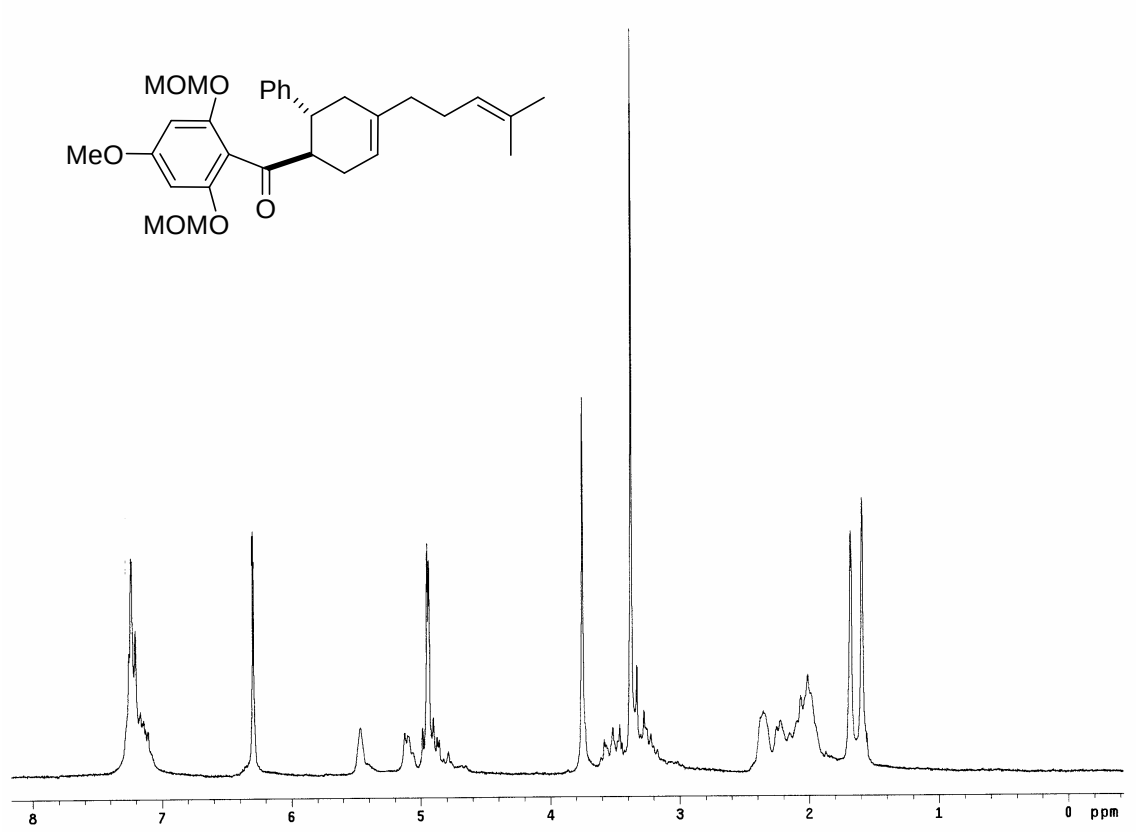
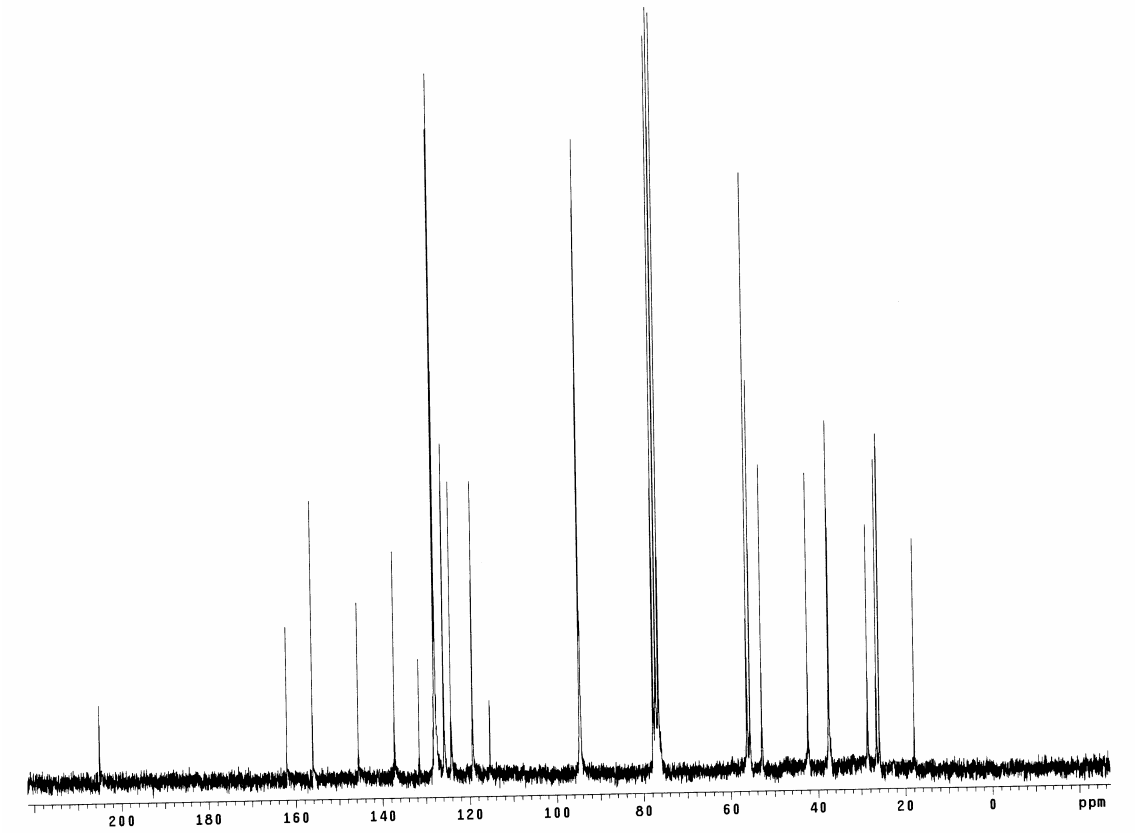
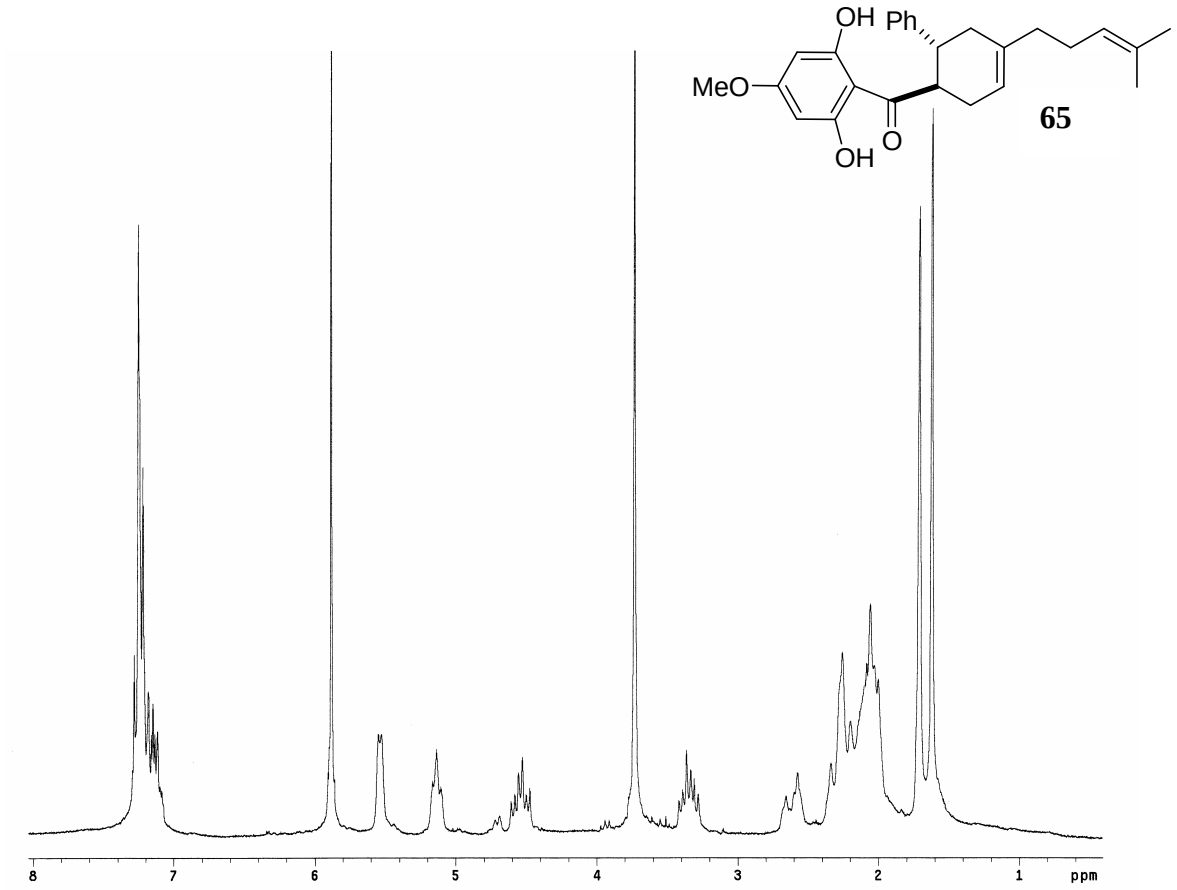
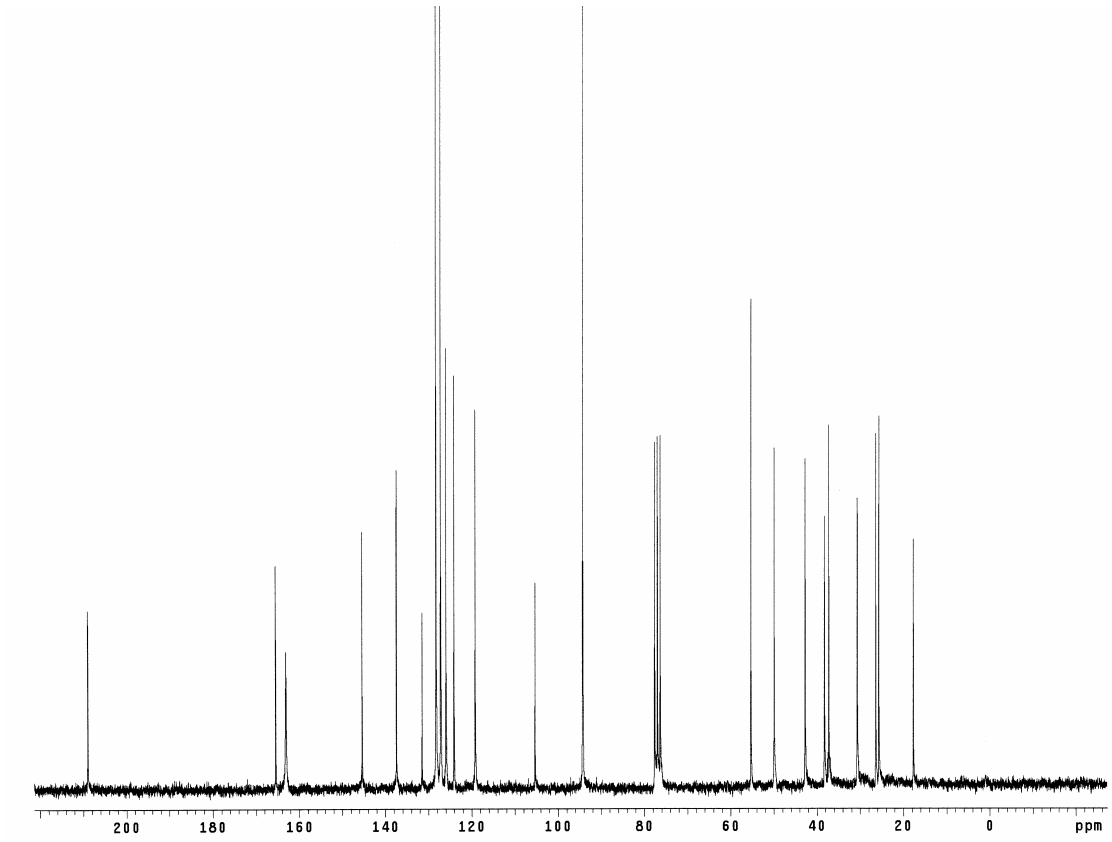
140
120
100
80
60
40
20
ppm


MOMO
Ph
MeO
O
MOMO
8
7
6
5
4
3
2
1
0 ppm


200
180
160
140
120
100
80
60
40
20
0
ppm


OH
Ph
MeO
O
OH
65
8
7
6
5
4
3
2
1
ppm


200
180
160
140
120
100
80
60
40
20
0
ppm