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Enantioselective Desymmetrization of Bisphenol Derivatives by Organocatalytic Sulfonylation

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Chiral 1,1-diarylalkanes are synthesized by enantioselective desymmetrization of bisphenol derivatives through an organocatalytic sulfonylation reaction. The methodology involves the selective sulfonylation of one enantiotopic hydroxyl group of a bisphenol using a sulfonyl chloride with a chiral thiourea catalyst in a $CHCl_3/H_2O$ system under basic conditions. The resulting products are obtained in good to high yields (up to 97%) with high enantioselectivity (up to 90.5:9.5 er). Remarkably, compounds that are almost enantiomerically pure can be obtained from the mother liquor after crystallization.

1. Introduction

Asymmetric catalysis is a fundamental strategy in chemical synthesis that enables the precise and selective formation of one enantiomer over the other another in chiral molecules.[1,2] This approach relies on the use of chiral catalysts—such as metal complexes, enzymes, or organocatalysts—to create a stereochemically controlled environment that directs reaction pathways. In this context, asymmetric desymmetrization[3–5] is a powerful method in asymmetric catalysis that converts prochiral or meso compounds into chiral products with high enantioselectivity. By selectively modifying one of two identical enantiotopic functional groups, this approach enables the conversion of relatively simple achiral starting materials to high-value stereochemically-defined rich products. In recent decades, asymmetric desymmetrization has played a crucial role in pharmaceutical synthesis,[6,7] natural product development,[8,9] and materials science, providing an efficient and sustainable route to enantiomerically pure chiral compounds. In this field, the catalytic desymmetrization of diol-type substrates has been extensively studied,[10,11] including enantioselective acylation, sulfonylation, phosphorylation, and silylation reactions (**Scheme 1**A). However, only a few examples of desymmetrization reactions of bisphenols derivatives have been reported, since as differentiating remote enantiotopic sites presents a significant challenge. This inherent difficulty makes the desymmetrization of these compounds particularly complex and less explored (Scheme 1B). Moreover, the reported examples of the desymmetrization of bisphenols by reaction of one hydroxyl group are limited to acylation reactions. Miller and coworkers described the asymmetric desymmetrization of bisphenols using anhydrides and catalyzed by a peptide.[12–14] In 2017, Zhao's group[15] reported the acylative desymmetrization of bisphenols using aliphatic aldehydes via NHC-catalysis. Afterward, in 2018, Li and coworkers described NHC-catalyzed desymmetrization of bisphenols through an acylation reaction with aromatic aldehydes.[16] Moreover, other desymmetrizations of bisphenols via electrophilic aromatic substitution of the electron-rich aromatic system using *N*-bromosuccinimide as electrophilic bromination reagent have been also described.[17–19] However, the enantioselective desymmetrization of bisphenols through a sulfonylation reaction has been used only to generate a sulfur stereogenic center.[20] Despite this elegant work, there is no report on the synthesis of chiral bisphenol compounds bearing a stereogenic carbon using a desymmetrizing asymmetric sulfonylation strategy. Therefore, herein we report a strategy for the asymmetric desymmetrization of bisphenols through a selective sulfonylation catalyzed by a bifunctional organocatalyst (Scheme 1C). This methodology enables the enantioselective synthesis of chiral 1,1-diarylalkanes.

2. Results and Discussion

Our initial investigation was carried out with 2,2′-(2,2-dimethylpropane-1,1-diyl)bis(4-methylphenol) (**1a**) and TsCl (**2a**) as the model substrates, 10 mol% Takemoto's thiourea[21,22] **A** as the catalyst[23] in the presence of K_3PO_4 as the base and CH_2Cl_2 as solvent at room temperature. Under these conditions, we obtained the chiral compound **3aa** in 81% yield, but with very low enantioselectivity (entry 1, **Table 1**). To dissolve better the inorganic base, we decided to add water as cosolvent to perform the reaction in a biphasic system, obtaining a lower yield (59%) but the enantiomeric ratio was increased to 61:39. Next, we

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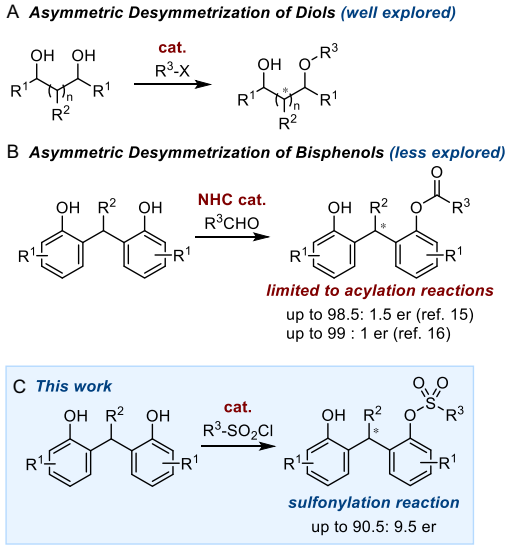
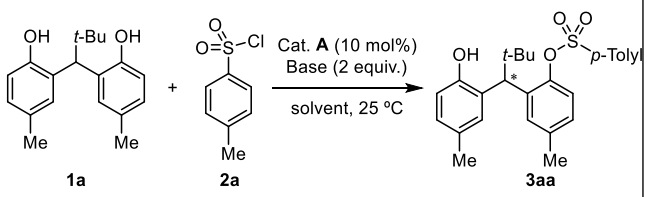


Scheme 1. Asymmetric desymmetrization of diols and bisphenols.

Table 1. Optimization of the reaction conditions.

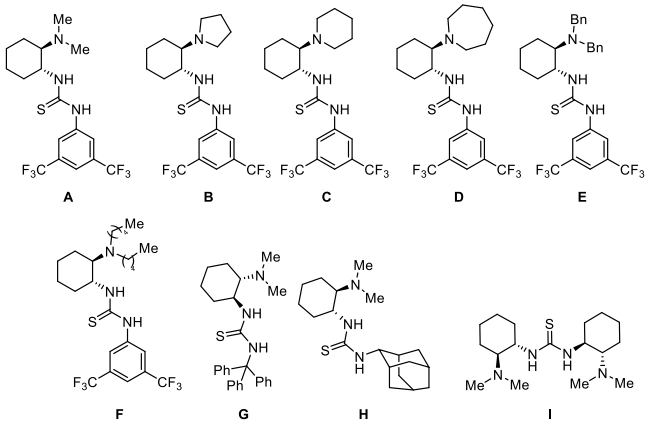


Entry[a]	Solvent	Base	*t* (days)	Yield [%][b]	er[c]
1	CH_2Cl_2	$K_3PO_4{\cdot}3H_2O$	3	81	54:46
2	CH_2Cl_2:H_2O[d]	$K_3PO_4{\cdot}3H_2O$	2	59	61:39
3	$CHCl_3$:H_2O[d]	$K_3PO_4{\cdot}3H_2O$	3	60	66:34
4	$CHCl_3$:H_2O[d]	$Na_3PO_4{\cdot}12H_2O$	1	51	78:26
5	$CHCl_3$:H_2O[d]	$K_2HPO_4{\cdot}3H_2O$	1	47	82:18
6	$CHCl_3$:H_2O[d]	$NaHPO_4$	1	38	81:19
7	$CHCl_3$:H_2O[d]	Cs_2CO_3	1	65	59:41
8	$CHCl_3$:H_2O[d]	K_2CO_3	1	45	76:24
9	$CHCl_3$:H_2O[d]	Na_2CO_3	1	51	78:22
10	$CHCl_3$:H_2O[d]	Li_2CO_3	1	54	80:20
11	$CHCl_3$:H_2O[d]	$MgCO_3$	1	39	83:17
12	$CHCl_3$:H_2O[d]	$CaCO_3$	1	46	83:17
13	$CHCl_3$:H_2O[d]	$(NH_4)_2CO_3$	1	52	83:17
14	$CHCl_3$:H_2O[d]	$NaHCO_3$	1	56	83:17
15	$CHCl_3$:H_2O[d]	NaOH	1	75	51:49
16[e]	$CHCl_3$:H_2O[d]	$MgCO_3$	3	68	85:15
17[e]	$CHCl_3$:H_2O[d]	$CaCO_3$	3	57	85:15
18[e]	$CHCl_3$:H_2O[d]	$(NH_4)_2CO_3$	3	55	81:19
19[e]	$CHCl_3$:H_2O[d]	$NaHCO_3$	3	44	84:16

[a]Reaction conditions: **1a** (0.07 mmol), **2a** (0.07 mmol), base (0.14 mmol), and catalyst **A** (10 mol%) in 1 mL of solvent at rt. [b]Isolated yield after column chromatography. [c]Determined by HPLC using chiral stationary phase. [d]The proportion of solvents was: 1 mL of solvent and 0.2 mL of H_2O. [e]The reaction was performed at 4 °C.

evaluate different organic solvents,[24] obtaining the best enantioselectivity when $CHCl_3$ was used (entry 3). At this point, we decided to study the effect of the basicity of different inorganic bases (entries 3–15). We observed an increase in the enantiomeric ratio when the inorganic base used had a pK_a value of ≈10 or lower, such as carbonates, hydrogen carbonate, or hydrogen phosphate. We also observed that the highest enantiomeric ratios were achieved when the cation of the inorganic base was sodium, calcium or magnesium. As a summary and analyzing the results of Table 1, we obtained product **3aa** with the best enantiomeric ratio (83:17) using $MgCO_3$, $CaCO_3$, $(NH_4)_2CO_3$, or $NaHCO_3$ as inorganic base (entries 11–14). Next, we decided to test the influence of the temperature with these 4 bases (entries 16–17), improving the enantiomeric ratio of compound **3aa** to 85:15 when $MgCO_3$ or $CaCO_3$ was used at 4 °C. We decided to continue the optimization with the magnesium salt because the desired product was obtained with a higher yield (68% vs 57% yield).

The next step in the optimization process was to evaluate other catalysts that are structurally similar to Takemoto's thiourea (**Scheme 2**).[24] The results are summarized in the entries 1–9, **Table 2**. The substituents in the tertiary amine moiety have some influence in the enantioselectivity and the conversion of the reaction. In general, organocatalysts bearing cyclic amines (**B–D**) gave good results similar to catalyst **A**, while a dibenzyl (**E**) or a dipentyl (**F**) substituent at the basic nitrogen afforded product **3aa** with lower enantioselectivity. Sterically demanding substituents, such as adamantyl or trityl groups at the thiourea moiety (**G** and **H**), negatively impacted the reaction's progress (entries 7 and 8, respectively). Finally, when C_2-symmetric thiourea **I** was used, the tosylated product **3aa** was obtained with good yield but with lower enantiomeric ratio. Therefore, we decided to continue the optimization process with the commercially available catalyst **A**. Using lower quantity of water (0.1 mL instead of 0.2 mL, entry 10) had a little influence on the reaction, but the experimental process to isolate **3aa** was more straightforward. We also evaluate the effect of increasing or decreasing the catalyst loading (entries 11 and 12), observing a lower yield for **3aa** but same er when 5 mol% of **A** was used. When a 20 mol% of A was employed, the er slightly increased from 85:15 to 86:14. Since we were working on a small scale (0.07 mmol), we attempted to scale up the



Scheme 2. Structure of the organocatalysts tested.

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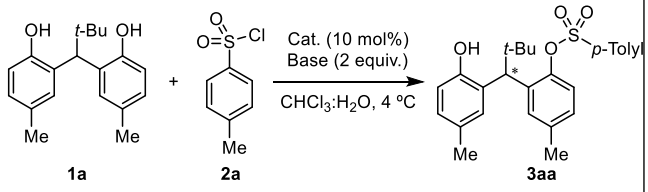
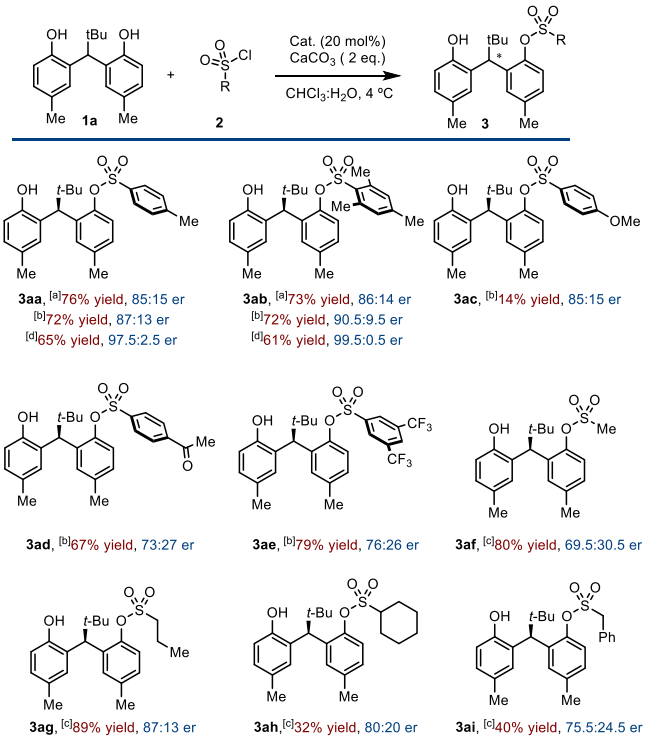
Table 2. Optimization of the reaction conditions.



Entry[a]	Catalyst	Base	*t* (days)	Yield (%)[b]	er[c]
1	**A** (10 mol%)	$MgCO_3$	3	68	85:15
2	**B** (10 mol%)	$MgCO_3$	3	86	86:14
3	**C** (10 mol%)	$MgCO_3$	3	75	84:16
4	**D** (10 mol%)	$MgCO_3$	3	82	83:17
5	**E** (10 mol%)	$MgCO_3$	3	13	75:25
6	**F** (10 mol%)	$MgCO_3$	3	71	54:46
7	**G** (10 mol%)	$MgCO_3$	3	24	54:46
8	**H** (10 mol%)	$MgCO_3$	3	58	62:38
9	**I** (10 mol%)	$MgCO_3$	3	74	68:32
10[d]	**A** (10 mol%)	$MgCO_3$	3	72	85:15
11[d]	**A** (5 mol%)	$MgCO_3$	3	27	85:15
12[d]	**A** (20 mol%)	$MgCO_3$	3	68	86:14
13[e]	**A** (10 mol%)	$MgCO_3$	3	50	85:15
14[f]	**A** (10 mol%)	$MgCO_3$	3	81	81:19
15[f]	**A** (20 mol%)	$MgCO_3$	3	81	84:16
16[f]	**A** (10 mol%)	$CaCO_3$	3	69	85:15
17[f]	**A** (20 mol%)	$CaCO_3$	3	76	85:15
18[f]	**B** (20 mol%)	$CaCO_3$	3	72	87:13

[a]Reaction conditions: **1a** (0.07 mmol), **2a** (0.07 mmol), base (0.14 mmol), and catalyst (10 mol%) in $CHCl_3$:H_2O (1:0.2) at 4 °C. [b]Isolated yield after column chromatography. [c]Determined by HPLC using chiral stationary phase. [d]The proportion of solvents was: 1 mL of $CHCl_3$ and 0.1 mL of H_2O. [e]Reaction conditions: **1a** (0.15 mmol), **2a** (0.15 mmol), base (0.30 mmol), and catalyst in $CHCl_3$:H_2O (2 mL:0.2 mL) at 4 °C. [f]Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), base (0.30 mmol) and catalyst in $CHCl_3$:H_2O (1:0.1) at 4 °C.



Scheme 3. Scope of the desymmetrization reaction of bisphenols with different sulfonyl chlorides. [a] Reaction conditions: **1a** (0.15 mmol), **2** (0.18 mmol), **A** (20 mol%), $CaCO_3$ (0.3 mmol) in a mixture of $CHCl_3$:H_2O at 4 °C for 3 days. Isolated yield after column chromatography. [b] 20 mol% of **B** instead of **A**. [c] **2** (0.3 mmol) and **B** (20 mol%). [d] Yield and er of the product obtained from the mother liquors after crystallization of a nearly racemic mixture. Isolated yield after column chromatography. Enantiomeric ratios determined by high-performance liquid chromatography (HPLC) using chiral stationary phase.

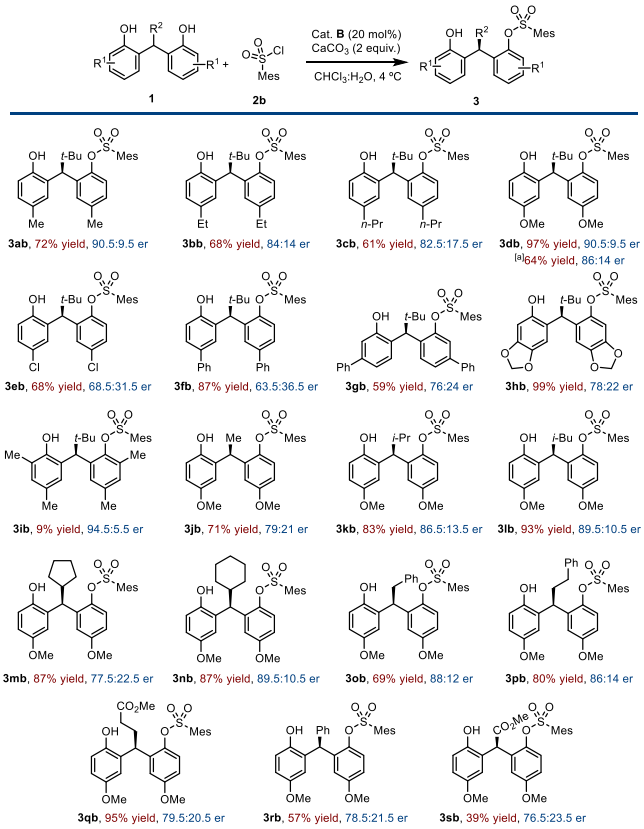
reaction to 0.15 mmol. However, this resulted in a lower yield of product **3aa** (50%, entry 13). Therefore, we increased the concentration from 0.07 to 0.14 M (entry 14), which improved the yield to 81% but the enantiomeric ratio decreased to 81:19. We achieved a similar yield while enhancing the enantioselectivity (84:16 er) by increasing the catalyst loading to 20 mol% (entry 15). We could also increase slightly the enantiomeric ratio by changing the base to $CaCO_3$ (entries 16 and 17). And finally, using 20 mol% of catalyst **B**, we could obtain compound **3aa** with the best enantioselectivity (87:13 er), and a good yield (72%). Thus, with the conditions outlined in entry 18, we decided to evaluate the scope and limitations of our methodology. At this point, it is important to highlight that this reaction is particularly challenging due to the existence of a potential background reaction associated with the use of an inorganic base. Indeed, both the inorganic base and the tertiary amine present in the organocatalyst, which have similar basicity, compete to promote the transformation.

With the optimized reaction conditions in hand, the scope of the desymmetrization of bisphenols through the sulfonylation reaction was studied. First, we evaluated the influence of the sulfonyl chloride **2** with bisphenol **1a** (**Scheme 3**). As the obtained results using the conditions of entry 17 and 18 were similar, we decided to evaluate both conditions with other sulfonyl chlorides. When mesityl sulfonyl chloride **2b** was used, we observed an enhancement in the enantiomeric ratio obtained. Specially, when catalyst **B** was used, the corresponding chiral compound **3ab** was obtained with 90.5:9.5 er and 72% yield. Consequently, we decided to use catalyst **B** for the rest of sulfonyl chlorides. The presence of strong electron-donating groups such as MeO did not influence the enantioselectivity of the reaction, but the conversion was very poor (14% yield). On the contrary, sulfonyl chlorides bearing electron-withdrawing groups delivered the corresponding products **3ad** and **3ae** in good yields but lower enantiomeric ratios. Next, aliphatic sulfonyl chlorides (Me, Pr, cyclohexyl, and Bn) were also evaluated, but in this case, we had to increase the amount of these electrophiles to reach better conversions. The higher reactivity of aliphatic sulfonyl chlorides with water could explain the necessity of using more equivalents. Looking at the results of Scheme 3, we obtained a high yield (89%) and good enantioselectivity (87:13 er) for compound **3ag**, with a propyl substituent in the sulfonyl chloride. As a general conclusion of the results of Scheme 3, mesityl sulfonyl chloride **2b** afforded the corresponding product **3ab** with the best

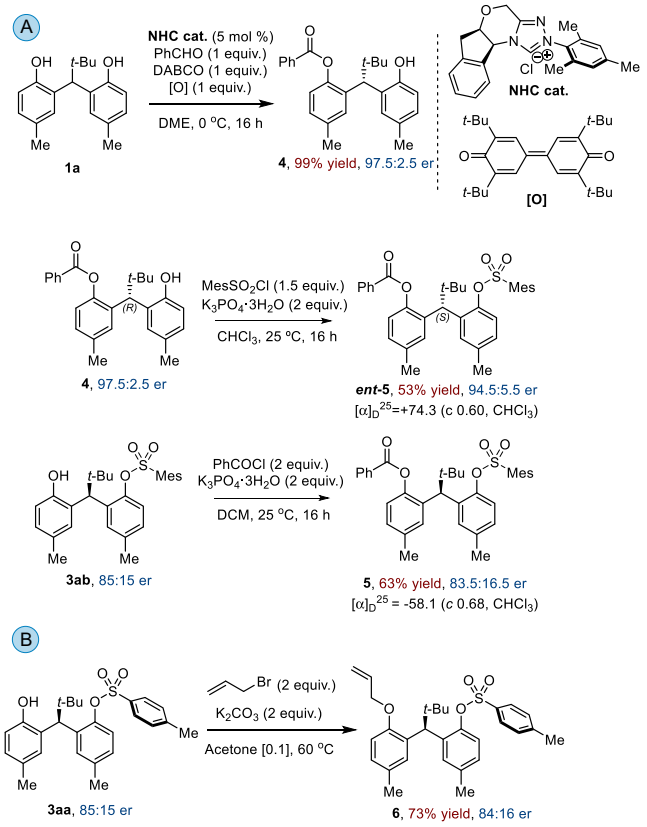
enantioselectivity, therefore we decide to further evaluate the scope of the reaction using **2b** as a reagent. The higher crystallinity of the racemic versus the enantioenriched product, allowed that the enantiomeric ratios of compounds **3aa** and **3ab** could be increased to 97.5:2.5 and 99.5:0.5 er, respectively, by evaporation of the mother liquors that are obtained after a crystallization by vapor diffusion of pentane over a $CHCl_3$ solution.

As shown in **Scheme 4** (**3ab**–**3ib**), the position and the electronic character of the substituents had an influence in the observed enantioselectivity. Bisphenols bearing electron-donating groups at *para* position afforded the corresponding mesylated product **3** with good enantiomeric ratios. On the contrary, the presence of electron-withdrawing groups (Cl) or a phenyl group diminished the enantioselectivity. Moreover, when the substituents are present at *meta* position, the corresponding products (**3gb** and **3hb**) were obtained in excellent yields but with lower enantiomeric ratios. Interestingly, the presence of a substituent in ortho position to the hydroxyl group enhanced the enantioselectivity to 94.5:5.5 er, but the product was obtained with a very low yield (9%), probably due to an increase of the steric hindrance. Afterward, we decided to study the influence of the substituent at the benzylic position (**3jb**–**3sb**). First, we evaluated the effect of the steric hindrance of the substituent. For example, changing from *t*-butyl to methyl, a diminution in the steric hindrance is reflected in a lower enantiomeric ratio (79:21 er), but other substituents such as *i*-propyl, *i*-butyl, cyclohexyl, benzyl, or phenethyl afforded the corresponding chiral compounds **3** with higher enantiomeric ratios. Unfortunately, bisphenols containing aromatic substituents such as phenyl or alkyl chains bearing esters moieties gave the corresponding products with lower enantioselectivity. The reaction between **1d** and **2b** could be performed on a 1 mmol scale. However, the desired product **3db** was obtained in a lower yield (64%) and with reduced enantioselectivity (86:14 er) compared to the reaction carried out on a 0.15 mmol scale.

The establishment of the absolute configuration of the chiral sulfonylated compounds **3** was achieved by chemical correlation (**Scheme 5**). Following the methodology for the asymmetric desymmetrization of bisphenols described by Li,[16] we prepared the (*R*)-2-(1-(2-hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-5-methylphenyl benzoate **4** in 99% yield and 97.5:2.5 er by reacting bisphenol **1a** and benzaldehyde with 5 mol% of the NHC-catalyst and DABCO as a base in DME at 0 °C under Ar. Then, compound **4** was reacted with 2,4,6-trimethylbenzenesulfonyl chloride (**2b**) in the presence of K_3PO_4 affording the product ***ent*-5** in 53% yield and 94.5:5.5 er. In contrast, benzoylation of compound **3ab** could be achieved by treatment with benzoyl chloride in CH_2Cl_2 in the presence of K_3PO_4. By this method, compound **5**, which exhibits



Scheme 4. Scope of the desymmetrization reaction of bisphenols with different sulfonyl chlorides. Reaction conditions: **1a** (0.15 mmol), **2** (0.18 mmol), **B** (20 mol%), and $CaCO_3$ (0.3 mmol) in a mixture of $CHCl_3$:H_2O at 4 °C for 3 days. [a] Reaction conditions: **1a** (1 mmol), **2** (1.2 mmol), **B** (20 mol%), and $CaCO_3$ (2 mmol) in a mixture of $CHCl_3$:H_2O (7 mL: 0.7 mL) at 4 °C for 3 days. Isolated yield after column chromatography. Isolated yield after column chromatography. Enantiomeric ratios determined by HPLC using chiral stationary phase.



Scheme 5. A) Absolute configuration assignment for **3ab**. Isolated yield after column chromatography. B) Synthetic transformations. Enantiomeric ratios determined by HPLC using chiral stationary phase.

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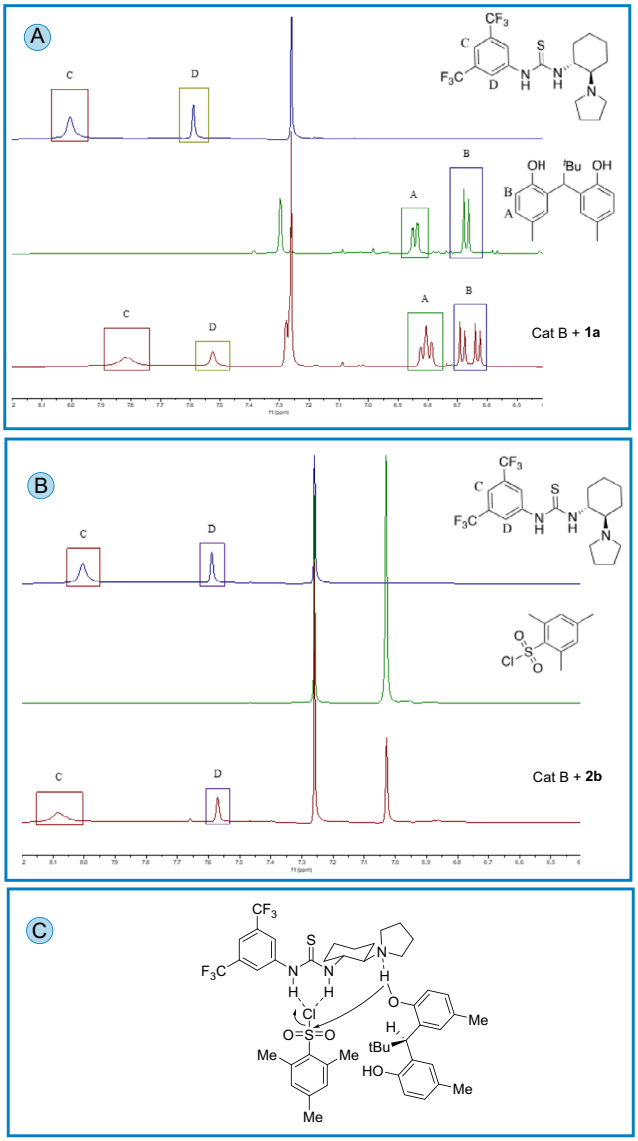
identical spectral features than ***ent*-5**, was obtained in 63% yield and 83.5:16.5 er. Comparison of both optical rotation values and chiral HPLC retention times allowed us to establish the absolute stereochemistry of the major enantiomer of the product prepared from **3ab** to be *R*. The absolute stereochemistry of all chiral product **3** was assigned by analogy.

We have tried several transformations with the chiral compounds **3**, including palladium-catalyzed reductions,[25,26] Suzuki coupling,[27] and the Buchwald–Hartwig reaction.[28] Unfortunately, none of these methods yielded the expected products. As an alternative approach, compound **3aa** was protected using allyl bromide, affording compound **6** in a 73% yield while preserving the optical purity of the starting material. Subsequent attempts to carry out the Claisen rearrangement with compound **6** under various reaction conditions were also unsuccessful, as the desired product was not observed.



Scheme 6. A) NMR studies of **Cat-B** and **1a**. B) NMR studies of **Cat-B** and **2b**. C) Plausible transition state for the desymmetrization sulfonylation reaction of bisphenols.

To elucidate the possible mechanism, we have conducted different nuclear magnetic resonance (NMR) experiments combining **Cat-B** with substrates **1a** and **2b** (**Scheme 6**). As shown in Scheme 6A, **Cat-B** is capable of desymmetrizing bisphenol **1a**, as the aromatic signals A and B split, and the C and D protons of **Cat-B** shift. Therefore, one of the hydroxyl groups of bisphenol **1b** can interact with **Cat-B**, most likely through hydrogen bonding.

In contrast, when compound **2b** is combined with **Cat-B**, the aromatic protons C and D of the catalyst also shift (Scheme 6B), which may indicate an interaction between $MesSO_2Cl$ and the organocatalyst.[29,30] Thus, we believe that in the reaction mechanism, the catalyst acts as a bifunctional catalyst (Scheme 6C), activating both the bisphenol through hydrogen bonding with the tertiary amine and the sulfonyl chloride **2b** via the thiourea, also through hydrogen bonding.[31] Considering the absolute configuration of **3ab**, when one of the phenol groups of **1a** coordinates with the catalyst, the *tert*-butyl group would remain on the opposite face, most likely due to steric hindrance.

3. Conclusion

In summary, we have successfully developed an organocatalytic desymmetrization reaction of bisphenols **1** using a sulfonylating reagent **2**, catalyzed by a bifunctional squaramide organocatalyst. This approach yields the corresponding chiral compounds **3**, which feature two aromatic rings, with moderate-to-excellent yields (up to 97%) and enantioselectivities ranging from low to outstanding (up to 94.5:5.5 er) under mild reaction conditions. Ongoing studies in our laboratory aim to further expand the scope of this transformation.

Acknowledgements

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: asymmetric catalysis · desymmetrizations · organocatalysis · phenols · sulfonylation

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Enantioselective Desymmetrization of Bisphenol Derivatives *via* Organocatalytic Sulfonylation

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General Experimental Methods

Unless otherwise noted, reactions were carried out in regular 5 mL-vials. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm.

NMR spectra were run at 300 MHz (Bruker Avance III 300) for ^{1}H and at 75 MHz for ^{13}C NMR using residual non-deuterated solvent as internal standard ($CDCl_3$: 7.26 and 77.00 ppm respectively) and at 282 MHz for ^{19}F NMR. Also, some NMR spectra were run at 500 MHz (Bruker Neo500) for ^{1}H and at 126 for ^{13}C. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments.

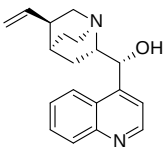
High resolution mass spectra (ESI) were recorded on a AB SCIEX Triple TOFTM spectrometer equipped with an electrospray source with a capillary voltage of 4.5 kV(ESI).

Sulfonyl chlorides were commercially available and used as received. Bisphenols **1** were prepared following reported methods.[18]

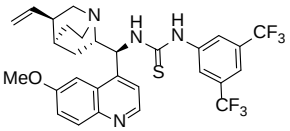
Optimization of the reaction conditions.

Organocatalyst Screening

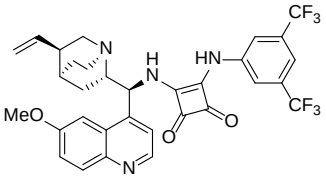
Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $K_3PO_4.3H_2O$ (0.14 mmol, 2 equiv.), and the proper organocatalyst (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in DCM (1 mL) or in a DCM:H_2O 10:2 mixture (1 mL of DCM and 0.2 mL of H_2O) and stirred continuously for the indicated time at 25 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.



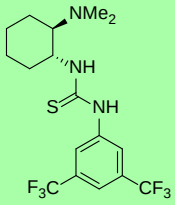
w/DCM; 3 d, 39% yield, 50:50 er



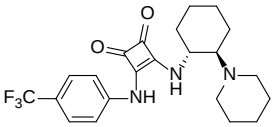
w/DCM; 4 d, 59% yield, 50.5:49.5 er
w/DCM:H_2O; 1 d, 58% yield, 53.5:46.5 er



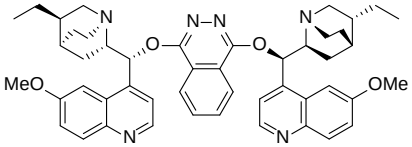
w/DCM; 4 d, 89% yield, 51:49 er
w/DCM:H_2O; 2 d, 63% yield, 50.5:49.5 er



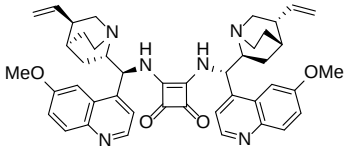
Organocatalyst **A**
w/DCM; 3 d, 81% yield, 54:46 er
w/DCM:H_2O; 1 d, 59% yield, 61:39 er



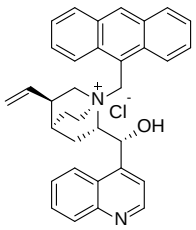
w/DCM; 3 d, 76% yield, 52:48 er
w/DCM:H_2O; 1 d, 68% yield, 51:49 er



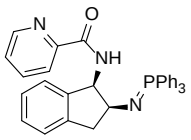
w/DCM; 4 d, 87% yield, 50.5:49.5 er
w/DCM:H_2O; 2 d, 73% yield, 51:49 er



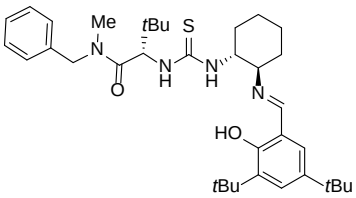
w/DCM; 2 d, 84% yield, 50.5:49.5 er



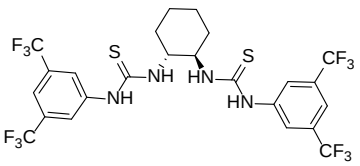
w/DCM; 4 d, 74% yield, 55:45 er
w/DCM:H_2O; 1 d, 75% yield, 52.5:47.5 er



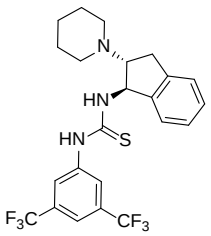
w/DCM; 3 d, 78% yield, 51:49 er
w/DCM:H_2O; 1 d, 58% yield, 50.5:49.5 er



w/DCM:H_2O; 1 d, 53% yield, 51.5:48.5 er



w/DCM:H_2O; 1 d, 71% yield, 51:49 er



w/DCM:H_2O; 1 d, 70% yield, 51.5:48.5 er

Solvent Screening

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $K_3PO_4.3H_2O$ (0.14 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a solvent:H_2O 10:2 mixture (1 mL of solvent and 0.2 mL of H_2O) and stirred continuously for the indicated time at 25 °C. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	Solvent	t (days)	Yield (%)	er (%)
1	CH_2Cl_2	2	59	61:39
2	$ClCH_2CH_2Cl$	1	73	58:42
3	$CHCl_3$	3	60	66:34
4	CCl_4	3	74	55:45
5	Toluene	1	75	55.5:44.5
6	PhCl	3	58	57:43
7	$PhCF_3$	3	71	53:47
8	cyclohexane	1	62	55.5:45.5
9	Et_2O	1	33	50.5:49.5
10	*t*-BuOMe	3	36	51.5:48.5
11	AcOEt	1	30	50:50

Inorganic Base Screening

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), inorganic base (0.14 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:2 mixture (1 mL of solvent and 0.2 mL of H_2O) and stirred continuously for the indicated time at 25 °C. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	Base	t (days)	Yield (%)	er (%)
1	$K_3PO_4 \cdot 3H_2O$	3	60	66:34
2	$Na_3PO_4 \cdot 12H_2O$	1	51	74.5:25.5
3	$K_2HPO_4 \cdot 3H_2O$	1	47	81.5:18.5
4	Na_2HPO_4	1	38	80.5:19.5
5	Cs_2CO_3	1	65	59:41
6	K_2CO_3	1	45	75.5:24.5
7	Na_2CO_3	1	51	77.5:22.5

8	Li_2CO_3	1	54	80:20
9	$MgCO_3$	1	39	83:17
10	$CaCO_3$	1	46	83:17
11	$NaHCO_3$	1	56	82.5:17.5
12	NaOH	1	75	51.5:48.5
13	$(NH_4)_2CO_3$	1	52	82:18

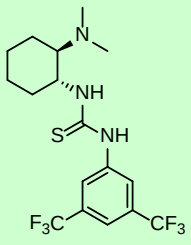
Temperature Screening.

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), inorganic base (0.14 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:2 mixture (1 mL of solvent and 0.2 mL of H_2O) and stirred continuously for the indicated time at the indicated temperature. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

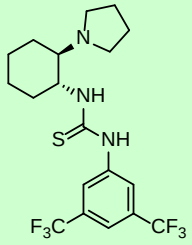
Entry	Base	T (ºC)	t (days)	Yield (%)	er (%)
1	$CaCO_3$	25	1	46	83:17
2	$CaCO_3$	4	3	57	85:15
3	$CaCO_3$	-20	7	15	86:14
4	$NaHCO_3$	25	1	56	82.5:17.5
5	$NaHCO_3$	4	2	44	83.5:16.5
6	$NaHCO_3$	-20	7	16	84.5:15.5
7	$MgCO_3$	25	1	39	83:17
8	$MgCO_3$	4	2	68	85:15
9	$MgCO_3$	-20	7	15	87:13
10	$(NH_4)_2CO_3$	25	1	52	82:18
11	$(NH_4)_2CO_3$	4	2	55	81:19

Further organocatalyst screening

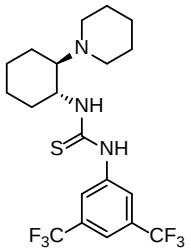
Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.15 mmol), tosyl chloride **2a** (0.18 mmol, 1.2 equiv.), $CaCO_3$ (0.3 mmol, 2 equiv.), and organocatalyst (0.03 mmol, 20 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 3 days at 4 ^oC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.



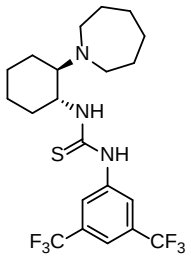
Organocatalyst **A**
3 d, 81% yield, 84:16 er



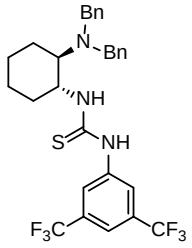
Organocatalyst **B**
3 d, 72% yield, 87:13 er



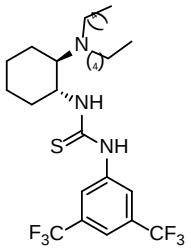
Organocatalyst **C**
3 d, 75% yield, 84:16 er



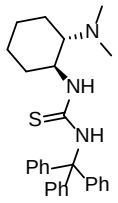
Organocatalyst **D**
3 d, 82% yield, 82.5:17.5 er



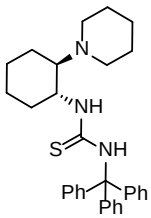
Organocatalyst **E**
3 d, 13% yield, 75.5:24.5 er



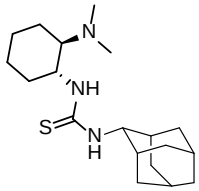
Organocatalyst **F**
3 d, 71% yield, 53.5:46.5 er



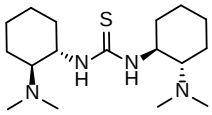
Organocatalyst **G**
3 d, 24% yield, 53.5:46.5 er



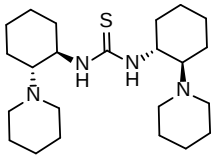
Organocatalyst **H**
3 d, 50% yield, 52:48 er



Organocatalyst **I**
3 d, 58% yield, 62:38 er



Organocatalyst **J**
3 d, 74% yield, [c] 68:32 er



Organocatalyst **K**
3 d, 76% yield, 65.5:34.5 er

Study of the equivalents of $MgCO_3$.

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $MgCO_3$ (0.14 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:2 mixture (1 mL of $CHCl_3$ and 0.2 mL of H_2O) and stirred continuously for 3 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	$MgCO_3$ (x equiv.)	Yield (%)	er (%)
1	1.2	66	84.5:15.5
2	1.5	61	83:17
3	2.0	68	85:15
4	3.0	70	83.5:16.5

Study of the amount of water

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $MgCO_3$ (0.2 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O mixture (1 mL of $CHCl_3$ and the indicated volume of H_2O) and stirred continuously for 3 days at 4 ^oC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	H_2O (mL)	Yield (%)	er (%)
1	0.0	19	85:15
2	0.1	72	85:15
3	0.2	68	85:15
4	0.5	74	84:16

Study of the concentration

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $MgCO_3$ (0.2 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O mixture (the indicated volume of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 3 days at 4 ^oC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	mL $CHCl_3$	Yield (%)	er (%)
1	0.5	77	84:16
2	1.0	72	85:15
3	2.0	47	84:16

Study of the organocatalyst loading

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a** (0.07 mmol, 1 equiv.), $MgCO_3$ (0.2 mmol, 2 equiv.), and organocatalyst **A** are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 3 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	Organocatalyst A (x mol %)	Yield (%)	er (%)
1	5	27	85.5:14.5
2	10	72	85:15
3	20	68	86:14

Study of the amount of tosyl chloride 2a

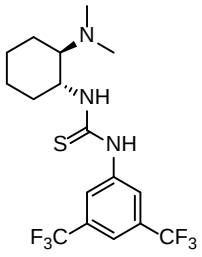
Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.07 mmol), tosyl chloride **2a**, $MgCO_3$ (0.2 mmol, 2 equiv.), and organocatalyst **A** (0.007 mmol, 10 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 3 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	2a (x equiv.)	Yield (%)	er (%)
1	1.0	72	85:15
2	1.2	69	84.5:15.5

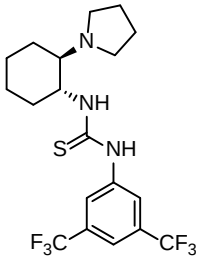
Study of scalability of the reaction

Synthetic procedure: In a regular glass vial, bisphenol **1a** (0.15 mmol, 1 equiv.), tosyl chloride **2a**, the indicated base (2 equiv.), and the indicated organocatalyst are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O mixture and stirred continuously for 3 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:AcOEt to obtain tosylated bisphenol **3aa**.

Entry	Base	2a (mmol)	H_2O (x mL)	$CHCl_3$ (x mL)	Organocatalyst (x mol %)	Yield (%)	er (%)
1	$MgCO_3$	0.15	0.2	2.0	A (10)	50	84.5:15.5
2	$MgCO_3$	0.18	0.1	1.0	A (10)	81	81.5:18.5
3	$MgCO_3$	0.18	0.1	1.0	A (20)	81	84:16
4	$CaCO_3$	0.18	0.1	1.0	A (10)	69	85:15
5	$CaCO_3$	0.18	0.1	1.0	A (10)	76	85:15
6	$CaCO_3$	0.18	0.1	1.0	B (20)	72	87:13

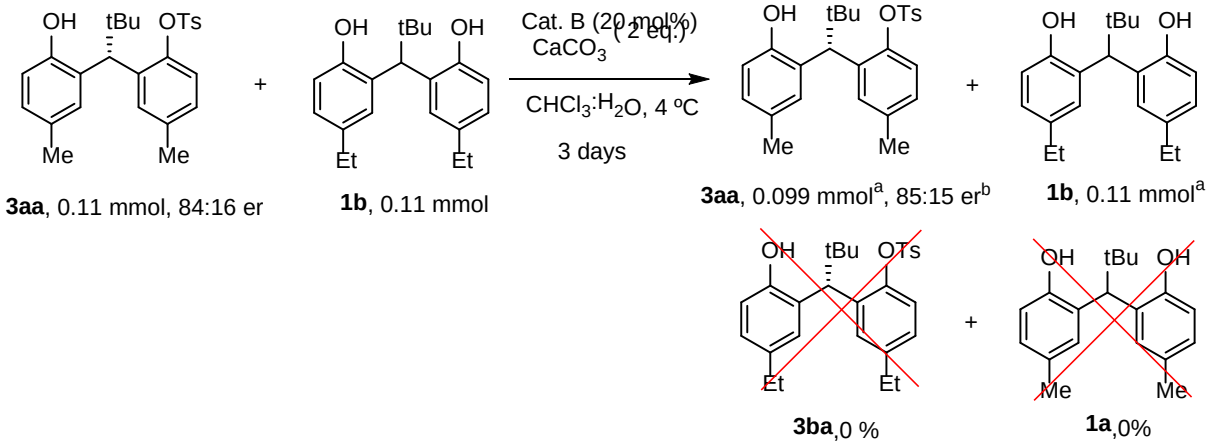


Organocatalyst **A**



Organocatalyst **B**

Control experiment to assess potential scrambling of the sulfonyl group between the starting material and the product



3aa, 0.11 mmol, 84:16 er

1b, 0.11 mmol

3aa, 0.099 mmol[a], 85:15 er[b]

1b, 0.11 mmol[a]

3ba,0 %

1a,0%

a. Isolated yield after column chromatography.
b. Enantiomeric ratios determined by HPLC using chiral stationary phase.

Synthetic Procedures for the Sulfonylation of Bisphenols

1. General Procedure for the non-enantioselective sulfonylation of bisphenols (GP-1)

In a regular glass vial, bisphenol **1** (0.07 mmol), sulfonyl chloride **2** (0.07 mmol, 1 equiv.), and $K_3PO_4 \cdot 3H_2O$ (0.14 mmol, 2 equiv.) are added. Next, the reaction mixture is dissolved in DCM (1 mL) and stirred at room temperature. The progress of reaction was monitored by TLC and directly purified by column chromatography using mixtures of hexane:DCM or hexane:AcOEt as eluent to obtain sulfonylated bisphenol **3**.

2. General Procedure for the Enantioselective sulfonylation of bisphenols using organocatalyst **A** (GP-2)

In a regular glass vial, bisphenol **1** (0.15 mmol), sulfonyl chloride **2** (0.18 mmol, 1.2 equiv.), $CaCO_3$ (0.30 mmol, 2 equiv.), and catalyst **A** (0.03 mmol, 20 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 4 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:DCM or hexane:AcOEt to obtain sulfonylated bisphenol **3**.

3. General Procedure for the Enantioselective sulfonylation of bisphenols using organocatalyst **B** (GP-3)

In a regular glass vial, bisphenol **1** (0.15 mmol), sulfonyl chloride **2** (0.18 mmol, 1.2 equiv.), $CaCO_3$ (0.30 mmol, 2 equiv.), and catalyst **B** (0.03 mmol, 20 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 4 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:DCM or hexane:AcOEt to obtain sulfonylated bisphenol **3**.

4. General Procedure for the Enantioselective sulfonylation of bisphenols using organocatalyst **B** (GP-4)

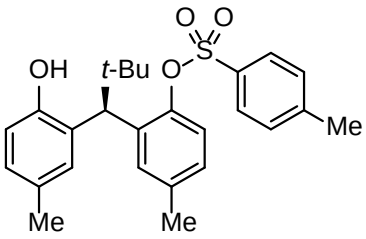
In a regular glass vial, bisphenol **1** (0.15 mmol), sulfonyl chloride **2** (0.45 mmol, 3 equiv.), $CaCO_3$ (0.30 mmol, 2 equiv.), and catalyst **B** (0.03 mmol, 20 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (1 mL of $CHCl_3$ and 0.1 mL of H_2O) and stirred continuously for 4 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:DCM or hexane:AcOEt to obtain sulfonylated bisphenol **3**.

5. Procedure for the Enantioselective sulfonylation of bisphenol **1d** using organocatalyst **B** at 1 mmol scale (GP-5)

In a regular glass vial, bisphenol **1d** (316.4 mg, 1 mmol), sulfonyl chloride **2b** (262, 4 mg, 1.5 mmol, 1.5 equiv.), $CaCO_3$ (200.2 mg, 2 mmol, 2 equiv.), and catalyst **B** (87.9 mg, 0.2 mmol, 20 mol %) are added. The reaction mixture is then dissolved in a $CHCl_3$:H_2O 10:1 mixture (7 mL of $CHCl_3$ and 0.7 mL of H_2O) and stirred continuously for 4 days at 4 ºC. Finally, the reaction mixture is evaporated and directly purified by column chromatography using mixtures of hexane:DCM to obtain sulfonylated bisphenol **3db**.

Characterization of the Products

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 4-methyl benzenesulfonate (3aa)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and 4-methylbenzenesulfonyl chloride (**2a**, 34.3 mg, 0.18 mmol), in accordance with GP-2, product **3aa** was obtained (50.0 mg, 0.114 mmol, 76% yield, white solid). Product **3aa** is also obtained following GP-3 (47.4 mg, 0.108 mmol, 72% yield, white solid). All characterization data below is generated from the product obtained from GP-2.

m.p.: 95 °C.

$[\alpha]_D^{25}$=-29.7 (*c* = 0.94, $CHCl_3$).

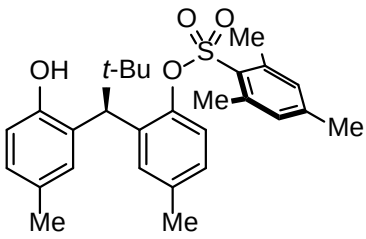
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 2.1 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 2.1 Hz, 1H), 6.91– 6.87 (m, Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.56 (s, 1H), 4.61 (s, 1H), 2.45 (s, 3H), 2.34 (s, 3H), 2.25 (s, 3H), 0.99 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.8 (C), 146.4 (C), 145.4 (C), 136.0 (C), 135.9 (C), 133.1 (C), 131.1 (CH), 131.0 (CH), 129.8 (CH), 129.3 (C), 128.7 (C), 128.5 (CH), 127.8 (CH), 127.6 (CH), 121.4 (CH), 117.7 (CH), 44.3 (CH), 36.0 (C), 29.2 (CH_3), 21.7 (CH_3), 21.4 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 12.82 min, t_R (minor) = 22.01 min, 85:15 er with GP-2, 87:13 er with GP-3. The mother liquor obtained after crystallization via pentane diffusion into a $CHCl_3$ solution of **3aa** (from GP-2) gave 97.5:2.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{26}H_{34}NO_4S^+$ 456.2203; found 456.2196.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 2,4,6-trimethylbenzenesulfonate (3ab)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-2, product **3ab** was obtained (51.1 mg, 0.110 mmol, 73% yield, yellowish oil). Product **3ab** is also obtained following GP-3 (50.4 mg, 0.108 mmol, 72% yield, yellowish oil). All characterization data below is generated from the product obtained from GP-2.

$[\alpha]_D^{25}$=-33.6 (*c* = 0.84, $CHCl_3$).

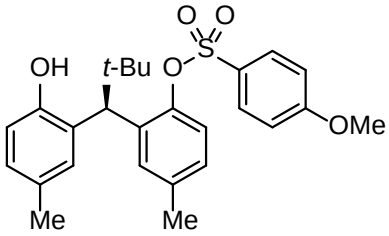
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.1 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 7.02 (s, 2H), 6.90 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.83 – 6.80 (m, 2H), 6.42 (d, *J* = 8.2 Hz, 1H), 5.67 (s, 1H), 4.76 (s, 1H), 2.60 (s, 6H), 2.36 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H), 1.08 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.0 (C), 146.6 (C), 143.9 (C), 140.0 (C), 135.88 (C), 135.86 (C), 131.94 (C), 131.85 (CH), 131.5 (CH), 130.8 (CH), 129.2 (C), 128.8 (C), 127.8 (CH), 127.6 (CH), 120.4 (CH), 117.9 (CH), 44.4 (CH), 36.3 (C), 29.3 (CH_3), 22.7 (CH_3), 21.4 (CH_3), 21.1 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 13.50 min, t_R (minor) = 18.02 min, 86:14 er with GP-2, 90.5:9.5 er with GP-3. The mother liquor obtained after crystallization via pentane diffusion into a $CHCl_3$ solution of **3ab** (from GP-2) gave 99.5:0.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{28}H_{38}NO_4S^+$ 484.2516; found 484.2510.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 4-methoxybenzenesulfonate (3ac)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and 4-methoxybenzene sulfonyl chloride (**2c**, 37.2 mg, 0.18 mmol), in accordance with GP-3, product **3ac** was obtained (9.5 mg, 0.021 mmol, 14% yield, white solid).

m.p.: 165 °C.

$[\alpha]_D^{25}$=-33.2 (*c* = 0.24, $CHCl_3$).

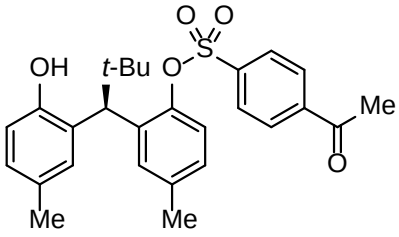
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.0 Hz, 2H), 7.54 (d, *J* = 2.1 Hz, 1H), 7.16 (d, *J* = 2.1 Hz, 1H), 6.99 (d, *J* = 9.0 Hz, 2H), 6.91 – 6.87 (m, 2H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.63 (s, 1H), 4.62 (s, 1H), 3.88 (s, 3H), 2.34 (s, 3H), 2.26 (s, 3H), 1.00 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 164.2 (C), 151.8 (C), 146.4 (C), 136.0 (C), 135.8 (C), 131.1 (CH), 131.0 (CH), 130.8 (CH), 129.3 (C), 128.8 (C), 127.8 (CH), 127.6 (CH), 127.3 (C), 121.4 (CH), 117.7 (CH), 114.4 (CH), 55.7 (CH_3), 44.3 (CH), 36.0 (C), 29.2 (CH_3), 21.4 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 19.67 min, t_R (minor) = 31.42 min, 85:15 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{26}H_{34}NO_5S^+$ 472.2152; found 472.2140.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 4-acetylbenzenesulfonate (3ad)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and 4-acetylbenzene sulfonyl chloride (**2d**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3ad** was obtained (46.9 mg, 0.101 mmol, 67% yield, white solid).

m.p.: 155 °C

$[\alpha]_D^{25}$=-16.5 (*c* = 0.93, $CHCl_3$).

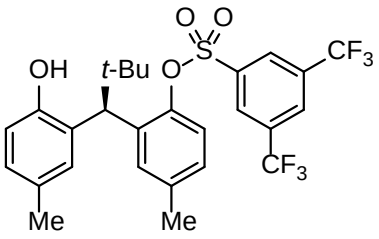
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 4H), 7.56 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 2.2 Hz, 1H), 6.93 – 6.88 (m, 2H), 6.86 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.61 (s, 1H), 2.65 (s, 3H), 2.35 (s, 3H), 2.23 (s, 3H), 0.97 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 196.6 (C), 151.6 (C), 146.3 (C), 141.1 (C), 139.9 (C), 136.3 (C), 135.9 (C), 131.2 (CH), 131.1 (CH), 129.3 (C), 128.9 (CH), 128.8 (CH), 128.3 (C), 127.8 (CH), 127.7 (CH), 121.1 (CH), 117.1 (CH), 44.1 (CH), 35.9 (C), 29.2 (CH_3), 26.9 (CH_3), 21.4 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 19.81 min, t_R (minor) = 34.66 min, 73:27 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{27}H_{34}NO_5S^+$ 484.2152; found 484.2158.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 3,5-bis(trifluoromethyl)benzenesulfonate (3ae)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and 3,5-bis(trifluoromethyl) benzenesulfonyl chloride (**2e**, 56.3 mg, 0.18 mmol), in accordance with GP-3, product **3ae** was obtained (66.7 mg, 0.119 mmol, 79% yield, white solid).

m.p.: 118 °C

$[\alpha]_D^{25}$=-7.7 (*c* = 0.95, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 2H), 8.05 (s, 1H), 7.54 (d, *J* = 2.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.96 – 6.87 (m, 2H), 6.75 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 4.76 (s, 1H), 4.43 (s, 1H), 2.31 (s, 3H), 2.13 (s, 3H), 0.86 (s, 9H).

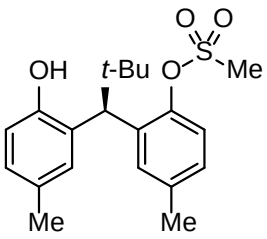
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.1 (C), 146.0 (C), 138.9 (C), 136.8 (C), 136.0 (C), 132.9 (q, J_{C-F} = 34.6 Hz, C), 131.2 (CH), 131.2 (CH), 129.4 (C), 128.9 (q, J_{C-F} = 3.9 Hz, CH), 127.8 (CH), 127.7 (CH), 127.7 (C), 127.6 - 127.5 (m, CH), 122.3 (q, J_{C-F} = 273.6 Hz, CF_3), 121.3 (CH), 116.2 (CH), 43.9 (CH), 35.7 (C), 29.0 (CH_3), 21.4 (CH_3), 20.9 (CH_3).

^{19}F{^{1}H} RMN (471 MHz, $CDCl_3$) δ - 62.92.

HPLC: chiral stationary column OD-H, mobile phase hexane/iPrOH = 99/1, 1.0 mL/min, 25 °C, t_R (major) = 10.7 min, t_R (minor) = 16.25 min, 76:24 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{27}H_{30}F_6NO_4S^+$ 578.1794; found 578.1801.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl methanesulfonate (3af)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and methanesulfonyl chloride (**2f**, 35 uL, 0.45 mmol), in accordance with GP-4, product **3af** was obtained (43.5 mg, 0.120 mmol, 80% yield, white solid).

m.p.: 150 ^oC

$[\alpha]_D^{25}$=-16.4 (*c* = 0.87, $CHCl_3$).

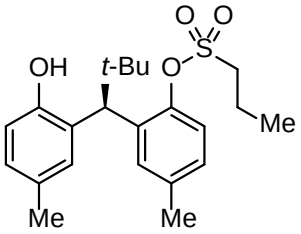
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 2.2 Hz, 1H), 7.02 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.87 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.71 (d, *J* = 8.1 Hz, 1H), 5.24 (s, 1H), 4.74 (s, 1H), 3.04 (s, 3H), 2.38 (s, 3H), 2.26 (s, 3H), 1.07 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.4 (C), 146.0 (C), 136.2 (C), 135.4 (C), 131.24 (CH), 131.15 (CH), 129.6 (C), 128.5 (C), 127.9 (CH), 127.8 (CH), 121.2 (CH), 116.8 (CH), 43.8 (CH), 37.6 (C), 36.1 (CH_3), 29.2 (CH_3), 21.4 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 7.65 min, t_R (minor) = 9.90 min, 69.5:30.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{20}H_{30}NO_4S^+$ 380.1890; found 380.1898.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl propane-1-sulfonate (3ag)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and propane-1-sulfonyl chloride (**2g**, 20 uL, 0.18 mmol), in accordance with GP-4, product **3ag** was obtained (48.1 mg, 0.134 mmol, 89% yield, white solid).

m.p.: 94 ^oC

$[\alpha]_D^{25}$=-11.2 (*c* = 0.87, $CHCl_3$).

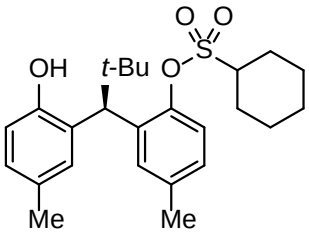
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.2 Hz, 1H), 7.25 (d, *J* = 2.1 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 7.02 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.88 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 5.49 (s, 1H), 4.70 (s, 1H), 3.39 – 3.17 (m, 2H), 2.37 (s, 3H), 2.27 (s, 3H), 2.04 – 1.96 (m, 2H), 1.15 – 0.99 (m, 12H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.7 (C), 145.6 (C), 136.1 (C), 135.4 (C), 131.3 (CH), 130.9 (CH), 129.5 (C), 128.6 (C), 127.9 (CH), 127.8 (CH), 121.6 (CH), 117.3 (CH), 52.8 (CH_2), 44.0 (CH), 36.1 (C), 29.2 (CH_3), 21.4 (CH_3), 21.0 (CH_3), 17.1 (CH_2), 12.9 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 7.49 min, t_R (minor) = 11.25 min, 87:13 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{22}H_{34}NO_4S^+$ 408.2203; found 408.2192.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl cyclohexanesulfonate (3ah)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and cyclohexanesulfonyl chloride (**2h**, 24 uL, 0.18 mmol), in accordance with GP-4, product **3ah** was obtained (20.7 mg, 0.048 mmol, 32% yield, colorless oil).
$[\alpha]_D^{25}$=+38.2 (*c* = 0.30, $CHCl_3$).

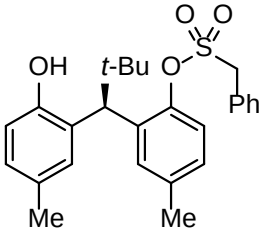
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 2.1 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 1H), 7.01 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.90 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 5.79 (s, 1H), 4.65 (s, 1H), 3.36 (tt, *J* = 12.0, 3.5 Hz, 1H), 2.49 – 2.38 (m, 2H), 2.36 (s, 3H), 2.29 (s, 3H), 1.99 – 1.95 (m, 2H), 1.84 – 1.71 (m, 3H), 1.50 – 1.19 (m, 3H), 1.06 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 151.9 (C), 145.2 (C), 136.1 (C), 135.4 (C), 131.4 (CH), 130.6 (CH), 129.4 (C), 128.7 (C), 127.9 (CH), 122.3 (CH), 117.9 (CH), 61.2 (CH), 44.0 (CH), 36.3 (C), 29.1 (CH_3), 26.49 (CH_2), 26.45 (CH_2), 25.02 (CH_2), 24.97 (CH_2), 24.9 (CH_2), 21.4 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 8.53 min, t_R (minor) = 11.40 min, 80:20 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{25}H_{38}NO_4S^+$ 484.2516; found 484.2514.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl phenylmethanesulfonate (3ai)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis (4-methyl phenol) (**1a**, 42.6 mg, 0.15 mmol) and phenylmethanesulfonyl chloride (**2i**, 34.4 mg, 0.18 mmol), in accordance with GP-4, product **3ai** was obtained (26.3 mg, 0.060 mmol, 40% yield, white solid).

m.p.: 145 °C

$[\alpha]_D^{25}$=+17.8 (*c* = 0.38, $CHCl_3$).

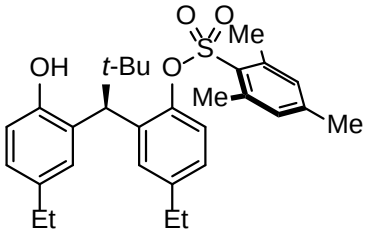
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 2.2 Hz, 1H), 7.46 – 7.44 (m, 2H), 7.41 – 7.40 (m, 3H), 7.23 (d, *J* = 2.2 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.2 Hz, 1H), 6.92 – 6.86 (m, 2H), 6.77 (d, *J* = 8.1 Hz, 1H), 5.41 (s, 1H), 4.65 (s, 1H), 4.51 (d, *J* = 2.7 Hz, 2H), 2.35 (s, 3H), 2.27 (s, 3H), 1.04 (s, 9H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.7 (C), 145.7 (C), 136.1 (C), 135.5 (C), 131.2 (CH), 131.0 (CH), 130.9 (CH), 129.5 (C), 129.3 (CH), 129.0 (CH), 128.5 (C), 127.88 (CH), 127.86 (CH), 127.1 (C), 121.7 (C), 117.3 (C), 57.2 (CH_2), 44.1 (CH), 36.1 (C), 29.1 (CH_3), 21.39 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 5.44 min, t_R (minor) = 8.42 min, 75.5:24.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{26}H_{34}NO_4S^+$ 456.2203; found 456.2209.

(*R*)-4-Ethyl-2-(1-(5-ethyl-2-hydroxyphenyl)-2,2-dimethylpropyl)phenyl 2,4,6-trimethylbenzenesulfonate (3bb)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4-ethylphenol) (**1b**, 46.9 mg, 0.15 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3bb** was obtained (50.5 mg, 0.102 mmol, 68% yield, white solid).

m.p.: 148 °C

$[\alpha]_D^{25}$=-24.2 (*c* = 0.84, $CHCl_3$).

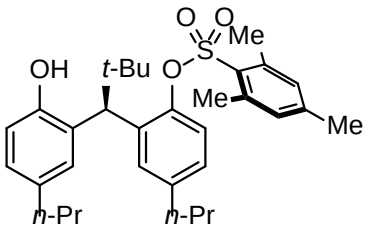
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 2.2 Hz, 1H), 7.37 (d, *J* = 2.1 Hz, 1H), 7.02 (s, 2H), 6.93 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.88 – 6.79 (m, 2H), 6.46 (d, *J* = 8.2 Hz, 1H), 5.70 (s, 1H), 4.78 (s, 1H), 2.65 – 2.56 (m, 10H), 2.36 (s, 3H), 1.29 – 1.16 (m, 6H), 1.08 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.2 (C), 146.6 (C), 143.9 (C), 142.0 (C), 140.0 (C), 135.8 (C), 135.7 (C), 131.94 (C), 131.85 (CH), 130.5 (CH), 129.6 (CH), 128.9 (C), 126.6 (CH), 126.4 (CH), 120.5 (CH), 117.8 (CH), 44.5 (CH), 36.5 (C), 29.3 (CH_3), 28.5 (CH_2), 28.4 (CH_2), 22.7 (CH_3), 21.1 (CH_3), 15.9 (CH_3), 15.4 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 9.80 min, t_R (minor) = 12.95 min, 86:14 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{30}H_{42}NO_4S^+$ 512.2829; found 512.2833.

(*R*)-2-(1-(2-Hydroxy-5-propylphenyl)-2,2-dimethylpropyl)-4-propylphenyl 2,4,6-trimethylbenzenesulfonate (3cb)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4-propylphenol) (**1c**, 51.1 mg, 0.15 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3cb** was obtained (47.8 mg, 0.092 mmol, 61% yield, colorless oil).

$[\alpha]_D^{25}$=-22.8 (*c* = 0.85, $CHCl_3$).

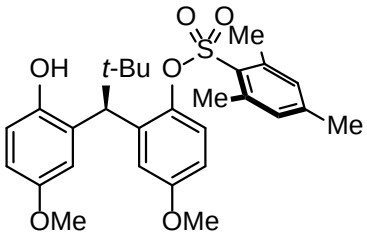
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.2 Hz, 1H), 7.32 (d, *J* = 2.1 Hz, 1H), 7.02 (s, 2H), 6.90 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.81 (d, *J* = 8.1 Hz, 2H), 6.45 (d, *J* = 8.3 Hz, 1H), 5.67 (s, 1H), 4.75 (s, 1H), 2.60 (s, 6H), 2.52 (td, *J* = 7.5, 1.9 Hz, 4H), 2.36 (s, 3H), 1.72 – 1.50 (m, 4H), 1.07 (s, 9H), 0.98 – 0.82 (m, 6H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.2 (C), 146.6 (C), 143.8 (C), 140.5 (C), 140.1 (C), 135.8 (C), 134.1 (C), 131.93 (C), 131.85 (CH), 131.1 (CH), 130.4 (CH), 128.7 (C), 127.2 (CH), 126.9 (CH), 120.5 (CH), 117.8 (CH), 44.5 (CH), 37.61 (CH_2), 37.55 (CH_2), 36.5 (C), 29.4 (CH_3), 24.8 (CH_2), 24.4 (CH_2), 22.7 (CH_3), 21.1 (CH_3), 13.7 (CH_3), 13.6 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 9.41 min, t_R (minor) = 11.19 min, 82.5:17.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{32}H_{46}NO_4S^+$ 540.3142; found 540.3149.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)-2,2-dimethylpropyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3db)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4-methoxy phenol) (**1d**, 47.4 mg, 0.15 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3db** was obtained (72.6 mg, 0.146 mmol, 97% yield, yellowsih oil).

$[\alpha]_D^{25}$=-45.5 (*c* = 0.90, $CHCl_3$).

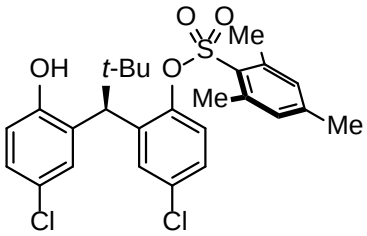
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, *J* = 3.0 Hz, 1H), 7.08 (d, *J* = 3.0 Hz, 1H), 7.02 (s, 2H), 6.88 (d, *J* = 8.8 Hz, 1H), 6.67 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.52 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.41 (d, *J* = 8.9 Hz, 1H), 5.29 (s, 1H), 4.80 (s, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 2.59 (s, 6H), 2.35 (s, 3H), 1.09 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3 (C), 153.3 (C), 148.2 (C), 144.0 (C), 142.3 (C), 140.1 (C), 137.6 (C), 131.9 (CH), 131.6 (C), 130.6 (C), 121.4 (CH), 118.9 (CH), 117.0 (CH), 116.7 (CH), 111.6 (CH), 111.2 (CH), 55.6 (CH_3), 55.4 (CH_3), 44.9 (CH), 36.4 (C), 29.2 (CH_3), 22.7 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 35.63 min, t_R (minor) = 39.91 min, 90.5:9.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{28}H_{38}NO_6S^+$ 516.2414; found 516.2418.

(*R*)-4-Chloro-2-(1-(5-chloro-2-hydroxyphenyl)-2,2-dimethylpropyl)phenyl 2,4,6-trimethylbenzenesulfonate (3eb)



Using 2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4-chlorophenol) (**1e**, 48.8 mg, 0.15 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3eb** was obtained (70.8 mg, 0.140 mmol, 93% yield, yellowsih oil).

$[\alpha]_D^{25}$=-14.4 (*c* = 0.88, $CHCl_3$).

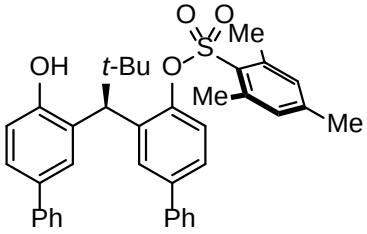
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 2.6 Hz, 1H), 7.35 (d, *J* = 2.5 Hz, 1H), 7.15 – 6.93 (m, 4H), 6.82 (d, *J* = 8.6 Hz, 1H), 6.46 (d, *J* = 8.7 Hz, 1H), 5.69 (s, 1H), 4.80 (s, 1H), 2.58 (s, 6H), 2.36 (s, 3H), 1.08 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 152.8 (C), 147.2 (C), 144.4 (C), 140.1 (C), 137.9 (C), 132.0 (CH), 131.4 (C), 130.7 (CH), 130.2 (C), 129.9 (CH), 127.5 (CH), 127.4 (CH), 125.4 (C), 122.0 (CH), 119.2 (CH), 44.7 (CH), 36.3 (C), 29.1 (CH_3), 22.7 (CH_3), 21.2 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 8.60 min, t_R (minor) = 9.65 min, 68.5:31.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{26}H_{32}Cl_2NO_4S^+$ 524.1424; found 524.1428.

(*R*)-3-(1-(4-Hydroxy-[1,1'-biphenyl]-3-yl)-2,2-dimethylpropyl)-[1,1'-biphenyl]-4-yl 2,4,6-trimethylbenzenesulfonate (3fb)



Using 3,3''-(2,2-dimethylpropane-1,1-diyl)bis([1,1'-biphenyl]-4-ol) (**1f**, 61.3 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3fb** was obtained (77.1 mg, 0.131 mmol, 87% yield, white solid).

m.p.: 186 °C

$[\alpha]_D^{25}$=-8.1 (*c* = 1.10, $CHCl_3$).

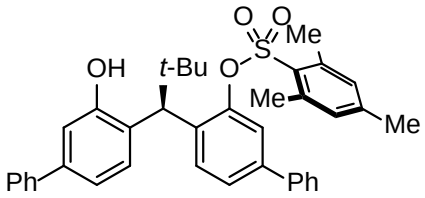
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 2.3 Hz, 1H), 7.83 (d, *J* = 2.3 Hz, 1H), 7.58 – 7.50 (m, 4H), 7.50 – 7.22 (m, 8H), 7.07 (s, 2H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.88 (s, 1H), 4.95 (s, 1H), 2.67 (s, 6H), 2.40 (s, 3H), 1.21 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 154.0 (C), 148.2 (C), 144.1 (C), 141.4 (C), 140.3 (C), 140.1 (C), 139.2 (C), 136.4 (C), 133.3 (C), 132.0 (CH), 131.9 (C), 129.9 (CH), 129.3 (CH), 129.0 (C), 128.9 (CH), 128.7 (CH), 127.5 (CH), 127.1 (CH), 126.7 (CH), 126.5 (CH), 126.2 (CH), 125.9 (CH), 121.1 (CH), 118.2 (CH), 45.0 (CH), 36.5 (C), 29.5 (CH_3), 22.8 (CH_3), 21.2 (CH_3).

HPLC: chiral stationary column AD-H, mobile phase hexane/iPrOH = 98/2, 1.0 mL/min, 25 °C, t_R (minor) = 41.28 min, t_R (major) = 70.78 min, 36.5:63.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{38}H_{42}NO_4S^+$ 608.2829; found 608.2819.

(*R*)-4-(1-(3-Hydroxy-[1,1'-biphenyl]-4-yl)-2,2-dimethylpropyl)-[1,1'-biphenyl]-3-yl 2,4,6-trimethylbenzenesulfonate (3gb)



Using 4,4''-(2,2-dimethylpropane-1,1-diyl)bis([1,1'-biphenyl]-3-ol) (**1g**, 61.3 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3gb** was obtained (52.3 mg, 0.089 mmol, 59% yield, yellowsih oil).

$[\alpha]_D^{25}$=-27.9 (*c* = 0.93, $CHCl_3$).

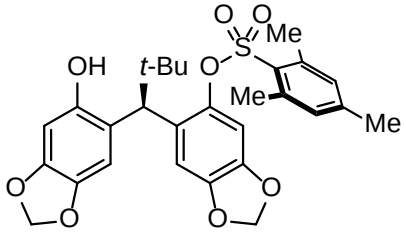
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.49 – 7.28 (m, 7H), 7.27 – 7.21 (m, 2H), 7.21 – 7.16 (m, 2H), 7.08 (s, 2H), 6.71 (d, *J* = 1.9 Hz, 1H), 6.03 (s, 1H), 4.92 (s, 1H), 2.64 (s, 6H), 2.39 (s, 3H), 1.17 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 154.6 (C), 148.9 (C), 144.2 (C), 140.5 (C), 140.4 (C), 140.2 (C), 140.0 (C), 139.1 (C), 135.1 (C), 132.0 (CH), 131.5 (C), 131.4 (CH), 130.7 (CH), 128.7 (CH), 128.6 (CH), 127.9 (C), 127.7 (CH), 127.2 (CH), 126.8 (CH), 126.6 (CH), 124.8 (CH), 119.6 (CH), 119.0 (CH), 116.4 (CH), 44.3 (CH), 36.6 (C), 29.4 (CH_3), 22.8 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 30.65 min, t_R (minor) = 39.35 min, 76:24 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{38}H_{42}NO_4S^+$ 608.2829; found 608.2822.

(*R*)-6-(1-(6-Hydroxybenzo[*d*][1,3]dioxol-5-yl)-2,2-dimethylpropyl)benzo[*d*][1,3]dioxol-5-yl 2,4,6-trimethylbenzenesulfonate (3hb)



Using 6,6'-(2,2-dimethylpropane-1,1-diyl)bis(benzo[*d*][1,3] dioxol-5-ol) (**1h**, 61.7 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3hb** was obtained (78.2 mg, 0.149 mmol, 99% yield, orange solid).

m.p.: 166 °C

$[\alpha]_D^{25}$=-27.9 (*c* = 0.90, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (s, 1H), 7.03 (s, 2H), 6.95 (s, 1H), 6.51 (s, 1H), 6.04 (s, 1H), 5.94 - 5.84 (m, 4H), 5.64 (s, 1H), 4.63 (s, 1H), 2.62 (s, 6H), 2.36 (s, 3H), 1.06 (s, 9H).

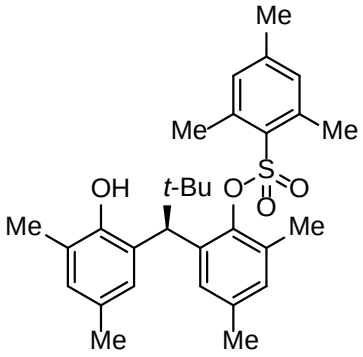
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 148.8 (C), 146.0 (C), 145.8 (C), 145.7 (C), 144.2 (C), 142.1 (C), 141.4 (C), 139.9 (C), 132.0 (CH), 131.6 (C), 129.8 (C), 121.4 (C), 109.6 (CH), 108.8 (CH), 102.2

(CH), 101.8 (CH_2), 100.9 (CH_2), 100.6 (CH), 44.5 (CH), 36.5 (C), 29.2 (CH_3), 22.7 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (major) = 56.34 min, t_R (minor) = 66.33 min, 78:22 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{28}H_{34}NO_8S^+$ 544.2000; found 544.1995.

(*R*)-2-(1-(2-Hydroxy-3,5-dimethylphenyl)-2,2-dimethylpropyl)-4,6-dimethylphenyl 2,4,6-trimethylbenzenesulfonate (3ib)



Using 6,6'-(2,2-dimethylpropane-1,1-diyl)bis(2,4-dimethyl phenol) (**1i**, 46.9 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3ib** was obtained (6.7 mg, 0.014 mmol, 9% yield, colorless oil).

$[\alpha]_D^{25}$=-8.9 (*c* = 0.11, $CHCl_3$).

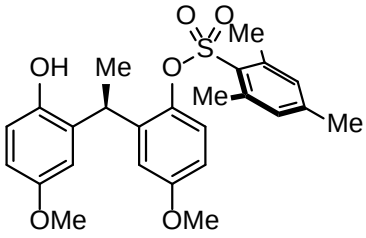
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.2 Hz, 1H), 6.98 (s, 2H), 6.85 (d, *J* = 2.2 Hz, 1H), 6.78 (d, *J* = 2.1 Hz, 1H), 6.77 (d, *J* = 2.1 Hz, 1H), 6.31 (s, 1H), 4.67 (s, 1H), 2.64 (s, 6H), 2.32 (s, 6H), 2.22 (s, 3H), 2.17 (s, 3H), 1.66 (s, 3H), 1.12 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 150.3 (C), 146.4 (C), 143.5 (C), 139.0 (C), 137.7 (C), 135.7 (C), 133.4 (C), 131.8 (CH), 130.8 (C), 130.0 (CH), 129.4 (CH), 128.9 (CH), 128.1 (CH), 127.8 (C), 126.6 (C), 126.0 (C), 46.1 (CH), 36.3 (C), 29.5 (CH_3), 22.6 (CH_3), 21.4 (CH_3), 21.1 (CH_3), 20.9 (CH_3), 17.3 (CH_3), 17.1 (CH_3).

HPLC: chiral stationary column IC, mobile phase hexane/iPrOH = 95/5, 1.0 mL/min, 25 °C, t_R (minor) = 4.64 min, t_R (major) = 6.32 min, 5.5:95.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{30}H_{42}NO_4S^+$ 512.2829; found 512.2833.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)ethyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3jb)



Using 2,2'-(ethane-1,1-diyl)bis(4-methoxyphenol) (**1j**, 41.1 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3jb** was obtained (48.6 mg, 0.107 mmol, 71% yield, yellowish oil).

$[\alpha]_D^{25}$=-39.3 (*c* = 1.03, $CHCl_3$).

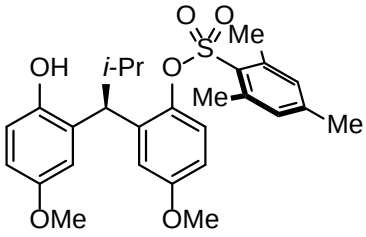
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, *J* = 1.1 Hz, 2H), 6.88 (d, *J* = 2.9 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 1H), 6.72 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.49 – 6.43 (m, 2H), 6.33 – 6.27 (m, 1H), 5.68 (s, 1H), 4.70 (q, *J* = 7.0 Hz, 1H), 3.78 (s, 3H), 3.59 (s, 3H), 2.56 (s, 6H), 2.34 (s, 3H), 1.53 (d, *J* = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.4(C), 153.3(C), 148.2(C), 144.2(C), 141.0(C), 140.8(C), 140.6(C), 131.9(CH), 130.7(C), 129.4(C), 122.1(CH), 117.0(CH), 114.2(CH), 114.0(CH), 112.3(CH), 111.8(CH), 55.8 (CH_3), 55.3 (CH_3), 33.0 (CH), 22.8(CH_3), 21.2(CH_3), 20.3(CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (major) = 31.51 min, t_R (minor) = 39.58 min, 79:21 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{25}H_{32}NO_6S^+$ 474.1945; found 474.1939.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)-2-methylpropyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3kb)



Using 2,2'-(2-methylpropane-1,1-diyl)bis(4-methoxyphenol) (**1k**, 45.4 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3kb** was obtained (53.0 mg, 0.110 mmol, 73% yield, yellowish oil).

$[\alpha]_D^{25}$=-4.5 (*c* = 1.21, $CHCl_3$).

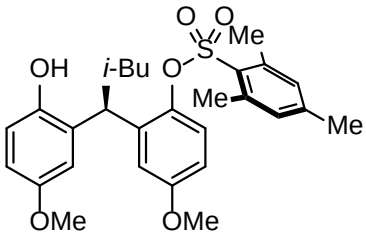
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (s, 2H), 6.95 (d, *J* = 3.0 Hz, 1H), 6.86 (d, *J* = 3.0 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 1H), 6.65 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.50 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.41 (d, *J* = 8.9 Hz, 1H), 5.56 (s, 1H), 4.25 (d, *J* = 10.6 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 2.61 (s, 6H), 2.36 (s, 3H), 1.01 – 0.84 (m, 6H)

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.0 (C), 153.7 (C), 148.1 (C), 144.0 (C), 142.0 (C), 140.2 (C), 138.6 (C), 131.9 (CH), 131.6 (C), 130.4 (C), 121.5 (CH), 118.0 (CH), 115.0 (CH), 114.5 (CH), 111.9 (CH), 111.4. (CH), 55.6 (CH_3), 55.4 (CH_3), 44.8 (CH), 32.4 (CH), 22.8 (CH_3), 21.5 (CH_3), 21.1 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (major) = 14.62 min, t_R (minor) = 16.38 min, 86.5:13.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{27}H_{36}NO_6S^+$ 502.2258; found 502.2252.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)-3-methylbutyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3lb)



Using 2,2'-(3-methylbutane-1,1-diyl)bis(4-methoxyphenol) (**1l**, 47.5 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3lb** was obtained (69.6 mg, 0.140 mmol, 93% yield, colorless oil).

$[\alpha]_D^{25}$=-24.6 (*c* = 1.04, $CHCl_3$).

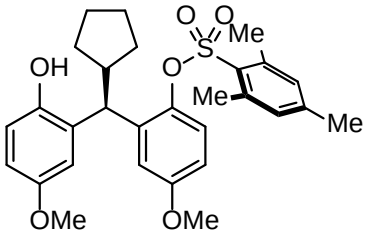
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 2H), 6.88 – 6.79 (m, 2H), 6.71 (dd, J = 8.8, 3.0 Hz, 1H), 6.54 (d, J = 3.0 Hz, 1H), 6.45 (dd, J = 8.9, 3.1 Hz, 1H), 6.32 (d, J = 8.8 Hz, 1H), 5.82 (s, 1H), 4.69 (dd, J = 10.2, 3.9 Hz, 1H), 3.78 (s, 3H), 3.61 (s, 3H), 2.57 (s, 6H), 2.34 (s, 3H), 2.02 – 1.84 (m, 1H), 1.72 – 1.52 (m, 2H), 0.93-0.91 (m, 6H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.2 (C), 153.2 (C), 148.7 (C), 144.1 (C), 140.9 (C), 140.43 (C), 140.40 (C), 131.9 (CH), 130.9 (C), 127.7 (C), 121.9 (CH), 117.4 (CH), 115.0 (CH), 114.5 (CH), 112.2 (CH), 111.4 (CH), 55.7 (CH_3), 55.3 (CH_3), 44.1 (CH_2), 35.7 (CH), 25.6 (CH), 23.5 (CH_3), 22.7 (CH_3), 21.4 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (minor) = 11.76 min, t_R (major) = 18.39 min, 10.5:89.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{28}H_{38}NO_6S^+$ 516.2414; found 516.2419.

(*R*)-2-(Cyclopentyl(2-hydroxy-5-methoxyphenyl)methyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3mb)



Using 2,2'-(cyclopentylmethylene)bis(4-methoxyphenol) (**1m**, 49.3 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3mb** was obtained (42.1 mg, 0.082 mmol, 55% yield, colorless oil).

$[\alpha]_D^{25}$=-13.2 (*c* = 1.11, $CHCl_3$).

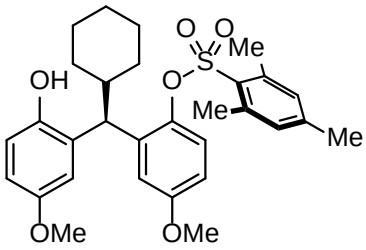
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (s, 2H), 6.95 (d, *J* = 3.0 Hz, 1H), 6.86 (d, *J* = 3.0 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.65 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.49 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.38 (d, *J* = 8.9 Hz, 1H), 5.61 (s, 1H), 4.38 (d, *J* = 10.9 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 2.84 – 2.48 (m, 7H), 2.36 (s, 3H), 1.76 – 1.34 (m, 8H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 153.6 (C), 147.8 (C), 144.0 (C), 141.7 (C), 140.2 (C), 139.2 (C), 131.9 (CH), 131.5 (C), 130.9 (C), 121.4 (CH), 118.0 (CH), 115.3 (CH), 114.9 (CH), 111.8 (CH), 111.3 (CH), 55.6 (CH_3), 55.4 (CH_3), 45.1 (CH), 43.1 (CH), 31.7 (CH_2), 31.2 (CH_2), 25.4 (CH_2), 25.1 (CH_2), 22.8 (CH_3), 21.2 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (minor) = 14.83 min, t_R (major) = 16.06 min, 22.6:77.4 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{29}H_{38}NO_6S^+$ 528.2414; found 528.2414.

(*R*)-2-(Cyclohexyl(2-hydroxy-5-methoxyphenyl)methyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3nb)



Using 2,2'-(cyclohexylmethylene)bis(4-methoxyphenol) (**1n**, 51.4 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3nb** was obtained (68.5 mg, 0.131 mmol, 87% yield, colorless oil).

$[\alpha]_D^{25}$=-9.7 (*c* = 1.08, $CHCl_3$).

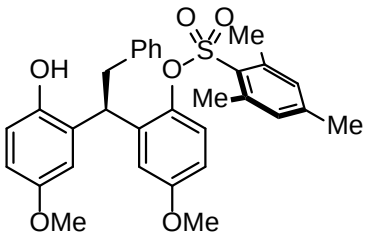
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 2H), 6.93 (d, *J* = 3.0 Hz, 1H), 6.82 (d, *J* = 3.0 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 1H), 6.62 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.48 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.39 (d, *J* = 8.9 Hz, 1H), 5.53 (s, 1H), 4.28 (d, *J* = 10.6 Hz, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 2.58 (s, 6H), 2.33 (s, 3H), 2.08 – 1.87 (m, 1H), 1.74 – 1.48 (m, 5H), 1.30 – 0.87 (m, 5H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.0 (C), 153.7 (C), 148.2 (C), 144.0 (C), 142.2 (C), 140.2 (C), 138.1 (C), 131.9 (CH), 131.6 (C), 130.0 (C), 121.5 (CH), 118.0 (CH), 115.1 (CH), 114.6 (CH), 111.7 (CH), 111.2 (CH), 55.6 (CH_3), 55.4 (CH_3), 43.6 (CH), 41.8 (CH), 31.6 (CH_2), 31.0 (CH_2), 26.5 (CH_2), 26.44 (CH_2), 26.36 (CH_2), 22.8 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (major) = 14.39 min, t_R (minor) = 16.36 min, 89.5:10.5 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{30}H_{40}NO_6S^+$ 542.2571; found 542.2578.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)-2-phenylethyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3ob)



Using 2,2'-(2-phenylethane-1,1-diyl)bis(4-methoxyphenol) (**1o**, 52.6 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3ob** was obtained (55.1 mg, 0.104 mmol, 69% yield, yellowish oil).

$[\alpha]_D^{25}$=+21.2 (*c* = 1.11, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 – 7.07 (m, 5H), 7.01 (s, 2H), 6.98 (d, *J* = 2.9 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 1H), 6.72 – 6.62 (m, 2H), 6.53 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.40 (d, *J* = 8.9 Hz, 1H), 5.69

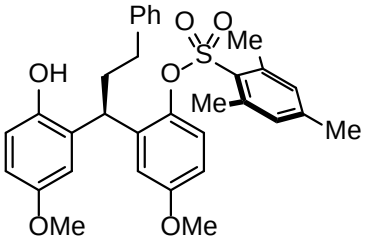
(s, 1H), 5.07 – 4.78 (m, 1H), 3.77 (s, 3H), 3.66 (s, 3H), 3.42 – 3.09 (m, 2H), 2.53 (s, 6H), 2.36 (s, 3H).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.3 (C), 153.2 (C), 148.4 (C), 144.1 (C), 141.0 (C), 140.4 (C), 139.1 (C), 139.0 (C), 131.8 (CH), 130.9 (C), 129.0 (CH), 128.1 (CH), 127.7 (C), 126.0 (CH), 122.0 (CH), 117.4 (CH), 115.1 (CH), 114.7 (CH), 112.6 (CH), 111.9 (CH), 55.7 (CH_3), 55.4 (CH_3), 40.9 (CH_2), 39.7 (CH), 22.7 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 85/15, 1.0 mL/min, 25 °C, t_R (minor) = 17.20 min, t_R (major) = 33.04 min, 12:88 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{31}H_{36}NO_6S^+$ 550.2258; found 550.2263.

(*R*)-2-(1-(2-Hydroxy-5-methoxyphenyl)-3-phenylpropyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3pb)



Using 2,2'-(3-phenylpropane-1,1-diyl)bis(4-methoxyphenol) (**1p**, 56.7 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3pb** was obtained (65.6 mg, 0.120 mmol, 80% yield, yellowish oil).
$[\alpha]_D^{25}$=-3.4 (*c* = 1.10, $CHCl_3$).

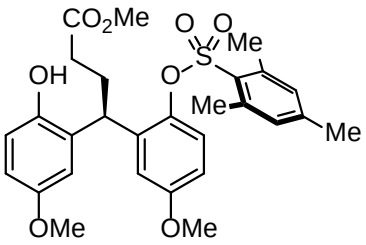
^1H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 2H), 7.22 – 7.12 (m, 3H), 7.02 (s, 2H), 6.91 (d, *J* = 3.0 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.74 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.66 (d, *J* = 3.0 Hz, 1H), 6.51 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.42 (d, *J* = 8.9 Hz, 1H), 5.70 (s, 1H), 4.68 - 4.64 (m, 1H), 3.79 (s, 3H), 3.65 (s, 3H), 2.90 – 2.62 (m, 2H), 2.59 (s, 6H), 2.36 (s, 3H), 2.32 – 2.17 (m, 2H).

$^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 158.3 (C), 153.5 (C), 148.5 (C), 144.1 (C), 141.9 (C), 141.0 (C), 140.4 (C), 139.4 (C), 131.9 (CH), 131.0 (C), 128.3 (CH), 128.2 (CH), 128.01 (C), 125.8 (CH), 122.1 (CH), 117.6 (CH), 114.8 (CH), 114.1 (CH), 112.4 (CH), 111.7 (CH), 55.7 (CH_3), 55.4 (CH_3), 38.0 (CH), 36.7 (CH_2), 34.2 (CH_2), 22.8 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 85/15, 1.0 mL/min, 25 °C, t_R (minor) = 13.57 min, t_R (major) = 15.86 min, 14:86 er.

HRMS (ESI$^+$) *m/z:* $[M + NH_4]^+$ Calcd for $C_{32}H_{38}NO_6S^+$ 564.2414; found 564.2411.

(*R*)-Methyl 4-(2-hydroxy-5-methoxyphenyl)-4-(2-((mesitylsulfonyl)oxy)-5-methoxyphenyl) butanoate (3qb)



Using methyl 4,4-bis(2-hydroxy-5-methoxyphenyl)butanoate (**1q**, 52.0 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3qb** was obtained (75.3 mg, 0.143 mmol, 95% yield, yellowish oil).

$[\alpha]_D^{25}$=-7.5 (*c* = 1.07, $CHCl_3$).

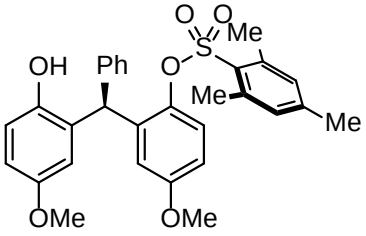
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (s, 2H), 6.82 (d, *J* = 9.1 Hz, 1H), 6.75 – 6.66 (m, 3H), 6.54 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.44 (d, *J* = 8.9 Hz, 1H), 4.62 (t, *J* = 7.0 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.67 (s, 3H), 2.55 (s, 6H), 2.45 – 2.35 (m, 2H), 2.34 (s, 3H), 2.32 – 2.12 (m, 2H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 174.0 (C), 158.3 (C), 153.4 (C), 148.5 (C), 144.1 (C), 141.3 (C), 140.5 (C), 138.3 (C), 131.9 (CH), 130.9 (C), 128.1 (C), 122.5 (CH), 117.7 (CH), 114.8 (CH), 114.0 (CH), 112.5 (CH), 112.0 (CH), 55.7 (CH_3), 55.5 (CH_3), 51.8 (CH_3), 37.1 (CH), 32.0 (CH_2) , 29.7 (CH_2), 22.8 (CH_3), 21.2 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 80/20, 1.0 mL/min, 25 °C, t_R (minor) = 16.98 min, t_R (major) = 28.75 min, 20.5:79.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{28}H_{36}NO_8S^+$ 546.2156; found 546.2153.

(*R*)-2-((2-Hydroxy-5-methoxyphenyl)(phenyl)methyl)-4-methoxyphenyl 2,4,6-trimethylbenzenesulfonate (3rb)



Using methyl 2,2'-(phenylmethylene)bis(4-methoxyphenol) (**1r**, 50.5 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3rb** was obtained (44.3 mg, 0.086 mmol, 57% yield, yellowish oil).

$[\alpha]_D^{25}$=+15.7 (*c* = 1.16, $CHCl_3$).

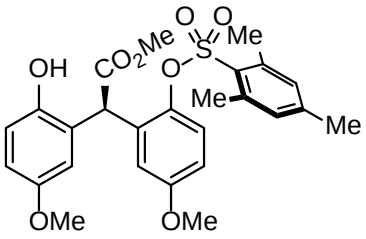
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.16 (m, 3H), 7.00 – 6.96 (m, 2H), 6.95 (s, 2H), 6.79 (d, *J* = 8.7 Hz, 1H), 6.68 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.56 (dd, *J* = 8.8, 3.1 Hz, 1H), 6.51 (d, *J* = 3.0 Hz, 1H), 6.47 (d, *J* = 8.8 Hz, 1H), 6.21 (d, *J* = 3.0 Hz, 1H), 5.96 (s, 1H), 5.48 (s, 3H), 3.61 (d, *J* = 5.7 Hz, 3H), 2.48 (s, 6H), 2.31 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.1(C), 153.1(C), 148.0(C), 144.1(C), 141.4(C), 140.5(C), 140.4(C), 137.4(C), 131.9(CH), 130.8(C), 129.3(CH), 129.1(C), 128.5(CH), 126.8(CH), 122.8(CH), 117.0(CH), 116.6(CH), 116.6(CH), 112.5(CH), 112.1(CH), 55.5(CH_3), 55.4(CH_3), 45.2(CH), 22.8(CH_3), 21.1(CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (minor) = 22.82 min, t_R (major) = 32.28 min, 21.5:78.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{30}H_{34}NO_6S^+$ 536.2101; found 536.2108.

(*R*)-Methyl 2-(2-hydroxy-5-methoxyphenyl)-2-(2-((mesitylsulfonyl)oxy)-5-methoxyphenyl)acetate (3sb)



Using methyl 2,2-bis(2-hydroxy-5-methoxyphenyl)acetate (**1s**, 47.7 mg, 0.15 mmol) and 2,4,6-trimethyl benzenesulfonyl chloride (**2b**, 39.4 mg, 0.18 mmol), in accordance with GP-3, product **3sb** was obtained (44.3 mg, 0.059 mmol, 39% yield, yellowish oil).

$[\alpha]_D^{25}$=+2.9 (*c* = 0.59, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (d, *J* = 8.8 Hz, 1H), 6.79 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.72 – 6.66 (m, 2H), 6.62 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.55 (d, *J* = 8.9 Hz, 1H), 5.44 (s, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.66 (s, 3H), 2.57 (s, 6H), 2.34 (s, 3H).

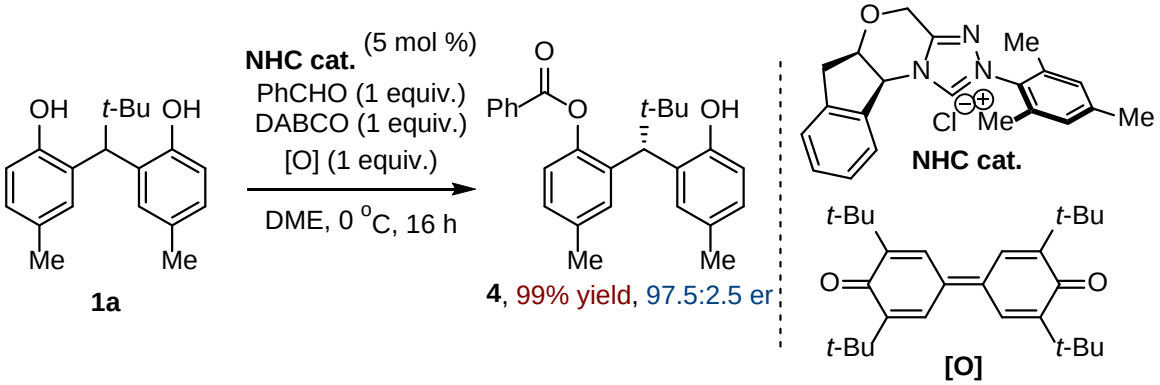
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 173.9 (C), 158.0 (C), 153.6 (C), 148.7 (C), 144.1 (C), 141.2 (C), 140.6 (C), 131.9 (CH), 131.0 (C), 122.5 (C), 122.34 (CH), 118.4 (CH), 116.00 (CH), 115.97 (CH), 115.0 (CH), 113.2 (CH), 55.7 (CH_3), 55.4 (CH_3), 52.9 (CH_3), 48.8 (CH), 22.7 (CH_3), 21.1(CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 80/20, 1.0 mL/min, 25 °C, t_R (minor) = 21.65 min, t_R (major) = 39.47 min, 23.5:76.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{26}H_{32}NO_8S^+$ 518.1843; found 518.1844.

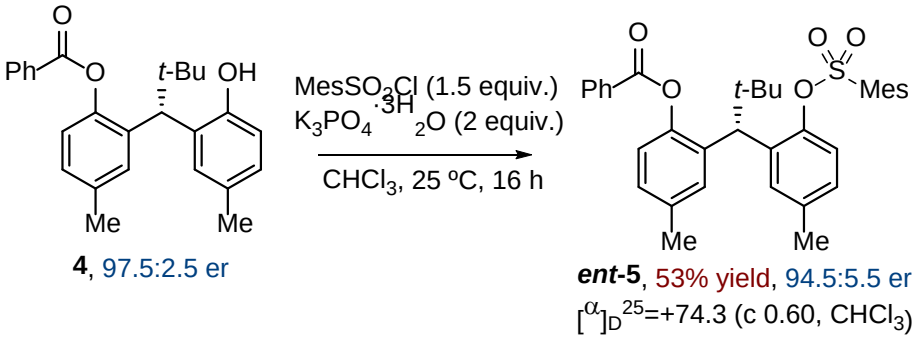
Determination of the Absolute Configuration and transformations

The inability to obtain enantiopure single crystals through either vapor diffusion or solvent layering prevented the determination of the absolute configuration of the major enantiomer of sulfonylated bisphenols **3** by means of X-Ray diffraction. Thus, we decided to determine the absolute configuration by comparison with a reported product. We used the conditions reported by Li in 2018 to prepare product **4** using NHC catalysis. [16]



Scheme S1: Acylation of bisphenol **1a** using the conditions reported by Li and coworkers.

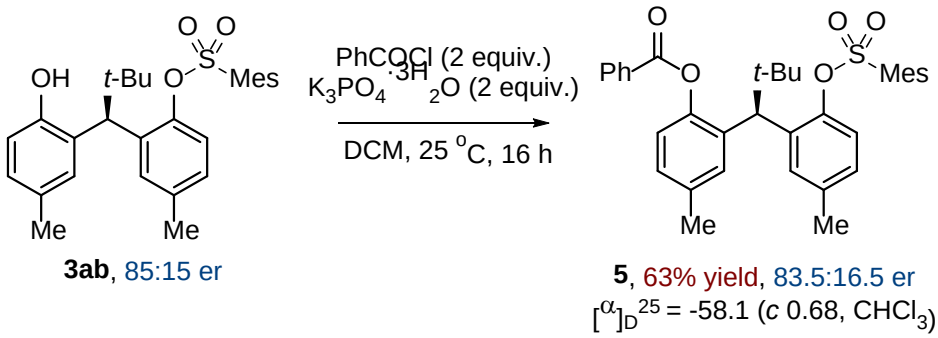
It is important to note that, whereas Li and coworkers used the NHC with (*5S, 10R*) absolute configuration and BF_4^- as anion (CAS 1061311-82-7), and the NHC precursor that was available in our laboratories was the one with (*5R, 10S*) absolute configuration and with Cl^- as anion (CAS 903571-02-8). Consequently, with the reaction conditions depicted in Scheme S1, the major enantiomer in acylated bisphenol **4** was the (*R*). Then, product **4** was derivatized using mesityl sulfonyl chloride (Scheme S2), obtaining bisphenol ***ent*-5** whose major enantiomer has (*S*) absolute configuration.



Scheme S2: Sulfonylation of bisphenol **4** with mesityl sulfonyl chloride.

Bisphenol ***ent*-5** displayed a $[\alpha]_D^{25}$ value of +74.3 (*c* 0.60, $CHCl_3$), and the major HPLC peak using an AD-H column in 98:2 hexane:*i*-PrOH appeared at 11.16 min, whereas the minor peak appeared at 13.42 min.

In parallel, compound **5** was also prepared by derivatizing bisphenol **3ab** via a benzoylation reaction with benzoyl chloride, obtaining it in 63% yield and with 83.5:16.5 er (Scheme S3).



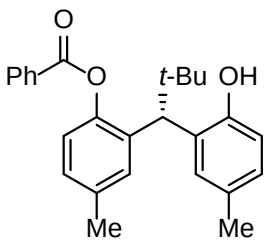
3ab, 85:15 er

5, 63% yield, 83.5:16.5 er
$[\alpha]_D^{25}$ = -58.1 (*c* 0.68, $CHCl_3$)

Scheme S3: Benzoylation of bisphenol **3ab** with benzoyl chloride.

The $[\alpha]_D^{25}$ of **5** was measured, obtaining a value of -58.1 (*c* 0.68, $CHCl_3$), therefore showing that the major enantiomer obtained by derivatization of sulfonylated bisphenol **3ab** is the opposite than the one obtained using the protocol outlined in Scheme S1 and S2. Chiral HPLC also confirmed this observation, since the major and the minor peak of bisphenol **5** appeared at 14.07 min and 11.70 min, respectively, when using an AD-H column in 98:2 hexane:*i*-PrOH.

(*R*)-2-(1-(2-Hydroxy-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl benzoate (4)



In an ovendried Schlenk tube, (5a*R*, 10b*S*)-5a, 10b-Dihydro-2-(2′2, 4′,6′-trimethylphenyl)-4*H*, 6*H*-indeno[2,1-*b*]-1,2,4-triazolo[4, 3-*d*]-1,4-oxazinium chloride (CAS 903571-02-8, 0.005 mmol, 5 mol %), bisphenol **1a** (0.1 mmol, 1 equiv.), DABCO (0.1 mmol, 1 equiv.) and 3,3',5,5'-tetra-tert-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione (0.1 mmol, 1 equiv.) were added. The flask was subjected to three vacuum/N2 cycles. Then, dry DME (1 mL) was added as solvent, and the reaction mixture was cooled down to 0 °C. After 5 minutes, benzaldehyde (0.1 mmol, 1 equiv.) was added, and the resulting mixture was stirred for 16 h at 0 °C. Afterwards, the reaction mixture was directly purified by column chromatography using hexane:EtOAc mixtures to obtain bisphenol **4** (0.099 mmol, 99% yield).

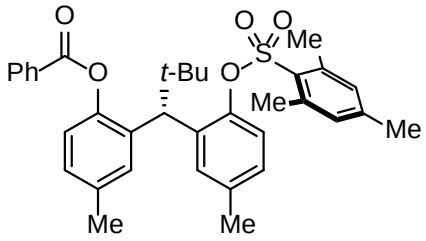
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$=+56.9 (*c* 0.79, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 – 8.21 (m, 2H), 7.71 – 7.59 (m, 1H), 7.59 – 7.46 (m, 2H), 7.40 (d, *J* = 2.1 Hz, 2H), 7.05 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.82 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 4.73 (s, 1H), 4.60 (s, 1H), 2.35 (s, 3H), 2.26 (s, 3H), 1.10 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 165.8 (C), 151.6 (C), 147.2 (C), 134.9 (C), 134.2 (C), 133.5 (CH), 131.5 (CH), 130.4 (CH), 130.2 (CH), 129.8 (C), 129.2 (C), 129.1 (C), 128.6 (CH), 127.7 (CH), 127.5 (CH), 122.3 (CH), 116.2 (CH), 44.4 (CH), 35.6 (C), 29.4 (CH_3), 21.4 (CH_3), 21.0 (CH_3).

HPLC: chiral stationary column AD, mobile phase hexane/iPrOH = 90/10, 1.0 mL/min, 25 °C, t_R (major) = 5.90 min, t_R (minor) = 8.59 min, 97.5:2.5 er.

(*S*)-2-(1-(2-((Mesitylsulfonyl)oxy)-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl benzoate (*ent*-5)



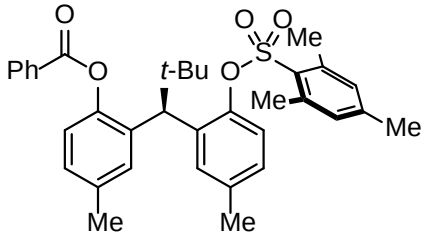
In a screwed test tube containing a stir bar, bisphenol **4** (0.099 mmol, 97.5:2.5 er), $K_3PO_4 \cdot 3H_2O$ (0.2 mmol, 2 equiv.) and $MesSO_2Cl$ (**1b**, 0.15 mmol, 1.5 equiv.) are added. $CHCl_3$ (1 mL) is added, and the reaction mixture is stirred at 25 °C for 16 h. Then, the solvent is removed under reduced pressure and the residue directly purified by column chromatography using a hexane:EtOAc 95:5 mixture to get benzoylated bisphenol ***ent*-5** (30.1 mg, 0.053 mmol, 53% yield) as a colorless oil.

$[\alpha]_D^{25}$=+74.3 (*c* 0.60, $CHCl_3$).

^{1}H- and ^{13}C-NMR data match with those reported for compound **5** (*see below*).

HPLC: chiral stationary column AD, mobile phase hexane/iPrOH = 98/2, 1.0 mL/min, 25 °C, t_R (major) = 11.16 min, t_R (minor) = 13.42 min, 94.5:5.5 er.

(*R*)-2-(1-(2-((Mesitylsulfonyl)oxy)-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl benzoate (5)



In a screwed test tube containing a stir bar, bisphenol **3ab** (0.063 mmol, 85:15 er) and $K_3PO_4 \cdot 3H_2O$ (0.13 mmol, 2 equiv.) are added. The flask is purged with a steam of N_2 and dry DCM (1 mL) and benzoyl chloride (0.126 mmol, 2 equiv.) are added. The reaction mixture is stirred at 25 °C for 16 h. Then, the solvent is removed under reduced pressure and the residue directly purified by column chromatography using a hexane:EtOAc 95:5 mixture to get benzoylated bisphenol **5** (21.8 mg, 0.038 mmol, 63% yield) as a colorless oil.

$[\alpha]_D^{25}$=-58.1 (*c* 0.68, $CHCl_3$).

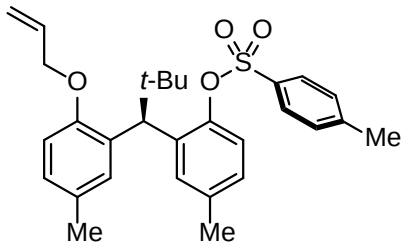
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 7.0 Hz, 2H), 7.68 (s, 1H), 7.65 – 7.58 (m, 1H), 7.56 – 7.48 (m, 2H), 7.18 (s, 1H), 7.11 – 6.98 (m, 2H), 6.93 (s, 2H), 6.74 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.26 (d, *J* = 8.3 Hz, 1H), 4.97 (s, 1H), 2.48 (s, 6H), 2.31 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H), 1.13 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 165.4 (C), 147.2 (C), 143.3 (C), 139.8 (C), 136.0 (C), 135.1 (C), 134.0 (C), 133.2 (CH), 132.8 (C), 132.6 (CH), 132.2 (C), 131.7 (CH), 131.2 (CH), 130.5 (CH), 130.1 (C), 128.4 (CH), 127.5 (CH), 127.4 (CH), 122.7 (CH), 119.9 (CH), 35.7 (C), 29.6 (CH_3), 22.6 (CH), 21.2 (CH_3), 21.2 (CH_3), 21.1 (CH_3).

HPLC: chiral stationary column AD, mobile phase hexane/iPrOH = 98/2, 1.0 mL/min, 25 °C, t_R (major) = 14.07 min, t_R (minor) = 11.70 min, 16.5:83.5 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{35}H_{42}NO_5S^+$ 588.2778; found 588.2783.

(*R*)-2-(1-(2-(Allyloxy)-5-methylphenyl)-2,2-dimethylpropyl)-4-methylphenyl 4-methylbenzenesulfonate (6)



In a screwed test tube containing a stir bar, tosylated bisphenol **3aa** (0.05 mmol, 85:15 er) and K_2CO_3 (0.1 mmol, 2 equiv.) are added. The flask is purged with a steam of N_2 and dry acetone (0.5 mL) and allyl bromide (0.1 mmol, 2 equiv.) are added. The reaction mixture is stirred at 60 ^{o}C for 16 h. Then, the solvent is removed under reduced pressure and the residue directly purified by column chromatography using a hexane:EtOAc 95:5 mixture to get allylated bisphenol **6** (14.5 mg, 0.037 mmol, 73% yield) as a colorless oil.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$=-49.2 (*c* = 0.25, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.59 (s, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.04 – 6.94 (m, 2H), 6.94 – 6.83 (m, 2H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.31 – 6.05 (m, 1H), 5.44 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.29 (dd, *J* = 10.5, 1.6 Hz, 1H), 4.85 (s, 1H), 4.64 (dd, *J* = 13.3, 5.1 Hz, 1H), 4.50 (dd, *J* = 13.2, 5.3 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 2.20 (s, 3H), 0.93 (s, 9H).

^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 154.6 (C), 146.9 (C), 144.8 (C), 136.5 (C), 135.1 (C), 134.4 (CH), 133.7 (C), 131.7 (CH), 130.9 (CH), 129.7 (C), 129.5 (CH), 128.6 (CH), 128.4 (C), 127.2 (CH), 127.1 (CH), 120.8 (CH), 116.8 (CH_2), 111.7 (CH), 69.3 (CH_2), 35.3 (C), 29.2 (CH_3), 21.6 (CH_3), 21.4 (CH_3), 20.8 (CH_3).

HPLC: chiral stationary column IG, mobile phase hexane/iPrOH = 98/2, 1.0 mL/min, 25 °C, t_R (minor) = 8.95 min, t_R (major) = 11.03 min, 84.16 er.

HRMS (ESI$^+$) *m/z:* [M + NH_4]$^+$ Calcd for $C_{29}H_{38}NO_4S^+$ 496.2516; found 496.2521.

NMR Studies

^{1}H-NMR spectra of $CDCl_3$ solutions containing equimolar amounts of bisphenol **1a** + Cat **B** and $MesSO_2Cl$ (**1b**) + Cat **B** have been recorded in a 500 MHz NMR unit.

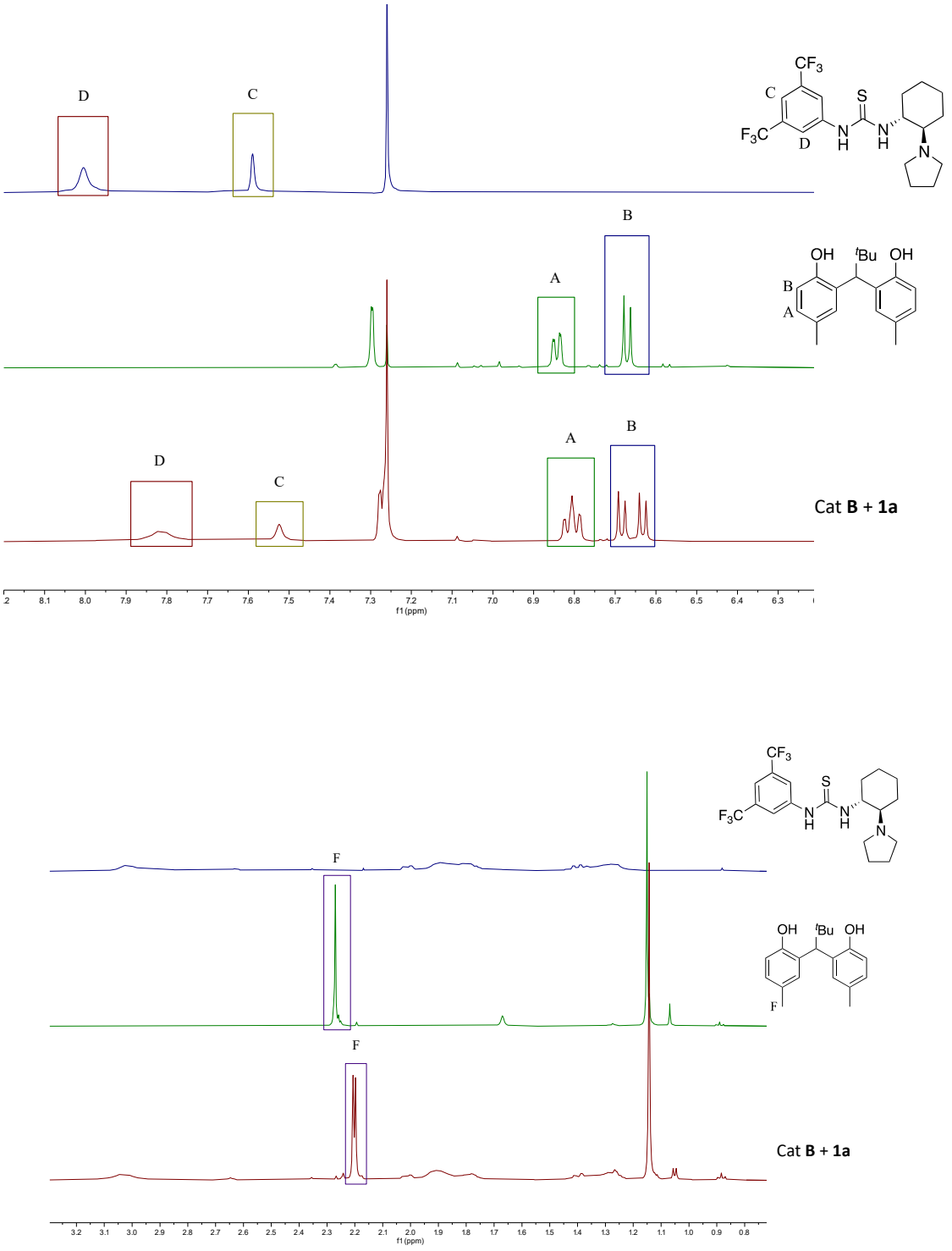


Figure S1: ^{1}H-NMR spectra of catalyst **B**, bisphenol **1a** and a mixture of catalyst **B** and bisphenol **1a**.

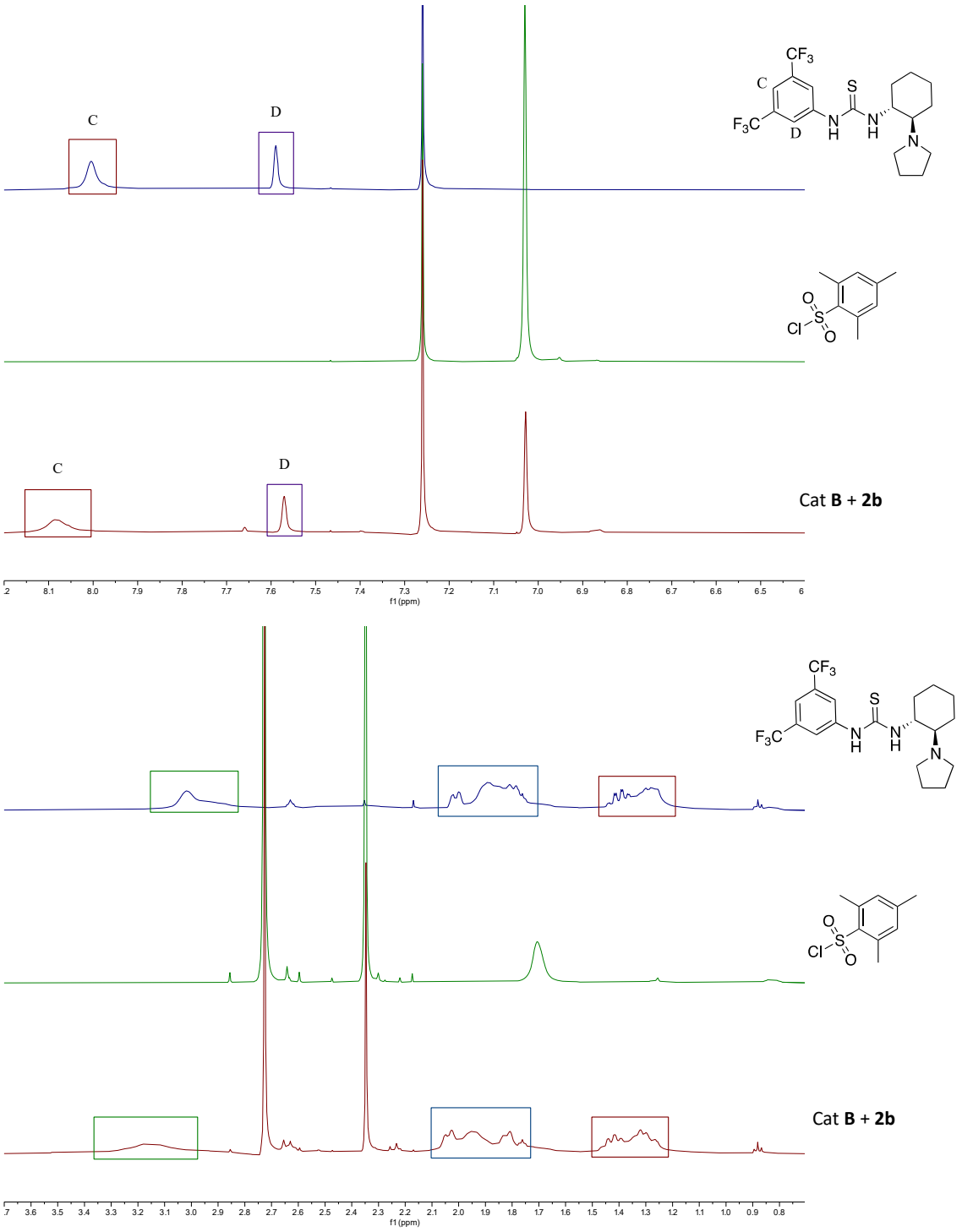


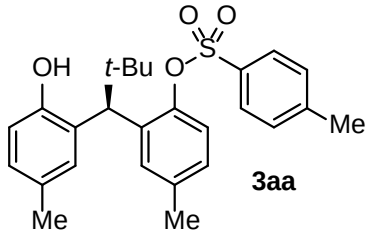
Figure S2: ^{1}H-NMR spectra of catalyst **B**, sulfonyl chloride **2b** and a mixture of catalyst **B** and sulfonyl chloride **2b**.

References

[18] Lu, S.; Song, X.; Poh, S. B.; Yang, H.; Wong, M. W.; Zhao, Y. *Chem. Eur. J.* **2017**, *23*, 2275–2281.

[16] S. Li, B. Liu, L. Chen, X. Li, J.-P. Cheng, *Org. Chem. Front.*, **2018**, *5*, 1101-1107.

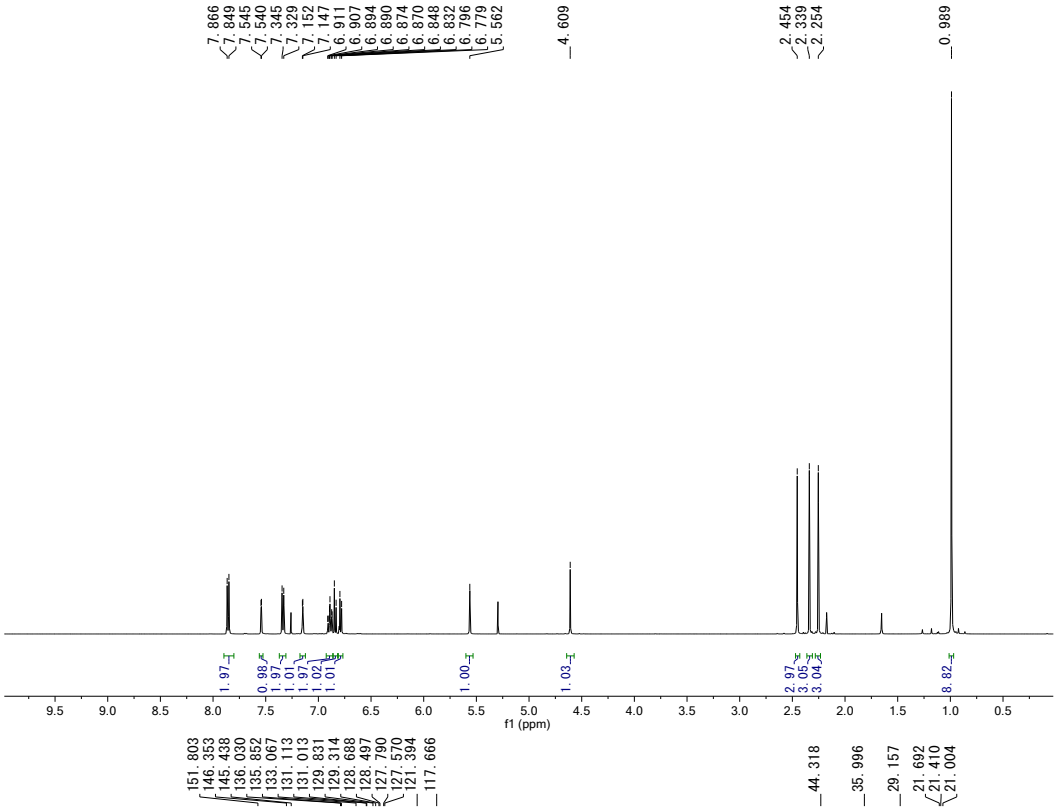
NMR Spectra

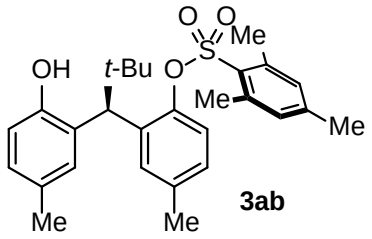


3aa

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)

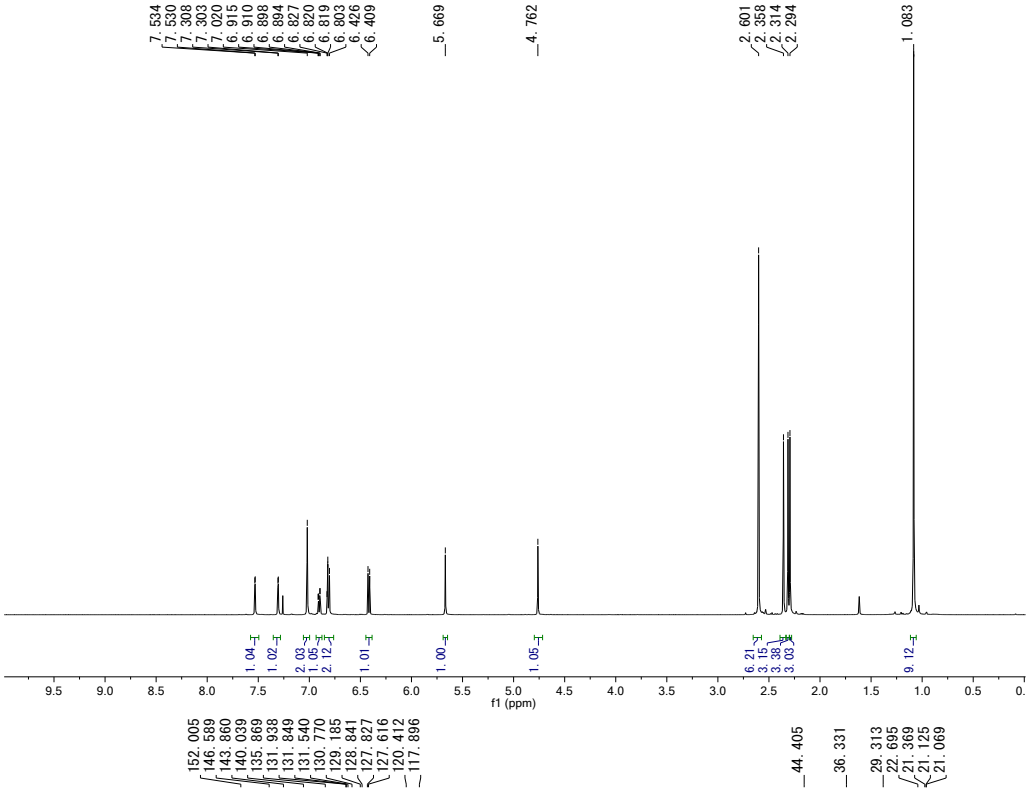


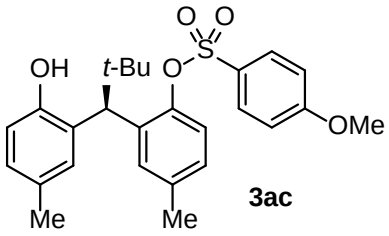


3ab

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)

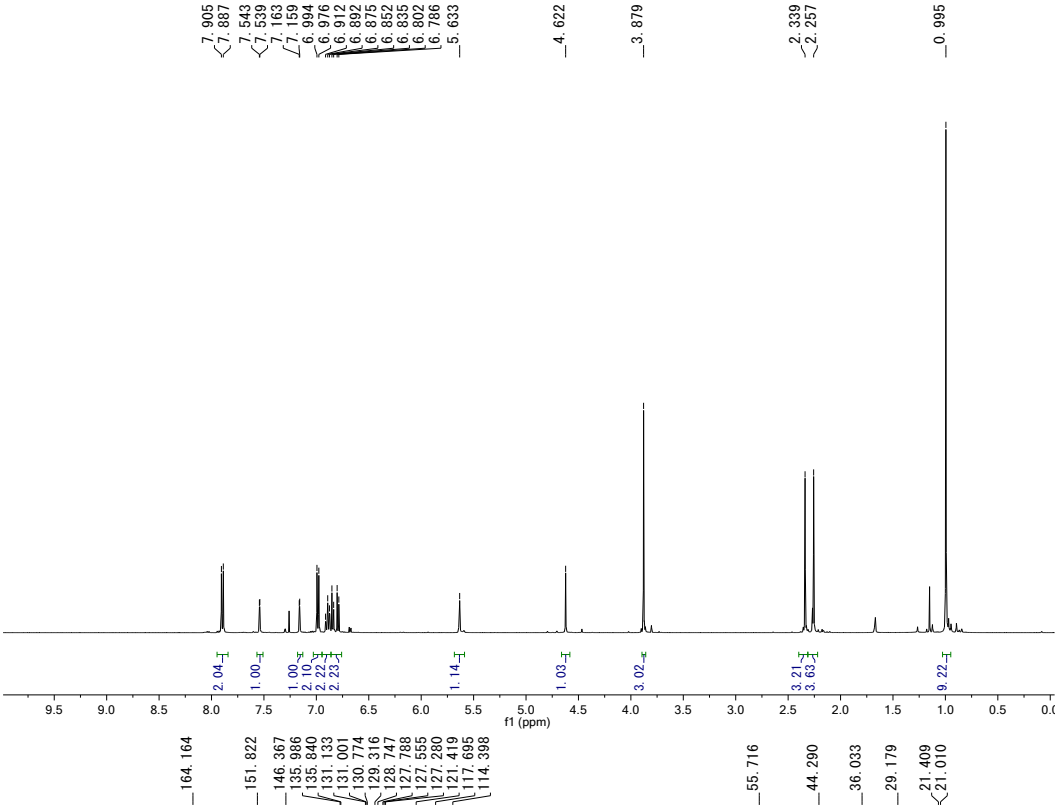


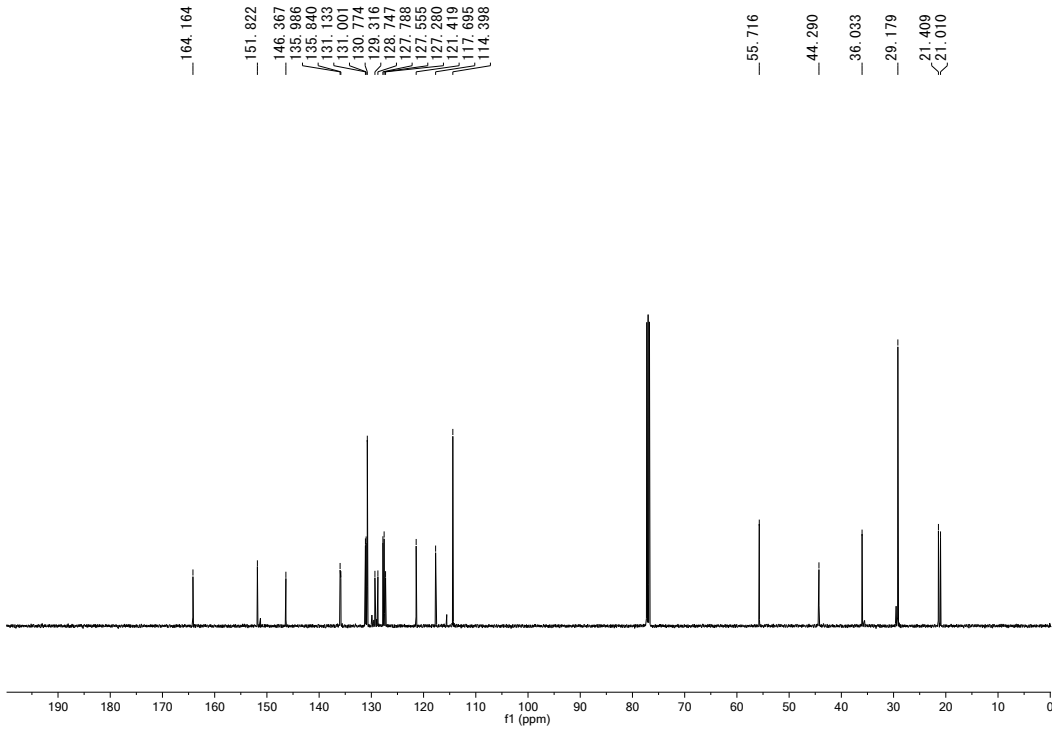


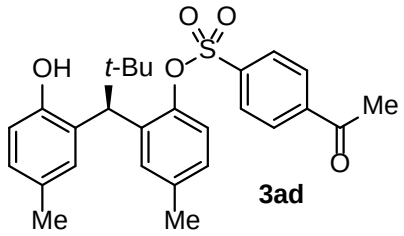
3ac

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)



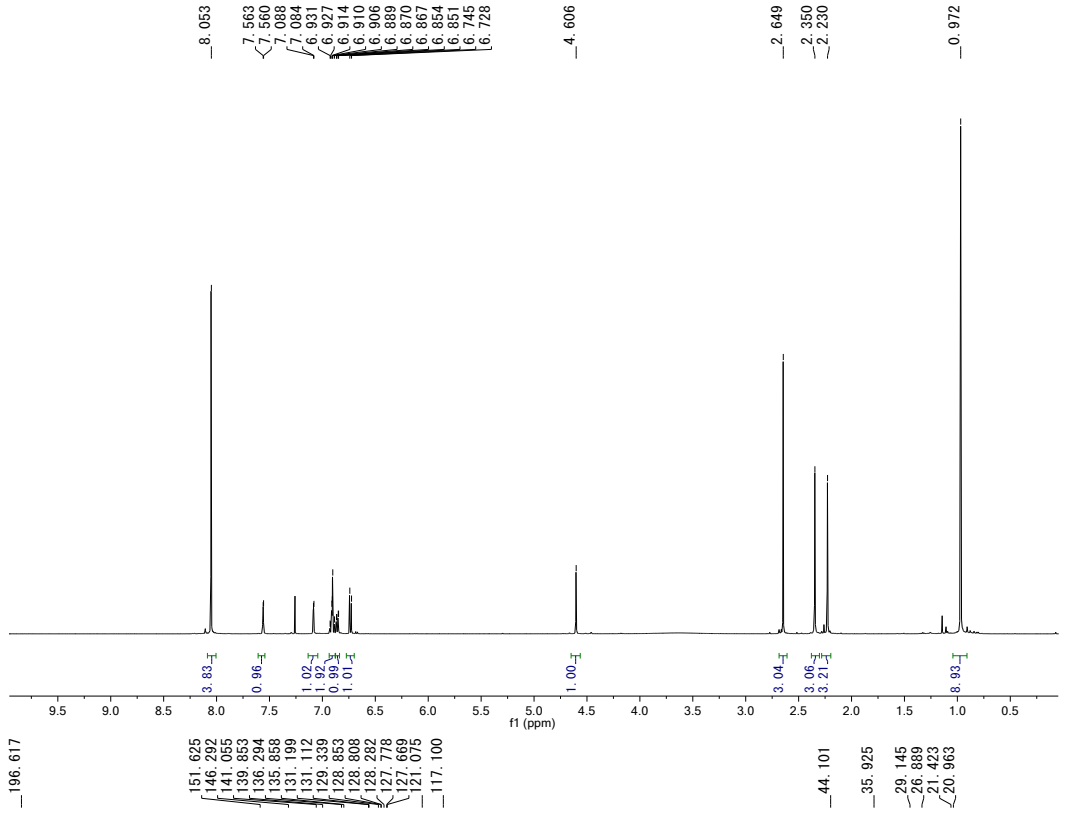


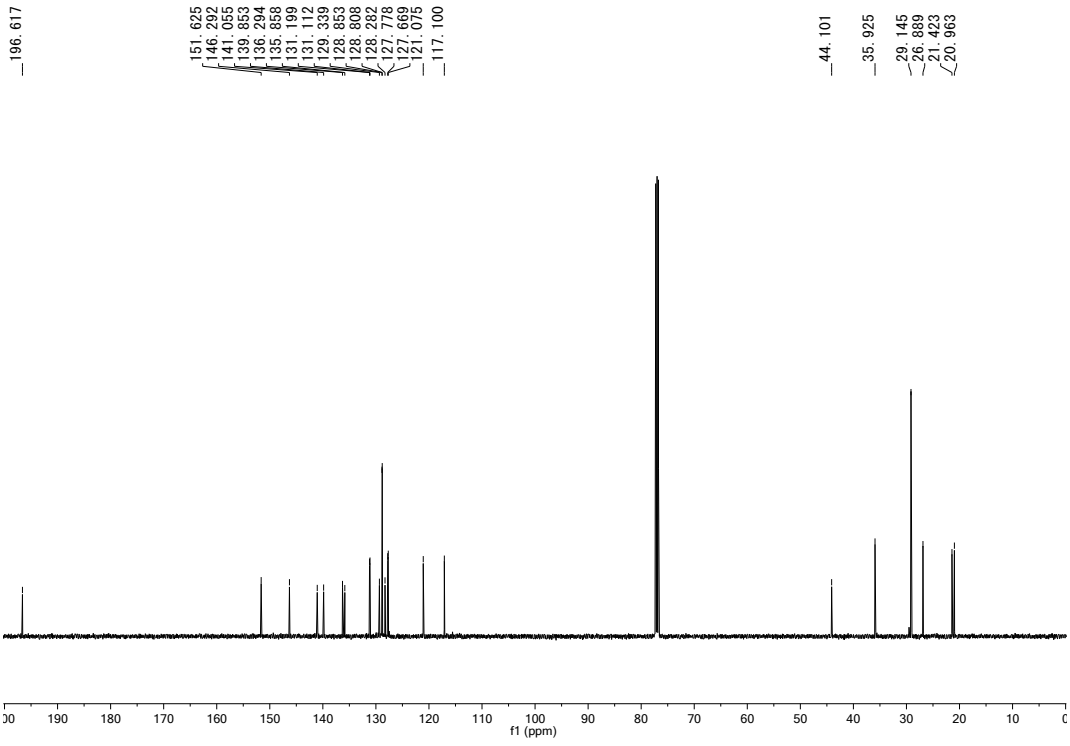


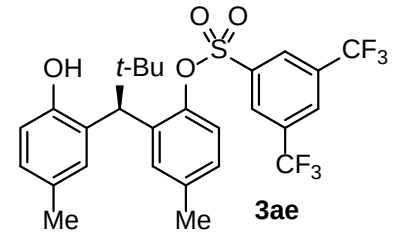
3ad

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)





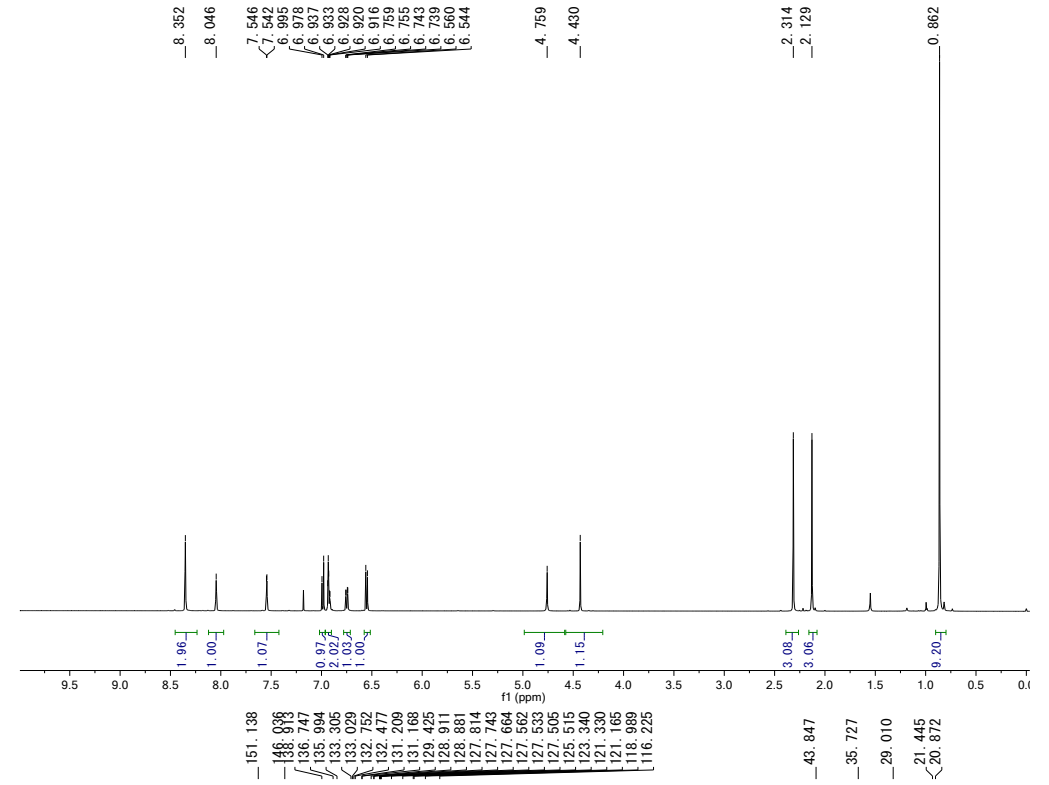


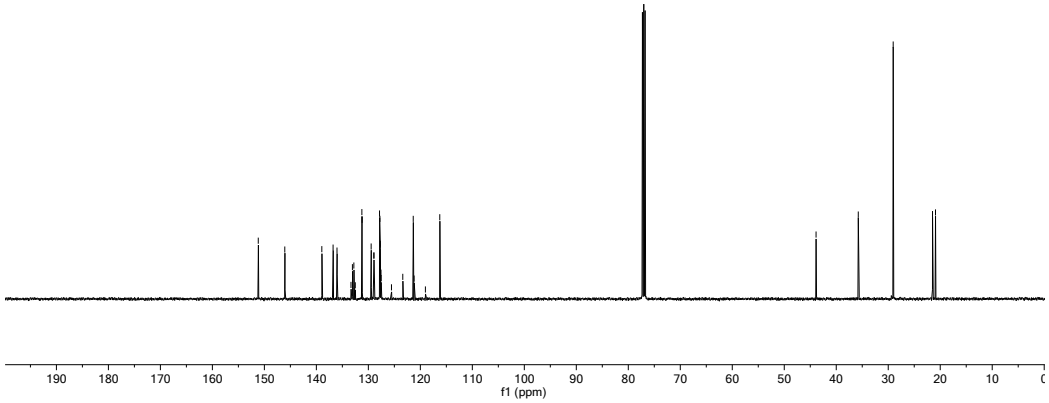
3ae

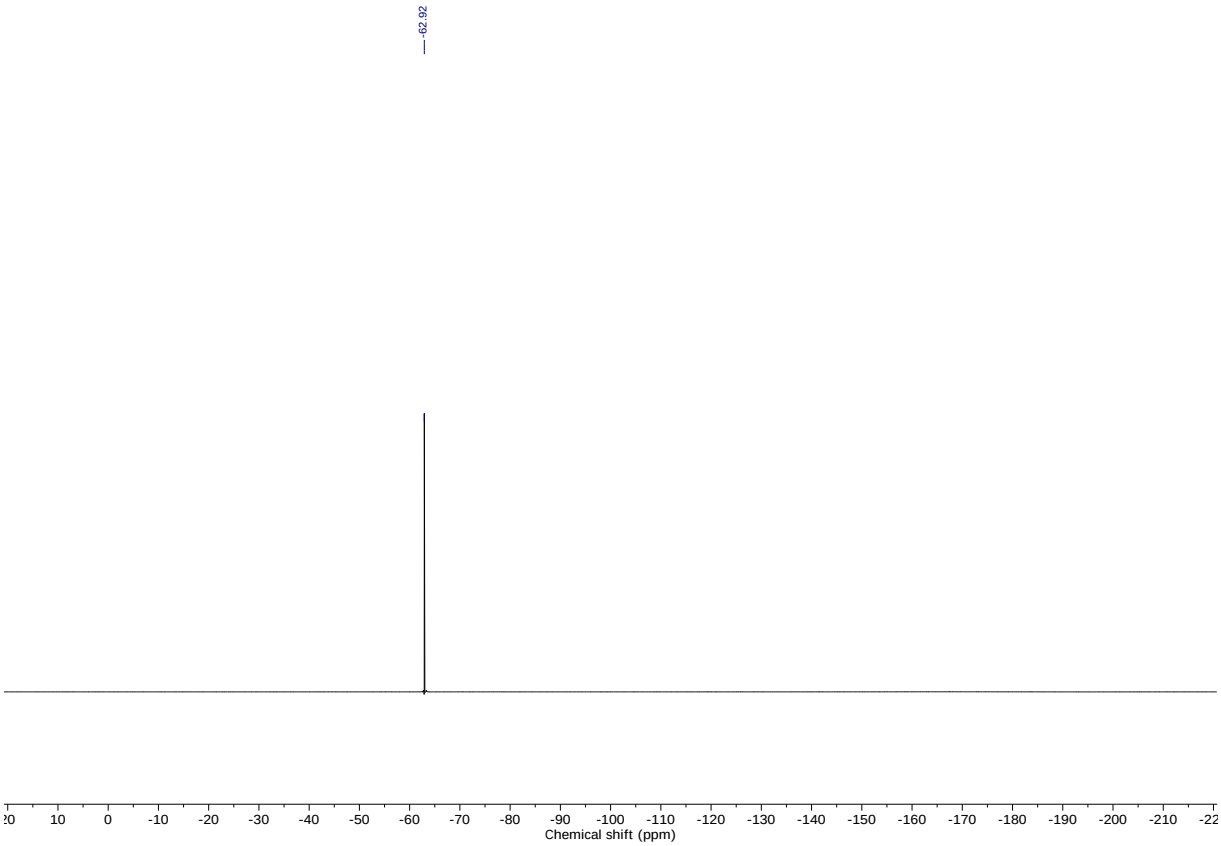
^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

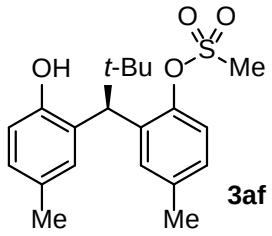
$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)

$^{19}F\{^{1}H\}$-NMR (471 MHz, 298 K, $CDCl_3$)





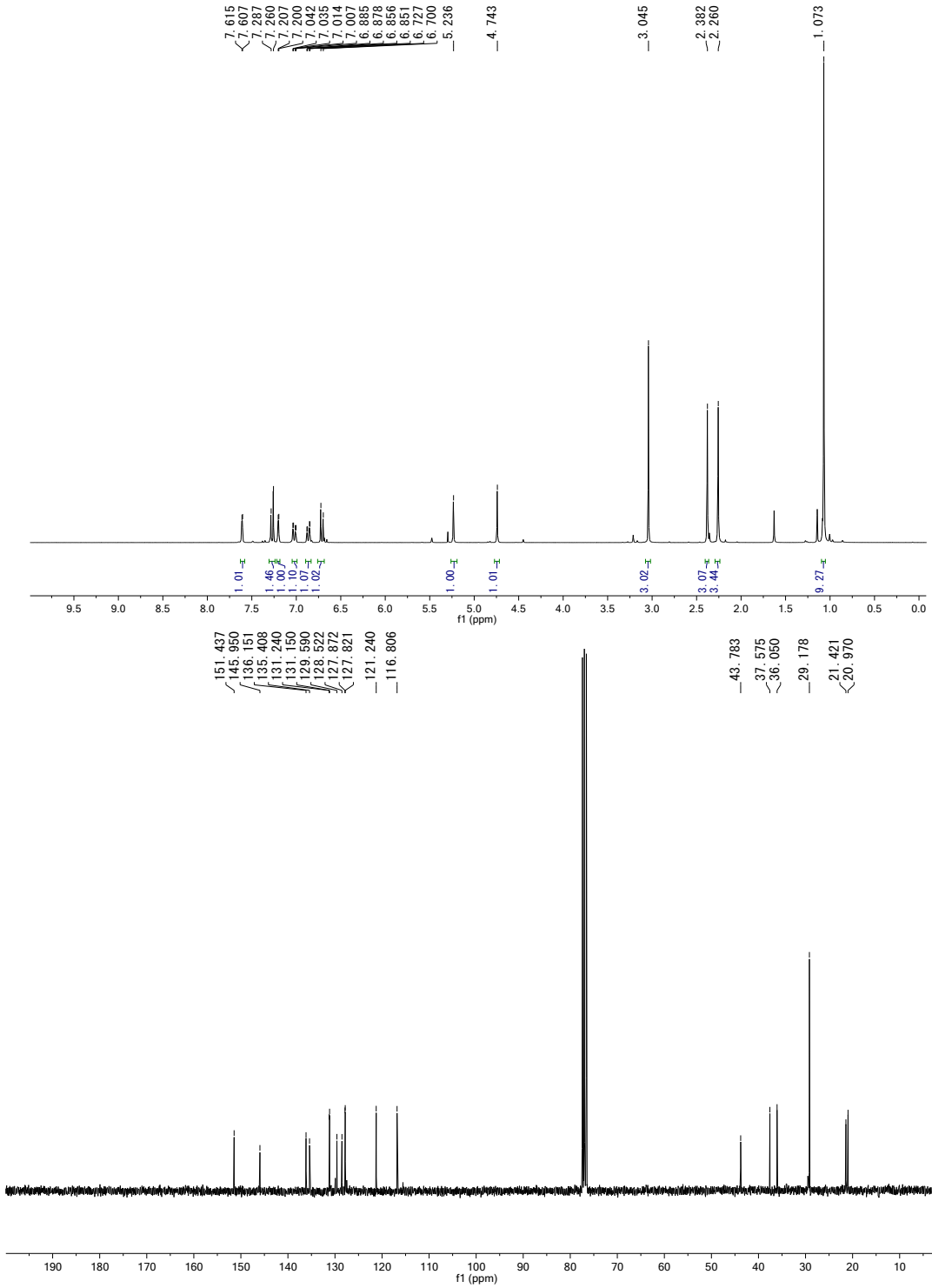

-62.92
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -22
Chemical shift (ppm)

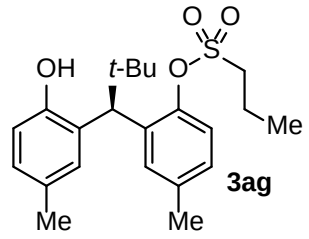


3af

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

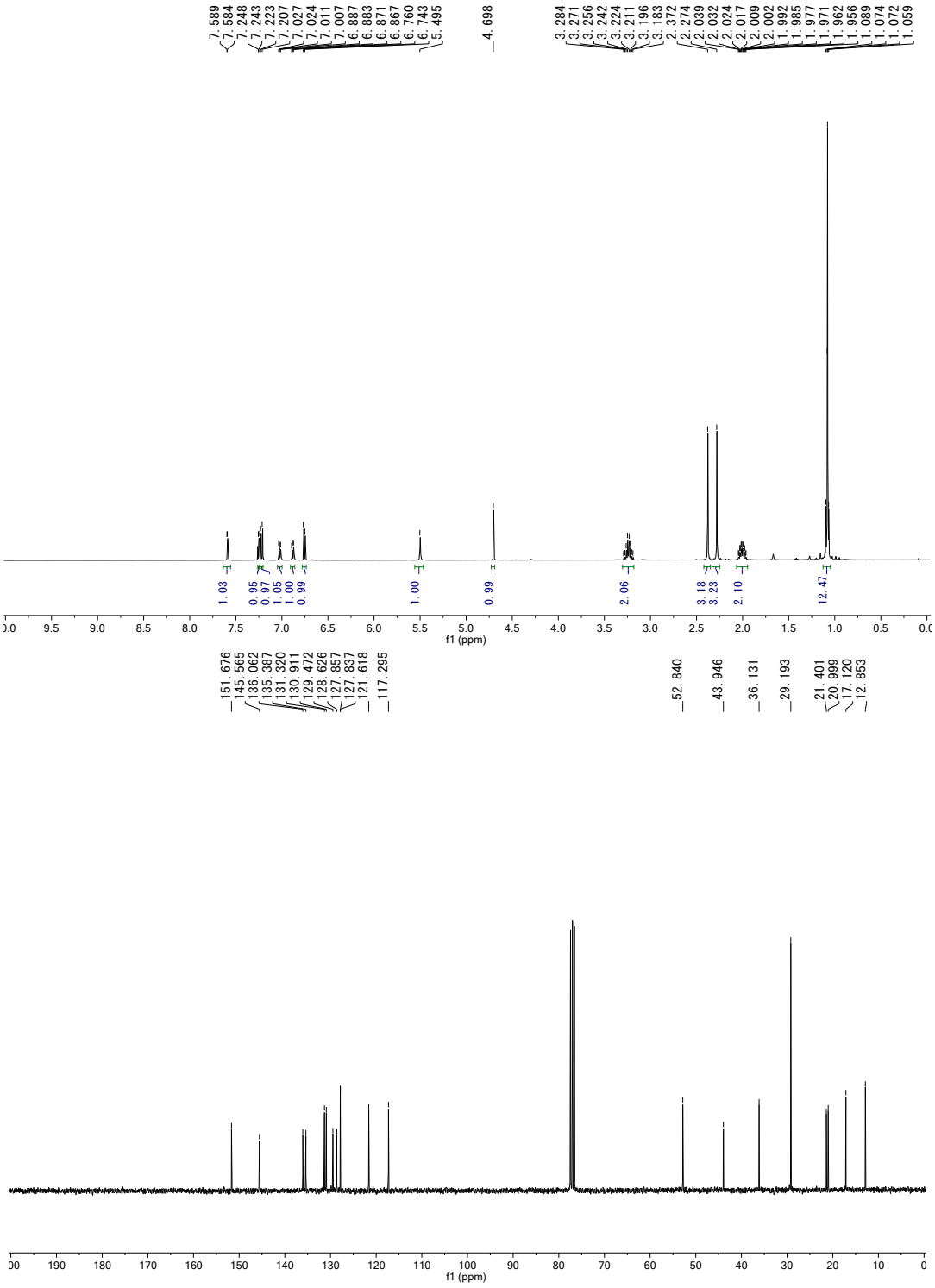


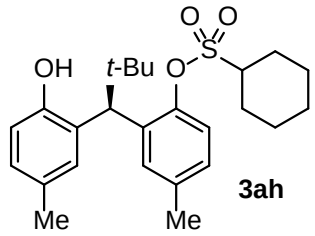


3ag

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

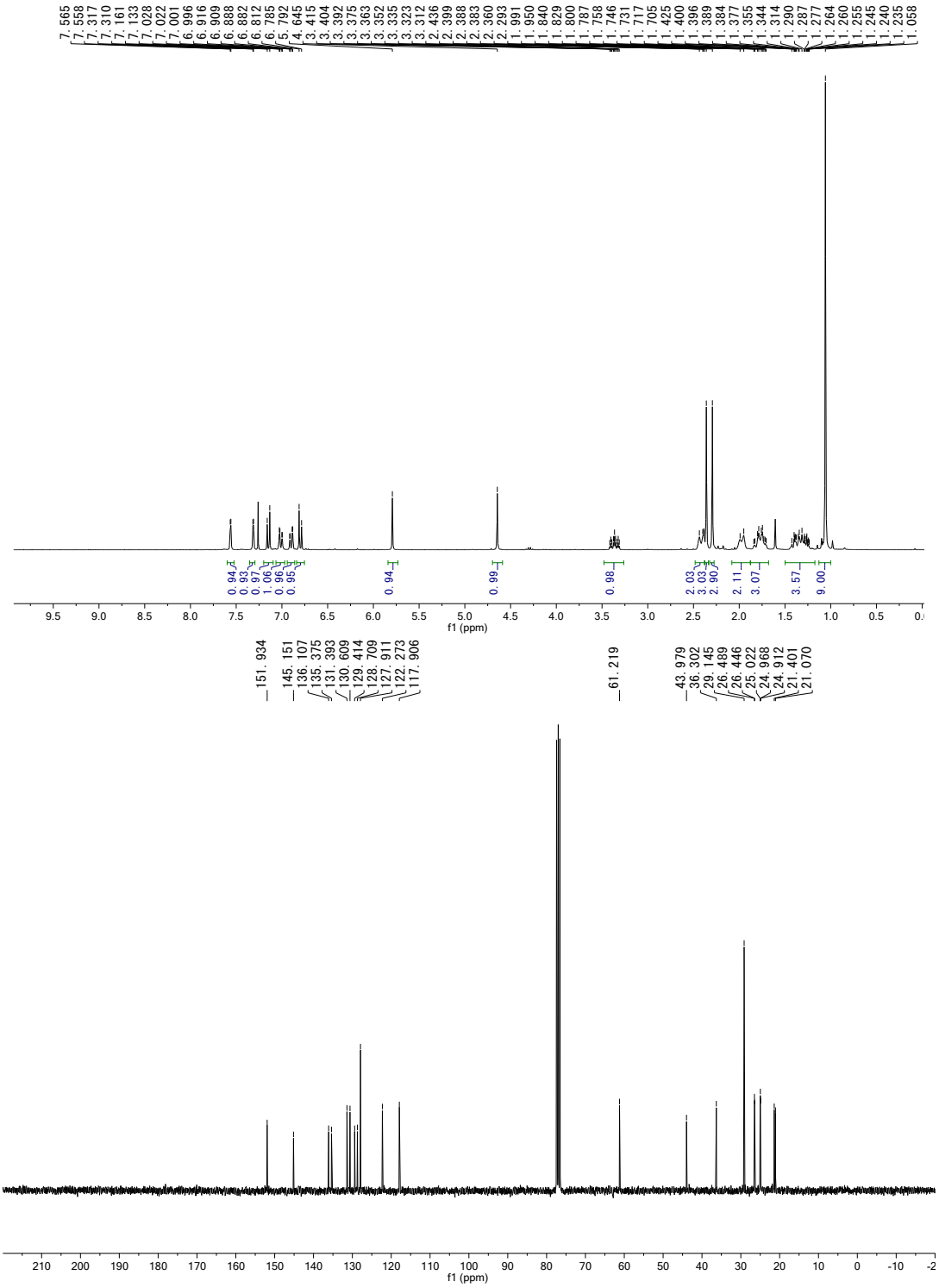


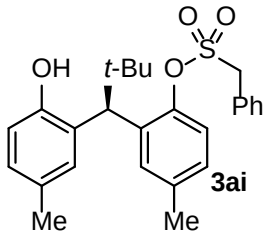


3ah

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

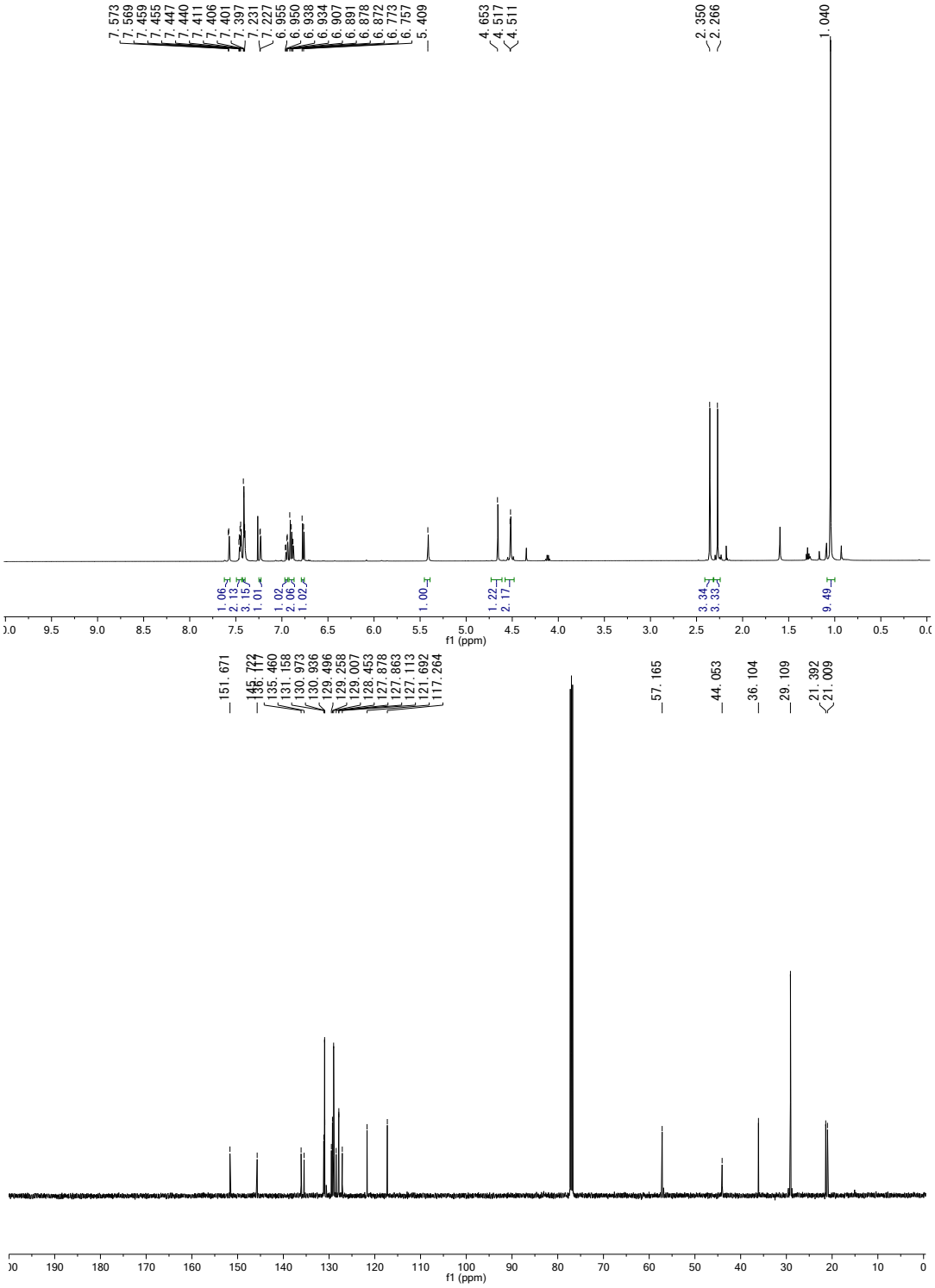


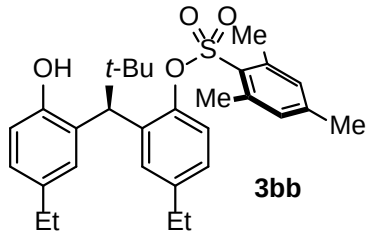


3ai

^{1}H-NMR (500 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (126 MHz, 298 K, $CDCl_3$)

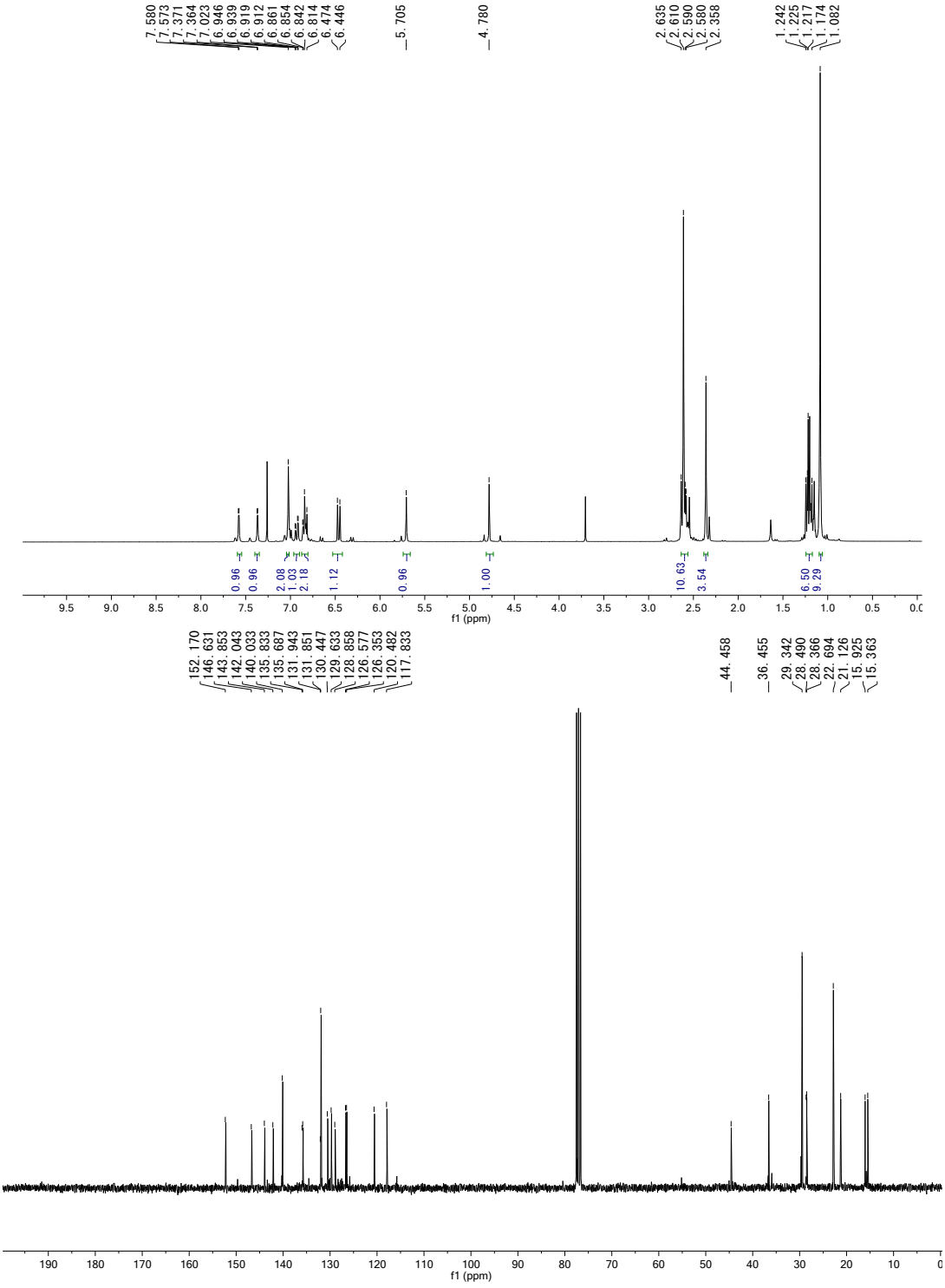


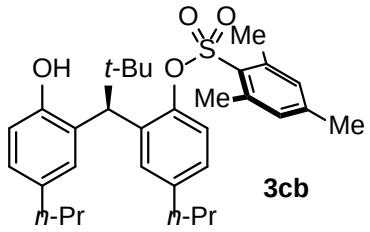


3bb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

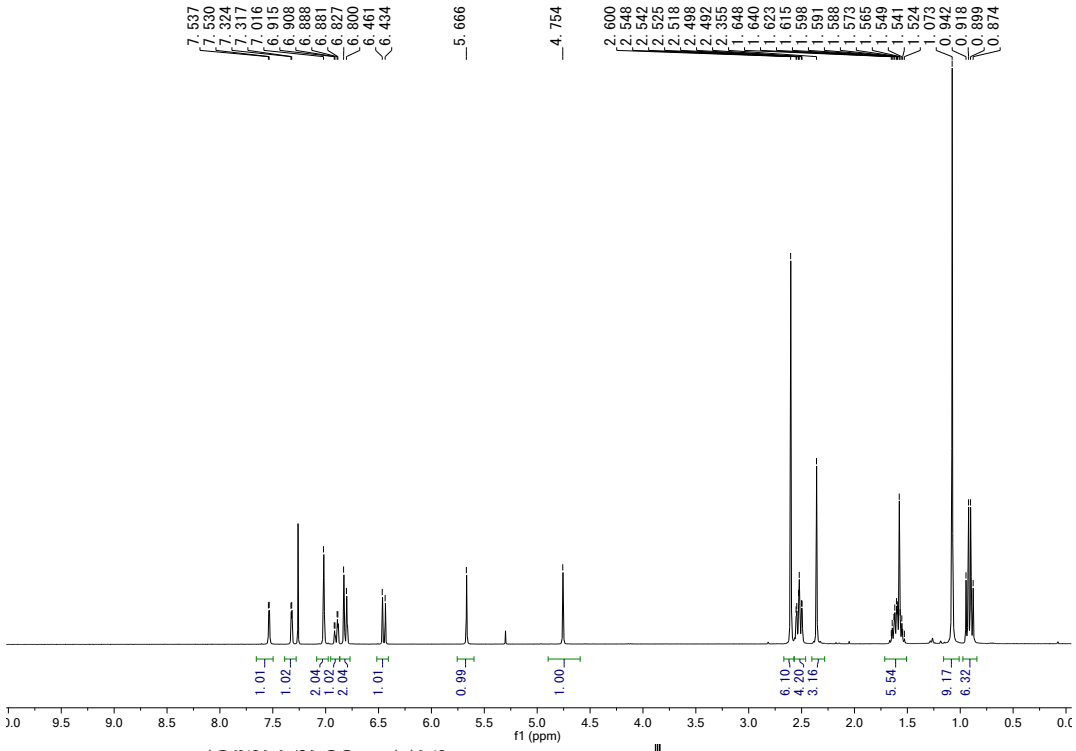


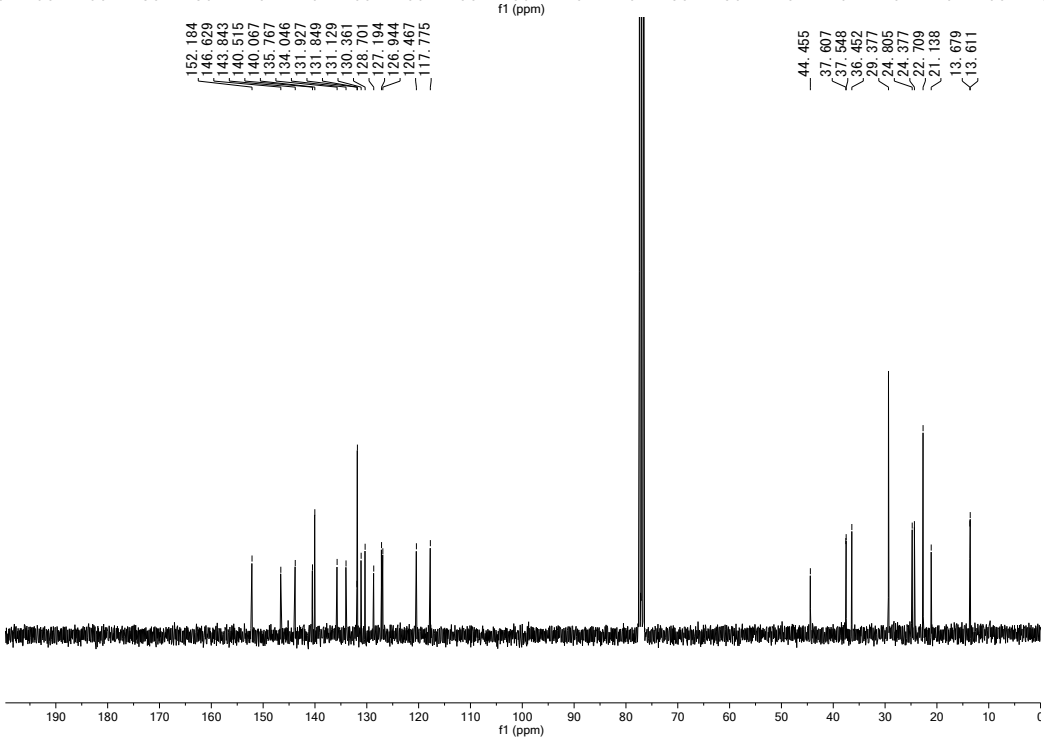


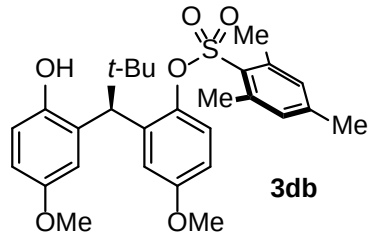
3cb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



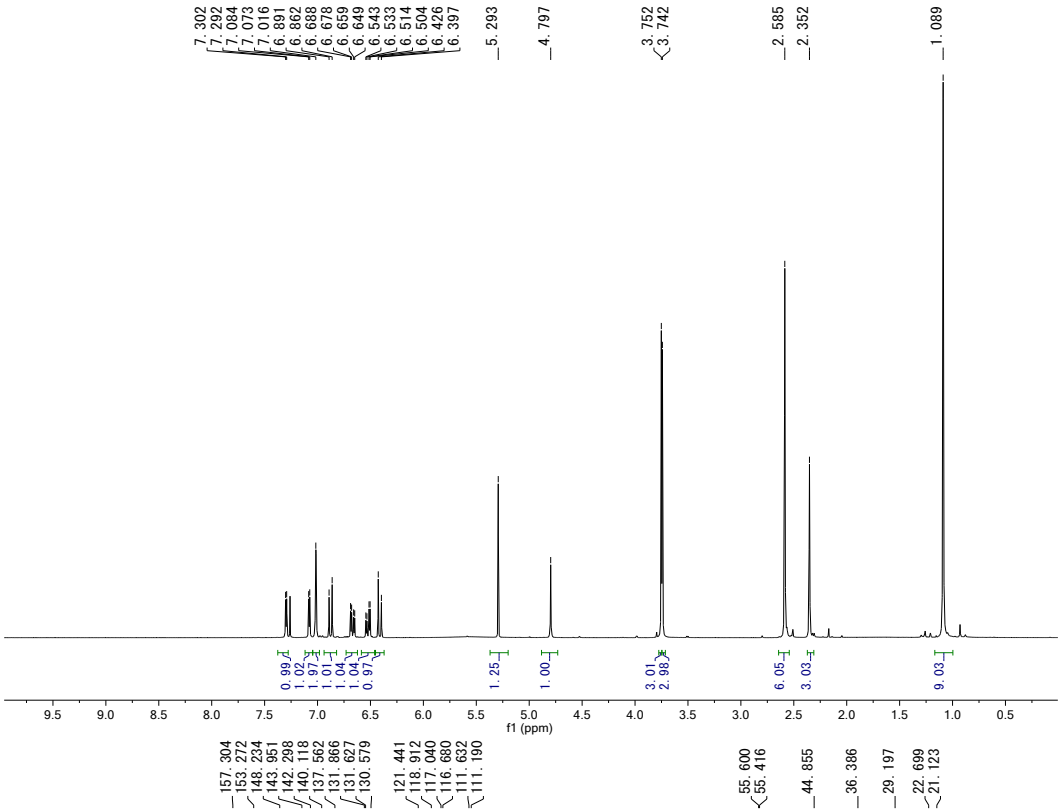


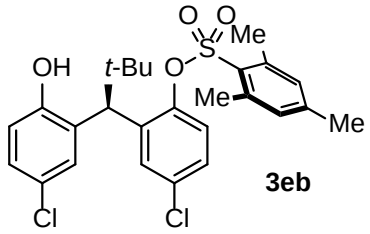


3db

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

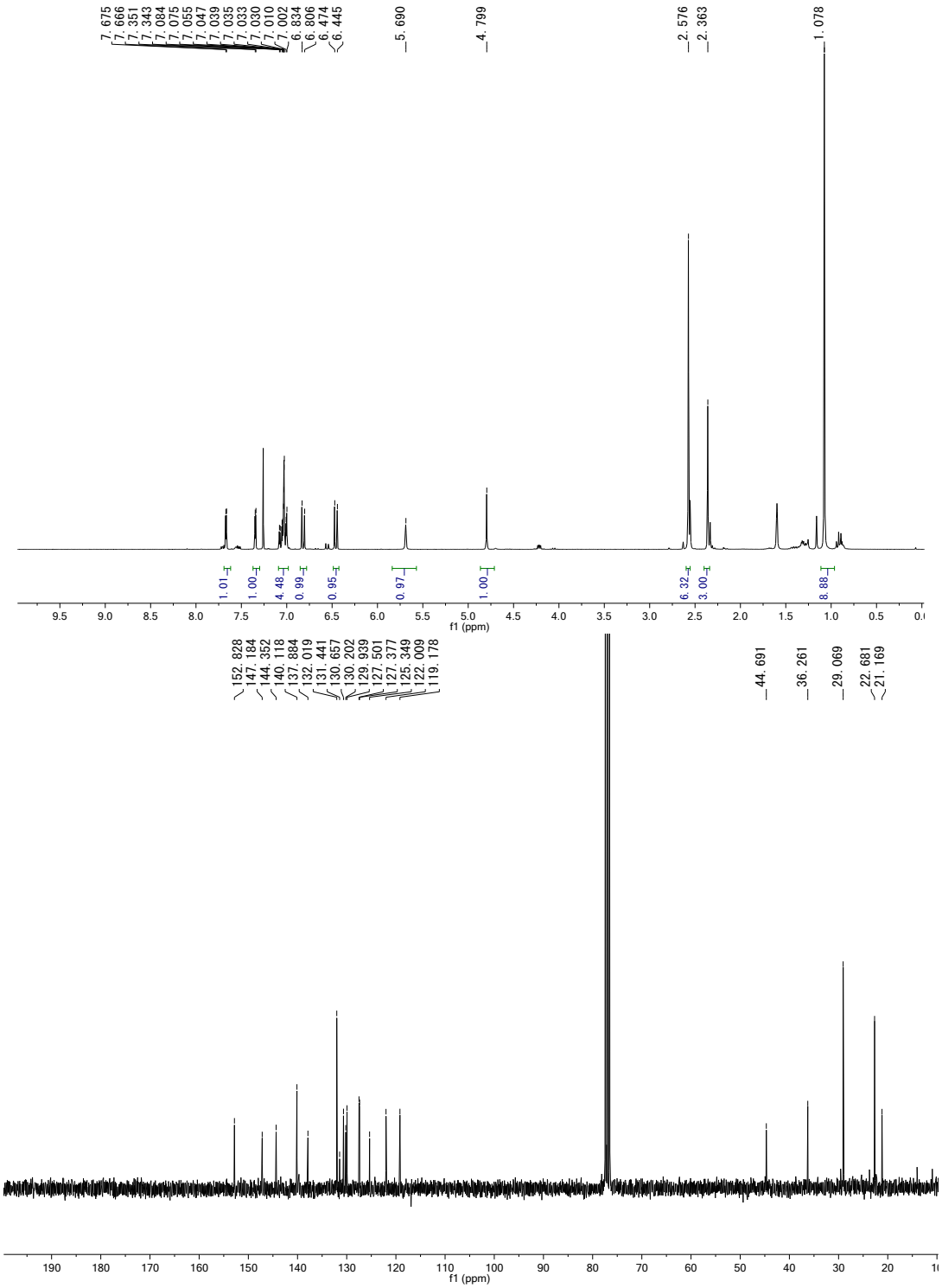


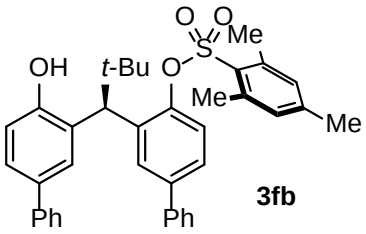


3eb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

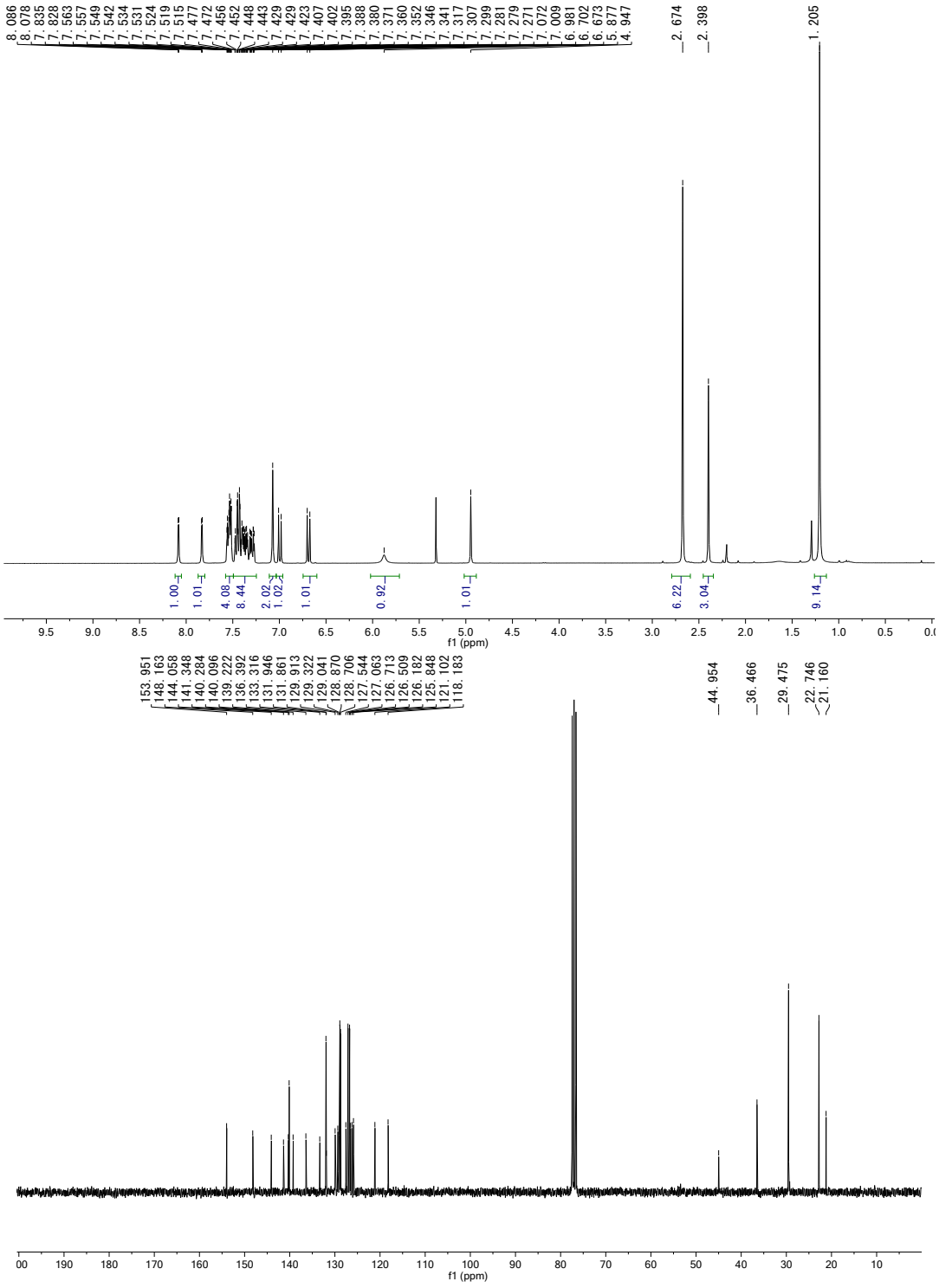


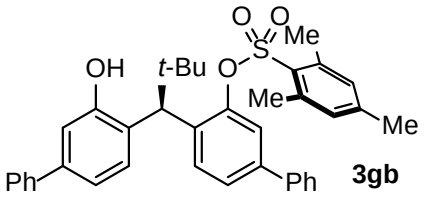


3fb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

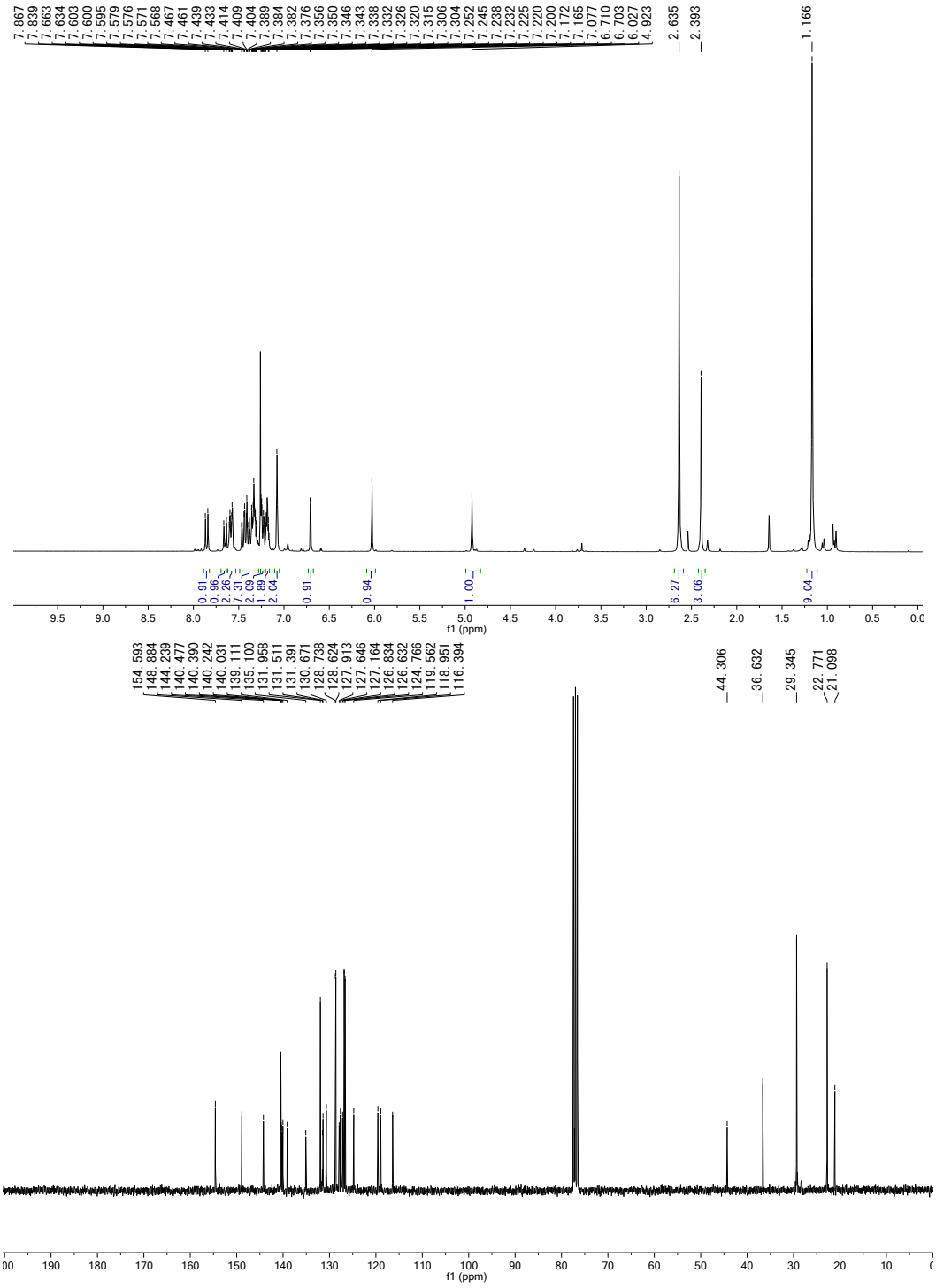


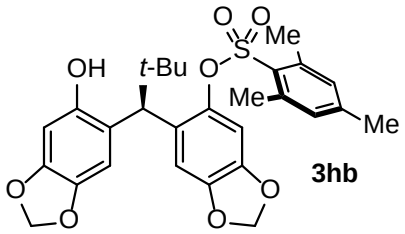


3gb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

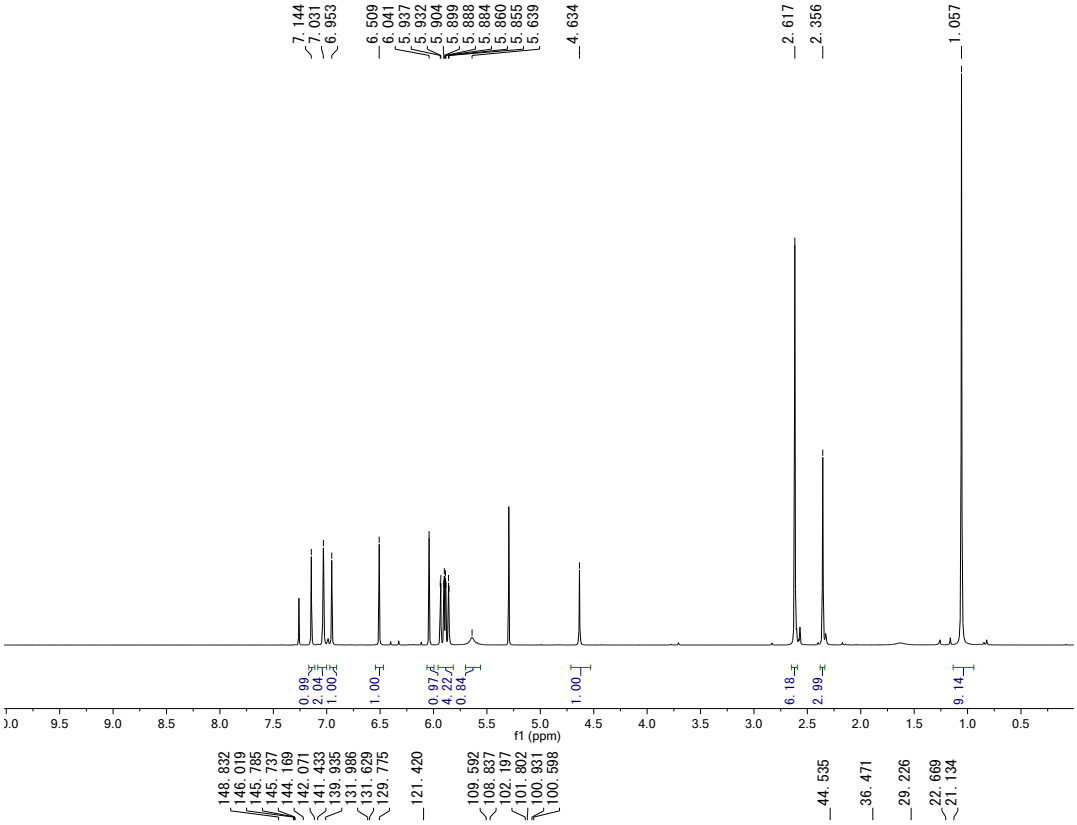


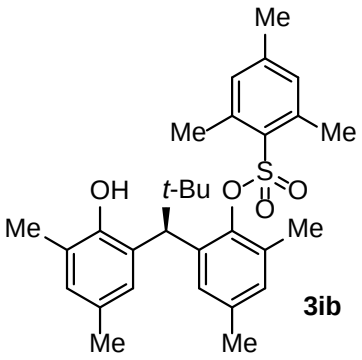


3hb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

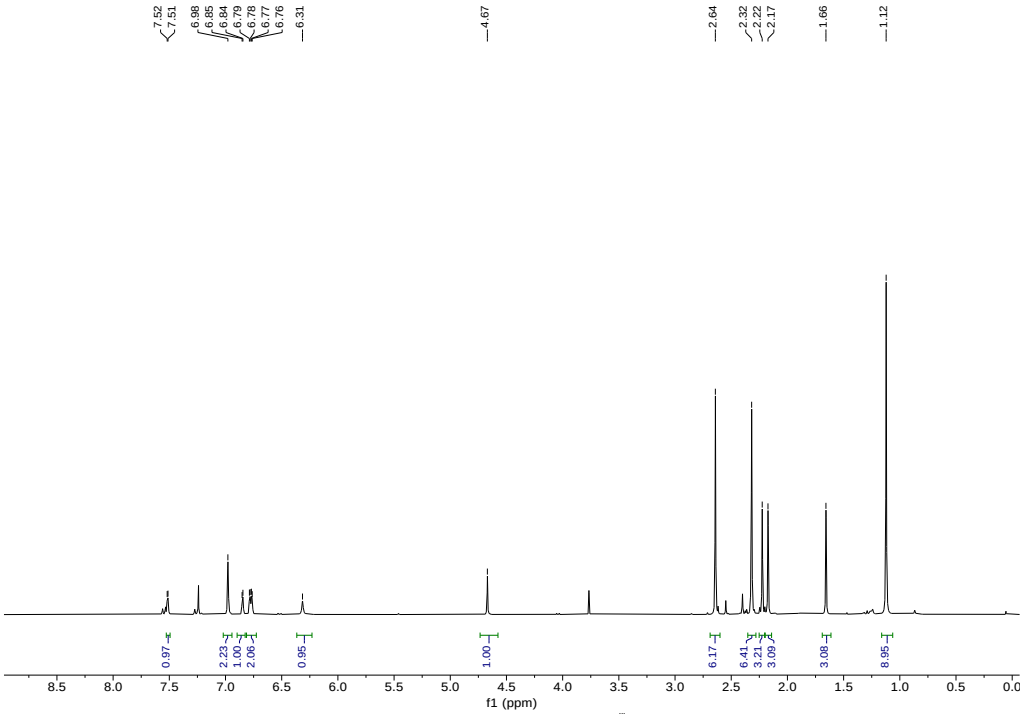


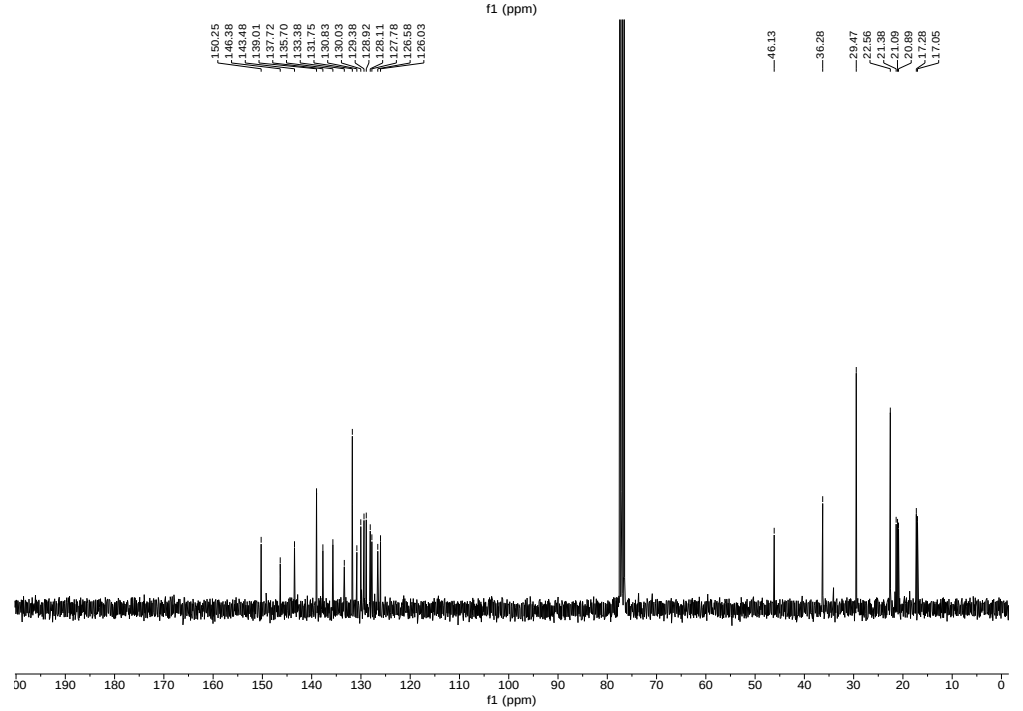


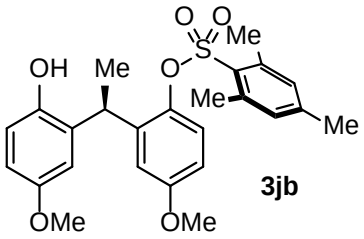
3ib

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



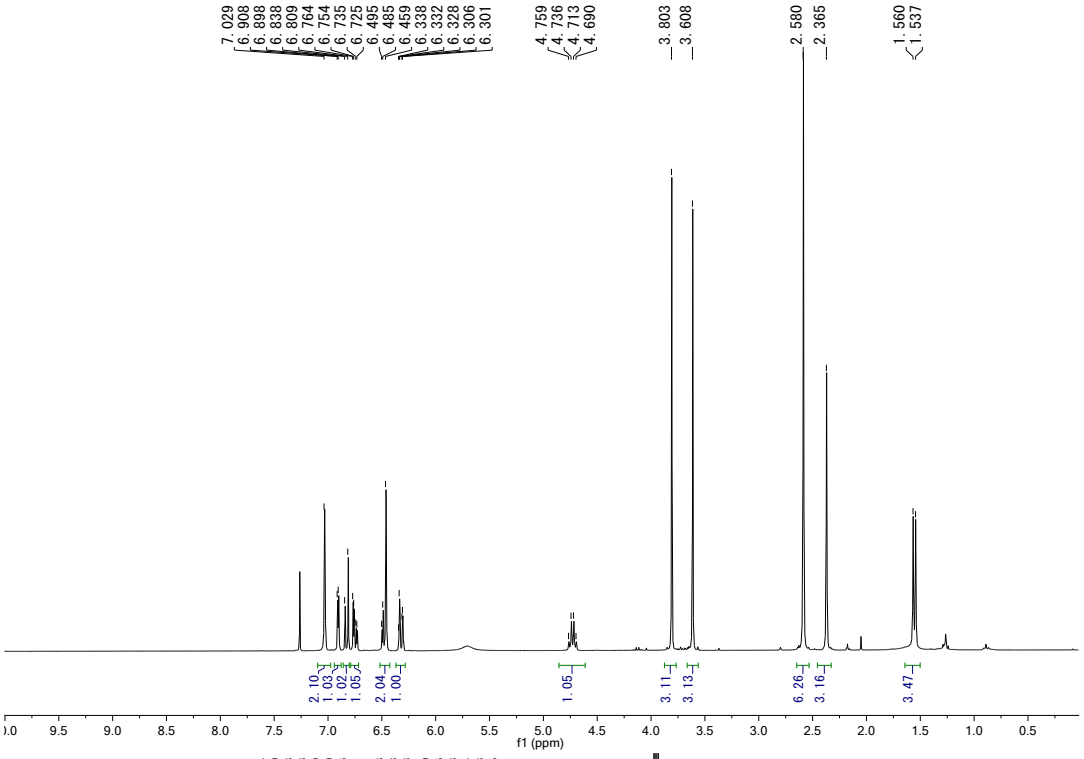


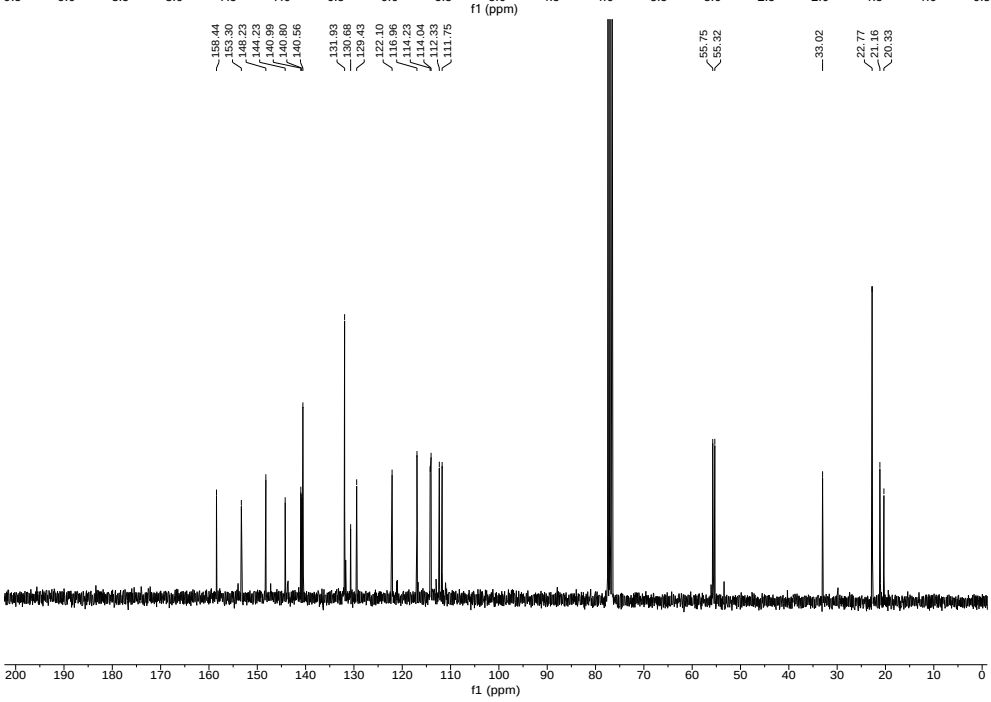


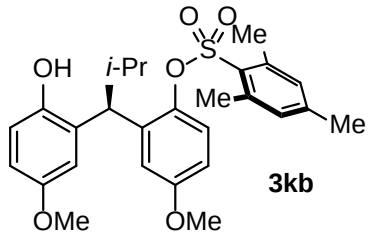
3jb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



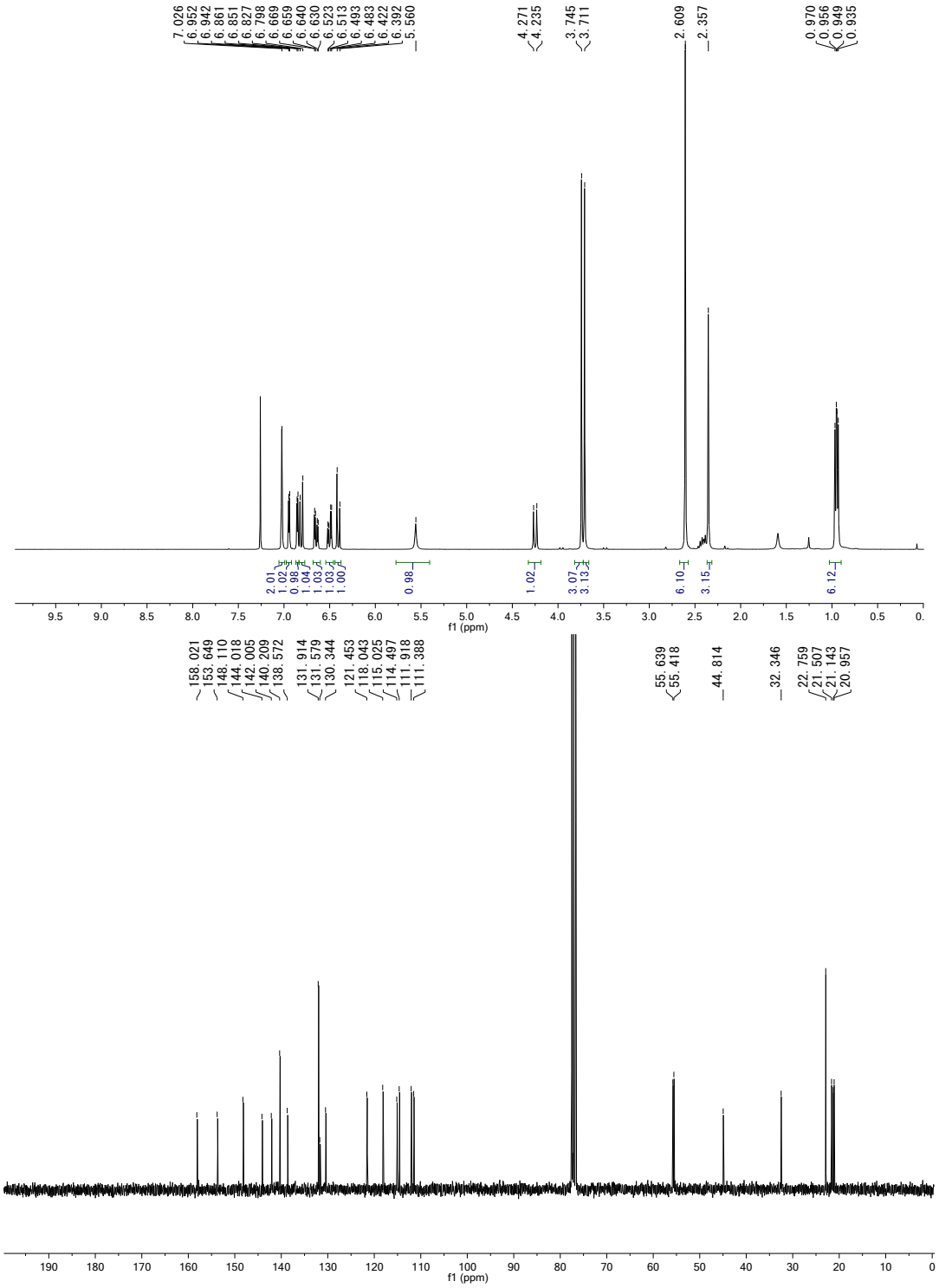


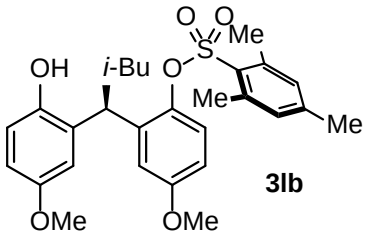


3kb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

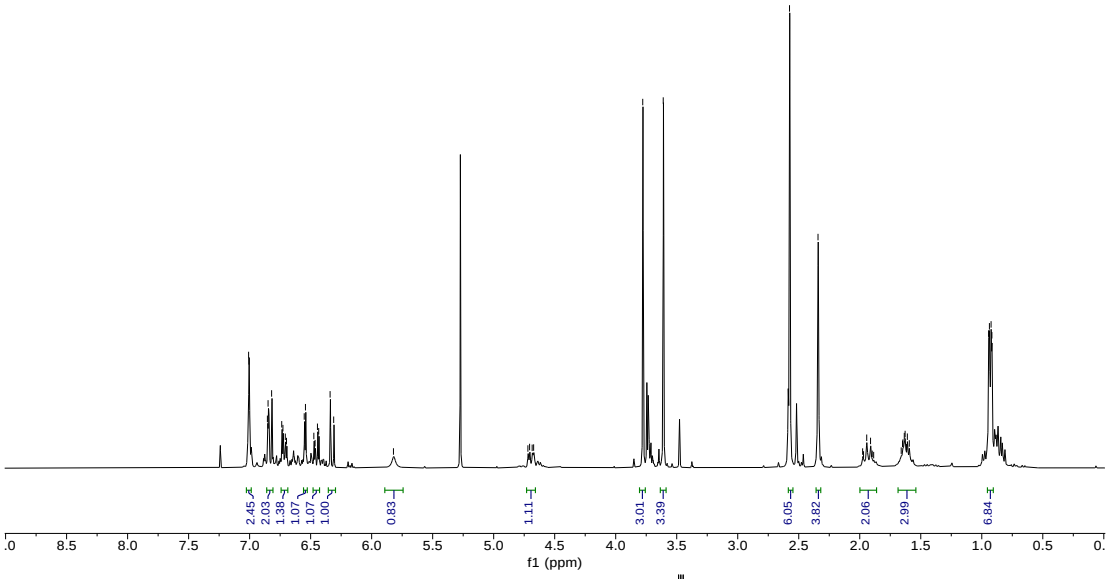


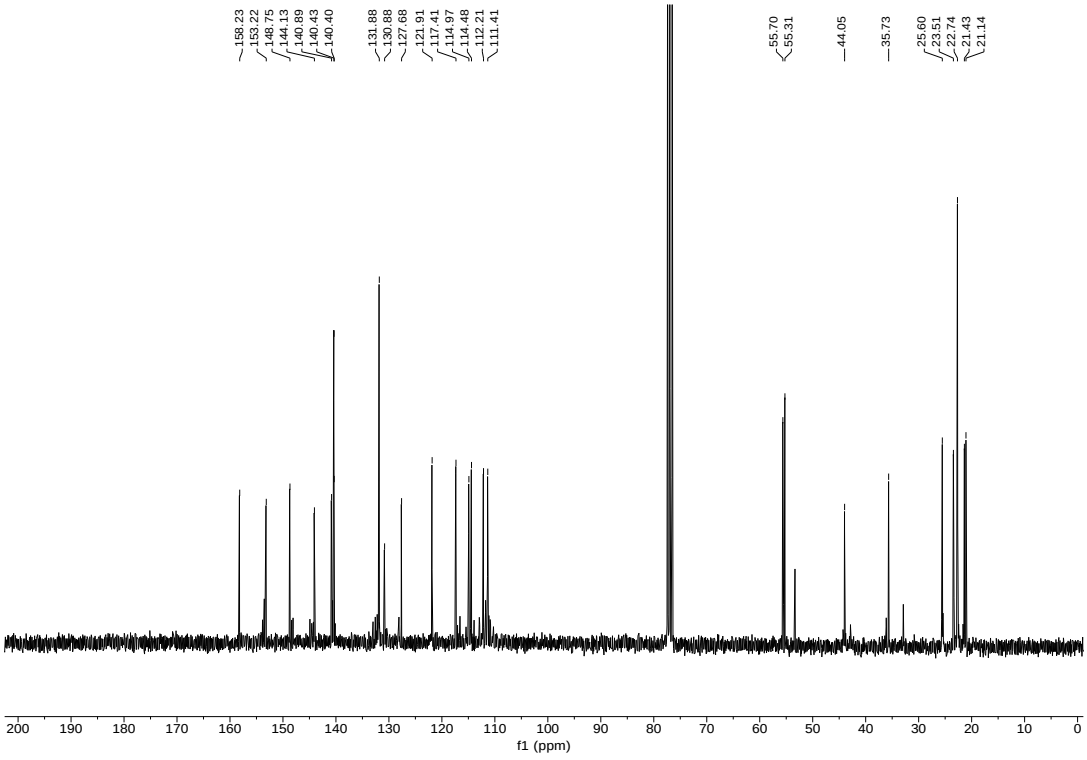


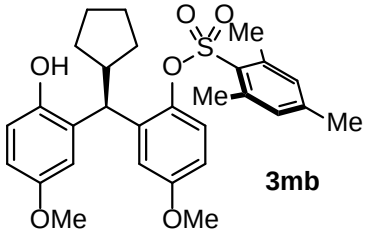
3Ib

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



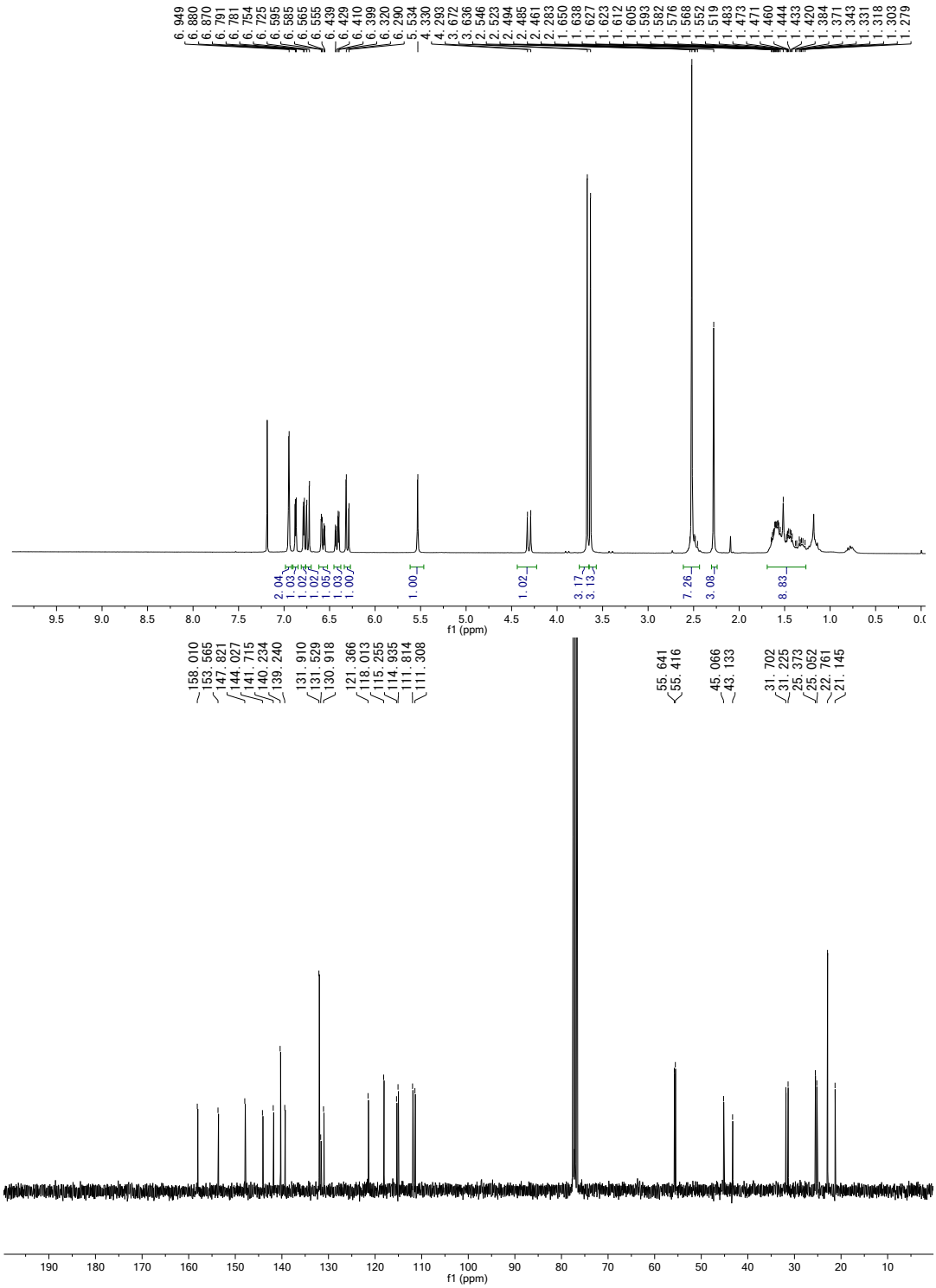


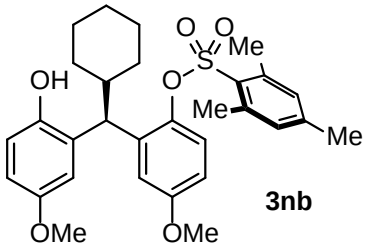


3mb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

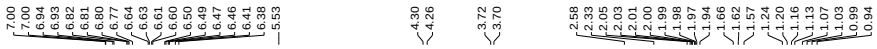


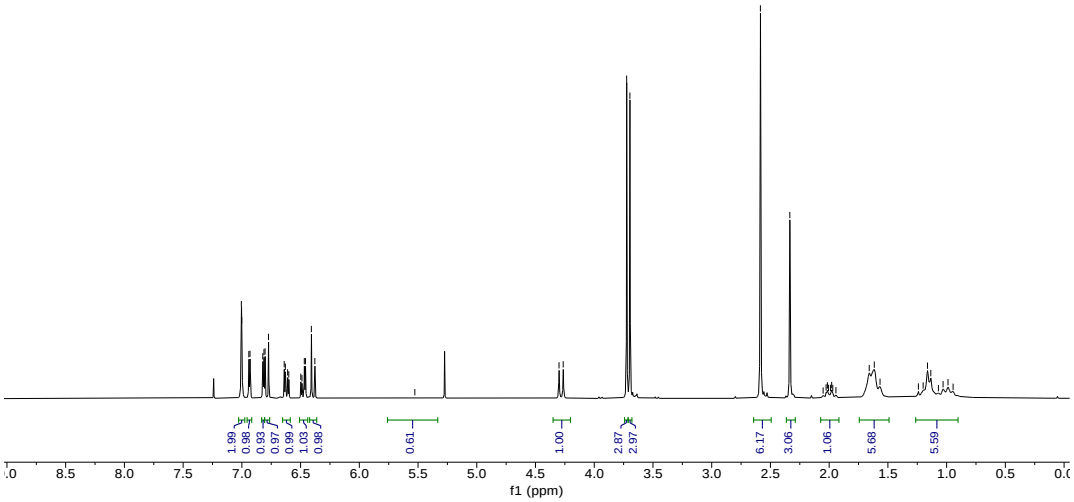


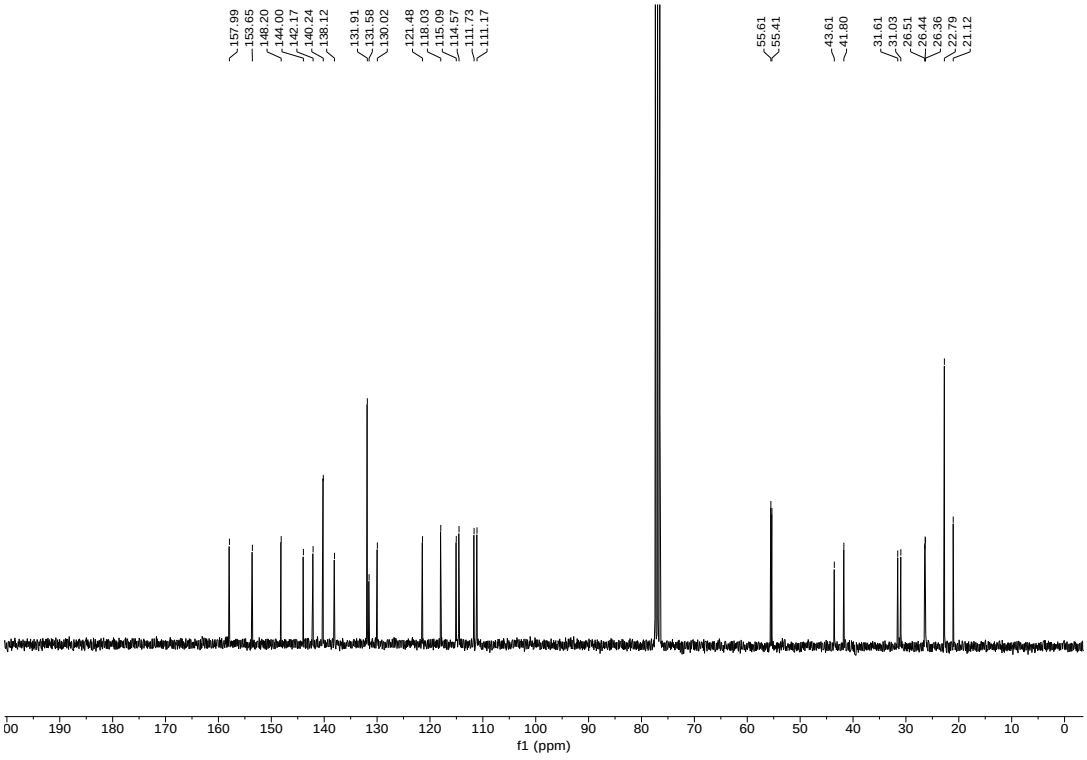
3nb

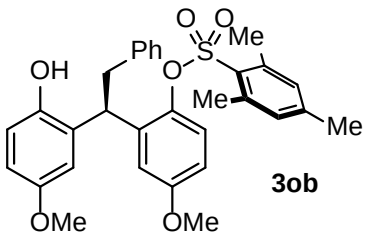
^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)





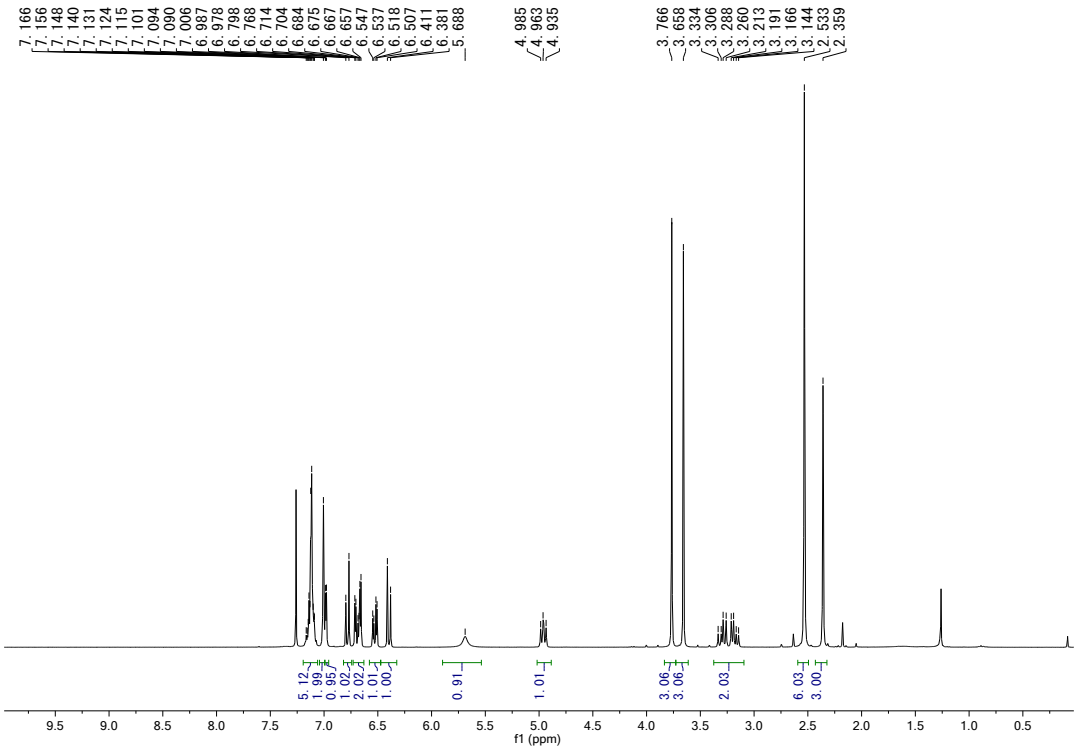


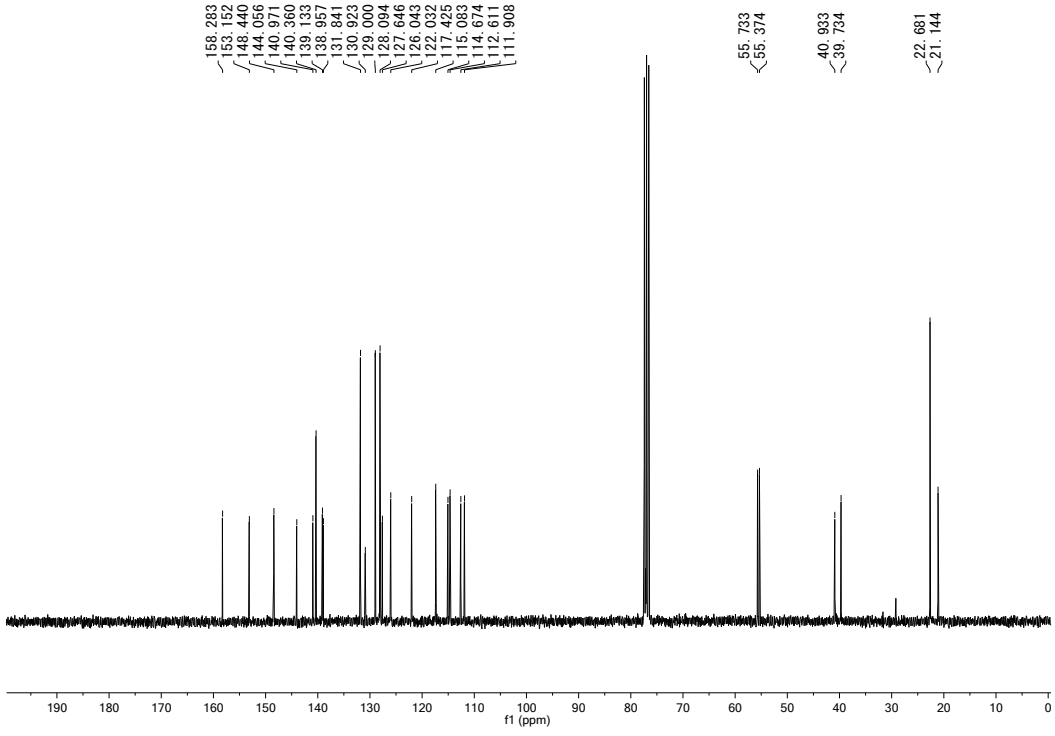


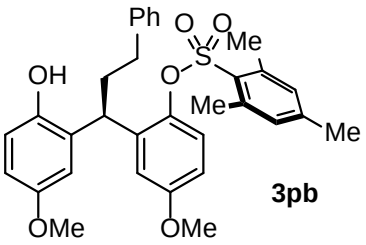
3ob

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



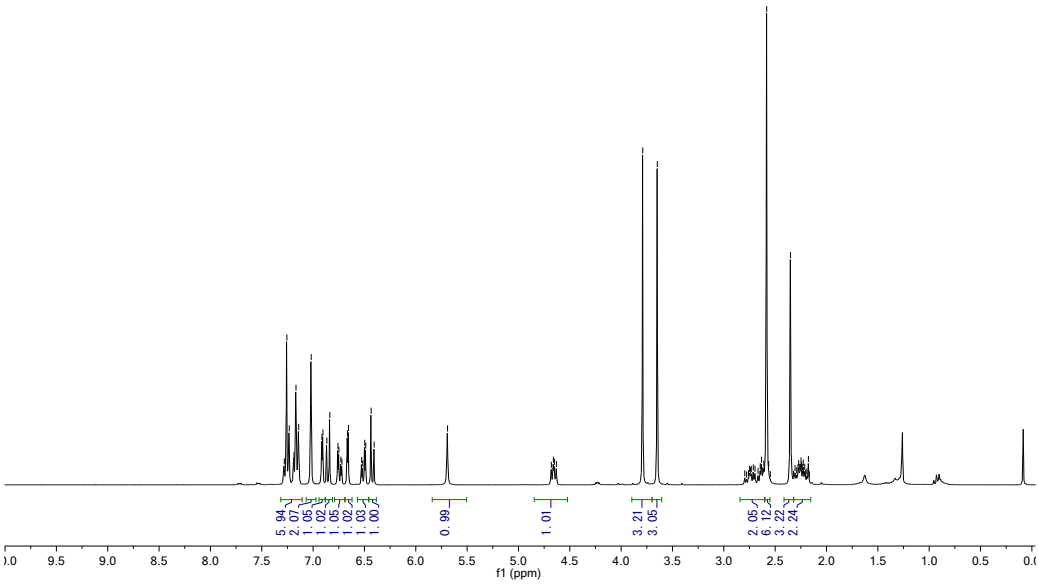


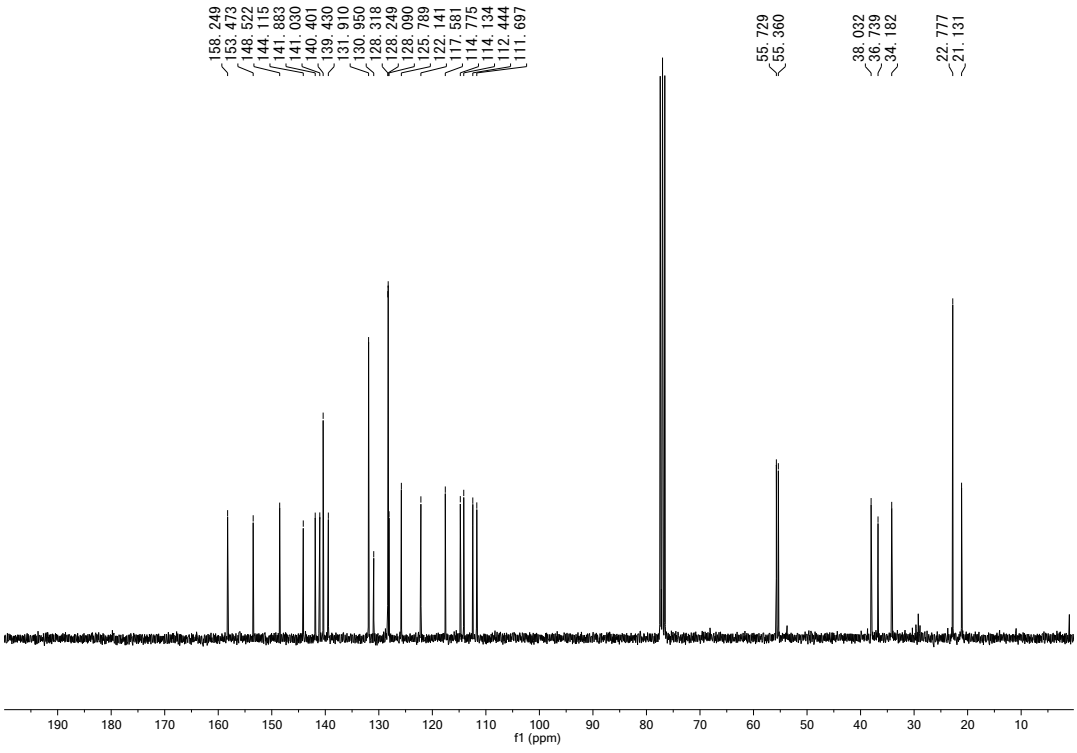


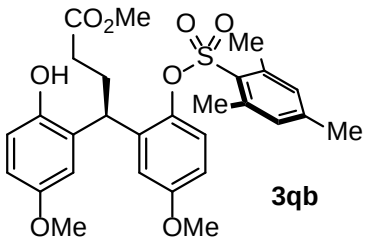
3pb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)



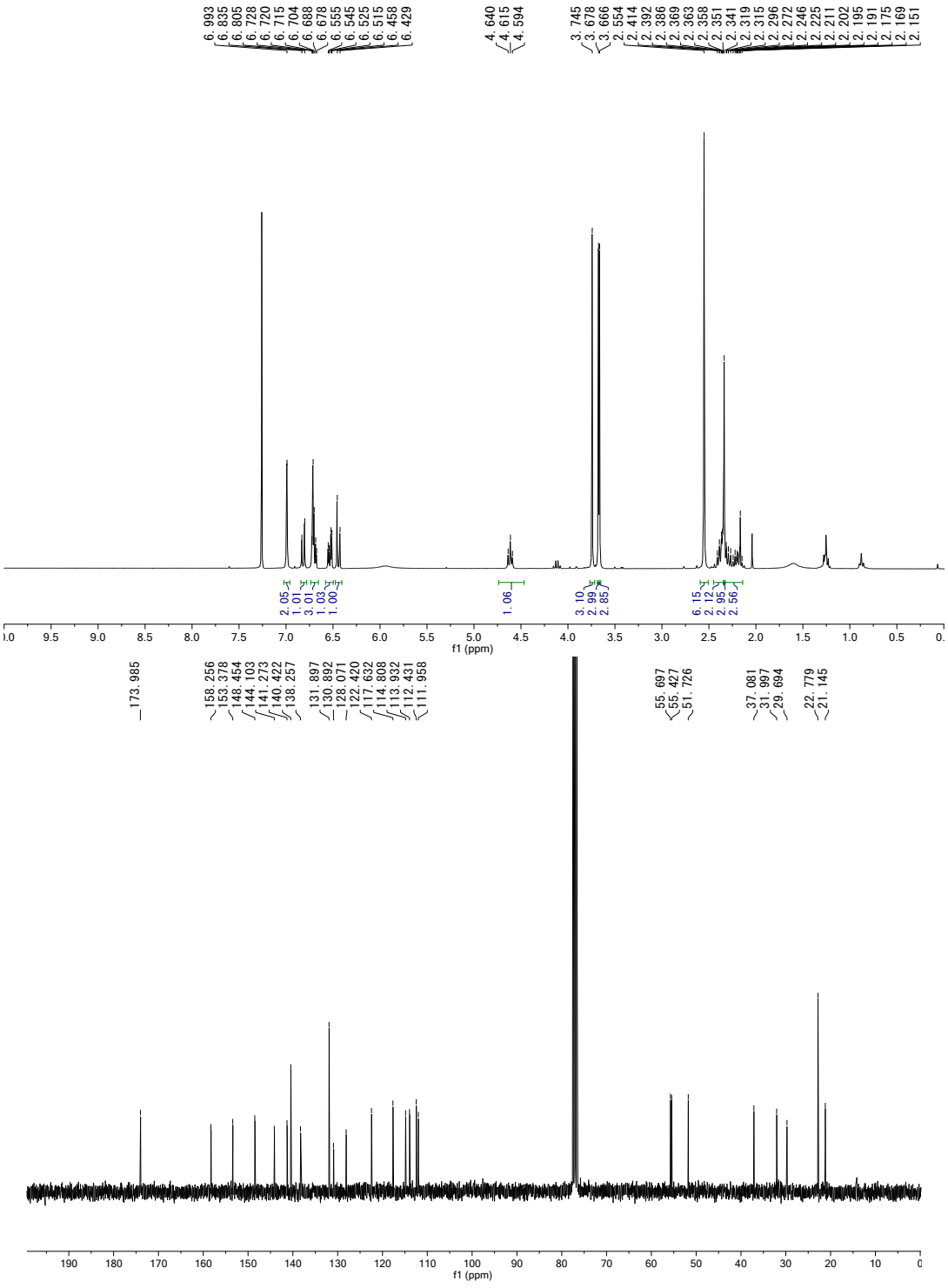


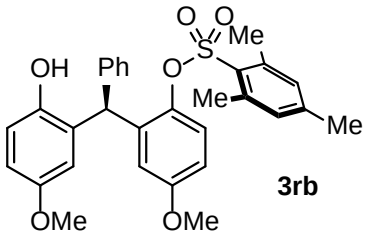


3qb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

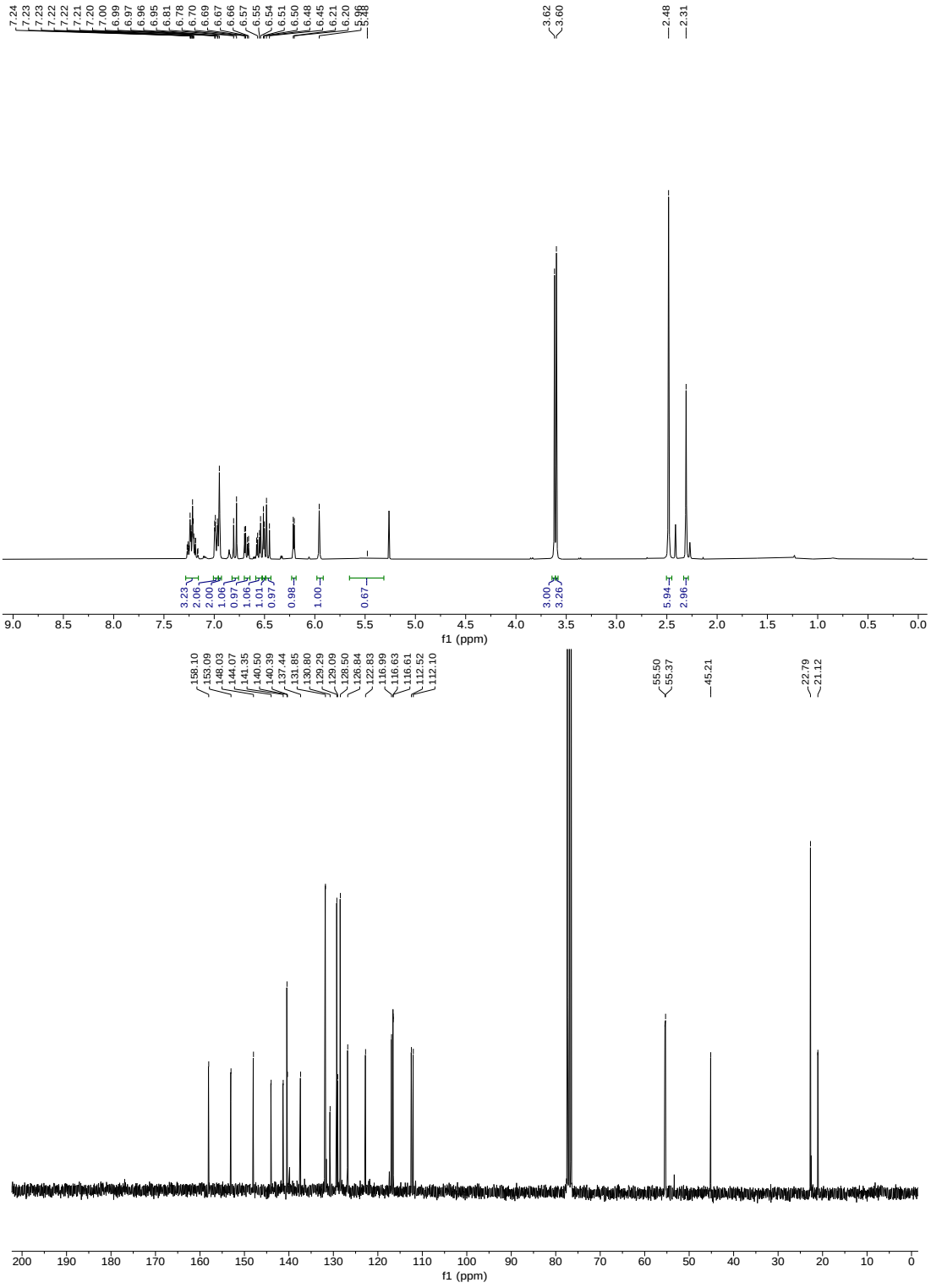


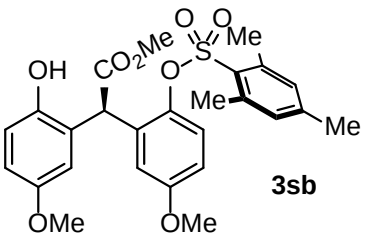


3rb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

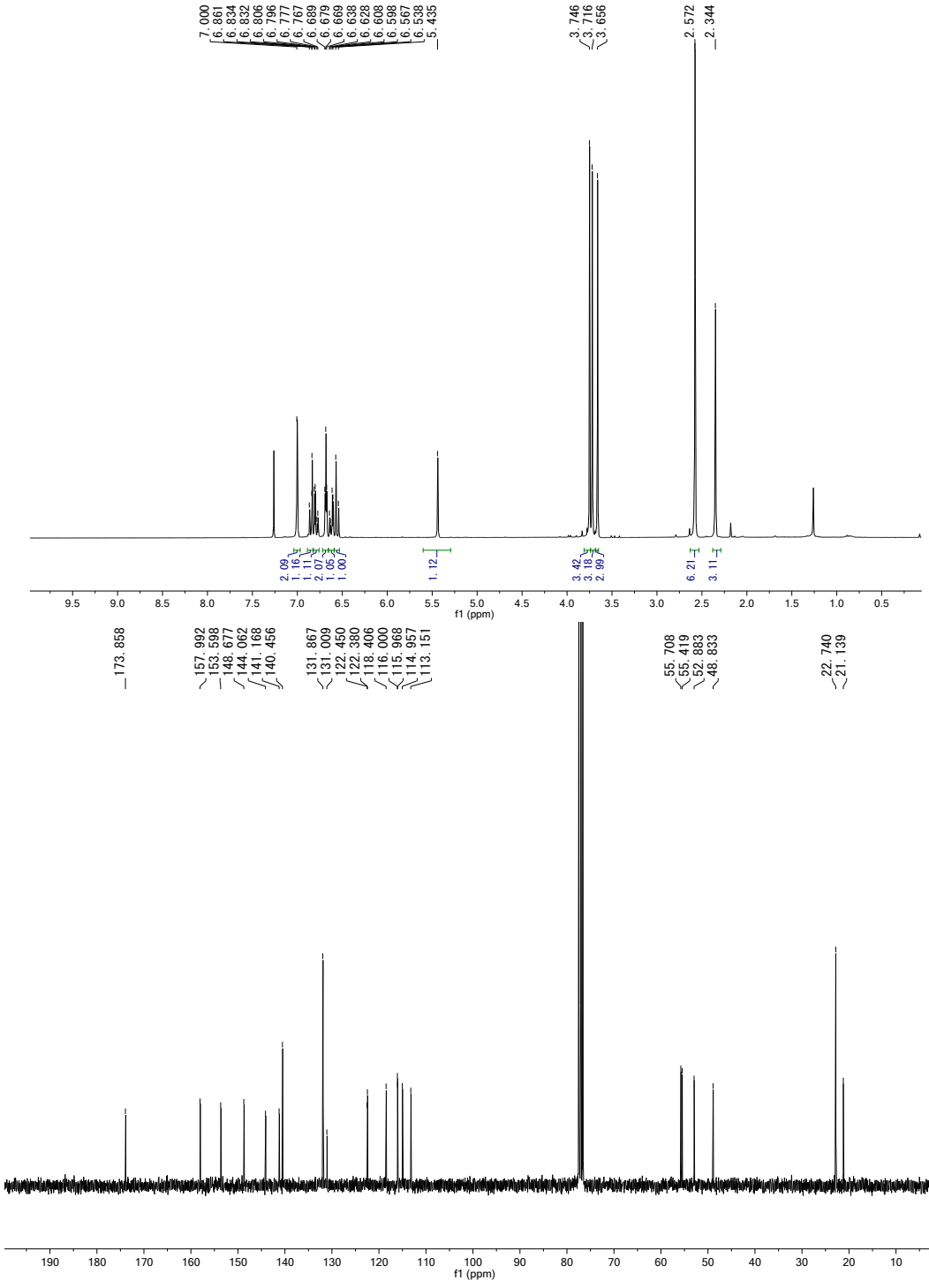


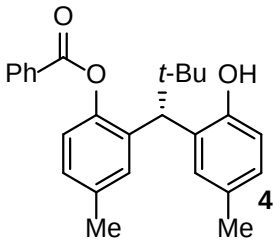


3sb

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

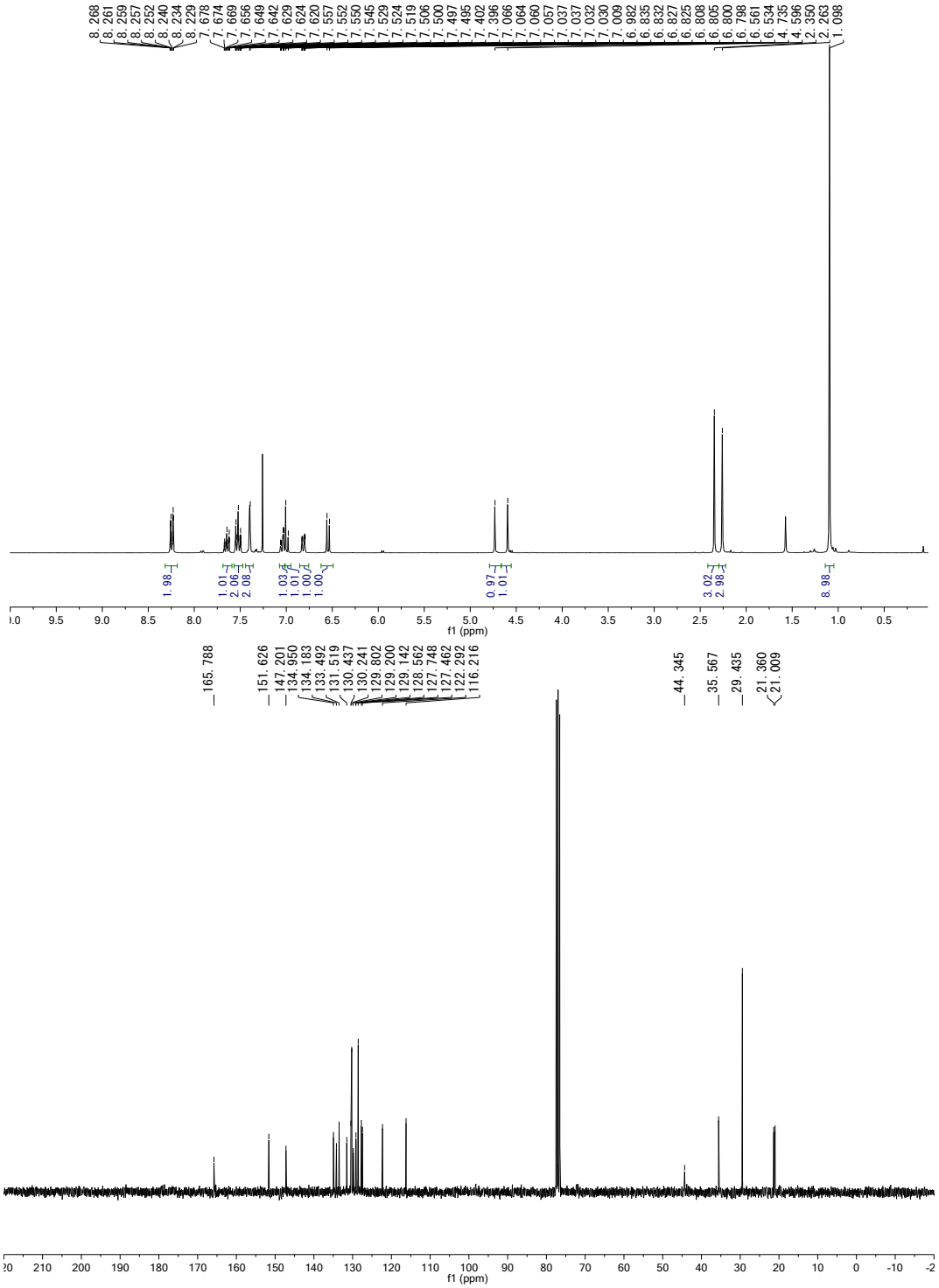
$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

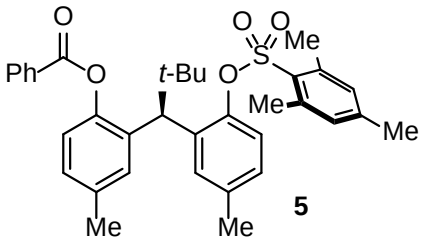




^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

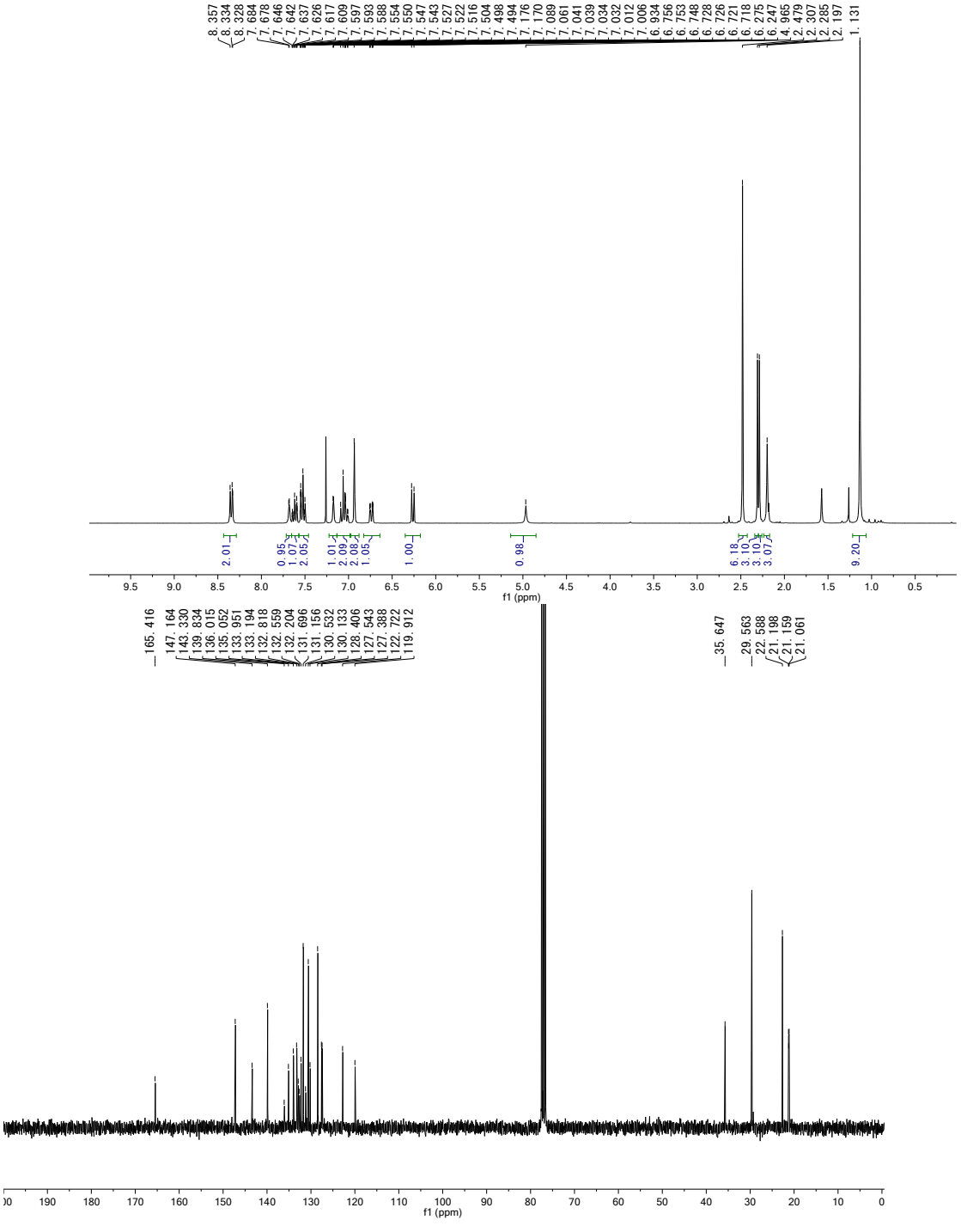


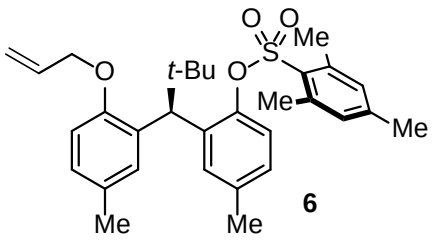


5

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

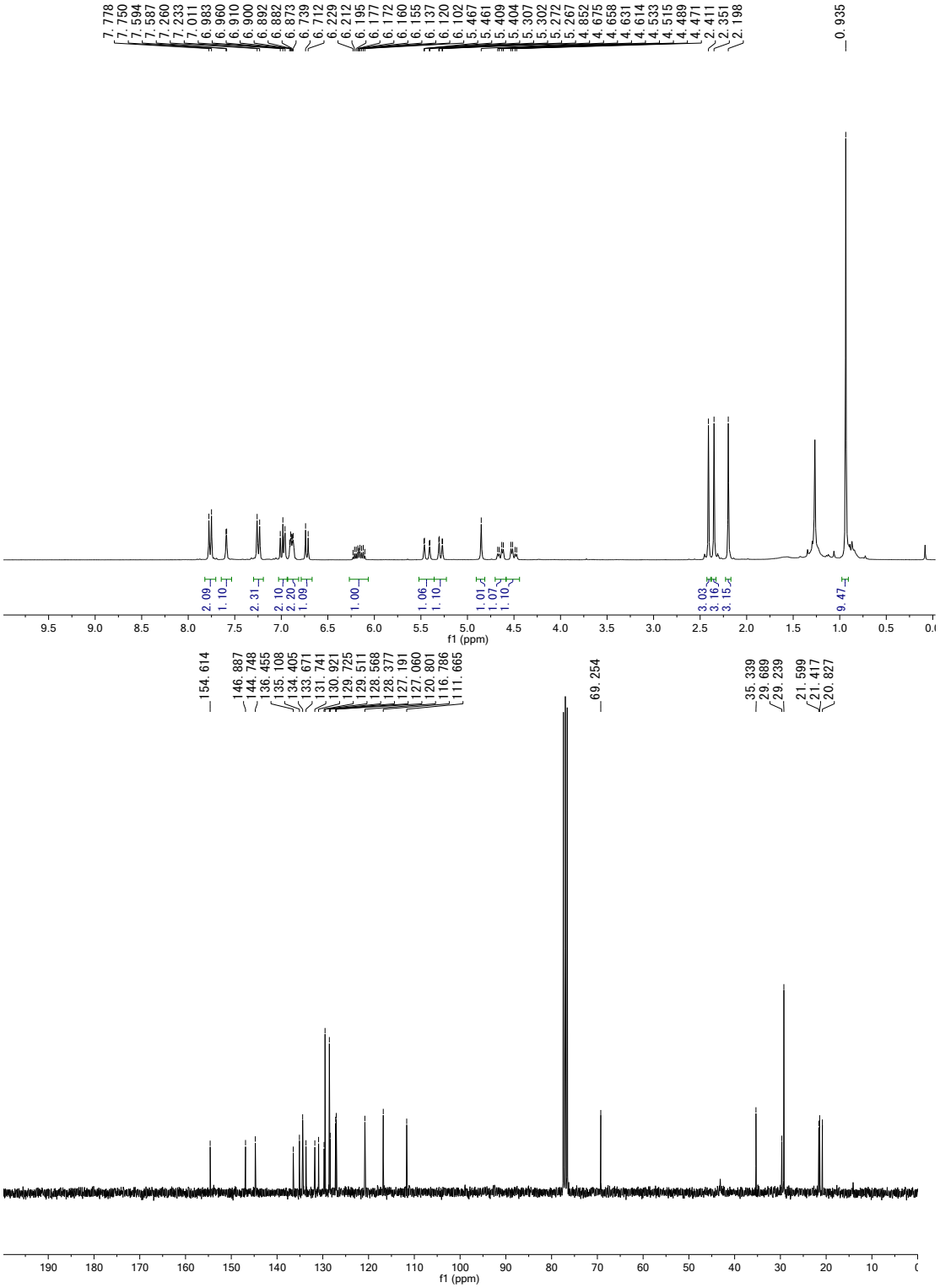




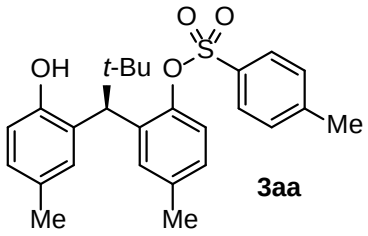
6

^{1}H-NMR (300 MHz, 298 K, $CDCl_3$)

$^{13}C\{^{1}H\}$-NMR (75 MHz, 298 K, $CDCl_3$)

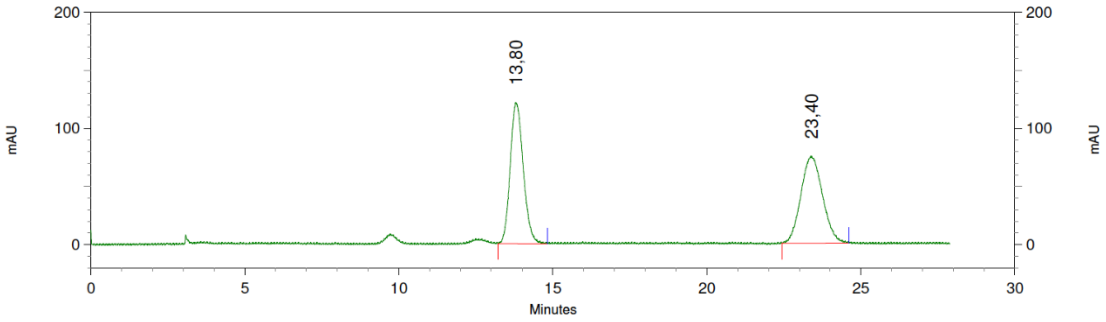


HPLC Traces



3aa

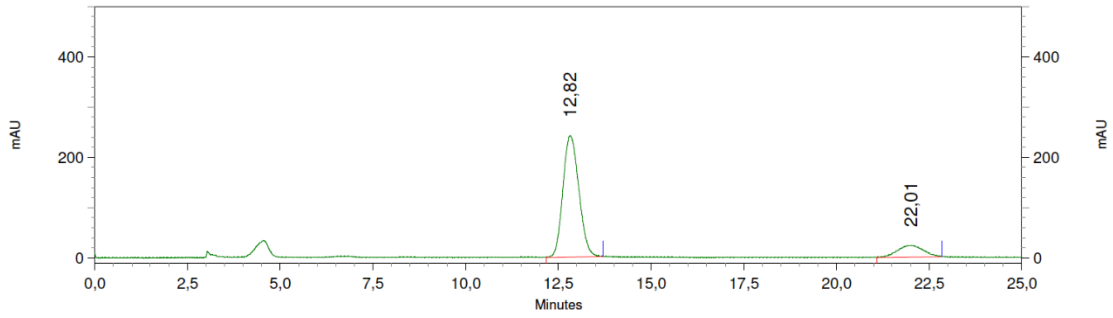
- Non enantioselective reaction



22: 285 nm, 4 nm
Results

Retention Time	Area	Area Percent
13,80	14357547	49,499
23,40	14648352	50,501

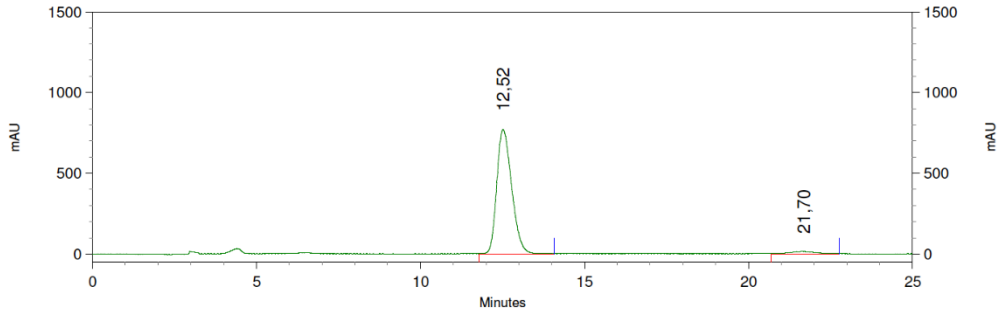
- Enantioselective reaction



19: 290 nm, 4 nm
Results

Retention Time	Area	Area Percent
12,82	28965758	86,371
22,01	4570862	13,629

- Mother liquors



43: 239 nm, 4 nm
Results

Retention Time	Area	Area Percent
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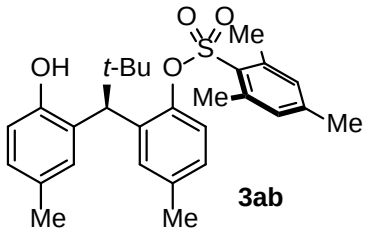
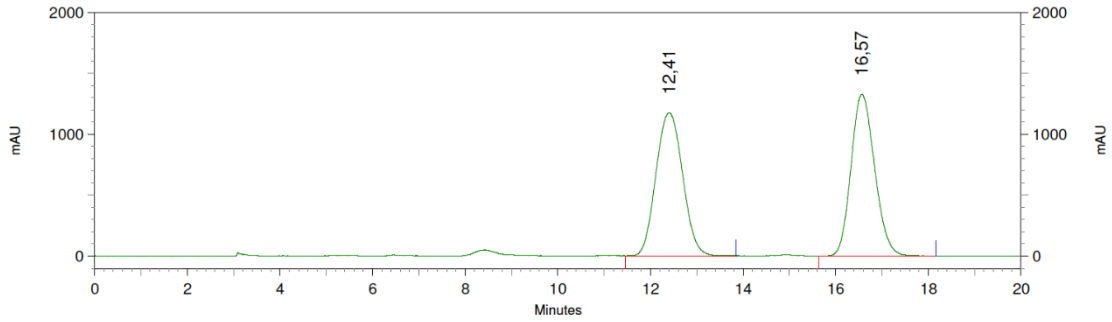
21,70	2848059	2,849



3ab

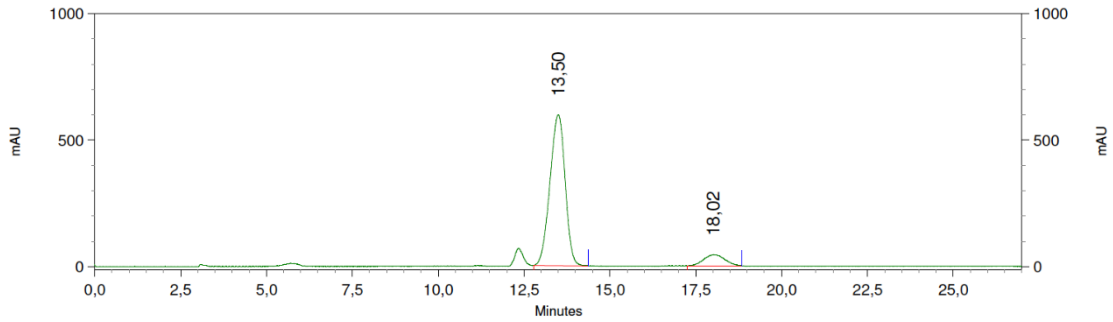
- Non enantioselective reaction



2: 220 nm, 4 nm Results

Retention Time	Area	Area Percent
12,41	188596152	49,957
16,57	188922764	50,043

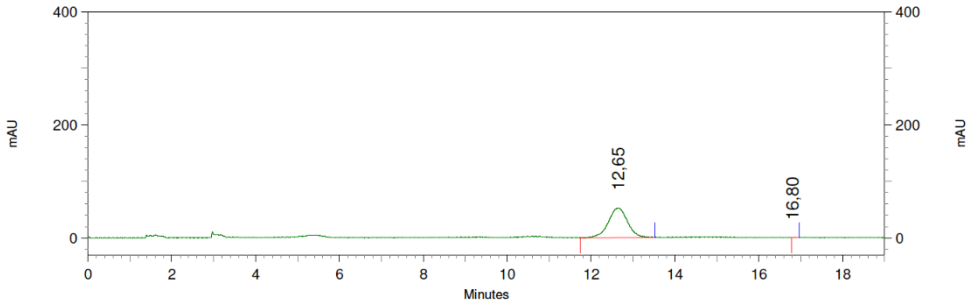
- Enantioselective reaction



18: 280 nm, 4 nm Results

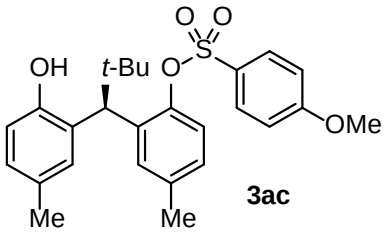
Retention Time	Area	Area Percent
13,50	73405211	90,542
18,02	7667910	9,458

- Mother liquors



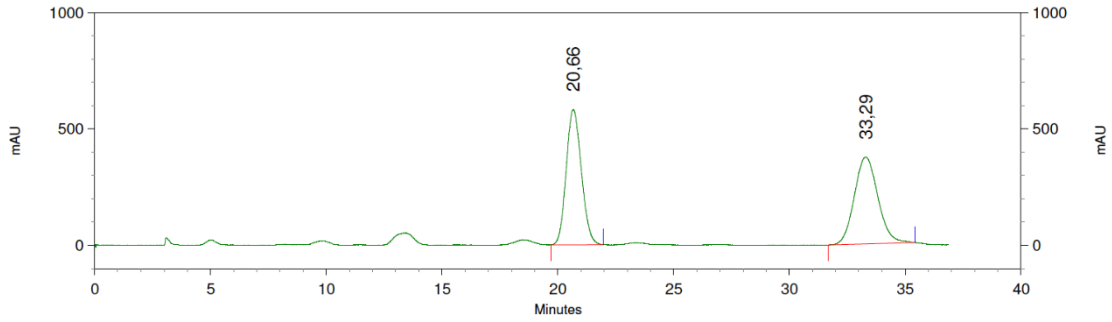
45: 294 nm, 4 nm
Results

Retention Time	Area	Area Percent
12,65	6785184	99,608
16,80	26733	0,392



3ac

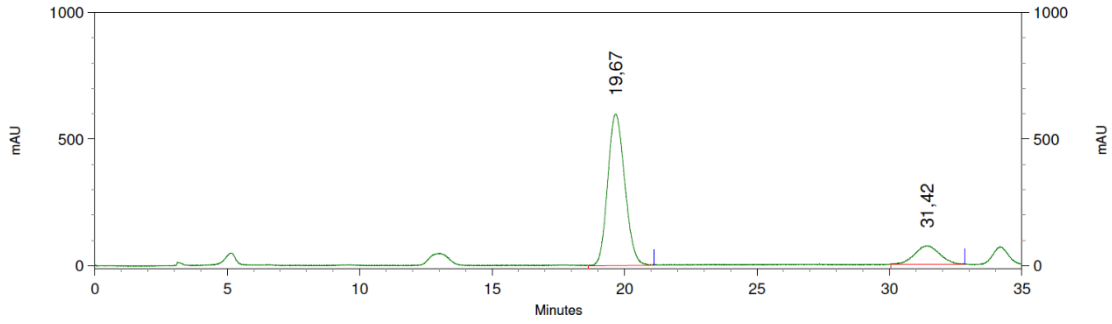
- Non enantioselective reaction



4: 214 nm, 4 nm Results

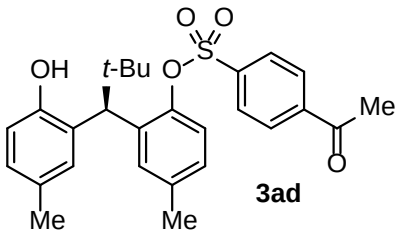
Retention Time	Area	Area Percent
20,66	105979641	50,014
33,29	105920713	49,986

- Enantioselective reaction



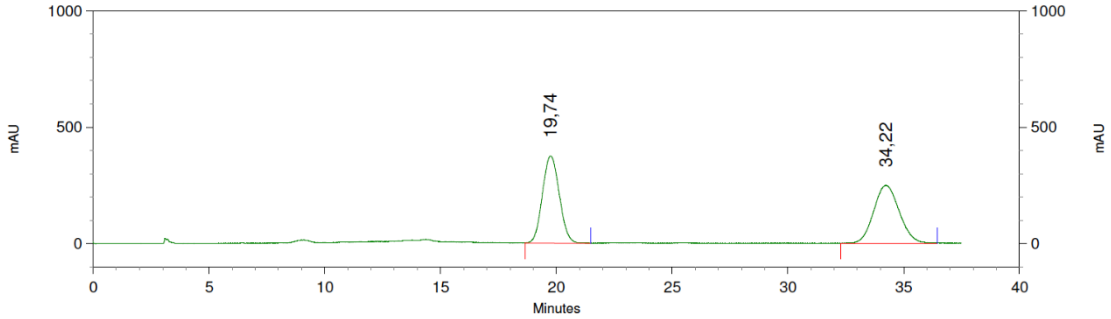
6: 244 nm, 4 nm Results

Retention Time	Area	Area Percent
19,67	106966187	84,519
31,42	19591897	15,481



3ad

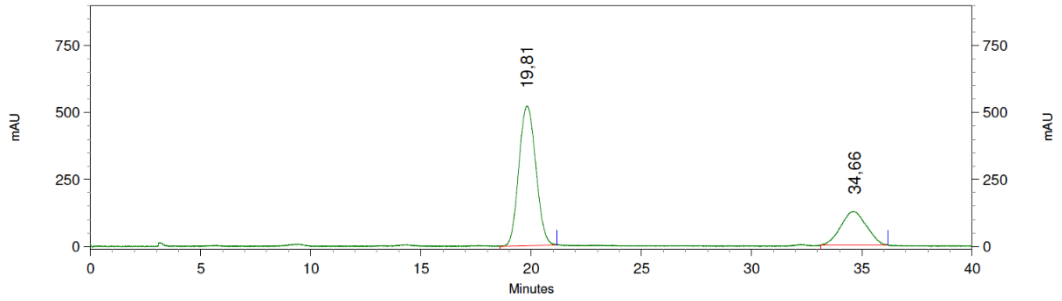
- Non enantioselective reaction



2: 220 nm, 4 nm Results

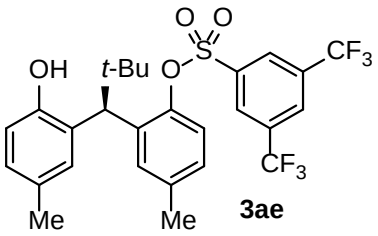
Retention Time	Area	Area Percent
19,74	75836622	49,828
34,22	76360121	50,172

- Enantioselective reaction



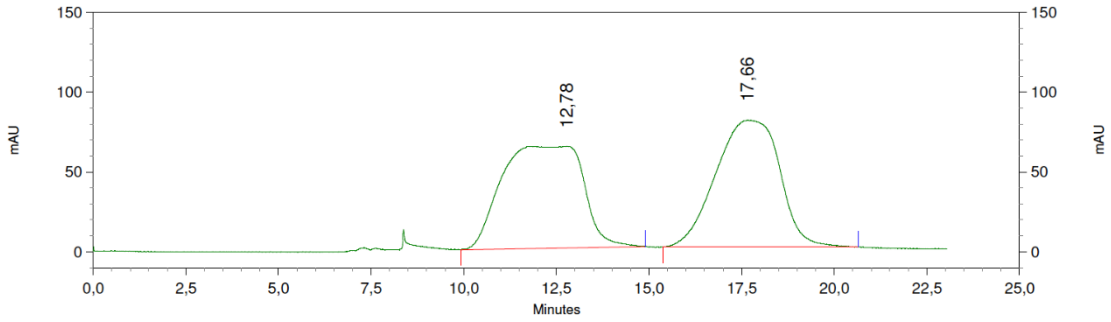
12: 240 nm, 4 nm
Results

Retention Time	Area	Area Percent
19,81	112118286	73,117
34,66	41222786	26,883



3ae

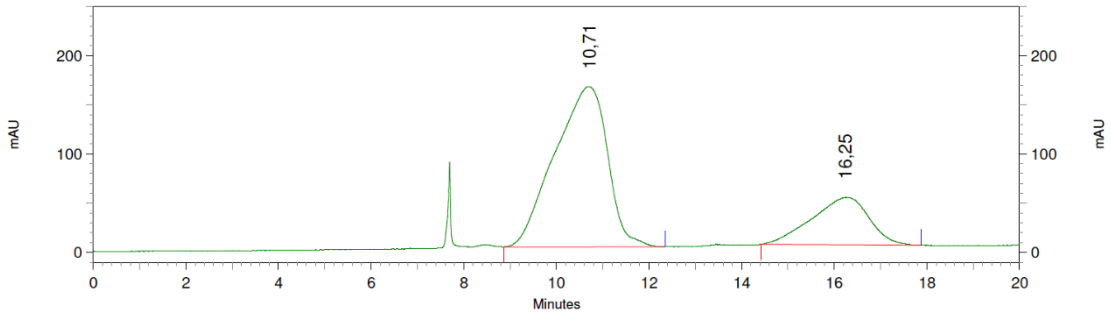
- Non enantioselective reaction



14: 221 nm, 4 nm
Results

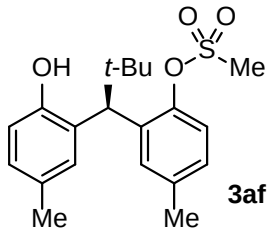
Retention Time	Area	Area Percent
12,78	39254301	50,609
17,66	38309342	49,391

- Enantioselective reaction



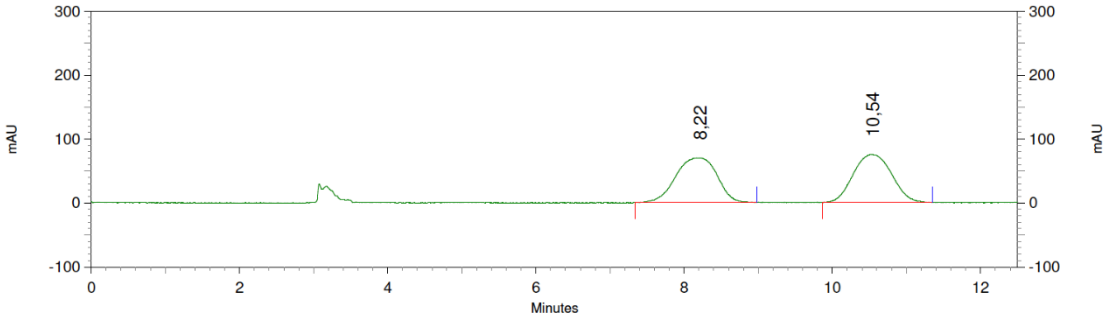
18: 280 nm, 4 nm
Results

Retention Time	Area	Area Percent
10,71	51892218	75,880
16,25	16494658	24,120



3af

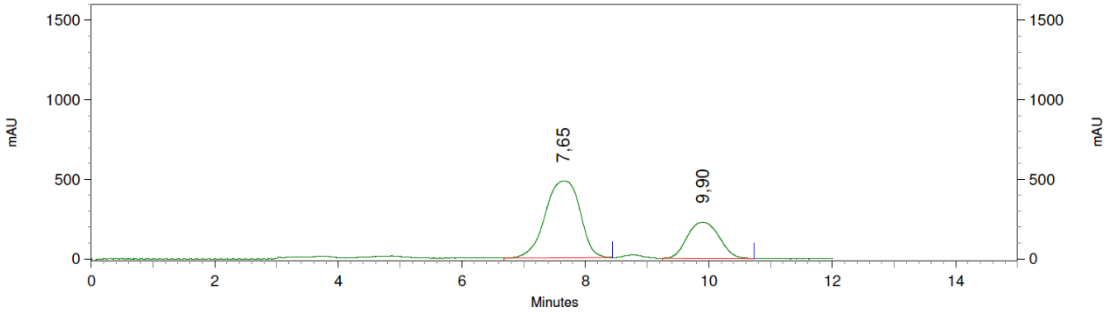
- Non enantioselective reaction



4: 214 nm, 4 nm Results

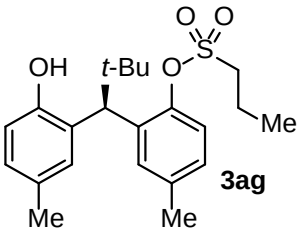
Retention Time	Area	Area Percent
8,22	10896783	50,045
10,54	10877264	49,955

- Enantioselective reaction



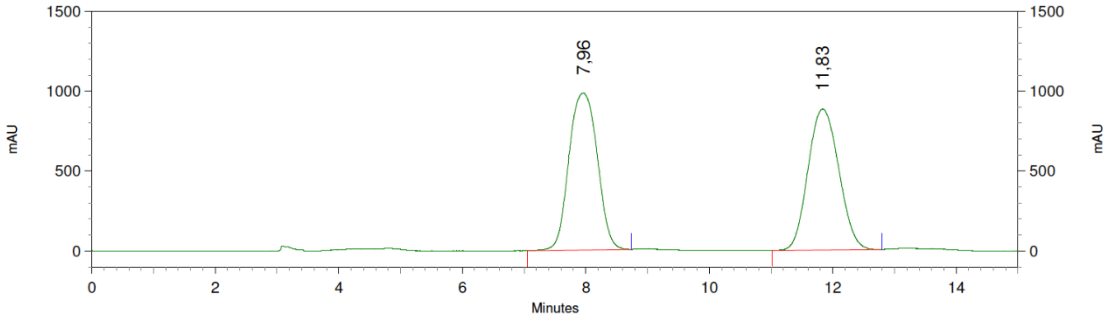
19: 290 nm, 4 nm Results

Retention Time	Area	Area Percent
7,65	75590538	69,660
9,90	32923124	30,340



3ag

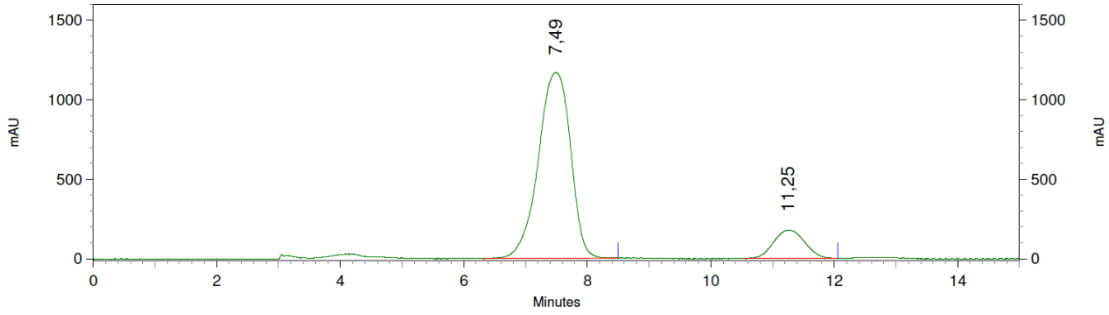
- Non enantioselective reaction



4: 214 nm, 4 nm Results

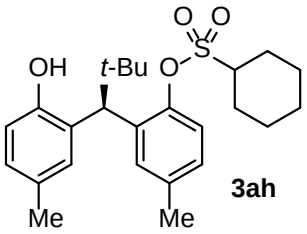
Retention Time	Area	Area Percent
7,96	125259160	50,576
11,83	122408154	49,424

- Enantioselective reaction



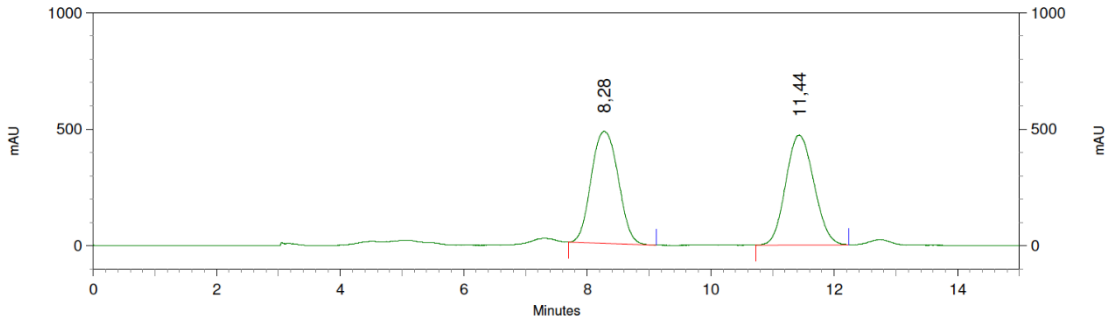
2: 220 nm, 4 nm Results

Retention Time	Area	Area Percent
7,49	169899499	87,125
11,25	25106667	12,875



3ah

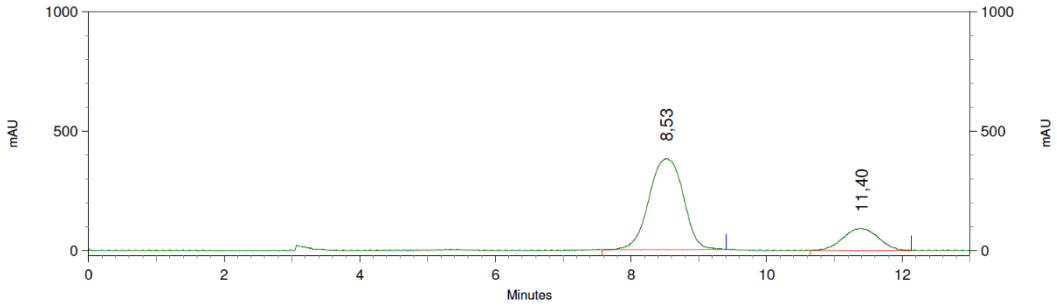
- Non enantioselective reaction



13: 230 nm, 4 nm
Results

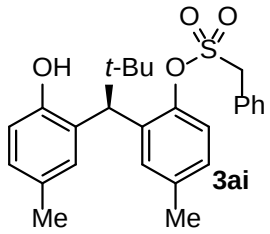
Retention Time	Area	Area Percent
8,28	58596678	49,434
11,44	59938077	50,566

- Enantioselective reaction



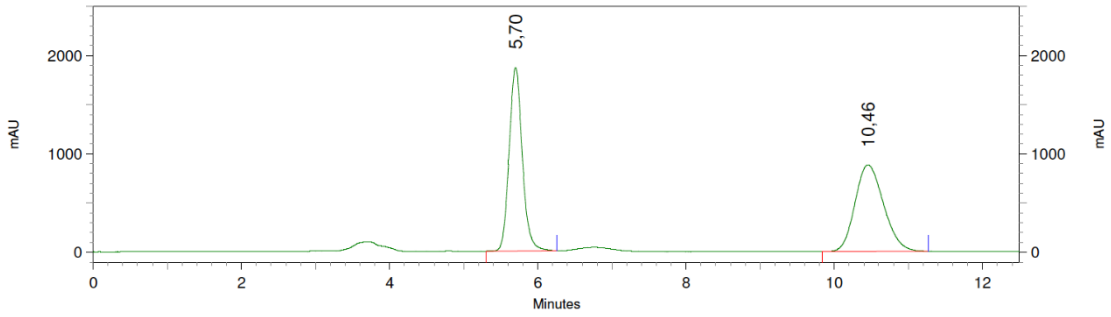
4: 229 nm, 4 nm Results

Retention Time	Area	Area Percent
8,53	53426214	79,679
11,40	13625361	20,321



3ai

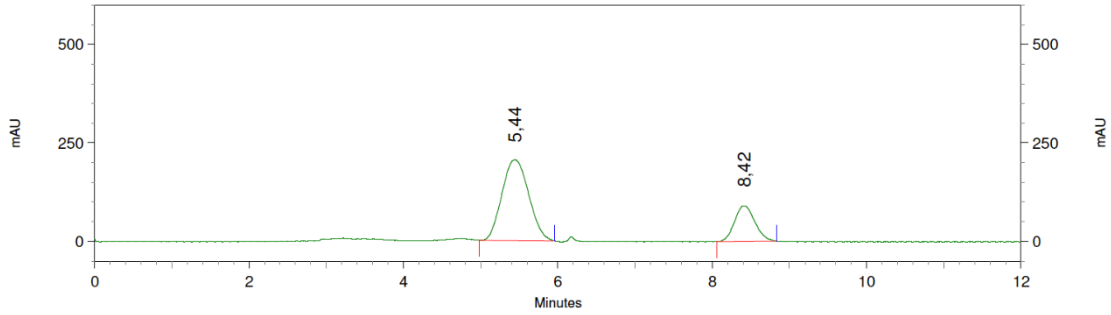
- Non enantioselective reaction



1: 230 nm, 4 nm Results

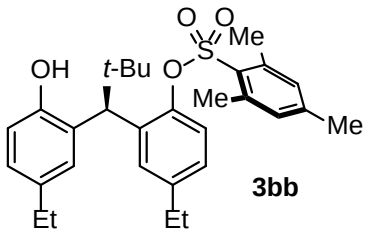
Retention Time	Area	Area Percent
5,70	91741961	49,308
10,46	94316958	50,692

- Enantioselective reaction



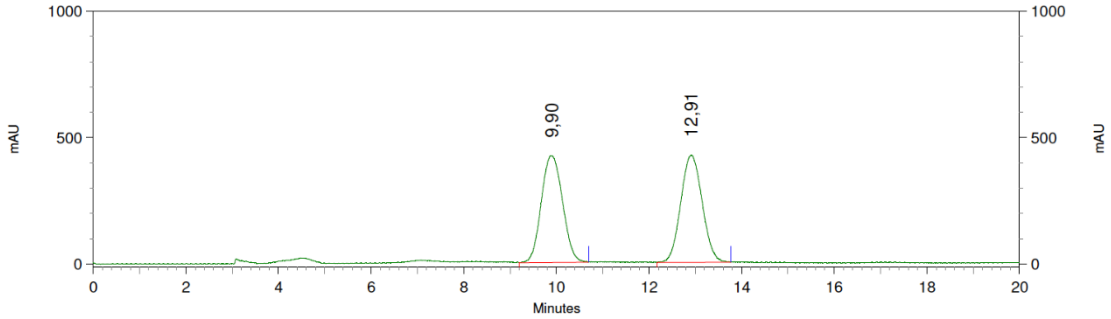
17: 287 nm, 4 nm
Results

Retention Time	Area	Area Percent
5,44	19813252	75,070
8,42	6579900	24,930



3bb

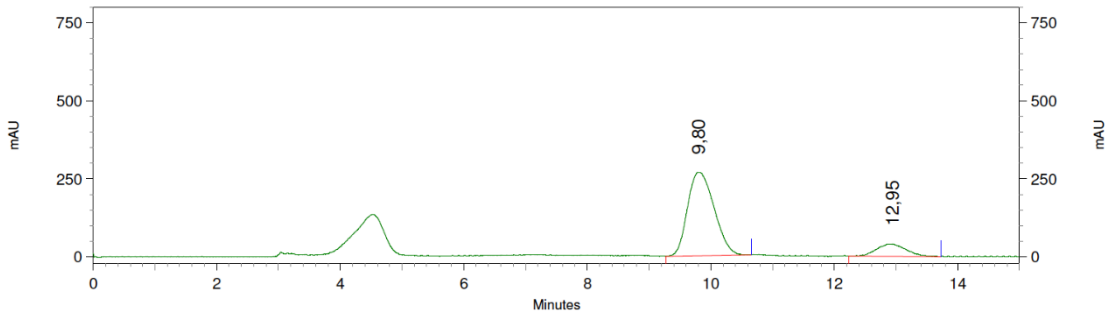
- Non enantioselective reaction



8: 228 nm, 4 nm Results

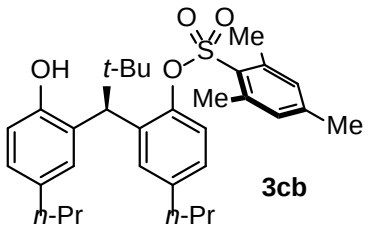
Retention Time	Area	Area Percent
9,90	53729426	49,652
12,91	54481705	50,348

- Enantioselective reaction



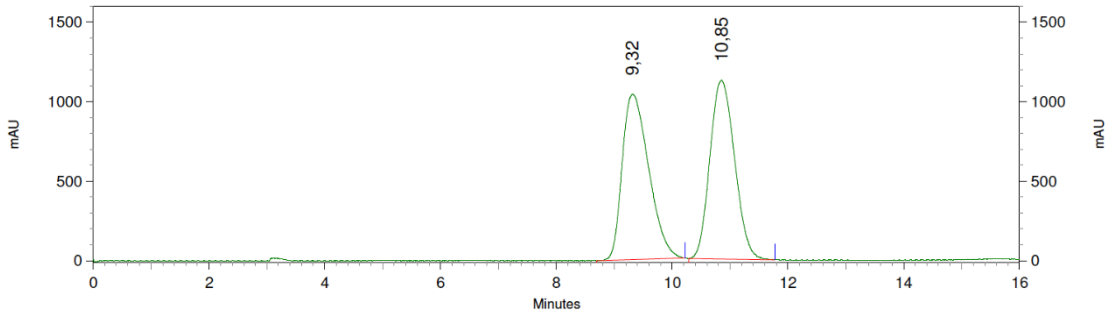
28: 298 nm, 4 nm
Results

Retention Time	Area	Area Percent
9,80	32019962	85,790
12,95	5303651	14,210



3cb

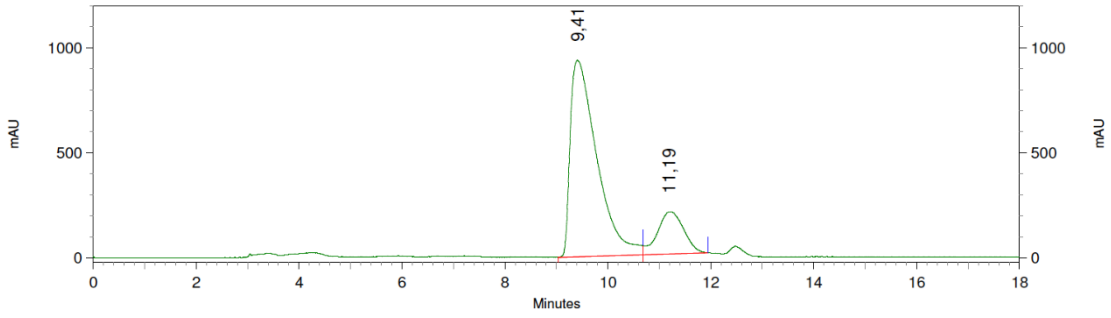
- Non enantioselective reaction



8: 228 nm, 4 nm Results

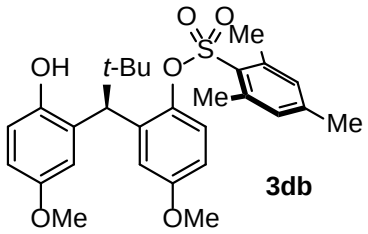
Retention Time	Area	Area Percent
9,32	132552303	49,811
10,85	133558093	50,189

- Enantioselective reaction



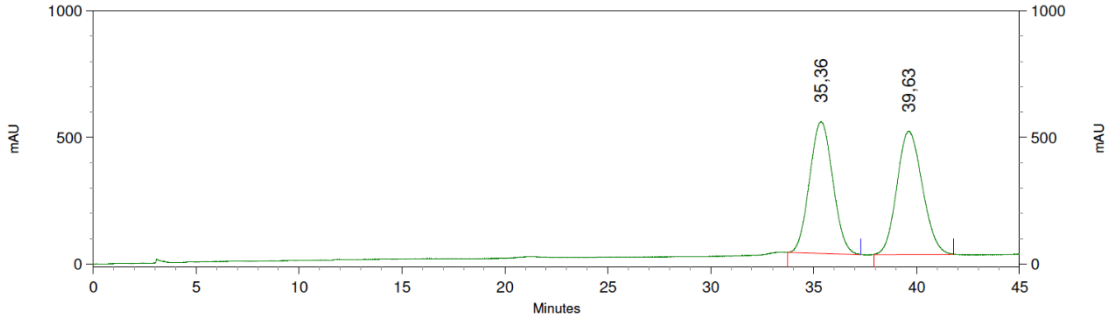
16: 251 nm, 4 nm Results

Retention Time	Area	Area Percent
9,41	134190141	82,605
11,19	28258218	17,395



3db

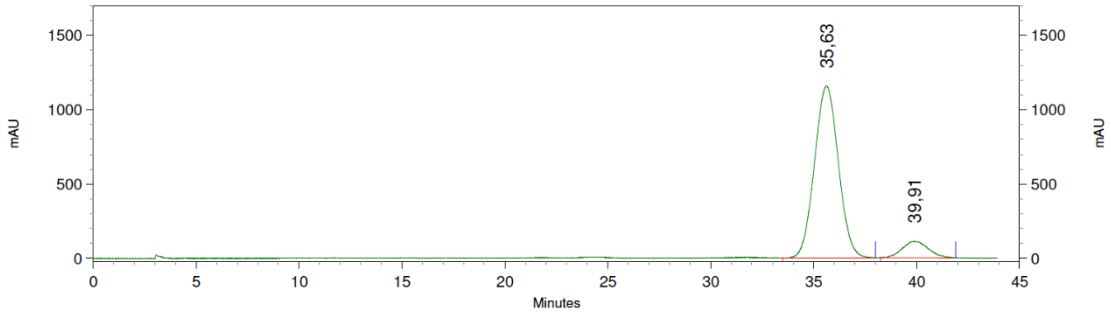
- Non enantioselective reaction



8: 228 nm, 4 nm Results

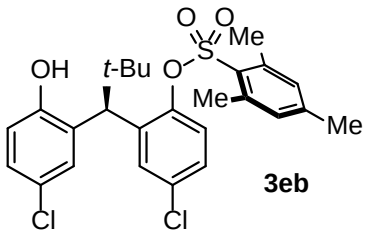
Retention Time	Area	Area Percent
35,36	163210766	49,395
39,63	167207986	50,605

- Enantioselective reaction



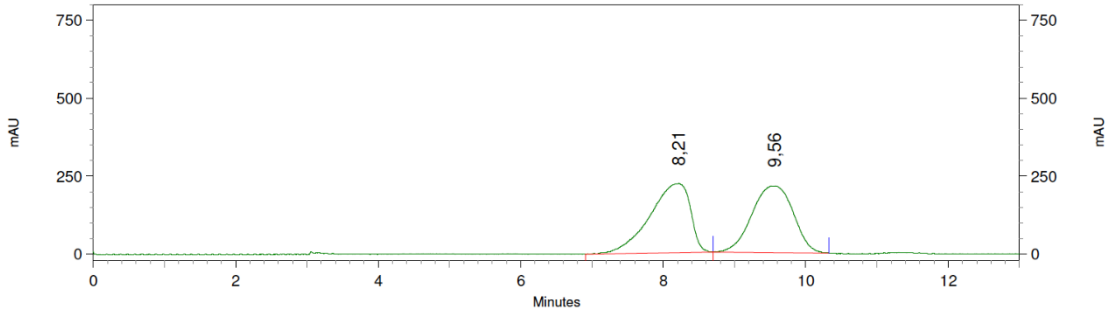
14: 221 nm, 4 nm Results

Retention Time	Area	Area Percent
35,63	373031614	90,562
39,91	38873744	9,438



3eb

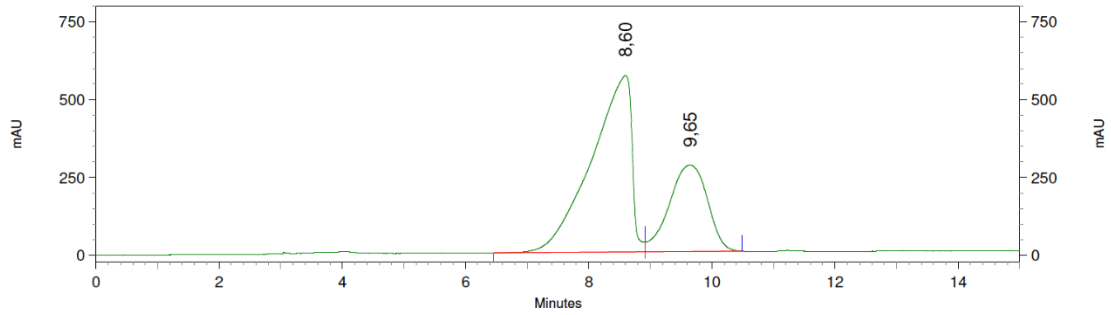
- Non enantioselective reaction



28: 298 nm, 4 nm
Results

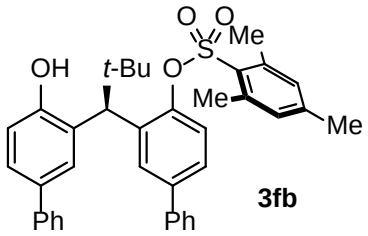
Retention Time	Area	Area Percent
8,21	35078321	50,419
9,56	34494715	49,581

- Enantioselective reaction



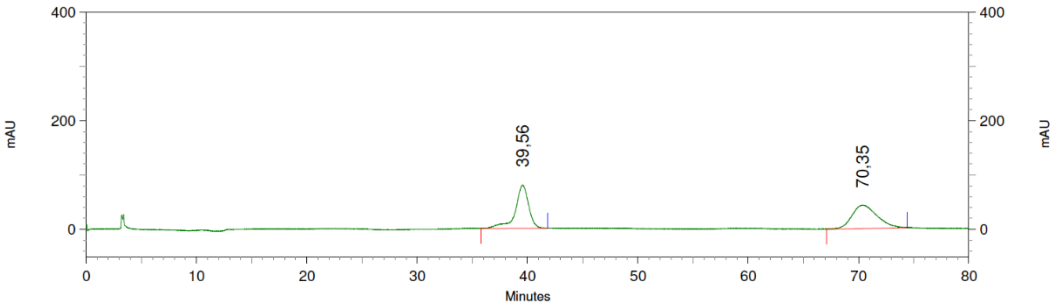
28: 298 nm, 4 nm
Results

Retention Time	Area	Area Percent
8,60	102958590	68,263
9,65	47867769	31,737



3fb

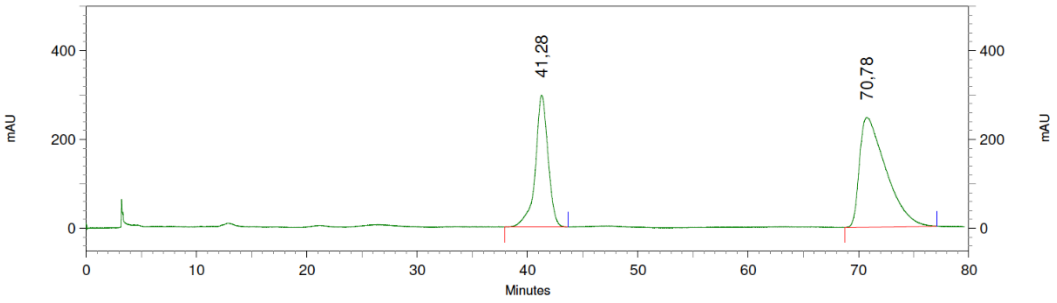
- Non enantioselective reaction



11: 231 nm, 4 nm
Results

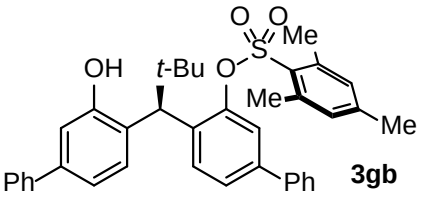
Retention Time	Area	Area Percent
39,56	27161836	49,617
70,35	27580786	50,383

- Enantioselective reaction



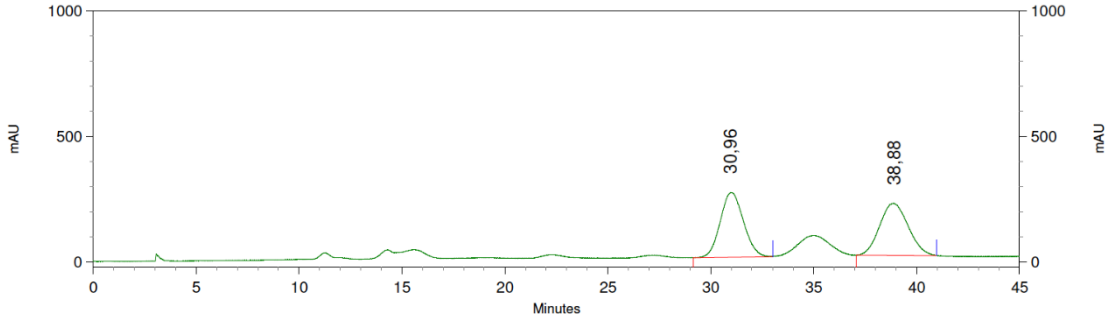
11: 231 nm, 4 nm
Results

Retention Time	Area	Area Percent
41,28	95805650	36,712
70,78	165158636	63,288



3gb

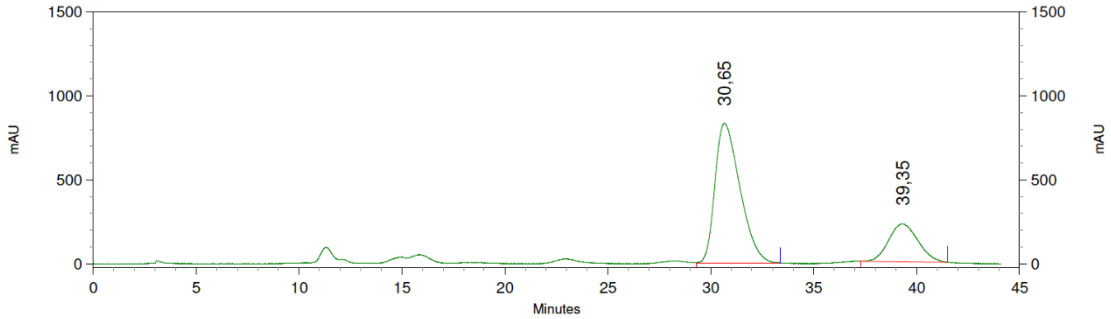
- Non enantioselective reaction



15: 217 nm, 4 nm
Results

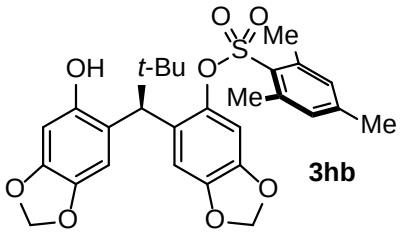
Retention Time	Area	Area Percent
30,96	80883050	50,311
38,88	79883213	49,689

- Enantioselective reaction



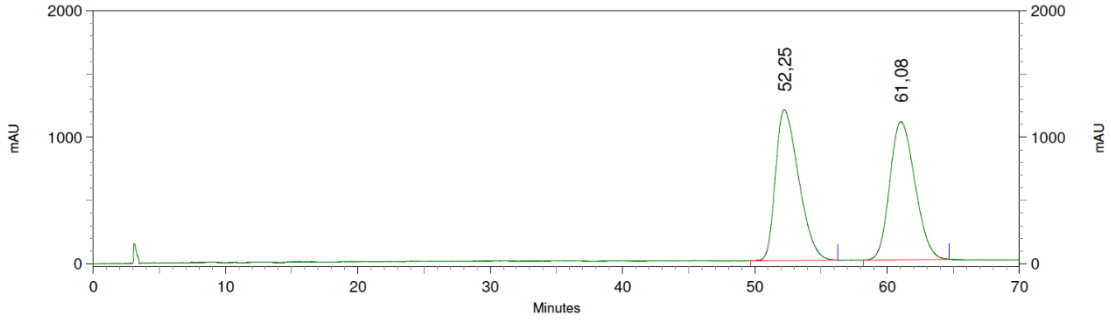
22: 285 nm, 4 nm
Results

Retention Time	Area	Area Percent
30,65	280109878	75,808
39,35	89390803	24,192



3hb

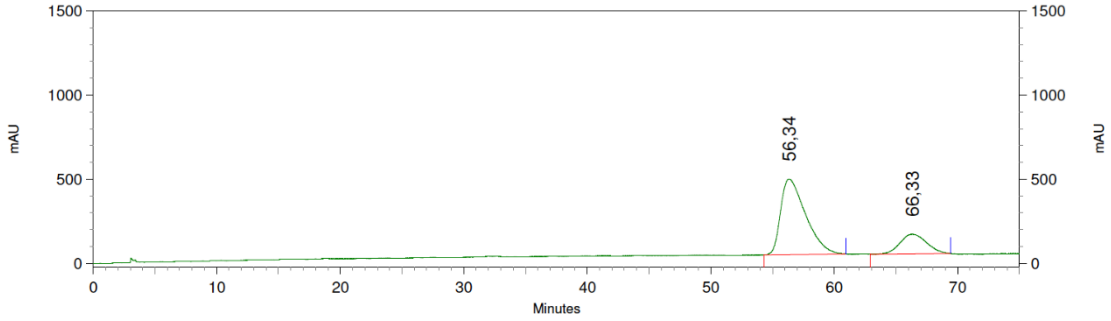
- Non enantioselective reaction



23: 205 nm, 4 nm
Results

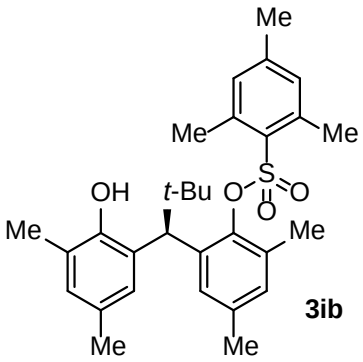
Retention Time	Area	Area Percent
52,25	582166513	50,107
61,08	579678960	49,893

- Enantioselective reaction



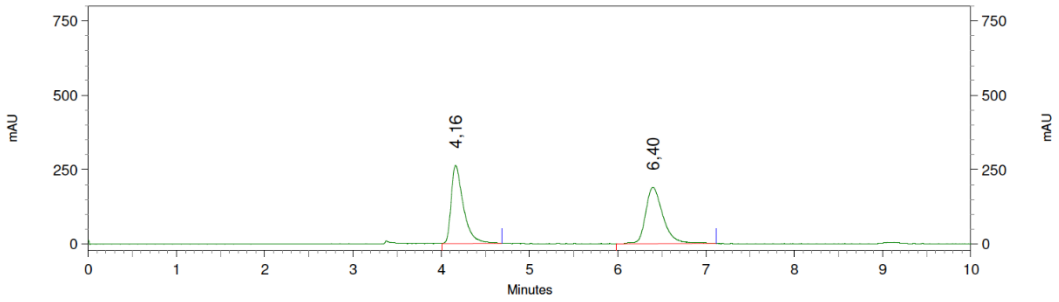
15: 217 nm, 4 nm
Results

Retention Time	Area	Area Percent
56,34	252246991	78,170
66,33	70444570	21,830



3ib

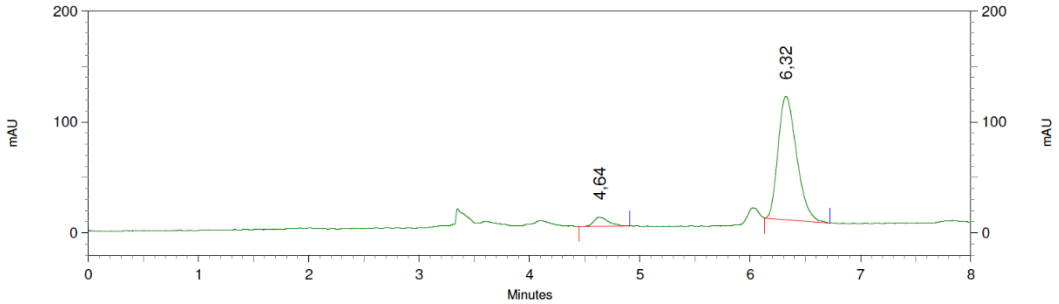
- Non enantioselective reaction



33: 291 nm, 4 nm
Results

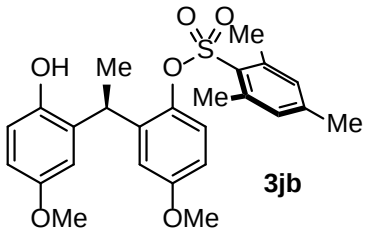
Retention Time	Area	Area Percent
4,16	10059743	49,273
6,40	10356514	50,727

- Enantioselective reaction



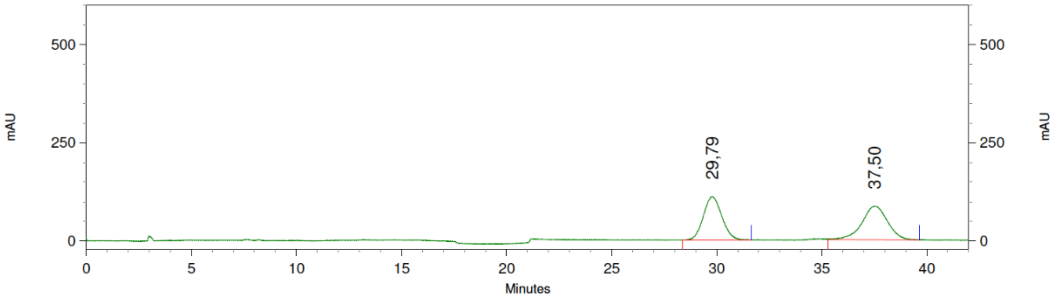
24: 231 nm, 4 nm
Results

Retention Time	Area	Area Percent
4,64	305333	5,517
6,32	5229454	94,483



3jb

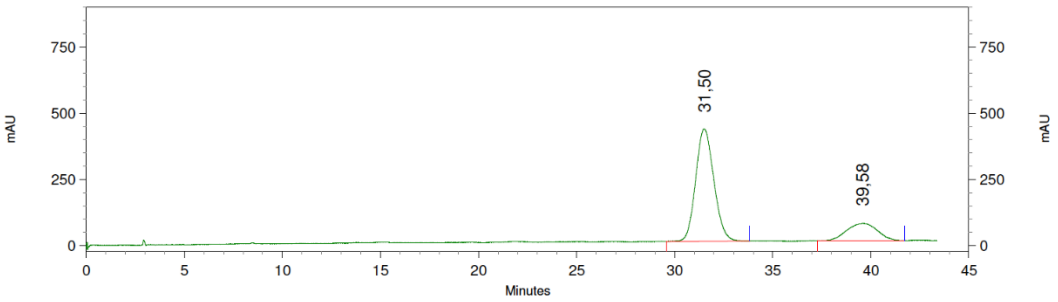
- Non enantioselective reaction



29: 229 nm, 4 nm
Results

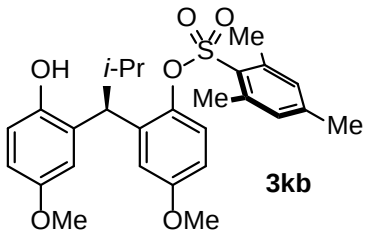
Retention Time	Area	Area Percent
29,79	27380587	48,635
37,50	28918079	51,365

- Enantioselective reaction



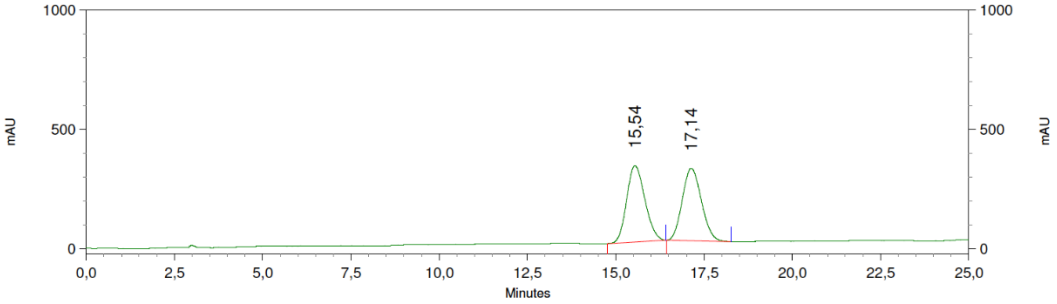
16: 218 nm, 4 nm
Results

Retention Time	Area	Area Percent
31,50	109397413	79,121
39,58	28867964	20,879



3kb

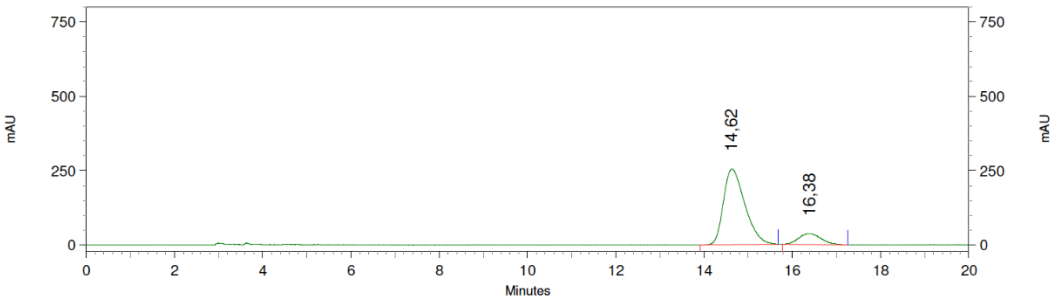
- Non enantioselective reaction



18: 224 nm, 4 nm
Results

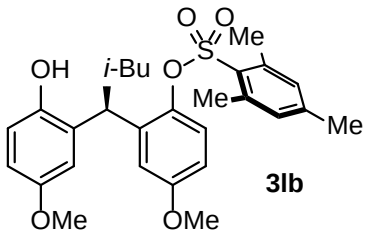
Retention Time	Area	Area Percent
15,54	45959969	50,040
17,14	45886269	49,960

- Enantioselective reaction



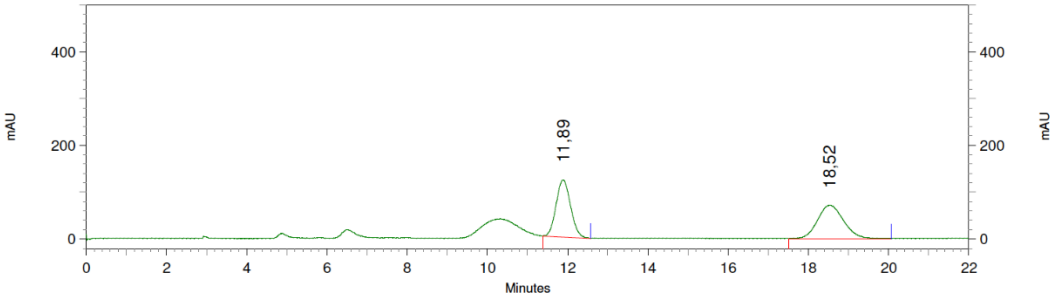
32: 251 nm, 4 nm
Results

Retention Time	Area	Area Percent
14,62	34470803	86,701
16,38	5287407	13,299



3lb

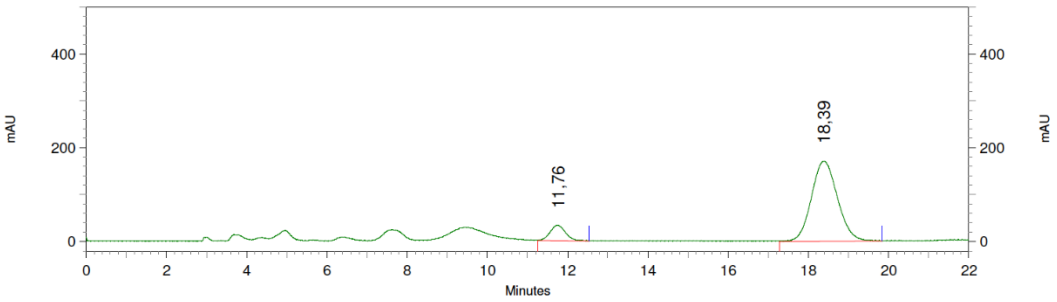
- Non enantioselective reaction



33: 291 nm, 4 nm
Results

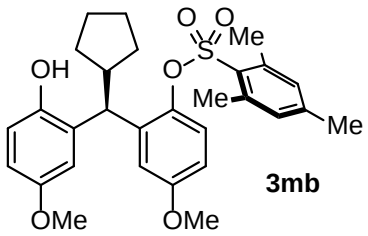
Retention Time	Area	Area Percent
11,89	12327089	48,547
18,52	13065210	51,453

- Enantioselective reaction



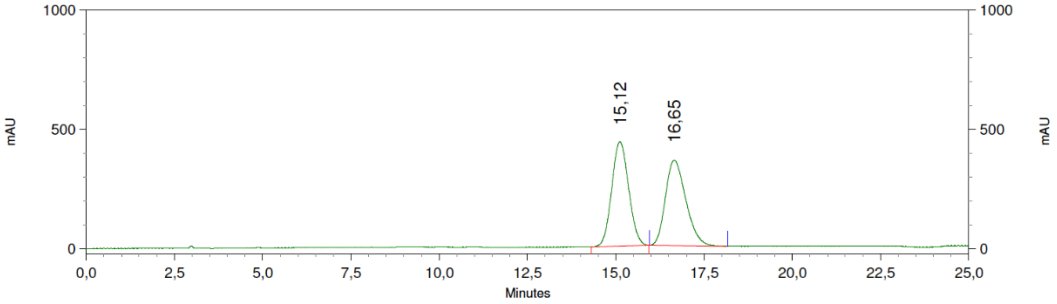
40: 236 nm, 4 nm
Results

Retention Time	Area	Area Percent
11,76	3529149	10,277
18,39	30812651	89,723



3mb

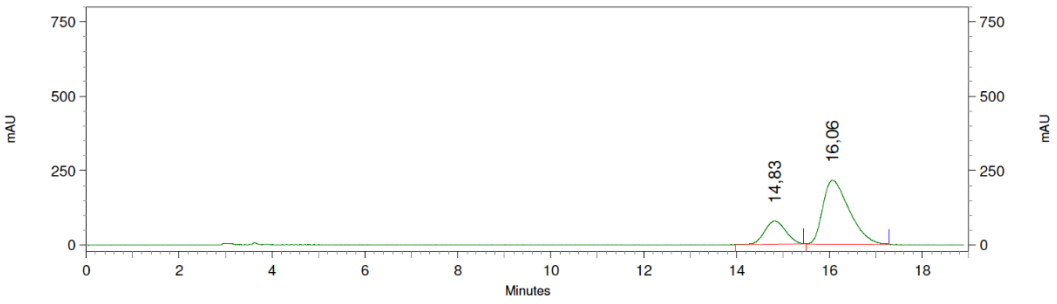
- Non enantioselective reaction



18: 224 nm, 4 nm
Results

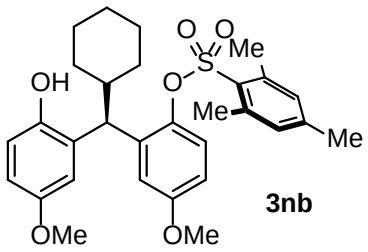
Retention Time	Area	Area Percent
15,12	58297111	50,220
16,65	57786241	49,780

- Enantioselective reaction



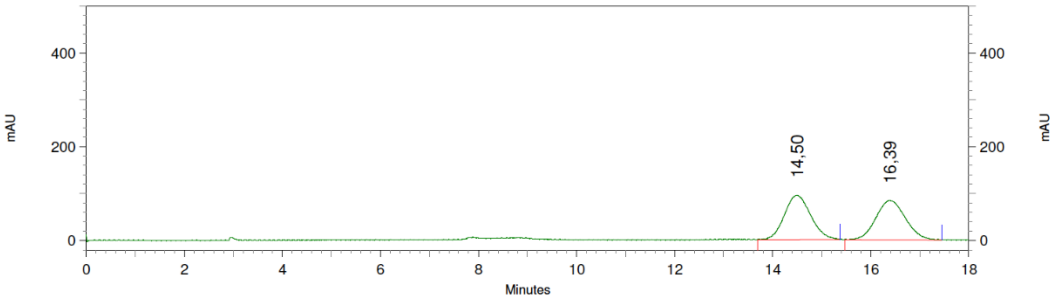
32: 251 nm, 4 nm
Results

Retention Time	Area	Area Percent
14,83	9885575	22,556
16,06	33942042	77,444



3nb

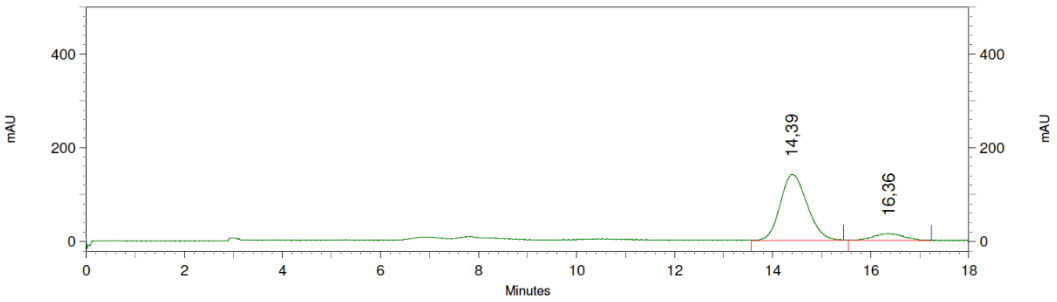
- Non enantioselective reaction



30: 248 nm, 4 nm
Results

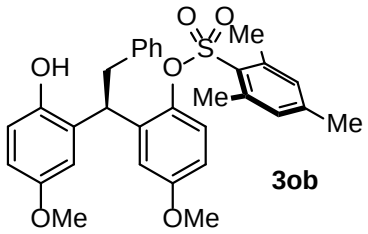
Retention Time	Area	Area Percent
14,50	14160713	50,017
16,39	14150921	49,983

- Enantioselective reaction



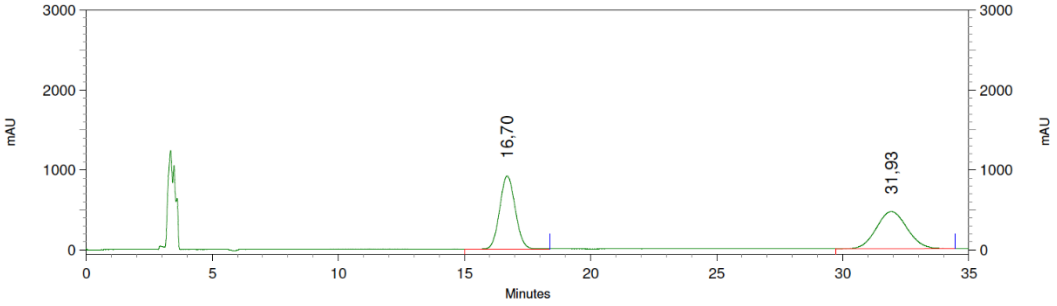
41: 252 nm, 4 nm
Results

Retention Time	Area	Area Percent
14,39	21365037	89,185
16,36	2590946	10,815



3ob

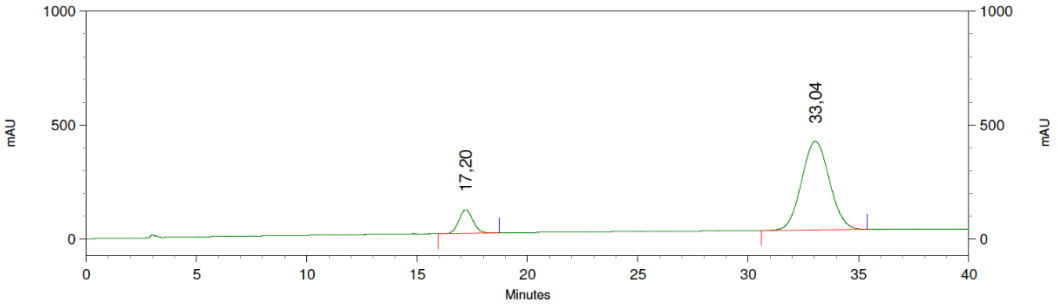
- Non enantioselective reaction



10: 206 nm, 4 nm
Results

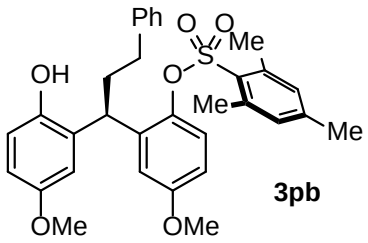
Retention Time	Area	Area Percent
16,70	157421627	49,905
31,93	158022849	50,095

- Enantioselective reaction



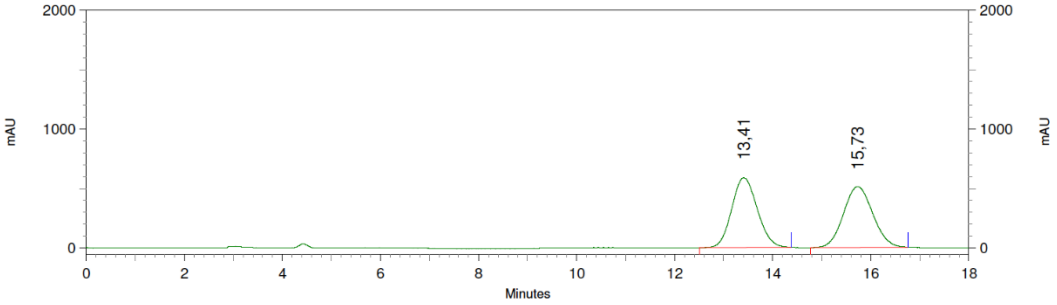
10: 223 nm, 4 nm
Results

Retention Time	Area	Area Percent
17,20	18227847	11,786
33,04	136429226	88,214



3pb

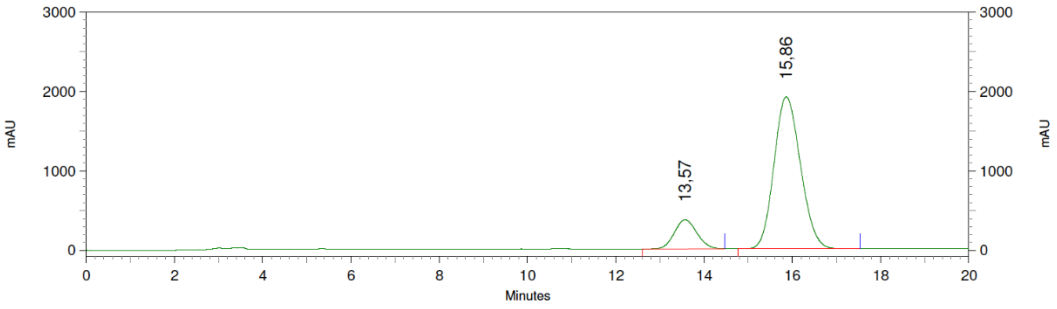
- Non enantioselective reaction



18: 227 nm, 4 nm
Results

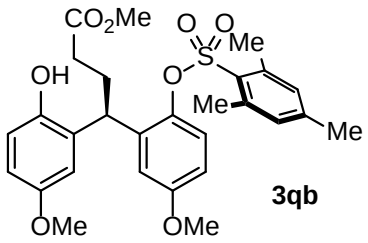
Retention Time	Area	Area Percent
13,41	85081146	50,073
15,73	84831937	49,927

- Enantioselective reaction



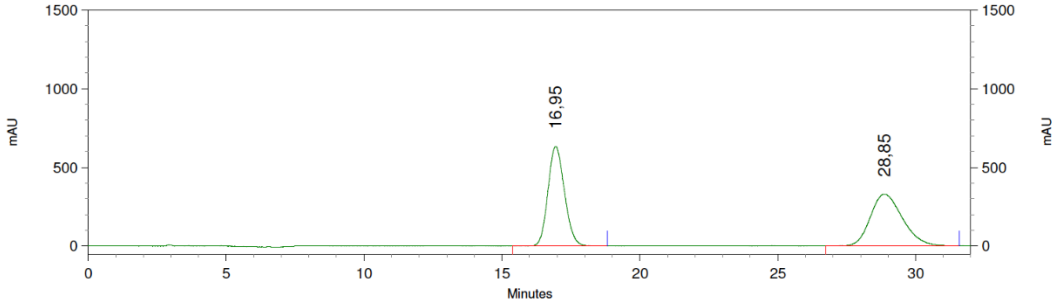
10: 223 nm, 4 nm
Results

Retention Time	Area	Area Percent
13,57	52326652	14,051
15,86	320066793	85,949



3qb

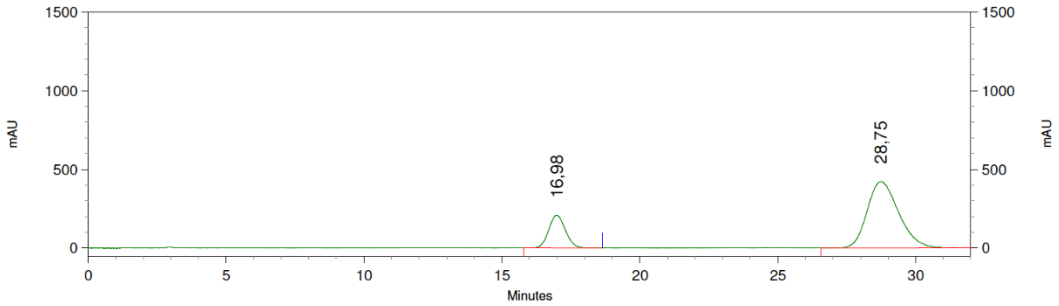
- Non enantioselective reaction



11: 231 nm, 4 nm
Results

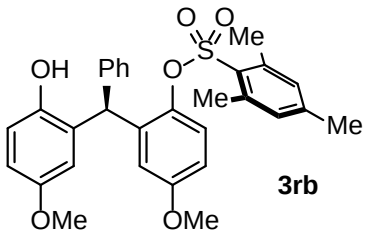
Retention Time	Area	Area Percent
16,95	105437325	49,842
28,85	106104468	50,158

- Enantioselective reaction



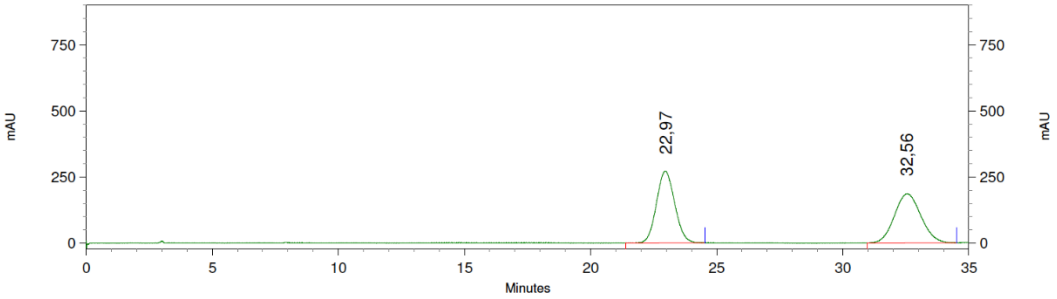
11: 231 nm, 4 nm
Results

Retention Time	Area	Area Percent
16,98	34925682	20,651
28,75	134201059	79,349



3rb

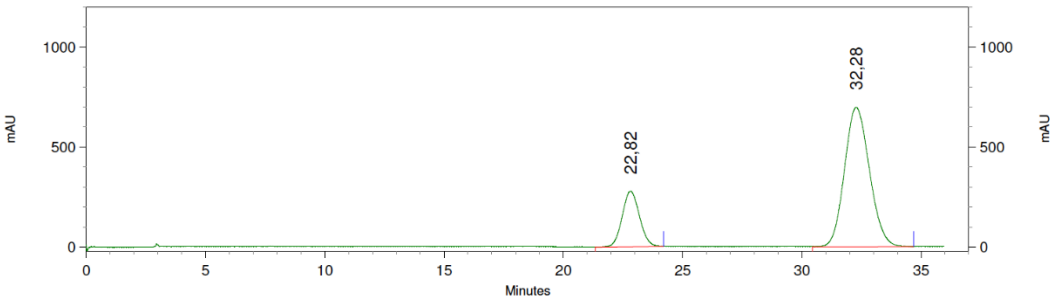
- Non enantioselective reaction



16: 218 nm, 4 nm
Results

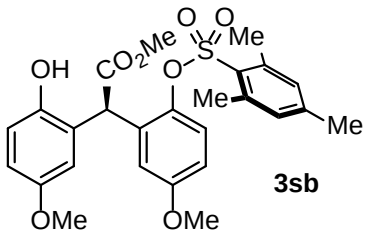
Retention Time	Area	Area Percent
22,97	55075835	50,227
32,56	54578053	49,773

- Enantioselective reaction



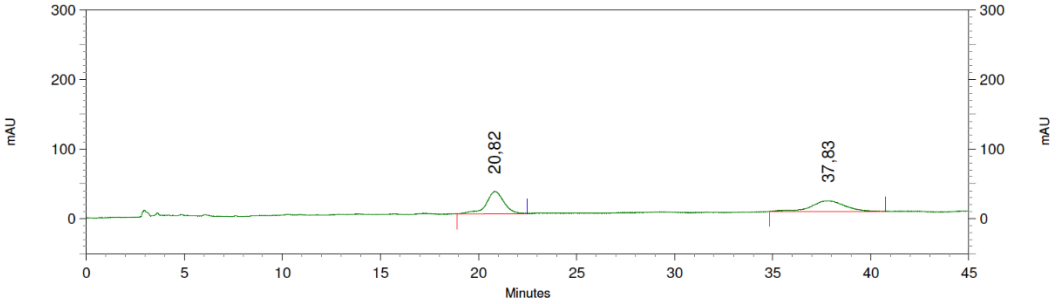
16: 218 nm, 4 nm
Results

Retention Time	Area	Area Percent
22,82	56013840	21,583
32,28	203515401	78,417



3sb

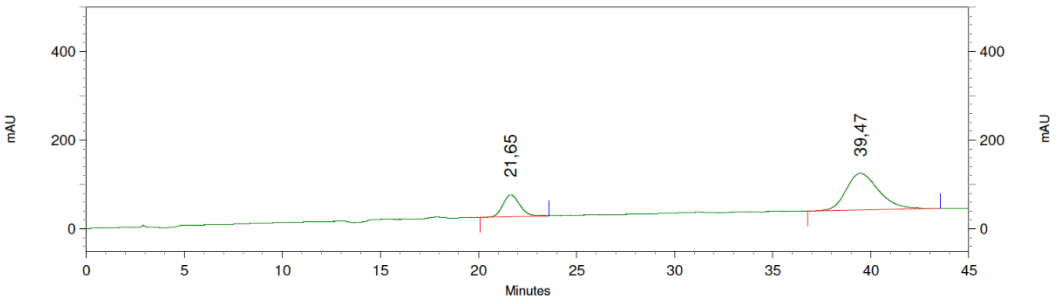
- Non enantioselective reaction



11: 231 nm, 4 nm
Results

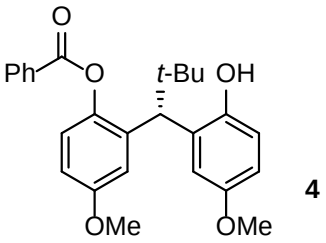
Retention Time	Area	Area Percent
20,82	8074551	50,963
37,83	7769336	49,037

- Enantioselective reaction



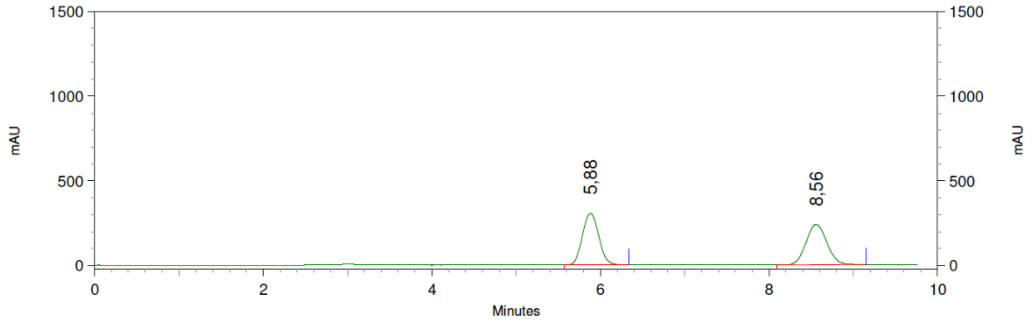
11: 231 nm, 4 nm
Results

Retention Time	Area	Area Percent
21,65	11729727	23,435
39,47	38323507	76,565



4

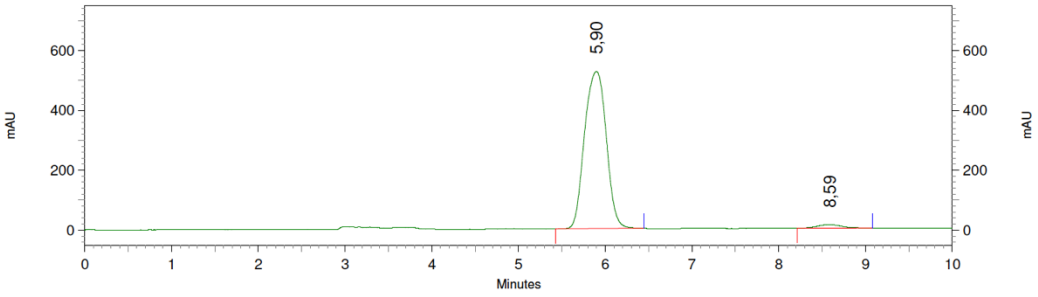
- Non enantioselective reaction



40: 236 nm, 4 nm
Results

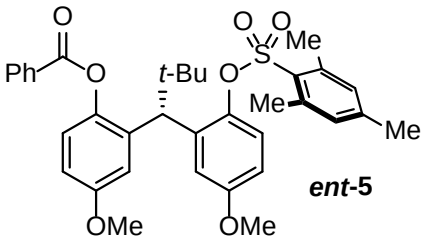
Retention Time	Area	Area Percent
5,88	16384921	50,095
8,56	16323085	49,905

- Enantioselective reaction



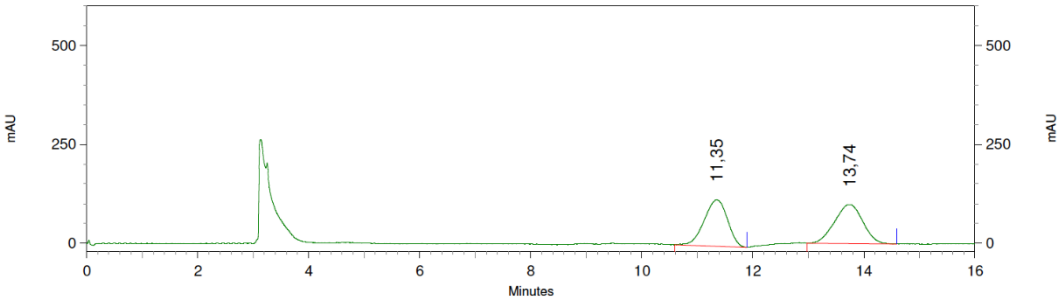
10: 232 nm, 4 nm
Results

Retention Time	Area	Area Percent
5,90	36475714	97,662
8,59	873364	2,338



***ent*-5**

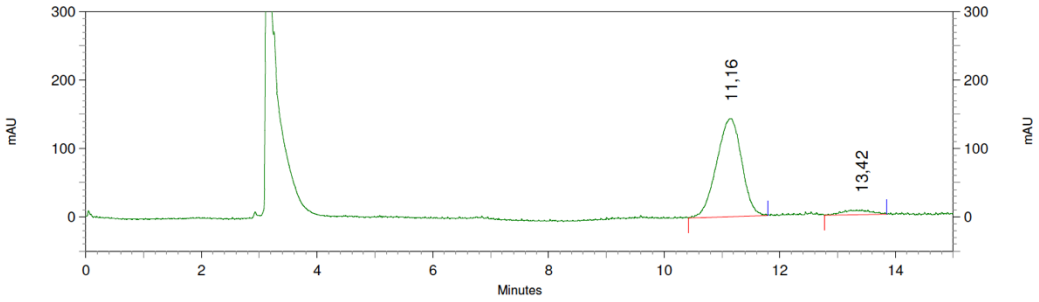
- Non enantioselective reaction



23: 205 nm, 4 nm
Results

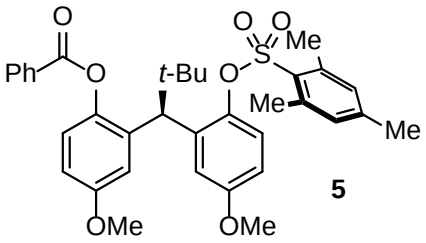
Retention Time	Area	Area Percent
11,35	13688633	49,263
13,74	14098486	50,737

- Enantioselective reaction



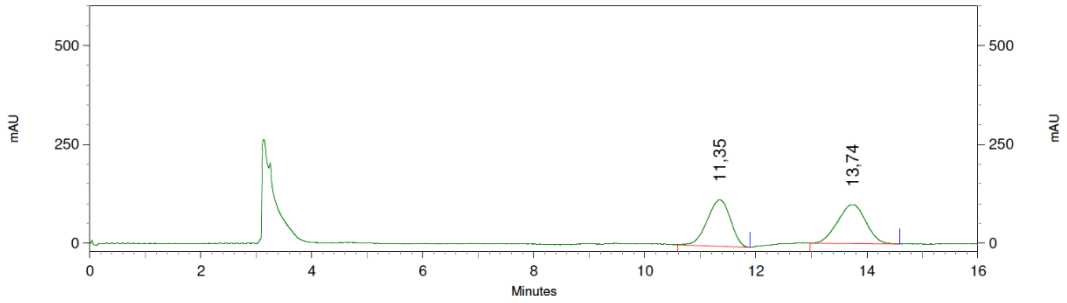
10: 202 nm, 4 nm
Results

Retention Time	Area	Area Percent
11,16	17275483	94,624
13,42	981550	5,376



5

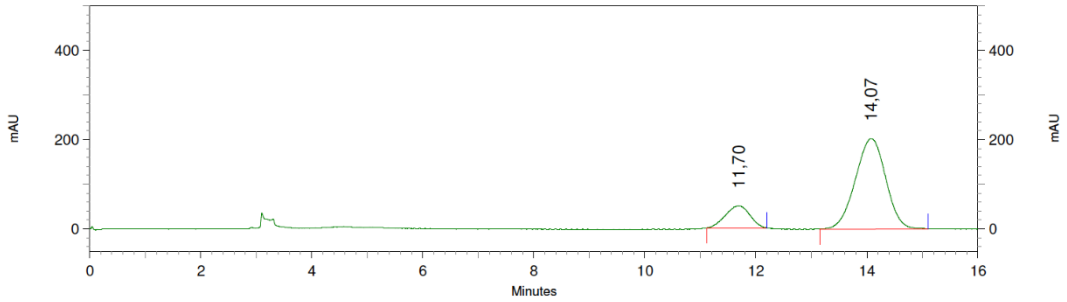
- Non enantioselective reaction



23: 205 nm, 4 nm
Results

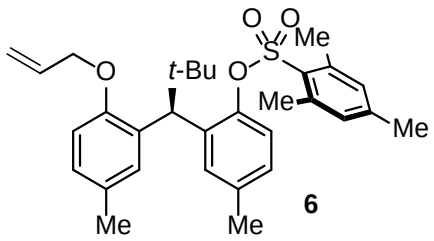
Retention Time	Area	Area Percent
11,35	13688633	49,263
13,74	14098486	50,737

- Enantioselective reaction



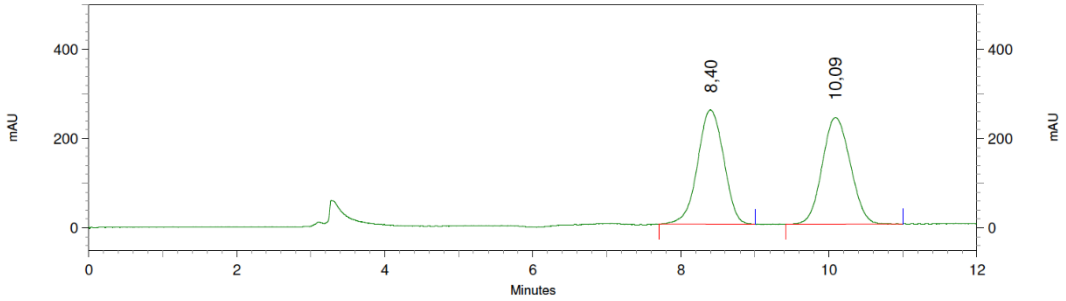
3: 216 nm, 4 nm Results

Retention Time	Area	Area Percent
11,70	6082299	16,496
14,07	30788679	83,504



6

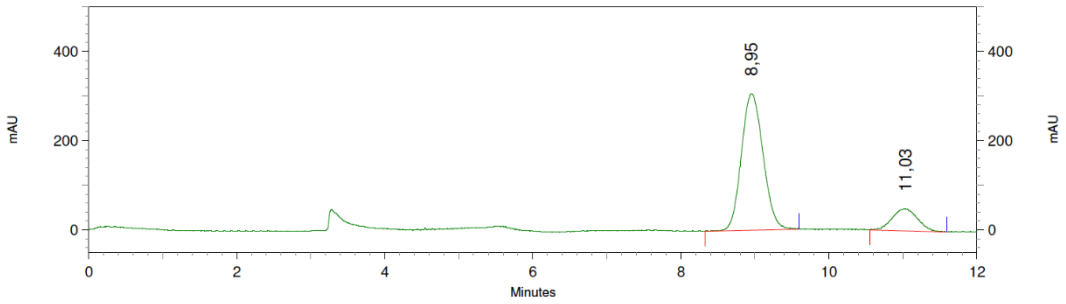
- Non enantioselective reaction



3: 216 nm, 4 nm Results

Retention Time	Area	Area Percent
8,40	25209901	49,935
10,09	25275509	50,065

- Enantioselective reaction



5: 220 nm, 4 nm Results

Retention Time	Area	Area Percent
8,95	24934482	84,001
11,03	4749164	15,999