Chapter 3

syn-Diastereoselective Synthesis of Chroman-Fused Tetralins via Ar–C Bond-Forming Intramolecular Friedel–Crafts Epoxide-Arene Cyclization Reaction

Work of this Chapter has resulted in the following publication:

Gogoi, D.,[#] Devi, R.,[#] Pahari, P., Sarma, B., and Das, S. K. *cis*-Diastereoselective synthesis of chroman-fused tetralins as B-ring-modified analogues of brazilin. *Beilstein Journal of Organic Chemistry*, 12:2816-2822, 2016. ([#]equal contributions)

3.1. Introduction

(+)-Brazilin **1** and (−)-haematoxylin **2** are two structurally-related tetracyclic homoisoflavonoid natural products embedded with a chroman ring (Figure 3.1) [1-3]. Their des-(angular)hydroxyl synthetic derivatives (+)-brazilane **3** and haematoxylane **4** have also been reported in the literature (Figure 3.1) [1-3]. Among these brazilin family of natural products, brazilin **1** occupies the most prominent position as it has been demonstrated to have a number of potentially important biological activities including anticancer activity, anti-inflammatory activity, hypoglycemic activity, antihepatotoxicity, inhibition of protein kinase C activity, antiplatelet aggregation, and induction of immunological tolerance [4]. Also, haematoxylin **2** has recently been demonstrated to be a potent inhibitor of protein tyrosine kinase [4].

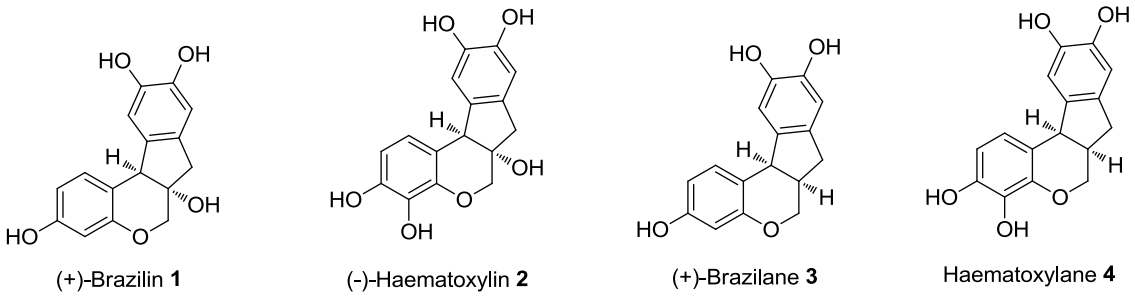


Figure 3.1. **Brazilin family of natural products**

Given the broad and interesting biological activities of these two natural products, significant efforts have been devoted for their stereoselective syntheses [5-12]. Moreover, Friedrich and Fies reported the synthesis of tetralin analogs of brazilin and haematoxylin (Figure 3.2) [13].

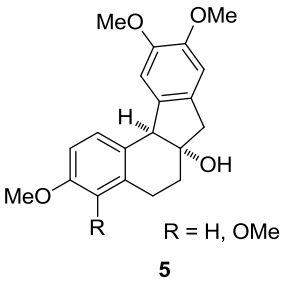


Figure 3.2. Tetralin analogs of brazilin and haematoxylin

More recently in 2010, Zhang and co-workers synthesized lactone, lactam and tetrahydroquinline analogs of brazilin (Figure 3.3) [14].

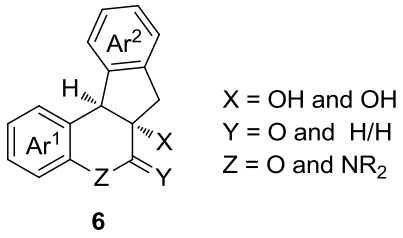


Figure 3.3. Lactone, lactam and tetrahydroquinline analogs of brazilin/brazilane

Despite all these synthetic works on brazilin, haematoxylin and their analogs, many possibilities remain unexplored especially for executing new design and synthetic strategies to generate their analogues and broaden the diversity.

3.2. Background and Objectives

Combination of two privileged scaffolds in one molecule gives a "hybrid" compounds, often with superior or unexpected biological profile through a synergistic effect [15]. Therefore, the development of a concise and efficient strategy leading to molecular systems containing two or more privileged scaffolds has gained significant attention for identifying novel and efficient ligands for various biological targets.

On the other hand, like the chroman scaffold, the tetralin unit has also been recognized as privileged structure [16]. However, to the best of our knowledge, the stereoselective synthesis of chroman-fused tetralins having an angular –OH group has never been reported. The aim of the research work described in this chapter was to synthesize, through the fusion of chroman and tetralin motifs, 6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-c]chromen-6a-ols **7** as brazilin-like molecules (Figure 3.4).

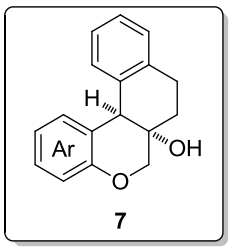
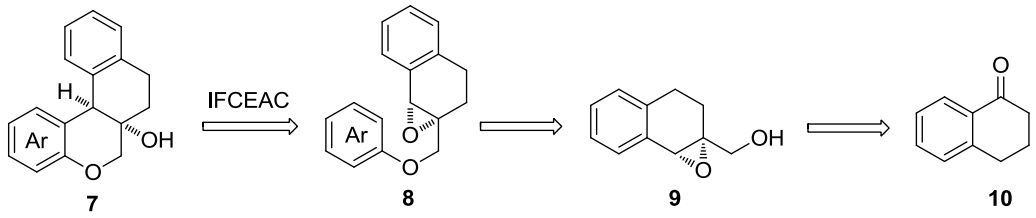


Figure 3.4. Chroman-fused tetralins as B-ring-modified analogues of brazilin

3.3. Results and Discussion

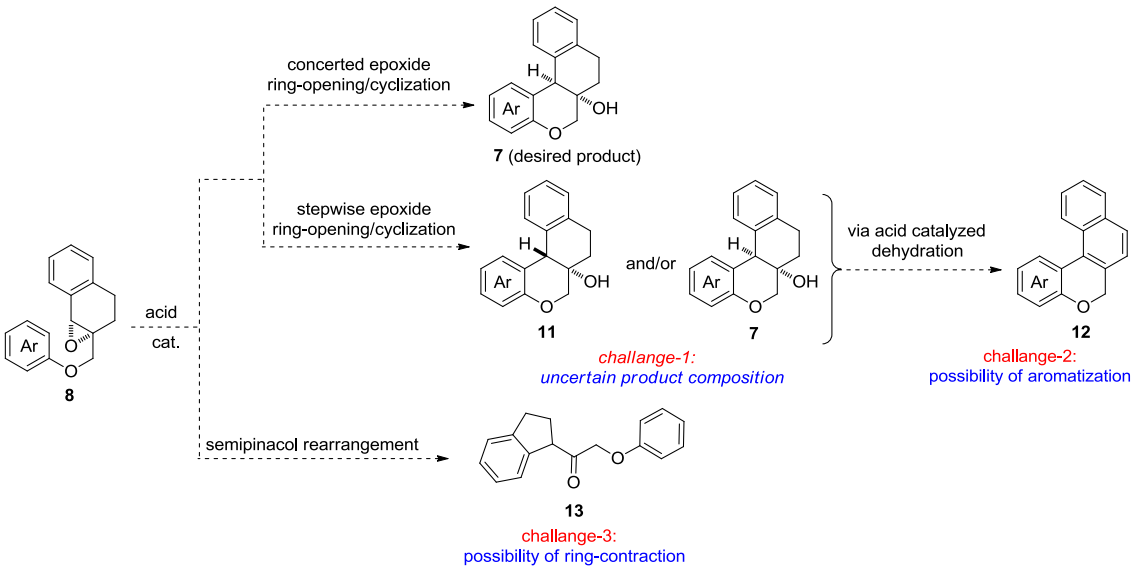
3.3.1. Retrosynthetic Analysis and Synthetic Challenges

Based on our previously developed protocols for the synthesis of *trans*-4-arylchroman-3-ols (Chapter 2), we envisioned that compounds **7** could be achieved from tetralin-based epoxy ethers **8** via the intramolecular Friedel-Crafts epoxide-arene cyclization (IFCEAC) strategy (Scheme 3.1). Compounds **8** could be synthesized from tetralin-based epoxy alcohol **9** and different phenols. Commercially available 1-tetralones **10** could be used as the starting materials to obtain compound **9**.



Scheme 3.1. Retrosynthetic analysis of the chroman-fused tetralins

Nonetheless, one major synthetic challenge associated with **7** would be the preferential construction of the *syn*-fused 6,6-ring system over the corresponding *anti*-fused ring system. While the stereochemical obligation makes sure that the 6,5-ring system in brazilin and related natural products remains *syn*-fused, its corresponding 6,6-ring system in **7** can have *syn* or *anti* stereochemistry at the ring junction. It was not obvious how the planned IFCEAC onto the pre-existing 6-membered ring, in case of stepwise-epoxide ring opening, would influence the product diastereoselectivity (Scheme 3.2). Thus, we were concerned about the possibility of getting mixture of **7** and **11** under the planned IFCEAC of **8**.

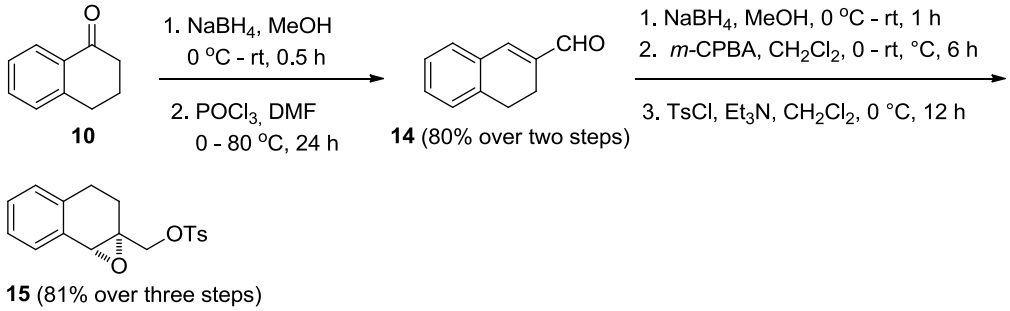


Scheme 3.2. Challenges associated with the synthesis of 7 via IFCEAC of 8

Another major issue came to our mind before the synthesis of **7** could be started. The Lewis/Brønsted acidic conditions employed during the IFCEA cyclization might activate the *tertiary*-OH group of **7** and/or **11**, leading to the formation of a stable 3^o carbocation which might further undergo dehydration ─ aromatization to generate compound **12**. Finally, in the presence of Lewis/ Brønsted acids, substrates **8** might undergo competitive semi-pinacol rearrangement to give ring contracted product **13**.

3.3.2. Synthesis of Tetralin-Embedded Epoxy Tosylate

We commenced our work with the synthesis of tetralin-embedded epoxy tosylate **15** that would serve as the key intermediate for the synthesis of **8**. Thus, $NaBH_4$ reduction of commercially available tetralone **10** followed by one-pot dehydration ─ Vilsmeier-Haack formylation of the resulting crude alcohol furnished α,β-unsaturated aldehyde **14** in 80% yield over two steps (Scheme 3.3). Next, $NaBH_4$ reduction of **14** followed by epoxidation of the resulting unsaturated alcohol by *m*-CPBA provided the corresponding epoxy alcohol which on tosylation furnished epoxy tosylate **15** in 81% yield over three steps.

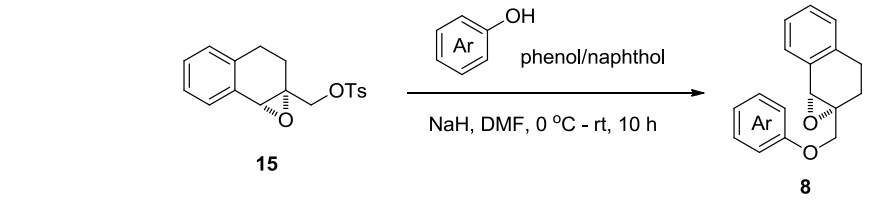


Scheme 3.3. Synthesis of tetralin-embedded epoxy tosylate 15

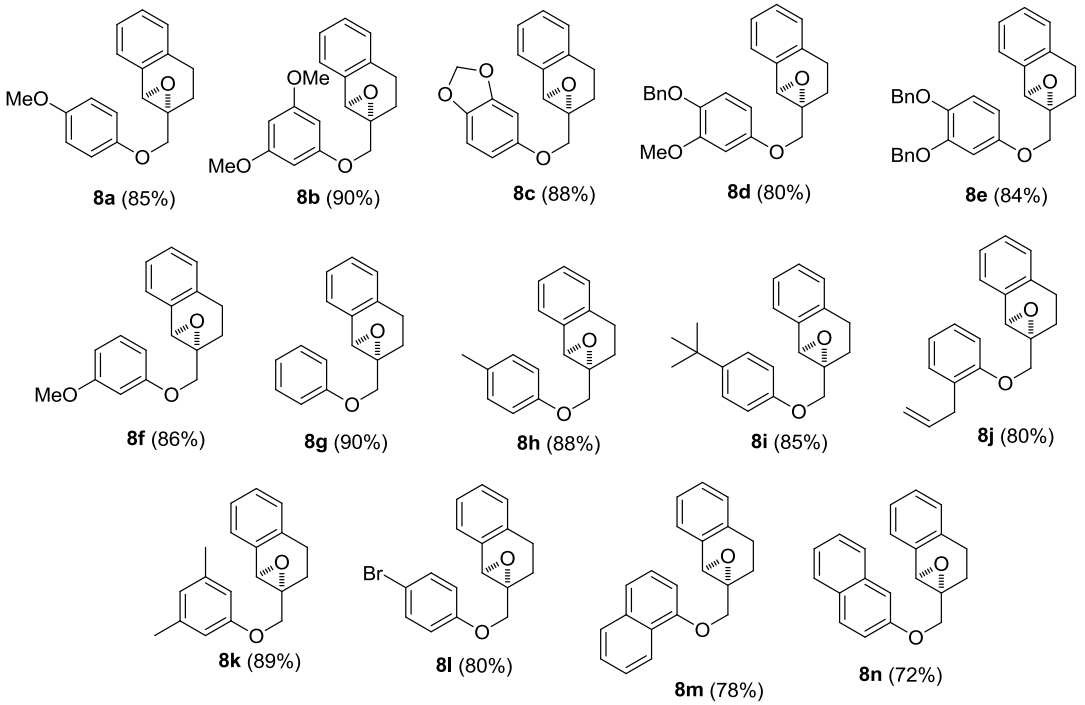
3.3.3. Synthesis of Tetralin-Embedded Glycidyl Ethers

With the key epoxy tosylate **15** in place, the stage was set for the alkylation of different phenols/naphthols with **15**. Fourteen different phenols/naphthols were treated with **15** in the presence of NaH to obtain the corresponding glycidyl ethers **8a-n** in good to high yields (Table 3.1).

Table 3.1. Synthesis of tetralin-embedded glycidyl ethers 8a-n[a,b]



15 8



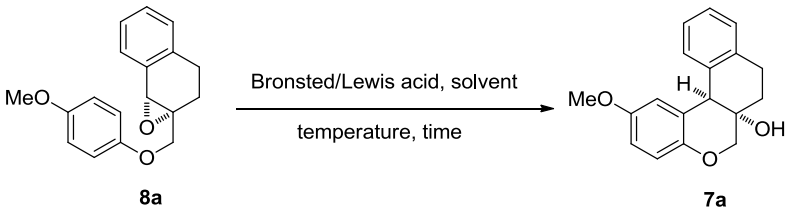
[a]Reaction conditions: phenol/naphthol (1.0 mmol), **15** (1.05 mmol) and NaH (1.5 mmol) in anh. DMF (3 mL). [b]The percentage values shown in parentheses indicate the respective isolated yields after column chromatography.

3.3.4. Screening of Reaction Conditions for IFCEAC Reaction

Our optimization study began with the IFCEAC of **8a** (Table 3.2). We first investigated this reaction using 1,1,3,3,3-hexafluoroisopropanol (HFIP) as reaction medium as well as reaction promoter. Unfortunately, refluxing a solution of **8a** in HFIP for 4 h (Table 3.2, entry 1) led to the formation of a mixture of two major isolable compounds, out of which one was the expected product **7a** (50 %), and the remaining one was hexafluoroisopropyl ether (generated from the nucleophilic addition of HFIP on the benzylic position). Next, a solution of **8a** in AR grade toluene containing 20 mol% of *p*-toluenesulfonic acid monohydrate ($TsOH \cdot H_2O$) as Brønsted acid catalyst was heated at 80 °C for 45 min. The desired product **7a** was obtained in 81% isolated yield (Table 3.2, entry 2). With 20 mol% of $TsOH \cdot H_2O$ in toluene, a significant increase or decrease in

temperature caused noticeable change in the product yields (entries 3 and 4). With 20 mol% of $TsOH \cdot H_2O$, we observed that the reaction efficiency was also dependent on the reaction medium, and toluene appeared to be the best one (entry 2) among the screened solvents (toluene, MeCN, DCE, and $MeNO_2$; entries 2-7).

Table 3.2. Screening of reaction conditions for IFCEAC of 8a leading to 7a[a]



8a **7a**

entry	catalyst (mol%)	solvent	temp (^oC)	time	yield (%)[b]
1	-	HFIP	reflux	4 h	50
2	**$TsOH \cdot H_2O$ (20)**	**toluene**	**80**	**45 min**	**81**
3	$TsOH \cdot H_2O$ (20)	toluene	115	45 min	75
4	$TsOH \cdot H_2O$ (20)	toluene	50	2 h	65
5	$TsOH \cdot H_2O$ (20)	MeCN	80	45 min	79
6	$TsOH \cdot H_2O$ (20)	DCE	80	45 min	70
7	$TsOH \cdot H_2O$ (20)	$MeNO_2$	80	45 min	75
8	TFA (20)	toluene	rt	45 min	74
9	TfOH (20)	toluene	rt	45 min	70
10	H_2SO_4 (20)	toluene	rt	45 min	75
11	$Sc(OTf)_2$ (20)	DCM	rt	60 min	78
12	$BF_3 \cdot Et_2O$ (100)	DCM	0	30 min	81
13	$FeBr_3$ (20)	DCM	rt	60 min	78
14	$AgSbF_6$ (20)	DCM	reflux	60 min	79
15	$TiCl_4$ (20)	DCM	reflux	60 min	78

[a]Reaction conditions: **8a** (0.4 mmol), acid catalyst, solvent (8 mL). [b]Isolated yields after silica gel column chromatography.

Lower yields of **7a** were obtained when stronger Brønsted acids like TFA, H_2SO_4 and TfOH were used as catalysts (entries 8-10) in toluene as the reaction medium. Among the five different Lewis acids we screened (entries 11-15), the best result was achieved

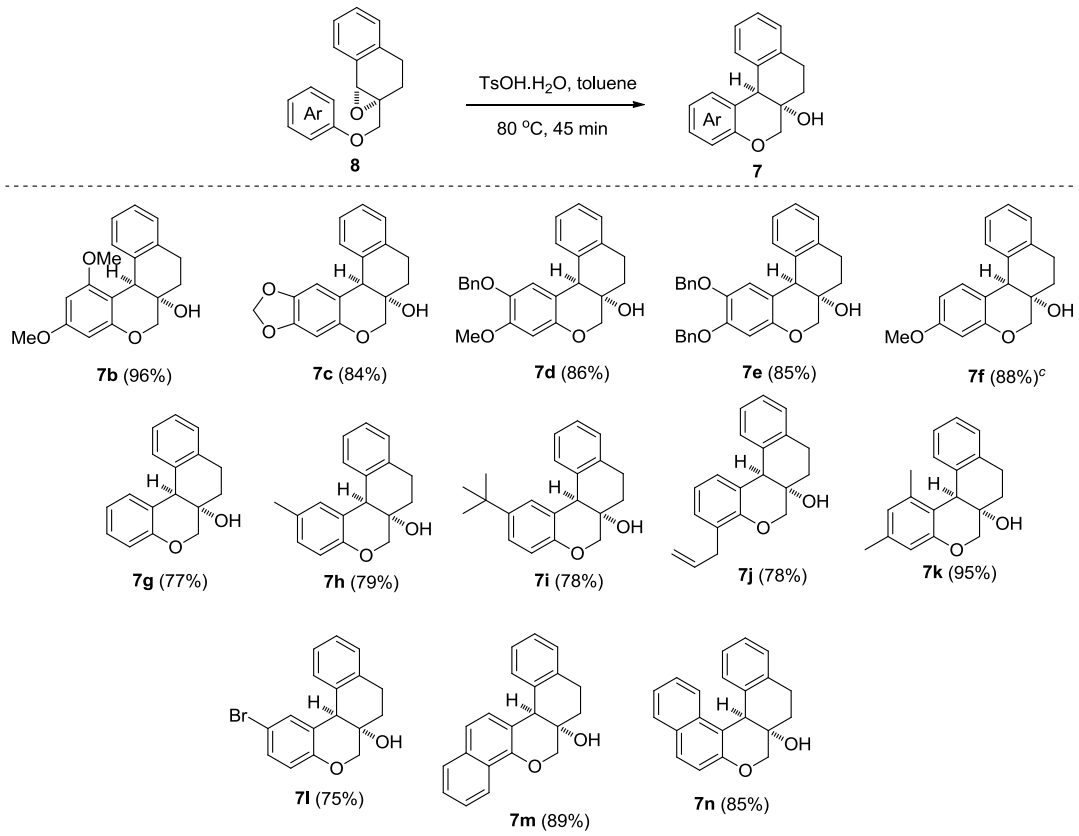
by using $BF_3 \cdot OEt_2$ (entry 12). Use of these Lewis acids required strict anh. conditions and some special attention to handle small amount of the catalyst. On the other hand, $TsOH \cdot H_2O$ is easily accessible, cheap, air stable, and even a minute amount can be weighed comfortably in an open atmosphere. It is important to mention that, among various acid catalyzed/promoted reactions described in the literature, on many occasions Brønsted acids have appeared as catalysts of choice under metal-free reaction conditions. On the basis of this fact and above investigations, we selected $TsOH \cdot H_2O$ (20 mol%) as catalyst in toluene at 80 °C as the optimized reaction conditions.

3.3.5. IFCEAC of 8b-n

We next subjected the remaining thirteen substrates **8b-n** to the optimized reaction conditions. The results are summarized in Table 3.3. All of these substrates could be effectively cyclized to give the corresponding chroman-fused tetralins **7b-n**, although the product yields were varied. Among the synthesized products, high yields were observed for **7b** (96%) and **7k** (95%), attributable to the high reactivity of symmetrical 3,5-dimethoxyphenoxy and 3,5-dimethylphenoxy groups in substrates **8b** and **8k**, respectively. Meanwhile, we witnessed somewhat lower (75-79%), but still synthetically useful, yields of products **7g**, **7h**, **7i**, **7j** and **7l** from the corresponding substrates, bearing moderately reactive arenoxy groups. But naphthochroman-fused tetralins **7m** and **7n** were obtained again in higher yields. Synthesis of **7j** was much significant as it has an allyl group which could be functionalized by diverse alkene chemistry. We believe that a large number of molecules similar to **7j** can also be synthesized using diverse 2-allylphenols (which are easily accessible via well-known Claisen rearrangement). Also, compound **7l** seems to have important synthetic potential for further diversification due to the presence of bromo substituent on the chroman-arene ring.

It is to be mentioned that, in each of the above-mentioned IFCEAC reactions, product was entirely the *syn*-isomer and no traces of the corresponding *anti*-isomers were detected in the ^{1}H NMR of the crude reaction mixtures. Stereochemical assignment at the ring junction of the products posed some initial challenge as it was not easy to confirm the *syn* relationship between the angular hydrogen and hydroxyl substituents with simple ^{1}D NMR spectroscopy. Alternative concrete evidences for the structural assignment were sought from X-ray crystallography.

Table 3.3: IFCEA cyclization on 8b-n leading to 7b-n[a,b]



[a]Reaction conditions: **8b-n** (0.4 mmol), TsOH·H_2O (20 mol%), toluene (8 mL), 80 °C, 45 min. [b]The numbers in parentheses represent isolated yields after silica gel column chromatography. [c]Yield of isolated mixture of the inseparable regioisomers.

Fortunately, we got the single crystals of **7k** by slow evaporation of its solution in hexanes/EtOAc. The molecular structure of **7k** was confirmed by X-ray diffraction analysis (Figure 3.4), confirming the *syn* relationship between H and OH at the ring junction. For the remaining products (**7a-j** and **7l-n**), this relative stereochemistry was confirmed by analogy.

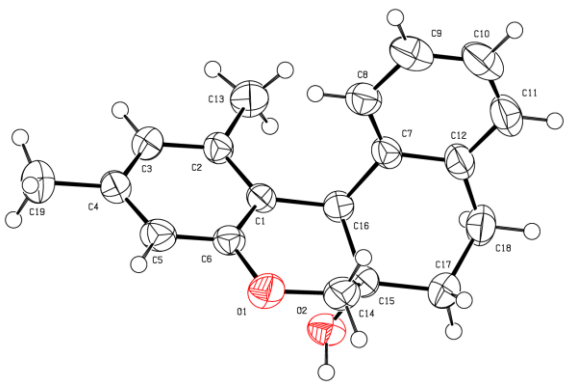
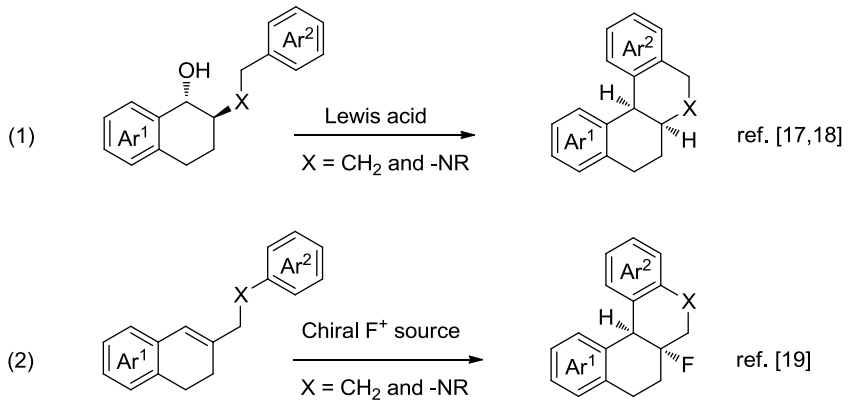


Figure 3.4. ORTEP diagram of **7k**

The observed *syn*-diastereoselectivity in this work was consistent with the reported synthesis of related-tetracyclic molecules via Friedel-Crafts cyclization promoted by metal-based Lewis acids (Scheme 3.4) [17-19]. Notably, none of the synthesized molecules described in these three reports contains angluar-OH group. We feel that our synthesis involves more challenging Friedel-Crafts cyclization (Scheme 3.2) and products are relevant in the field of the synthesis of natural-product-like small molecules (the synthesized molecules are close analogs of brazilin). Moreover, the use of $TsOH{\cdot}H_2O$ as an easily-accessible Brønsted acid catalyst with low loading under metal-free conditions and the operational simplicity render this transformation an attractive approach.



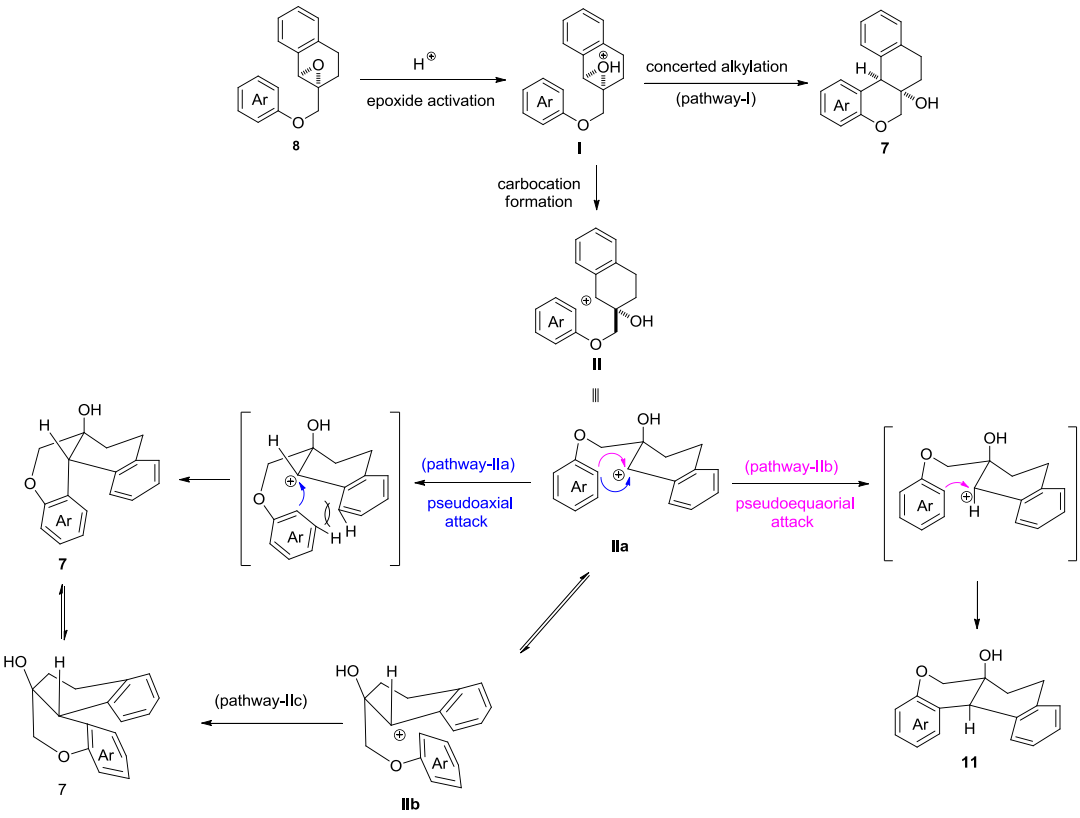
Scheme 3.4. Recent literature reports of *syn*-diastereoselective synthesis of tri- and tetracyclic molecules (containing two-fused six-membered rings) via IFCEAC

3.3.6. Proposed Reaction Mechanism

Our proposed mechanism of this IFCEAC is outlined in Scheme 3.5. First, substrate **8** gets activated in the presence of acid to afford protonated epoxide **I** onto which the electrophilic attack of the tethered arenoxy group may take place in concerted way, furnishing observed product **7** via 6-(arene-*endo*)-*endo*-epoxide cyclization (pathway-I, Scheme 3.5). Epoxide ring of the protonated epoxide **I** could also be opened to form benzylic carbocation intermediate **II** which can have two conformers **IIa** and **IIb**. The tethered arenoxy group in **IIa** can approach the electron deficient carbon atom either from the pseudoequatorial position (pathway-IIa) or from the pseudoaxial position (pathway-IIb), giving *anti*-product **11** and *syn*-product **7**, respectively. Formation of **7** as the sole IFCEAC product isomer clearly indicates the non-existence of pathway-IIb. This is in contrary to the fact that whereas pseudoequatorial approach of the arenoxy ring is

relatively free of steric or torsional strain, pseudoaxial attack may experience a steric hindrance from the benzene ring of tetralin moiety. Unfortunately, for the time being, we don't have a clear-cut answer for this anomaly. Nonetheless, reaction of conformer **IIb** can only provide the *syn*-fused product **7** (pathway-IIc).

Given the dual nature of the ring-opening of epoxide by arene (concerted by step-wise) and the unknown conformational preferences of carbocation **II** (**IIa** vs **IIb**), the attempted rationalization described above for the stereochemical result must be considered tentative. Also it is important to mention that this explanation is essentially an intermediate-based analysis and does not take into account the relative thermodynamic stability of the products **7** and **11**. In explaining the stereochemical outcome of the reaction, the relative thermodynamic stability of **7** and **11** may play an important role.

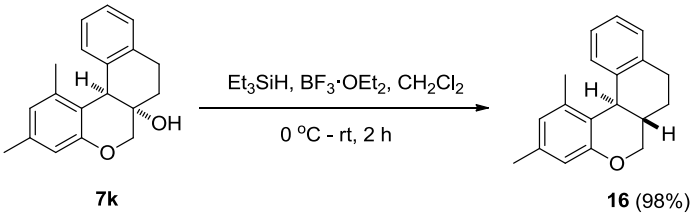


Scheme 3.5. Proposed reaction mechanism

3.4.7. Synthesis of a Chroman-Fused Tetralin with *trans*-Stereochemistry at the Ring Junction

In an additional work, the angular -OH group of **7k** was reductively removed on treatment with Et_3SiH and boron trifluoride etherate to get chroman-fused tetralin **16** with the two angular H atoms being positioned in *trans* fashion (Scheme 3.6); no *cis*-

isomer was formed. In the ^{1}H NMR spectrum of **16**, the benzylic angular methine proton appeared as a doublet with J = 10.5 Hz at δ 3.97. In the related previously known *cis*-fused tetracycles, the benzylic angular methine proton appeared as a doublet with coupling constant J = 4–6 Hz [20], whereas that in *trans*-fused ones appeared as a doublet with coupling constant J = 9–11 Hz [21]. Thus, the *trans*-stereochemistry at the ring junction in **16** was confirmed.



Scheme 3.6. Stereoselective reductive dehydroxylation of 7k

Such a stereoselective reductive removal of –OH group should be useful in preparing library of chroman-fused tetralins with *trans*-stereochemistry at the ring junction.

3.5. Conclusion

In conclusion, we have developed a convenient Brønsted acid-catalyzed, metal-free, *syn*-diastereoselective synthesis of 6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ols as B-ring-modified analogues of brazilin using starting materials derived from 1-tetralone and phenols/naphthols. Our worries concerning the formation *syn-anti* mixture of 6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ols and their probable conversion to of naphthopyran derivatives via dehydration of *tertiary*-OH group were laid to rest. To the best of our knowledge, this is the first example of the generation of such type of chroman-fused tetralins. The easy accessibility of the starting materials, the mild reaction conditions, and the importance of products as B-ring-modified analogues of brazilin should make this synthetic work a useful addition in the diversity-oriented synthesis of natural-product like molecules.

3.6. Experimental Section

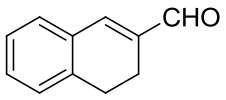
3.6.1. General Remarks

Same as described in the **Chapter 2**, **Section 2.6.1** of this thesis.

3.6.2. Preparation of Compounds

Synthesis of Tetralin-Embedded Epoxy Tosylate from 1-Tetralone (Scheme 3.3)

3,4-Dihydronaphthalene-2-carbaldehyde (14):



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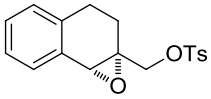
To a stirred solution of α-tetralone **10** (6.0 g, 41.0 mmol) in MeOH (60 mL) was slowly added $NaBH_4$ (3.78 g, 102.6 mmol) at 0 °C and then the resulting mixture was stirred for 30 min at rt. The reaction was carefully quenched by the addition aq. saturated NH_4Cl solution (20 mL) at 0 °C. The resulting mixture was then concentrated in a rotary evaporator until the almost whole methanol got removed. The residue was dissolved in EtOAc (80 mL) and the mixture was diluted with H_2O (50 mL). The organic layer was separated and then washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude 1,2,3,4-tetrahydronaphth-1-ol was virtually pure (TLC) and used for the next step without further purification.

To an ice-cooled solution of this crude product in anh. DMF (25.0 ml) was added $POCl_3$ (12.0 ml) dropwise and the resulting mixture was then stirred at rt for 1 h and finally at 80 °C overnight. After cooling to room temperature, the reaction was quenched with ice water (50 mL) and made basic with 1N NaOH and the resulting mixture was extracted with EtOAc (100 ml). The aqueous phase was extracted with EtOAc (3 x 50 mL) and the combined organic fractions were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (0-10% EtOAc in hexanes) to give **14** (5.19 g, 80% over two steps) as a as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (s, 1H), 7.35-7.19 (m, 5H), 2.89 (t, *J* = 8.2 Hz, 2H), 2.58 (t, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.9, 145.8, 139.3, 138.2, 132.2, 130.6, 128.9, 128.1, 127.0, 27.0, 19.3. The physical and spectral data matched with the literature data [22].

((1a*R,7b*R**)-1a,2,3,7b-Tetrahydronaphtho[1,2-*b*]oxiren-1a-yl)methyl 4-methyl benzenesulfonate (15):**



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To a stirred solution of 3,4-dihydronaphthalene-2-carbaldehyde **14** (5.0 g, 31.6 mmol) in MeOH (50 mL) was slowly added $NaBH_4$ (3.0 g, 79.0 mmol) at 0 °C and then the resulting mixture was stirred for 1 h at rt. The reaction was carefully quenched by the addition aq. saturated NH_4Cl solution (20 mL) at 0 °C. The resulting mixture was then concentrated in a rotary evaporator until the almost whole methanol got removed. The residue was dissolved in EtOAc (70 mL) and the mixture was diluted with H_2O (50 mL). The organic layer was separated and then washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude (3,4-dihydronaphthalen-2-yl)methanol was virtually pure (TLC) and used for the next step without further purification.

To a stirred solution of this alcohol in CH_2Cl_2 (50 mL) was added *m*-CPBA (70% purity, 8.2 g, 33.42 mmol) at 0 ^oC. The reaction mixture was stirred overnight at room temperature. The mixture was washed successively with aq. solutions of Na_2SO_3 (50 mL) and $NaHCO_3$ (50 mL). The combined aqueous phases were extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude epoxy alcohol was used for the next step without further purification.

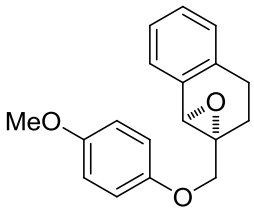
To a stirred solution of above epoxy alcohol in CH_2Cl_2 (50 mL) at 0 ^oC was added triethyl amine (4.5 mL, 31.41 mmol) followed by tosyl chloride (5.0 g, 26.17 mmol) and kept in the refrigerator for 12 h. The reaction mixture was diluted with H_2O (100 mL), and extracted with CH_2Cl_2 (2× 50 mL). The combined organic layers were washed with brine (100 mL) and dried over anh. Na_2SO_4. After filtration, the solvent was removed under reduced pressure. The crude product was recrystallized from EtOAc/hexanes to obtain epoxy tosylate **15** as an off-white solid. Yield: 81% (8.05 g; over three steps); ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.38-7.05 (m, 6H), 4.32 (d, *J* = 11.0 Hz, 1H), 4.20 (d, *J* = 11.0 Hz, 1H), 3.71 (s, 1H), 2.78 (td, *J* = 6.8, 14.7 Hz, 1H), 2.58-2.52 (m, 1H), 2.43 (s, 3H), 2.31-2.25 (m, 1H), 1.78 (td, *J* = 5.5, 14.0 Hz, 1H); Anal. Calcd. for $C_{18}H_{18}O_4S$: C, 65.43; H, 5.49, found: C, 65.32; H, 5.51.

General Procedure A: Synthesis of Tetralin-Embedded Glycidyl Ethers 8a-n (Table 3.1):

To a stirred suspension of NaH (35 mg, 1.5 mmol) in anh. DMF (3 mL) was added a solution of appropriate phenol (1.0 mmol) in anh. DMF (5 mL) at 0 °C under N_2 atmosphere. The resulting mixture was stirred for 5 min, and then a solution of 15 (345

mg, 1.1 mmol) in DMF (5 mL) was added dropwise. The solution was stirred for an additional 10 h at 0 ºC. The reaction was terminated by the addition of 10% aqueous ammonium chloride (10 mL) and diethyl ether (50 mL) was added. The organic layer was separated, washed by brine (50 mL) and dried over anhyd. Na_2SO_4. After filtration, the solution was evaporated to anh.ness under reduced pressure. The residue was subjected to silica gel column chromatography (with EtOAc/hexanes as the eluent) to afford the desired tetralin-based epoxy ethers 8a-n.

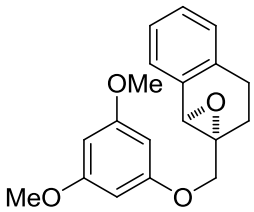
(1a*R,7b*R**)-1a-((4-Methoxyphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8a)**:



8a

Following the **general procedure A**, compound **8a** was prepared from epoxy tosylate **15** and 4-methoxyphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as a white solid; m.p.: 95-96 °C; Yield: 85% (239 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.3 Hz, 1H), 7.29-7.25 (m, 1H), 7.22-7.19 (m, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 9.1 Hz, 2H), 6.84 (d, *J* = 9.1 Hz, 2H), 4.26 (d, *J* = 10.7 Hz, 1H), 4.16 (d, *J* = 10.7 Hz, 1H), 3.92 (s, 1H), 3.77 (s, 3H), 2.88 (td, *J* = 6.4, 14.9 Hz, 1H), 2.65-2.61 (m, 1H), 2.48-2.44 (m, 1H), 1.94 (td, *J* = 5.5, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 137.0, 132.0, 129.5, 128.6, 128.3, 126.2, 115.7, 114.6, 71.5, 62.5, 57.1, 55.7, 25.2, 22.9; Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43, found: C, 76.54; H, 6.50.

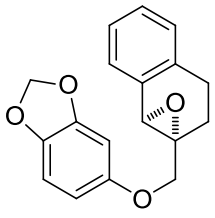
(1a*R,7b*R**)-1a-((3,5-Dimethoxyphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho [1,2-*b*]oxirene (8b)**:



8b

Following the **general procedure A**, compound **8b** was prepared from epoxy tosylate **15** and 3,5-dimethoxyphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as an off-white solid; m.p.: 45-46 °C; Yield: 90% (281 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 1H), 7.29-7.26 (m, 1H), 7.21 (t, *J* = 7.3 Hz, 1H),7.13 (d, *J* = 7.3 Hz, 1H), 6.14 (d, *J* = 2.2 Hz, 2H), 6.10 (t, *J* = 2.2 Hz, 1H), 4.27 (d, *J* = 10.7 Hz, 1H), 4.16 (d, *J* = 10.4 Hz, 1H), 3.92 (s, 1H), 3.76 (s, 6H), 2.88 (td, *J* = 6.4, 14.7 Hz, 1H), 2.65-2.61 (m, 1H), 2.48-2.44 (m, 1H), 1.96 (td, *J* = 5.5, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 160.5, 136.9, 131.9, 129.5, 128.7, 128.3, 126.2, 93.48, 93.45, 70.7, 62.3, 57.2, 55.3, 25.2, 22.9; Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45, found: C, 72.99; H, 6.55.

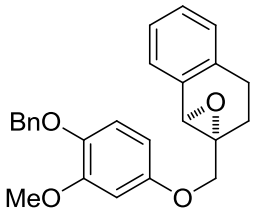
(1a*R,7b*R**)-1a-((Benzo[d][1,3]dioxol-5-yloxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8c)**:



8c

Following the **general procedure A**, compound **8c** was prepared from epoxy tosylate **15** and sesamol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 82-83°C; Yield: 88% (260 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.3 Hz, 1H), 7.30-7.28 (m, 1H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.52 (d, *J* = 2.7 Hz, 1H), 6.38 (dd, *J* = 2.7, 8.7 Hz, 1H), 5.93 (s, 2H), 4.24(d, *J* = 10.5 Hz, 1H), 4.14 (d, *J* = 10.5 Hz, 1H), 3.92 (s, 1H), 2.89 (td, *J* = 6.4, 14.7 Hz, 1H), 2.67-2.61 (m, 1H), 2.49-2.44 (m, 1H), 1.94 (td, *J* = 5.5, 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.3, 136.9, 131.9, 129.5, 128.7, 128.3, 126.2, 107.9, 105.8, 101.2, 98.3, 87.1, 71.7, 62.4, 57.1, 25.2, 22.9; Anal. Calcd. for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44, found: C, 73.02; H, 5.53.

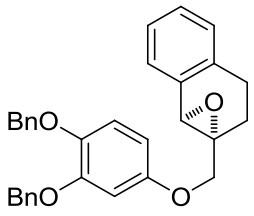
(1a*R,7b*R**)-1a-((4-(Benzyloxy)-3-methoxyphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8d)**:



8d

Following the **general procedure A**, compound **8d** was prepared from epoxy tosylate **15** and 3-methoxy-4-benzyloxyphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 105-106°C; Yield: 80% (310 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.0 Hz, 2H), 7.41-7.35 (m, 3H), 7.32-7.27 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 1H),7.13 (d, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 6.62 (d, *J* = 2.7 Hz, 1H), 6.38 (dd, *J* = 2.7, 8.5 Hz, 1H), 5.09 (s, 2H), 4.26 (d, *J* = 10.7 Hz, 1H), 4.15 (d, *J* = 10.7 Hz, 1H), 3.93 (s, 1H), 3.87 (s, 3H), 2.89 (td, *J* = 6.1, 14.6 Hz, 1H), 2.66-2.62 (m, 1H), 2.49-2.45 (m, 1H), 1.95 (td, *J* = 5.5, 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.8, 150.7, 142.7, 137.4, 136.9, 129.4, 128.7, 128.4, 128.3, 127.7, 127.4, 126.2, 126.1, 115.4, 104.0, 101.2,72.0, 71.2, 62.4, 57.1, 55.9, 25.1, 22.9; Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23, found: C, 77.35; H, 6.28.

(1a*R,7b*R**)-1a-((3,4-bis(Benzyloxy)phenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8e)**:

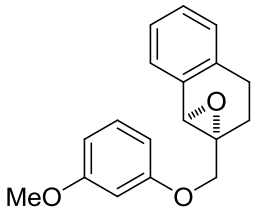


8e

Following the **general procedure A**, compound **8e** was prepared from epoxy tosylate **15** and 3,4-dibenzyloxyphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 102-103°C; Yield: 84% (390 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46-7.20 (m, 13H), 7.13 (d, *J* = 7.1 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.65 (d, *J* = 3.0 Hz, 1H), 6.42 (dd, *J* = 3.0, 8.8 Hz, 1H), 5.13 (s, 2H), 5.09 (s, 2H), 4.22 (d, *J* = 10.7 Hz, 1H), 4.11 (d, *J* = 10.7 Hz, 1H), 3.89 (s, 1H), 2.87 (td, *J* = 6.4, 14.7 Hz, 1H), 2.65-2.61 (m, 1H), 2.46-2.42 (m, 1H), 1.91 (td, *J* = 5.5, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.9, 150.2, 143.4, 137.5, 137.0, 136.9, 132.0, 129.5, 128.7,

128.5, 128.4, 128.3, 127.8, 127.7, 127.5, 127.3, 126.2, 116.9, 105.4, 103.6, 72.5, 71.3, 71.1, 62.4, 57.1, 25.2, 22.9; Anal. Calcd. for $C_{31}H_{28}O_4C$, 80.15; H, 6.08, found: C, 80.18; H, 6.13.

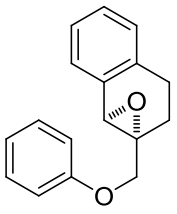
(1a*R,7b*R**)-1a-((3-Methoxyphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8f)**:



8f

Following the **general procedure A**, compound **8f** was prepared from epoxy tosylate **15** and 3-methoxyphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as colourless gum. Yield: 86% (242 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.29-7.17 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 1H), 6.55-6.52 (m, 3H), 4.28 (d, *J* = 10.7 Hz, 1H), 4.17 (d, *J* = 10.7 Hz, 1H), 3.92 (s, 1H), 3.79 (s, 3H), 2.89 (td, *J* = 6.4, 14.9 Hz, 1H), 2.66-2.62 (m, 1H), 2.50-2.45 (m, 1H), 1.95 (td, *J* = 5.5, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 159.8, 132.0, 129.9, 129.5, 128.7, 128.3, 126.2, 106.9, 106.7, 101.1, 70.7, 62.3, 57.2, 55.3, 25.2, 22.9; Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43, found: C, 76.67; H, 6.52.

(1a*R,7b*R**)-1a-(Phenoxymethyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8g)**:

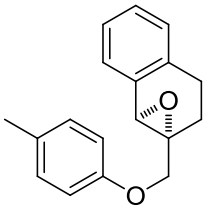


8g

Following the **general procedure A**, compound **8g** was prepared from epoxy tosylate **15** and phenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 105-106°C; Yield: 90% (227 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 6.9 Hz, 1H), 7.31-7.19 (m, 4H), 7.13 (d, *J* = 7.3 Hz, 1H), 6.99-6.94 (m, 3H), 4.30 (d, *J* = 10.5 Hz, 1H), 4.20 (d, *J* = 10.5 Hz, 1H), 3.93 (s,

1H), 2.88 (td, *J* = 6.4, 14.7 Hz, 1H), 2.66-2.61 (m, 1H), 2.50-2.45 (m, 1H), 1.95 (td, *J* = 5.5, 13.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 136.9, 131.9, 129.5, 128.6, 128.3, 126.2, 121.1, 114.6, 87.0, 70.6, 62.4, 57.1, 25.1, 22.9; Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39, found: C, 80.96; H, 6.41.

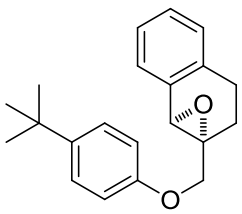
(1a*R,7b*R**)-1a-((*p*-Tolyloxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8h)**:



8h

Following the **general procedure A**, compound **8h** was prepared from epoxy tosylate **15** and *p*-cresol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 95-96°C; Yield: 88% (234 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 1H), 7.29-7.27 (m, 1H), 7.21 (t, 1H, *J* = 7.3 Hz, 1H), 7.13 (d, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.27 (d, *J* = 10.7 Hz, 1H), 4.18 (d, *J* = 10.7 Hz, 1H), 3.93 (s, 1H), 2.89 (td, *J* = 6.4, 15.2 Hz, 1H), 2.66-2.61 (m, 1H), 2.49-2.45 (m, 1H), 2.29 (s, 3H), 1.94 (td, *J* = 5.5, 14.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 137.0, 132.0, 130.4, 129.9, 129.5, 128.6, 128.3, 126.2, 114.5, 70.8, 62.4, 57.2, 25.2, 22.9, 20.5; Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81; Found: C, 81.26; H, 6.88.

(1a*R,7b*R**)-1a-((4-(*tert*-Butyl)phenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8i)**:

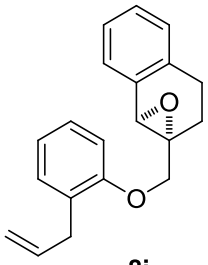


8i

Following the **general procedure A**, compound **8i** was prepared from epoxy tosylate **15** and 4-*tert*-butylphenol. Column chromatography: 1-10% EtOAc in hexanes. This

compound was isolated as a white solid; m.p.: 98-99°C; Yield: 85% (262 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 1H), 7.32-7.25 (m, 3H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.28 (d, *J* = 10.7 Hz, 1H), 4.19 (d, *J* = 10.7 Hz, 1H), 3.92 (s, 1H), 2.88 (td, *J* = 6.4, 15.0 Hz, 1H), 2.65-2.61 (m, 1H), 2.49-2.45 (m, 1H), 1.95 (td, *J* = 5.5, 14.0 Hz, 1H), 1.3 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 143.8, 137.0, 132.0,129.5, 128.6, 128.3, 126.3, 126.2, 114.0, 70.8, 62.4, 57.2, 34.1, 31.5, 25.2, 22.9; Anal. Calcd. for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84, found: C, 81.82; H, 7.77.

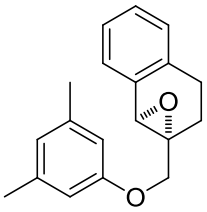
((1a*R,7b*R**)-1a-((2-Allylphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8j)**:



8j

Following the **general procedure A**, compound **8j** was prepared from epoxy tosylate **15** and 2-allylphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as colourless semi-solid. Yield: 80% (234 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.28-7.21 (m, 5H), 6.92 (t, *J* = 7.3 Hz, 1H), 6.86 (d, *J* = 7.9 Hz, 1H), 6.05-5.94 (m, 1H), 5.09-5.02 (m, 2H), 4.28 (d, *J* = 10.4 Hz, 1H), 4.19 (d, *J* = 10.9 Hz, 1H), 3.92 (s, 1H), 3.43 (d, *J* = 6.7 Hz, 1H), 2.88 (td, *J* = 6.4, 15.0 Hz, 1H), 2.65-2.60 (m, 1H), 2.49-2.45 (m, 1H), 1.94 (td, *J* = 5.5, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 136.9, 136.8, 132.0, 129.8, 129.4, 128.8, 128.6, 128.3, 127.3, 126.1, 121.0, 115.5, 111.4, 70.8, 62.4, 57.1, 34.4, 25.2, 22.9; Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89, found: C, 82.01; H, 6.97.

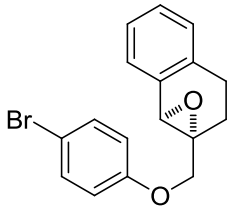
((1a*R,7b*R**)-1a-((3,5-Dimethylphenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8k)**:



8k

Following the **general procedure A**, compound **8k** was prepared from epoxy tosylate **15** and 3,5-dimethylphenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as a colourless semi-solid. Yield: 89% (250 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.3 Hz, 1H), 7.29-7.19 (m, 2H), 7.12 (d, *J* = 7.3 Hz, 1H), 6.62 (s, 1H), 6.58 (s, 2H), 4.26 (d, *J* = 10.5 Hz, 1H), 4.17 (d, *J* = 10.9 Hz, 1H), 3.91 (s, 1H), 2.88 (td, *J* = 6.4, 15.6 Hz, 1H), 2.65-2.60 (m, 1H), 2.48-2.42 (m, 1H), 2.28 (s, 6H), 1.94 (td, *J* = 5.5, 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 139.2, 136.9, 132.0, 129.5, 128.6, 128.3, 126.1, 122.9, 112.4, 70.6, 62.4, 57.2, 25.2, 22.9, 21.4; Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19, found: C, 81.44; H, 7.22.

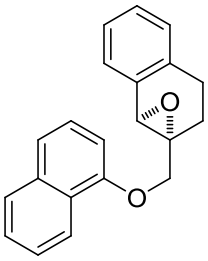
((1a*R,7b*R**)-1a-((4-Bromophenoxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8l)**:



8l

Following the **general procedure A**, compound **8l** was prepared from epoxy tosylate **15** and 4-bromophenol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as a colourless semi-solid. Yield: 80% (265 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.38 (m, 3H), 7.31-7.28 (m, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.30 (d, *J* = 10.5 Hz, 1H), 4.17 (d, *J* = 10.9 Hz, 1H), 3.93 (s, 1H), 2.89 (td, *J* = 6.4, 15.1 Hz, 1H), 2.68-2.62 (m, 1H), 2.50-2.44 (m, 1H), 1.94 (td, *J* = 5.5, 14.2 Hz, 1H); Anal. Calcd. for $C_{17}H_{15}BrO_2$:C, 61.65; H, 4.56, found: C, 61.56; H, 4.62.

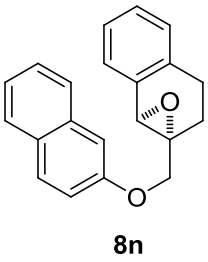
(((1a*R,7b*R**)-1a-((Naphthalen-1-yloxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8m)**:



8m

Following the **general procedure A**, compound **8m** was prepared from epoxy tosylate **15** and 1-naphthol. Column chromatography: 1-10% EtOAc in hexanes.
This compound was isolated as white solid; m.p.: 97-98°C; Yield: 78% (236 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31-8.29 (m, 1H), 7.81-7.79 (m, 1H), 7.51-7.42 (m, 4H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.31-7.21 (m, 2H), 7.15 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.3 Hz, 1H), 4.45 (d, *J* = 10.4 Hz, 1H), 4.38 (d, *J* = 10.4 Hz, 1H), 4.01 (s, 1H), 2.94 (td, *J* = 6.4, 14.7 Hz, 1H), 2.70-2.65 (m, 1H), 2.60-2.56 (m, 1H), 2.07 (td, *J* = 5.5, 13.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 136.9, 134.5, 132.0, 129.6, 128.7, 128.4, 127.5, 126.5, 126.2, 125.7, 125.5, 125.3, 122.0, 120.8, 104.9, 71.1, 62.4, 57.4, 25.2, 23.1; Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00, found: C, 83.49; H, 6.02.

((((1a*R,7b*R**)-1a-((Naphthalen-2-yloxy)methyl)-1a,2,3,7b-tetrahydronaphtho[1,2-*b*]oxirene (8n)**:



8n

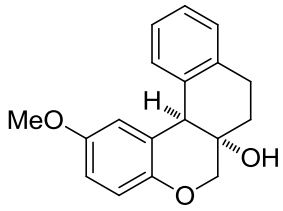
Following the **general procedure A**, compound **8n** was prepared from epoxy tosylate **15** and 2-naphthol. Column chromatography: 1-10% EtOAc in hexanes. This compound was isolated as white solid; m.p.: 148-149 °C; Yield: 72% (218 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.83 (m, 3H), 7.47-7.42 (m, 2H), 7.37-7.28 (m, 2H), 7.25-7.20 (m, 3H), 7.16 (d, *J* = 7.3 Hz, 1H), 4.44 (d, *J* = 10.4 Hz, 1H), 4.33 (d, *J* = 10.4 Hz, 1H), 4.01 (s, 1H), 2.93 (td, *J* = 6.4, 14.4 Hz, 1H), 2.69-2.65 (m, 1H), 2.56-2.52 (m, 1H), 2.01 (td, *J* = 5.5, 13.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 137.0, 134.4, 132.0, 129.55,

129.50, 129.1, 128.7, 128.4, 127.6, 126.8, 126.4, 126.2, 70.7, 62.4, 57.2, 25.2, 23.0; Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00, found: C, 83.46; H, 5.92.

General procedure B: preparation of chroman-fused tetralins 7a-n via IFCEAC reactions:

To a stirred solution of glycidyl ethers **8** (0.4 mmol) in AR grade toluene (8 mL) was added TsOH·H_2O (16 mg, 0.084 mmol). The resulting mixture was then heated at 80 °C. When the reaction was completed (approx. 45 min), the mixture was cooled to room temperature, and then poured in beaker containing EtOAc (30 mL) and saturated aq. $NaHCO_3$ solution (25 mL) with vigorous stirring. The combined organic layers was washed with brine (30 mL) and dried over anh. Na_2SO_4. After filtration, the solution was evaporated to anh.ness under reduced pressure. The residue was subjected to silica gel column chromatography (with EtOAc/hexanes as the eluent) to afford the desired chroman-fused tetralins **7a-n**.

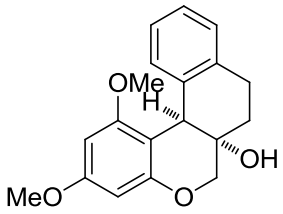
(6a*S,12b*R**)-2-Methoxy-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7a)**:



7a

Following the **general procedure B**, compound **7a** was prepared from glycidyl ether **8a**. Column chromatography: 5-12% EtOAc in hexanes; Isolated as a colourless gum; Yield: 81% (92 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.13 (m, 4H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.79 (dd, *J* = 2.7, 8.7 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 3.91-3.87 (m, 2H), 3.75-3.72 (m, 4H), 3.07-2.99 (m, 1H), 2.83-2.76 (m, 1H), 2.31 (s, 1H), 2.15-2.09 (m, 1H), 1.82-1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.7, 146.8, 136.9, 136.8, 129.1, 128.0, 126.9, 126.2, 122.0, 117.5, 116.2, 114.3, 71.4, 68.1, 55.7, 47.6, 31.5, 26.4; Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43, found: C, 76.68; H, 6.48.

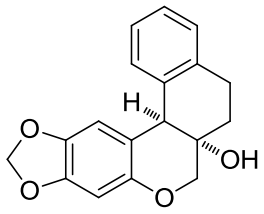
(6a*S,12b*R**)-1,3-Dimethoxy-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7b)**:



7b

Following the **general procedure B**, compound **7b** was prepared from glycidyl ether **8b**. Column chromatography: 5-15% EtOAc in hexanes; Isolated as a light-brown solid; m.p.: 155-156 °C. Yield: 96% (120 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J* = 3.9 Hz, 2H), 7.10-7.07 (m, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.21 (d, *J* = 2.4 Hz, 1H), 6.14 (d, *J* = 2.4 Hz, 1H), 3.94 (s, 1H), 3.81 (s, 3H), 3.78 (dd, *J* = 2.7, 11.3 Hz, 1H), 3.75 (s, 3H), 3.51 (d, *J* = 11.3 Hz, 1H), 3.10-3.03 (m, 1H), 2.81-2.75 (m, 1H), 2.39 (s, 1H), 2.31-2.26 (m, 1H), 1.57-1.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5, 160.3, 154.3, 138.5, 137.2, 127.8, 127.0, 126.2, 126.1, 101.8, 93.2, 92.0, 70.1, 68.2, 55.4, 55.3, 41.5, 33.3, 27.1; Anal. Calcd. for $C_{19}H_{20}O_4$:C, 73.06; H, 6.45, found: C, 73.09; H, 6.35.

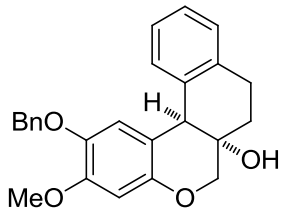
(6a*S,13b*R**)-6,6a,7,13b-Tetrahydro-5*H*-[1,3]dioxolo[4,5-*g*]naphtho[2,1-*c*]chromen-6a-ol (7c)**:



7c

Following the **general procedure B**, compound **7c** was prepared from glycidyl ether **8c**. Column chromatography: 5-15% EtOAc in hexanes; Isolated as a colourless semi-solid. Yield: 84% (100 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.18 (m, 3H), 7.13-7.11 (m, 1H), 6.60 (s, 1H), 6.46 (s, 1H), 5.92 (s, 2H), 3.87 (dd, *J* = 1.6, 10.6 Hz, 1H), 3.78 (s, 1H), 3.68 (d, *J* = 11.0 Hz, 1H), 3.04-2.97 (m, 1H), 2.80-2.75 (m, 1H), 2.14-2.09 (m, 1H), 1.79-1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.7, 147.4, 141.9, 137.4, 136.9, 128.9, 127.9, 126.8, 126.2, 112.5, 110.0, 101.1, 98.5, 71.3, 68.1, 47.3, 31.6, 26.4; Anal. Calcd. for $C_{18}H_{16}O_4$:C, 72.96; H, 5.44, found: C, 73.08; H, 5.49.

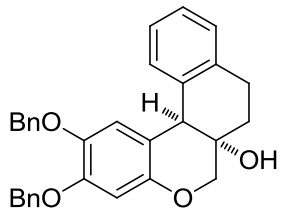
(6a*S,12b*R**)-2-(Benzyloxy)-3-methoxy-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7d)**:



7d

Following the **general procedure B**, compound **7d** was prepared from glycidyl ether **8d**. Column chromatography: 5-15% EtOAc in hexanes; Isolated as a colourless white solid; m.p.: 103-104 °C. Yield: 86% (133 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.30 (m, 5H), 7.19-7.14 (m, 2H), 7.09-7.06 (m, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.64 (s, 1H), 6.49 (s, 1H), 5.10-5.04 (m, 2H), 3.87 (s, 3H), 3.85 (dd, *J* = 1.8, 11.0 Hz, 1H), 3.70 (s, 1H), 3.65 (d, *J* = 11.0 Hz, 1H), 3.01-2.95 (m, 1H), 2.78-2.72 (m, 1H), 2.32 (sbr, 1H), 2.13-2.08 (m, 1H), 1.73-1.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 147.3, 141.9, 137.4, 137.2, 136.7, 128.6, 128.4, 127.8, 127.7, 127.5, 126.6, 126.1, 118.1, 111.4, 100.9, 71.7, 71.1, 68.1, 55.9, 46.6, 31.7, 26.4; Anal. Calcd. for $C_{25}H_{24}O_4$:C, 77.30; H, 6.23, found: C, 77.20; H, 6.16.

(6a*S,12b*R**)-2,3-bis(Benzyloxy)-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7e)**:

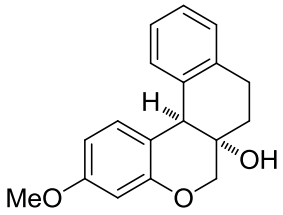


7e

Following the **general procedure B**, compound **7e** was prepared from glycidyl ether **8e**. Column chromatography: 5-15% EtOAc in hexanes; Isolated as a colourless semi-solid. Yield: 85% (157 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.30 (m, 10H), 7.21-7.09 (m, 3H), 6.88 (d, *J* = 7.3 Hz, 1H), 6.71 (s, 1H), 6.55 (s, 1H), 5.15 (s, 2H), 5.13-5.06 (m, 2H), 3.83 (dd, *J* = 1.8, 11.0 Hz, 1H), 3.71 (s, 1H), 3.64 (d, *J* = 10.4 Hz, 1H), 3.02-2.95 (m, 1H), 2.79-2.72 (m, 1H), 2.28 (s br, 1H), 2.13-2.07 (m, 1H), 1.74-1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.5, 147.5, 142.4, 137.33, 137.31, 136.9, 136.7, 128.7,

128.5, 128.4, 127.83, 127.80, 127.7, 127.6, 127.2, 126.6, 126.1, 119.4, 112.3, 103.0, 72.2, 71.0, 70.8, 68.0, 46.6, 31.6, 26.4; Anal. Calcd. for $C_{31}H_{28}O_4$:C, 80.15; H, 6.08, found: C, 80.22; H, 6.16.

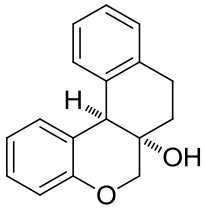
(6a*S,12b*R**)-3-Methoxy-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7f)**:



7f

Following the **general procedure B**, compound **7f** was prepared from glycidyl ether **8f**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a ca. 3:1 mixture of inseparable regioisomers as judged by ^{1}H NMR analysis. Colourless semi-solid; Yield: 88% (99 mg); Major isomer (**7f**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.10 (m, 4H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.55 (dd, *J* = 2.5, 8.6 Hz, 1H), 6.47 (d, *J* = 2.5 Hz, 1H), 3.92 (dd, *J* = 1.5, 11.0 Hz, 1H), 3.82 (s, 1H), 3.78-3.76 (m, 4H), 3.05-2.98 (m, 1H), 2.88 (s, 1H), 2.81-2.76 (m, 1H), 2.13-2.08 (m, 1H), 1.82-1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 153.6, 137.2, 136.5, 132.1, 129.1, 127.9, 126.6, 126.03, 126.01, 107.8, 101.4, 71.3, 67.9, 55.2, 46.6, 31.3, 26.2; Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43, found: C, 76.52; H, 6.51.

(6a*S,12b*R**)-6a,7,8,12b-Tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7g)**:

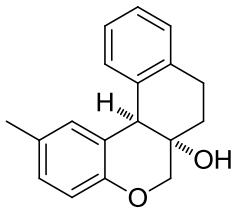


7g

Following the **general procedure B**, compound **7g** was prepared from glycidyl ether **8g**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a colourless semi-solid. Yield: 77% (77 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24-7.16 (m, 5H), 7.12-7.09 (m, 1H), 6.97-6.91 (m, 2H), 3.95 (dd, *J* = 1.8, 11.0 Hz, 1H), 3.90 (s, 1H), 3.80 (d, *J* = 11.0 Hz, 1H), 3.09-2.99 (m, 1H), 2.82-2.76 (m, 1H), 2.33 (br s, 1H),

2.15-2.08 (m, 1H), 1.85-1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 136.9, 132.0, 129.5, 128.7, 129.5, 128.7, 128.3, 126.2, 105.8, 101.2, 87.1, 71.7, 62.4, 57.1, 25.2, 22.9; Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39, found: C, 80.99; H, 6.33.

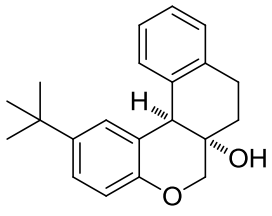
(6a*S,12b*R**)-2-Methyl-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7h)**:



7h

Following the **general procedure B**, compound **7h** was prepared from glycidyl ether **8h**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a white solid; m.p.: 110-112 °C. Yield: 79% (84 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.17 (m, 3H), 7.11-7.10 (m, 1H), 7.01 (dd, *J* = 1.8, 8.5 Hz, 1H), 6.96 (s, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 3.90 (dd, *J* = 1.5, 11.0 Hz, 1H), 3.85 (s, 1H), 3.75 (d, *J* = 11.0 Hz, 1H), 3.05-2.98 (m, 1H), 2.81-2.76 (m, 1H), 2.28 (s, 3H), 2.27 (br s, 1H), 2.14-2.09 (m, 1H), 1.82-1.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.6, 137.1, 136.7, 131.9, 130.0, 129.2, 129.0, 127.9, 126.7, 126.0, 120.8, 116.6, 71.2, 68.1, 47.2, 31.5, 26.3, 20.6; Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81, found: C, 81.11; H, 6.76.

(6a*S,12b*R**)-2-(*tert*-Butyl)-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7i)**:

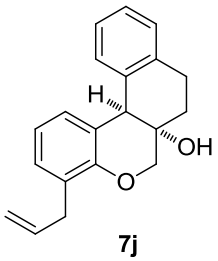


7i

Following the **general procedure B**, compound **7i** was prepared from glycidyl ether **8i**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a colourless gum. Yield: 78% (96 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.14 (m, 5H), 7.03 (d, *J* = 6.7 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 3.88-3.83 (m, 2H), 3.85 (s, 1H), 3.65 (d, *J*= 10.4 Hz, 1H), 3.04-2.98 (m, 1H), 2.79-2.74 (m, 1H), 2.48 (br s, 3H), 2.15-

2.10 (m, 1H), 1.71-1.65 (m, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 143.4, 137.6, 137.0, 128.8, 128.7, 127.7, 126.6, 126.0, 125.4, 119.9, 116.2, 71.0, 68.3, 47.2, 34.0, 31.8, 31.4, 26.5; Anal. Calcd. for $C_{21}H_{24}O_2$:C, 81.78; H, 7.84, found: C, 81.85; H, 7.92.

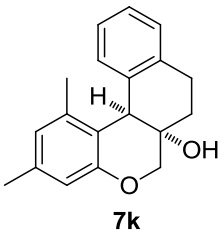
(6a*S,12b*R**)-4-Allyl-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7j)**:



7j

Following the **general procedure B**, compound **7j** was prepared from glycidyl ether **8j**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a colourless semi-solid. Yield: 78% (91 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.16 (m, 3H), 7.10-7.03 (m, 3H), 6.89 (t, *J* = 7.8 Hz, 1H), 6.07-5.99 (m, 1H), 5.09-5.04 (m, 2H), 3.96 (dd, *J* = 1.8, 11.0 Hz, 1H), 3.88 (s, 1H), 3.79 (d, *J* = 11.0 Hz, 1H), 3.40 (d, *J* = 6.4 Hz, 1H), 3.05-2.97 (m, 1H), 2.81-2.74 (m, 1H), 2.33 (br s, 1H), 2.14-2.07 (m, 1H), 1.82-1.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 137.3, 136.7, 136.6, 129.7, 129.2, 128.5, 128.1, 127.9, 126.6, 126.0, 120.8, 120.3, 115.4, 71.3, 67.9, 47.4, 34.2, 31.4, 26.3; Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89, found: C, 82.19; H, 6.98.

(6a*S,12b*R**)-1,3-Dimethyl-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7k)**:

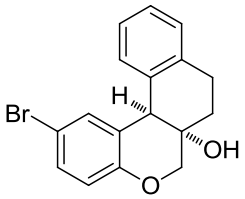


7k

Following the **general procedure B**, compound **7k** was prepared from glycidyl ether **8k**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a white solid; m.p.: 161-162 °C; Yield: 95% (107 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.14 (m, 2H), 7.10-7.07 (m, 1H), 6.75 (s, 1H), 6.65 (s, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 3.80 (s, 1H), 3.71 (dd, *J* = 2.5, 11.0 Hz, 1H), 3.40 (d, *J* = 11.0 Hz, 1H), 3.12-3.07 (m, 1H), 2.81-2.76 (m, 1H), 2.50 (br s, 3H), 2.34-2.29 (m, 4H), 1.46-1.40 (m, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$): δ 153.0, 139.8, 138.3, 138.1, 138.0, 127.1, 126.9, 126.5, 126.3, 124.1, 115.5, 115.2, 69.9, 69.1, 44.3, 33.4, 27.1, 21.0, 18.8. Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19, found: C, 81.36; H, 7.26.

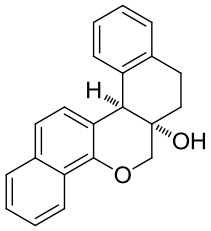
(6a*S,12b*R**)-2-Bromo-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromen-6a-ol (7l)**:



7l

Following the **general procedure B**, compound **7l** was prepared from glycidyl ether **8l**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a white solid; m.p.: 152-153 °C; Yield: 75% (99 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.16 (m, 5H), 7.9-7.06 (m, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 3.93 (dd, *J* = 1.4, 11.0 Hz, 1H), 3.84 (s, 1H), 3.78 (d, *J* = 11.0 Hz, 1H), 3.03-2.95 (m, 1H), 2.80-2.73 (m, 1H), 2.16 (br s, 3H), 2.09-2.02 (m, 1H), 1.83-1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.0, 136.3, 136.0, 133.7, 131.2, 129.4, 128.3, 127.1, 126.3, 123.8, 118.7, 112.9, 71.5, 67.6, 47.1, 31.2, 26.1; Anal. Calcd. for $C_{17}H_{15}BrO_2$: C, 61.65; H, 4.56, found: C, 61.72; H, 4.59.

(6a*S,12b*R**)-6a,7,8,12b-tetrahydro-6*H*-benzo[*h*]naphtho[2,1-*c*]chromen-6a-ol (7m)**:

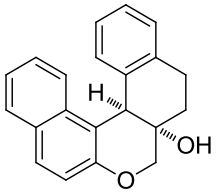


7m

Following the **general procedure B**, compound **7m** was prepared from glycidyl ether **8m**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a white solid; m.p.: 152-153 °C; Yield: 89% (107 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23-8.21 (m, 1H), 7.80-7.78 (m, 1H), 7.50-7.43 (m, 3H), 7.27-7.24 (m, 1H), 7.18-7.11 (m, 3H), 7.06 (d, *J*= 7.6 Hz, 1H), 4.09 (dd, *J* = 1.8, 11.0 Hz, 1H), 3.96 (s, 1H), 3.84 (d, *J* = 11.0 Hz, 1H), 3.07-3.01 (m, 1H), 2.81-2.77 (m, 1H), 2.24-2.20 (m, 2H), 1.76-1.71 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 138.0, 137.3, 133.7, 129.2, 128.8, 127.7,

127.4, 126.7, 126.4, 126.2, 125.5, 124.9, 121.9, 120.3, 114.4, 71.3, 68.3, 47.3, 32.2, 26.7; Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00, found: C, 83.36; H, 6.09.

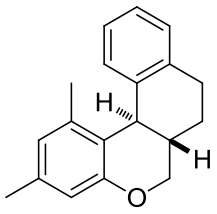
(4a*S,10b*R**)-4a,5,6,10b-Tetrahydro-4*H*-benzo[*f*]naphtho[2,1-*c*]chromen-4a-ol (7n)**:



7n

Following the **general procedure B**, compound **7n** was prepared from glycidyl ether **8n**. Column chromatography: 5-15% EtOAc in hexanes. This compound was obtained as a white solid; m.p.: 152-153 °C; Yield: 85% (102 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.83 (m, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.42-7.36 (m, 2H), 7.23-7.15 (m, 3H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 4.34 (s, 1H), 3.88 (dd, *J* = 2.4, 11.0 Hz, 1H), 3.62 (d, *J* = 11.0 Hz, 1H), 3.24-3.18 (m, 1H), 2.90-2.85 (m, 1H), 2.53 (br s, 1H), 2.43-2.39 (m, 1H), 1.56-1.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0, 138.2, 138.1, 134.4, 129.5, 129.4, 128.5, 128.3, 126.9, 126.8, 126.6, 126.2, 123.6, 123.0, 118.7, 111.8, 70.2, 68.7, 47.3, 33.6, 27.2; Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00, found: C, 83.50; H, 6.04.

Preparation of (6a*S,12b*R**)-1,3-Dimethyl-6a,7,8,12b-tetrahydro-6*H*-naphtho[2,1-*c*]chromene (16) (Scheme 3.6):**



16

$BF_3{\cdot}Et_2O$ (0.25 mL, 1.50 mmol) was added drop-wise to a solution of **7k** (200 mg, 0. 71 mmol) and triethylsilane (0.19 ml, 1.5 mmol) in anh. CH_2Cl_2 (222 mL) at 0 °C under nitrogen atmosphere and then stirred for 2 h at rt. The reaction mixture was cooled on an ice bath, then quenched with aq. saturated $NaHCO_3$ solution (10 mL). The resulting mixture extracted with CH_2Cl_2 (2 x15 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The crude product was purified by column chromatography (5% EtOAc in hexanes) to afford **16** as a colorless gum. Yield: 98% (185 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.16 (m, 3H), 7.06 (d, *J* = 6.4 Hz, 1H), 6.60 (d, *J* = 8.7 Hz, 2H), 3.97 (d, *J* = 10.5 Hz, 1H), 3.91 (dd, *J* = 10.2, 2.3 Hz, 1H), 2.99 (dd, *J* = 10.2, 2.3 Hz, 1H), 2.88 (d, *J* = 16.5 Hz, 1H), 2.64 (d, *J* = 16.5 Hz, 1H), 2.27-2.21 (m, 4H), 2.15 (s, 3H), 1.91-1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1, 146.8, 143.9, 137.6, 136.6, 127.4, 126.7, 124.8, 123.2, 123.0, 117.4, 114.6, 71.7, 45.7, 35.4, 35.0, 29.9, 20.9, 19.0; Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63, found: C, 86.25; H, 7.71.

3.6.3. X-ray crystallography:

X-ray reflections were collected on a Bruker APEX-II, CCD diffractometer using Mo Kα (λ = 0.71073 Å) radiation. Data reduction was performed using Bruker SAINT Software [23]. Intensities for absorption were corrected using SADABS. Structures were solved and refined using SHELXL-2014 with anisotropic displacement parameters for non-H atoms. Hydrogen atom on O was experimentally located in the crystal structure. All C–H atoms were fixed geometrically using the HFIX command in SHELX-TL [24]. A check of the final CIF file using PLATON did not show any missed symmetry [25,26].

Compound **7k** was crystallized in monoclinic space group $P2_1/n$ with 1 symmetry independent molecules in the crystal lattice. The ORTEP diagram of **7k** is shown below.

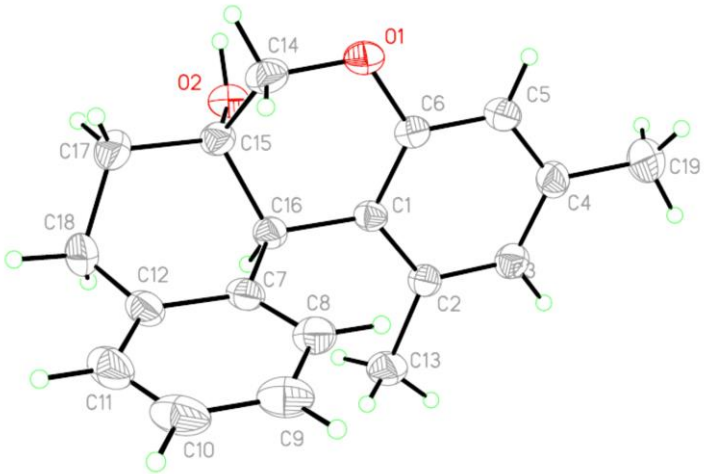


Figure 3.6. ORTEP diagram of 7k with 35% probability ellipsoid

Crystal data are summarized in Table 3.4.

Table 3.4. Crystal data parameter

Crystal Data	
Formula unit	$C_{19}H_{20}O_2$
Formula wt.	280.35
Crystal system	Monoclinic
T [K]	100
a [Å]	9.1569(9)
b [Å]	7.0032(6)
c [Å]	23.2281(18)
α [°]	90
β [°]	95.727(18)
γ [°]	90
Volume [Å^3]	1482.1(2)
Space group	$P2_1/n$
Z	4
D_{calc} [g cm^{-3}]	1.256
μ/mm^{-1}	0.080
Reflns. Collected	4566
Unique reflns.	1689
Observed reflns.	1330
R_1 [I>2σ(I)], wR_2	0.0428; 0.1161
GOF	1.004
Instrument	Bruker APEX-II
X-ray	MoK\α; λ=0.71073
CCDC Reference No.	1485292

3.6. References

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2.7. NMR Spectra of Selected Compounds

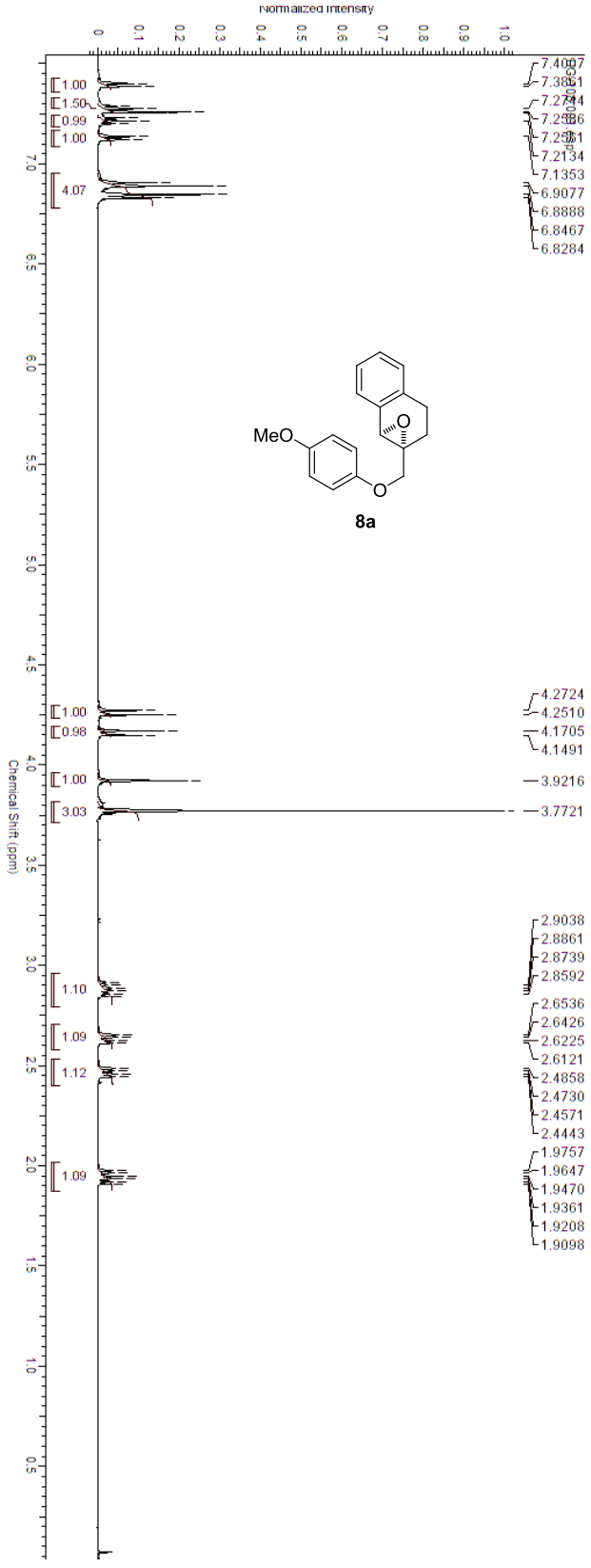

Figure 3.5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 8a

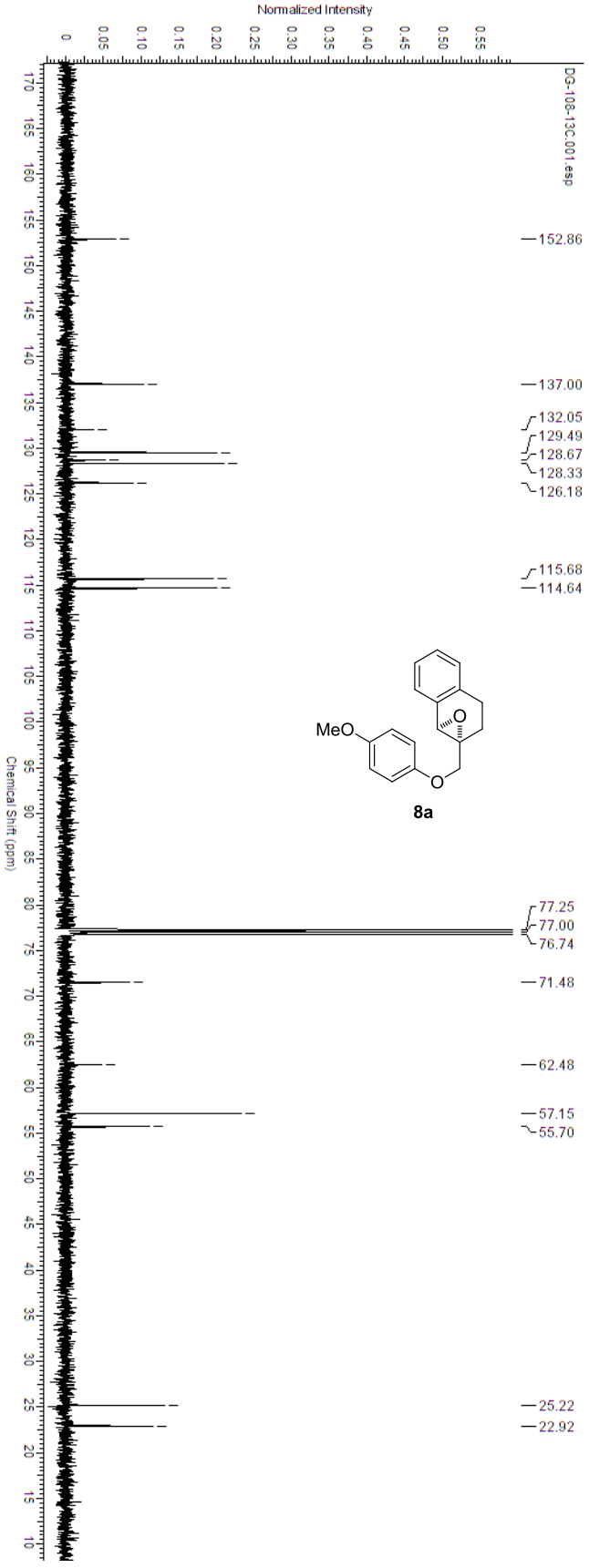

Figure 3.6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 8a

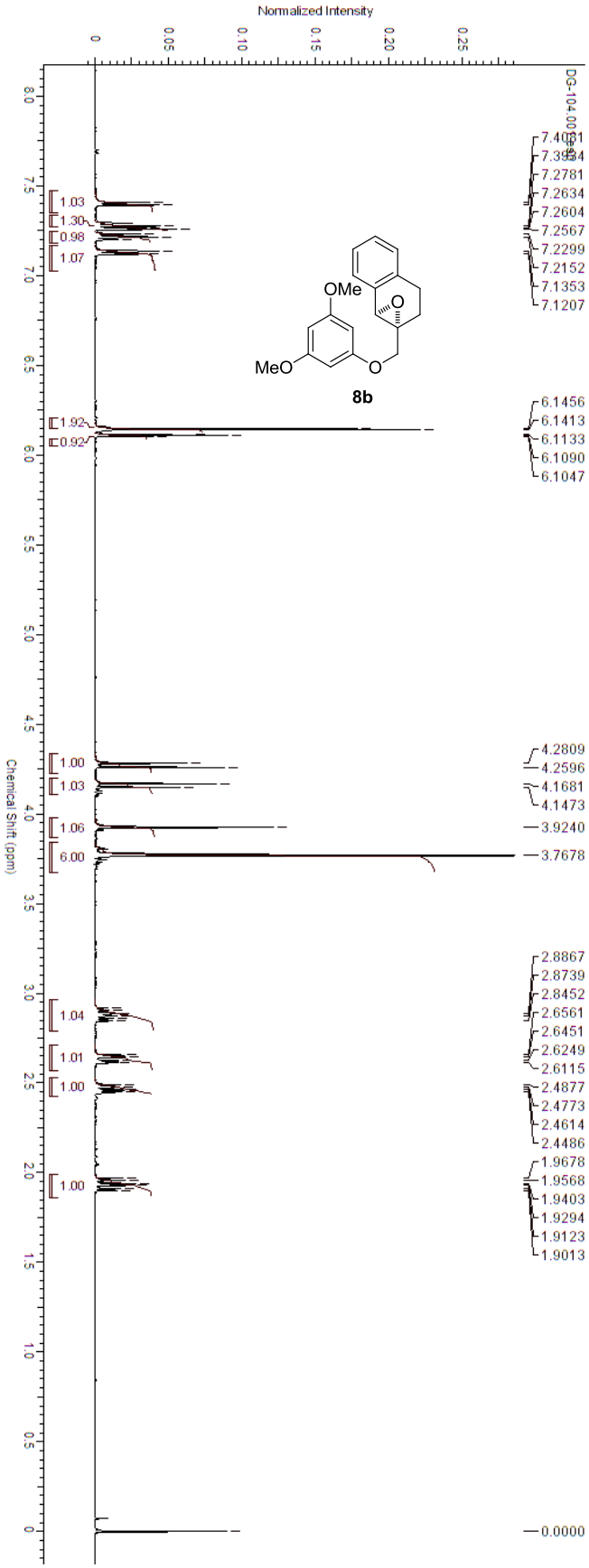

Figure 3.7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 8b

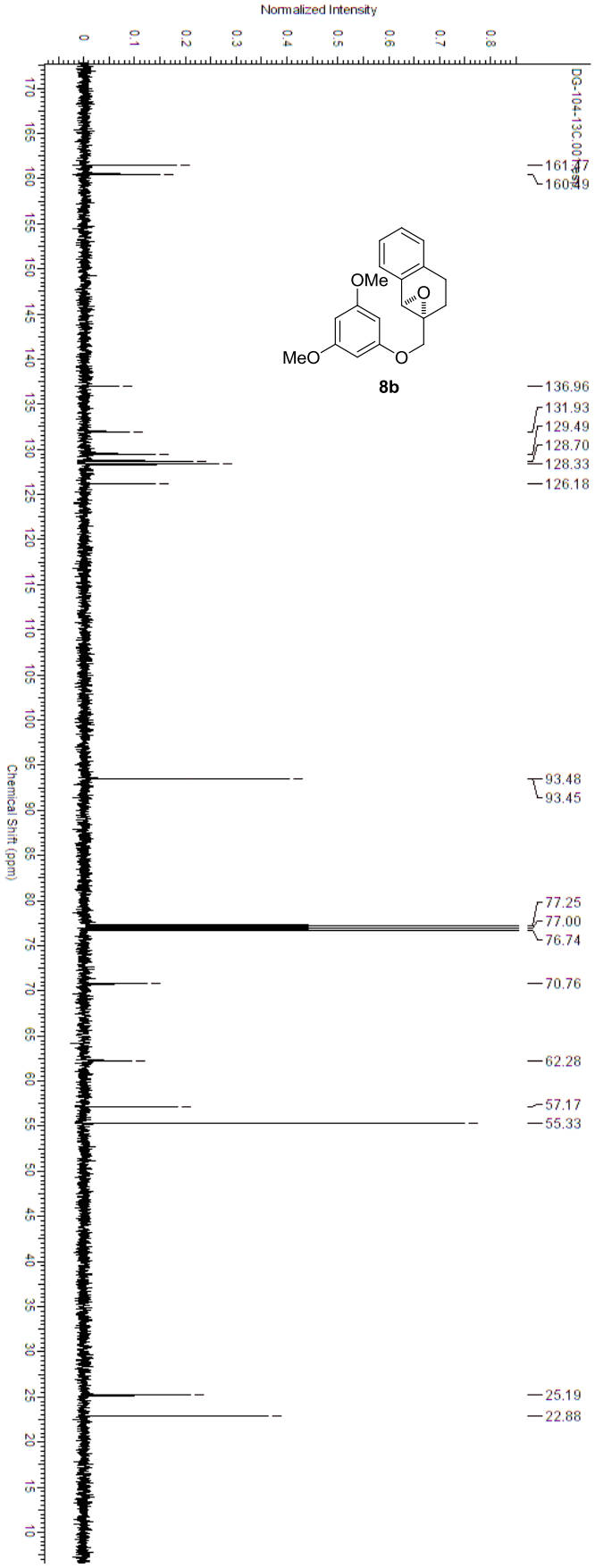

Figure 3.8. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 8b

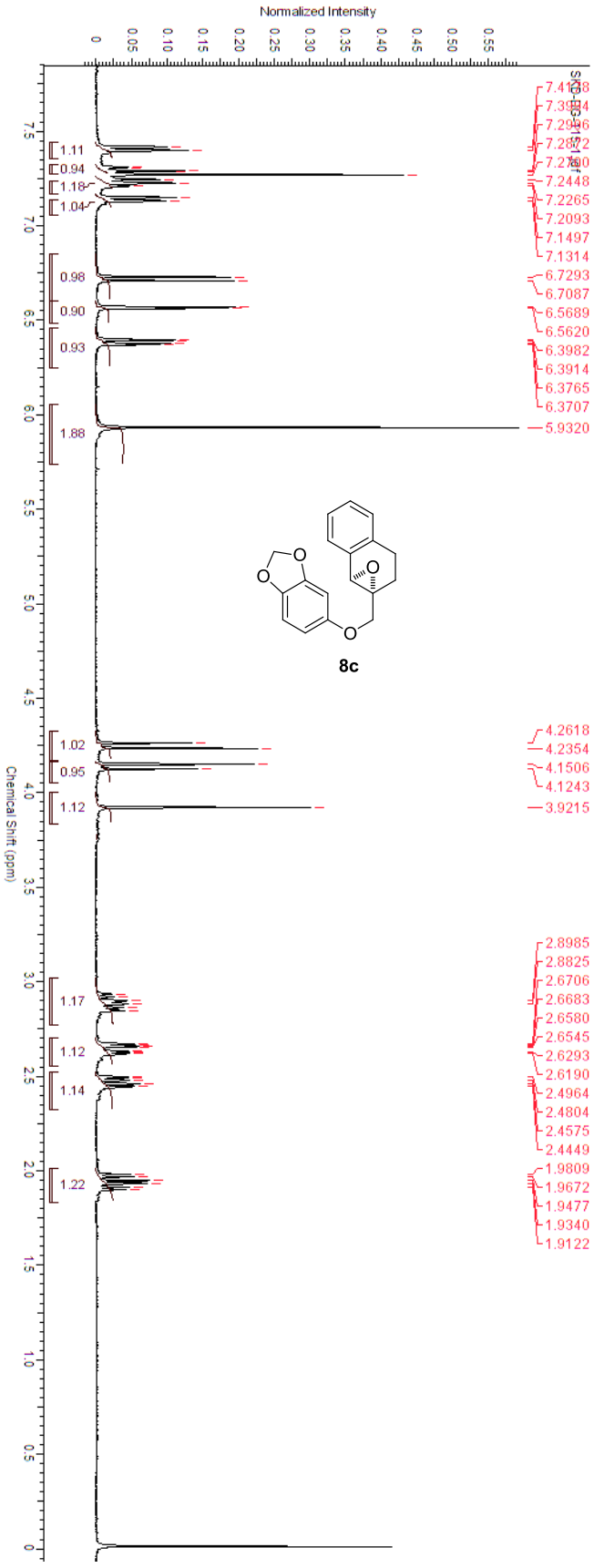

Figure 3.9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 8c

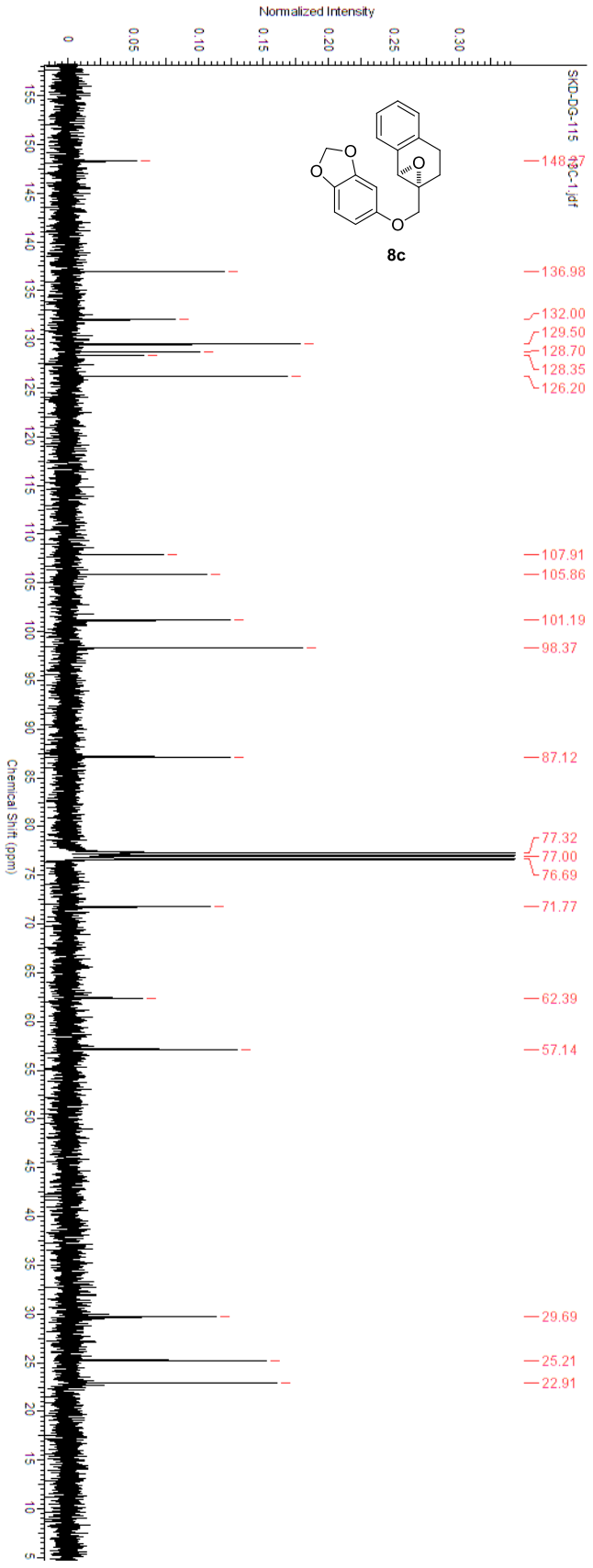

Figure 3.10. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 8c

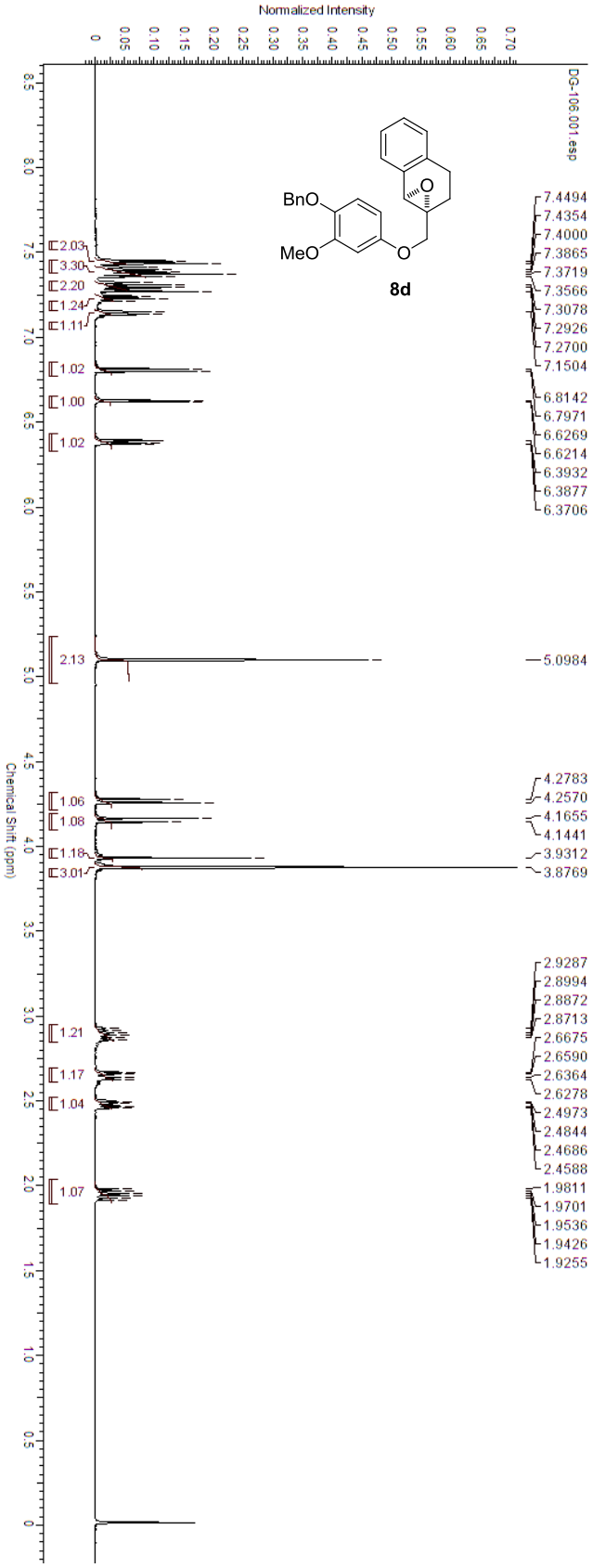

Figure 3.11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 8d

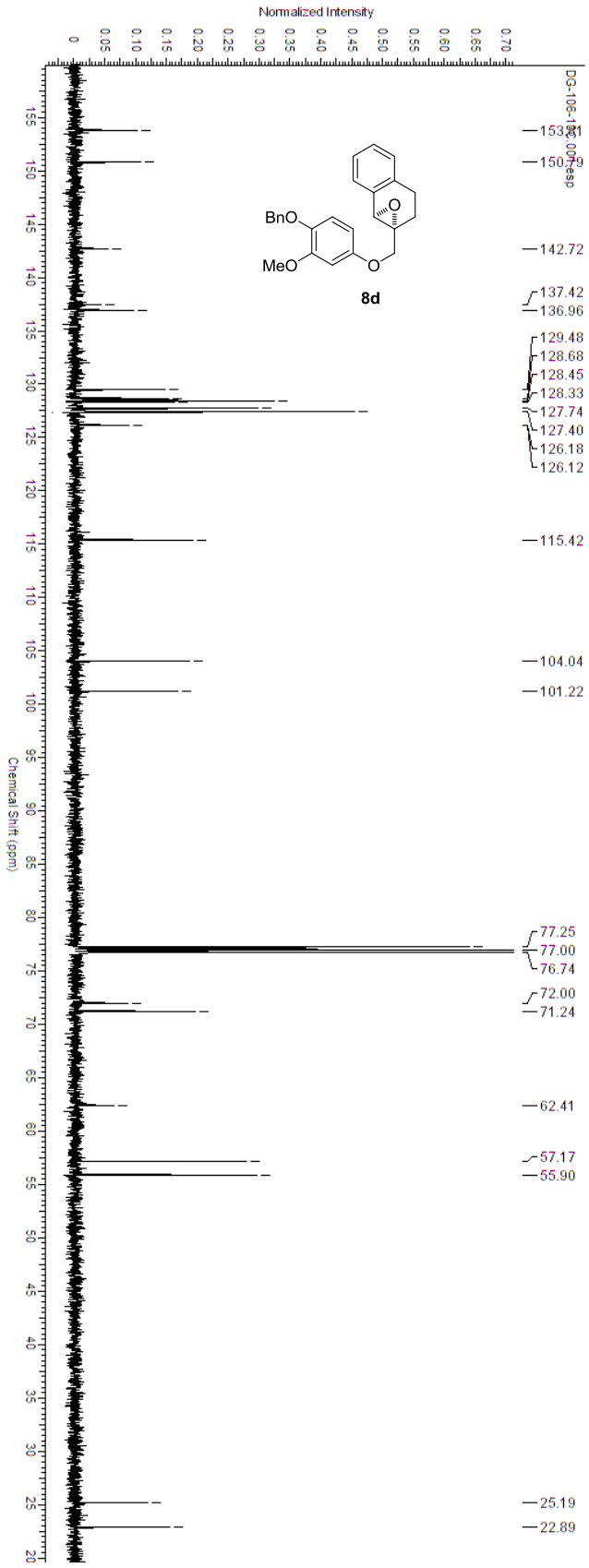

Figure 3.12. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 8d

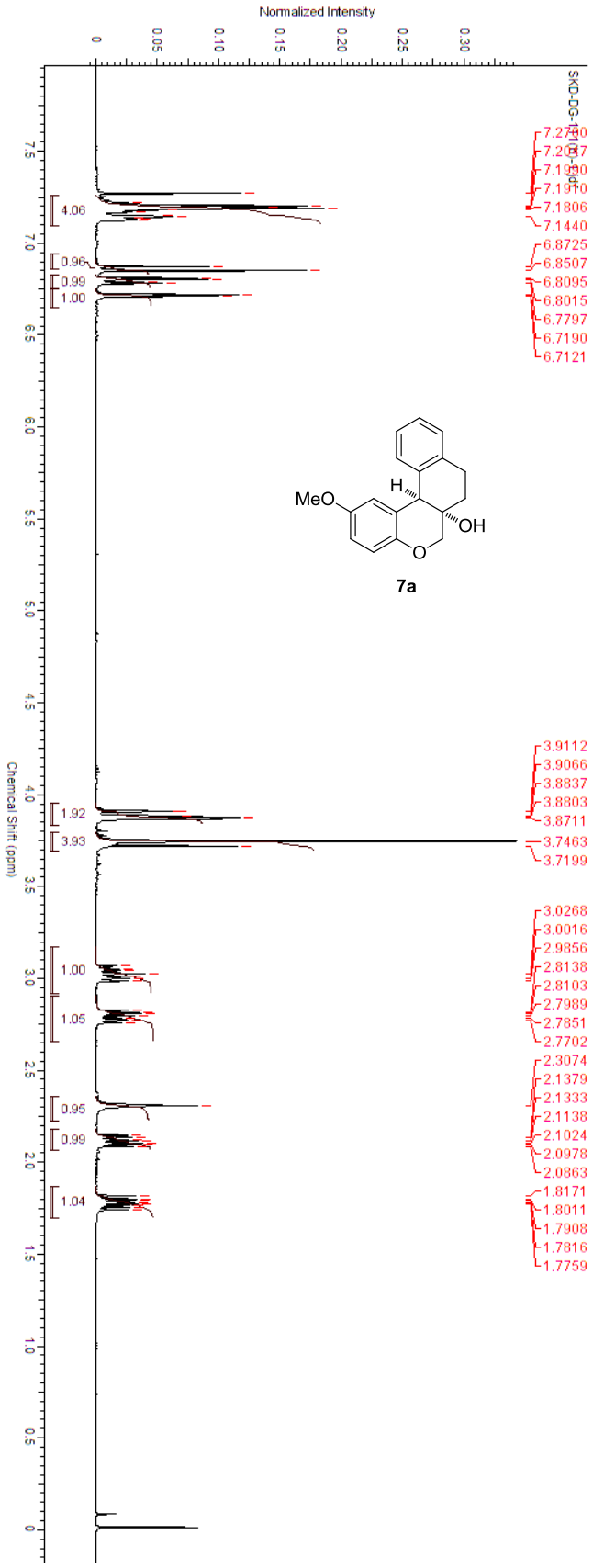

Figure 3.13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 7a

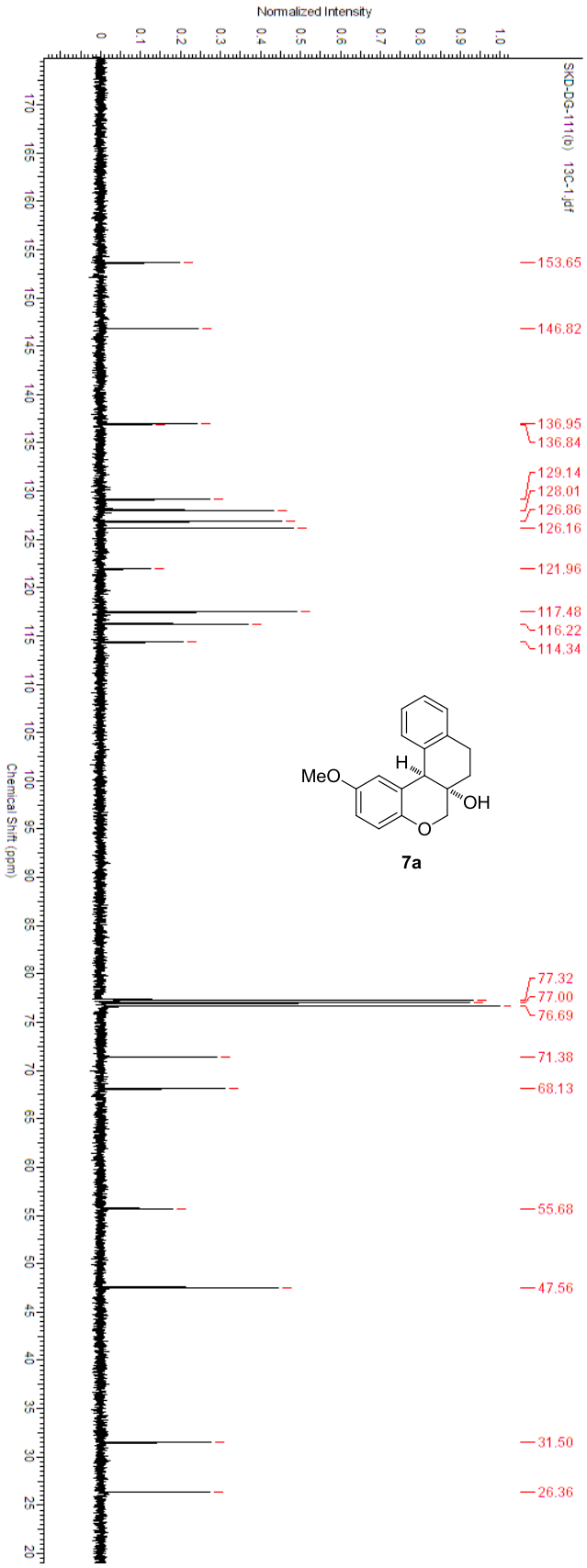

Figure 3.14. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 7a

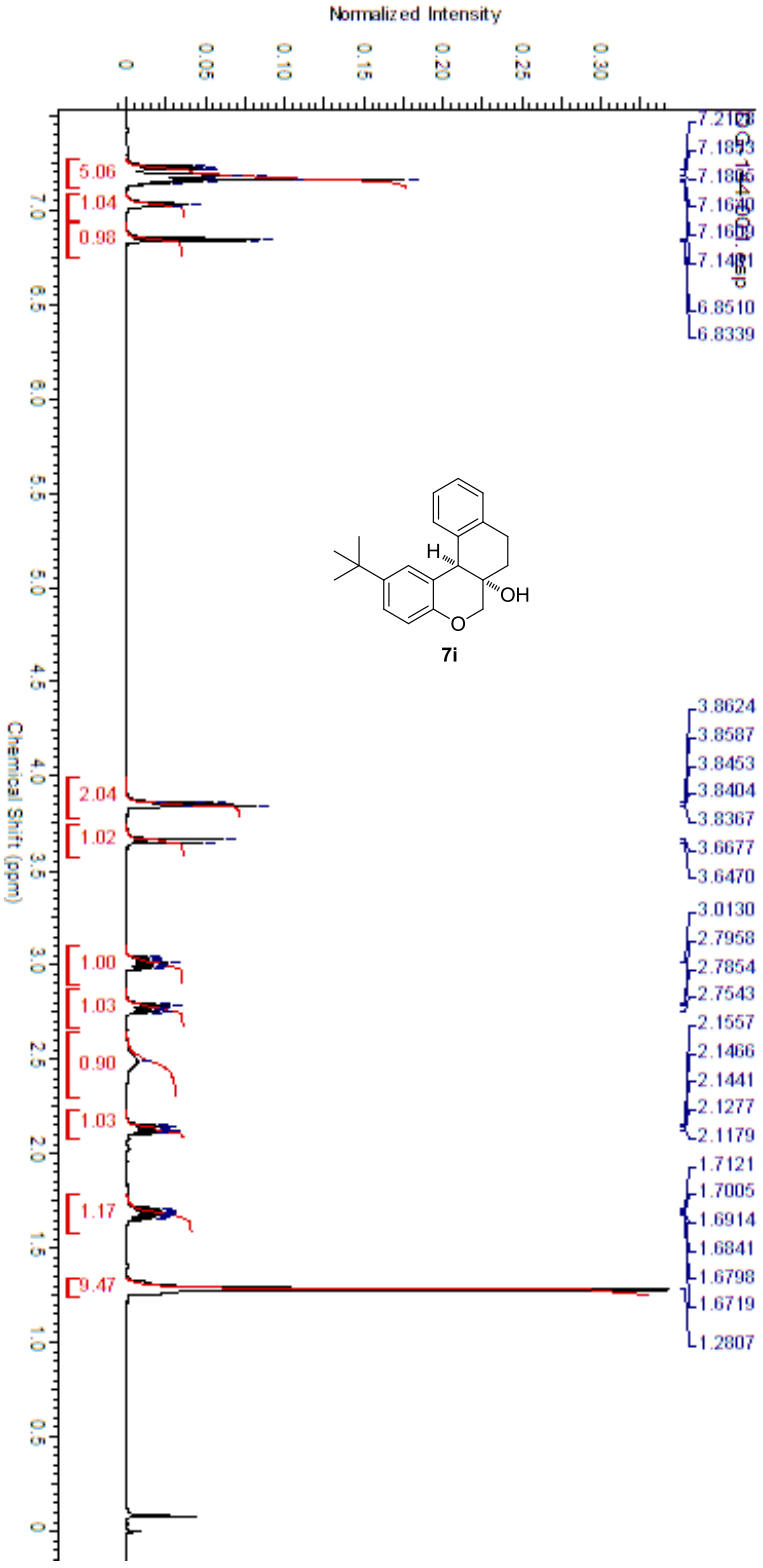

Figure 3.15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 7i

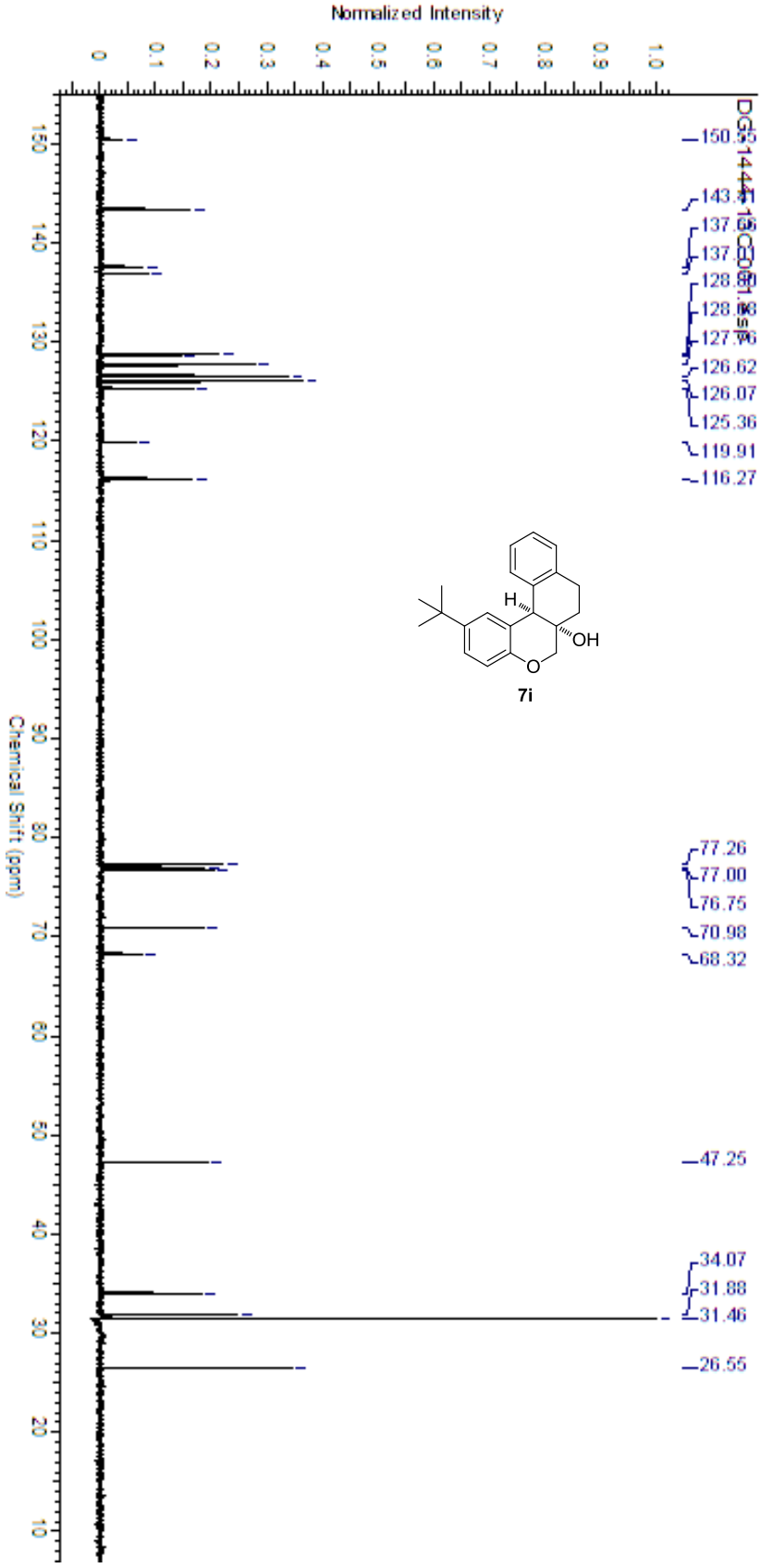

Figure 3.16. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 7i

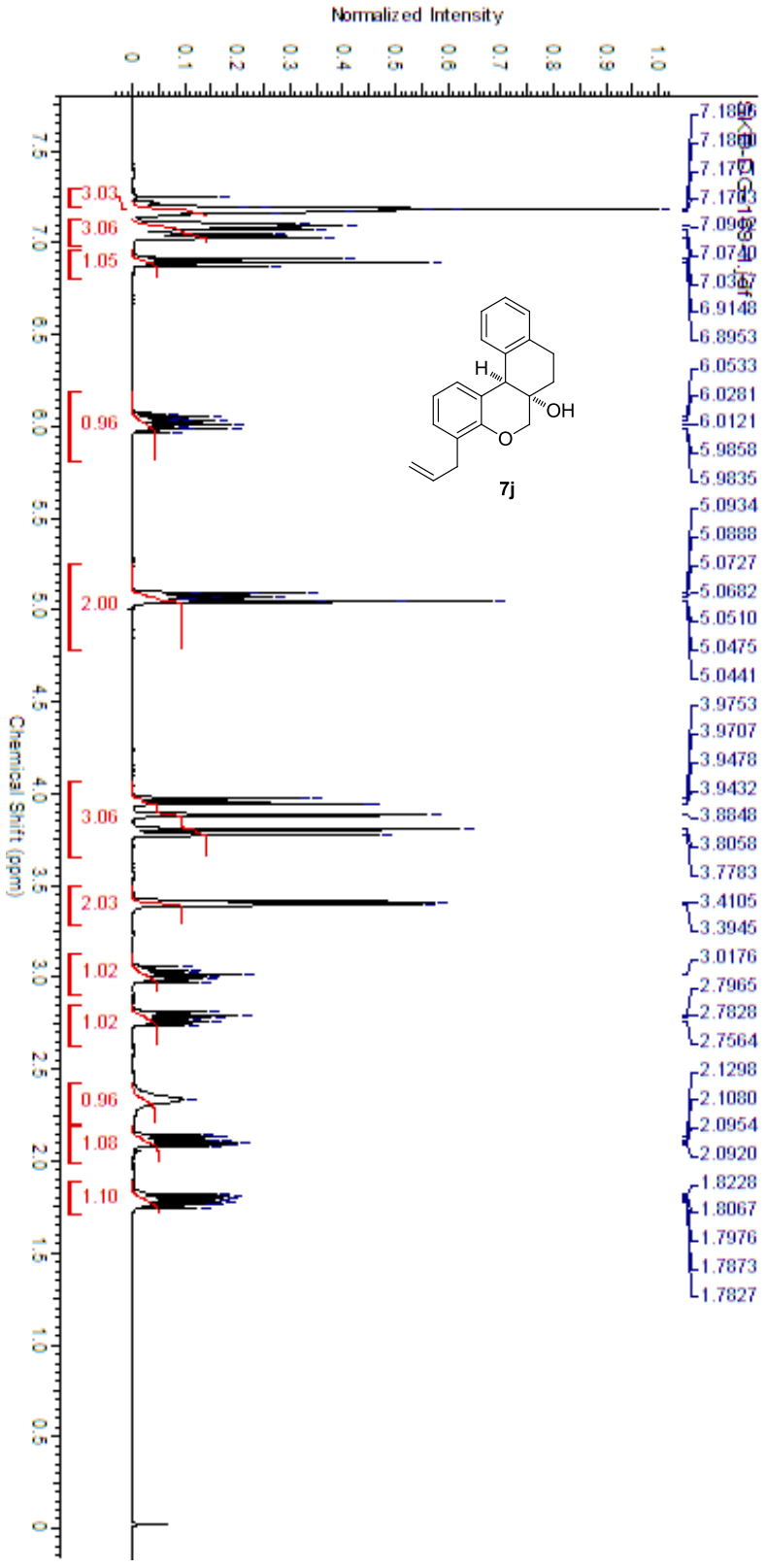

Figure 3.17. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 7j

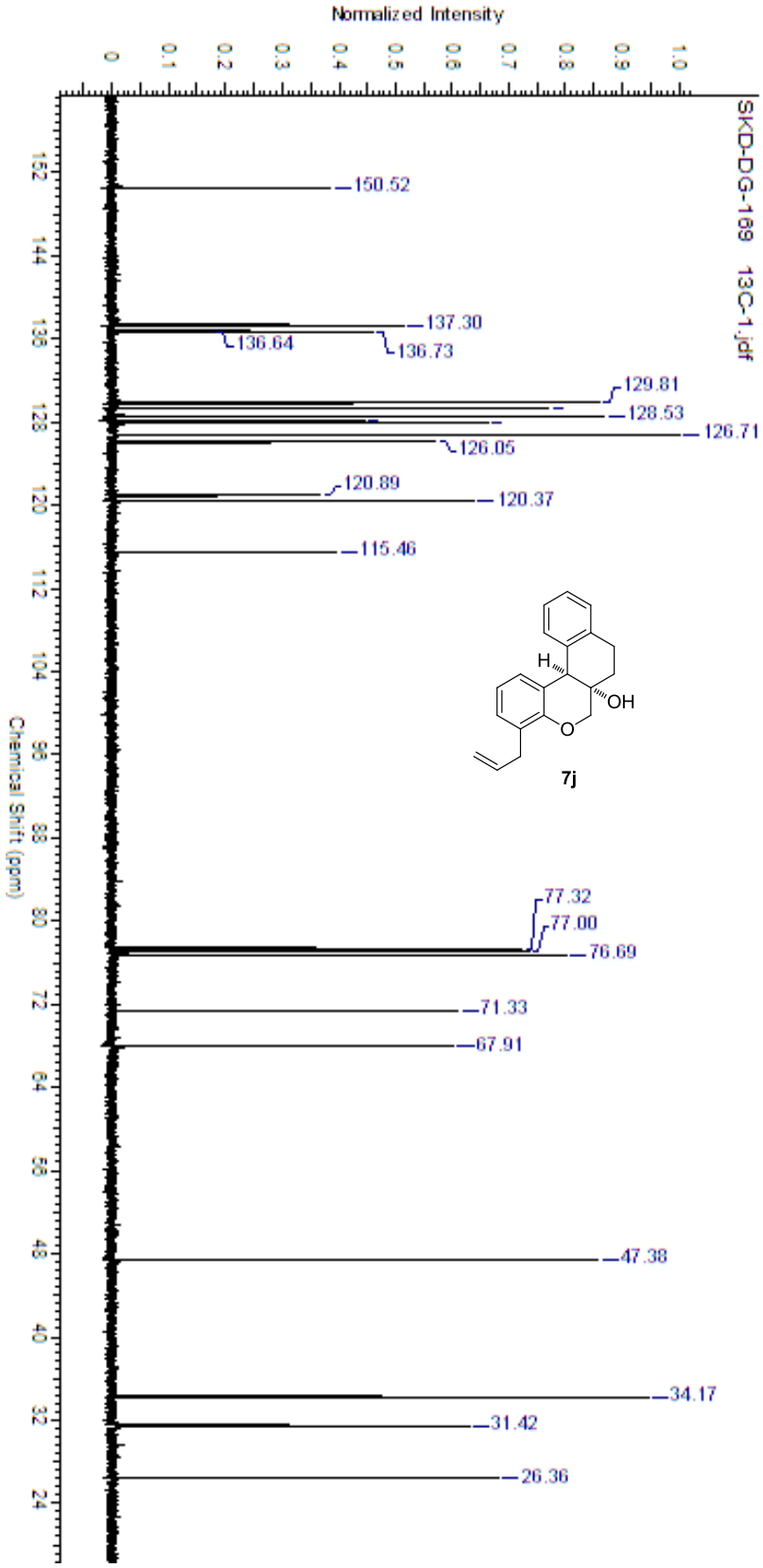

Figure 3.18. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 7j

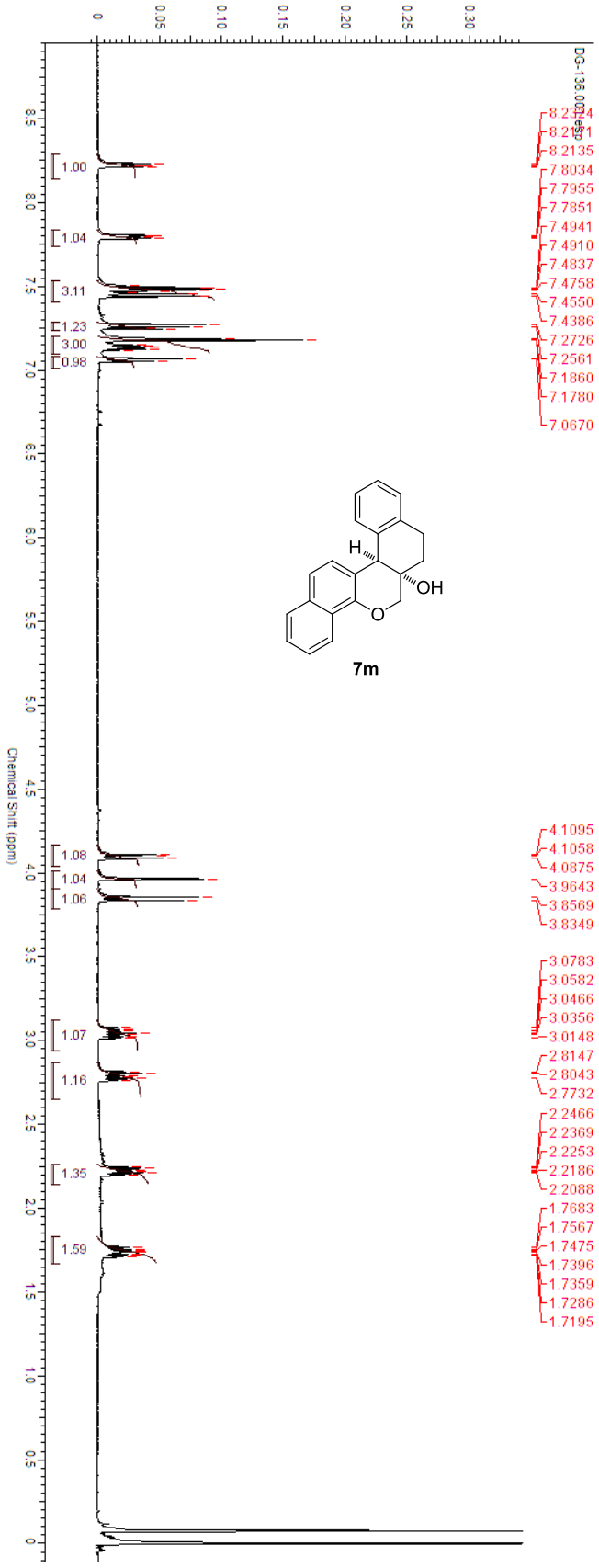

Figure 3.19. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 7m

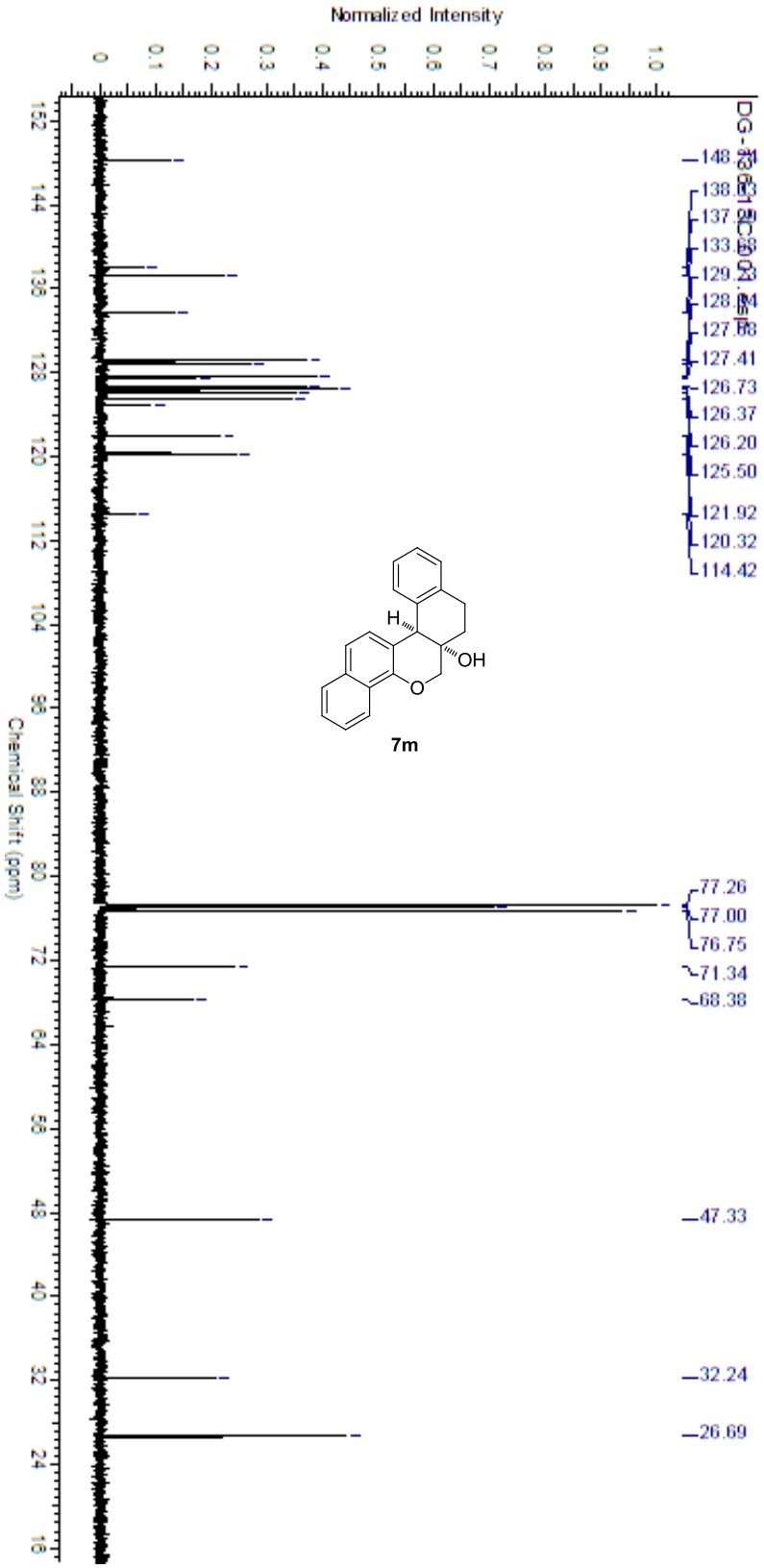

Figure 3.20. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 7m

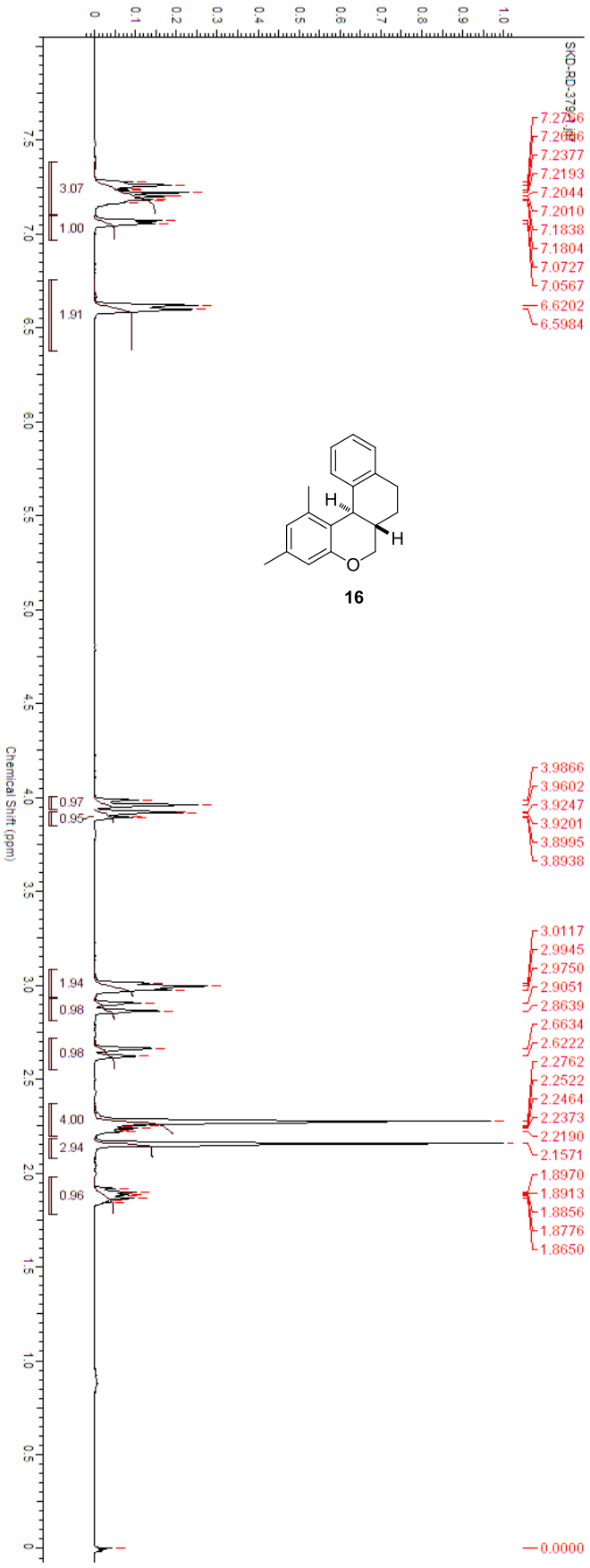

Figure 3.21. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound 16

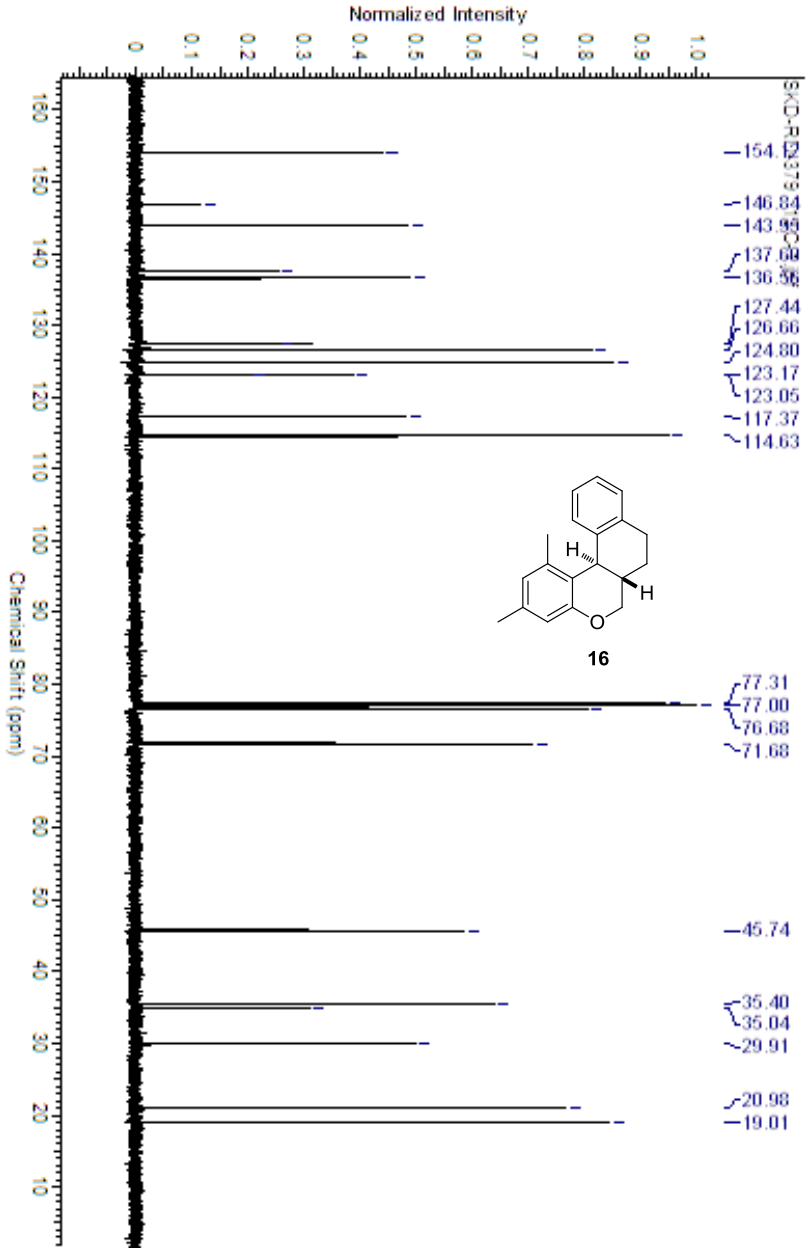

Figure 3.22. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound 16