

1,3-Dianionic annulation of ketones with ketene dithioacetal: A modified route to 3-aryl/cyclopropyl-5-thiomethyl-phenols and 1-(methylthio)-9,10-dihydrophenanthren-3-ols

Ranjay Shaw,^a Prasoon Prakash,^b Ismail Althagafi,^c Nand Gopal Giri,^d Ramendra Pratap^{d*}

^a Department of Chemistry, GLA University, Mathura, U.P., India-281406

^b Department of Kinesiology and Educational Psychology, Washington State University, Pullman, WA, USA-99164

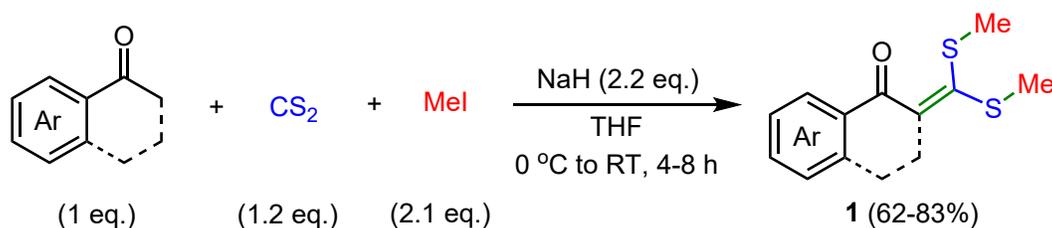
^c Department of Chemistry, Faculty of Science, Umm Al-Qura University, Makkah, Saudi Arabia

^d Department of Chemistry, Shivaji College, University of Delhi, Raja Garden, New Delhi-110027, India

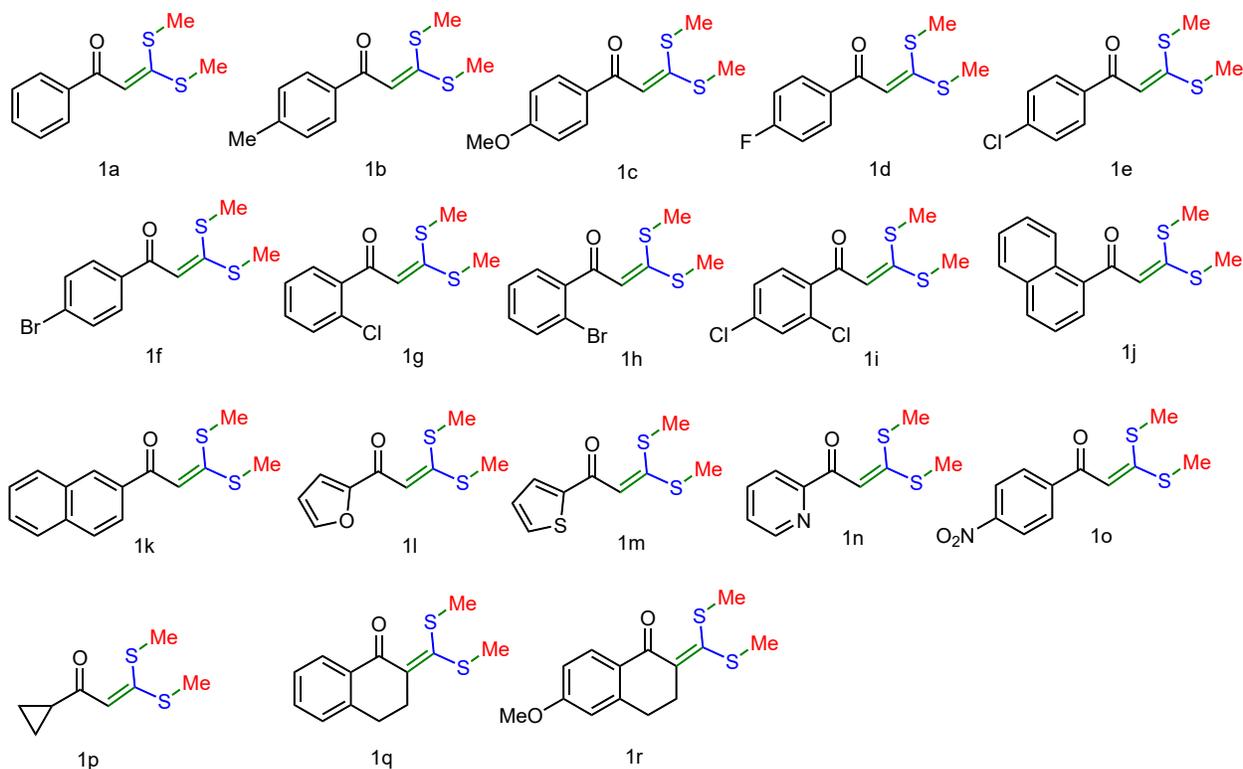
^e Department of Chemistry, University of Delhi, North Campus, Delhi, India-110007

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1. General method for synthesis of precursors: [3,3-bis(methylthio)-1-arylprop-2-en-1-ones]
(1)¹



To a stirred solution of NaH (44 mmol) in THF (50 mL) at 0°C, alkyl aryl ketone (20 mmol) was added dropwise manner (in 8-10 minutes) through a dropping funnel. The suspension was stirred for 20 minutes, and carbon disulfide (CS₂) (24 mmol) was added in dropwise over 8-10 minutes. The reaction mixture (RM) was allowed to stir for 30 min, then MeI (42 mmol) was added dropwise over 12-15 minutes. The RM was slowly brought up to room temperature (RT) and stirring continued for another 4-8 hours with monitoring by TLC. After completion of the reaction, RM was poured into crushed ice. Most of the 3,3-bis(methylthio)-1-arylprop-2-en-1-ones were precipitated in crushed ice. The precipitate was filtered and washed with ice-cold water and dried overnight inside a vacuum hood. Few 3,3-bis(methylthio)-1-arylprop-2-en-1-ones were not precipitated on crushed ice, which was extracted with ethyl acetate in ice-cooled water, dried with Na₂SO₄ and concentrated under reduced pressure. The crude mixture was recrystallized with ethyl acetate and n-hexane.



2. General information on experimental:

Commercially available reagents and solvents from Alfa Aesar, Spectrochem, Sigma Aldrich, Fischer Scientific and TCI Chemicals were used without further purification. ¹H and ¹³C NMR spectra were recorded on a 400 MHz and 100 MHz NMR spectrometer (Jeol and Bruker instrument) respectively, and CDCl₃ (from Eurisotop) was used as solvent. Chemical shifts for all the compounds are reported in parts per million (ppm) shifts (δ-value). One singlet at δ 7.26 ppm of ¹H and a triplet at 77.00 ppm of ¹³C NMR for CDCl₃ were taken as an internal standard. Signal patterns are mentioned as s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet and bm, broad multiplet. The coupling constant (*J*) for protons are given in hertz (Hz). Infrared (IR) spectra were recorded on a Perkin Elmer AX-1 spectrophotometer and reported in wave number (cm⁻¹). HRMS is reported for the peak of (M+H)⁺ using Agilent G6530AA (LC-HRMS-Q-TOF) spectrometer. Reagent-grade solvents were used for extraction and chromatography. The yield of the product was reported as chromatographically isolated pure materials.

3. Crystal data of product 5h:

Crystal Preparation: The product is a sticky solid at room temperature. To grow the crystal, a highly concentrated (saturated) solution of the compound **5h** was prepared by dissolving it in hot methanol. After that, the compound was cooled to room temperature and kept in the fridge for 3 days. After 3 days of cooling small crystals were generated (with minimum exposure of room temperature).

X-ray structure analysis: Intensity data for the compound **5h** was collected at 288 K on an XtaLAB Synergy, Single source at home/near, HyPix diffractometer using graphite monochromated Mo-K α radiation $\lambda = 0.71073$ Å. The structure was solved by Using Olex2² with SHELXT³ structure solution program using Intrinsic Phasing and refined with the olex2 refine⁴ refinement package using Gauss-Newton minimisation. The hydrogen atoms were placed at the calculated positions and included in the last cycles of the refinement. The graphics for publication were prepared by using Mercury software. Crystallographic data collection and structure solution parameters are summarized in Table 1.

Table S1: Crystallographic data of **5h**

<i>Empirical formula</i>	$C_{21}H_{20}O_3S$
CCDC	2297558
<i>Formula weight</i>	352.44
<i>Temperature/K</i>	288
<i>Crystal system</i>	monoclinic
<i>Space group</i>	C2/c
<i>a/Å</i>	22.2427(13)
<i>b/Å</i>	5.4882(4)
<i>c/Å</i>	29.653(2)
$\alpha/^\circ$	90
$\beta/^\circ$	90.096(6)
$\gamma/^\circ$	90
<i>Volume/Å³</i>	3619.8(4)
<i>Z</i>	68
ρ_{calc}/cm^3	1.293
μ/mm^{-1}	0.195
<i>F(000)</i>	1489.9
<i>Crystal size/mm³</i>	0.1 × 0.1 × 0.1
<i>Radiation</i>	Mo K α ($\lambda = 0.71073$)

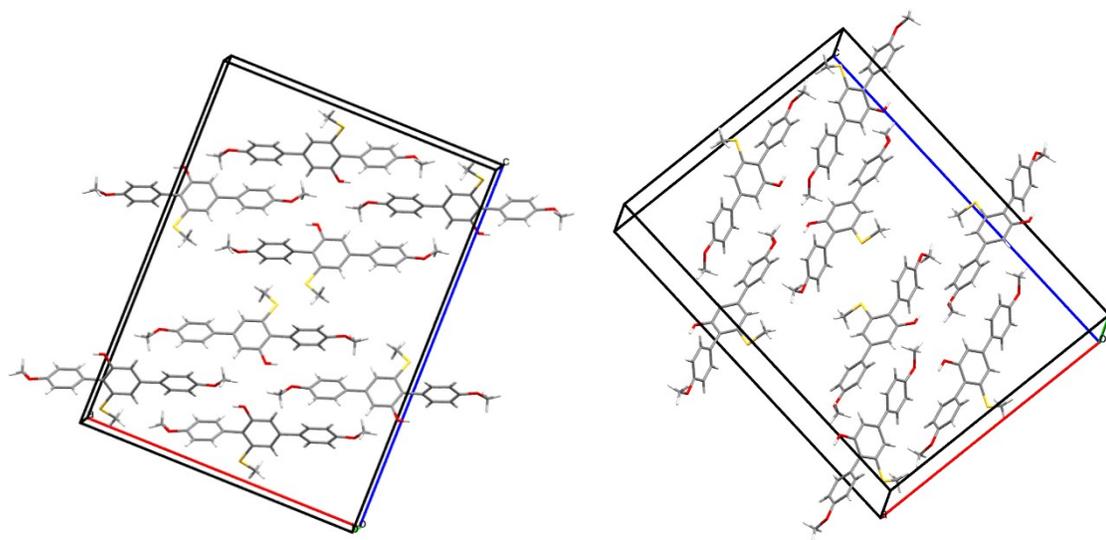


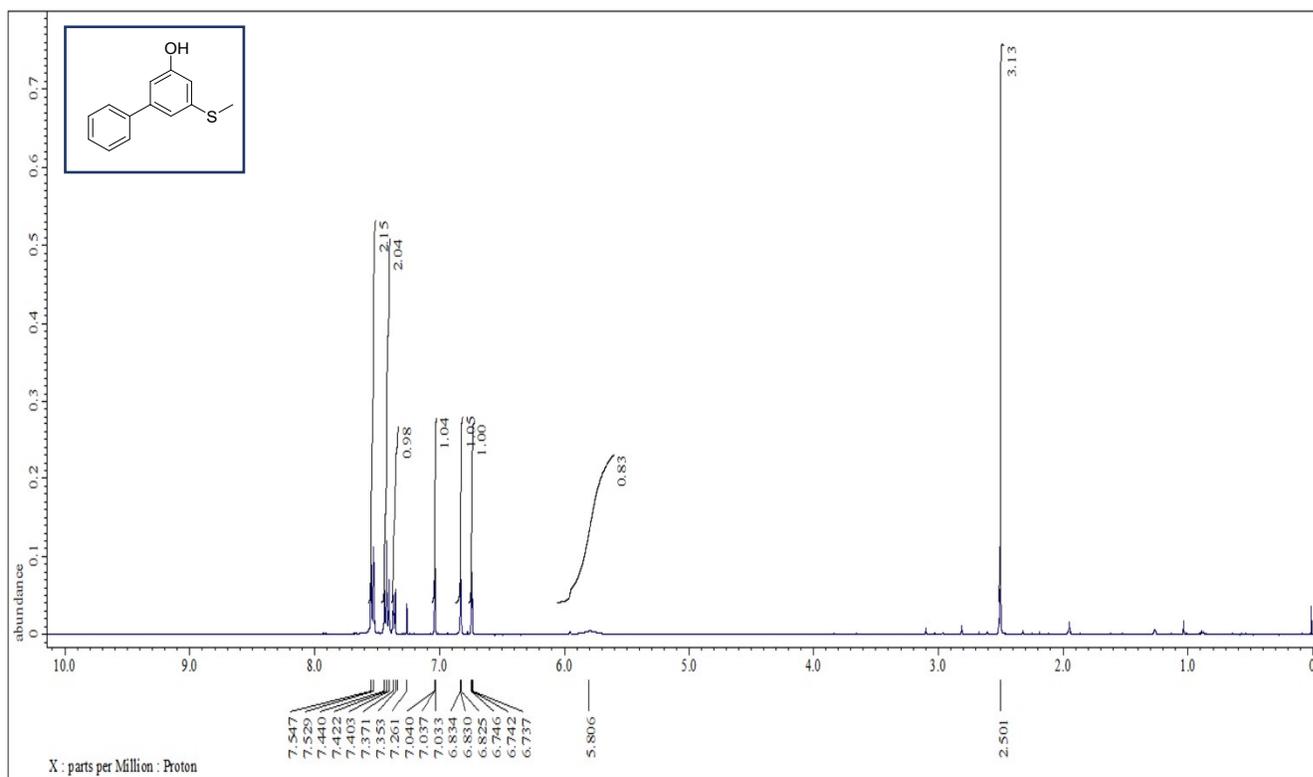
Figure 2. Packing structure of 5h in a unit cell.

4. References:

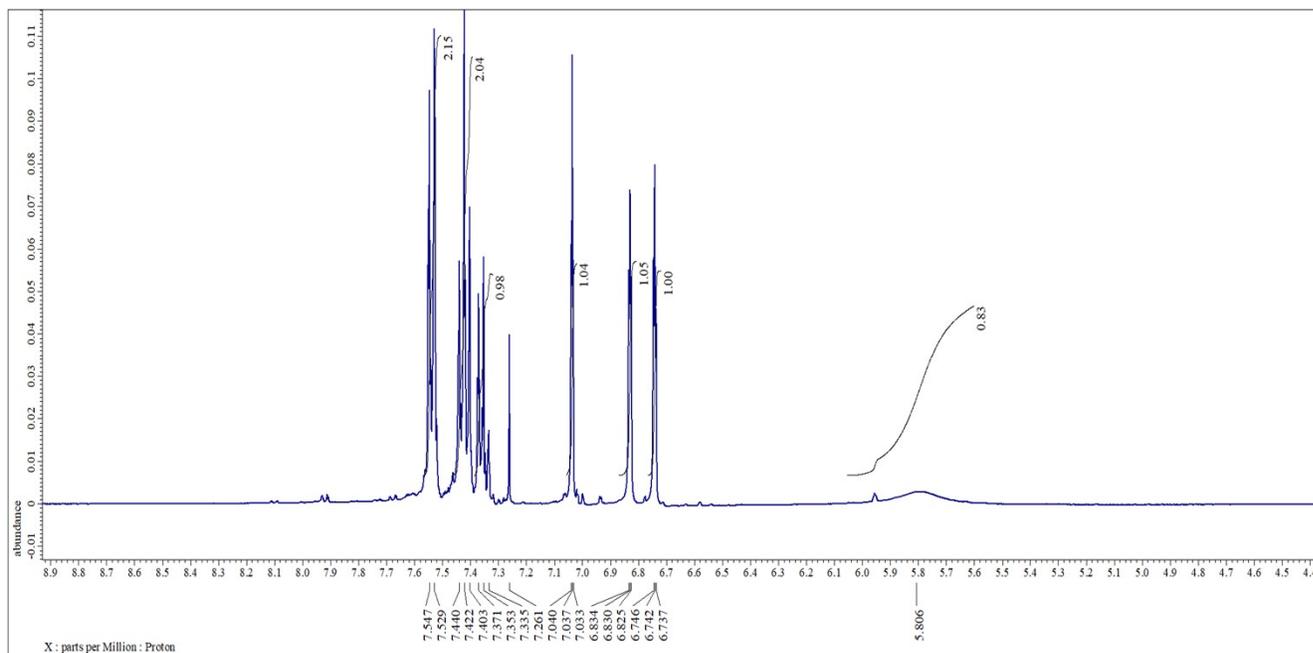
1. (a) Verma, S.; Sharon, S. Intramolecular cyclization to fused pyranoisoxazoles and molecular packing motifs identification through X-ray structural studies. *J. Indian Chem. Soc.*, **2021**, *98*, 100135; (b) Shaw, R.; Pratap, R. A Green and Base-Free Arylation of Thiomethylated 2-pyranones and Ketene Dithioacetals via Liebeskind-Srogl Coupling in Water. *Asian J. Org. Chem.*, **2022**, *11*, e202200078.
2. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K. & Puschmann, H. (2009), *J. Appl. Cryst.* *42*, 339-341.
3. Sheldrick, G.M. (2015). *Acta Cryst.* *A71*, 3-8.
4. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). *Acta Cryst.* *A71*, 59-75.

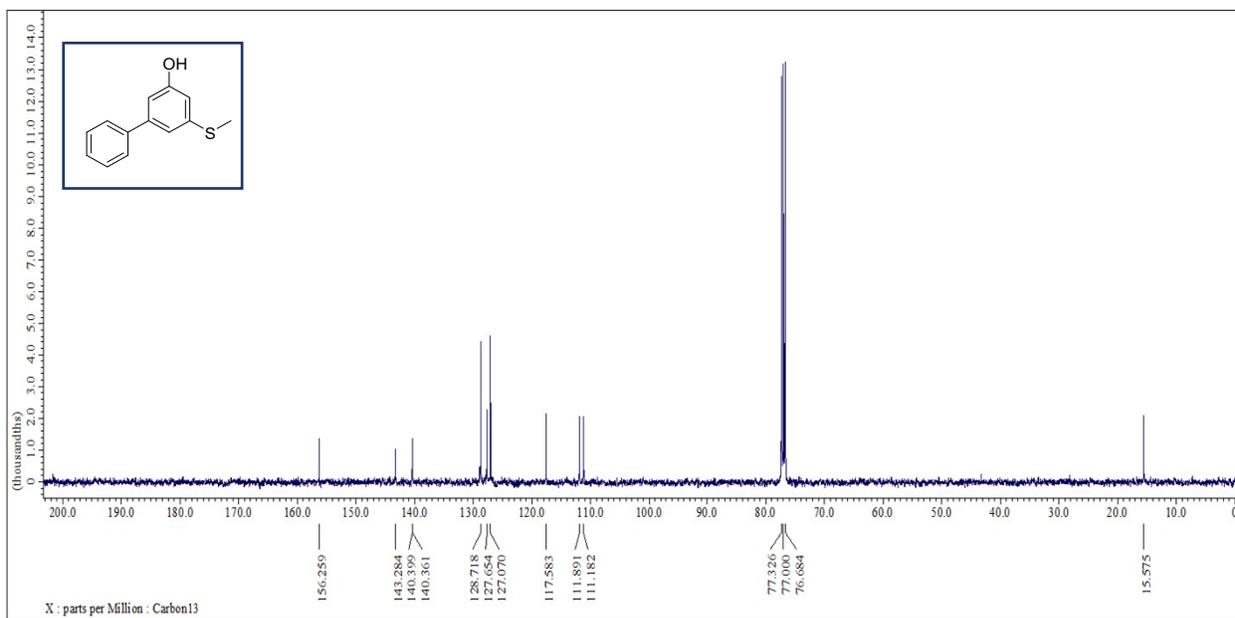
5. ^1H and ^{13}C NMR spectra of products

3a. 5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR

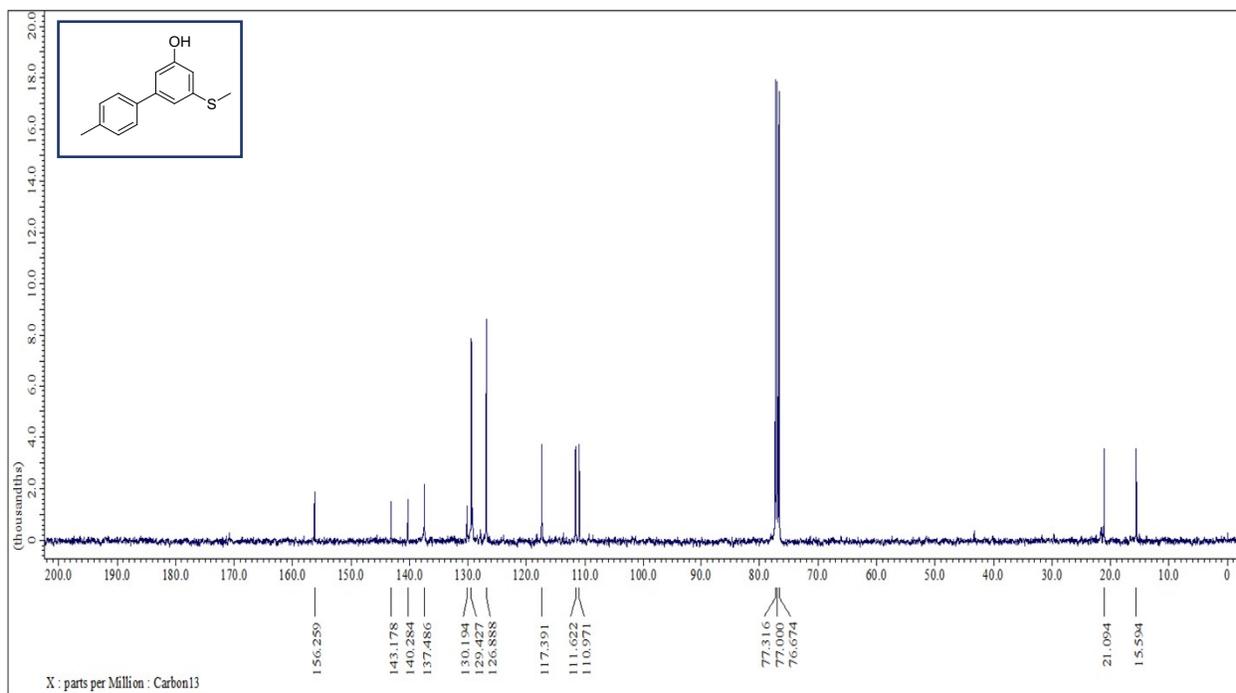
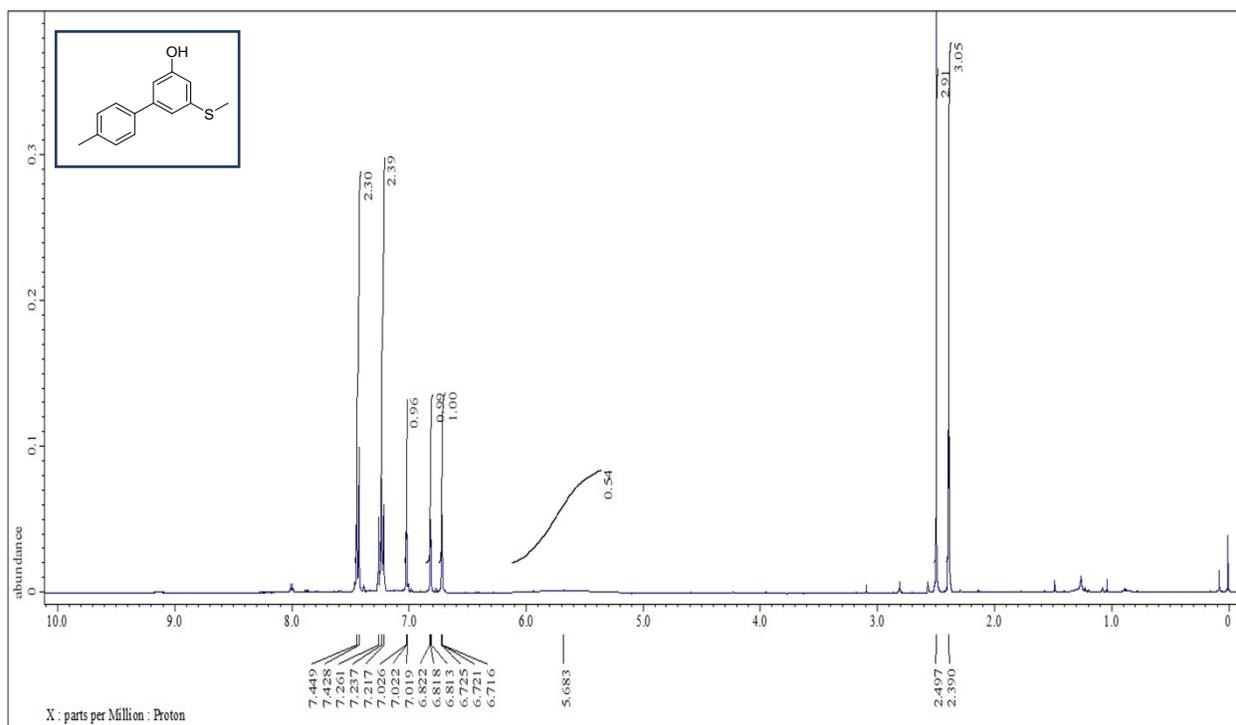


Expanded view for aromatic and phenolic proton.

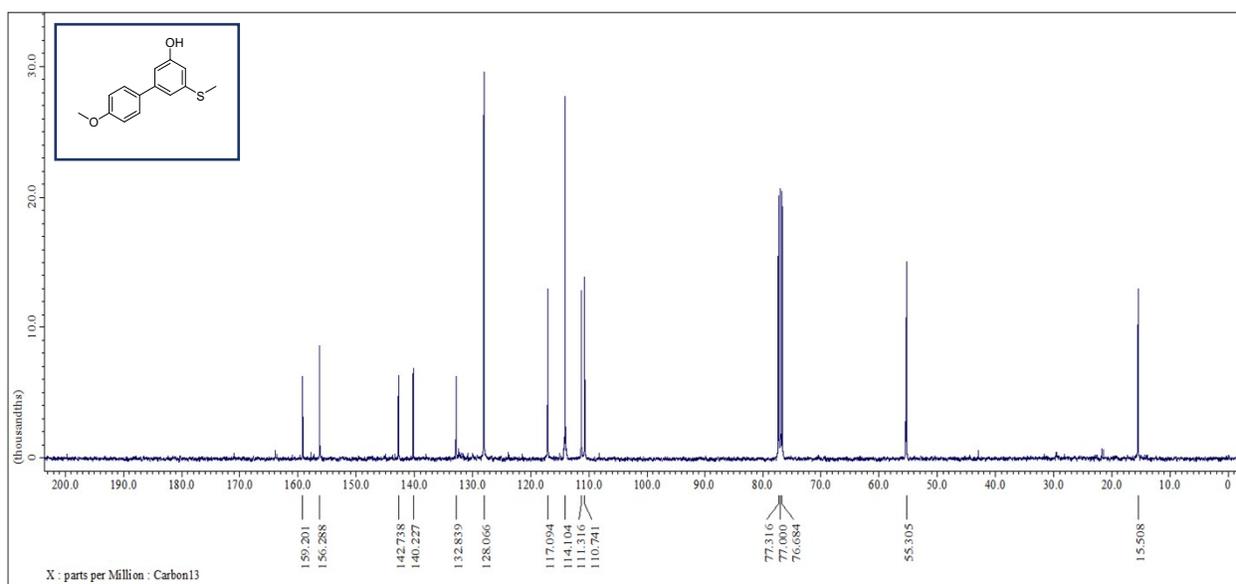
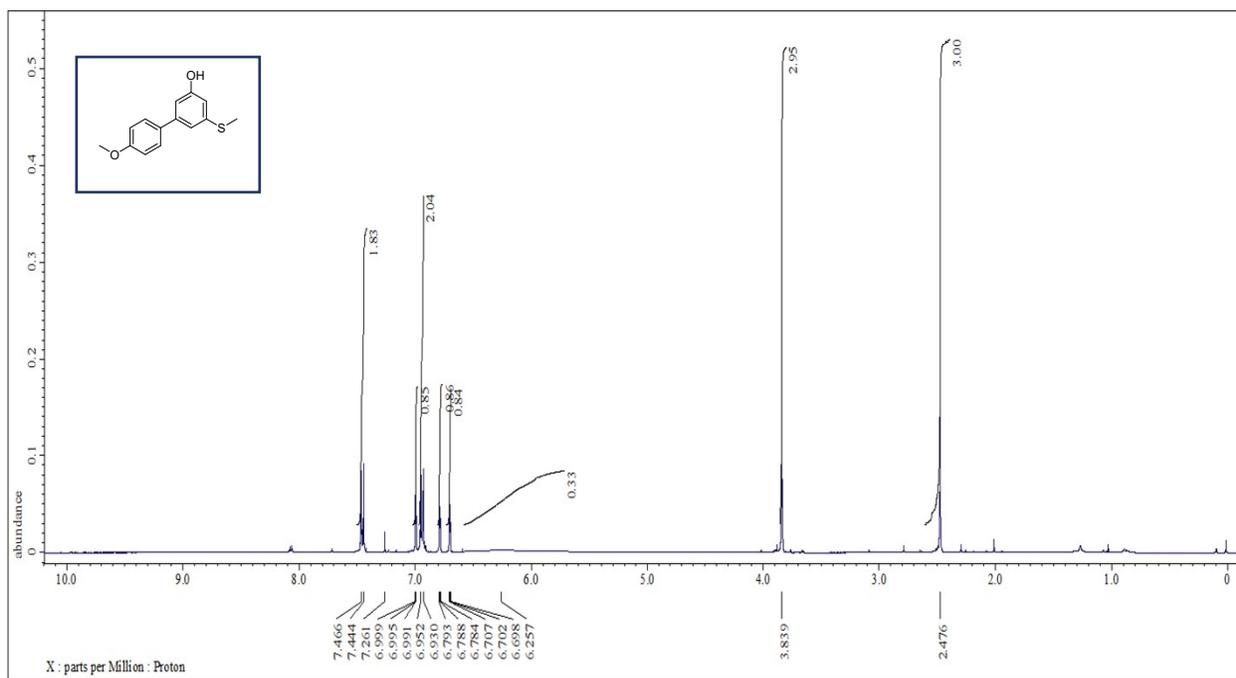




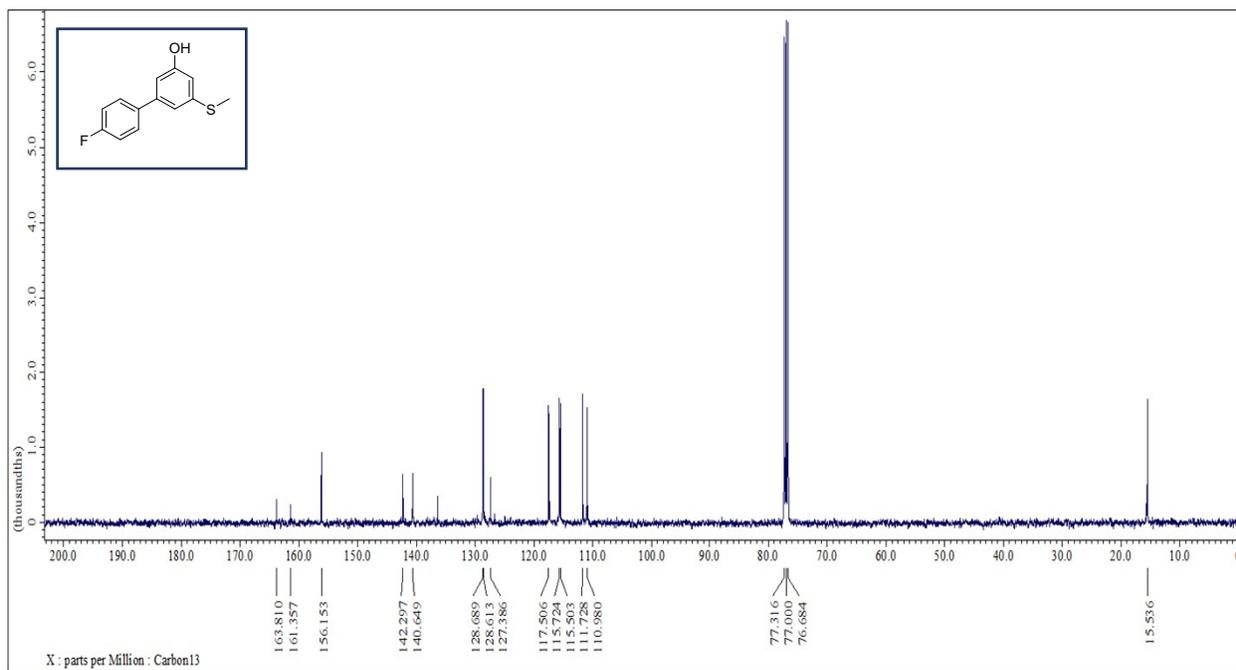
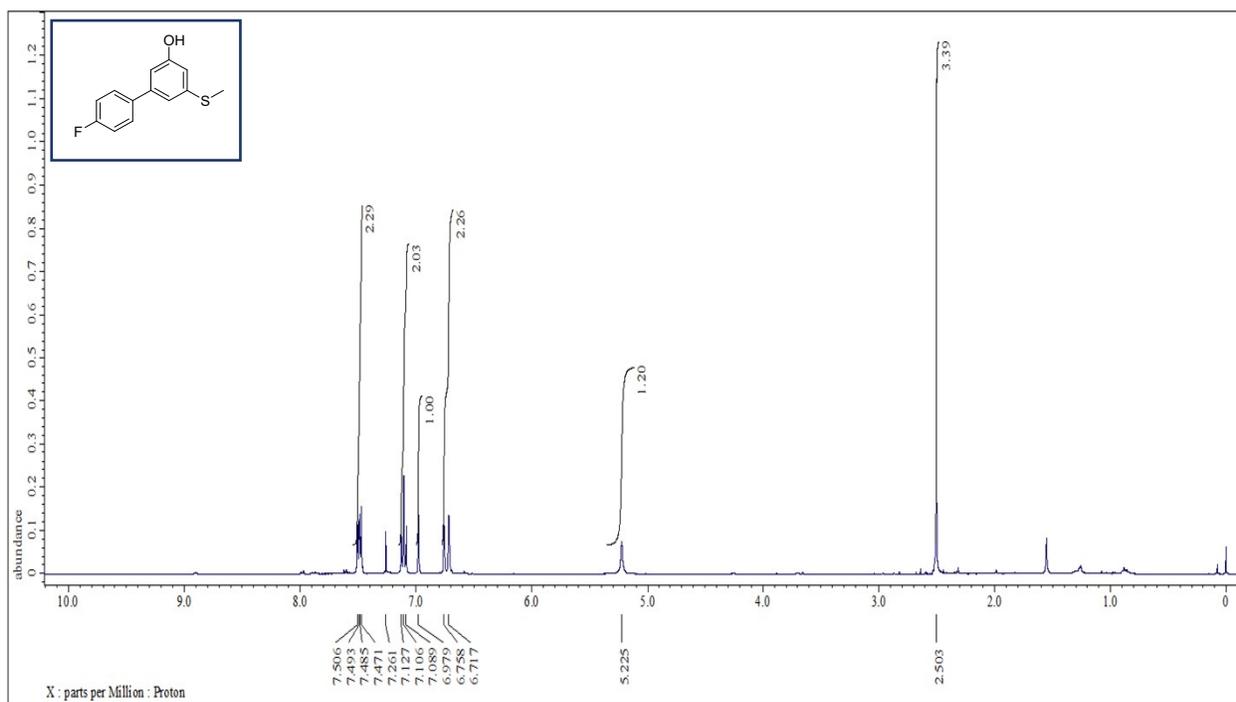
3b. 4'-methyl-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



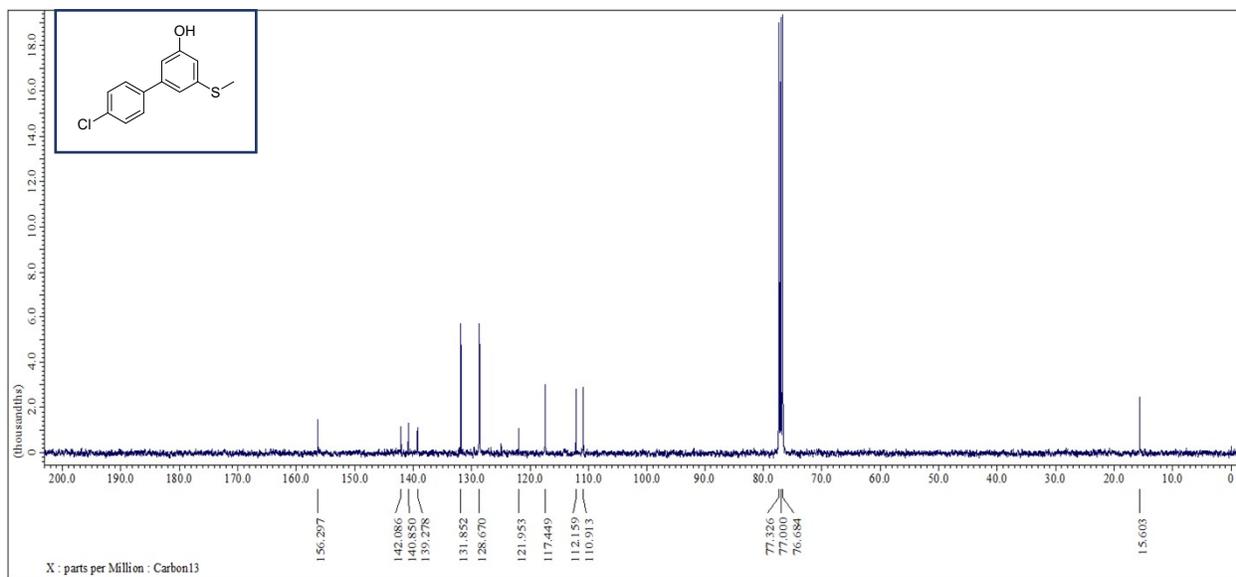
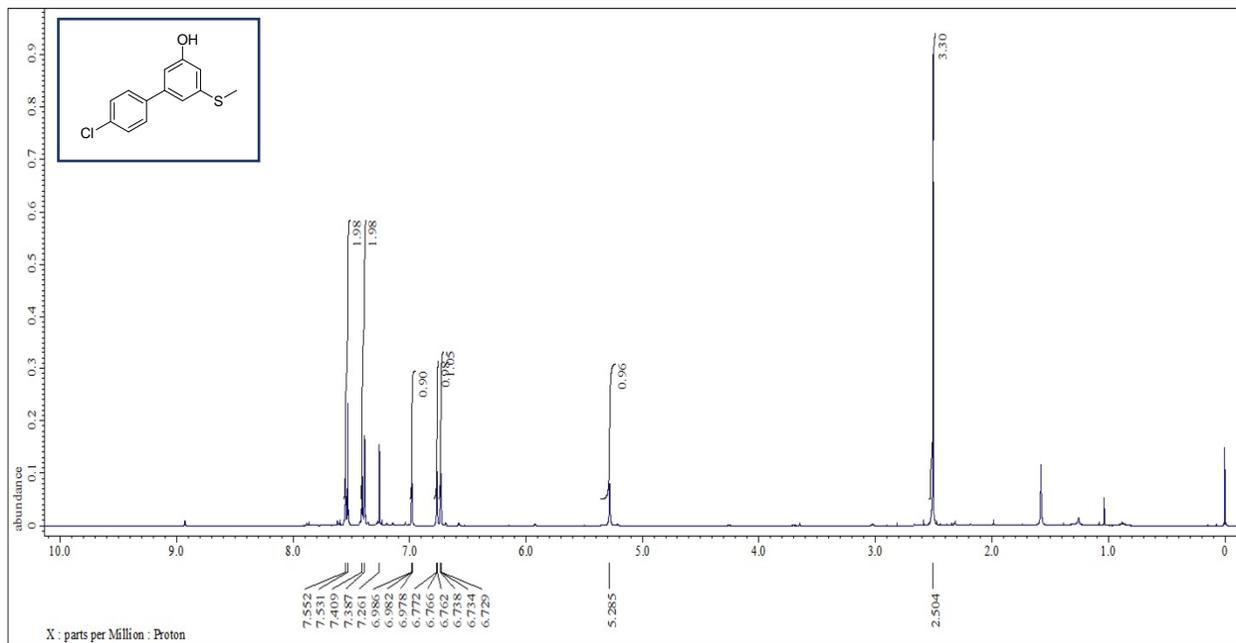
3c. 4'-methoxy-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



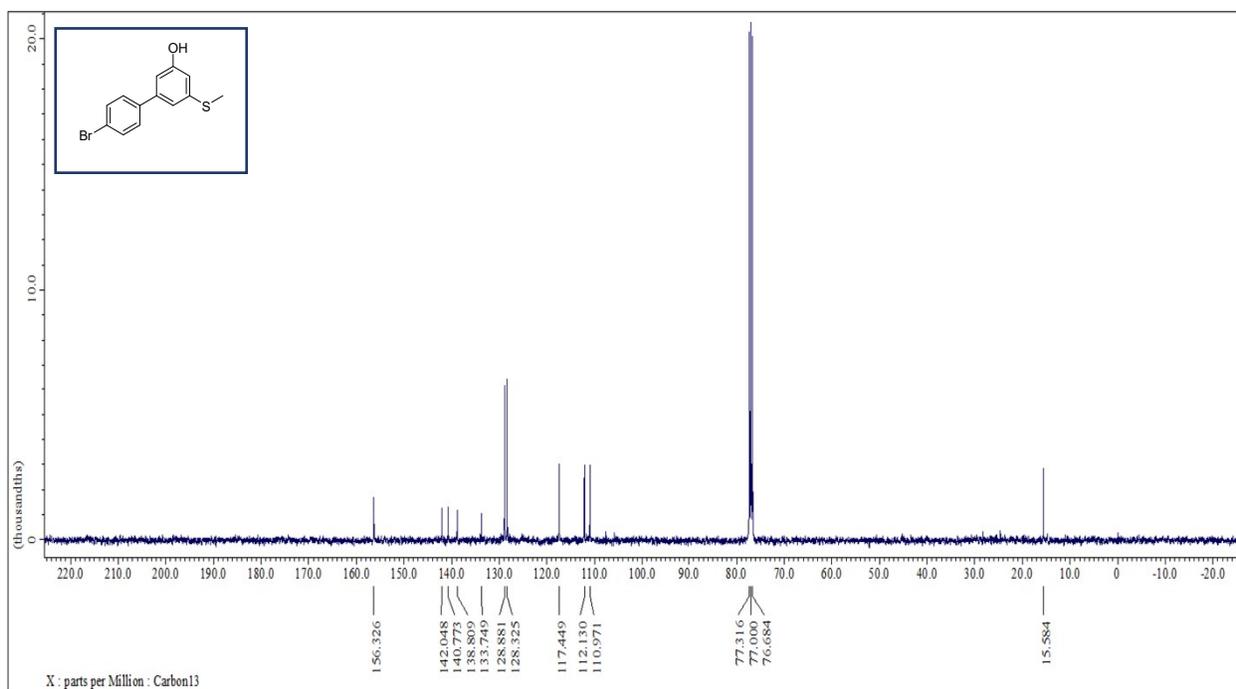
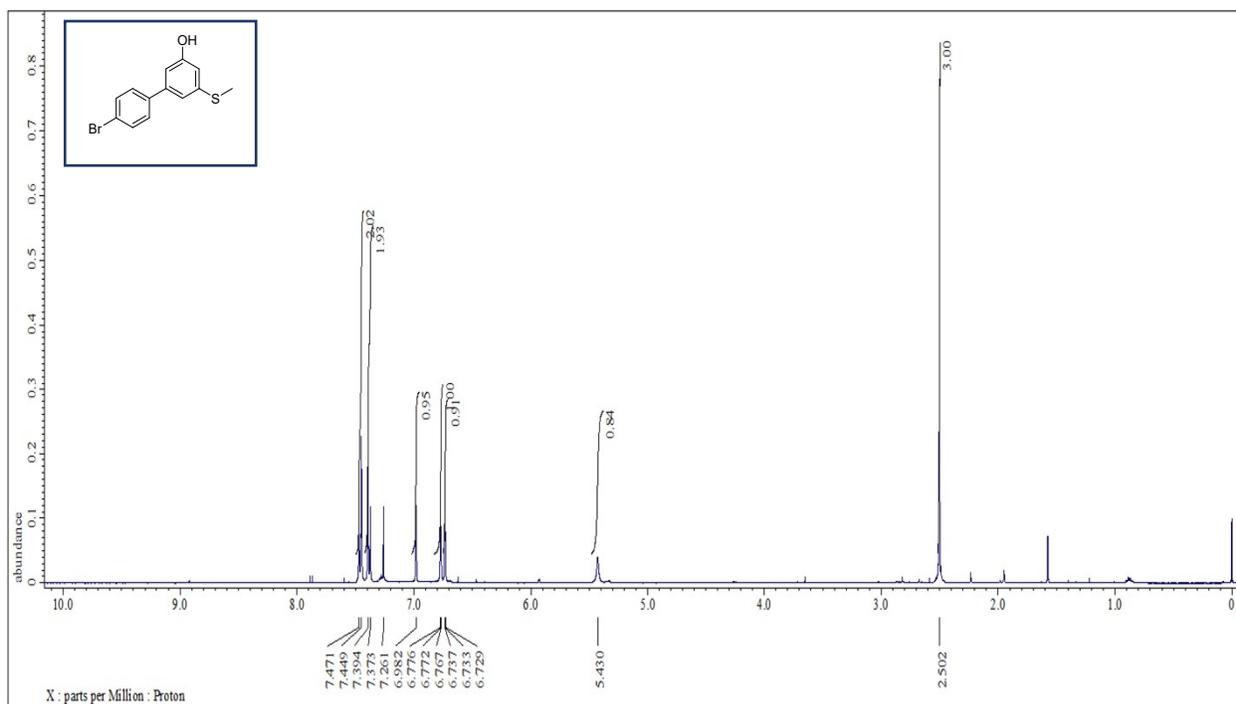
3d. 4'-fluoro-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



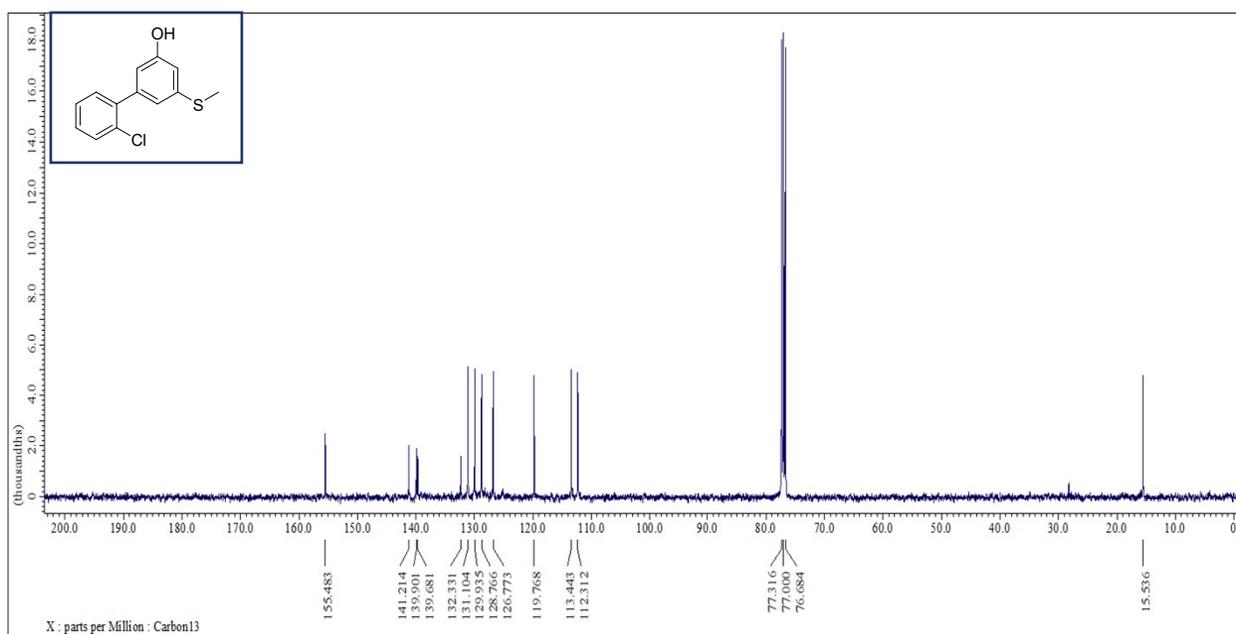
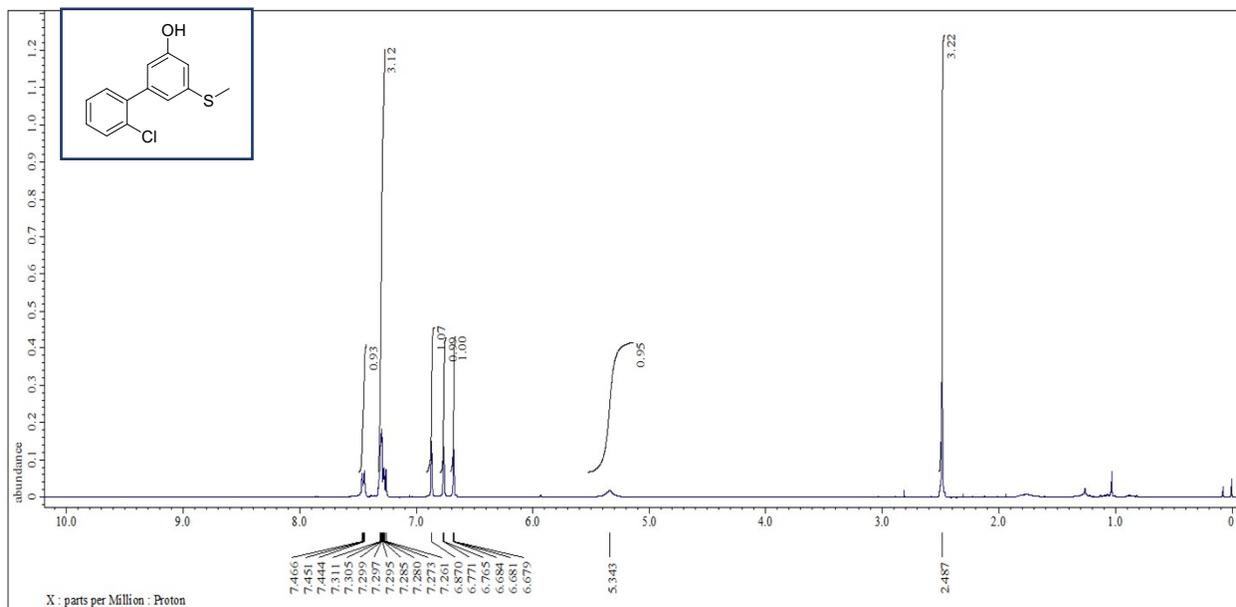
3e. 4'-chloro-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



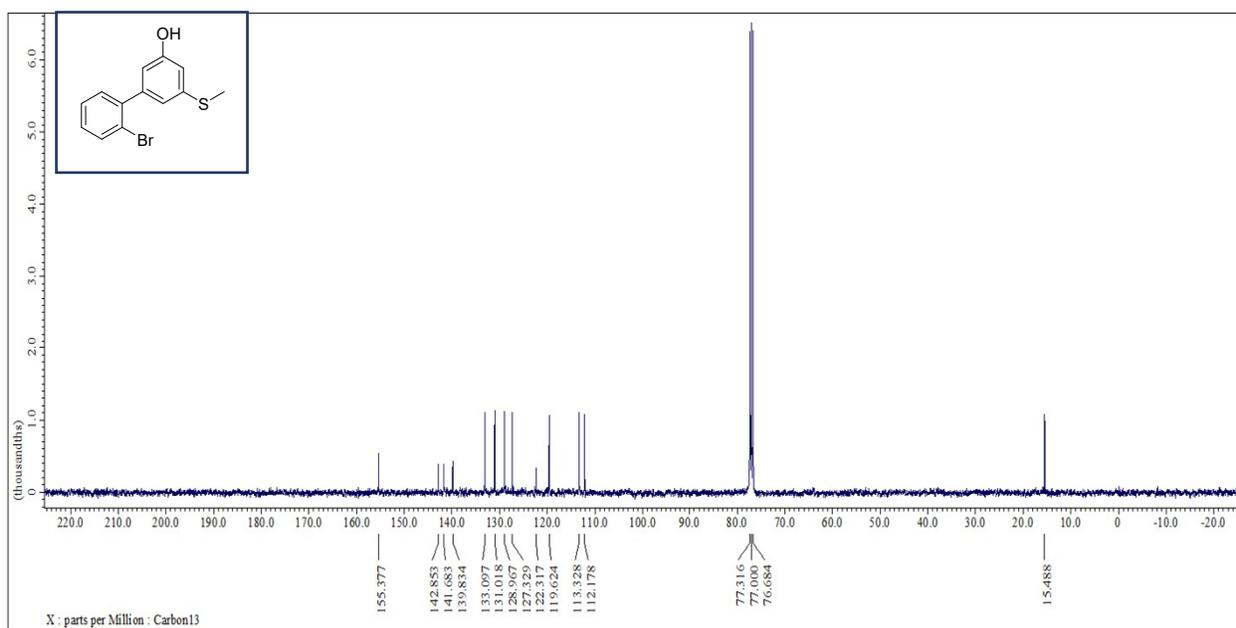
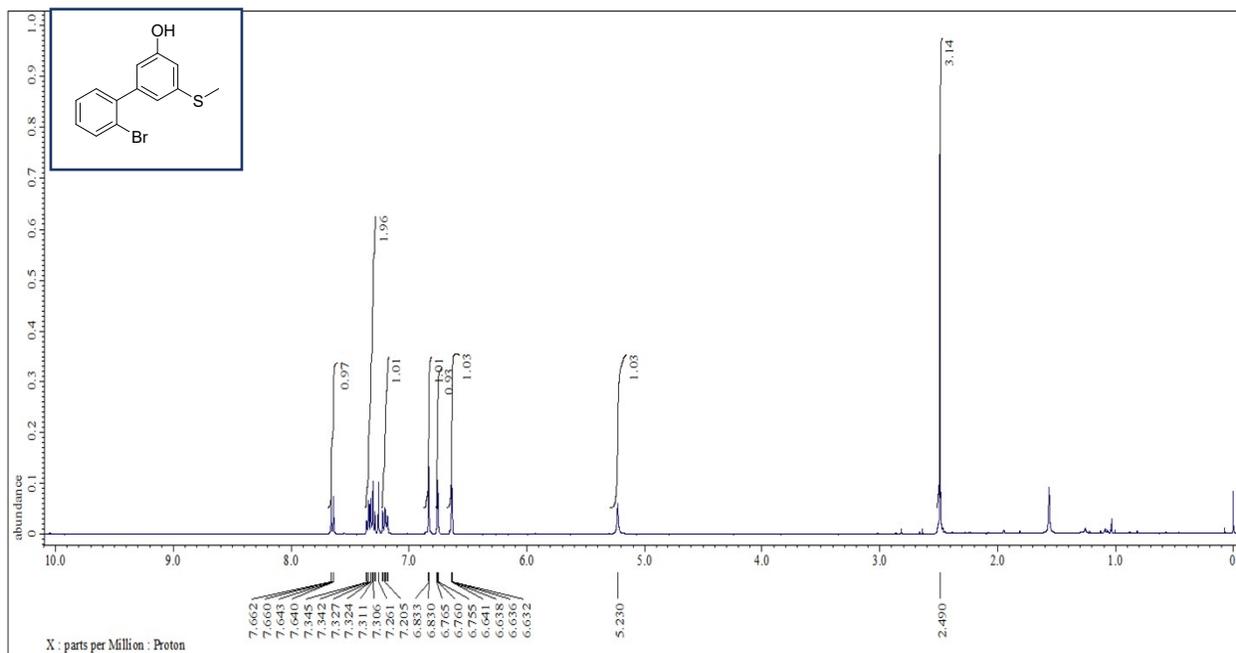
3f. 4'-bromo-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



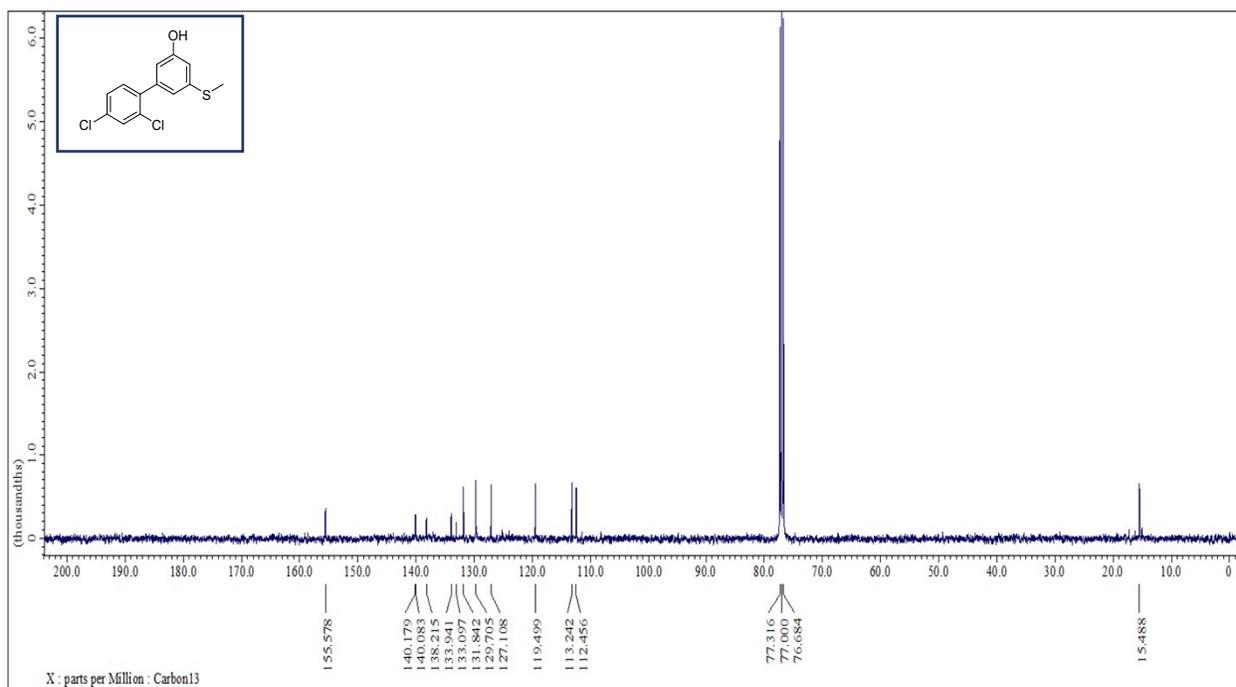
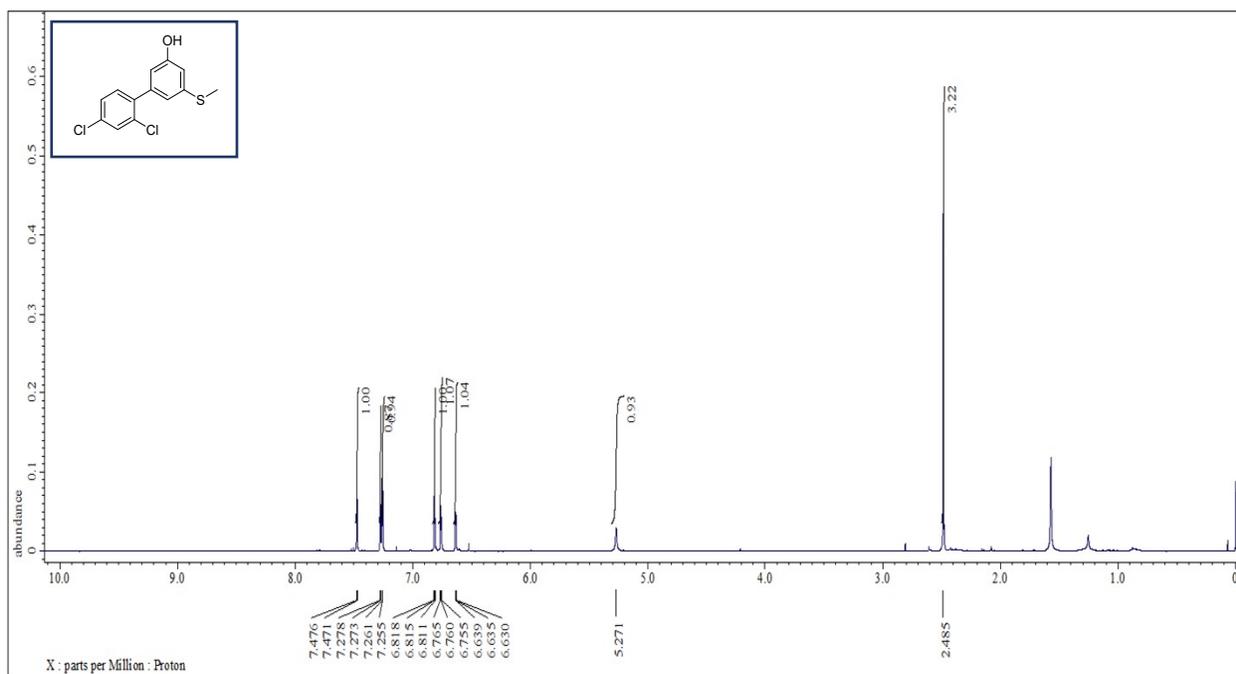
3g. 2'-chloro-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



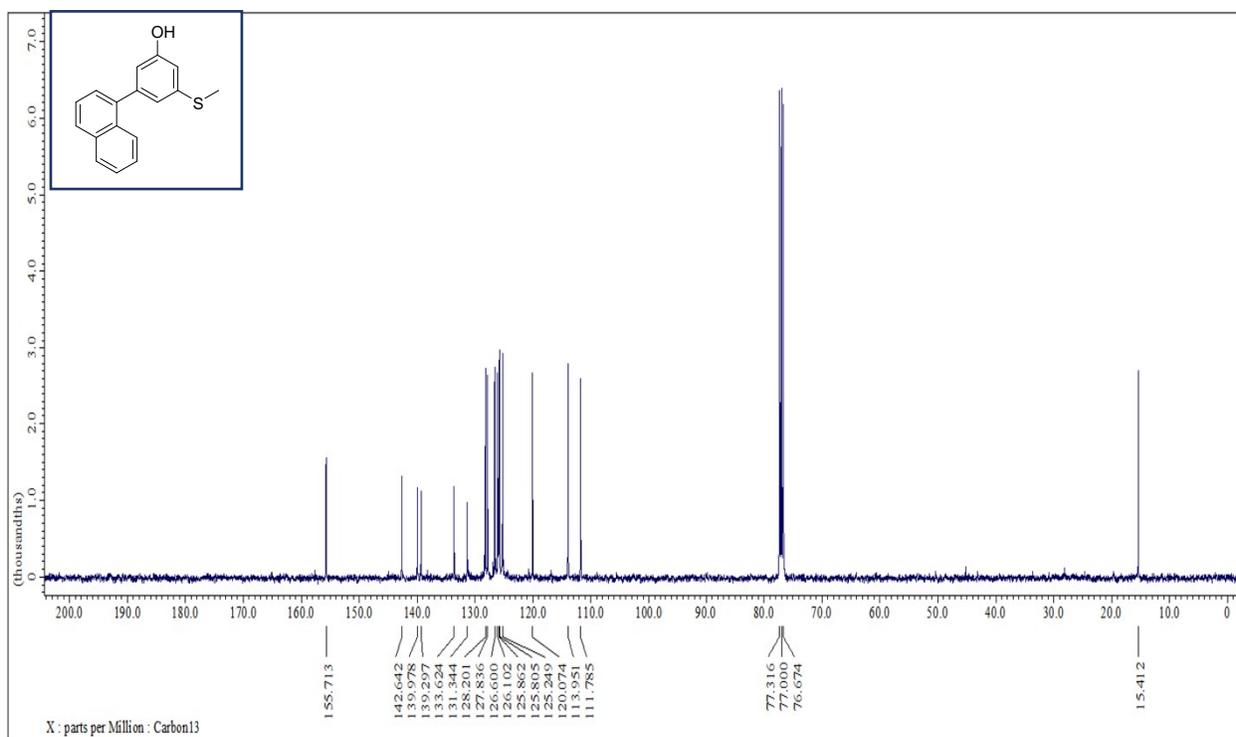
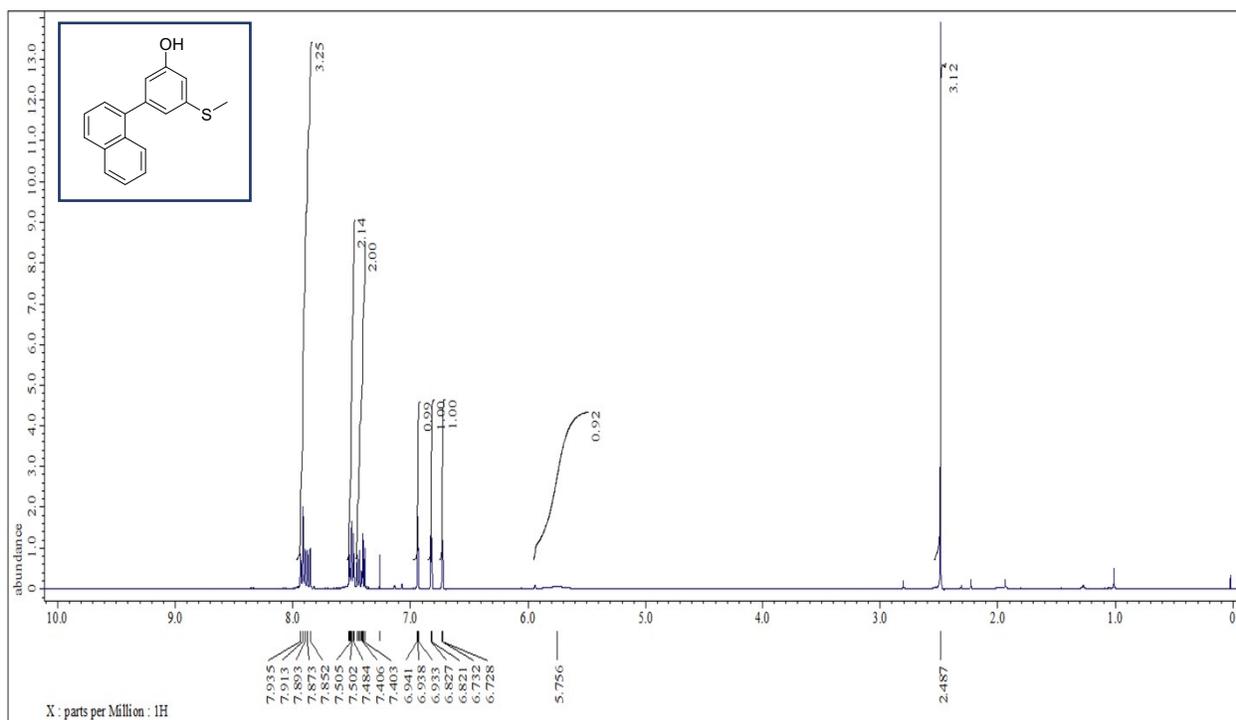
3h. 2'-bromo-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



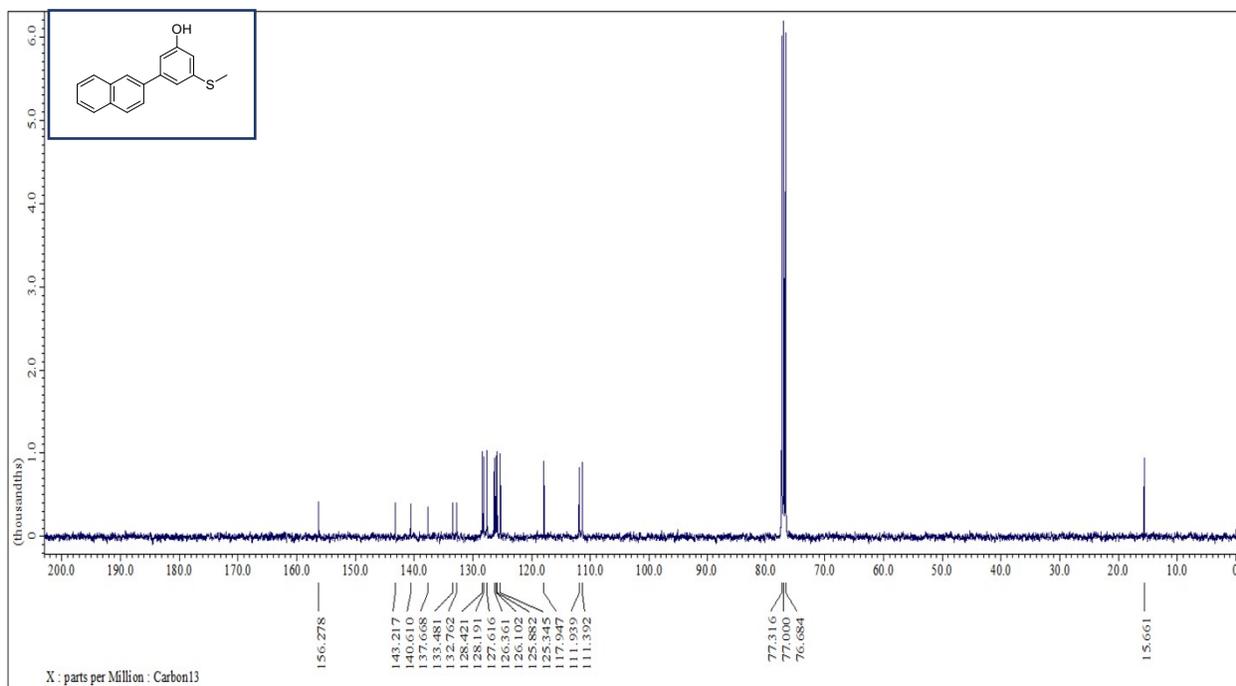
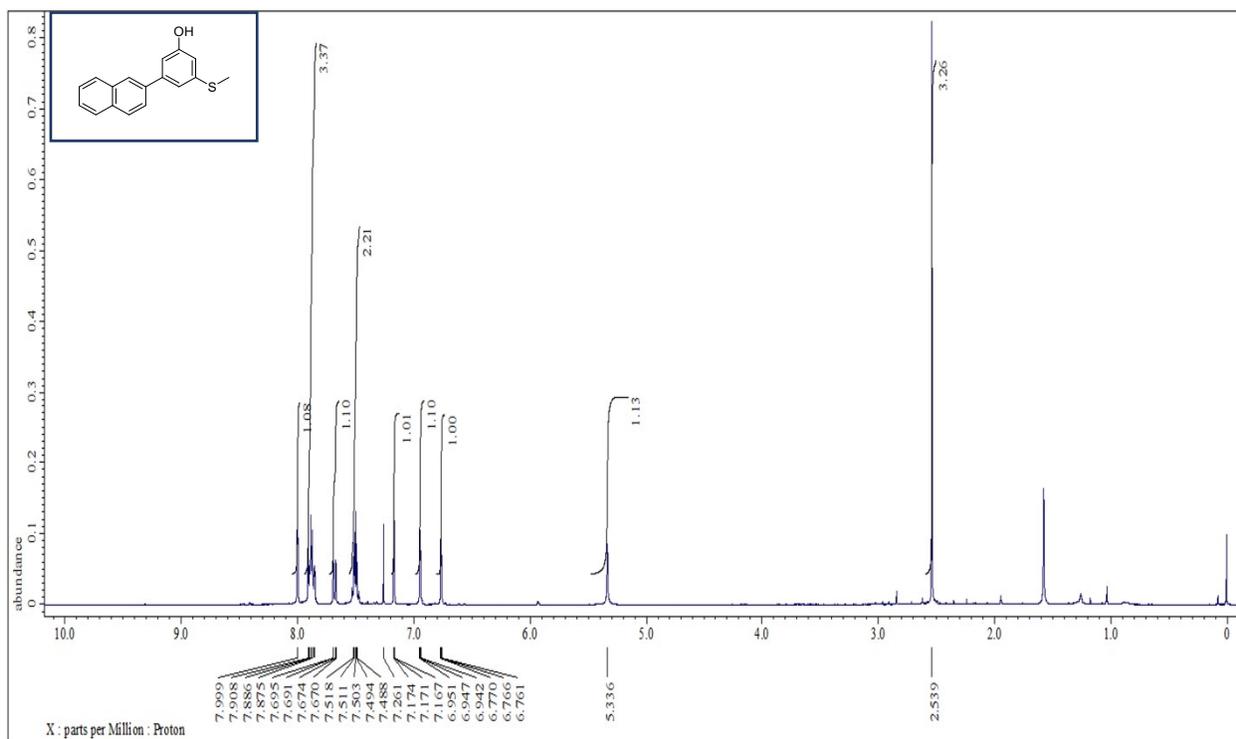
3i. 2',4'-dichloro-5-(methylthio)-[1,1'-biphenyl]-3-ol: ¹H and ¹³C NMR



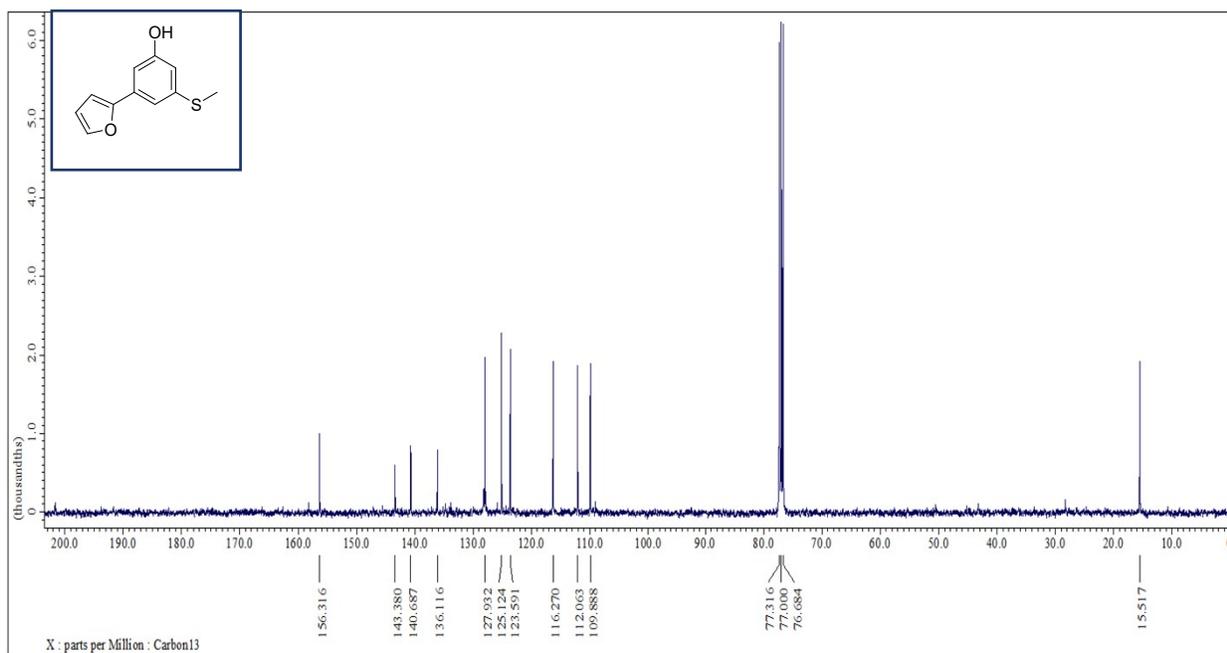
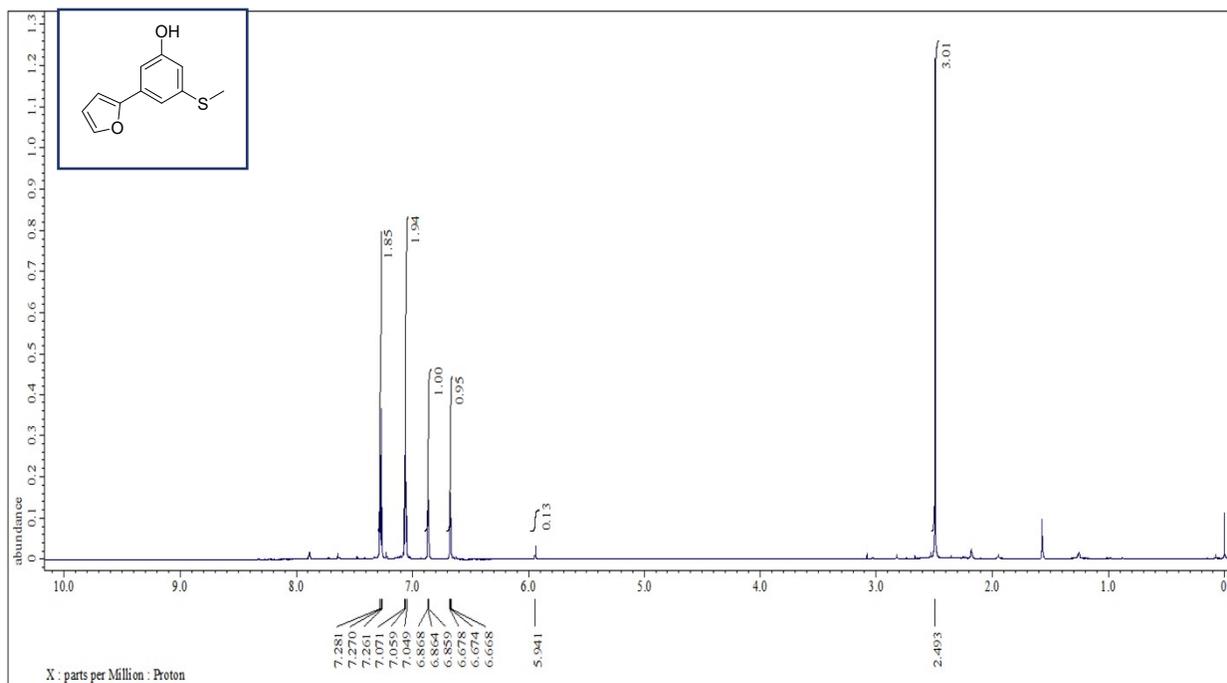
3j. 3-(methylthio)-5-(naphthalen-1-yl)phenol: ^1H and ^{13}C NMR



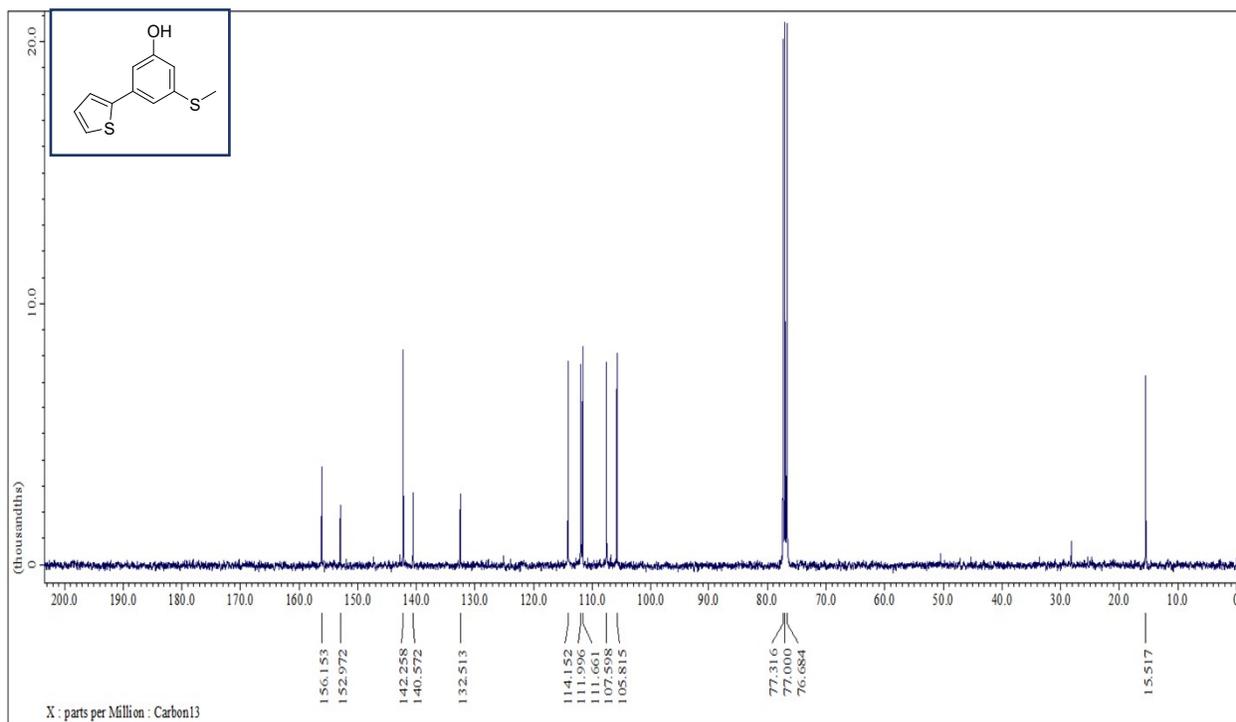
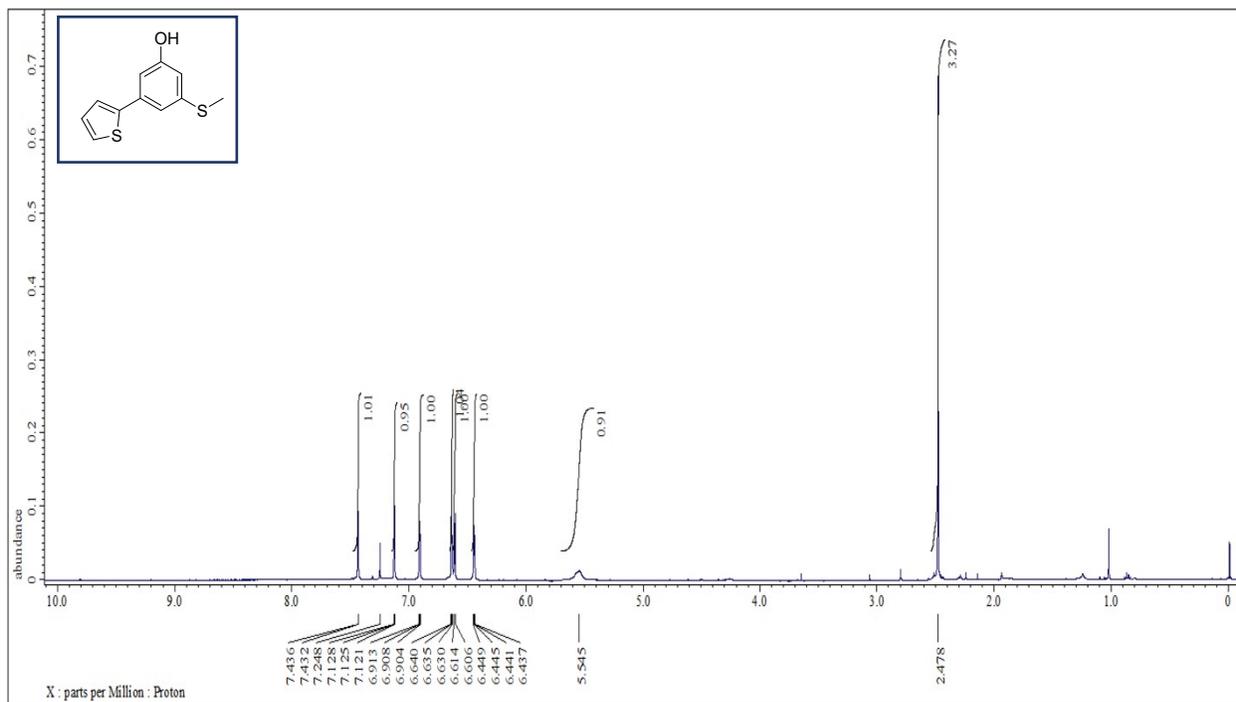
3k. 3-(methylthio)-5-(naphthalen-2-yl)phenol: ^1H and ^{13}C NMR



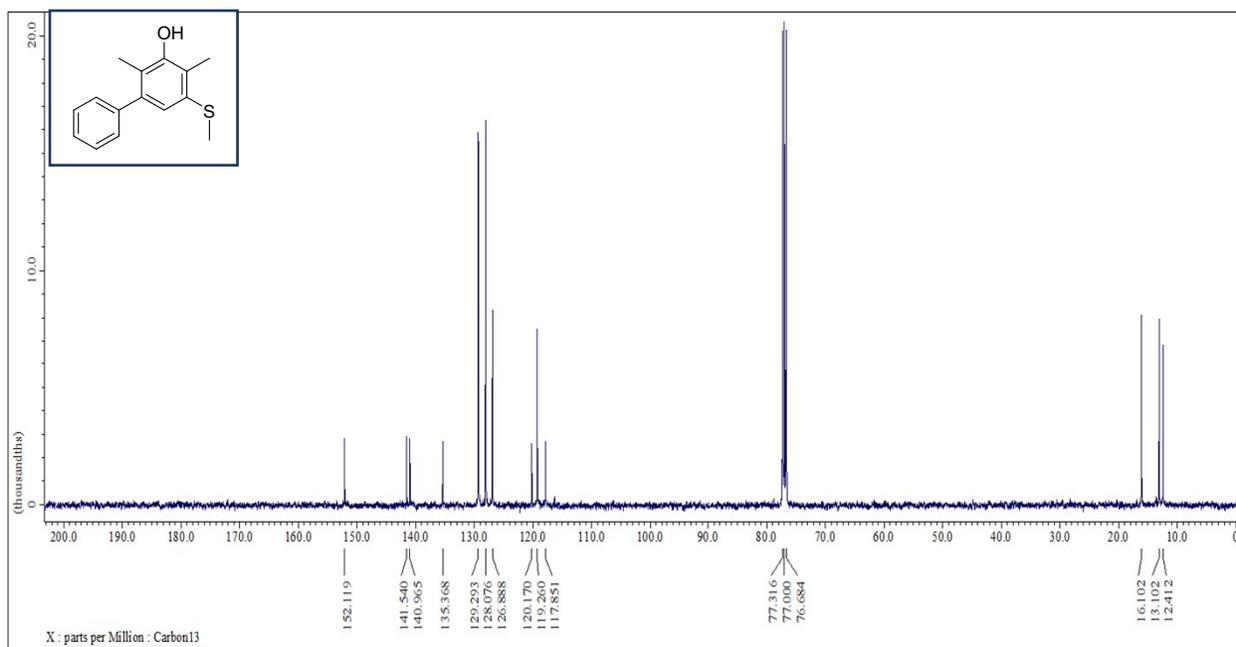
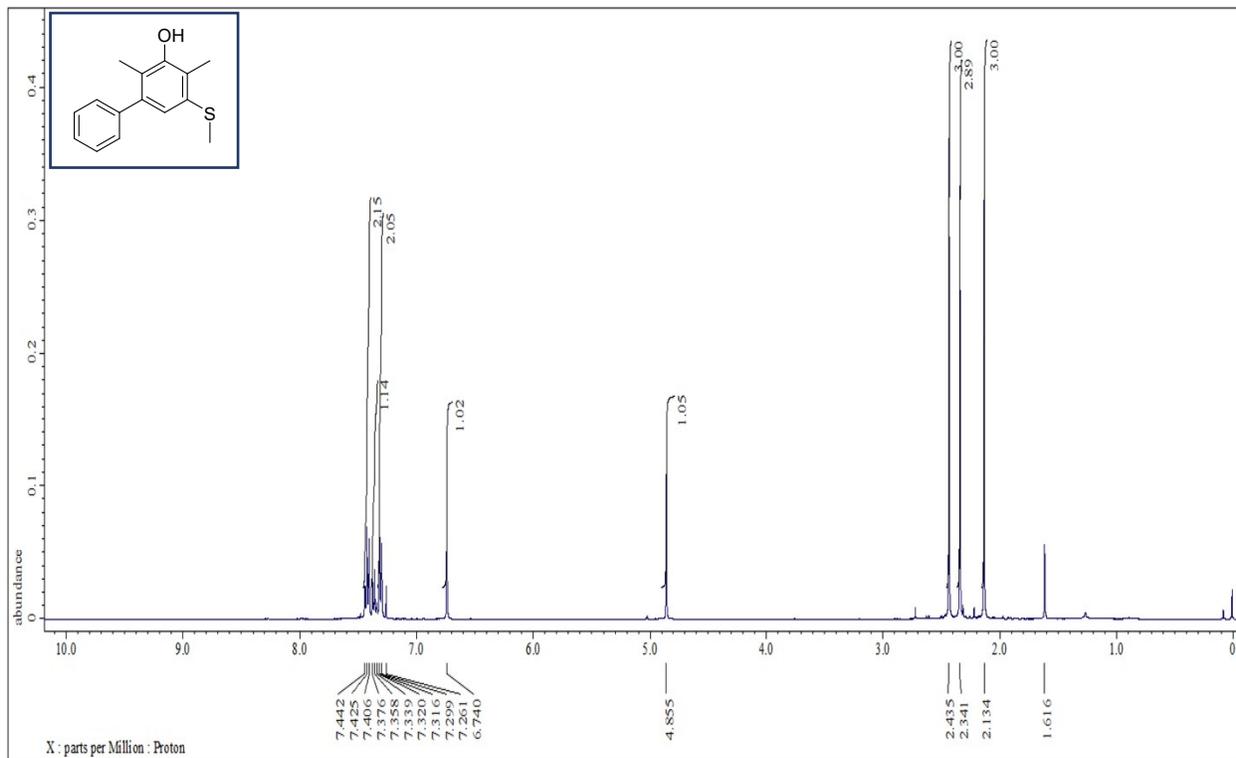
3l. 3-(furan-2-yl)-5-(methylthio)phenol: ^1H and ^{13}C NMR



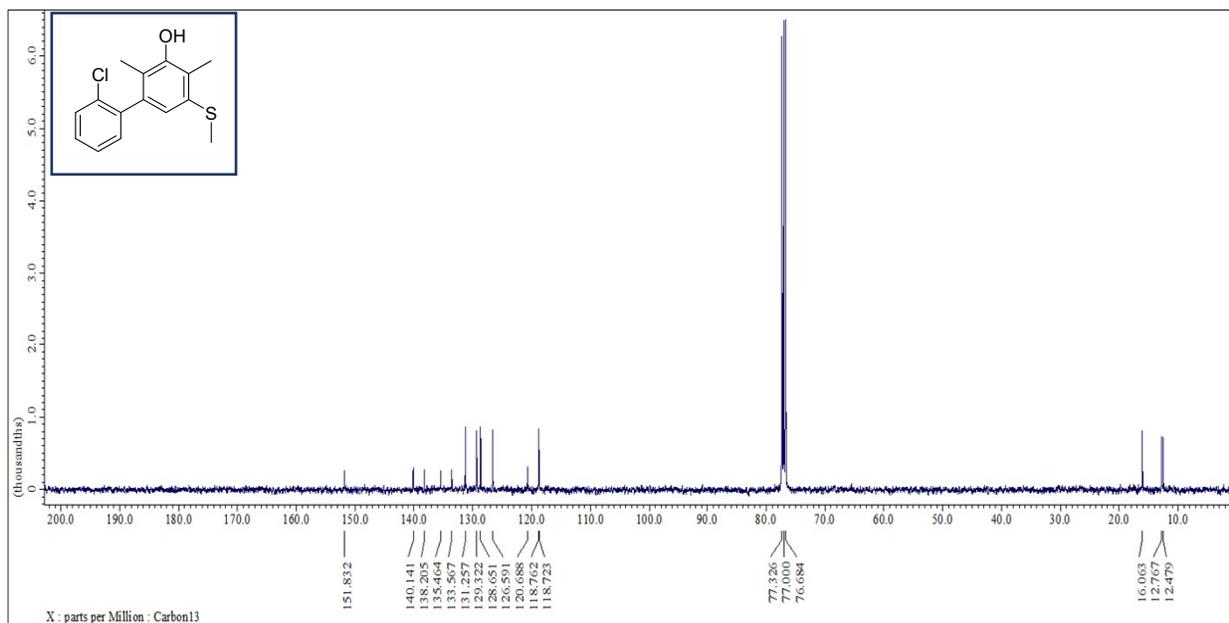
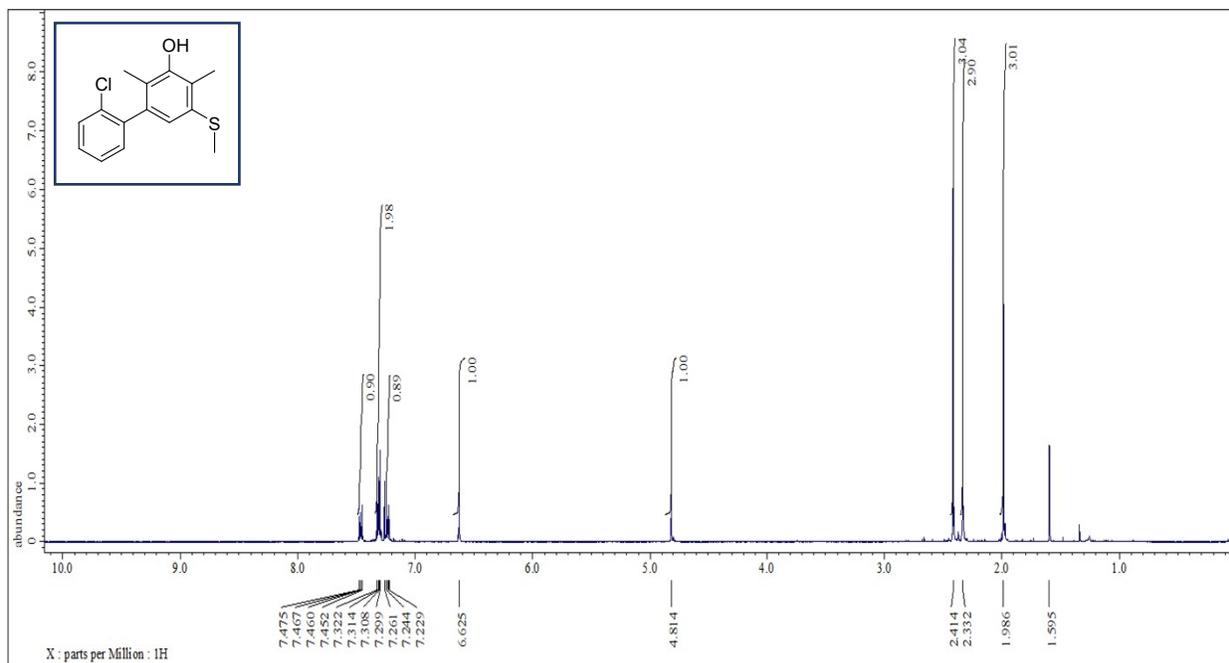
3m. 3-(methylthio)-5-(thiophen-2-yl)phenol: ^1H and ^{13}C NMR



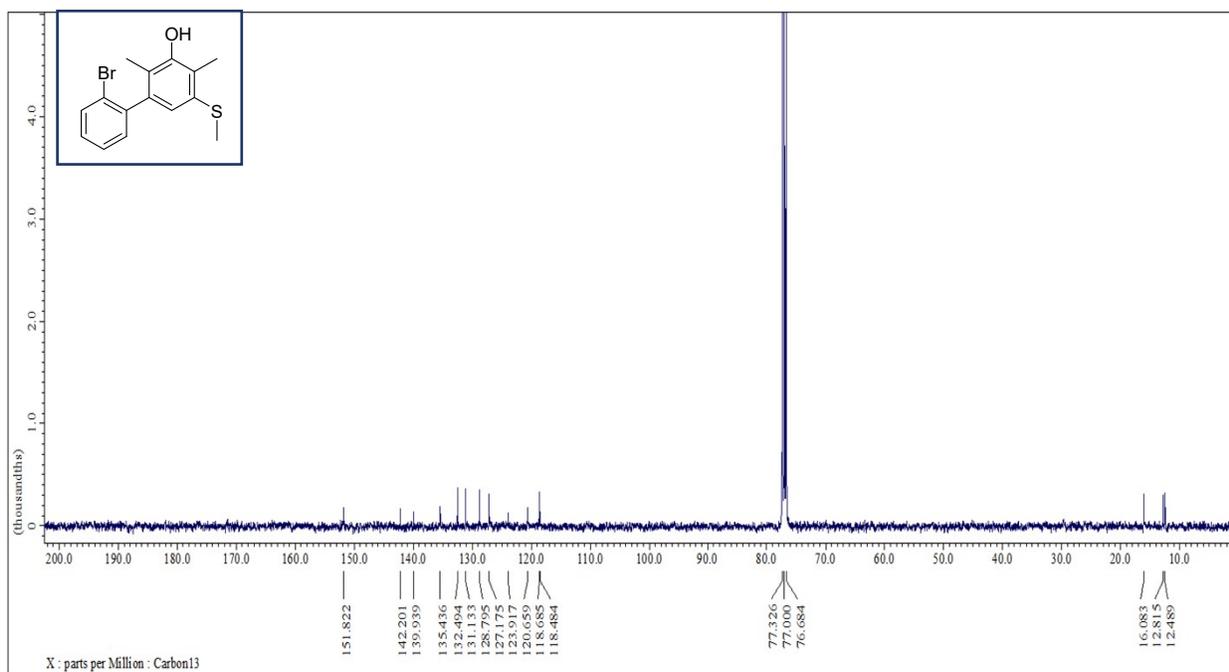
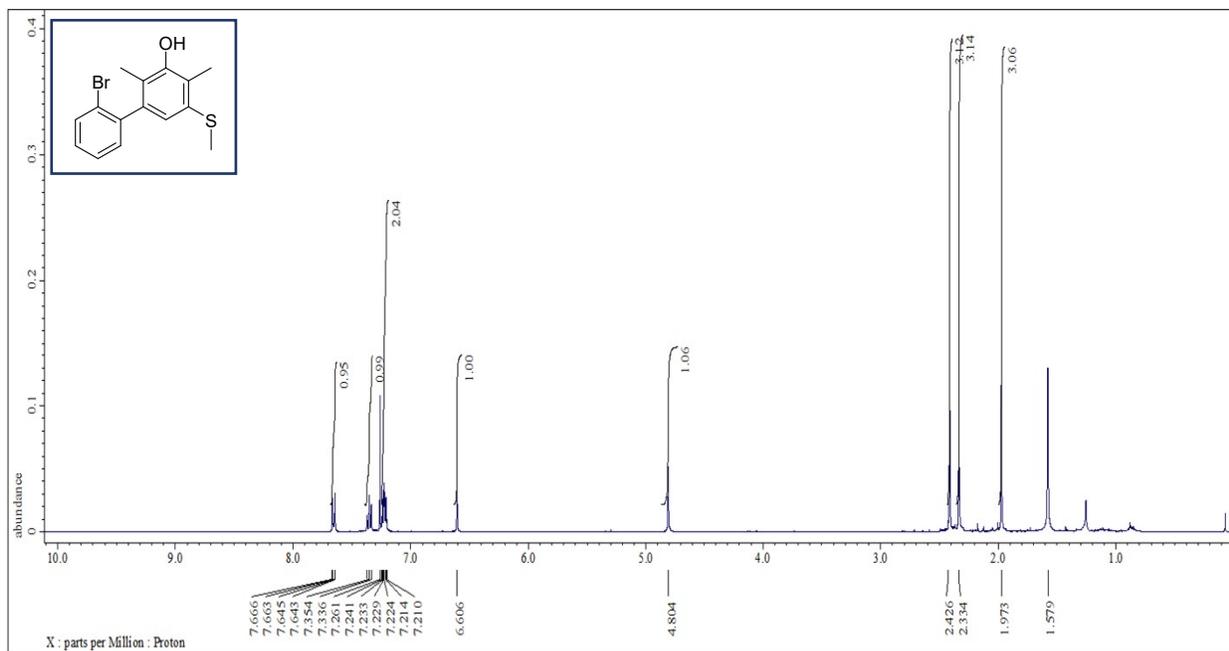
5a. 2,4-dimethyl-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



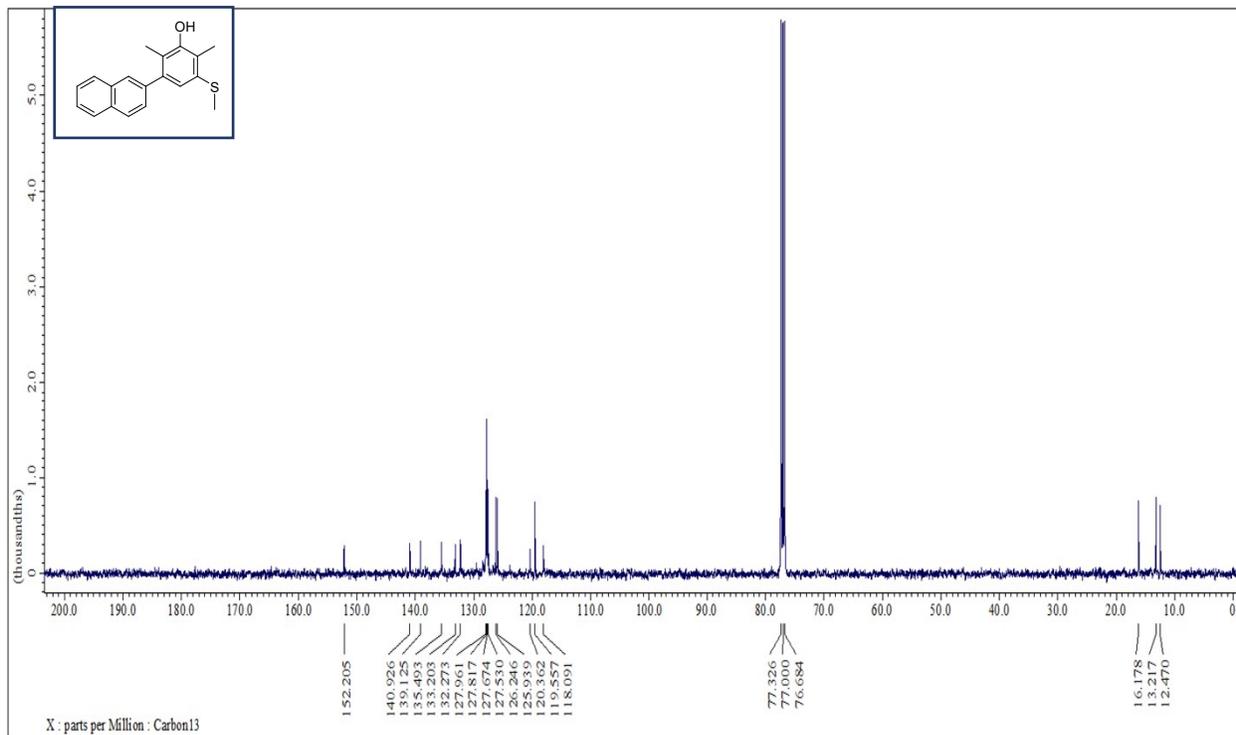
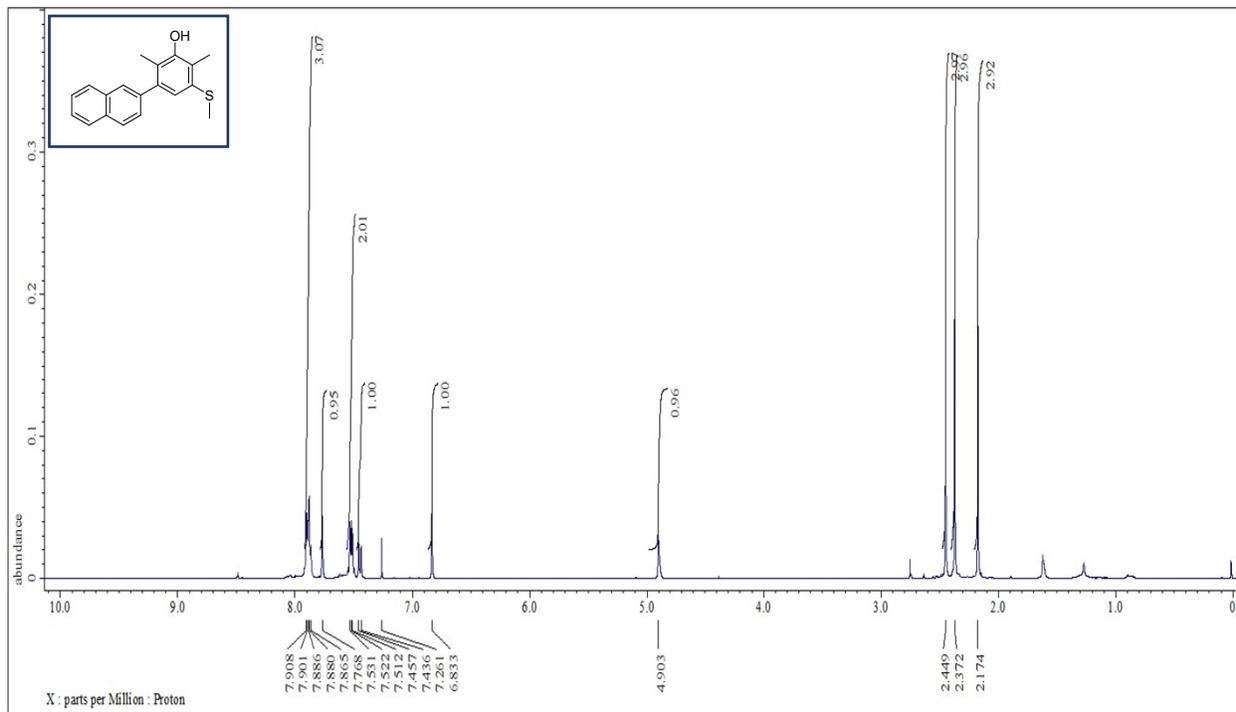
5b. 2'-chloro-2,4-dimethyl-5-(methylthio)-[1,1'-biphenyl]-3-ol: ¹H and ¹³C NMR



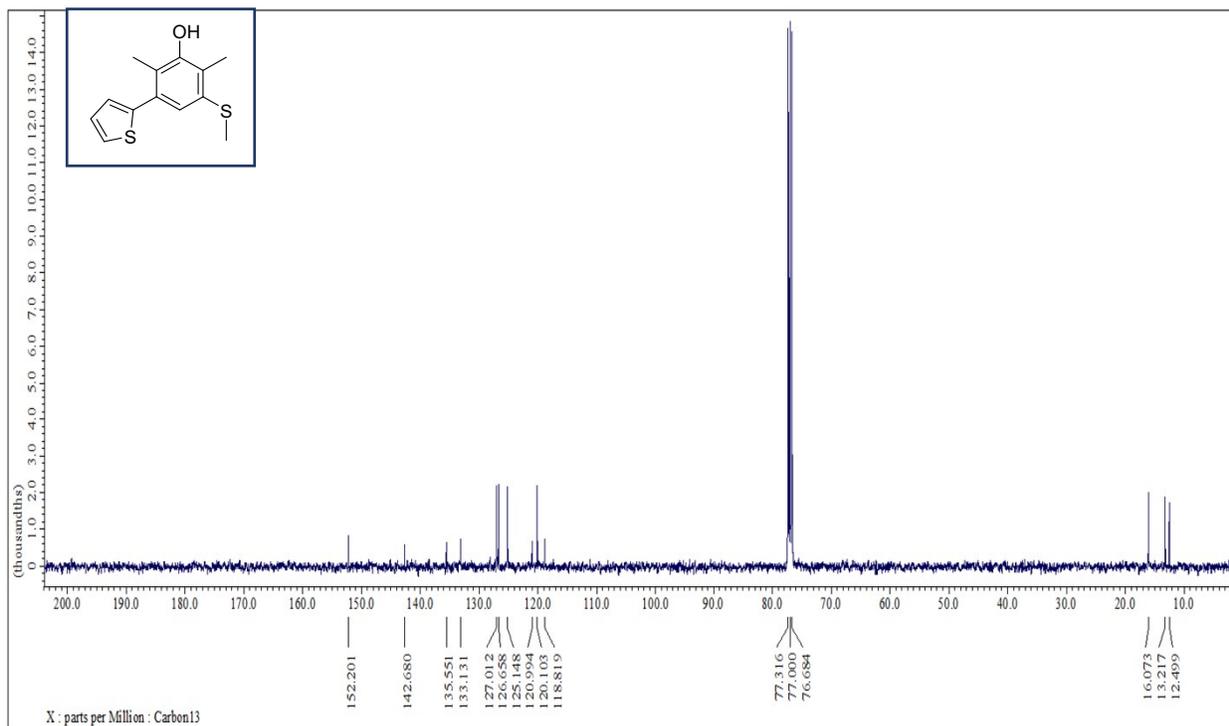
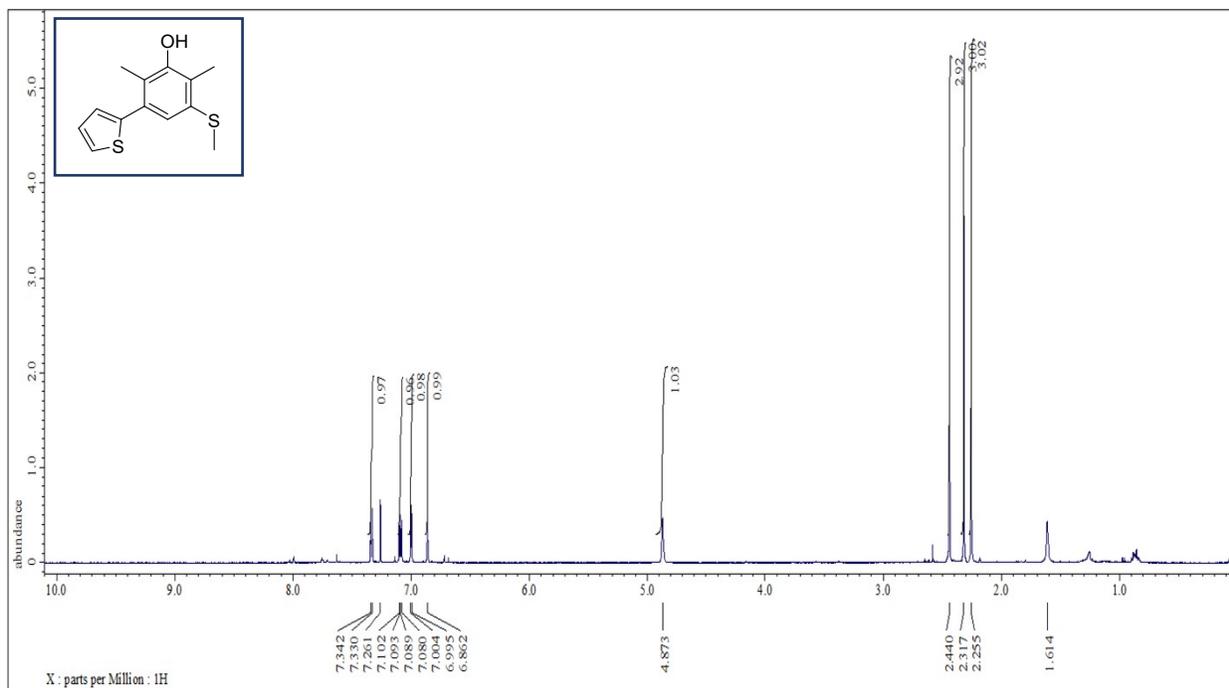
5c. 2'-bromo-2,4-dimethyl-5-(methylthio)-[1,1'-biphenyl]-3-ol: ^1H and ^{13}C NMR



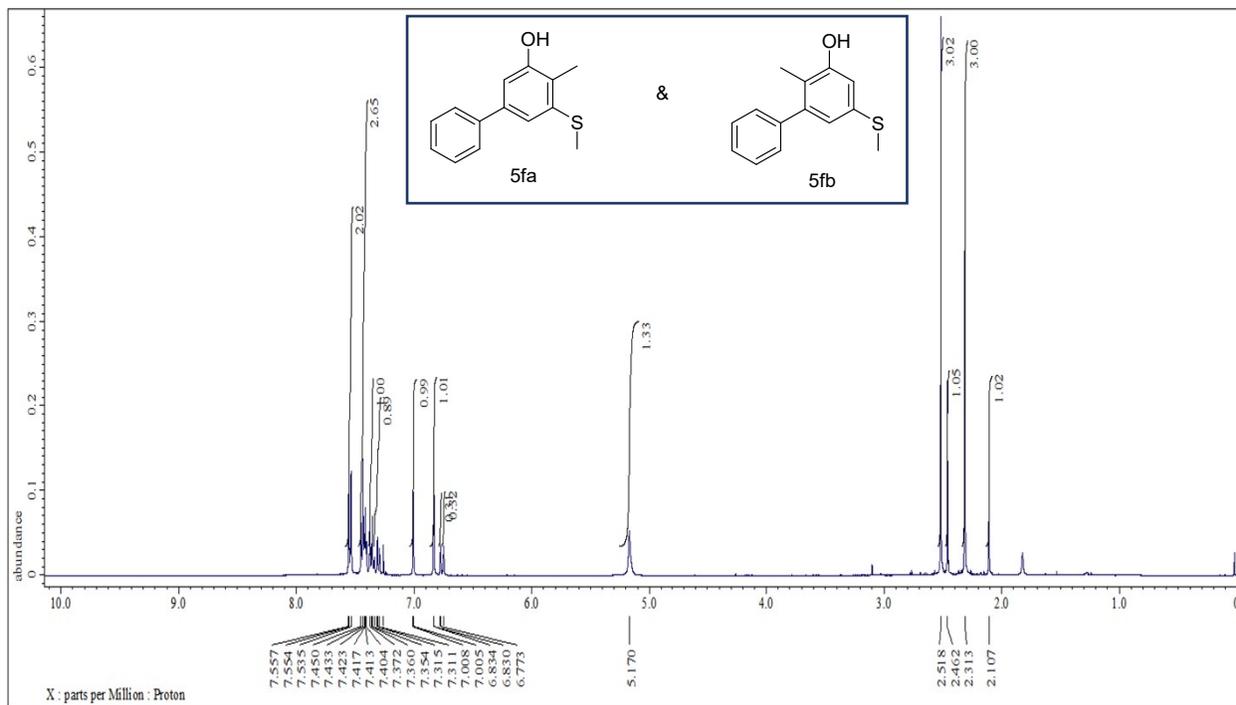
5d. 2,6-dimethyl-3-(methylthio)-5-(naphthalen-2-yl)phenol: ^1H and ^{13}C NMR



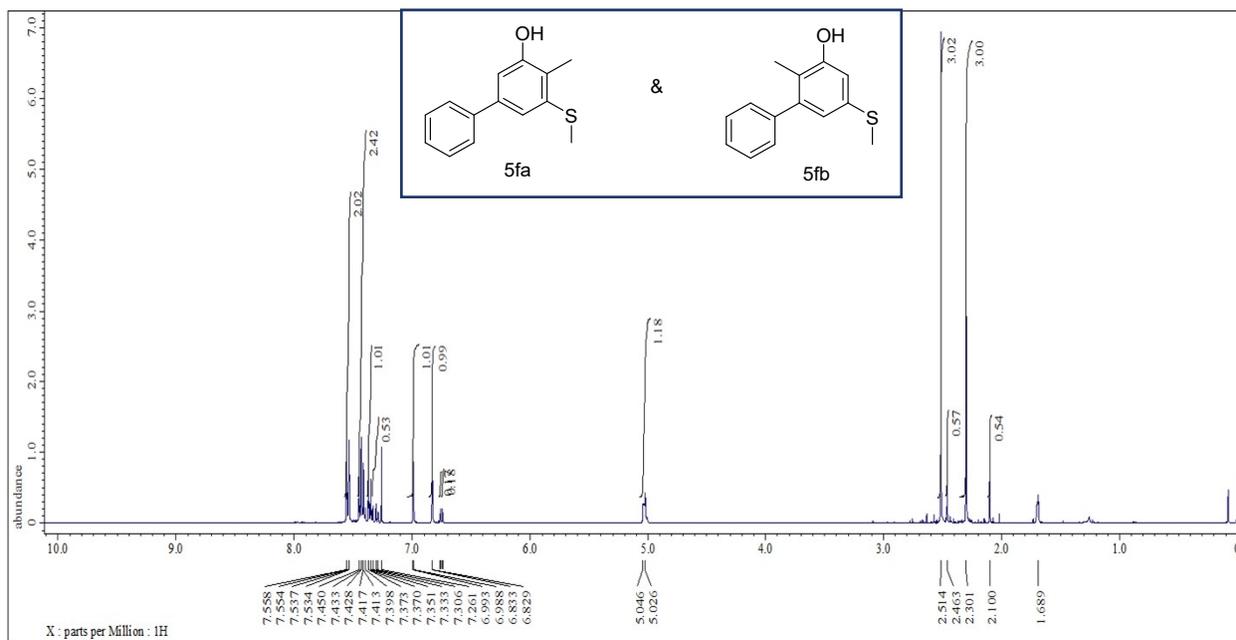
5e. 2,6-dimethyl-3-(methylthio)-5-(thiophen-2-yl)phenol: ¹H and ¹³C NMR

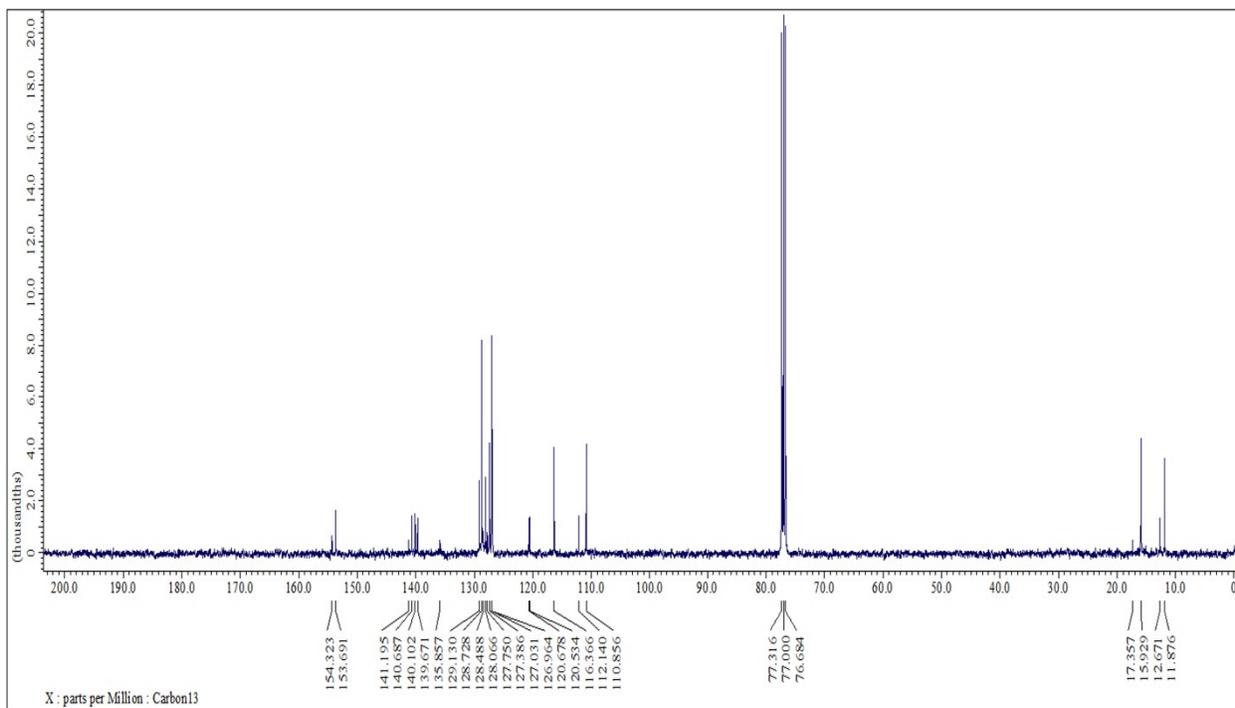


5fa and 5fb. 4-methyl-5-(methylthio)-[1,1'-biphenyl]-3-ol and 2-methyl-5-(methylthio)-[1,1'-biphenyl]-3-ol: ¹H NMR (When prepared in NaH, 5fa:5fb = 10;3): ¹H and ¹³C NMR

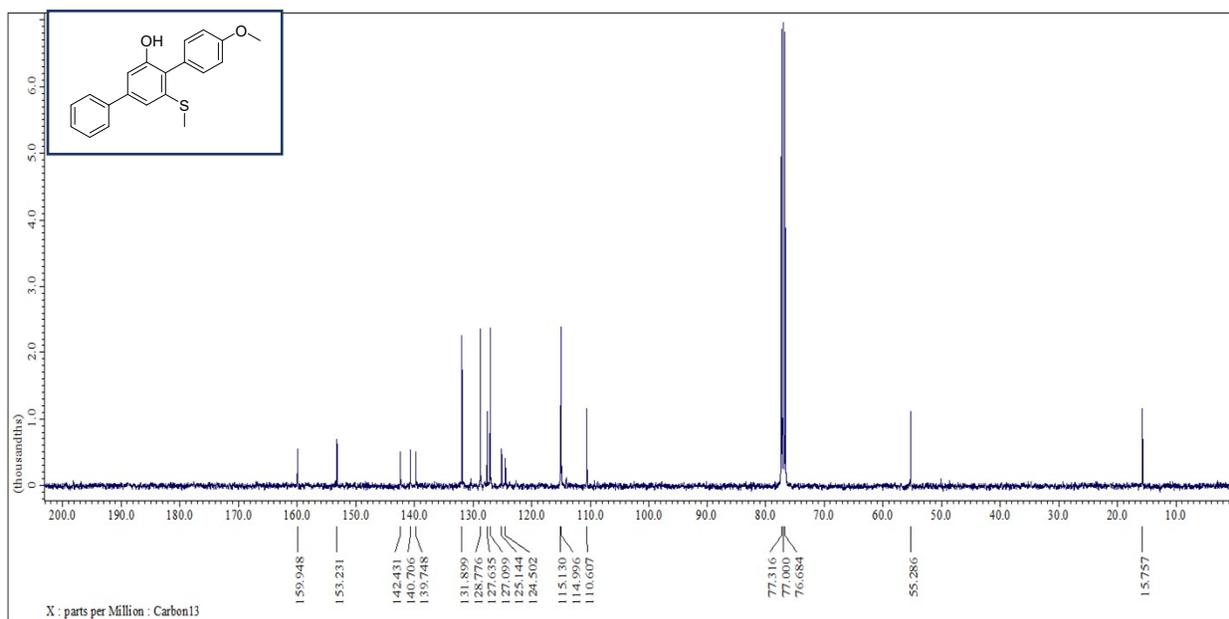
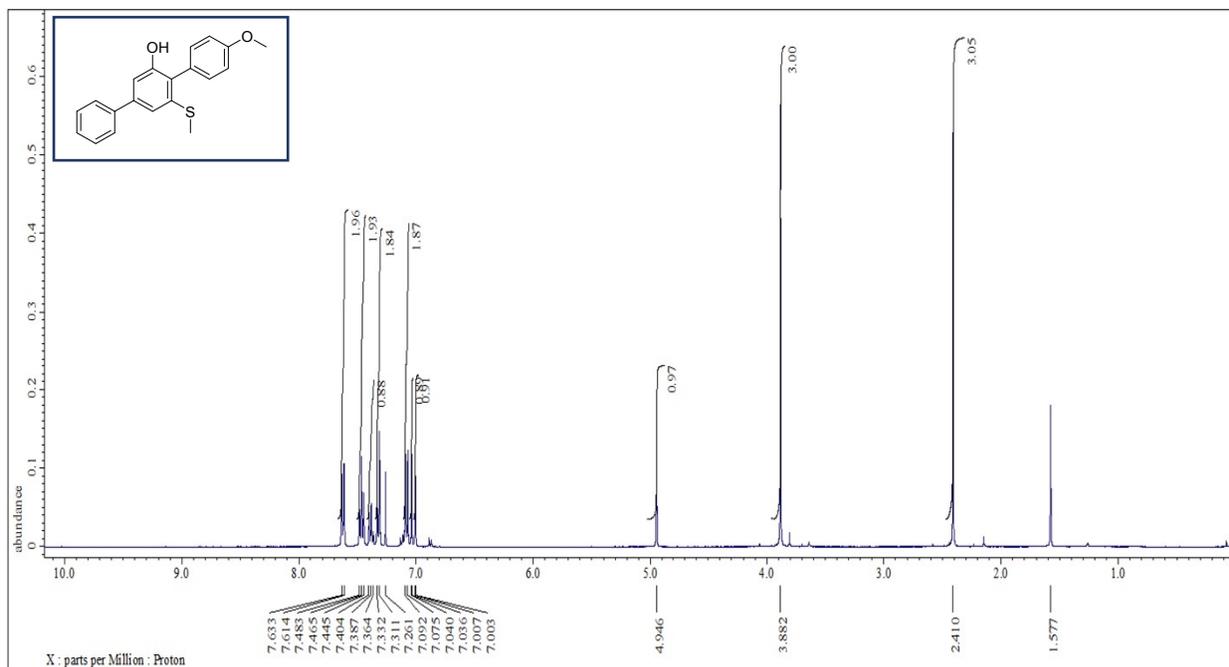


¹H NMR of 5fa and 5fb (When prepared in ^tBuOK, 5fa:5fb = 5;1)

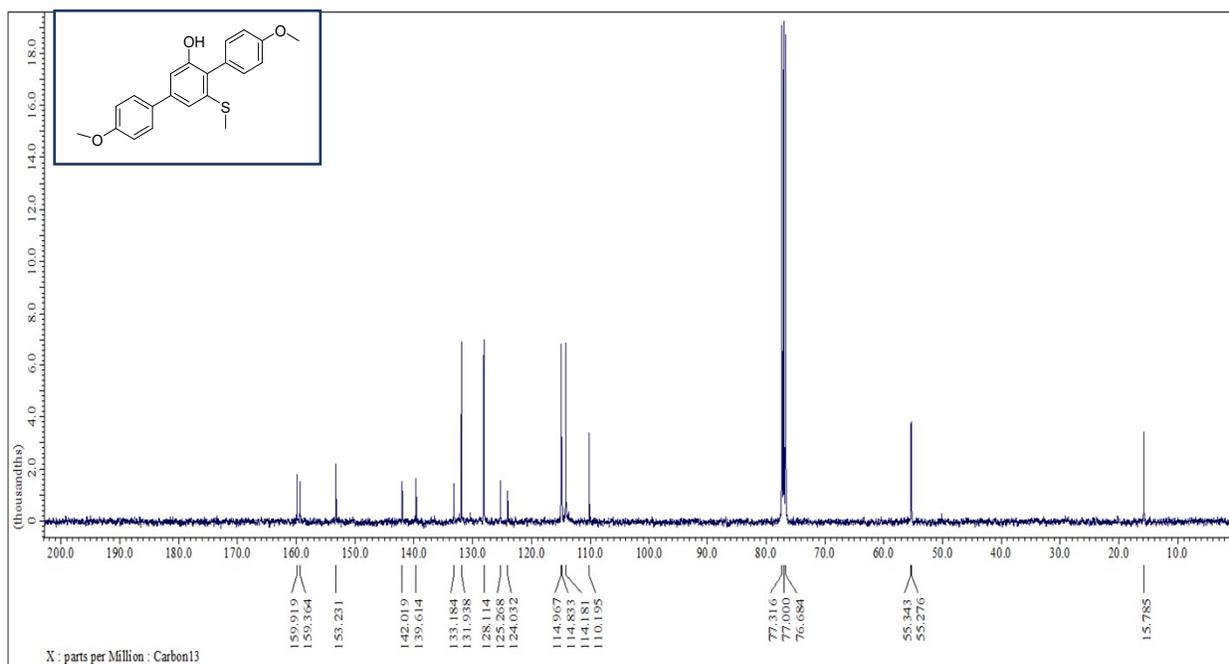
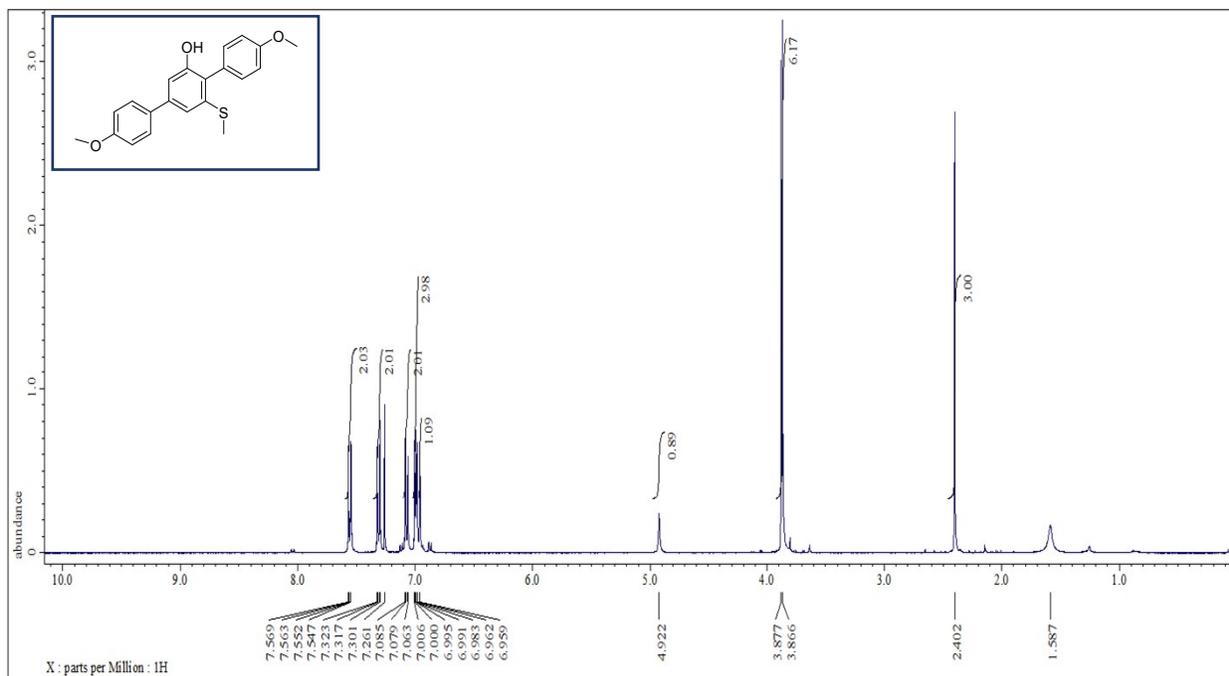




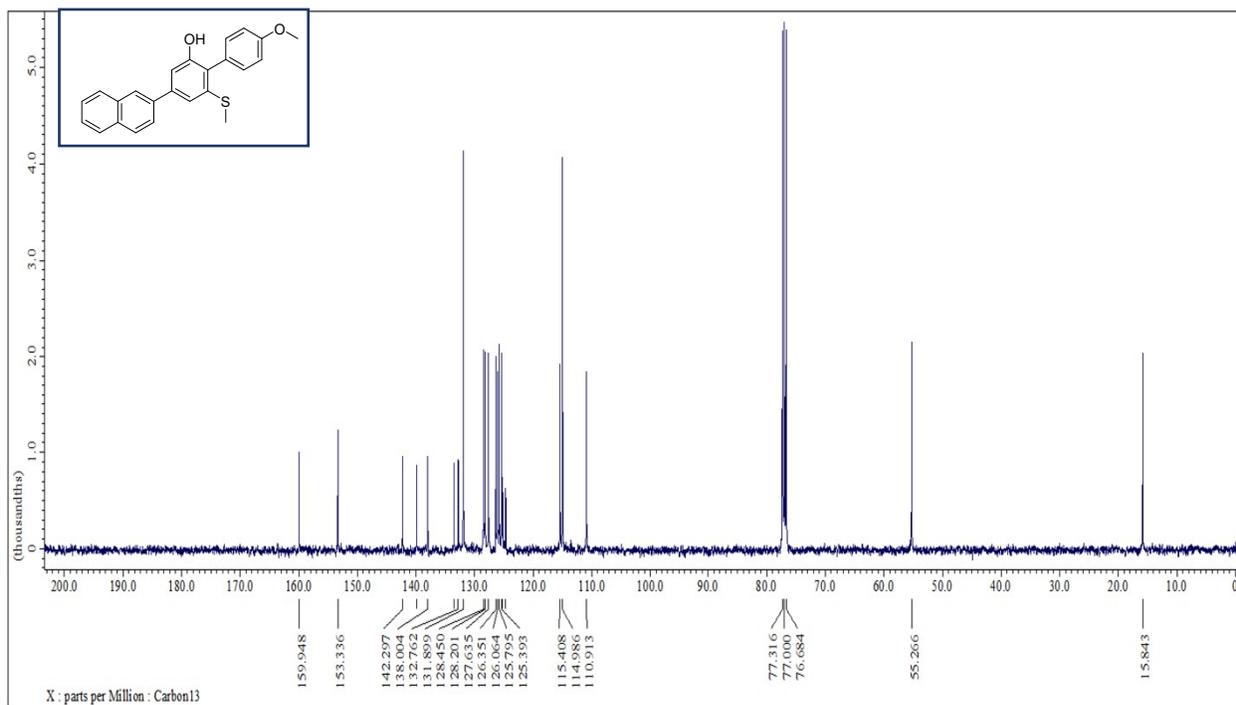
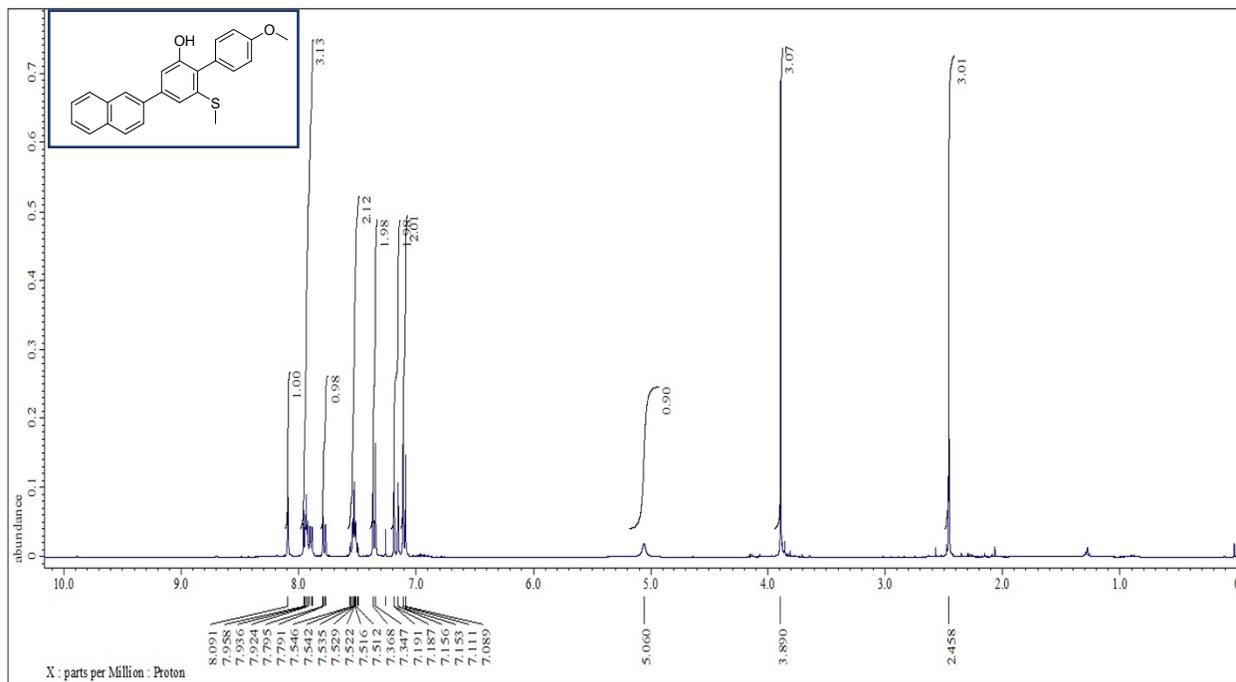
5g. 4-methoxy-6'-(methylthio)-[1,1':4',1''-terphenyl]-2'-ol: ^1H and ^{13}C NMR



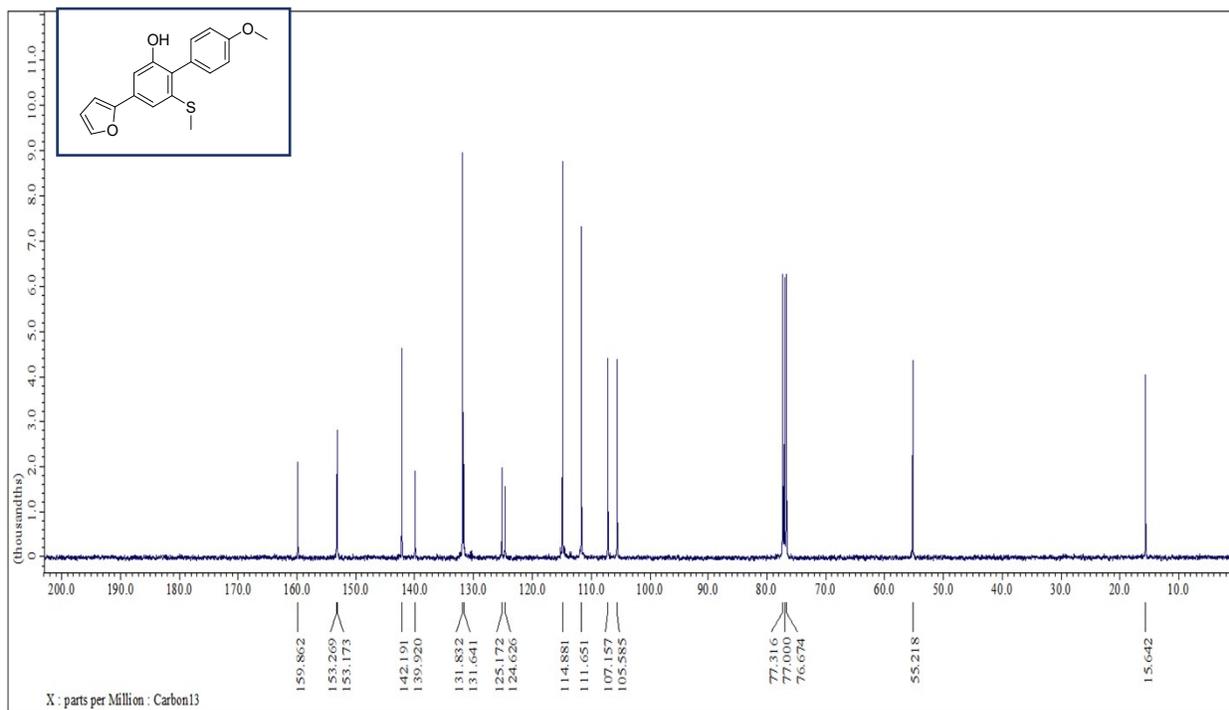
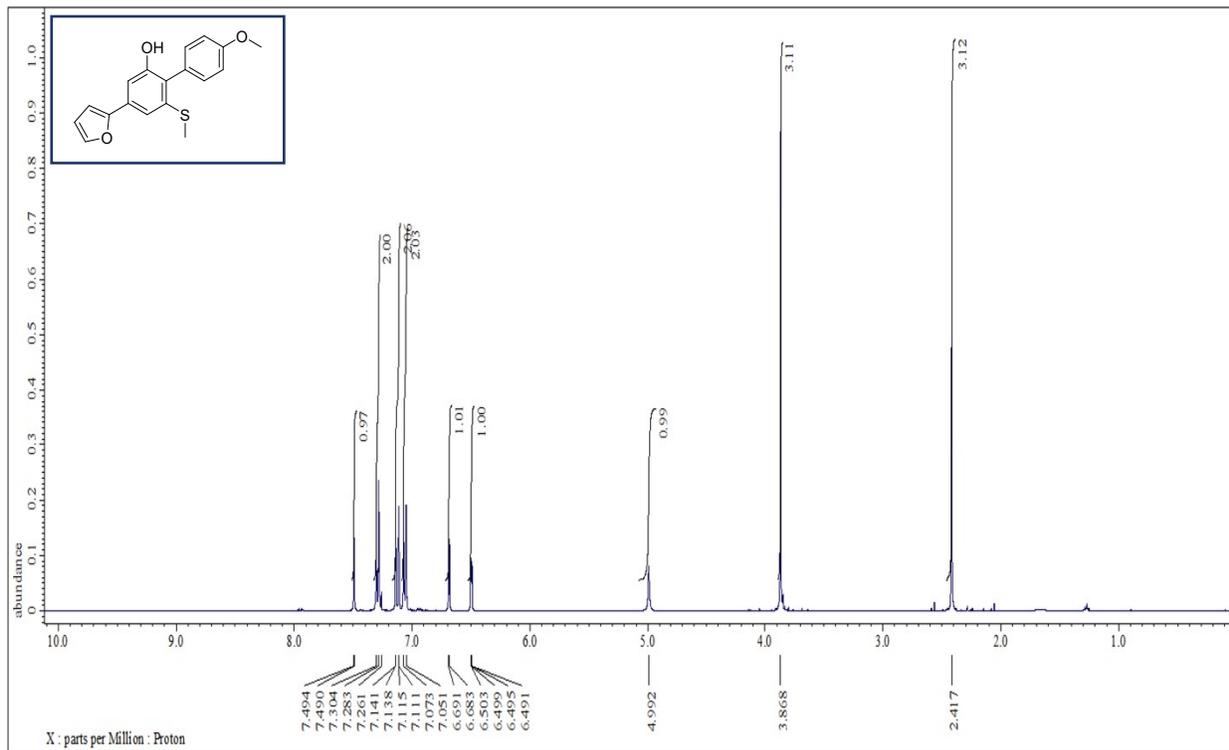
5h. 4,4''-dimethoxy-6'-(methylthio)-[1,1':4',1''-terphenyl]-2'-ol: ¹H and ¹³C NMR



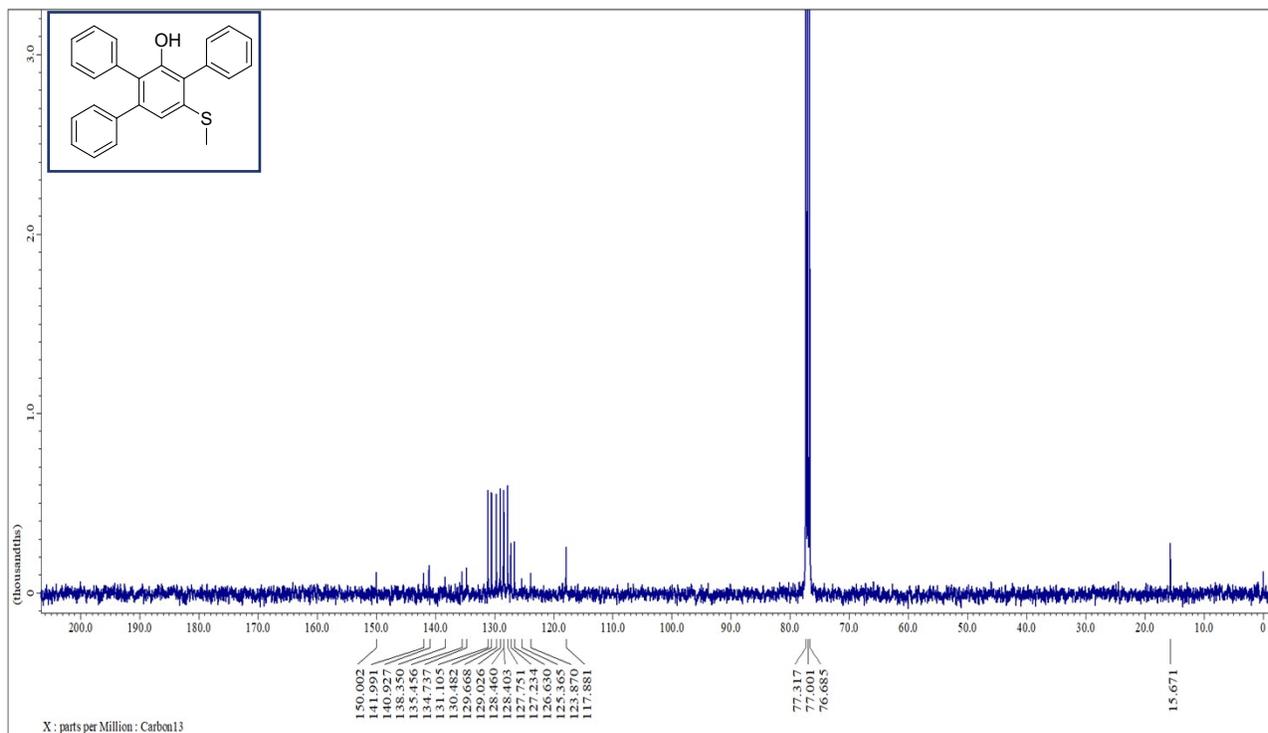
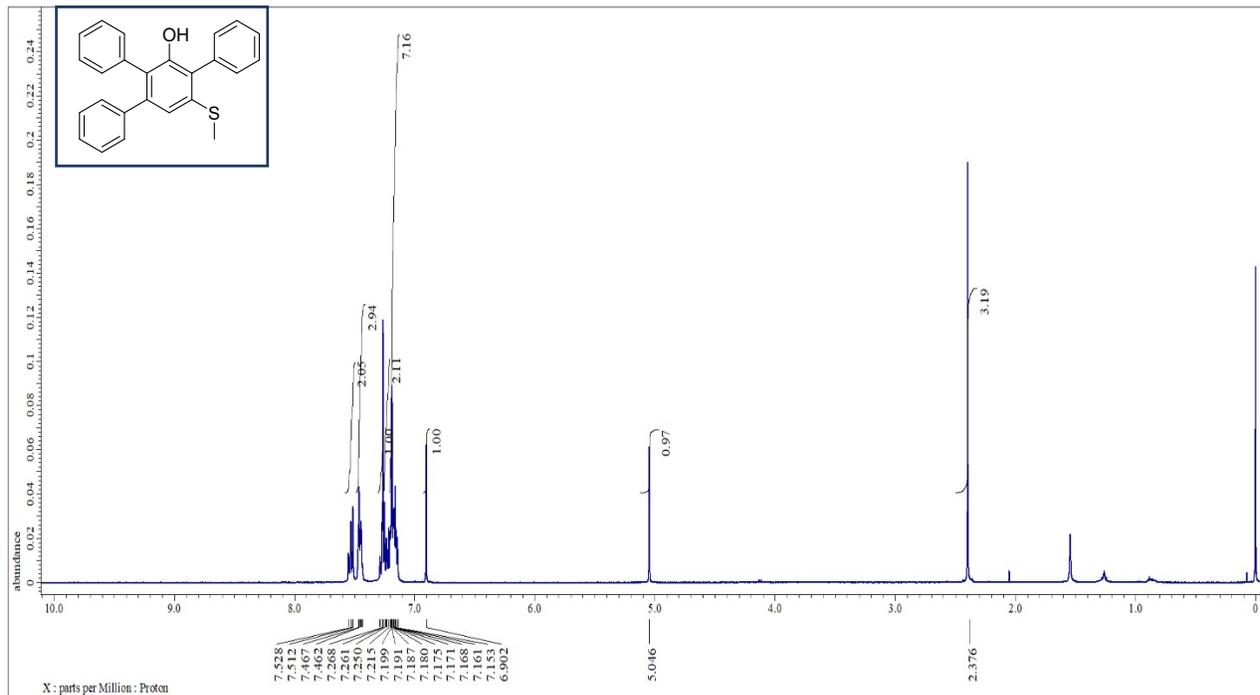
5i. 4'-methoxy-6-(methylthio)-4-(naphthalen-2-yl)-[1,1'-biphenyl]-2-ol: ^1H and ^{13}C NMR



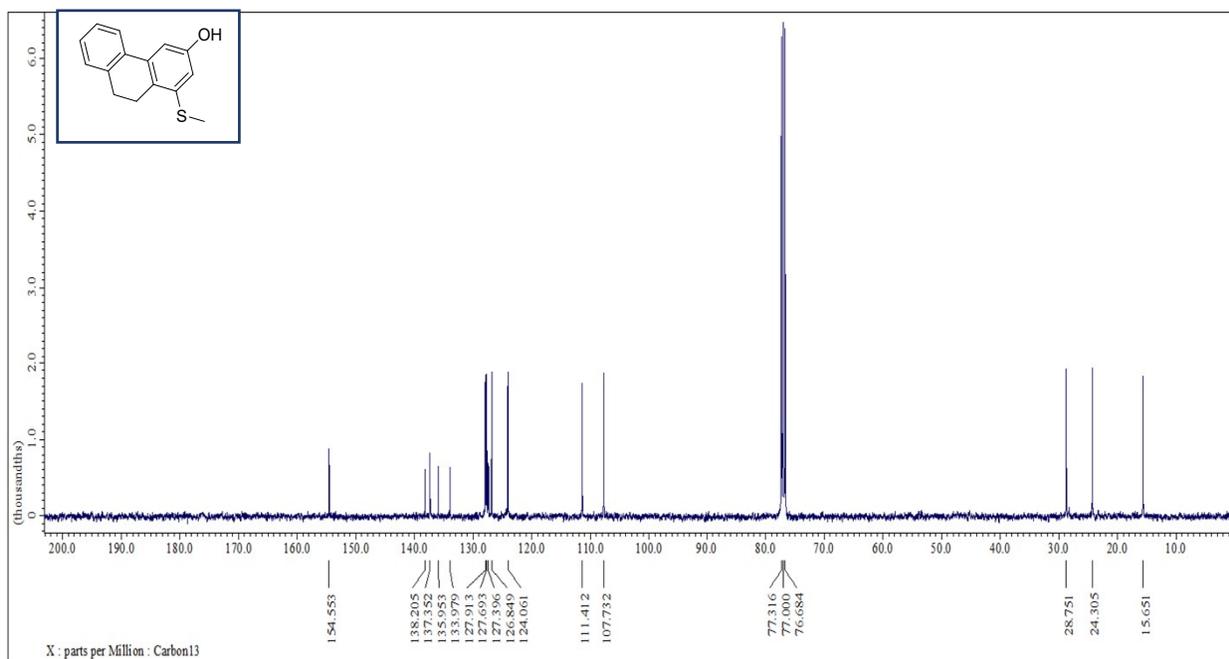
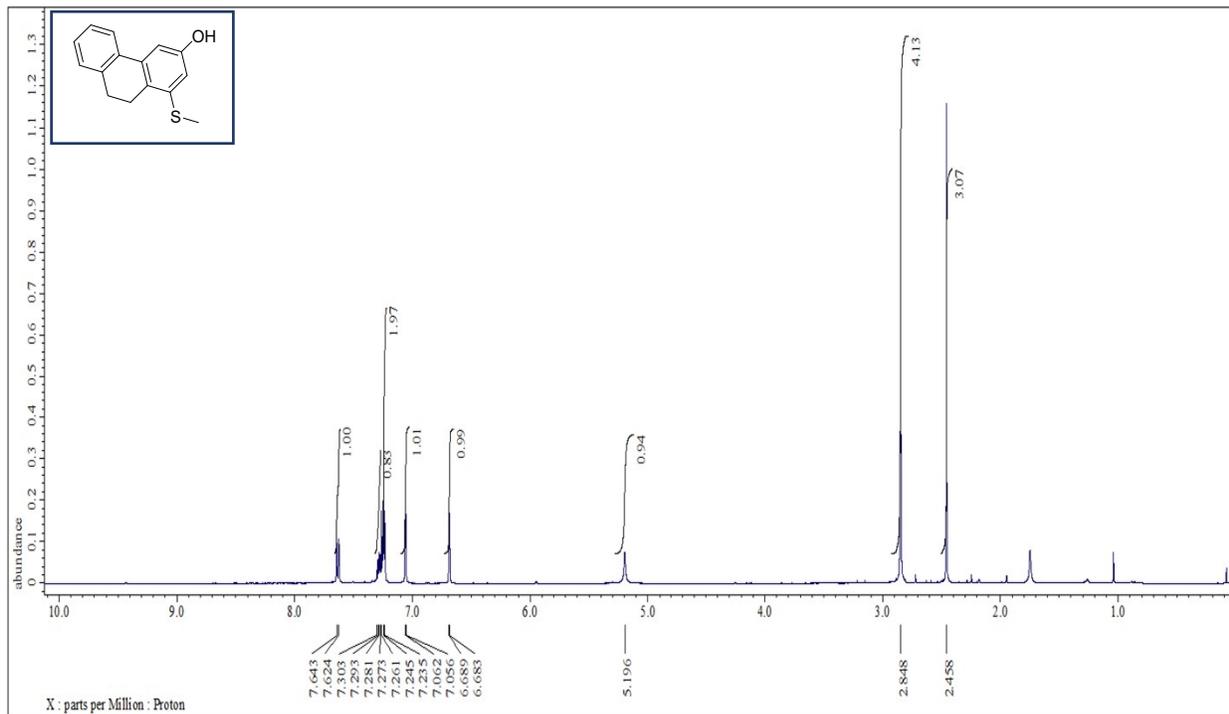
5j. 4-(furan-2-yl)-4'-methoxy-6-(methylthio)-[1,1'-biphenyl]-2-ol: ¹H and ¹³C NMR



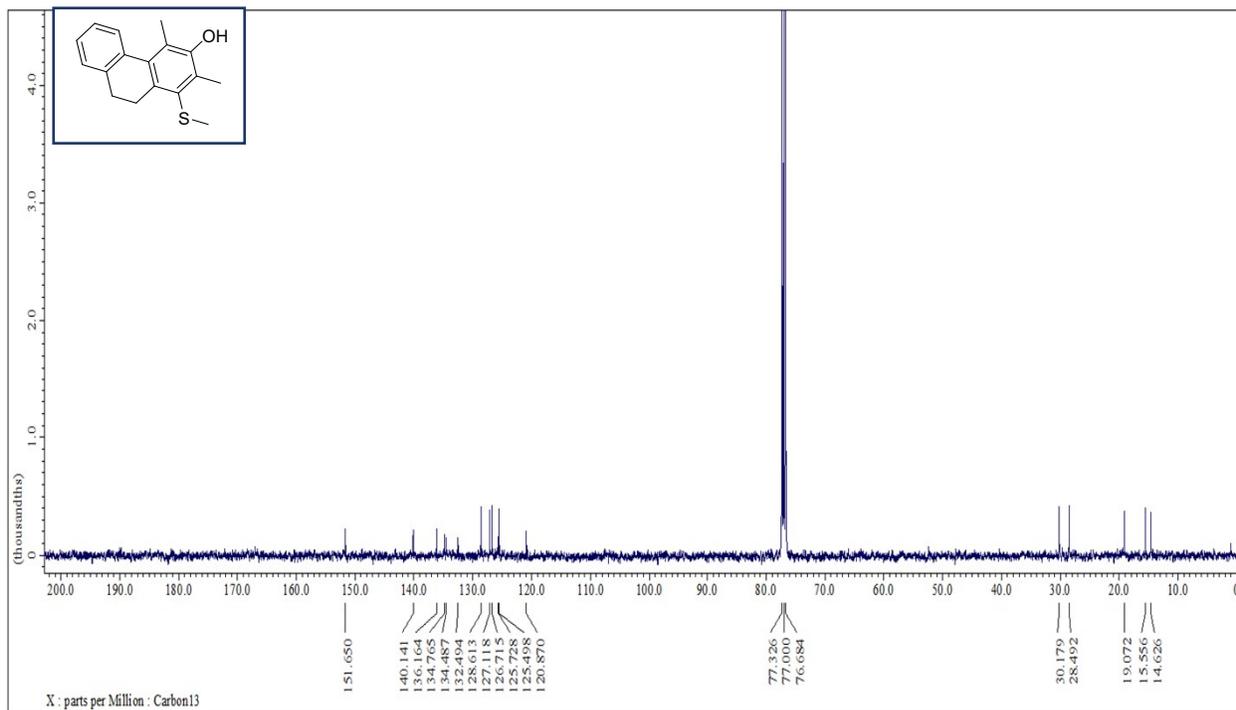
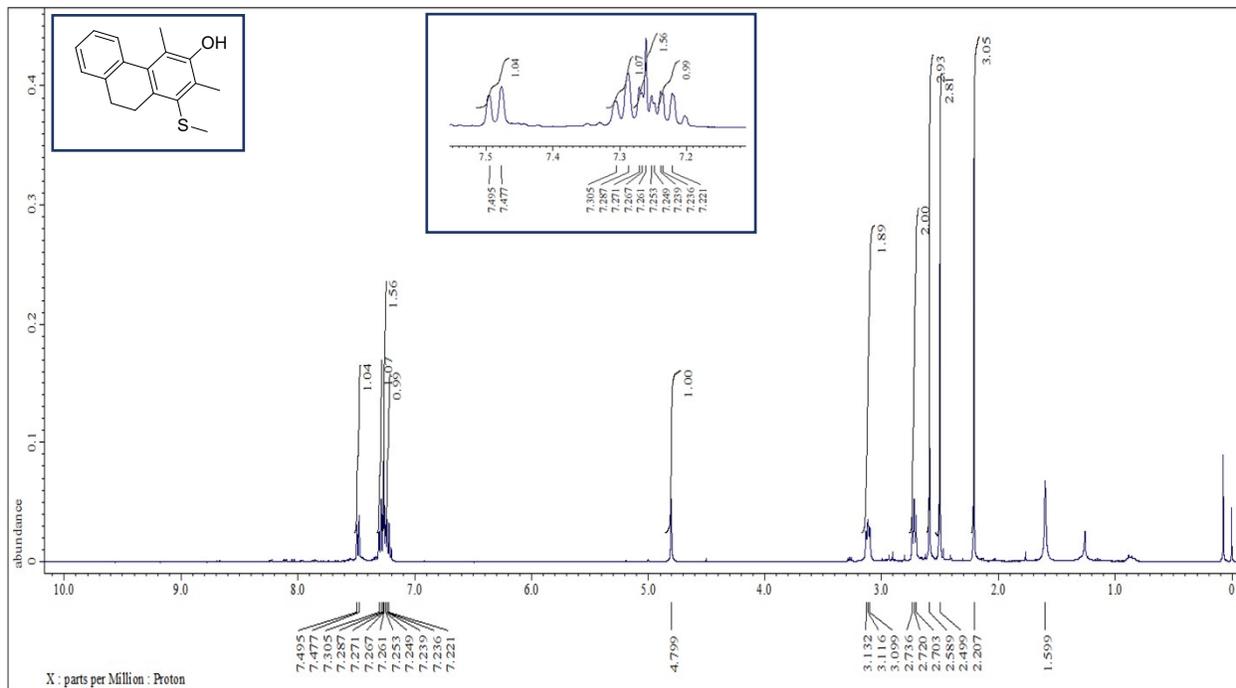
5k. 5'-(methylthio)-4'-phenyl-[1,1':2',1''-terphenyl]-3'-ol: ^1H and ^{13}C NMR



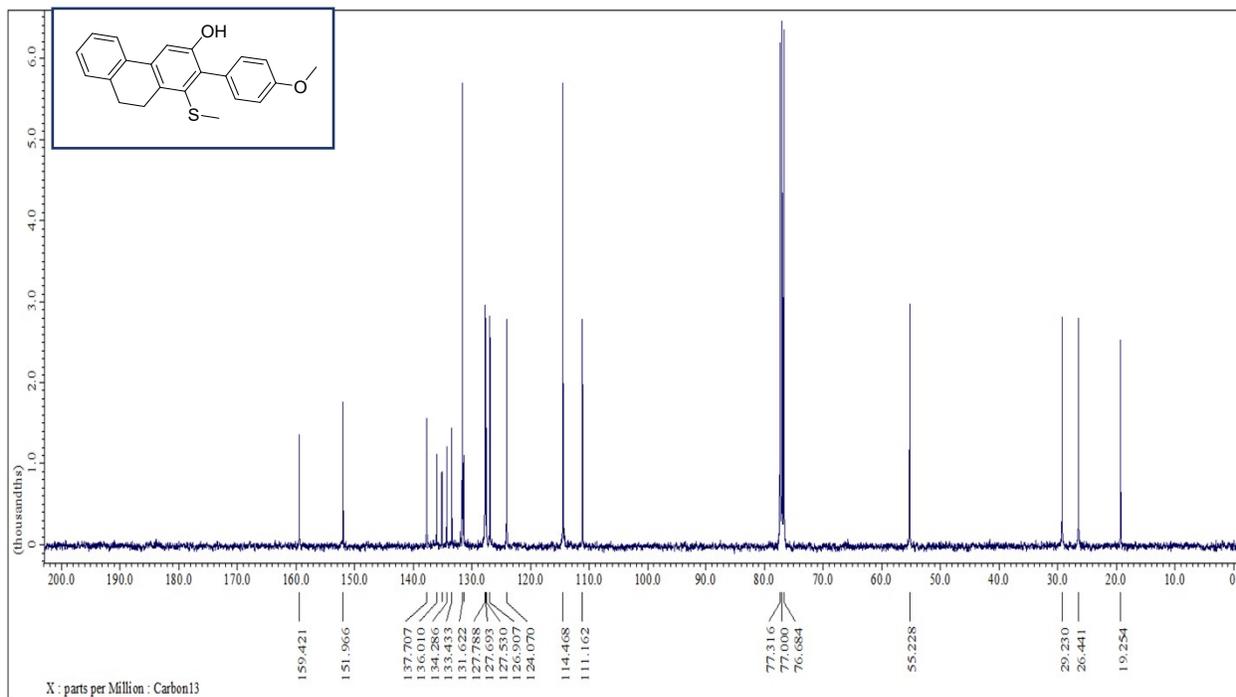
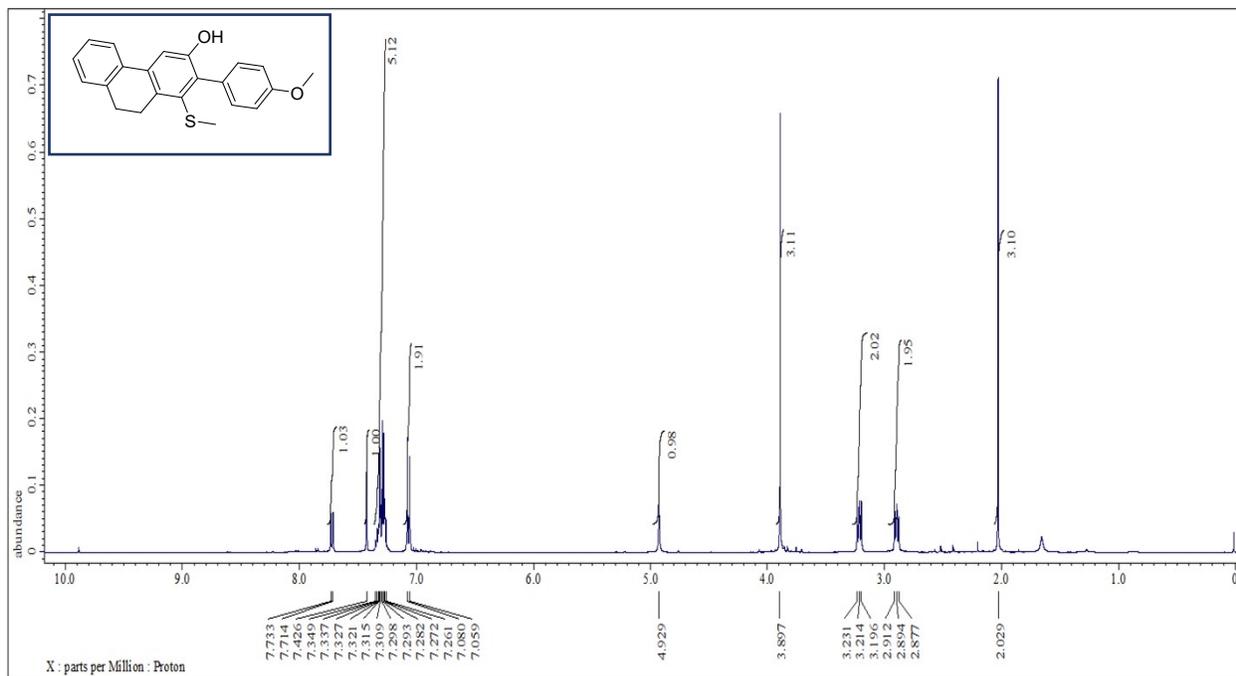
6a. 1-(methylthio)-9,10-dihydrophenanthren-3-ol: ^1H and ^{13}C NMR



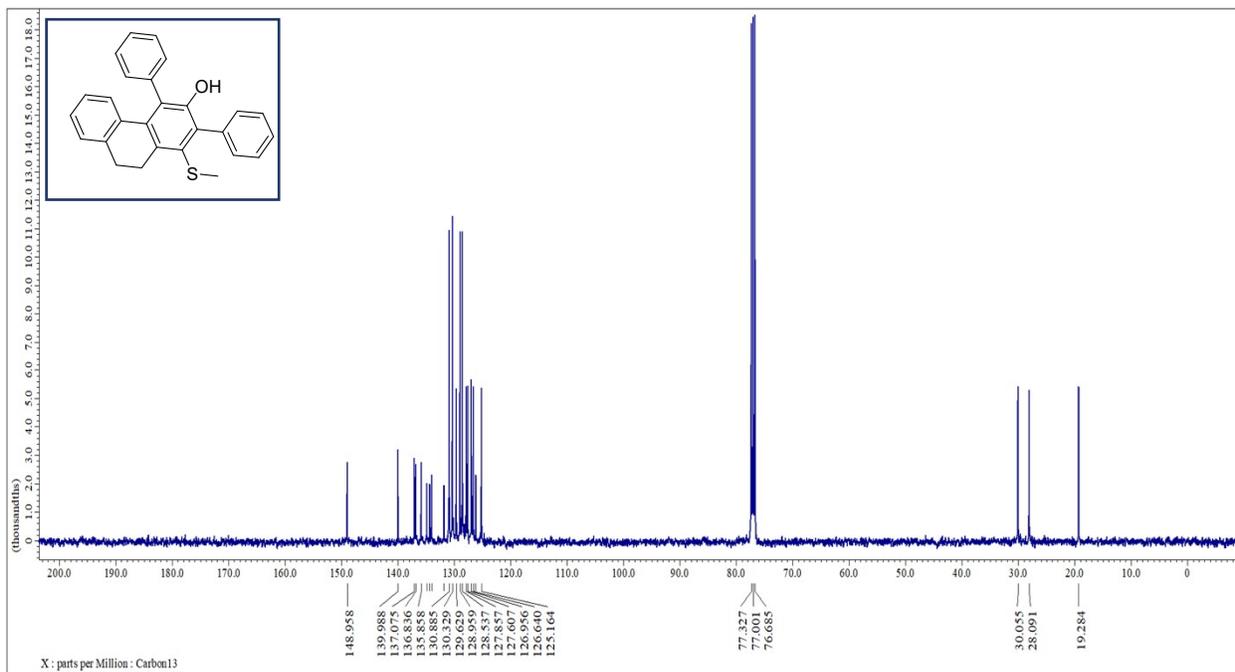
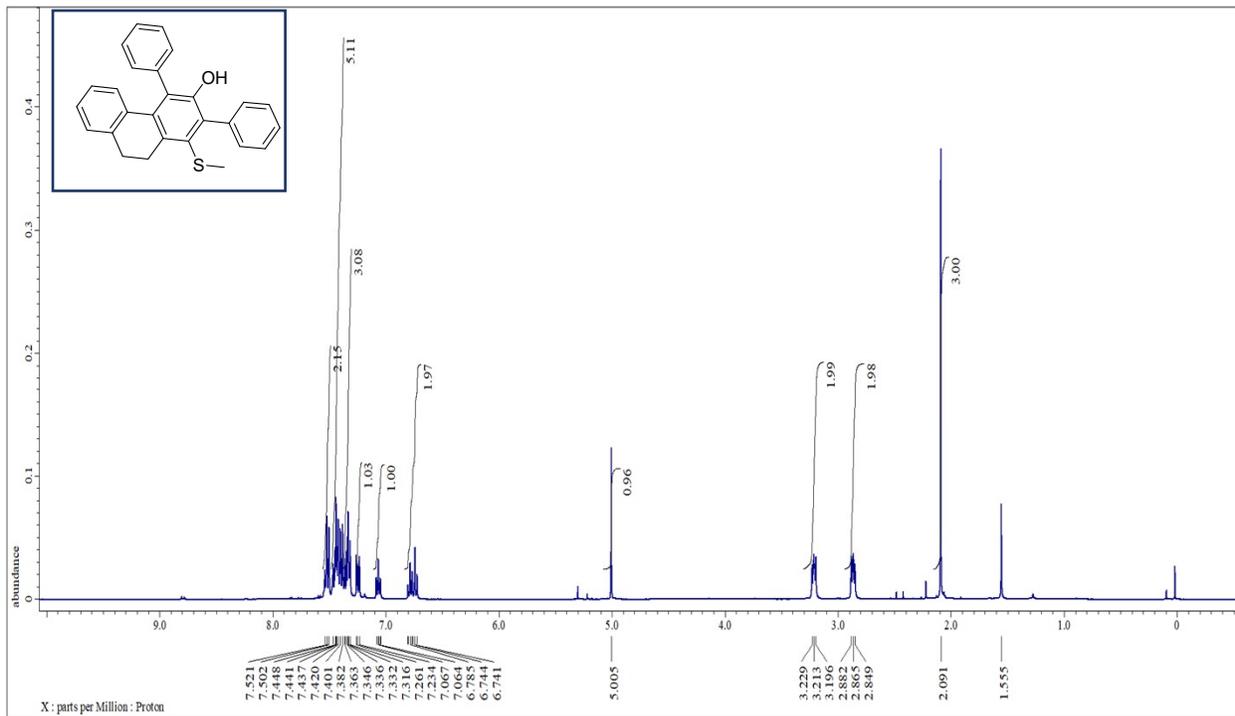
6b. 2,4-dimethyl-1-(methylthio)-9,10-dihydrophenanthren-3-ol: ^1H and ^{13}C NMR



6c. 2-(4-methoxyphenyl)-1-(methylthio)-9,10-dihydrophenanthren-3-ol: ^1H and ^{13}C NMR

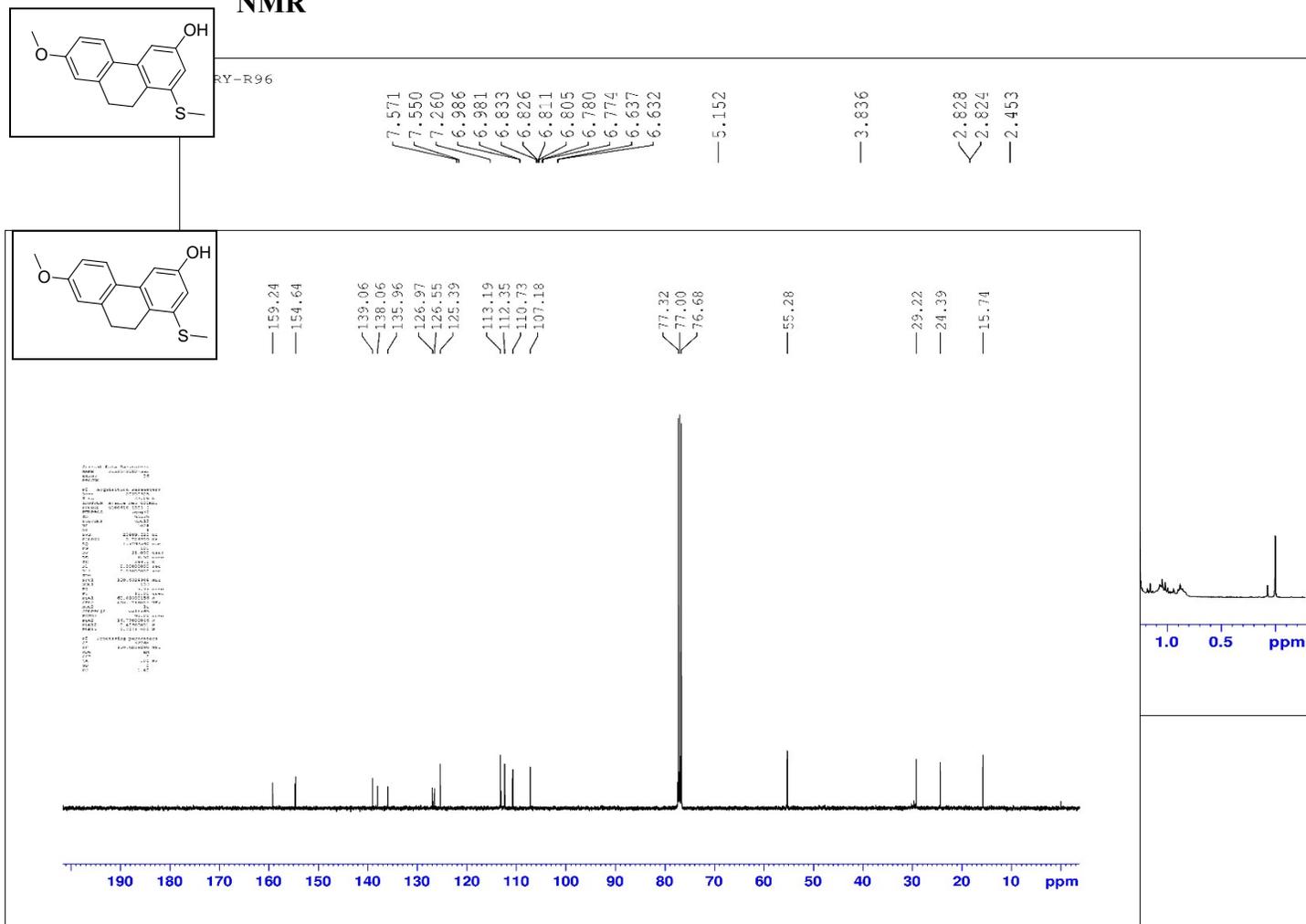


6d. 1-(methylthio)-2,4-diphenyl-9,10-dihydrophenanthren-3-ol: ¹H and ¹³C NMR

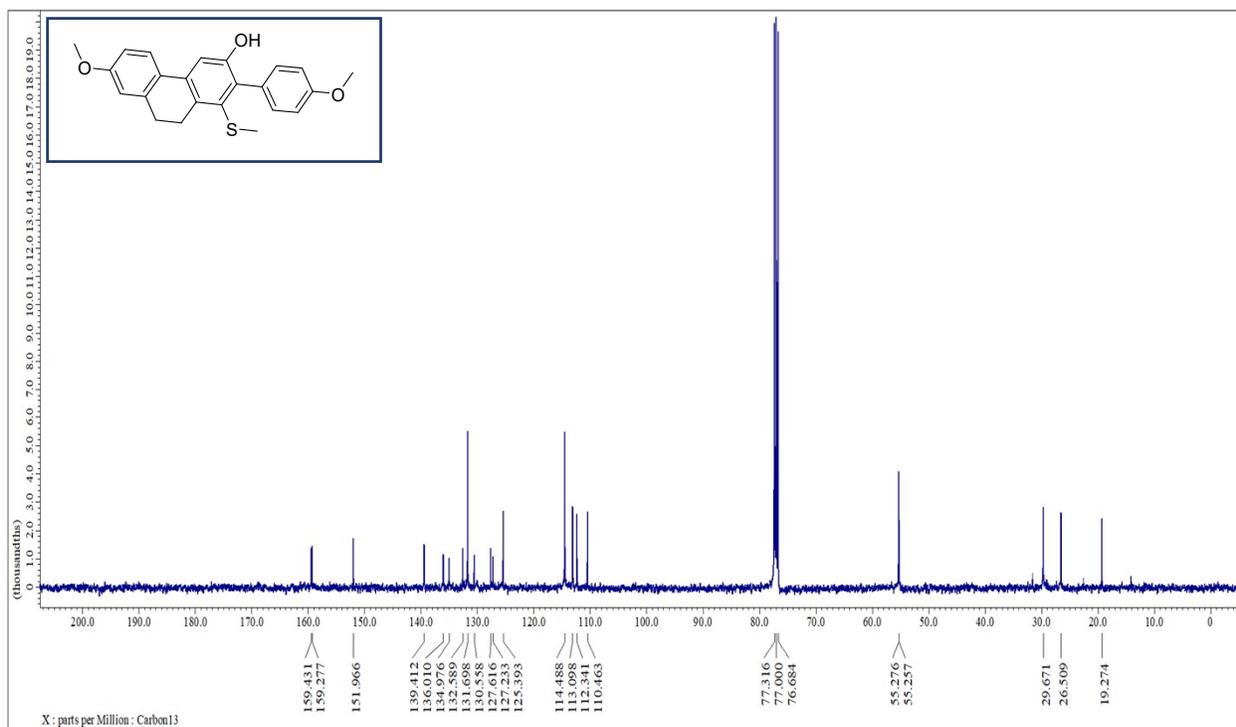
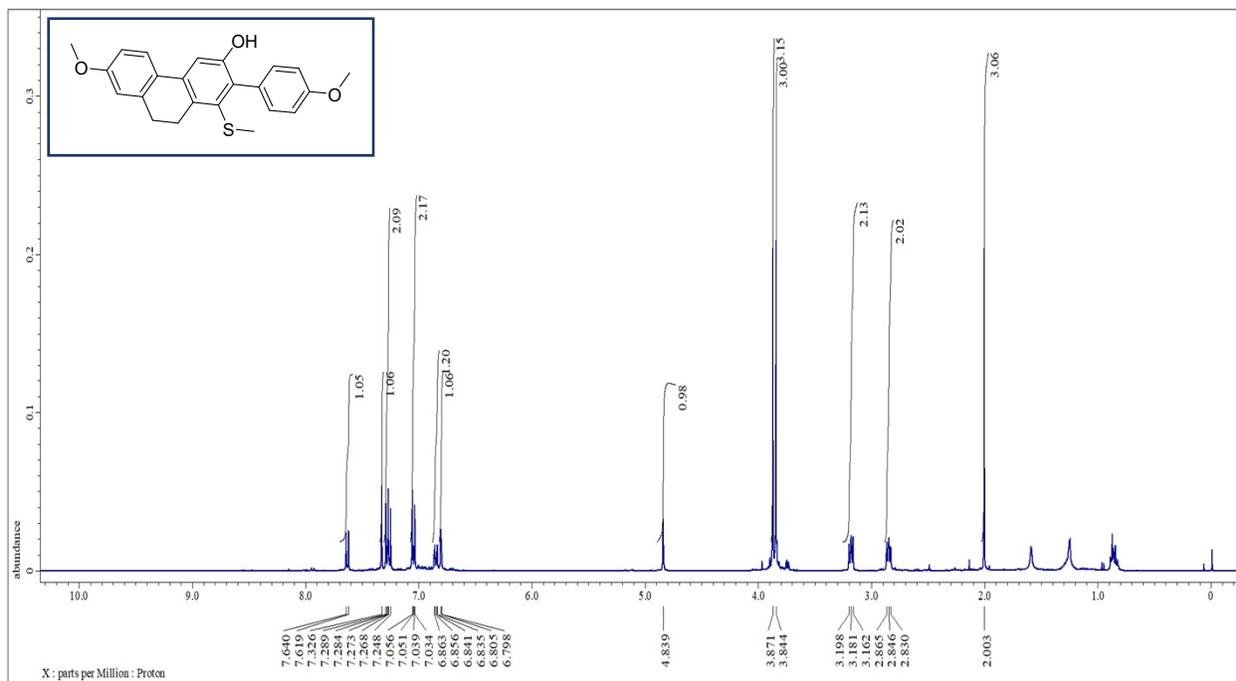


6e. 7-Methoxy-1-(methylthio)-9,10-dihydrophenanthren-3-ol: ¹H and ¹³C

NMR



6f. 7-Methoxy-2-(4-methoxyphenyl)-1-(methylthio)-9,10-dihydrophenanthren-3-ol: ¹H and ¹³C NMR



7. 3-cyclopropyl-5-(methylthio)phenol: ¹H and ¹³C NMR

