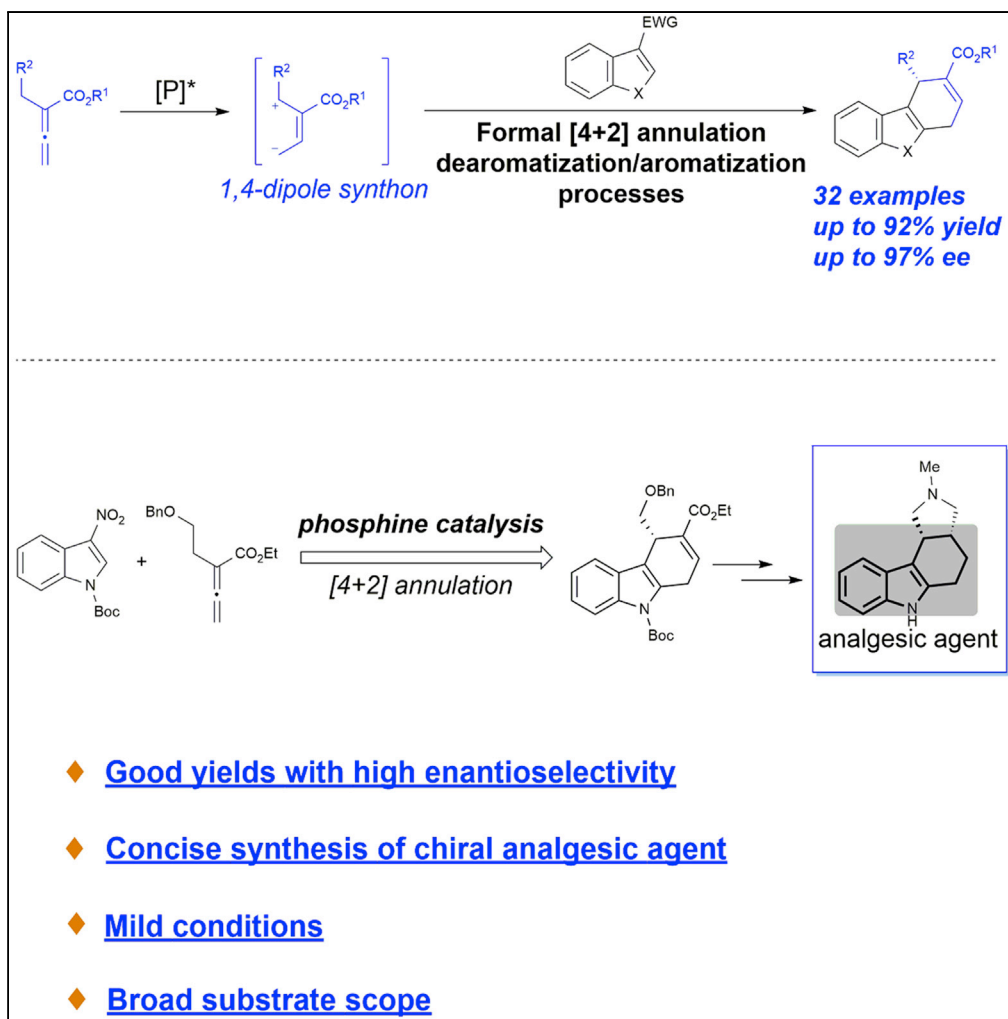


Article

Enantioselective [4+2] Annulation to the Concise Synthesis of Chiral Dihydrocarbazoles



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HIGHLIGHTS

High regio-, chemo-, and enantioselectivity

Broad substrate scope

Dearomatization/
aromatization steps
proceed under mild
conditions

Concise synthesis of chiral
analgesic agent

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Article

Enantioselective [4+2] Annulation to the Concise Synthesis of Chiral Dihydrocarbazoles

Haiyang Wang,¹ Qingdong Hu,¹ Mingxu Wang,¹ and Chang Guo^{1,2,*}**SUMMARY**

A highly efficient phosphine-catalyzed enantioselective [4 + 2] annulation of allenates with 3-nitroindoles or 3-nitrobenzothiophenes has been developed. The protocol represents a unique dearomatization-aromatization process to access functionalized dihydrocarbazoles or dihydrodibenzothiophenes with high optical purity (up to 97% ee) under mild reaction conditions. The synthetic utility of the highly enantioselective [4 + 2] annulation enables a concise synthesis of analgesic agent.

INTRODUCTION

Fused polycyclic indoles are common structural motifs found in a vast array of natural and biologically active molecules (Saxton, 1996; Knölker and Reddy, 2002; Schmidt et al., 2012; Tan and Cheng, 2019), such as kopsihainanine A, isoelliptitoxin, and analgesic agents (Scheme 1A) (Madalengoitia and Macdonald, 1993; Carmosin et al., 2000; Chen et al., 2011). In this regard, the development of efficient methods for enantioselective construction of hydrocarbazole skeleton is still highly demanded (Sings et al., 2001; Lu et al., 2012; Zhou et al., 2015; Gu et al., 2016). The group of Jørgensen disclosed a novel [4 + 2] annulation by trienamine catalysis, thus obtaining dihydrocarbazoles in good yields and enantioselectivities (Li et al., 2016b). In this context, we hypothesized that the development of new methods through the enantioselective phosphine-catalyzed [4 + 2] dearomatization would provide practical and efficient approach to this class of enantioenriched heterocycles (Scheme 1B).

Phosphine catalysis has been recognized as a reliable tool for the development of unique transformations of allenates, allowing for the discovery of novel asymmetric synthetic methodology (Lu et al., 2001; Methot and Roush, 2004; Ye et al., 2008; Cowen and Miller, 2009; Wei and Shi, 2010, 2017; Fan and Kwon, 2013; Wang et al., 2014, 2016; López and Mascareñas, 2014; Xie and Huang, 2015; Li and Zhang, 2016a; Li and Lu, 2017; Ni et al., 2018; Guo et al., 2018). Considerable research efforts have been devoted to the development of new methods for the phosphine-catalyzed enantioselective reactions. The use of phosphine catalysts has introduced a set of elementary steps that operate via discrete reactive species, allowing access to natural products and pharmaceuticals (Tran and Kwon, 2005; Andrews and Kwon, 2012; Han et al., 2012; Wang and Krische, 2003; Cai et al., 2016). One particularly versatile and reactive species is the phosphine-mediated 1,4-dipole generated upon addition of the phosphine catalyst to an allenate substrate, thus providing a concise approach for accessing enantioselective annulations. Specially, Kwon group reported the result of their pioneering studies toward the development of a novel [4 + 2] annulation reaction of allenates and *N*-tosylimines in the presence of phosphine catalyst (Zhu et al., 2003). Later, Fu group reported the phosphine-catalyzed highly enantioselective [4 + 2] annulation of *N*-tosylimines with allenates (Wurz and Fu, 2005). Although great achievements have been made, concise syntheses of useful heterocycles involving phosphine-catalyzed [4 + 2] annulations in asymmetric versions were still rare (Tran and Kwon, 2007; Wang and Ye, 2010; Tran et al., 2011; Xiao et al., 2011; Baskar et al., 2011; Yu and Ma, 2012; Zhong et al., 2012; Takizawa et al., 2014; Yu et al., 2014; Liu et al., 2016; Wang and Guo, 2019a). Moreover, the development of an enantioselective phosphine-catalyzed [4 + 2] dearomatization reaction would provide an attractive and complementary approach for construction of privileged motifs, which will be of great value for the synthesis of bioactive molecules (Scheme 1C).

Enantioselective dearomatization reactions of heteroaromatic compounds are very powerful transformations because they provide direct access to a wide variety of chiral heterocycles (You, 2016; Roche and Porco, 2011; Zhuo et al., 2012; Zhuo et al., 2014; Zheng and You, 2016; Sun et al., 2016; Wu et al., 2016). In recent years, 3-nitroindole was demonstrated to be a good substrate for various dearomatization

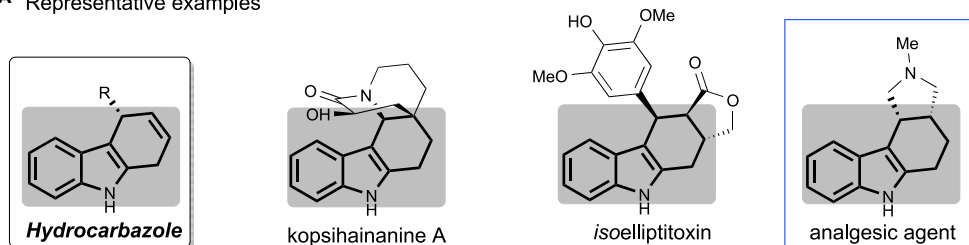
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²Lead Contact

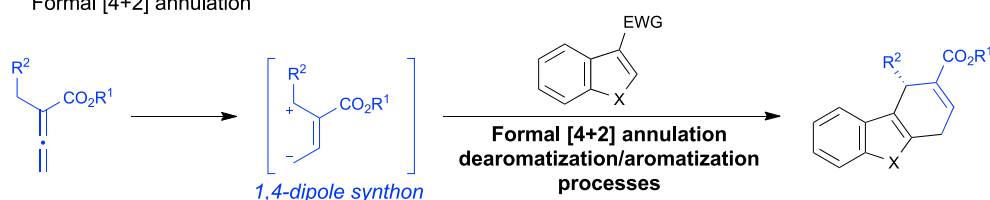
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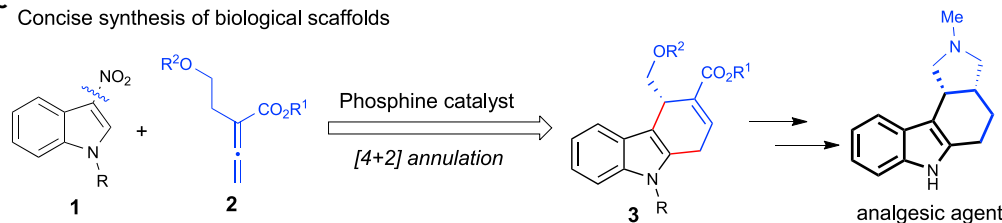
A Representative examples



B Formal [4+2] annulation



C Concise synthesis of biological scaffolds



Scheme 1. Phosphine-catalyzed [4 + 2] Dearomatization/Aromatization Reactions for the Formation of Enantioenriched Heterocycles

(A) Representative examples of chiral hydrocarbazole derivatives.
 (B) Formal [4 + 2] annulation for the preparation of hydrocarbazole.
 (C) Concise approach to the enantioselective synthesis of analgesic agent.

processes, and a number of enantioselective approaches have been reported (Awata and Arai, 2014; Zhao et al., 2015a, 2015b, 2018, 2019; Gerten and Stanley, 2016; Trost et al., 2014; Cheng et al., 2018; Zhang et al., 2018; Sun et al., 2018; Yue et al., 2017; Yang et al., 2019). Importantly, Lu group (Li et al., 2019) and Zhang group (Wang et al., 2019b) independently reported the efficient phosphine-catalyzed enantioselective [3 + 2] annulation of 3-nitroindoles with allenates to afford cyclopentaindoline products in high yields and excellent enantioselectivities. We envisaged that heteroaromatic systems bearing an electron-withdrawing group could react with phosphine-mediated zwitterionic intermediate in a process involving the [4 + 2] reaction to achieve the chiral dihydrocarbazole scaffold (Scheme 1C). With this objective in mind, a readily available 3-nitroindole derivative was selected as a model substrate to investigate the optimum reaction condition for the enantioselective [4 + 2] dearomatization reaction using a phosphine catalyst.

RESULTS AND DISCUSSION

Based on our previous work on phosphine chemistry (Wang and Guo, 2019a), we initiated the study by investigating the reaction between **1a** and **2a** in the presence of the phosphine **4a** (Table 1, entry 1). Initially, diverse chiral phosphine catalysts were examined (entries 1–5). However, the catalyst **4a** to **4c** did not work for this reaction (entries 1–3). To our great delight, the desired dihydrocarbazole **3a** could be obtained when the chiral phosphine **4d** was employed (entry 4). After surveying an array of additives, we determined that silica gel can promote elimination of HNO_2 for the aromatization process to afford the corresponding adduct in 92% yield with 94% ee (entry 4) (So and Mattson, 2012; Long et al., 2016). Other additives, such as $\text{Sc}(\text{OTf})_3$, Et_3N , and SnCl_2 led to byproducts (for further details, see Table S1 in the Supplemental Information). Furthermore, the ee values of the **3a** decreased to 80% with low yield in the presence of **4e** as catalyst (entry 5). Varying the solvents led to no improvement in the reaction, and toluene was proven to be the best choice (entries 4 vs 6–8). Further optimization studies revealed that the protection group of the 3-nitroindole was also sensitive to the reaction, and the variation of the *N*-substituent of the 3-nitroindole **1a'** or **1a''** generated no product at all (entries 9 and 10) (Rivinoja et al., 2017; Suo et al., 2018).

Entry	1	4	Solvent	Yield (%) ^a	ee (%) ^b
1	1a	4a	Toluene	nr	–
2	1a	4b	Toluene	nr	–
3	1a	4c	Toluene	nr	–
4	1a	4d	Toluene	92	94
5	1a	4e	Toluene	26	80
6	1a	4d	CH ₂ Cl ₂	23	73
7	1a	4d	THF	73	84
8	1a	4d	Dioxane	57	90
9	1a'	4d	Toluene	nr	–
10	1a''	4d	Toluene	nr	–

Table 1. Optimization of Reaction Conditions

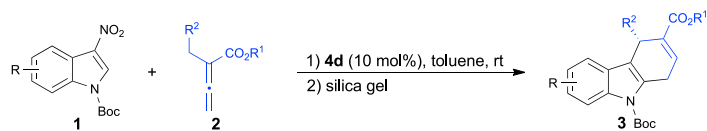
Unless indicated otherwise, the reaction were conducted with **1** (0.1 mmol), **2a** (0.15 mmol), and **4** (0.01 mmol) in toluene (1.0 mL) at room temperature for 18 h. Then silica gel (200 mg) was added to the reaction mixture to complete elimination of HNO₂. nr = no reaction.

^aYield of isolated product.

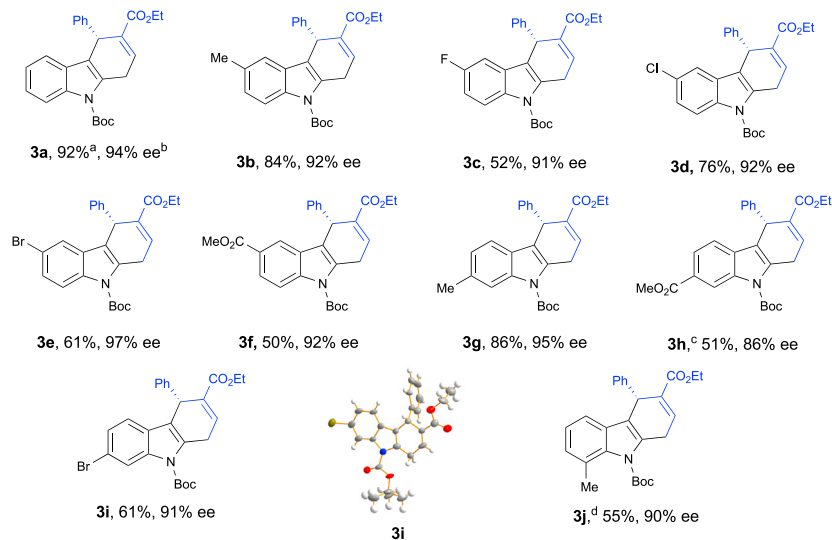
^bDetermined by HPLC analysis.

With the optimal reaction conditions in hand, we set out to explore the substrate scope of the procedure. As shown in [Scheme 2](#), various electron-withdrawing or donating groups on the indole were well tolerated and resulted in excellent levels of enantioselectivities ranging from 86% to 97% ee (**3a–3j**). The extension of the protocol to the 3-nitroindole with a variety of substitution patterns at the 5-position was successful to afford corresponding adducts with excellent enantioselectivities (**3b–3f**). To our delight, substrates bearing substituents on different positions of the indole ring also facilitate the annulation with high yields and ee values (**3b**, **3g**, and **3j**). The absolute configuration of the enantiopure **3i**, recrystallized from ethyl acetate and petroleum ether, was assigned by single-crystal X-ray diffraction analysis.

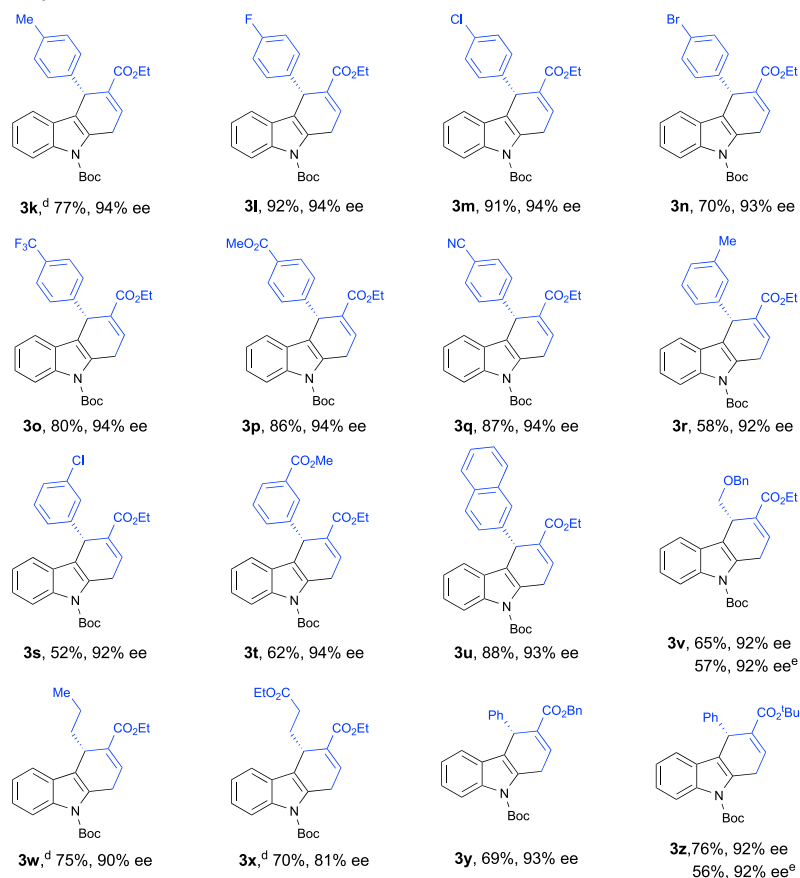
The generality of the reaction with respect to the scope of the allenates **2** was also investigated using 3-nitroindole **1a** as the reaction partner under the optimized conditions. A diverse array of allenates (**2**) with a variety of functional groups (methyl, fluoro, chloro, bromo, ester, trifluoromethyl, and cyano) performed well in this annulation reaction, and the corresponding products were isolated in good yields with high ee values (**3k–3q**). Remarkably, this method was compatible with alkyl allenates, affording the desired products in good yields with good enantioselectivity (**3v–3x**). Additionally, all reactions with different esters attached to the allenates proceeded smoothly, giving the corresponding products in good yields and excellent ee (**3y** and **3z**). To test the synthetic utility of the current annulation, we performed the reaction on a 1 mmol scale with the formation of **3z** in 56% yield and 92% ee.



The scope of 3-nitroindoles 1:



The scope of allenates 2:



Scheme 2. Substrate Scope of Enantioselective [4 + 2] Annulation

Unless indicated otherwise, the reactions were conducted with **1** (0.1 mmol), **2** (0.15 mmol), and catalyst **4d** (0.01 mmol) in toluene at room temperature for 12–48 h. Then silica gel was added to the reaction mixture to complete elimination of HNO₂.

^aYield of the isolated product after purification by chromatography on silica gel.

^bEnantiomeric excess determined by HPLC analysis.

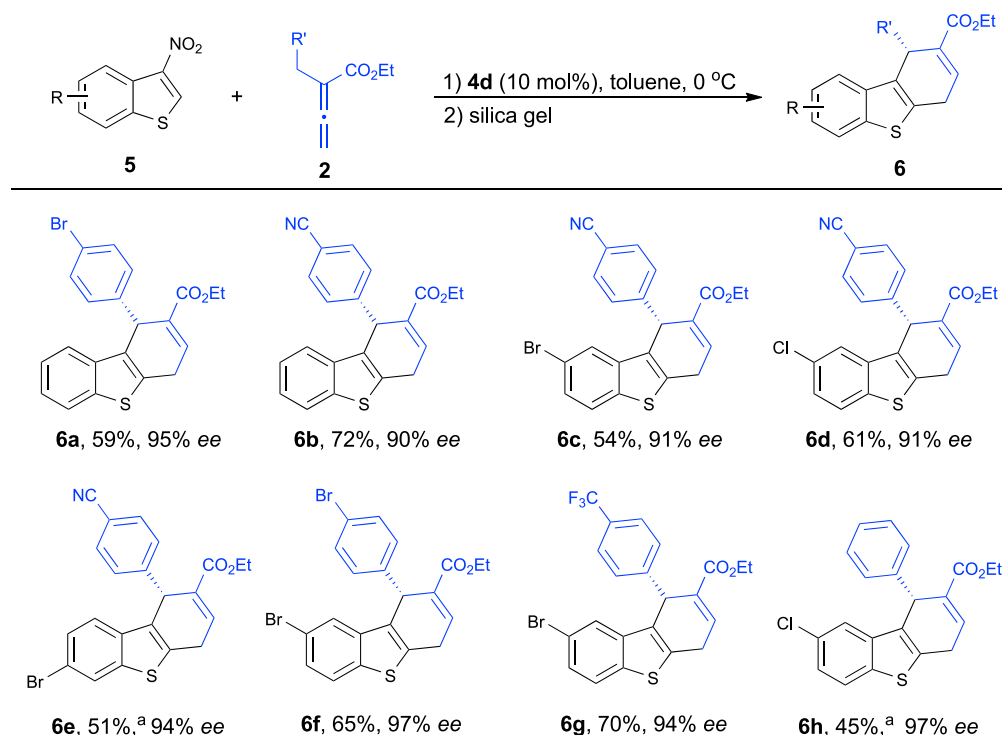
^cAromatization process was performed at 50°C.

^d20 mol% of **4d**.

^eThe reaction was performed on 1 mmol scale.

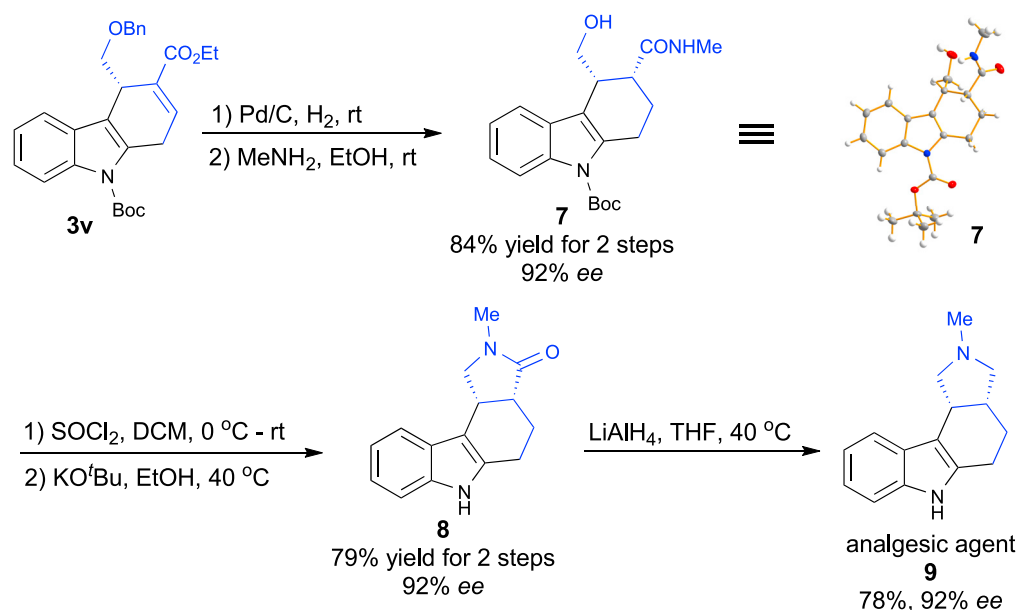
Encouraged by the excellent results with various 3-nitroindoles, we then investigated the [4 + 2] annulation reaction with a range of 3-nitrobenzothiophenes (**5**). Remarkably, process where the 3-nitrobenzothiophene as a reactive partner for asymmetric annulation has been much less studied (Tran and Kwon, 2007; Wang and Ye, 2010; Tran et al., 2011; Xiao et al., 2011; Baskar et al., 2011; Yu and Ma, 2012; Zhong et al., 2012; Takizawa et al., 2014; Yu et al., 2014; Liu et al., 2016; Wang and Guo, 2019a; Cheng et al., 2000; Cheng et al., 2017; Suo et al., 2018; Yue et al., 2018; Chen et al., 2019). Using phosphine **4d** in toluene at 0°C, we were able to access dihydrodibenzothiophene products **6** (Scheme 3). Under the optimized reaction condition (for further details, see Table S2 in the Supplemental Information), a broad range of allenates **2** and 3-nitrobenzothiophenes **5** were investigated. Allenates with different substituents on the aromatic ring underwent this catalytic transformation smoothly in good yields with excellent ee (**6a** and **6b**). Furthermore, various substitutions of 3-nitrobenzothiophenes **5** at the aromatic ring had little impact on the reactions (**6c–6h**, 91%–97% ee).

To highlight the synthetic potential of the present method, the dihydrocabazole **3v**, which was obtained from the enantioselective [4 + 2] annulation, can be easily converted into analgesic agent **9** (Scheme 4). In 2000, Carosin and co-workers obtained the racemic analgesic agent **9** via the Diels-Alder reaction,

**Scheme 3. Enantioselective [4 + 2] Annulation of 3-Nitrobenzothiophene 5**

Unless indicated otherwise, the reactions was conducted with **5** (0.1 mmol), **2** (0.15 mmol), and catalyst **4d** (0.01 mmol) in toluene (1.0 mL) at 0°C for 48–60 h. Then silica gel was added to the reaction mixture to complete elimination of HNO₂. Yield of the isolated product after purification by chromatography on silica gel. Enantiomeric excess determined by HPLC analysis.

^a0.02 mmol of **4d** was used.



Scheme 4. Enantioselective Synthesis of Analgesic Agent 9

and the optical product was obtained by using preparative chromatography (Carmosin et al., 2000). Taking advantage of our current phosphine-catalyzed enantioselective [4 + 2] reaction, we can easily obtain the analgesic agent **9** with excellent enantioselectivity. Hydrogenation of **3v** in the presence of a catalytic amount of Pd/C, followed by amidation with MeNH₂ gave rise to the desired amide **7** in 84% yield over two steps. The configuration of compound **7** was assigned by X-ray analysis. The subsequent chlorination of alcohol, deprotection of the N-Boc group and cyclization furnished **8** in good yield. Finally, the amide **8** was reduced to generate the corresponding analgesic agent **9** in 78% yield and 92% ee.

The proposed catalytic cycle for the enantioselective [4 + 2] annulation is illustrated in Figure 1. The addition of phosphine catalyst **4d** to the allenolate **2** gives the intermediate **A**, which could react with the 3-nitroindole **1** or 3-nitrobenzothiophenes **5** to form the intermediate **B**. Following migration and intramolecular conjugate addition give rise to the intermediate **D** and regenerate the phosphine **4d**. This species **D** then undergoes elimination of HNO₂ through the aromatization process to furnish the final dihydrocarbazole **3** or dihydrodibenzothiophene **6**.

In summary, we have developed simple and efficient synthetic routes to highly enriched hydrocarbazoles through chiral phosphine-catalyzed [4 + 2] annulation utilizing 3-nitroindole and allenolates as starting materials. This phosphine-catalyzed enantioselective [4 + 2] annulation procedure involving tandem dearomatization and aromatization steps proceeds under mild conditions. This reaction displays a broad substrate scope with respect to the substituents. Additionally, the obtained dihydrocarbazole could be efficiently transformed to an analgesic agent containing polycyclic indole frameworks.

Limitations of the Study

The synthesis of the products needs two steps in one pot. No product was formed with the initial addition of silica gel.

METHODS

All methods can be found in the accompanying [Transparent Methods supplemental file](#).

DATA AND CODE AVAILABILITY

Crystallographic data for the structures reported in this article have been deposited at the Cambridge Crystallographic Data Center (CCDC) under accession numbers CCDC 1938371 (**3i**) and CCDC 1955757 (**7**). Copies of the data can be obtained free of charge from www.ccdc.cam.ac.uk/structures/.

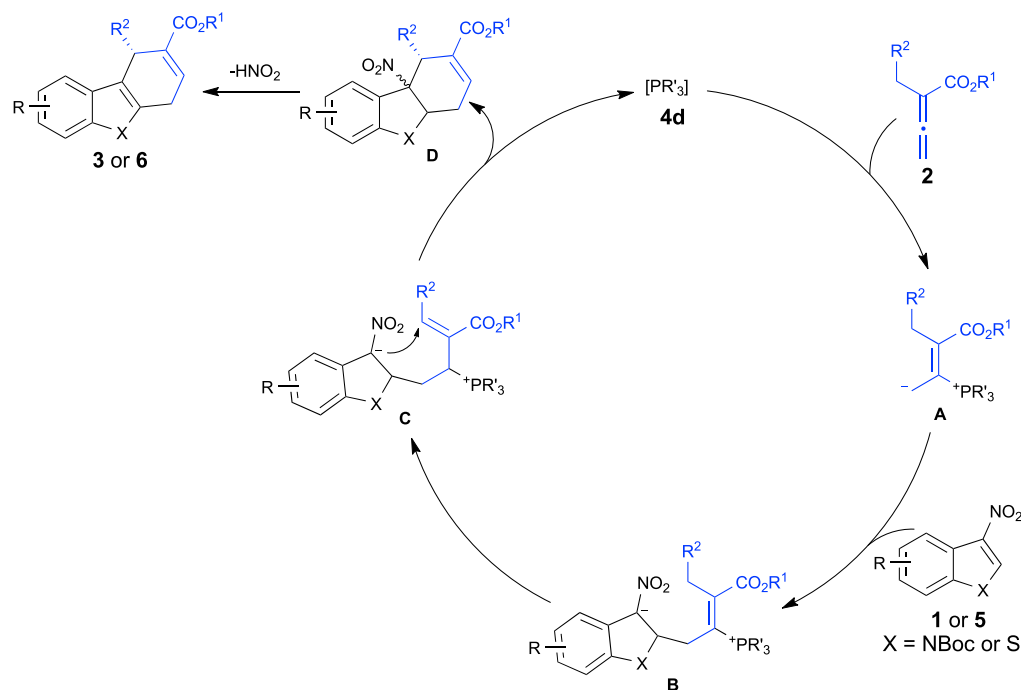


Figure 1. Proposed Mechanism

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.isci.2020.100840>.

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AUTHOR CONTRIBUTIONS

H.W. carried out the experimental and data analysis work. Q.H. and M.W. prepared some starting materials. C.G. designed the reaction and directed the project. The paper was written by C.G. with assistance of H.W., Q.H., and M.W.

DECLARATION OF INTERESTS

The authors declare no conflict of interest.

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Supplemental Information

Enantioselective [4+2] Annulation to the Concise Synthesis of Chiral Dihydrocarbazoles

Haiyang Wang, Qingdong Hu, Mingxu Wang, and Chang Guo

Supplemental Figures for NMR spectrums:

Figure S1. ¹H NMR spectrum of 3a, related to Scheme 2.

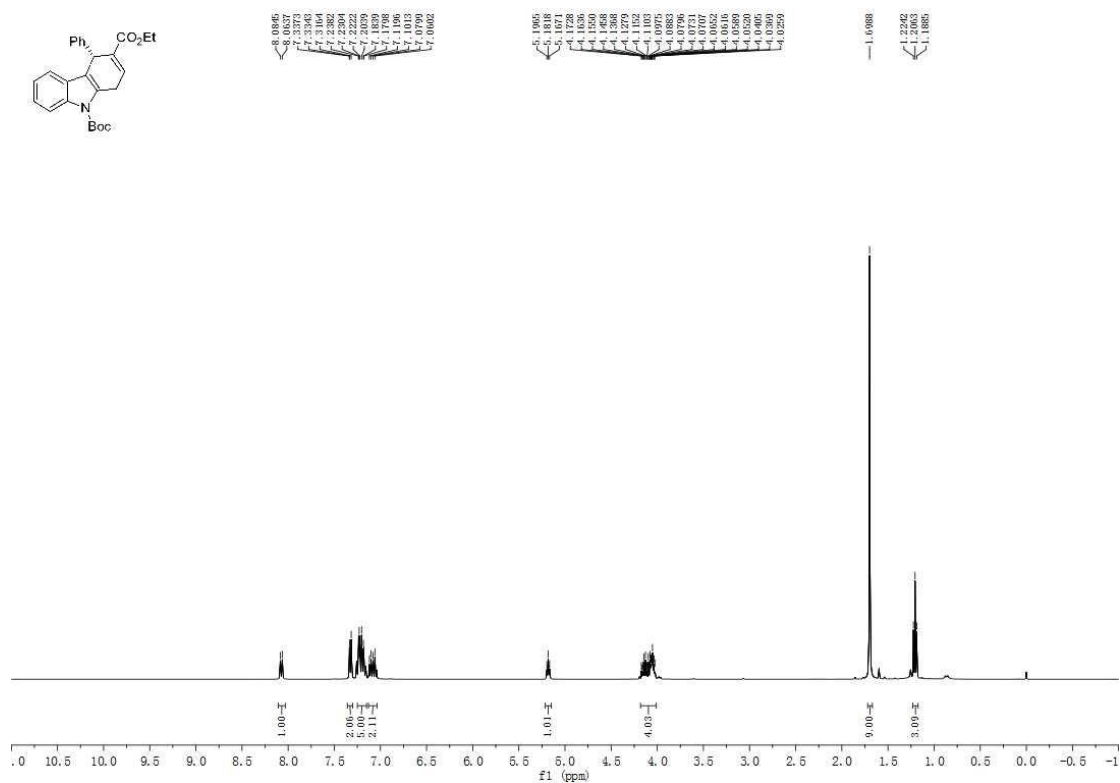


Figure S2. ¹³C NMR spectrum of 3a, related to Scheme 2.

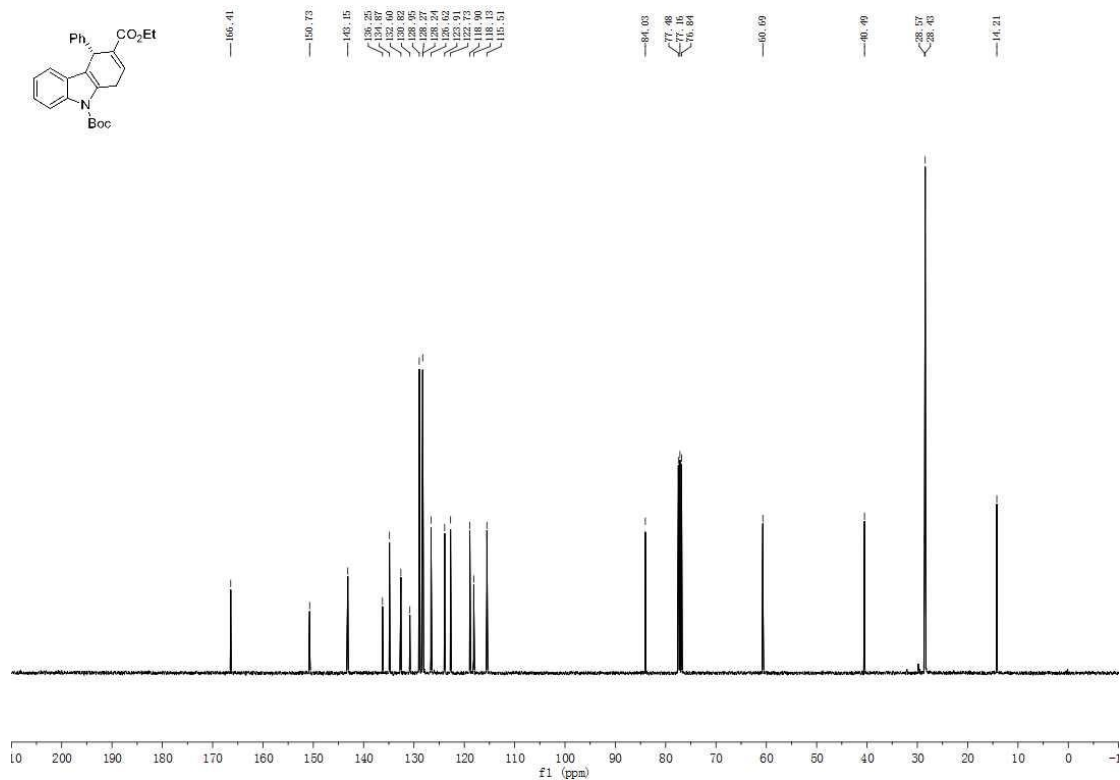


Figure S3. ¹H NMR spectrum of **3b**, related to Scheme 2.

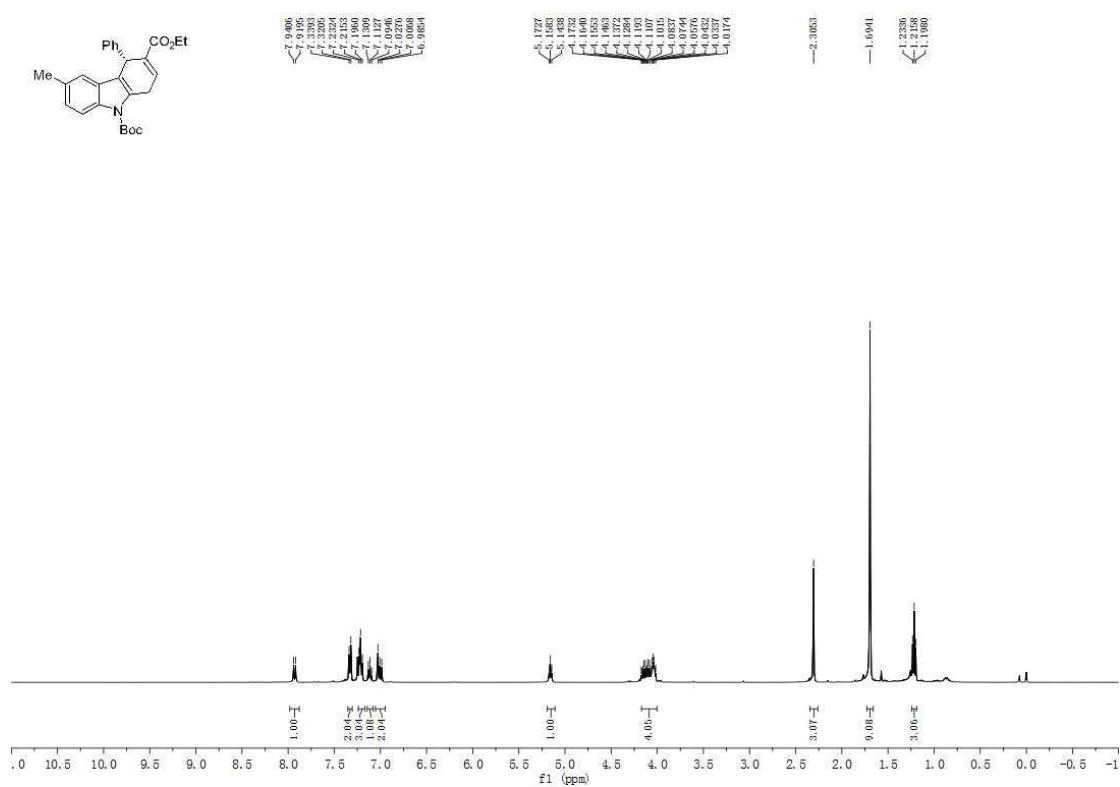


Figure S4. ¹³C NMR spectrum of **3b**, related to Scheme 2.

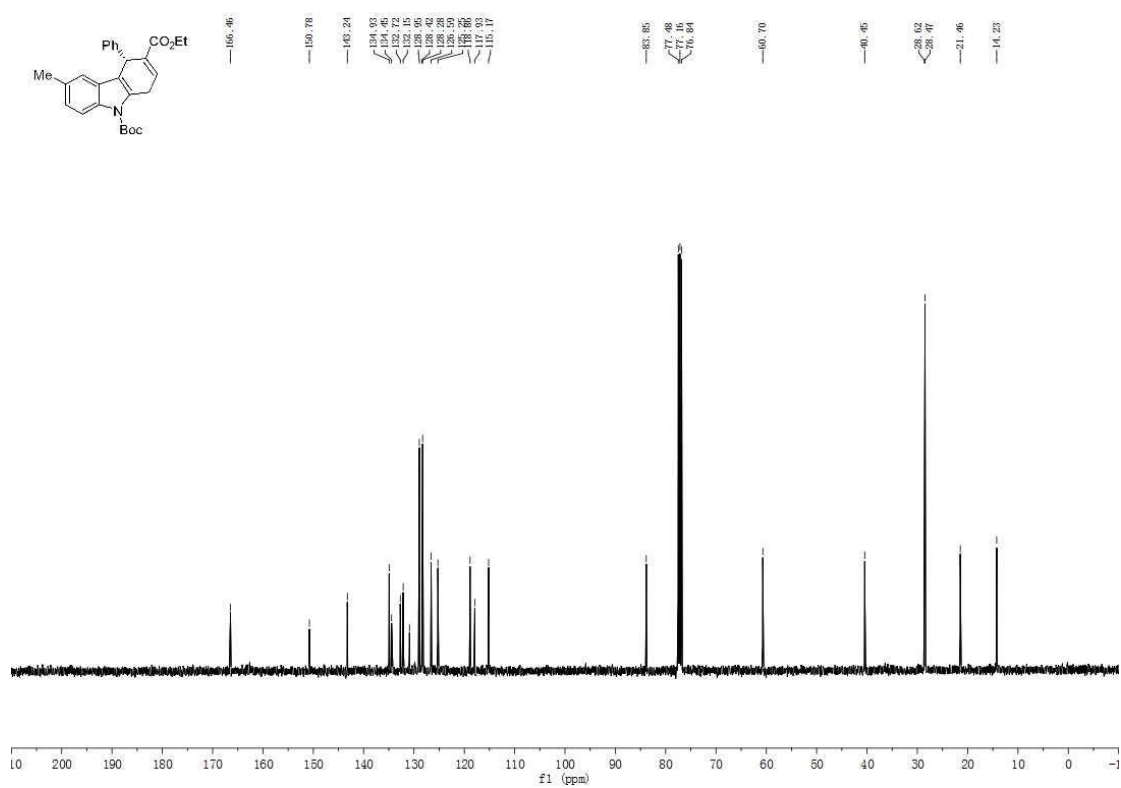


Figure S5. ¹H NMR spectrum of **3c**, related to Scheme 2.

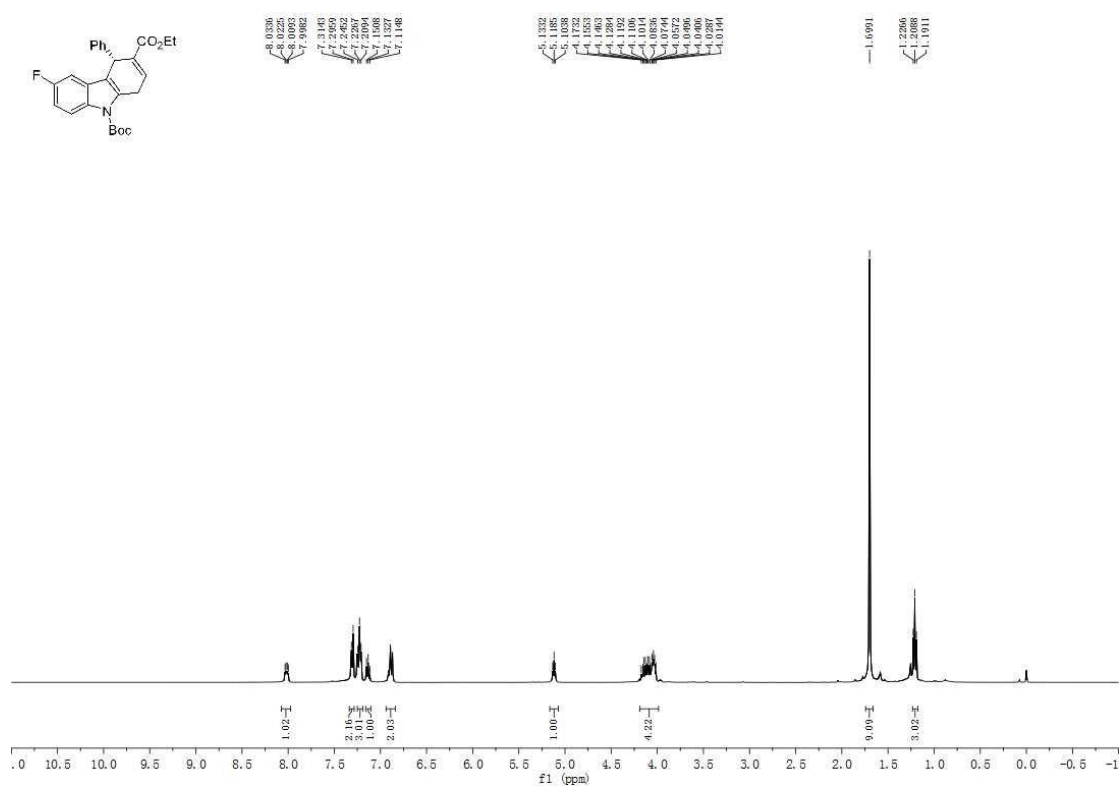


Figure S6. ¹³C NMR spectrum of **3c**, related to Scheme 2.

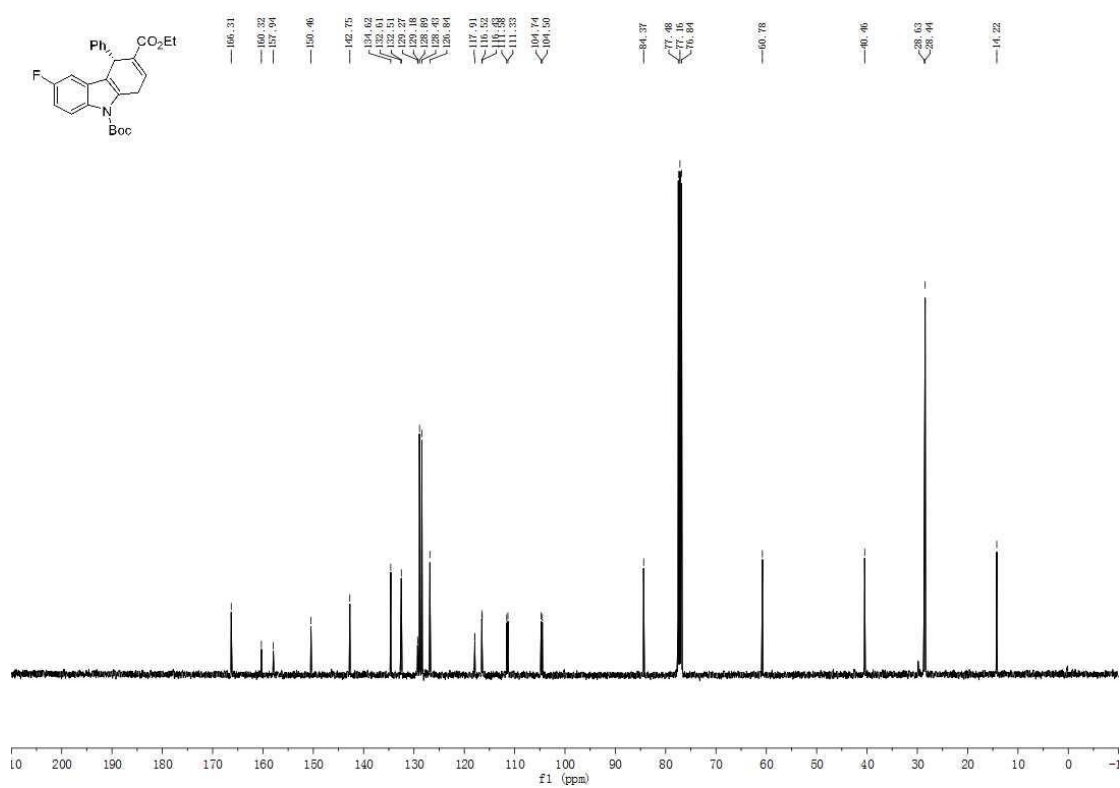


Figure S7. ^{19}F NMR spectrum of **3c**, related to **Scheme 2**.

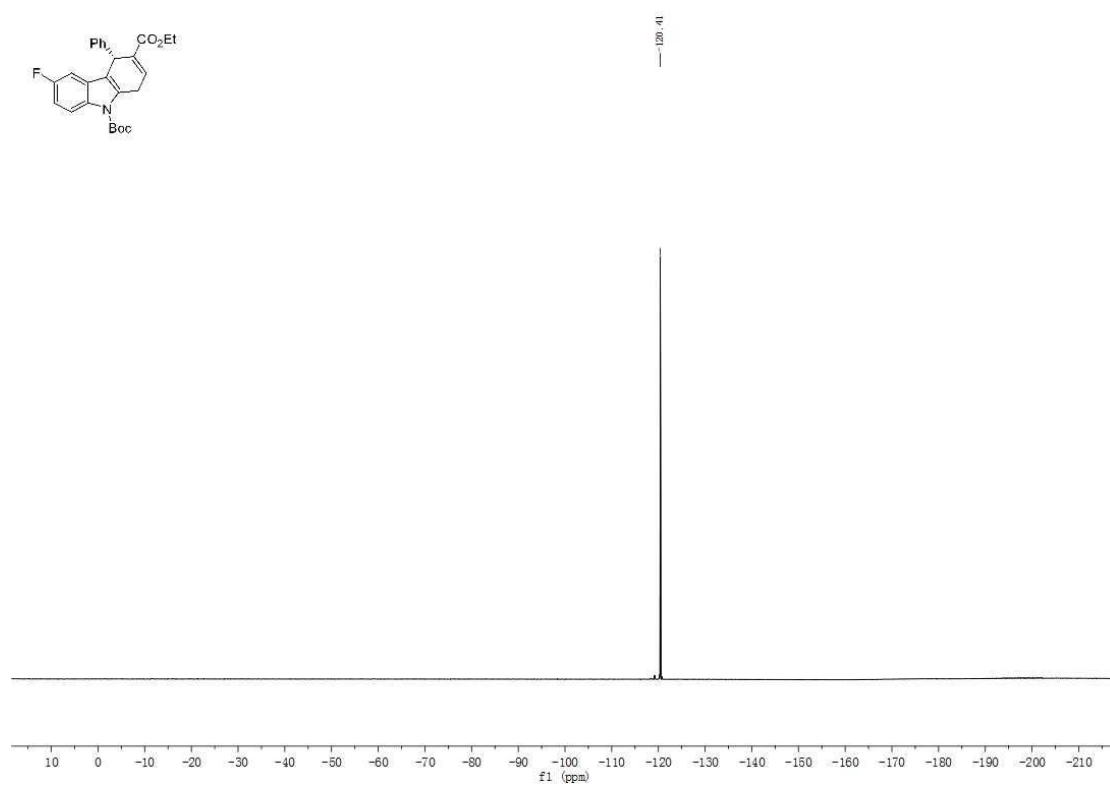


Figure S10. ¹H NMR spectrum of **3e**, related to Scheme 2.

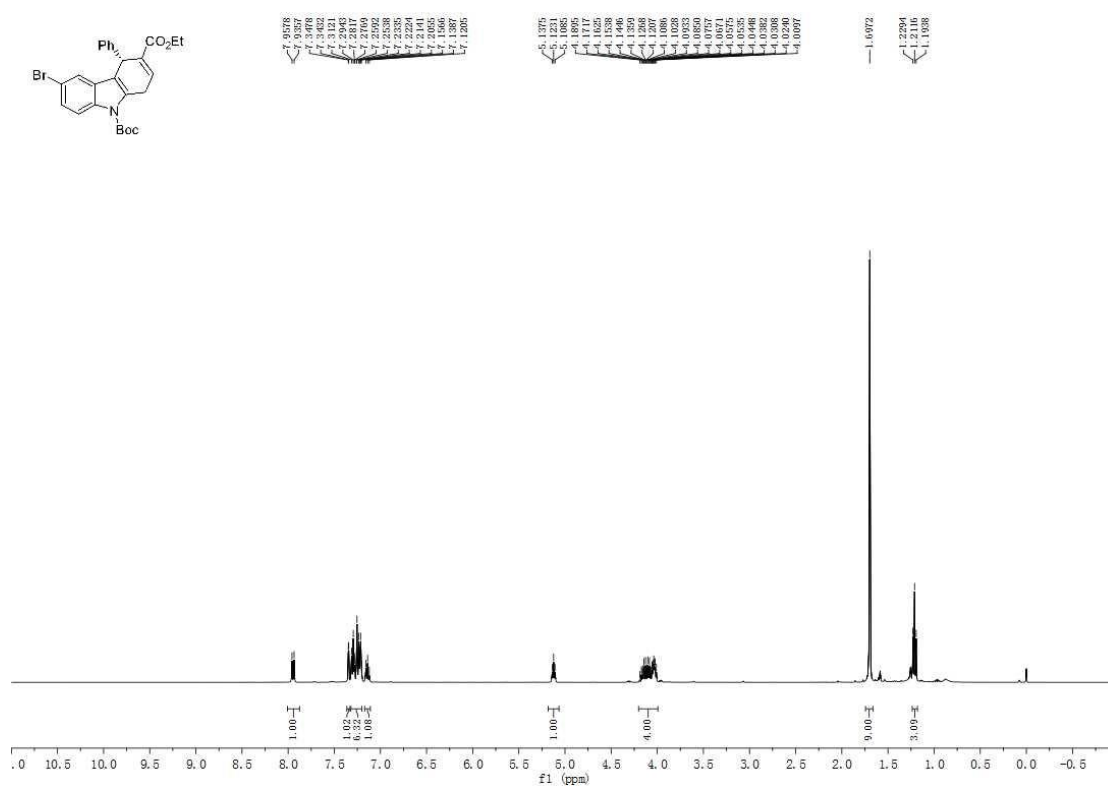


Figure S11. ¹³C NMR spectrum of **3e**, related to Scheme 2.

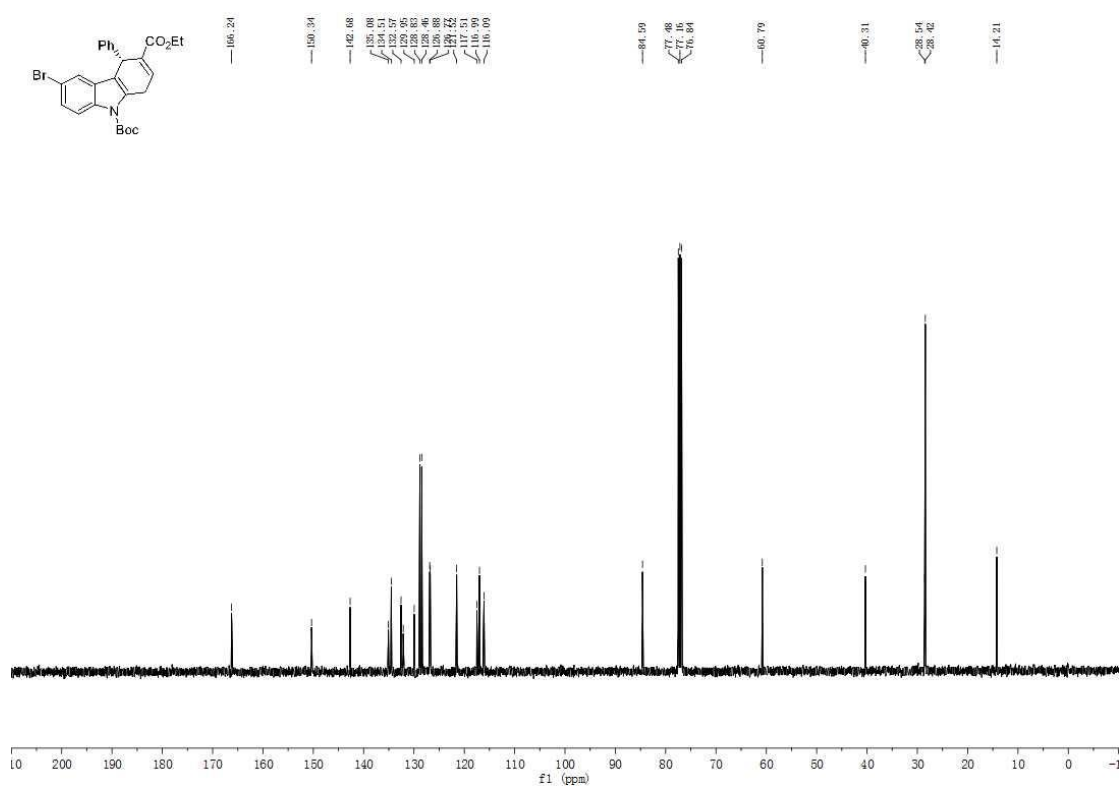


Figure S12. ¹H NMR spectrum of **3f**, related to Scheme 2.

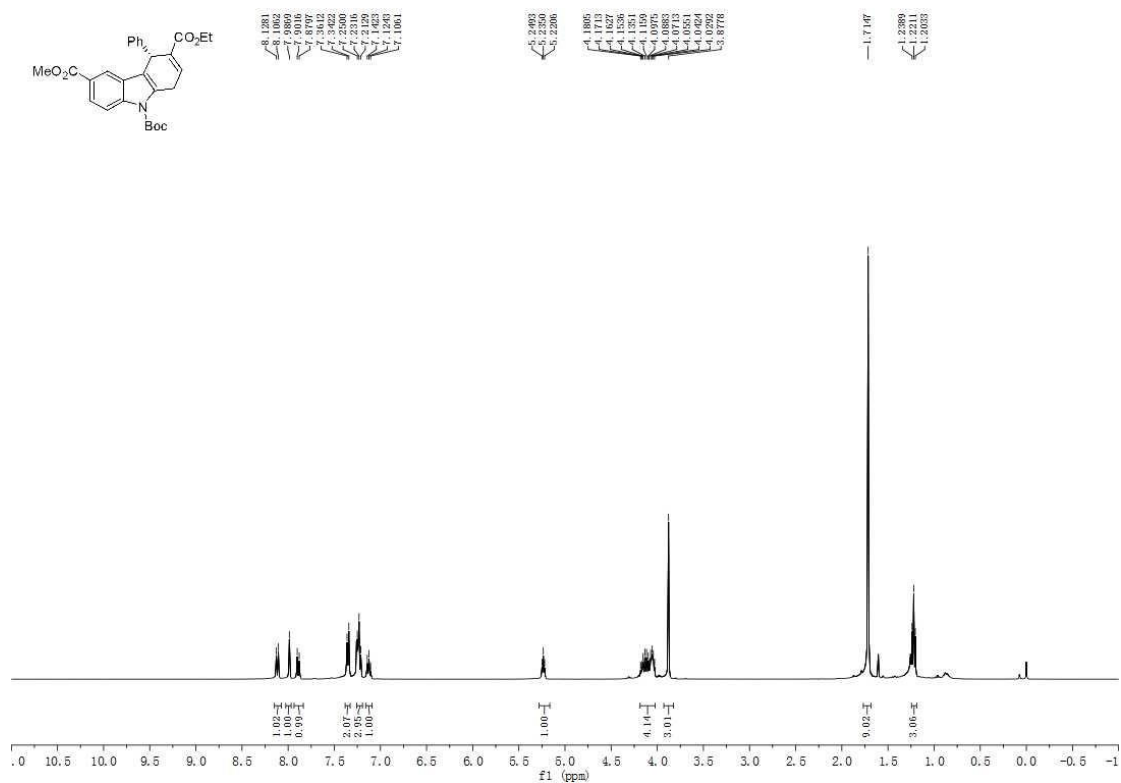


Figure S13. ¹³C NMR spectrum of **3f**, related to Scheme 2.

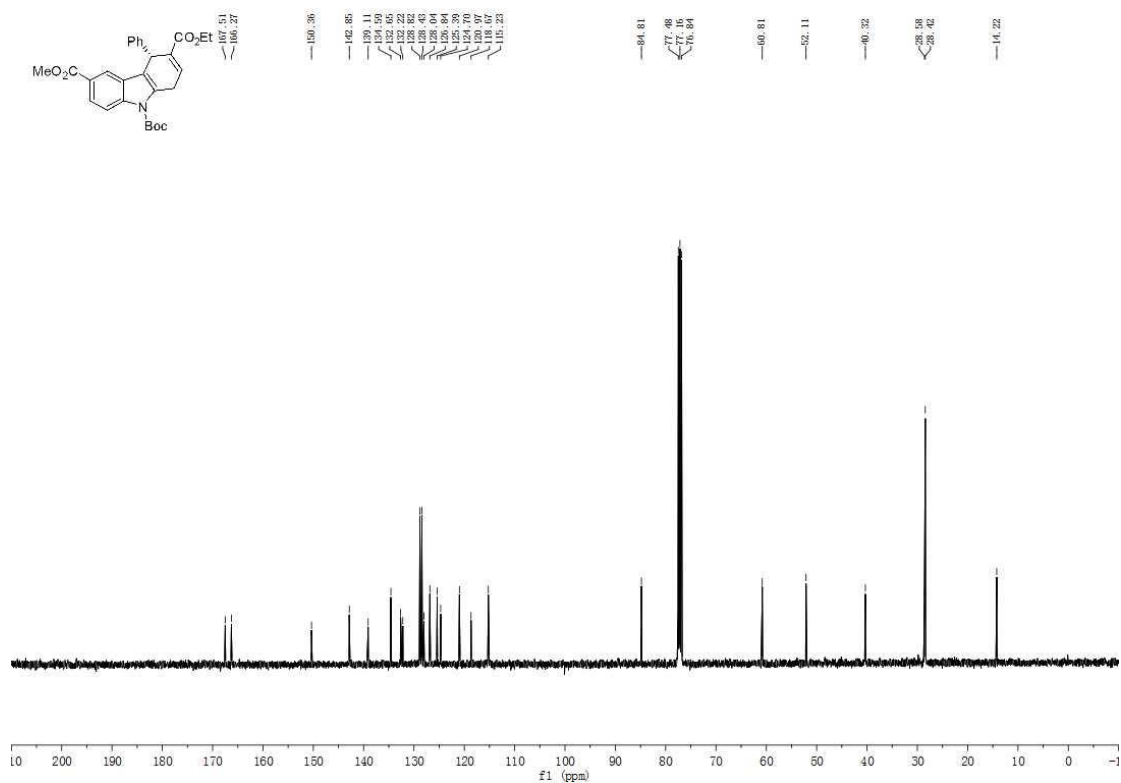


Figure S14. ¹H NMR spectrum of **3g**, related to Scheme 2.

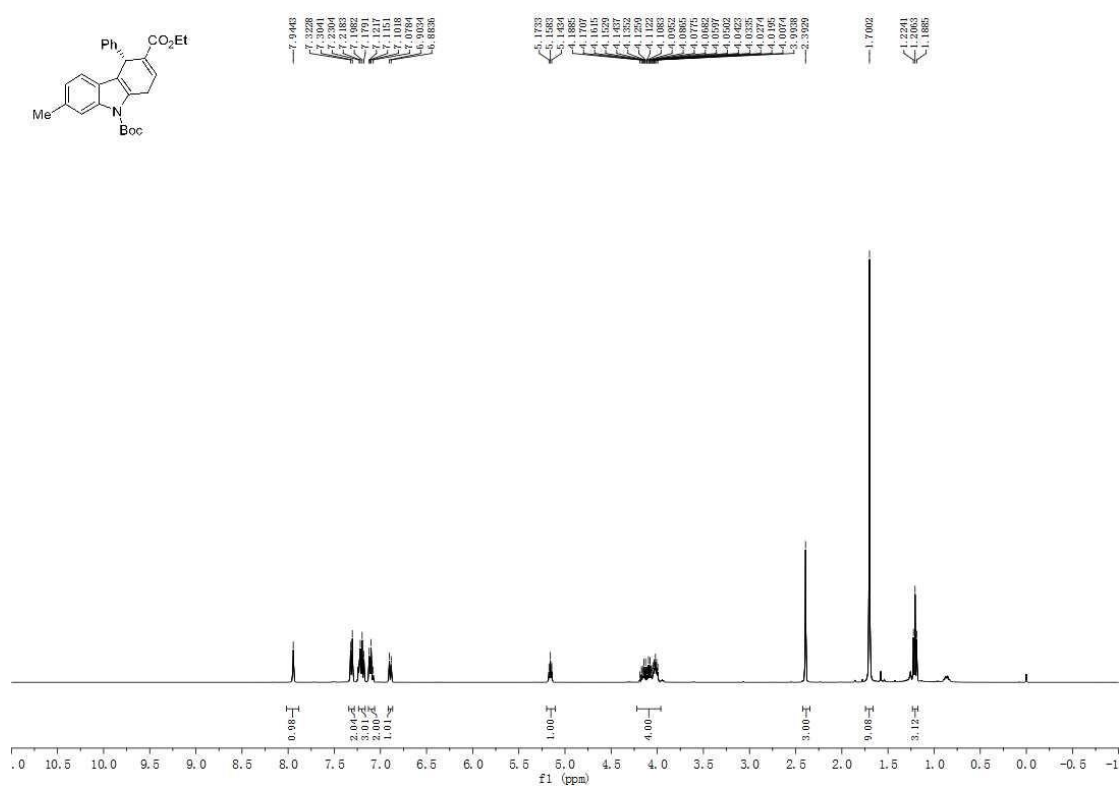


Figure S15. ¹³C NMR spectrum of **3g**, related to Scheme 2.

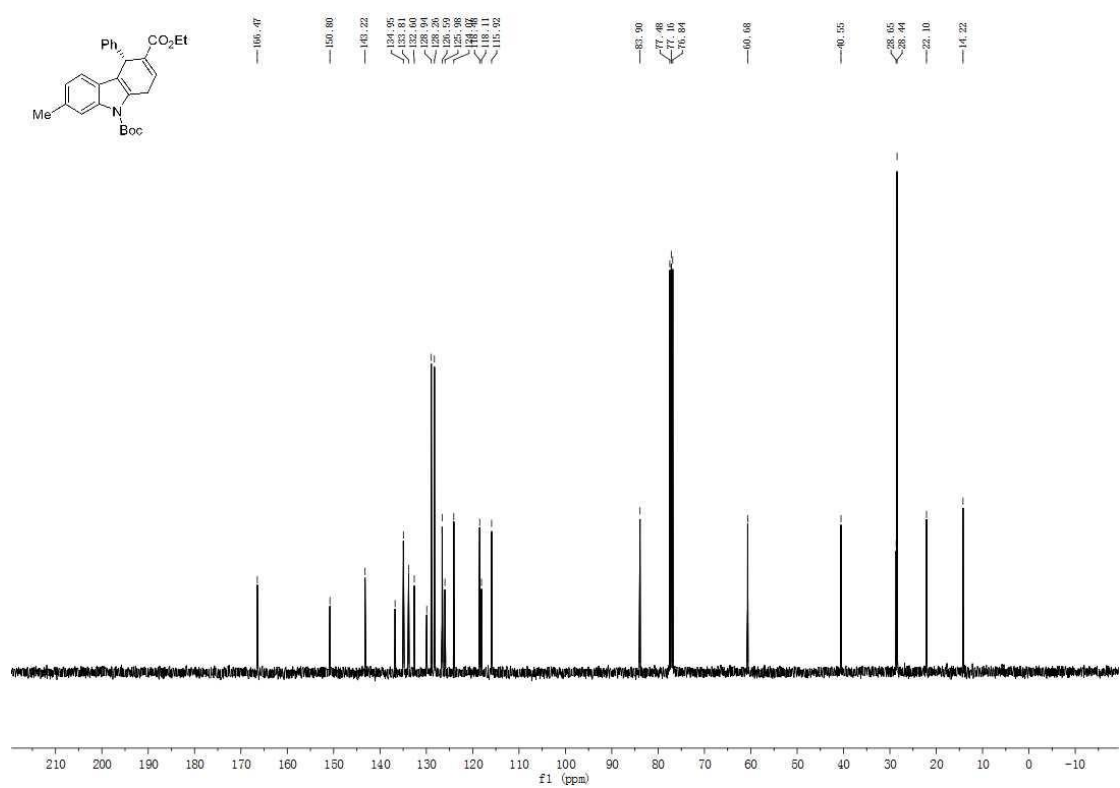


Figure S16. ¹H NMR spectrum of **3h**, related to Scheme 2.

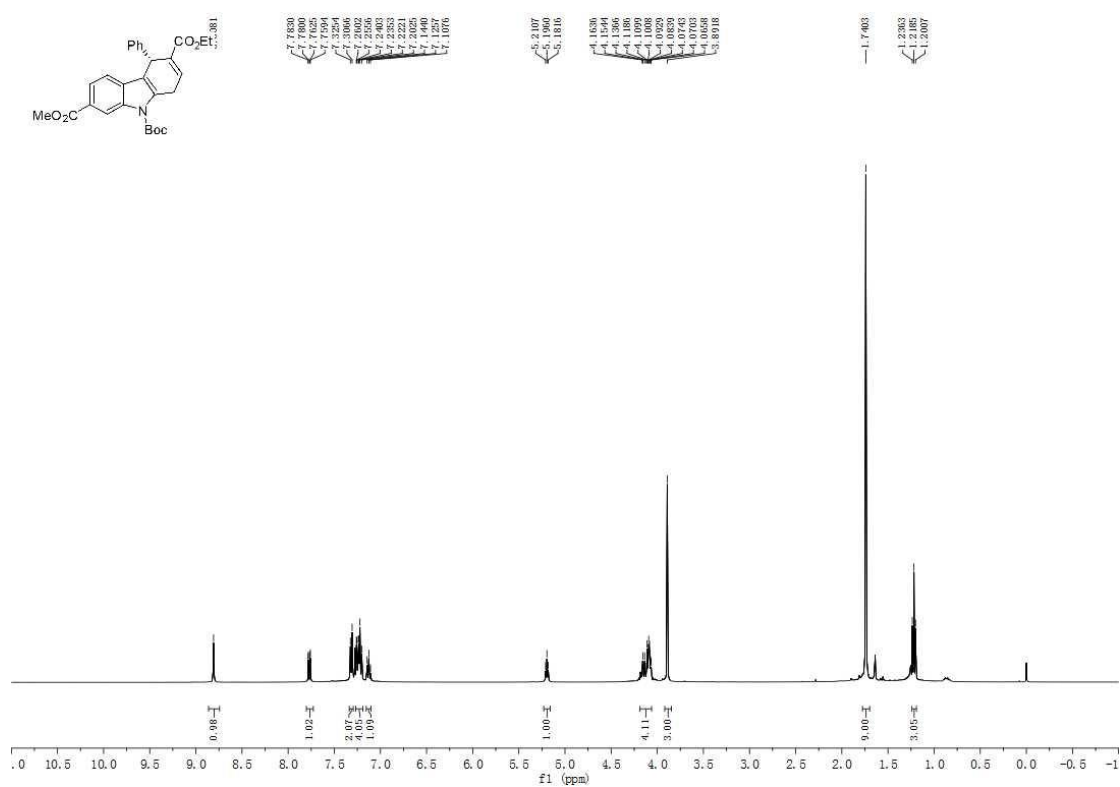


Figure S17. ¹³C NMR spectrum of **3h**, related to Scheme 2.

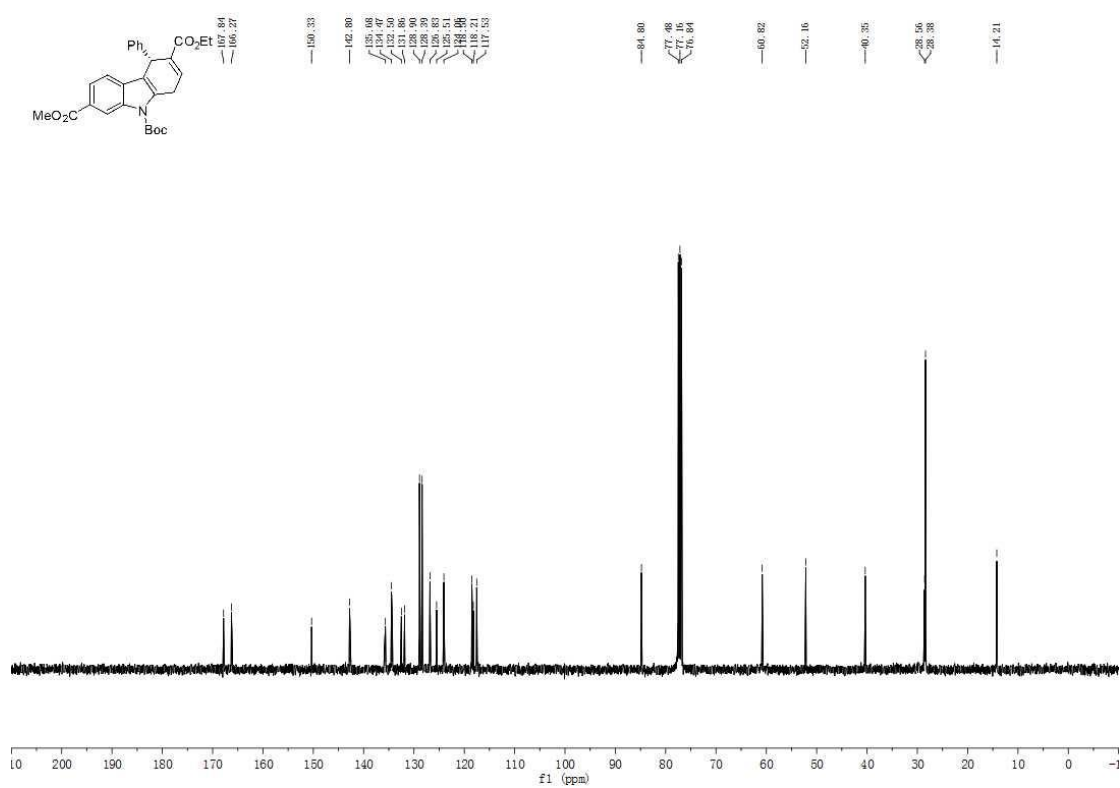


Figure S18. ¹H NMR spectrum of **3i**, related to Scheme 2.

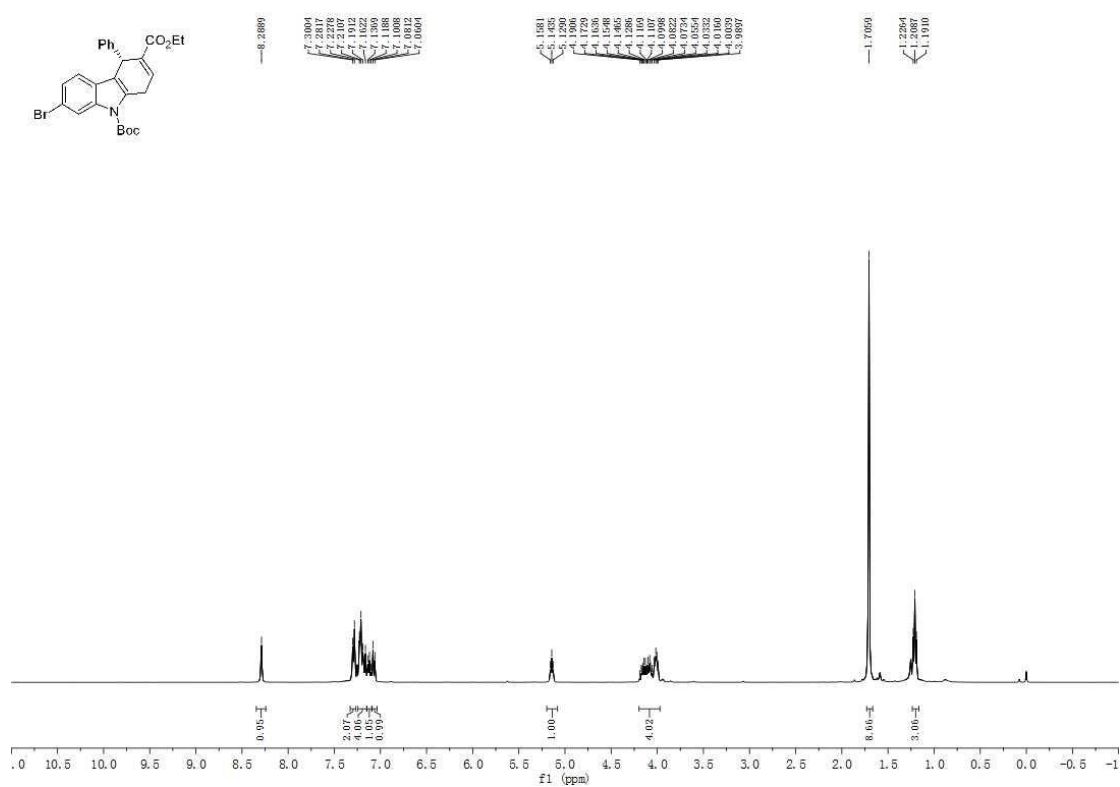


Figure S19. ¹³C NMR spectrum of **3i**, related to Scheme 2.

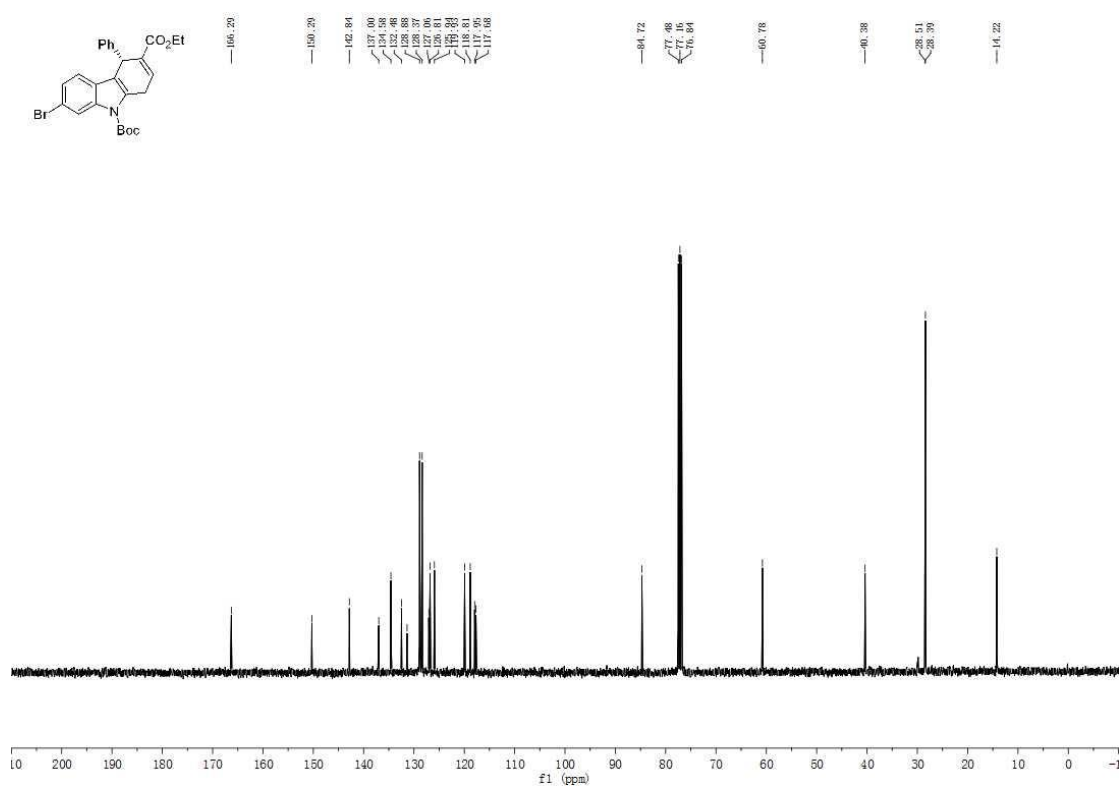


Figure S20. ¹H NMR spectrum of **3j**, related to Scheme 2.

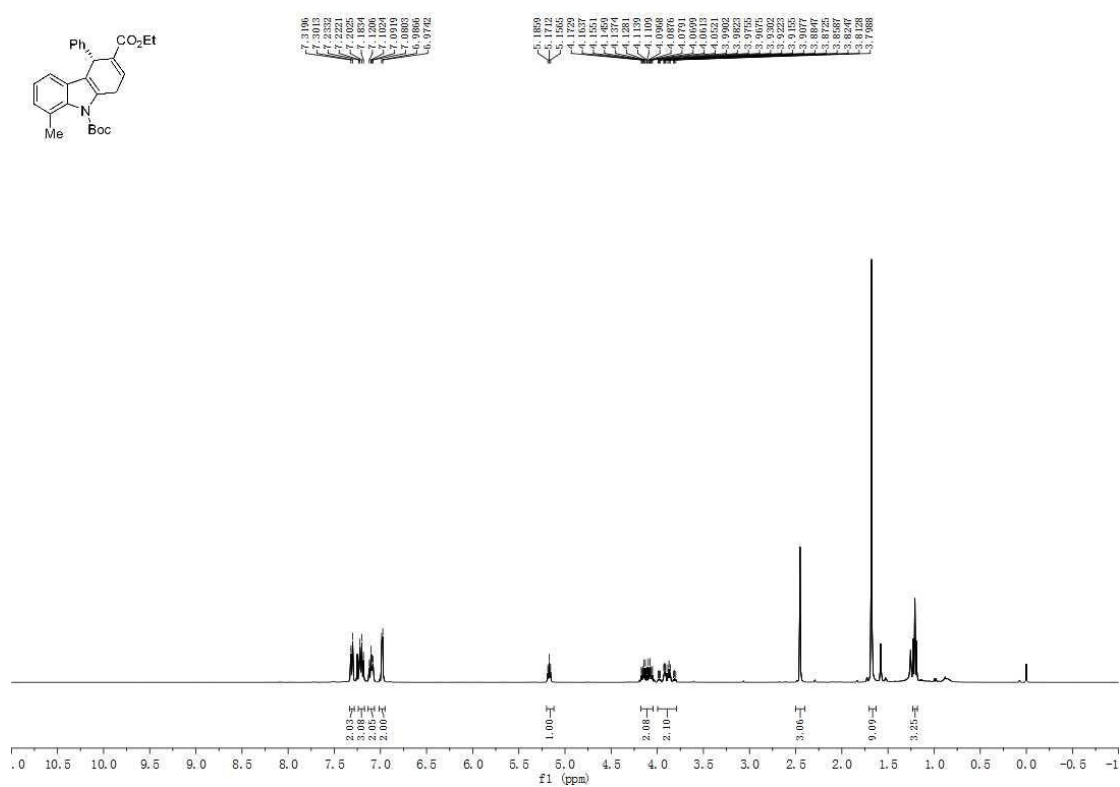


Figure S21. ¹³C NMR spectrum of **3j**, related to Scheme 2.

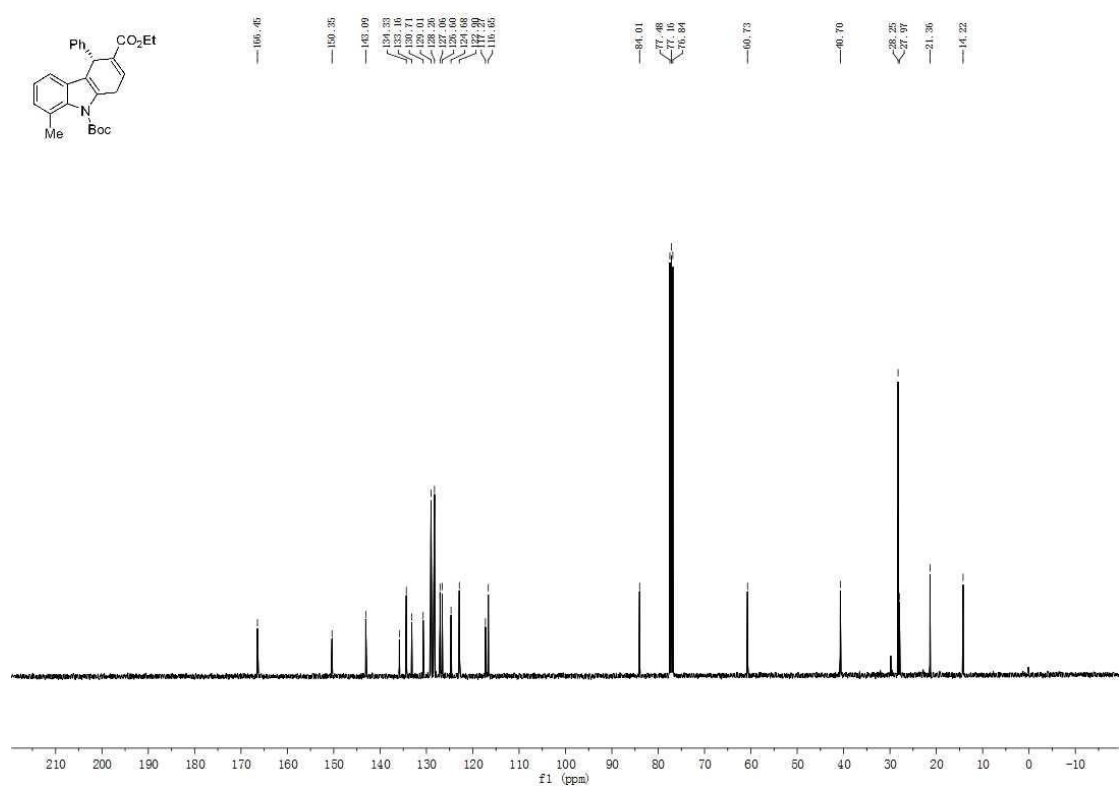


Figure S24. ¹H NMR spectrum of **3I**, related to Scheme 2.

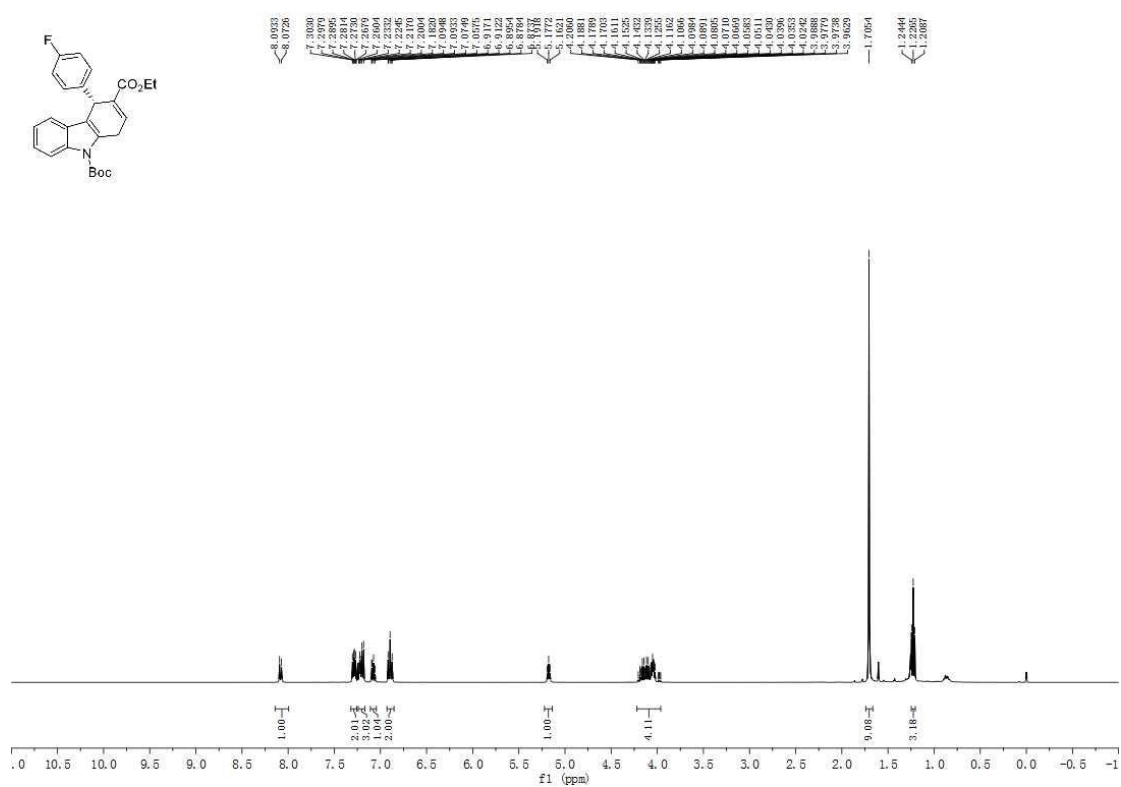


Figure S25. ¹³C NMR spectrum of **3I**, related to Scheme 2.

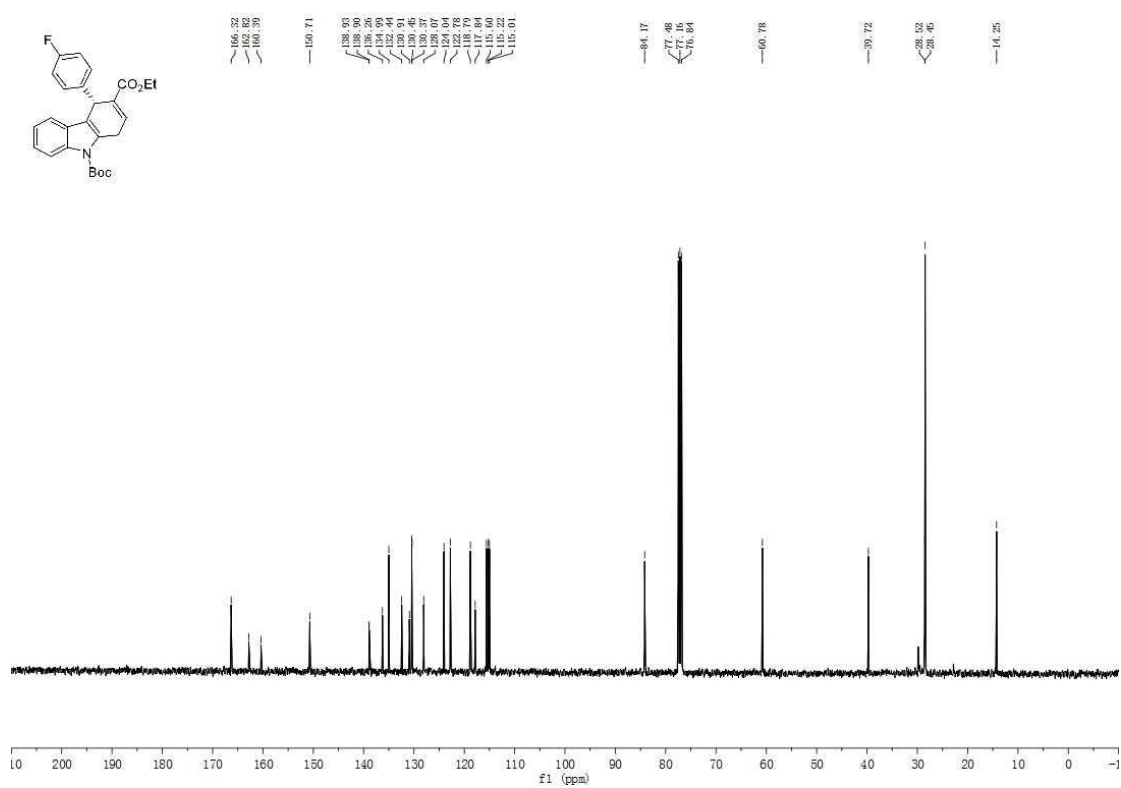


Figure S26. ^{19}F NMR spectrum of **3I**, related to **Scheme 2**.

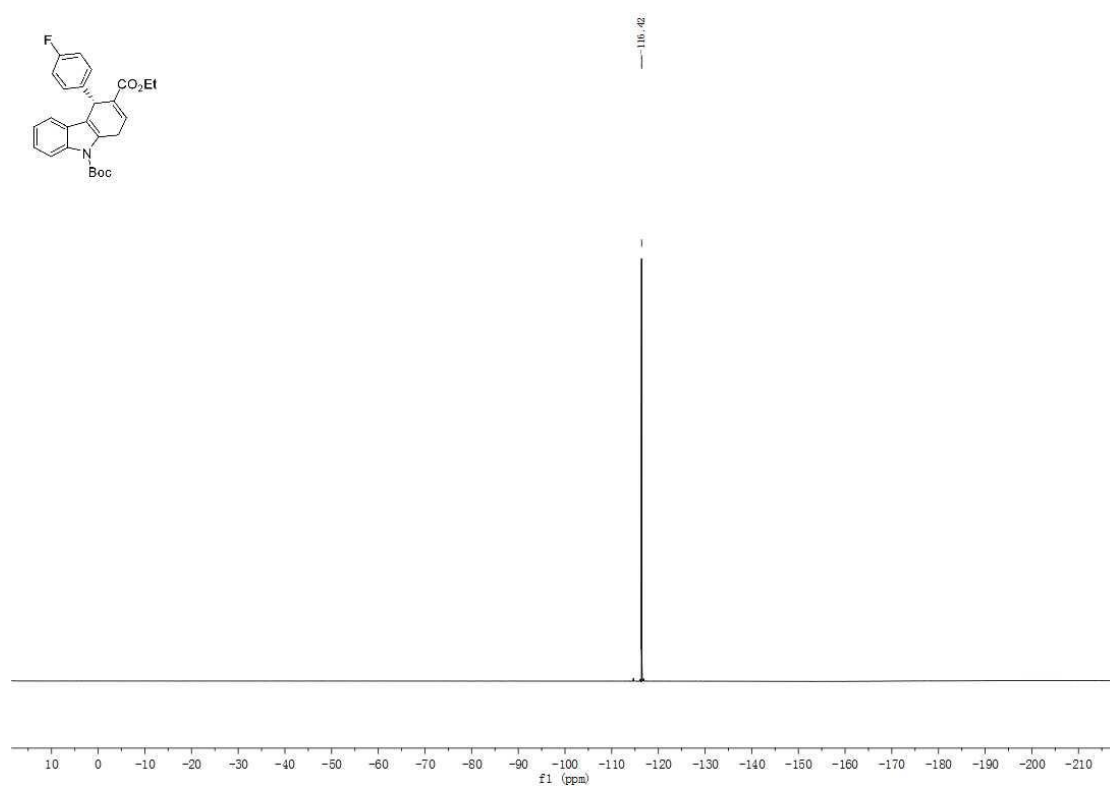


Figure S27. ¹H NMR spectrum of **3m**, related to Scheme 2.

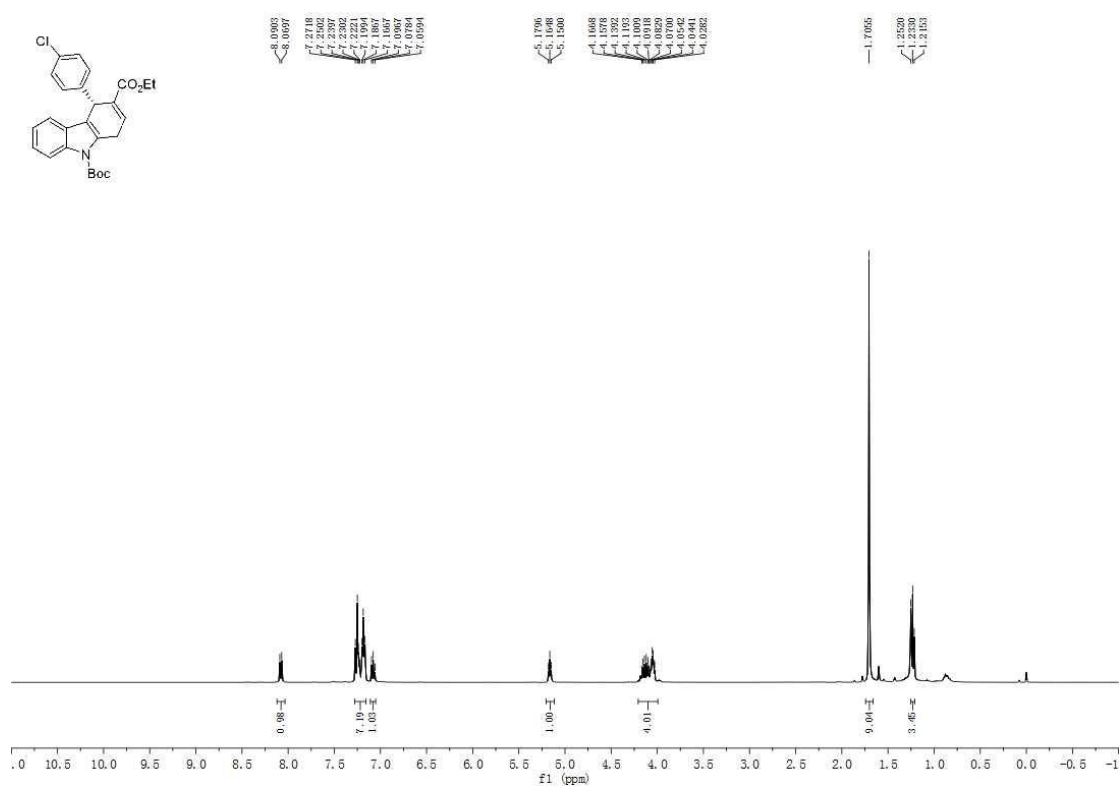


Figure S28. ¹³C NMR spectrum of **3m**, related to Scheme 2.

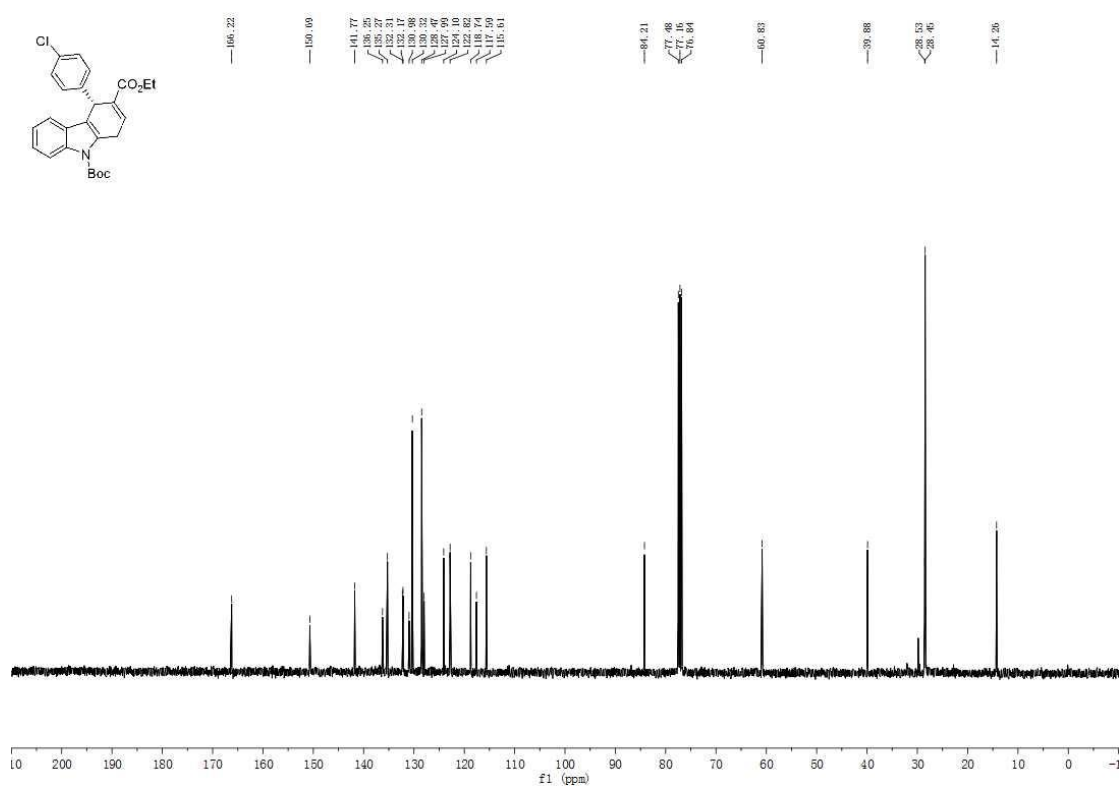


Figure S29. ¹H NMR spectrum of **3n**, related to Scheme 2.

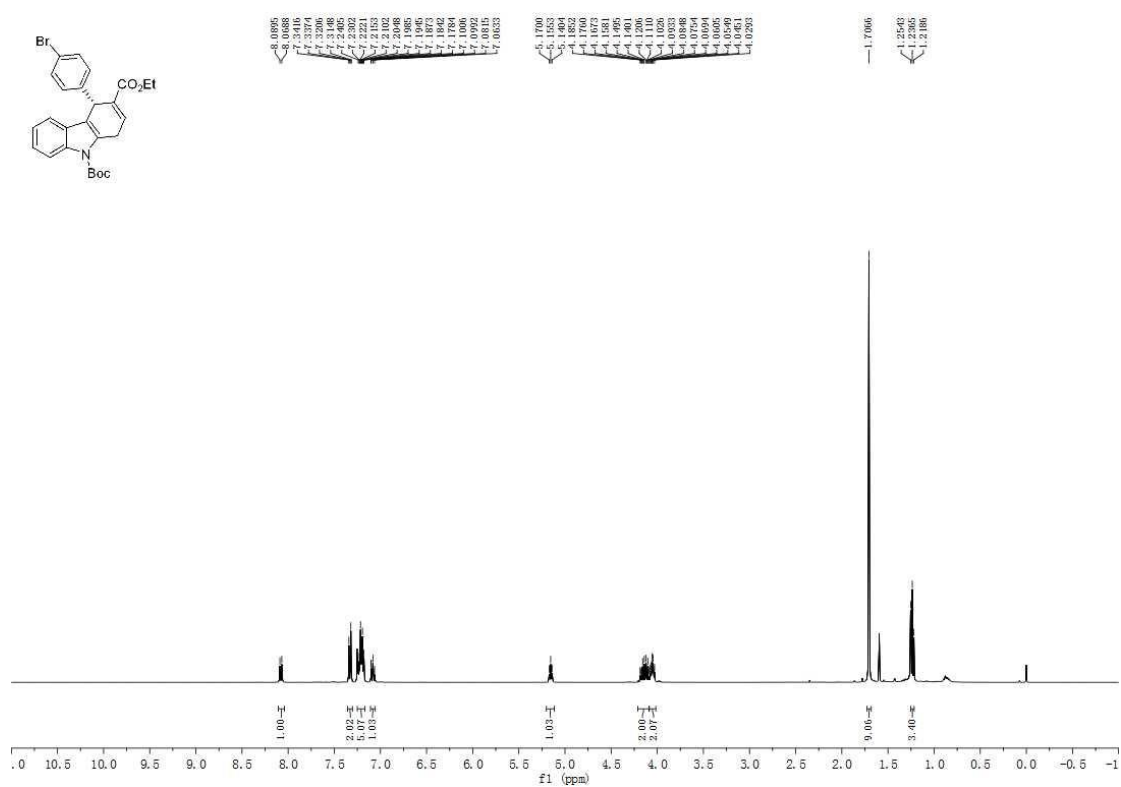


Figure S30. ¹³C NMR spectrum of **3n**, related to Scheme 2.

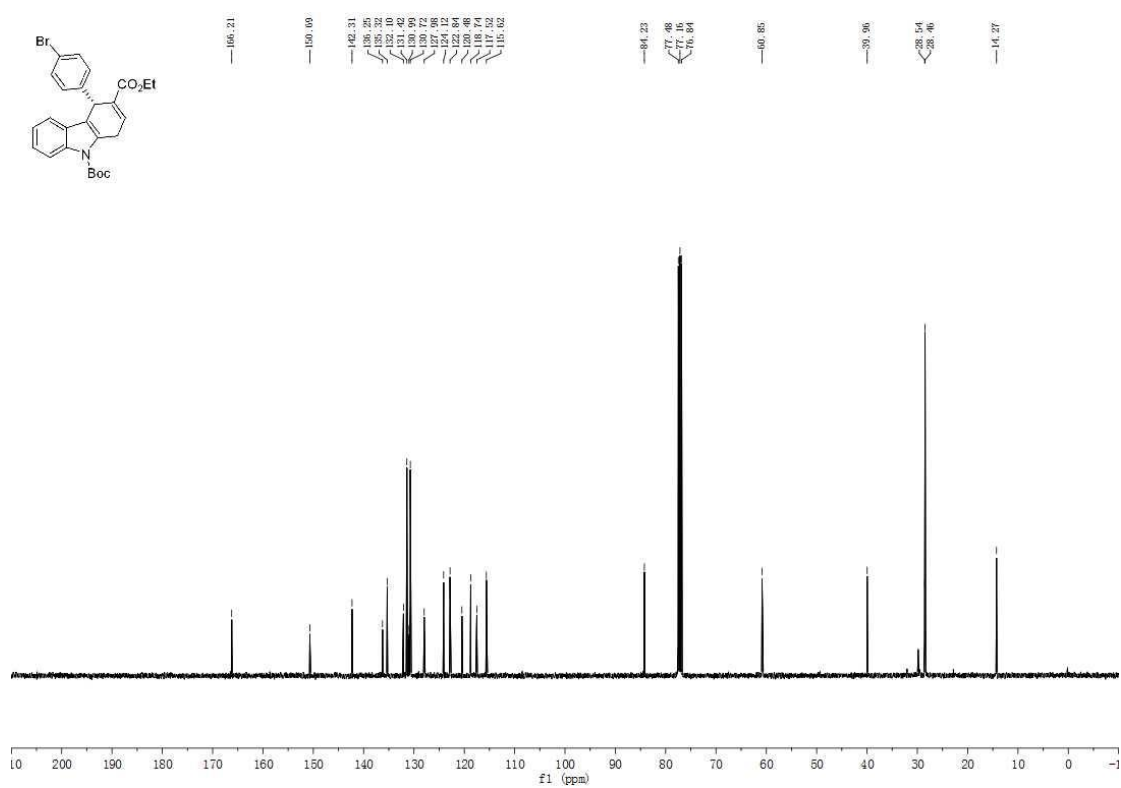


Figure S33. ^{19}F NMR spectrum of **3o**, related to **Scheme 2**.

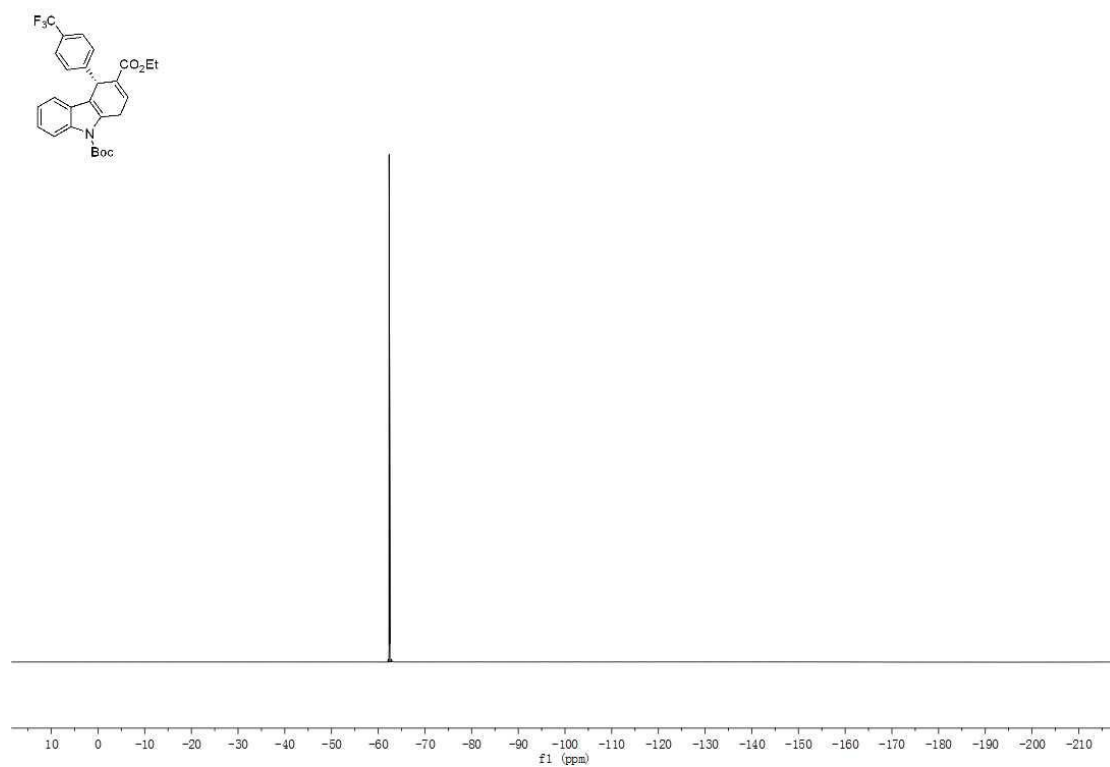


Figure S36. ¹H NMR spectrum of **3q**, related to Scheme 2.

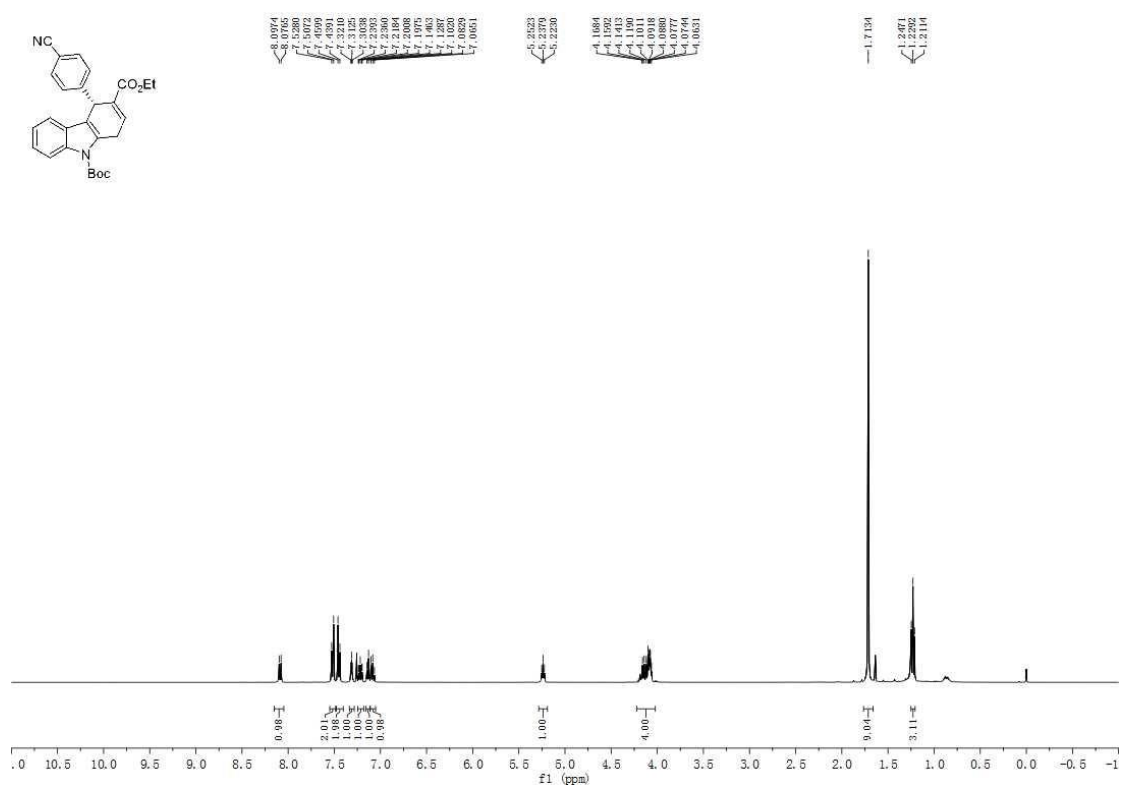


Figure S37. ¹³C NMR spectrum of **3q**, related to Scheme 2.

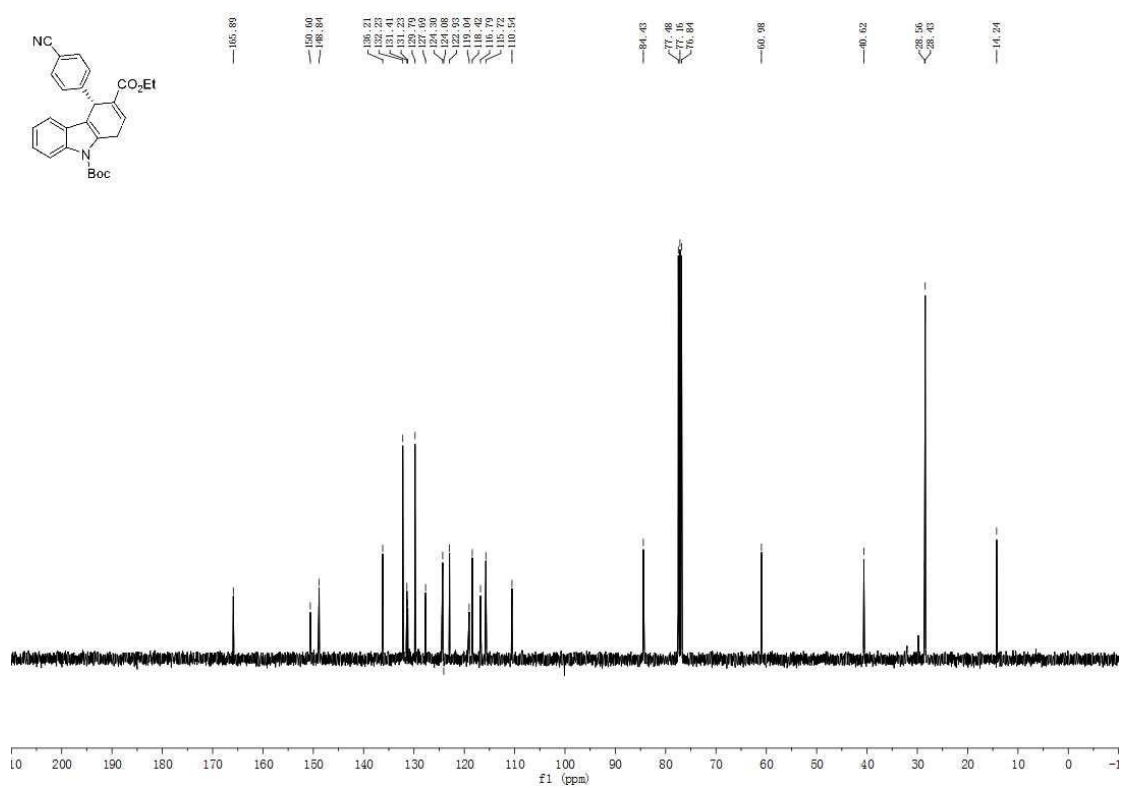


Figure S38. ¹H NMR spectrum of **3r**, related to Scheme 2.

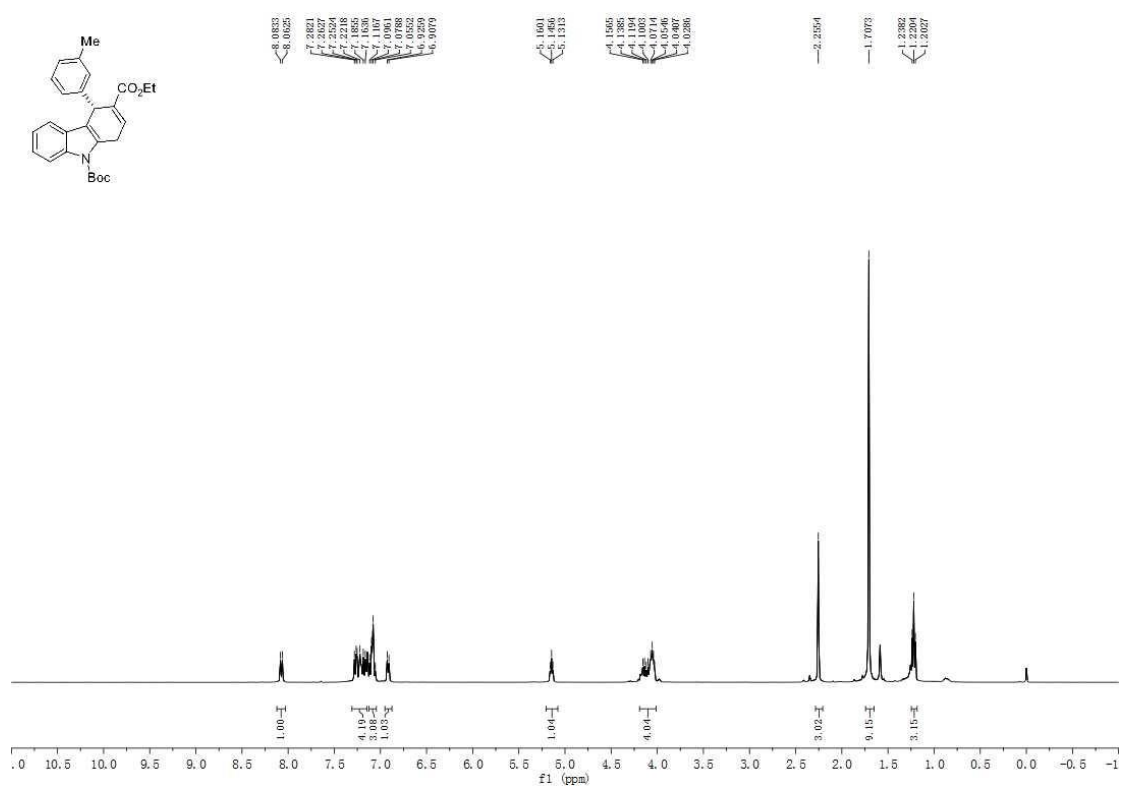


Figure S39. ¹³C NMR spectrum of **3r**, related to Scheme 2.

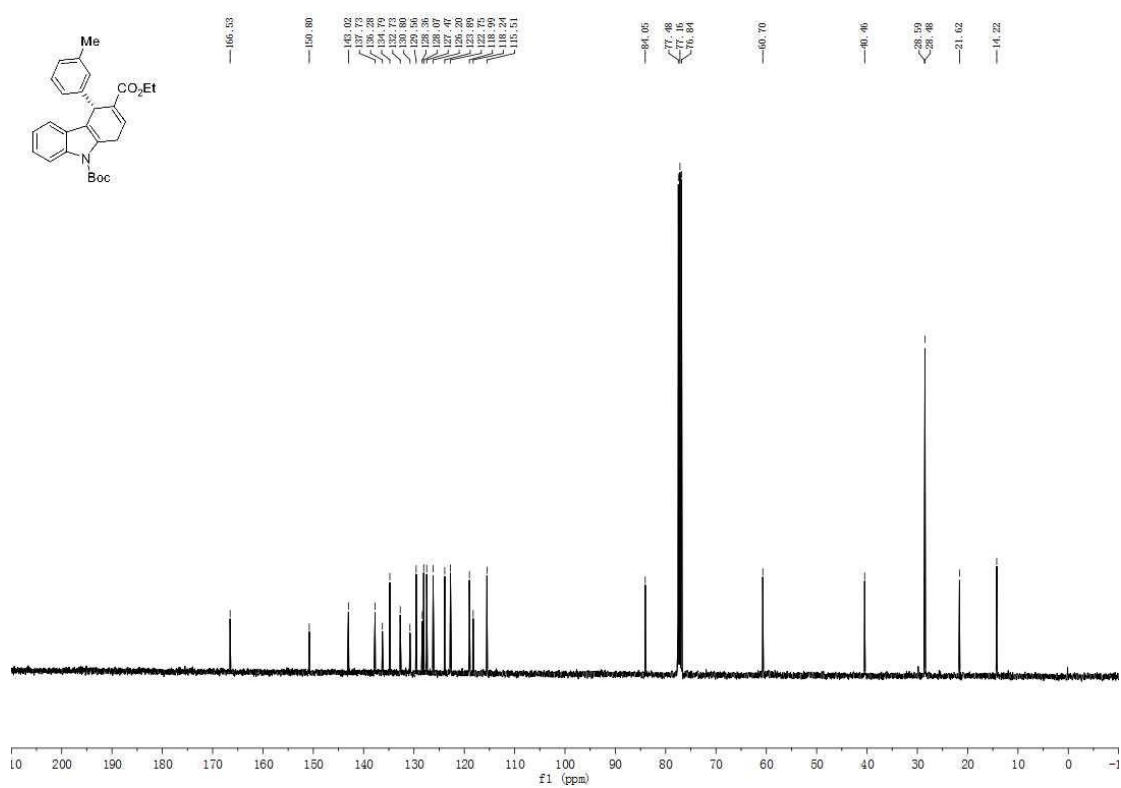


Figure S40. ¹H NMR spectrum of **3s**, related to Scheme 2.

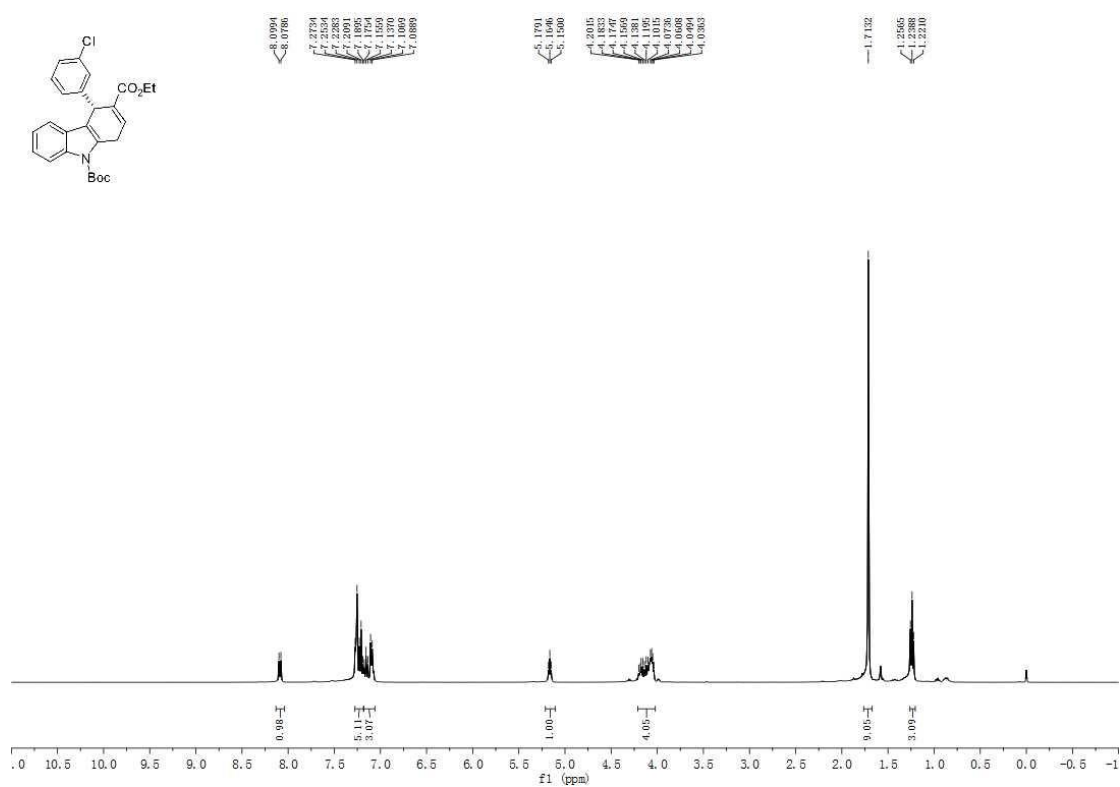


Figure S41. ¹³C NMR spectrum of **3s**, related to Scheme 2.

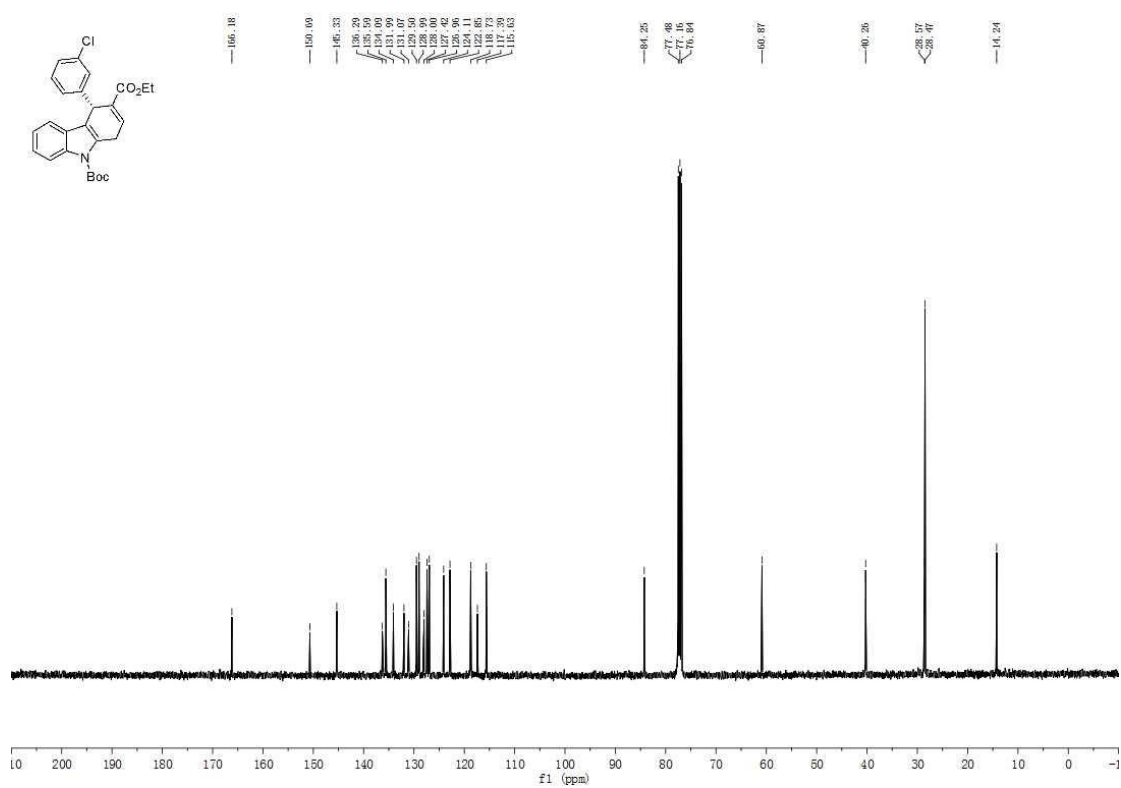


Figure S42. ¹H NMR spectrum of **3t**, related to Scheme 2.

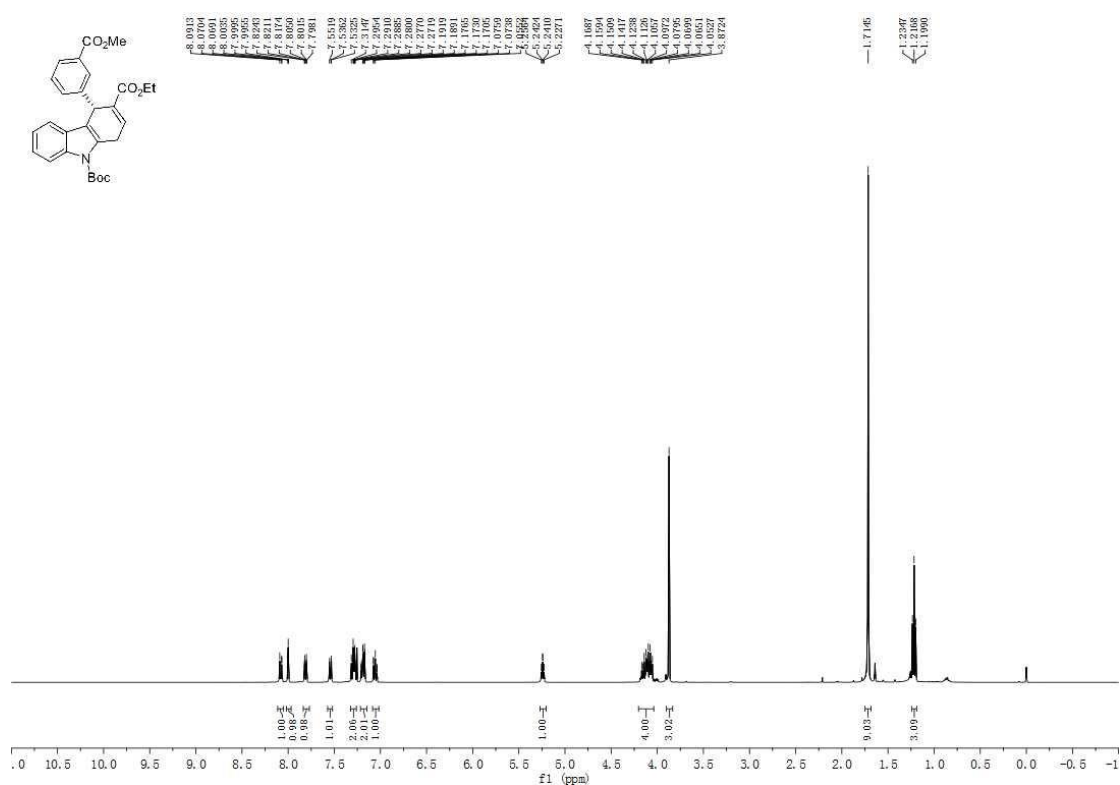


Figure S43. ¹³C NMR spectrum of **3t**, related to Scheme 2.

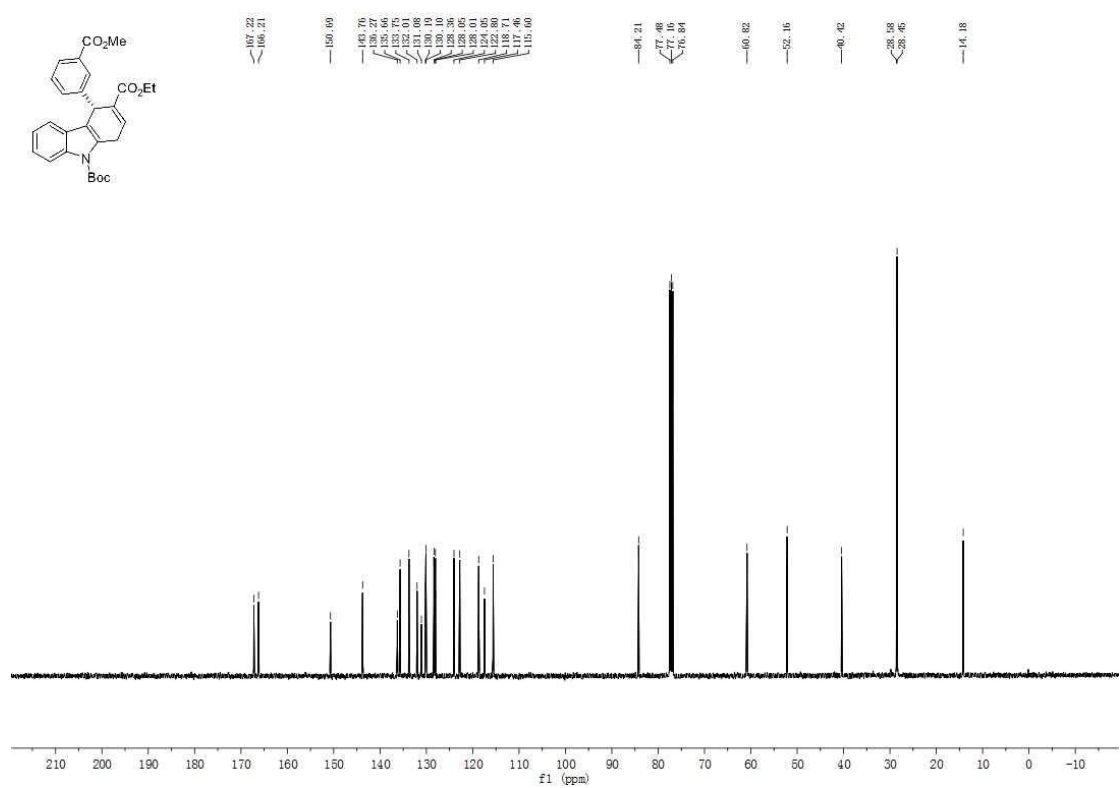


Figure S44. ¹H NMR spectrum of **3u**, related to Scheme 2.

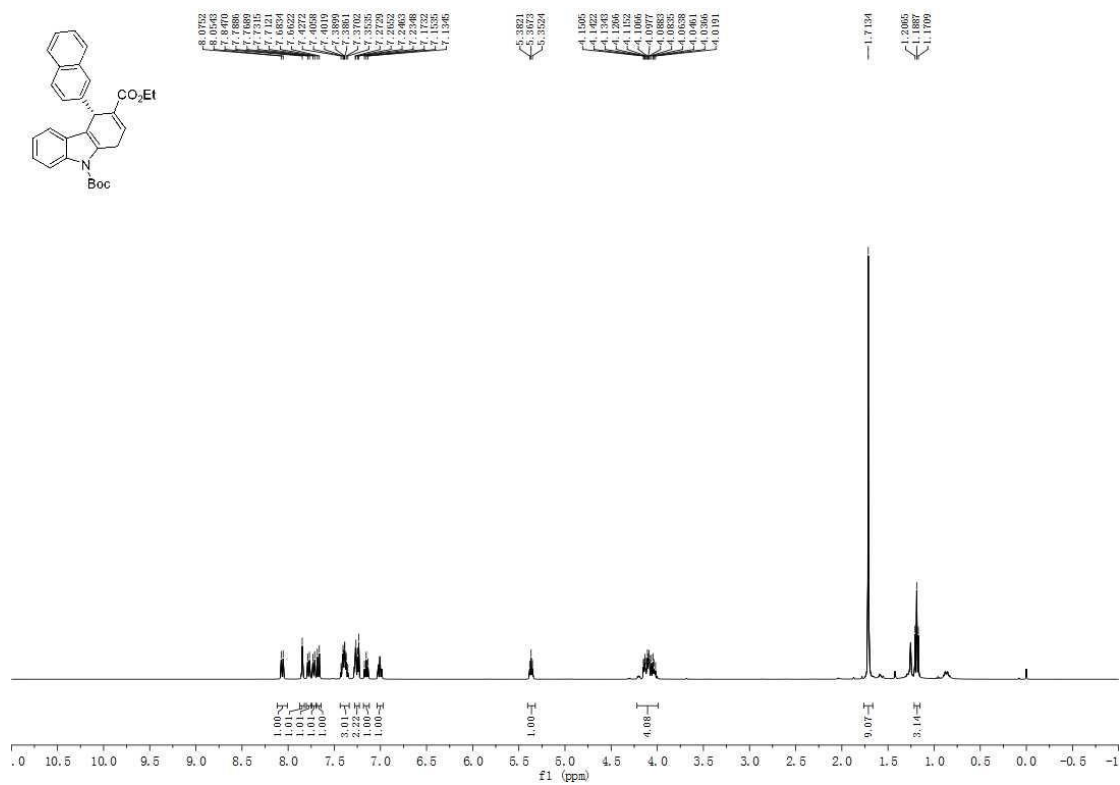


Figure S45. ¹³C NMR spectrum of **3u**, related to Scheme 2.

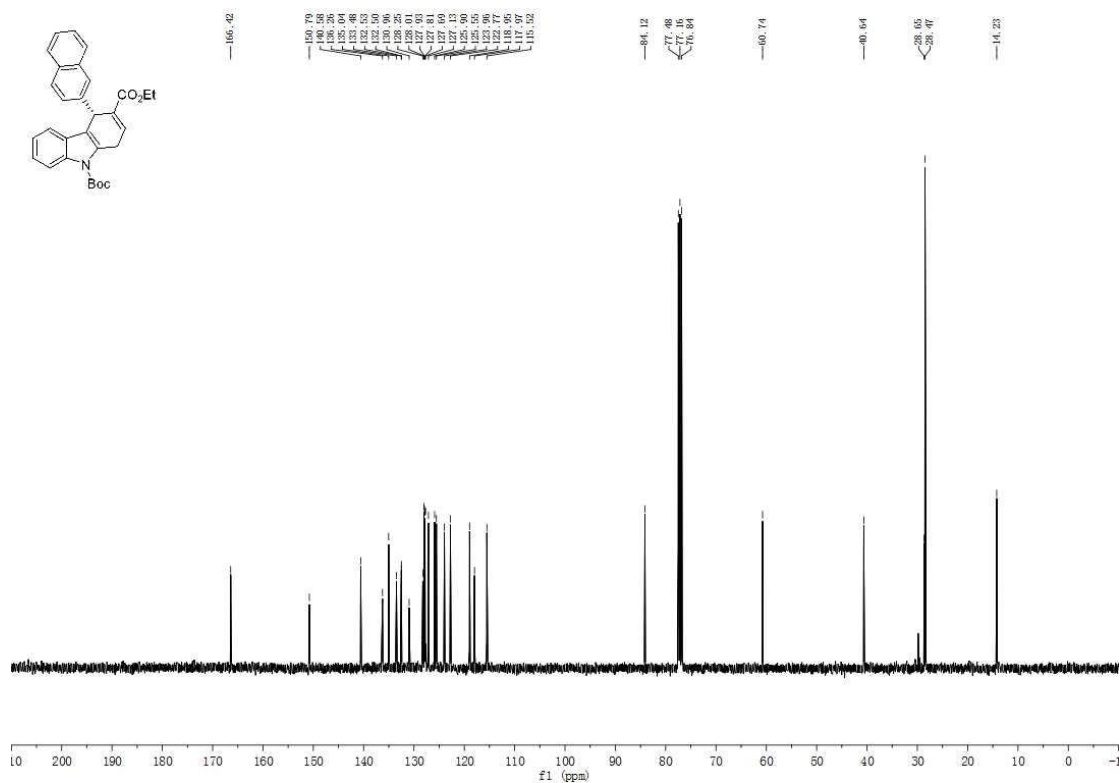


Figure S46. ¹H NMR spectrum of **3v**, related to Scheme 2.

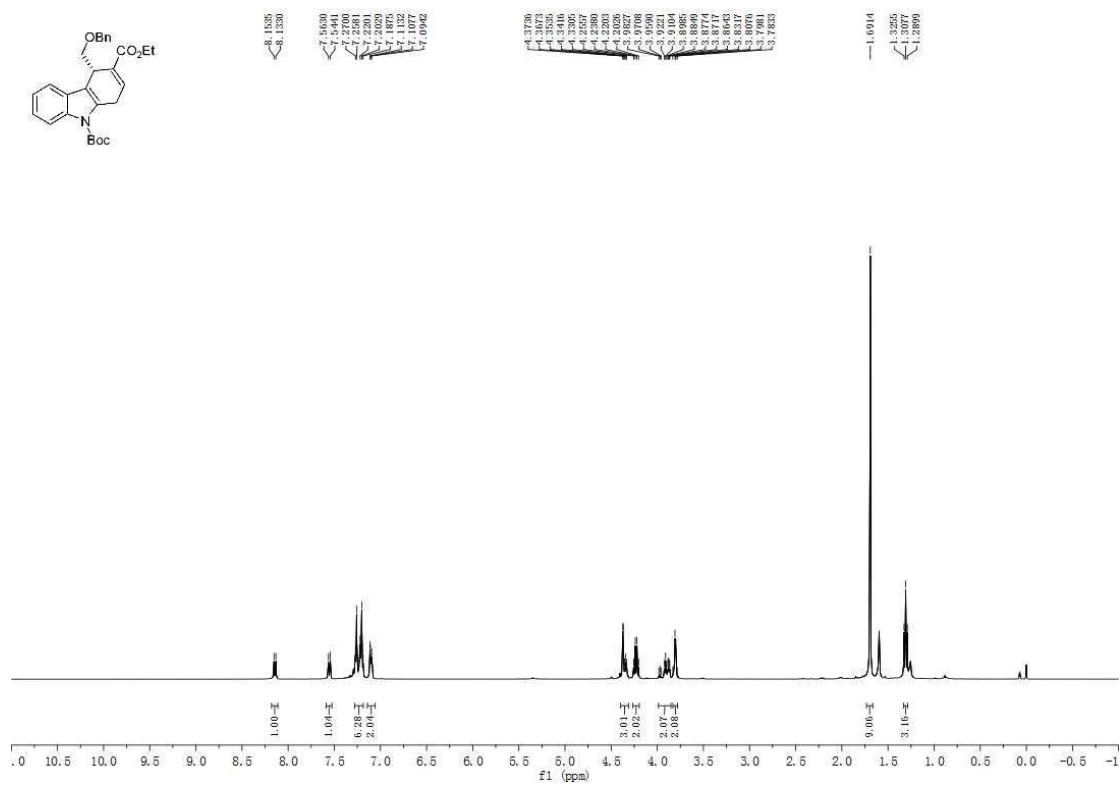


Figure S47. ¹³C NMR spectrum of **3v**, related to Scheme 2.

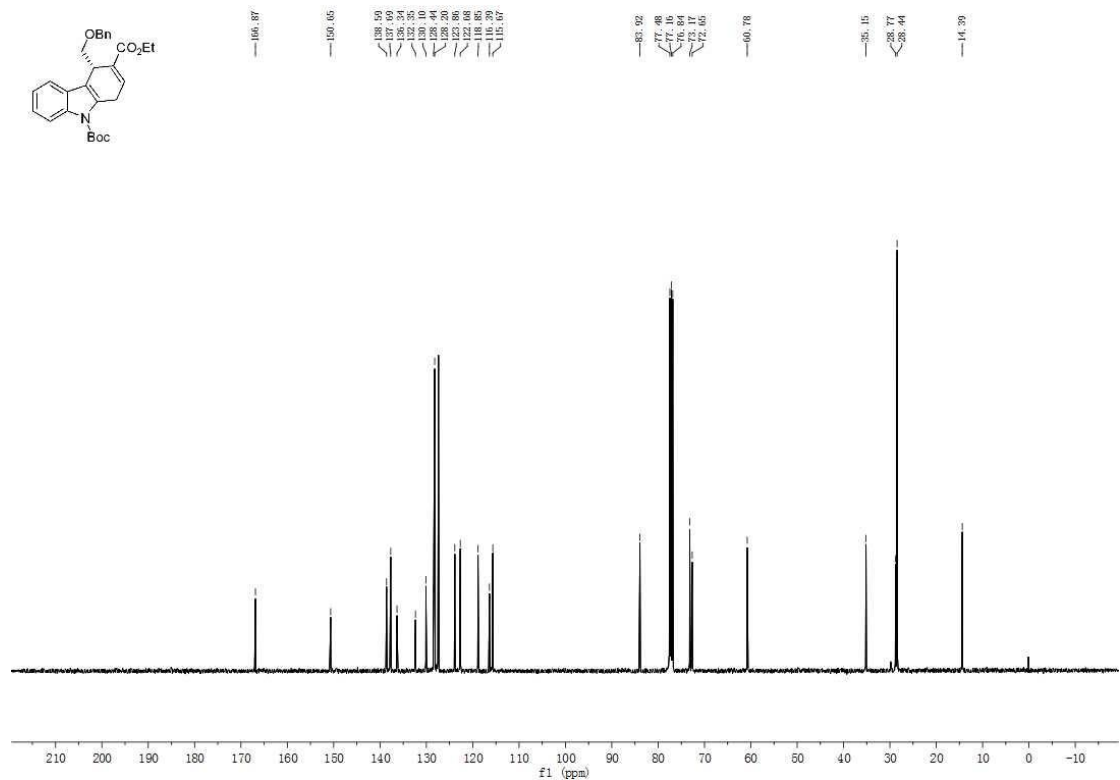


Figure S48. ¹H NMR spectrum of **3w**, related to Scheme 2.

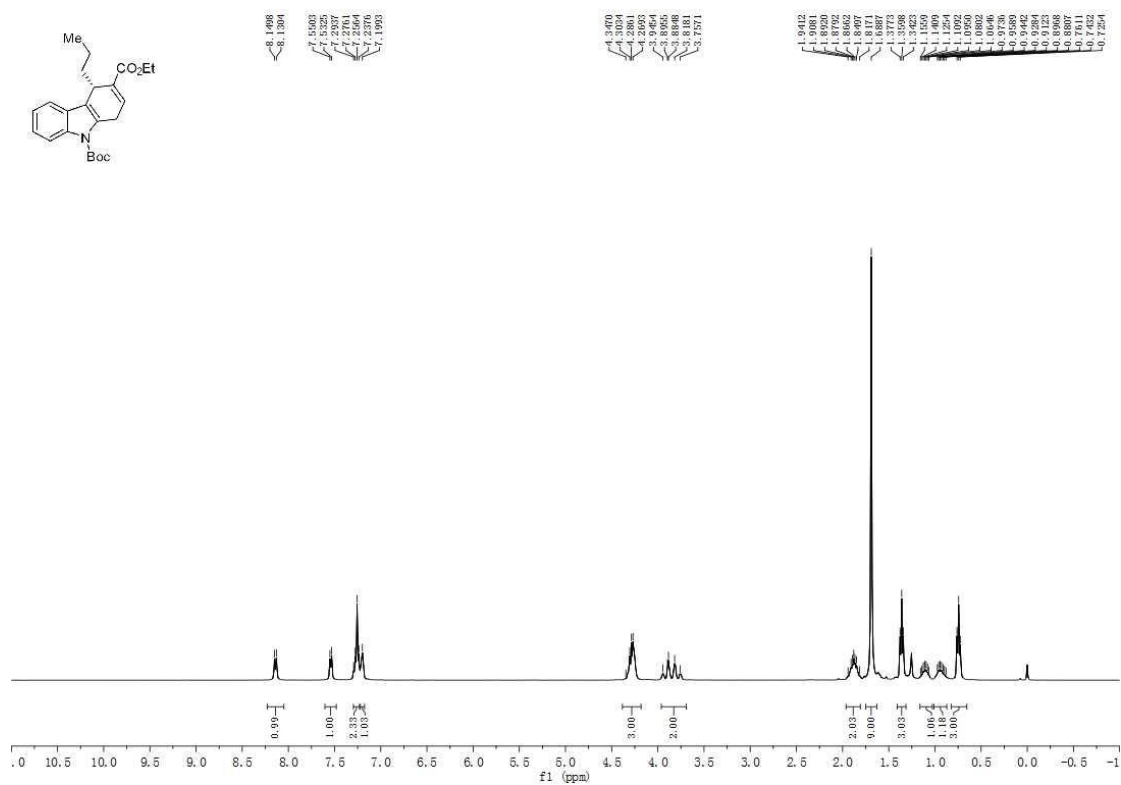


Figure S49. ¹³C NMR spectrum of **3w**, related to Scheme 2.

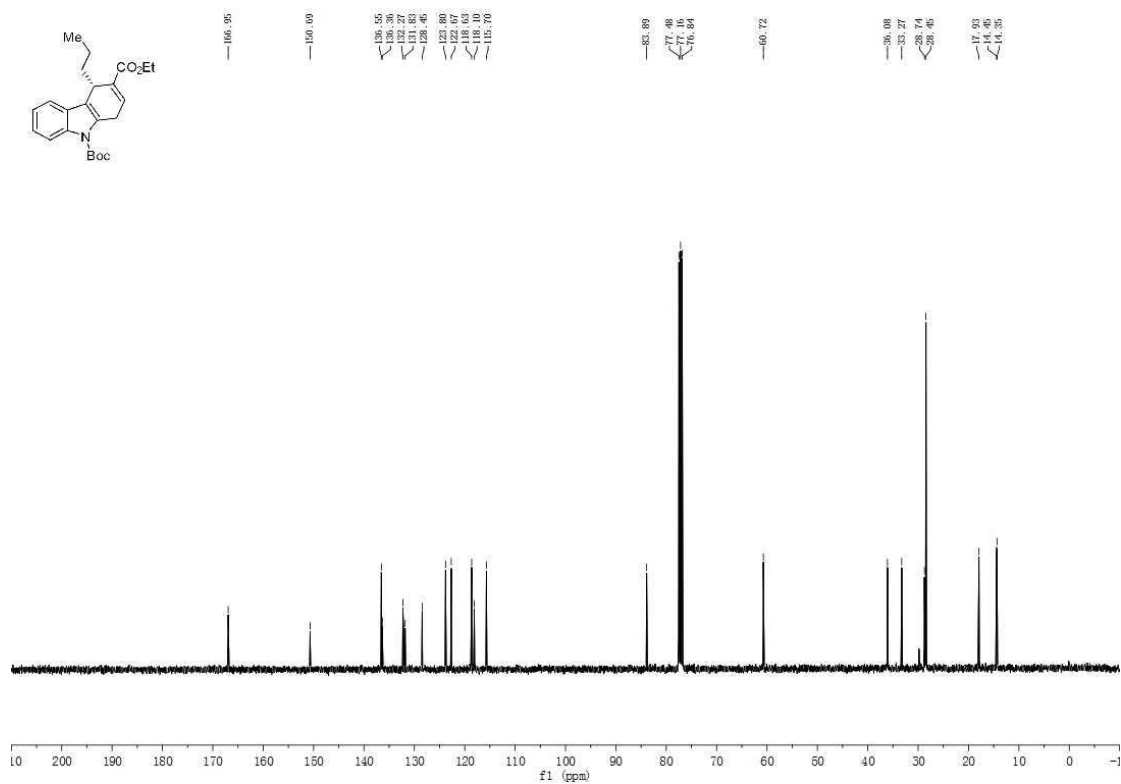


Figure S50. ¹H NMR spectrum of **3x**, related to Scheme 2.

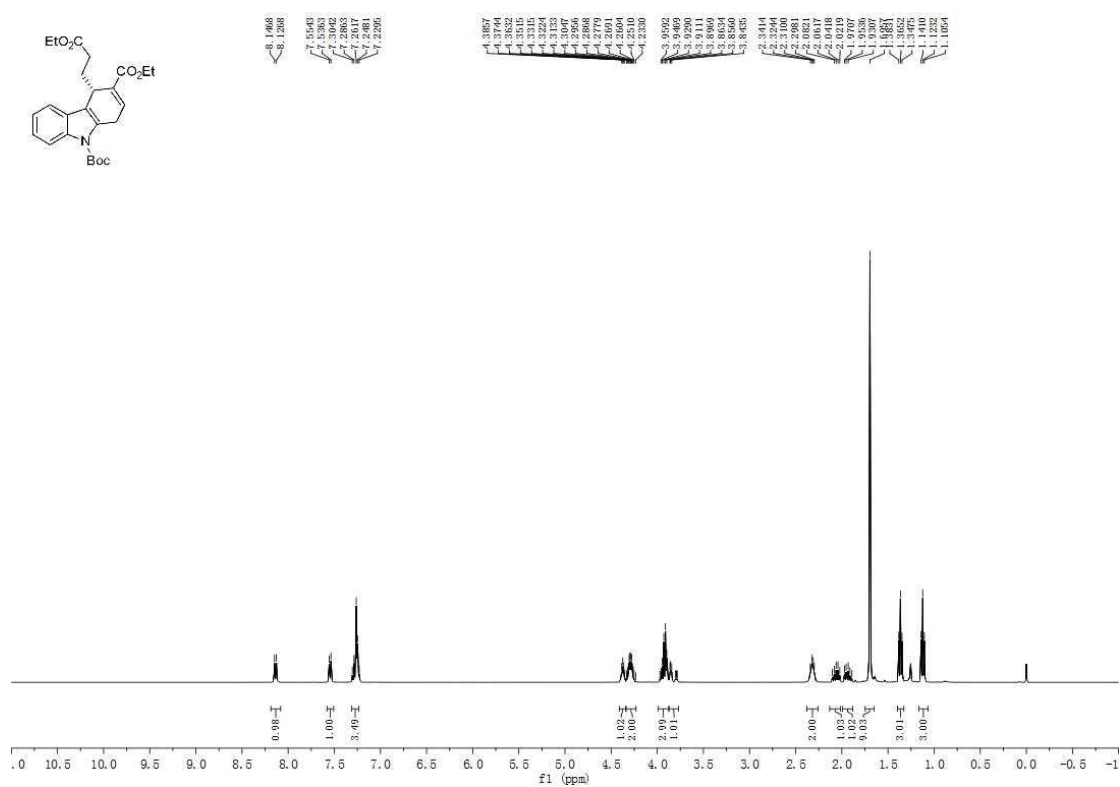


Figure S51. ¹³C NMR spectrum of **3x**, related to Scheme 2.

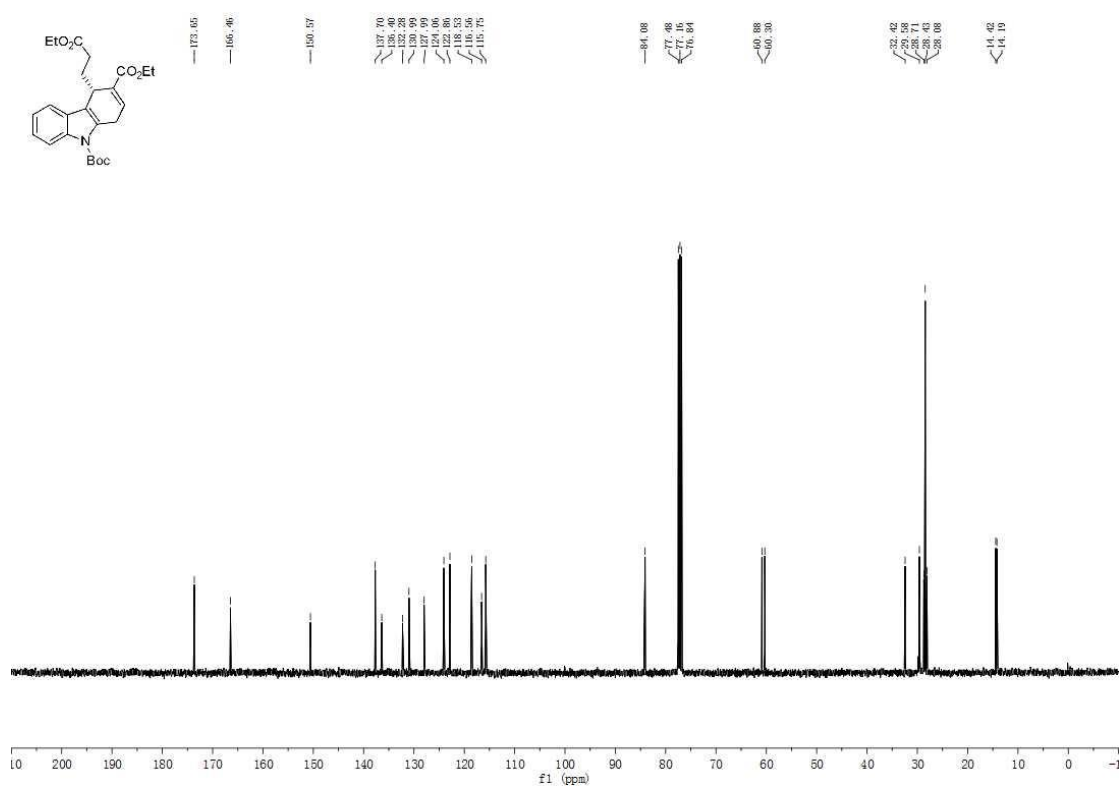


Figure S52. ¹H NMR spectrum of **3y**, related to Scheme 2.

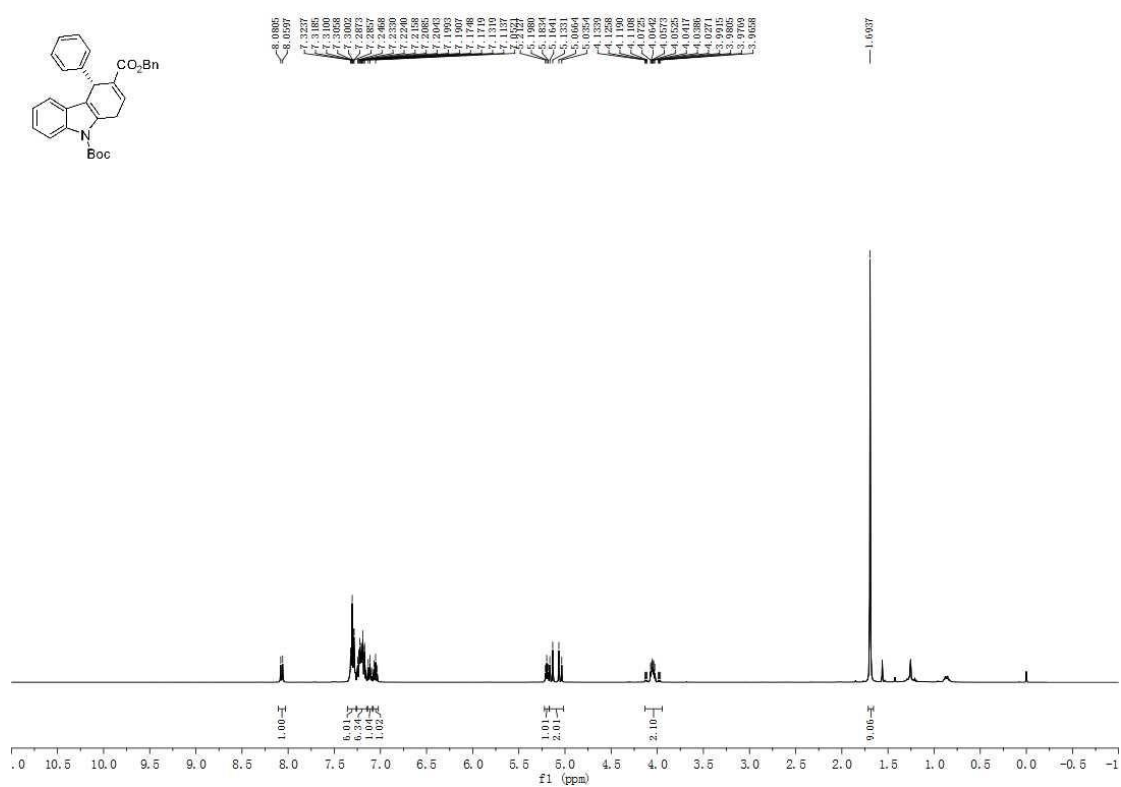


Figure S53. ¹³C NMR spectrum of **3y**, related to Scheme 2.

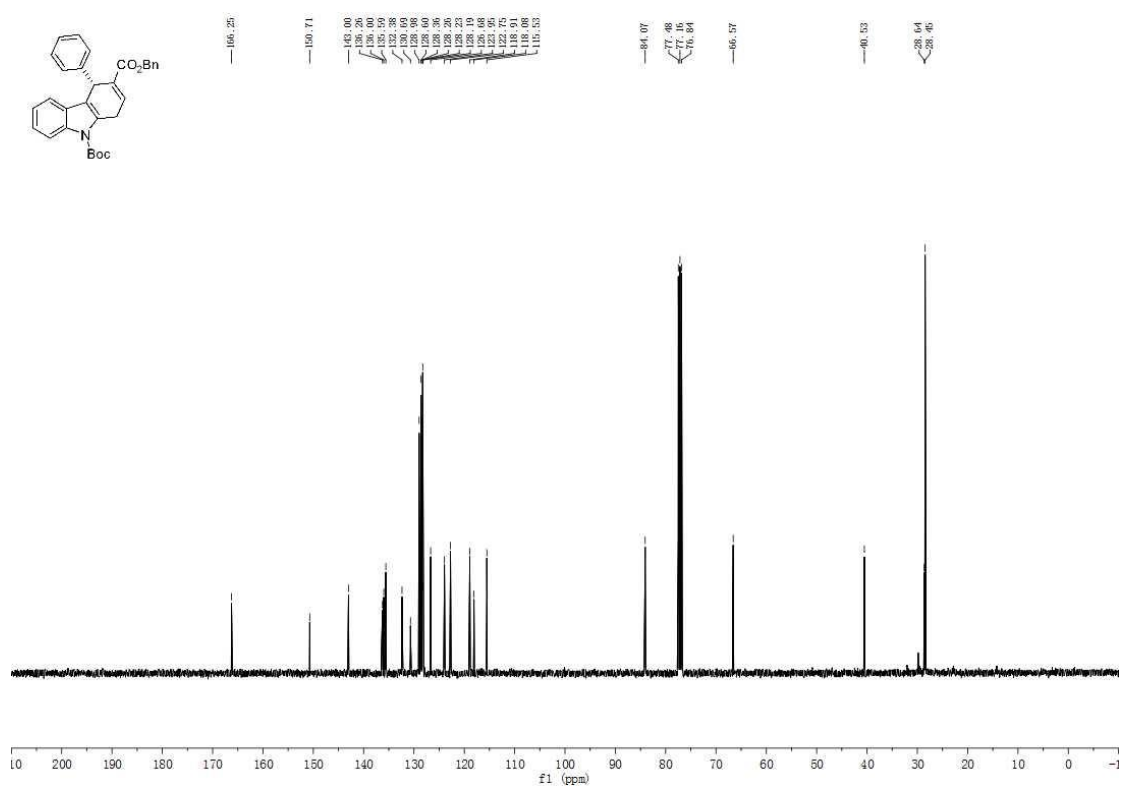


Figure S54. ¹H NMR spectrum of **3z**, related to Scheme 2.

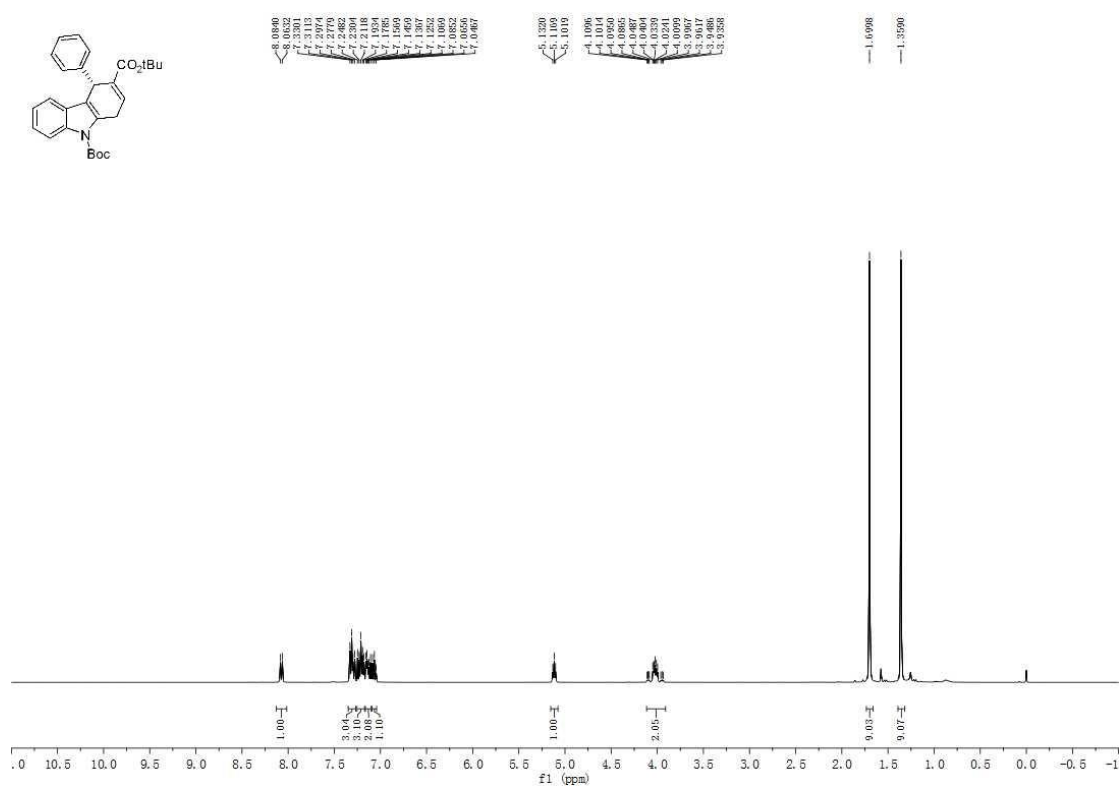


Figure S55. ¹³C NMR spectrum of **3z**, related to Scheme 2.

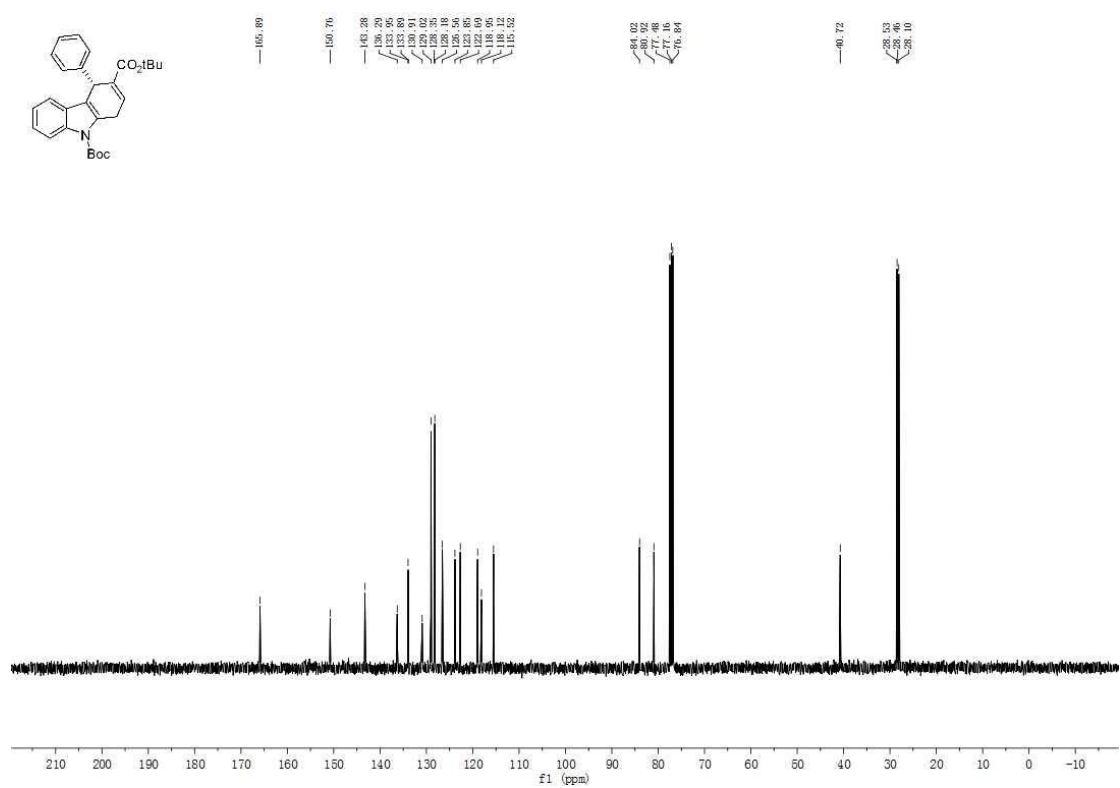


Figure S56. ¹H NMR spectrum of **6a**, related to Scheme 3.

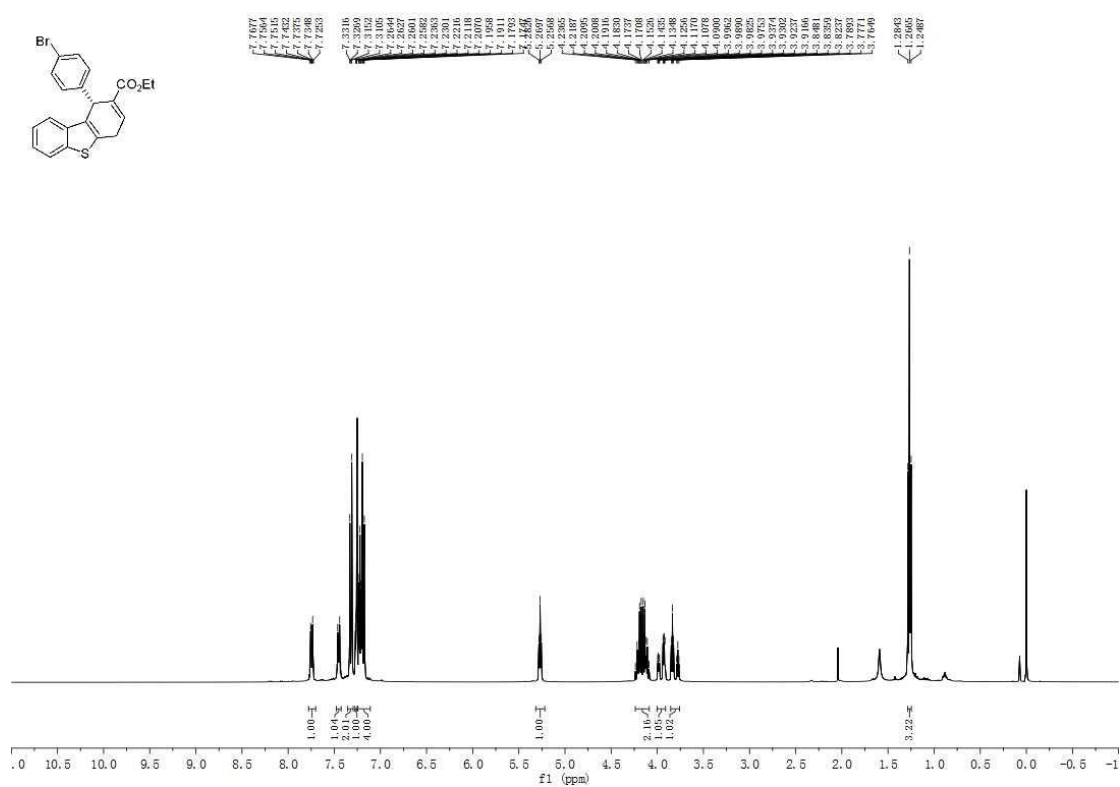


Figure S57. ¹³C NMR spectrum of **6a**, related to Scheme 3.

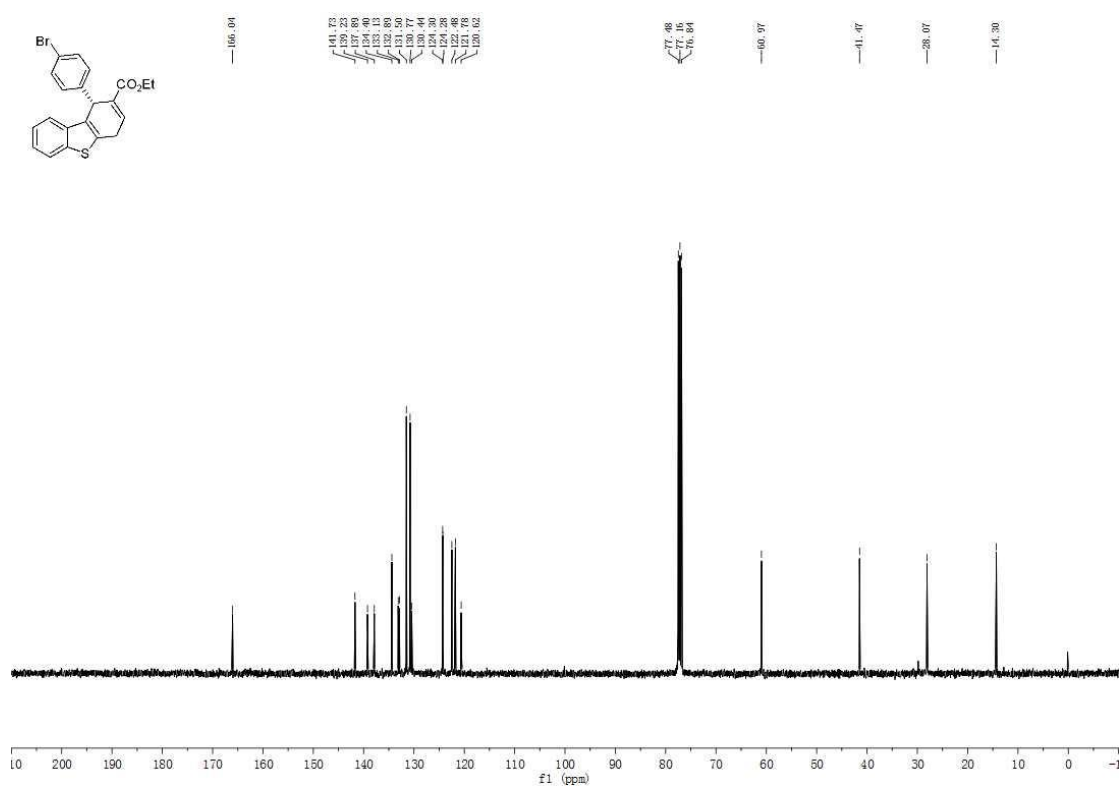


Figure S58. ¹H NMR spectrum of **6b**, related to Scheme 3.

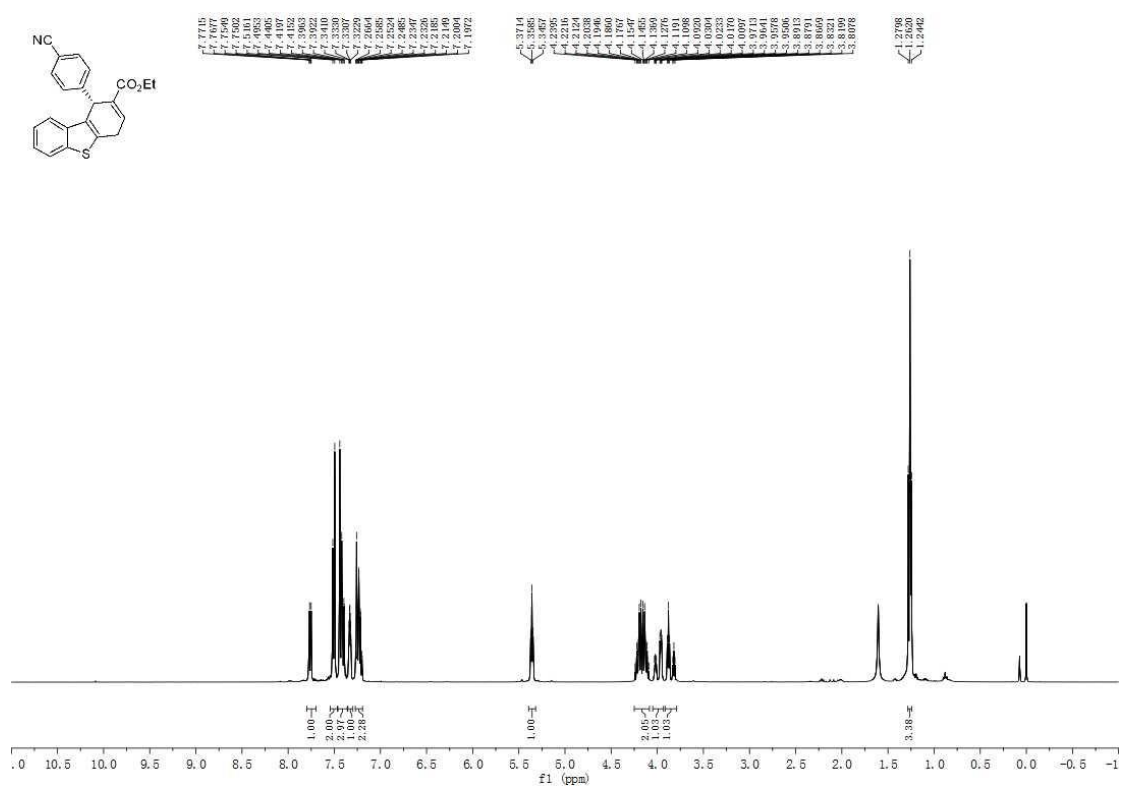


Figure S59. ¹³C NMR spectrum of **6b**, related to Scheme 3.

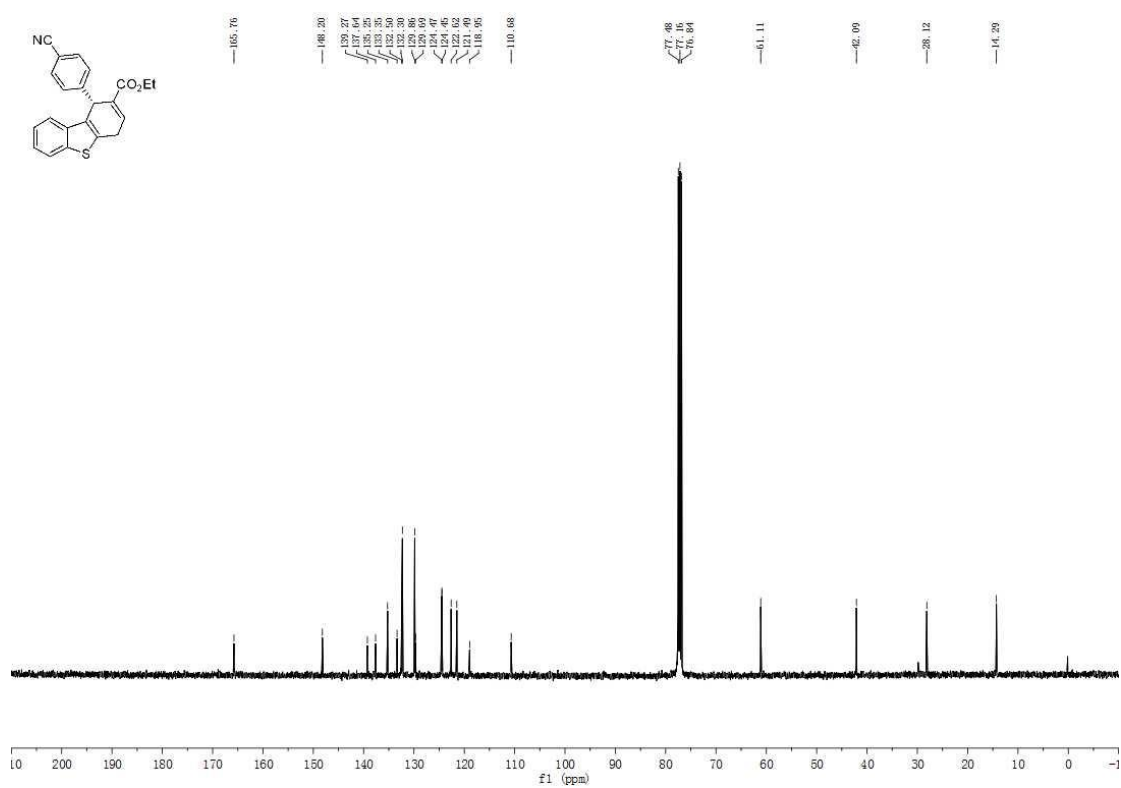


Figure S60. ¹H NMR spectrum of **6c**, related to Scheme 3.

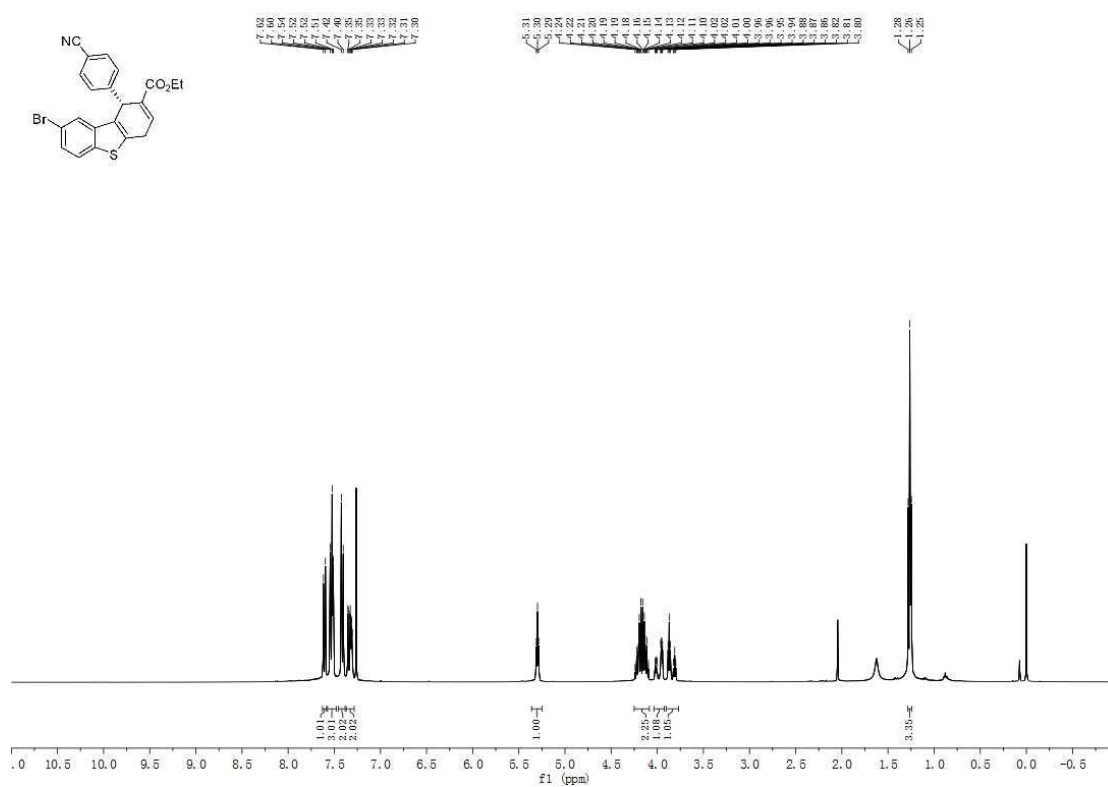


Figure S61. ¹³C NMR spectrum of **6c**, related to Scheme 3.

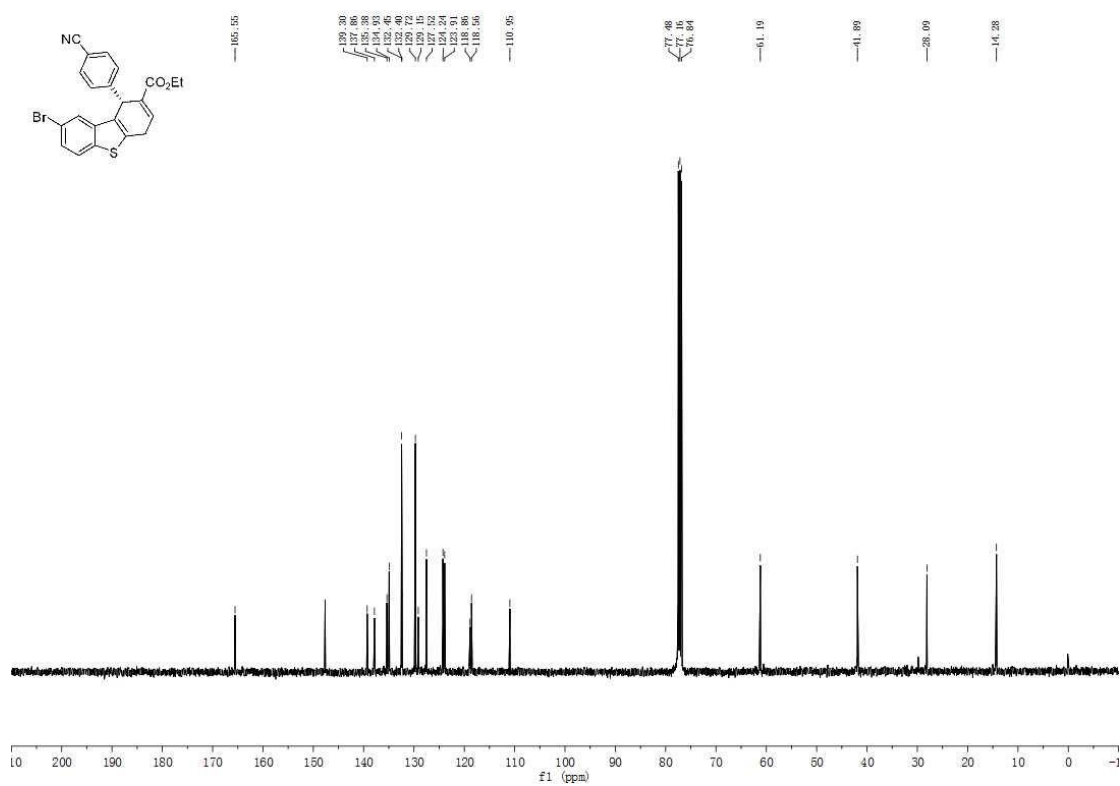


Figure S62. ¹H NMR spectrum of **6d**, related to Scheme 3.

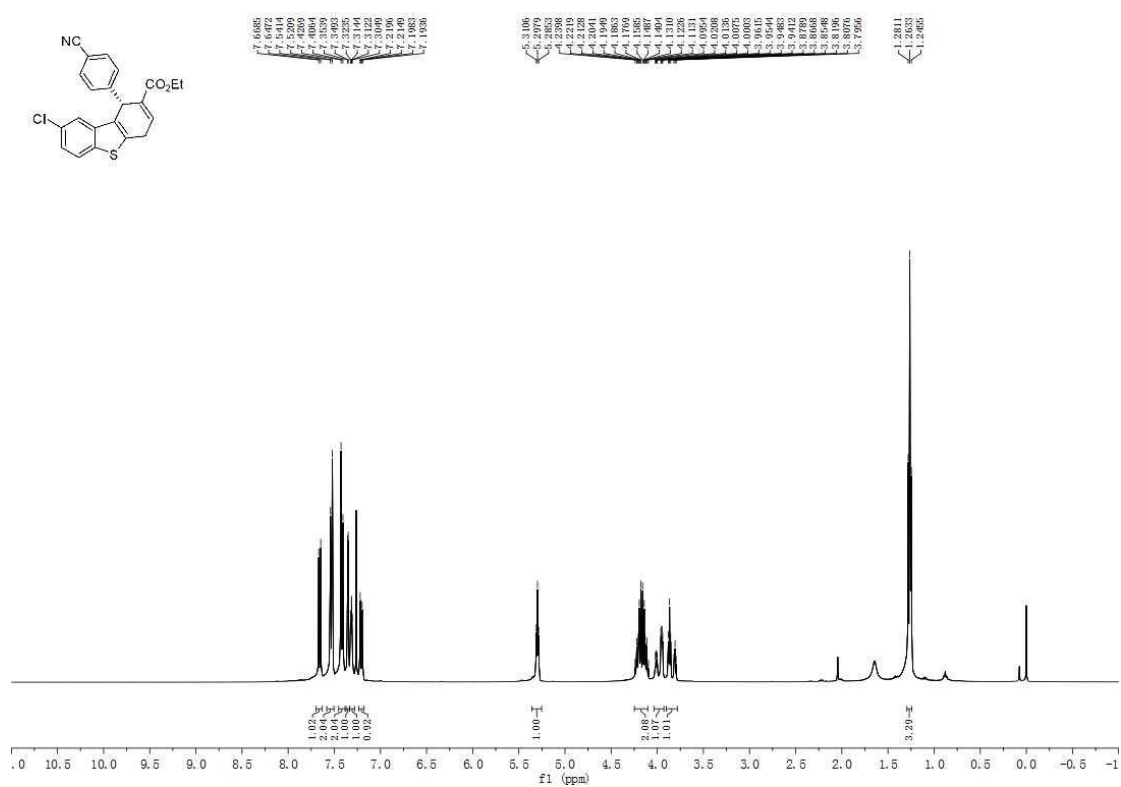


Figure S63. ¹³C NMR spectrum of **6d**, related to Scheme 3.

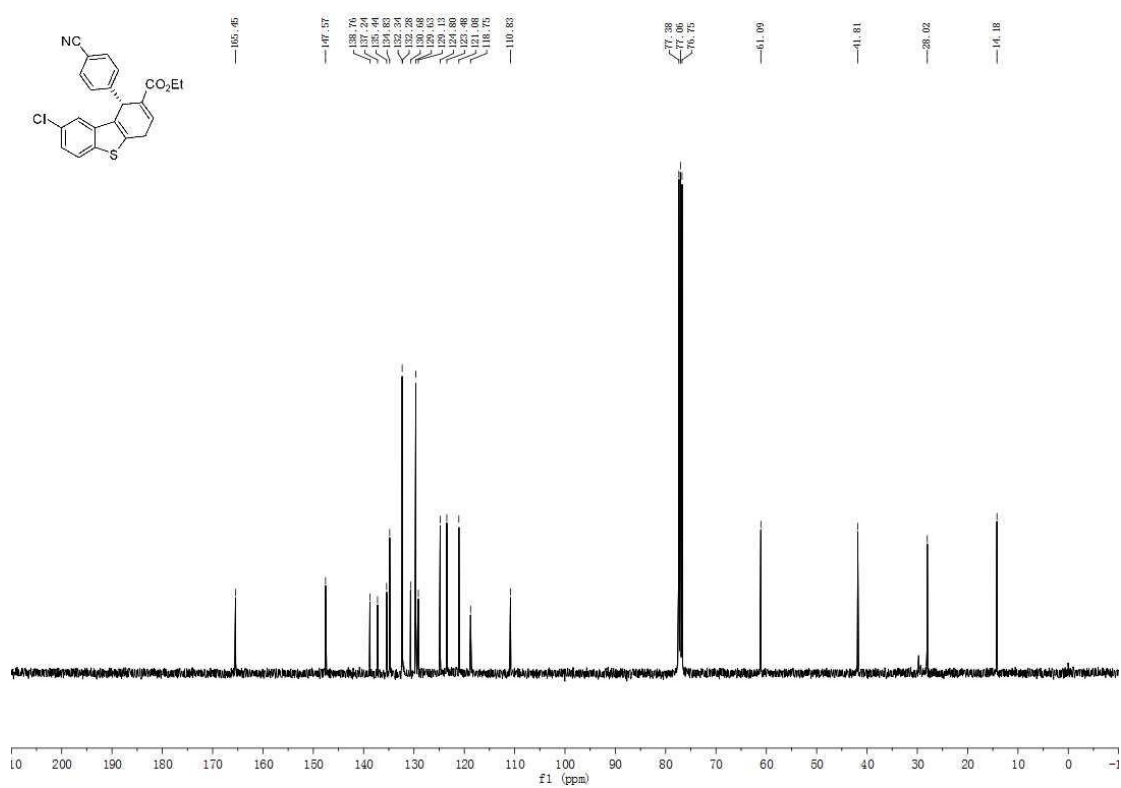


Figure S66. ¹H NMR spectrum of **6f**, related to Scheme 3.

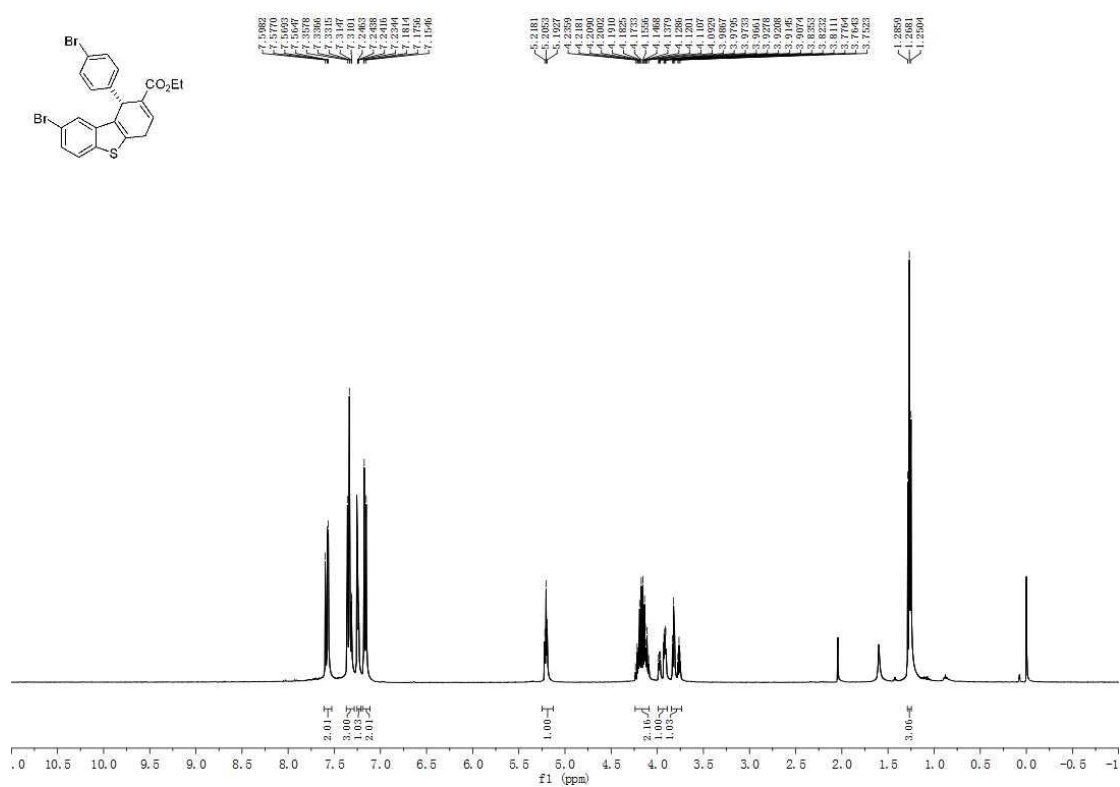


Figure S67. ¹³C NMR spectrum of **6f**, related to Scheme 3.

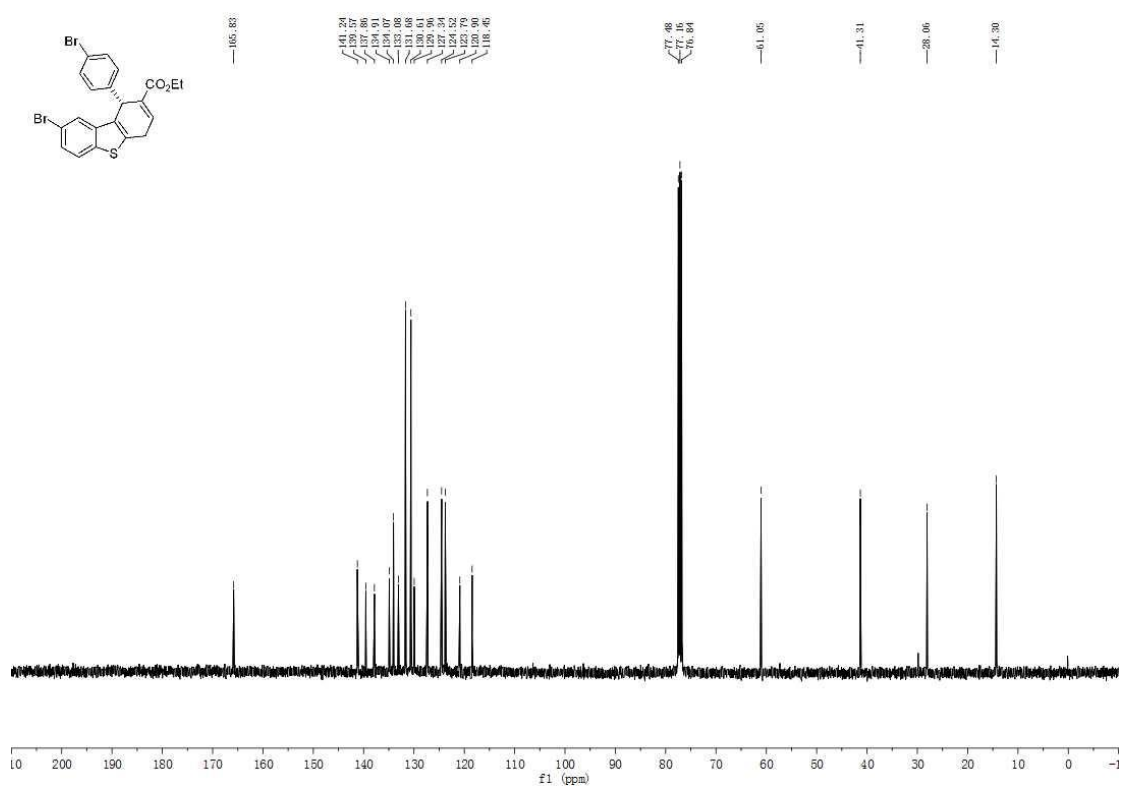


Figure S68. ¹H NMR spectrum of **6g**, related to Scheme 3.

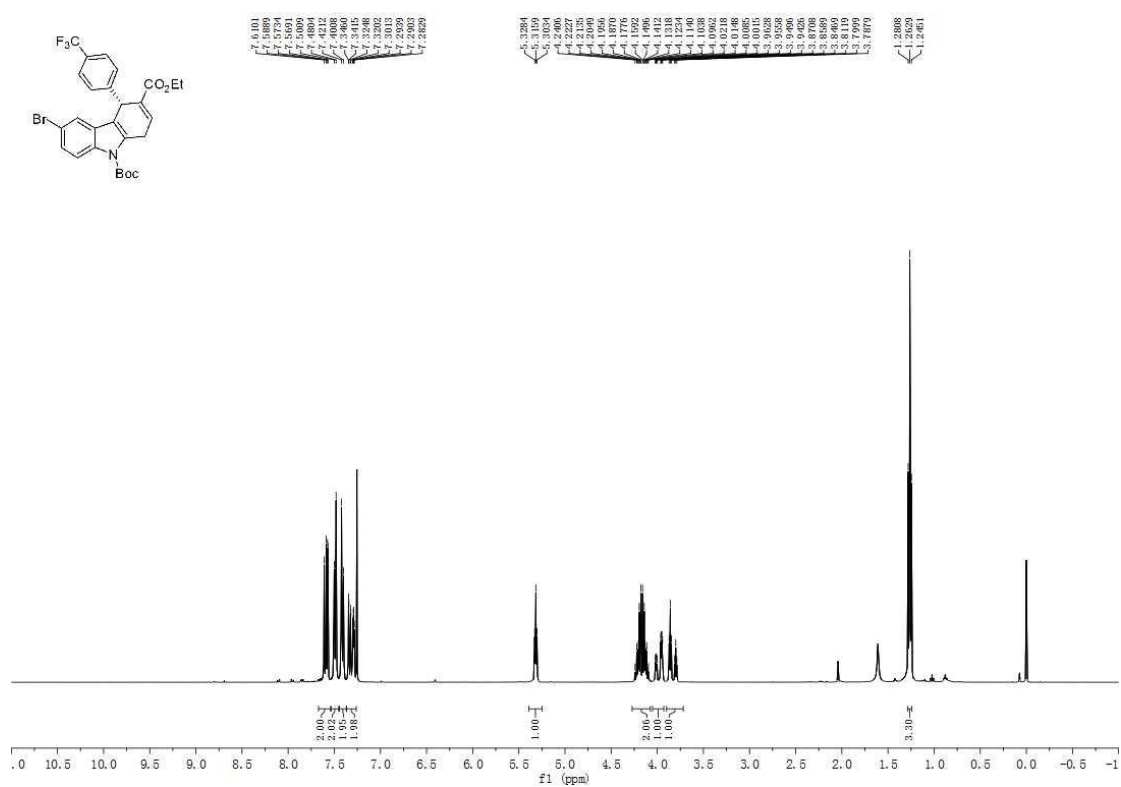


Figure S69. ¹³C NMR spectrum of **6g**, related to Scheme 3.

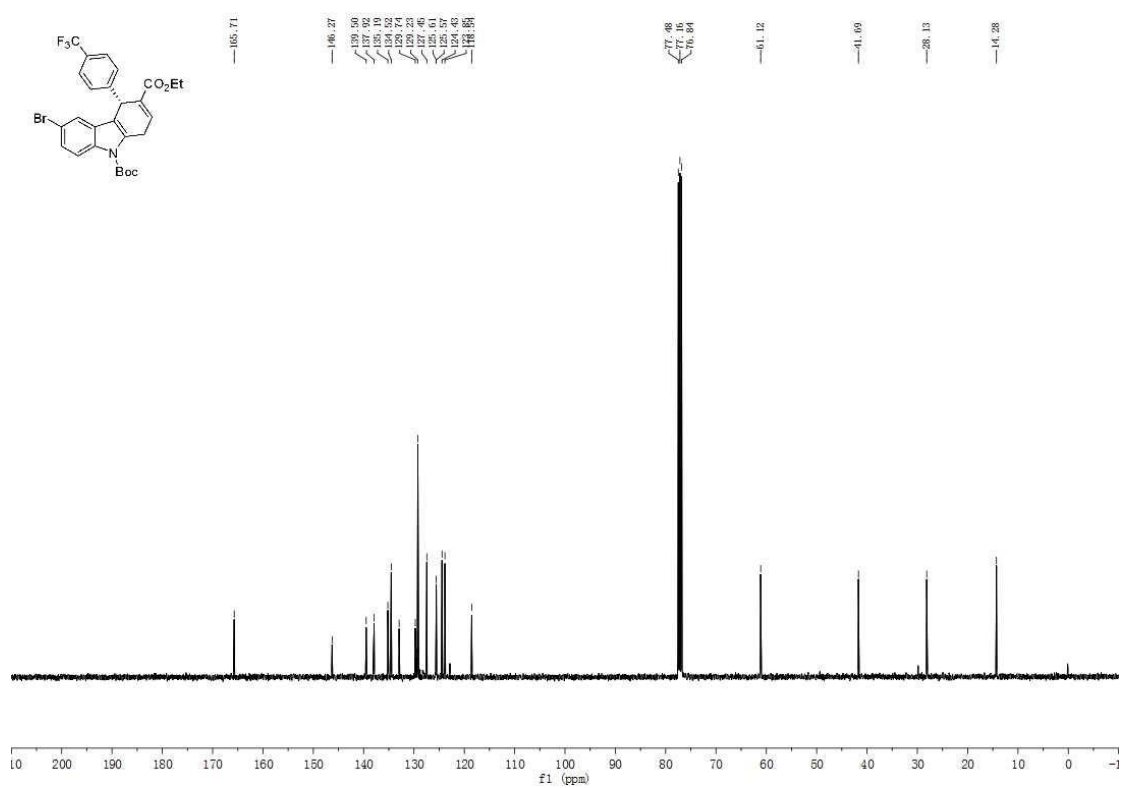


Figure S70. ^{19}F NMR spectrum of **6g**, related to **Scheme 3**.

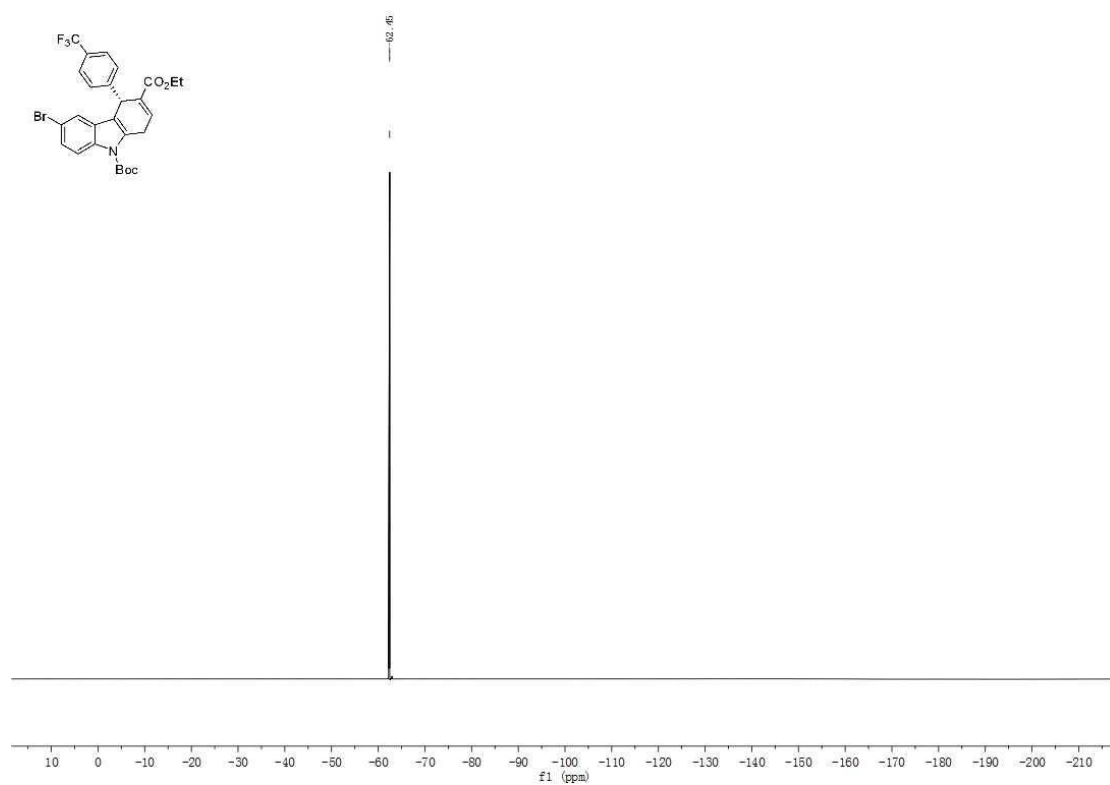


Figure S71. ¹H NMR spectrum of **6h**, related to Scheme 3.

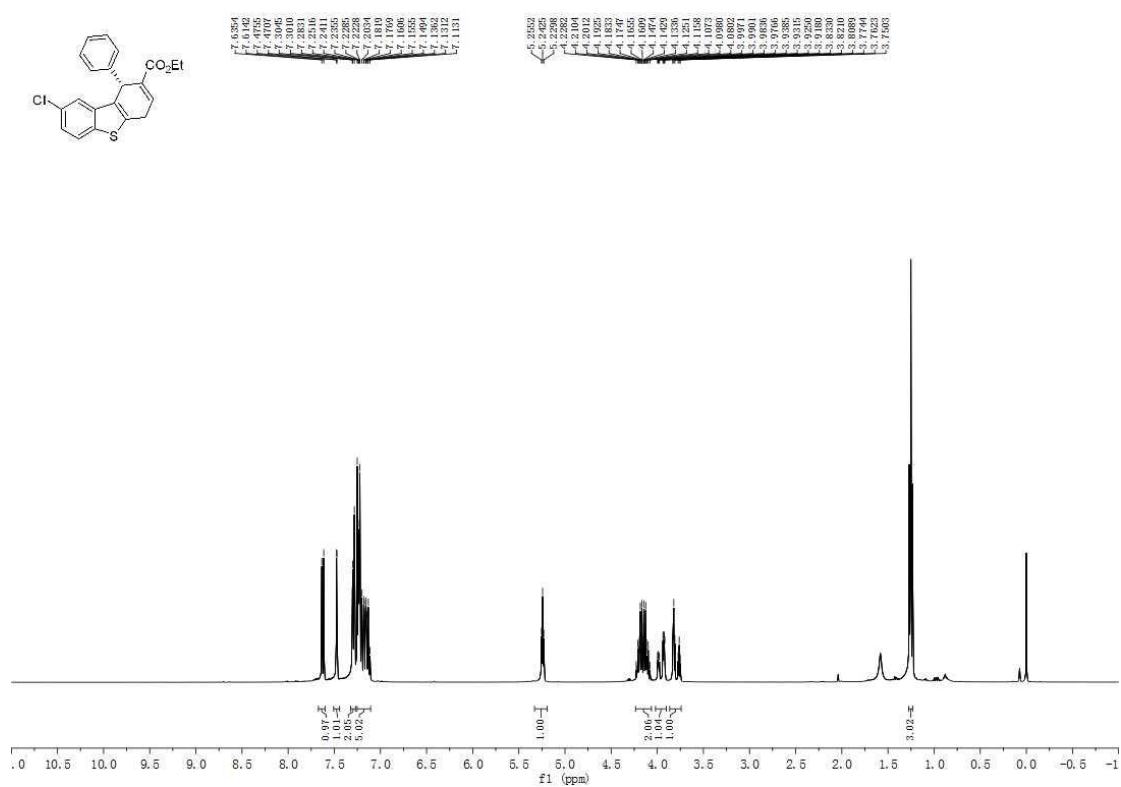


Figure S72. ¹³C NMR spectrum of **6h**, related to Scheme 3.

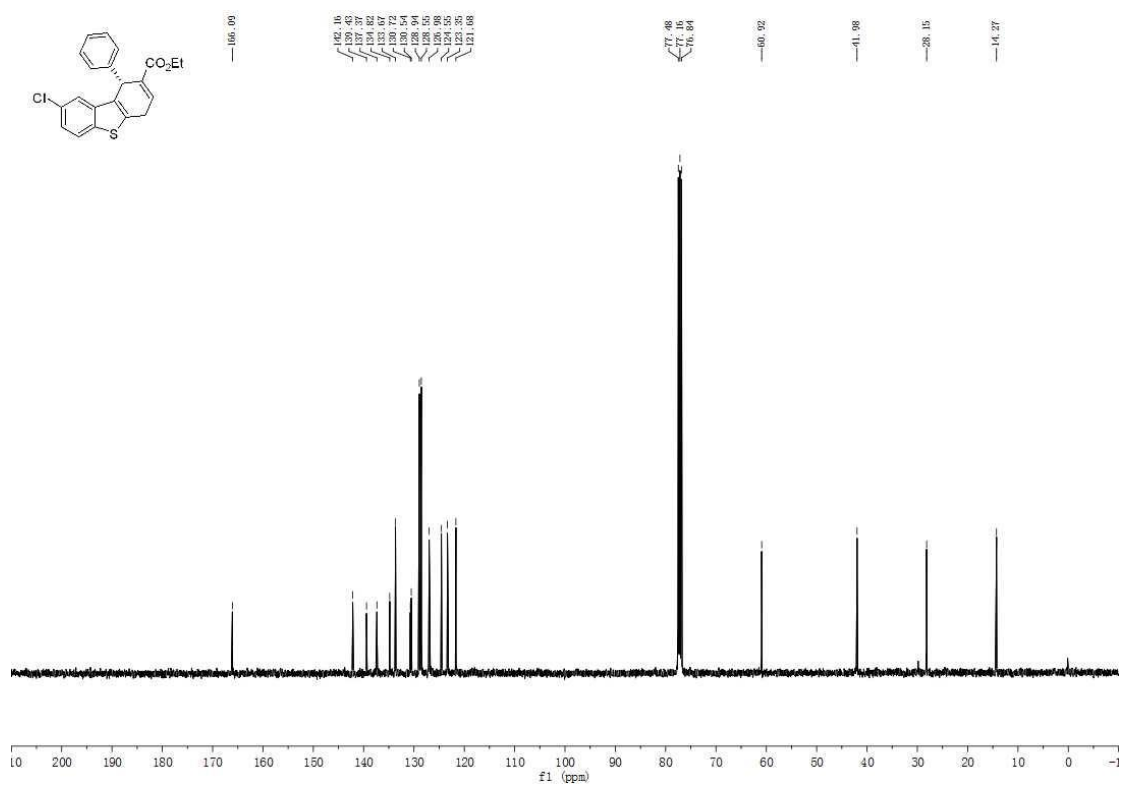


Figure S73. ¹H NMR spectrum of **7**, related to Scheme 4.

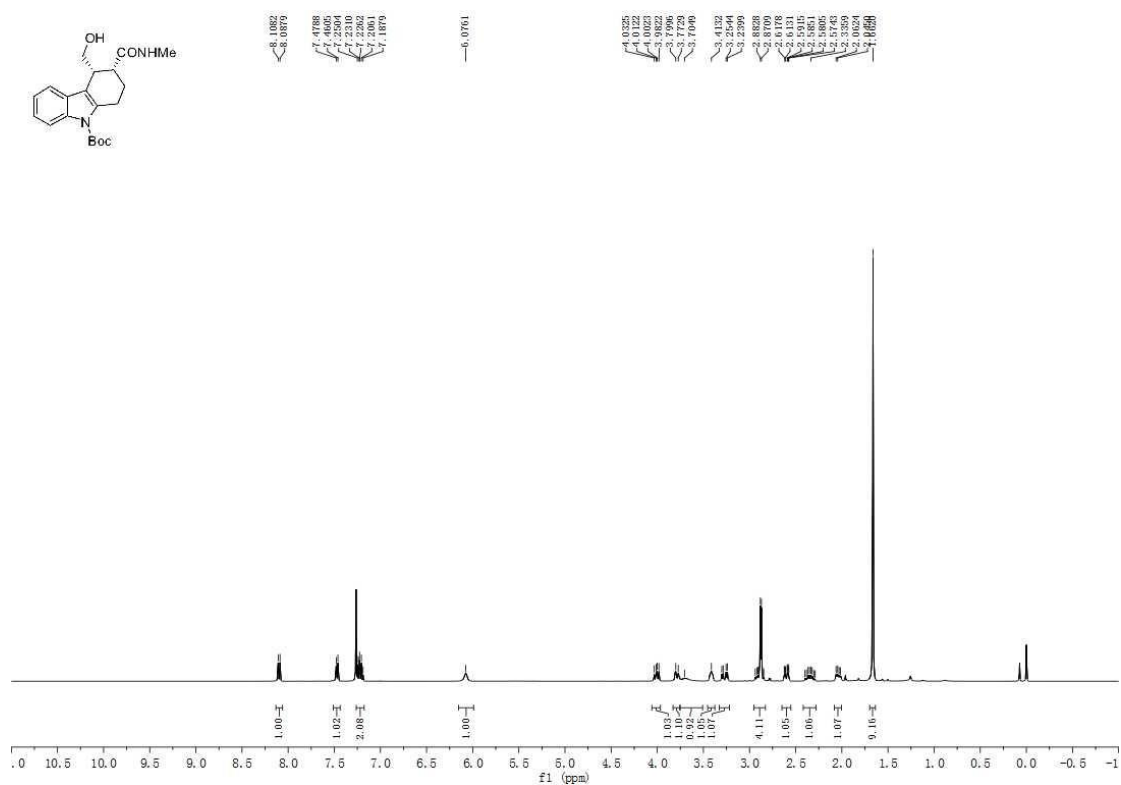


Figure S74. ¹³C NMR spectrum of **7**, related to Scheme 4.

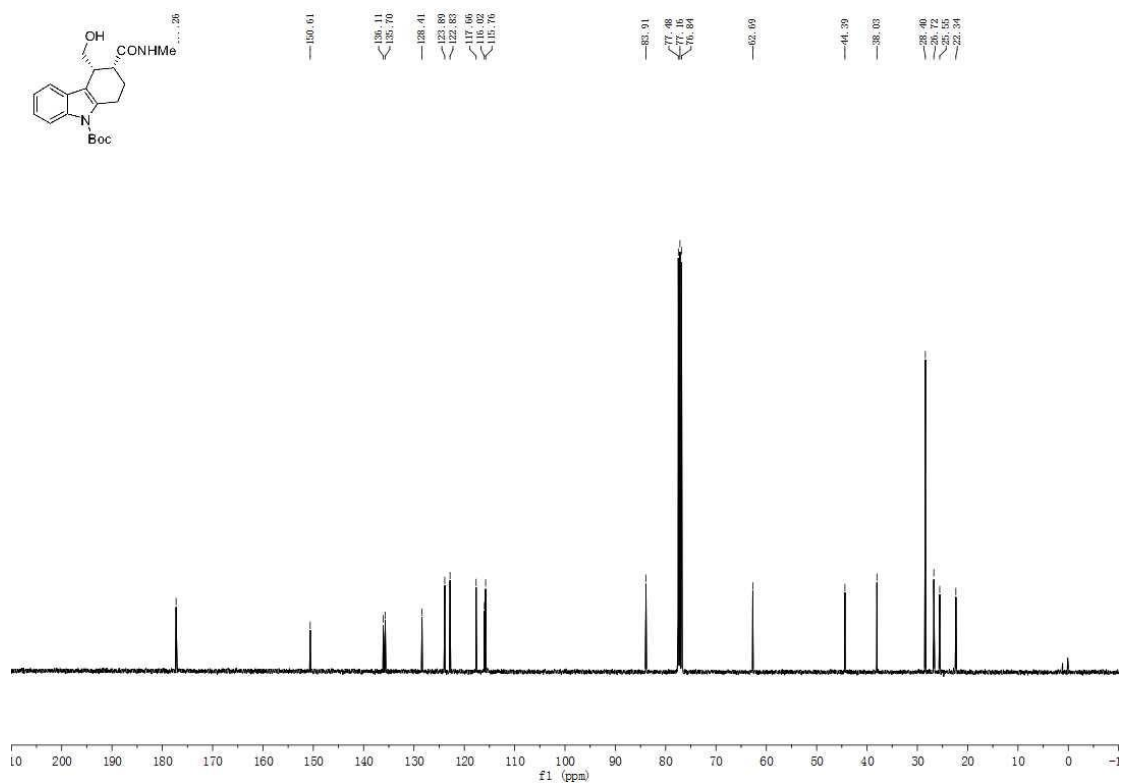


Figure S77. ¹H NMR spectrum of **9**, related to Scheme 4.

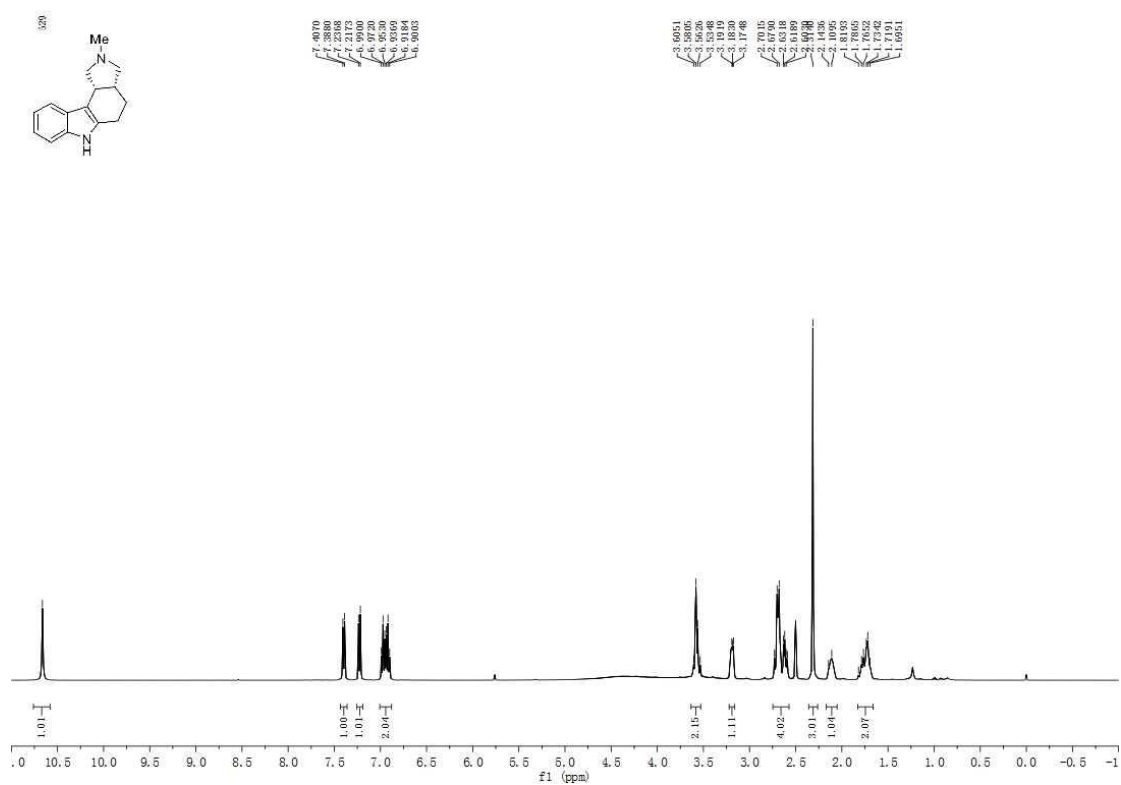


Figure S78. ¹³C NMR spectrum of **9**, related to Scheme 4.

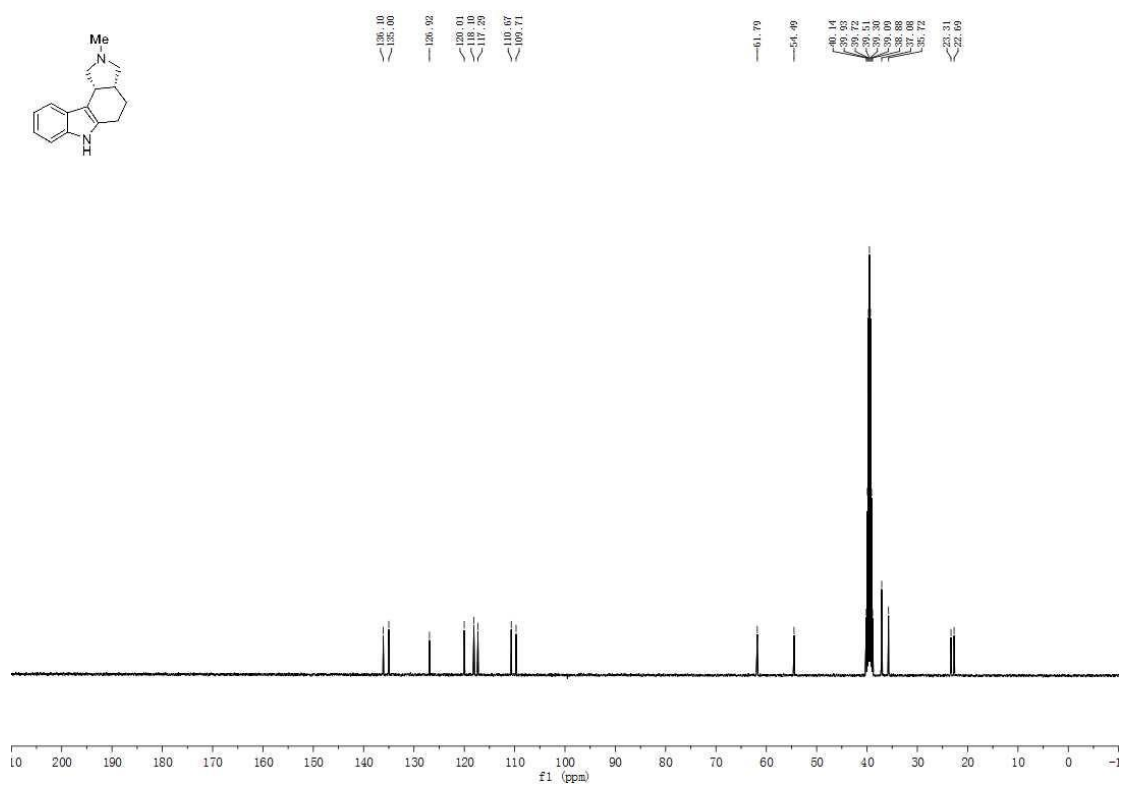


Figure S79. ¹H NMR spectrum of **10**, related to Table 1.

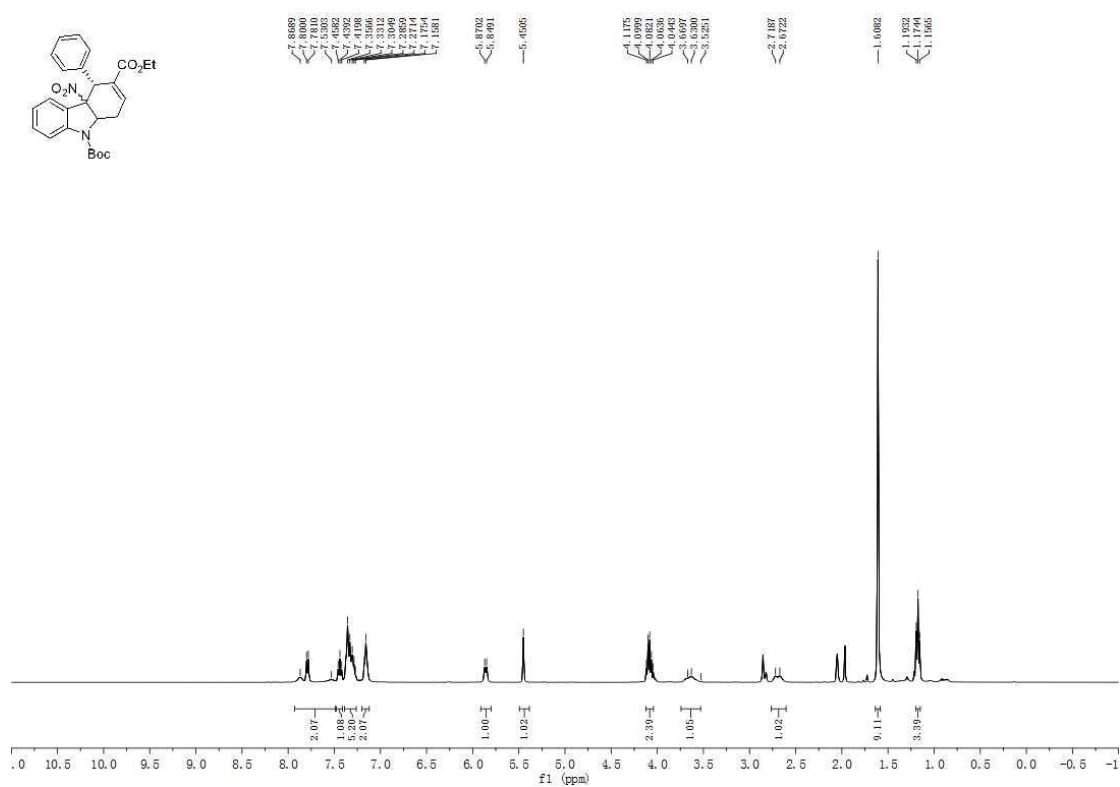
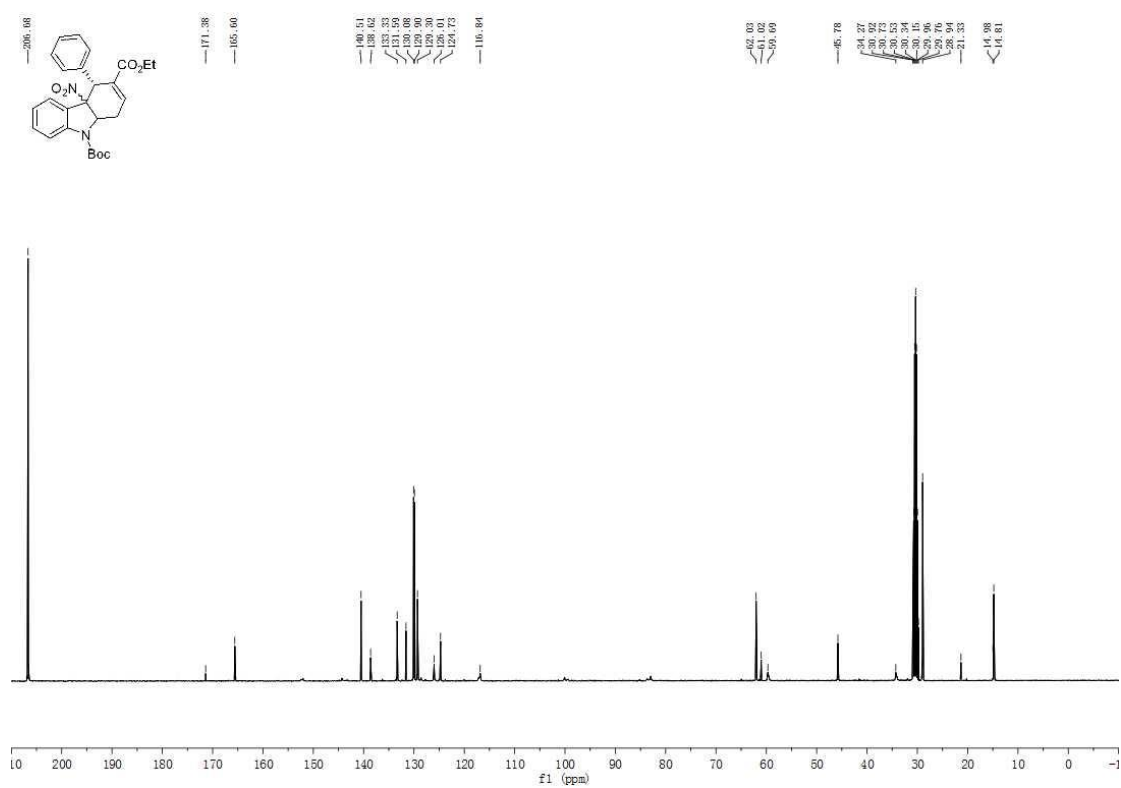


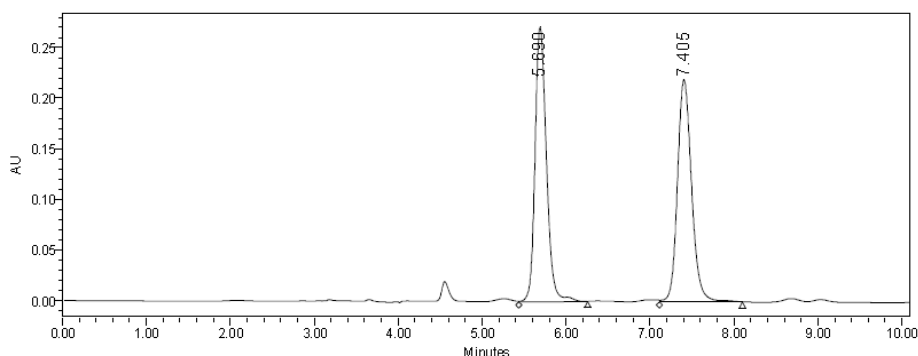
Figure S80. ¹³C NMR spectrum of **10**, related to Table 1.



Supplemental Figures for HPLC spectra

Figure S81. HPLC spectra of *rac*-3a, related to Scheme 2.

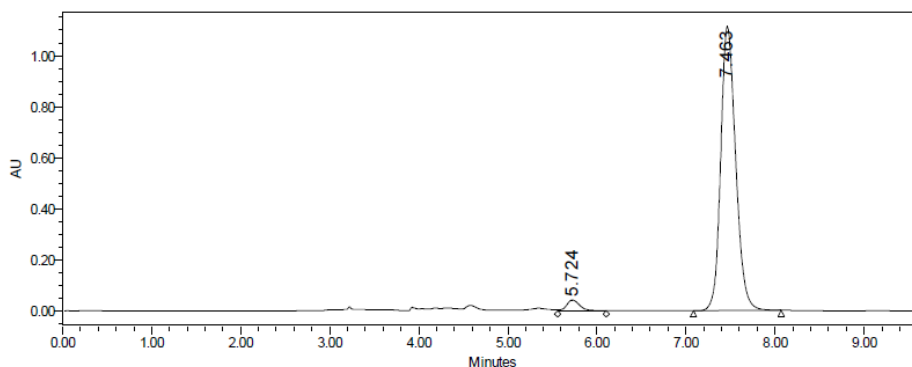
SAMPLE INFORMATION			
Sample Name:	why-g05-72-5-rac-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	61	Acq. Method Set:	3%
Injection #:	2	Processing Method	5 72 5 RAC
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	9/24/2019 2:39:18 PM CST		
Date Processed:	9/24/2019 2:53:07 PM CST		



	RT	Area	% Area	Height
1	5.690	2580919	50.07	271284
2	7.405	2554055	49.93	219595

Figure S82. HPLC spectra of 3a, related to Scheme 2.

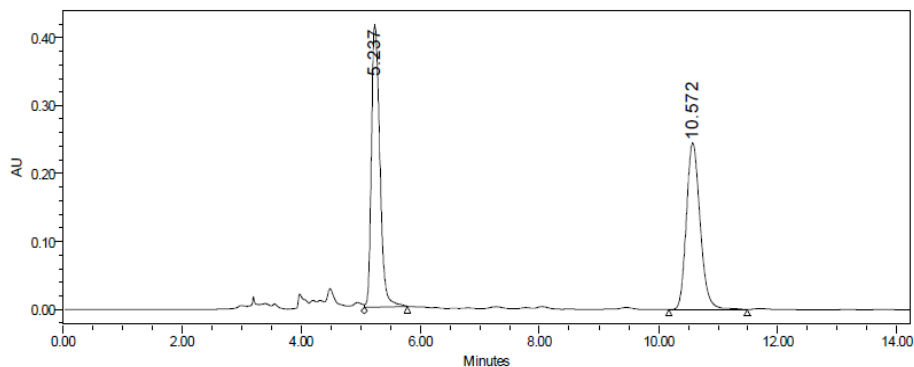
SAMPLE INFORMATION			
Sample Name:	why-g05-72-5-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	37	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 72 5
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/13/2019 4:32:02 PM CST		
Date Processed:	7/19/2019 4:19:16 PM CST		



	RT	Area	% Area	Height
1	5.724	434402	3.24	42393
2	7.463	12978962	96.76	1111415

Figure S83. HPLC spectra of *rac-3b*, related to **Scheme 2**.

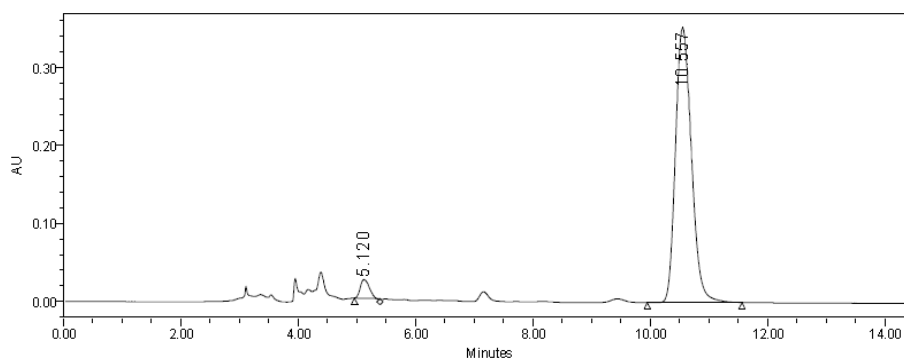
SAMPLE INFORMATION			
Sample Name:	why-g05-102-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	45	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 102 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/5/2019 4:48:39 PM CST		
Date Processed:	7/19/2019 4:24:54 PM CST		



	RT	Area	% Area	Height
1	5.237	4069692	50.92	415006
2	10.572	3922670	49.08	245275

Figure S84. HPLC spectra of **3b**, related to **Scheme 2**.

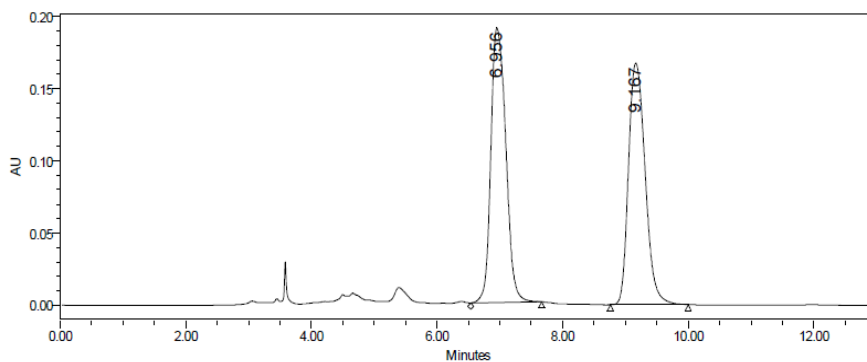
SAMPLE INFORMATION			
Sample Name:	why-g05-102-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	80	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 102 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/7/2019 3:50:53 PM CST		
Date Processed:	9/23/2019 8:46:36 PM CST		



	RT	Area	% Area	Height
1	5.120	260126	3.78	24045
2	10.557	6618616	96.22	352534

Figure S85. HPLC spectra of *rac*-**3c**, related to Scheme 2.

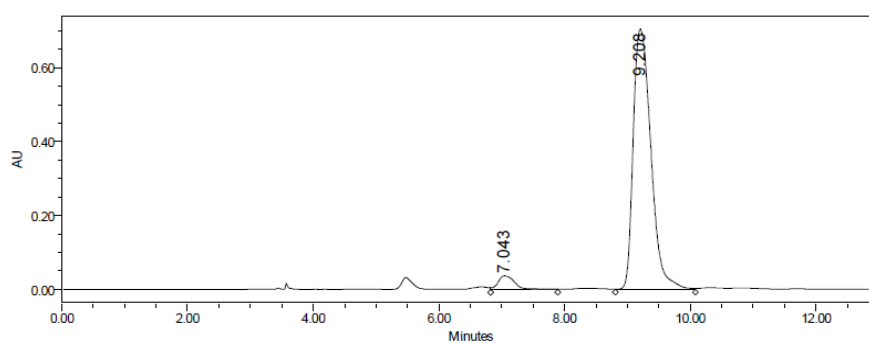
SAMPLE INFORMATION			
Sample Name:	why-g05-118-1-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	7	Acq. Method Set:	1.5%
Injection #:	1	Processing Method:	5.118.1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/23/2019 10:26:54 AM CST		
Date Processed:	7/19/2019 4:27:37 PM CST		



	RT	Area	% Area	Height
1	6.956	3151355	50.36	189896
2	9.167	3106347	49.64	167240

Figure S86. HPLC spectra of **3c**, related to Scheme 2.

SAMPLE INFORMATION			
Sample Name:	why-g05-118-2-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	43	Acq. Method Set:	1.5%
Injection #:	1	Processing Method:	5.118.2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/23/2019 10:41:01 AM CST		
Date Processed:	7/19/2019 4:28:16 PM CST		



	RT	Area	% Area	Height
1	7.043	663366	4.57	36756
2	9.208	13837500	95.43	702659

Figure S87. HPLC spectra of *rac*-**3d**, related to **Scheme 2**.

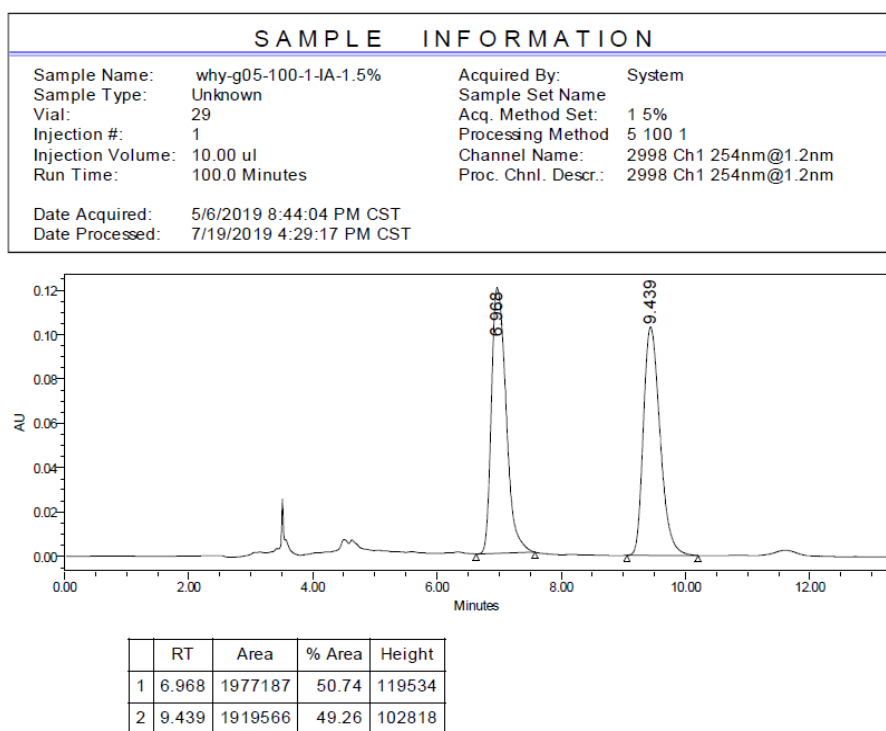


Figure S88. HPLC spectra of **3d**, related to **Scheme 2**.

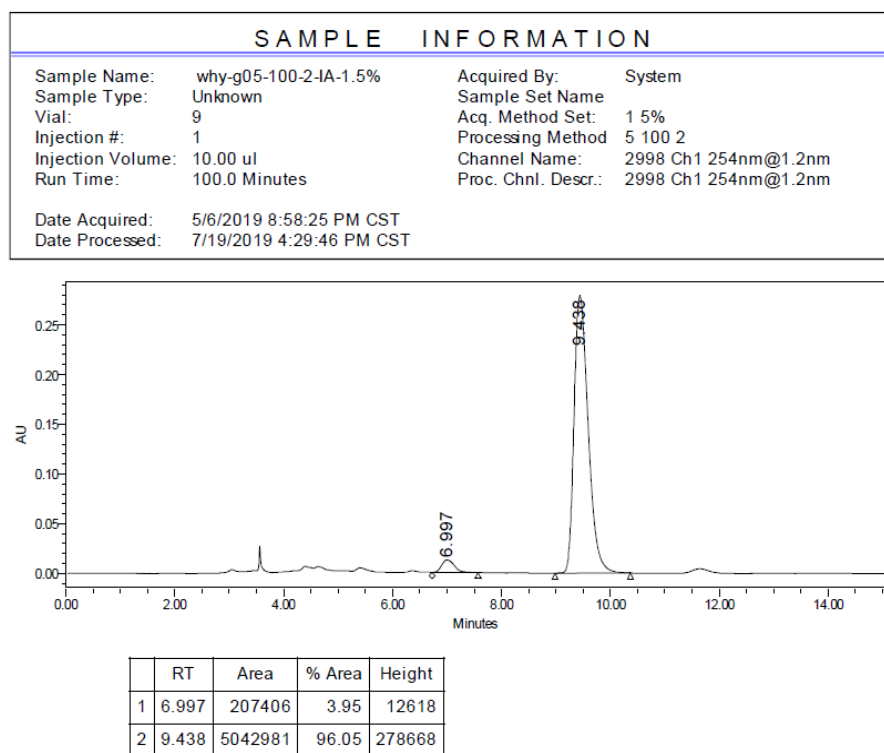
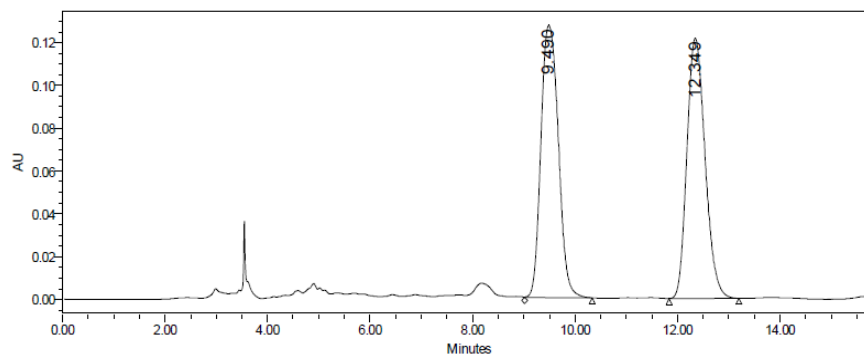


Figure S89. HPLC spectra of *rac*-**3e**, related to **Scheme 2**.

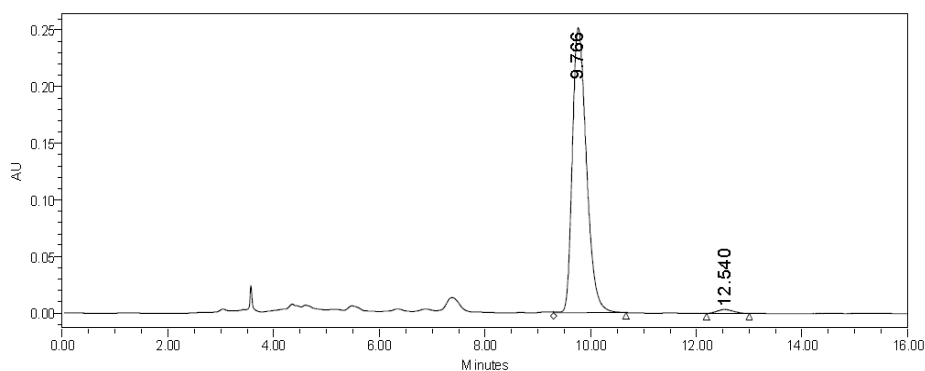
SAMPLE INFORMATION			
Sample Name:	why-g05-101-1-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	37	Acq. Method Set:	1 5%
Injection #:	1	Processing Method:	5 101 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/4/2019 8:54:53 PM CST		
Date Processed:	7/19/2019 4:31:14 PM CST		



	RT	Area	% Area	Height
1	9.490	3002746	50.01	127223
2	12.349	3001033	49.99	121658

Figure S90. HPLC spectra of **3e**, related to **Scheme 2**.

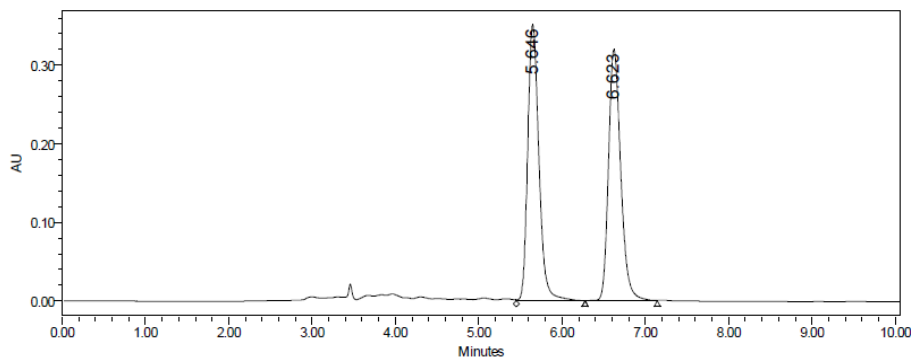
SAMPLE INFORMATION			
Sample Name:	why-g05-101-2-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	20190506
Vial:	10	Acq. Method Set:	1 5%
Injection #:	1	Processing Method:	5 101 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	16.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/6/2019 8:06:10 PM CST		
Date Processed:	8/4/2019 2:53:57 PM CST		



	RT	Area	% Area	Height
1	9.766	4614701	98.50	251558
2	12.540	70049	1.50	3342

Figure S91. HPLC spectra of *rac*-**3f**, related to **Scheme 2**.

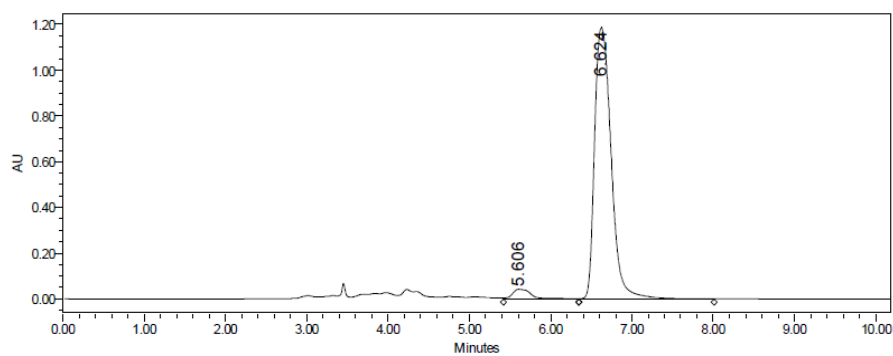
SAMPLE INFORMATION			
Sample Name:	why-g05-103-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	46	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 103 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/5/2019 5:09:33 PM CST		
Date Processed:	7/19/2019 4:32:50 PM CST		



	RT	Area	% Area	Height
1	5.646	3262228	50.18	350856
2	6.623	3238870	49.82	319764

Figure S92. HPLC spectra of **3f**, related to **Scheme 2**.

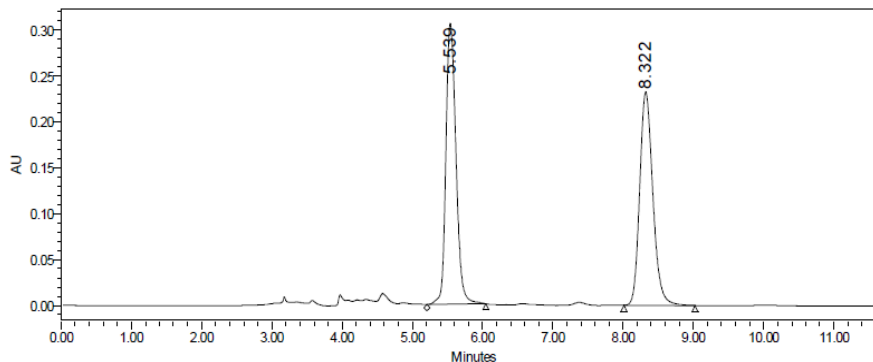
SAMPLE INFORMATION			
Sample Name:	why-g05-103-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	105	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 103 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/8/2019 8:52:48 PM CST		
Date Processed:	7/19/2019 4:33:25 PM CST		



	RT	Area	% Area	Height
1	5.606	719834	4.09	42857
2	6.624	16862017	95.91	1186073

Figure S93. HPLC spectra of *rac*-**3g**, related to **Scheme 2**.

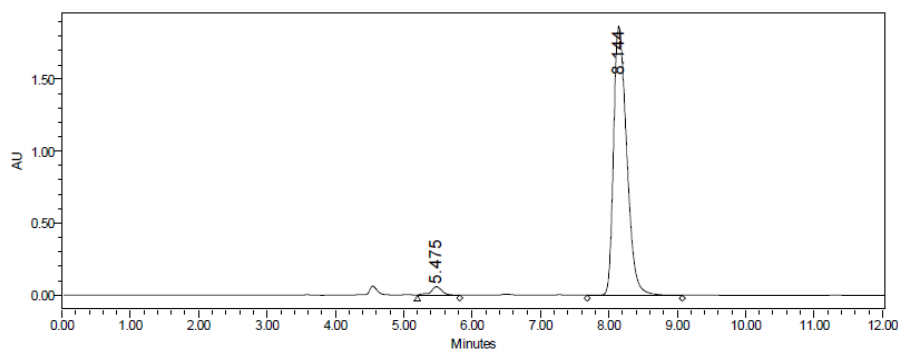
SAMPLE INFORMATION			
Sample Name:	why-g05-104-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	117	Acq. Method Set:	3%
Injection #:	2	Processing Method	5 104 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/8/2019 8:09:13 PM CST		
Date Processed:	7/19/2019 4:34:27 PM CST		



	RT	Area	% Area	Height
1	5.539	3070027	50.27	305813
2	8.322	3037606	49.73	232393

Figure S94. HPLC spectra of **3g**, related to **Scheme 2**.

SAMPLE INFORMATION			
Sample Name:	why-g05-104-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	3	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 104 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/10/2019 2:32:38 PM CST		
Date Processed:	7/19/2019 4:35:27 PM CST		



	RT	Area	% Area	Height
1	5.475	619159	2.43	57367
2	8.144	24875543	97.57	1866265

Figure S95. HPLC spectra of *rac*-**3h**, related to **Scheme 2**.

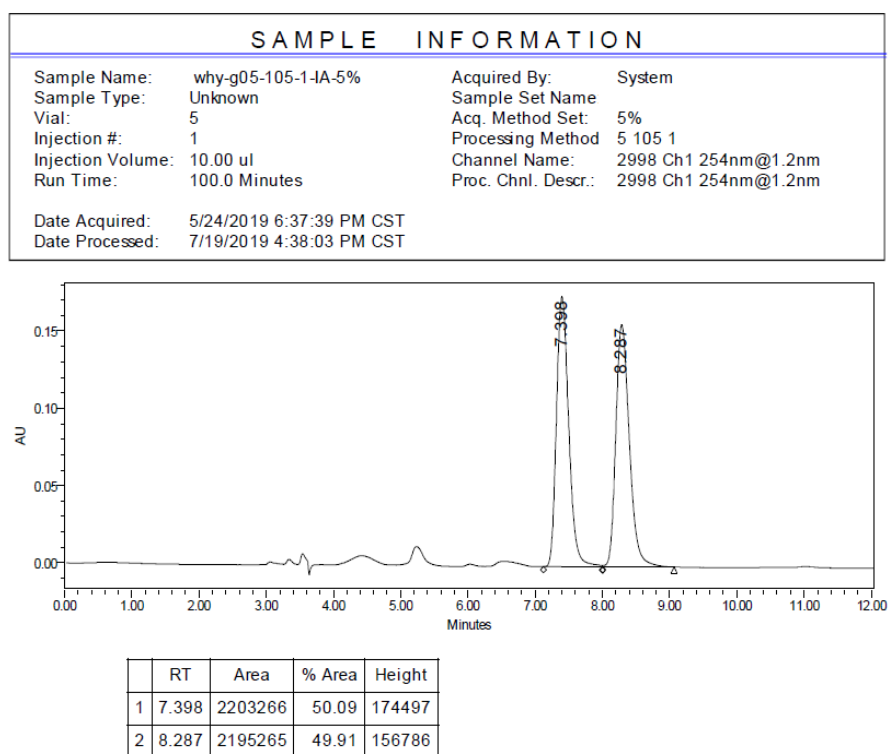


Figure S96. HPLC spectra of **3h**, related to **Scheme 2**.

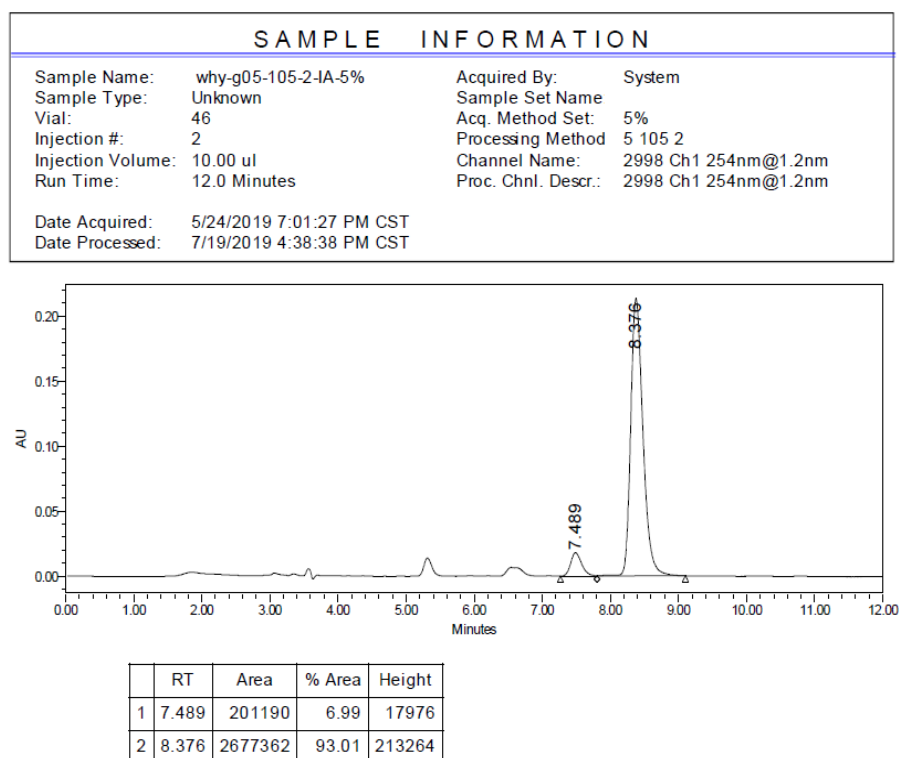


Figure S97. HPLC spectra of *rac*-3i, related to Scheme 2.

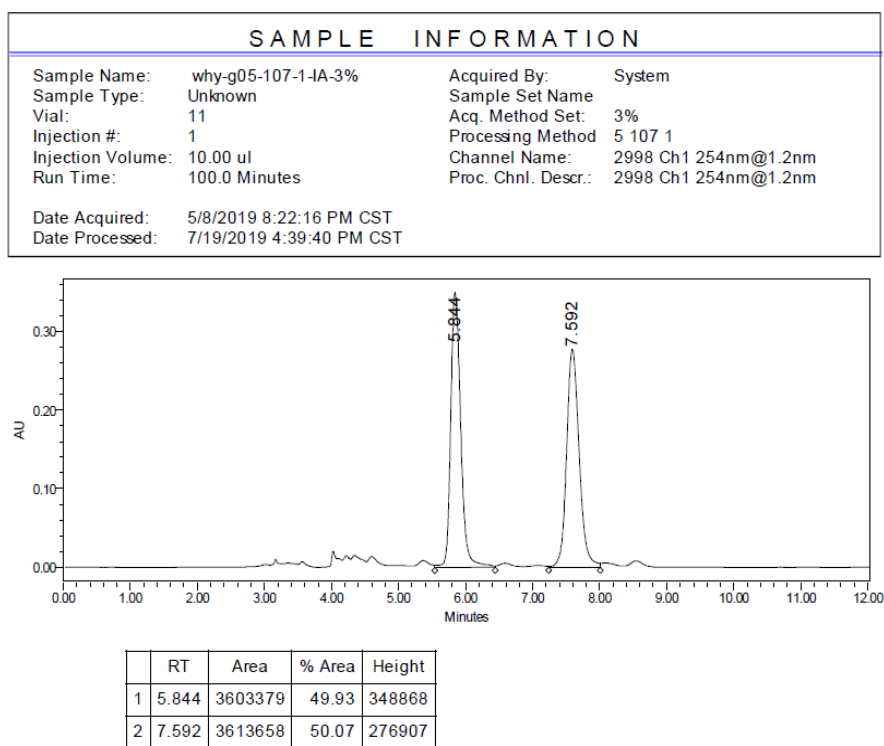


Figure S98. HPLC spectra of 3i, related to Scheme 2.

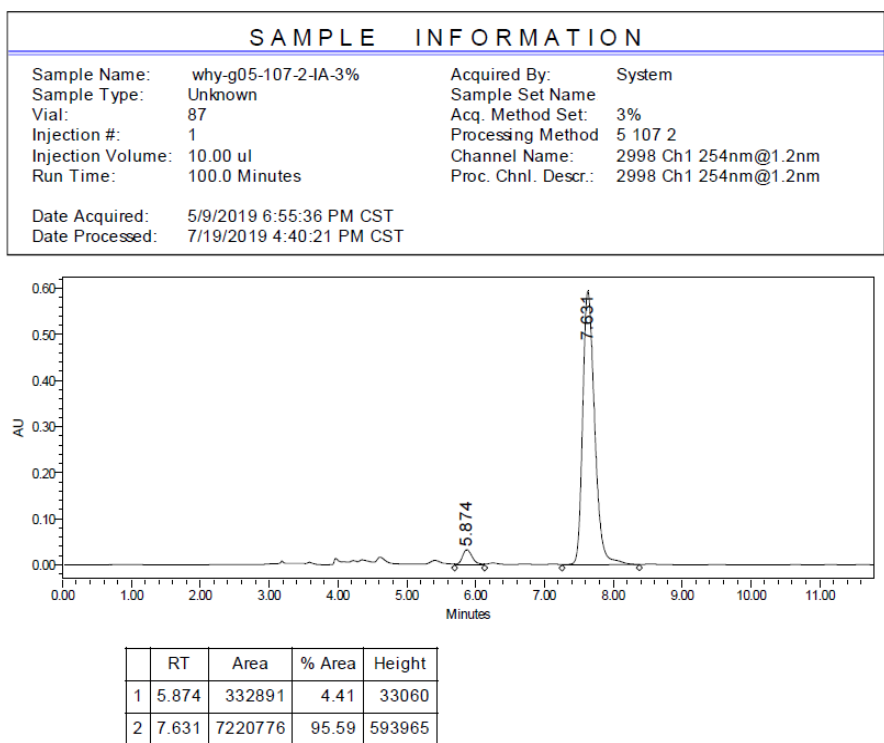
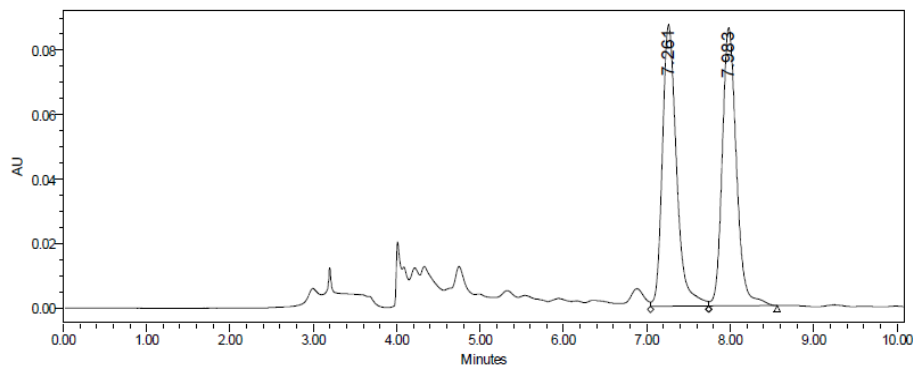


Figure S99. HPLC spectra of *rac*-3j, related to Scheme 2.

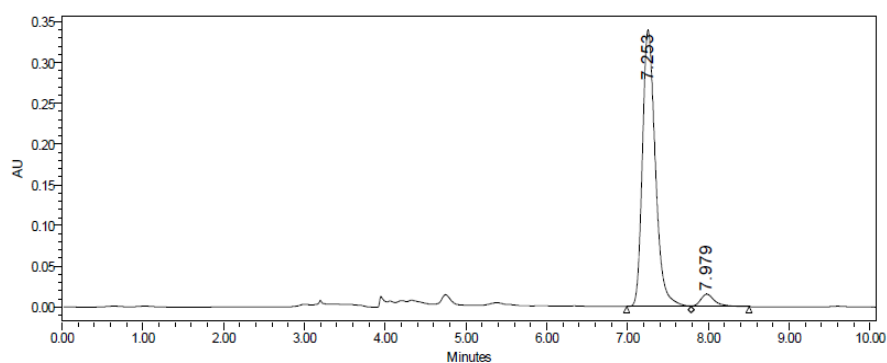
SAMPLE INFORMATION			
Sample Name:	why-g05-81-2-1A-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	60	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 81 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/22/2019 4:50:13 PM CST		
Date Processed:	7/19/2019 4:44:40 PM CST		



	RT	Area	% Area	Height
1	7.261	1026355	50.26	87261
2	7.983	1015759	49.74	86324

Figure S100. HPLC spectra of 3j, related to Scheme 2.

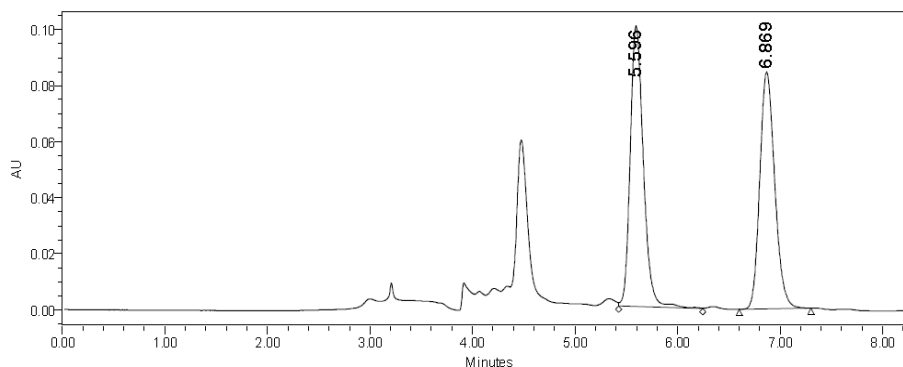
SAMPLE INFORMATION			
Sample Name:	why-g05-81-1-1A-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	3	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 81 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/22/2019 5:01:20 PM CST		
Date Processed:	7/19/2019 4:45:09 PM CST		



	RT	Area	% Area	Height
1	7.253	3759068	95.17	338669
2	7.979	190617	4.83	15191

Figure S101. HPLC spectra of *rac-3k*, related to **Scheme 2**.

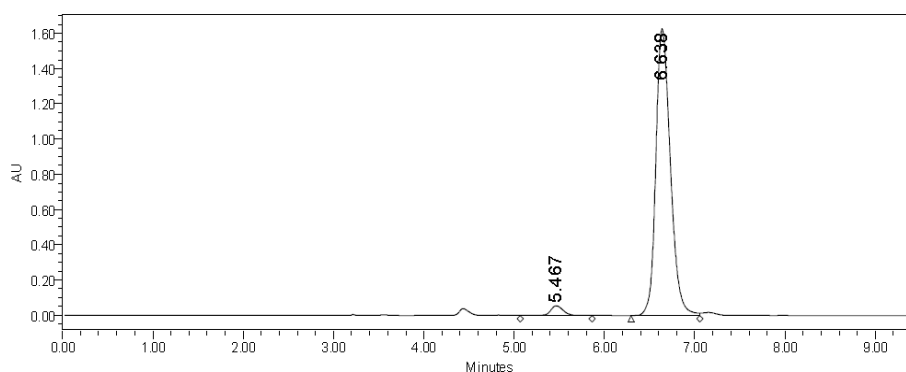
SAMPLE INFORMATION			
Sample Name:	why-g05-77-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	17	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 77 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/18/2019 7:20:40 PM CST		
Date Processed:	7/19/2019 4:52:42 PM CST		



	RT	Area	% Area	Height
1	5.596	897583	51.14	100114
2	6.869	857680	48.86	84508

Figure S102. HPLC spectra of **3k**, related to **Scheme 2**.

SAMPLE INFORMATION			
Sample Name:	why-g05-77-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	61	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 77 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/23/2019 4:09:48 PM CST		
Date Processed:	8/5/2019 4:15:42 PM CST		



	RT	Area	% Area	Height
1	5.467	548142	2.91	54996
2	6.638	18266140	97.09	1626763

Figure S103. HPLC spectra of *rac*-**3I**, related to **Scheme 2**.

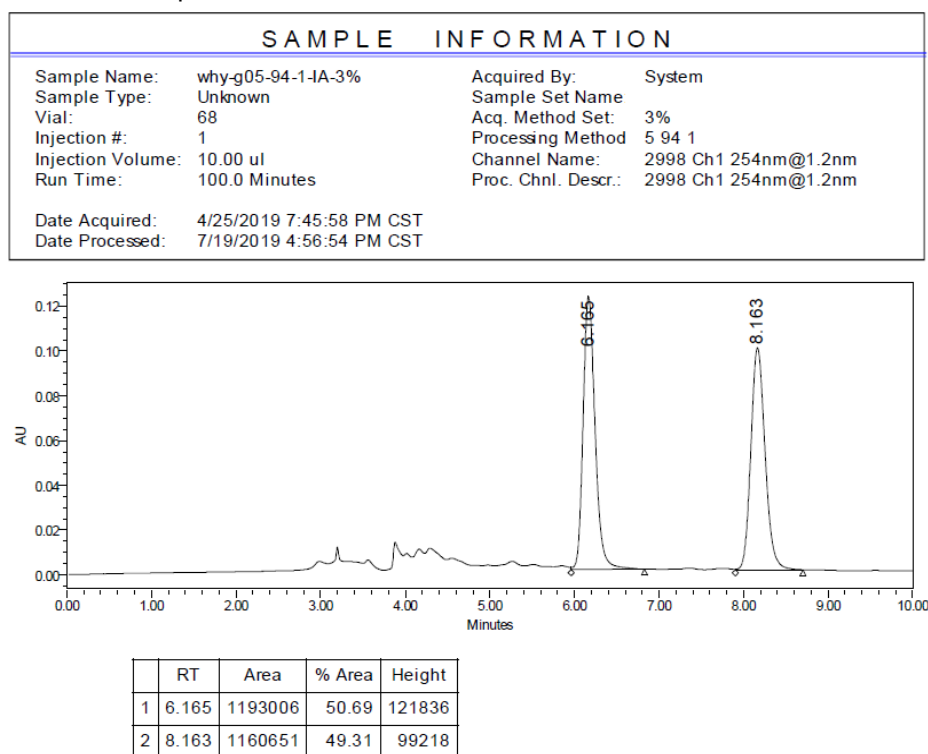


Figure S104. HPLC spectra of **3I**, related to **Scheme 2**.

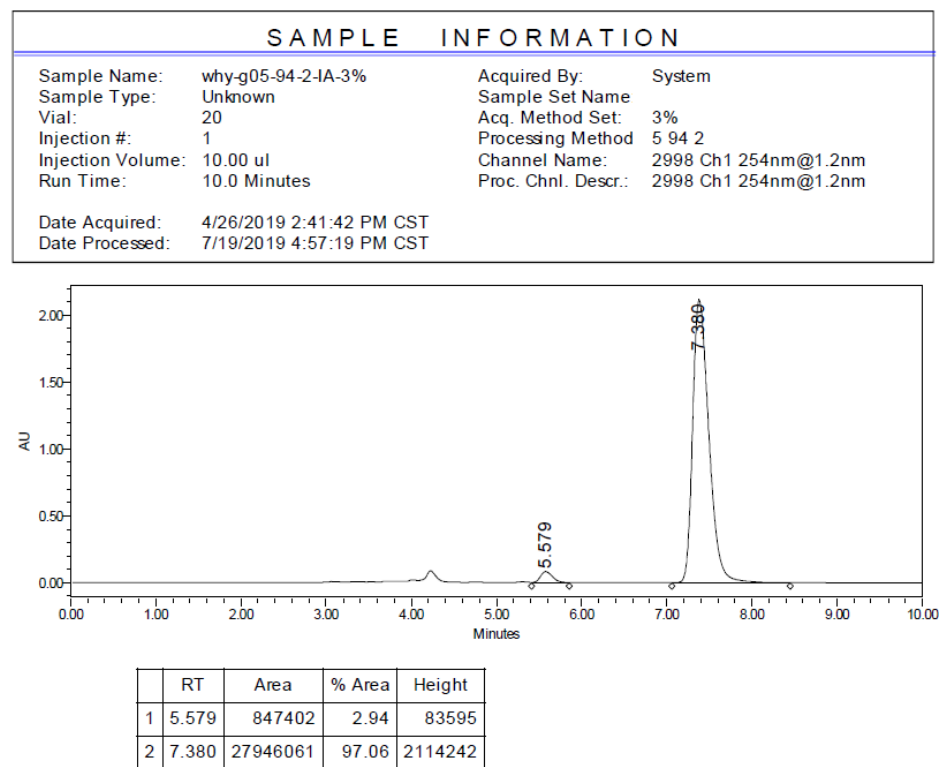
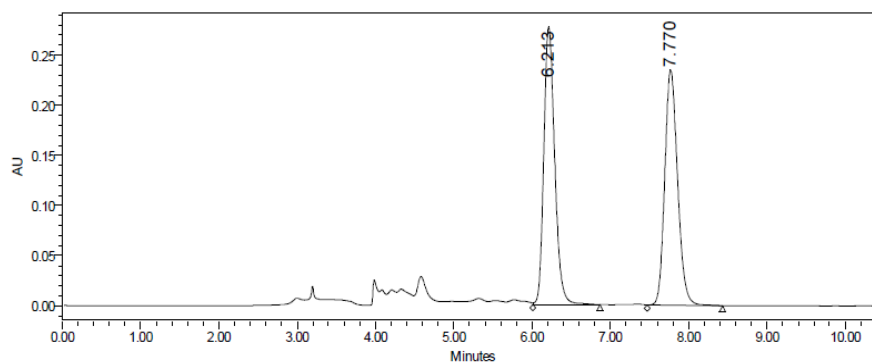


Figure S105. HPLC spectra of *rac-3m*, related to **Scheme 2**.

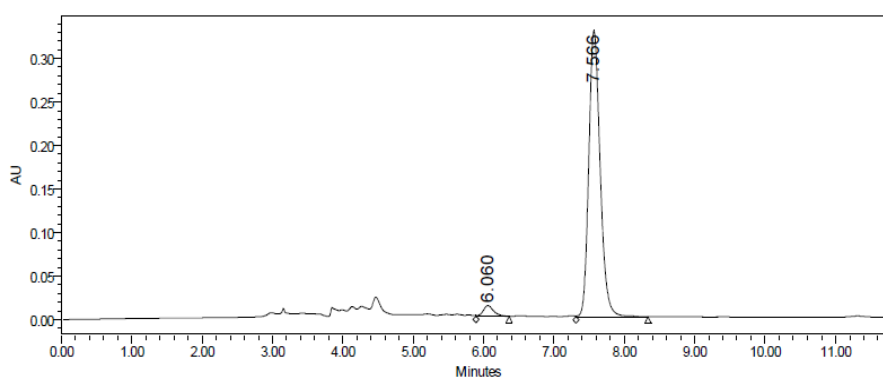
SAMPLE INFORMATION			
Sample Name:	why-g05-93-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	93	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 93 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/24/2019 7:21:42 PM CST		
Date Processed:	7/19/2019 4:55:33 PM CST		



	RT	Area	% Area	Height
1	6.213	2689605	50.26	276948
2	7.770	2661667	49.74	234692

Figure S106. HPLC spectra of **3m**, related to **Scheme 2**.

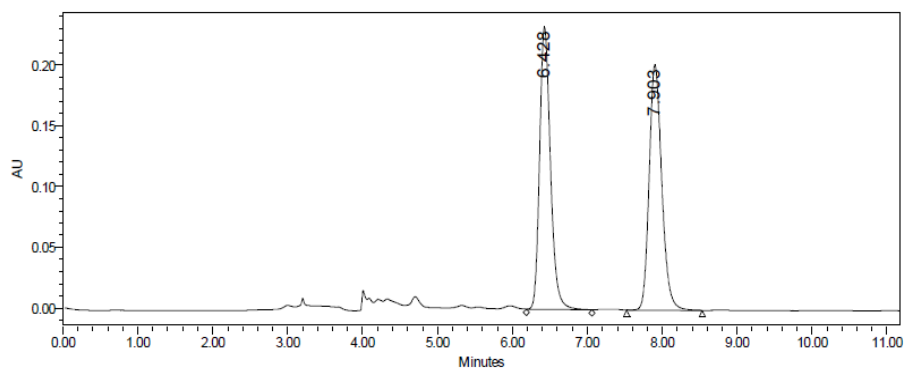
SAMPLE INFORMATION			
Sample Name:	why-g05-93-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	39	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 93 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/25/2019 7:28:12 PM CST		
Date Processed:	7/19/2019 4:56:19 PM CST		



	RT	Area	% Area	Height
1	6.060	122657	3.21	12140
2	7.566	3695531	96.79	328030

Figure S107. HPLC spectra of *rac*-**3n**, related to **Scheme 2**.

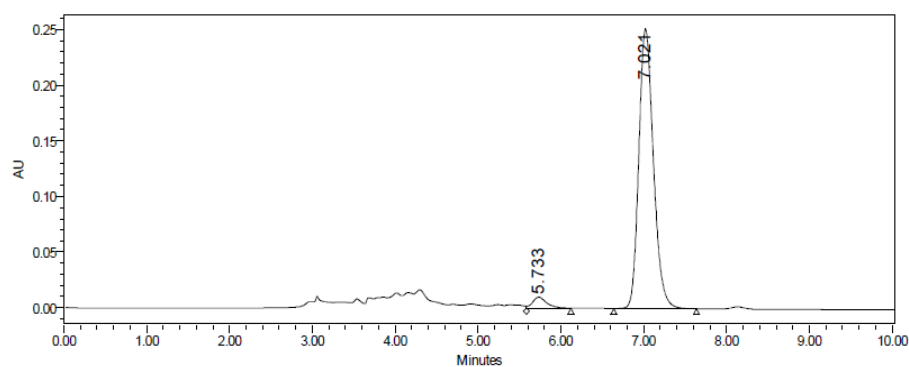
SAMPLE INFORMATION			
Sample Name:	why-g05-92-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	62	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 92 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/24/2019 7:33:32 PM CST		
Date Processed:	7/19/2019 4:54:10 PM CST		



	RT	Area	% Area	Height
1	6.428	2345053	49.77	232209
2	7.903	2367186	50.23	202032

Figure S108. HPLC spectra of **3n**, related to **Scheme 2**.

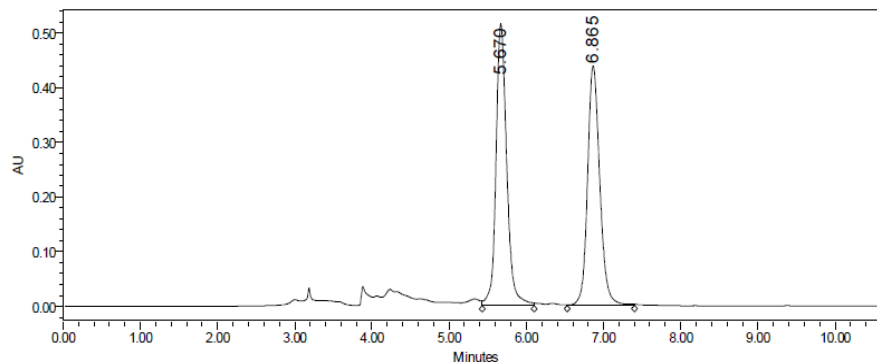
SAMPLE INFORMATION			
Sample Name:	why-g05-92-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	7	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 92 2 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/25/2019 2:53:22 PM CST		
Date Processed:	7/19/2019 4:54:40 PM CST		



	RT	Area	% Area	Height
1	5.733	112010	3.49	9656
2	7.021	3096909	96.51	251145

Figure S109. HPLC spectra of *rac-3o*, related to **Scheme 2**.

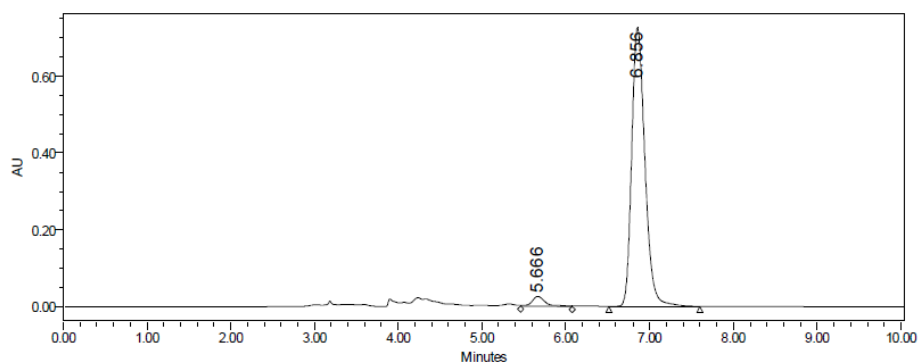
SAMPLE INFORMATION			
Sample Name:	why-g05-108-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	29	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 108 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/8/2019 8:35:18 PM CST		
Date Processed:	7/19/2019 5:00:18 PM CST		



	RT	Area	% Area	Height
1	5.670	5001622	50.69	514650
2	6.865	4864935	49.31	

Figure S110. HPLC spectra of **3o**, related to **Scheme 2**.

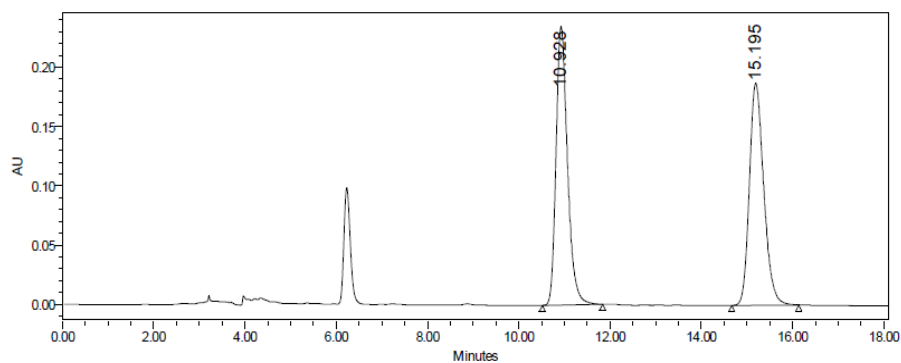
SAMPLE INFORMATION			
Sample Name:	why-g05-108-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	54	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 108 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/9/2019 6:44:31 PM CST		
Date Processed:	7/19/2019 5:00:44 PM CST		



	RT	Area	% Area	Height
1	5.666	262467	3.21	25190
2	6.856	7924180	96.79	724173

Figure S111. HPLC spectra of *rac*-**3p**, related to **Scheme 2**.

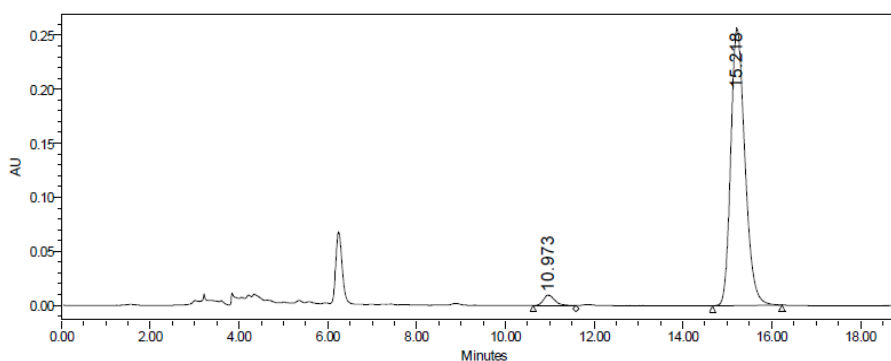
SAMPLE INFORMATION			
Sample Name:	why-g05-78-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	18	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 78 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/18/2019 7:29:57 PM CST		
Date Processed:	7/19/2019 4:58:20 PM CST		



	RT	Area	% Area	Height
1	10.928	4064719	49.84	234399
2	15.195	4090337	50.16	

Figure S112. HPLC spectra of **3p**, related to **Scheme 2**.

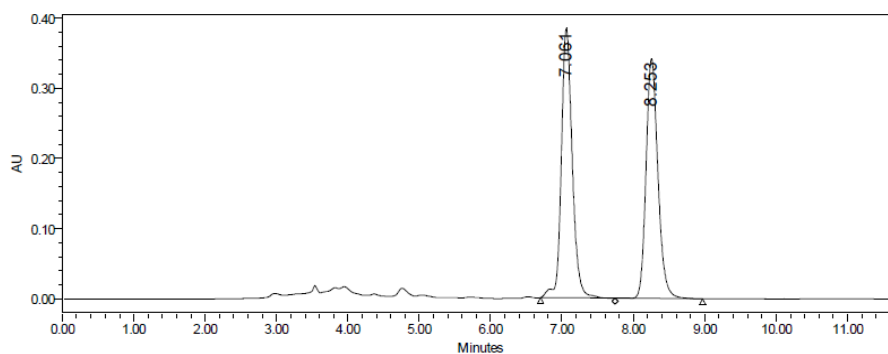
SAMPLE INFORMATION			
Sample Name:	why-g05-78-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	28	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 78 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/18/2019 7:59:30 PM CST		
Date Processed:	7/19/2019 4:58:55 PM CST		



	RT	Area	% Area	Height
1	10.973	171013	2.94	9718
2	15.218	5652888	97.06	256407

Figure S113. HPLC spectra of *rac*-3q, related to Scheme 2.

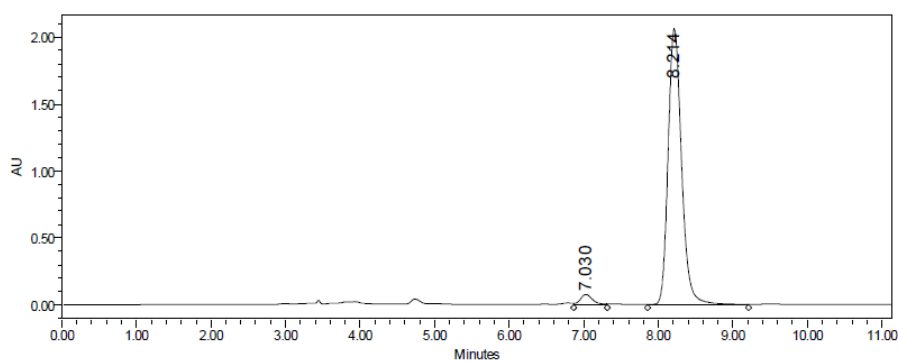
SAMPLE INFORMATION			
Sample Name:	why-g05-95-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	95	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 95 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/25/2019 8:49:00 PM CST		
Date Processed:	7/19/2019 5:02:52 PM CST		



	RT	Area	% Area	Height
1	7.061	4062898	50.61	383542
2	8.253	3964240	49.39	341550

Figure S114. HPLC spectra of 3q, related to Scheme 2.

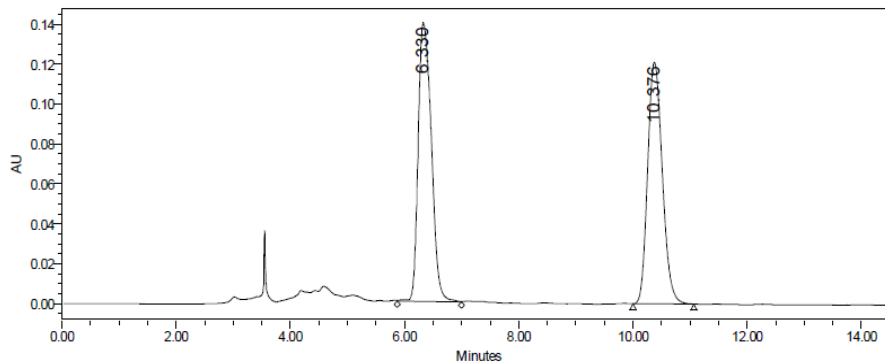
SAMPLE INFORMATION			
Sample Name:	why-g05-95-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	25	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 95 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/26/2019 7:23:15 PM CST		
Date Processed:	7/19/2019 5:03:23 PM CST		



	RT	Area	% Area	Height
1	7.030	827616	3.15	74981
2	8.214	25472113	96.85	2056802

Figure S115. HPLC spectra of *rac-3r*, related to **Scheme 2**.

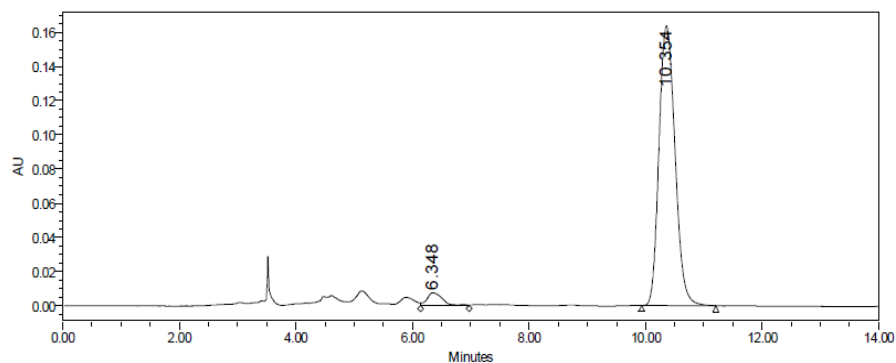
SAMPLE INFORMATION			
Sample Name:	why-g05-97-1-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	5	Acq. Method Set:	1.5%
Injection #:	1	Processing Method:	5.97.1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/27/2019 8:11:01 PM CST		
Date Processed:	7/19/2019 5:03:57 PM CST		



	RT	Area	% Area	Height
1	6.330	2216005	50.51	139512
2	10.376	2171620	49.49	

Figure S116. HPLC spectra of **3r**, related to **Scheme 2**.

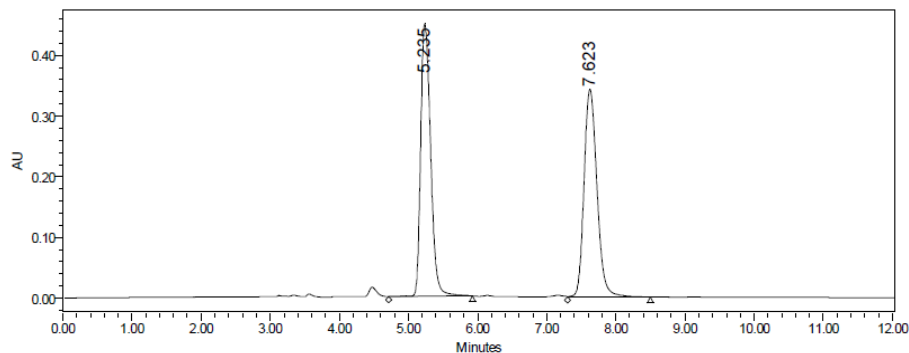
SAMPLE INFORMATION			
Sample Name:	why-g05-97-2-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	4	Acq. Method Set:	1.5%
Injection #:	1	Processing Method:	5.97.2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	14.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/27/2019 8:26:29 PM CST		
Date Processed:	7/19/2019 5:04:21 PM CST		



	RT	Area	% Area	Height
1	6.348	132661	4.09	7406
2	10.354	3111023	95.91	163191

Figure S117. HPLC spectra of *rac*-3s, related to Scheme 2.

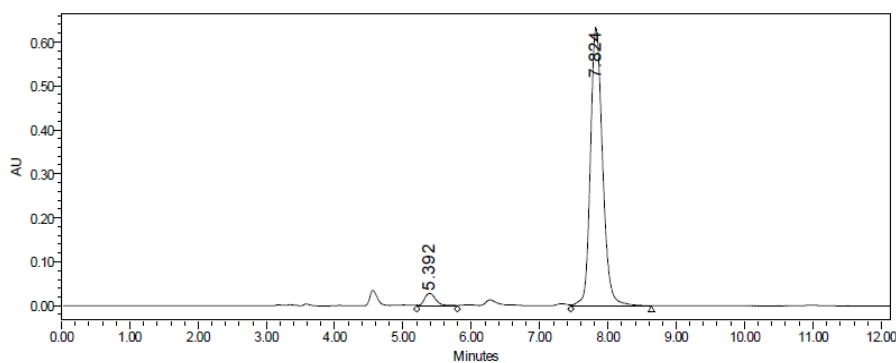
SAMPLE INFORMATION			
Sample Name:	why-g05-115-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	51	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 115 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/20/2019 8:55:09 PM CST		
Date Processed:	7/19/2019 5:05:32 PM CST		



	RT	Area	% Area	Height
1	5.235	4473670	50.07	448631
2	7.623	4461737	49.93	342190

Figure S118. HPLC spectra of 3s, related to Scheme 2.

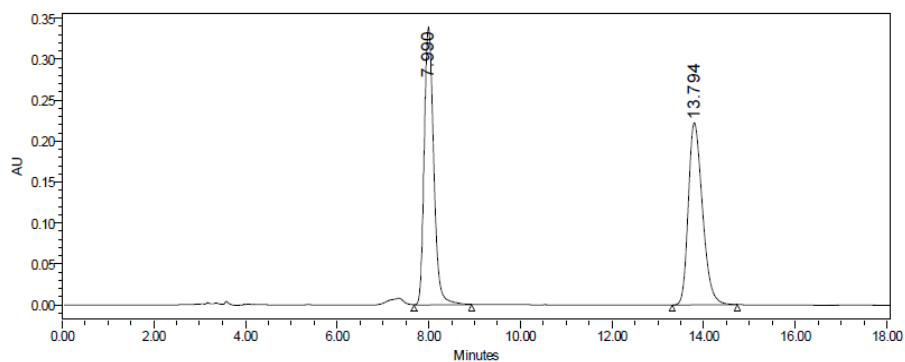
SAMPLE INFORMATION			
Sample Name:	why-g05-115-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	110	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 115 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/21/2019 8:08:57 PM CST		
Date Processed:	7/19/2019 5:06:16 PM CST		



	RT	Area	% Area	Height
1	5.392	322979	3.95	28062
2	7.824	7850224	96.05	631496

Figure S119. HPLC spectra of *rac*-**3t**, related to **Scheme 2**.

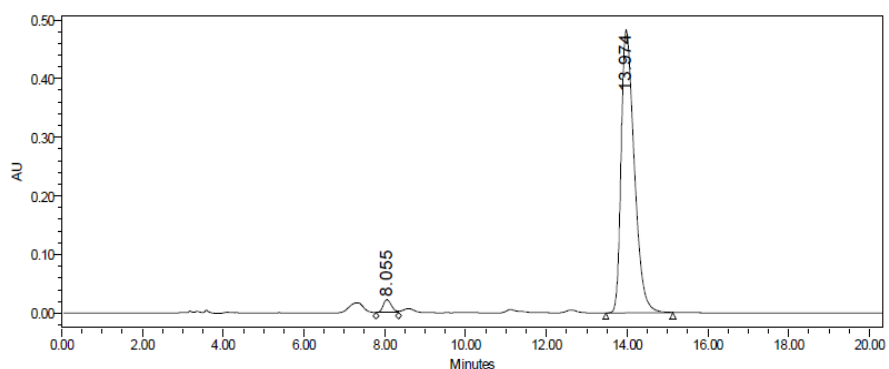
SAMPLE INFORMATION			
Sample Name:	why-g05-116-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	75	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 116 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/20/2019 9:53:04 PM CST		
Date Processed:	7/19/2019 5:06:54 PM CST		



	RT	Area	% Area	Height
1	7.990	4847139	50.24	338076
2	13.794	4801700	49.76	222331

Figure S120. HPLC spectra of **3t**, related to **Scheme 2**.

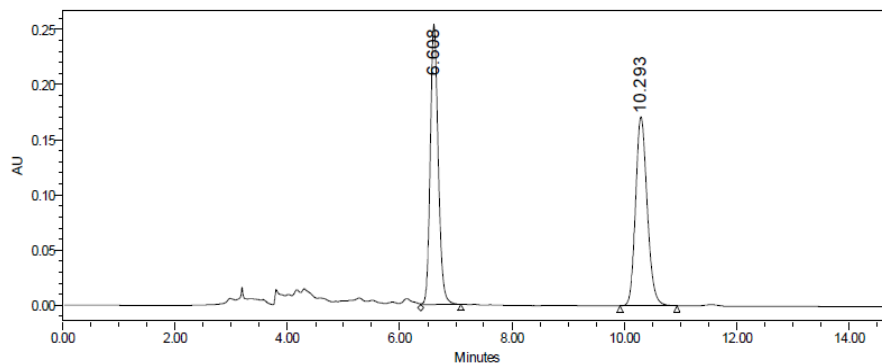
SAMPLE INFORMATION			
Sample Name:	why-g05-116-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	21	Acq. Method Set:	3%
Injection #:	1	Processing Method	5 116 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/21/2019 8:52:38 PM CST		
Date Processed:	7/19/2019 5:08:01 PM CST		



	RT	Area	% Area	Height
1	8.055	318489	2.85	21925
2	13.974	10860475	97.15	481624

Figure S121. HPLC spectra of *rac*-3u, related to Scheme 2.

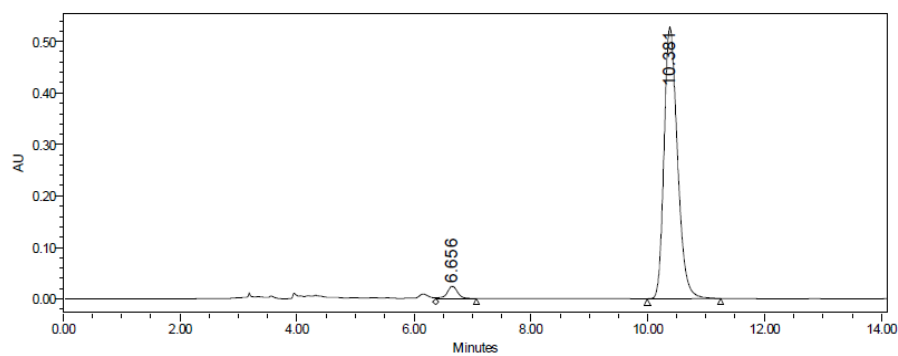
SAMPLE INFORMATION			
Sample Name:	why-g05-98-1-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	46	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 98 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/27/2019 9:57:01 AM CST		
Date Processed:	7/19/2019 4:47:50 PM CST		



	RT	Area	% Area	Height
1	6.608	2497231	50.16	253252
2	10.293	2481349	49.84	171382

Figure S122. HPLC spectra of 3u, related to Scheme 2.

SAMPLE INFORMATION			
Sample Name:	why-g05-98-2-IA-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	14	Acq. Method Set:	3%
Injection #:	1	Processing Method:	5 98 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	4/28/2019 4:33:51 PM CST		
Date Processed:	7/19/2019 4:48:45 PM CST		



	RT	Area	% Area	Height
1	6.656	294513	3.41	24072
2	10.381	8344780	96.59	526504

Figure S123. HPLC spectra of *rac-3v*, related to **Scheme 2**.

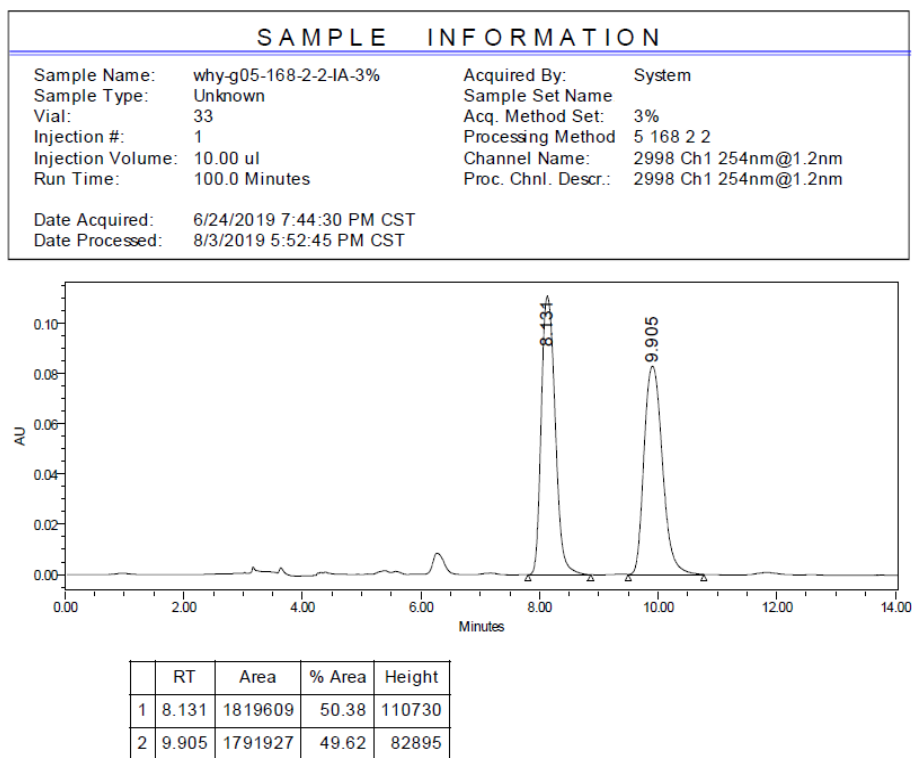


Figure S124. HPLC spectra of **3v**, related to **Scheme 2**.

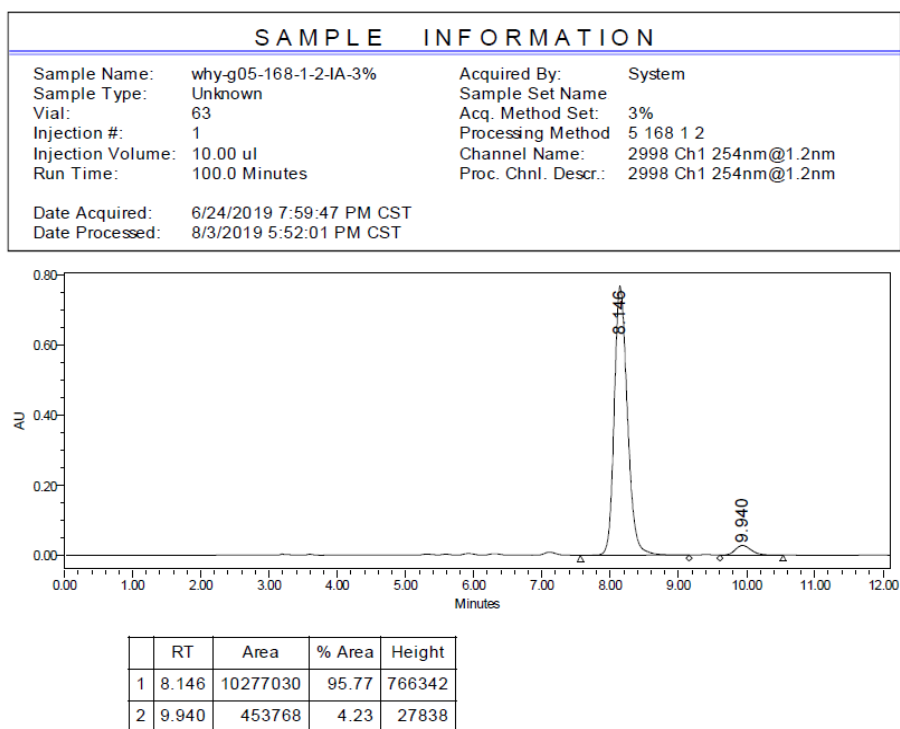
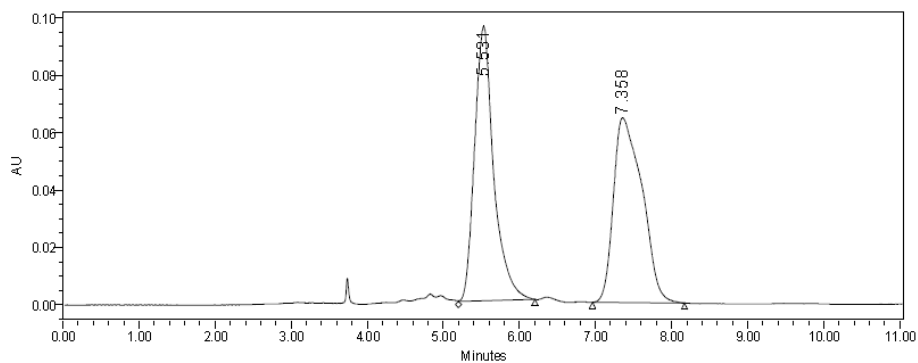


Figure S125. HPLC spectra of *rac*-3w, related to Scheme 2.

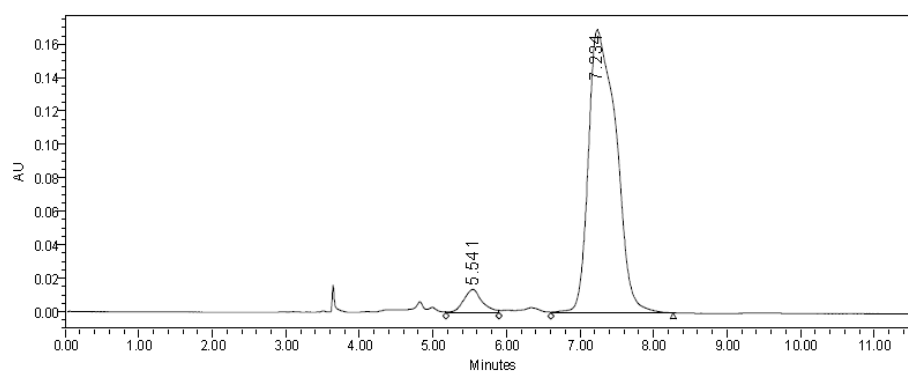
SAMPLE INFORMATION			
Sample Name:	why-g06-66-2-IA-1%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	115	Acq. Method Set:	1%
Injection #:	1	Processing Method	6 66 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/29/2019 9:46:58 PM CST		
Date Processed:	10/29/2019 7:56:09 PM CST		



	RT	Area	% Area	Height
1	5.531	1662937	49.74	95598
2	7.358	1680242	50.26	64357

Figure S126. HPLC spectra of 3w, related to Scheme 2.

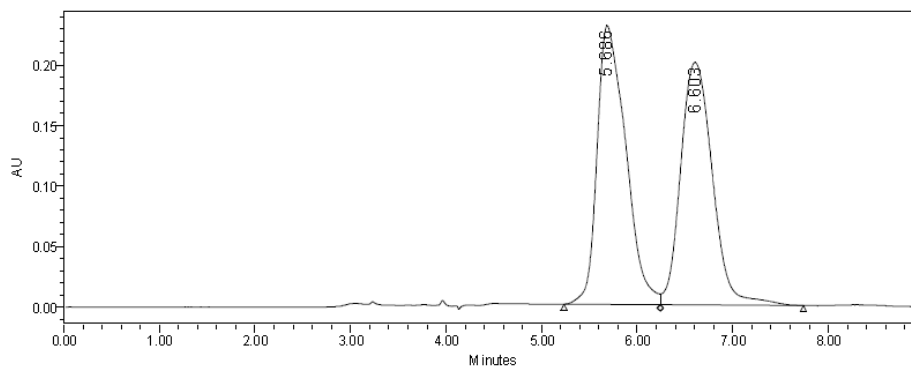
SAMPLE INFORMATION			
Sample Name:	why-g06-66-2-IA-1%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	96	Acq. Method Set:	1%
Injection #:	1	Processing Method	6 66 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/29/2019 12:01:45 PM CST		
Date Processed:	10/29/2019 12:19:04 PM CST		



	RT	Area	% Area	Height
1	5.541	243961	5.21	13942
2	7.234	4438154	94.79	169210

Figure S127. HPLC spectra of *rac-3x*, related to Scheme 2.

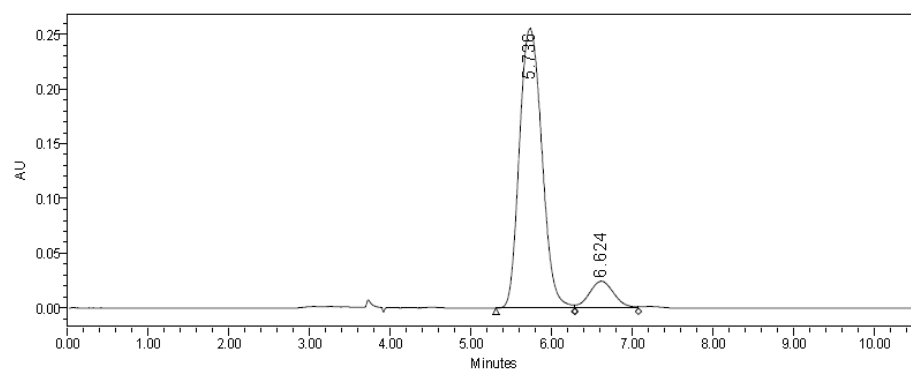
SAMPLE INFORMATION			
Sample Name:	why-g06-69-2-AS-H-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	30	Acq. Method Set:	3%
Injection #:	1	Processing Method	6 69 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/28/2019 5:30:58 PM CST		
Date Processed:	10/29/2019 8:31:18 PM CST		



	RT	Area	% Area	Height
1	5.686	4814427	50.89	230369
2	6.603	4646848	49.11	200356

Figure S128. HPLC spectra of *3x*, related to Scheme 2.

SAMPLE INFORMATION			
Sample Name:	why-g06-67-2-AS-H-3%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	117	Acq. Method Set:	3%
Injection #:	1	Processing Method	6 67 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/29/2019 12:21:53 PM CST		
Date Processed:	10/29/2019 8:29:38 PM CST		



	RT	Area	% Area	Height
1	5.736	4932155	90.43	255229
2	6.624	522203	9.57	24555

Figure S129. HPLC spectra of *rac*-**3y**, related to **Scheme 2**.

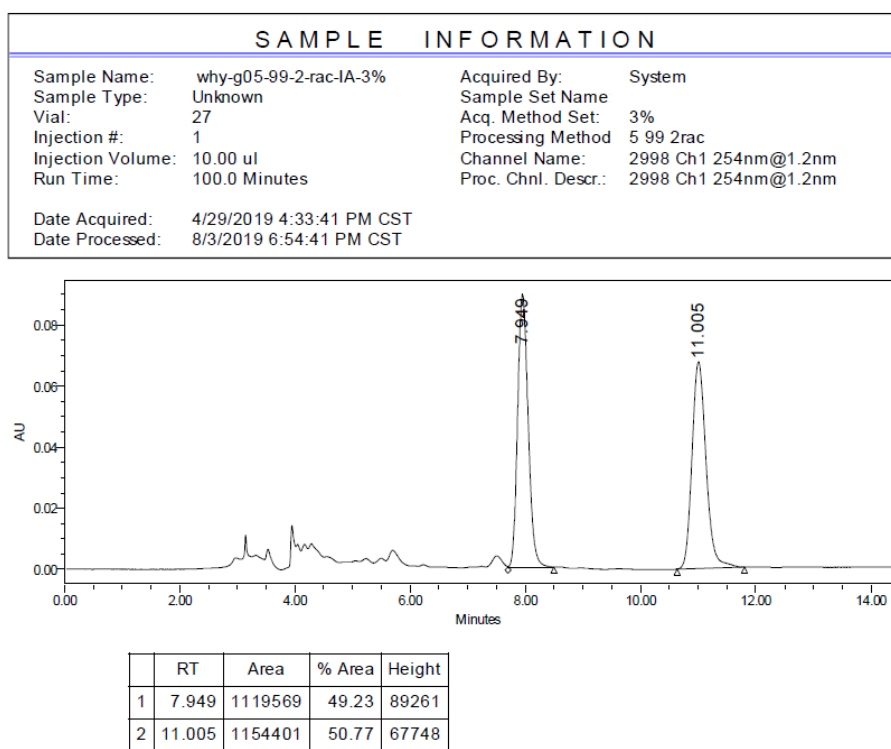


Figure S130. HPLC spectra of **3y**, related to **Scheme 2**.

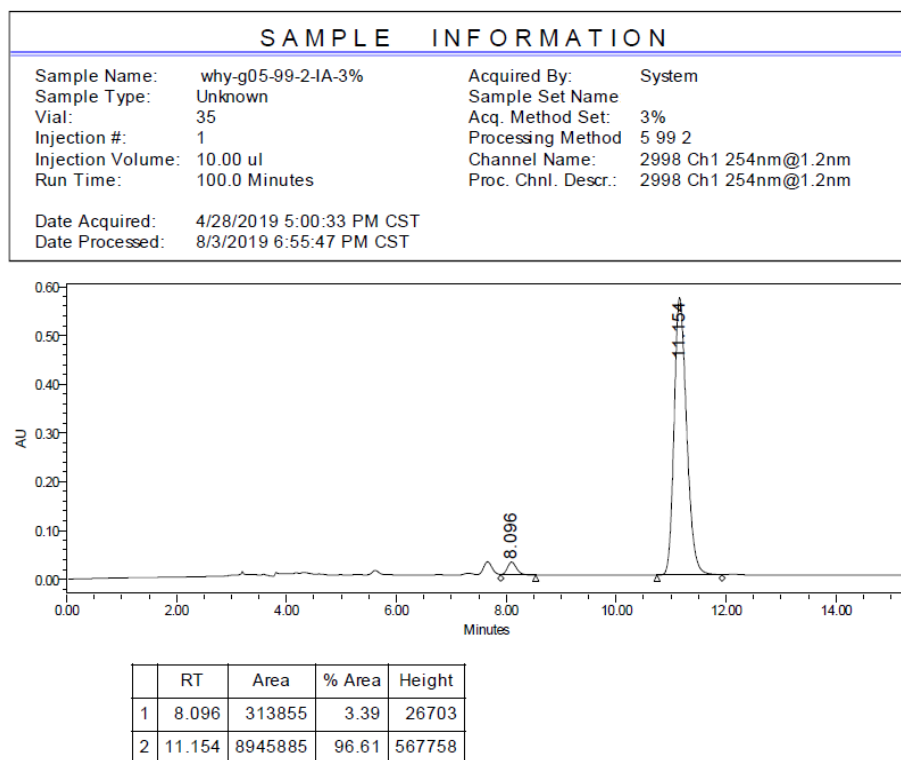
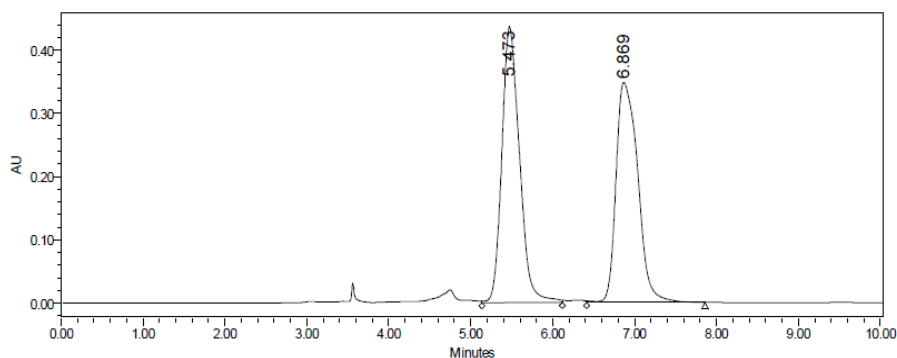


Figure S131. HPLC spectra of *rac*-**3z**, related to **Scheme 2**.

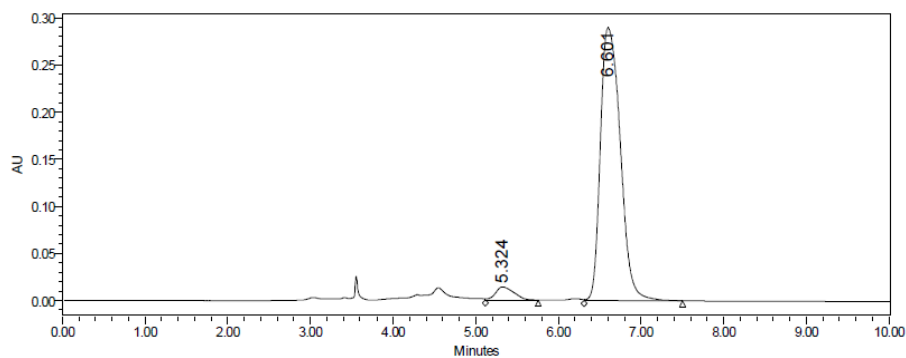
SAMPLE INFORMATION			
Sample Name:	why-g05-99-1-rac-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	44	Acq. Method Set:	1.5%
Injection #:	1	Processing Method	5 99 1 rac
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/5/2019 5:25:59 PM CST		
Date Processed:	7/19/2019 4:50:47 PM CST		



	RT	Area	% Area	Height
1	5.473	6503943	50.32	435332
2	6.869	6420979	49.68	347760

Figure S132. HPLC spectra of **3z**, related to Scheme 2.

SAMPLE INFORMATION			
Sample Name:	why-g05-99-1-IA-1.5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	99	Acq. Method Set:	1.5%
Injection #:	1	Processing Method	5 99 1 asy
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	5/6/2019 7:38:31 PM CST		
Date Processed:	7/19/2019 4:51:16 PM CST		



	RT	Area	% Area	Height
1	5.324	209937	4.16	13908
2	6.601	4839867	95.84	289449

Figure S133. HPLC spectra of *rac-6a*, related to **Scheme 3**.

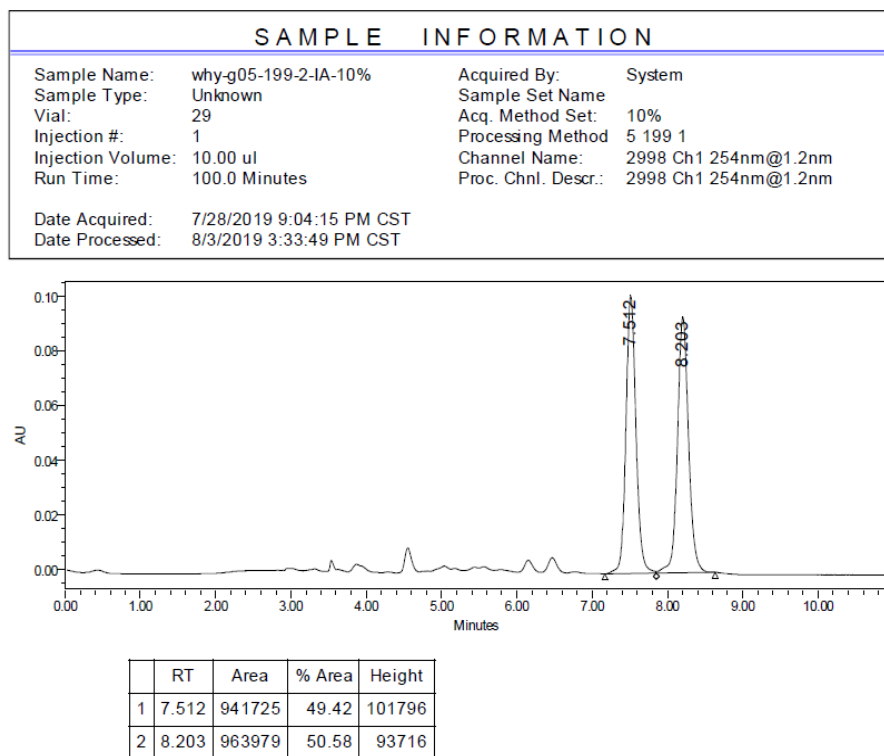


Figure S134. HPLC spectra of **6a**, related to **Scheme 3**.

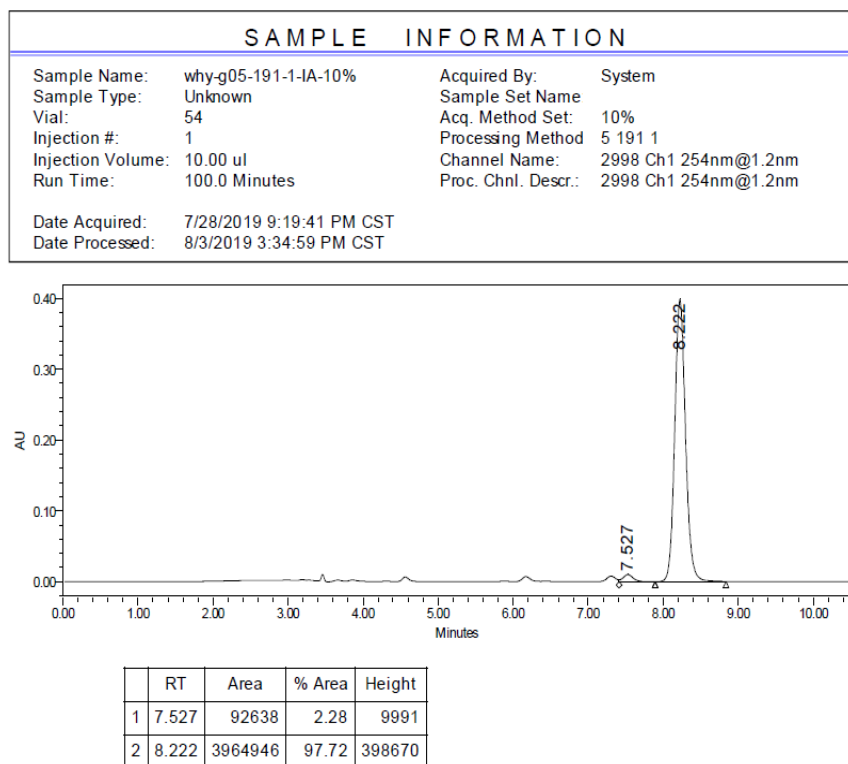
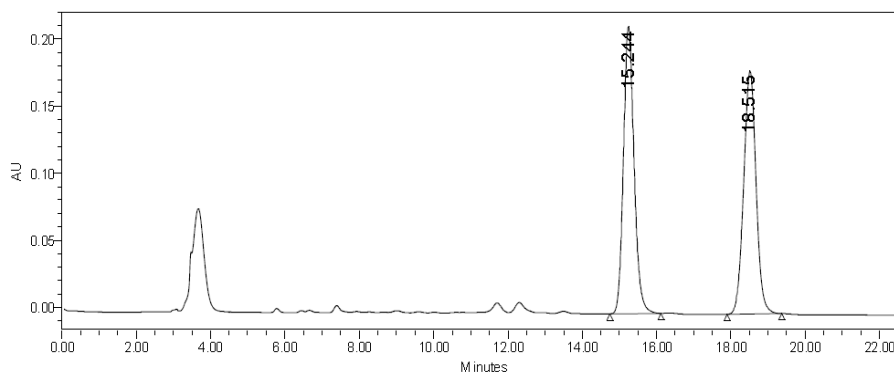


Figure S135. HPLC spectra of *rac*-6b, related to Scheme 3.

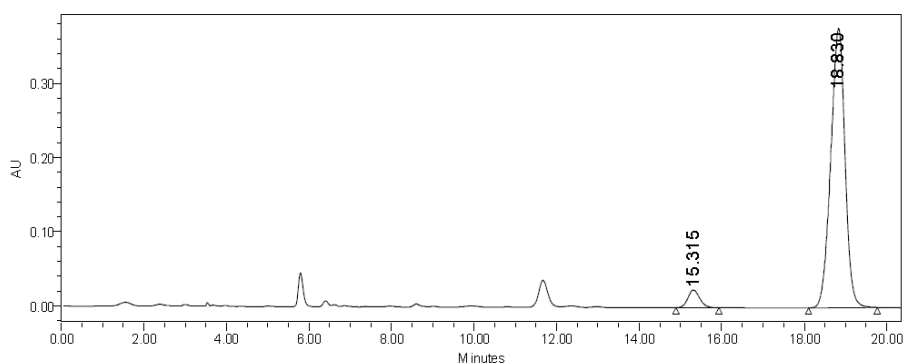
SAMPLE INFORMATION			
Sample Name:	why-g05-159-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	56	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 159 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	6/18/2019 6:54:46 PM CST		
Date Processed:	8/3/2019 3:26:09 PM CST		



	RT	Area	% Area	Height
1	15.244	4234718	50.08	213977
2	18.515	4220834	49.92	181236

Figure S136. HPLC spectra of 6b, related to Scheme 3.

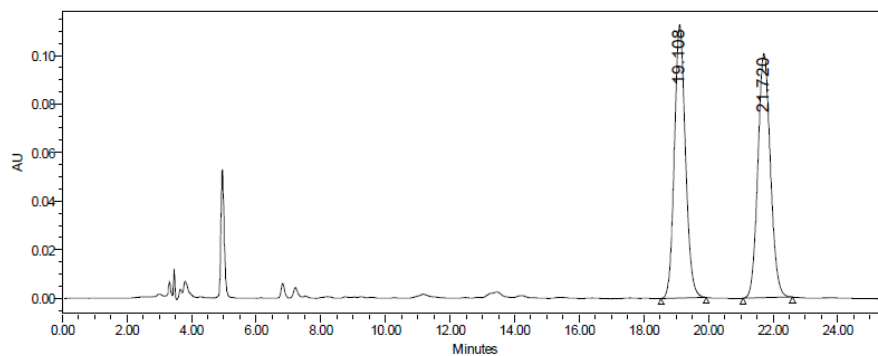
SAMPLE INFORMATION			
Sample Name:	why-g05-169-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	106	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 169 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	6/24/2019 6:55:34 PM CST		
Date Processed:	8/3/2019 3:28:10 PM CST		



	RT	Area	% Area	Height
1	15.315	467017	4.94	23666
2	18.830	8989230	95.06	376102

Figure S137. HPLC spectra of *rac-6c*, related to **Scheme 3**.

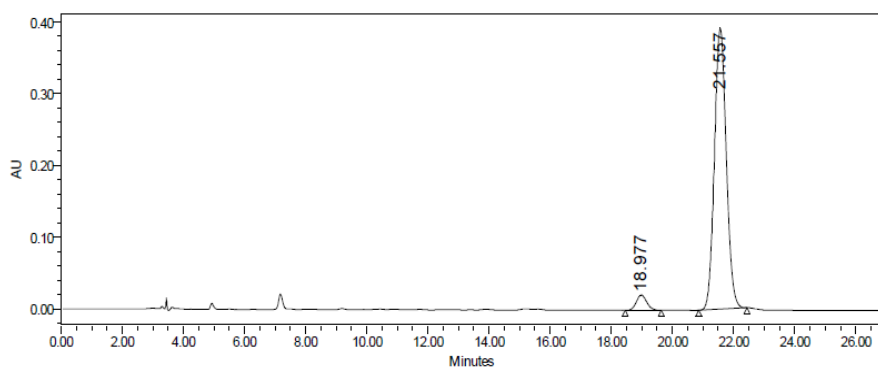
SAMPLE INFORMATION			
Sample Name:	why-g05-189-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	27	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 189 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/22/2019 8:16:51 PM CST		
Date Processed:	8/3/2019 3:32:13 PM CST		



	RT	Area	% Area	Height
1	19.108	2679165	49.92	112252
2	21.720	2687341	50.08	

Figure S138. HPLC spectra of **6c**, related to **Scheme 3**.

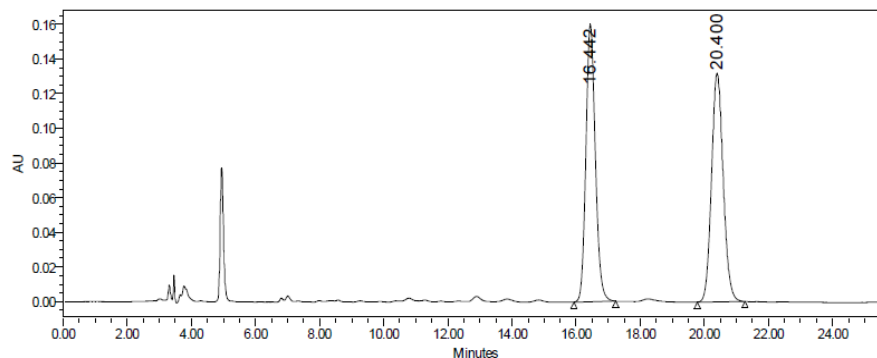
SAMPLE INFORMATION			
Sample Name:	why-g05-189-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	45	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 189 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/22/2019 2:30:04 PM CST		
Date Processed:	8/3/2019 3:32:41 PM CST		



	RT	Area	% Area	Height
1	18.977	504451	4.61	21417
2	21.557	10436432	95.39	391481

Figure S139. HPLC spectra of *rac*-**6d**, related to **Scheme 3**.

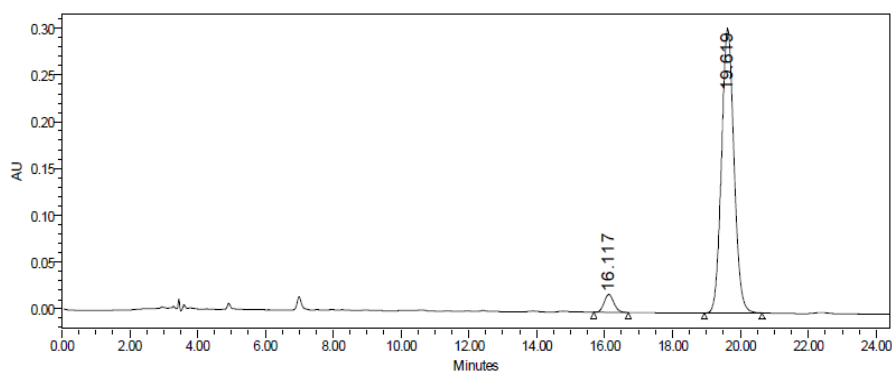
SAMPLE INFORMATION			
Sample Name:	why-g05-188-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	4	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 188 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/22/2019 7:50:10 PM CST		
Date Processed:	8/3/2019 3:31:12 PM CST		



	RT	Area	% Area	Height
1	16.442	3290513	49.87	159858
2	20.400	3307902	50.13	

Figure S140. HPLC spectra of **6d**, related to **Scheme 3**.

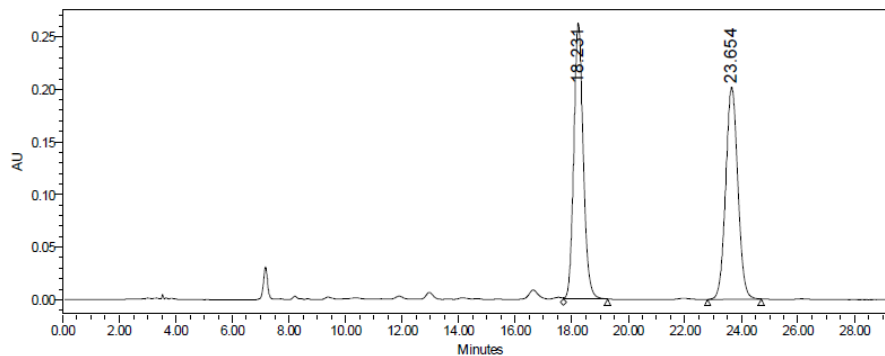
SAMPLE INFORMATION			
Sample Name:	why-g05-188-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	2	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 188 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/22/2019 2:03:03 PM CST		
Date Processed:	8/3/2019 3:31:41 PM CST		



	RT	Area	% Area	Height
1	16.117	385610	4.75	19275
2	19.619	7731158	95.25	303811

Figure S141. HPLC spectra of *rac-6e*, related to **Scheme 3**.

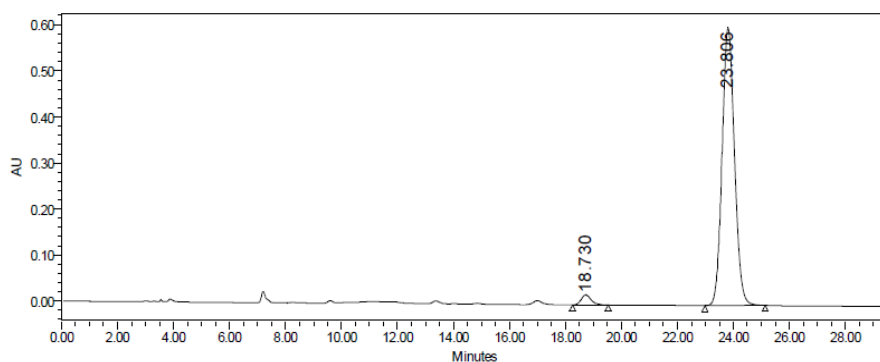
SAMPLE INFORMATION			
Sample Name:	why-g05-197-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	21	Acq. Method Set:	10%
Injection #:	1	Processing Method:	5 197 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/27/2019 6:48:52 PM CST		
Date Processed:	8/3/2019 3:38:05 PM CST		



	RT	Area	% Area	Height
1	18.231	6009022	50.18	261771
2	23.654	5965484	49.82	201754

Figure S142. HPLC spectra of **6e**, related to **Scheme 3**.

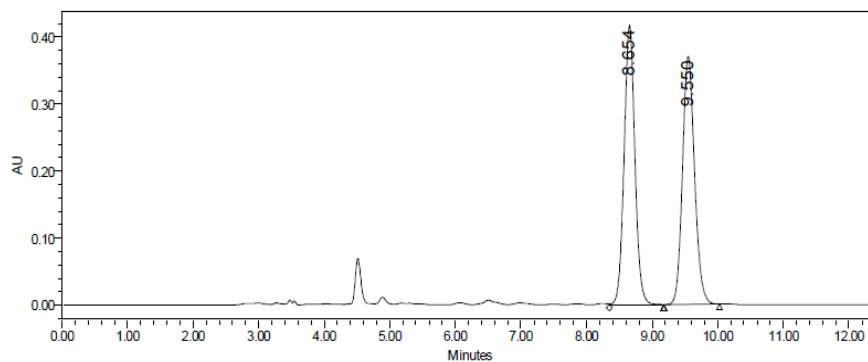
SAMPLE INFORMATION			
Sample Name:	why-g05-194-2-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	16	Acq. Method Set:	10%
Injection #:	1	Processing Method:	5 194 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/28/2019 9:52:27 AM CST		
Date Processed:	8/3/2019 3:38:37 PM CST		



	RT	Area	% Area	Height
1	18.730	536788	2.82	21793
2	23.806	18472791	97.18	602626

Figure S143. HPLC spectra of *rac-6f*, related to **Scheme 3**.

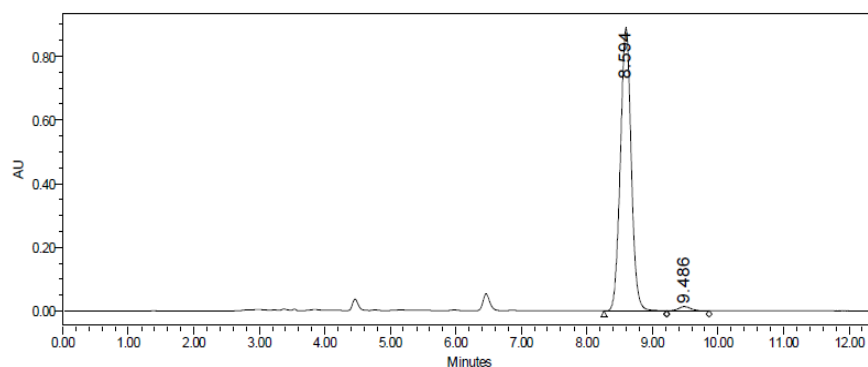
SAMPLE INFORMATION			
Sample Name:	why-g05-198-2-AD-H15%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	26	Acq. Method Set:	15%
Injection #:	1	Processing Method	5 198 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/27/2019 3:43:43 PM CST		
Date Processed:	8/3/2019 3:42:35 PM CST		



	RT	Area	% Area	Height
1	8.654	4775242	50.08	416049
2	9.550	4759319	49.92	370063

Figure S144. HPLC spectra of **6f**, related to **Scheme 3**.

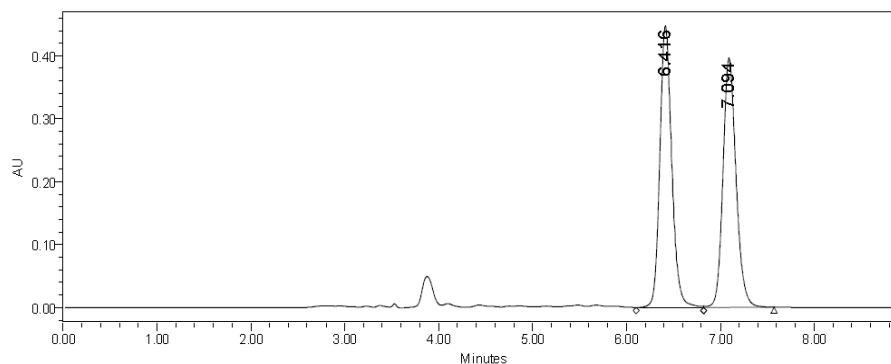
SAMPLE INFORMATION			
Sample Name:	why-g05-195-2-AD-H15%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	63	Acq. Method Set:	15%
Injection #:	1	Processing Method	5 195 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/27/2019 3:57:29 PM CST		
Date Processed:	8/3/2019 3:42:58 PM CST		



	RT	Area	% Area	Height
1	8.594	10249546	98.27	888091
2	9.486	180751	1.73	13529

Figure S145. HPLC spectra of *rac*-6g, related to **Scheme 3**.

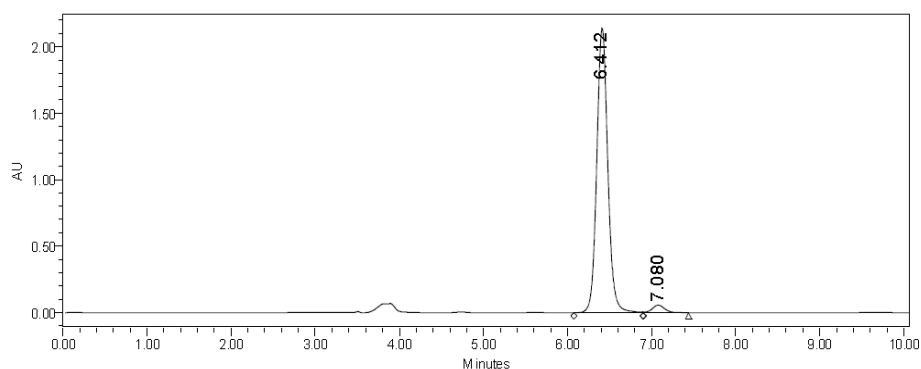
SAMPLE INFORMATION			
Sample Name:	why-g05-198-1-AD-H15%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	104	Acq. Method Set:	15%
Injection #:	1	Processing Method	5 198 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/27/2019 2:50:56 PM CST		
Date Processed:	8/3/2019 3:41:13 PM CST		



	RT	Area	% Area	Height
1	6.416	3934302	50.62	447162
2	7.094	3838527	49.38	395811

Figure S146. HPLC spectra of 6g, related to **Scheme 3**.

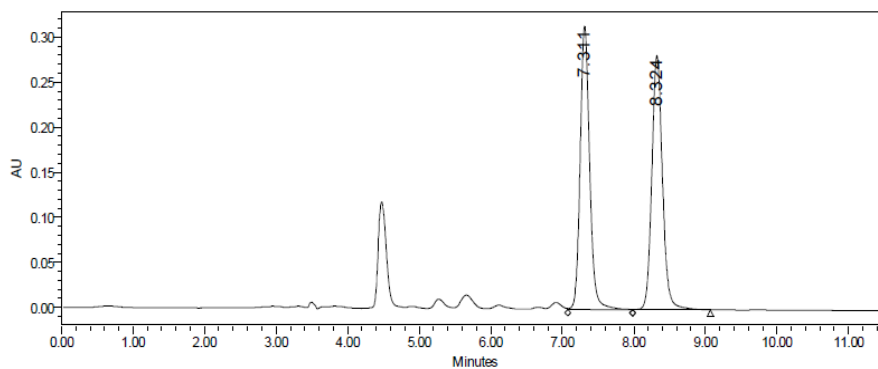
SAMPLE INFORMATION			
Sample Name:	why-g05-195-1-AD-H15%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	20	Acq. Method Set:	15%
Injection #:	1	Processing Method	5 195 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/27/2019 3:01:35 PM CST		
Date Processed:	8/3/2019 3:41:58 PM CST		



	RT	Area	% Area	Height
1	6.412	19561736	97.09	2137082
2	7.080	585287	2.91	57468

Figure S147. HPLC spectra of *rac-6h*, related to **Scheme 3**.

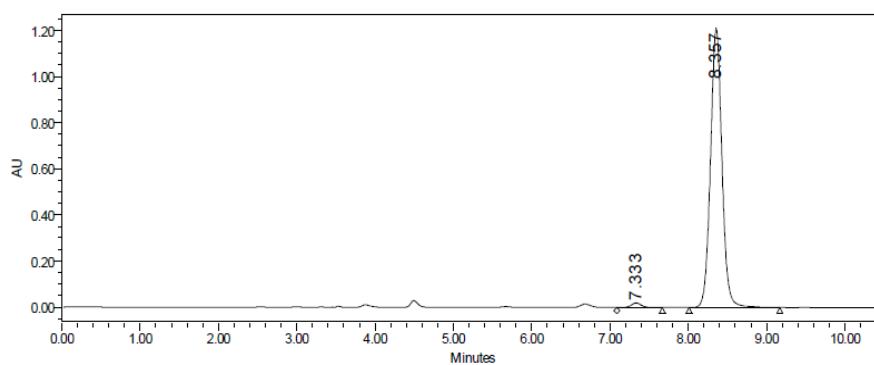
SAMPLE INFORMATION			
Sample Name:	why-g05-197-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	73	Acq. Method Set:	10%
Injection #:	2	Processing Method	5 197 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/28/2019 7:29:54 PM CST		
Date Processed:	8/3/2019 3:36:19 PM CST		



	RT	Area	% Area	Height
1	7.311	2912330	49.94	314167
2	8.324	2919807	50.06	281933

Figure S148. HPLC spectra of **6h**, related to **Scheme 3**.

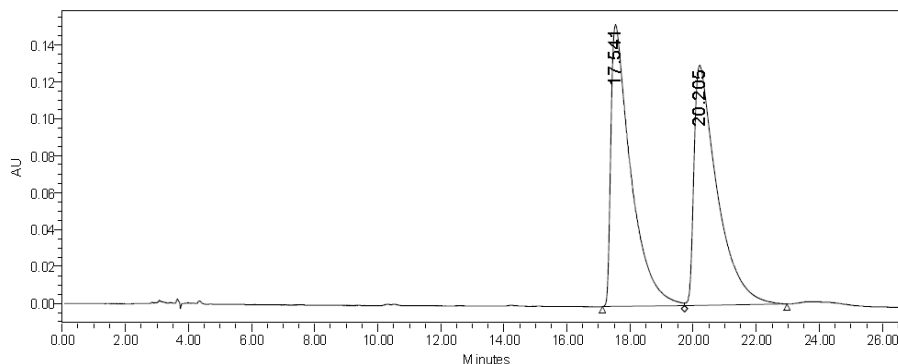
SAMPLE INFORMATION			
Sample Name:	why-g05-194-1-IA-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	97	Acq. Method Set:	10%
Injection #:	1	Processing Method	5 194 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	7/28/2019 7:42:43 PM CST		
Date Processed:	8/3/2019 3:37:24 PM CST		



	RT	Area	% Area	Height
1	7.333	176263	1.42	19997
2	8.357	12249569	98.58	1208965

Figure S149. HPLC spectra of *rac-7*, related to Scheme 4.

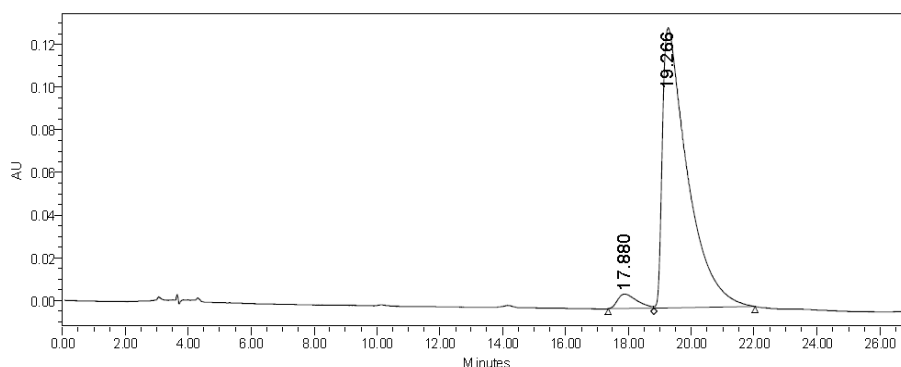
SAMPLE INFORMATION			
Sample Name:	why-g06-37-1-IA-5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	2	Acq. Method Set:	5%
Injection #:	1	Processing Method	6 37 1 rac
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	8/26/2019 8:45:50 PM CST		
Date Processed:	9/24/2019 2:55:43 PM CST		



	RT	Area	% Area	Height
1	17.541	6673637	50.20	152291
2	20.205	6620390	49.80	129656

Figure S150. HPLC spectra of **7**, related to Scheme 4.

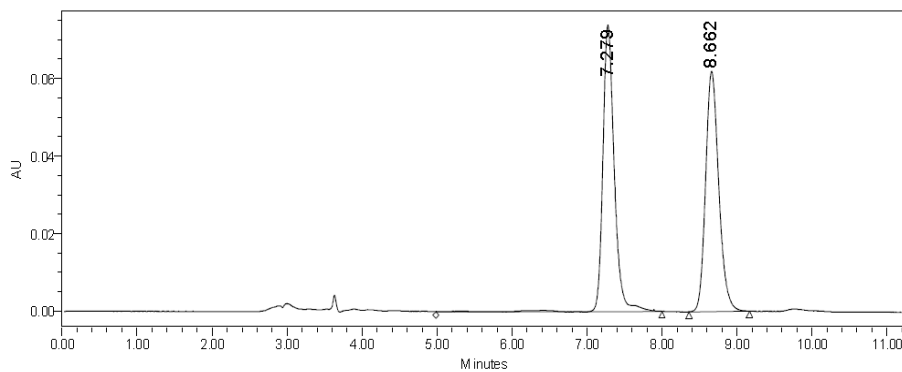
SAMPLE INFORMATION			
Sample Name:	why-g06-37-1-asy-IA-5%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	12	Acq. Method Set:	5%
Injection #:	1	Processing Method	6 37 1 asy
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	9/21/2019 10:09:33 AM CST		
Date Processed:	9/24/2019 3:03:36 PM CST		



	RT	Area	% Area	Height
1	17.880	289188	3.85	6737
2	19.266	7230632	96.15	131152

Figure S151. HPLC spectra of *rac*-8, related to Scheme 4.

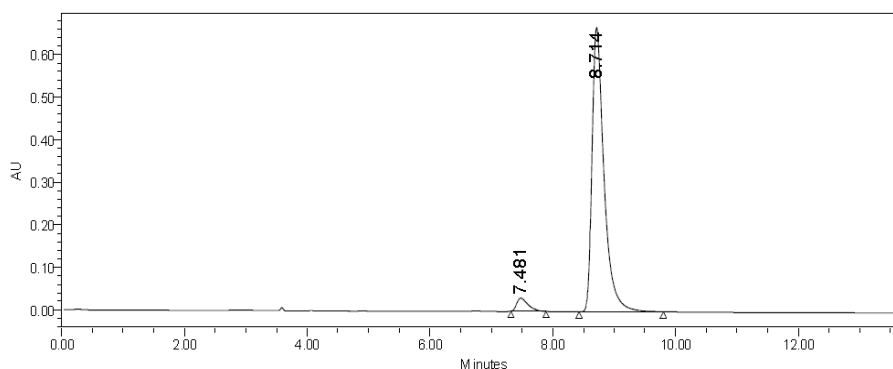
SAMPLE INFORMATION			
Sample Name:	why-g06-38-1-ADH-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	72	Acq. Method Set:	10%
Injection #:	1	Processing Method:	6 38 1 rac
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	8/28/2019 3:59:26 PM CST		
Date Processed:	9/24/2019 2:57:11 PM CST		



	RT	Area	% Area	Height
1	7.279	788784	50.95	73830
2	8.662	759429	49.05	61938

Figure S152. HPLC spectra of 8, related to Scheme 4.

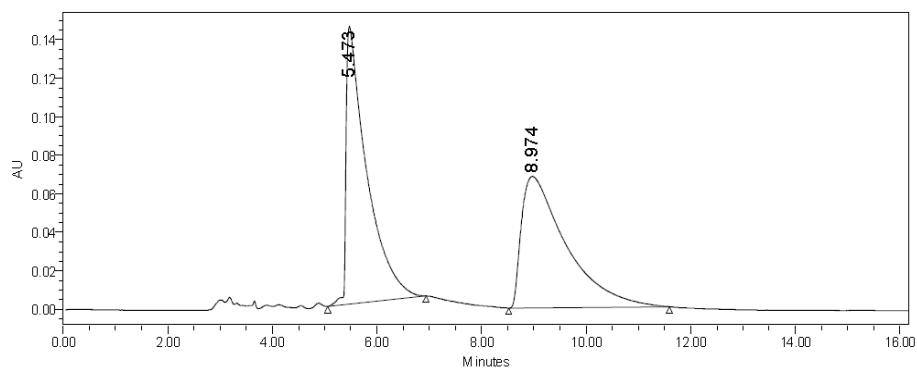
SAMPLE INFORMATION			
Sample Name:	why-g06-38-1-asy-ADH-10%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	
Vial:	2	Acq. Method Set:	10%
Injection #:	1	Processing Method:	6 38 1 ASY
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	9/23/2019 11:27:03 AM CST		
Date Processed:	9/23/2019 2:37:07 PM CST		



	RT	Area	% Area	Height
1	7.481	402073	4.23	30981
2	8.714	9113769	95.77	667895

Figure S153. HPLC spectra of *rac*-9, related to Scheme 4.

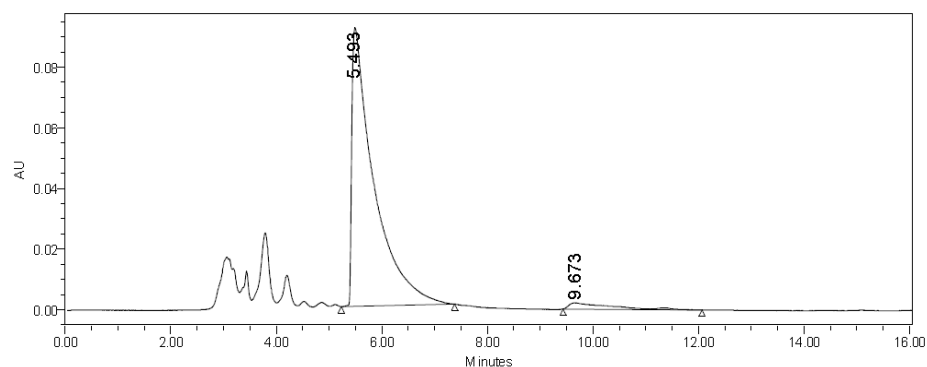
SAMPLE INFORMATION			
Sample Name:	why-g06-39-1- <i>rac</i> -AS-H-30%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	21	Acq. Method Set:	30%quanbo
Injection #:	1	Processing Method	6 39 1 <i>rac</i>
Injection Volume:	20.00 ul	Channel Name:	254.0nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 254.0 nm (2998)
Date Acquired:	9/20/2019 2:14:32 PM CST		
Date Processed:	9/24/2019 2:59:48 PM CST		



	RT	Area	% Area	Height
1	5.473	3973711	49.57	144135
2	8.974	4042019	50.43	68201

Figure S154. HPLC spectra of 9, related to Scheme 4.

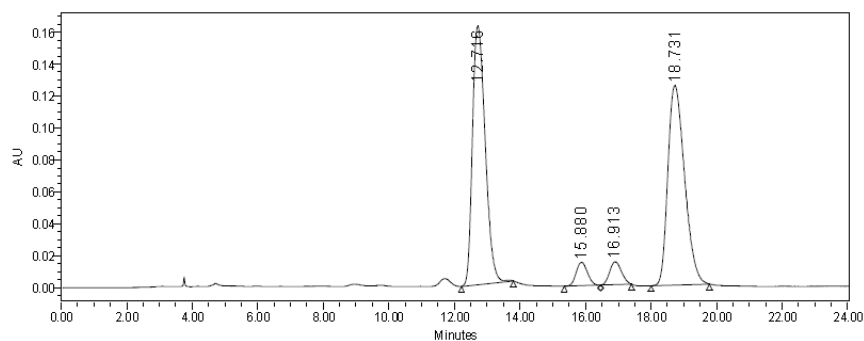
SAMPLE INFORMATION			
Sample Name:	why-g06-39-1- <i>asy</i> -AS-H-30%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	60	Acq. Method Set:	30%quanbo
Injection #:	1	Processing Method	6 39 1 <i>asy</i>
Injection Volume:	20.00 ul	Channel Name:	254.0nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 PDA 254.0 nm (2998)
Date Acquired:	9/20/2019 2:31:54 PM CST		
Date Processed:	9/24/2019 3:00:50 PM CST		



	RT	Area	% Area	Height
1	5.493	2669826	95.84	91846
2	9.673	115750	4.16	2036

Figure S155. HPLC spectra of *rac*-10, related to Table 1.

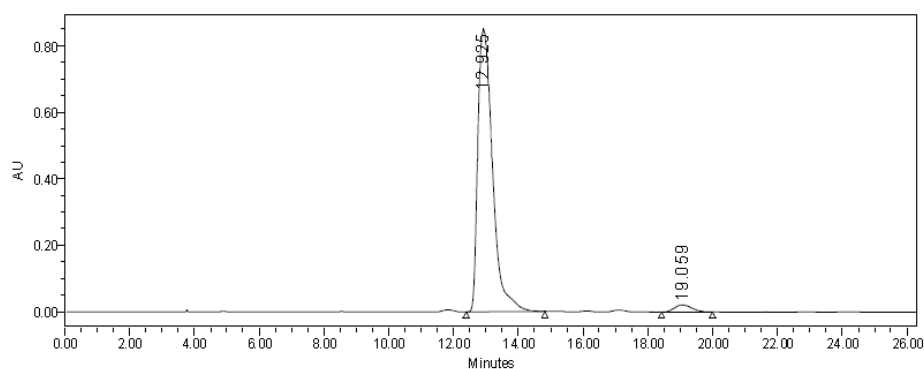
SAMPLE INFORMATION			
Sample Name:	why-g06-61-2--IA-1%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	1	Acq. Method Set:	1%
Injection #:	1	Processing Method	6 61 2
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/23/2019 7:49:52 PM CST		
Date Processed:	10/29/2019 7:48:57 PM CST		



	RT	Area	% Area	Height
1	12.716	4399203	46.14	161787
2	15.880	343025	3.60	14577
3	16.913	360347	3.78	14351
4	18.731	4431866	46.48	124940

Figure S156. HPLC spectra of 10, related to Table 1.

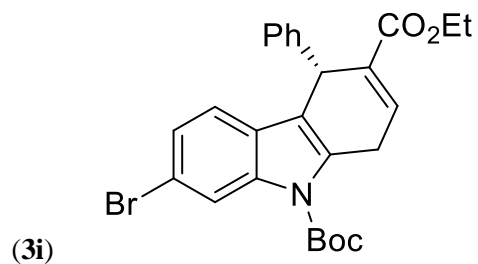
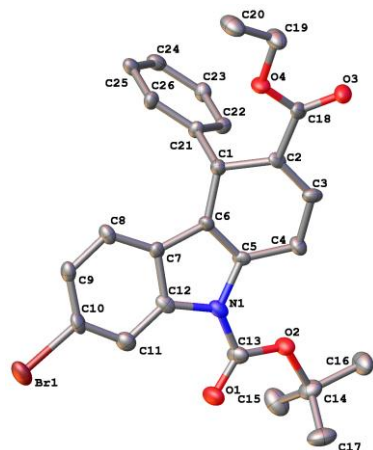
SAMPLE INFORMATION			
Sample Name:	why-g06-61-1--IA-1%	Acquired By:	System
Sample Type:	Unknown	Sample Set Name	
Vial:	50	Acq. Method Set:	1%
Injection #:	1	Processing Method	6 61 1
Injection Volume:	10.00 ul	Channel Name:	2998 Ch1 254nm@1.2nm
Run Time:	100.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 254nm@1.2nm
Date Acquired:	10/23/2019 4:46:41 PM CST		
Date Processed:	10/29/2019 7:53:12 PM CST		



	RT	Area	% Area	Height
1	12.925	26610987	97.04	850338
2	19.059	811472	2.96	21383

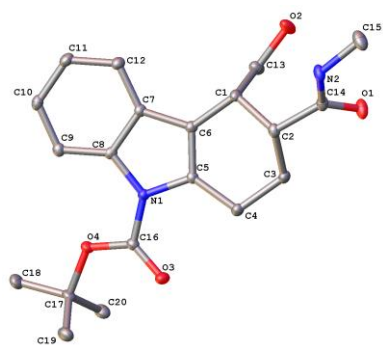
Supplemental figures and tables for X-Ray structures

Figure S157. X-Ray crystal data of **3i**, related to Scheme 2.

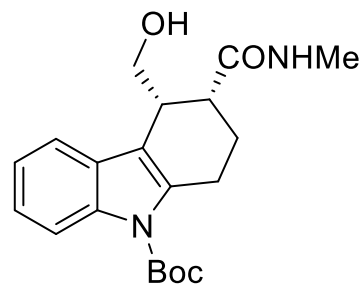


Chemical formula	$C_{26}H_{26}BrNO_4$
Formula weight	496.39
Space group	P1
Z	4
α , Å	9.1215(5)
b , Å	13.5175(7)
c , Å	19.4869(10)
α , °	99.498(3)
β , °	93.402(3)
γ , °	96.017(3)
V , Å ³	2349.5(2)
ρ , g/cm ³	1.403

Figure S158.. X-Ray crystal data of **7**, related to **Scheme 4**.



(7)



Chemical formula	C ₂₀ H ₂₆ N ₂ O ₄
Formula weight	358.43
Space group	P2 ₁ 2 ₁ 2 ₁
Z	4
α , Å	7.87500(10)
b , Å	10.1406(2)
c , Å	23.0161(4)
α , °	90
β , °	90
γ , °	90
V , Å ³	1838.00(5)
ρ , g/cm ³	1.295

Transparent Methods

General Information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. NMR spectra were recorded on a Bruker-400 MHz spectrometer. Chemical shifts (δ) are given in ppm relative to TMS. The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (CHCl_3 : δ 7.26 for proton and δ 77.16 for carbon; DMSO: δ 2.49 for proton and δ 39.51 for carbon; Acetone: δ 2.05 for proton and δ 206.68 for carbon). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublet of doublets); dt (doublet of triplets); m (multiplets); brs (broad signal). Coupling constants are reported as a J value in Hz. High resolution mass spectral analysis (HRMS) was performed on Waters XEVO G2 Q-TOF. The measurement of enantiomeric excesses was performed on Waters-Alliance (2998. Photodiode Array Detector, UV detection monitored at 254 nm). Chiralpak IA, AD-H and AS-H columns were purchased from Daicel Chemical Industries, LTD. The absolute configuration of **3i** and **7** were assigned by the X-ray analysis. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-343 polarimeter.

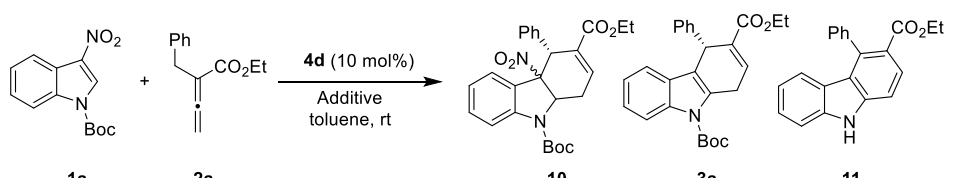
Preparation of Substrates

Preparation of 3-Nitroindoles **1** and 3-Nitrobenzothiophenes **5**

The 3-nitroindoles **1** (You et al, 2018), 3-nitrobenzothiophenes **5** (You et al, 2017) and Allenates **2** (Kwon et al, 2007) were synthesized according to the literature.

Optimize reaction conditions

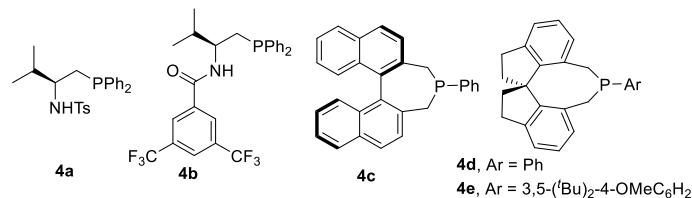
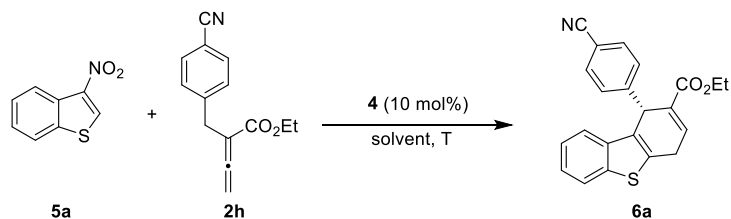
Table S1: Additives effect the reaction of 3-nitroindoles **1a and allenates **2a**, related to Table 1^[a].**



Entry	Additive	T (°C)	t (h)	10 [%] ^[b]	ee [%] ^[c]	3a [%] ^[b]	ee [%] ^[c]	11 [%] ^[b]
1	-	rt	-	74	94	21	94	-
2	Silica gel (200 mg)	rt	3	8	94	92	94	-
3	Sc(OTf) ₃ (20 mol%)	50	6	-	-	10	90	59
4	SnCl ₂ (20 mol%)	50	6	24	94	44	94	
5	PhCOOH (20 mol%)	50	3	67	94	15	94	
6	Et ₃ N (1.0 eqive)	50	3	66	94	16	94	
7	DABCO (1.0 eqive)	50	3	52	94	14	94	

[a] Reactions were conducted with **1a** (0.1 mmol), **2a** (0.15 mmol) and catalyst **4d** (0.01 mmol) in toluene (1.0 mL) at room temperature. [b] Yield of the isolated product after purification by chromatography on silica gel. [c] Enantiomeric excess determined by HPLC

Table S2: Optimization of the reaction of 3-nitrobenzothiophenes **5a and allenate **2h**, related to Scheme 3^[a].**



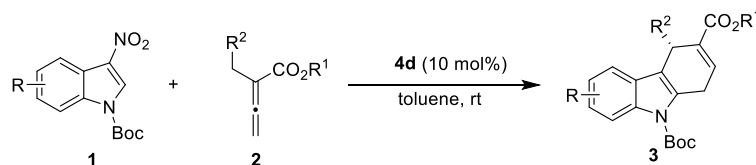
Entry	4	T (°C)	solvent	6a [%] ^[b]	ee [%] ^[d]
1	4a	rt	toluene	-	-
2	4b	rt	toluene	-	-
3	4c	rt	toluene	trace	-
4	4d	rt	toluene	50	82
5	4e	rt	toluene	24	12
6	4d	rt	THF	49	87
7	4d	rt	DCM	36	86
8	4d	rt	dioxane	trace	-
9	4d	0	THF	65	90
10	4d	0	toluene	72	90
11	4d	-20	toluene	trace	-

[a] Reactions were conducted with **5a** (0.1 mmol), **2h** (0.15 mmol) and catalyst **4** (0.01 mmol) in toluene (1.0 mL). [b] Yield of the isolated product after purification by chromatography on silica gel. [c] Enantiomeric excess determined by HPLC analysis.

General procedure

All the racemic products were obtained by use of Cy₃P as catalyst.

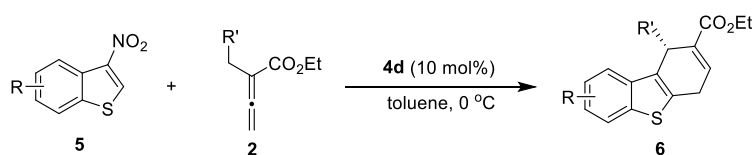
Scheme S1. General procedure for phosphine-catalyzed enantioselective [4+2] annulation reaction of 3-nitroindoles **1** and allenates **2**, related to Scheme 2.



A dried tube with a magnetic stir bar was charged with 3-nitroindole derivative **1** (0.10 mmol), allenolate derivative **2** (0.15 mmol, 1.5 equiv.), catalyst **4d** (10 mol%), followed by the addition of toluene (1.0 mL), and the reaction mixture was stirred at room temperature. When the reaction was finished (determined by TLC). The mixture was added silica gel and toluene (1.0 mL) continued stir at room temperature when the aromatization process was finished (determined by TLC). Then solvent was evaporated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the products **3**.

Scheme S2. General procedure for phosphine-catalyzed enantioselective [4+2]

annulation reaction of 3-nitrobenzothiophene **5** and allenoate **2**, related to Scheme 3.



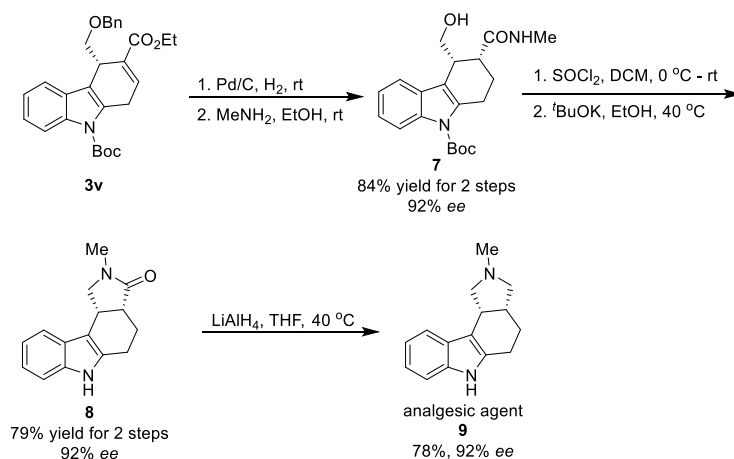
A dried tube with a magnetic stir bar was charged with 3-nitrobenzothiophenes derivative **5** (0.10 mmol), allenoate derivative **2** (0.15 mmol, 1.5 equiv.), catalyst **4d** (10 mol%), followed by the addition of toluene (1.0 mL), and the reaction mixture was stirred at 0 °C. When the reaction was finished (determined by TLC). The mixture were added silica gel and toluene (1.0 mL) continued stir at room temperature when the aromatization process was finished (determined by TLC). Then solvent was evaporated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the products **6**.

Scheme S3. 1-mol scale reaction, related to Scheme 2.



A dried tube with a magnetic stir bar was charged with 3-nitroindole derivative **1a** (1.0 mmol), allenoate derivative **2o** (1.5 mmol, 1.5 equiv.), catalyst **4d** (10 mol%), followed by the addition of toluene (10.0 mL), and the reaction mixture was stirred at room temperature. When the reaction was finished (determined by TLC). The mixture were added silica gel (2.0 g) and toluene (10.0 mL) continued stir at room temperature when the aromatization was finished (determined by TLC). Then solvent was evaporated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the products **3x** (251.4 mg, 56%, 92% ee).

Scheme S3. Synthesis procedure of derivatization reaction, related to Scheme 4.



A dried tube with a magnetic stir bar was charged with 3-nitroindole derivative **1a** (1.00 mmol), allenoate derivative **2m** (1.50 mmol, 1.5 equiv.), catalyst **4d** (10 mol%), followed by the addition

of toluene (10.0 mL), and the reaction mixture was stirred at room temperature. When the reaction was finished (determined by TLC). The mixture were added silica gel (2.0 g) and toluene (10.0 mL) continued stir at room temperature when the aromatization process was finished (determined by TLC). Then solvent was evaporated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the products **3v** (261.6 mg, 57%, 92% ee).

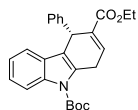
A suspension of **3v** (261.6 mg, 0.57 mmol) and 10% palladium on carbon (130.0 mg) in MeOH (10.0 mL) was maintained under an atmosphere of hydrogen gas for 8 h at rt. The insoluble solids were removed by filtration and the filtrate was concentrated. The residue was dissolved in MeNH₂ (30 wt. % in absolute EtOH 4.0 mL), and the resulting mixture was stirred 1 h. Then solvent was evaporated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to afford the product **7** (179.2 mg, 84%, 92% ee).

To a solution of **7** (179.2 mg, 0.48 mmol) in anhydrous DCM (5 mL) was slowly added SOCl₂ (1 mol/L in DCM, 2.0 mL) at 0 °C. The suspension was allowed to warm to room temperature and continues to stir 2 h. After that, the reaction mixture was reduced in vacuo. The residue was dissolved in EtOH (5.0 mL) and potassium tert-butoxide (336.0 mg, 3.0 mmol) was added and the reaction stirred at 40 °C for 36 h. The solvent was removed and the residue was purified by column chromatography using MeOH/DCM as the eluent to give **8** (91.2 mg, 79%, 92% ee).

To a solution of **7** (28.8 mg, 0.12 mmol) in anhydrous THF (5 mL) was added LiAlH₄ (45.6 mg, 1.2 mmol) at 0 °C. The suspension was allowed to warm to room temperature and continues to stir at 40 °C for 36 h. After that, saturated aqueous Na₂SO₄ (4 mL) was added. The solid formed was filtered and washed with DCM. The organic layers were combined and dried with MgSO₄. The solvent was removed and the residue was purified by column chromatography (DCM/MeOH/Et₃N = 100/5/1) to give **8** (21.2 mg, 78%, 92% ee).

Characterization of products

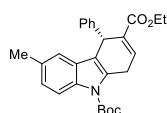
9-(Tert-butyl) 3-ethyl (S)-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (**3a**)



Step 1: 18 h; Step 2: 3 h (Silica gel 200 mg); Total yield: 38.4 mg (92%); ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.24 – 7.15 (m, 5H), 7.13 – 7.03 (m, 2H), 5.18 (t, *J* = 5.9 Hz, 1H), 4.18 – 4.00 (m, 4H), 1.70 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 166.41, 150.73, 143.15, 136.25, 134.87, 132.60, 130.82, 128.95, 128.27, 128.24, 126.62, 123.91, 122.73, 118.90, 118.13, 115.51, 84.03, 60.69, 40.49, 28.57, 28.43, 14.21. ESI-MS: calculated [C₂₆H₂₇NO₄ + Na]⁺: 440.1832, found: 440.1833. [α]_D²⁰ = 26.8 (c = 0.96, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 5.72 min, t₂(major) = 7.46 min.

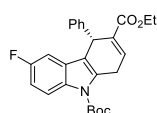
9-(Tert-butyl) 3-ethyl (S)-6-methyl-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxy-

late (3b)



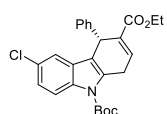
Step 1: 20 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 36.3 mg (84%); **¹H NMR (400 MHz, CDCl₃)** δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.24 – 7.17 (m, 3H), 7.14 – 7.08 (m, 1H), 7.05 – 6.97 (m, 2H), 5.16 (t, *J* = 5.8 Hz, 1H), 4.18 – 4.00 (m, 4H), 2.31 (s, 3H), 1.69 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.46, 150.78, 143.24, 134.93, 134.45, 132.72, 132.15, 130.89, 128.95, 128.42, 128.28, 126.59, 125.25, 118.86, 117.93, 115.17, 83.85, 60.70, 40.45, 28.62, 28.47, 21.46, 14.23. **ESI-MS: calculated [C₂₇H₂₉NO₄ + Na]⁺: 454.1989, found: 454.1989.** [α]²⁰_D = 4.8 (c = 0.98, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 5.12 min, t₂(major) = 10.56 min.

9-(Tert-butyl) 3-ethyl (S)-6-fluoro-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3c)



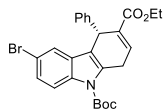
Step 1: 24 h; Step 2: 4 h (Silica gel 400 mg); Total yield: 22.8 mg (52%); **¹H NMR (400 MHz, CDCl₃)** δ 8.05 – 7.97 (m, 1H), 7.34 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 7.17 – 7.10 (m, 1H), 6.93 – 6.83 (m, 2H), 5.12 (t, *J* = 5.9 Hz, 1H), 4.18 – 3.99 (m, 4H), 1.70 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.31, 159.13 (*J* = 239.3 Hz), 150.46, 142.75, 134.62, 132.61, 132.51, 129.27, 129.18, 128.89, 128.43, 126.84, 117.93 (d, *J* = 3.8 Hz), 116.48 (d, *J* = 8.9 Hz), 111.46 (d, *J* = 24.8 Hz), 104.62 (d, *J* = 23.9 Hz), 84.37, 60.78, 40.46, 28.63, 28.44, 14.22. **¹⁹F NMR (377 MHz, CDCl₃)** δ -120.41. **ESI-MS: calculated [C₂₆H₂₇FNO₄ + H]⁺: 436.1919, found: 436.1924.** [α]²⁰_D = 21.3 (c = 1.07, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 91% ee (CHIRALPAK IA, hexane/*i*-PrOH = 98.5/1.5, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 7.04 min, t₂(major) = 9.21 min.

9-(Tert-butyl) 3-ethyl (S)-6-chloro-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3d)



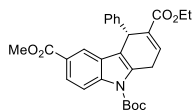
Step 1: 24 h; Step 2: 12 h (Silica gel 400 mg); Total yield: 34.4 mg (76%); **¹H NMR (400 MHz, CDCl₃)** δ 7.99 (d, *J* = 8.8 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.26 – 7.17 (m, 4H), 7.17 – 7.10 (m, 2H), 5.13 (t, *J* = 5.8 Hz, 1H), 4.18 – 3.99 (m, 4H), 1.70 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.25, 150.36, 142.70, 134.70, 134.53, 132.56, 132.26, 129.45, 128.85, 128.45, 128.32, 126.87, 124.06, 118.49, 117.59, 116.57, 84.55, 60.79, 40.34, 28.57, 28.42, 14.21. **ESI-MS: calculated [C₂₆H₂₆ClNO₄ + H]⁺: 452.1623, found: 452.1628.** [α]²⁰_D = 24.3 (c = 0.97, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK IA, hexane/*i*-PrOH = 98.5/1.5, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 7.00 min, t₂(major) = 9.44 min.

9-(Tert-butyl) 3-ethyl (S)-6-bromo-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3e)



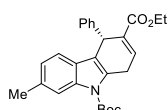
Step 1: 24 h; Step 2: 16 h (Silica gel 400 mg); Total yield: 30.3 mg (61%); **¹H NMR (400 MHz, CDCl₃)** δ 7.95 (d, *J* = 8.8 Hz, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.32 – 7.20 (m, 6H), 7.17 – 7.10 (m, 1H), 5.12 (t, *J* = 5.8 Hz, 1H), 4.21 – 3.99 (m, 4H), 1.70 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.24, 150.34, 142.68, 135.08, 134.51, 132.57, 132.13, 129.95, 128.83, 128.46, 126.88, 126.77, 121.52, 117.51, 116.99, 116.09, 84.59, 60.79, 40.31, 28.54, 28.42, 14.21. **ESI-MS: calculated [C₂₆H₂₆BrNO₄ + H]⁺: 496.1118, found: 496.1100.** [α]_D²⁰ = -38.3 (c = 1.01, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 97% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =98.5/1.5, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(major) = 9.77 min, t₂(minor) =12.54 min.

9-(Tert-butyl) 3-ethyl 6-methyl (S)-4-phenyl-1,4-dihydro-9H-carbazole-3,6,9-tricarboxylate (3f)



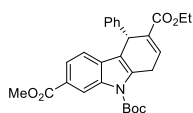
Step 1: 24 h; Step 2: 12 h (Silica gel 400 mg); Total yield: 23.8 mg (50%); **¹H NMR (400 MHz, CDCl₃)** δ 8.12 (d, *J* = 8.8 Hz, 1H), 7.99 (s, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 7.38 – 7.30 (m, 2H), 7.25 – 7.20 (m, 3H), 7.16 – 7.07 (m, 1H), 5.23 (t, *J* = 5.8 Hz, 1H), 4.19 – 4.02 (m, 4H), 3.88 (s, 3H), 1.71 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 167.51, 166.27, 150.36, 142.85, 139.11, 134.59, 132.65, 132.22, 128.82, 128.43, 128.04, 126.84, 125.39, 124.70, 120.97, 118.67, 115.23, 84.81, 60.81, 52.11, 40.32, 28.58, 28.42, 14.22. **ESI-MS: calculated [C₂₈H₂₉NO₆ + H]⁺: 476.2068, found:476.2068.** [α]_D²⁰ = -49.2 (c = 0.96, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) =5.61 min, t₂(major) =6.62 min.

9-(Tert-butyl) 3-ethyl (S)-7-methyl-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3g)



Step 1: 24 h; Step 2: 0.5 h (Silica gel 200 mg); Total yield: 37.3 mg (86%); **¹H NMR (400 MHz, CDCl₃)** δ 7.94 (s, 1H), 7.33 – 7.28 (m, 2H), 7.24 – 7.16 (m, 3H), 7.14 – 7.05 (m, 2H), 6.92 – 6.86 (m, 1H), 5.16 (t, *J* = 6.0 Hz, 1H), 4.20 – 3.97 (m, 4H), 2.39 (s, 3H), 1.70 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.47, 150.80, 143.22, 136.74, 134.95, 133.81, 132.60, 129.91, 128.94, 128.26, 126.59, 125.98, 124.07, 118.48, 118.11, 115.92, 83.90, 60.68, 40.55, 28.65, 28.44, 22.10, 14.22. **ESI-MS: calculated [C₂₇H₂₉NO₄ + H]⁺: 432.2169, found: 432.2170.** [α]_D²⁰ = 15.0 (c = 1.02, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 95% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 5.48min, t₂(major) =8.14 min.

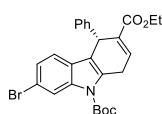
9-(Tert-butyl) 6-ethyl 2-methyl (S)-5-phenyl-5,8-dihydro-9H-carbazole-2,6,9-tricarboxylate (3h)



Step 1: 24 h; Step 2: 6 h (Silica gel 400 mg); Total yield: 24.4 mg (51%); **¹H NMR (400 MHz, CDCl₃)** δ 8.81 (s, 1H), 7.77 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.19 (m, 4H), 7.15 – 7.07 (m, 1H), 5.20 (t, *J* = 5.8 Hz, 1H), 4.19 – 4.06 (m, 4H), 3.89 (s, 3H), 1.74 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 167.84, 166.27, 150.33, 142.80, 135.68, 134.47, 134.28, 132.50, 131.86, 128.90, 128.39, 126.83, 125.51, 124.06, 118.50, 118.21, 117.53, 84.80, 60.82, 52.16, 40.35, 28.56, 28.38, 14.21. **ESI-MS: calculated [C₂₈H₂₉NO₆ + H]⁺: 476.2068, found: 476.2083.** [α]²⁰_D = 15.5 (*c* = 0.51, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 86% *ee* (CHIRALPAK IA, hexane/*i*-PrOH = 95/5, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(minor) = 7.49 min, *t*₂(major) = 8.38 min.

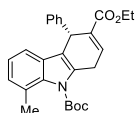
9-(Tert-butyl) 3-ethyl (S)-7-bromo-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3i)



Step 1: 24 h; Step 2: 6 h (Silica gel 200 mg); Total yield: 30.3 mg (61%); **¹H NMR (400 MHz, CDCl₃)** δ 8.29 (s, 1H), 7.32 – 7.27 (m, 2H), 7.24 – 7.15 (m, 4H), 7.15 – 7.09 (m, 1H), 7.09 – 7.04 (m, 1H), 5.14 (t, *J* = 5.8 Hz, 1H), 4.20 – 3.97 (m, 4H), 1.71 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)**

δ 166.29, 150.29, 142.84, 137.00, 134.58, 132.48, 131.37, 128.88, 128.37, 127.06, 126.81, 125.94, 119.93, 118.81, 117.95, 117.68, 84.72, 60.78, 40.38, 28.51, 28.39, 14.22. **ESI-MS: calculated [C₂₆H₂₆BrNO₄ + H]⁺: 496.1118, found: 496.1121.** [α]²⁰_D = -24.8 (*c* = 0.97, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 91% *ee* (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(minor) = 5.87 min, *t*₂(major) = 7.63 min.

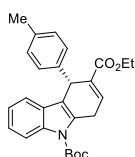
9-(Tert-butyl) 3-ethyl (S)-8-methyl-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3j)



Step 1: 18 h; Step 2: 6 h (Silica gel 400 mg); Total yield: 23.9 mg (55%); **¹H NMR (400 MHz, CDCl₃)** δ 7.33 – 7.28 (m, 2H), 7.24 – 7.17 (m, 3H), 7.13 – 7.06 (m, 2H), 7.00 – 6.95 (m, 2H), 5.17 (t, *J* = 5.9 Hz, 1H), 4.18 – 4.04 (m, 2H), 4.00 – 3.78 (m, 2H), 2.45 (s, 3H), 1.68 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)**

δ 166.45, 150.35, 143.09, 135.84, 134.33, 133.16, 130.71, 129.23, 129.01, 128.26, 127.06, 126.60, 124.68, 122.90, 117.27, 116.65, 84.01, 77.48, 77.16, 76.84, 60.73, 40.70, 28.25, 27.97, 21.36, 14.22. **ESI-MS: calculated [C₂₇H₂₉NO₄ + Na]⁺: 454.1989, found: 454.1993.** [α]²⁰_D = 21.5 (*c* = 0.51, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 90% *ee* (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(major) = 7.25 min, *t*₂(minor) = 7.98 min.

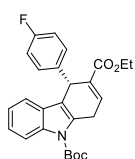
9-(Tert-butyl) 3-ethyl (S)-4-(p-tolyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3k)



Step 1: 24 h; Step 2: 3 h (Silica gel 200 mg); Total yield: 33.2 mg (77%); **¹H NMR (400 MHz, CDCl₃)** δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.23 – 7.15 (m, 4H), 7.09 – 7.04 (m, 1H), 7.01 (d, *J* = 7.9 Hz, 2H), 5.15 (t, *J* = 5.8 Hz, 1H), 4.20 – 4.00 (m, 4H), 2.24 (s, 3H), 1.70 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100**

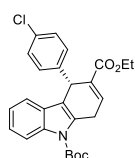
MHz, CDCl₃) δ 166.52, 150.78, 140.13, 136.28, 136.08, 134.70, 132.76, 130.76, 129.02, 128.76, 128.30, 123.90, 122.74, 118.94, 118.34, 115.52, 84.03, 60.71, 40.04, 28.59, 28.47, 21.19, 14.25. **ESI-MS: calculated [C₂₇H₂₉NO₄ + H]⁺: 432.2169, found: 432.21625.** $[\alpha]^{20}_D = 11.7$ (c = 0.38, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(minor) = 5.47 min, *t*₂(major) =6.64 min.

9-(Tert-butyl) 3-ethyl (S)-4-(4-fluorophenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3l)



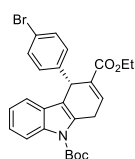
Step 1: 12 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 40.1 mg (92%); **¹H NMR (400 MHz, CDCl₃)** δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 7.11 – 7.05 (m, 1H), 6.93 – 6.86 (m, 2H), 5.18 (t, *J* = 5.9 Hz, 1H), 4.24 – 3.94 (m, 4H), 1.71 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.32, 161.60 (*J* = 244.5 Hz), 150.71, 138.91 (*J* = 3.0 Hz), 136.26, 134.99, 132.44, 130.91, 130.41 (*J* = 8.0 Hz), 128.07, 124.04, 122.78, 118.79, 117.84, 115.60, 115.11 (*J* = 21.4 Hz), 84.17, 60.78, 39.72, 28.52, 28.45, 14.25. **¹⁹F NMR (376 MHz, CDCl₃)** δ -116.42. **ESI-MS: calculated [C₂₆H₂₆FNO₄ + Na]⁺: 458.1738, found: 458.1746.** $[\alpha]^{20}_D = 27.6$ (c = 1.00, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(minor) = 5.58 min, *t*₂(major) =7.38 min.

9-(Tert-butyl) 3-ethyl (S)-4-(4-chlorophenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3m)



Step 1: 12 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 41.3 mg (91%); **¹H NMR (400 MHz, CDCl₃)** δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.28 – 7.16 (m, 7H), 7.11 – 7.03 (m, 1H), 5.16 (t, *J* = 5.9 Hz, 1H), 4.23 – 4.00 (m, 4H), 1.71 (s, 9H), 1.23 (d, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.22, 150.69, 141.77, 136.25, 135.27, 132.31, 132.17, 130.98, 130.32, 128.47, 127.99, 124.10, 122.82, 118.74, 117.59, 115.61, 84.21, 60.83, 39.88, 28.53, 28.45, 14.26. **ESI-MS: calculated [C₂₆H₂₆ClNO₄ + Na]⁺:474.1443, found:474.1443.** $[\alpha]^{20}_D = 13.5$ (c = 1.01, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), *t*₁(minor) = 6.06 min, *t*₂(major) =7.57 min.

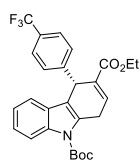
9-(Tert-butyl) 3-ethyl (S)-4-(4-bromophenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3n)



Step 1: 18 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 34.6 mg (70%); **¹H NMR (400 MHz, CDCl₃)** δ 8.08 (d, *J* = 8.3 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.26 – 7.15 (m, 5H), 7.11 – 7.03 (m, 1H), 5.16 (t, *J* = 5.9 Hz, 1H), 4.21 – 4.09 (m, 2H), 4.09 – 4.02 (m, 2H), 1.71 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.21, 150.69, 142.31, 136.25, 135.32, 132.10, 131.42, 130.99, 130.72, 127.98, 124.12, 122.84, 120.48, 118.74, 117.52, 115.62, 84.23, 60.85, 39.96, 28.54, 28.46, 14.27. **ESI-MS:**

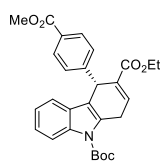
calculated $[\text{C}_{26}\text{H}_{26}\text{BrNO}_4 + \text{H}]^+$: 496.1118, found: 496.1111. $[\alpha]^{20}_{\text{D}} = 9.0$ ($c = 1.01$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), $t_1(\text{minor}) = 5.73$ min, $t_2(\text{major}) = 7.02$ min.

9-(Tert-butyl) 3-ethyl (S)-4-(4-(trifluoromethyl)phenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3o)



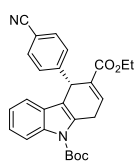
Step 1: 10 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 38.7 mg (80%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09 (d, $J = 8.3$ Hz, 1H), 7.52 – 7.40 (m, 4H), 7.32 – 7.27 (m, 1H), 7.24 – 7.16 (m, 2H), 7.13 – 7.05 (m, 1H), 5.26 (t, $J = 5.9$ Hz, 1H), 4.21 – 3.98 (m, 4H), 1.71 (s, 9H), 1.23 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 166.07, 150.67, 147.35, 136.27, 135.79, 131.88, 131.14, 129.29, 128.88 ($J = 32.2$ Hz), 127.88, 125.21 ($J = 3.7$ Hz), 124.30 ($J = 270.3$ Hz), 124.19, 122.88, 118.62, 117.30, 115.68, 84.32, 60.91, 40.36, 28.59, 28.45, 14.23. **ESI-MS: calculated $[\text{C}_{27}\text{H}_{26}\text{F}_3\text{NO}_4 + \text{H}]^+$: 486.1887, found: 486.1896.** $[\alpha]^{20}_{\text{D}} = 18.8$ ($c = 1.00$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), $t_1(\text{minor}) = 5.67$ min, $t_2(\text{major}) = 6.86$ min.

9-(Tert-butyl) 3-ethyl (S)-4-(4-(methoxycarbonyl)phenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3p)



Step 1: 8 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 40.9 mg (86%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.08 (d, $J = 8.5$ Hz, 1H), 7.90 (d, $J = 8.3$ Hz, 2H), 7.41 (d, $J = 8.3$ Hz, 2H), 7.28 (t, $J = 3.5$ Hz, 1H), 7.22 – 7.17 (m, 2H), 7.08 – 7.03 (m, 1H), 5.24 (t, $J = 5.9$ Hz, 1H), 4.19 – 4.03 (m, 4H), 3.85 (s, 3H), 1.71 (s, 9H), 1.19 (d, $J = 4.9$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 167.09, 166.15, 150.68, 148.58, 136.24, 135.68, 131.87, 131.03, 129.72, 129.07, 128.59, 127.96, 124.11, 122.83, 118.68, 117.33, 115.61, 84.26, 60.86, 52.10, 40.56, 28.58, 28.45, 14.23. **ESI-MS: calculated $[\text{C}_{28}\text{H}_{29}\text{NO}_6 + \text{H}]^+$: 476.2068, found: 476.2063.** $[\alpha]^{20}_{\text{D}} = 15.2$ ($c = 1.02$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), $t_1(\text{minor}) = 10.97$ min, $t_2(\text{major}) = 15.22$ min.

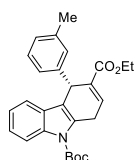
9-(Tert-butyl) 3-ethyl (S)-4-(4-cyanophenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3q)



Step 1: 12 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 38.4 mg (87%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09 (d, $J = 8.4$ Hz, 1H), 7.52 (d, $J = 8.3$ Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H), 7.31 (t, $J = 3.4$ Hz, 1H), 7.25 – 7.19 (m, 1H), 7.16 – 7.12 (m, 1H), 7.11 – 7.05 (m, 1H), 5.24 (t, $J = 5.9$ Hz, 1H), 4.20 – 3.99 (m, 4H), 1.71 (s, 9H), 1.23 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.89, 150.60, 148.84, 136.21, 132.23, 131.41, 131.23, 129.79, 127.69, 124.30, 124.08, 122.93, 119.04, 118.42, 116.79, 115.72, 110.54, 84.43, 60.98, 40.62, 28.56, 28.43, 14.24. **ESI-MS: calculated**

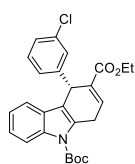
[C₂₇H₂₆N₂O₄ + H]⁺: 443.1965, found: 443.1966. [α]²⁰_D = 8.7 (c = 1.01, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH = 90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 7.03 min, t₂(major) = 8.21 min.

9-(Tert-butyl) 3-ethyl (S)-4-(m-tolyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3r)



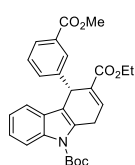
Step 1: 20 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 25.0 mg (58%); **¹H NMR (400 MHz, CDCl₃)** δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.15 (m, 4H), 7.13 – 7.03 (m, 3H), 6.92 (d, *J* = 7.2 Hz, 1H), 5.15 (t, *J* = 5.8 Hz, 1H), 4.19 – 4.01 (m, 4H), 2.26 (s, 3H), 1.71 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.53, 150.80, 143.02, 137.73, 136.28, 134.79, 132.73, 130.80, 129.56, 128.36, 128.07, 127.47, 126.20, 123.89, 122.75, 118.99, 118.24, 115.51, 84.05, 60.70, 40.46, 28.59, 28.48, 21.62, 14.22. **ESI-MS: calculated [C₂₇H₂₉NO₄ + Na]⁺: 454.1989, found: 454.2002. [α]²⁰_D = 27.5 (c = 0.94, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK IA, hexane/*i*-PrOH = 98.5/1.5, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 6.35 min, t₂(major) = 10.35 min.**

9-(Tert-butyl) 3-ethyl (S)-4-(3-chlorophenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3s)



Step 1: 12 h; Step 2: 2 h (Silica gel 100 mg); Total yield: 23.5 mg (52%); **¹H NMR (400 MHz, CDCl₃)** δ 8.09 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.18 (m, 5H), 7.18 – 7.06 (m, 3H), 5.16 (t, *J* = 5.8 Hz, 1H), 4.21 – 4.02 (m, 4H), 1.71 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.18, 150.69, 145.33, 136.29, 135.59, 134.09, 131.99, 131.07, 129.50, 128.99, 128.00, 127.42, 126.96, 124.11, 122.85, 118.73, 117.39, 115.63, 84.25, 60.87, 40.26, 28.57, 28.47, 14.24. **ESI-MS: calculated [C₂₆H₂₆ClNO₄ + H]⁺: 452.1623, found: 452.1616. [α]²⁰_D = 17.4 (c = 1.03, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 5.39 min, t₂(major) = 7.82 min.**

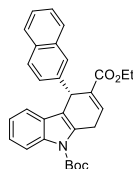
9-(Tert-butyl) 3-ethyl (S)-4-(3-(methoxycarbonyl)phenyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3t)



Step 1: 12 h; Step 2: 2 h (Silica gel 100 mg); Total yield: 29.4 mg (62%); **¹H NMR (400 MHz, CDCl₃)** δ 8.10 – 8.05 (m, 1H), 8.00 (t, *J* = 1.6 Hz, 1H), 7.85 – 7.78 (m, 1H), 7.57 – 7.51 (m, 1H), 7.34 – 7.26 (m, 2H), 7.22 – 7.15 (m, 2H), 7.09 – 7.02 (m, 1H), 5.26 – 5.22 (m, 1H), 4.19 – 4.05 (m, 4H), 3.87 (s, 3H), 1.71 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 167.22, 166.21, 150.69, 143.76, 136.27, 135.66, 133.75, 132.01, 131.08, 130.19, 130.10, 128.36, 128.05, 128.01, 124.05, 122.80, 118.71, 117.46, 115.60, 84.21, 60.82, 52.16, 40.42, 28.58, 28.45, 14.18. **ESI-MS: calculated [C₂₈H₂₉NO₆ + Na]⁺: 498.1887, found: 498.1890. [α]²⁰_D = 14.3 (c = 1.01, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee**

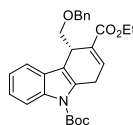
(CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min),
 t_1 (minor) = 8.06 min, t_2 (major) =13.97 min.

9-(Tert-butyl) 3-ethyl (S)-4-(naphthalen-2-yl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3u)



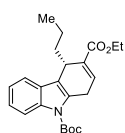
Step 1: 36 h; Step 2: 3 h (Silica gel 200 mg); Total yield: 41.0 mg (88%); **¹H NMR (400 MHz, CDCl₃)** δ 8.06 (d, *J* = 8.3 Hz, 1H), 7.85 (s, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.44 – 7.32 (m, 3H), 7.29 – 7.22 (m, 2H), 7.15 (t, *J* = 7.7 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 5.37 (t, *J* = 6.0 Hz, 1H), 4.21 – 3.98 (m, 4H), 1.71 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.42, 150.79, 140.58, 136.26, 135.04, 133.48, 132.53, 132.50, 130.96, 128.25, 128.01, 127.93, 127.81, 127.69, 127.13, 125.90, 125.55, 123.96, 122.77, 118.95, 117.97, 115.52, 84.12, 60.74, 40.64, 28.65, 28.47, 14.23. **ESI-MS: calculated [C₃₀H₂₉NO₄ + Na]⁺: 490.1989, found: 490.1994.** $[\alpha]_D^{20}$ = 48.3 (*c* = 0.99, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 93% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (minor) = 6.66 min, t_2 (major) =10.38 min.

9-(Tert-butyl) 3-ethyl (S)-4-((benzyloxy)methyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3v)



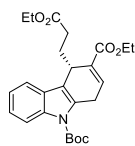
Step 1: 24 h; Step 2: 2 h (Silica gel 200 mg); Total yield: 30.2 mg (65%); **¹H NMR (400 MHz, CDCl₃)** δ 8.14 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.28 – 7.17 (m, 6H), 7.14 – 7.07 (m, 2H), 4.38 – 4.31 (m, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.99 – 3.85 (m, 2H), 3.84 – 3.77 (m, 2H), 1.69 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.87, 150.65, 138.59, 137.69, 136.34, 132.35, 130.10, 128.44, 128.20, 123.86, 122.68, 118.85, 116.39, 115.67, 83.92, 73.17, 72.65, 60.78, 35.15, 28.77, 28.44, 14.39. **ESI-MS: calculated [C₂₈H₃₁NO₅ + Na]⁺: 484.2094, found: 484.2103.** $[\alpha]_D^{20}$ = -34.2 (*c* = 1.15, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 92% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =97/3, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (major) = 8.15 min, t_2 (minor) =9.94 min.

9-(Tert-butyl) 3-ethyl (S)-4-propyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3w)



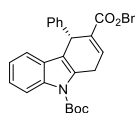
Step 1: 36 h; Step 2: 4 h (Silica gel 400 mg); Total yield: 28.9 mg (75%); **¹H NMR (400 MHz, CDCl₃)** δ 8.14 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.1 Hz, 1H), 7.32 – 7.23 (m, 3H), 7.20 (s, 1H), 4.36 – 4.20 (m, 3H), 3.97 – 3.72 (m, 2H), 1.95 – 1.80 (m, 2H), 1.69 (s, 9H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.17 – 1.04 (m, 1H), 1.00 – 0.87 (m, 1H), 0.74 (t, *J* = 7.2 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.95, 150.69, 136.55, 136.36, 132.27, 131.83, 128.45, 123.80, 122.67, 118.63, 118.10, 115.70, 83.89, 60.72, 36.08, 33.27, 28.74, 28.45, 17.93, 14.45, 14.35. **ESI-MS: calculated [C₂₃H₂₉NO₄ + H]⁺: 384.2169, found: 384.2161.** $[\alpha]_D^{20}$ = -71.1 (*c* = 0.39, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 90% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =99/1, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (minor) = 5.54 min, t_2 (major) =7.23 min.

9-(Tert-butyl) 3-ethyl (S)-4-(3-ethoxy-3-oxopropyl)-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3x)



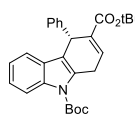
Step 1: 36 h; Step 2: 4 h (Silica gel 400 mg); Total yield: 30.8 mg (70%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.14 (d, $J = 8.0$ Hz, 1H), 7.55 (d, $J = 7.2$ Hz, 1H), 7.35 – 7.18 (m, 3H), 4.41 – 4.34 (m, 1H), 4.32 – 4.22 (m, 2H), 3.98 – 3.88 (m, 3H), 3.87 – 3.77 (m, 1H), 2.37 – 2.27 (m, 2H), 2.12 – 2.01 (m, 1H), 1.98 – 1.88 (m, 1H), 1.70 (s, 9H), 1.37 (t, $J = 7.1$ Hz, 3H), 1.12 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 173.65, 166.46, 150.57, 137.70, 136.40, 132.28, 130.99, 127.99, 124.06, 122.86, 118.53, 116.56, 115.75, 84.08, 60.88, 60.30, 32.42, 29.58, 28.71, 28.43, 28.08, 14.42, 14.19. **ESI-MS: calculated $[\text{C}_{25}\text{H}_{31}\text{NO}_6 + \text{H}]^+$: 442.2224, found: 442.2208.** $[\alpha]^{20}_{\text{D}} = -47.5$ ($c = 0.51$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 81% ee (CHIRALPAK AS-H, hexane/*i*-PrOH = 97/3, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (major) = 5.74 min, t_2 (minor) = 6.62 min.

3-Benzyl 9-(tert-butyl) (S)-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3y)



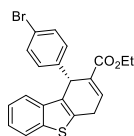
Step 1: 18 h; Step 2: 1.5 h (Silica gel 200 mg); Total yield: 32.9 mg (69%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 (d, $J = 8.3$ Hz, 1H), 7.34 – 7.27 (m, 6H), 7.26 – 7.15 (m, 6H), 7.14 – 7.09 (m, 1H), 7.08 – 7.02 (m, 1H), 5.20 (t, $J = 5.9$ Hz, 1H), 5.10 (dd, $J = 39.1, 12.4$ Hz, 2H), 4.15 – 3.95 (m, 2H), 1.69 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 166.25, 150.71, 143.00, 136.26, 136.00, 135.59, 132.38, 130.69, 128.98, 128.60, 128.36, 128.26, 128.23, 128.19, 126.68, 123.95, 122.75, 118.91, 118.08, 115.53, 84.07, 66.57, 40.53, 28.64, 28.45. **ESI-MS: calculated $[\text{C}_{31}\text{H}_{29}\text{NO}_4 + \text{Na}]^+$: 502.1989, found: 502.1987.** $[\alpha]^{20}_{\text{D}} = 24.5$ ($c = 0.97$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 93% ee (CHIRALPAK IA, hexane/*i*-PrOH = 97/3, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 8.10 min, t_2 (major) = 11.15 min.

Di-tert-butyl (S)-4-phenyl-1,4-dihydro-9H-carbazole-3,9-dicarboxylate (3z)



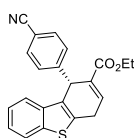
Step 1: 36 h; Step 2: 1.5 h (Silica gel 200 mg); Total yield: 33.7 mg (76%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 (d, $J = 8.3$ Hz, 1H), 7.34 – 7.27 (m, 3H), 7.26 – 7.17 (m, 3H), 7.17 – 7.10 (m, 2H), 7.09 – 7.04 (m, 1H), 5.12 (t, $J = 6.0$ Hz, 1H), 4.12 – 3.93 (m, 2H), 1.70 (s, 9H), 1.36 (s, 9H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.89, 150.76, 143.28, 136.29, 133.95, 133.89, 130.91, 129.02, 128.35, 128.18, 126.56, 123.85, 122.69, 118.95, 118.12, 115.52, 84.02, 80.92, 40.72, 28.53, 28.46, 28.10. **ESI-MS: calculated $[\text{C}_{28}\text{H}_{31}\text{NO}_4 + \text{H}]^+$: 446.2326, found: 446.2318.** $[\alpha]^{20}_{\text{D}} = 26.9$ ($c = 2.0$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK IA, hexane/*i*-PrOH = 98.5/1.5, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 5.32 min, t_2 (major) = 6.60 min.

Ethyl (R)-1-(4-bromophenyl)-1,4-dihydrodibenzo[b,d]thiophene-2-carboxylate (6a)



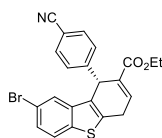
Step 1: 48 h; Step 2: 5 h (Silica gel 300 mg); Total yield: 24.4 mg (59%); **¹H NMR (400 MHz, CDCl₃)** δ 7.77 – 7.71 (m, 1H), 7.48 – 7.42 (m, 1H), 7.34 – 7.30 (m, 2H), 7.28 – 7.25 (m, 1H), 7.24 – 7.16 (m, 4H), 5.27 (t, *J* = 5.2 Hz, 1H), 4.26 – 4.06 (m, 2H), 4.02 – 3.89 (m, 1H), 3.87 – 3.74 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 166.04, 141.73, 139.23, 137.89, 134.40, 133.13, 132.89, 131.50, 130.77, 130.44, 124.30, 124.28, 122.48, 121.78, 120.62, 60.97, 41.47, 28.07, 14.30. **ESI-MS: calculated [C₂₁H₁₇BrN₂S + H]⁺: 413.0205, found: 413.0213.** [α]_D²⁰ = -36.9 (c = 0.81, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 95% ee (CHIRALPAK IA, hexane/*i*-PrOH =90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 7.53 min, t₂(major) =8.22min.

Ethyl (*R*)-1-(4-cyanophenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6b)



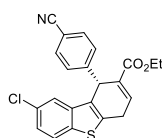
Step 1: 48 h; Step 2: 5 h (Silica gel 300 mg); Total yield: 25.7 mg (72%); **¹H NMR (400 MHz, CDCl₃)** δ 7.79 – 7.74 (m, 1H), 7.53 – 7.48 (m, 2H), 7.45 – 7.38 (m, 3H), 7.36 – 7.32 (m, 1H), 7.29 – 7.19 (m, 2H), 5.36 (t, *J* = 5.1 Hz, 1H), 4.25 – 4.08 (m, 2H), 4.03 – 3.94 (m, 1H), 3.91 – 3.78 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 165.76, 148.20, 139.27, 137.64, 135.25, 133.35, 132.50, 132.30, 129.86, 129.69, 124.47, 124.45, 122.62, 121.49, 118.95, 110.68, 61.11, 42.09, 28.12, 14.29. **ESI-MS: calculated [C₂₂H₁₇NO₂S + H]⁺: 360.1053, found: 360.1055.** [α]_D²⁰ = -34.2 (c = 1.15, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 90% ee (CHIRALPAK IA, hexane/*i*-PrOH =90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 15.32 min, t₂(major) = 18.83 min.

Ethyl (*R*)-8-bromo-1-(4-cyanophenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6c)



Step 1: 60 h; Step 2: 8 h (Silica gel 500 mg); Total yield: 23.7 mg (54%); **¹H NMR (400 MHz, CDCl₃)** δ 7.61 (d, *J* = 8.5 Hz, 1H), 7.56 – 7.50 (m, 3H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.29 (m, 2H), 5.30 (t, *J* = 5.1 Hz, 1H), 4.30 – 4.08 (m, 2H), 4.04 – 3.91 (m, 1H), 3.90 – 3.77 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 165.55, 139.30, 137.86, 135.38, 134.93, 132.45, 132.40, 129.72, 129.15, 127.52, 124.24, 123.91, 118.86, 118.56, 110.95, 61.19, 41.89, 28.09, 14.28. **ESI-MS: calculated [C₂₂H₁₆BrNO₂S + H]⁺: 438.0158, found: 438.0164.** [α]_D²⁰ = -100.3 (c = 0.74, CH₂Cl₂). The product was analyzed by HPLC to determine the enantiomeric excess: 91% ee (CHIRALPAK IA, hexane/*i*-PrOH =90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t₁(minor) = 18.98 min, t₂(major) =21.56 min.

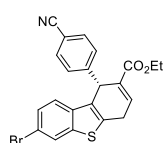
Ethyl (*R*)-8-chloro-1-(4-cyanophenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6d)



Step 1: 60 h; Step 2: 8 h (Silica gel 500 mg); Total yield: 24.2 mg (61%); **¹H NMR (400 MHz, CDCl₃)** δ 7.66 (d, *J* = 8.5 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 1.9 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.21 (dd,

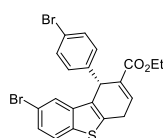
$J = 8.5, 1.9$ Hz, 1H), 5.30 (t, $J = 5.1$ Hz, 1H), 4.25 – 4.09 (m, 2H), 4.04 – 3.93 (m, 1H), 3.90 – 3.77 (m, 1H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.45, 147.57, 138.76, 137.24, 135.44, 134.83, 132.34, 132.28, 130.68, 129.63, 129.13, 124.80, 123.48, 121.08, 118.75, 110.83, 61.09, 41.81, 28.02, 14.18. **ESI-MS: calculated $[\text{C}_{22}\text{H}_{16}\text{ClNO}_2\text{S} + \text{H}]^+$: 394.0663, found: 394.0667.** $[\alpha]^{20}_{\text{D}} = -100.0$ ($c = 1.01, \text{CH}_2\text{Cl}_2$). The product was analyzed by HPLC to determine the enantiomeric excess: 91% ee (CHIRALPAK IA, hexane/*i*-PrOH = 90/10, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 16.12 min, t_2 (major) = 19.62 min.

Ethyl (*R*)-7-bromo-1-(4-cyanophenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6e)



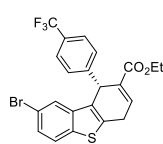
Step 1: 60 h; Step 2: 5 h (Silica gel 600 mg); Total yield: 22.5 mg (51%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.88 (d, $J = 1.6$ Hz, 1H), 7.51 (d, $J = 8.2$ Hz, 2H), 7.40 (d, $J = 8.3$ Hz, 2H), 7.34 – 7.28 (m, 2H), 7.23 (d, $J = 8.5$ Hz, 1H), 5.31 (t, $J = 5.2$ Hz, 1H), 4.27 – 4.07 (m, 2H), 4.03 – 3.89 (m, 1H), 3.89 – 3.75 (m, 1H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.59, 147.80, 140.74, 136.42, 134.91, 134.03, 132.35, 129.78, 129.48, 127.87, 125.16, 122.53, 118.80, 118.30, 110.89, 61.16, 41.97, 28.01, 14.27. **ESI-MS: calculated $[\text{C}_{22}\text{H}_{16}\text{NO}_2\text{S} + \text{H}]^+$: 438.0158, found: 438.0167.** $[\alpha]^{20}_{\text{D}} = -11.8$ ($c = 0.49, \text{CH}_2\text{Cl}_2$). The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH = 90/10, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 18.73 min, t_2 (major) = 23.81 min.

Ethyl (*R*)-8-bromo-1-(4-bromophenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6f)



Step 1: 60 h; Step 2: 24 h (Silica gel 600 mg); Total yield: 31.9 mg (65%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.61 – 7.52 (m, 2H), 7.37 – 7.29 (m, 3H), 7.25 – 7.23 (m, 1H), 7.19 – 7.14 (m, 2H), 5.21 (t, $J = 5.1$ Hz, 1H), 4.26 – 4.07 (m, 2H), 4.00 – 3.89 (m, 1H), 3.85 – 3.73 (m, 1H), 1.27 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.83, 141.24, 139.57, 137.86, 134.91, 134.07, 133.08, 131.68, 130.61, 129.96, 127.34, 124.52, 123.79, 120.90, 118.45, 61.05, 41.31, 28.06, 14.30. **ESI-MS: calculated $[\text{C}_{21}\text{H}_{16}\text{Br}_2\text{O}_2\text{S} + \text{H}]^+$: 492.9290, found: 492.9296.** $[\alpha]^{20}_{\text{D}} = -112.6$ ($c = 1.00, \text{CH}_2\text{Cl}_2$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% ee (CHIRALPAK AD-H, hexane/*i*-PrOH = 85/15, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (major) = 8.59 min, t_2 (minor) = 9.49 min.

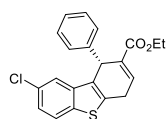
Ethyl (*R*)-8-bromo-1-(4-(trifluoromethyl)phenyl)-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6g)



Step 1: 60 h; Step 2: 24 h (Silica gel 600 mg); Total yield: 33.7 mg (70%); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.61 – 7.54 (m, 2H), 7.49 (d, $J = 8.2$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 7.35 – 7.27 (m, 2H), 5.32 (t, $J = 5.0$ Hz, 1H), 4.28 – 4.07 (m, 2H), 4.05 – 3.92 (m, 1H), 3.89 – 3.75 (m, 1H), 1.26 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 165.71, 146.27, 139.50, 137.92, 135.19, 134.52, 132.95, 129.74, 129.27

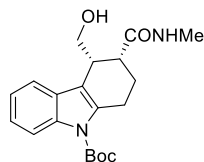
(d, $J = 32.4$ Hz), 129.23, 127.45, 125.59 (q, $J = 3.8$ Hz), 124.43, 123.85, 118.54, 61.12, 41.69, 28.13, 14.28. ^{19}F NMR (377 MHz, CDCl_3) δ -62.45. **ESI-MS: calculated $[\text{C}_{22}\text{H}_{16}\text{BrF}_3\text{O}_2\text{S} + \text{H}]^+$: 481.0079, found: 481.0090.** $[\alpha]^{20}_{\text{D}} = -57.1$ ($c = 0.99$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 94% *ee* (CHIRALPAK AD-H, hexane/*i*-PrOH =85/15, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 6.41min, t_2 (major) = 7.08 min.

Ethyl (*R*)-8-chloro-1-phenyl-1,4-dihydrodibenzo[*b,d*]thiophene-2-carboxylate (6h)



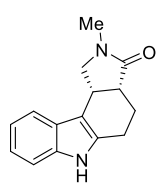
Step 1: 60 h; Step 2: 24 h (Silica gel 600 mg); Total yield: 16.7 mg (45%); ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, $J = 8.5$ Hz, 1H), 7.47 (d, $J = 1.9$ Hz, 1H), 7.32 – 7.27 (m, 2H), 7.26 – 7.10 (m, 5H), 5.24 (t, $J = 5.1$ Hz, 1H), 4.25 – 4.05 (m, 2H), 4.03 – 3.89 (m, 1H), 3.87 – 3.71 (m, 1H), 1.25 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 166.09, 142.16, 139.43, 137.37, 134.82, 133.67, 130.72, 130.54, 128.94, 128.55, 126.98, 124.55, 123.35, 121.68, 60.92, 41.98, 28.15, 14.27. **ESI-MS: calculated $[\text{C}_{21}\text{H}_{17}\text{ClO}_2\text{S} + \text{H}]^+$: 369.0711, found: 369.0712.** $[\alpha]^{20}_{\text{D}} = -109.0$ ($c = 0.52$, CH_2Cl_2). The product was analyzed by HPLC to determine the enantiomeric excess: 97% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =90/10, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 7.33min, t_2 (major) = 8.36 min.

Tert-butyl(3*R*,4*R*)-4-(hydroxymethyl)-3-(methylcarbamoyl)-1,2,3,4-tetrahydro-9*H*-carbazole-9-carboxylate (7)



^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.1$ Hz, 1H), 7.47 (d, $J = 7.3$ Hz, 1H), 7.25 – 7.13 (m, 2H), 6.08 (brs, 1H), 4.01 (dd, $J = 12.0, 8.1$ Hz, 1H), 3.79 (d, $J = 10.7$ Hz, 1H), 3.70 (brs, 1H), 3.41 (s, 1H), 3.27 (dd, $J = 18.4, 5.8$ Hz, 1H), 2.95 – 2.82 (m, 4H), 2.65 – 2.56 (m, 1H), 2.42 – 2.27 (m, 1H), 2.08 – 1.99 (m, 1H), 1.66 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 177.26, 150.61, 136.11, 135.70, 128.41, 123.89, 122.83, 117.66, 116.02, 115.76, 83.91, 62.69, 44.39, 38.03, 28.40, 26.72, 25.55, 22.34. **ESI-MS: calculated $[\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_4\text{S} + \text{H}]^+$: 359.1965, found: 359.1966.** The product was analyzed by HPLC to determine the enantiomeric excess: 92% *ee* (CHIRALPAK IA, hexane/*i*-PrOH =95/5, detector: 254 nm, $T = 30$ °C, flow rate: 1 mL/min), t_1 (minor) = 17.88min, t_2 (major) = 19.27 min.

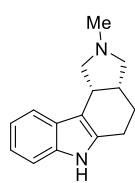
(3*aR*,10*cR*)-2-methyl-1,3*a*,4,5,6,10*c*-hexahydropyrrolo[3,4-*c*]carbazol-3(2*H*)-one (8)



^1H NMR (400 MHz, CDCl_3) δ 8.39 (brs, 1H), 7.43 (d, $J = 7.6$ Hz, 1H), 7.30 (d, $J = 7.8$ Hz, 1H), 7.12 (m, 2H), 4.62 – 4.36 (m, 2H), 3.89 – 3.76 (m, 1H), 3.22 – 3.08 (m, 1H), 2.96 (s, 3H), 2.92 – 2.80 (m, 1H), 2.70 – 2.57 (m, 1H), 2.41 – 2.27 (m, 1H), 2.10 – 1.95 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 165.58, 136.06, 135.49, 126.71, 121.58, 119.61, 117.60, 111.03, 107.64, 73.59, 39.37, 34.85, 34.12, 22.31, 19.60. **ESI-MS: calculated $[\text{C}_{15}\text{H}_{16}\text{N}_2\text{O} + \text{H}]^+$: 235.1335, found: 235.1331.** The product was analyzed by HPLC to determine the enantiomeric excess: 92% *ee* (CHIRALPAK

AD-H, hexane/*i*-PrOH =90/10, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (minor) = 7.48min, t_2 (major) =8.71 min.

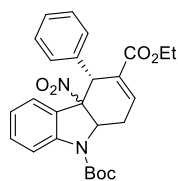
(3aR,10cR)-2-methyl-1,2,3,3a,4,5,6,10c-octahydropyrrolo[3,4-c]carbazole (9)



$^1\text{H NMR}$ (400 MHz, DMSO) δ 10.66 (s, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 7.01 – 6.86 (m, 2H), 3.62 – 3.52 (m, 2H), 3.25 – 3.14 (m, 1H), 2.76 – 2.58 (m, 4H), 2.31 (s, 3H), 2.17 – 2.04 (m, 1H), 1.83 – 1.65 (m, 2H). $^{13}\text{C NMR}$ (100 MHz, DMSO) δ 136.10, 135.00, 126.92, 120.01, 118.10, 117.29, 110.67, 109.71, 61.79, 54.49, 37.08, 35.72, 23.31, 22.69. **ESI-MS: calculated $[\text{C}_{15}\text{H}_{18}\text{N}_2 + \text{H}]^+$: 227.1543, found:227.1541.**

The product was analyzed by HPLC to determine the enantiomeric excess: 92% ee (CHIRALPAK AS-H, hexane/*i*-PrOH =70/30, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (major) = 5.49min, t_2 (minor) =9.67 min.

9-(Tert-butyl) 3-ethyl (4R)-4a-nitro-4-phenyl-1,4,4a,9a-tetrahydro-9H-carbazole-3,9-dicarboxylate (10)



Total yield: 34.6 mg (74%); $^1\text{H NMR}$ (400 MHz, Acetone) δ 7.92 – 7.49 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 7.40 – 7.26 (m, 5H), 7.19 – 7.12 (m, 2H), 5.86 (d, J = 8.5 Hz, 1H), 5.45 (s, 1H), 4.16 – 4.03 (m, 2H), 3.74 – 3.49 (m, 1H), 2.70 (d, J = 18.6 Hz, 1H), 1.61 (s, 9H), 1.17 (t, J = 7.4 Hz, 3H). $^{13}\text{C NMR}$ (100 MHz, Acetone) δ 171.38, 165.60, 140.51, 138.62, 133.33, 131.59, 130.08, 129.90, 129.30, 126.01, 124.73, 116.84, 62.03, 61.02, 59.69, 45.78, 34.27, 28.94, 21.33, 14.98, 14.81. **ESI-MS: calculated $[\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_6 + \text{Na}]^+$: 487.1845, found: 487.1869.** $[\alpha]^{20}_{\text{D}} = -246.5$ (c = 0.45, CH_2Cl_2).

The product was analyzed by HPLC to determine the enantiomeric excess: 94% ee (CHIRALPAK IA, hexane/*i*-PrOH =99/1, detector: 254 nm, T = 30 °C, flow rate: 1 mL/min), t_1 (major) = 12.93 min, t_2 (minor) =19.06 min.

Supplemental References

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3. Tran, Y. S., and Kwon, O. (2007). Phosphine-catalyzed [4 + 2] annulation: synthesis of cyclohexenes. *J. Am. Chem. Soc.* 129, 12632-12633.