Synthesis of Cyclopropanoids, and elaboration to Tetralones

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Certificate of Examination

This is to certify that the dissertation titled "***Synthesis of Cyclopropanoids, and elaboration to Tetralones***" submitted by Mr. Kaushalendra Patel (Reg. No. MP16012) for the partial fulfilment of MS degree programme of the Institute, has been examined by the thesis committee duly appointed by the Institute. The committee finds the work done by the candidate satisfactory and recommends that the report be accepted.

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Declaration

The work presented in this dissertation has been carried out by me under the guidance of **Dr. S. S. V. Ramasastry** at the Indian Institute of Science Education and Research Mohali.
This work has not been submitted in part or in full for a degree, a diploma, or a fellowship to any university or institute. Whenever contributions of others are involved, every effort is made to indicate this clearly, with due acknowledgement of collaborative research and discussion. This thesis is a bonafide record of original work done by me and all sources listed within have been detailed in the bibliography.

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In my capacity as the supervisor of the candidate's project work, I certify that the above statements by the candidate are true to the best of my knowledge.

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I am extremely thankful to all my lab-members for their help in learning the experimental techniques, which benefited me during the course of the project. I am thankful to IISER - Mohali for fellowship. Also, I would like to acknowledge all the faculties of Department of chemical sciences for their constant support. I am thankful to library, IR, NMR and HRMS facilities of IISER-Mohali.

Last but not the least, I would like to acknowledge my family for their unconditional love and support.

Contents

List of Figure

List of Tables

List of Schemes

Abbreviations

d	Doublet
δ	Chemical shift in ppm
dd	Doublet of doublet
ddd	Doublet of doublet of doublet
DMSO	Dimethylsuphoxide
DMF	Dimethylformamide
DOSM	Dimethyloxosulfonium methylide
dt	Doublet of triplet
EtOAc	Ethyl acetate
HRMS	High resolution mass spectroscopy
IR	Infra-red
m	Multiplet
M. P.	Melting point
NMR	Nuclear magnetic resonance
ppm	Parts per million
q	Quartet
s	Singlet
t	Triplet
td	Triplet of doublet
TLC	Thin layer chromatography

Abstract

Unexpected reactions triggered by the dimethyloxosulfonium methylide led to the discovery of unconventional approaches for the synthesis of cyclopropafused tetralones. These highly functionalized structures were further elaborated in one step to privileged scaffold such as tetralones. As a whole, the results presented herein establish new diversity-oriented folding pathways.

General introduction about cyclopropanoids

Cyclopropanes are structural units of several bioactive Natural products and pharmaceutically important compounds including many marketed drugs. Due to its unique electronic, conformational, and steric properties the cyclopropyl group is of great interest in medicinal chemistry.[1a-b] There are several challenges posed by the cyclic arrangement of three tetravalent carbons, ranging from the synthesis of highly strained molecules to gaining an understanding of the mode of action of biologically active cyclopropyl derivatives. Strain of approximately 27 kcal/mol associated with such rings leads to significant challenges for their construction and manipulation, resulting in certain tactical limitations.[1c-d]

Cyclopropanes are especially charismatic to synthetic chemists due to their presence in several biologically active natural products such as shagene A,[2] avenaol,[3] (–)-α- cubebene,[4] myrocine C,[5] saxagliptin,[6] crispatene,[7] chloranthalactone A,[8] (–)-nardoaristolone B[9] (fig. 1). Therefore, cyclopropanoids with impressive pharmacological properties and complex molecular architectures inspired several research groups to contribute significantly to their synthesis (see for example, Scheme-1a, 1b and 1c).[10,11a-11h]

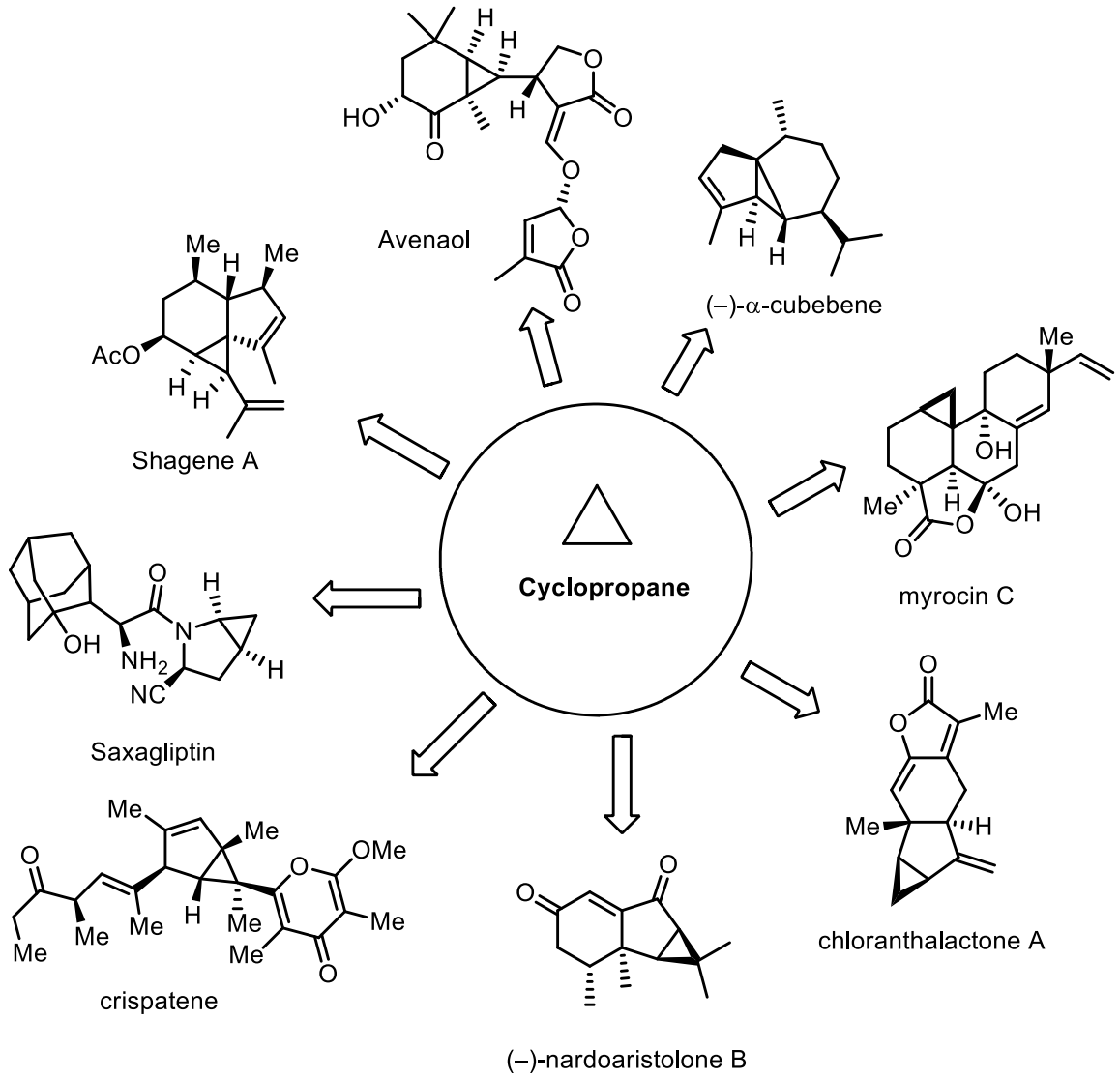
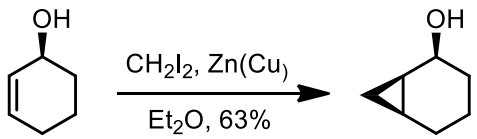


Fig. 1. Few examples of natural products and medicinally important compounds possessing cyclopropane framework.

Various strategies to access cyclopropanoids

a) *Simmon-Smith cyclopropanation of olefins*[11a]

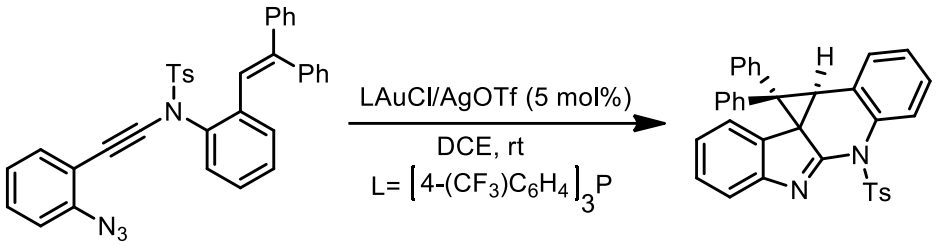


In 1958, H. E. Simmons and R. D. Smith discovered the formal cycloaddition of methylene and various olefins by treatment of diiodomethane with the zinc-copper couple. This reaction can be employed on the wide range of the olefins. Diastereocontrol is an important strategic feature in olefin cyclopropanation, it is mainly governed by steric factors. Additionally, a strong directing effect may be observed when the substrate bears Lewis basic heteroatoms in proximity to the olefin. Due to the complexity associated with the zinc-copper

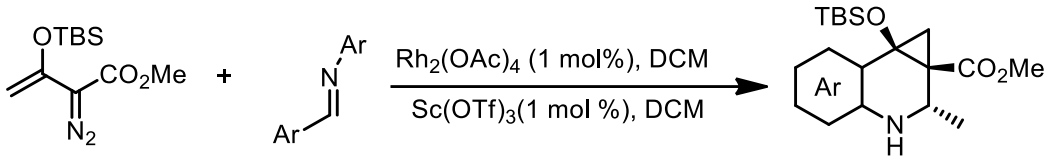
couple preparation and reproducibility problems caused by variation in surface features of alloy, other protocol for the generation of metal-carbenoid have been developed.

b) *Transition metal-catalyzed formation of cyclopropanes*

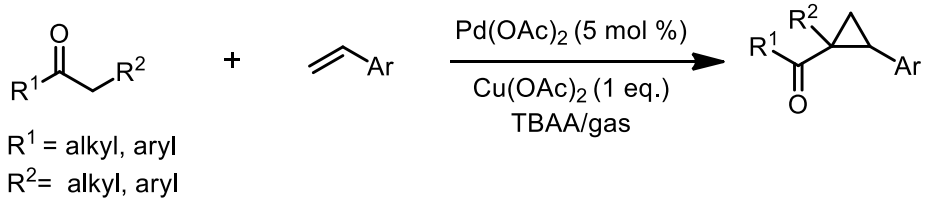
i) Au-catalyzed formation of cyclopropanes from ynamides[11b]



ii) Rh(II)/Lewis acid-catalyzed [4 + 2]-cycloaddition reaction between enoldiazoacetates and imines[11c]



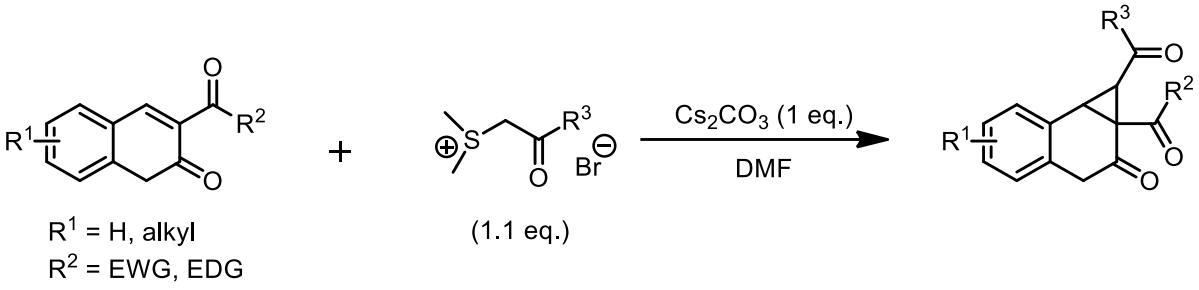
iii) Nacci and Monopoli's Pd(II)-catalyzed cyclopropanation reaction proceeding through a two-fold C-H activation[11d]



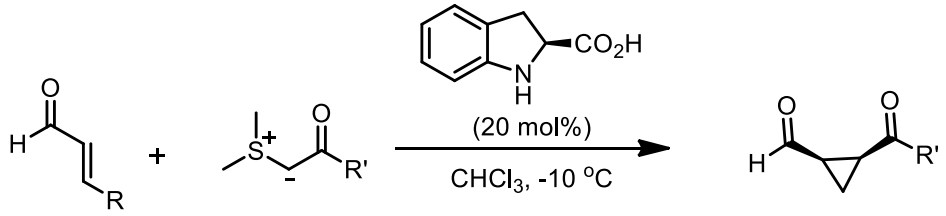
c) *Sulphur ylide mediated cyclopropanation*

Sulphur ylides are the most important and widely applied reagents for the cyclopropanation reactions. In 1961, A. William Johnson, E. J. Corey and M. Chaykovsky discovered the sulphur ylide mediated cyclopropanation of enone system.[11e] This reaction has pioneered the field of sulphur ylide chemistry. Nucleophilic 1,1'-dipolar nature of sulphur ylides attributes its impressive successes. Stabilized sulfonium ylides along with stabilized sulfoxonium ylides are being used for the enantioselective organocatalytic cyclopropanation of α,β-unsaturated aldehydes and ketones.[11f,11g]

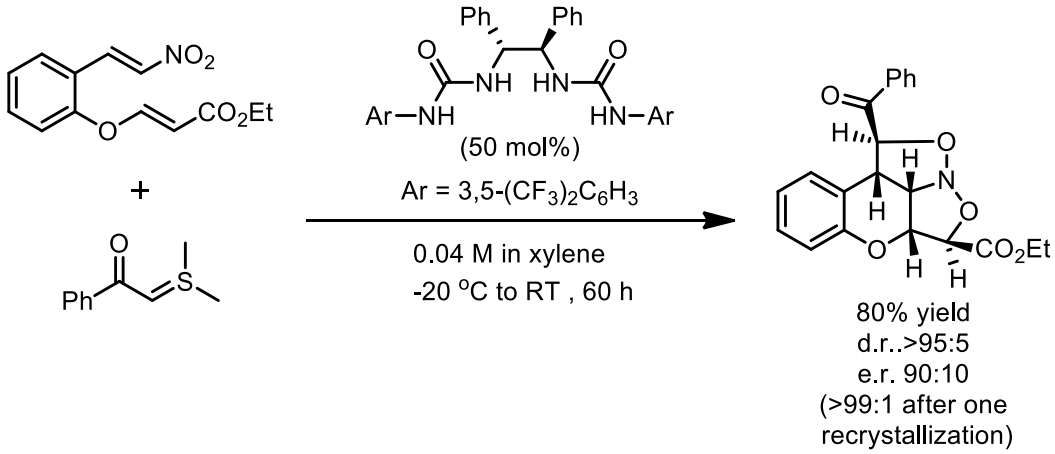
i) stabilized sulphur ylide mediated cyclopropanation[11f]



ii) Enantioselective cyclopropanations of sulfur ylides with α,β-unsaturated aldehydes[11g]



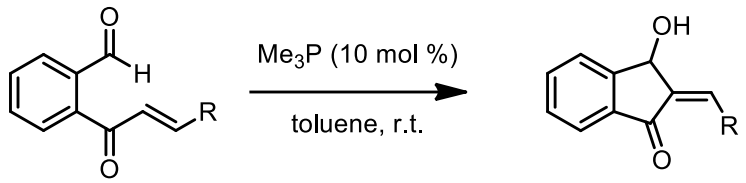
iii) Construction of fused heterocyclic architectures by formal [4+1]/[3+2] cycloaddition cascade of sulfur ylides and nitroolefins[11h]



Scheme 1. Synthesis of cyclopropanoids through various strategies.

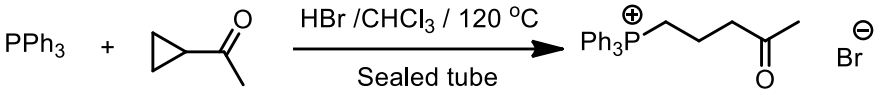
Our hypothesis

Recently, our group has reported phosphine catalysed intramolecular Morita-Baylis-Hillman (MBH) reaction of enone-aldehydes to generate a variety of cyclopenta[*b*]annulated arenes and heteroarenes in excellent enantiopurities and near-quantitative yields.[12a]



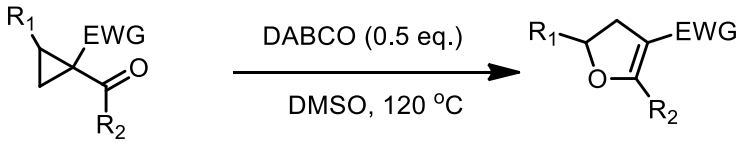
Scheme 2. Synthesis of cyclopenta[*b*]annulated arenes *via* intramolecular MBH reaction.

In 1987, Cristau *et al.*[12b] reported phosphine mediated ring-opening of cyclopropyl ketones to generate Wittig salt.



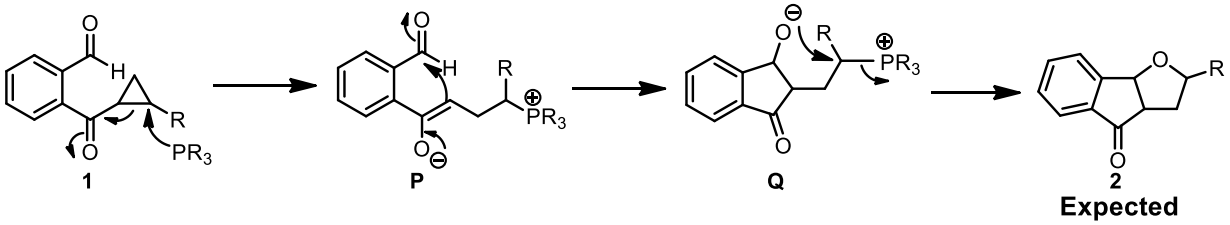
Scheme 3. Synthesis of Wittig salt *via* phosphine mediated ring-opening of cyclopropyl ketones.

In 2017, Xu *et al.*[12c] reported 1,4-diazabicyclo[2.2.2]octane (DABCO)-catalyzed ring expansion of cyclopropyl ketones to 2,3-dihydrofurans.[12c]



Scheme 4. Synthesis of 2,3-dihydrofurans *via* organocatalytic Cloke-Wilson rearrangement.

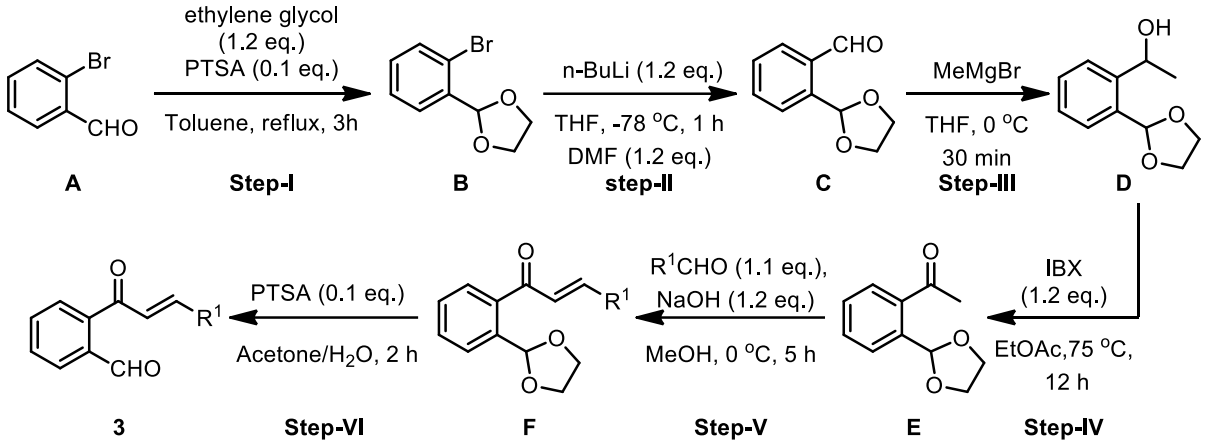
Therefore, motivated by the literature reports available on the organocatalytic cyclopropane ring-opening and our earlier work, we hypothesized organophosphine catalysed ring-opening of cyclopropyl keto-aldehydes.



It was envisioned that nucleophilic attack of the phosphine on cyclopropane may lead to the formation of enolate **P**. Further, intramolecular cyclization of **P** could afford alkoxide **Q**, which may enable the formation of **2** via the nucleophilic displacement of the phosphine.

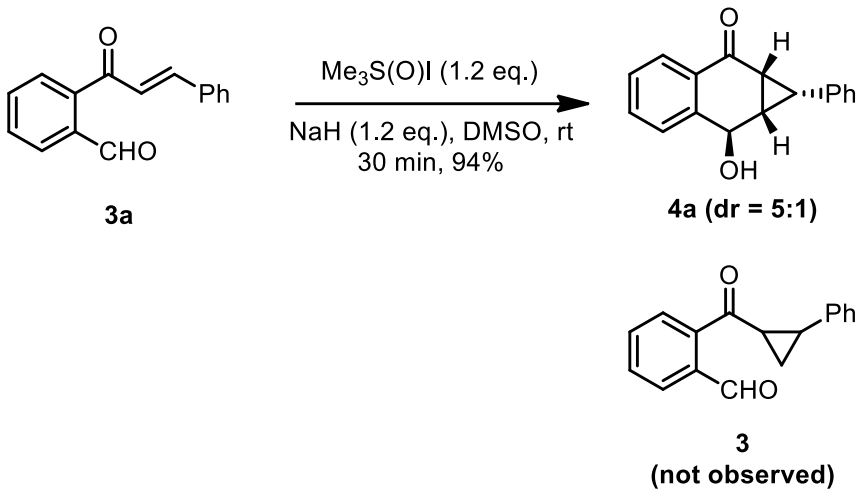
Result and Discussion

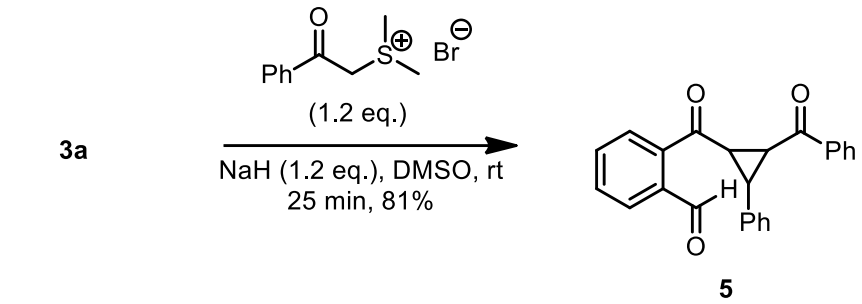
At the outset, the enone-aldehyde **3a-3e** were synthesized from the corresponding bromo-aldehydes in good to excellent yields (Scheme-5).



Scheme 5. Synthesis of the enone-aldehydes (**3a-3e**).

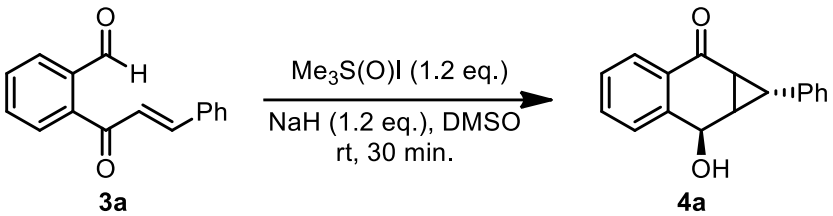
After getting the enone-aldehyde **3a**, we performed the reaction with the sulfoxonium ylide to get expected product cyclopropyl keto-aldehyde **3**. However, an unexpected product **4a** was isolated in 94% yield, as a separable mixture of diastereomers. Interestingly, when **3a** was treated with a stabilized sulfonium ylide, the cyclopropane **5** was realized.





After realizing the unprecedented formation of **4a** from **3a**, we initiated screening of various bases and solvents combinations with **3a** as the model substrate, with the intention to obtain the good yield of **4a**, table **1**.

Table 1: Optimization of reaction parameters with 3a

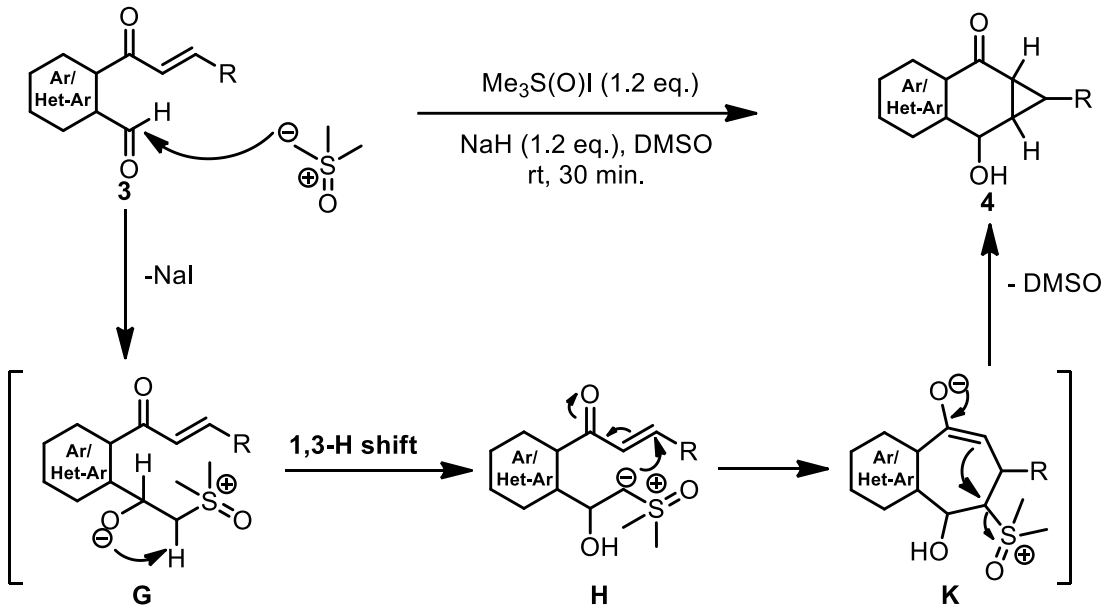


Entry	Base	Solvent	Time (h)	Yield[a] (%)
1	KOH	DMSO	1	53/10
2	K_2CO_3	DMSO	1	34/7
3	**NaH**	**DMSO**	**0.5**	**73/21**
4	K^{t}OBu	DMSO	0.5	70/16
5	NaH	DMF	1	71/19
6	NaH	THF	1	Trace/-
7	NaH	1,4-dioxane	1	-

8	NaH	Toluene	1	-
9	NaH	Nitroethane	1	-
10	NaH	Chloroform	1	Trace/-

[a]Isolated yields after column chromatography

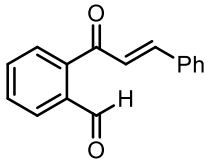
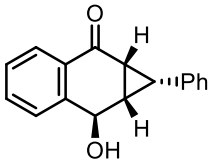
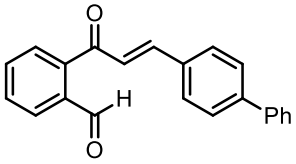
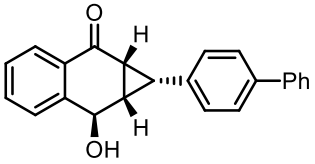
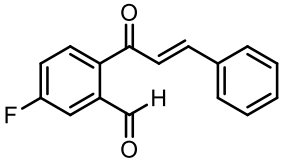
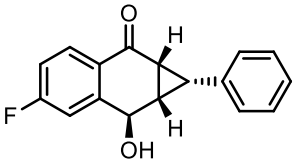
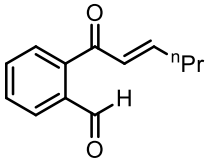
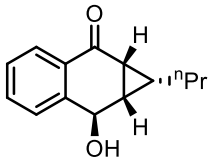
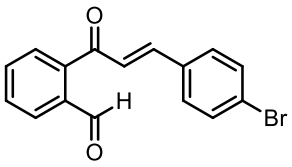
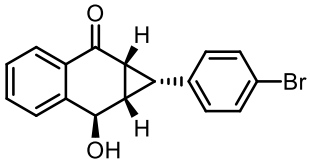
After having optimize condition, we turned towards the substrate scope. The reaction was well-tolerated with electron-withdrawing, highly electron donating as well as hetero-aromatic systems to give cyclopropa-fused tetralones.



Scheme 6. Mechanism for cyclopropa-fused tetralones.

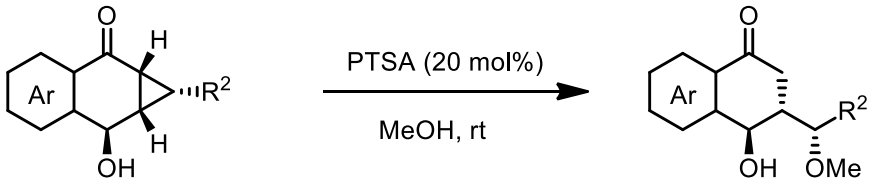
As of the mechanism of the formation of **4**, an initial aldol-type reaction of the ylide dimethyloxosulfonium methylide (DOSM) with **3** generates the 1,4-zwitterionic species **G**. A subsequent 1,3-proton shift followed by an intramolecular Michael addition to the enone functionality provides the enolate **K**, which enables the formation of **4** *via* the nucleophilic displacement of the dimethylsulfoxonium group.

Table 2. Substrate scope for cyclopropa-fused tetralones

Entry	Substrate	Product
1	 **3a**	 **4a, 94% (*dr* = 5:1)**
2	 **3b**	 **4b, 85% (*dr* = 5:1)**
3	 **3c**	 **4c, 85% (*dr* = 2.5:1)**
4	 **3d**	 **4d, 88% (*dr* = 2.5:1)**
5	 **3e**	 **4e, 83% (*dr* = 5:1)**

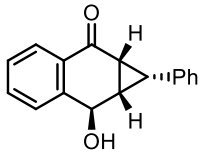
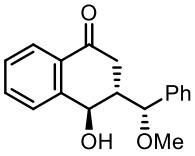
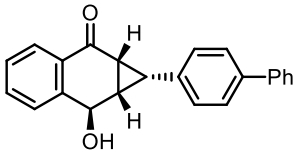
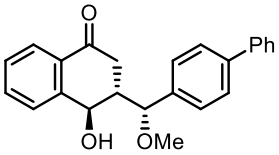
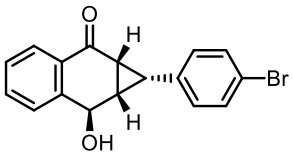
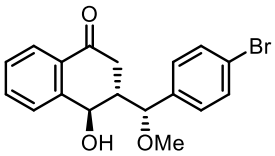
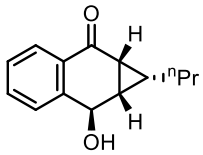
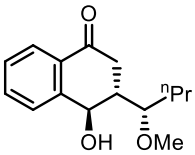
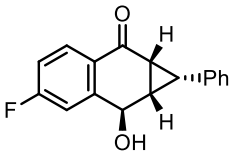
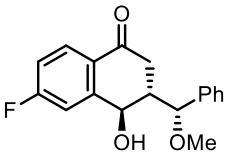
Synthetic application of cyclopropa-fused tetralones (4a-4e) to 1,2-disubstituted tetralones (6a-6e)

It was our hypothesis that the reaction of tetralones **4a** in the presence of an appropriate nucleophile under acidic conditions could possibly undergo ring opening of cyclopropane. Indeed, we were delighted to find that the reaction of **4a** in the presence of a catalytic amount of PTSA in methanol generated the *trans*-1,2-disubstituted tetralone **6a** possessing three contiguous stereogenic centers. Employing the same reaction conditions, tetralones **(6b-6e)** were also synthesized in good yields. These results indicate that the strategy could perhaps be applicable to other analogous nucleophile-mediated ring openings (e.g. 1,2-dicarbonyls) for the synthesis of a diverse range of tetralones.



Scheme 7. Synthesis of 1,2-disubstituted tetralones (**6a-6e**)

Table 3. Substrate scope for 1,2-disubstituted tetralones

Entry	Substrate	Product
1	 **4a**	 **6a, 25 h, 78%**
2	 **4b**	 **6b, 40 h, 79%**
3	 **4c**	 **6c, 22 h, 76%**
4	 **4d**	 **6d, 24 h, 63%**
5	 **4e**	 **6e, 42 h, 81%**

Summary

In conclusion, we presented an unprecedented diastereoselective transformations triggered by the DOSM for the synthesis of complex and otherwise difficult-to-access cyclopropanoids. Further, a one-step synthetic elaboration was established to access privileged structures such as tetralones incorporated with unusual substitution patterns. The methods described herein are operationally straightforward and mechanistically intriguing and symbolize novel substrate-based diversity-oriented strategies.

Experimental methods

General experimental methods: All the starting compounds and catalysts employed in this study were procured from Sigma-Aldrich and were used without further purification. For thin layer chromatography (TLC), silica aluminium foils with fluorescent indicator 254 nm (from Aldrich) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using SD Fine silica gel 100-200 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and stored over sodium wire. IR spectra were recorded on a Perkin–Elmer FT IR spectrometer as thin films or KBr pellet, as indicated, with ν_{max} in inverse centimetres. Melting points were recorded on a digital melting point apparatus Stuart SMP30 and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz BrukerBiospinAvance III FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$.Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm).

Experimental Procedure

General procedure-1: Synthesis of enone-aldehydes (3a-3e)

Enone-aldehydes **3a-3e** were synthesized following a six-step protocol starting from 2-bromobenzaldehydes **A** (Scheme 5). The reaction of **A** with ethylene glycol in the presence of a catalytic amount of PTSA afforded 2-bromoacetals **B**. *n*-Butyllithium-mediated formylation of **B** generated **C**, which upon treatment with MeMgBr yielded **D**. IBX oxidation afforded ketones **E**. Aldol condensation of **E** with appropriate aldehydes under basic condition delivered **F**. PTSA-mediated deprotection of the acetal functionality in **F** afforded desired enone-aldehydes **3a-3e**.

Representative procedure for step-I (Scheme 5): A 50 mL RB flask was charged with 2-bromobenzaldehydes **A** (500 mg, 2.70 mmol), toluene (10 mL), ethylene glycol (1.2 eq.) and PTSA (0.1 eq.) and the whole mixture was refluxed at 150 ^{o}C by connecting to a Dean-Stark set-up. The reaction continued until **A** disappeared (as monitored by TLC). The reaction

mixture was cooled to room temperature and quenched by the addition of aqueous sodium bicarbonate solution (5 mL). Majority of the volatile components were removed under reduced pressure and the residue was extracted with ethyl acetate (2x3 mL). The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using hexanes/ethyl acetate (9:1) as eluent to afford 2-bromoacetals **B** in 83-89%.

Representative procedure for step-II (Scheme 2): To a solution of **B** (600 mg, 2.62 mmol) in anhydrous THF (5 mL) at -78 ^{o}C was added *n*-BuLi (1.6 M in hexane, 1.9 mL, 3.14 mmol). After 15 min, DMF (0.24 ml, 3.14 mmol) at the same temperature was added and the reaction mixture was stirred for an additional 30 min. The mixture was warmed to room temperature over 30 min. The reaction progress was monitored by TLC. Reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as eluent to afford the aldehyde **C** in 72-78% yield.

Representative procedure for step-III (Scheme 2): To a solution of **C** (400 mg, 2.25 mmol) in THF (5 mL) at 0 ^{o}C under nitrogen atmosphere, MeMgBr (3 M in THF, 0.9 mL, 2.7 mmol) was added dropwise over 5 min and the reaction mixture was stirred for an additional 30 min. The reaction progress was monitored by TLC and the reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexanes/ethyl acetate (7:3) as eluent to afford alcohols **D** in 87-94%.

Representative procedure for step-IV (Scheme 2): Compound **D** (1.80 mmol) was dissolved in ethyl acetate (10 mL), and IBX (1.5 eq, 2.71 mmol) was introduced. The resulting reaction mixture was immersed in an oil bath and stirred at 75 °C until compound **D** disappeared as monitored by TLC. The reaction was cooled to room temperature and filtered through Buchner funnel. The filter cake was washed with ethyl acetate (3x2 mL). Organic extracts were combined and worked up using saturated sodium bicarbonate solution to remove excess iodobenzoic acid. The extract was dried over anhydrous sodium sulphate and concentrated under reduced vacuum. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (5:1) as eluent to afford the compound **E** in 70-75% yield.

Representative procedure for step-V (Scheme 2): The ketoacetal **E** (290 mg, 1.51 mmol) was dissolved in MeOH, and benzaldehyde (1.1 eq., 1.66 mmol) and NaOH (1.2 eq., 72.5 mg,

1.81 mmol) were introduced at 0 ^{o}C. The reaction mixture was then stirred at 0 ^{o}C until the reactant **E** disappeared as monitored by TLC. The reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate as eluent (5:1) to afford compound **F** in 75-80% yield.

Representative procedure for step-VI (Scheme 2): Compound **F** (280 mg, 1 mmol) was dissolved in acetone/water (5 mL, 3:1) mixture in an oven dried round bottom flask and PTSA (0.1 eq.) was added and stirred at rt until the reactant **F** disappeared as monitored by TLC. The reaction mixture was quenched with saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as eluent to afford compound **3** in 88-92% yield.

General procedure-2: Synthesis of cyclopropa-fused tetralones (4a-4e)

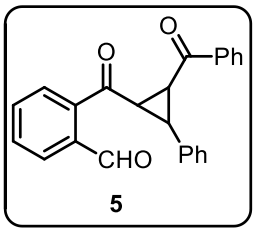
A mixture of sodium hydride (60% in oil, 20.3 mg, 0.51 mmol) and trimethyloxosulfonium iodide (111.8 mg, 0.51 mmol) was placed in an oven dried flask and DMSO (4 mL) was added to the mixture. After the evolution of hydrogen ceased, the milky solution turned clear and the reaction mixture was stirred for 15 min. The compound **3** (100 mg, 0.42 mmol) was dissolved in DMSO (1 mL) and was added to the clear solution dropwise over a period of 5-10 min and stirred at rt until the reactant **3** disappeared as monitored by TLC. The reaction mixture was quenched with ice-water and extracted with diethyl ether. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (5:1 to 3:2) as eluent to afford and **1'**.

General procedure-3: Synthesis of tetralones (6a-6e)

The compound **4a** (100 mg, 0.4 mmol) was dissolved in methanol in an oven dried round bottom flask and PTSA (12 mg, 0.08 mmol) was added and stirred at rt until **4a** disappeared as monitored by TLC. Then the reaction mixture was quenched by adding saturated aqueous sodium bicarbonate solution and the methanol solvent was removed by reduced pressure and the crude reaction mixture was extracted with ethyl acetate. The organic extracts were combined, dried over anhydrous sodium sulphate and concentrated. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (5:1 to 4:1) as eluent to afford compound **6a** in 78% yield (see scheme 4).

Spectroscopic data of all new compounds reported in this study

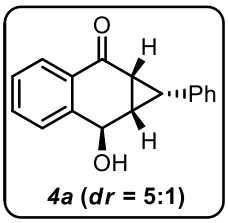
2-(2-Benzoyl-3-phenylcyclopropanecarbonyl)benzaldehyde (5).



5

This compound was isolated as brown solid. Following the reaction procedure-2 (with dimethyl(2-oxo-2-phenylethyl)sulfonium bromide ylide), 100 mg of **3a** afforded 122 mg of **5** (81% yield). M.P = 74-76 ^{o}C. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat): ν_{max}/cm^{-1}** 2923, 1688, 1451, 1219, 1013, 750, 695. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.16 (s, 1H), 8.02 (dd, *J* = 8.3 and 1 Hz, 2H), 7.97-7.93 (m, 1H), 7.89-7.84 (m, 1H), 7.67-7.63 (m, 2H), 7.62-7.57 (m, 1H), 7.50-7.43 (m, 2H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.37-7.31 (m, 3H), 3.51 (t, *J* = 6.2 Hz, 1H), 3.48-3.43 (m, 1H), 3.32 (dd, *J* = 9 and 6.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 197.7, 194.4, 192.4, 141.0, 137.8, 136.8, 136.0, 133.6, 132.9, 131.8, 129.3, 128.9 (2CH), 128.7 (2CH), 128.5, 128.4 (2CH), 127.5, 126.5 (2CH), 38.1, 37.8, 32.8. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{18}NaO_3$ (M + Na) $^{+}$: 377.1154, Found: 377.1163.

7-Hydroxy-1-phenyl-7,7a-dihydro-1*H*-cyclopropa[*b*]naphthalen-2(1a*H*)-one (4a).

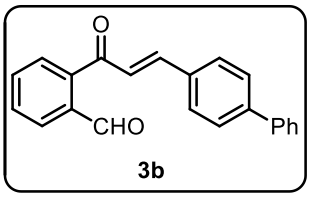


***4a* (*dr* = 5:1)**

Major: This compound was isolated as orange solid. Following the reaction procedure-2, 100 mg of **3a** afforded 77 mg of **4a** (73% yield). M.P = 120-123 ^{o}C. R_f = 0.5 (hexane/EtOAc = 4/6). **IR (thin film, neat):** ν_{max}/cm^{-1} 3398, 3061, 1661, 1597, 1348, 1009, 766. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.53 (d, *J* = 7.76 Hz, 1H), 7.22 (t, *J* = 7.48 Hz, 1H), 7.10-7.01 (m, 2H), 6.94-6.83 (m, 5H), 5.18 (s, 1H), 3.26 (br. s, 1H), 3.03 (t, *J* = 9.28 Hz, 1H), 2.63-2.51 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.6, 141.5, 133.5, 133.3, 131.9, 129.6 (2CH), 128.9, 128.5, 127.8 (2CH), 126.5, 125.9, 66.1, 29.5, 28.3, 27.3. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{15}O_2$ (M + H) $^{+}$: 251.1072, Found: 251.1081.

Minor: This compound was isolated as pale yellow solid. Following the reaction procedure-2, 100 mg of **3a** afforded 22 mg of **4a1** (21% yield). M.P = 139-143 ^{o}C. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3388, 2935, 1664, 1605, 1291, 1028, 748. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.1 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.33-7.21 (m, 3H), 7.11 (d, *J* = 7.1 Hz, 2H), 5.38 (d, *J* = 4.6 Hz, 1H), 2.68-2.56 (m, 2H), 2.55-2.49 (m, 1H), 2.43 (br. s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.2, 141.0, 138.3, 134.1, 129.1, 128.7 (2CH), 128.3, 127.0, 126.9, 126.7, 126.4 (2CH), 65.5, 36.1, 29.7, 29.2.

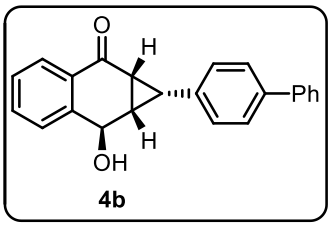
(*E*)-2-(3-([1,1'-biphenyl]-4-yl)acryloyl)benzaldehyde (3b).



3b

This compound was isolated as orange solid. Following the reaction procedure-1, 200 mg of **F** (R^1 = (*p*-C_6H_5)C_6H_4) afforded 153 mg of **3b** (87% yield). M.P = 122-126 ^oC. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3032, 1696, 1593, 1328, 1215, 984, 762. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.22 (s, 1H), 8.04 (d, *J* = 7.1 Hz, 1H), 7.75-7.62 (m, 9H), 7.55 (d, *J* = 15.9 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42 (d, *J* = 7.3 Hz, 1H), 7.29 (d, *J* = 16 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.3, 191.2, 146.6, 143.8, 141.8, 139.9, 135.6, 133.3, 133.1, 131.0, 129.6, 129.2 (2CH), 128.9 (2CH), 128.5, 128.1, 127.7 (2CH), 127.1 (2CH), 125.7. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{17}O_2$ $(M + H)^+$: 313.1229, Found: 313.1245.

1-([1,1'-Biphenyl]-4-yl)-7-hydroxy-7,7a-dihydro-1*H*-cyclopropa[*b*]naphthalen-2(1a*H*)-one (4b).



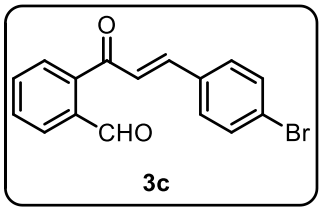
4b

Major: This compound was isolated as pale yellow liquid. Following the reaction procedure-2, 100 mg of **3b** afforded 68 mg of **4b** (65% yield). R_f = 0.5 (hexane/EtOAc = 4/6). **IR (thin film, neat):** ν_{max}/cm^{-1} 3394, 3031, 1659, 1488, 1348, 1007, 761. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.64 (dd, *J* = 7.9 and 1.3 Hz, 1H), 7.89-7.34 (m, 4H), 7.33-7.29 (m, 1H), 7.27-7.21 (m, 1H), 7.17-7.07 (m, 4H), 7.01 (d, *J* = 7.6 Hz, 2H), 5.25 (s, 1H), 3.09 (t, *J* = 9.3 Hz, 1H), 2.71 (ddd, *J* = 9.5, 7.3 and 1.2 Hz, 1H), 2.60 (ddd, *J* = 9, 7.4 and 1.5 Hz, 1H), 2.48 (br. s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.1, 141.3, 140.5, 139.3, 133.5, 132.4, 132.1, 130.1 (2CH), 128.8, 128.7, 128.6 (2CH), 127.2, 126.8 (2CH), 126.4 (2CH), 126.1, 66.3, 29.0, 28.3, 27.2. **HRMS (ESI):** *m/z* calcd for $C_{23}H_{19}O_2$ $(M + H)^+$: 327.1385, Found: 327.1371.

Minor: This compound was isolated as pale yellow solid. Following the reaction procedure-2, 100 mg of **3b** afforded 17 mg of **4b1** (16% yield). M.P = 191-195 ^oC. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3392, 3022, 1660, 1479, 1343, 1076, 759. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.95 (dd, *J* = 7.6 and 1.2 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.69 (td, *J* = 7.6 and 1.2 Hz, 1H), 7.61-7.52 (m, 4H), 7.47 (q, *J* = 7.8 Hz, 3H), 7.39-7.34 (m, 1H), 7.20 (d, *J* = 8.3 Hz, 2H), 5.42 (br. s, 1H), 2.73-2.63 (m, 2H), 2.58 (t, *J* = 4.7 Hz, 1H), 2.28 (br. s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.0, 140.9, 140.5, 139.9, 137.4,

134.1, 129.1, 128.8 (2CH), 128.3, 127.4, 127.3 (2CH), 127.0, 126.9 (2CH), 126.8 (2CH), 126.7, 65.5, 36.2, 29.4, 29.3.

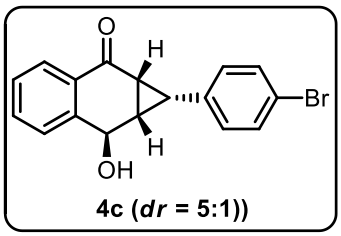
(*E*)-2-(3-(4-bromophenyl)acryloyl)benzaldehyde (3c).



3c

This compound was isolated as pale yellow solid. Following the reaction procedure-1, 200 mg of **F** (R^1 = (*p*-Br)C_6H_4) afforded 162 mg of **3c** (92% yield). M.P = 134-137 ^oC. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 2881, 1691, 1594, 1485, 1326, 1219, 981, 769. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 10.18 (s, 1H), 8.02 (d, *J* = 6.68 Hz, 1H), 7.75-7.63 (m, 3H), 7.56 (d, *J* = 8.28 Hz, 2H), 7.46-7.38 (m, 3H), 7.21 (d, *J* = 16.1 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 194.1, 191.1, 145.3, 141.5, 135.6, 133.4, 133.1, 132.3 (3CH), 131.1, 129.9 (2CH), 128.4, 126.3, 125.4. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{12}BrO_2$ $(M+H)^+$: 315.0021, Found: 315.0006.

1-(4-Bromophenyl)-7-hydroxy-7,7a-dihydro-1*H*-cyclopropa[*b*]naphthalen-2(1a*H*)-one (4c).

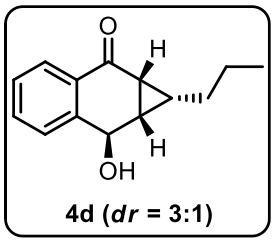


4c (*dr* = 5:1))

Major: This compound was isolated as white solid. Following the reaction procedure-2, 100 mg of **3c** afforded 65.5 mg of **4c** (63% yield). M.P = 195-197 ^oC. R_f = 0.5 (hexane/EtOAc = 4/6). **IR (thin film, neat):** ν_{max}/cm^{-1} 3399, 2950, 1659, 1489, 1348, 1295, 1009, 763. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.58 (dd, *J* = 7.7 and 1.2 Hz, 1H), 7.34- 7.28 (m, 1H), 7.16-7.08 (m, 2H), 7.05-7.00 (m, 2H), 6.84-6.73 (m, 2H), 5.16 (d, *J* = 4.6 Hz, 1H), 2.94 (t, *J* = 9.3 Hz, 1H), 2.77 (d, *J* = 6.6 Hz, 1H), 2.66-2.51 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.9, 141.2, 133.8, 132.4, 131.8, 131.2 (2CH), 130.9 (2CH), 128.92, 128.90, 126.0, 120.5, 66.0, 28.7, 28.1, 27.1. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}BrO_2$ $(M + H)^+$: 329.0177, Found: 329.0190.

Minor: This compound was isolated as orange semi solid. Following the reaction procedure-2, 100 mg of **3c** afforded 21 mg of **4c1** (20% yield). R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3444, 2928, 1663, 1491, 1289, 1072, 764. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.92 (d, *J* = 6.8 Hz, 1H), 7.78-7.39 (m, 2H), 7.50-7.39 (m, 3H), 7.0 (d, *J* = 8.6 Hz, 2H), 5.39 (t, *J* = 16.1 Hz, 1H), 2.64-2.53 (m, 2H), 2.49 (t, *J* = 4.6 Hz, 1H), 2.34 (d, *J* = 8.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 139.8, 140.8, 137.4, 134.2, 131.7 (2CH), 128.9, 128.4, 128.1 (2CH), 127.1, 126.7, 120.7, 65.3, 35.9, 29.2, 29.0.

7-Hydroxy-1-propyl-7,7a-dihydro-1*H*-cyclopropa[*b*]naphthalen-2(1a*H*)-one (4d).

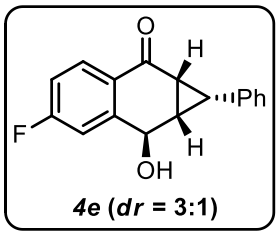


4d (*dr* = 3:1)

Major: This compound was isolated as pale yellow semisolid. Following the reaction procedure-2, 100 mg of **3d** afforded 72.5 mg of **4d** (68% yield). R_f = 0.5 (hexane/EtOAc = 4/6). **IR (thin film, neat):** ν_{max}/cm^{-1} 3398, 2959, 1661, 1353, 1291, 1009, 763. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.63-7.55 (m, 1H), 7.49-7.45 (m, 1H), 7.39 (td, *J* = 7.6 and 1.2 Hz, 1H), 5.06 (s, 1H), 2.90 (br. s, 1H), 2.26-2.15 (m, 2H), 1.69-1.58 (m, 1H), 1.28-1.14 (m, 2H), 1.09-0.97 (m, 1H), 0.94-0.82 (m, 1H), 0.70 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.6, 142.9, 134.1, 132.1, 129.2, 129.0, 126.1, 65.4, 27.9, 27.0, 26.2, 25.0, 22.8, 13.5. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{17}O_2$ $(M + H)^+$: 217.1229, Found: 217.1221.

Minor: This compound was isolated as pale brown semi solid. Following the reaction procedure-2, 100 mg of **3d** afforded 22.5 mg of **4d1** (21% yield). R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3415, 2958, 1662, 1457, 1339, 1292, 1020, 725. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.85 (dd, *J* = 7.7 and 1.1 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 5.26 (d, *J* = 4.6 Hz, 1H), 2.12-2.03 (m, 2H), 1.53-1.30 (m, 6H), 0.92 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.9, 141.1, 133.8, 129.5, 128.0, 126.8, 126.5, 65.8, 34.5, 32.8, 27.5, 26.4, 22.4, 13.8.

5-Fluoro-7-hydroxy-1-phenyl-7,7a-dihydro-1*H*-cyclopropa[b]naphthalen-2(1a*H*)-one (4e).

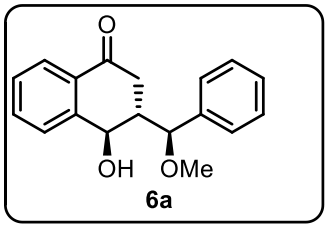


4e (*dr* = 3:1)

Major: This compound was isolated as pale yellow solid. Following the reaction procedure-2, 100 mg of **3e** afforded 68.5 mg of **4e** (65% yield). M.P = 100-104 ^oC. R_f = 0.5 (hexane/EtOAc = 6/4). **IR (thin film, neat):** ν_{max}/cm^{-1} 3399, 3056, 1662, 1606, 1494, 1351, 1249, 1009, 700. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.48 (dd, *J* = 8.7 and 5.7 Hz, 1H), 6.96-6.88 (m, 5H), 6.76 (dd, *J* = 8.8 and 2.4 Hz, 1H), 6.68 (td, *J* = 8.4 and 2.4 Hz, 1H), 5.12 (s, 1H), 3.71 (br. s, 1H), 3.05 (t, *J* = 9.28 Hz, 1H), 2.56 (d, *J* = 9.4 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.4, 165.5 (d, *J* = 254 Hz), 144.5 (d, *J* = 8.3 Hz), 133.0, 129.5 (2CH), 128.8 (d, *J* = 9.3 Hz), 128.5 (d, *J* = 2.6 Hz), 127.9 (2CH), 126.8, 115.9 (d, *J* = 21.9 Hz), 115.3 (d, *J* = 21.5 Hz), 65.7 (d, *J* = 0.8 Hz), 29.5, 28.1, 27.5. **HRMS (ESI):** *m/z* calcd for $C_{17}H_{14}FO_2$ $(M+H)^+$: 269.0978, Found: 269.0965.

Minor: This compound was isolated as pale brown liquid. Following the reaction procedure-2, 100 mg of **3e** afforded 25.5 mg of **4e1** (24% yield). R_f = 0.5 (hexane/EtOAc = 7/3). **IR (thin film, neat):** 3411, 2900, 1667, 1605, 1488, 1266, 1074, 755, 697. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.93 (dd, *J* = 8.6 and 5.8 Hz, 1H), 7.45 (dd, *J* = 9.6 and 2.1 Hz, 1H), 7.33-7.20 (m, 3H), 7.14-7.06 (m, 3H), 5.33 (br. s, 1H), 2.75 (d, *J* = 5.6 Hz, 1H), 2.65-2.58 (m, 1H), 2.56 (dd, *J* = 8.2 and 4.1 Hz, 1H), 2.50 (t, *J* = 7.8 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 192.9, 166.7 (d, *J* = 253.7 Hz), 144.4 (d, *J* = 8.3 Hz), 138.1, 130.1 (d, *J* = 9.4 Hz), 128.7 (2CH), 127.1, 126.3 (2CH), 125.5 (d, *J* = 2.8 Hz), 115.8 (d, *J* = 22 Hz), 113.9 (d. *J* = 23.2 Hz), 65.3 (d, *J* = 1 Hz), 35.8, 29.8, 29.0.

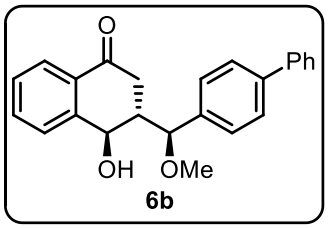
4-Hydroxy-3-(methoxy(phenyl)methyl)-3,4-dihydronaphthalen-1(2*H*)-one (3a).



6a

This compound was isolated as pale yellow solid. Following the general procedure-3, 100 mg of **4a** afforded 88 mg of **6a** (78% yield). M.P = 105-107 ^{o}C. R_f = 0.5 (hexane/EtOAc = 4/1). **IR (thin film, neat):** ν_{max}/cm^{-1} 3424, 2933, 1677, 1601, 1297, 1102, 1001, 766. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.96 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.63 (td, *J* = 7.6 and 1.2 Hz, 1H), 7.44-7.37 (m, 3H), 7.32-7.30 (m, 3H), 4.97 (d, *J* = 9.3 Hz, 1H), 4.65 (d, *J* = 3.4 Hz, 1H), 3.64 (br. s, 1H), 3.37 (s, 3H), 2.67-2.55 (m, 2H), 2.50-2.37 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 197.0, 145.9, 137.6, 134.2, 130.5, 128.6 (2CH), 128.1, 127.7, 127.2 (2CH), 126.5, 126.4, 83.8, 68.7, 57.6, 48.5, 37.6. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{17}O_3$ $(M-H)^+$: 281.1178, Found: 281.1154.

3-([1,1'-Biphenyl]-4-yl(methoxy)methyl)-4-hydroxy-3,4-dihydronaphthalen-1(2*H*)-one (6b).

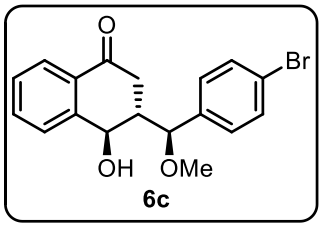


6b

This compound was isolated as pale brown solid. Following the reaction procedure-3, 100 mg of **4b** afforded 86.5 mg of **6b** (79% yield). M.P = 156-158 ^{o}C. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3441, 2927, 1676, 1600, 1298, 1098, 764. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.98 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.67-7.59 (m, 5H), 7.51-7.44 (m, 2H), 7.43-7.36 (m, 4H), 5.02 (dd, *J* = 9 and 2.9 Hz, 1H), 4.71 (d, *J* = 3.2 Hz, 1H), 3.64 (d, *J* = 4.2 Hz, 1H), 3.41 (s, 3H), 2.71-2.60 (m, 2H), 2.65-2.45 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.9, 145.9, 141.1, 140.6, 136.7, 134.2, 130.6, 128.8

(2CH), 127.7, 127.6 (2CH), 127.5, 127.4 (2CH), 127.1 (2CH), 126.6, 126.5, 83.6, 68.7, 57.7, 48.6, 37.7. **HRMS (ESI):** *m/z* calcd for $C_{24}H_{22}NaO_3$ $(M+Na)^+$: 381.1467, Found: 381.1486.

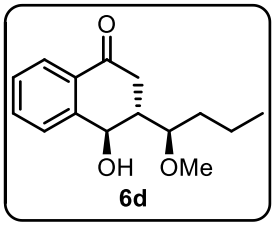
3-(4-Bromophenyl)(methoxy)methyl)-4-hydroxy-3,4-dihydronaphthalen-1(2*H*)-one (6c).



6c

This compound was isolated as pale yellow solid. Following the reaction procedure-3, 100 mg of **4c** afforded 82 mg of **6c** (75% yield). M.P = 140-142 ^oC. R_f = 0.5 (hexane/EtOAc = 8/2). **IR (thin film, neat):** ν_{max}/cm^{-1} 3422, 2926, 1679, 1599, 1298, 1099, 764. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.97 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.64 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.58-7.52 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.23-7.18 (m, 2H), 4.96 (d, *J* = 7.1 Hz, 1H), 4.64 (d, *J* = 2.9 Hz, 1H), 3.36 (s, 3H), 3.31 (d, *J* = 3.4 Hz, 1H), 2.61-2.43 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.7, 145.6, 137.1, 134.3, 131.8 (2CH), 130.5, 128.8 (2CH), 127.9, 126.7, 126.4, 121.9, 82.7, 68.7, 57.7, 48.7, 37.2. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{18}BrO_3$ $(M+H)^+$: 361.0439, Found: 361.0421.

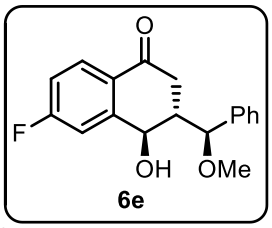
4-Hydroxy-3-(1-methoxybutyl)-3,4-dihydronaphthalen-1(2*H*)-one (6d).



6d

This compound was isolated as pale yellow liquid. Following the reaction procedure-3, 100 mg of **4d** afforded 72 mg of **6d** (63% yield). R_f = 0.5 (hexane/EtOAc = 7.5/2.5). **IR (thin film, neat):** ν_{max}/cm^{-1} 3433, 2932, 1681, 1601, 1458, 1299, 1090, 769. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.02 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.65 (td, *J* = 7.6 and 1.5 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 5.07 (d, *J* = 7.6 Hz, 1H), 3.70 (d, *J* = 3.4 Hz, 1H), 3.51 (ddd, *J* = 8.6, 4.2 and 2 Hz, 1H), 3.47 (s, 3H), 2.67-2.58 (m, 1H), 2.55-2.48 (m, 2H), 1.79-1.69 (m, 1H), 1.62-1.36 (m, 3H), 1.0 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 196.9, 146.4, 134.2, 130.5, 127.6, 126.6, 126.1, 82.3, 69.3, 58.3, 44.3, 38.3, 32.1, 19.5, 14.1. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{20}NaO_3$ $(M+Na)^+$: 271.1310, Found: 271.1337.

6-Fluoro-4-hydroxy-3-(methoxy(phenyl)methyl)-3,4-dihydronaphthalen-1(2*H*)-one (3e).

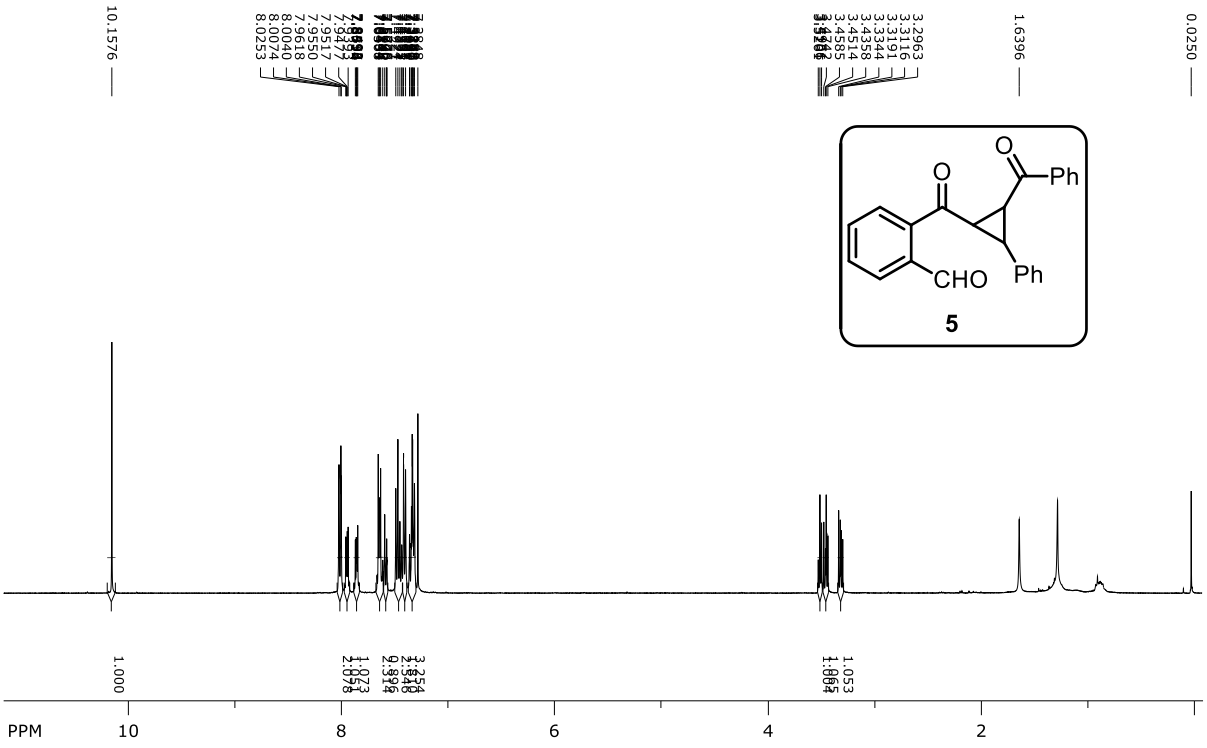


6e

This compound was isolated as pale yellow solid. Following the reaction procedure-3, 100 mg of **4e** afforded 91 mg of **6e** (81% yield). M.P = 116-118 ^oC. R_f = 0.5 (hexane/EtOAc = 7.5/2.5). **IR (thin film, neat):** ν_{max}/cm^{-1} 3414, 2895, 1676, 1605, 1452, 1258, 1101, 830, 708. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.96 (dd, *J* = 8.8 and 5.9 Hz, 1H), 7.48-7.38 (m, 3H), 7.37-

7.30 (m, 3H), 7.03 (td, *J* = 8.4 and 2.3 Hz, 1H), 4.94 (dd, *J* = 9.7 and 2.6 Hz, 1H), 4.69 (d, *J* = 3.2 Hz, 1H), 4.10 (d, *J* = 4.2 Hz, 1H), 3.36 (s, 3H), 2.62-2.53 (m, 2H), 2.45-2.34 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 195.7, 166.6 (d, *J* = 254.4 Hz), 149.74 (d, *J* = 8.7 Hz), 137.4, 129.70 (d, *J* = 9.6 Hz), 128.7 (2CH), 128.1, 127.1 (2CH), 127.06 (d, *J* = 2.5 Hz), 115.23 (d, *J* = 22.1 Hz), 113.27 (d, *J* = 22.9 Hz), 83.47 (d, *J* = 6.8 Hz), 68.5, 57.6, 48.4, 37.5. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{18}FO_3$ $(M+H)^+$: 301.1240, Found: 301.1256.

NMR Spectra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3.4358
3.4514
3.4585
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CHO
Ph
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1.053
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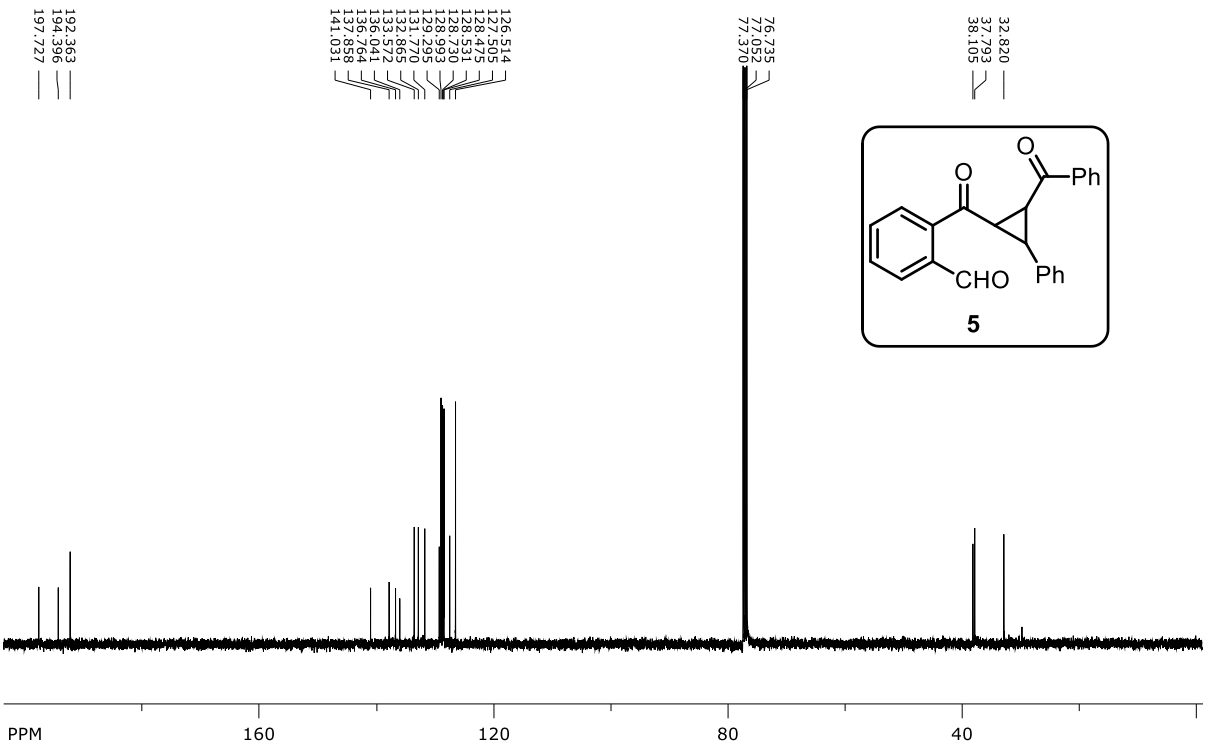
10
8
6
4
2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136.041
136.764
137.858
141.031
76.735
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CHO
Ph
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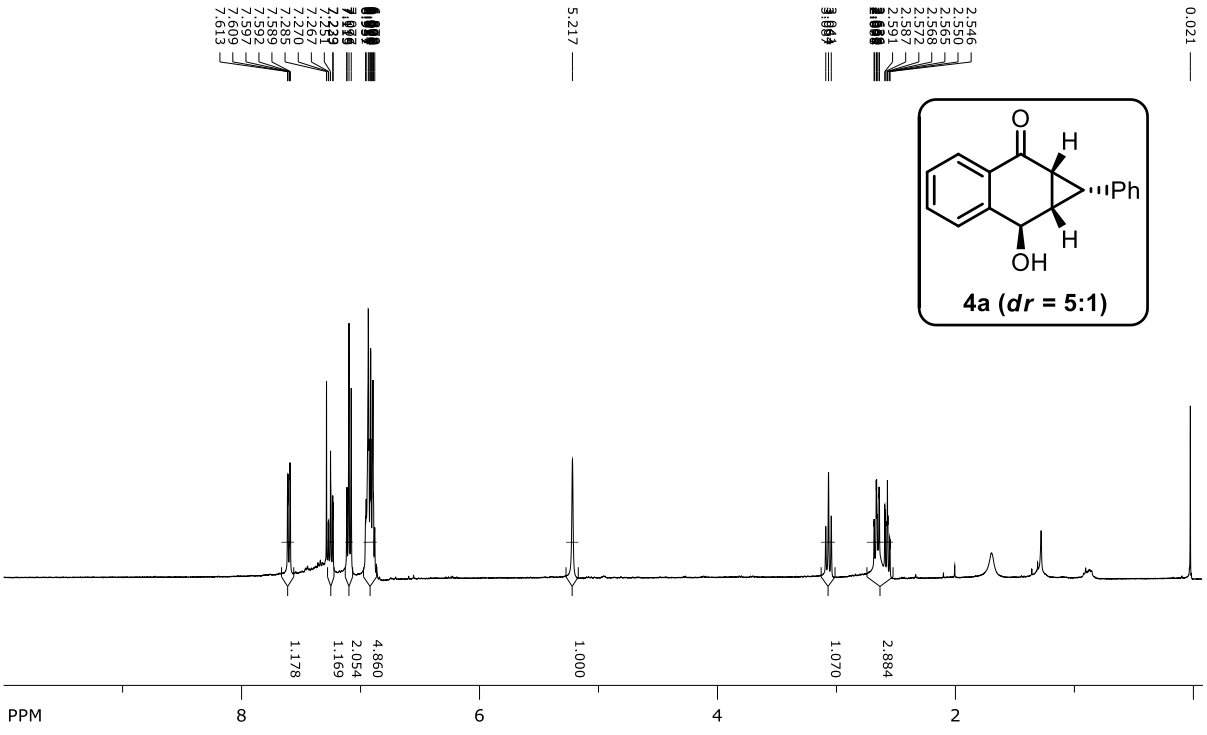
80
40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Ph
H
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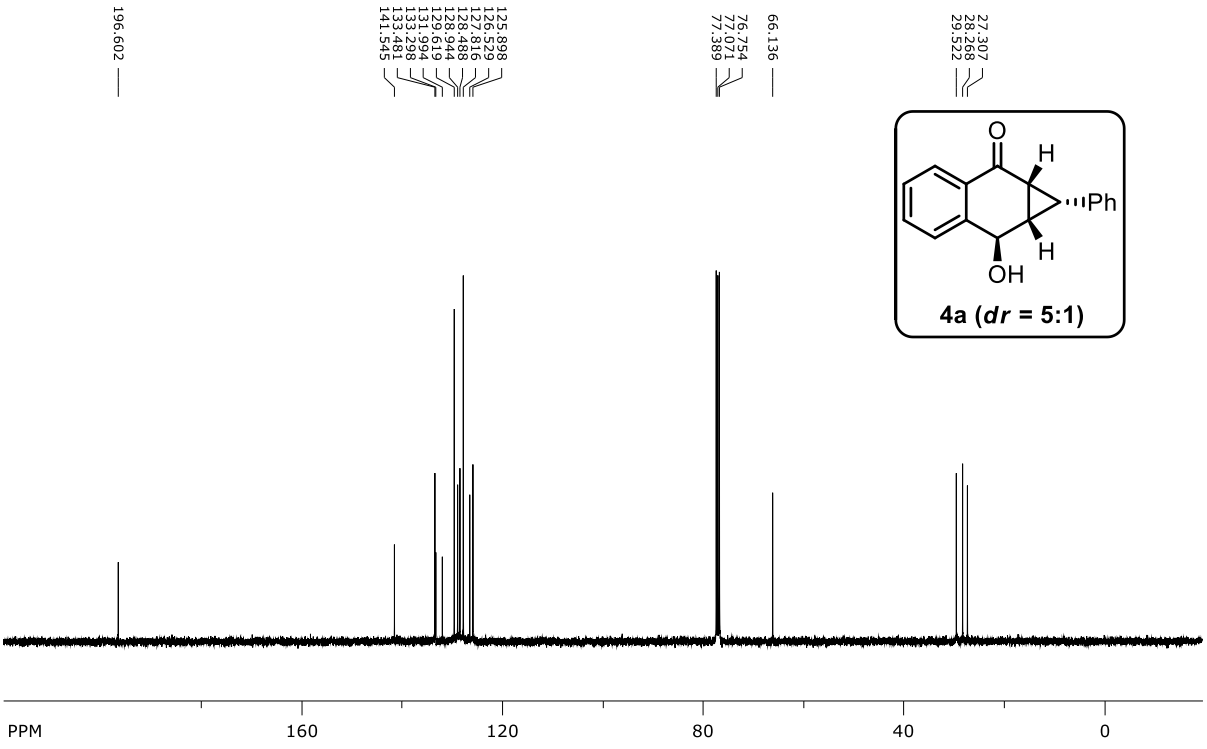
4
2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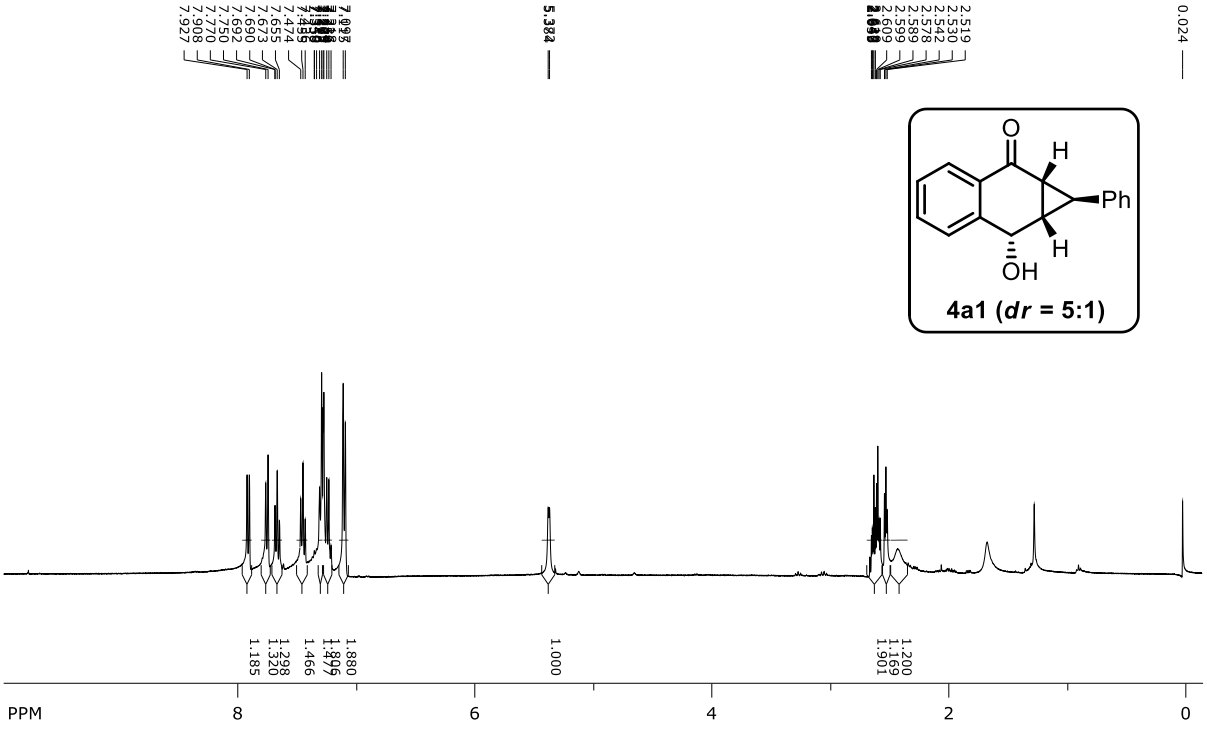
120
80
40
0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Ph
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OH
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2
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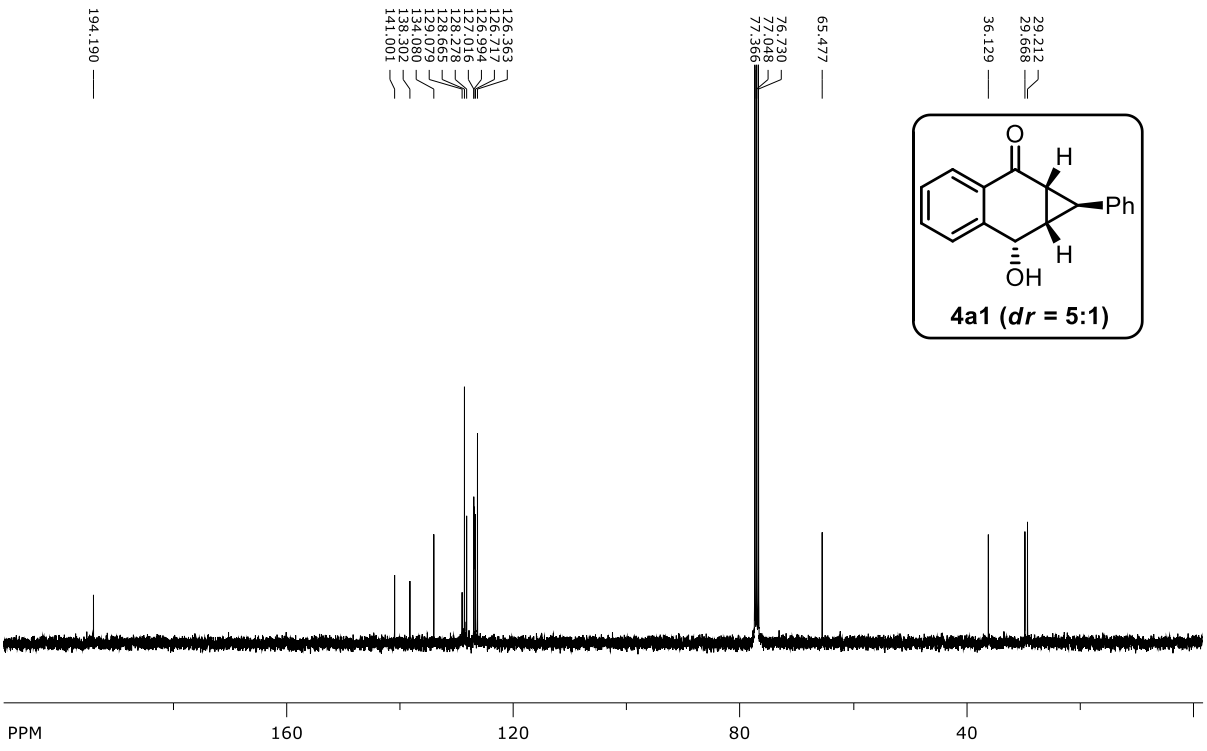
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76.730
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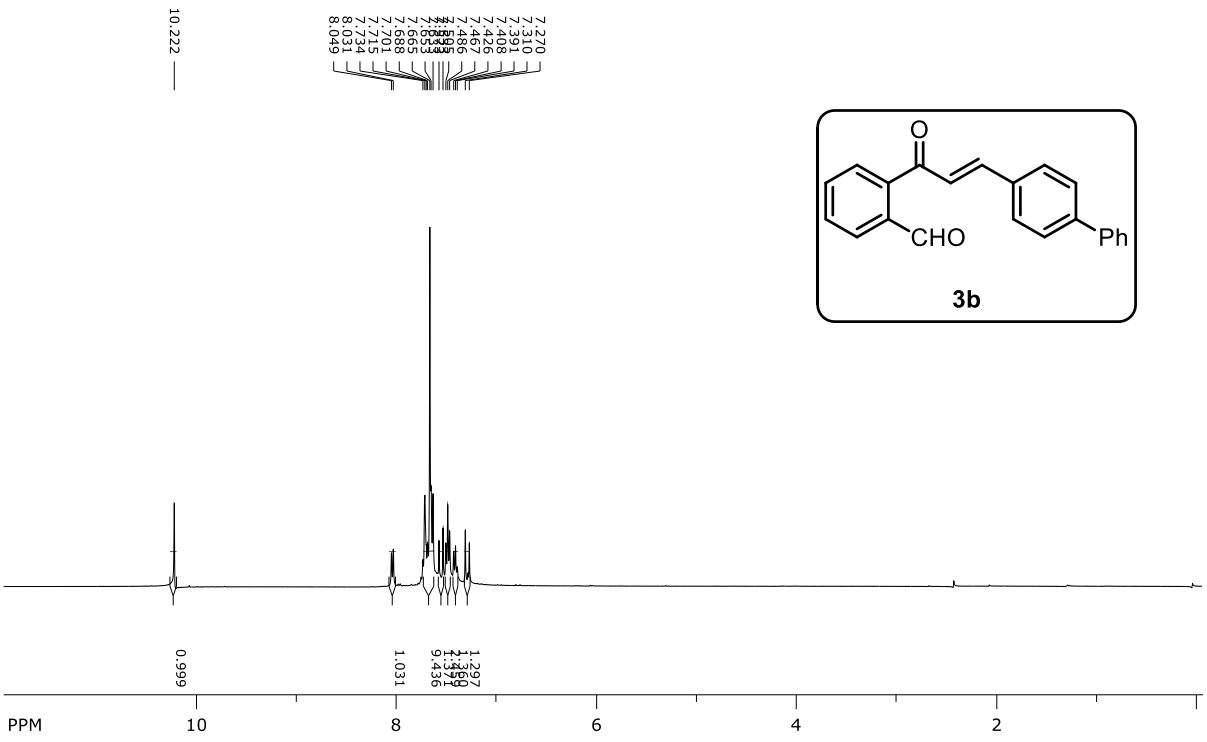
120
80
40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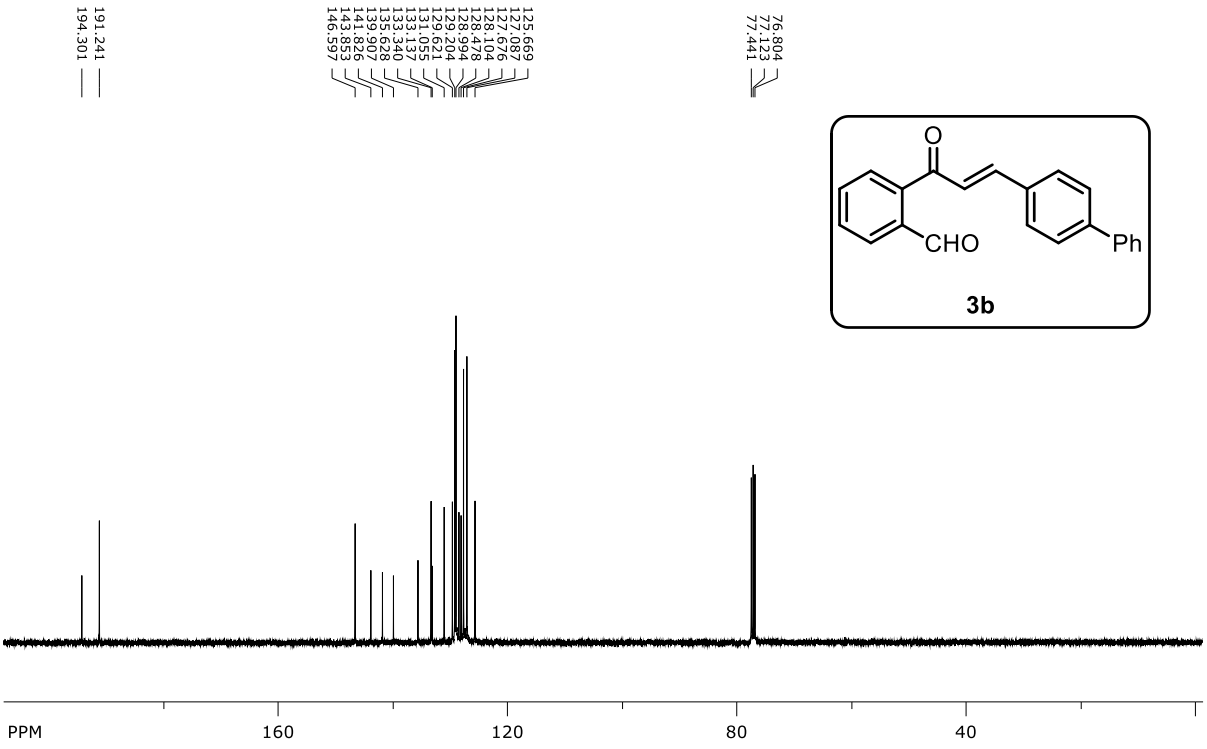
9.436
PPM
10
8
6
4
2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CHO
Ph
3b
PPM
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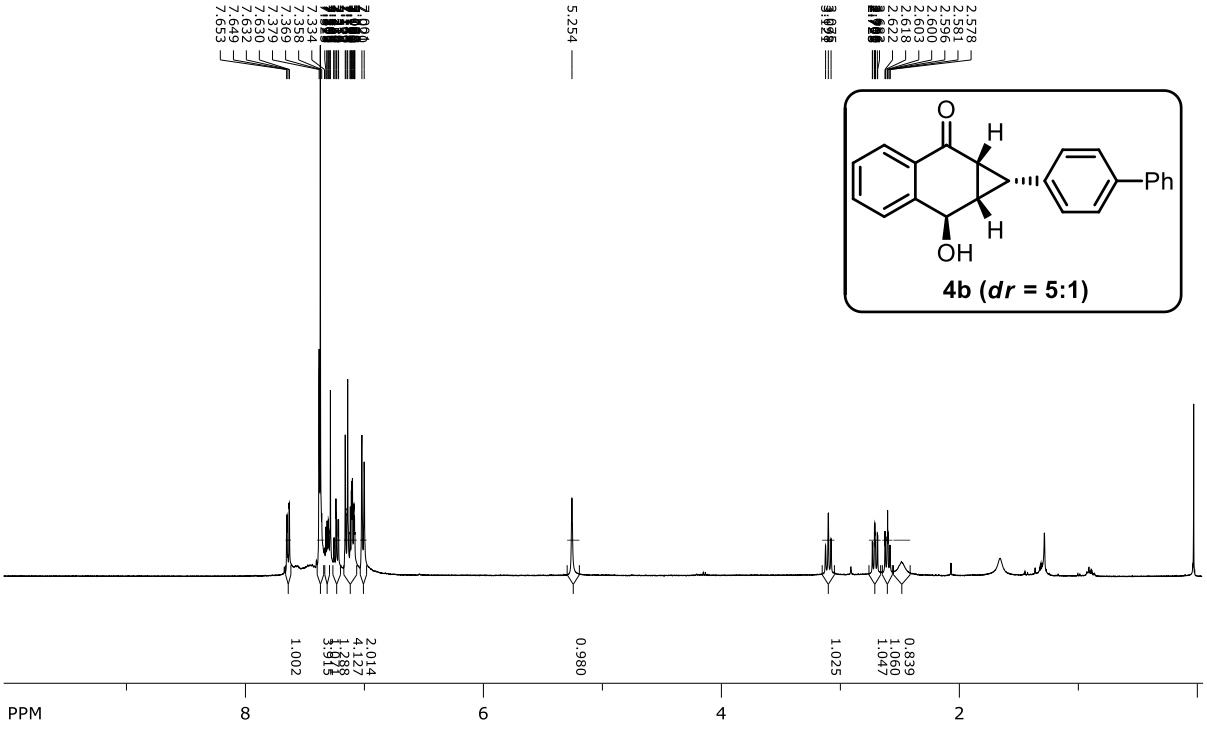
120
80
40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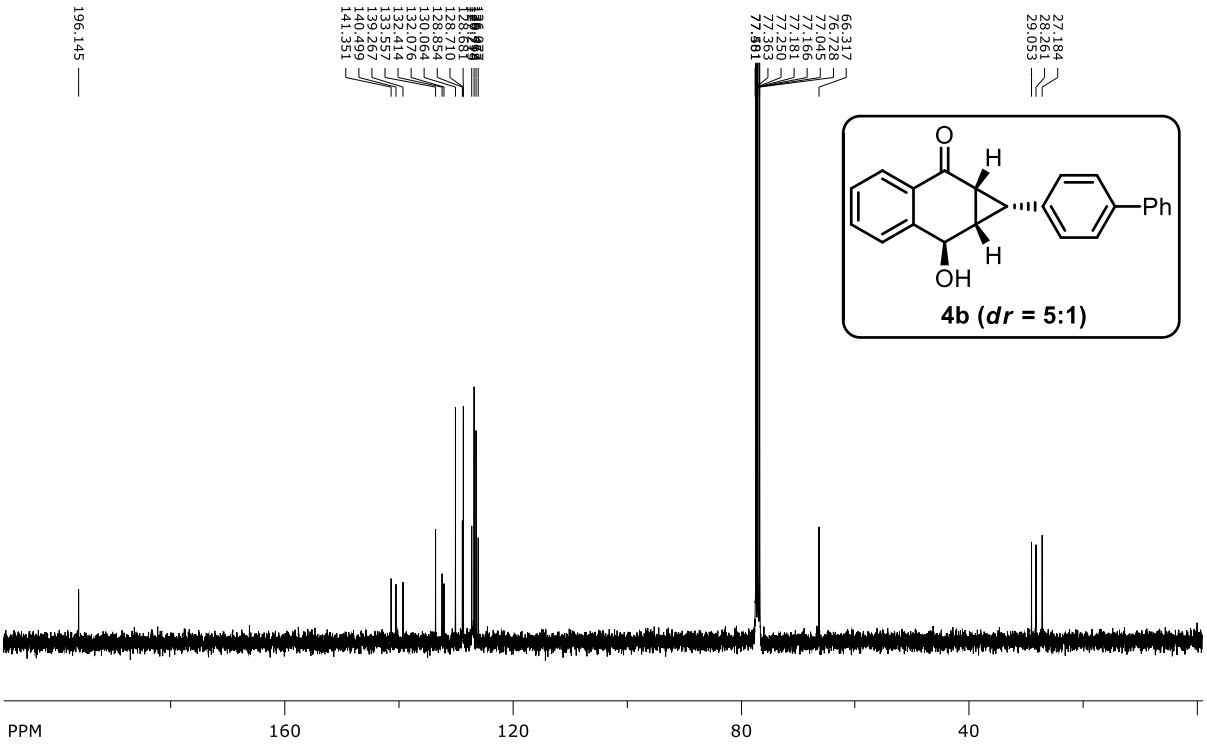
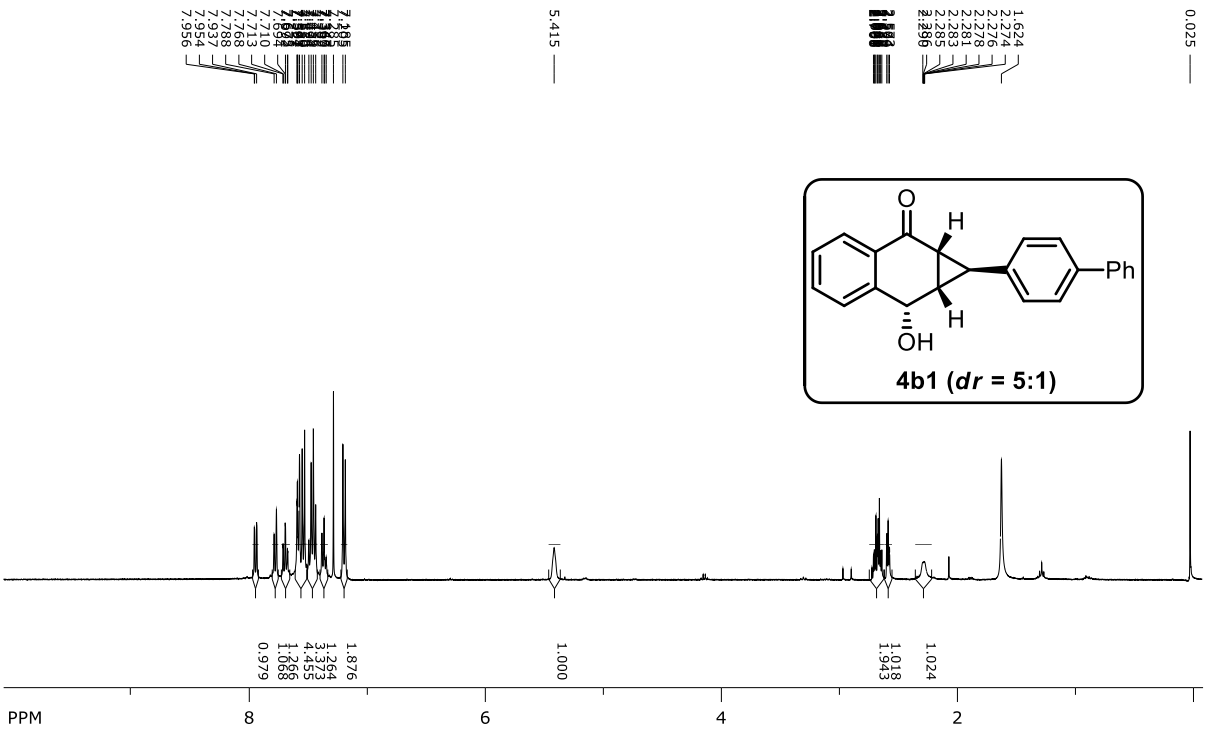
7.369
7.358
7.334
5.254
2.578
2.581
2.596
2.600
2.603
2.618
2.622
1.002
2.014
4.127
0.980
1.025
0.839
1.060
1.047
PPM
8
6
4
2
O
H
Ph
H
OH
4b (dr = 5:1)


196.145
141.351
140.499
139.267
133.557
132.414
132.076
130.064
128.854
66.317
76.728
77.045
77.166
77.181
77.250
77.363
27.184
28.261
29.053
PPM
160
120
80
40
O
H
Ph
H
OH
4b (dr = 5:1)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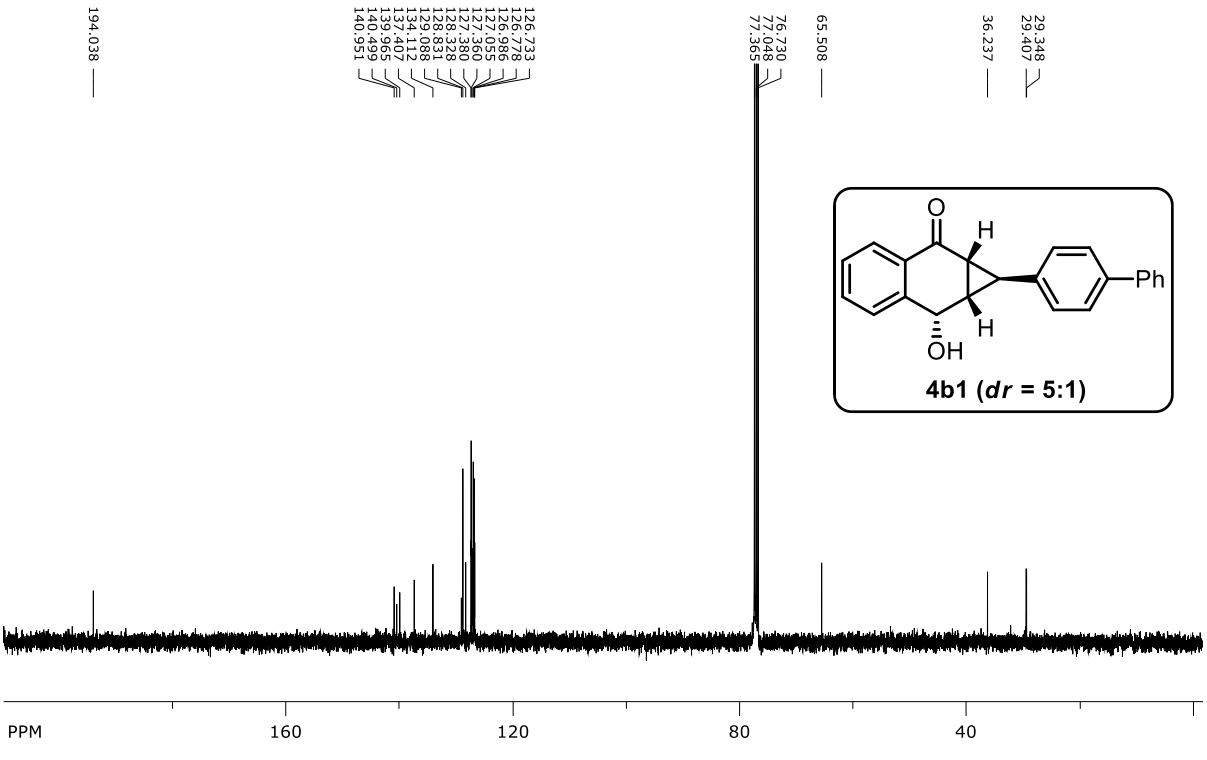
7.954
7.937
7.788
7.713
7.710
5.415
1.624
2.274
2.276
2.278
2.281
2.285
2.386
0.025
O
H
Ph
H
OH
4b1 (dr = 5:1)
0.979
1.068
1.265
4.455
3.373
1.264
1.876
1.000
1.018
1.943
1.024
PPM
8
6
4
2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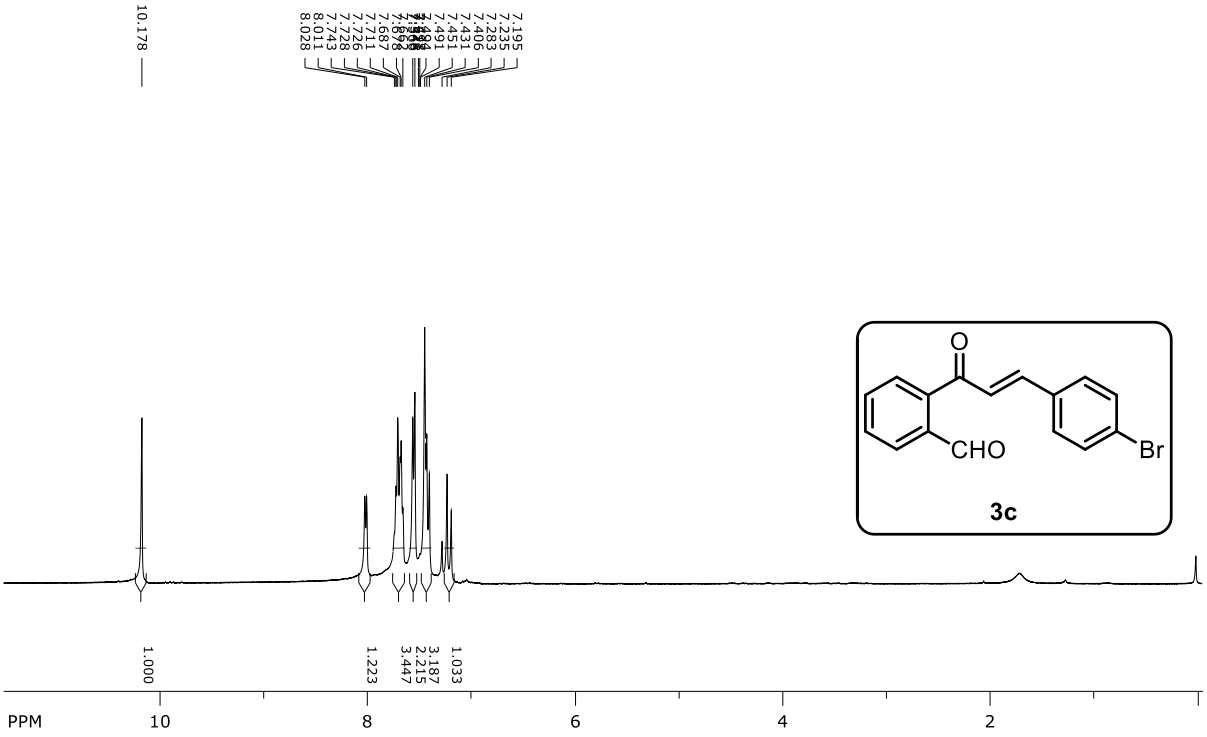
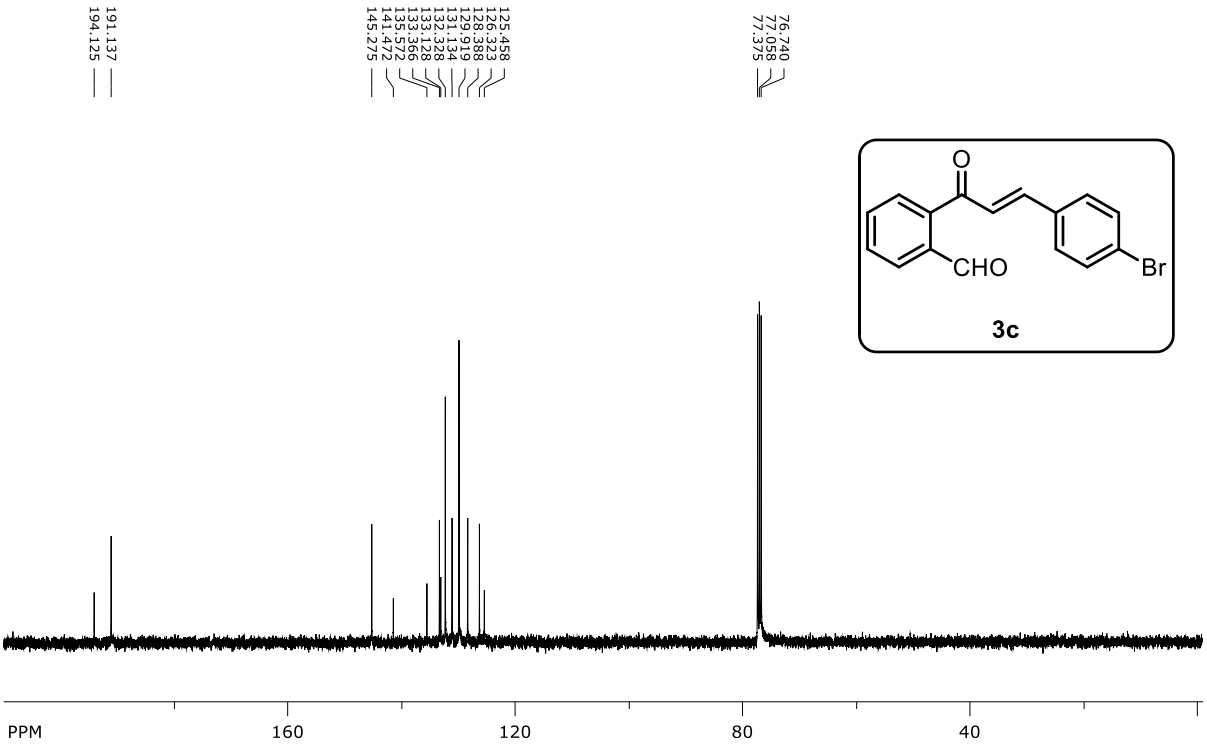
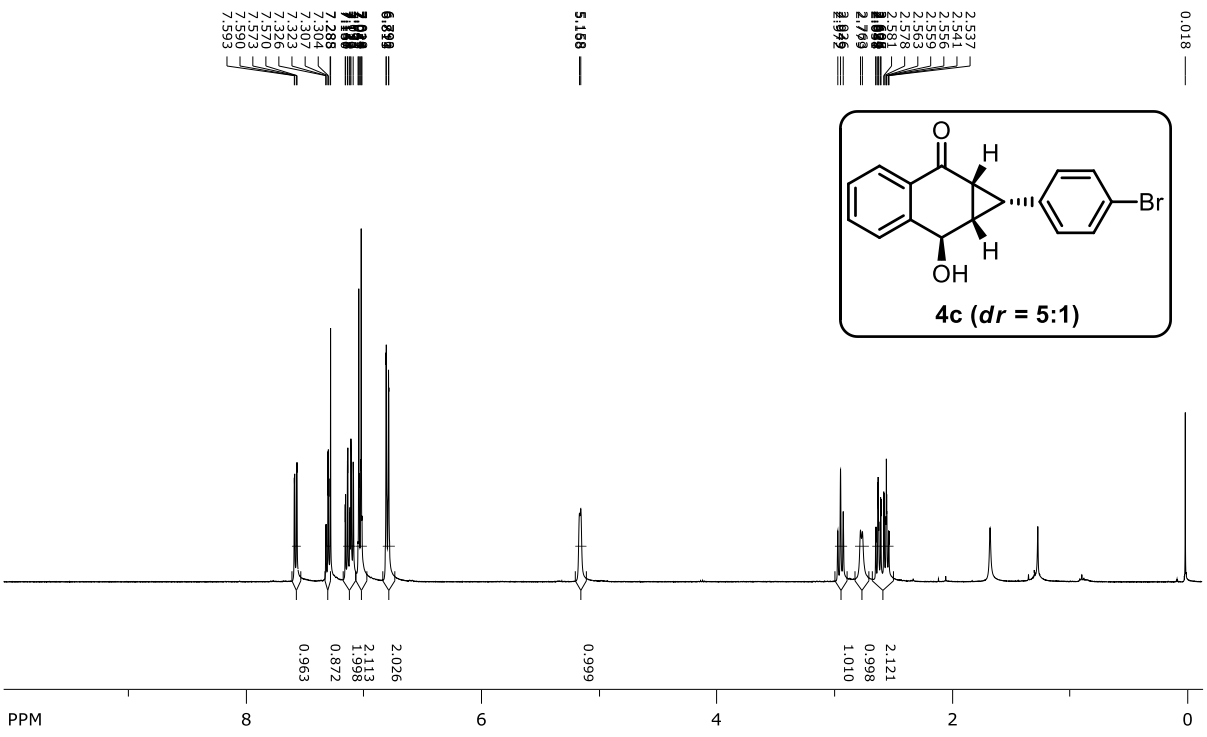
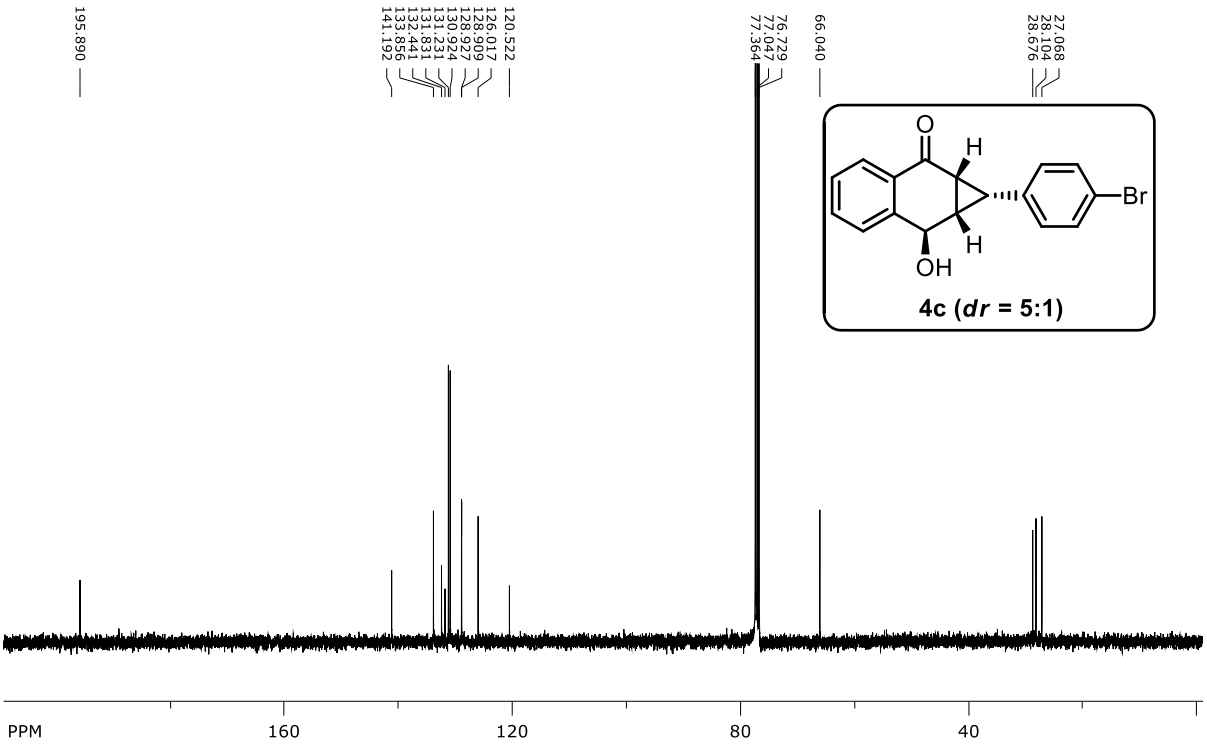
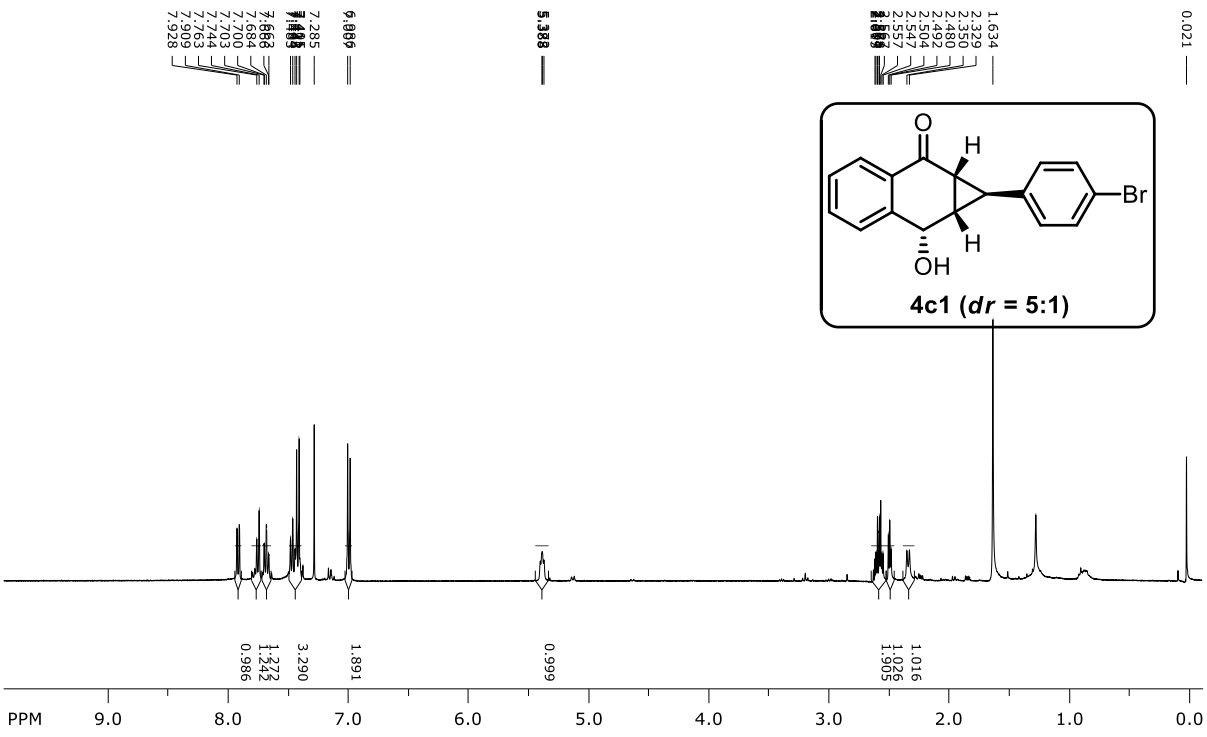
140.951
140.499
139.965
137.407
134.112
129.088
128.831
128.328
127.360
127.055
126.986
126.778
126.733
77.365
77.048
76.730
65.508
36.237
29.407
29.348
O
H
Ph
H
OH
4b1 (dr = 5:1)
PPM
160
120
80
40

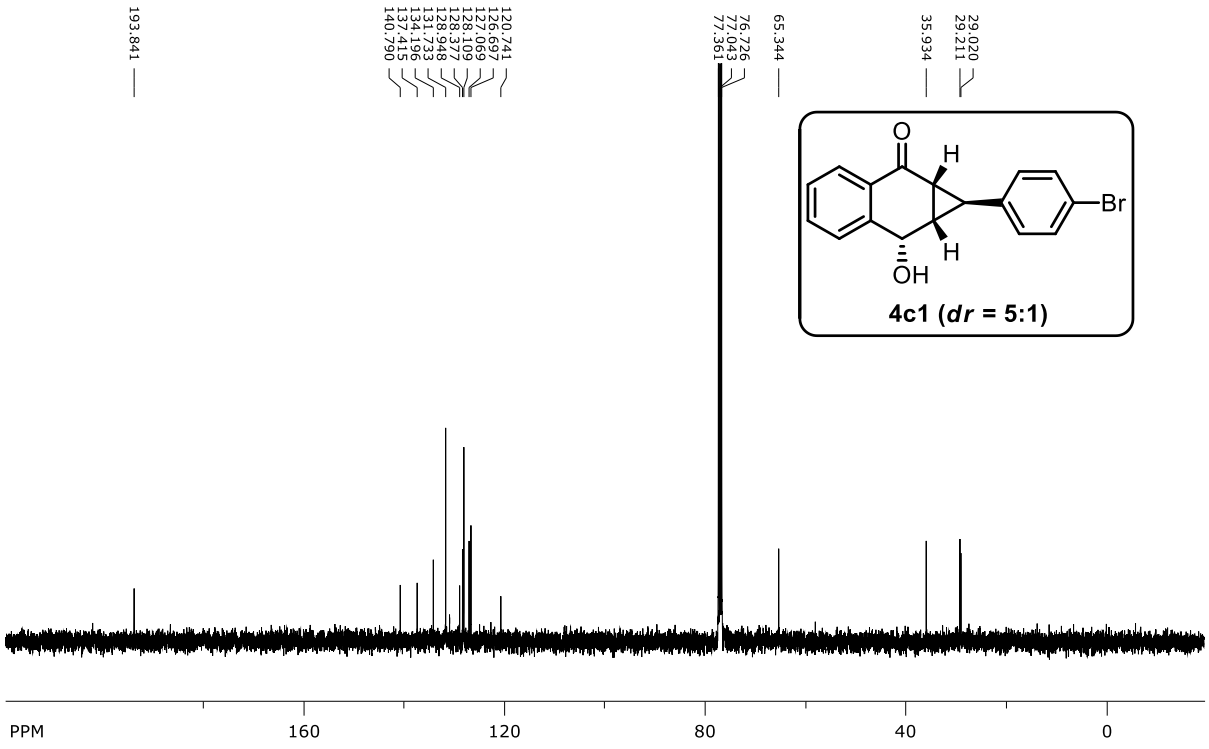

10.178
8.028
8.011
7.743
7.728
7.726
7.711
7.687
7.491
7.451
7.431
7.406
7.235
7.195
O
CHO
Br
3c
1.000
1.223
3.187
2.215
3.447
1.033
PPM
10
8
6
4
2

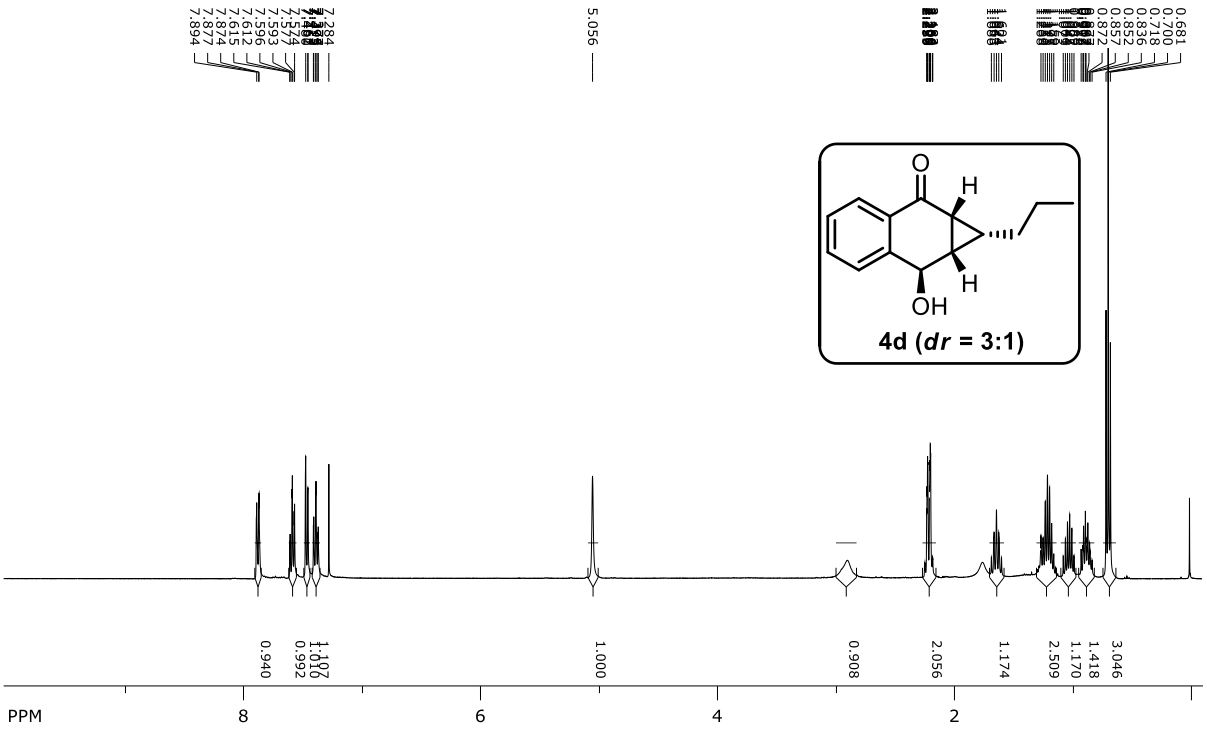

191.137
194.125
145.275
141.472
135.572
133.366
133.128
132.328
131.134
129.919
128.388
127.233
125.458
77.375
76.740
O
CHO
Br
3c
PPM
160
120
80
40

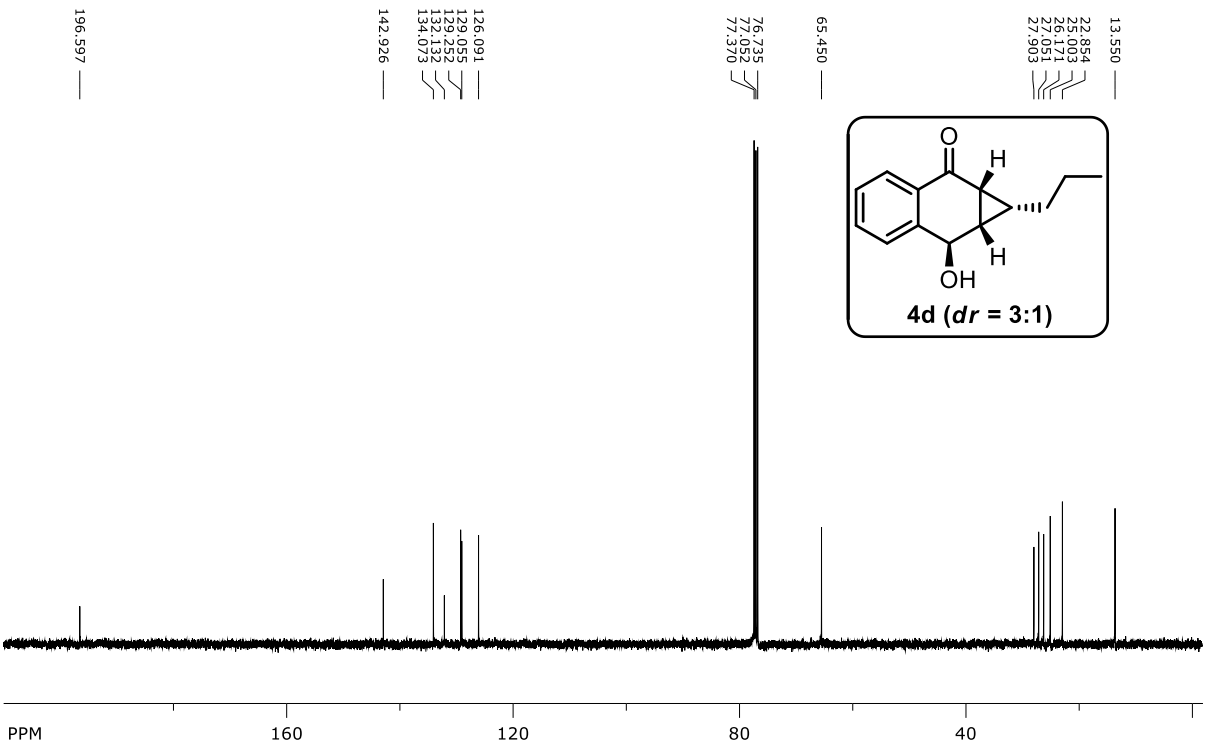

7.593
7.560
7.570
7.326
7.323
7.307
7.304
7.288
6.899
5.168
2.578
2.563
2.559
2.556
2.541
2.537
0.018
O
H
H
OH
Br
4c (dr = 5:1)
0.963
0.872
1.998
2.113
2.026
0.999
1.010
0.998
2.121
PPM
8
6
4
2
0


195.890
141.192
133.856
132.441
131.831
131.231
130.924
128.927
128.909
126.017
120.522
77.364
77.047
76.729
66.040
28.676
28.104
27.068
O
H
H
OH
Br
4c (dr = 5:1)
PPM
160
120
80
40


7.928
7.909
7.763
7.703
7.700
7.684
7.663
7.285
5.388
2.557
2.504
2.492
2.480
2.350
2.329
1.634
0.021
O
H
H
OH
Br
4c1 (dr = 5:1)
0.986
1.242
1.272
3.290
1.891
0.999
1.905
1.026
1.016
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


193.841
140.790
137.415
134.196
131.733
128.948
128.377
128.109
127.069
120.741
77.361
76.726
65.344
35.934
29.211
29.020
O
H
H
OH
Br
4c1 (dr = 5:1)
PPM
160
120
80
40
0


7.894
7.877
7.874
7.615
7.612
7.596
7.593
5.056
0.681
0.700
0.718
0.836
0.852
0.857
0.872
O
H
H
OH
4d (dr = 3:1)
0.940
0.992
1.000
0.908
2.056
1.174
2.509
1.418
1.170
3.046
PPM
8
6
4
2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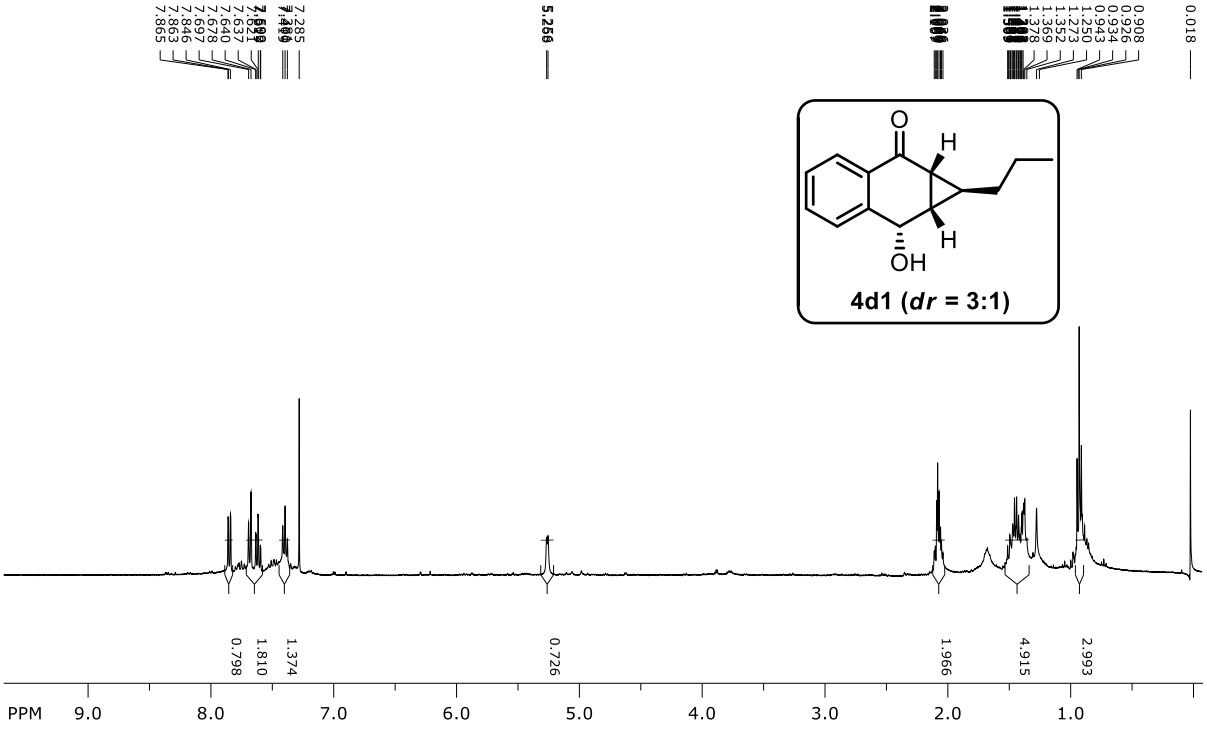
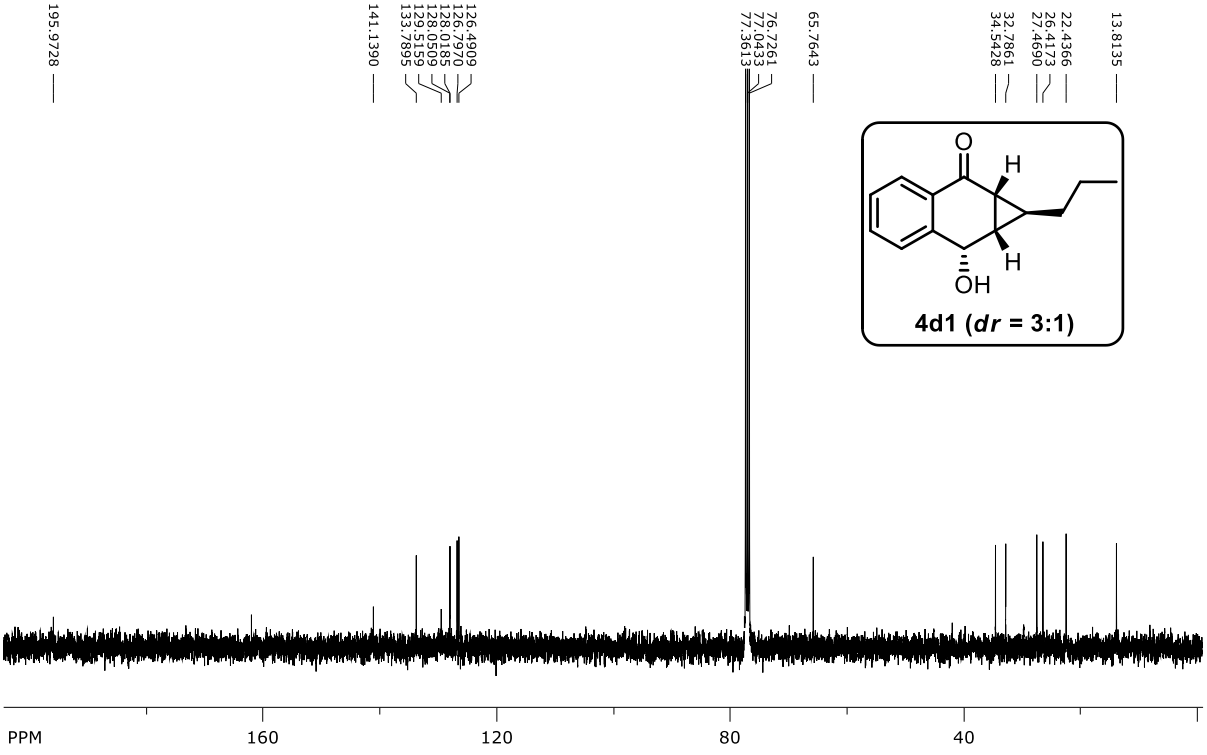
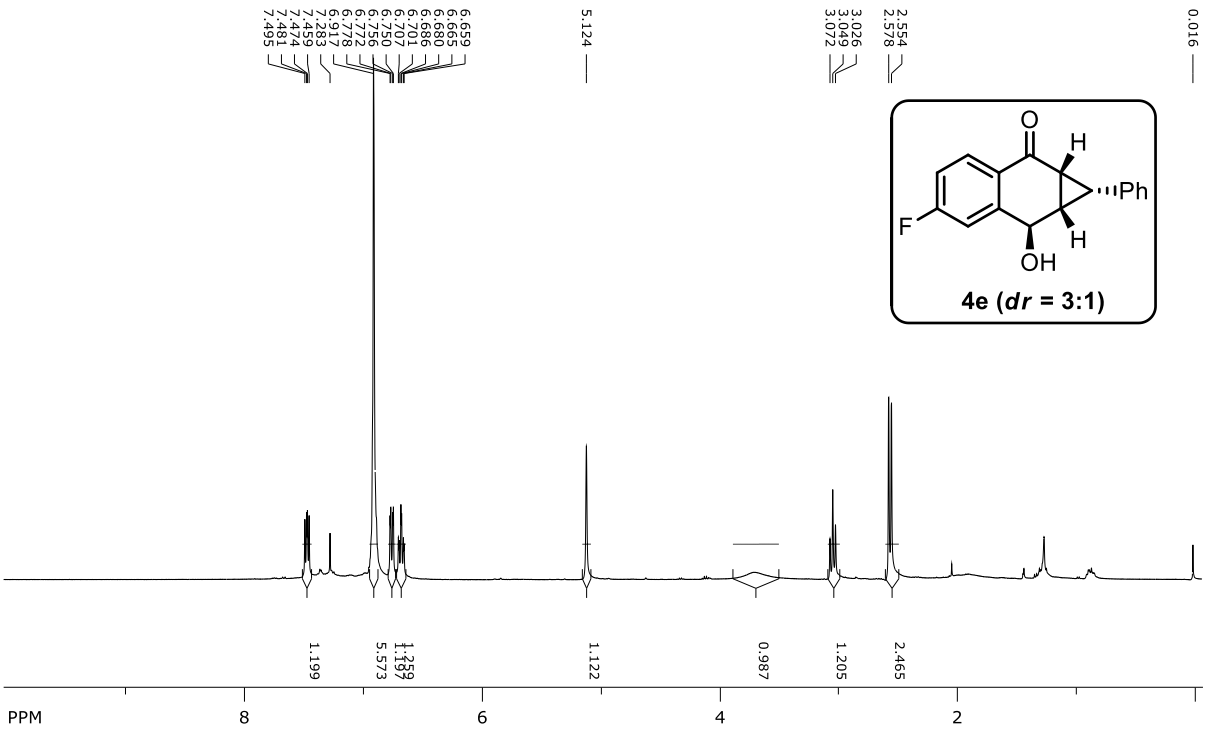
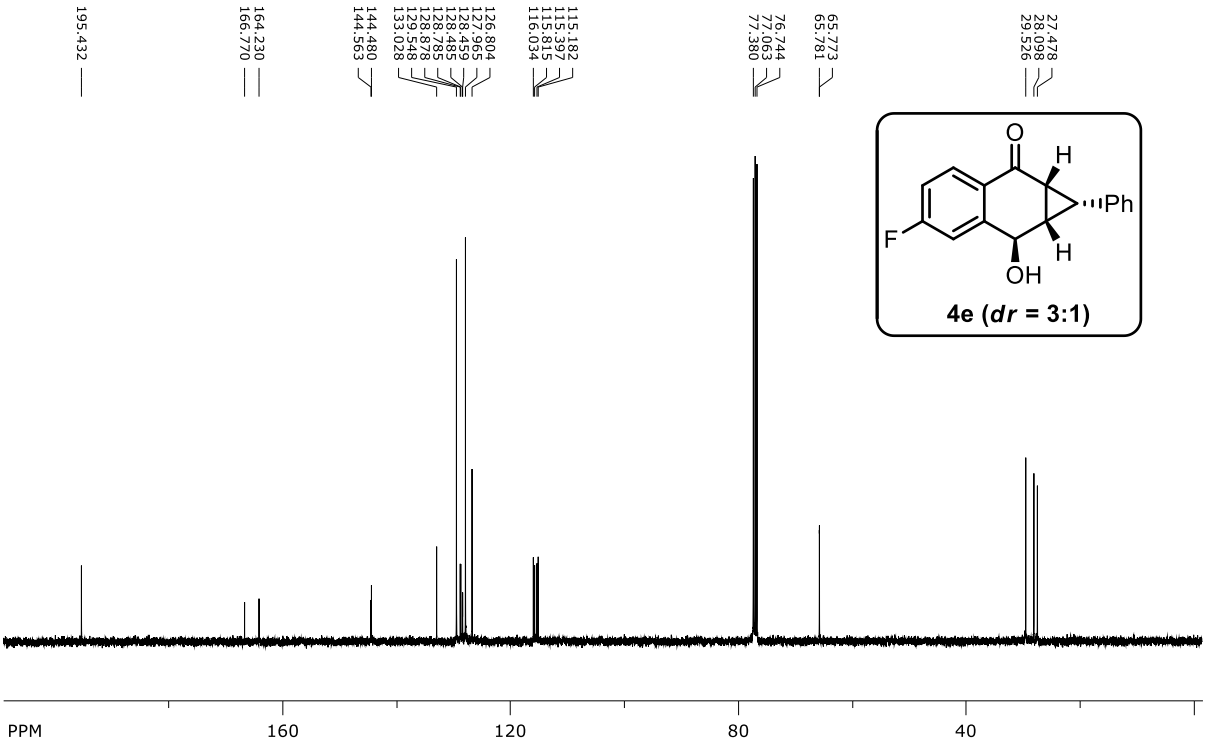
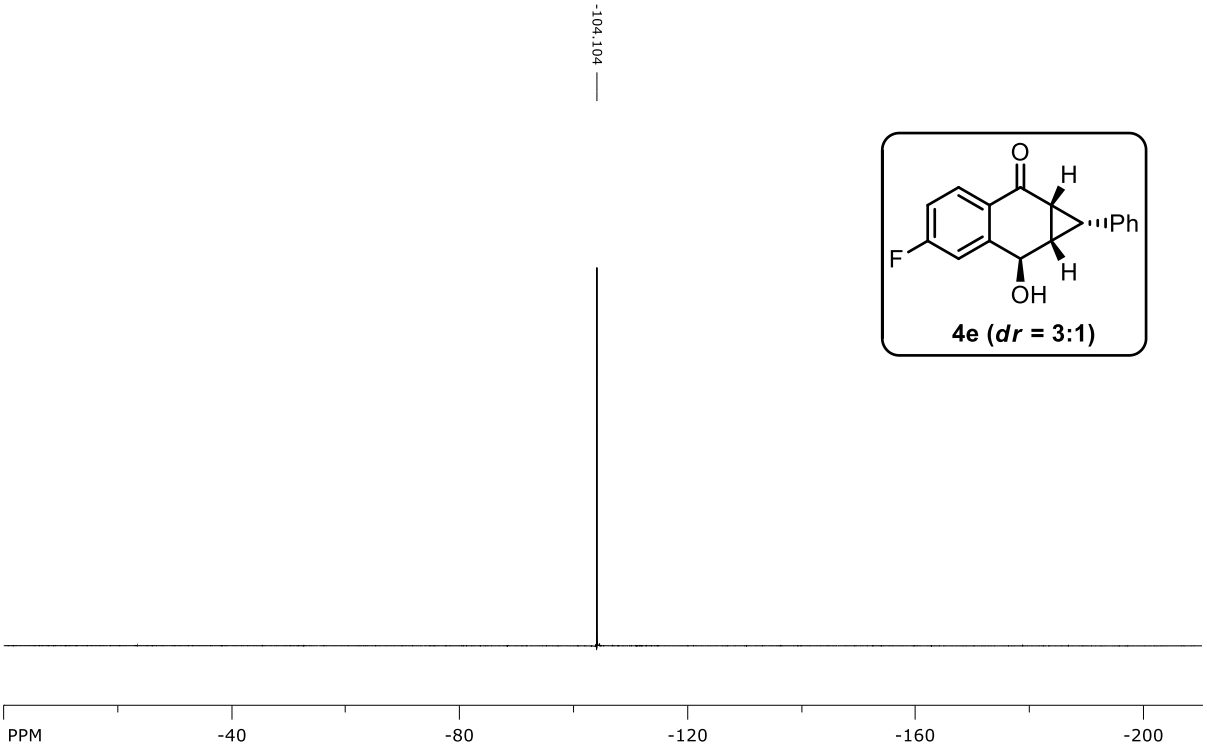
142.926
134.073
132.132
129.055
126.091
77.370
77.052
76.735
65.450
27.903
27.051
26.171
25.003
22.854
13.550
O
H
H
OH
4d (dr = 3:1)
PPM
160
120
80
40


7.865
7.863
7.846
7.697
7.648
7.637
7.621
7.285
5.256
0.908
0.926
0.934
0.943
1.250
1.273
1.352
1.369
1.378
0.018
4d1 (dr = 3:1)
0.798
1.810
1.374
0.726
1.966
4.915
2.993
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

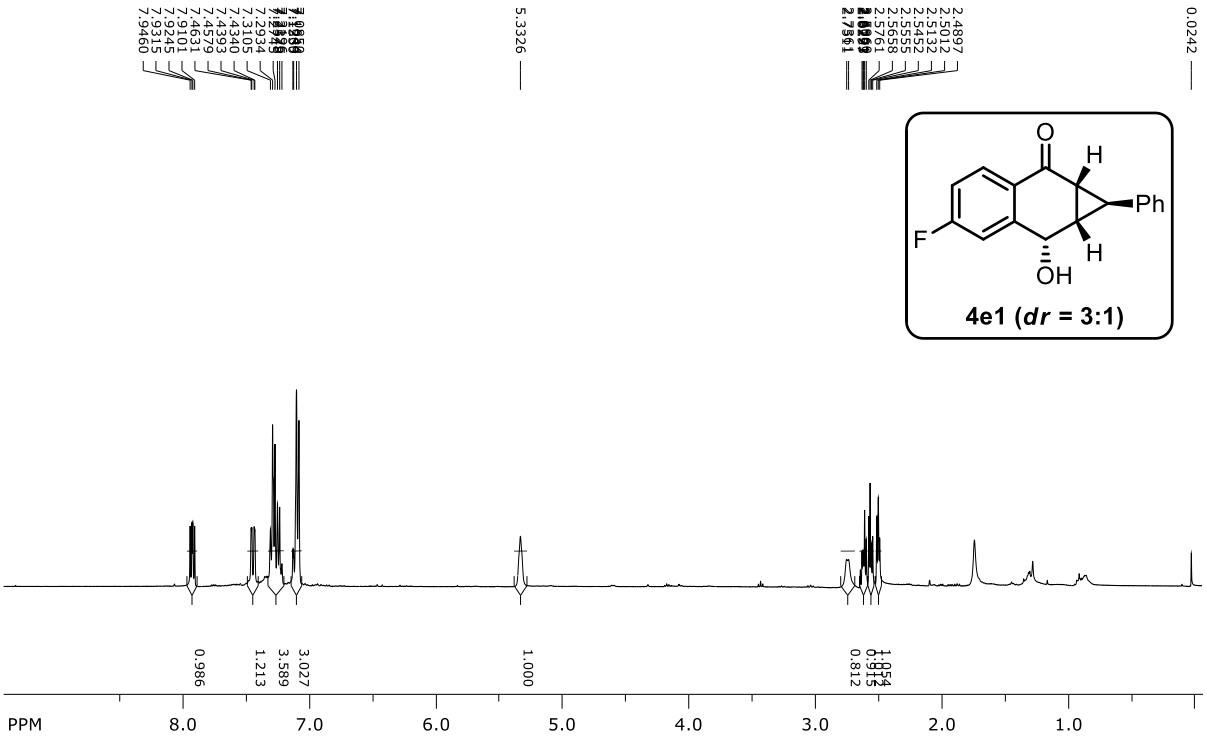

195.9728
141.1390
133.7895
129.5159
128.0509
128.0185
126.7970
126.4909
77.3613
77.0433
76.7261
65.7643
34.5428
32.7861
27.4690
25.4173
22.4366
13.8135
4d1 (dr = 3:1)
PPM
160
120
80
40


7.495
7.481
7.474
7.459
7.283
6.917
6.778
6.772
6.756
6.750
6.707
6.701
6.686
6.680
6.665
6.659
5.124
3.072
3.049
3.026
2.578
2.554
0.016
O
H
Ph
F
H
OH
4e (dr = 3:1)
1.199
5.573
1.122
0.987
1.205
2.465
PPM
8
6
4
2

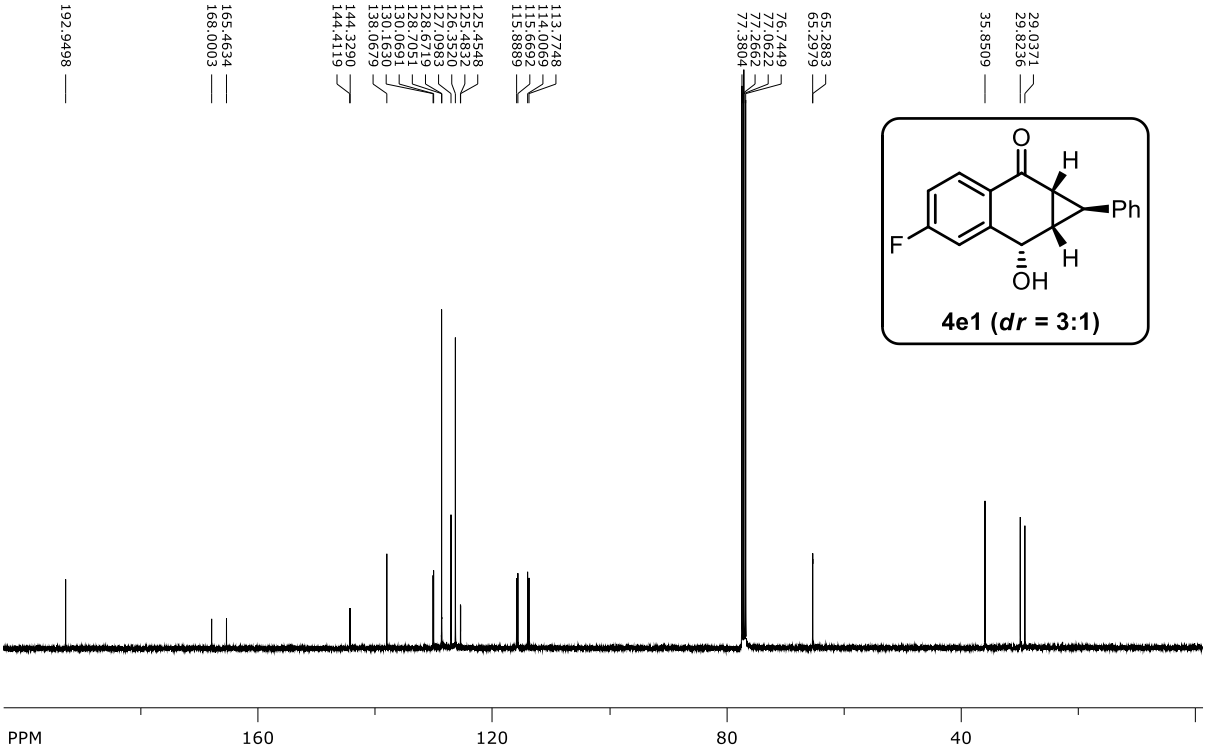

195.432
166.770
164.230
144.563
144.480
133.028
129.548
128.878
128.785
128.485
128.455
126.804
116.034
115.815
115.397
115.182
77.380
77.063
76.744
65.781
29.526
28.098
27.478
O
H
Ph
F
H
OH
4e (dr = 3:1)
PPM
160
120
80
40



4e (*dr* = 3:1)



4e1 (*dr* = 3:1)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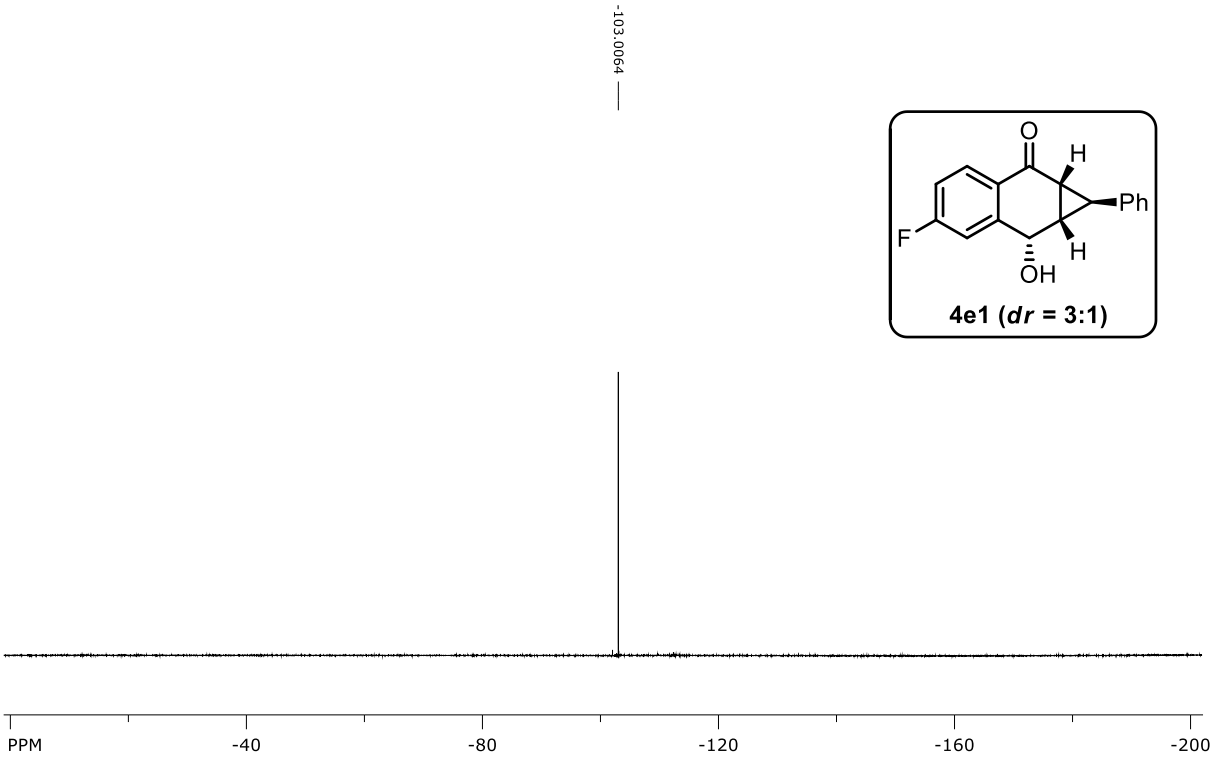
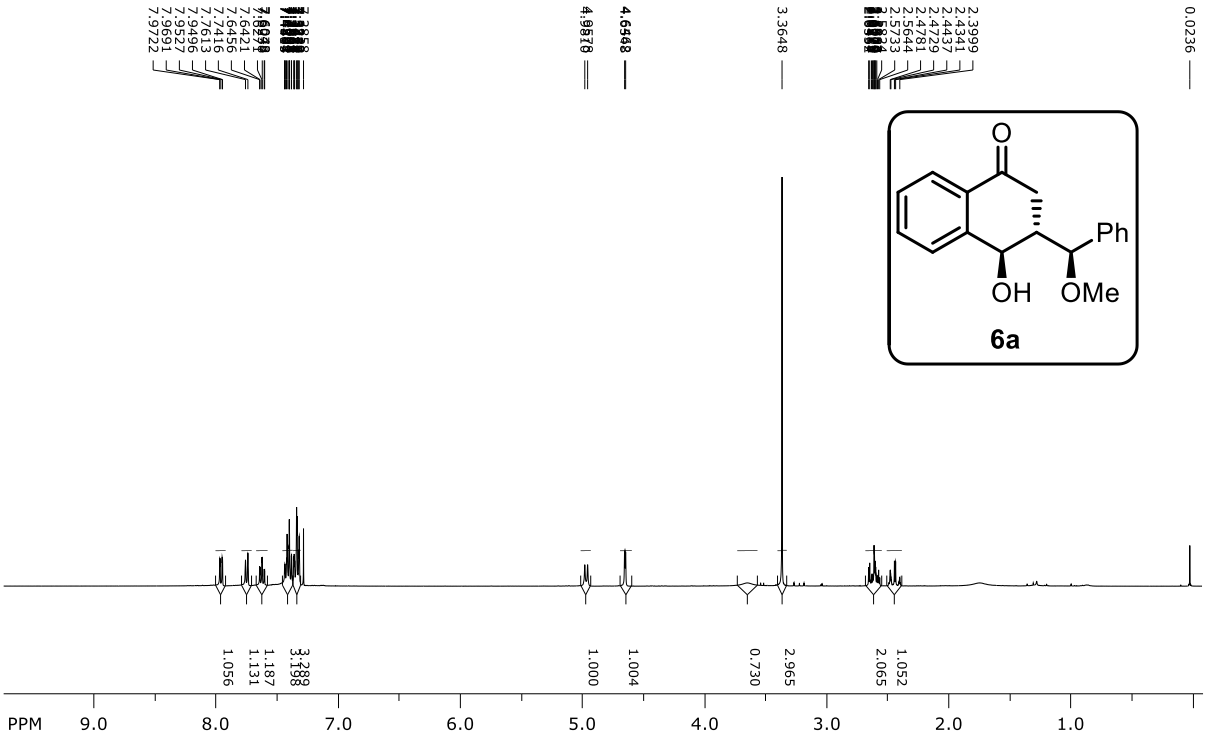
165.4634
168.0003
144.3290
144.4119
138.0679
130.1630
130.0691
128.7051
128.6719
127.0983
126.3520
125.4832
125.4548
113.7748
114.0069
115.6692
115.8889
77.3804
77.2662
77.0622
76.7449
65.2883
65.2979
35.8509
29.8236
29.0371
PPM
160
120
80
40
4e1 (dr = 3:1)


-103.0064
PPM
-40
-80
-120
-160
-200
4e1 (dr = 3:1)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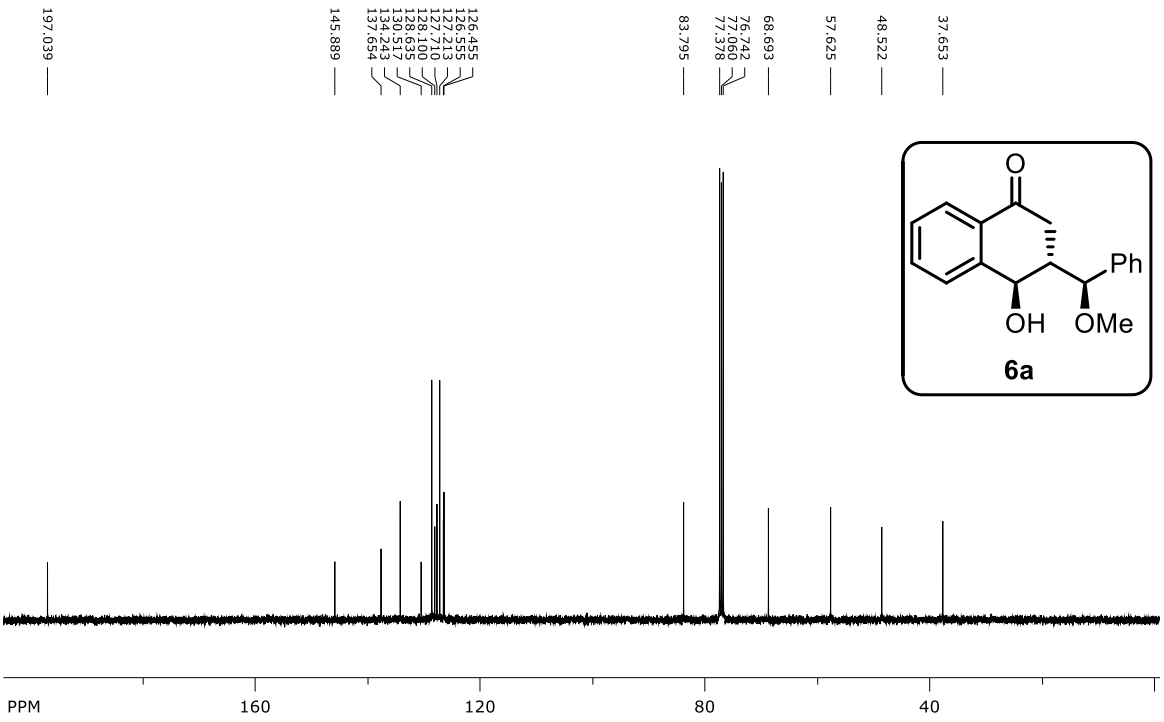
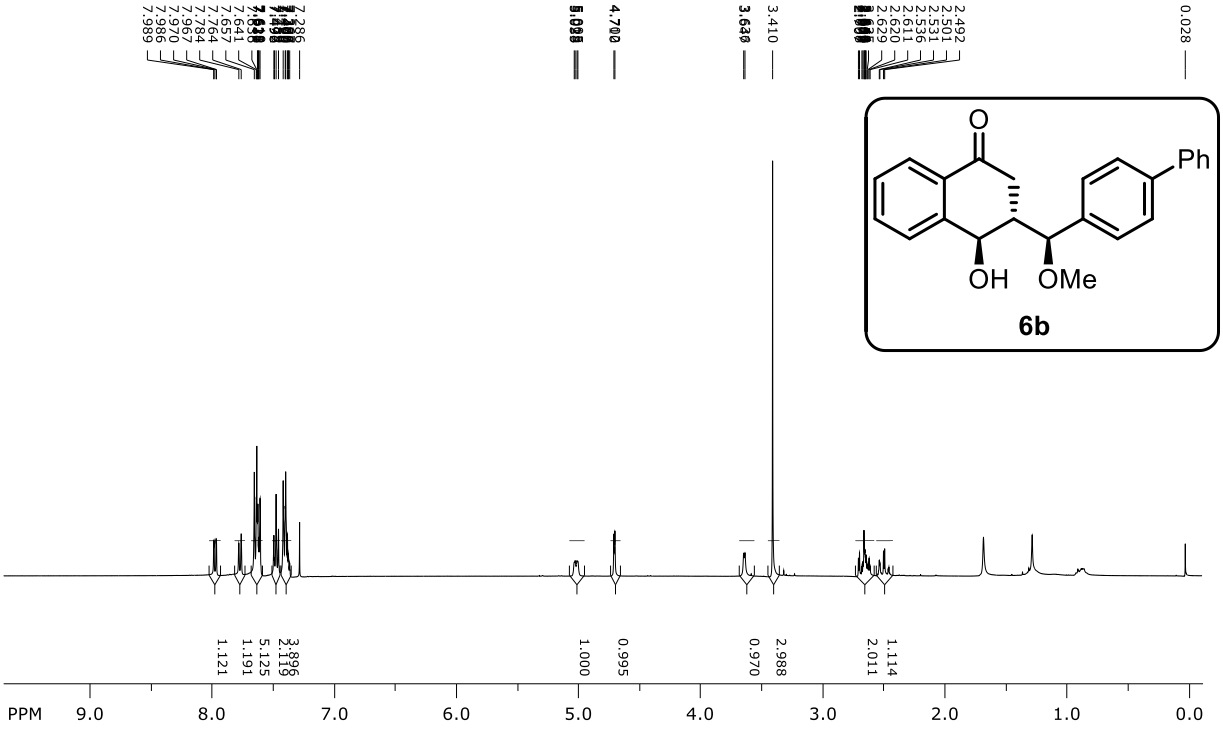
7.9691
7.9527
7.9496
7.7613
7.7416
7.6456
7.6421
4.9570
4.6548
3.3648
2.4729
2.4781
2.5644
2.5733
2.3999
2.4341
2.4437
0.0236
O
Ph
OH
OMe
6a
1.056
1.131
1.187
1.000
1.004
0.730
2.965
2.065
1.052
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


197.039
145.889
137.654
134.243
130.517
128.639
127.710
127.213
126.555
126.455
83.795
77.378
76.742
77.060
68.693
57.625
48.522
37.653
O
Ph
OH
OMe
6a
PPM
160
120
80
40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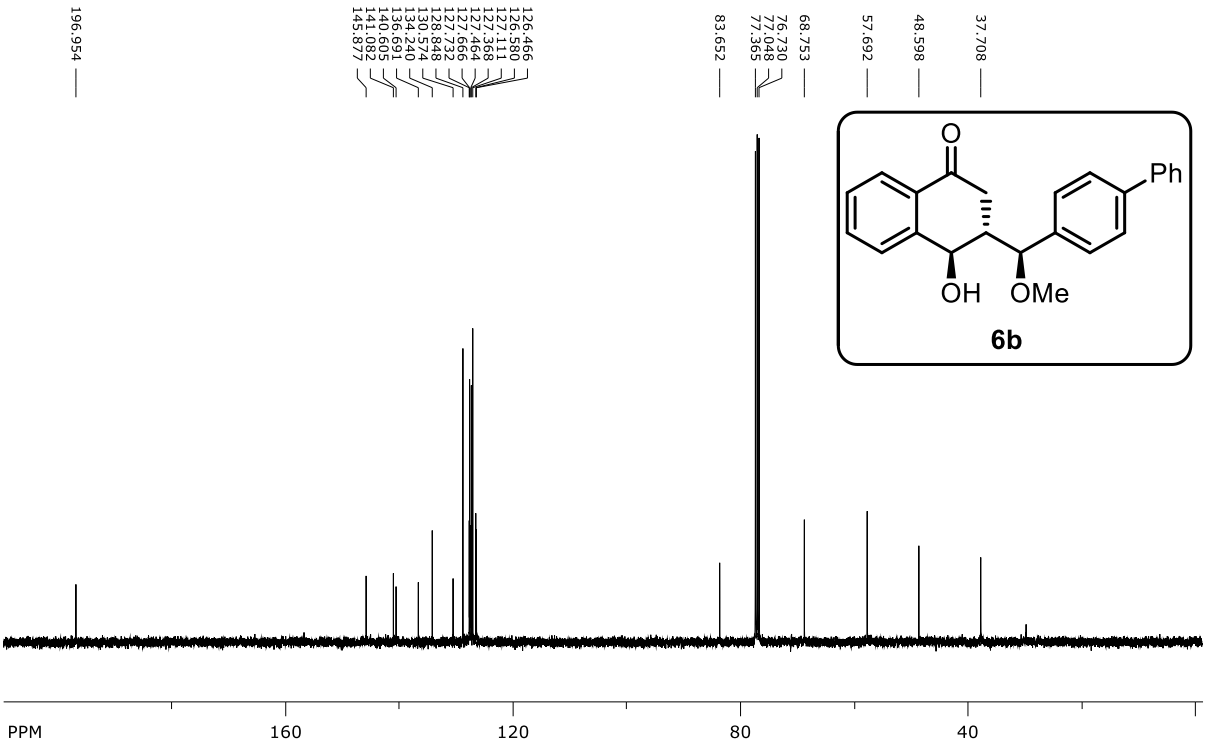
7.986
7.970
7.967
7.784
7.764
7.657
4.700
3.634
3.410
2.492
2.501
2.531
2.536
2.611
2.620
2.629
0.028
O
Ph
OH
OMe
6b
1.121
1.191
5.125
1.000
0.995
0.970
2.988
1.114
2.011
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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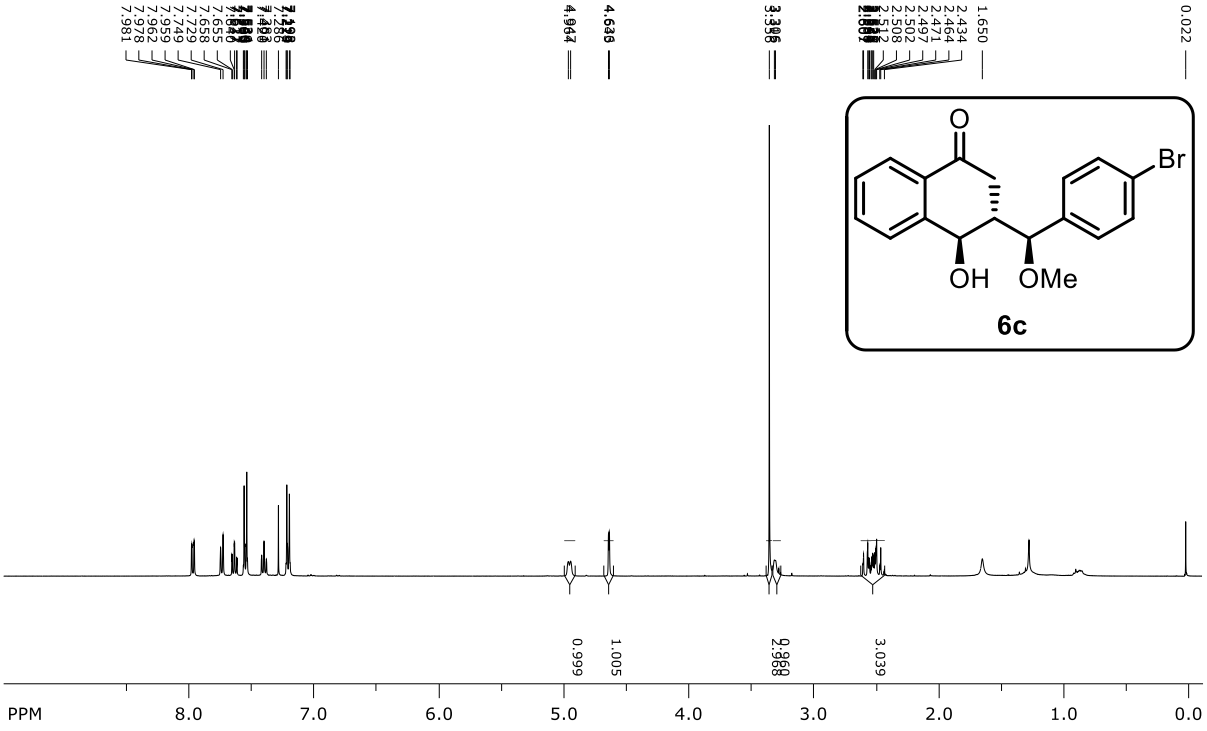
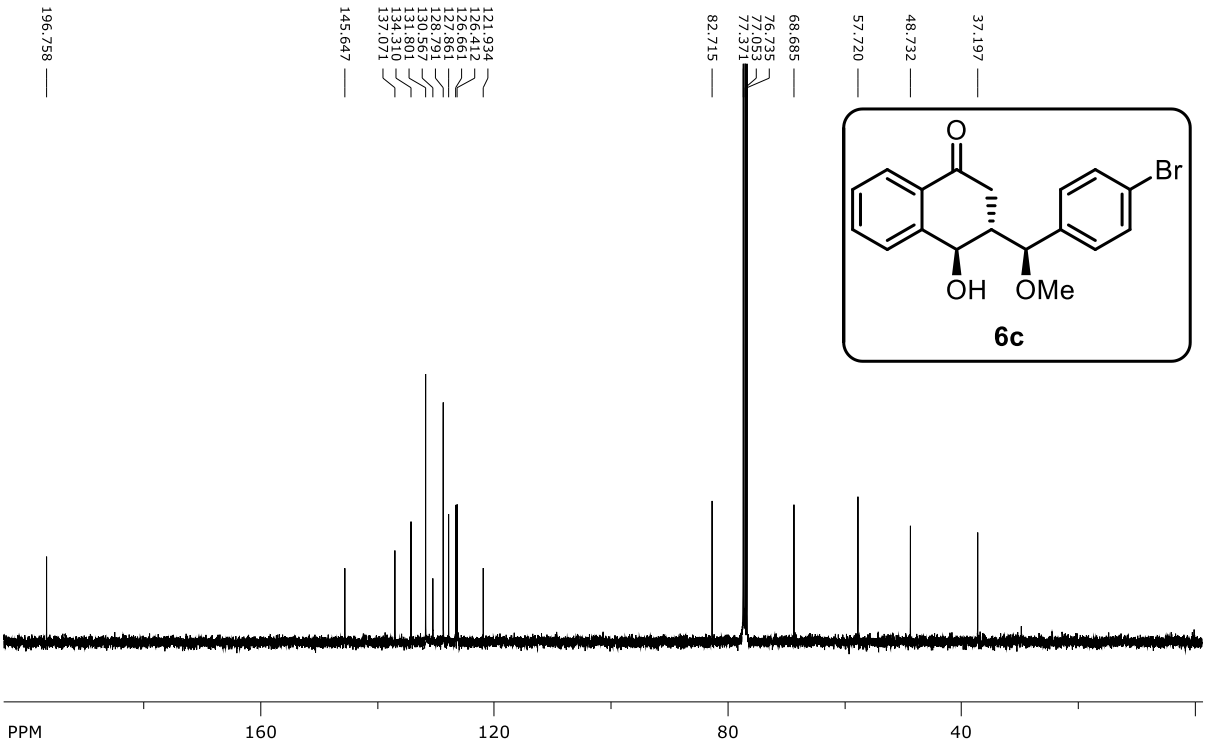
145.877
141.082
140.605
136.691
134.240
130.574
128.848
127.696
127.464
127.368
127.111
126.580
126.466
83.652
77.365
77.048
76.730
68.753
57.692
48.598
37.708
O
Ph
OH
OMe
6b
PPM
160
120
80
40


7.981
7.978
7.962
7.959
7.749
7.729
7.658
7.655
4.964
4.638
3.336
2.434
2.464
2.471
2.497
2.502
1.650
0.022
O
Br
OH
OMe
6c
0.999
1.005
2.968
3.039
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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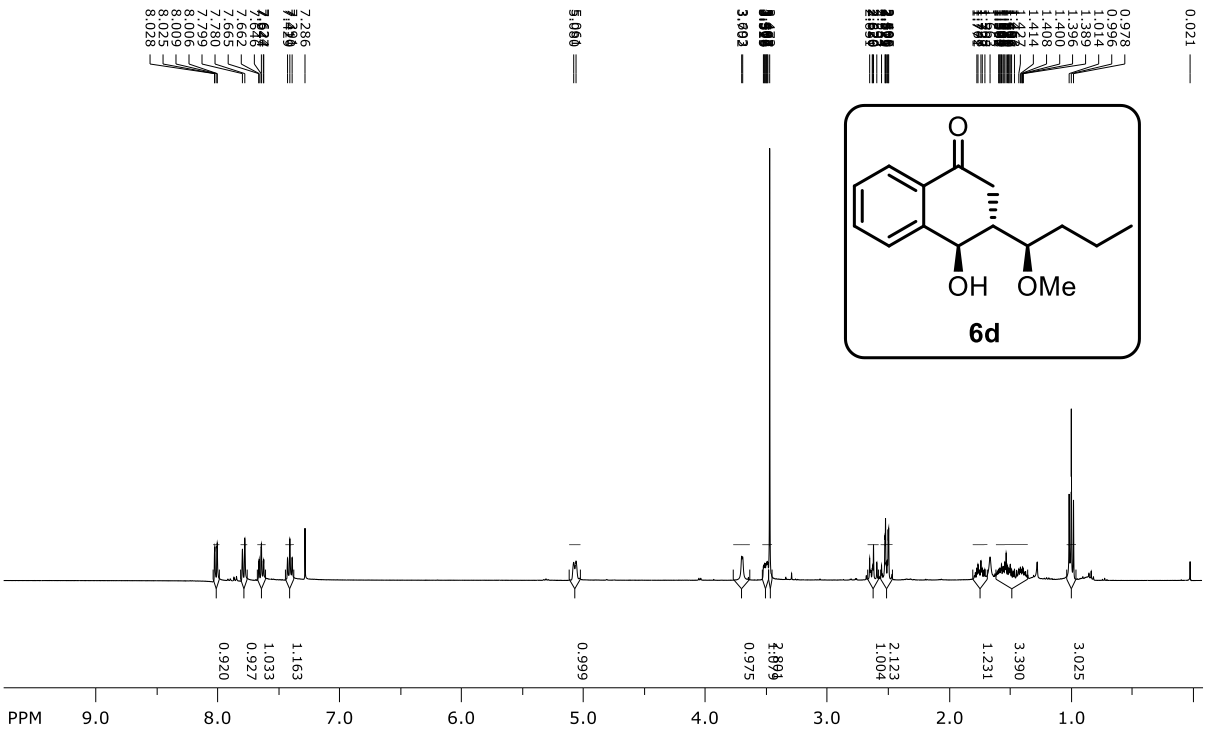
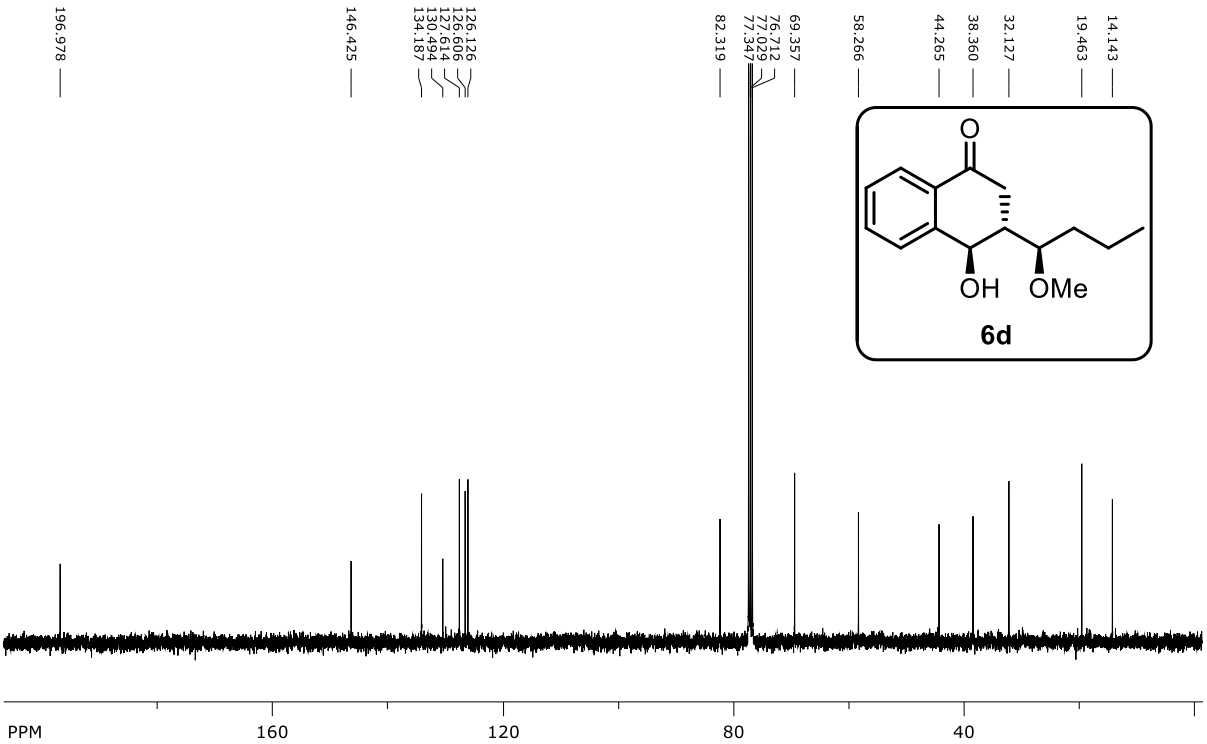
134.310
131.801
130.567
128.781
126.661
126.412
121.934
82.715
77.371
76.735
68.685
57.720
48.732
37.197
O
Br
OH
OMe
6c
PPM
160
120
80
40


8.028
8.025
8.009
8.006
7.799
7.780
7.665
7.662
7.286
5.060
3.893
0.978
0.996
1.014
1.389
1.396
1.400
1.408
1.414
0.021
O
OH
OMe
6d
0.920
0.927
1.033
1.163
0.999
0.975
2.123
1.004
1.231
3.390
3.025
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0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146.425
134.187
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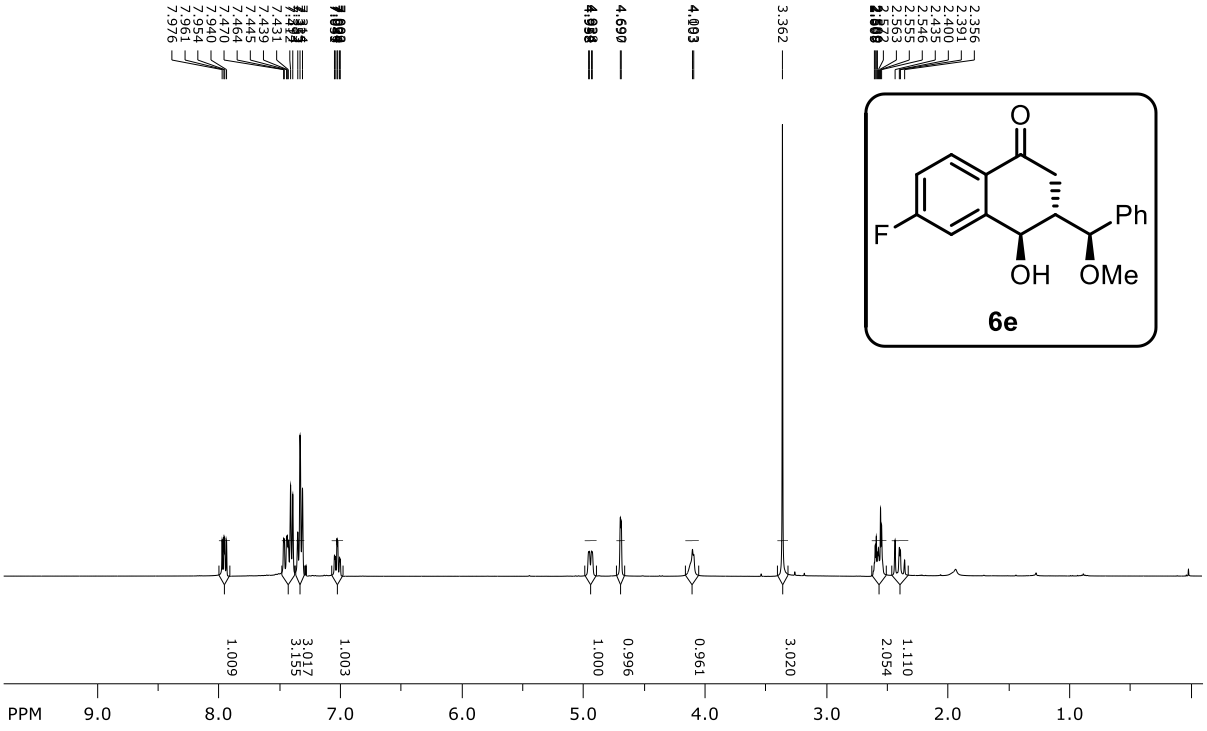
127.614
126.606
126.126
82.319
77.347
77.029
76.712
69.357
58.266
44.265
38.360
32.127
19.463
14.143
O
OH
OMe
6d
PPM
160
120
80
40


7.976
7.961
7.954
7.470
7.464
7.445
7.439
7.431
4.690
4.003
3.362
2.356
2.391
2.400
2.435
2.546
2.555
O
F
Ph
OH
OMe
6e
1.009
3.017
3.155
1.003
1.000
0.996
0.961
3.020
1.110
2.054
PPM
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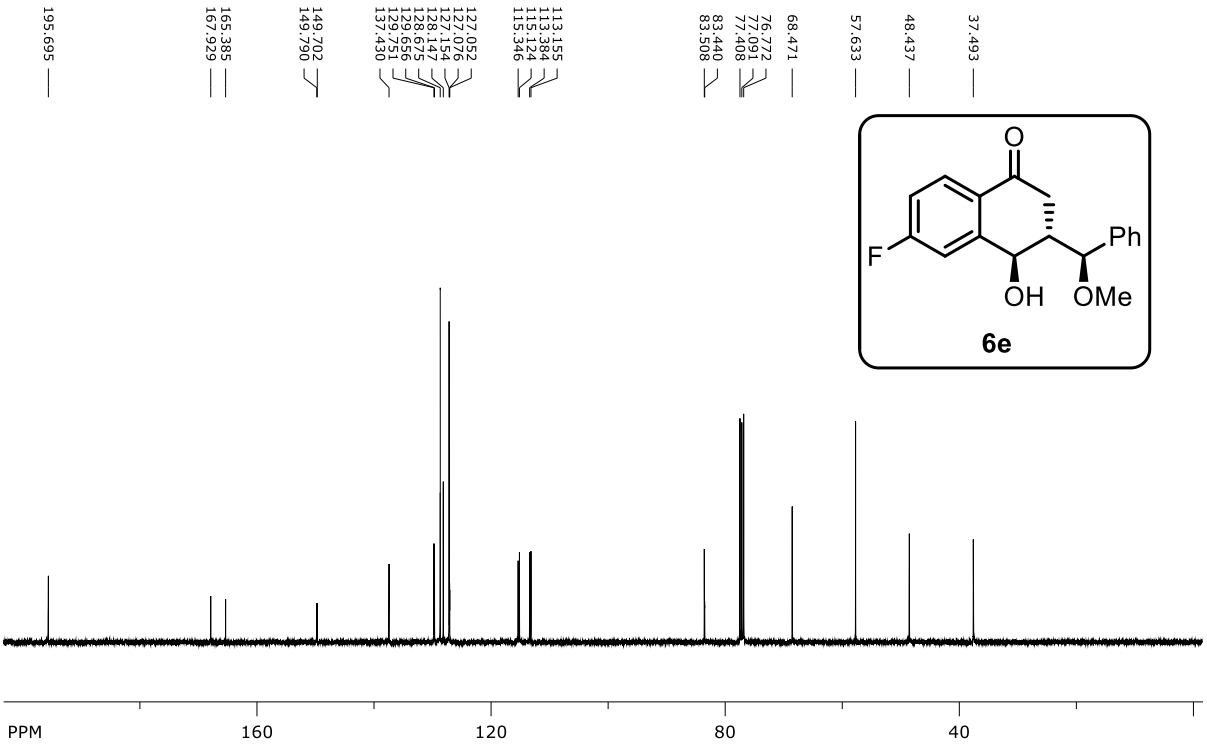
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0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167.929
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149.790
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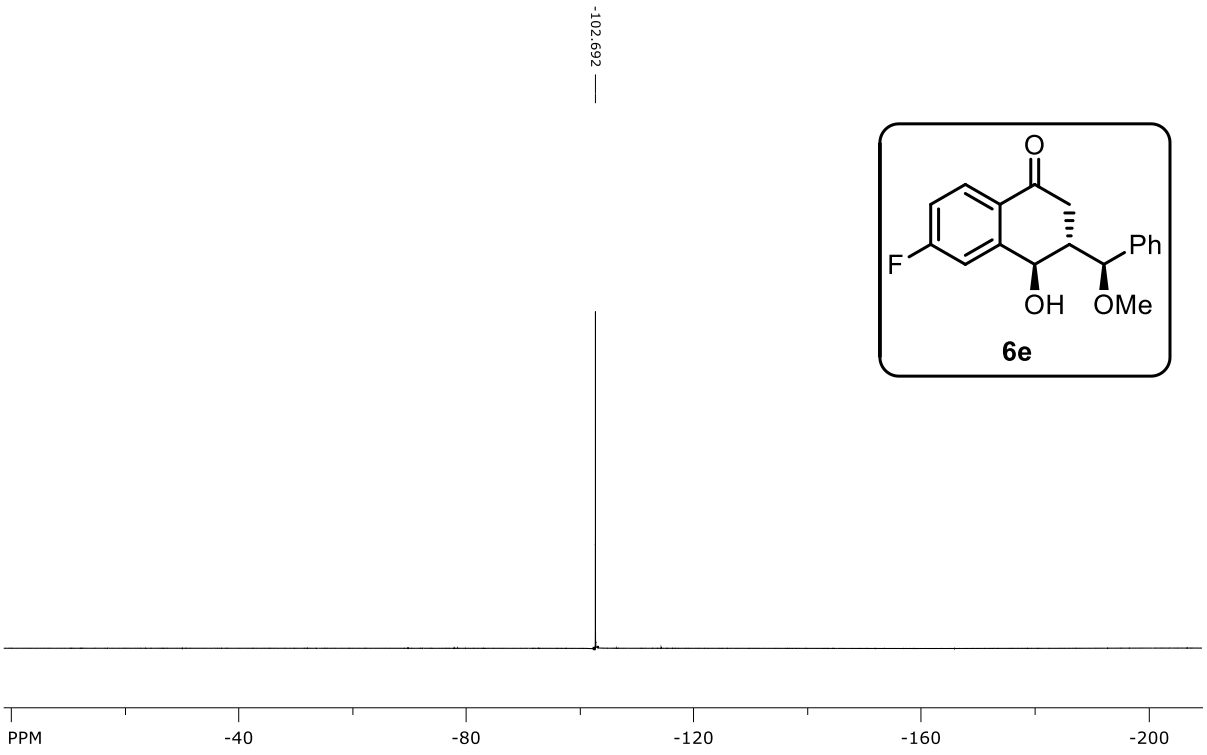
128.147
127.154
127.052
127.076
115.346
113.155
113.384
115.124
83.508
83.440
76.772
77.091
77.408
68.471
57.633
48.437
37.493
O
F
Ph
OH
OMe
6e
PPM
160
120
80
40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Ph
OH
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6e
PPM
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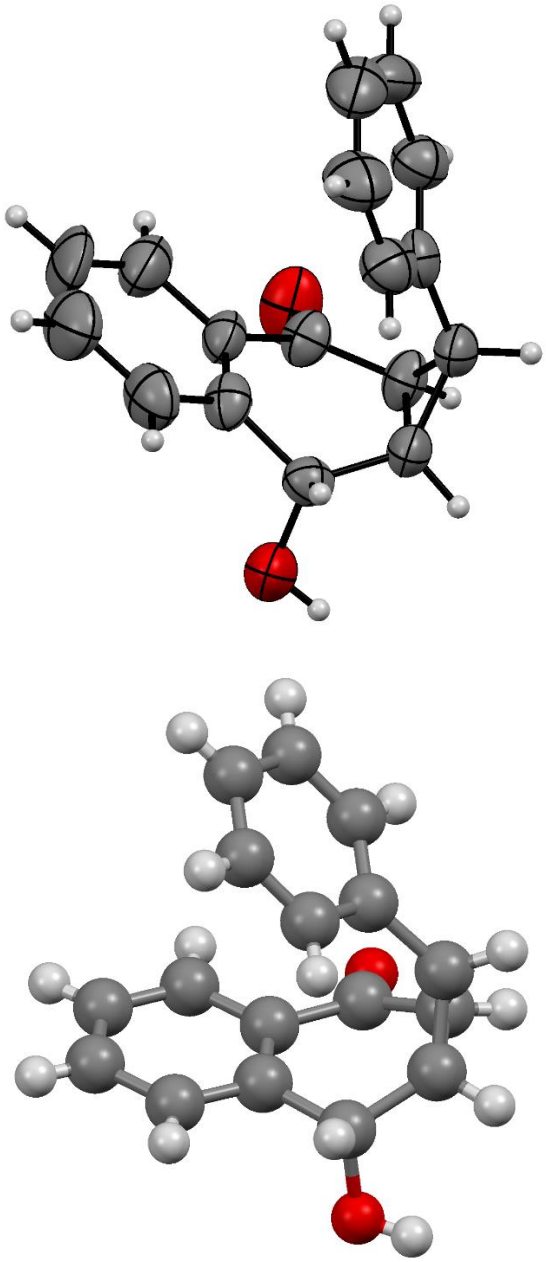
-80
-120
-160
-200

Table 4: General data and structure refinement parameters for cyclopropa-fused tetralone 4a

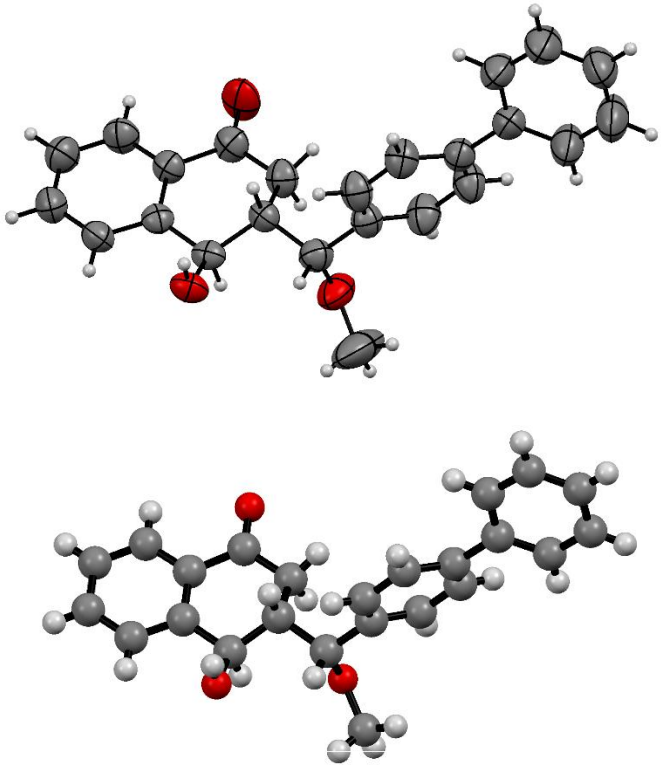


Crystal Data for $C_{17}H_{14}O_2$ (*M* =250.28 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 12.550(4) Å, *b* = 8.868(2) Å, *c* = 12.114(4) Å, *β* = 105.063(11)°, *V* = 1301.9(6) Å^3, *Z* = 4, *T* = 298 K, μ(MoKα) = 0.083 mm^{-1}, *Dcalc* = 1.277 g/cm^3, 6620 reflections measured (6.724° ≤ 2Θ ≤ 54.964°), 2925 unique (R_{int} = 0.0829, R_{sigma} = 0.1229) which were used in all calculations. The final R_1 was 0.0839 (I > 2σ(I)) and wR_2 was 0.2604 (all data).

Table 5: Crystal data and structure refinement for 4a.

Identification code	4a
Empirical formula	$C_{17}H_{14}O_2$
Formula weight	250.28
Temperature/K	298
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	12.550(4)
b/Å	8.868(2)
c/Å	12.114(4)
α/°	90
β/°	105.063(11)
γ/°	90
Volume/Å^3	1301.9(6)
Z	4
ρ_{calc}g/cm^3	1.277
μ/mm^{-1}	0.083
F(000)	528.0
Crystal size/mm^3	0.3 × 0.2 × 0.2

Table 6: General data and structure refinement parameters for cyclopropa-fused tetralone 6b



Crystal Data for $C_{24}H_{22}O_3$ (*M* =358.41 g/mol): triclinic, space group P-1 (no. 2), *a* = 10.929(4) Å, *b* = 11.823(4) Å, *c* = 17.435(6) Å, *α* = 101.104(9)°, *β* = 97.099(9)°, *γ* = 116.493(8)°, *V* = 1921.3(11) Å^3, *Z* = 4, *T* = 298.00(2) K, μ(MoKα) = 0.081 mm^{-1}, *Dcalc* =

1.239 g/cm^3, 22995 reflections measured ($4.008° \leq 2\Theta \leq 49.992°$), 6732 unique ($R_{int}$ = 0.0790, R_{sigma} = 0.0909) which were used in all calculations. The final R_1 was 0.0575 ($I > 2\sigma(I)$) and wR_2 was 0.1846 (all data).

Table 7: Crystal data and structure refinement for 6b

Identification code	6b
Empirical formula	$C_{24}H_{22}O_3$
Formula weight	358.41
Temperature/K	298.00(2)
Crystal system	triclinic
Space group	P-1
a/Å	10.929(4)
b/Å	11.823(4)
c/Å	17.435(6)
α/°	101.104(9)
β/°	97.099(9)
γ/°	116.493(8)
Volume/Å^3	1921.3(11)
Z	4
ρ_{calc}g/cm^3	1.239
μ/mm^{-1}	0.081
F(000)	760.0
Crystal size/mm^3	0.3 × 0.2 × 0.2

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