

Supporting Information

Kinetic Separation and Asymmetric Reactions of Norcaradiene Cycloadducts: Facilitated Access via H₂O-Accelerated Cycloaddition

William D. Mackay and Jeffrey S. Johnson*

Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-3290, United States

jsj@unc.edu

Table of Contents:	Page
Methods and Materials	S1
General Procedure A for the preparation of cycloheptatrienes/norcaradienes (1a-k)	S2
Table S1. Optimization of the Buchner reaction.	S7
Rationale for regioselectivity in the intermolecular Buchner reaction	S8
General Procedure B for the Buchner/Diels-Alder sequence of benzene and mesitylene	S10
Separation difficulties for 2cb/3ca	S13
General Procedure C for the Buchner/Diels-Alder/hydrolysis sequence	S15
Further transformations of the Diels-Alder products	S19
HPLC traces for S3a,b (derived from hemiesters 11a,b)	S24
References	S26
NMR data	S27
X-ray crystallographic data for 2a	S63

Methods

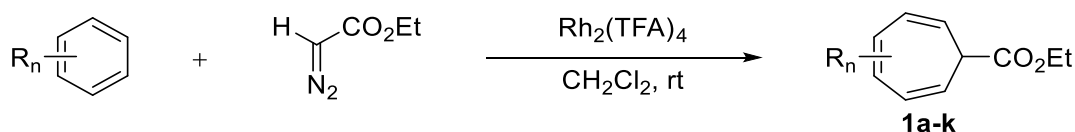
Proton and carbon magnetic resonance spectra (¹H NMR and ¹³C NMR) were recorded on either a Bruker model DRX 400 or 600 spectrometer (¹H NMR at 400 or 600 MHz and ¹³C NMR at 100 or 150 MHz) with solvent resonance as the internal standard (¹H NMR: CDCl₃ at 7.28 ppm and ¹³C NMR: CDCl₃ at 77.0 ppm). ¹H NMR data are reported as follows: chemical shift, multiplicity (abbreviations: s = singlet, br s = broad singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, dt = doublet of triplets, t = triplet, td = triplet of doublets, tt = triplet of triplets, qt = quintet, and m = multiplet), coupling constant (Hz) and integration. Melting points (mp) were determined using a Thomas Hoover Capillary Melting Point Apparatus and are uncorrected. Infrared (IR) spectra were obtained using a Jasco 260 Plus Fourier Transform Infrared Spectrometer. High resolution mass spectrometry (HRMS) was performed using a Thermo Scientific LTQ FT Ultra mass spectrometer S2 with direct infusion in either the positive or negative ion mode. Samples were prepared in HPLC grade methanol. All reported masses obtained in the positive ion mode correspond to the protonated molecular ion (M+H) unless otherwise noted, and all reported masses obtained in the negative ion mode correspond to the deprotonated molecular ion (M-H), unless otherwise noted. High performance liquid chromatography (HPLC) was performed on a Perkin Elmer Flexar® HPLC system equipped with a Chiracel IA column. Samples were eluted with HPLC grade hexanes with the indicated percentage of ⁱPrOH with an oven temperature of 40 °C. Optical rotations were measured using a 2 mL cell with a 1 dm path length on a Jasco DIP 1000 digital polarimeter. Microwave reactions were

performed using a 300 W CEM Discover System with internal temperature monitoring via infrared sensing, in sealed 10 mL pressure vessels with a maximum ramp time of 2 min. Reactions performed “on water” were run in either conventional round-bottomed flasks or 1 or 5 dram vials with rapid agitation, either by vigorous manual shaking, or stirring (>900 rpm); we noticed no noticeable difference in the two methods. Thin layer chromatography (TLC) was performed on Sorbtech plastic-backed 0.20 mm silica gel 60 plates. Visualization was accomplished with UV light and either an aqueous ceric ammonium molybdate (CAM) or potassium permanganate (KMnO₄) solution, followed by heating. Flash chromatography was performed under positive air pressure using Siliaflash-P60 silica gel (40-63 μm) purchased from Silicycle. Unless otherwise specified, all crude materials were introduced to the chromatography column after dissolution in the specified eluent (plus a few drops dichloromethane, if required). Yields and diastereomeric ratios (dr’s) are reported herein for a specific experiment and as a result may differ slightly from those found in the tables, which are averages of at least two experiments.

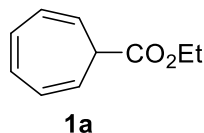
Materials

Nitrogen was dried by passage through anhydrous calcium sulfate with 3% cobalt chloride as indicator (commercial Drierite). Ethyl diazoacetate,¹ *N*-benzylmaleimide,² and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD)³ were prepared according to known literature procedures. The cycloheptatrienes **1a-k** were prepared by a modified literature procedure.⁴⁻⁶ The ethyl diazoacetate was stored at room temperature as a solution (>80% w/w) in CH₂Cl₂ in a brown bottle to exclude light. While we experienced no difficulties in handling ethyl diazoacetate, care must be taken at all times when handling diazo compounds.¹ All aromatic substrates were purified by distillation prior to use. In all reactions run on water, solid reagents (maleic anhydride, *N*-benzylmaleimide, naphthoquinone) were ground into fine powders prior to use. All other reagents and solvents were purchased from commercial sources and used as received.

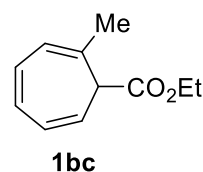
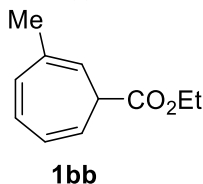
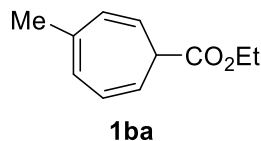
General Procedure A for the preparation of cycloheptatrienes/norcaradienes (**1a-1k**)



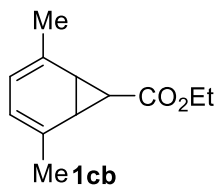
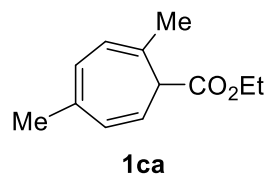
To a 25 mL round-bottomed flask charged with Rh₂(TFA)₄ (6.6 mg, 0.01 equiv), the aromatic substrate (20 equiv), and CH₂Cl₂ (2.5 mL) was added a 2.5 mL solution of ethyl diazoacetate (114 mg, 1 mmol) in CH₂Cl₂ via syringe pump addition over 3 h. After complete addition, the brown solution was stirred for an additional hour at room temperature, at which time the CH₂Cl₂ was removed by rotary evaporation, and the excess arene was removed and could be recovered by distillation under reduced pressure with gentle heating (<40 °C). Analytically pure material was obtained following purification by silica gel chromatography. Complete analytical data are reported for new compounds; only ¹H NMR data are reported for known compounds. In cases where multiple regioisomers were formed, the isomers are listed in decreasing order of percent composition of the isolated mixture, and when possible, the resonances are identified for each isomer. The percentage shown in parentheses after identification of the regioisomer reflects the percent composition of that isomer in the regioisomeric mixture of the product mixture. Also indicated are the cases where the norcaradiene (NCD) is the predominant isomer by ¹H NMR analysis.



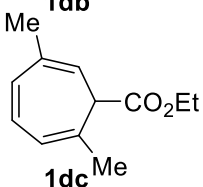
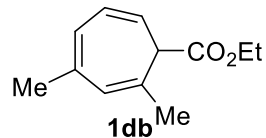
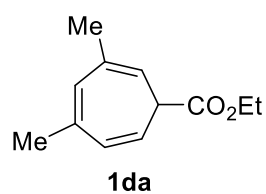
Ethyl cyclohepta-1,3,5-triene-7-carboxylate (1a): The title compound was prepared according to General Procedure A using benzene (1.78 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (94 mg, 57%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.68 (m, 2H), 6.28 (m, 2H), 5.46 (dd, $J = 9.2, 5.6$ Hz, 2H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.56 (t, $J = 5.6$ Hz, 1H), 1.33 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.59$.



Ethyl 3-methylcyclohepta-1,3,5-triene-7-carboxylate (1b): The title compound was prepared according to General Procedure A using toluene (2.13 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 1 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (105 mg, 64%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**1ba, 3-Me, 60%**) 6.44 (m, 1H), 6.20 (m, 1H), 6.10 (m, 1H), 5.40 – 5.32 (m, 2H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.57 (t, $J = 5.6$ Hz, 1H), 2.09 (s, 3H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1bb, 2-Me, 27%**) 6.44 (m, 2H), 6.20 (m, 1H), 5.05 (m, 1H), 4.75 (m, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.26 (t, $J = 5.2$ Hz, 1H), 1.97 (s, 3H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1bc, 1-Me, 13%**) 6.55 (m, 2H), 6.24 (dd, $J = 9.1, 4.8$ Hz, 1H), 6.12 (d, $J = 4.2$ Hz, 1H), 5.72 (dd, $J = 9.1, 7.0$ Hz, 1H), 5.36 (m, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.85 (d, $J = 7.0$ Hz, 1H), 1.99 (s, 3H), 1.32 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.60$.

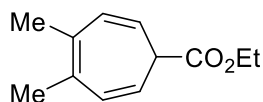


Ethyl 1,4-dimethylcyclohepta-1,3,5-triene-7-carboxylate (1c): The title compound was prepared according to General Procedure A using *p*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (115 mg, 60%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**1ca, 1,4-Me, 70%**) 6.33 (d, $J = 3.2$ Hz, 1H), 6.07 (d, $J = 6.0$ Hz, 1H), 6.01 (d, $J = 3.2$ Hz, 1H), 5.69 (dd, $J = 6.0, 4.4$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.89 (d, $J = 4.4$ Hz, 1H), 2.05 (s, 3H), 1.95 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); (**1cb, 2,5-Me (NCD), 30%**) 6.05 (s, 2H), 4.25 (q, $J = 7.2$ Hz, 2H), 3.79 (br s, 2H), 1.97 (s, 6H), 1.59 (m, 1H), 1.31 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.62$.

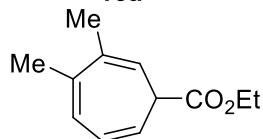


Ethyl 2,4-dimethylcyclohepta-1,3,5-triene-7-carboxylate (1d): The title compound was prepared according to General Procedure A using *m*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (93 mg, 48%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**1da, 2,4-Me, 50%**) 6.16 (br s, 1H), 5.94 (br s, 1H), 4.73 (m, 1H), 4.43 (br s, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.11 (t, $J = 5.2$ Hz, 1H), 1.99 (s, 3H), 1.96 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); (**1db, 1,3-Me, 35%**) 6.36 (d, $J = 5.6$ Hz, 1H), 6.14 (m, 1H), 5.96 (br s, 1H), 5.65 (dd, $J = 9.2, 6.7$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.89 (d, $J = 6.7$ Hz, 1H), 2.05 (s, 3H), 1.95 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); (**1dc, 1,5-Me, 15%**) 6.44 (m, 2H), 6.01 (m, 1H), 5.47 (d, $J = 6.8$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.84 (d,

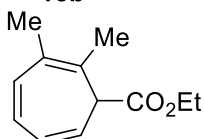
$J = 6.8$ Hz, 1H), 1.96 (s, 3H), 1.94 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.62$.



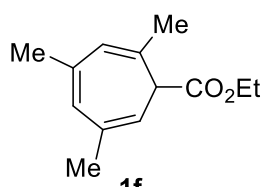
1ea



1eb

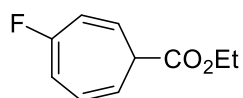


1ec

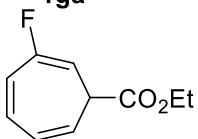


1f

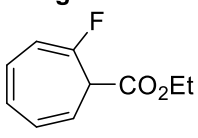
Ethyl 1,3,5-trimethylcyclohepta-1,3,5-triene-7-carboxylate (1f): The title compound was prepared according to General Procedure A using mesitylene (2.78 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (129 mg, 62%). Analytical data: $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.25 (s, 1H), 5.84 (s, 1H), 5.38 (d, $J = 6.8$ Hz, 1H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.87 (d, $J = 6.8$ Hz, 1H), 2.01 (s, 3H), 1.93 (s, 3H), 1.90 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.64$.



1ga

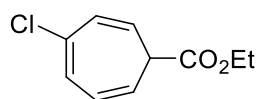


1gb



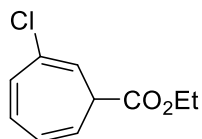
1gc

Ethyl 3-fluorocyclohepta-1,3,5-triene-7-carboxylate (1g): The title compound was prepared according to General Procedure A using fluorobenzene (1.88 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (99 mg, 54%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**1ga, 3-F, 67%**) 6.40 (m, 1H), 6.24 (m, 2H), 5.69 (m, 1H), 5.388 (dd, $J = 9.0, 5.4$ Hz, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.69 (m, 1H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1gb, 2-F, 20%**) 6.60 (ddd, $J = 10.8, 6.0, 4.2$ Hz, 1H), 6.40 (m, 1H), 6.17 (dd, $J = 9.6, 6.0$ Hz, 1H), 5.43 (dd, $J = 7.8, 6.0$ Hz, 1H), 5.03 (dd, $J = 12.6, 6.0$ Hz, 1H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.69 (m, 1H), 1.30 (t, $J = 7.2$ Hz, 3H); (**1gc, 1-F, 13%**) 6.47 (dd, $J = 11.7, 5.7$ Hz, 1H), 6.34 (dd, $J = 9.6, 5.7$ Hz, 1H), 6.29 (ddd, $J = 12.9, 11.7, 6.6$ Hz, 1H), 6.06 (dd, $J = 12.9, 7.2$ Hz, 1H), 5.69 (m, 1H), 4.16 (m, 2H), 3.71 (dd, $J = 18.0, 7.8$ Hz, 1H), 1.24 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.54$.

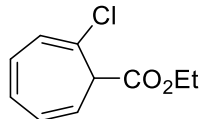


1ha

Ethyl 3-chlorocyclohepta-1,3,5-triene-7-carboxylate (1h): The title compound was prepared according to General Procedure A using chlorobenzene (2.03 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (113 mg, 57%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**1ha, 3-Cl, 70%**) 6.82

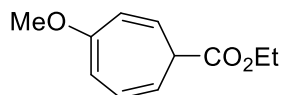


1hb

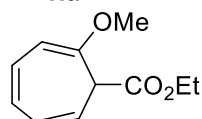


1hc

(dd, $J = 6.6, 1.2$ Hz, 1H), 6.26 – 6.20 (m, 2H), 5.53 (dd, $J = 9.6, 6.0$ Hz, 1H), 5.50 (dd, $J = 9.6, 5.4$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.72 (dd, $J = 6.0, 5.4$ Hz, 1H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1hb**, **2-Cl**, **18%**) 6.54 (dd, $J = 10.2, 5.4$ Hz, 1H), 6.50 (d, $J = 10.2$ Hz, 1H), 6.23 (m, 1H), 5.21 (m, 1H), 5.18 (ddd, $J = 8.4, 5.4, 1.8$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 2.50 (dd, $J = 6.6, 5.4$ Hz, 1H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1hc**, **1-Cl**, **11%**) 6.61 (dd, $J = 10.8, 5.4$ Hz, 1H), 6.47 (d, $J = 6.0$ Hz, 1H), 6.42 (dd, $J = 10.8, 6.6$ Hz, 1H), 6.34 (dd, $J = 9.6, 6.0$ Hz, 1H), 5.78 (dd, $J = 9.0, 7.8$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 3.48 (d, $J = 7.8$ Hz, 1H), 1.28 (t, $J = 7.2$ Hz, 3H); **TLC** (20% EtOAc/hexanes) $R_f = 0.54$.

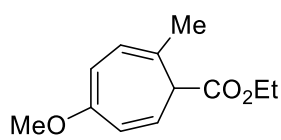


1ia

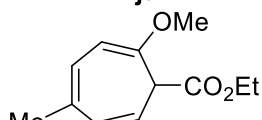


1ib

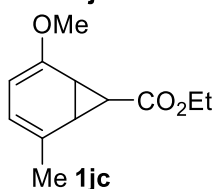
Ethyl 3-methoxycyclohepta-1,3,5-triene-7-carboxylate (1i): The title compound was prepared according to General Procedure A using anisole (2.17 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (73 mg, 37%). Analytical data: **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ (**1ia**, **3-OMe**, **74%**) 6.23 (m, 1H), 6.10 (dt, $J = 10.0$ Hz, 1.6 Hz, 1H), 5.89 (dd, $J = 6.8, 2.0$ Hz, 1H), 5.65 (m, 1H), 5.29 (m, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 3.69 (s, 3H), 2.71 (t, $J = 5.6$ Hz, 1H), 1.33 (t, $J = 7.2$ Hz, 3H); (**1ib**, **1-OMe**, **26%**) 6.49 (dd, $J = 10.8, 6.6$ Hz, 1H), 6.36 (dd, $J = 10.8, 5.7$ Hz, 1H), 6.31 (dd, $J = 9.3, 5.7$ Hz, 1H), 5.66 (dd, $J = 9.3, 7.2$ Hz, 1H), 5.53 (d, $J = 6.6$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 3.66 (s, 3H), 3.34 (d, $J = 7.2$ Hz, 1H), 1.33 (t, $J = 7.2$ Hz, 3H). **TLC** (20% EtOAc/hexanes) $R_f = 0.51$.



1ja

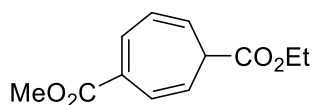


1jb



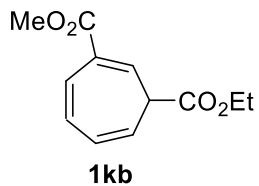
Me 1jc

Ethyl 3-methoxy-6-methylcyclohepta-1,3,5-triene-7-carboxylate (1j): The title compound was prepared according to General Procedure A using 4-methylanisole (2.52 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10% EtOAc/hexanes) provided a clear oil (95 mg, 46%). Analytical data: **$^1\text{H NMR}$** (600 MHz, CDCl_3) δ (**1ja**, **3-OMe**, **6-Me**, **51%**) 6.07 (d, $J = 9.9$ Hz, 1H), 6.01 (dd, $J = 6.6, 1.2$ Hz, 1H), 5.86 (dd, $J = 9.9, 7.2$ Hz, 1H), 5.77 (d, $J = 6.6$ Hz, 1H), 4.20 (d, $J = 7.2$ Hz, 2H), 3.64 (s, 3H), 2.91 (d, $J = 7.2$ Hz, 1H), 1.91 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H); (**1jb**, **1-OMe**, **4-Me**, **31%**) 6.24 (d, $J = 6.9$ Hz, 1H), 6.12 (d, $J = 9.6$ Hz, 1H), 5.64 (dd, $J = 9.6, 7.4$ Hz, 1H), 5.39 (d, $J = 6.9$ Hz, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 3.61 (s, 3H), 3.31 (d, $J = 7.4$ Hz, 1H), 2.02 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); (**1jc**, **2-OMe**, **5-Me (NCD)**, **19%**) 5.83 (br s, 1H), 5.26 (br s, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 3.62 (s, 3H), 1.95 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H); **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ (**1ja**, **3-OMe**, **6-Me**) 172.2, 158.7, 124.9, 122.4, 122.3, 121.2, 103.9, 60.5, 54.7, 48.6, 20.0, 14.2; (**1jb**, **1-OMe**, **4-Me**) 170.3, 148.1, 133.2, 129.8, 124.9, 117.4, 96.7, 60.8, 56.4, 48.5, 23.6, 14.1; **IR** (thin film, cm^{-1}) 2980, 2937, 2836, 1740, 1616, 1550, 1463, 1369, 1315, 1034; **TLC** (20% EtOAc/hexanes) $R_f = 0.54$; **HRMS** (ESI⁺) Calcd. for $\text{C}_{12}\text{H}_{16}\text{NaO}_3$: 231.0992, Found: 231.0993.

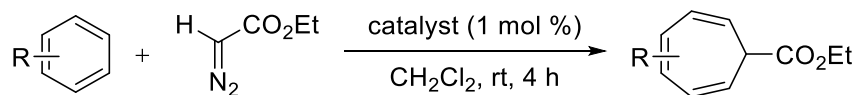


1ka

7-ethyl 3-methyl cyclohepta-1,3,5-triene-3,7-dicarboxylate (1k): The title compound was prepared according to General Procedure A using methyl benzoate (2.51 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), and $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol). Flash chromatography (10%



EtOAc/hexanes) provided a colored oil (50 mg, 23%). Analytical data: ^1H NMR (400 MHz, CDCl_3) δ (**1ka**, **3-CO₂Me**, **57%**) 7.63 (d, $J = 6.0$ Hz, 1H), 6.85 (d, $J = 9.6$ Hz, 1H), 6.42 (m, 1H), 5.55 (ddd, $J = 9.0, 5.4, 1.2$ Hz, 1H), 5.34 (ddd, $J = 9.0, 5.4, 1.2$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 3.85 (s, 3H), 2.42 (dd, $J = 5.4, 5.4$ Hz, 1H), 1.32 (t, $J = 7.2$ Hz, 3H); (**1kb**, **2-CO₂Me**, **43%**) 7.19 (d, $J = 10.2$ Hz, 1H), 6.64 (dd, $J = 10.2, 6.6$ Hz, 1H), 6.39 (m, 1H), 5.72 (ddd, $J = 5.4, 3.0, 1.0$ Hz, 1H), 4.82 (ddd, $J = 8.4, 5.5, 3.0$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 3.81 (s, 3H), 2.10 (dd, $J = 5.4, 5.4$ Hz, 1H), 1.33 (t, $J = 7.2$ Hz, 3H).

Table S1. Optimization of the Buchner reaction.^a

entry	substrate	catalyst	product	yield (%)	rr
1	benzene	Rh ₂ (TFA) ₄	1a	90	-
2		Rh ₂ (OAc) ₄	1a	40	-
3		Cu(hfacac) ₂	1a	<2	-
5	<i>p</i> -xylene	Rh ₂ (TFA) ₄	1c	73	70:30
6		Rh ₂ (OAc) ₄	1c	36	84:16
7		Rh ₂ (oct) ₄	1c	15	93:7
8		Rh ₂ (esp) ₂	1c	13	96:4

^aAll reactions were run on 1 mmol scale. Yields are ¹H NMR yields and were determined by ¹H NMR using 1,4-dimethylterephthalate as internal standard. Regioisomeric ratio (rr) was determined by ¹H NMR.

Using benzene, Rh₂(TFA)₄ was quickly identified as the optimal catalyst to generate high yields of the CHT product, as rhodium diacetate dimers bearing electron-deficient ligands are reported to provide higher activity in the intermolecular Buchner reaction (entry 1).⁴ Copper catalysts (entry 3) were ineffective at promoting this reaction. In order to investigate the role of the catalyst in the regioselectivity of the reaction, we focused on *p*-xylene as a model substrate, since only two possible regioisomers could arise. As shown in Table S1, although more electron-deficient ligands provided higher yields in the Buchner reaction, lower rr was observed (entry 5). Conversely, using the electron-rich Rh₂(esp)₂ (entry 8), we observed excellent regioselectivity, albeit in poor yields. Variation in reaction temperature, concentration, and catalyst loading were ineffective in providing higher regioselectivity in the reaction. In light of these findings, we decided to use Rh₂(TFA)₄ throughout our screening, with the caveat that downstream separation of the multiple regioisomers would be required.

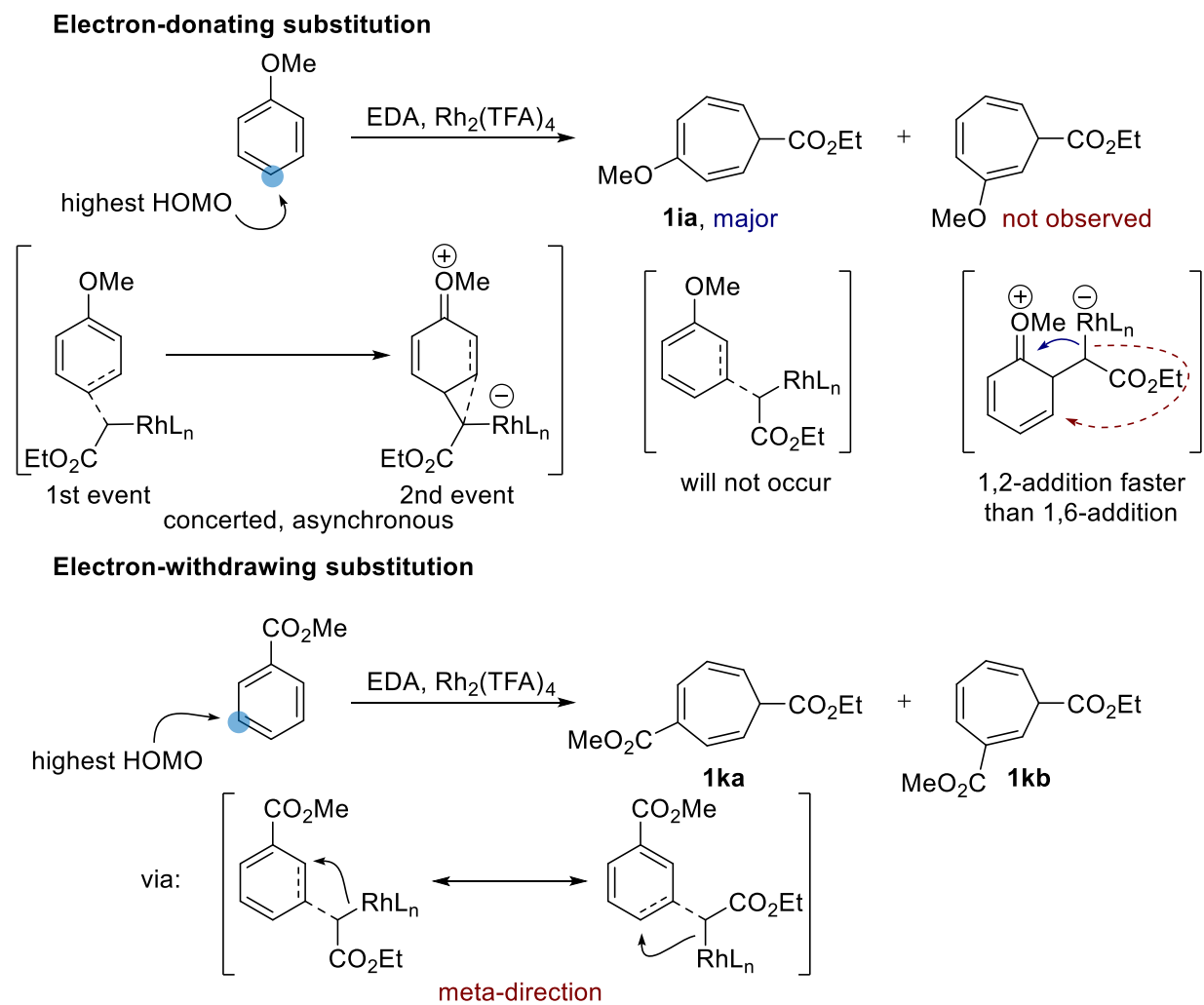
Rationale for the regioselectivity in the intermolecular Buchner reaction

There were two key aspects to the factors that governed the regioselectivity of the Buchner reaction: steric and electronic effects. In alkyl substituted aromatic compounds, the steric effects seemed to govern the regioselectivity, since, using toluene to generate the cycloheptatriene mixture **1b**, the least sterically encumbered site was the major product, with decreasing product yields approaching the methyl group. The steric impact was so great such that 1,4-bis-hydroxymethyl-substituted arenes did not undergo the Buchner reaction, regardless of the protecting group on the primary alcohols. At the same time, a simple steric argument was insufficient to completely describe this reaction, since the non-symmetrical CHT **1ca** was the major isomer using *p*-xylene as substrate, even when it appeared to arise from cyclopropanation at the more congested site.

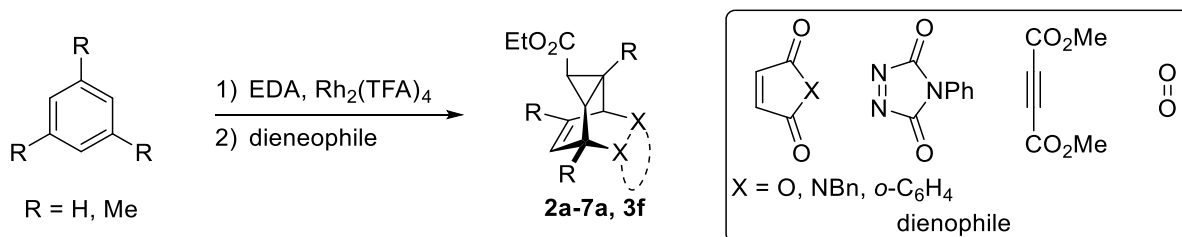
It has been suggested⁵ that there is a significant electronic component to the regioselectivity of this reaction. Cyclopropanation reactions involving dirhodium carboxylate carbenoid intermediates are thought to proceed via a concerted process; however, the bond forming steps are not necessarily synchronous. In the context of this reaction, the mechanism of cycloaddition was reasonable to consider a concerted, asynchronous process. With that in mind, the first bond forming “event” should occur at the position on the aromatic substrate with the highest HOMO, since the intermediate carbenoid was electrophilic. Upon reaction with anisole, one would expect initial addition to either the *ortho*- or *para*-positions. Initial attack at the *para*-position provided the major product (**1ia**). Initial attack at the *ortho*-position, however, could result in either the 1,2-addition product (Scheme S1), providing **1ib**, or the 1,6-addition product to give the 2-methoxy-substituted cycloheptatriene. Since the latter product was not observed, it was evident that the 1,2-addition pathway was significantly more facile than the 1,6-pathway.

Along these lines, using an electron-deficient aromatic substrate, such as methyl benzoate, we should expect a statistical mixture of the 2- and 3-substituted products, owing to the lack of direction by initial attack at the *meta*-position. In the event, we observed a 56:44 ratio of **1ka/1kb**, which was congruent with such an analysis.

Scheme S1. The regiochemical outcome of the Buchner reaction.

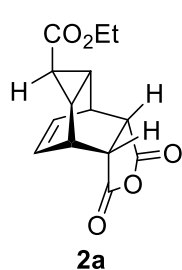


General Procedure B for the Buchner/Diels-Alder sequence of benzene and mesitylene



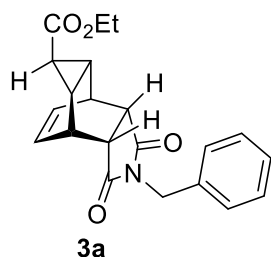
To a 25 mL round-bottomed flask charged with $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 equiv), the aromatic substrate (20 equiv), and CH_2Cl_2 (2.5 mL) was added a 2.5 mL solution of ethyl diazoacetate (114 mg, 1 mmol) in CH_2Cl_2 via syringe pump addition over 3 h. After complete addition, the brown solution was stirred for an additional hour at room temperature, at which time the CH_2Cl_2 was removed by rotary evaporation, and the excess arene was removed and could be recovered by distillation under reduced pressure, yielding a brown oil. The following conditions were employed for the appropriate dienophile:

For maleic anhydride and *N*-benzylmaleimide: To the resultant oil was then added the dienophile (3 equiv) and saturated brine (NaCl) solution (10 mL), and the mixture was rapidly stirred at room temperature until the reaction was complete (2 – 30 min). The products were extracted with Et_2O (2 × 5 mL), dried over MgSO_4 , filtered, concentrated, and purified by chromatography. **For naphthoquinone:** To the resultant oil was then added naphthoquinone (3 equiv) and saturated brine (NaCl) solution (3 mL), and the mixture was heated under microwave irradiation (300 W, 100 °C, 1 h). Then the reaction mixture was diluted with EtOAc (25 mL), filtered through a short pad of activated charcoal and Celite, dried over MgSO_4 , filtered, concentrated, and purified by chromatography. **For dimethyl acetylenedicarboxylate (DMAD):** To the resultant oil was then added DMAD (10 equiv) and saturated brine (NaCl) solution (3 mL), and the mixture was heated under microwave irradiation (300 W, 100 °C, 1 h). The products were extracted with EtOAc (2 × 10 mL), dried over Na_2SO_4 , filtered, concentrated, and purified by chromatography. **For 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD):** To the resultant oil was then added PTAD (1.1 equiv) with 5 mL Et_2O . After stirring for 10 min, the solvent was removed by rotary evaporation, and the residue was purified by chromatography. **For $\text{O}=\text{O}$:** To the resultant oil was added rose bengal (0.01 equiv), and the mixture was dissolved in CCl_4/MeOH (20:1, 5 mL) and cooled to 0 °C. Then a steady stream of O_2 was bubbled through the solution and the mixture was irradiated with a Hg lamp with a Pyrex filter. After stirring for 7 – 24 h, the solvent was removed by rotary evaporation at room temperature, and the crude material was purified by chromatography.

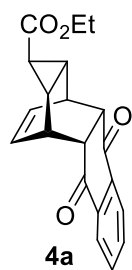


Ethyl -1,3-dioxo-3,3a,4,4a,5,5a,6,6a-octahydro-1H-4,6-ethenocyclopropa-[f]isobenzofuran-5-carboxylate (2a): The title compound was prepared according to General Procedure B using benzene (17.8 mL, 200 mmol), ethyl diazoacetate (1.14 g, 10 mmol), $\text{Rh}_2(\text{TFA})_4$ (65.8 mg, 0.1 mmol), and maleic anhydride (2.94 g, 30 mmol). Flash chromatography (40% EtOAc /hexanes) provided a white solid (2.32 g, 88%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.97 (tt, $J = 4.2, 3.6$ Hz, 2H), 4.08 (q, $J = 7.2$ Hz, 2H), 3.57 (m, 2H), 3.32 (tt, $J = 4.2, 1.8$ Hz, 2H), 1.76 (dt, $J = 2.7, 2.4$ Hz, 2H), 1.38 (t, $J = 2.7$ Hz, 1H), 1.23 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ

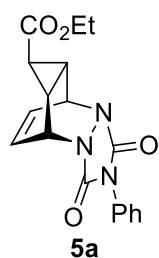
171.7, 171.5, 129.1, 60.8, 45.2, 32.8, 20.3, 19.6, 14.1; **mp** 129–130 °C; **IR** (thin film, cm^{-1}) 2981, 1861, 1838, 1779, 1721, 1420, 1297, 1229, 1173, 926; **TLC** (20% EtOAc/hexanes) $R_f = 0.07$; **HRMS** (ESI⁺) Calcd. for $\text{C}_{14}\text{H}_{13}\text{O}_5$: 261.0768, Found: 261.0770.



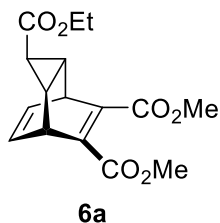
Ethyl -2-octyl-1,3-dioxo-1,2,3,3a,4,4a,5,5a,6,6a-decahydro-4,6-ethenocyclopropa-[f]isoindole-5-carboxylate (3a): The title compound was prepared according to General Procedure B using benzene (1.8 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol), and *N*-benzylmaleimide (234 mg, 1.25 mmol). Flash chromatography (30% EtOAc/hexanes) provided a white solid (260 mg, 74%). Analytical data: **¹H NMR** (600 MHz, CDCl_3) δ 7.29 – 7.22 (m, 5H), 5.69 (t, $J = 4.2$ Hz, 2H), 4.53 (s, 2H), 4.09 (q, $J = 7.2$ Hz, 2H), 3.50 (br s, 2H), 3.01 (br s, 2H), 1.74 (dd, $J = 5.4, 3.0$ Hz, 2H), 1.35 (t, $J = 3.0$ Hz, 1H), 1.23 (t, $J = 7.2$ Hz, 3H); **¹³C NMR** (150 MHz, CDCl_3) δ 177.3, 17.2, 135.6, 128.5, 128.3, 128.2, 127.6, 60.6, 44.5, 42.0, 32.8, 20.3, 19.9, 14.1; **mp** 172–173 °C; **IR** (thin film, cm^{-1}) 2978, 1702, 1419, 1397, 1335, 1290, 1247, 1173, 1070, 910; **TLC** (20% EtOAc/hexanes) $R_f = 0.08$; **HRMS** (ESI⁺) Calcd. for $\text{C}_{21}\text{H}_{22}\text{NO}_4$: 352.1543, Found: 352.1564.



Ethyl -3,8-dioxo-1a,2,2a,3,8,8a,9,9a-octahydro-1H-2,9-ethenocyclopropa-[b]anthracene-1-carboxylate (4a): The title compound was prepared according to General Procedure B using benzene (1.8 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol), and naphthoquinone (474 mg, 3.0 mmol). Flash chromatography (20% EtOAc/hexanes) provided a brown solid (139 mg, 43%). Analytical data: **¹H NMR** (600 MHz, CDCl_3) δ 8.03 (dd, $J = 6.0, 3.0$ Hz, 2H), 7.71 (dd, $J = 6.0, 3.0$ Hz, 2H), 5.80 (dd, $J = 4.2, 3.9$ Hz, 2H), 4.11 (q, $J = 7.2$ Hz, 2H), 3.76 (br s, 2H), 3.29 (s, 2H), 1.89 (dd, $J = 4.8, 3$ Hz, 2H), 1.26 (t, $J = 3.0$ Hz, 1H), 1.26 (t, $J = 7.2$ Hz, 3H); **¹³C NMR** (150 MHz, CDCl_3) δ 196.8, 172.9, 135.3, 134.2, 129.8, 126.9, 60.6, 49.5, 36.7, 20.6, 18.0, 14.2; **mp** 127–128°C; **IR** (thin film, cm^{-1}) 3065, 2980, 1717, 1678, 1592, 1418, 1274, 1161, 709; **TLC** (20% EtOAc/hexanes) $R_f = 0.13$; **HRMS** (ESI⁺) Calcd. for $\text{C}_{20}\text{H}_{17}\text{O}_4$: 321.1132, Found: 321.1144.

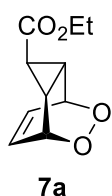


Ethyl -1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5a): The title compound was prepared according to General Procedure B using benzene (1.8 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (175 mg, 1.1 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (241 mg, 71%). Analytical data: **¹H NMR** (600 MHz, CDCl_3) δ 7.43 (m, 4H), 7.35 (m, 1H), 6.17 (t, $J = 4.2$ Hz, 2H), 5.26 (m, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 2.23 (m, 2H), 1.45 (t, $J = 3.0$ Hz, 1H), 1.26 (t, $J = 7.2$ Hz, 3H); **¹³C NMR** (150 MHz, CDCl_3) δ 170.2, 156.4, 131.1, 129.0, 128.2, 126.0, 125.4, 61.1, 52.1, 23.5, 15.3, 14.0; **mp** 167–168°C; **IR** (thin film, cm^{-1}) 3066, 2982, 2937, 1770, 1715, 1503, 1407, 1319, 1235, 1177, 1048; **TLC** (20% EtOAc/hexanes) $R_f = 0.08$; **HRMS** (ESI⁺) Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_4$: 340.1292, Found: 340.1311.

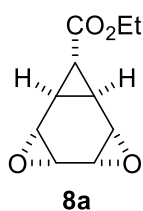


3-Ethyl-6,7-dimethyl-tricyclo[3.2.2.02,4]nona-6,8-diene-3,6,7-tricarboxylate

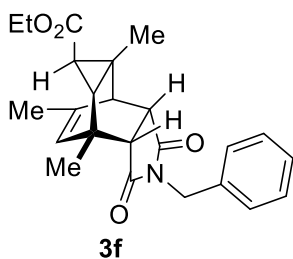
(6a): The title compound was prepared according to General Procedure B using benzene (1.8 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and dimethyl acetylenedicarboxylate (1.2 mL, 10 mmol). Flash chromatography (20% EtOAc/hexanes) provided a clear oil (178.2 mg, 58%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 6.16 (t, *J* = 4.2 Hz, 2H), 4.25 (m, 2H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 6H), 2.07 (dt, *J* = 2.4, 2.4 Hz, 2H), 1.76 (t, *J* = 2.4 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 170.9, 166.2, 147.1, 130.8, 60.6, 52.3, 40.6, 30.6, 26.8, 14.1; **IR** (thin film, cm⁻¹) 3065, 2985, 2953, 2844, 1714, 1637, 1601, 1278, 1061, 731; **TLC** (20% EtOAc/hexanes) R_f = 0.17; **HRMS** (ESI⁺) Calcd. for C₁₆H₁₉O₆: 307.1176, Found: 307.1176.



Ethyl-6,7-dioxatricyclo[3.2.2.02,4]non-8-ene-3-carboxylate (7a): The title compound was prepared according to General Procedure B using benzene (1.8 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and rose bengal (10 mg, 0.01 mmol), under irradiation for 7 h. Flash chromatography (30% EtOAc/hexanes) provided a white solid (104 mg, 53%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 6.32 (t, *J* = 6.0 Hz, 2H), 4.98 (m, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.24 (m, 2H), 1.29 – 1.22 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 171.3, 127.8, 72.0, 61.0, 21.7, 14.3, 14.1; **IR** (thin film, cm⁻¹) 2984, 1724, 1455, 1370, 1311, 1241, 1182, 1056, 877; **TLC** (20% EtOAc/hexanes) R_f = 0.15; **HRMS** (ESI⁺) Calcd. for C₁₀H₁₃NaO₄: 219.0628, Found: 219.0634.



Ethyl-3,6-dioxatetracyclo[6.1.0.02,4.05,7]nonane-9-carboxylate (8a): The title compound was prepared according to General Procedure B using benzene (17.8 mL, 200 mmol), ethyl diazoacetate (1.14 g, 10 mmol), Rh₂(TFA)₄ (65.8 mg, 0.1 mmol), and rose bengal (103 mg, 0.1 mmol) under irradiation for 20 h. Flash chromatography (20% EtOAc/hexanes) provided a pink solid (976 mg, 49%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 4.19 (q, *J* = 7.2 Hz, 2H), 3.31 (s, 4H), 2.12 (d, *J* = 4.4 Hz, 2H), 1.76 (t, *J* = 4.4 Hz, 1H), 1.31 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 171.1, 61.0, 47.4, 47.0, 22.6, 21.2, 14.0; **mp** 89–90 °C; **IR** (thin film, cm⁻¹) 2987, 1718, 1455, 1372, 1311, 1184, 1059, 1005, 945; **TLC** (20% EtOAc/hexanes) R_f = 0.05; **HRMS** (ESI⁺) Calcd. for C₁₀H₁₃NaO₄: 219.0628, Found: 219.0633.



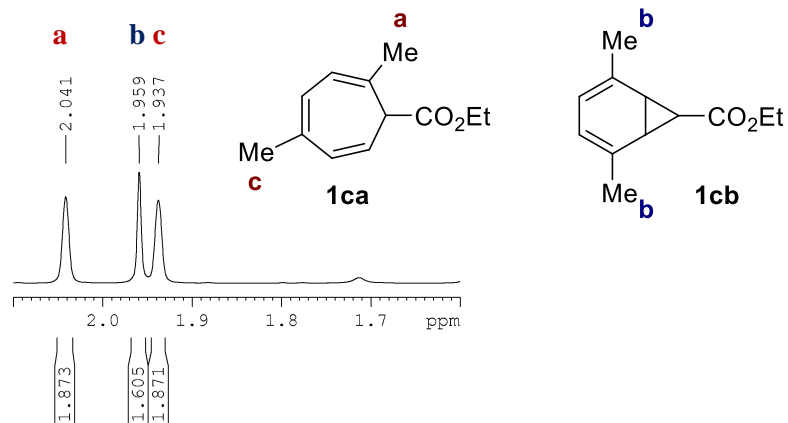
Ethyl-4,5a,7-trimethyl-2-octyl-1,3-dioxo-1,2,3,3a,4,4a,5,5a,6,6a-decahydro-4,6-ethenocyclopropa[f]isoindole-5-carboxylate (3f):

The title compound was prepared according to General Procedure B using mesitylene (2.78 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and *N*-benzylmaleimide (562 mg, 3 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (210 mg, 53%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.27 – 7.22 (m, 5H), 4.96 (s, 1H), 4.57 (d, *J* = 14.1 Hz, 1H), 4.48 (d, *J* = 14.1 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.26 (dd, *J* = 7.5, 3.6 Hz, 1H), 2.94 (m, 1H), 2.65 (d, *J* = 7.5 Hz, 1H), 1.51 (s, 3H), 1.45 (d, *J* = 1.2 Hz, 3H), 1.38 (m, 2H), 1.29 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 177.5, 176.6, 171.6, 136.8, 135.8, 128.4, 128.3, 127.6, 125.9, 60.5, 49.0, 45.2, 43.8, 41.9, 39.9, 33.7, 24.6, 24.1, 21.5, 20.5, 14.2, 13.2; **mp** 134–135 °C; **IR** (thin film, cm⁻¹) 2933, 2874, 1770, 1698, 1397, 1327, 1180; **TLC** (20% EtOAc/hexanes) R_f = 0.18; **HRMS** (ESI⁺) Calcd. for C₂₁H₂₂NO₄: 394.2013, Found: 394.2036.

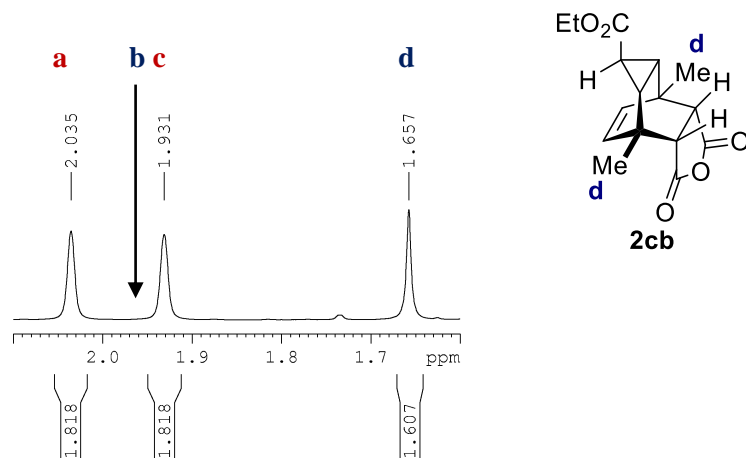
Separation difficulties for 2cb/3ca

Figure S1. Kinetic separation of 1c using maleic anhydride on water

Before addition of maleic anhydride to 1c

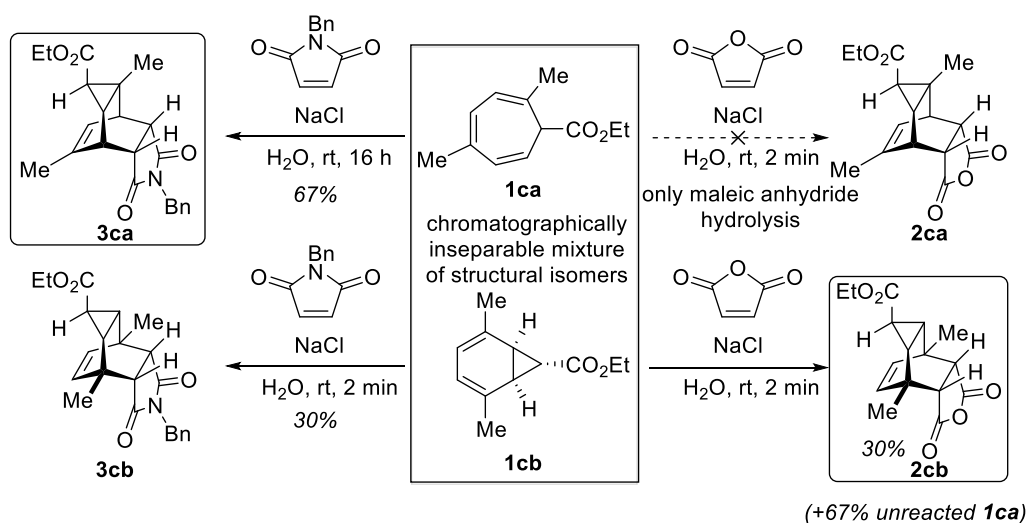


After 2 min in brine with maleic anhydride



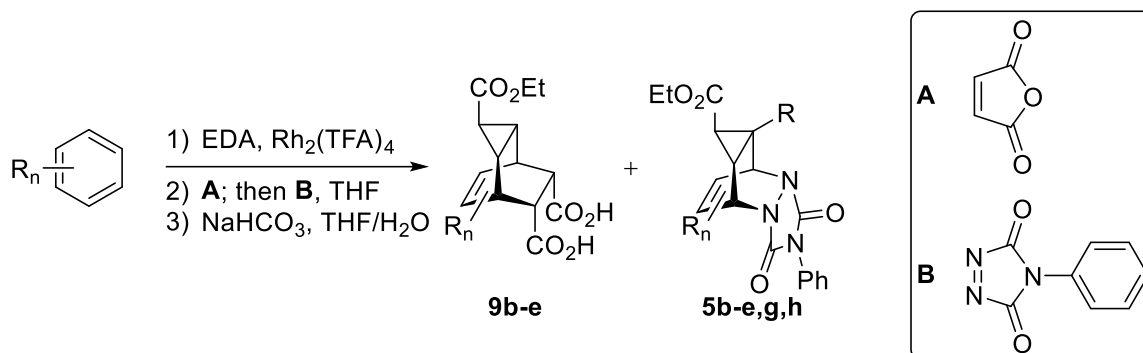
As shown in Figure S1, treatment of the regioisomeric mixture **1c** with maleic anhydride in brine provided complete conversion of **1cb** in under 2 min, while only trace conversion of **1ca** (<3%) was observed. While this analysis was feasible with any of the protons, the methyl peaks provided the cleanest separation. The vinyl protons in **1cb** (6.03 ppm) and **2cb** (5.67 ppm) both overlap peaks in **1ca**. 1,4-Dimethylterephthalate was used as an internal standard, with the resonance at 8.11 ppm (aryl C–H) set to 4.00, and the singlet at 3.96 ppm (–CO₂Me) provided internal consistency with an integration of 6.00.

Scheme S2. Kinetic separation of inseparable regioisomers via successive Diels-Alder reactions.

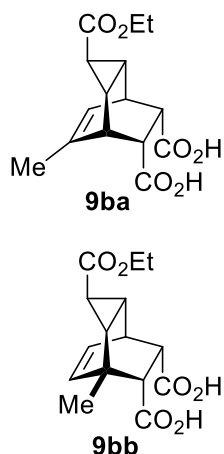


The originally-proposed two-step reaction sequence relied on the facile separation of the anhydride Diels-Alder product **2cb** and the maleimide Diels-Alder product **3ca**. This method was successful in providing orthogonal reactivity by treating the **1ca/1cb** mixture successively with maleic anhydride and *N*-benzylmaleimide, providing clean identification of **2cb** and **3ca** by ¹H NMR; however, this route proved infeasible for a number of reasons. First, **2cb** was non-UV active and does not stain with any conventional TLC stains. Even KMnO₄ was unable to oxidize the alkene. Furthermore, **3ca** was only faintly UV active, and it also did not stain. Not only do the two products elute at similar times (R_f difference <0.05 in 20% EtOAc/hexanes) but also the excess maleimide coeluted with the products, so the inability to discern which fractions contained which products made both mass recovery and pure isolation of the products challenging. Switching to *N*-octylmaleimide did provide a noticeable R_f difference; however, the analogous octyl-substituted maleimide Diels-Alder product was not UV active, and did not stain, so it faced the same challenges of “flying blind” as running a column on **2cb**. Therefore, PTAD was selected as the second dieneophile in this reaction sequence since it was not hydrolytically stable, so any excess PTAD would be destroyed in an aqueous workup, and the urazole moiety was both UV active, and the Diels-Alder products **5** stained in KMnO₄.

General Procedure C for the Buchner/Diels-Alder/hydrolysis sequence



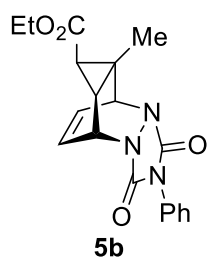
To a 25 mL round-bottomed flask charged with $Rh_2(TFA)_4$ (6.6 mg, 0.01 equiv), the aromatic substrate (20 equiv), and CH_2Cl_2 (2.5 mL) was added a 2.5 mL solution of ethyl diazoacetate (114 mg, 1 mmol) in CH_2Cl_2 via syringe pump addition over 3 h. After complete addition, the brown solution was stirred for an additional hour at room temperature, at which time the CH_2Cl_2 was removed by rotary evaporation, and the excess arene was removed and could be recovered by distillation under reduced pressure. At this point the crude mixture was analyzed by 1H NMR spectroscopy to determine yield and regioisomeric ratio, using 1,4-dimethylterephthalate as an internal standard. To the brown oil was added finely ground maleic anhydride (300 mg, 3 equiv), and the neat mixture stood at room temperature for 30 min, after ensuring that the oil permeated the powder, after which, the mixture was dissolved in THF (5 mL) and treated with PTAD (1.1 equiv, relative to the regioisomers that had not reacted with maleic anhydride), and the red solution was rapidly stirred for 1 h. After stirring for 1 h, brine was added (5 mL), and the mixture was rapidly stirred for 30 min. The products were extracted with EtOAc (2×10 mL), and washed with $NaHCO_3$, water, and brine (1×10 mL ea), dried over $MgSO_4$, filtered, and concentrated. The brown residue was subsequently partitioned between THF (10 mL) and saturated aqueous $NaHCO_3$ solution (10 mL) and rapidly stirred for 16 h, after which time the mixture was extracted with EtOAc (2×10 mL), and the combined organic layer was washed sequentially with $NaHCO_3$, water, and brine (1×10 mL ea), dried over Na_2SO_4 , filtered, and concentrated, and then purified by chromatography, yielding the urazole **5**. The aqueous washes were combined and cooled to 0 °C and acidified with conc. HCl (about 7 mL). Then the acidic medium was extracted with Et_2O (3×25 mL), and the combined organic layer was dried over $MgSO_4$, filtered, and concentrated. The solid residue was then triturated with CH_2Cl_2 , and the white solid **9** was collected by vacuum filtration and dried in vacuo. **Note**: it was necessary to perform a preliminary aqueous workup to remove the maleic acid resulting from the hydrolysis of maleic anhydride in order to maximize the yield and purity of the diacid product. Maleic acid was not removed in the CH_2Cl_2 trituration, but it could be removed via trituration with EtOAc; however, the diacid products had higher solubility in EtOAc, so yields were diminished without removing the maleic acid halfway through the synthetic route. Notably, the anhydride in the Diels-Alder products was significantly more stable toward hydrolysis than maleic anhydride, so the maleic anhydride could be selectively hydrolyzed under the conditions reported. Below, in cases where an inseparable mixture of regioisomers were isolated, both structures are shown, and when possible, the resonances for both structures are identified. All spectra were recorded in $CDCl_3$; however, the diacids required approx. 10 drops of CD_3OD for dissolution.



3-(Ethoxycarbonyl)-8-methyltricyclo[3.2.2.0.2,4]non-8-ene-6,7-dicarboxylic acid

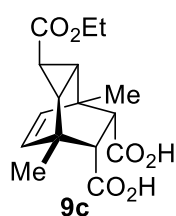
(9b): The title compound was prepared according to General Procedure C using toluene (2.13 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and maleic anhydride (294 mg, 3 mmol), yielding a white solid (54 mg, 20%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ (**9ba**, 47%) 5.51 (d, *J* = 6.6 Hz, 1H), 4.02 (q, *J* = 7.2 Hz, 2H), 3.12 – 2.92 (m, 4H), 1.71 (s, 3H), 1.58 (m, 1H), 1.36 (m, 1H), 1.19 (m, 1H), 1.18 (t, *J* = 7.2 Hz, 3H); (**9bb**, 53%) 5.93 (t, *J* = 7.8 Hz, 1H), 5.53 (d, *J* = 7.8 Hz, 1H), 4.02 (q, *J* = 7.2 Hz, 2H), 3.18 (br s, 1H), 3.12 – 2.92 (m, 2H), 1.58 (m, 1H), 1.54 (m, 1H), 1.31 (m, 4H), 1.18 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ (**9ba**, 47%) 175.1, 175.0, 173.5, 132.6, 120.8, 60.6, 53.6, 47.1, 38.8, 33.3, 21.7, 20.7, 20.1, 18.2, 13.9; (**9bb**, 53%) 174.9, 174.6, 173.5, 136.7, 127.3, 60.6, 50.2, 47.2, 38.8, 32.3, 26.7, 21.9, 21.5, 17.7, 13.9; **mp** 170–172 °C; **IR** (thin film, cm⁻¹) 3445, 1716, 1653, 1419, 1317, 1282, 1219, 1168; **HRMS**

(ESI) Calcd. for C₁₅H₁₇O₆: 293.1031, Found: 293.1034.



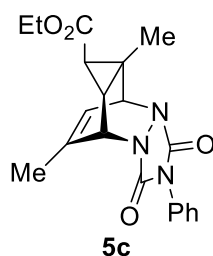
Ethyl-5a-methyl-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5b):

The title compound was prepared according to General Procedure C using toluene (2.13 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol) Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (35 mg, 0.2 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (36 mg, 8%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.45 (m, 4H), 7.38 (m, 1H), 6.27 (ddd, *J* = 7.2, 5.1, 1.5 Hz, 1H), 6.18 (ddd, *J* = 7.2, 6.0, 1.2 Hz, 1H), 5.24 (ddd, *J* = 5.1, 4.5, 1.2 Hz, 1H), 4.96 (dd, *J* = 6.0, 1.5 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.10 (dd, *J* = 4.5, 3.9 Hz, 1H), 1.61 (d, *J* = 3.9 Hz, 1H), 1.53 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 169.7, 157.1, 156.7, 131.2, 129.1, 128.3, 126.7, 125.7, 125.5, 61.1, 58.7, 52.7, 28.3, 20.4, 20.3, 14.2, 12.6; **mp** 140–142 °C; **IR** (thin film, cm⁻¹) 3065, 2982, 2932, 1774, 1715, 1503, 1405, 1335, 1232; **TLC** (20% EtOAc/hexanes) R_f = 0.13; **HRMS** (ESI⁺) Calcd. for C₁₉H₂₀N₃O₄: 354.1448, Found: 354.1469.



3-(Ethoxycarbonyl)-1,5-dimethyltricyclo[3.2.2.0.2,4]non-8-ene-6,7-dicarboxylic acid

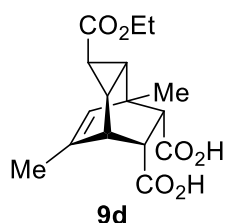
(9c): The title compound was prepared according to General Procedure C using *p*-xylene (24.6 mL, 200 mmol), ethyl diazoacetate (1.14 g, 10 mmol), Rh₂(TFA)₄ (65.8 mg, 0.1 mmol), and maleic anhydride (2.94 g, 30 mmol), yielding a white solid (409 mg, 14%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 5.57 (s, 3H), 3.98 (q, *J* = 7.2 Hz, 2H), 2.95 (s, 2H), 1.33, (d, *J* = 2.4 Hz, 2H), 1.31 (s, 6H), 1.30 (t, *J* = 2.4 Hz, 1H), 1.16 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 174.0, 173.7, 131.7, 60.6, 56.0, 38.0, 28.1, 21.7, 17.1, 13.8; **mp** 188–189 °C; **IR** (thin film, cm⁻¹) 3420, 2967, 1716, 1417, 1306, 1243, 1163; **HRMS** (ESI) Calcd. for C₁₆H₁₉O₆: 307.1187, Found: 307.1191



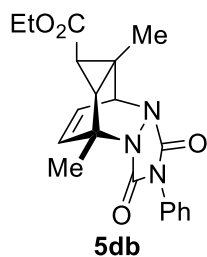
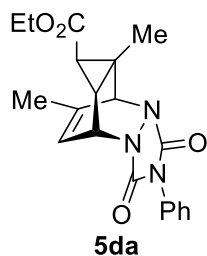
Ethyl-5a,9-dimethyl-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5c):

The title compound was prepared according to General Procedure C using *p*-xylene (24.6 mL, 200 mmol), ethyl diazoacetate (1.14 g, 10 mmol) Rh₂(TFA)₄ (65.8 mg, 0.1 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (1.40 g, 8 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (1.85 g, 50%).

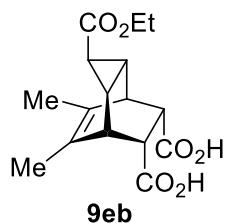
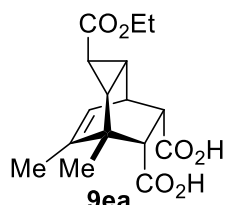
Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.46 (m, 4H), 7.37 (m, 1H), 5.83 (m, 1H), 5.00 (dd, $J = 5.1, 1.8$ Hz, 1H), 4.86 (d, $J = 6.0$ Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 2.05 (dd, $J = 5.1, 3.6$ Hz, 1H), 1.88 (d, $J = 1.8$ Hz, 3H), 1.53 (d, $J = 3.6$ Hz, 1H), 1.51 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 169.8, 157.4, 156.9, 136.3, 131.3, 129.1, 128.2, 125.4, 118.5, 61.1, 59.6, 57.0, 28.0, 21.7, 20.0, 19.5, 14.2, 12.7; **mp** 126–127 °C; **IR** (thin film, cm^{-1}) 3063, 2981, 2935, 1772, 1716, 1504, 1404, 1227, 1158; **TLC** (20% EtOAc/hexanes) $R_f = 0.13$; **HRMS** (ESI^+) Calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_4$: 368.1605, Found: 368.1630.



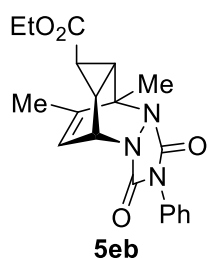
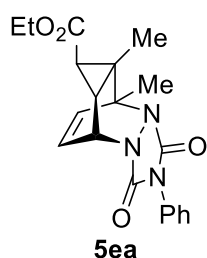
3 - (Ethoxycarbonyl)-1,9-dimethyltricyclo[3.2.2.0,2,4]non-8-ene-6,7-dicarboxylic acid (9d): The title compound was prepared according to General Procedure C using *m*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol), and maleic anhydride (294 mg, 3 mmol), yielding a white solid (57 mg, 20%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.15 (s, 1H), 4.01 (q, $J = 7.2$ Hz, 2H), 3.05 (d, $J = 9.9$ Hz, 1H), 3.00 (br s, 1H), 2.90 (d, $J = 9.9$ Hz, 1H), 1.78 (s, 3H), 1.57 (br s, 1H), 1.30 (m, 1H), 1.26 (s, 3H), 1.21 – 1.15 (m, 4H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 174.9, 174.6, 173.7, 135.9, 125.8, 60.6, 53.5, 49.8, 38.8, 37.3, 27.9, 21.9, 21.4, 20.5, 17.7, 13.9; **mp** 159–160 °C; **IR** (thin film, cm^{-1}) 3432, 2091, 1646, 1636, 1456, 1418, 1274, 1173; **HRMS** (ESI^-) Calcd. for $\text{C}_{16}\text{H}_{19}\text{O}_6$: 307.1187, Found: 307.1192



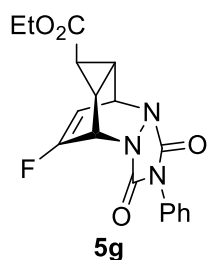
Ethyl -5a,10-dimethyl-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine - 6 - carboxylate (5d): The title compound was prepared according to General Procedure C using *m*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol) $\text{Rh}_2(\text{TFA})_4$ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (105 mg, 0.6 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (114 mg, 31%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ (**5da, 74%**) 7.44 (m, 4H), 7.42 (m, 1H), 5.75 (d, $J = 5.4$ Hz, 1H), 5.14 (t, $J = 5.4$ Hz, 1H), 4.73 (s, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 2.05 (m, 1H), 1.92 (s, 3H), 1.52 (s, 3H), 1.49 (d, $J = 3.6$ Hz, 1H), 1.29 (t, $J = 7.2$ Hz, 3H); (**5db, 26%**) 7.41 (m, 1H), 7.36 (m, 4H), 6.18 (dd, $J = 7.5, 6.0$ Hz, 1H), 5.99 (d, $J = 7.5$ Hz, 1H), 4.94 (d, $J = 6.0$ Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 2.04 (s, 3H), 1.89 (d, $J = 3.6$ Hz, 1H), 1.59 (d, $J = 3.6$ Hz, 1H), 1.52 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ (**5da, 74%**) 169.8, 157.3, 156.9, 137.2, 131.2, 129.0, 128.2, 125.3, 117.7, 63.1, 61.0, 53.6, 27.7, 22.0, 20.0, 19.6, 14.2, 12.6; (**5db, 26%**) 169.8, 155.9, 155.4, 131.4, 131.2, 129.0, 128.2, 125.7, 125.0, 62.8, 61.0, 58.0, 28.0, 27.7, 21.8, 21.6, 14.2, 12.5; **mp** 110–112 °C; **IR** (thin film, cm^{-1}) 3064, 2980, 2934, 1771, 1716, 1504, 1404, 1227, 1173; **TLC** (20% EtOAc/hexanes) $R_f = 0.13$; **HRMS** (ESI^+) Calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_4$: 368.1605, Found: 368.1628.



3-(Ethoxycarbonyl)-1,8-dimethyltricyclo[3.2.2.0,2,4]non-8-ene-6,7-dicarboxylic acid (9e): The title compound was prepared according to General Procedure C using *o*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and maleic anhydride (294 mg, 3 mmol), yielding a white solid (37 mg, 12%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ (**9ea**, 77%) 5.58 (d, *J* = 6.6 Hz, 1H), 3.96 (q, *J* = 7.2 Hz, 2H), 3.08 (m, 1H), 2.96 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.87 (d, *J* = 10.8 Hz, 1H), 1.56 (d, *J* = 0.6 Hz, 3H), 1.50 (m, 1H), 1.28 (dd, *J* = 8.4, 2.4 Hz, 1H), 1.25 (s, 3H), 1.16–1.12 (m, 4H); (**9eb**, 23%) 3.96 (q, *J* = 7.2 Hz, 2H), 2.93 (br s, 2H), 2.89 (br s, 2H), 1.58 (s, 6H), 1.48 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H), 0.96 (t, *J* = 2.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ (**9ea**, 77%) 174.8, 174.5, 173.7, 137.9, 121.2, 60.5, 53.8, 41.0, 32.0, 26.9, 21.9, 20.0, 18.1, 17.5, 16.8, 13.8; (**9eb**, 23%) 175.0, 173.7, 127.4, 60.5, 47.0, 39.3, 21.6, 18.2, 13.8; **mp** 120–121°C; **IR** (thin film, cm⁻¹); 3420, 1716, 1698, 1652, 1540, 1276, 1174; **HRMS** (ESI⁺) Calcd. for C₁₆H₁₉O₆: 307.1187, Found: 307.1193.

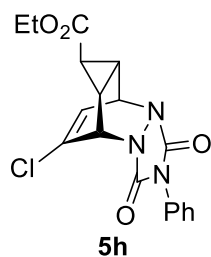


Ethyl 5,5a-dimethyl-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5e): The title compound was prepared according to General Procedure C using *o*-xylene (2.47 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (44 mg, 0.25 mmol), yielding a white solid (31 mg, 9%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ (**5ea**, 76%) 7.44 (m, 4H), 7.36 (m, 1H), 6.14 (dd, *J* = 7.8, 6.0 Hz, 1H), 6.04 (dd, *J* = 7.8, 1.5 Hz, 1H), 5.23 (ddd, *J* = 6.0, 1.5, 1.5 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.12 (dd, *J* = 3.6, 1.5 Hz, 1H), 1.99 (s, 3H), 1.65 (d, *J* = 3.6 Hz, 1H), 1.43 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H); (**5eb**, 24%) 7.44 (m, 4H), 7.36 (m, 1H), 6.24 (dd, *J* = 4.2, 3.6 Hz, 1H), 4.90 (dd, *J* = 4.2, 3.6 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 1.65 (m, 5H), 1.50 (s, 3H), 1.30–1.27 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ (**5ea**, 76%) 169.9, 155.7, 155.4, 132.5, 131.3, 129.0, 128.2, 125.7, 124.7, 65.9, 61.1, 61.8, 28.2, 24.0, 22.7, 19.1, 14.2, 10.1; **mp** 131–132°C; **IR** (thin film, cm⁻¹) 2981, 2929, 1771, 1715, 1504, 1404, 1223, 1188; **TLC** (20% EtOAc/hexanes) R_f = 0.13; **HRMS** (ESI⁺) Calcd. for C₂₀H₂₂N₃O₄: 368.1605, Found: 368.1627.

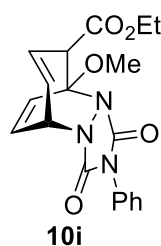


Ethyl 9-fluoro-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5g): The title compound was prepared according to General Procedure C using fluorobenzene (1.88 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (193 mg, 1.1 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white solid (167 mg, 47%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.46 (m, 4H), 7.38 (m, 1H), 5.46 (m, 1H), 5.38 (m, 1H), 5.352 (ddd, *J* = 8.4, 5.4, 3.0, Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.30 (m, 1H), 2.22 (m, 1H), 1.61 (t, *J* = 2.7 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 169.8, 156.4, 156.2 (d, *J* = 3.3 Hz), 154.2, 130.9, 129.1, 128.4, 125.3, 98.6 (d, *J* = 3.5 Hz), 61.4, 54.3 (d, *J* = 26.7 Hz), 52.7 (d, *J* = 6.3 Hz), 23.2, 16.8, 14.9 (d, *J* = 2.6 Hz), 14.0; **mp** 132–133°C; **IR** (thin film, cm⁻¹) 3064, 2987,

2932, 1717, 1663, 1404, 1226, 1165, 1050; **TLC** (20% EtOAc/hexanes) $R_f = 0.16$; **HRMS** (ESI⁺) Calcd. for C₁₈H₁₇FN₃O₄: 358.1198, Found: 358.1217.



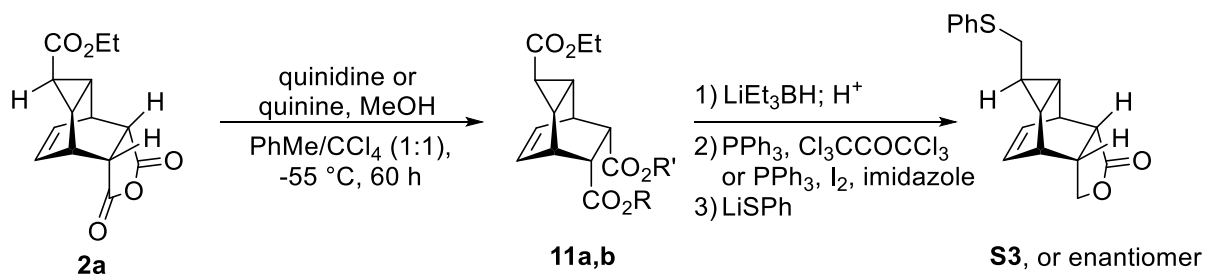
Ethyl 9-chloro-1,3-dioxo-2-phenyl-2,3,5a,6,6a,7-hexahydro-1H,5H-5,7-ethenocyclopropa[d][1,2,4]triazolo[1,2-a]pyridazine-6-carboxylate (5h): The title compound was prepared according to General Procedure C using chlorobenzene (2.03 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (193 mg, 1.1 mmol). Flash chromatography (20% EtOAc/hexanes) provided a white foam (191 mg, 51%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.46 (m, 4H), 7.39 (m, 1H), 6.13 (dd, $J = 6.6, 2.4$ Hz, 1H), 5.33 (dd, $J = 6.6, 5.8$ Hz, 1H), 5.30 (dd, $J = 4.8, 2.4$ Hz, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 2.31 (ddd, $J = 8.1, 4.8, 3.0$, Hz, 1H), 2.23 (ddd, $J = 8.1, 4.8, 3.0$ Hz, 1H), 1.52 (t, $J = 3.0$ Hz, 1H), 1.29 (t, $J = 7.2$ Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 169.8, 156.4, 156.0, 130.9, 129.1, 128.5, 128.4, 125.3, 120.8, 61.4, 59.1, 53.5, 23.3, 16.5, 15.3, 14.1; **IR** (thin film, cm⁻¹) 3065, 2981, 2932, 1772, 1716, 1646, 1505, 1404, 1224; **TLC** (20% EtOAc/hexanes) $R_f = 0.15$; **HRMS** (ESI⁺) Calcd. for C₁₈H₁₇ClN₃O₄: 374.0902, Found: 374.0911.



Ethyl 5-methoxy-1,3-dioxo-2-phenyl-2,3,6,9-tetrahydro-1H,5H-5,9-etheno[1,2,4]triazolo[1,2-a][1,2]diazepine-6-carboxylate (10i): The title compound was prepared according to General Procedure C using anisole (2.17 mL, 20 mmol), ethyl diazoacetate (114 mg, 1 mmol), Rh₂(TFA)₄ (6.6 mg, 0.01 mmol), and 4-phenyl-1,2,4-triazoline-3,5-dione (53 mg, 0.3 mmol). Flash chromatography (20% EtOAc/hexanes) provided a yellow oil (34 mg, 9%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.53 (d, $J = 7.9$ Hz, 2H), 7.47 (dt, $J = 7.9, 7.3$ Hz, 2H), 7.38 (t, $J = 7.3$ Hz, 1H), 6.78 (dd, $J = 9.6, 7.2$ Hz, 1H), 6.34 (d, $J = 9.6$ Hz, 1H), 6.21 (ddd, $J = 11.1, 7.2, 2.4$ Hz, 1H), 5.77 (dd, $J = 11.1, 4.4$ Hz, 1H), 5.02 (dd, $J = 7.2, 7.2$ Hz, 1H), 4.28 (dd, $J = 4.4, 2.4$ Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 3.60 (s, 3H), 1.27 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 167.0, 154.4, 150.8, 132.5, 131.2, 131.1, 129.3, 129.0, 128.2, 126.5, 125.5, 91.2, 61.4, 53.7, 52.0, 50.3, 14.0; **IR** (thin film, cm⁻¹) 3067, 2981, 2938, 1772, 1715, 1498, 1409, 1247, 1187; **TLC** (20% EtOAc/hexanes) $R_f = 0.10$; **HRMS** (ESI⁺) Calcd. for C₁₉H₂₀N₃O₅: 370.1397, Found: 370.1419.

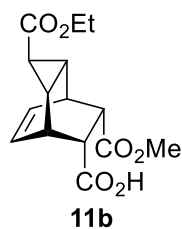
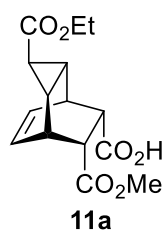
Further transformations of Diels-Alder products

Method to obtain HPLC traces of 11a,b



Note: The title procedure was required to assay the enantiomeric ratio (er) of the initial desymmetrization products **11a,b** owing to their poor UV activity. The desymmetrization could also be performed using benzyl alcohol without any loss in reactivity; however, this product was also poorly UV active.

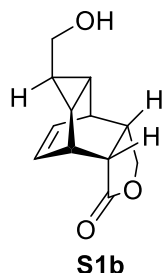
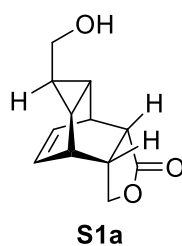
Furthermore, it was required to convert the hemiester into the respective lactone, since the acid functionality inhibited elution on silica. Due to the conformational rigidity of the hemiester, and the intermediates to **S3**, we presume that no loss of enantiomeric purity was observed in this sequence.



(1S,2S,4R,5R,6R,7S) -3-(ethoxycarbonyl)-7-(methoxycarbonyl)tricyclo[3.2.2.0]oct-8-ene-6-carboxylic acid (11a/11b):

The anhydride (262 mg, 1 mmol) was added to a flame-dried round-bottomed flask containing the cinchona alkaloid (357 mg, 1.1 mmol), and the solid was suspended in 1:1 toluene/ CCl_4 (5 mL for quinidine, 20 mL for quinine). Then methanol (121 μL , 3 mmol) was added and the mixture was cooled to $-55\text{ }^\circ\text{C}$, where it stirred for 60 h. The mixture was warmed to room temperature and concentrated, and the residue was taken up in Et_2O (10 mL) and washed with 1 M HCl ($3 \times 10\text{ mL}$). The combined aqueous layer was extracted with Et_2O ($2 \times 10\text{ mL}$). **Note:** the cinchona alkaloid could be recovered from the acidic aqueous layer by basifying with Na_2CO_3 and extracting with Et_2O . The combined organic layer was then extracted with Na_2CO_3 ($2 \times 20\text{ mL}$). The resultant aqueous layer was then acidified with conc. HCl (approx. 10 mL), and the organics were extracted with Et_2O ($2 \times 25\text{ mL}$), washed with brine, dried over MgSO_4 , filtered, and concentrated, yielding a white solid of good purity: for quinine (**11a**, 272 mg, 93%), for quinidine (**11b**, 290 mg, 99%). Analytical

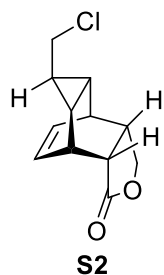
data: $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 10.16 (br s, 1H), 6.01 (t, $J = 6.8\text{ Hz}$, 1H), 5.93 (t, $J = 6.8\text{ Hz}$, 1H), 4.09 (q, $J = 7.2\text{ Hz}$, 2H), 3.59 (s, 3H), 3.00 (m, 2H), 3.17 (dd, $J = 10.4, 1.6\text{ Hz}$, 1H), 3.12 (dd, $J = 10.4, 2.0\text{ Hz}$, 1H), 1.67 (m, 2H), 1.37 (dd, $J = 2.8, 2.4\text{ Hz}$, 1H), 1.24 (t, $J = 7.2\text{ Hz}$, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 178.2, 173.0, 172.8, 128.7, 127.8, 60.6, 51.6, 47.4, 47.2, 33.8, 33.3, 20.3, 20.2, 18.4, 14.1; **mp** 114–116 $^\circ\text{C}$; $[\alpha]_{\text{D}} = (\mathbf{11a}) +0.5^\circ$ ($c = 5.21, \text{CH}_2\text{Cl}_2$), (**11b**) -1.4° ($c = 11.79, \text{CH}_2\text{Cl}_2$); **IR** (thin film, cm^{-1}) 3446, 2984, 1732, 1717, 1698, 1419, 1280, 1161, 1047; **HRMS** (ESI) Calcd. for $\text{C}_{15}\text{H}_{17}\text{O}_6$: 293.1031, Found: 293.1031.



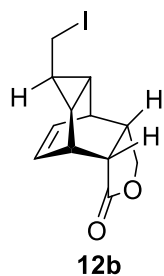
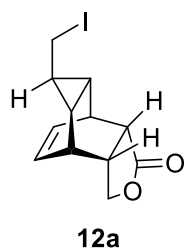
(3aS,4S,4aS,5aR,6R,6aR)-5-(hydroxymethyl)-3,3a,4,4a,5,5a,6,6a-octahydro-1H-4,6-ethenocyclopropa[f]isobenzofuran-1-one (S1):

The hemiester **11a** (290 mg, 1 equiv) was added to a flame-dried 25 mL round-bottomed flask under nitrogen atmosphere and cooled to $0\text{ }^\circ\text{C}$. A solution of LiEt_3BH (1.0 M in THF, 6 mL, 6 equiv) was then added dropwise over 3 min. After stirred for 15 min at $0\text{ }^\circ\text{C}$, the ice bath was removed, and the solution warmed to room temperature while stirred for 6 h. The reaction was then carefully quenched with 1 M HCl (10 mL) under nitrogen atmosphere, and the mixture stirred for an additional 2 h. The organics were then extracted with Et_2O ($2 \times 10\text{ mL}$), dried over MgSO_4 , filtered, and concentrated. The crude material was purified by column chromatography (40% EtOAc /hexanes), yielding a pungent smelling, white solid (132 mg, 71%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.99 (dd, $J = 7.8, 6.6\text{ Hz}$, 1H), 5.93 (dd, $J = 7.2, 7.2\text{ Hz}$, 1H), 4.38 (dd, $J = 9.6, 9.0\text{ Hz}$, 1H), 3.89 (dd, $J = 9.6, 4.8\text{ Hz}$, 1H), 3.51 (dd, $J = 11.4, 6.6\text{ Hz}$, 1H), 3.45 (dd, $J = 11.4, 7.2\text{ Hz}$, 1H), 3.38 (m, 1H), 3.04 (m, 1H), 2.92 (dd, $J = 9.6, 3.6\text{ Hz}$, 1H), 2.85 (dddd, $J = 9.6, 9.6, 3.6, 3.6\text{ Hz}$, 1H), 1.04 (ddd, $J = 7.2, 3.0, 3.0\text{ Hz}$, 1H),

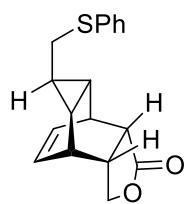
0.97–0.91 (m, 2H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 178.3, 130.8, 128.8, 71.8, 64.0, 45.7, 39.1, 34.5, 33.1, 20.3, 15.5, 15.4; **mp** 115–117 $^\circ\text{C}$; $[\alpha]_{\text{D}} = (\mathbf{S1a}) +43.8^\circ$ ($c = 2.90, \text{CH}_2\text{Cl}_2$), (**S1b**) -53.6° ($c = 6.27, \text{CH}_2\text{Cl}_2$); **IR** (thin film, cm^{-1}) 3420, 2851, 1748, 1652, 1541, 1396, 1190, 1038; **TLC** (20% EtOAc /hexanes) $R_f = 0.05$; **HRMS** (ESI $^+$) Calcd. for $\text{C}_{12}\text{H}_{15}\text{O}_3$: 207.1016, Found: 207.1021



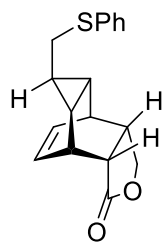
(3a*S*,4*S*,4a*R*,5a*S*,6*R*,6a*R*)- 5- (chloromethyl) - 3,3a,4,4a,5,5a,6,6a - octahydro - 1*H* - 4,6-ethenocyclopropa[*f*]isobenzofuran-1-one (S2**):** Hexachloroacetone (0.6 mL, 6 equiv) was added to a 25 mL round-bottomed flask with 2 mL CH₂Cl₂, and the flask was cooled to 0 °C. Triphenylphosphine (185 mg, 1.1 equiv) was added, and the mixture stirred for 5 min. The intermediate alcohol **S1** (132 mg, 1 equiv) was added in 3 mL CH₂Cl₂, and the clear solution stirred for 5 min at 0 °C and 2 h at room temperature. The reaction was concentrated and immediately purified by column chromatography (20% EtOAc/hexanes), yielding a white solid (107 mg, 74%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 5.96 (dd, *J* = 7.8, 6.6 Hz, 1H), 5.92 (dd, *J* = 7.8, 6.6 Hz, 1H), 4.35 (t, *J* = 9.6 Hz, 1H), 3.85 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.45 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.38 – 3.32 (m, 2H), 3.04 (m, 1H), 2.88 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.82 (m, 1H), 1.13 (m, 1H), 1.06 – 0.99 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 178.0, 130.6, 128.8, 71.6, 46.8, 45.3, 38.8, 34.3, 33.0, 20.2, 18.1, 18.0; **mp** 99–100 °C; **IR** (thin film, cm⁻¹) 3050, 2934, 2867, 1759, 1636, 1377, 1182, 1007; **TLC** (20% EtOAc/hexanes) *R_f* = 0.05; **HRMS** (ESI⁺) Calcd. for C₁₂H₁₄ClO₂: 225.0677, Found: 225.0677.



(3a*S*,4*S*,4a*R*,5a*S*,6*R*,6a*R*)- 5- (iodomethyl) - 3,3a,4,4a,5,5a,6,6a - octahydro - 1*H* - 4,6-ethenocyclopropa[*f*]isobenzofuran-1-one (12**):** A 25 mL round-bottomed flask was charged with triphenylphosphine (412 mg, 2.05 equiv) and imidazole (261 mg, 5 equiv). The solids were dissolved in CH₂Cl₂ (5 mL) and cooled to 0 °C. Iodine (389 mg, 2 equiv) was added, and the yellow-orange solution stirred at 0 °C for 10 min. The intermediate alcohol **S1** (158 mg, 0.8 mmol) was added in 10 mL of CH₂Cl₂, and the reaction was allowed to gradually warm to room temperature as it stirred for 16 h. Then the reaction was quenched with saturated Na₂S₂O₃ (8 mL), and the reaction was stirred at room temperature for 15 min. The product were then extracted with CH₂Cl₂ (3 × 10 mL), and washed with brine (1 × 20 mL), dried over Na₂SO₄, filtered, and concentrated, and immediately purified by column chromatography (40% EtOAc/hexanes), yielding a white solid (88 mg, 36%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 5.96 (dd, *J* = 7.2, 6.6 Hz, 1H), 5.92 (dd, *J* = 7.2, 6.6 Hz, 1H), 4.34 (dd, *J* = 9.6, 9.0 Hz, 1H), 3.85 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.36 (m, 1H), 3.13 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.07 – 2.99 (m, 2H), 2.87 (dd, *J* = 9.6, 3.0 Hz, 1H), 2.08 (dddd, *J* = 9.6, 9.6, 4.2, 4.2 Hz, 1H), 1.08 (m, 2H), 0.97 (m, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 177.9, 130.6, 128.7, 71.5, 45.1, 38.6, 34.6, 33.3, 23.3, 23.0, 22.3, 9.4; **mp** 98–99 °C; [α]_D²⁰ = (**12a**) +47.3° (*c* = 2.00, CH₂Cl₂), (**12b**) -43.0° (*c* = 4.60, CH₂Cl₂); **IR** (thin film, cm⁻¹) 3054, 2859, 2359, 1756, 1484, 1437, 1182, 1119, 998, 750; **TLC** (20% EtOAc/hexanes) *R_f* = 0.06; **HRMS** (ESI⁺) Calcd. for C₁₂H₁₄IO₂: 317.0033, Found: 317.0035.



S3a

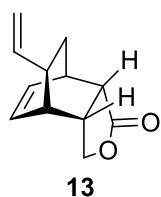
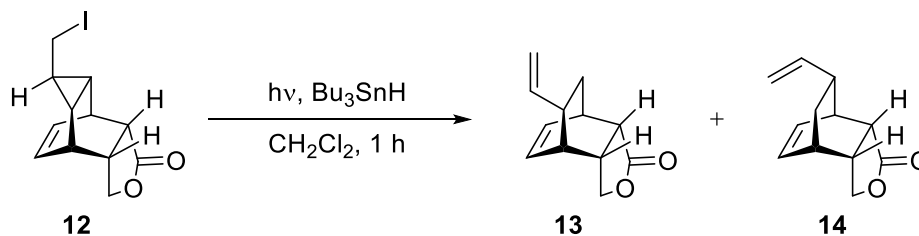


S3b

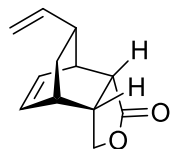
(3a*S*,4a*S*,4a*R*,5a*S*,6*R*,6a*R*)-5-((phenylthio)methyl)-3,3a,4,4a,5,5a,6,6a-octahydro-1H-4,6-ethenocyclopropa[f]isobenzofuran-1-one (S3): *n*-BuLi (2.61 M in hexanes, 0.36 mL, 2 equiv) was added dropwise to a flame-dried 25 mL round-bottomed flask containing thiophenol (0.15 mL, 3 equiv) in anhydrous THF cooled to 0 °C. After complete addition, the solution was warmed to room temperature, where it stirred for 15 min. The alkyl chloride **S3** (107 mg, 1 equiv) was added with 4 mL anhydrous THF, and the clear solution stirred until deemed complete by TLC (16 h). The reaction was then concentrated and immediately purified by column chromatography (20% EtOAc/hexanes), yielding a white solid (61 mg, 59%). The enantiomeric ratio (**S3a**: 94:6; **S3b**, 6:94) was determined by chiral HPLC (column IA, 90:10 hexanes/^{*i*}PrOH). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ 7.35 (m, 2H), 7.29 (m, 2H), 7.21 (m, 1H), 5.94 (t, *J* = 7.2 Hz, 1H), 5.88 (t, *J* = 7.2 Hz, 1H), 4.35 (dd, *J* = 9.6, 9.0 Hz, 1H), 3.85 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.32 (m, 1H), 2.99 (m, 1H), 2.89 – 2.83 (m, 2H), 2.81 – 2.85 (m, 2H), 1.00 (ddd, *J* = 7.5, 3.0, 3.0 Hz, 1H), 0.91 (ddd, *J* = 7.5, 3.6, 3.6 Hz, 1H), 0.87 (dddd, *J* = 6.6, 6.6, 3.6, 3.0 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 178.3, 136.2, 130.6, 130.0, 128.8, 128.7, 126.3, 71.7, 45.5, 38.9, 36.3, 34.6, 33.2, 18.04, 18.00, 17.5;

mp 96–97 °C; [α]_D = (**S1a**) +22.5° (*c* = 0.98, CH₂Cl₂), (**S1b**) -21.0° (*c* = 0.18, CH₂Cl₂); **IR** (thin film, cm⁻¹) 3053, 2948, 1758, 1647, 1584, 1479, 1377, 1183, 1015; **TLC** (20% EtOAc/hexanes) *R*_f = 0.11; **HRMS** (ESI⁺) Calcd. for C₁₈H₁₉O₂S: 299.1100, Found: 299.1110.

Cyclopropylmethyl radical-promoted ring-opening of **12**



13



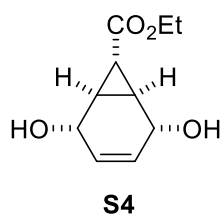
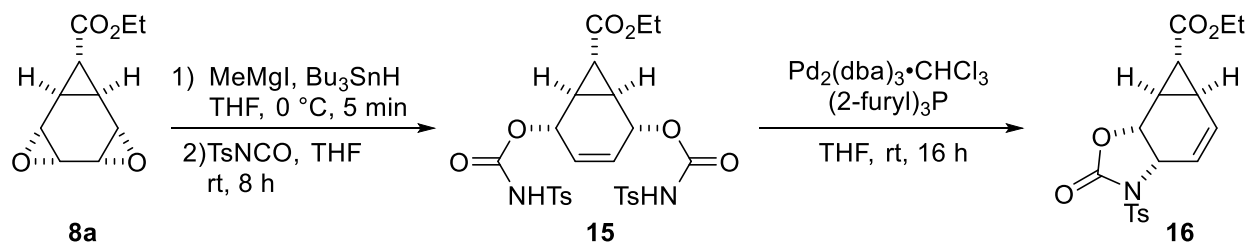
14

9-vinyl-3a,4,7,7a-tetrahydro-4,7-ethanoisobenzofuran-1(3H)-one and 9-vinyl-3a,4,7,7a-tetrahydro-4,7-ethanoisobenzofuran-3(1H)-one (13/14): The alkyl iodide **12** (38 mg, 0.12 mmol) was added to a flame-dried 5 dram vial under nitrogen atmosphere. Then the Bu₃SnH (0.13 mL, 4 equiv) was added, and the mixture was dissolved in anhydrous CH₂Cl₂ (10 mL). The vial was then subjected to irradiation by a Hg lamp/Pyrex filter for 1 h. After 1 h, the lamp was turned off and the reaction was concentrated and purified by column chromatography (20% EtOAc/hexanes), yielding a clear oil as a mixture of regioisomers (23 mg, >99%). Analytical data: ¹H NMR (600 MHz, CDCl₃) δ (**13**, **56%**) 6.42 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.21 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.56 (m, 1H), 4.98 (m, 1H), 4.91 (m, 1H), 4.37 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.87 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.11 (m, 1H), 2.84 – 2.77 (m, 2H), 2.76 – 2.68 (m, 1H), 2.38 (m, 1H), 1.91 (ddd, *J* = 12.6, 9.6, 2.4 Hz, 1H), 1.19 (ddd, *J* = 13.2, 4.8, 3.6 Hz, 1H); (**14**, **44%**)

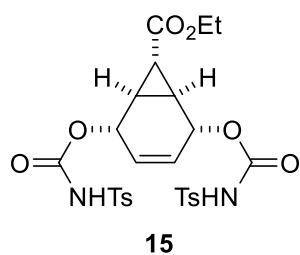
6.36 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.26 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.56 (m, 1H), 4.98 (m, 1H), 4.91 (m, 1H), 4.37 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.87 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.07 (m, 1H), 2.87 (dd, *J* = 10.2, 3.6 Hz, 1H), 2.76 – 2.68 (m, 2H), 2.45 (m, 1H), 1.83 (ddd, *J* = 12.6, 9.6, 2.4 Hz, 1H), 1.15 (ddd, *J* = 13.2, 5.4, 3.0

Hz, 1H); ^{13}C NMR (150 MHz, CDCl_3) δ (**13**, **56%**) 179.1, 143.0, 134.9, 130.7, 113.5, 71.9, 44.1, 40.6, 39.4, 38.5, 32.3, 31.3; (**14**, **44%**) 178.9, 142.8, 133.2, 132.4, 113.6, 72.3, 45.1, 40.3, 37.4, 37.3, 34.0, 31.3; **IR** (thin film, cm^{-1}) 3048, 2934, 2867, 1759, 1636, 1377, 1182, 1007; **TLC** (20% EtOAc/hexanes) $R_f = 0.16$; **HRMS** (ESI $^+$) Calcd. for $\text{C}_{12}\text{H}_{14}\text{NaO}_2$: 213.0886, Found: 213.0890.

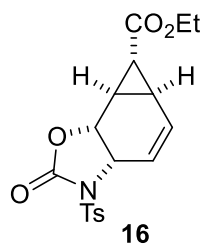
Desymmetrization of bis-epoxide **8a**



Ethyl -2,5-dihydroxybicyclo[4.1.0]hept-3-ene-7-carboxylate (S4): The bis-epoxide **8a** (250 mg, 1.3 mmol) and Bu_3SnH (1.4 mL, 4 equiv) were added to a flame-dried 25 mL round-bottomed flask under nitrogen atmosphere and dissolved in anhydrous THF (10 mL). Then the reaction was cooled to 0 °C before the MeMgI (3.0 M in Et_2O , 0.53 mL, 1.25 equiv) was added dropwise over 5 min. After complete addition of MeMgI , the reaction was immediately quenched with saturated NH_4Cl (5 mL) under nitrogen atmosphere. The product was extracted with Et_2O (2 \times 5 mL), dried over MgSO_4 , filtered, and concentrated. The crude material was purified by column chromatography (50% EtOAc/hexanes \rightarrow 100% EtOAc \rightarrow 90% EtOAc/MeOH) yielding a golden oil (221 mg, 87%). **Note:** the reaction was slow to proceed if run in Et_2O , and it failed when MeMgBr was used instead. The inclusion of Bu_3SnH minimizes THF polymerization, although the reaction proceeds without it as an additive. Analytical data: ^1H NMR (600 MHz, CDCl_3) δ 5.87 (br s, 2H), 4.42 (br s, 2H), 4.32 (br s, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 2.04 (d, $J = 4.2$ Hz, 2H), 1.38 (t, $J = 4.2$ Hz, 1H), 1.27 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 172.8, 128.3, 61.8, 61.0, 25.9, 21.3, 14.2; **IR** (thin film, cm^{-1}) 3391, 2983, 2905, 1716, 1447, 1302, 1198, 1013, 801; **TLC** (20% EtOAc/hexanes) $R_f = 0.02$; **HRMS** (ESI) Calcd. for $\text{C}_{10}\text{H}_{14}\text{NaO}_4$: 221.0784, Found: 221.0789.



Ethyl-2,5-bis((tosylcarbamoyl)oxy)bicyclo[4.1.0]hept-3-ene-7-carboxylate (15): The diol **S4** (53 mg, 0.26 mmol) was added to a flame-dried 10 mL round-bottomed flask under nitrogen atmosphere and dissolved in anhydrous THF (2.5 mL). The *p*-toluenesulfonyl isocyanate (81 μL , 2.01 equiv) was then added, and the reaction was allowed to stir at room temperature for 8 h. The reaction was then concentrated and flushed through a short pad of silica first with 20% EtOAc/hexanes (40 mL) then with EtOAc (100 mL). The fractions containing the product were collected and concentrated, yielding a white solid (158 mg, >99%). Analytical data: ^1H NMR (600 MHz, CDCl_3) δ 7.93 (m, 4H), 7.34 (m, 4H), 5.93 (br s, 2H), 5.42 (m, 2H), 4.13 (q, $J = 7.2$ Hz, 2H), 2.46 (s, 6H), 1.95 (m, 2H), 1.43 (t, $J = 4.2$ Hz, 1H), 1.25 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 171.2, 150.0, 145.2, 135.3, 129.6, 128.4, 127.4, 66.2, 61.4, 21.7, 21.4, 21.1, 14.1; **mp** 87–89 °C; **IR** (thin film, cm^{-1}) 3248, 2985, 2875, 1716, 1597, 1456, 1353, 1161, 853; **TLC** (20% EtOAc/hexanes) $R_f = 0.01$; **HRMS** (ESI $^-$) Calcd. for $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_{10}\text{S}_2$: 591.1113, Found: 591.1160.



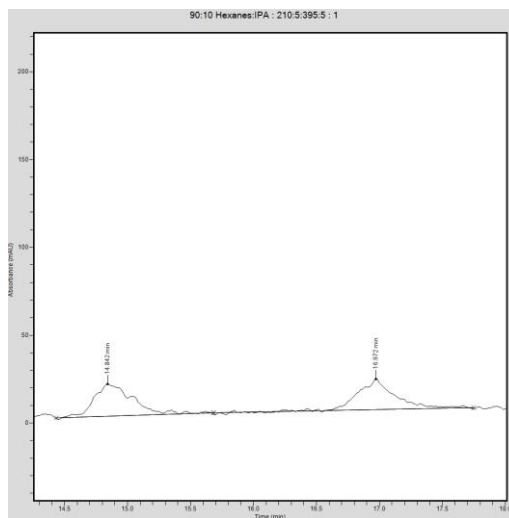
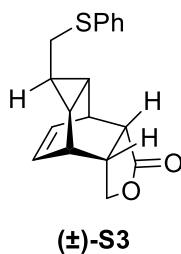
Ethyl -2-oxo-3-tosyl-3,3a,5a,6,6a,6b-hexahydro-2H-cyclopropa[3,4]benzo[1,2-d]oxazole-6-carboxylate (16): A flame-dried 10 mL round-bottomed flask was charged with $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (10 mg, 0.05 equiv) and tris-(2-furyl)phosphine (5 mg, 0.1 equiv) in a nitrogen-filled glovebox. The solids were then dissolved in anhydrous THF (2.5 mL), and the dark mixture stirred for 1 h. Then the bis-carbamate **15** (114 mg, 0.19 mmol) was added with anhydrous THF (2.5 mL), and the reaction was allowed to stir at room temperature for 16 h. Once the reaction was deemed complete

by TLC analysis, the reaction was concentrated and immediately subjected to column chromatography (30% EtOAc/hexanes) to yield a white foam (55 mg, 76%). Analytical data: $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.96 (d, $J = 8.4$ Hz, 2H), 7.37 (d, $J = 8.4$ Hz, 2H), 6.28 (ddd, $J = 7.2, 5.4, 1.8$ Hz, 1H), 5.63 (ddd, $J = 7.2, 3.6, 1.8$ Hz, 1H), 5.14 (dd, $J = 7.8, 1.5$ Hz, 1H), 4.71 (ddd, $J = 7.8, 3.6, 1.8$ Hz, 1H), 4.16 (q, $J = 7.2$ Hz, 2H), 2.46 (s, 3H), 2.28 (ddd, $J = 7.8, 4.8, 1.5$ Hz, 1H), 2.08 (ddd, $J = 7.8, 5.4, 3.6$ Hz, 1H), 1.56 (dd, $J = 4.8, 3.6$ Hz, 1H), 1.27 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 170.4, 150.7, 145.7, 135.3, 129.9, 129.1, 128.4, 119.5, 70.4, 61.4, 53.0, 29.7, 21.8, 20.2, 18.6, 14.2; **IR** (thin film, cm^{-1}) 3058, 2984, 1780, 1717, 1647, 1366, 1300, 1193, 1015, 814; **TLC** (20% EtOAc/hexanes) $R_f = 0.14$; **HRMS** (ESI $^+$) Calcd. for $\text{C}_{18}\text{H}_{19}\text{NNaO}_6\text{S}$: 400.0825, Found: 400.0851.

HPLC traces for **S3a,b** (derived from hemiesters **11a,b**)

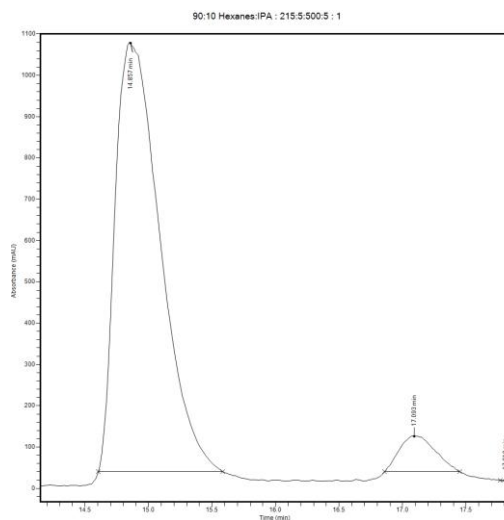
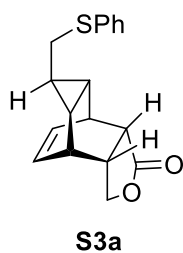
S3 (rac):

Peak #	RT (min)	Area (mAU \times s)	Height (mAU)	Area(%)
1	14.842	390454.38	18414.06	52.9
2	16.972	347299.13	17470.47	47.1



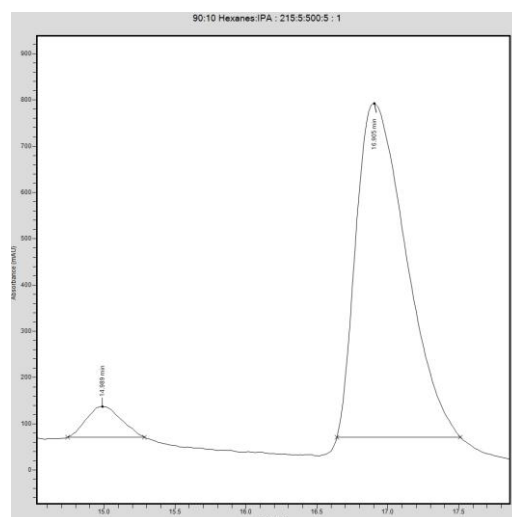
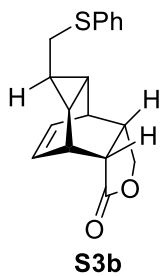
S3a (quinine):

Peak #	RT (min)	Area (mAU × s)	Height (mAU)	Area(%)
1	14.857	25553519.61	1041017.51	93.7
2	17.093	1705684.86	86778.97	6.3



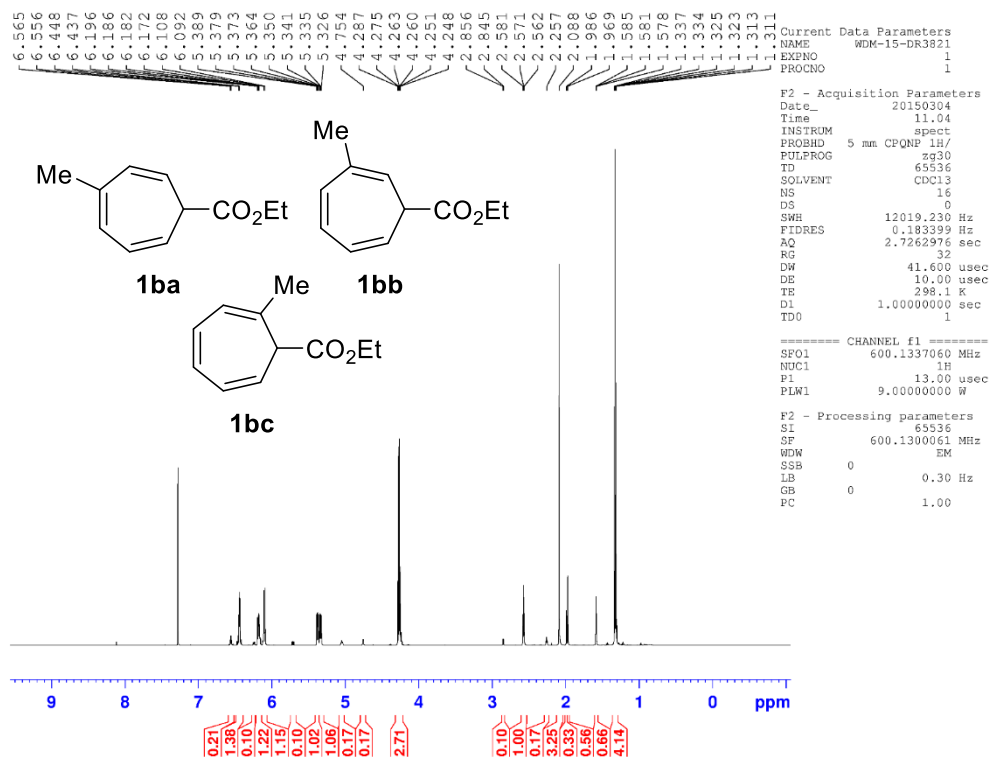
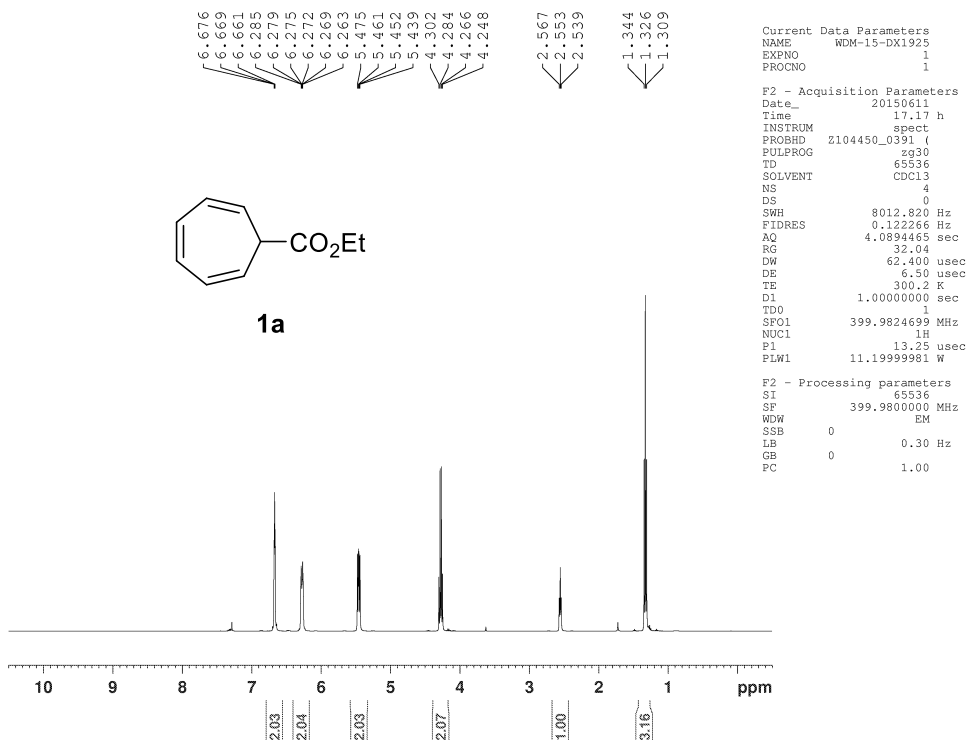
S3b (quinidine):

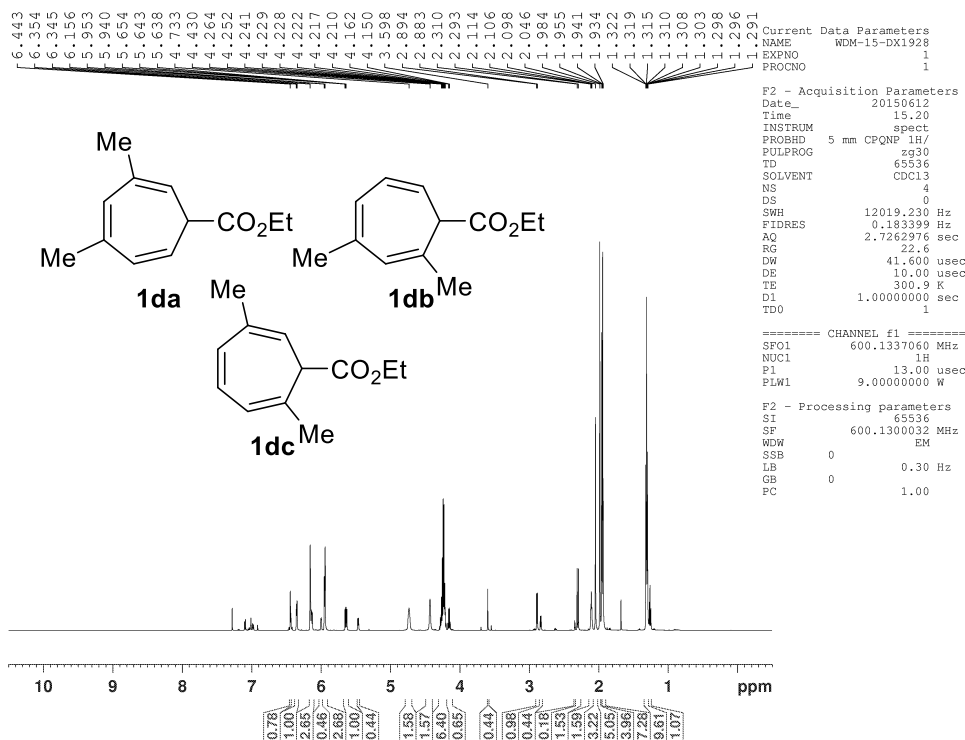
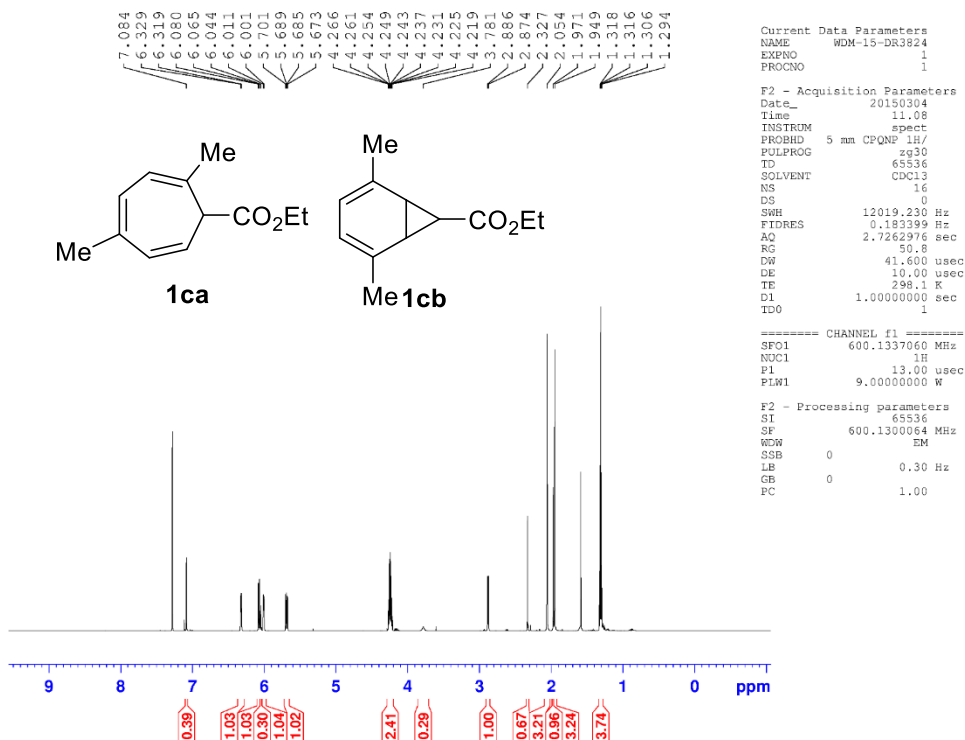
Peak #	RT (min)	Area (mAU × s)	Height (mAU)	Area(%)
1	14.989	1182560.66	67685.57	6.3
2	16.905	17686664.05	724177.58	93.7

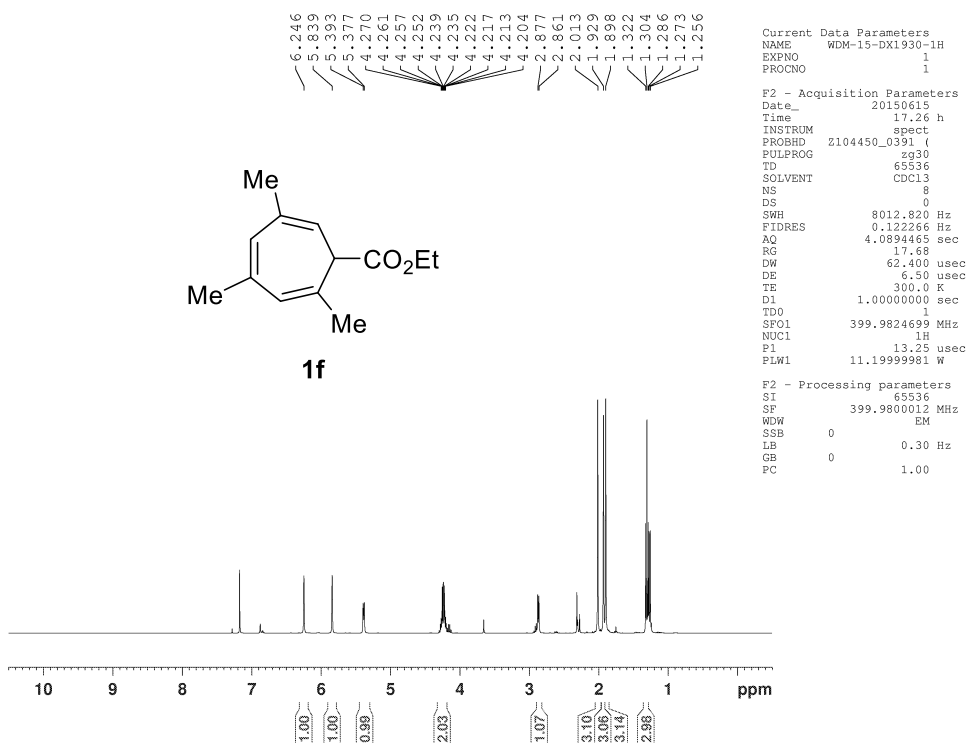
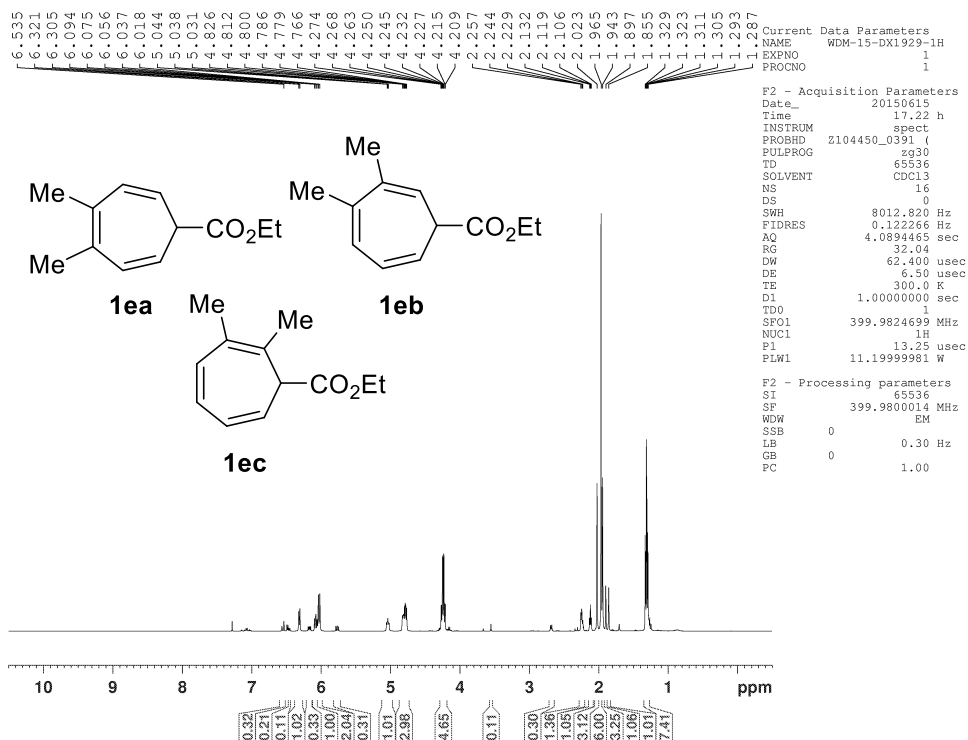


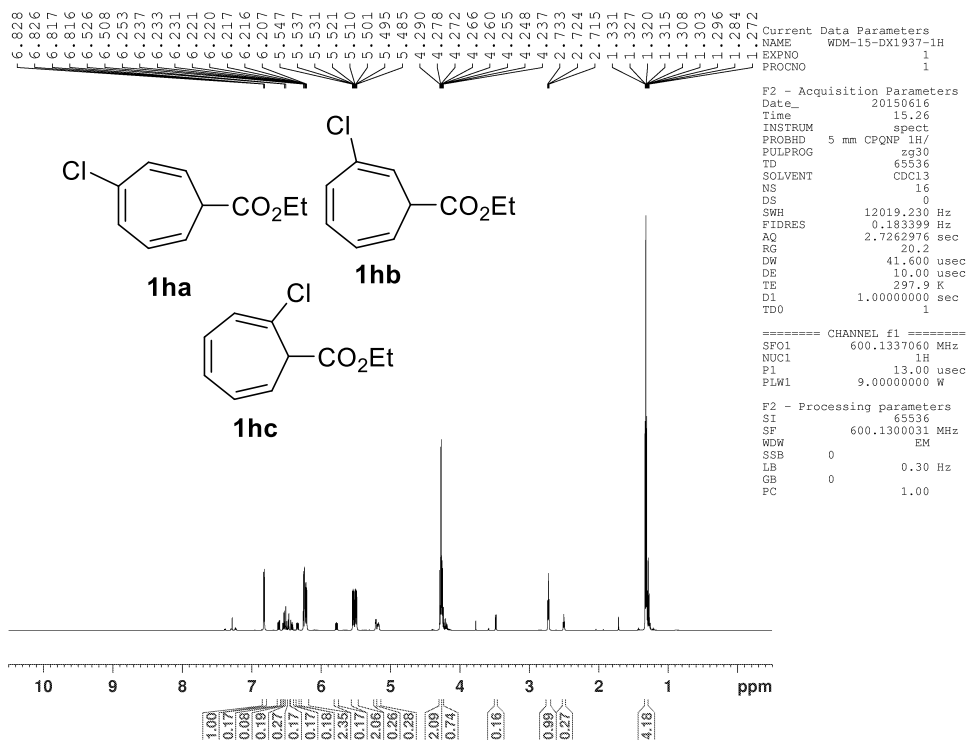
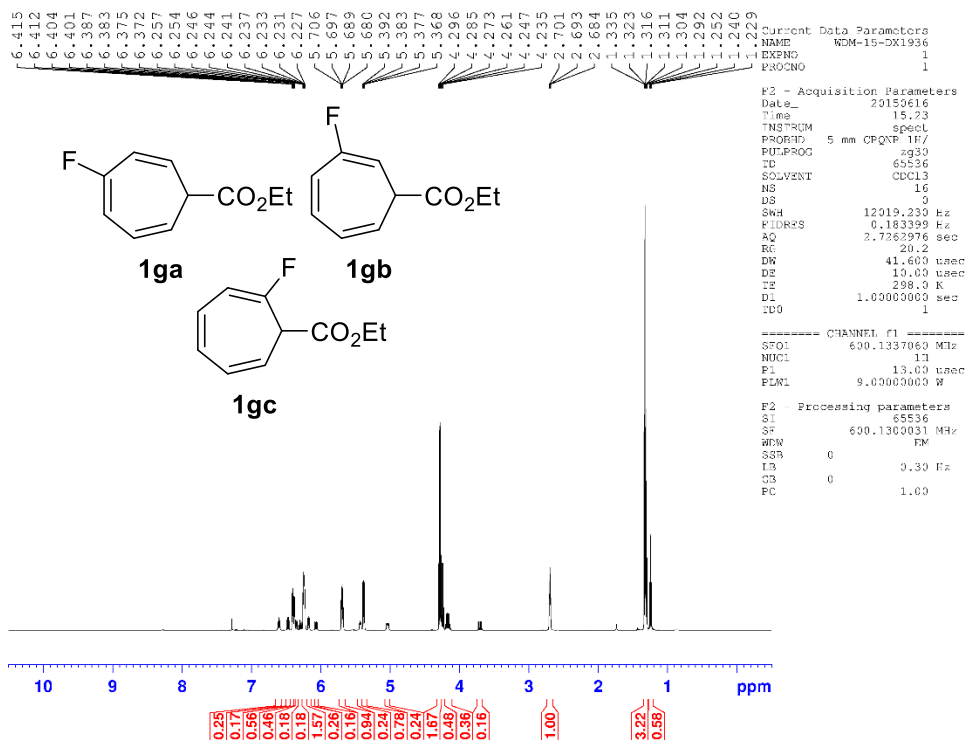
References

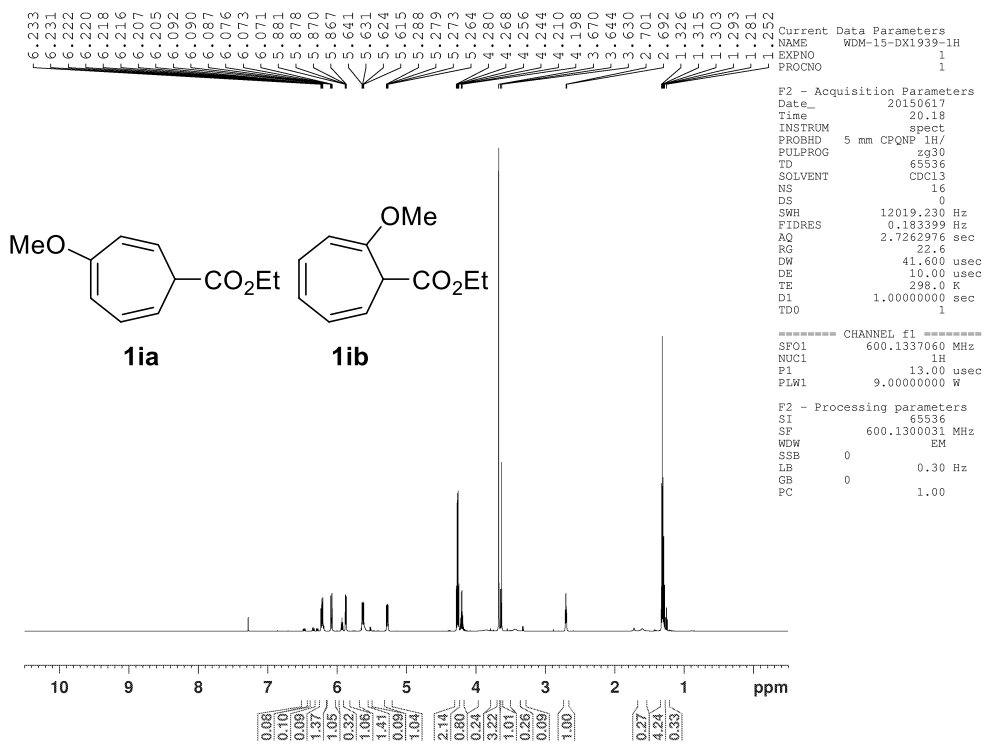
1. Searle, N. E. *Org. Synth.* **1956**, *36*, 25.
2. Wang, Z.; Kim, C.; Facchetti, A.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 13362.
3. Cookson, R. C.; Gupte, S. S.; Stevens, D. R.; Watts, C. T. *Org. Synth.* **1971**, *51*, 121.
4. Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Hubert, A. J.; Warin, R.; Teyssie, P. *J. Org. Chem.* **1981**, *46*, 873.
5. Wyatt, E. E.; Galloway, W. R. J. D.; Spring, D. R. *Synlett* **2011**, *10*, 1449.
6. Matsumoto, M.; Shiono, T.; Mutoh, H.; Amano, M.; Arimitsu, S. *J. Chem. Soc., Chem. Commun.* **1995**, *24*, 101.

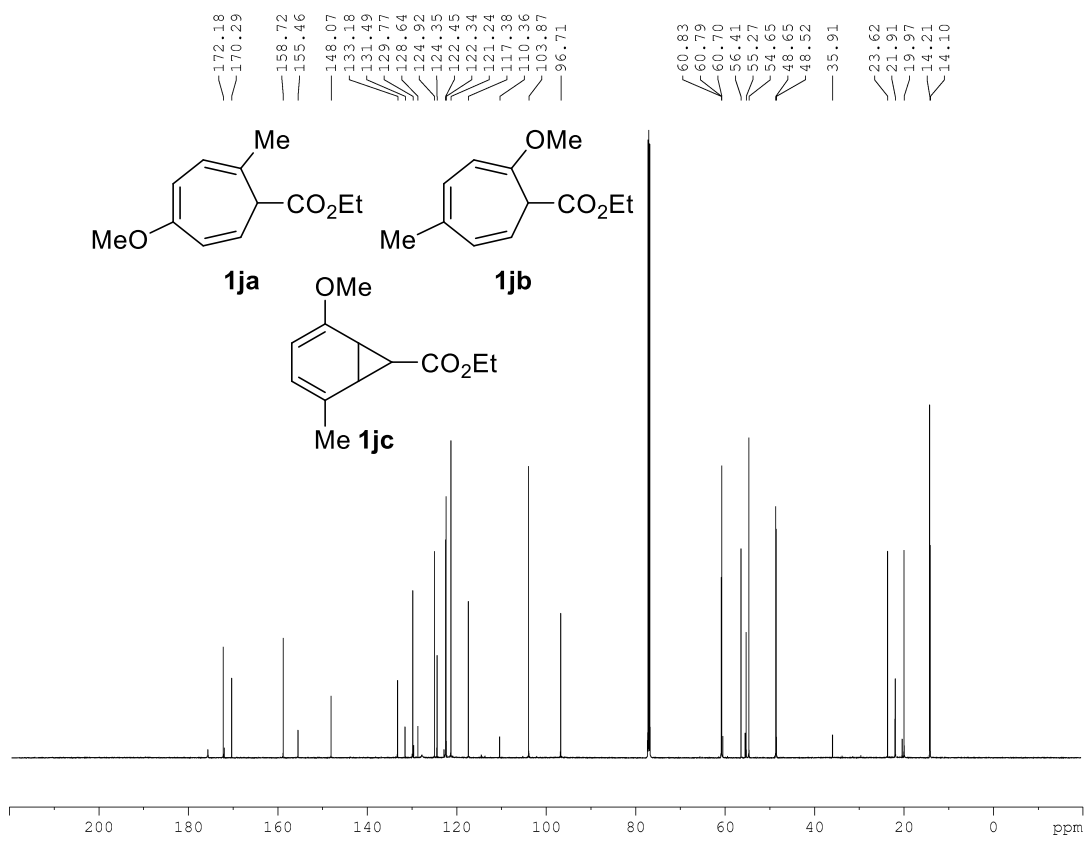
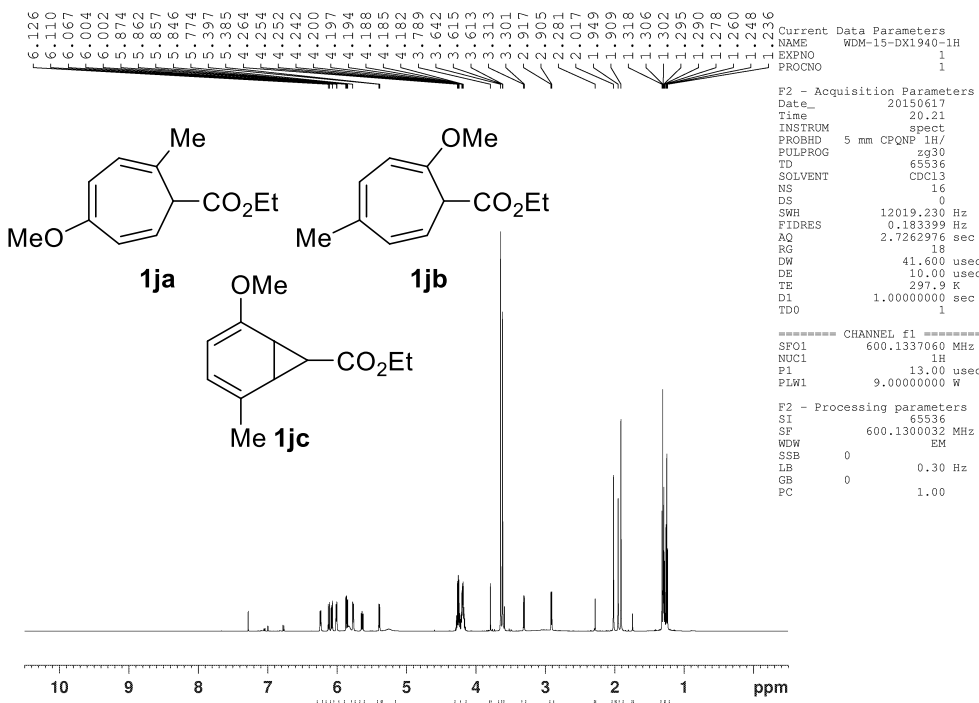


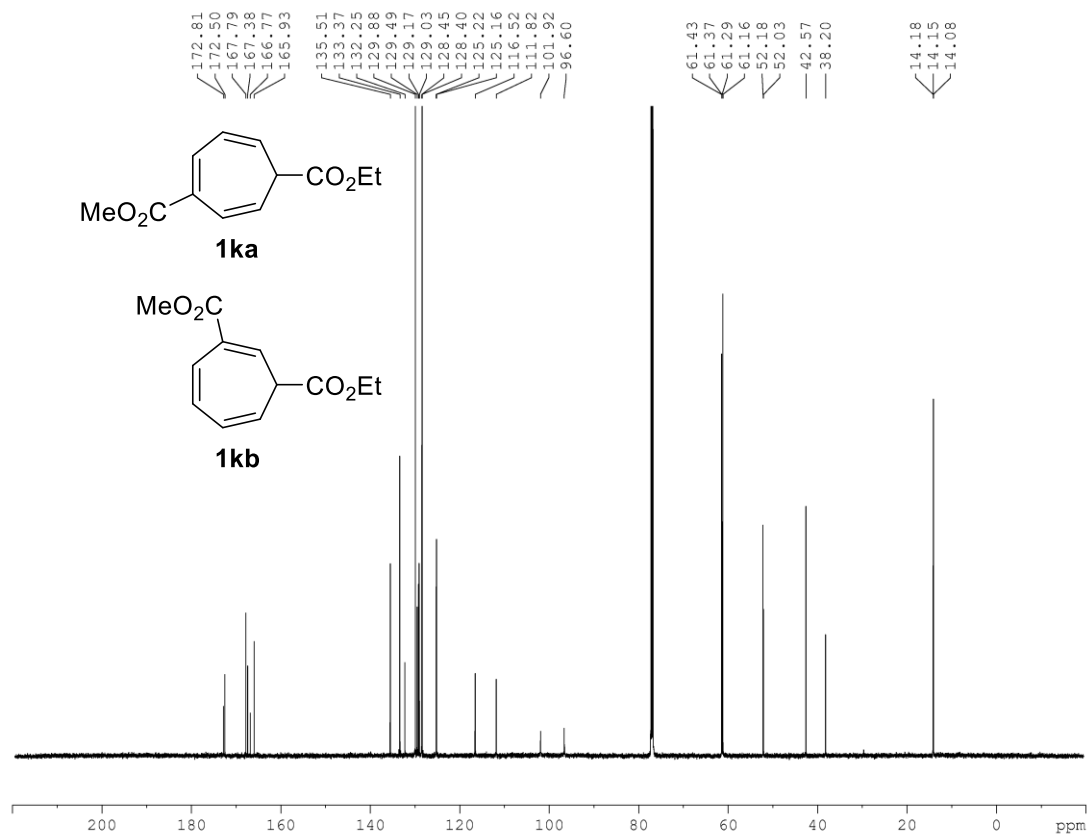
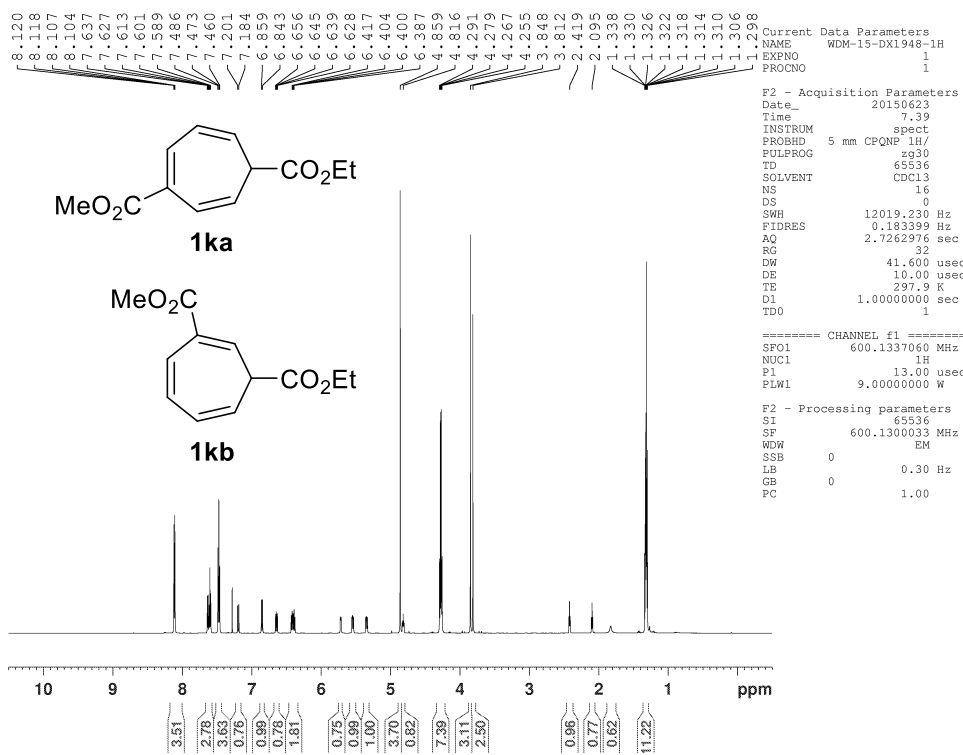


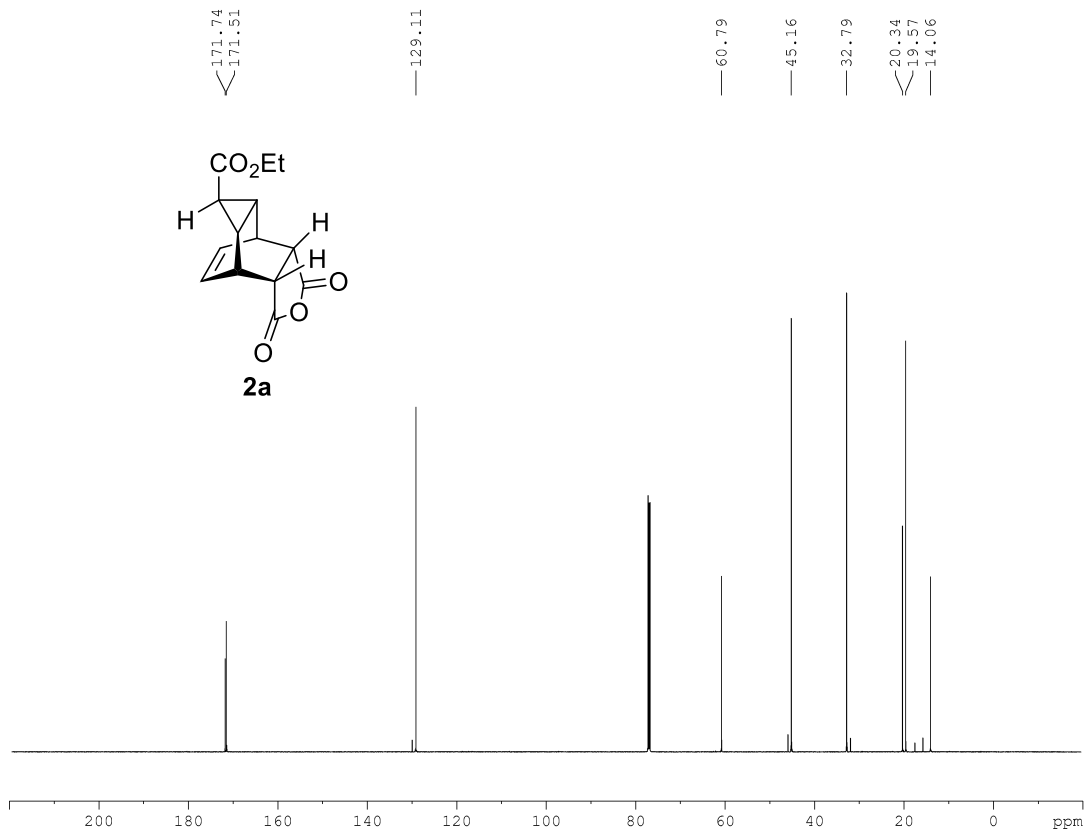
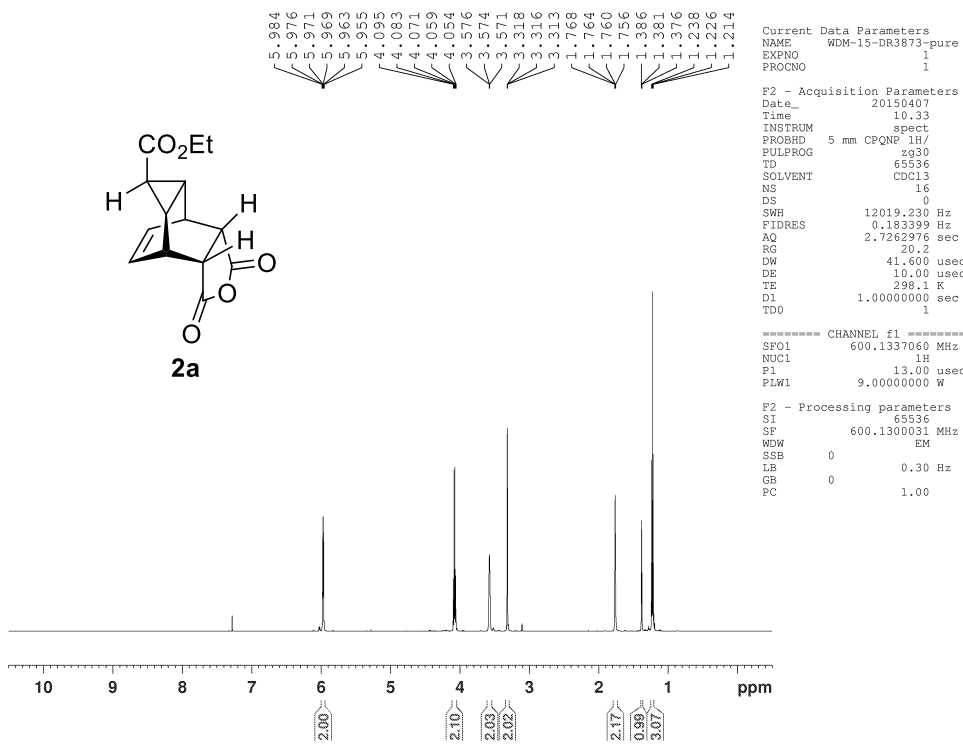


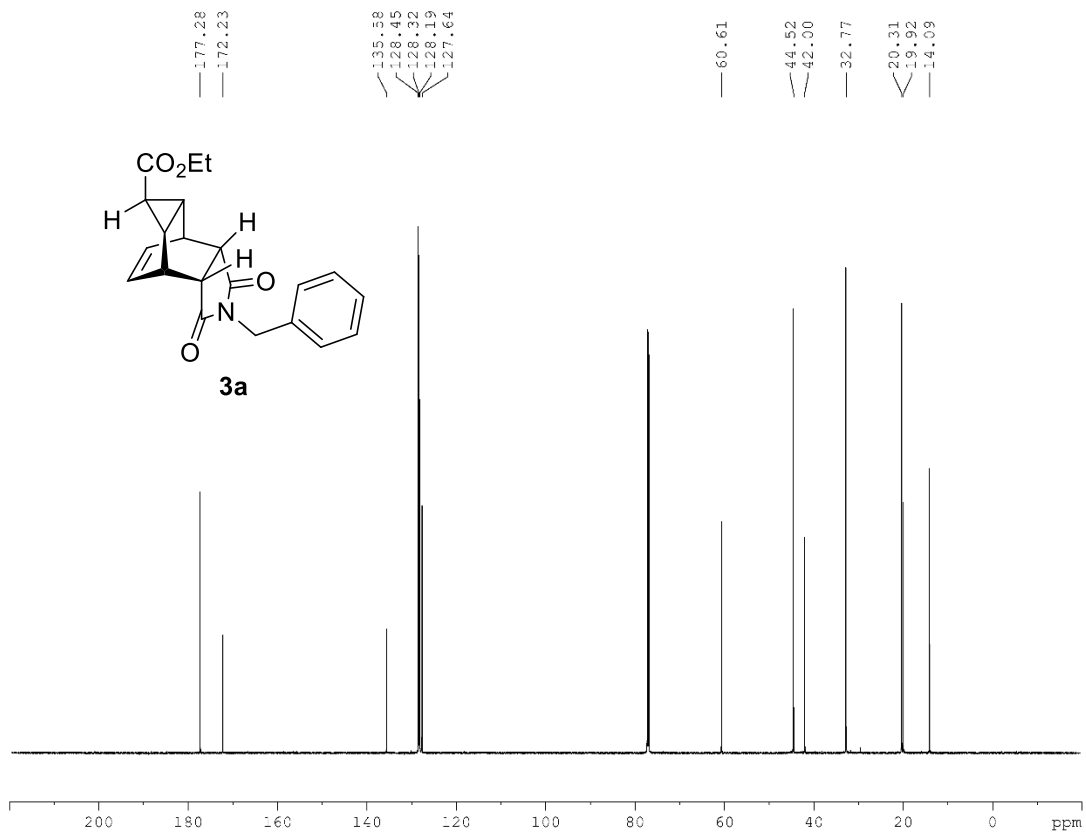
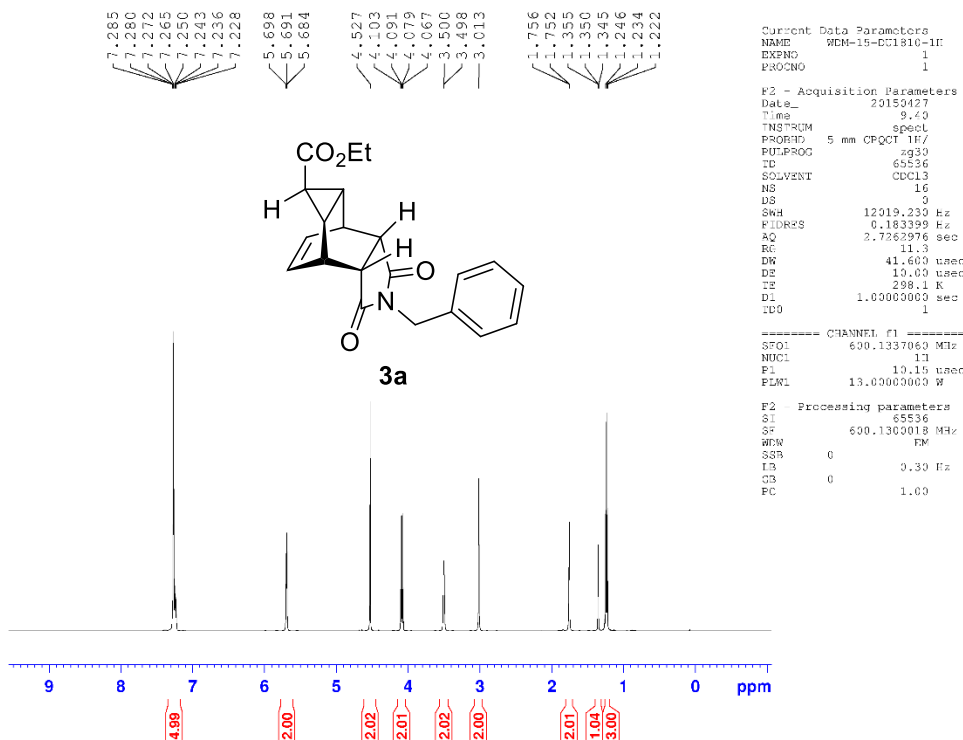


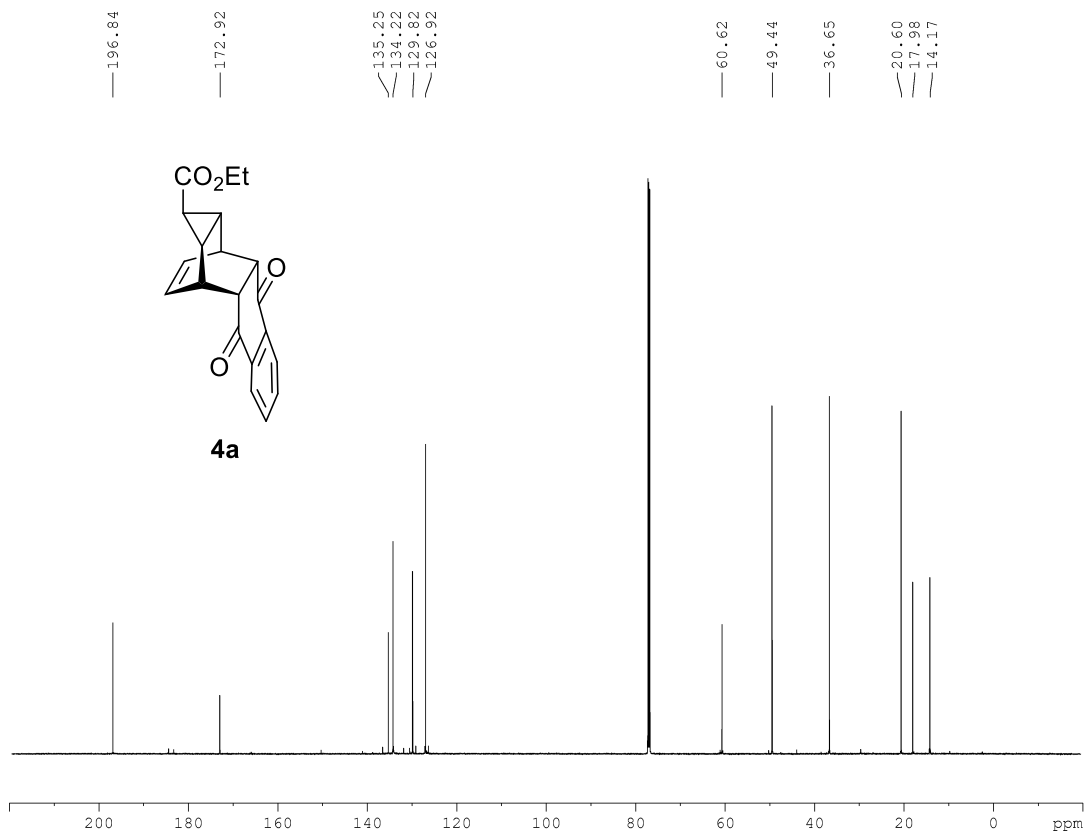
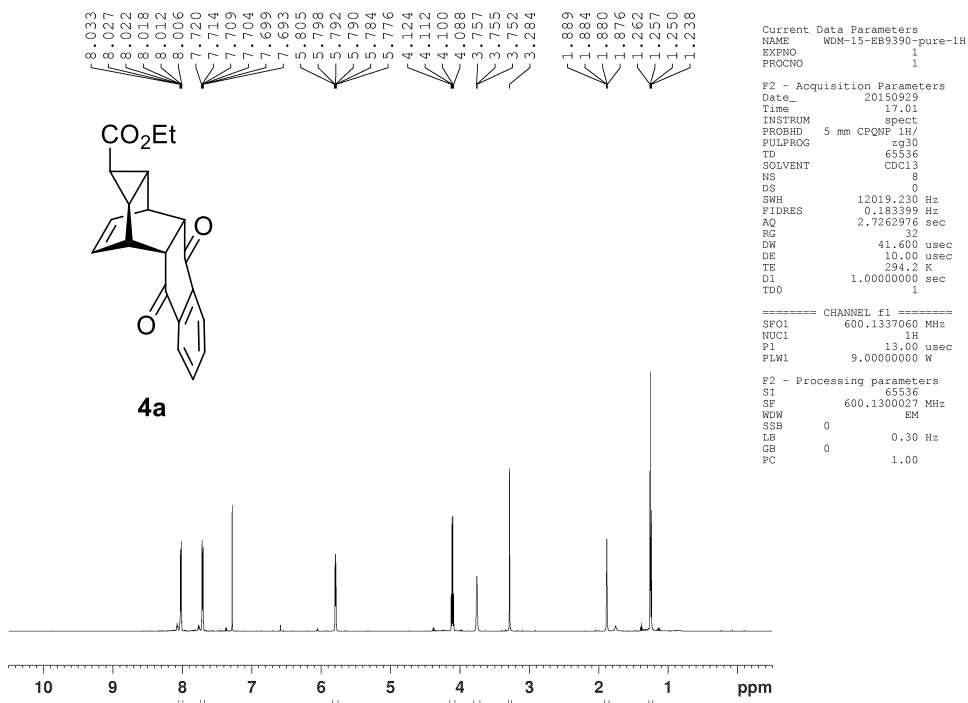


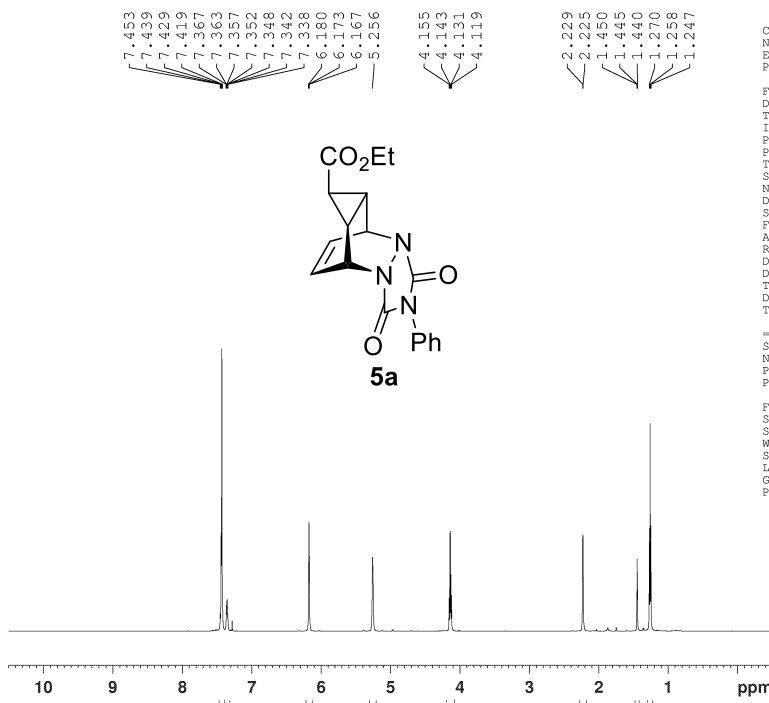










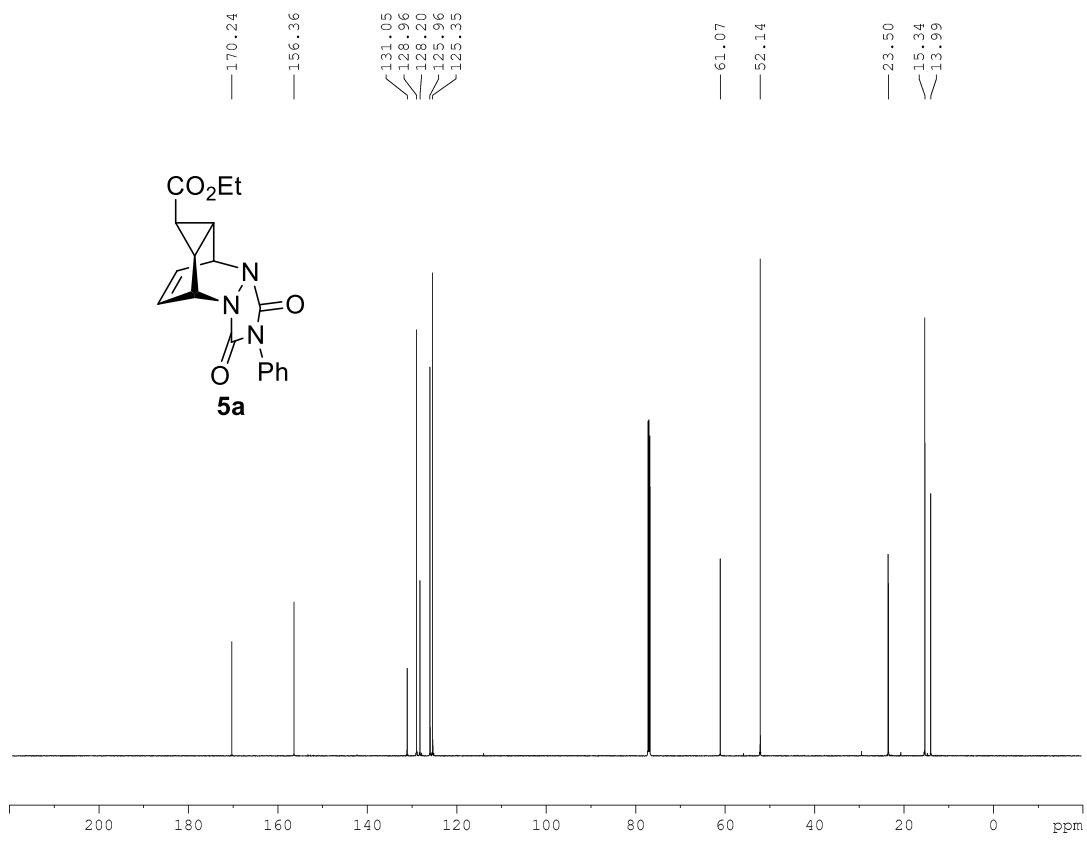


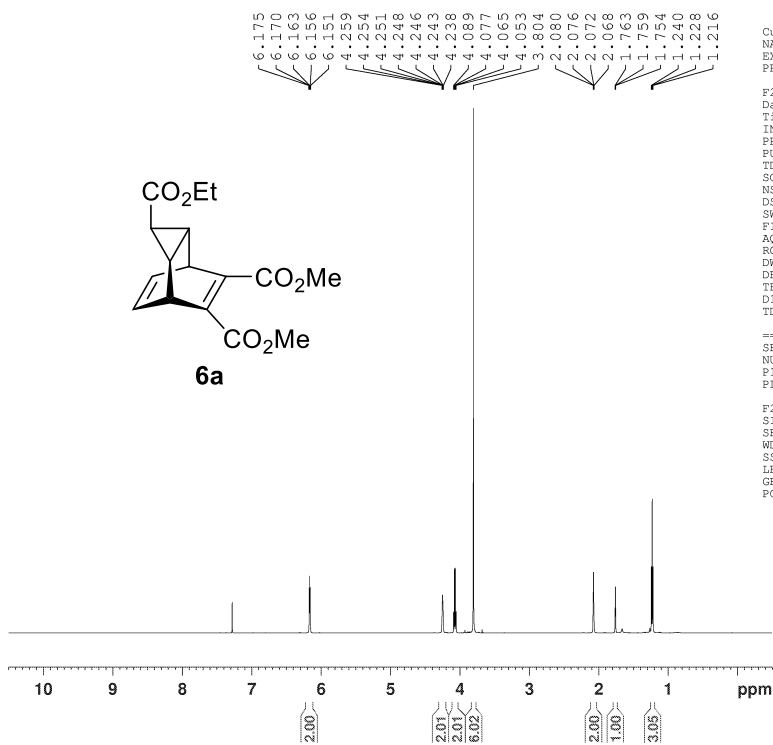
Current Data Parameters
 NAME WDM-15-DX1913-1H
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150608
 Time 15.35
 INSTRUM spect
 PROBHD 5 mm CPQNP 1H/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 20.2
 DW 41.600 usec
 DE 10.00 usec
 TE 298.0 K
 D1 1.00000000 sec
 TDO 1

===== CHANNEL f1 =====
 SFO1 600.1337060 MHz
 NUCL1 1H
 P1 13.00 usec
 PLW1 9.00000000 W

F2 - Processing parameters
 SI 65536
 SF 600.1300033 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



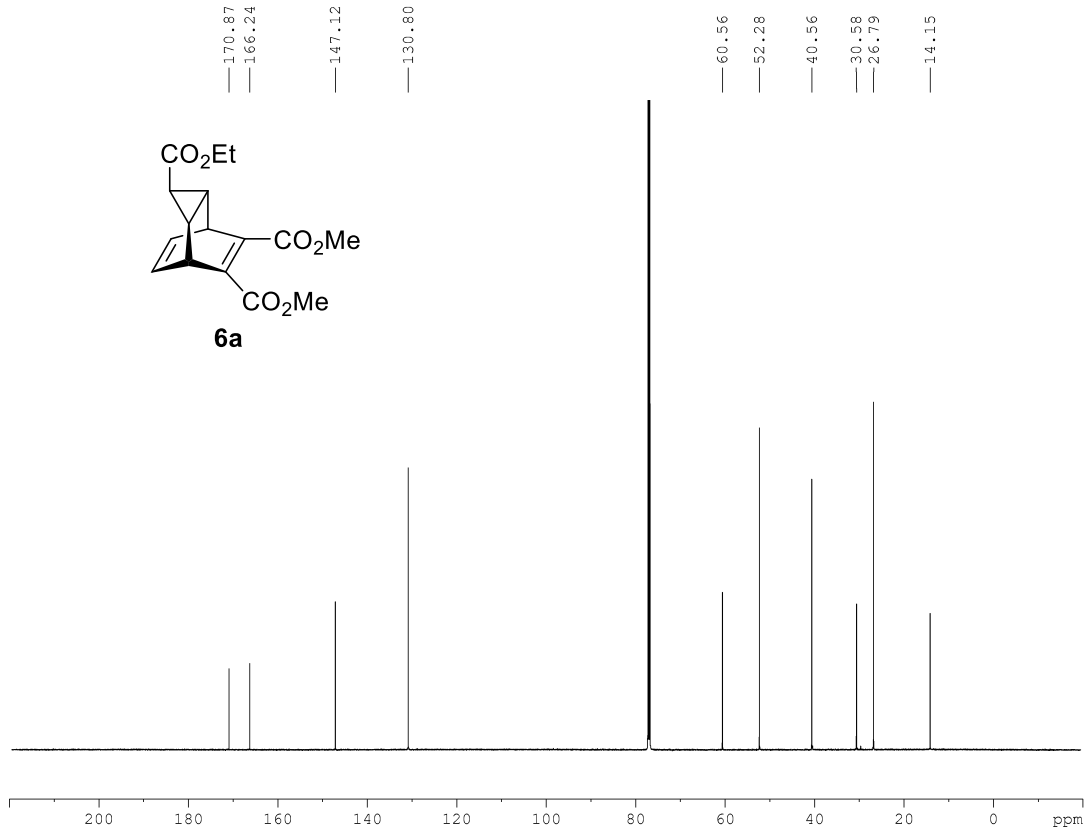


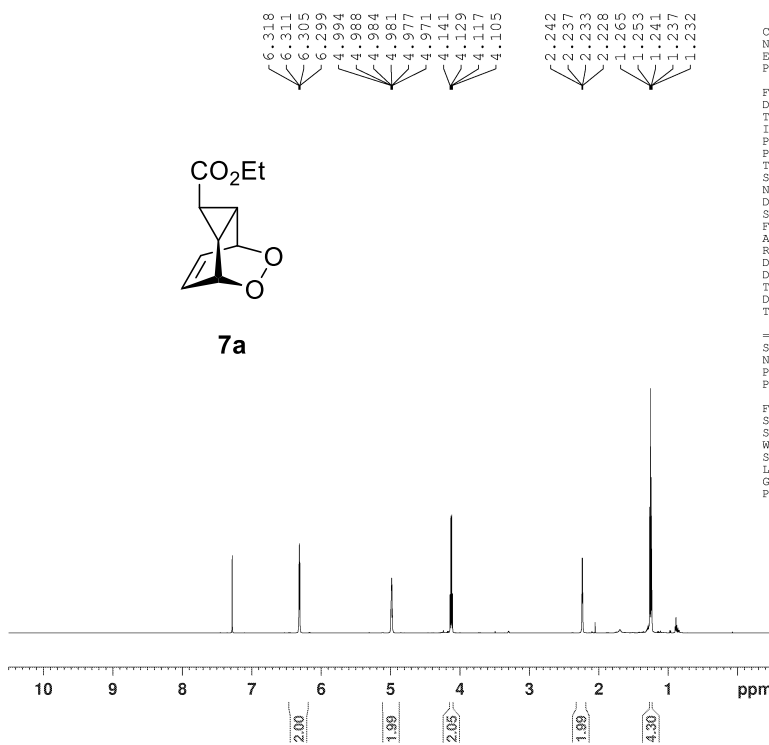
Current Data Parameters
NAME WDM-15-EF1919A-1H
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20151019
Time 14.02
INSTRUM spect
PROBHD 5 mm CPNP 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl₃
NS 16
DS 0
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 32
DW 41.600 usec
DE 10.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====
SFO1 600.1337060 MHz
NUC1 1H
P1 13.00 usec
PLW1 9.00000000 W

F2 - Processing parameters
SI 65536
SF 600.1300027 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



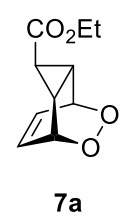


Current Data Parameters
 NAME WDM-15-RF1907-1H
 EXPNO 1
 PROCNO 1

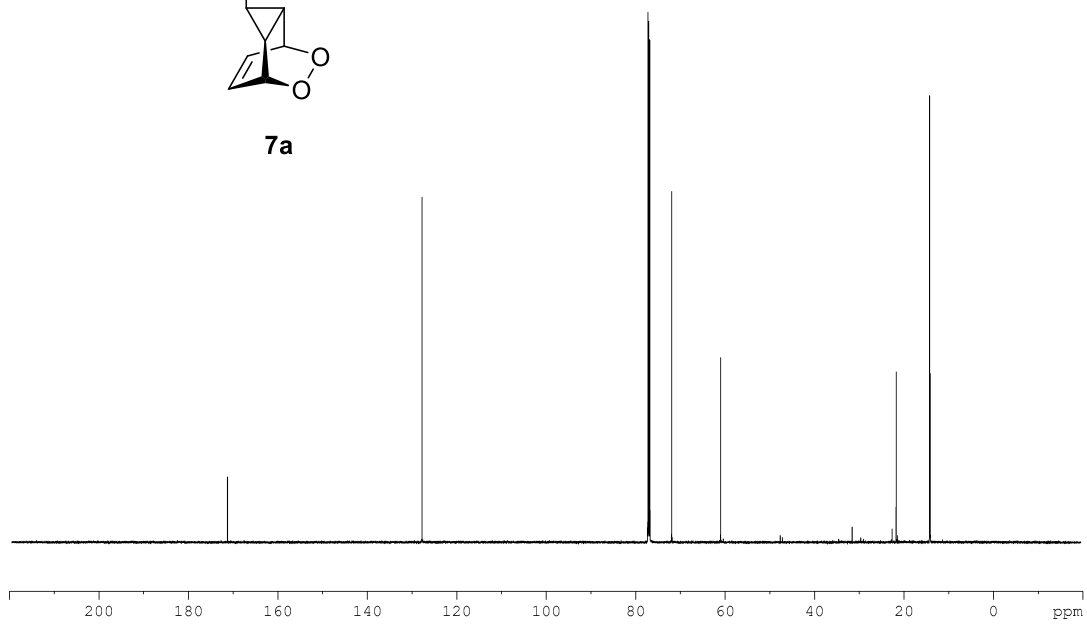
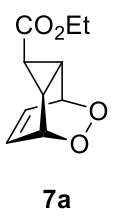
F2 - Acquisition Parameters
 Date_ 20151012
 Time 17.15
 INSTRUM spect
 PROBHD 5 mm CPNP 1H/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 8
 DS 2
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 32
 DW 41.600 usec
 DE 10.00 usec
 TE 294.2 K
 DI 1.00000000 sec
 TDO 1

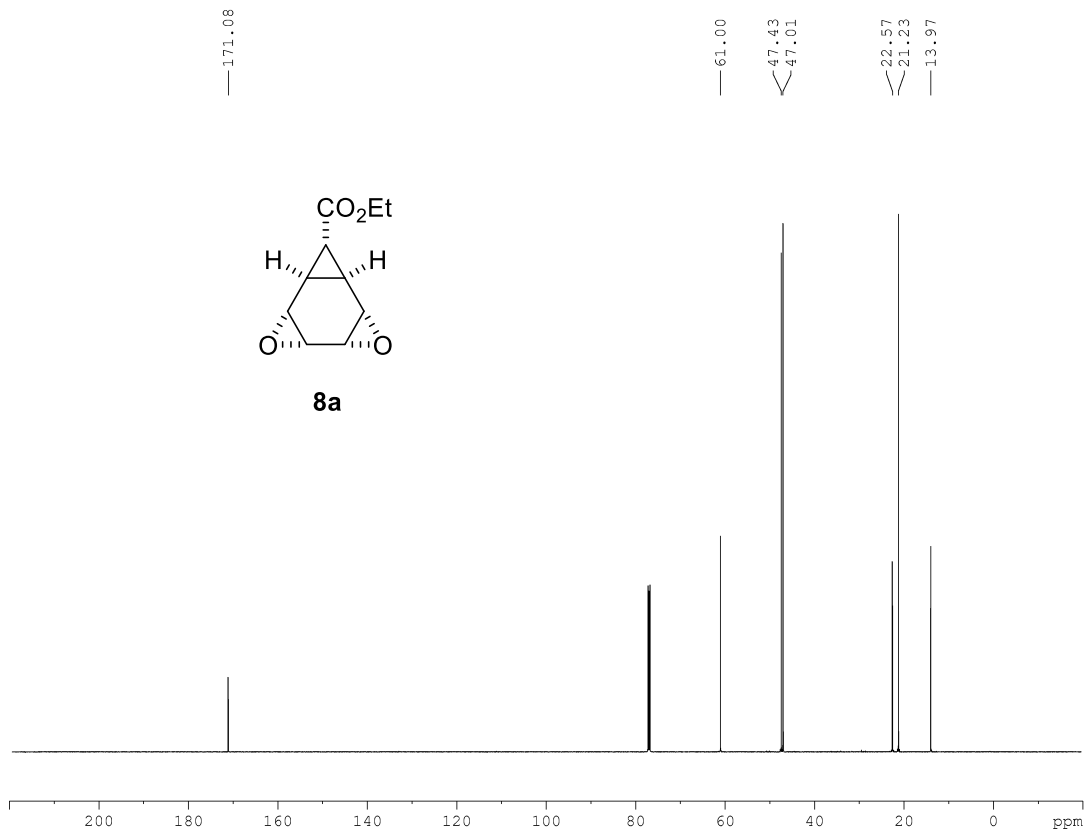
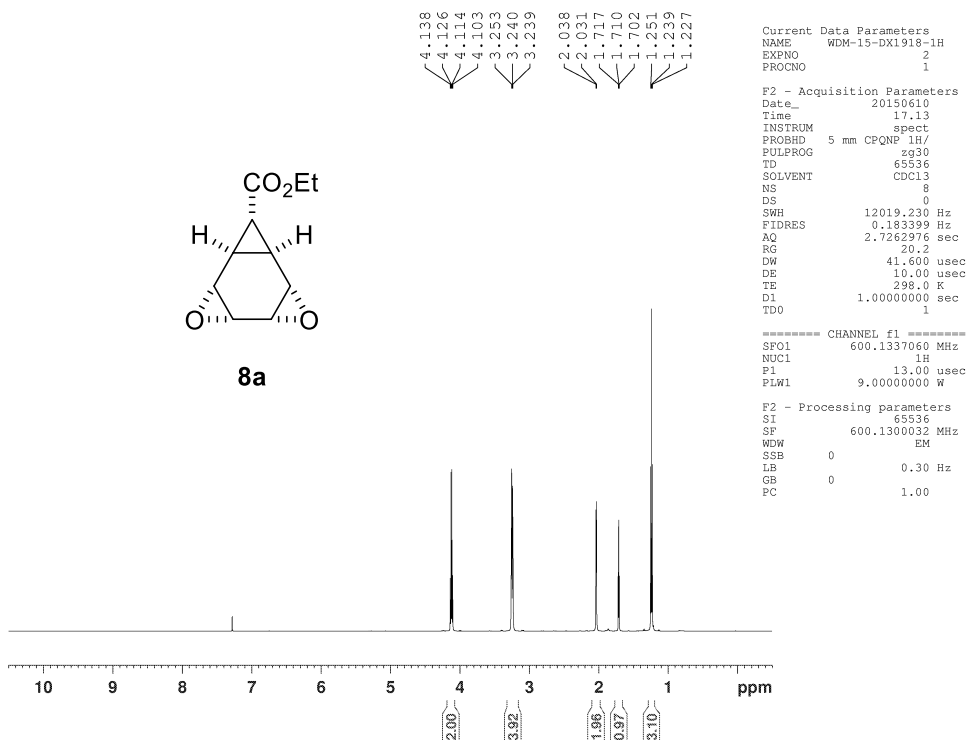
===== CHANNEL f1 =====
 SFO1 600.1337060 MHz
 NUC1 1H
 P1 13.00 usec
 PLW1 9.00000000 W

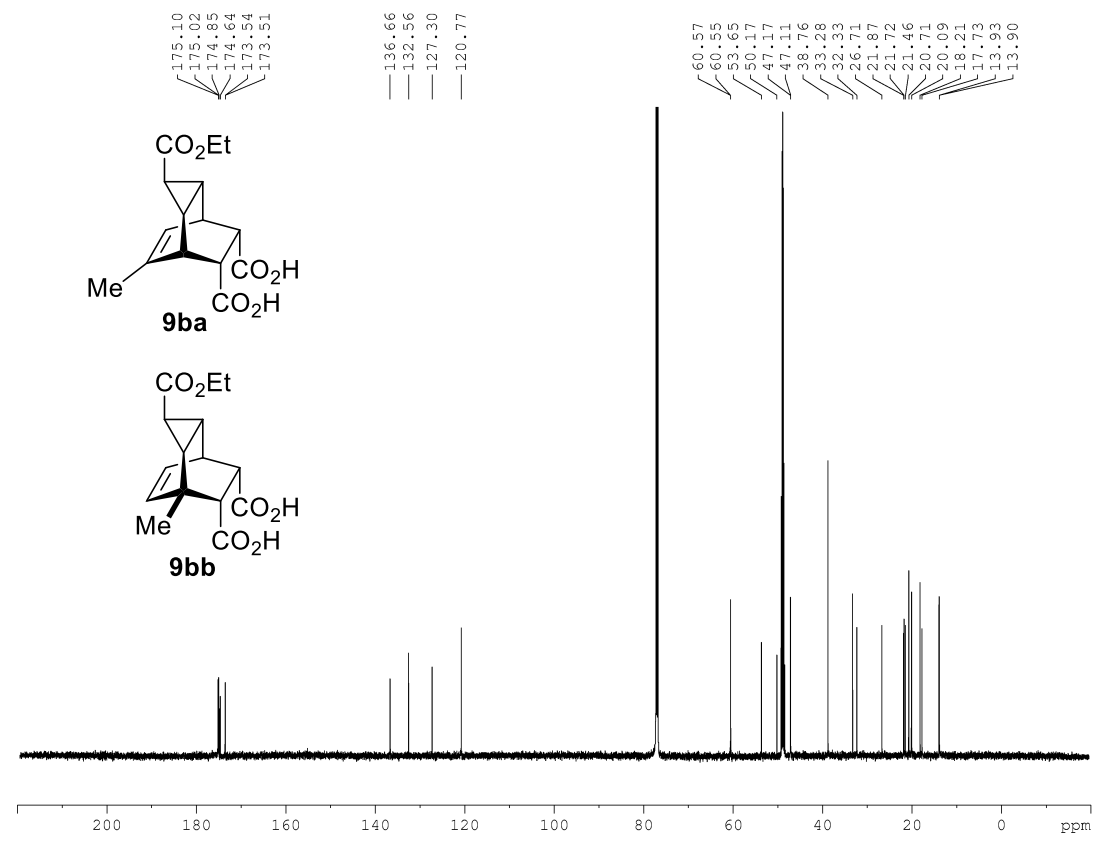
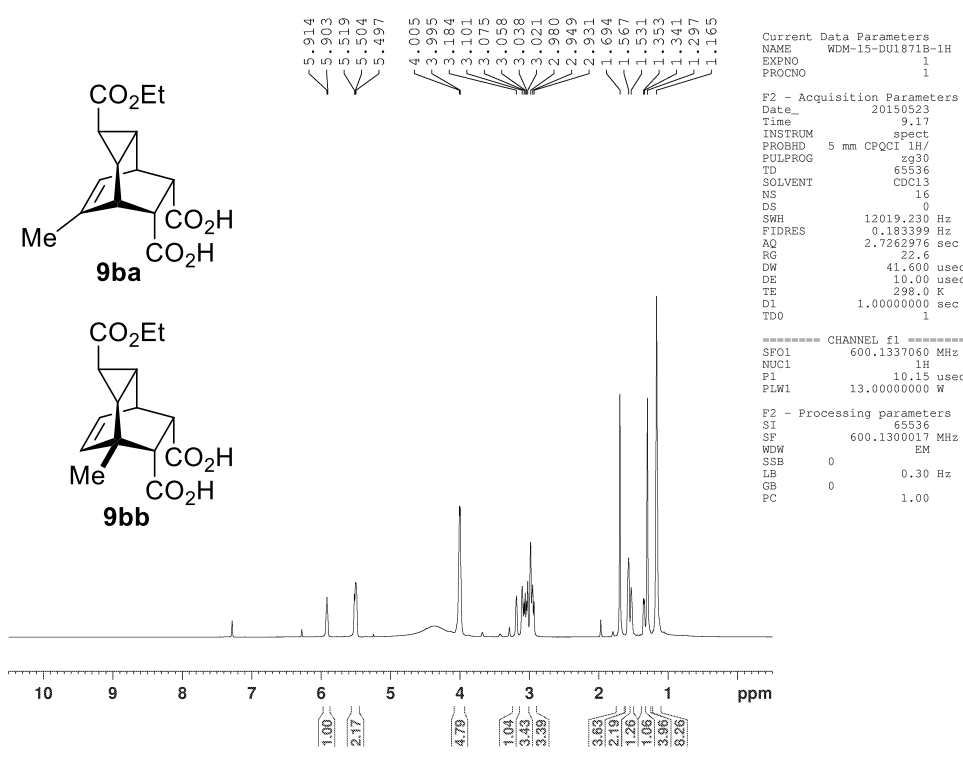
F2 - Processing parameters
 SI 65536
 SF 600.1300028 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

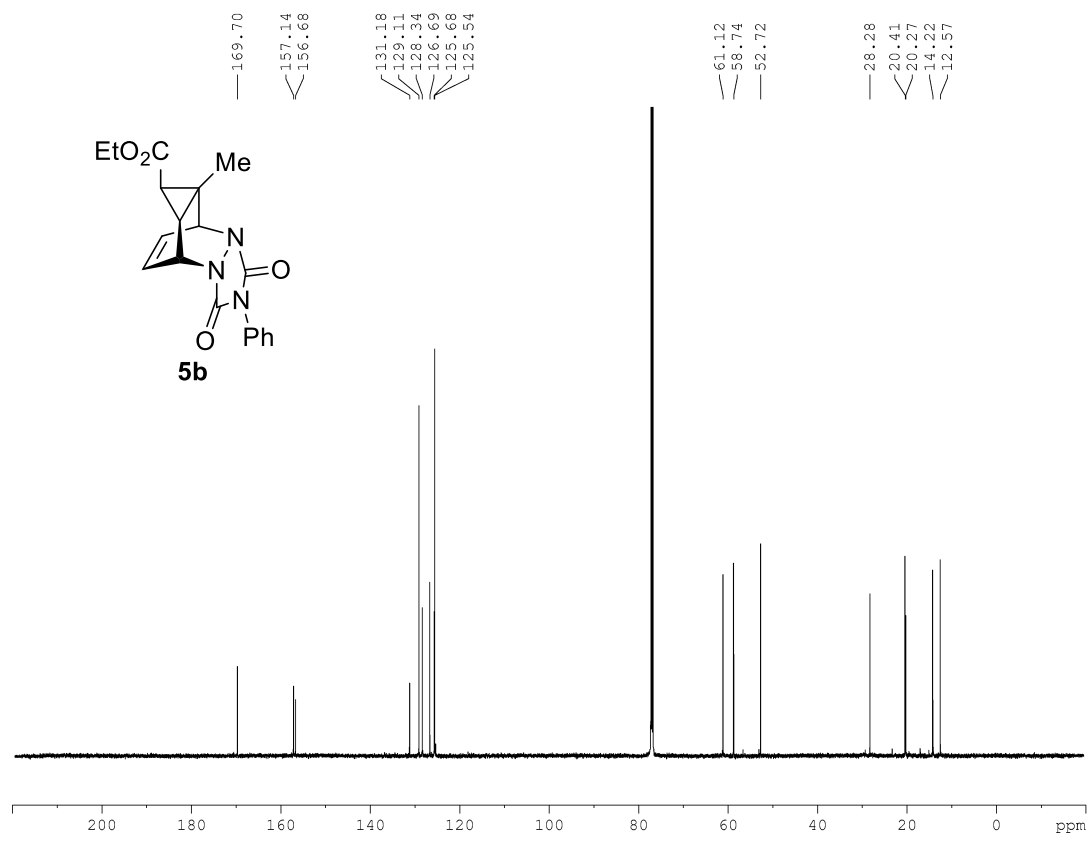
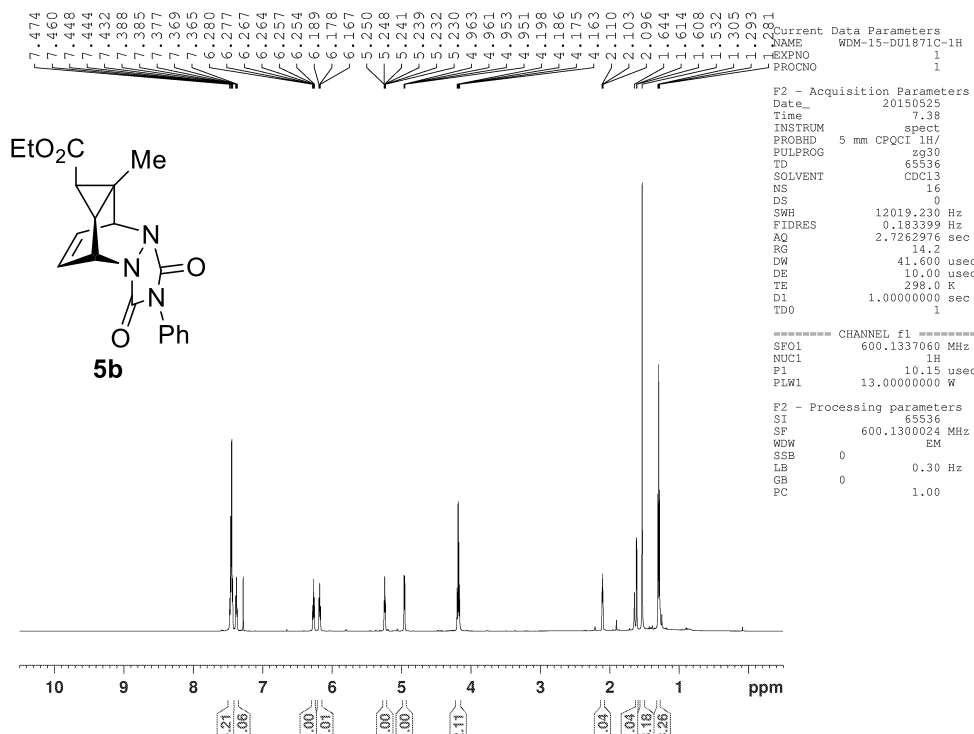


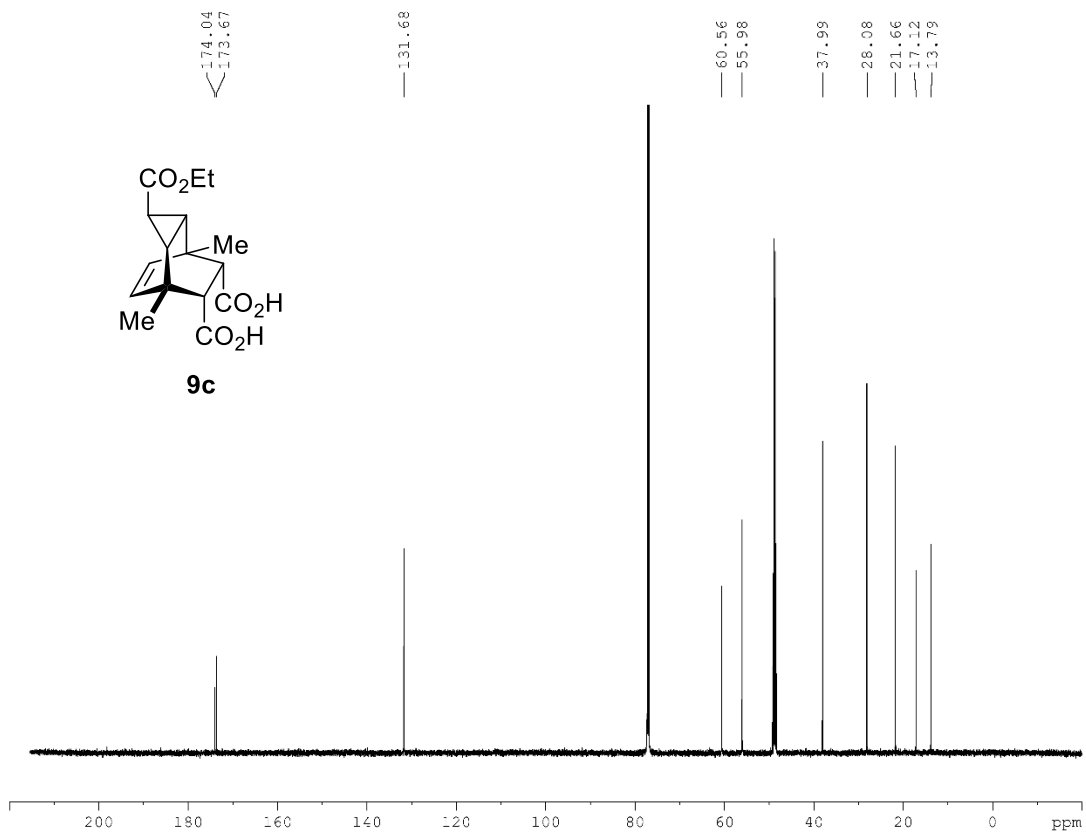
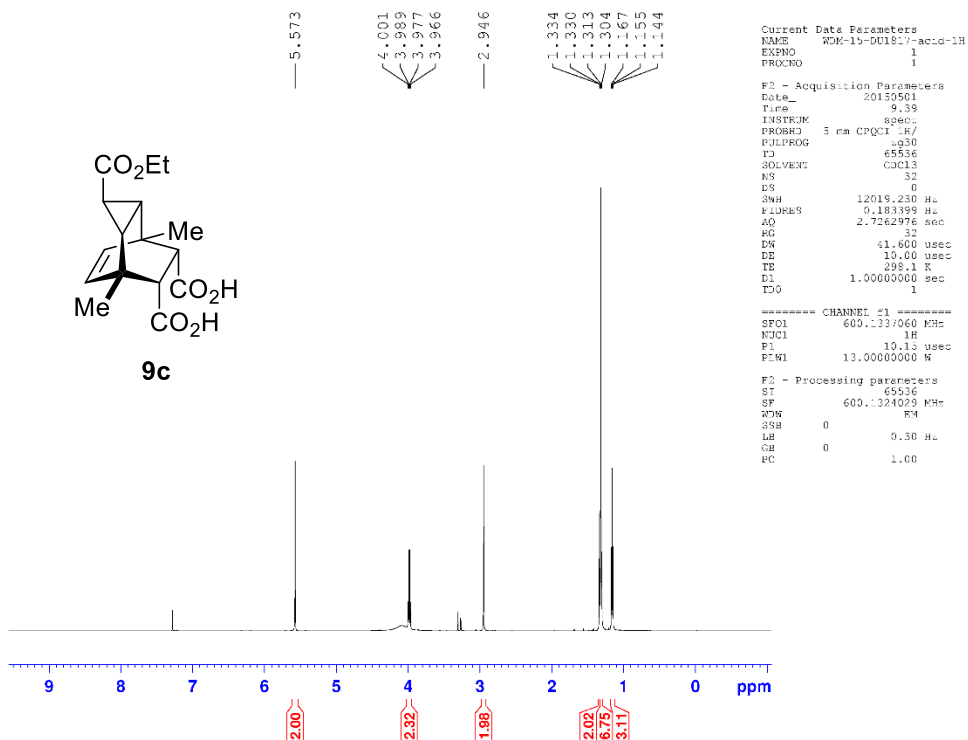
Chemical shifts (ppm): 171.21, 127.72, 71.90, 60.91, 21.67, 14.22, 14.10.

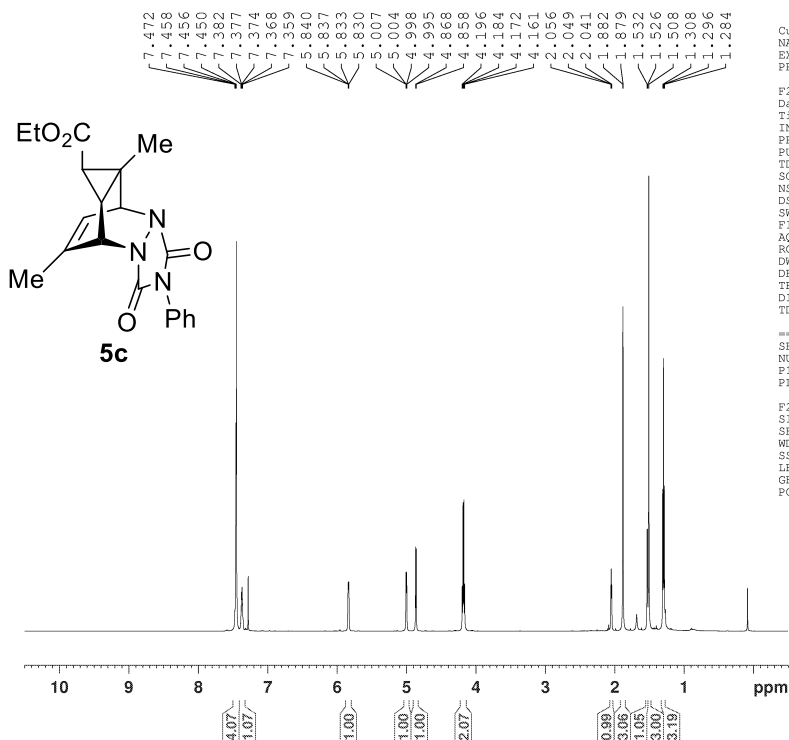












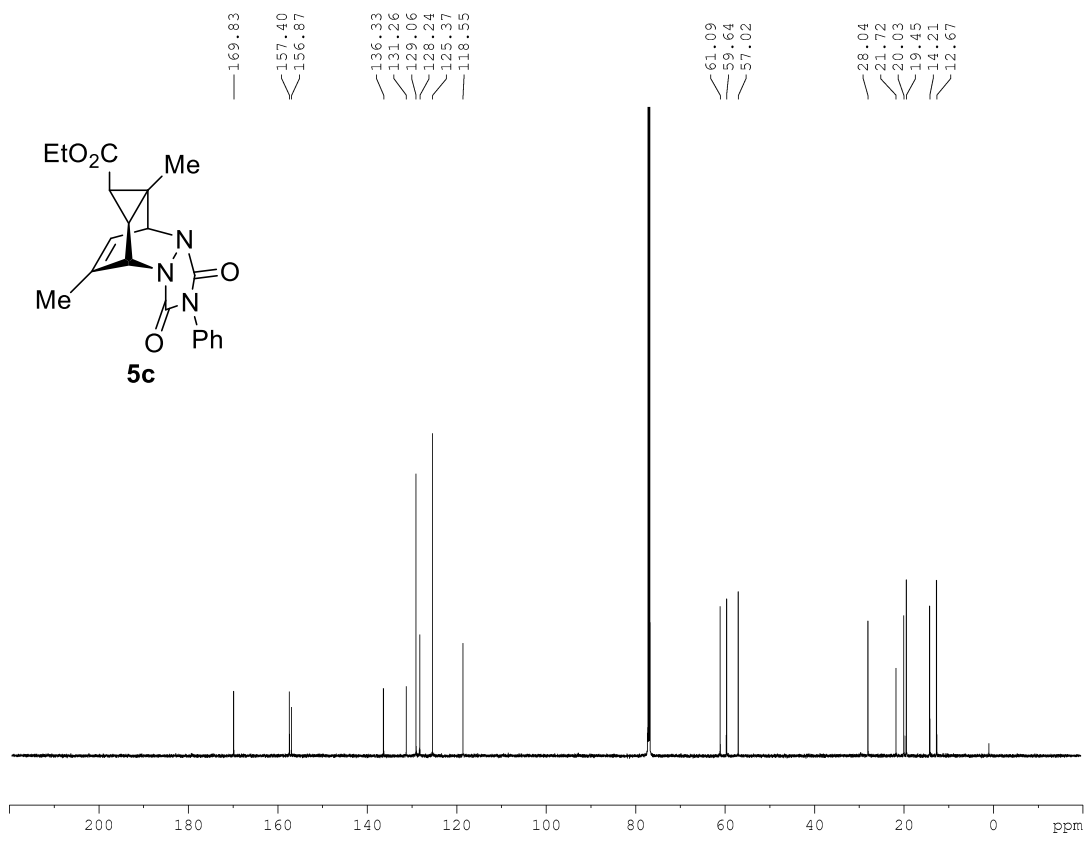
```

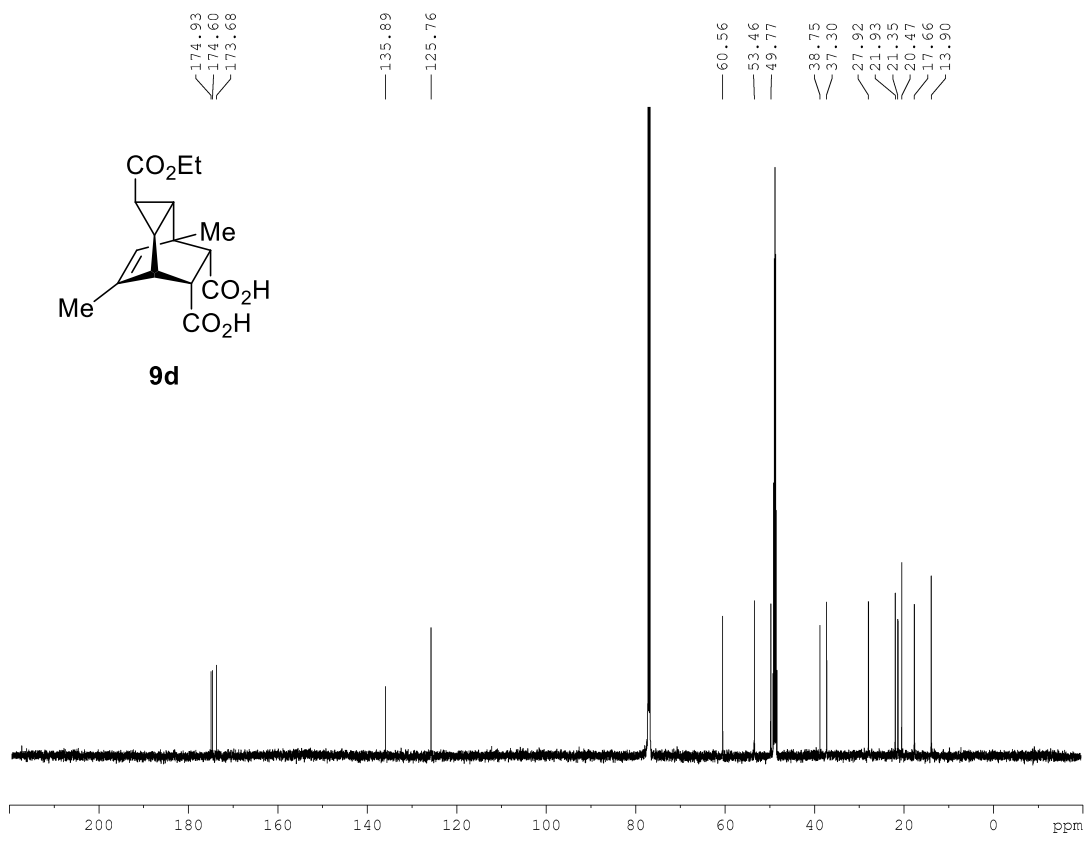
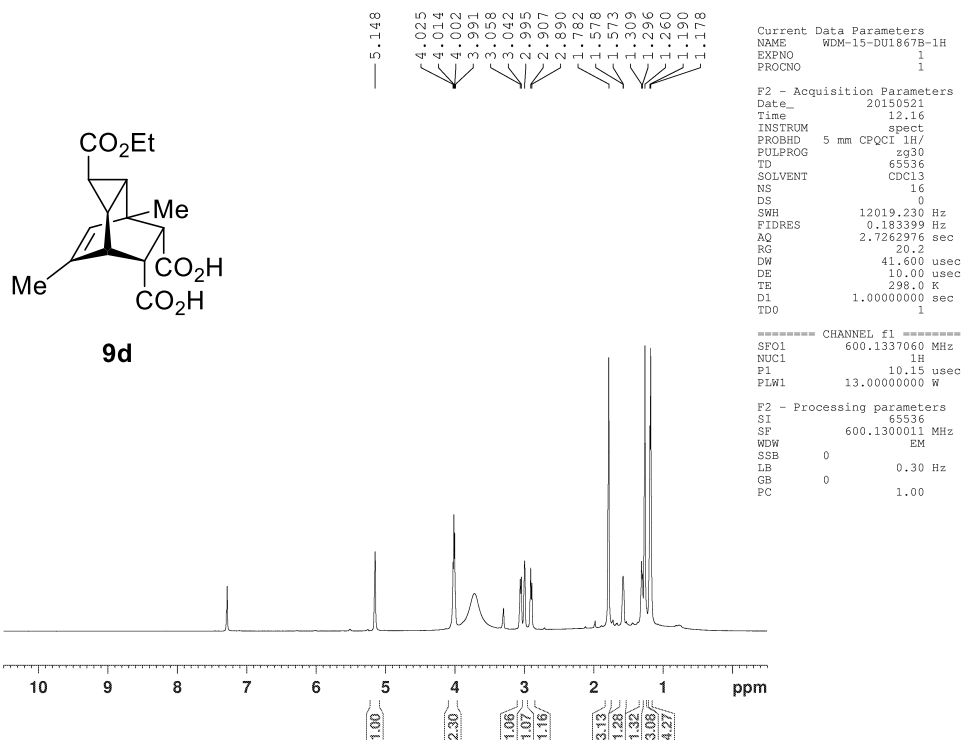
Current Data Parameters
NAME      WDM-15-DU1853A-1H
EXPNO    1
PROCNO   1

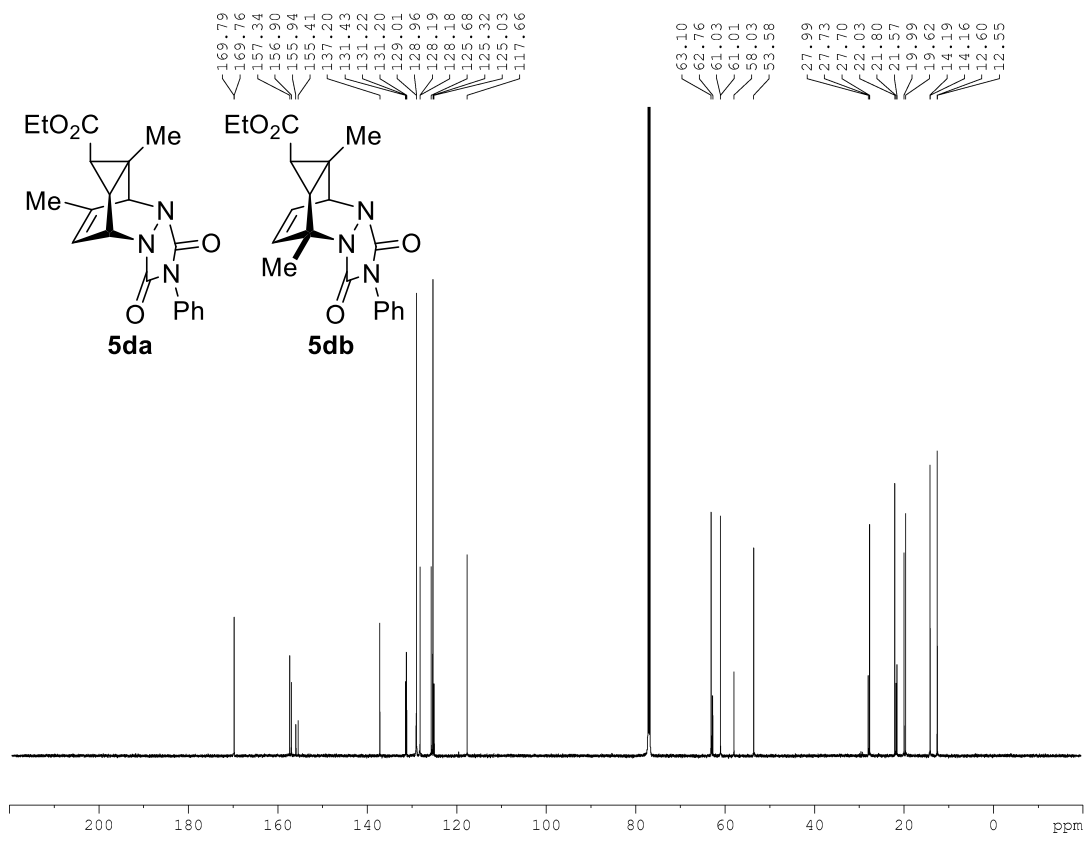
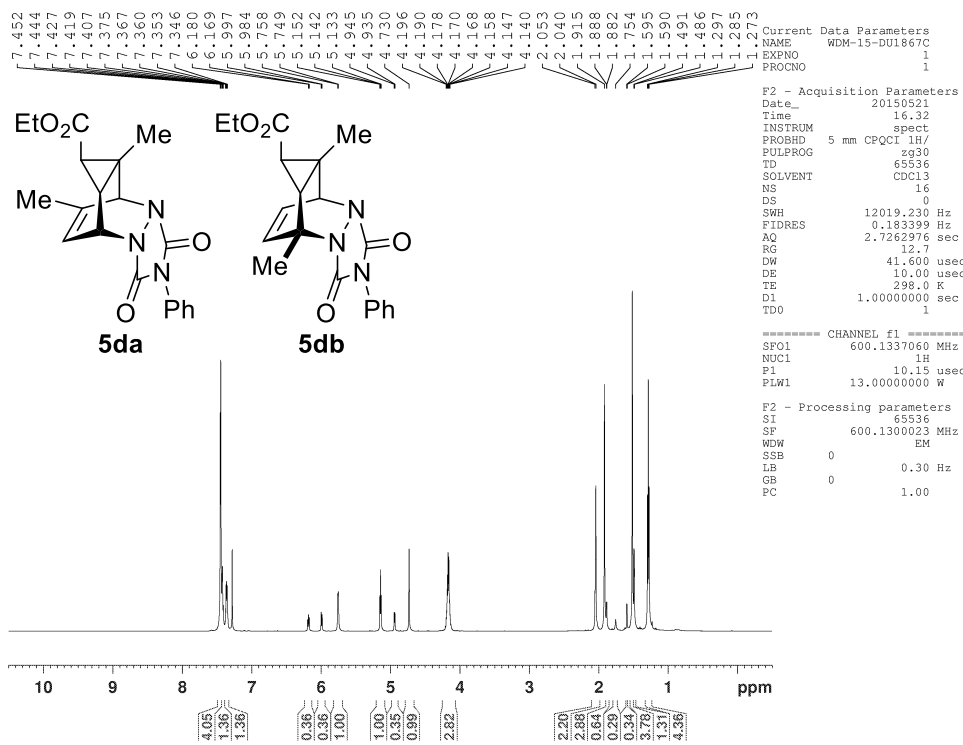
F2 - Acquisition Parameters
Date_    20150318
Time     8.54
INSTRUM  spect
PROBHD   5 mm CPQCI 1H/
PULPROG  zg30
TD        65536
SOLVENT  CDCl3
NS        16
DS        0
SWH       12019.230 Hz
FIDRES    0.183399 Hz
AQ         2.7262976 sec
RG         16
DW         41.600 usec
DE         10.00 usec
TE         298.0 K
D1         1.00000000 sec
TDO        1

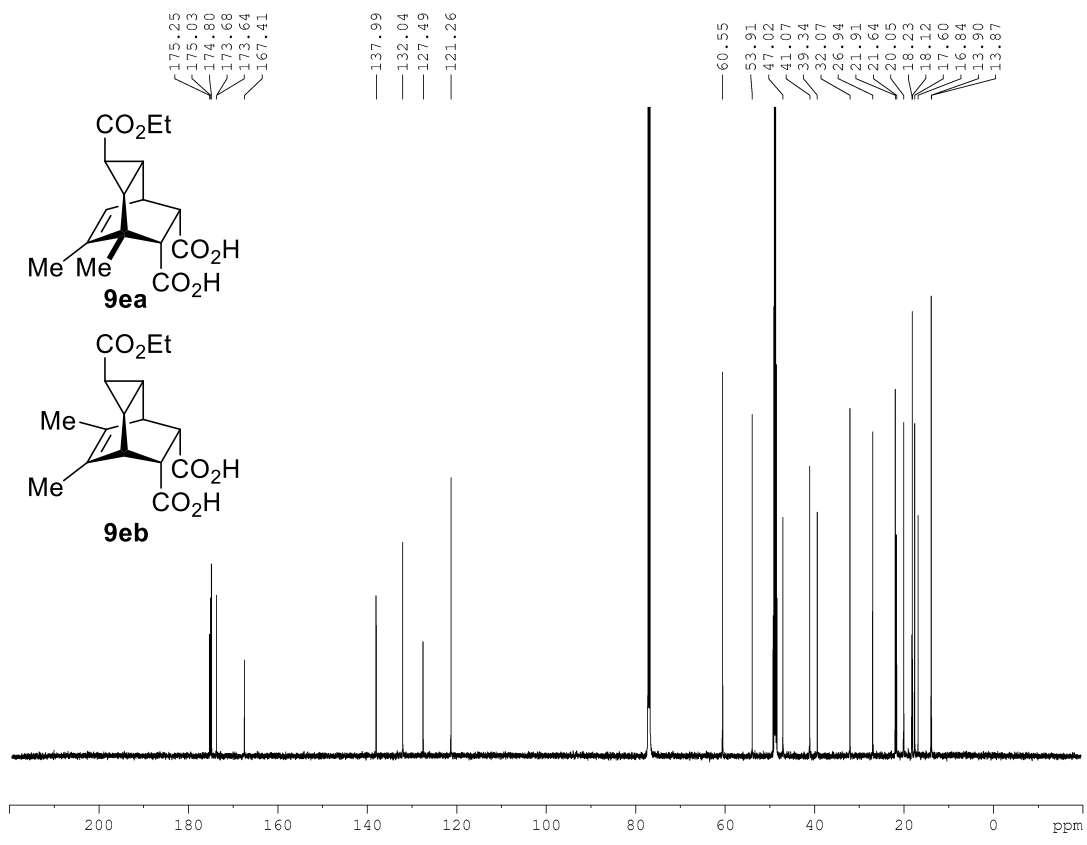
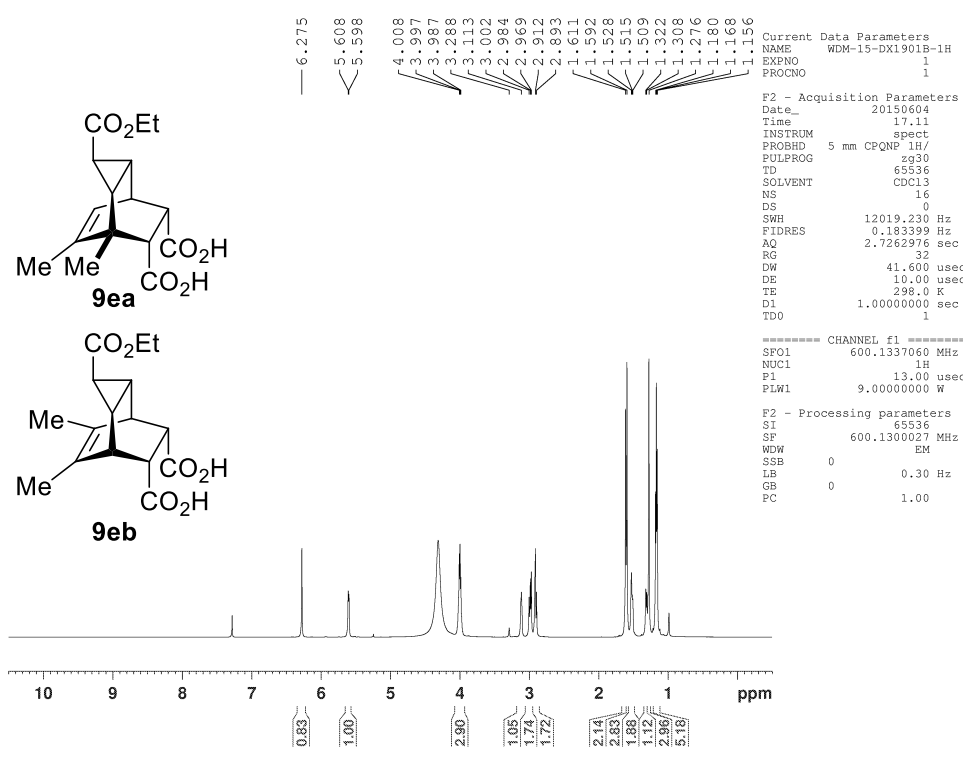
===== CHANNEL f1 =====
SFO1     600.1337060 MHz
NUC1      1H
P1        10.15 usec
PLW1     13.00000000 W

F2 - Processing parameters
SI        65536
SF        600.1300022 MHz
WDW       EM
SSB       0
LB        0.30 Hz
GB        0
PC        1.00
  
```





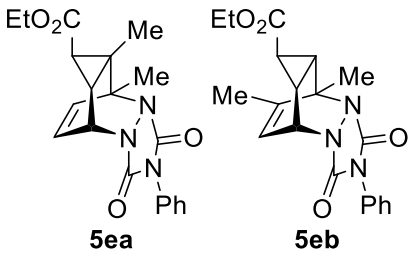




7.465
7.852
7.840
7.427
7.415
7.378
7.367
7.355
6.852
6.845
6.839
6.814
6.742
6.731
6.050
6.038
5.239
5.231
5.222
4.900
4.894
4.202
4.196
4.191
4.184
4.173
4.163
4.151
4.137
2.120
2.113
2.105
1.986
1.849
1.843
1.804
1.750
1.701
1.690
1.681
1.678
1.670
1.640

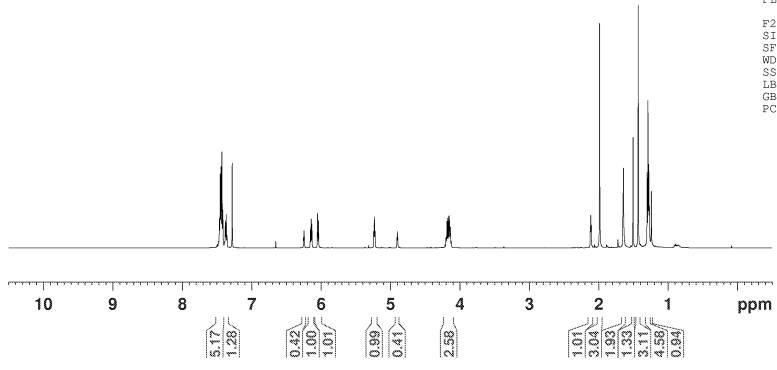
Current Data Parameters
NAME WDM-15-DX1996B-1H
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150715
Time 12.01
INSTRUM spect
PROBHD 5 mm CPNP 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 32
DW 41.600 usec
DE 10.00 usec
TE 294.1 K
D1 1.00000000 sec
TDO 1

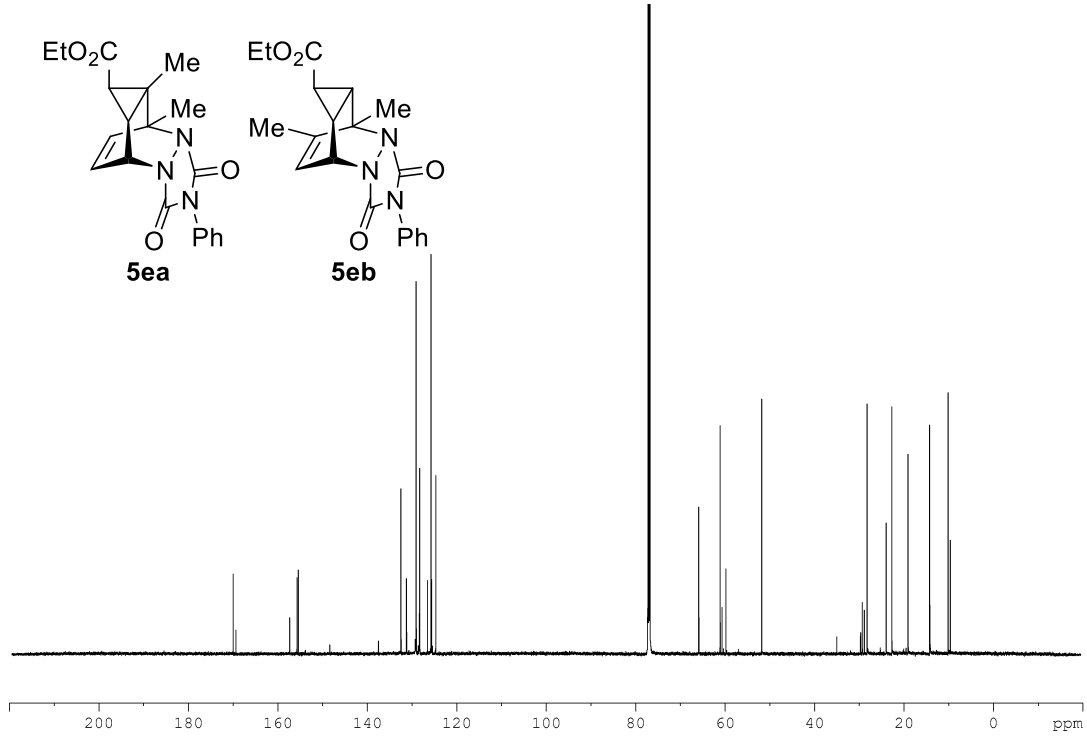
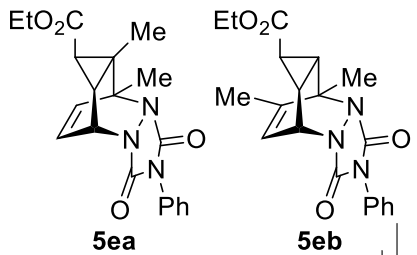


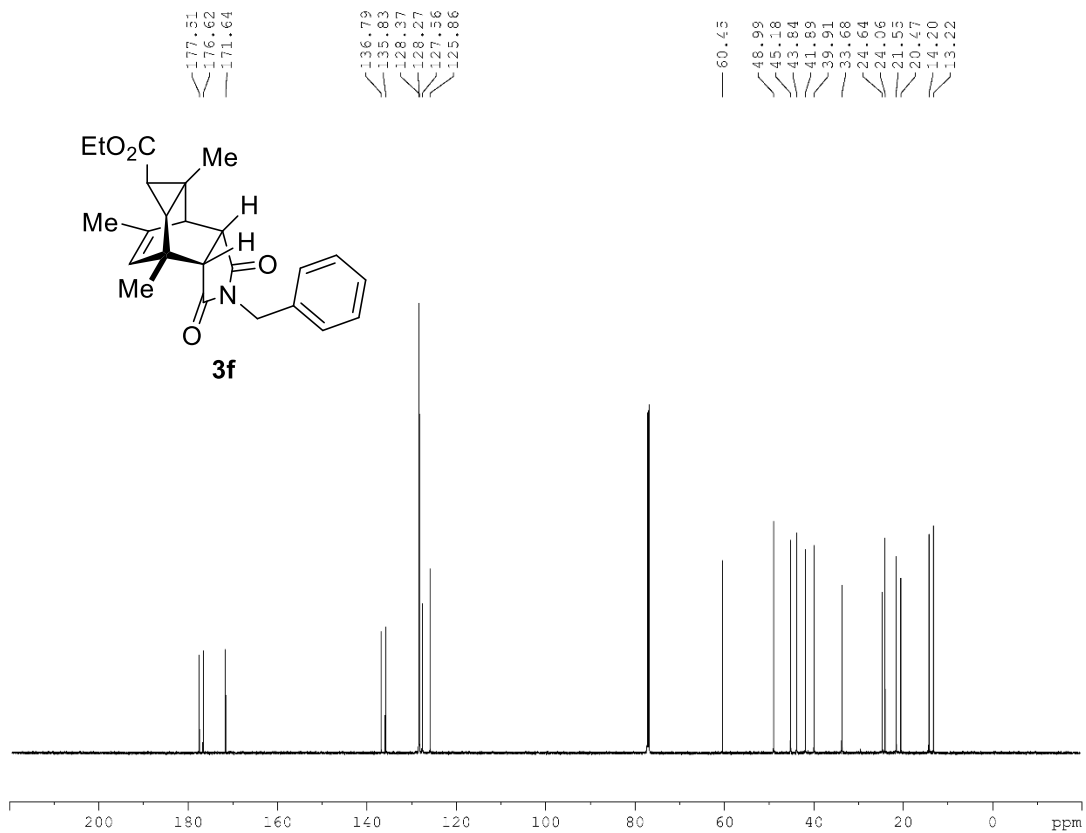
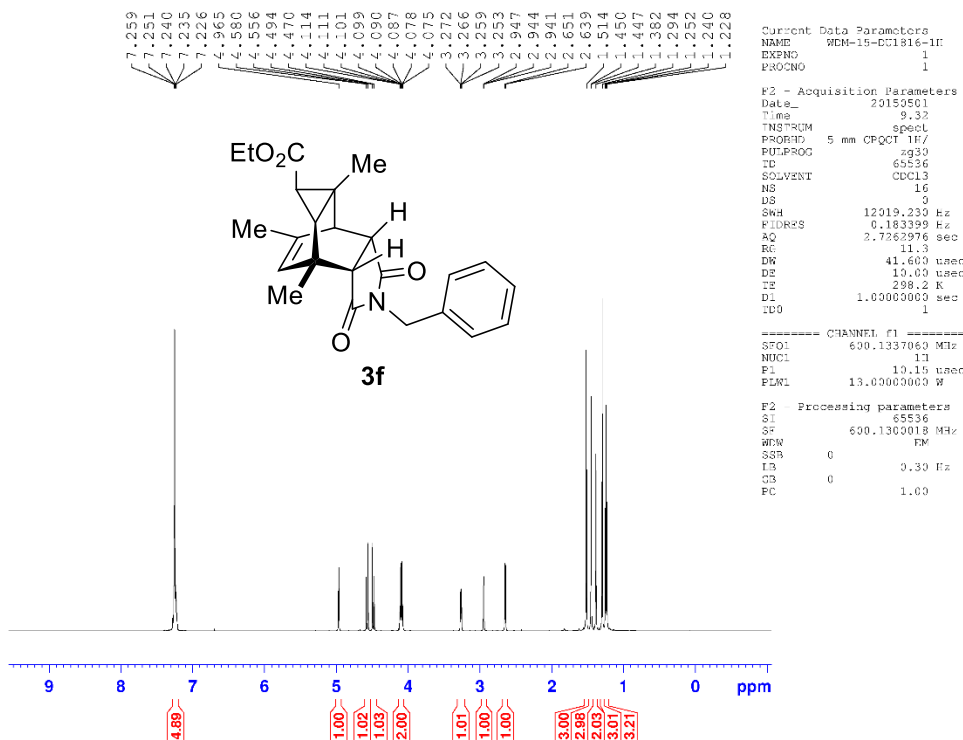
===== CHANNEL f1 =====
SFO1 600.1337060 MHz
NUC1 1H
P1 13.00 usec
PLW1 9.00000000 W

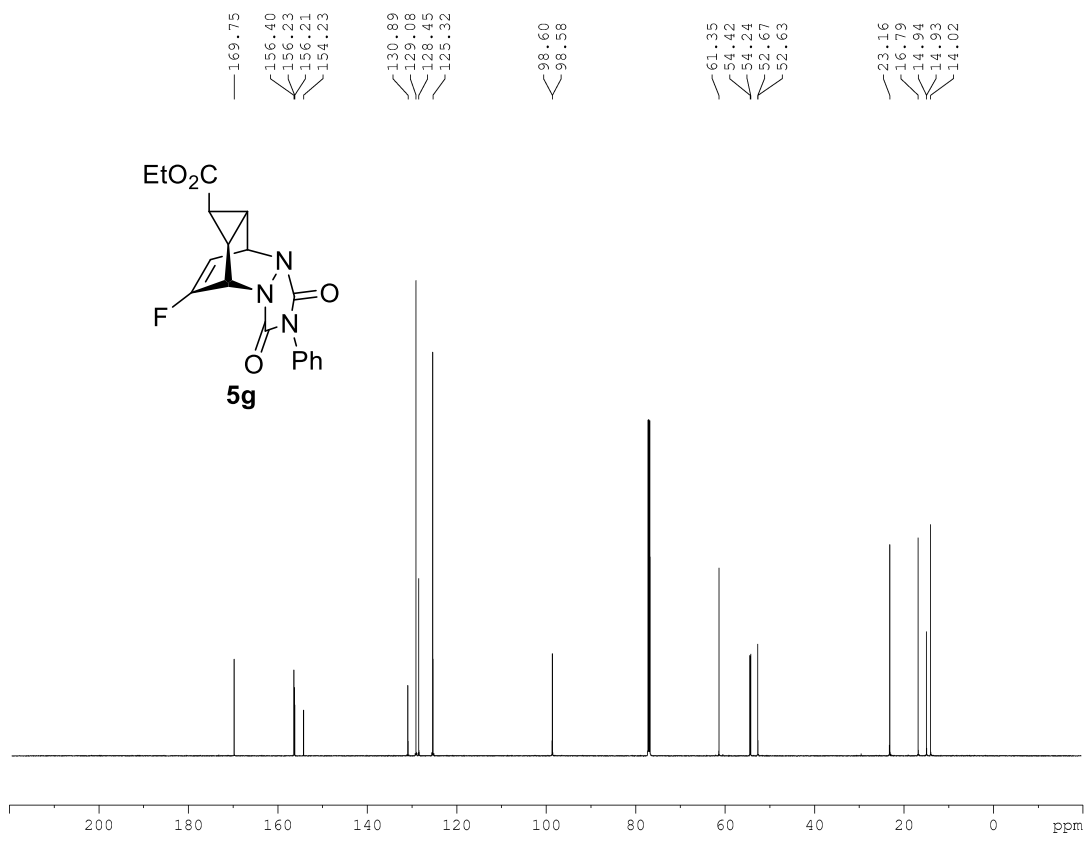
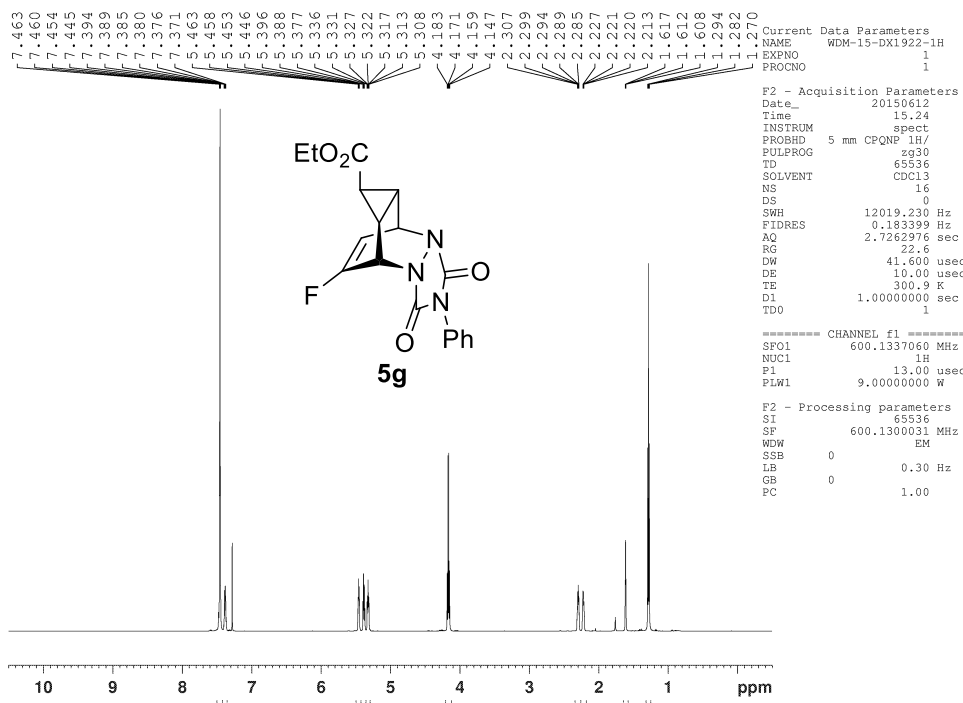
F2 - Processing parameters
SI 65536
SF 600.1300036 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

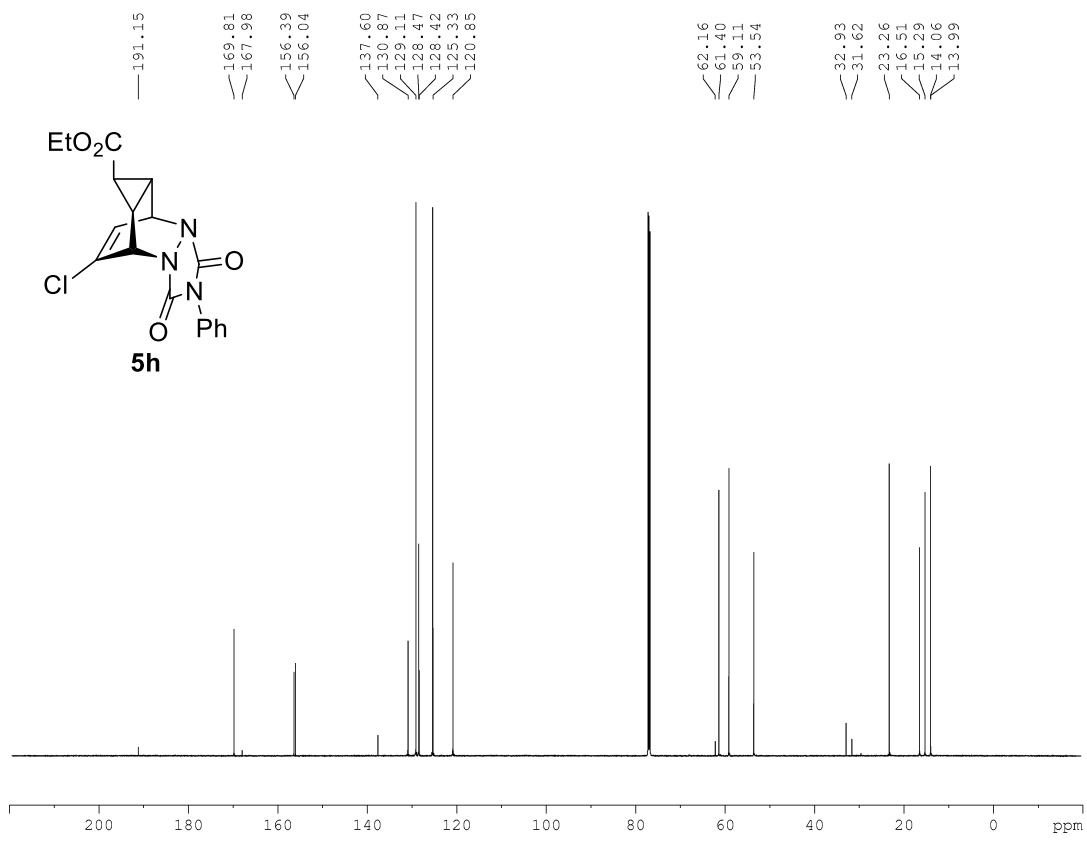
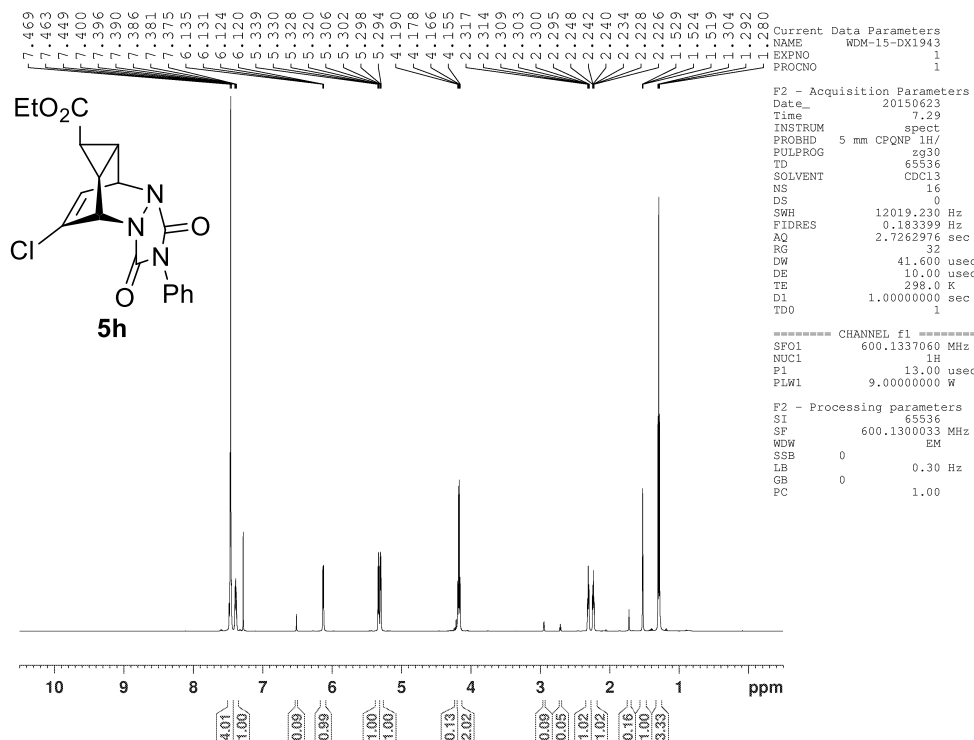


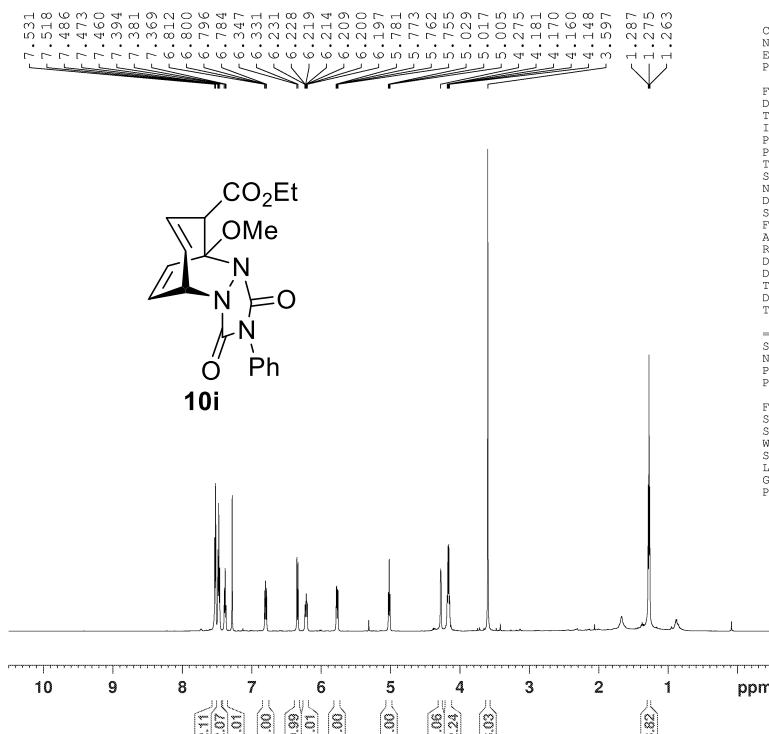
169.92
169.32
157.30
155.64
155.36
132.44
131.22
131.16
129.12
129.04
128.35
128.25
126.49
125.74
125.58
124.65
65.84
61.09
60.62
59.76
51.78
34.97
29.67
29.32
28.81
28.19
23.97
22.67
22.65
19.09
14.22
10.12
9.61









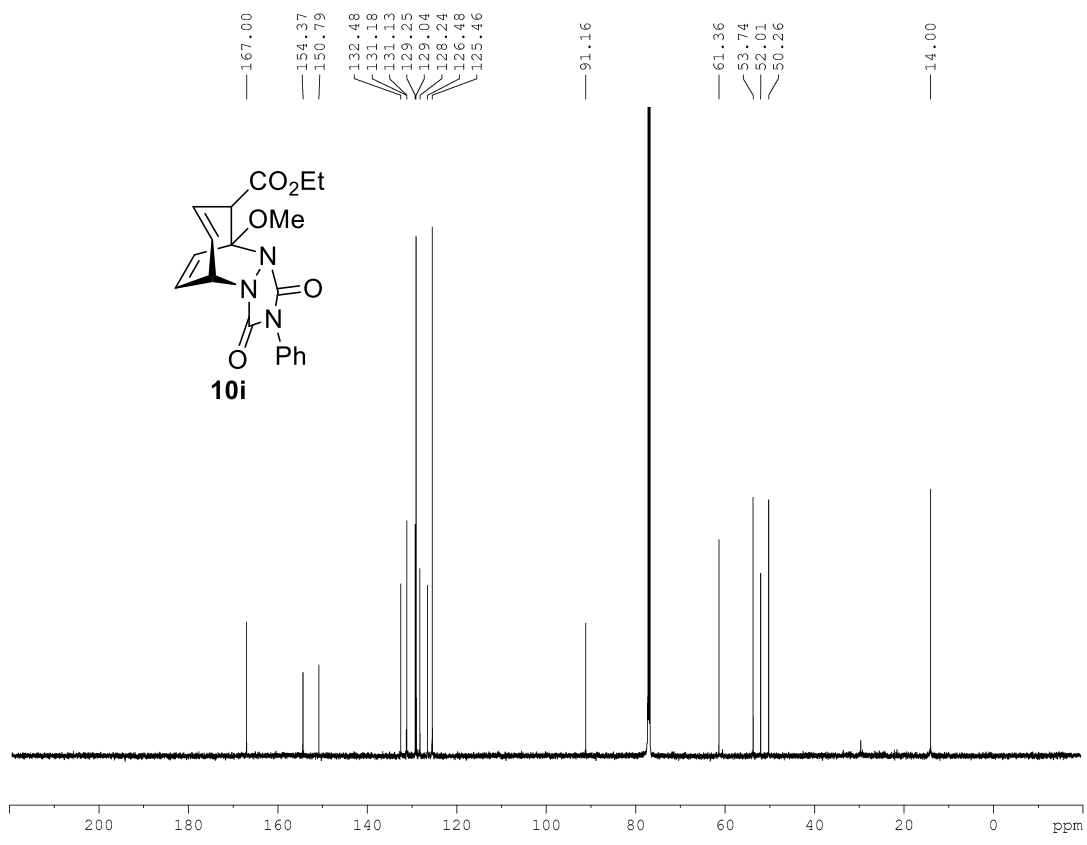


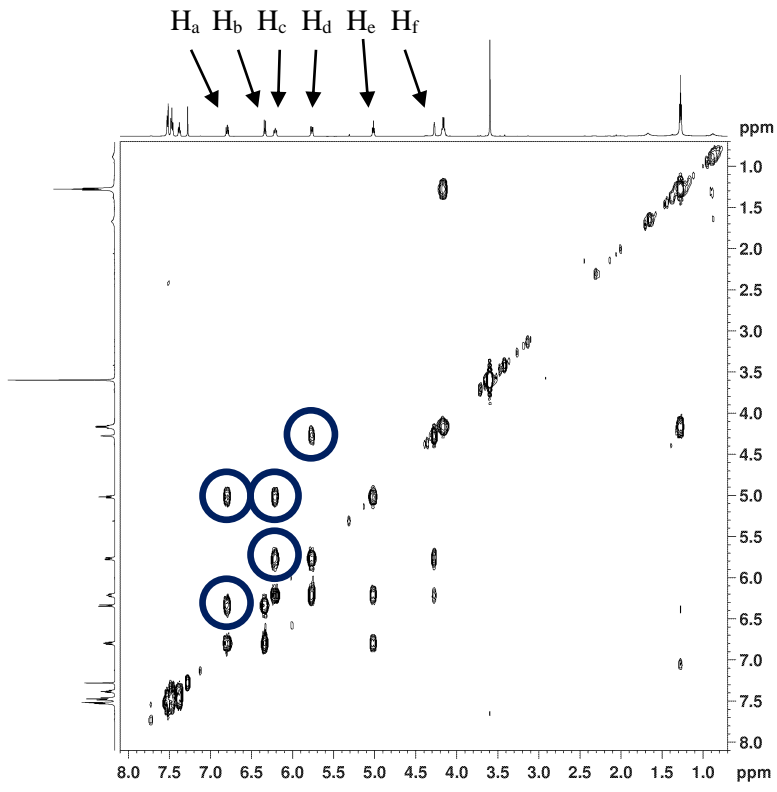
Current Data Parameters
 NAME WDM-15-DU1874C-1H
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150526
 Time 17.32
 INSTRUM spect
 PROBHD 5 mm CPQCI 1H/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 16
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 22.6
 DW 41.600 usec
 DE 10.00 usec
 TE 298.0 K
 D1 1.00000000 sec
 TDO 1

===== CHANNEL f1 =====
 SFO1 600.1337060 MHz
 NUC1 1H
 P1 10.15 usec
 PLW1 13.00000000 W

F2 - Processing parameters
 SI 65536
 SF 600.1300024 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



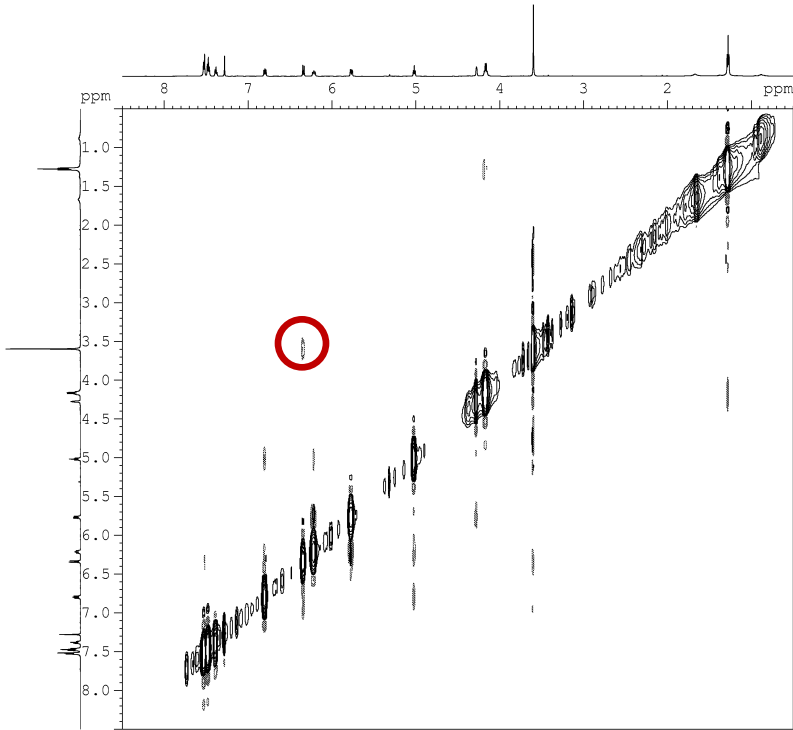
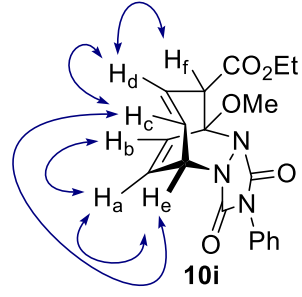


```

Current Data Parameters
NAME      WGM-15-0019194-COSY
EXPNO     1
PROCNO    1

F2 - Acquisition Parameters
Date_     20150527
Time      12.09
INSTRUM   spect
PROBHD    5 mm CPQCI 131
PULPROG   cosypprogf
TD         2048
SOLVENT   CDCl3
NS         1
DS         4
SWH        8012.820 Hz
FIDRES     3.912510 Hz
AQ         0.127182 sec
RG         641
AQ         0.127182 sec
RG         64
DM          62.400 usec
DE         10.00 usec
TE         298.2 K
D0         0.0000000 sec
D1         2.0000000 sec
D11        0.0000000 sec
D12        0.0000000 sec
D13        0.0000000 sec
D14        0.0002000 sec
D16        0.0002000 sec
IN0        0.00012480 sec
  
```

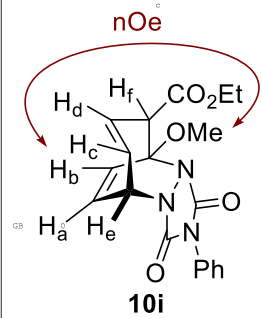
COSY correlations



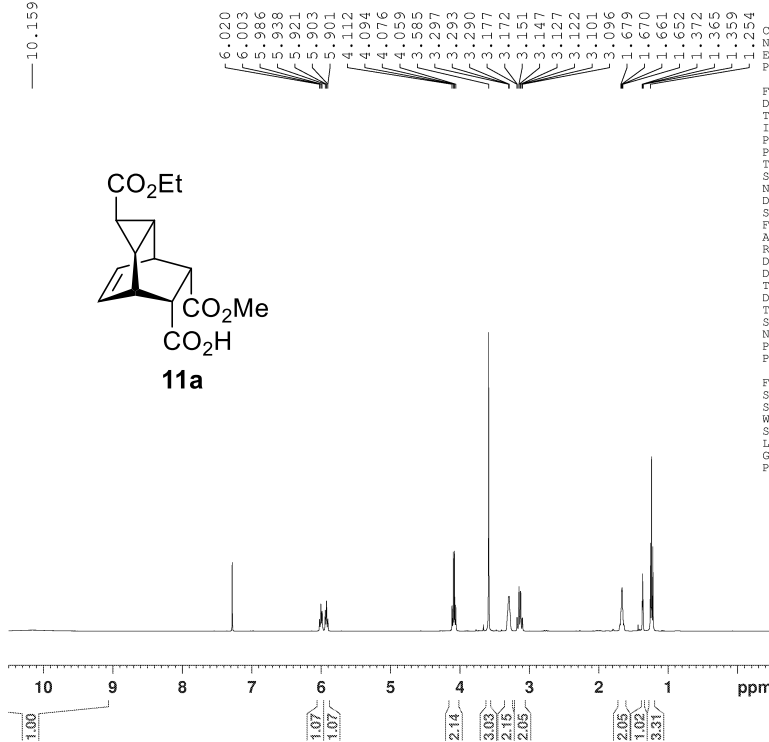
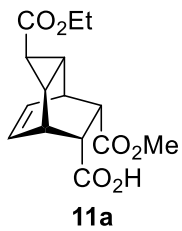
```

Current Data Parameters
NAME      WGM-15-001874C-NOESY
EXPNO     1
PROCNO    1

F2 - Acquisition Parameters
Date_     20150527
Time      12.14
INSTRUM   spect
PROBHD    5 mm CPQCI 131
PULPROG   noesypprogf
TD         2048
SOLVENT   CDCl3
NS         4
DS         4
SWH        6009.615 Hz
FIDRES     2.934382 Hz
AQ         0.1703936 sec
RG         64
DM          83.200 usec
DE         10.00 usec
TE         298.2 K
D0         0.0007020 sec
D1         2.0000000 sec
D11        0.3000000 sec
D12        0.0000000 sec
D14        0.0002000 sec
D16        0.0002000 sec
IN0        0.00016640 sec
  
```



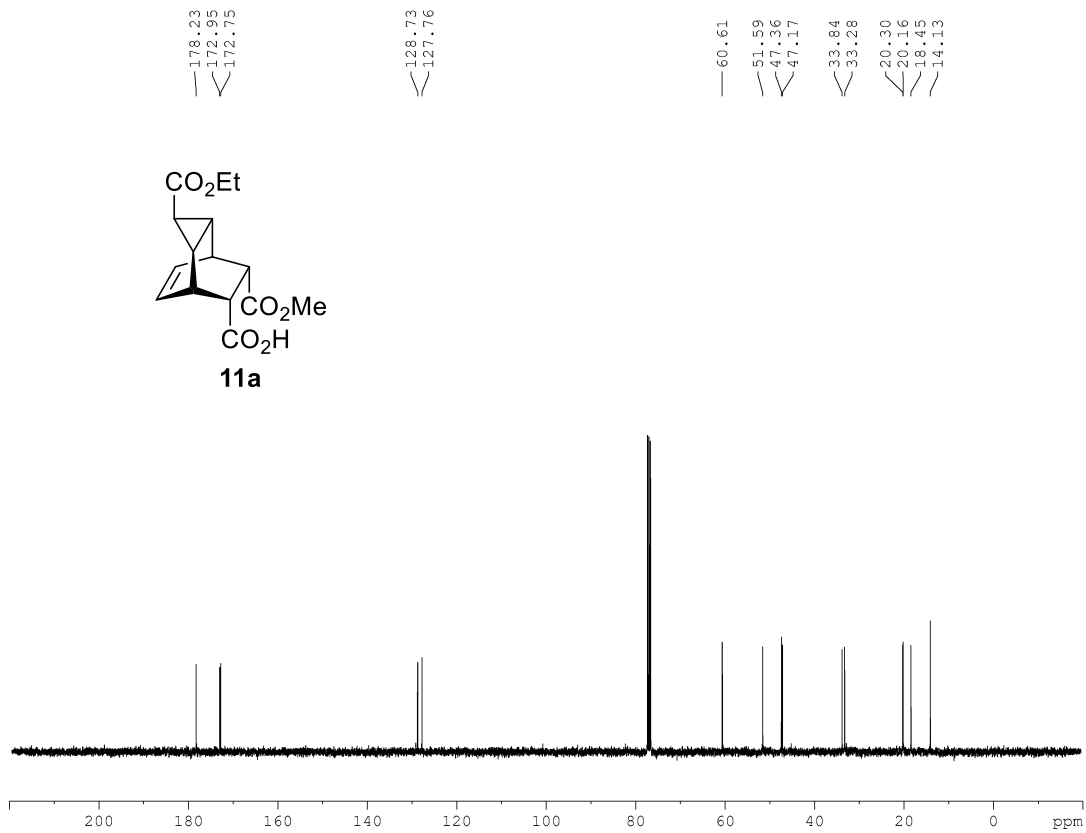
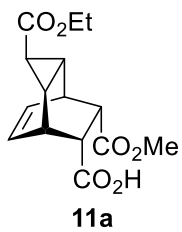
10.159

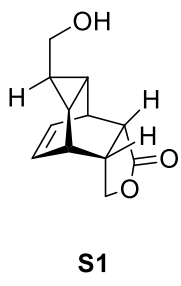
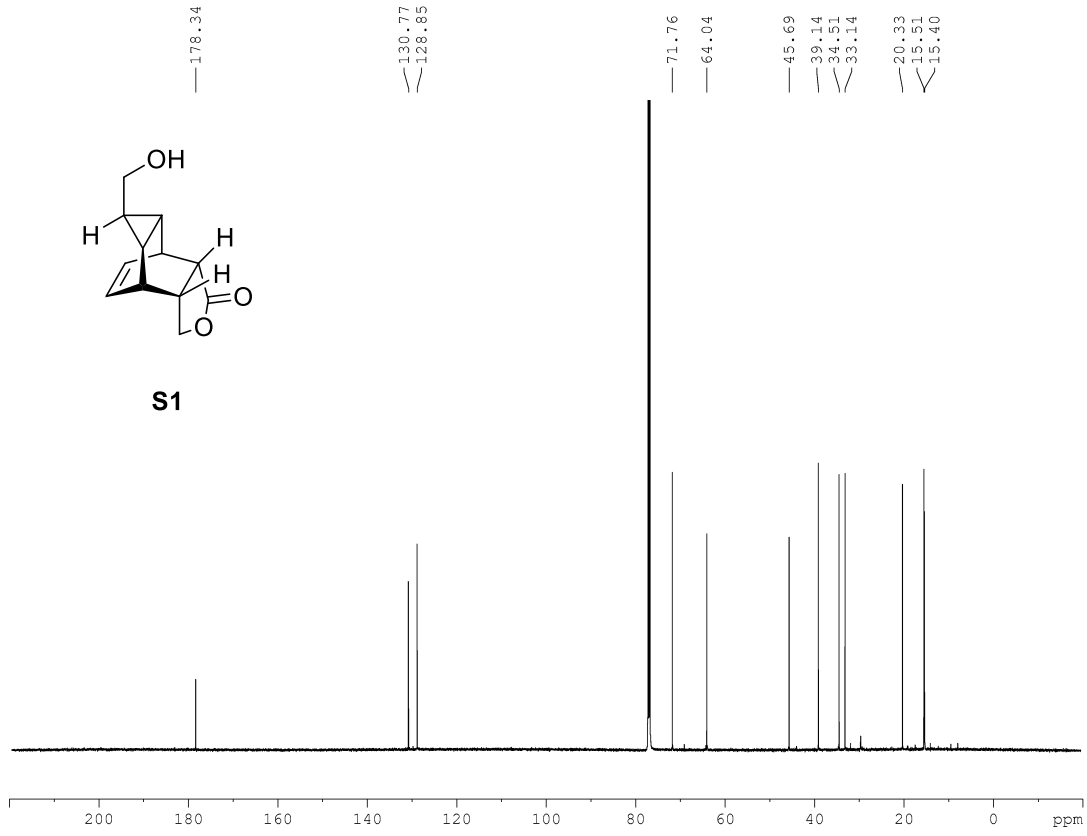
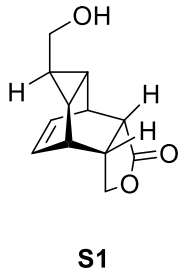
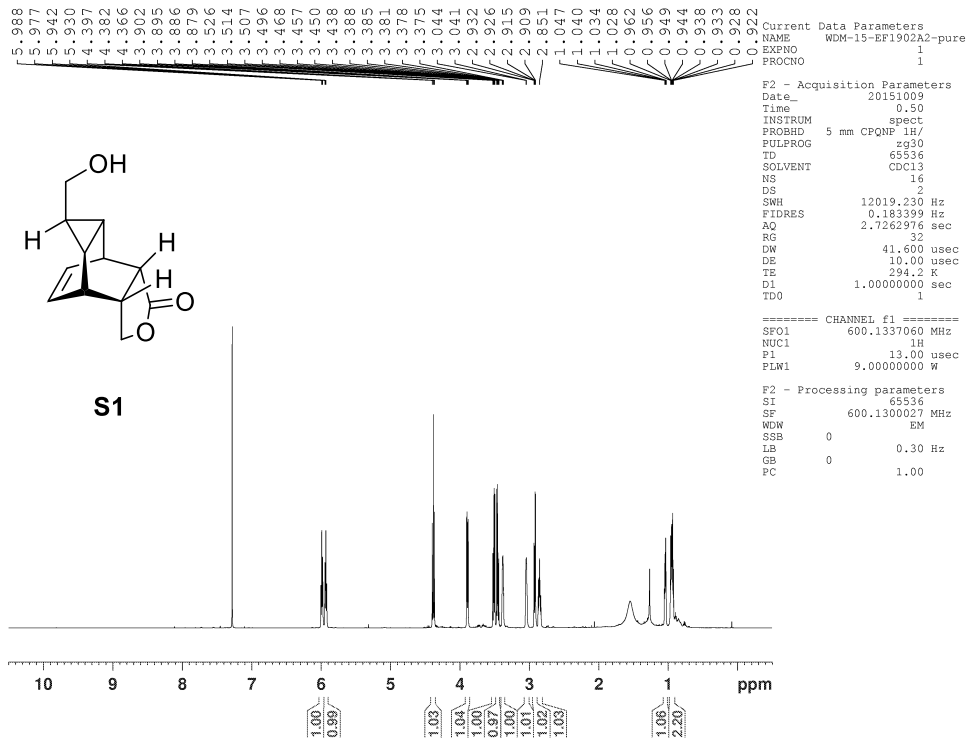


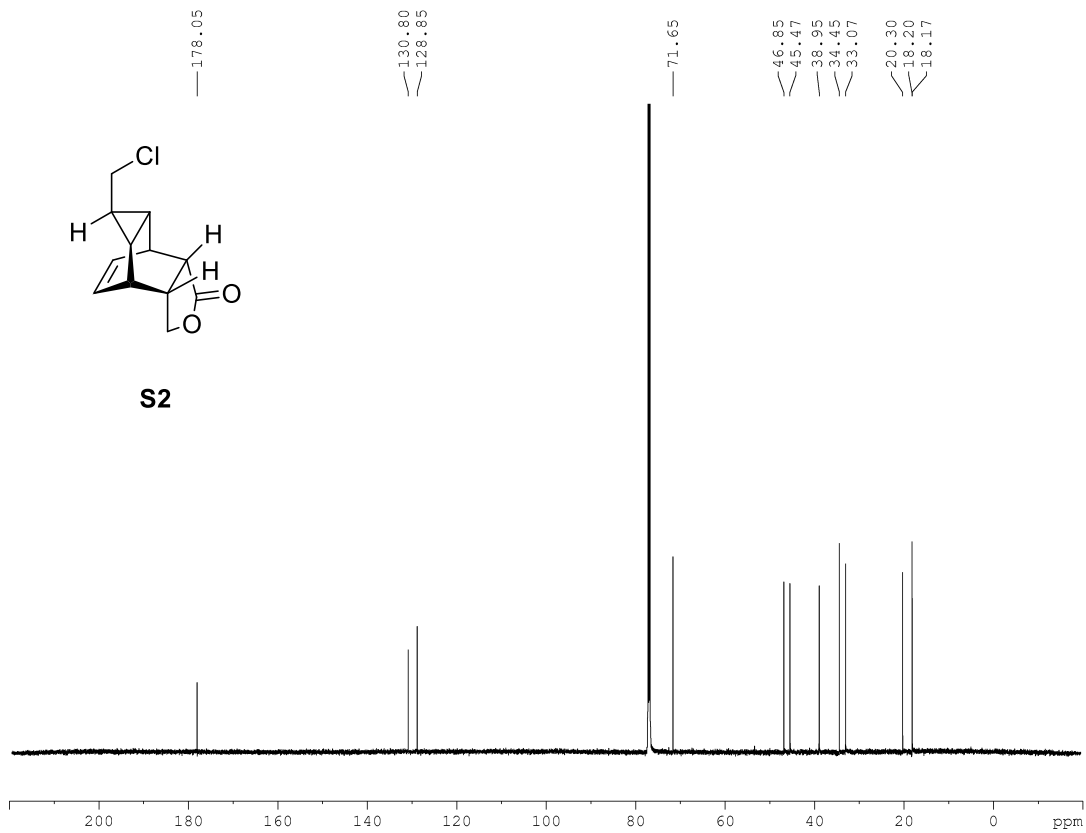
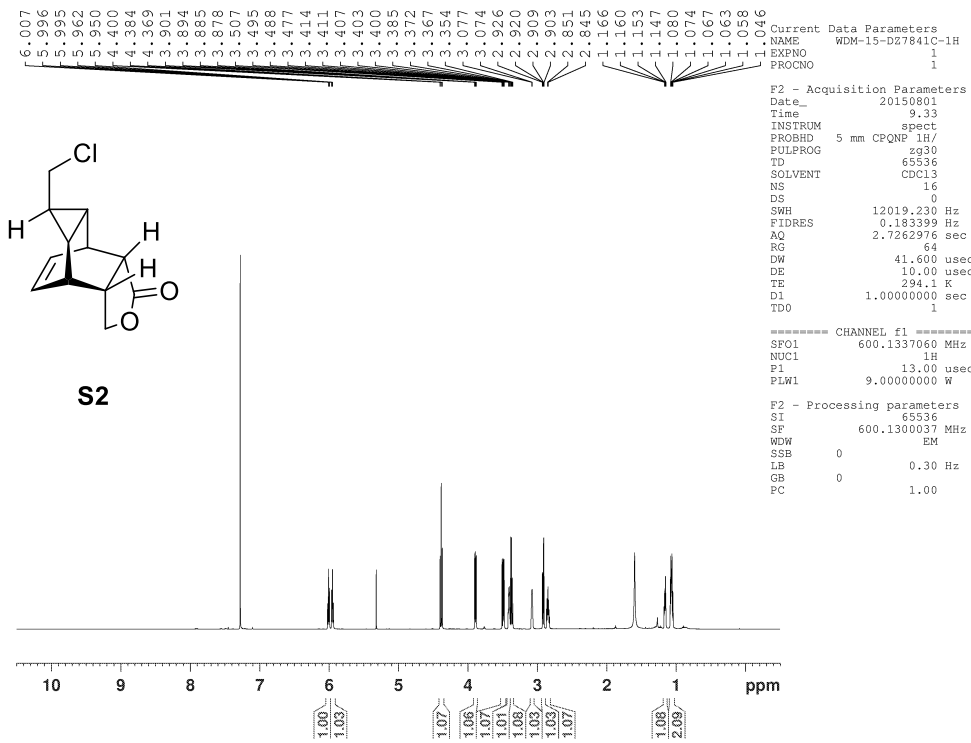
Current Data Parameters
NAME WDM-15-DX1985B
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150713
Time 9.21 h
INSTRUM spect
PROBHD Z104450_0391 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 0
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 59.75
DW 62.400 usec
DE 6.50 usec
TE 297.0 K
D1 1.00000000 sec
TDO 1
SFO1 399.9824699 MHz
NUC1 1H
P1 13.25 usec
PLW1 11.19999981 W

F2 - Processing parameters
SI 65536
SF 399.9800017 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00







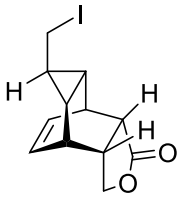
5.967
5.955
5.931
5.920
5.908
4.364
4.349
4.333
3.863
3.856
3.847
3.840
3.377
3.366
3.350
3.138
3.134
3.122
3.057
3.053
3.042
3.037
3.023
3.007
2.884
2.878
2.867
2.861
2.824
2.814
2.808
2.802
1.105
1.100
1.095
1.089
1.077
0.988
0.982
0.976
0.970
0.963

Current Data Parameters
NAME WDM-15-D27870-1H
EXPNO 1
PROCNO 1

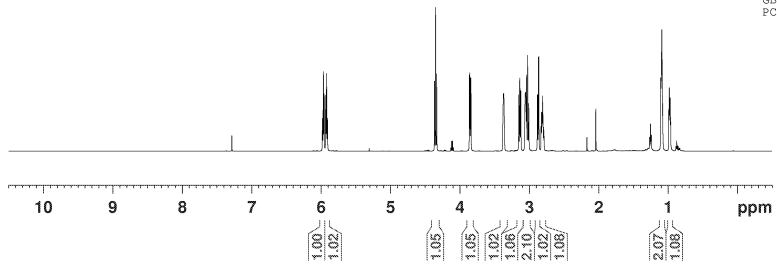
F2 - Acquisition Parameters
Date_ 20150813
Time 15.27
INSTRUM spect
PROBHD 5 mm CPQNP 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 0
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 22.6
DW 41.600 usec
DE 10.00 usec
TE 294.2 K
D1 1.00000000 sec
TDO 1

===== CHANNEL f1 =====
SFO1 600.1337060 MHz
NUC1 1H
P1 13.00 usec
PLW1 9.00000000 W

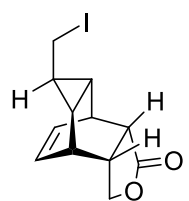
F2 - Processing parameters
SI 65536
SF 600.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



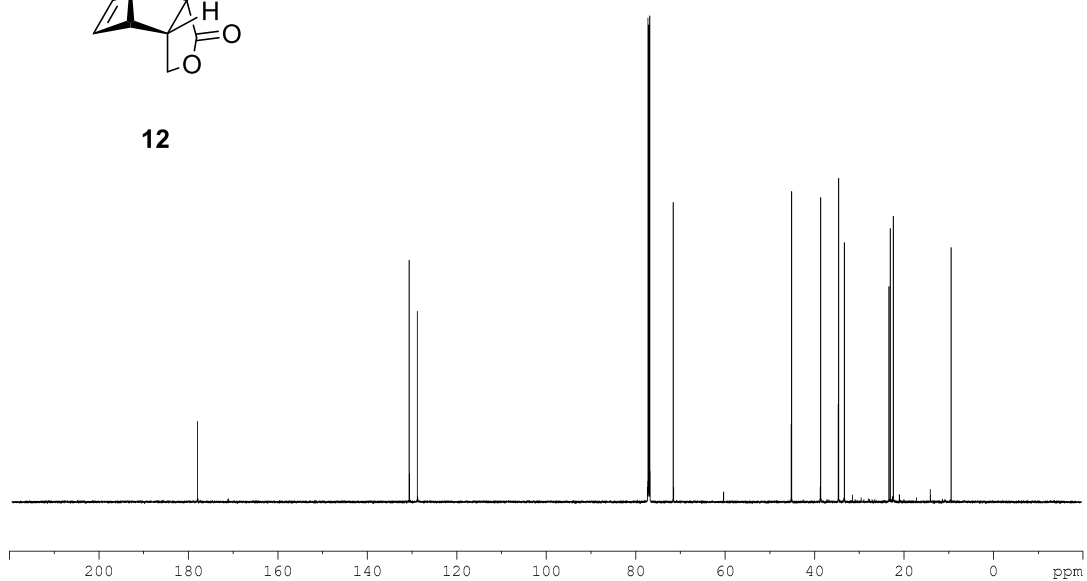
12

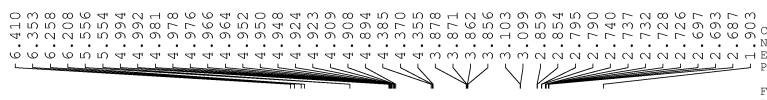


177.87
130.55
128.72
71.52
45.10
38.59
34.59
33.28
23.31
22.31
9.42

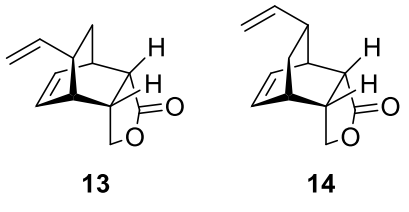


12





6.410
6.353
6.358
6.308
6.556
5.554
4.994
4.992
4.981
4.978
4.976
4.966
4.964
4.952
4.950
4.948
4.924
4.923
4.909
4.908
4.894
4.885
4.370
4.355
3.876
3.871
3.862
3.856
3.103
3.099
2.859
2.854
2.785
2.780
2.740
2.737
2.732
2.728
2.726
2.697
2.693
2.687
1.903

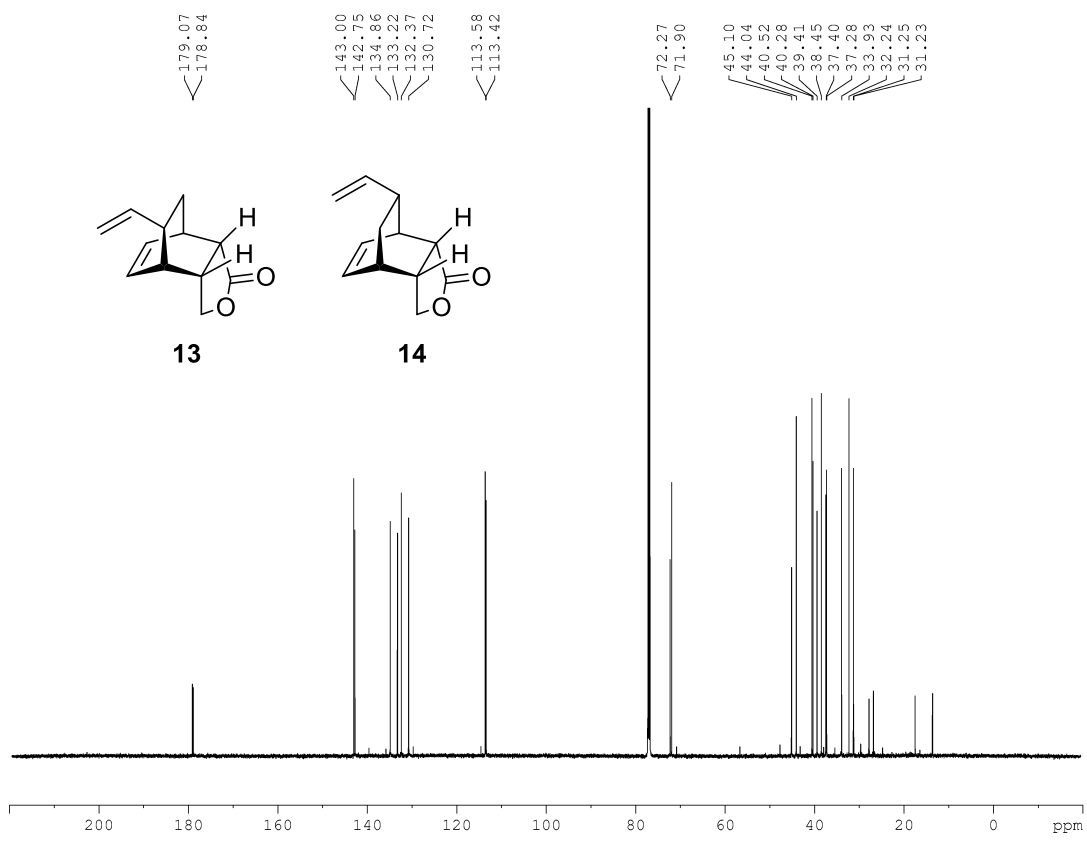
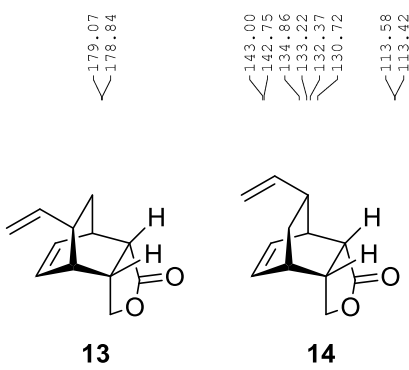
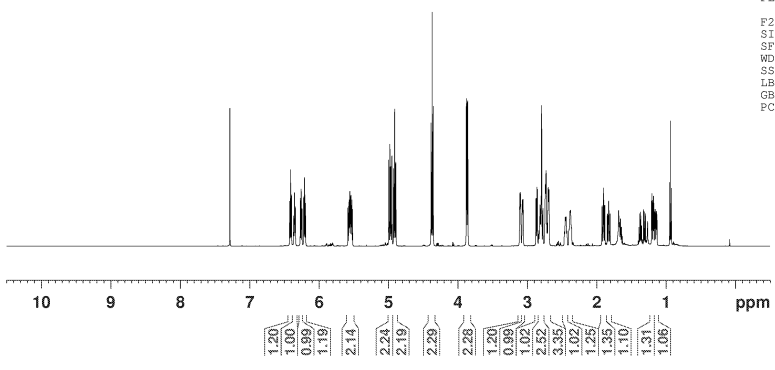


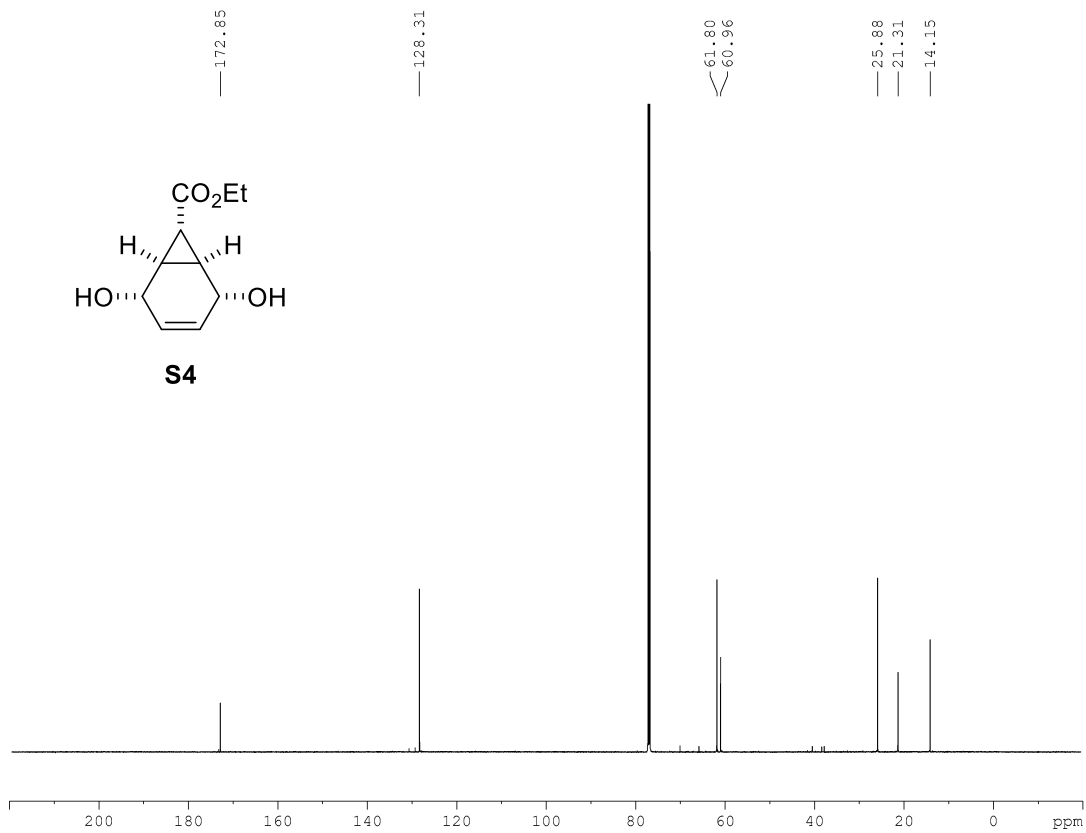
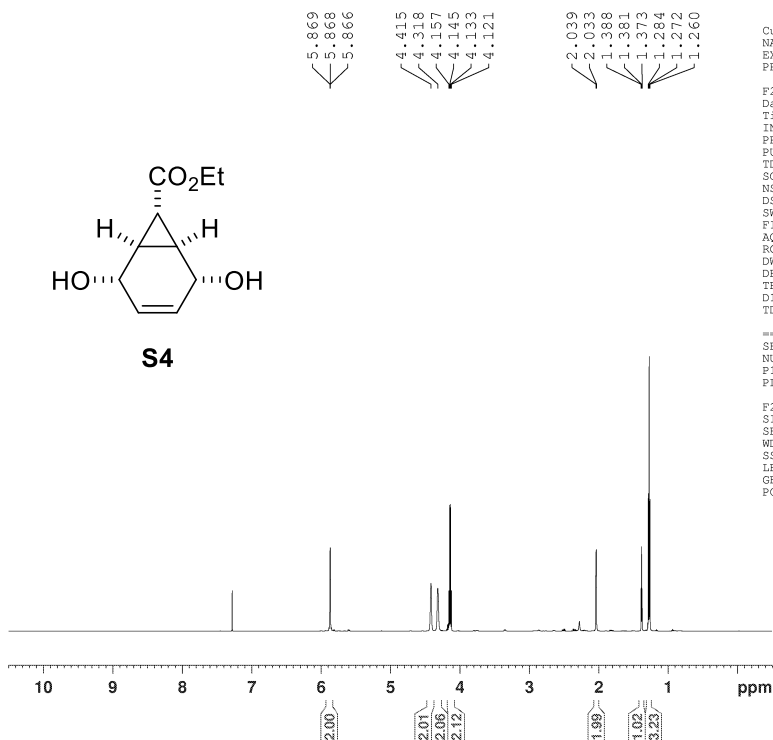
Current Data Parameters
 NAME WDM-15-EB9389
 EXPNO 1
 PROCNO 1

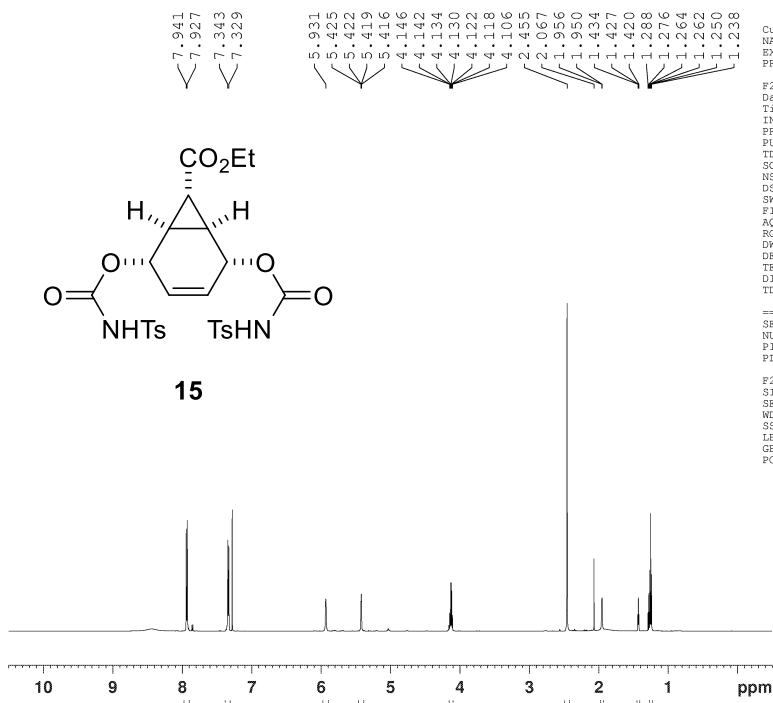
F2 - Acquisition Parameters
 Date_ 20150329
 Time 16.59
 INSTRUM spect
 PROBHD 5 mm CPQNP 1H/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 8
 DS 0
 SWH 12019.230 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RG 32
 DW 41.600 usec
 DE 10.00 usec
 TE 294.2 K
 DI 1.00000000 sec
 TDO 1

===== CHANNEL f1 =====
 SFO1 600.1337060 MHz
 NUC1 1H
 P1 13.00 usec
 PLW1 9.00000000 W

F2 - Processing parameters
 SI 65536
 SF 600.1300000 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00



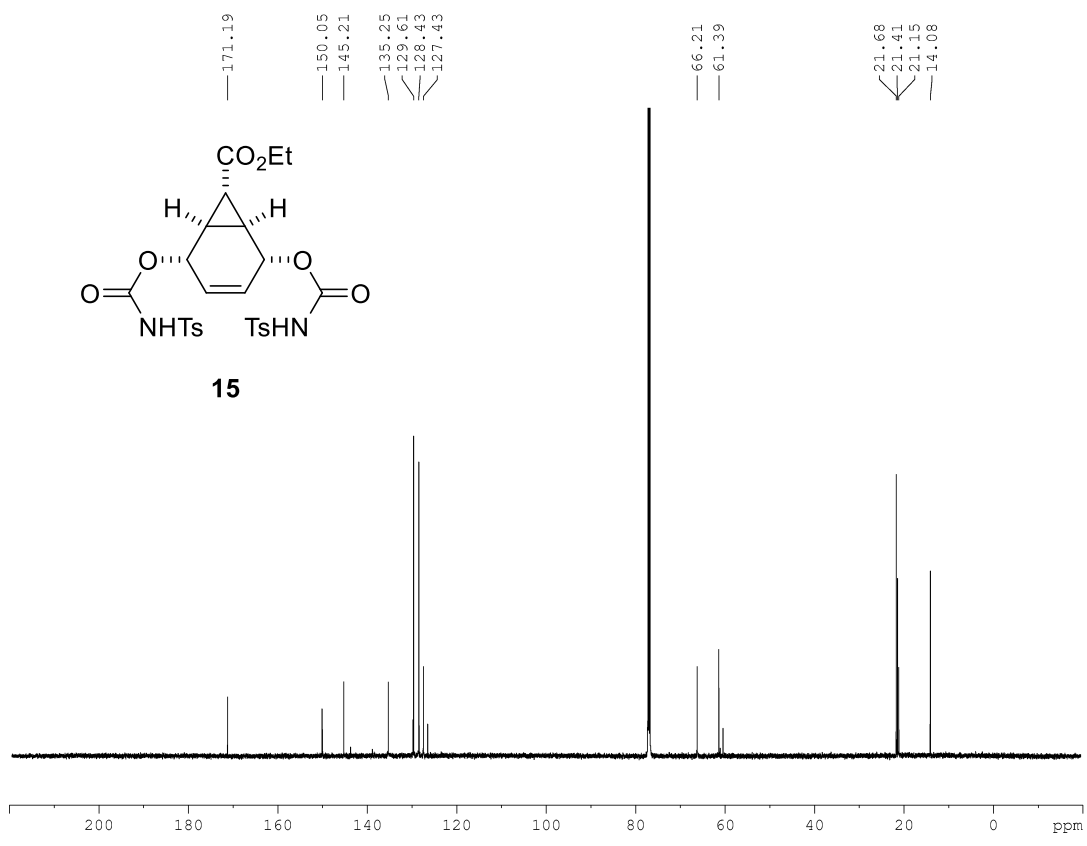


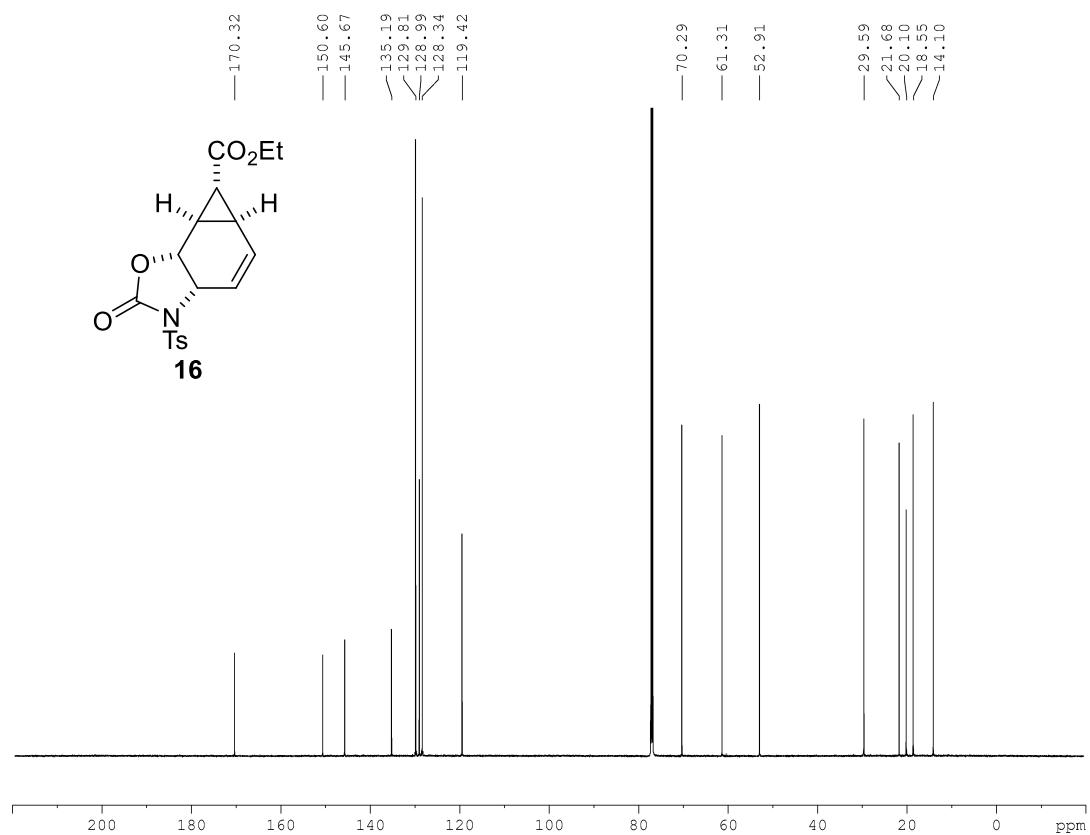
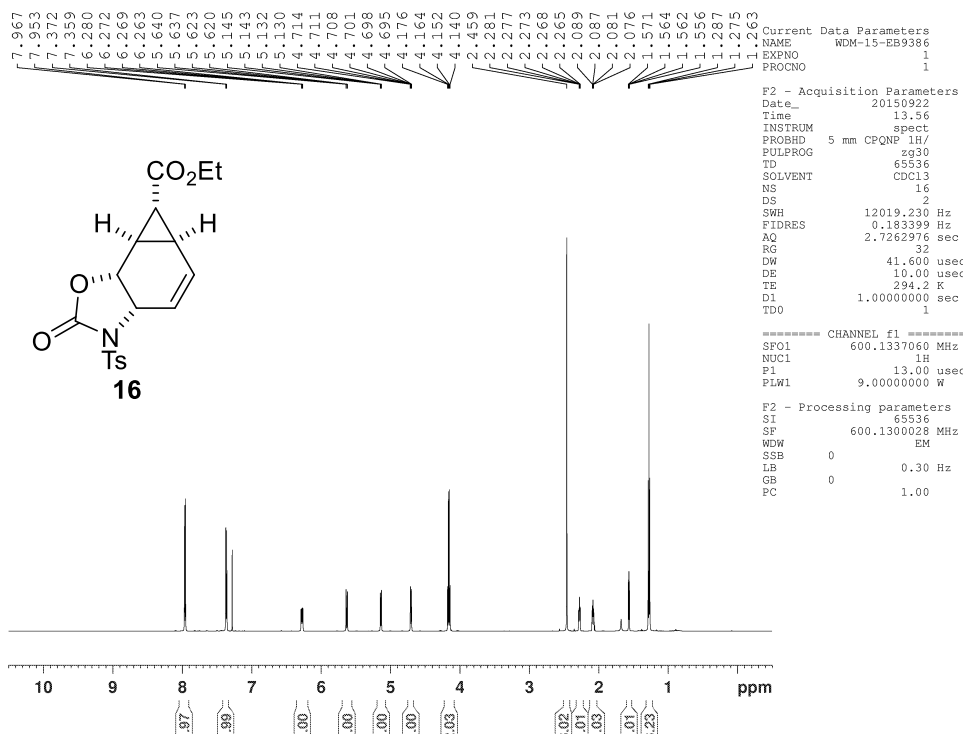


Current Data Parameters
 NAME WDM-15-EB9387-pure-1H
 EXFNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20150929
 Time 16.51
 INSTRUM spect
 PROBHD 5 mm CPQNP 1H/
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 8
 DS 0
 SWH 12019.226 Hz
 FIDRES 0.183399 Hz
 AQ 2.7262976 sec
 RC 32
 DW 41.600 usec
 DE 10.00 usec
 TE 294.2 K
 D1 1.0000000 sec
 TDO

===== CHANNEL f1 =====
 SF01 600.1337060 MHz
 NUCL1 1H
 P1 13.00 usec
 PLW1 9.00000000 W
 F2 - Processing parameters
 S1 65536
 SF 600.1300029 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00





X-ray crystallographic data for 2a

Suitable single crystals of compound **2a** were selected and analyzed on a Bruker APEX-II CCD diffractometer. Crystals were kept at 100 K during data collection. Using Olex2,¹ structures were solved with the olex2.solve² structure solution program using Charge Flipping and refined with the XL³ refinement package using Least Squares minimization. Thermal ellipsoid plots of this structure is included below.

1. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339–341.
2. Bourhis, L. J.; Dolomanov, O. V.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *Acta. Cryst.* **2015**, *A71*, 59–75.
3. Sheldrick, G. M. *Acta. Cryst.* **2008**, *A64*, 112–122.

