Supporting Information

Silver Nanoparticle-Catalyzed Diels-Alder Cycloadditions of 2'-Hydroxychalcones

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I. General Information

A. Instrumentation and methods

^{1}H NMR spectra were recorded at 400 or 500 MHz at ambient temperature with $CDCl_3$ (Cambridge Isotope Laboratories, Inc.) as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded at 100 MHz at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to $CDCl_3$ (^{1}H, δ 7.24; ^{13}C, δ 77.0). Data for ^{1}H NMR are reported as follows: chemical shift, integration, multiplicity (br = broad, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. All ^{13}C NMR spectra were recorded with complete proton decoupling. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. High-resolution mass spectra were obtained at the Boston University Chemical Instrumentation Center using a Waters Q-TOF mass spectrometer. Melting points were recorded on a Mel-temp apparatus (Laboratory Devices). Analytical liquid chromatography and quantitative kinetic monitoring were performed using a Waters ACQUITY UPLC® system equipped with PDA, ELS, and SQ detectors. Analytical thin layer chromatography (TLC) was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 200-400 mesh silica gel (Sorbent Technologies, Inc.). Preparative TLC was conducted with glass backed 250 μm or 1000 μm silica gel 60-F plates (Silicycle, Inc.) Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Diels-Alder reactions were conducted in Teflon® capped, heavy wall sealed vials (Chemglass CG-1880, 15 mL or CG-4920-01 Complete Package) to minimize solvent/reagent evaporation. All other reactions were carried out in oven-dried glassware under an argon/nitrogen atmosphere unless otherwise noted. The Arthur™ Suite Reaction Planner (Symyx Technologies, Inc.) was used for experimental procedure planning.

Transmission electron microscope (TEM) and energy-dispersive X-ray spectroscopy (EDS) were conducted at the Boston University Department of Biology using a JEOL 2010 TEM (operating at 80 kV), and at the MIT Center for Materials Science and Engineering (CMSE) using a JEOL 2010F TEM (operating at 200 kV) equipped with an Oxford Instruments INCA EDS system. Silver content of samples measured by inductively coupled plasma mass spectrometry (ICP-MS) was conducted at the Boston University Department of Earth Sciences using a VG Plasma Quad ExCell ICP-MS system. UV-Vis spectra were recorded using a Varian Cary 100 Bio UV-visible spectrophotometer under ambient conditions with a quartz cuvette (path length 1.0 cm). X-ray photoelectron spectroscopy (XPS) spectra were collected on a Kratos AXIS Ultra Imaging X-ray Photoelectron Spectrometer with monochromatic Al Kα X-ray source (Kratos Analytical, Inc.) at the MIT CMSE. A charge

neutralizer was employed during the XPS measurements. Electron paramagnetic resonance (EPR) spectra were conducted at the MIT Department of Chemistry using a Bruker EMX EPR spectrometer operating at 9.81 GHz and room temperature.

B. Chemical reagents and solvents

HPLC grade tetrahydrofuran, methylene chloride, diethyl ether, toluene, acetonitrile, and benzene were purchased from Fisher and VWR and were purified and dried by passing through a PURE SOLV® solvent purification system (Innovative Technology, Inc.). Silver salts and Bu_4NBH_4 were purchased from Aldrich. Silver powder (1-3 microns) was purchased from Strem Chemicals, Inc. Other reagents were purchased from Strem, Aldrich, Acros, TCI America, Indofine, and Alfa Aesar and were used as received. Chromatography grade silica gel (200-400 mesh) from Sorbent Technologies, Inc. was used as received for preparation of the supported AgNP catalyst.

II. Experimental Procedures and Compound Characterization

A. General experimental procedures for Diels-Alder cycloadditions*: In situ-generated AgNP catalyst:*

General condition A: To a reaction vial equipped with a stirbar were sequentially added $AgBF_4$ (5.8 mg, 0.03 mmol, 30 mol%), Bu_4NBH_4 (2.6 mg, 0.01 mmol, 10 mol%), and anhydrous CH_2Cl_2 (1.0 mL) in a N_2 glove box. To the resulting black suspension were added 2'-hydroxychalcone derivative (0.1 mmol, 1.0 equiv) and diene (4 – 22 equiv.). The vial was sealed with a Teflon® cap and removed from the glove box. After stirring under the conditions (temperature/time) as indicated in the manuscript and/or SI, the reaction mixture was directly concentrated *in vacuo*. Purification using silica gel or preparative TLC (hexane/ethyl acetate) afforded the Diels-Alder cycloadduct.

General condition B: To a reaction vial equipped with a stirbar were sequentially added $AgBF_4$ (11.7 mg, 0.06 mmol, 60 mol%), Bu_4NBH_4 (7.7 mg, 0.03 mmol, 30 mol%), and anhydrous CH_2Cl_2 (1.0 mL) in a N_2 glove box. To the resulting black suspension were added 2'-hydroxychalcone derivative (0.1 mmol, 1.0 equiv) and diene (4 – 22 equiv.). The vial was sealed with a Teflon® cap and removed from the glove box. After stirring under the conditions (temperature/time) as indicated in the manuscript and/or SI, the reaction mixture was directly concentrated *in vacuo*. Purification using silica gel or preparative TLC (hexane/ethyl acetate) afforded the Diels-Alder cycloadduct.
The *in situ*-generated AgNP's can be prepared in N_2-purged vials with equal catalytic

activities. Use of a glove box is not necessary. However, the highly hydroscopic compound Bu_4NBH_4 should better be stored and used in a glove box to extend its shelf life.

Preparation of an in situ-generated, catalytically active AgNP supernatant in CH_2Cl_2:
To a reaction vial equipped with a stirbar were sequentially added $AgBF_4$ (5.8 mg, 0.03 mmol), Bu_4NBH_4 (2.6 mg, 0.01 mmol), and anhydrous CH_2Cl_2 (1.0 mL) in a N_2 glove box. The vial was sealed with a Teflon® cap and removed from the glove box. After stirring at room temperature (25 ^oC) for 1 h, the vial was transferred into the glove box and opened. The clear supernatant was separated and collected by filtration through a short cotton plug.

Preparation of the silica-supported AgNP catalyst:[S1] To a reaction vial equipped with a stirbar were sequentially added $AgBF_4$ (29.2 mg, 0.15 mmol), Bu_4NBH_4 (12.9 mg, 0.05 mmol), and anhydrous CH_2Cl_2 (5.0 mL) in a N_2 glove box. The vial was sealed with a Teflon® cap and removed from the glove box. After stirring at room temperature (25 ^oC) for 1 h, the vial was opened to the air. The black precipitate contained in the vial was separated from the clear supernatant by filtration through a short cotton plug. Chromatography grade silica gel (500 mg) was added to the supernatant and stirred at room temperature (25 ^oC) for 3 h before the solid in the suspension was collected by filtration. The solid was then dried at 220 ^oC for 2 h in air followed by at 220 ^oC for 10 h under vacuum to afford the silica-supported AgNP catalyst as a fine, light brown powder (***Figure S5***). The silver content was determined by ICP-MS to be $2.7\pm0.6 \times 10^2$ ppm (0.27 μg Ag per 1 mg of supported catalyst).

Silica-supported AgNP catalyst:

General condition C: To a reaction vial equipped with a stirbar were added silica-supported AgNP catalyst (100 mg, containing 27 μg Ag, 0.25 mol%), 2'-hydroxychalcone (0.1 mmol, 1.0 equiv), diene (4 – 22 equiv.), and CH_2Cl_2 (1.0 mL, ACS grade) in air. The vial was sealed with a Teflon® cap. After stirring under the conditions (temperature/time) as indicated in the manuscript and/or SI, the reaction mixture was filtered and concentrated *in vacuo*. Purification using silica gel or preparative TLC (hexane: ethyl acetate) afforded the Diels-Alder cycloadduct.

Recycling the silica-supported AgNP catalyst:
At the workup step of general condition C, silica-supported AgNP catalyst was separated and collected by filtration. The recovered catalyst was washed with EtOAc and dried under vacuum for 2 h prior to the next use (according to general condition C).

B. Characterization of AgNP catalysts

[S1] Zheng, N.; Stucky, G. D. *J. Am. Chem. Soc.* **2006**, *128*, 14278–14280.

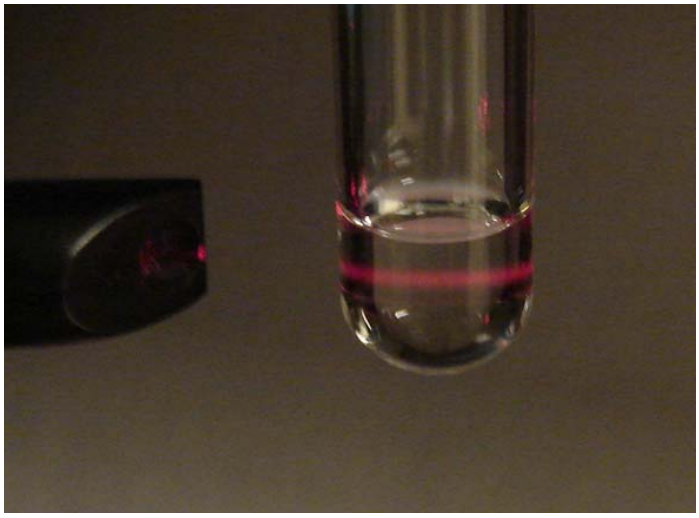


Figure S1. Tyndall effect of the catalytically active supernatant (prepared from 3:1 $AgBF_4/Bu_4NBH_4$ following the procedure described in Section II-A) under a laser beam, suggesting the presence of *in situ*-generated AgNP's.

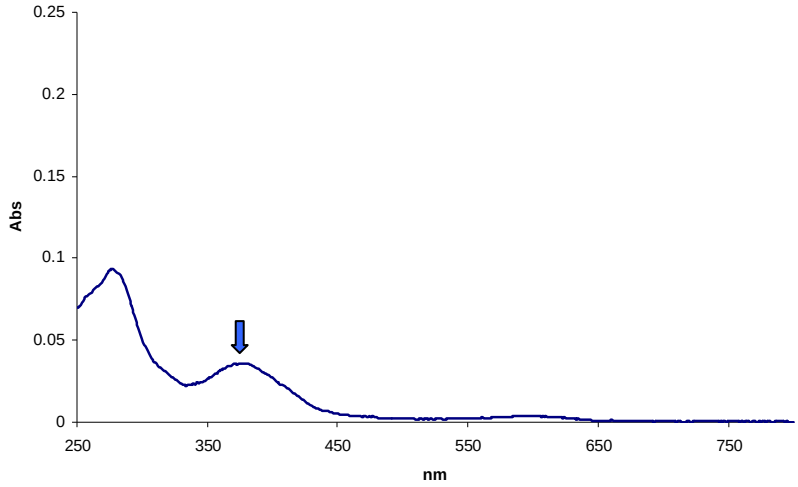


Figure S2. UV-Vis spectrum of the catalytically active supernatant (prepared from 3:1 $AgBF_4/Bu_4NBH_4$ following the procedure described in Section II-A) showing a plasmon resonance absorption (λ_{max} = 381 nm) which is consistent with literature reported data for AgNP's.[S2] The test sample was diluted five times with CH_2Cl_2 prior to analysis.

[S2] Evanoff, D. D., Jr.; Chumanov, G. *ChemPhysChem* **2005**, *6*, 1221–1231.

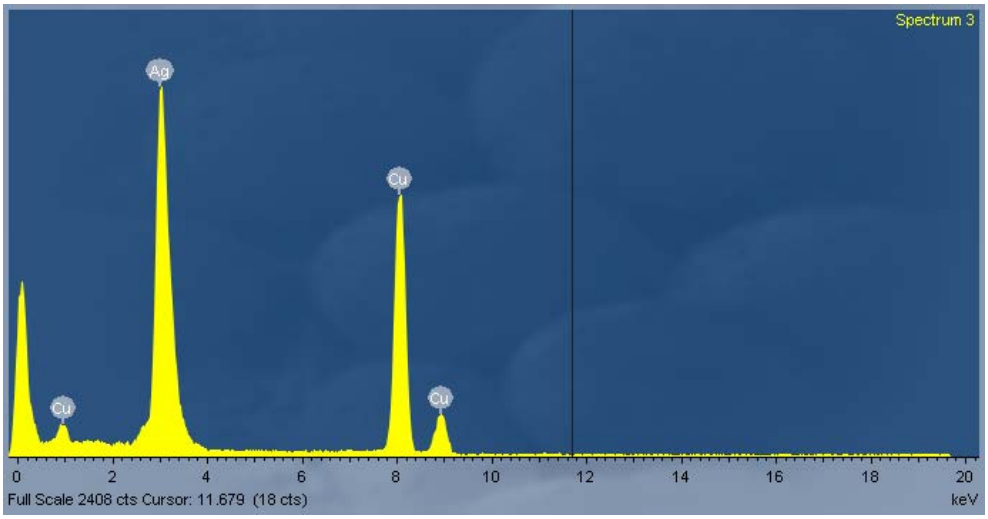


Figure S3. Representative EDS spectrum of the *in situ*-generated AgNP catalyst (prepared from 3:1 $AgBF_4/Bu_4NBH_4$). Analysis was conducted on a carbon-coated copper TEM grid.

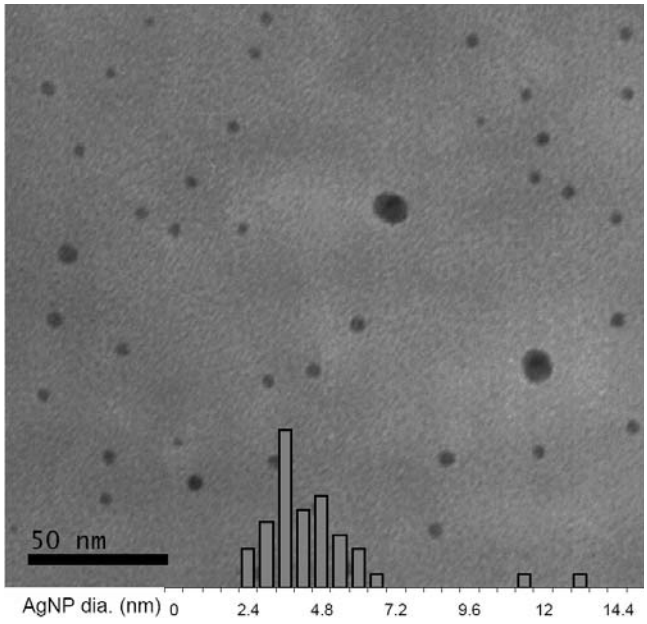


Figure S4. TEM image with particle size distribution histogram of AgNP catalyst generated *in situ* from 2:1 $AgBF_4/Bu_4NBH_4$ showing an average particle size of 4.5 nm. (Corresponding to general condition B described in Section II-A, *cf.* Table S2)

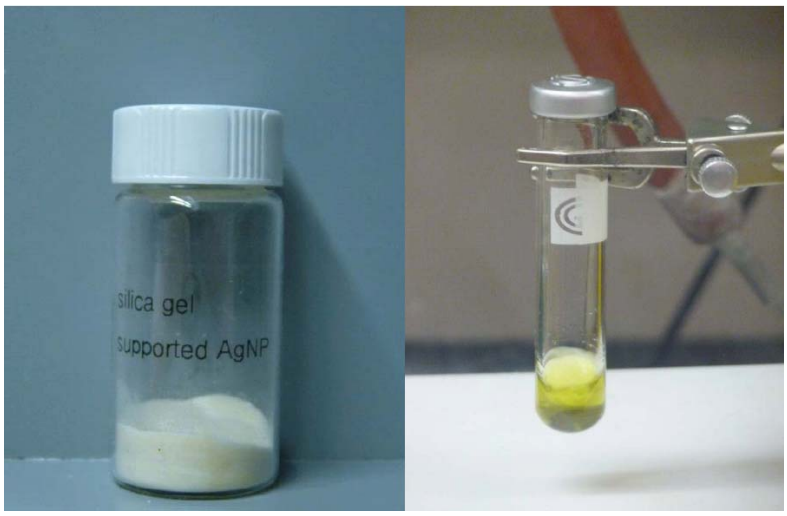
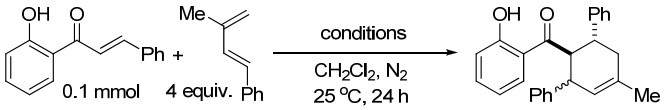


Figure S5. Left: silica-supported AgNP catalyst. Right: A typical cycloaddition reaction catalyzed by silica-supported AgNP catalyst.

C. Additional experiments

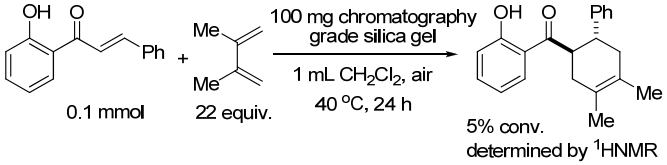
Table S1. Control experiments showing that μm-sized silver clusters are inactive.



condition	conv.
60 mol% Ag powder[a]	<2% (no product observed)
60 mol% Ag powder[a], 60 mol% Bu_4NBF_4	<2% (no product observed)

[a]Commercially available Ag powder (1-3 microns) was washed with 3 M HNO_3, water, and acetone (three times each), then dried under vacuum for overnight prior to use.

Scheme S1. Control experiments showing that silica gel is inactive.



Scheme S2. Catalyst filtration experiment.

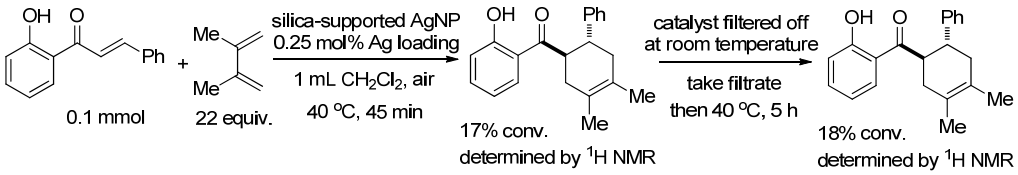
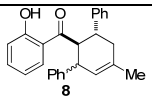
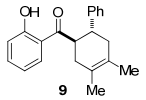
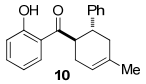
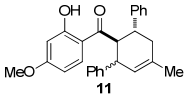
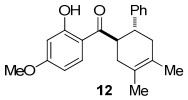
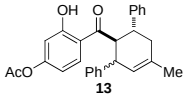
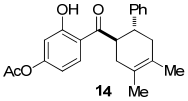
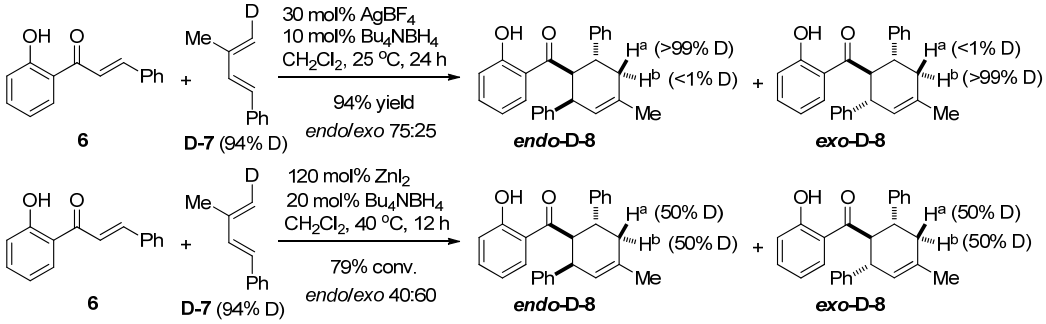


Table S2. Substrate scope using the *in situ* generated AgNP catalyst.

entry	product	condition	yield(%)[a]
1	 **8**	Gen. condition A, 25 °C, 24 h	98(75:25)
2	 **9**	Gen. condition A, 40 °C, 24 h	96
3	 **10**	Gen. condition A, 40 °C, 24 h	92
4	 **11**	Gen. condition B, 40 °C, 36 h	63(83:17)
5	 **12**	Gen. condition B, 40 °C, 36 h	65
6	 **13**	Gen. condition B, 40 °C, 36 h	74(74:26)
7	 **14**	Gen. condition B, 40 °C, 36 h	85

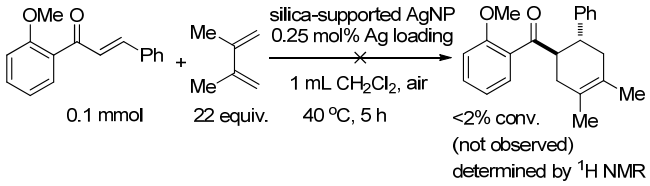
[a]Isolated yields are shown with *endo/exo* ratio in parentheses. A single regioisomer was observed for unsymmetrical dienes.

Scheme S3. Cycloadditions using a deuterium-labeled diene.[a]

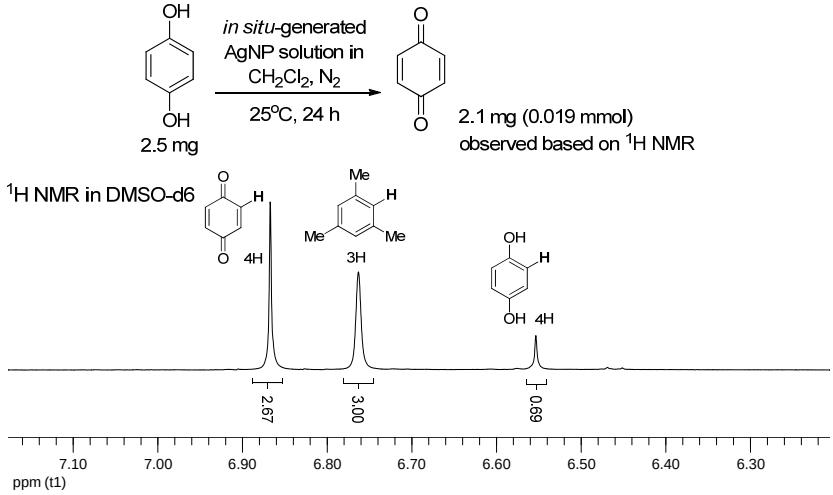


[a]Isolated cycloadducts contained a trace amount of **3** (less than 10%) due to the presence of approximately 6% non-deuterium-labeled diene in starting material **D-2**.

Scheme S4. Cycloadditions using 2'-methoxychalcone as a dienophile.



Scheme S5. Converting *p*-hydroquinone to *p*-benzoquinone using an *in situ*-generated AgNP solution in the absence of an external oxidant.



To a reaction vial equipped with a stirbar were added an *in situ*-generated solution of AgNP's in CH_2Cl_2 (27 mL, prepared from 3:1 $AgBF_4/Bu_4NBH_4$ following the procedure described in Section II-A) and *p*-hydroquinone (2.5 mg, 0.022 mmol) in a N_2 glove box. The vial was sealed with a Teflon® cap and removed from the glove box. After stirring at room temperature (25 °C) for 24 h, the reaction mixture was directly concentrated *in vacuo*. The presence and quantity of the oxidized product *p*-benzoquinone was determined by ^{1}H NMR analysis immediately (within 15 min) using DMSO-d6 as a solvent and mesitylene as internal standard. The reaction mixture was kept under a N_2 atmosphere during the entire experiment. ^{1}H NMR (500 MHz, DMSO-d6): *p*-hydroquinone δ 8.60 (2H, s), 6.55 (4H, s); *p*-benzoquinone δ 6.87 (4H, s); mesitylene δ 6.77 (3H, s), 2.21 (9H, s).

Control experiments conducted under air with otherwise identical conditions afforded comparable conversion as under nitrogen. Control experiments conducted without AgNP's (in CH_2Cl_2, solvent only) failed to afford *p*-benzoquinone either under N_2 or air.

Based on the above experiments, the partial conversion observed for *p*-hydroquinone to *p*-benzoquinone supports the oxidative properties of the *in situ*-generated AgNP's which in this case may serve as a stoichiometric oxidant. Based on our previous ICP-MS data, 1 mL of the AgNP solution contains approximately ~150 μg of Ag. Accordingly, our rough estimate is that 27 mL of the AgNP solution may contain 4.1 mg Ag (0.038 mmol) which led to the

production of 2.1 mg (0.019 mmol) of *p*-benzoquinone from 2.5 mg (0.022 mmol) of *p*-hydroquinone (Scheme S5).

D. Preliminary kinetic studies

General experimental procedures for kinetic measurements: To a reaction vial equipped with a stirbar were added the silica-supported AgNP catalyst (100.0 ± 0.5 mg, containing 27 μg Ag), 2'-hydroxychalcone (0.025-0.2 mmol), 4,4'-di-*tert*-butylbiphenyl (internal standard, 3.5 mg), and CH_2Cl_2 (ACS grade) in air. The mixture was stirred for 10 seconds before 2,3-dimethylbutadiene (25-250 μL) was injected to initiate the reaction. The vial was quickly sealed with a Teflon® septum and was vigorously stirred. Test samples were taken using a clean microliter syringe at the recorded time (10-15 μL aliquot each time) and were quickly transferred to a clean, dry 2 mL HPLC vial. The solvent and the remaining diene in the test sample were evaporated immediately under a strong flow of compressed air to terminate the reaction. The vial was then added 1 mL of CH_3CN, sealed and kept at -20°C, and analyzed by UPLC. At least five test samples were taken for each reaction before the overall conversion reached 10%. The initial rates of reactions were determined by measuring the change of the concentration of cycloadduct as a function of reaction time.

E. UV-Vis absorbance measurements

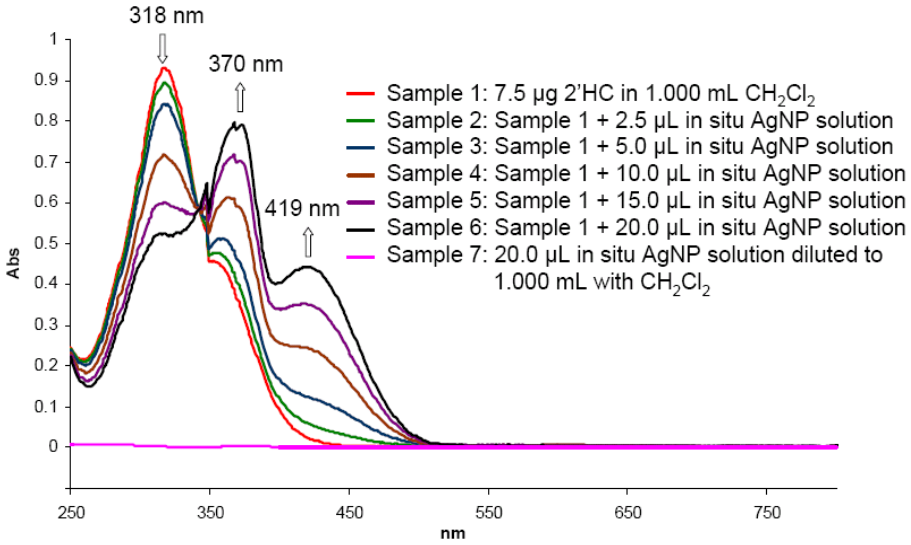


Figure S6. UV-Vis spectra of 2'-hydroxychalcone (2'HC) in the presence of various amounts of the *in situ*-generated AgNP's in CH_2Cl_2 (prepared from 3:1 $AgBF_4/Bu_4NBH_4$ following the procedure described in Section II-A). The arrows indicate the direction of the spectral changes with the addition of AgNP solution.

As shown in ***Figure S6***, the contribution of the AgNP surface plasmon resonance (Sample 7)

to the UV-Vis absorption related to the 2'-hydroxychalcone is negligible under the experimental conditions. Upon sequential addition of the AgNP solution, the changes of the UV-Vis absorption are due to interactions between 2'-hydroxychalcone and AgNP. The new absorption bands at 370 nm and 419 nm result from red-shifting of the original chalcone absorption at 318 nm and ~350 nm (shoulder), respectively. Control experiments showed that the adsorption spectrum of 2'-hydroxychalcone did not change upon addition of $AgBF_4$ solution in CH_2Cl_2. Overall, the observed absorption changes are consistent with literature results on the adsorption of small organic molecules to nanoparticles.[S3]

F. XPS measurements of the silica-supported AgNP catalyst

In order to shorten the XPS collection time, the silica-supported AgNP sample for XPS measurements was prepared with a higher silver loading following the procedure described in Section II-A. Details are provided below.

To a reaction vial equipped with a stirbar were added sequentially $AgBF_4$ (29.2 mg, 0.15 mmol), Bu_4NBH_4 (12.9 mg, 0.05 mmol), and anhydrous CH_2Cl_2 (5.0 mL) in a N_2 glove box. The vial was sealed with a Teflon® cap and removed from the glove box. After stirring at room temperature (25 °C) for 1 h, the vial was opened to the air. The black precipitate contained in the vial was separated from the clear supernatant by filtration through a short cotton plug. Chromatography grade silica gel (50 mg) was added to the supernatant and stirred at room temperature (25 °C) for 3 h before the solid in the suspension was collected by filtration. The solid was then dried at 220 °C for 2 h in air followed by at 220 °C for 10 h under vacuum to afford the silica-supported AgNP catalyst as a fine, brown powder.

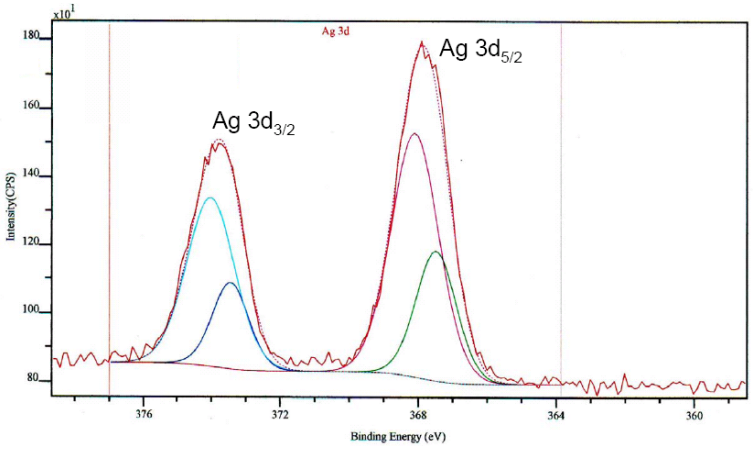


Figure S7. XPS spectrum for Ag 3d peaks.

[S3] (a) Lim, I. S.; Goroleski, F.; Mott, D.; Kariuki, N.; Ip, W.; Luo, J.; Zhong, C.-J. *J. Phys. Chem. B* **2006**, *110*, 6673–6682. (b) Nawrocka, A.; Krawczyk, S. *J. Phys. Chem. A* **2008**, *112*, 10233–10241.

Table S3. XPS data for Ag $3d_{5/2}$ peaks.

sample	BE $3d_{5/2}$ (eV)	area %
Ag (standard)	368.2	----
Ag_2O (standard)	367.6	----
AgNP sample	367.8	100
fitted curves	368.1	72
	367.5	28

All binding energies (BE) were calibrated using the Si 2p peak (silica gel, 103.4 eV) as an internal standard. The high resolution data was collected using a pass energy of 20 eV with a takeoff angle of 0^o. The binding energies for the Ag $3d_{5/2}$ peak of the test sample (367.8 eV) are between the standard values for Ag(0) and Ag(I) oxidation states (Comprehensive XPS data can be found at NIST XPS database: http://srdata.nist.gov/xps/intro.aspx and literature reports.[S4] We choose average BE values for metallic silver and Ag_2O as standards to determine the relative compositions of Ag(0) and Ag(I), respectively. See ***Figure S7*** and ***Table S3***). Curve fitting of the Ag $3d_{5/2}$ peak shows that the supported AgNP's are composed of approx. 70% Ag(0) and 30% Ag(I).

G. Electron paramagnetic resonance (EPR) spin trapping measurements

The samples for EPR measurements were prepared in a nitrogen-filled, dry glove box using dry, deoxygenated methylene chloride (distilled over CaH_2) at 25 ^oC. The EPR spectrometer settings were as follows: modulation frequency, 100 kHz; modulation amplitude, 2.0 G; microwave power, 40 mW; receiver gain, 5.02e+4; time constant, 10.240 ms; conversion time, 20.48 ms; magnetic field scan 150 G. Simulations were conducted using WinSim (http://www.niehs.nih.gov/research/resources/software/tools/index.cfm), a free software from the National Institute of Environmental Health Sciences (NIEHS).

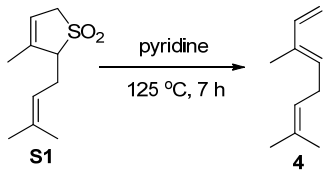
H. Preparation of substrates

1-Phenyl-3-methylbutadiene **7**,[S5] acetylated chalcones,[S6] and deuterium-labeled diene **D-7**[S7] were prepared according to literature procedures.

[S4] Select references: (a) Bielmann, M.; Schwaller, P.; Ruffieux, P.; Groning, O.; Schlapbach, L.;. Groning, P. *Phys. Rev. B* **2002**, *65*, 235431. (b) G. I. N. Waterhouse, G. A. Bowmaker, J. B. Metson, *Appl. Surf. Sci.* **2001**, *183*, 191–204. (c) Chaki, N. K.; Sharma, J.; Mandle, A. B.; Mulla, I. S.; Pasricha, R.; Vijayamohanan, K. *Phys. Chem. Chem. Phys.* **2004**, *6*, 1304–1309. (d) Erol, M.; Han, Y.; Stanley, S. K.; Stafford, C. M.; Du, H.; Sukhishvili. S. *J. Am. Soc. Chem.* **2009**, *131*, 7480–7481.

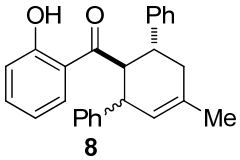
[S5] Lebel, H.; Guay, D.; Paquet, V.; Huard, K. *Org. Lett.* **2004**, *6*, 3047–3050. We utilized method F in the Supporting Information for preparation of **7**.

[S6] Cong, H.; Ledbetter, D.; Rowe, G. T.; Caradonna, J. P.; Porco, J. A. Jr., *J. Am. Soc. Chem.* **2008**, *130*, 9214–9215.



***Trans*-β-ocimene (4).** To a reaction vial equipped with a stirbar were added sulfone **S1**[S8] (215 mg, 1.07 mmol) and anhydrous pyridine (2.0 mL) in air and the vial was sealed with a Teflon® cap. After stirred at 125 °C for 7 h, the reaction mixture was cooled and transferred with the aid of 10 mL pentane to a separation funnel containing 20 mL 0.05 M HCl. The aqueous layer was further extracted with 2 x 5 mL pentane. The combined organic phase was washed twice with saturated aq. $CuSO_4$ and twice with brine. The organic phase was then filtered through a short silica gel pad with the aid of pentane. The combined pentane solution was carefully concentrated *in vacuo* to afford **4** (125 mg, 85%) as a colorless oil. Characterization data were identical with those reported in the literature.[S9]

I. Preparation of Diels-Alder cycloadducts



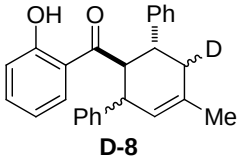
Diels-Alder cycloadduct 8.[S6]

In situ-generated AgNP catalyst: Prepared using general condition A at 25 °C for 24 h employing 22.2 mg (0.099 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (5% CH_2Cl_2 in hexane followed by 2% EtOAc in hexane), the desired cycloadduct **8** (35.8 mg, 98%) was isolated as a white solid and was shown to be a single regioisomer and 3.0/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

Silica-supported AgNP catalyst: Prepared using general condition C at 25 °C for 5 h employing 22.1 mg (0.099 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **8** (35.2 mg, 96%) was isolated as a white solid and was shown to be a single regioisomer and 2.0/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

[S7] Herndon, J. W.; Hill, D. K.; McMullen, L. *Tetrahedron Lett.* **1995**, *36*, 5687–5690.
[S8] Desai, S. R.; Gore, V. K.; Bhat, S. V. *Synth. Commun.* **1990**, *20*, 523–533.
[S9] (a) Chou, T.-S.; Tso, H.-H.; Chang, L.-J. *J. Chem. Soc. Chem., Comm.* **1984**, 1323–1324. (b) Tanaka, S.; Yasuda, A.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1975**, *97*, 3252–3254.

A pure sample of each diastereomer was obtained by further separation using preparative TLC (5% EtOAc in hexane). Characterization data were identical with those reported in the literature.[S6]



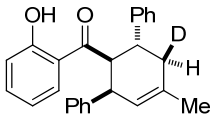
D-8

Deuterio-Diels-Alder cycloadduct D-8.

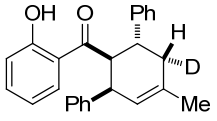
In situ-generated AgNP catalyst: Prepared using general condition A at 25 °C for 24 h employing 21.4 mg (0.096 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 55 mg (0.38 mmol, 4 equiv.) of deuterium-labeled diene **D-7** (94% D). After chromatography on silica gel (5% CH_2Cl_2 in hexane followed by 2% EtOAc in hexane), the desired cycloadduct **D-8** (33.1 mg, 94%) was isolated as a white solid and was shown to be a single regioisomer and 3.0/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

Silica-supported AgNP catalyst: Prepared using general condition C at 25 °C for 5 h employing 21.8 mg (0.097 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 55 mg (0.38 mmol, 4 equiv.) of deuterium-labeled diene **D-7** (94% D). After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **D-8** (34.8 mg, 97%) was isolated as a white solid and was shown to be a single regioisomer and 1.9/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

A pure sample of each diastereomer was obtained by further separation using preparative TLC (5% EtOAc in hexane).



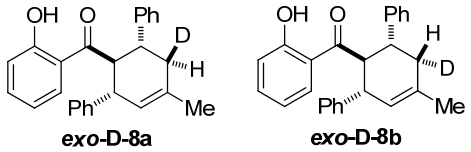
***endo*-D-8a**



***endo*-D-8b**

The deuterio-*endo* isomer from both conditions above afforded exclusively ***endo*-D-8a**, with no ***endo*-D-8b** observed based on ^{1}H NMR. Isolated *endo* isomer contained trace amount of *endo*-**8** (less than 10%) due to the 6% non-deuterium-labeled diene in starting material **D-7**.

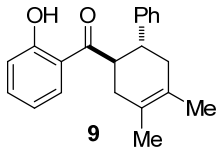
***endo*-D-8a**: white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.77 (1H, s), 8.01 (1H, d, J = 8.0 Hz, 1.2 Hz), 7.46 (1H, ddd, J = 7.8 Hz, 7.8 Hz, 1.6 Hz), 7.15-7.20 (7H, m), 7.07 (1H, m), 6.96 (1H, dd, J = 7.6 Hz, 7.6 Hz), 6.88 (3H, m), 5.57 (1H, br, s), 4.44 (1H, dd, J = 11.2 Hz, 5.6 Hz), 4.00 (1H, br, m), 3.44 (1H, dd, J = 11.4 Hz, 11.4 Hz), 2.24 (1H, d, J = 11.2 Hz), 1.85 (3H, s); HRMS (ESI+) m/z calculated for $C_{26}H_{24}DO_2$ ($M + H^+$) 370.1912, found 370.1939.



***exo*-D-8a** ***exo*-D-8b**

The deuterio-*exo* isomer from both conditions above afforded exclusively ***exo*-D-8b**, with no ***exo*-D-8a** observed based on ^{1}H NMR. Isolated *exo* isomer contained trace amount of *exo*-**8** (less than 10%) due to the 6% non-deuterium-labeled diene in starting material **D-7**.

exo-D-8b: white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.18 (1H, s), 6.95-7.13 (12H, m), 6.59 (1H, dd, *J* = 8.4 Hz, 0.8 Hz), 6.40 (1H, dd, *J* = 7.2 Hz, 7.2 Hz), 5.53 (1H, br, s), 3.89 (1H, m); 3.84 (1H, dd, *J* = 10.6 Hz, 10.6 Hz), 3.44 (1H, dd, *J* = 10.4 Hz, 5.2 Hz), 2.32 (1H, br), 1.82 (3H, s); HRMS (ESI+) m/z calculated for $C_{26}H_{24}DO_2$ ($M + H^+$) 370.1912, found 370.1935.

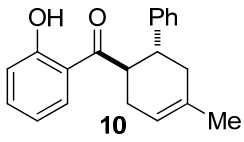


9

Diels-Alder cycloadduct 9.[S6]

In situ-generated AgNP catalyst: Prepared using general condition A at 40 °C for 24 h employing 21.9 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 250 μL (2.2 mmol, 22 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **9** (28.7 mg, 96%) was isolated as a light yellow oil. Characterization data were identical with those reported in the literature.[S6]

Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 5 h employing 22.0 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 250 μL (2.2 mmol, 22 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **9** (28.6 mg, 95%) was isolated as a light yellow oil. Characterization data were identical with those reported in the literature.[S6]



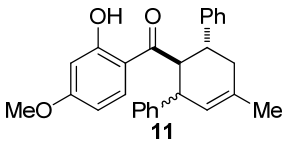
10

Diels-Alder cycloadduct 10.[S6]

In-situ generated AgNP catalyst: Prepared using general condition A at 40 °C for 24 h employing 22.1 mg (0.099 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 250 μL (2.5 mmol, 25 equiv.) of isoprene. After chromatography on silica gel (5% CH_2Cl_2 in hexane), the desired cycloadduct **10** (26.4 mg, 92%) was isolated as a light yellow solid and as a single regioisomer. Characterization data were identical with those reported in the literature.[S6]

Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 10 h employing 22.4 mg (0.10 mmol, 1.0 equiv.) of 2'-hydroxychalcone and 250 μL (2.5 mmol, 25 equiv.) of isoprene. After chromatography on silica gel (2% EtOAc in hexane), the desired

cycloadduct **10** (28.0 mg, 96%) was isolated as a light yellow solid and as a single regioisomer. Characterization data were identical with those reported in the literature.[S6]



11

Diels-Alder cycloadduct 11.

In situ-generated AgNP catalyst: Prepared using general condition B at 40 °C for 36 h employing 25.7 mg (0.101 mmol, 1.0 equiv.) of 2'-hydroxy-4'-methoxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (5% CH_2Cl_2 in hexane followed by 2% EtOAc in hexane), the desired cycloadduct **11** (25.3 mg, 63%) was isolated as a white solid and was shown to be a single regioisomer and 4.9/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

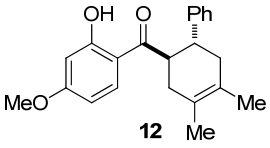
Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 18 h employing 24.8 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxy-4'-methoxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **11** (37.2 mg, 96%) was isolated as a white solid and was shown to be a single regioisomer and 2.0/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

A pure sample of each diastereomer was obtained by further separation using preparative TLC (5% EtOAc in hexane).

***endo*-11**: white solid. mp: 108-110°C; R_f: 0.54 (20% EtOAc in hexane);
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.30 (1H, s), 7.90 (1H, d, *J* = 8.8 Hz), 7.12-7.20 (7H, m), 7.04-7.08 (1H, m), 6.89 (2H, m), 6.50 (1H, dd, *J* = 8.8 Hz, 2.4 Hz), 6.33 (1H, d, *J* = 2.4 Hz), 5.56 (1H, br), 4.31 (1H, dd, *J* = 11.6 Hz, 5.6 Hz), 3.94 (1H, br), 3.82 (3H, s), 3.42 (1H, ddd, *J* = 11.6 Hz, 11.6 Hz, 6.0 Hz), 2.47 (1H, dd, *J* = 18.0 Hz, 5.6 Hz), 2.25 (1H, dd, *J* = 18.4 Hz, 12.0 Hz), 1.83 (3H, s); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 204.2, 165.7, 165.4, 145.2, 139.9, 135.0, 130.8, 129.2, 128.4, 127.9, 127.10, 127.07, 126.0, 122.2, 114.5, 107.7, 101.1, 55.5, 50.3, 45.8, 40.1, 36.6, 23.2; IR ν_{max} (film): 3026, 1627, 1376, 1238, 1212 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{27}H_{27}O_3$ ($M + H^+$) 399.1960, found 399.1978.

***exo*-11**: white solid. mp: 125-128°C; R_f: 0.54 (20% EtOAc in hexane);
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.85 (1H, s), 6.97-7.13 (10H, m), 6.88 (1H, d, *J* = 9.2 Hz), 6.05 (1H, d, *J* = 2.4 Hz), 5.94 (1H, dd, *J* = 8.8 Hz, 2.4 Hz), 5.51 (1H, s), 3.88 (1H, br); 3.71 (1H, dd, *J* = 10.6 Hz, 10.6 Hz), 3.65 (3H, s), 3.44 (1H, ddd, *J* = 11.4 Hz, 11.4 Hz, 5.2 Hz), 2.44 (1H, dd, *J* = 17.6 Hz, 11.6 Hz), 2.32 (1H, dd, *J* = 17.6 Hz, 5.6 Hz), 1.81 (3H, s); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 207.7, 165.4, 164.9, 143.6, 142.9, 134.2, 131.6, 128.4, 128.3,

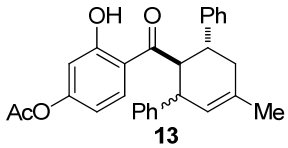
127.7, 127.5, 126.6, 126.5, 124.5, 115.2, 106.9, 99.9, 55.3, 54.0, 48.3, 44.7, 38.8, 23.2; IR ν_{max} (film): 2909, 1621, 1372, 1233, 1210 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{27}H_{27}O_3$ ($M + H^+$) 399.1960, found 399.1946.



Diels-Alder cycloadduct 12.[S6]

In situ-generated AgNP catalyst: Prepared using general condition B at 40 °C for 36 h employing 24.9 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxy-4'-methoxychalcone and 250 μL (2.2 mmol, 22 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (5% CH_2Cl_2 in hexane followed by 2% EtOAc in hexane), the desired cycloadduct **12** (21.3 mg, 65%) was isolated as a light yellow oil. Characterization data were identical with those reported in the literature.[S6]

Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 36 h employing 24.7 mg (0.097 mmol, 1.0 equiv.) of 2'-hydroxy-4'-methoxychalcone and 250 μL (2.2 mmol, 23 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **12** (29.0 mg, 89%) was isolated as a light yellow oil. Characterization data were identical with those reported in the literature.[S6]



Diels-Alder cycloadduct 13.

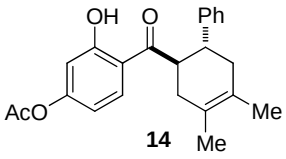
In situ-generated AgNP catalyst: Prepared using general condition B at 40 °C for 36 h employing 27.6 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxy-4'-acetoxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (2% EtOAc in hexane), the desired cycloadduct **13** (30.9 mg, 74%) was isolated as a colorless oil and was shown to be a single regioisomer and 2.8/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 6 h employing 27.6 mg (0.098 mmol, 1.0 equiv.) of 2'-hydroxy-4'-acetoxychalcone and 58 mg (0.4 mmol, 4 equiv.) of 1-phenyl-3-methylbutadiene. After chromatography on silica gel (5% EtOAc in hexane), the desired cycloadduct **13** (39.8 mg, 95%) was isolated as a colorless oil and was shown to be a single regioisomer and 1.9/1 mixture of *endo/exo* diastereomers (determined by ^{1}H NMR integration).

A pure sample of each diastereomer was obtained by further separation using preparative TLC (10% EtOAc in hexane).

***endo*-13**: colorless oil; R_f: 0.44 (20% EtOAc in hexane);
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.00 (1H, s), 8.02 (1H, d, *J* = 8.8 Hz), 7.05-7.22 (8H, m), 6.89 (2H, m), 6.74 (1H, dd, *J* = 8.8 Hz, 2.4 Hz), 6.64 (1H, d, *J* = 2.0 Hz), 5.57 (1H, br), 4.37 (1H, dd, *J* = 11.8 Hz, 5.8 Hz), 3.97 (1H, br), 3.43 (1H, ddd, *J* = 11.4 Hz, 11.4 Hz, 5.6 Hz), 2.48 (1H, dd, *J* = 18.0 Hz, 6.0 Hz), 2.30 (3H, s), 2.24 (1H, dd, *J* = 18.0 Hz, 11.8 Hz), 1.84 (3H, s); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 205.4, 168.5, 164.1, 156.2, 144.9, 139.6, 135.1, 130.4, 129.2, 128.5, 128.0, 127.2, 127.1, 126.2, 122.0, 118.1, 112.8, 111.4, 50.8, 45.7, 40.0, 36.6, 23.1, 21.2; IR ν_{max} (film): 3027, 1766, 1638, 1195, 1128 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{28}H_{27}O_4$ ($M + H^+$) 427.1909, found 427.1907.

***exo*-13**: colorless oil; R_f: 0.44 (20% EtOAc in hexane);
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.38 (1H, s), 6.95-7.13 (11H, m), 6.37 (1H, d, *J* = 2.0 Hz), 6.18 (1H, dd, *J* = 8.8 Hz, 2.0 Hz), 5.52 (1H, s), 3.88 (1H, br), 3.76 (1H, dd, *J* = 10.6 Hz, 10.6 Hz), 3.44 (1H, ddd, *J* = 11.2 Hz, 11.2 Hz, 5.6 Hz), 2.46 (1H, dd, *J* = 18.4 Hz, 11.2 Hz), 2.33 (1H, dd, *J* = 18.0 Hz, 5.4 Hz), 2.18 (3H, s), 1.82 (3H, s); ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 209.3, 168.1, 163.2, 155.8, 143.3, 142.6, 134.4, 131.2, 128.5, 128.4, 127.6, 127.4, 126.8, 126.7, 124.4, 118.9, 111.7, 110.0, 54.7, 48.4, 44.8, 38.7, 23.2, 21.2; IR ν_{max} (film): 2909, 1768, 1629, 1192, 1128 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{28}H_{27}O_4$ ($M + H^+$) 427.1909, found 427.1922.

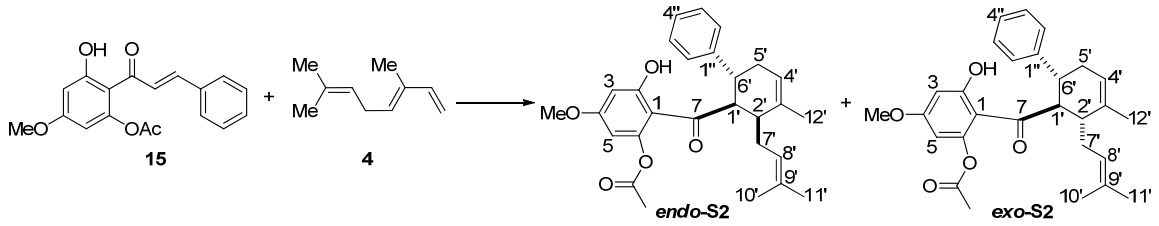


14

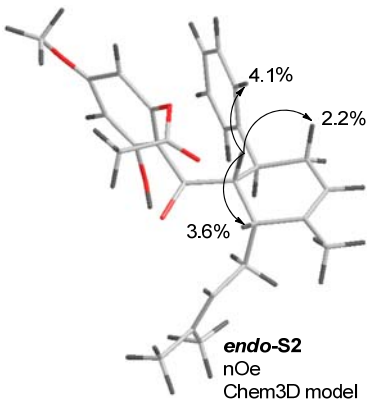
Diels-Alder cycloadduct 14.[S6]
In situ-generated AgNP catalyst: Prepared using general condition B at 40 °C for 36 h employing 27.1 mg (0.096 mmol, 1.0 equiv.) of 2'-hydroxy-4'-acetoxychalcone and 250 μL (2.2 mmol, 23 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (5% CH_2Cl_2 in hexane followed by 4% EtOAc in hexane), the desired cycloadduct **14** (29.6 mg, 85%) was isolated as a colorless oil. Characterization data were identical with those reported in the literature.[S6]

Silica-supported AgNP catalyst: Prepared using general condition C at 40 °C for 10 h employing 27.8 mg (0.099 mmol, 1.0 equiv.) of 2'-hydroxy-4'-acetoxychalcone and 250 μL (2.2 mmol, 22 equiv.) of 2,3-dimethylbutadiene. After chromatography on silica gel (5% EtOAc in hexane), the desired cycloadduct **14** (33.3 mg, 93%) was isolated as a colorless oil. Characterization data were identical with those reported in the literature.[S6]

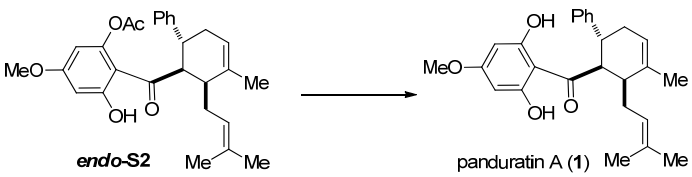
J. Total synthesis of panduratin A



To a reaction vial equipped with a stirbar were added silica-supported AgNP catalyst (500 mg, containing 135 μg Ag, 0.54 mol%), acetylated chalcone **15** (71.8 mg, 0.23 mmol, 1.0 equiv), *trans*-β-ocimene (150 mg, 1.1 mmol, 4.8 equiv.) and CH_2Cl_2 (2.0 mL) in air. The vial was sealed with a Teflon® cap. After stirred at 50 °C for 48 h, the reaction mixture was filtered and concentrated *in vacuo*. Purification using silica gel (2.5% EtOAc in hexane) afforded the cycloadduct (87.2 mg, 85%) as colorless oil. The isolated product contained the desired cycloadduct ***endo*-S2** and a minor product (approx. 95:5 ratio as determined by ^{1}H NMR). We assigned the minor product as ***exo*-S2** since a trace amount of nicolaioidesin A was observed after saponification (***Figure S8***).



***endo*-S2**: colorless oil; R_f: 0.31 (20% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.43 (1H, s), 7.09-7.22 (5H, m), 6.23 (1H, d, *J* = 2.8 Hz), 6.16 (1H, d, *J* = 2.8 Hz), 5.44 (1H, s), 4.80 (1H, t, *J* = 7.0 Hz), 4.08 (1H, dd, *J* = 11.6 Hz, 4.4 Hz), 3.77 (3H, s), 3.41 (1H, ddd, *J* = 11.2 Hz, 11.2 Hz, 6.0 Hz), 2.38-2.49 (2H, m), 2.35 (3H, s), 2.23 (1H, m), 1.97-2.10 (2H, m), 1.78 (3H, s), 1.50 (3H, s), 1.49 (3H, s); NOED (400 MHz, $CDCl_3$) Irradiation at δ (H-1'): 4.1% enhancement at H-2'', 3.6% enhancement at H-2', 2.2% enhancement at H-5'a; ^{13}C NMR (100.0 MHz, $CDCl_3$) δ 204.8, 168.5, 167.2, 164.3, 151.5, 146.2, 136.9, 132.4, 128.5, 126.8, 125.8, 123.6, 121.3, 108.5, 103.1, 99.3, 55.6, 54.1, 43.2, 36.9, 36.2, 28.7, 25.6, 22.6, 21.2, 17.9; IR ν_{max} (film): 2916, 1777, 1624, 1576, 1185, 1154 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{28}H_{33}O_5$ ($M + H^+$) 449.2328, found 449.2318.



To a reaction vial equipped with a stirbar were added the acetylated cycloadduct ***endo*-S2** (11.2 mg, 0.025 mmol), MeOH (1 mL) and saturated aqueous $NaHCO_3$ (2 mL) in air. The resulting pale yellow suspension was stirred at 40 °C for 6 h. The reaction mixture was adjusted to pH 4 by adding 1M HCl, extracted with EtOAc, washed with brine, dried over

Na_2SO_4, and concentrated *in vacuo*. Purification using silica gel (15% EtOAc in hexane) afforded recovered starting material (1.2 mg) and panduratin A (8.8 mg, 87%, 98% based on recovered starting material) as a pale yellow solid.

After saponification, crude panduratin A contained a trace amount of nicolaioidesin A[S10] (***Figure S8***) which was generated by saponification of ***exo*-S2** (minor product in the previous step). Further purification of panduratin A was carried out by recrystallization in CH_2Cl_2/hexane at -20 °C.

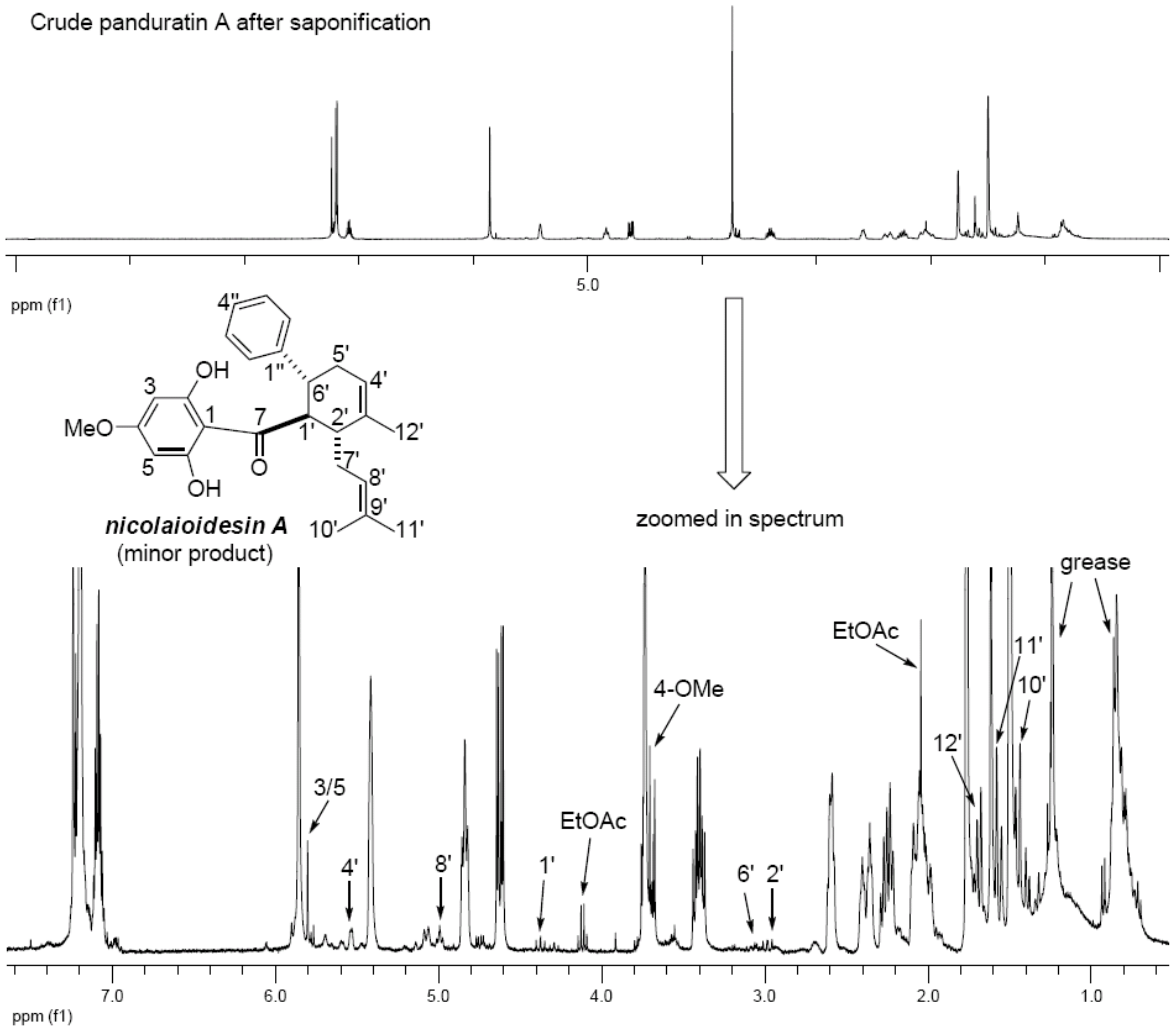
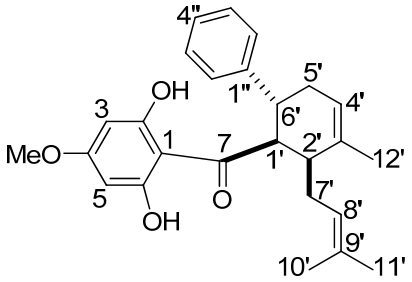


Figure S8. Analysis of ^{1}H NMR (400 MHz) traces of the minor product (nicolaioidesin A).

[S10] Gu, J-Q; Park, E. J.; Vigo, J. S.; Graham, J. G.; Fong, H. H. S.; Pezzuto, J. M.; Kinghorn, A. D. *J. Nat. Prod.* **2002**, *65*, 1616–1620.

Panduratin A (1): pale yellow solid. mp: 153-155 ^{o}C (Lit.[S 11] mp: 157–157.5 ^{o}C, recrystallized from hexane/ether); R_f: 0.20 (20% EtOAc in hexane); IR ν_{max} (film): 3311(br), 1626, 1588, 1210, 1162 cm^{-1}; HRMS (ESI+) m/z calculated for $C_{26}H_{31}O_4$ ($M + H^+$) 407.2222, found 407.2225.

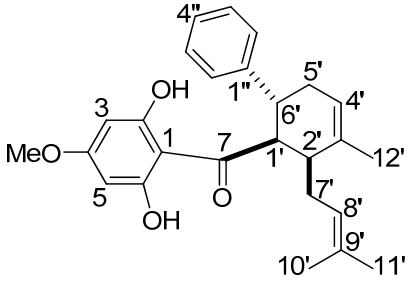
Table S4. ^{1}H NMR analysis of synthetic panduratin A in comparison to literature data[S10,11,12]



Position	δ (J_{H-H} in Hz)	
	literature (500 MHz, $CDCl_3$)	synthetic (500 MHz, $CDCl_3$)
3/5	5.87 (s)	5.86 (s)
1’	4.66 (dd, *J* = 11.3, 4.6)	4.61 (dd, *J* = 11.5, 4.5)
2’	2.63 (m)	2.59 (m)
4’	5.43 (s, br)	5.42 (s, br)
5’a	2.03 (m)	2.00 (m, overlapping)
5’b	2.40 (m)	2.38 (m)
6’	3.43 (ddd, *J* = 11, 11, 6.3)	3.40 (ddd, *J* = 11.0, 11.0, 6.5)
7’a	2.09 (m)	2.06 (m, overlapping)
7’b	2.28 (m)	2.25 (m)
8’	4.87 (t, *J* = 6.7)	4.84 (t, *J* = 6.8)
10’/11’	1.52 (s)	1.50 (s)
12’	1.78 (s)	1.76 (s)
2’’/6’’, 3’’/5’’	7.21 (m)	7.18-7.21 (m)
4’’	7.10 (m)	7.08 (m)
OMe-4	3.74 (s)	3.74 (s)
OH-2	---	not detected
OH-6	---	not detected

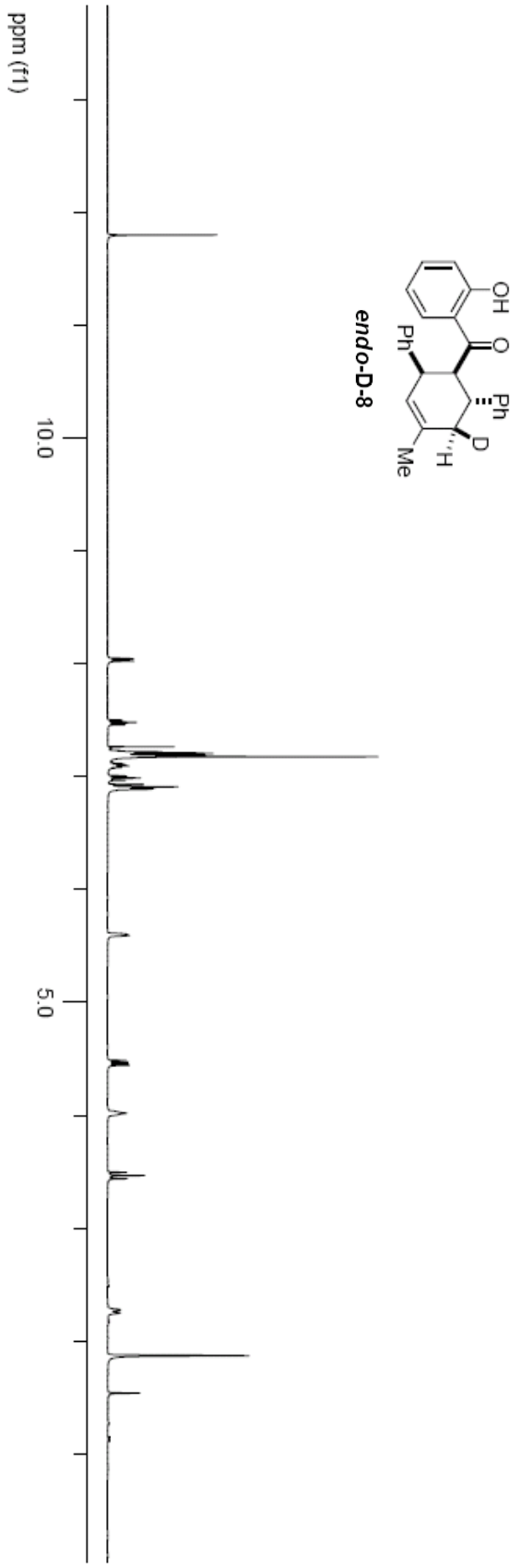
[S11] Tuntiwachwuttikul, P.; Pancharoen, O.; Reutrakul, V.; Byrne, L. T. *Aust. J. Chem.* **1984**, *37*, 449–453.
[S 12] Yoshikawa, M.; Morikawa, T.; Funakoshi, K.; Ochi, M.; Pongpiriyadacha, Y.; Matsuda, H. *Heterocycles* **2008**, *75*, 1639–1650.

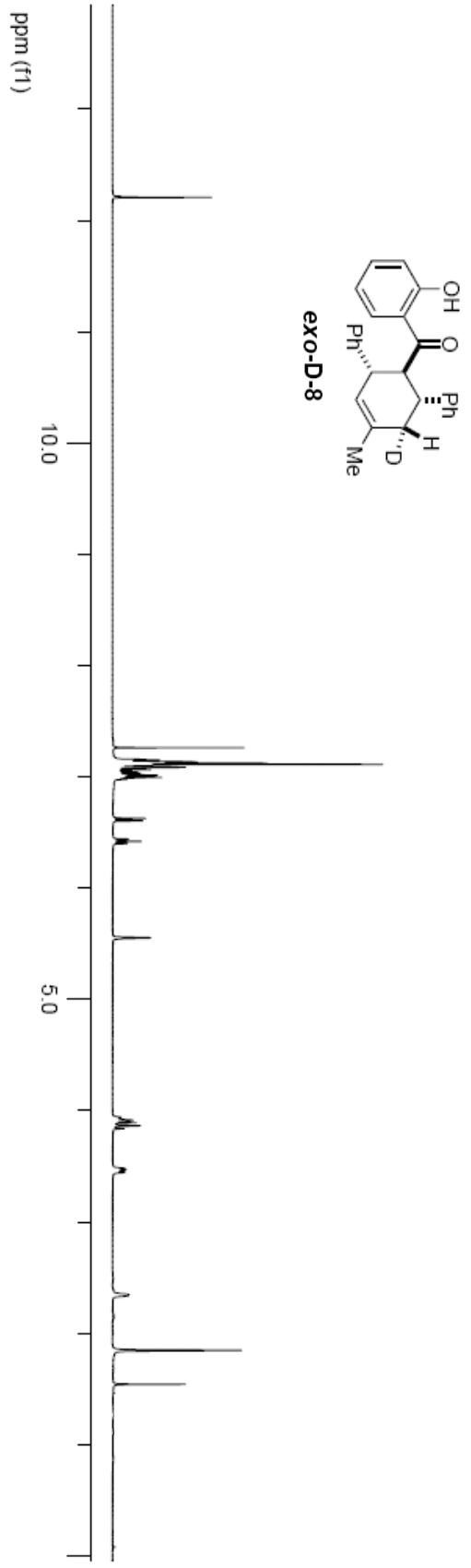
Table S5. ^{13}C NMR analysis of synthetic panduratin A in comparison to literature data[S10,11,12]

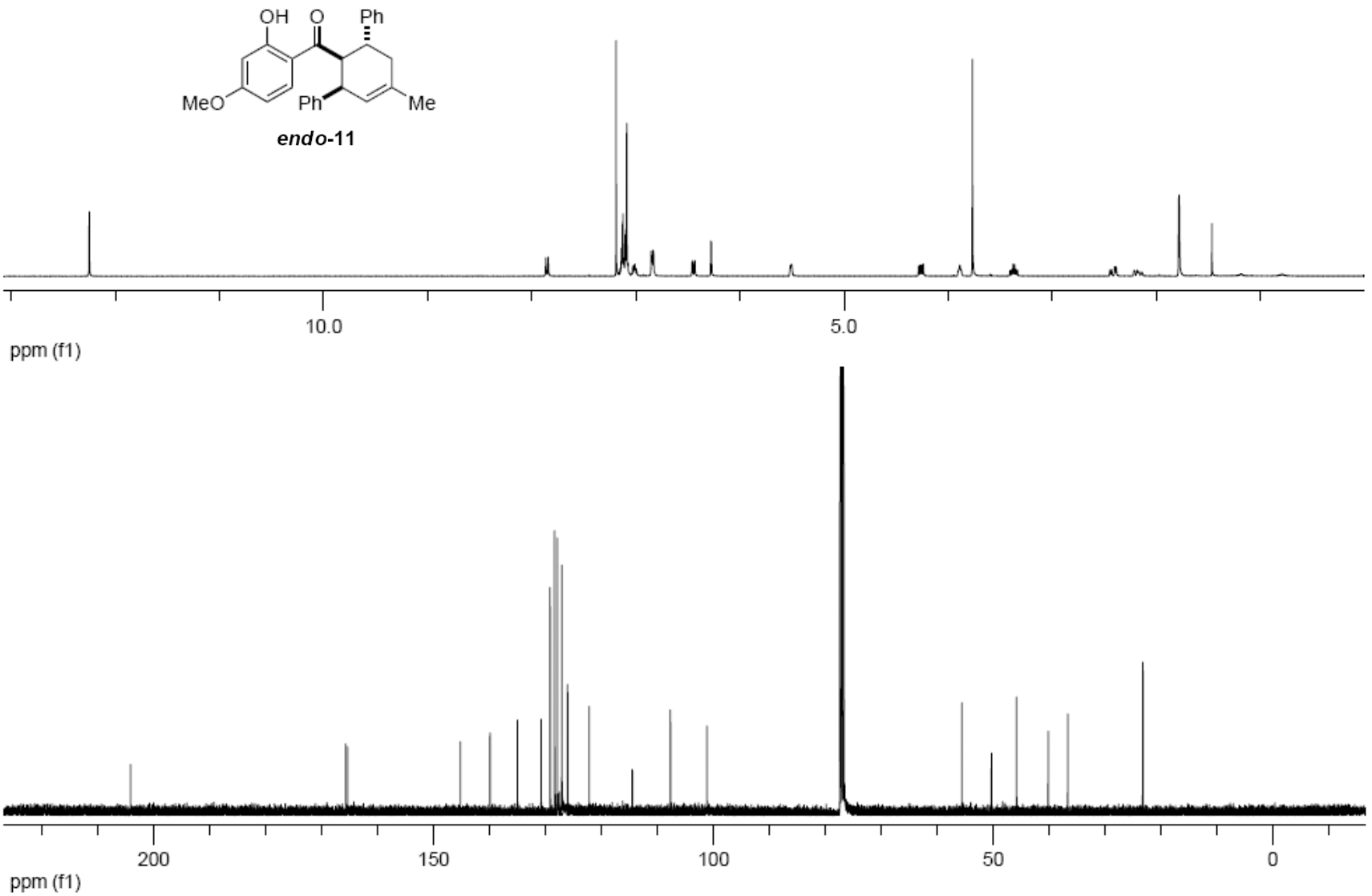


Position	δ	
	literature (125 MHz, $CDCl_3$)	synthetic (100 MHz, $CDCl_3$)
1	105.7	105.6
2/6	165.0	164.9
3/5	94.5	94.5
4	165.0	164.9
7	206.4	206.2
1’	53.9	53.9
2’	42.6	42.6
3’	137.1	137.1
4’	121.1	121.1
5’	35.9	35.8
6’	37.0	37.0
7’	28.8	28.8
8’	124.2	124.1
9’	131.9	131.9
10’	25.6	25.7
11’	17.9	17.9
12’	22.7	22.7
1’’	147.0	146.9
2’’/6’’	127.0	127.0
3’’/5’’	128.3	128.3
4’’	125.6	125.6
OMe-4	55.4	55.4

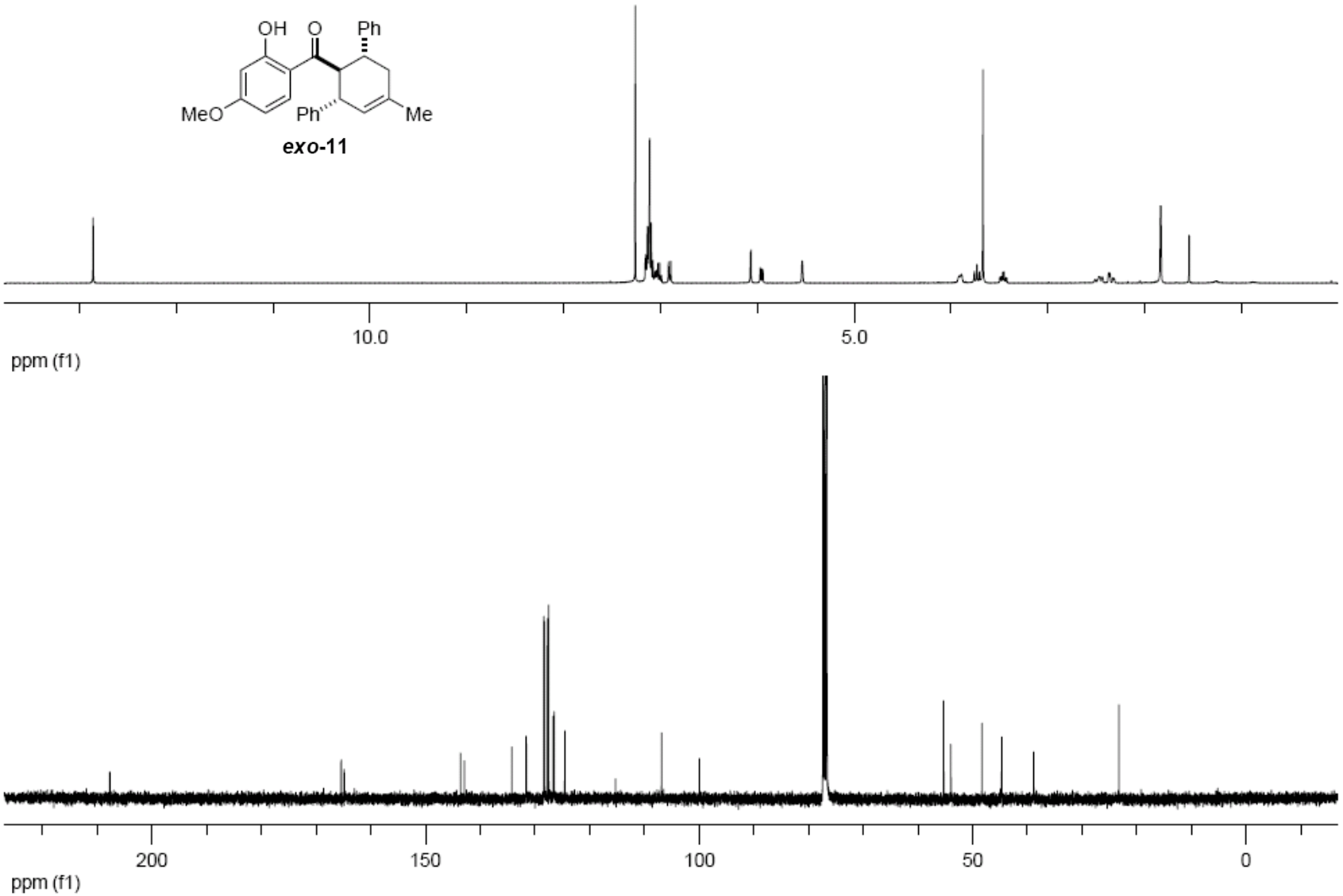
III. Select NMR Spectra



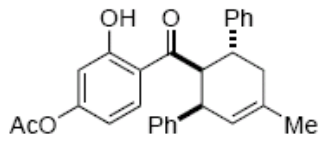




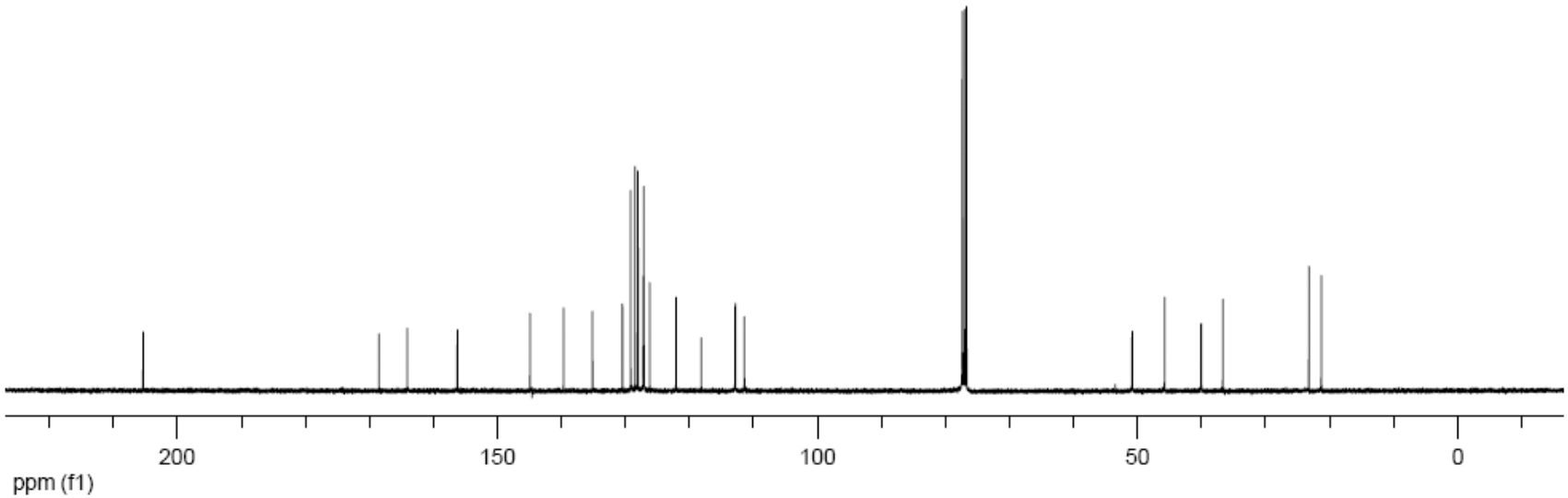
***endo*-11**

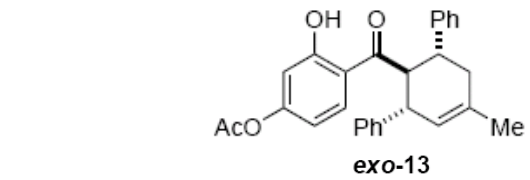


***exo*-11**

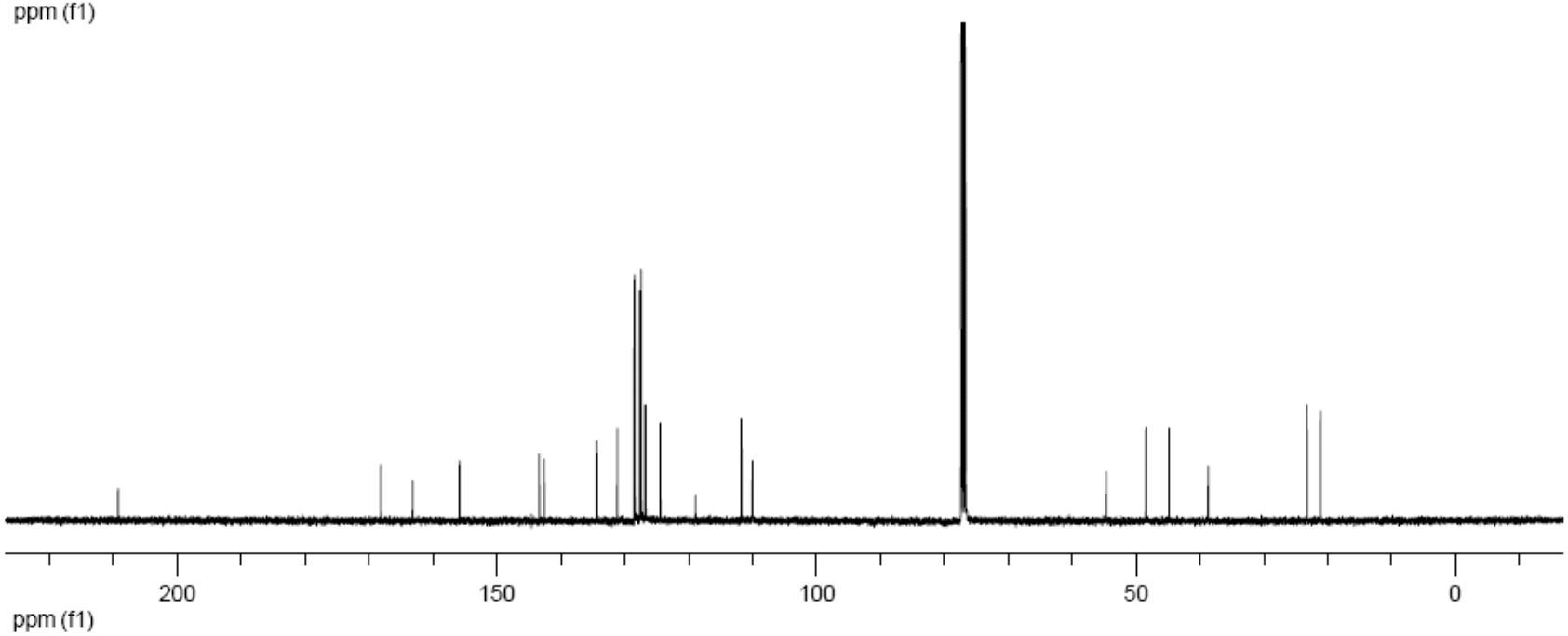


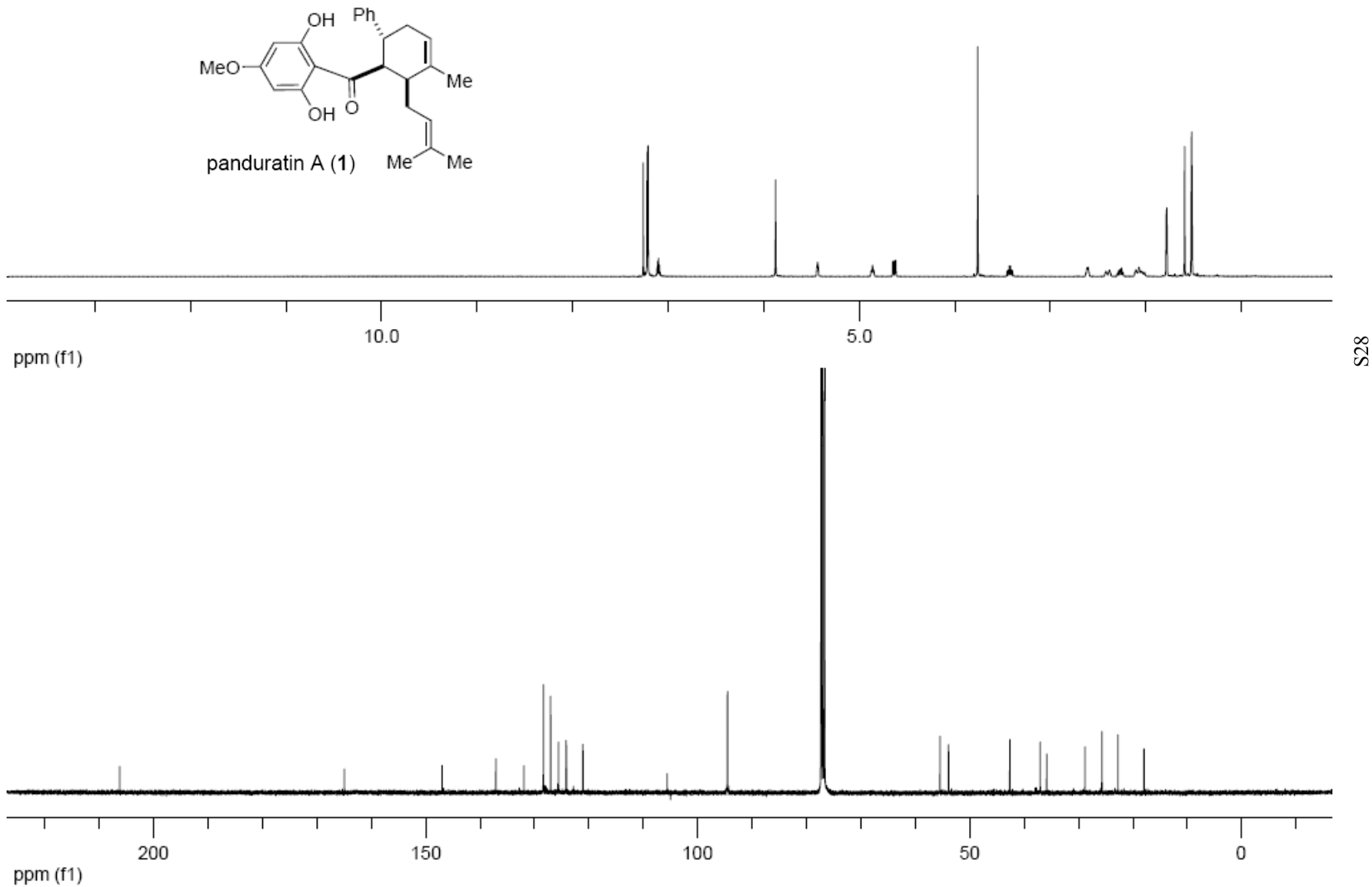
***endo*-13**





***exo*-13**




OH
Ph
MeO
Me
O
OH
Me
Me
panduratin A (1)
10.0
5.0
ppm (f1)
200
150
100
50
0
ppm (f1)