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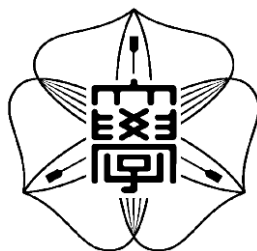
Cyclic amins from aldehydes and “roofed” mono-*N*-sulfonyl *cis*-diamines

(アルデヒドと屋根付きモノ-*N*-スルホニル シス型ジアミンとの環状アミナル)

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PhD Thesis



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Abbreviations

[Compounds]

DMPEDA; *N,N'*-dimethyl-1,2-diphenyl ethylene diamine

MBNC: 2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acid

RDA; "roofed" *cis*-diamine, rel-(11*R*,12*S*)-9,10-dihydro-9,10-ethanoanthracene-11,12-

Diamine, RDA-Ms; *N*-(12-amino-9,10-dihydro-9,10-ethanoanthracen-11-yl)-methyl-

Sulfonamide, RDA-Ts; *N*-(12-amino-9,10-dihydro-9,10-ethanoanthracen-11-yl)-4-

methylbenzenesulfonamide, RDA-1Nps; *N*-(12-amino-9,10-dihydro-9,10-ethanoanthracen-

11-yl)-1-naphthylsulfonamide, RDA-2Nps; *N*-(12-amino-9,10-dihydro-9,10-

ethanoanthracen-11-yl)-2-naphthylsulfonamide

TMS; trimethylsilane, HCl; hydrochloric acid, MeOH; methanol, EtOAc; ethyl Acetate

Me; methyl, Et; ethyl, Ms; methylsulfonyl, Ts; *p*-toluenesulfonyl, Nps; naphthylsulfonyl,

TEA; triethylamine

[Isolation, analysis]

Mp; melting point, MS; Mass Spectrometry, EI; Electron Ionization, FD; Field Desorption,

HR; High Resolution, TLC; Thin Layer Chromatography, NMR; Nuclear Magnetic

Resonance, ee; enantiomeric excess, *R*_f; Retention factor

S; singlet, br s; broad singlet, d; doublet, dd; double doublet, m; multiplet,

J; coupling constant

NOE; Nuclear Overhauser Effect, NOESY; Nuclear Overhauser Effect Spectroscopy,

COSY; Correlation Spectroscopy, HSQC; Heteronuclear Single-Quantum Correlation

Spectroscopy, HMBC; Heteronuclear Multiple-Bond Correlation Spectroscopy

[Reaction condition]

Aq; aqueous, conc.; concentrated, h; hour(s), min; minute(s), refl.; reflux, eq; equivalent(s),

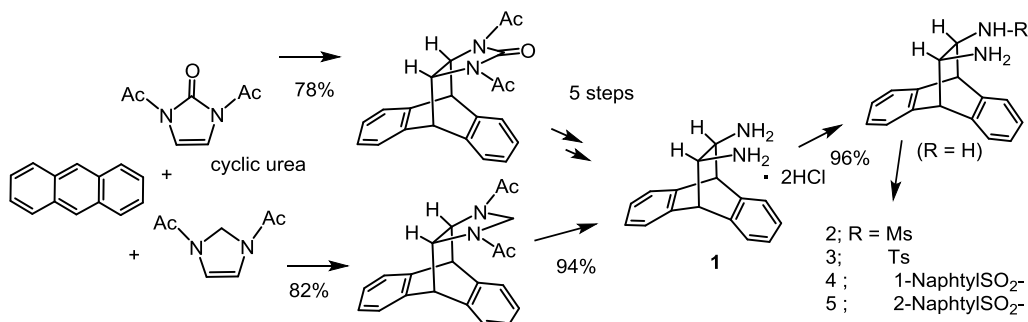
rt; room temperature

Summary

A most popular strategy for optical resolution (resolution of enantiomers) is based on the different physical properties of diastereomers. New mono-*N*-sulfonyl *cis*-diamine reagents were created as chiral derivatizing reagents for racemic aldehydes in this research. Racemic aldehydes are converted into mixture of diastereomers by using the new “roofed” *cis*-diamine reagents. Most of resulting five-membered diastereomeric amins are stable on silica-gel TLC plate and well separated by silica-gel chromatography. The absolute configuration of aldehyde moiety in each separated diastereomer is determined by two-dimensional NMR analyses. The new reagents react smoothly with aldehydes under mild and neutral condition.

1. New synthetic process for “roofed” *cis*-diamine skeleton

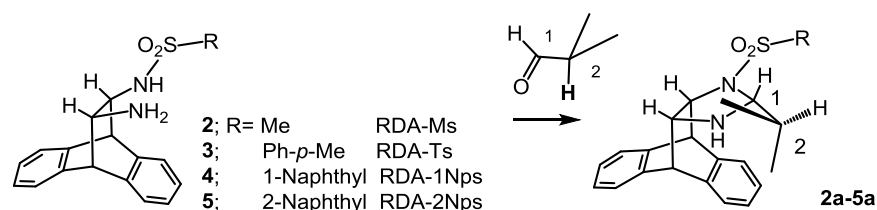
The “roofed” *cis*-diamine skeleton [*rel*-(11*R*,12*S*)-9,10-dihydro-9,10-ethanoanthracene-11,12-diamine hydrochloride (1:2) **1**] was synthesized conventionally by Diels–Alder reaction of anthracene and cyclic urea (1,3-diacetyl-2-imidazolone) as the first step. The bicyclic imidazolidinone was converted to the “roofed” *cis*-diamine hydrochloride **1** through five serial reactions. The cyclic urea was replaced to a cyclic aminal derivative (1,3-diacetyl-2,3-dihydro-1*H*-Imidazole) in this research. By Diels–Alder reaction of anthracene and the cyclic aminal derivative to afford a new intermediate (“roofed” 1,3-diacetyl-2-imidazolidine), which was hydrolyzed under refluxing in conc. HCl /MeOH solution to give the same “roofed” *cis*-diamine hydrochloride **1** in high yield (94 %). The treatment of the salt **1** with base liberated the free diamine in 96 % yield. I introduced sulfonyl substituents to **1** to provide the stereoselectivity in the amination. Mono-*N*-sulfonyl *cis*-diamines (**2-5**) were prepared from **1** and corresponding sulfonyl chloride.



Scheme 1. Preparation of mono-*N*-sulfonyl *cis*-diamines (**2-5**).

2. Preparation of diastereomeric amins from aldehydes and “roofed” mono-*N*-sulfonyl *cis*-diamine reagents 2-5

The mono-*N*-sulfonyl *cis*-diamine reagents **2-5** were reacted with isobutyraldehyde to form cyclic amins **2a-5a**.



Scheme 2. Amino derivatives (**2a-5a**) from **2-5** and isobutyraldehyde.

One methyl proton signal in each amino is apt to shift upfield. The chemical shift differences of geminal carbon signals in four amins are more than 8 ppm. In the stable conformation of amins, the methine proton (the smallest substitution group) faces sulfonyl moiety. As the result, one methyl group will get closer to one benzene ring of the reagent. Due to the diamagnetic effect of the benzene ring, the methyl proton signal should appear upfield. NOE experimental data supports the conformation.

Table 1. Selected chemical shifts, $\Delta\delta$ of geminal methyl protons, and coupling constants for “roofed” amins (**2a-5a**).

	2a	3a	4a	5a
¹ H NMR				
geminal Me	0.82	0.79	0.82	0.81
	-0.01	0.03	0.02	0.05
$\Delta\delta$	0.83	0.76	0.80	0.76
methine	2.22	2.39	2.58	2.50
² J _{H-H} (Hz)	3.1	3.5	2.7	3.1
¹³ C NMR				
geminal Me	19.44	19.50	19.60	19.53
	11.18	11.37	11.29	11.41
$\Delta\delta$	8.26	8.13	8.31	8.21
methine	28.21	28.31	28.74	28.36
(500 MHz/126 MHz, CDCl ₃)				

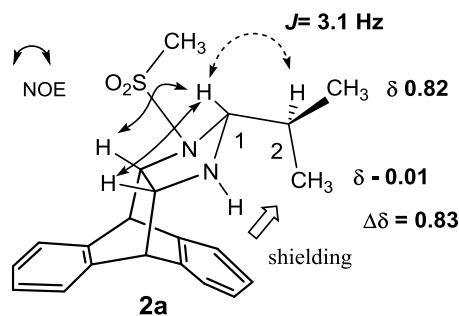


Fig.1. Predicted conformation of **2a**.

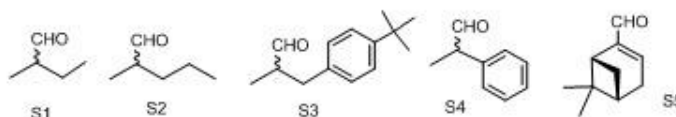
3. Preparation of chiral reagents (2-5) and diastereomeric amins from racemic aldehydes

Aldehydes **S1-S5** were reacted with reagents (2-5) to afford diastereomeric amins. These diastereomers were well separated on silica-gel TLC plates.

Table 2. R_f values of diastereomeric amins (**2a-5a**) from racemic reagent (2-5) and aldehydes (**S1-S5**).

Reagents/aldehydes	S1	S2	S3	S4	S5
2; RDA-Ms	B 0.45/0.49	B 0.57/0.68	B 0.63/0.73	B 0.61/0.72	B 0.55/0.63
	C 0.44/0.47	C 0.58/0.60	C 0.59/0.65	C 0.59/0.66	C 0.57/0.68
3; RDA-Ts	A 0.30/0.36	A 0.35/0.45	A 0.39/0.53	A 0.33/0.46	A 0.33/0.36
	E 0.56/0.62	E 0.43/0.58	D 0.40/0.57	D 0.49/0.53	E 0.41/0.43
4; RDA-1Nps	A 0.34/0.41	A 0.39/0.47	A 0.41/0.54	A 0.36/0.46	A 0.34/0.41
	E 0.56/0.62	E 0.42/0.58	D 0.41/0.56	D 0.51/0.57	E 0.39/0.52
5; RDA-2Nps	A 0.39/0.45	A 0.44/0.53	A 0.49/0.63	A 0.43/0.52	A 0.41/0.45
	E 0.61/0.69	E 0.51/0.66	D 0.50/0.67	D 0.43/0.57	E 0.50/0.57

Silica-gel TLC plate: Merck 60F₂₅₄ 5715
 Solvent combinations: A: Hexane/EtOAc (2:1), B: EtOAc, C: CHCl₃/MeOH (10:1), D: Toluene/EtOAc (20:1), E: Toluene/EtOAc (10:1).



Diastereomeric amins **4b** (high R_f) and **4c** (low R_f), which were synthesized from racemic RDA-1Nps **4** and racemic 2-methylbutanal **S1**, were analyzed by 1D and 2D-NMR (COSY, HSQC, HMBC, and NOESY).

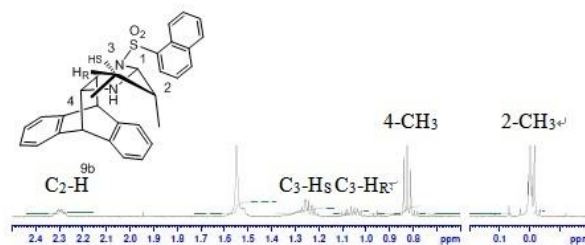


Fig.2. Partial ^1H NMR spectrum (500 MHz; CDCl_3) for **4b** from RDA-1Nps **4** and **6**.

It is worthy of notice that each amins derivative can be confirmed its relative configuration by NMR.

Chiral reagents were obtained by acidic hydrolysis of amins which were prepared from (1*R*)-(-)-myrtenal **S5** and racemic reagents (2-5). The whole structure of each amins was determined by two-dimensional NMR analyses.

I submit here a configurational correlation model for the amins from (12*R*)-mono-*N*-sulfonyl RDA reagents and α -disubstituted racemic aldehydes as shown in **Fig. 3**. The model can explain the chemical shift difference ($\Delta\delta$) of diastereomers, and predict the absolute configurations of separated aldehydes.

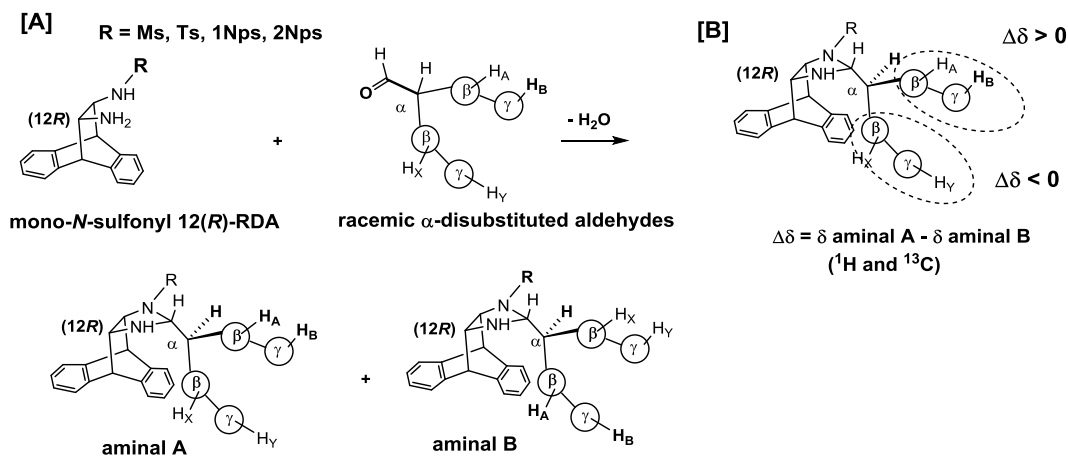


Fig. 3. (A) Configurational correlation model for the amins from (12*R*)-mono-*N*-sulfonyl RDAs and α -disubstituted racemic aldehydes. (B) $\text{H}_{\text{A,B}}$ and $\text{H}_{\text{X,Y}}$ are on the far and near sides to the faced benzene ring of reagent in aminal A, respectively.

The developing pattern of a pair of diastereomeric amins from α -disubstituted aldehydes on a silica-gel TLC plate may be predicted by the following steps using **Fig. 4**.

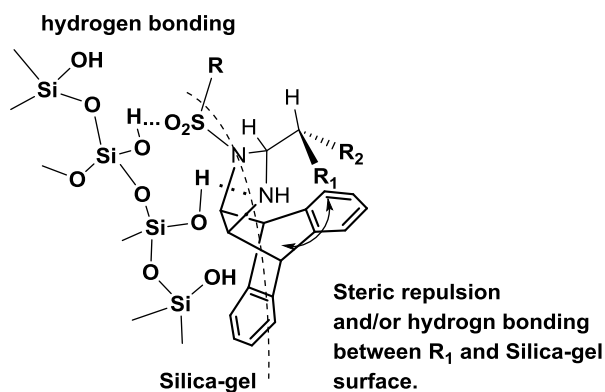


Fig. 4. A schematic view of the interaction of (12*R*)-RDA reagents with silica-gel stationary phase.

“Roofed” *cis*-diamine **1** was synthesized in a short step. The new method using “roofed” mono-*N*-sulfonyl *cis*-diamines, **2-5** could be useful for determination of absolute configuration of chiral aldehydes.

CHAPTER 1

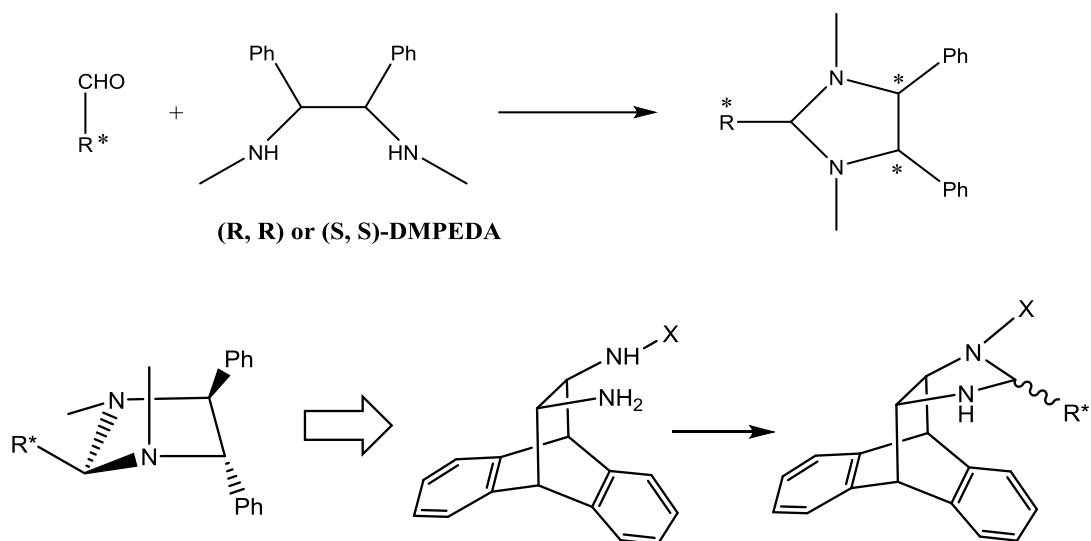
1. Introduction

1.1. Background

Enantioselective synthesis remains as constant challenge for chemists. The broad utility of chiral molecules in optically pure form as biologically active compounds (pharmaceuticals and agrochemicals), as additives for modification of polymer properties and in electronic and optical devices explains the importance of chirality and methods of obtaining enantiopure compounds. Tremendous advances have been made in asymmetric synthesis, but the preparation of racemic mixture followed by its resolution can still be practical alternative, especially when both enantiomers are required¹⁾.

NMR spectroscopy is a well-documented method of determining optical purities and absolute configurations of partially resolved enantiomers, chiral shift reagents, chiral solvating reagents/ chiral solvents, and diastereomeric derivatives have been the subject of countless articles³⁾.

A most popular strategy for optical resolution is based on the different physical properties of diastereomers¹⁾. Several reagents have been developed for the configurational analysis of aldehydes by forming cyclic derivatives such as 2-substituted thiazoline²⁾, 2-substituted oxazoline³⁾, and imidazolidine^{4, 5)}. Especially, the enantiomeric purities of aldehydes were determined by NMR or chromatographic methods of imidazolidine derivatives with *N,N'*-dimethyl-1,2-diphenyl ethylene diamine (DMPEDA)⁴⁾. My interest is to develop chiral recognition reagents⁶⁾ 9,10-dihydro-9,10-ethanoanthracene 11,12-diamine; “roofed” *cis*-diamine as a new skeleton for chiral analysis of aldehydes.



Scheme 1. Proposal of a new skeleton for chiral analysis of aldehydes next to DMPEDA⁴⁾

1.2. Objective and Thesis Outlines

1.2.1. Objective

The objective of this study is to develop a new method for optical resolution of aldehydes and to determinate absolute configuration of aldehydes.

1.2.2. Thesis Outlines

This thesis is divided into 4 chapters: Introduction, Results and Discussions, Conclusion, and Experimental Section. The current chapter, Chapter 1 (Introduction) introduces the background, objectives, and outlines of this study. Chapter 2 (Results and Discussions) reports the results and provides discussions of this study. Chapter 3 (Conclusion) provides conclusion of this study. Chapter 4 (Experimental Section) describes the materials, reaction conditions for preparing compounds, and interpretation of spectrum. Any entry tables, spectrum data, and TLC separation figure are attached in the appendix.

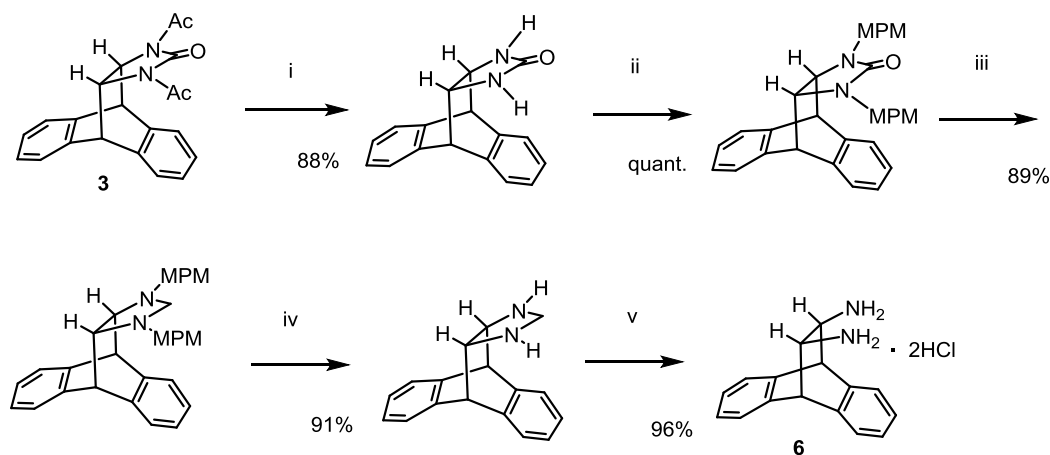
CHAPTER 2

2. Results and Discussion

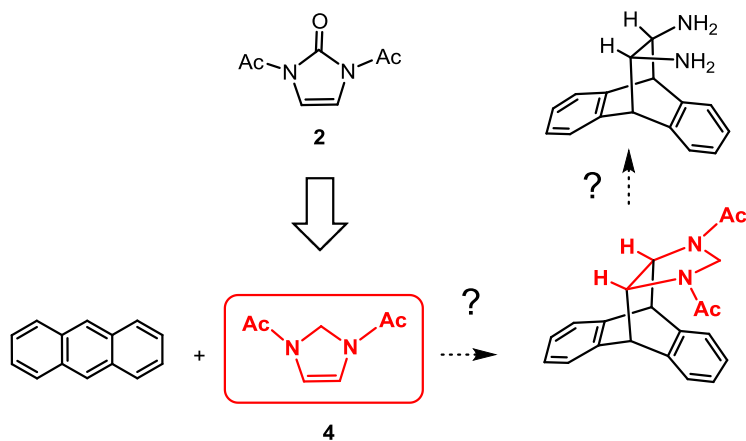
2.1. Diastomeric amins from racemic aldehydes and new reagents

2.1.1. Synthesis of “roofed” *cis*-diamine by an improved route

The “roofed” *cis*-diamine skeleton **3** was synthesized conventionally by Diels–Alder reaction of anthracene **1** and 1,3-diacetyl-2-imidazolone **2** as the first step⁷. The bicyclic imidazolidinone **3** was converted to **6** through five serial reactions⁸.



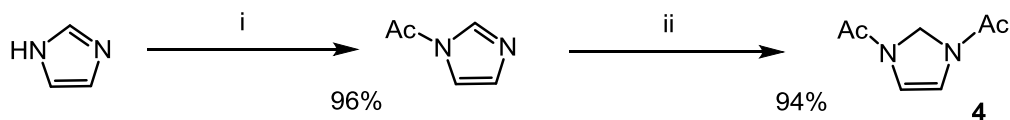
Scheme 2. Synthetic route of roofed *cis*-diamine reagent⁸. Reagents and conditions : i) NaH, MeOH, CH₂Cl₂, rt; ii) NaH, MPMCl, DMF, 0°C to 25°C; iii) LAH, THF, 50°C; iv) TFA, 40°C; v) TMSCl, MeOH, heat, 6h



I estimated that compound **2** could be replaced by 1,3-diacetyl-2,3-dihydro-1H-imidazole⁹ **4** for convenience.

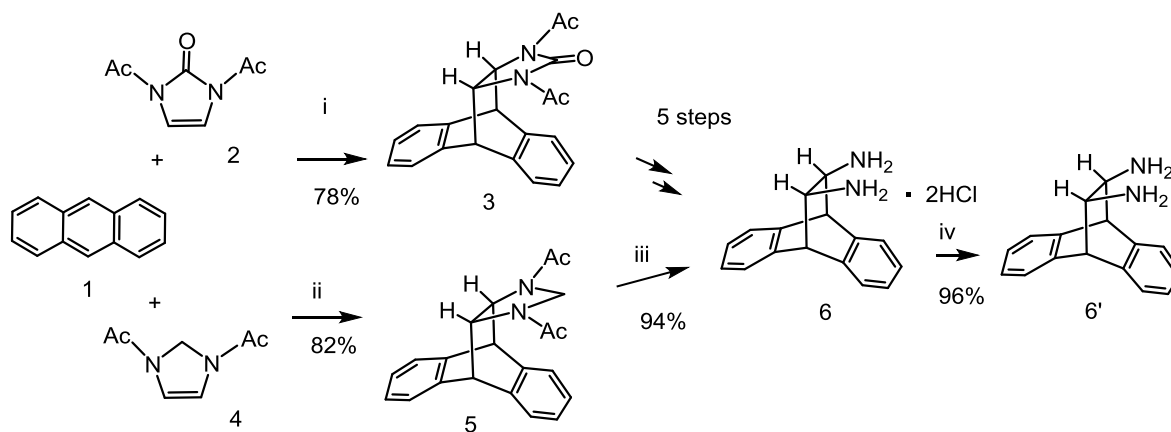
Scheme 3. Hypothetical new synthetic route of “roofed” *cis*-diamine

Compound **4** was synthesized from *N*-acetylimidazole in 94% yield by my improved method. *N*-Acetylimidazole was prepared from imidazole and acetic anhydride in 96% yield¹⁰).



Scheme 4. New synthetic route of compound **4**. Reagents and conditions : i) Ac_2O , toluene, 30°C , 1h; ii) AcOH , NaBH_4 , Ac_2O , 0°C , 10 min, then adding MeOH

Diels–Alder reaction of anthracene **1** and **4** to afford a “roofed” 1,3-diacetyl-2-imidazolidine derivative **5** in 82 % yield, which exists as two major rotamers at *N*-Ac bonds (symmetric:asymmetric = 1:2) in CDCl_3 . Compound **5** was hydrolyzed under refluxing in conc. HCl /MeOH solution to give **6** in 94 % yield. The treatment of the salt **6** with base liberated the free diamine **6'** in 96 % yield.



Scheme 5. Synthetic route of “roofed” *cis*-diamine reagent (via imidazolidinone)⁸⁾ (top), and our new synthetic route (bottom). Reagents and conditions : i) xylene, 180°C ⁷⁾ ii) *o*-dichlorobenzene, *p*-hydroquinone, refl, 15h; iii) MeOH, conc. HCl , refl, 3h; iv) CHCl_3 , TEA, rt, 30 min

2.1.2. Aminals from “roofed” *cis*-diamine and isobutyraldehyde

Compound **6'** was reacted with isobutyraldehyde to form two diastomeric aminals **6a** (endo), **6b** (exo) at a ratio 4:1. These aminals were detected on NMR data, but could not be separated on a silica-gel TLC plate.

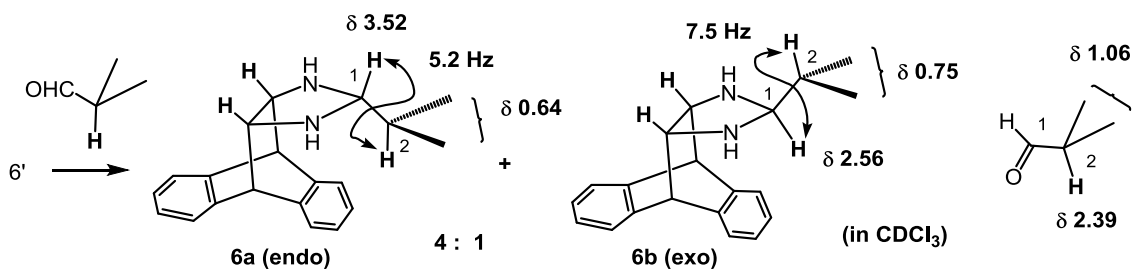
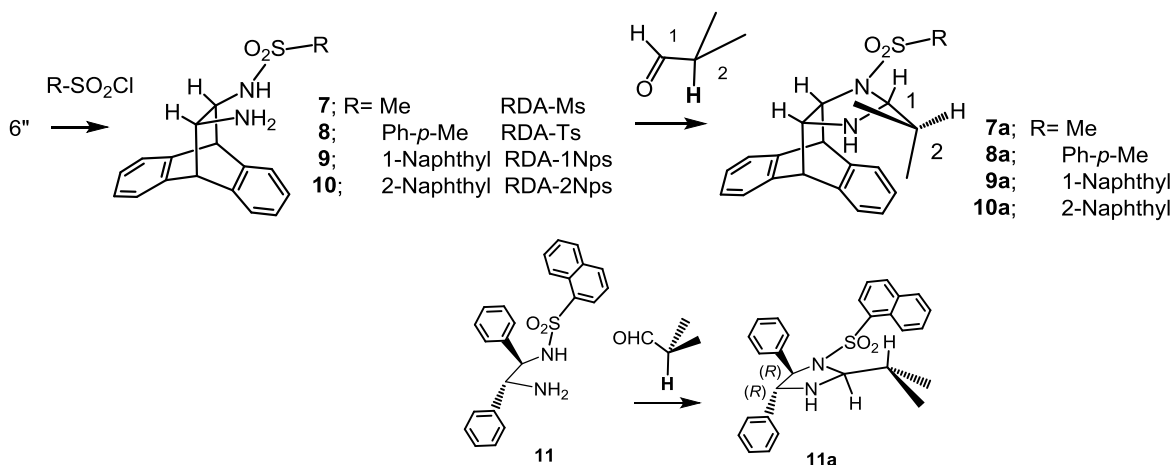


Fig.1. Stable conformations for **6a** and **6b**.

The geminal methyl protons in **6a** and **6b** show an upfield shift at 0.64 and 0.75 ppm, respectively. The coupling constants between the vicinal methine protons (C₁-H and C₂-H) of aldehyde moiety in **6a** and **6b** are 5.2 and 7.5 Hz, respectively, which indicate that both conformations of the two protons are predominantly *anti* form.

2.1.3. Preparation of RDA reagents and amins with isobutyraldehyde

Sulfonyl groups were introduced to **6'** to improve the stereoselectivity of amination. Mono-*N*-sulfonyl “roofed” *cis*-diamines (**7**¹¹, **8**^{11, 12}, **9**¹¹, **10**¹³) were prepared from **6** and corresponding sulfonyl chlorides.



Scheme 6. Preparation of racemate mono-*N*-sulfonyl “roofed” *cis*-diamines (**7-10**) and amination derivatives with isobutyraldehyde (**7a-10a**), **11a** for comparison.

The mono-*N*-sulfonyl *cis*-diamines (**7-10**) were reacted with isobutyraldehyde to form stereoselectively endo-type cyclic amins (imidzolidines) **7a-10a**. For comparison, the amina **11a** was prepared from (*R,R*)-*N*-(1-naphthylsulfonyl)-1,2-diphenylethylenediamine¹⁴ **11** and isobutyraldehyde. The chemical shifts of selected proton and carbon signals in these amins are summarized in Table.1.

Table 1. Selected chemical shifts, $\Delta\delta$ of geminal methyl protons, and coupling constants for ‘roofed’ amins (**6a**, **6b** and **7a-11a**).

	6a	6b	7a	8a	9a	10a	11a
¹ H NMR							
geminal Me	0.64	0.75	0.82 -0.01	0.79 0.03	0.82 0.02	0.81 0.05	1.04 0.99
$\Delta\delta$	0	0	0.83	0.76	0.80	0.76	0.05
methine	1.34	1.31	2.22	2.39	2.58	2.50	2.13
³ J _{HH} (Hz)	5.2	7.5	3.1	3.5	2.7	3.1	8.9
¹³ C NMR							
geminal Me	17.88	19.12	19.44 11.18	19.50 11.37	19.60 11.29	19.53 11.41	19.47 19.20
$\Delta\delta$	0	0	8.26	8.13	8.31	8.21	0.27
methine	30.81	33.19	28.21	28.31	28.74	28.36	32.53

[270 MHz/67.5 MHz or 500 MHz/126 MHz (¹H/¹³C)] in CDCl₃

The conformation of *N*-Ms amina **7a** was revealed as shown in Fig. 1. Because of the steric hindrance of Ms group, endo-oriented aminalization occurs stereoselectively and the C₂-methine proton of aldehyde moiety faces to the Ms group. The coupling constant between the vicinal methine protons (C₁-H and C₂-H) of aldehyde moiety in **7a** is 3.1 Hz, which indicates that the two protons are *gauche* form. As a result, one methyl group gets close to one benzene ring of the reagent. This methyl appears at – 0.01 ppm, supposed to be is affected by the strong anisotropy of the faced benzene ring. The NOESY spectrum supports the above conformation. The methyl proton of Ms shows NOE with underlined protons in Fig. 2. C₁-H (N-CH₁-N) shows NOE with 4-CH₃ (strong) and 3-CH₃ (weak). The broad NH proton at 1.5 ppm shows NOE with the 3-CH₃ (strong) and 4-CH₃ (moderate). In addition, 3-CH₃ shows NOE with C₁'-H, C₂'-H, C₃'-H, and C₄'-H. The NMR spectral data of **8a-10a**

support the same conformation of them. Additionally, the aromatic rings of sulfonyl moieties seem to be hardly affected the chemical shifts of proton signals in aldehyde moieties.

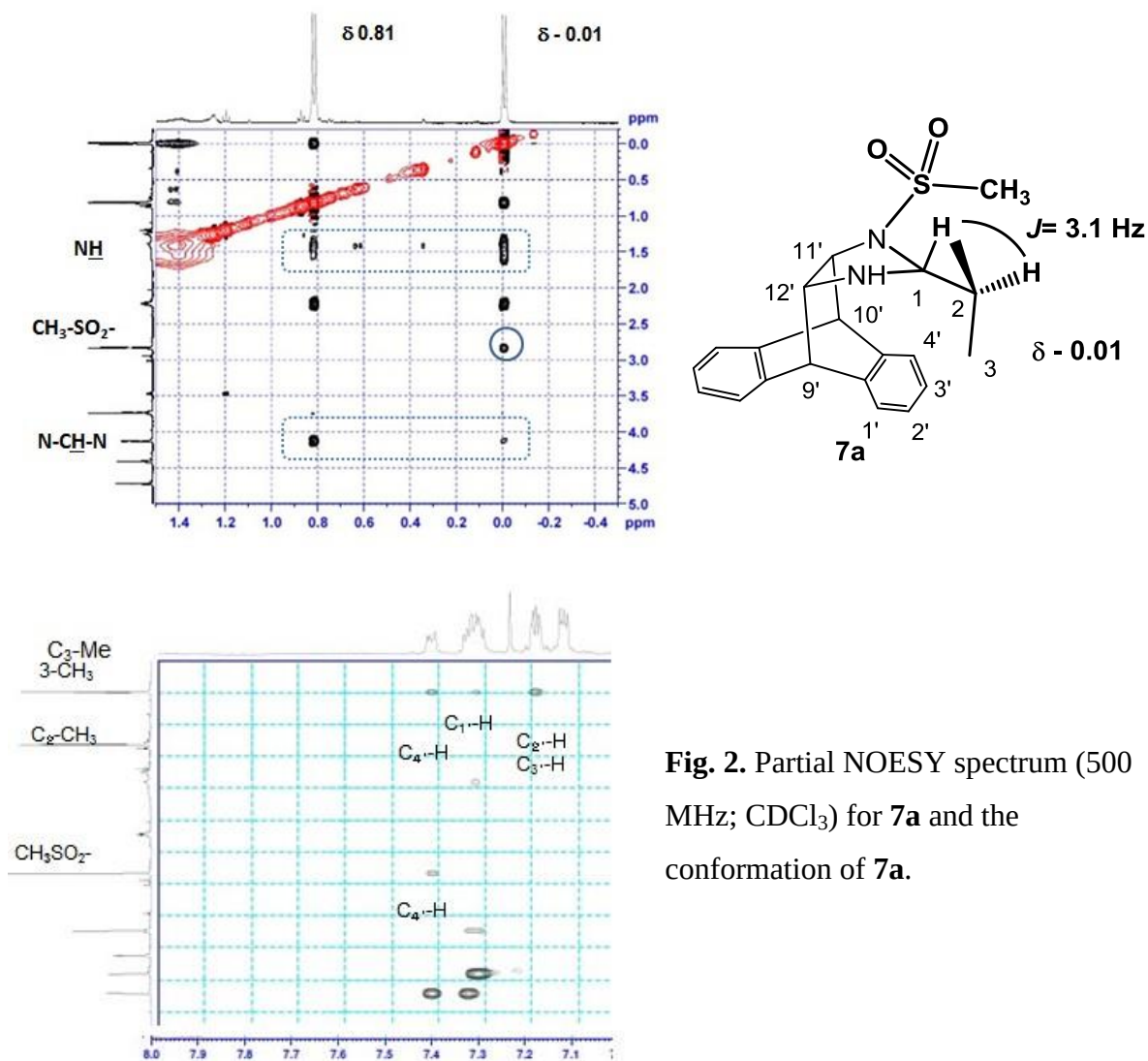


Fig. 2. Partial NOESY spectrum (500 MHz; CDCl₃) for **7a** and the conformation of **7a**.

2.1.4 TLC separation of diastereomeric amins from RDA reagents

The RDA reagents **7-10** were reacted with α -disubstituted racemic aldehydes (**S1-S4**) and an α,β -unsaturated chiral terpene **S5** shown in **Fig. 3** to afford diastereomeric amins. These diastereomers were well separated on silica-gel TLC plates (**Table 2**).

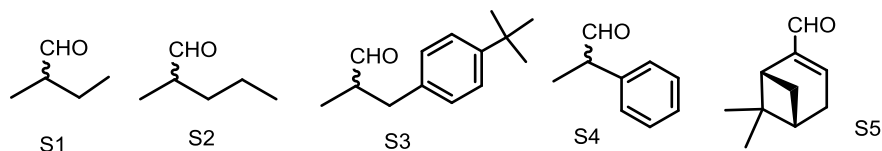


Fig. 3. Structure of tested racemic α -disubstituted aldehydes (**S1-S4**) and an α,β -unsaturated chiral terpene **S5**

Table 2. Separation pattern of amination derivatives from RDA reagents (**7-10**) with tested aldehydes (**S1-S5**).

Reagents/aldehydes	S1	S2	S3	S4	S5
7 ; RDA- Ms	B 0.45/0.49	B 0.57/0.68	B 0.63/0.73	B 0.61/0.72	B 0.55/0.63
	C 0.44/0.47	C 0.58/0.60	C 0.59/0.65	C 0.59/0.66	C 0.57/0.68
8 ; RDA- Ts	A 0.30/0.36	A 0.35/0.45	A 0.39/0.53	A 0.33/0.46	A 0.33/0.36
	E 0.56/0.62	E 0.43/0.58	D 0.40/0.57	D 0.49/0.53	E 0.41/0.43
9 ; RDA- 1Nps	A 0.34/0.41	A 0.39/0.47	A 0.41/0.54	A 0.36/0.46	A 0.34/0.41
	E 0.56/0.62	E 0.42/0.58	D 0.41/0.56	D 0.51/0.57	E 0.39/0.52
10 ; RDA- 2Nps	A 0.39/0.45	A 0.44/0.53	A 0.49/0.63	A 0.43/0.52	A 0.41/0.45
	E 0.61/0.69	E 0.51/0.66	D 0.50/0.67	D 0.43/0.57	E 0.50/0.57

Condition: Silica-gel TLC plate: Merck 60F254 5715.

Solvent combinations: A: Hexane/EtOAc (2:1), B: EtOAc, C: CHCl₃/MeOH (10:1),

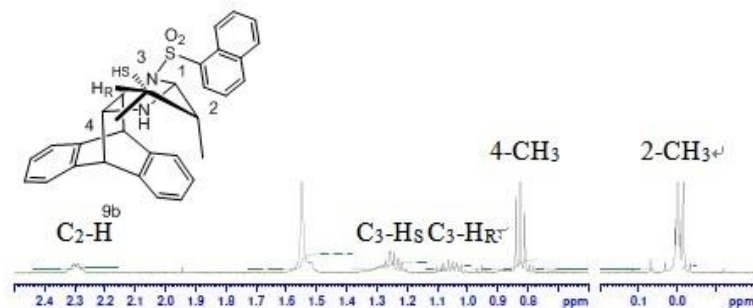
D: Toluene/EtOAc (20:1), E: Toluene/EtOAc (10:1).

2.2 NMR analysis of diastereomeric amins

2.2.1 Diastereomeric amins from 2-methylbutanal **S1** and RDA-**1Nps 9**

Diastereomeric amins **9b** (high R_f) and **9c** (low R_f), which were synthesized from racemic RDA-**1Nps 9** and 2-methylbutanal **S1**, were analyzed by 1D and 2D-NMR (COSY, HSQC, HMBC, and NOESY).

(A)



(B)

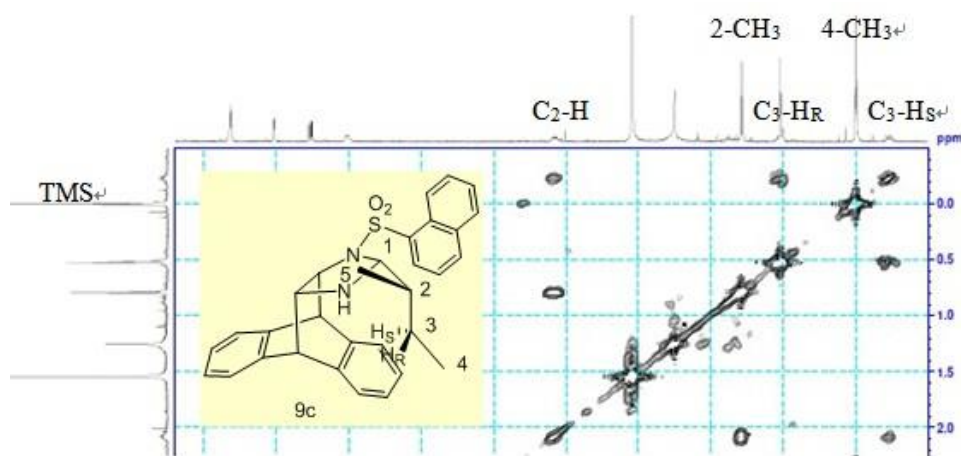


Fig. 4. Partial ^1H NMR spectrum (500 MHz; CDCl_3) for **9b** (A) and COSY spectrum (B) for **9c** and the conformations of **9b**, **c**.

	9b	9c	$\Delta\delta = \delta_{9b} - \delta_{9c}$	S1
Proton				
C ₁ -H	4.34	4.32	+ 0.02	9.63
C ₂ -H	2.30	2.08	+ 0.22	2.36
C ₂ -CH ₃	-0.01	0.79	- 0.80	1.1
C ₃ -H _R	1.25	0.52	+ 0.73	1.34*
C ₃ -H _S	1.06	-0.24	+ 1.30	1.70*
4-CH ₃	0.82	0.51	+ 0.31	0.96
Carbon				
C ₁	83.3	85.0	- 1.7	205.2
C ₂	35.6	35.9	- 0.3	47.8
C ₂ -CH ₃	9.1	16.3	- 7.2	12.9
C ₃	27.3	18.3	+ 9.0	23.6
C ₄	12.2	10.8	+ 1.4	11.4

*; exchangeable

Table 3. Proton and carbon chemical shifts (δ in ppm) for 2-methylbutanal moieties of **9b**, **9c**, and 2-methylbutanal.

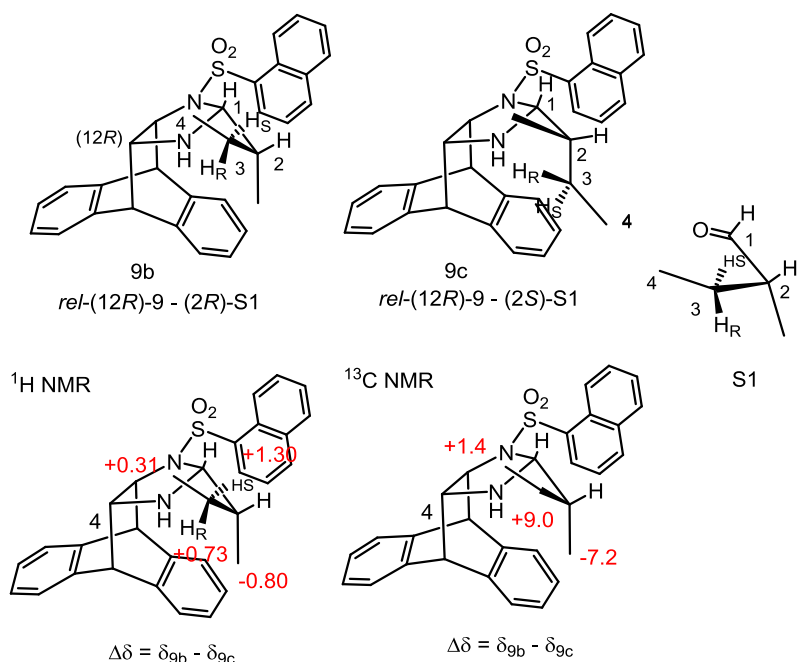


Fig 5. Chemical shift difference (^1H and ^{13}C) of amina derivatives **9b**, **9c** and 2-isobutyraldehyde **S1**

The $\text{C}_3\text{-H}_s$ and $\text{C}_2\text{-CH}_3$ are affected by the strong anisotropy of the faced benzene ring of reagent in both amina. The chemical shift difference ($\Delta\delta = \delta_{9b} - \delta_{9c}$) also supports the relative structures for **9b** and **9c**. Especially, the chemical shift difference of C_3 is 9.0 ppm.

2.2.2 Diastereomeric amina from lial S3 and RDA-2Nps 10

Diastereomeric amina **10b** (high R_f) and **10c** (low R_f), which were synthesized from racemic RDA-2Nps **10** and lial **S3**, were analyzed by 1D and 2D-NMR (COSY, HSQC, HMBC, and NOESY). Their relative structures could be easily determined by the chemical shifts and NOEs. The chemical shift difference ($\Delta\delta = \delta_{10b} - \delta_{10c}$) shows quite regularity for long distance.

	10b	10c	$\Delta\delta = \delta_{10b} - \delta_{10c}$	lilial (S3)
Proton				
C ₁ -H	3.76	3.92	- 0.16	9.71
C ₂ -H	2.81	2.59	+ 0.22	2.66
C ₂ -CH ₃	0.15	0.71	- 0.56	1.09
C ₃ -H _R	2.39*	0.88	+ 1.51	3.06*
C ₃ -H _S	2.42*	2.16	+ 0.26	2.57*
C _{2',6'} -H	7.11	6.94	+ 0.17	7.10
C _{3',5'} -H	7.28	7.20	+ 0.08	7.30
C ₄ -t-Bu	1.34	1.29	+ 0.05	1.30
Carbon				
C ₁	81.9	84.5	- 2.6	204.5
C ₂	35.5	35.9	- 0.4	48.0
C ₂ -CH ₃	10.2	16.4	- 6.2	13.3
C ₃	39.9	31.38	+ 8.52	36.1
C _{1'}	137.1	137.6	- 0.5	135.7
C _{2',6'}	128.7	128.7	0.0	125.4
C _{3',5'}	125.2	124.9	+ 0.3	126.8
C _{4'}	148.7	148.3	+ 0.4	149.2
t-Bu (Me)	31.5	31.41	+ 0.09	31.3
t-Bu (C)	34.4	34.3	+ 0.1	34.4

Table 4. Proton and carbon chemical shifts (δ in ppm) for lilial (**S3**) moieties of **10b**, **10c**, and lilial **S3**.

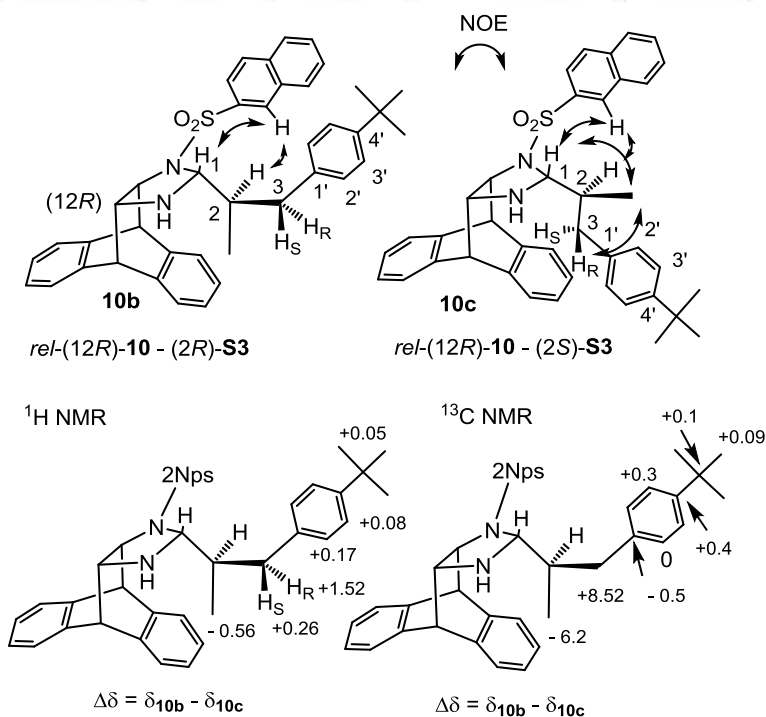


Fig . 6. Selected NOE correlation and chemical shift difference (^1H and ^{13}C) for aminal derivatives **10b** and **10c**.

2.2.3 Diastereomeric amins from (1*R*)- **5** and RDA reagents **7**-**10**.

Racemic **7** was reacted with (1*R*)- **5** (around 1.3 equivalent amount of **7**) to afford **7b** and **7c**. The R_f values for **7b** and **7c** on a silica-gel TLC plate developed using EtOAc are 0.63 (high) and 0.55 (low), respectively. Other diastereomeric amins (**8b**, **8c**, **9d**, **9e**, **10d**, and **10e**) were prepared and numbered in the same way. All amins so far synthesized could be detected as distinct spots on silica-gel TLC plates. I could separate all diastereomeric amins by silica-gel flash chromatography. Surprisingly, only amins **8b** and **10d**, which were synthesized from racemic RDA-Ts **8** and RDA-2Nps **10** with (1*R*)-myrtenal **5**, were gradually hydrolyzed during silica-gel chromatography.

Compound **7c** exists predominantly as one aminal conformer in CDCl₃. The C₁-H, C₇-H signals of myrtenal moiety in **7c** show upfield shift at 0.72 and 2.19 ppm, respectively. The NOESY spectrum of **7c** showed NOEs between (CH₃SO₂/C₁-H, C₃-H, C₇-H_n), (NH/C₁-H, 9-CH₃), (C₁-H/C₃-H), and (C₈-CH₃/C₂'-H, C₃'-H). These data indicate that compound **7c** is the aminal with (12*S*)-**7**. Contrarily, **7b** exists as an isomeric mixture of more than two aminal rotamers and one (*E*)-imine in CDCl₃ as shown in **Fig. 7** and **8**.

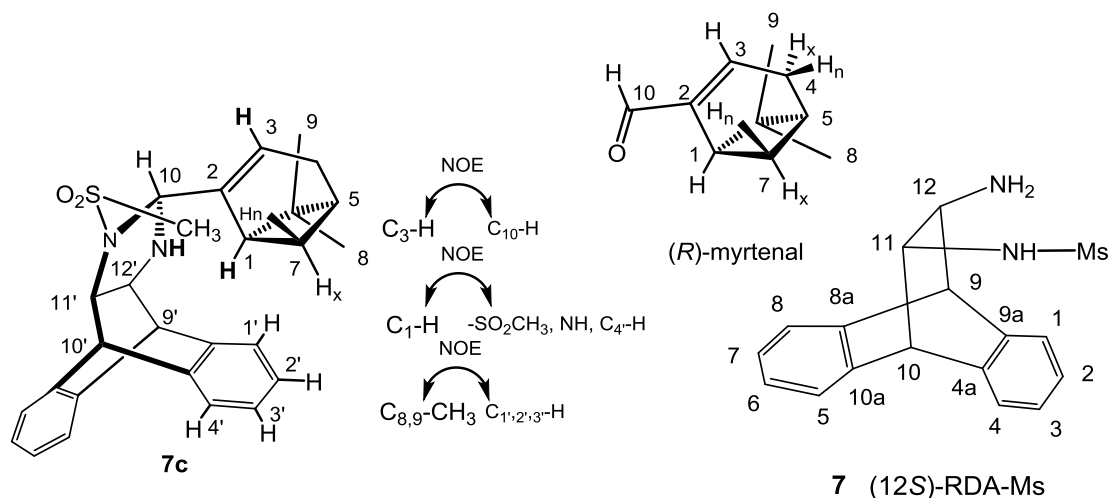


Fig. 7. (A) Selected NOE correlation and absolute configuration for aminal derivatives **7c**. (B) Carbon numbering of myrtenal and (12*S*)-RDA-Ms, **7**.

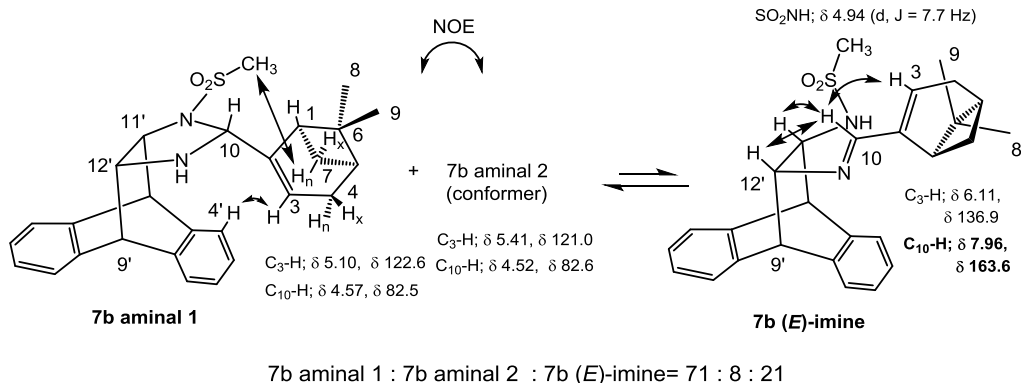


Fig. 8. Selected NOE correlation and absolute configuration for aminal derivatives **7b** (aminal), **7b** (imine).

Table 5. Proton and carbon chemical shifts (δ in ppm) for myrtenal moieties and selected mother skeleton of **7b**, **7c**, **7d**, and myrtenal, **5S**.

Proton	7b (aminal)	7b (imine)	7c	Myrtenal
H-1	1.13	2.59	0.72	2.85
H-3	5.10	6.11	5.60	6.70
H-4 _n	2.13	2.49	2.26	2.52
H-4 _x	2.05	2.39	2.09	2.58
H-5	1.94	2.12	1.95	2.18
H-7 _n	0.85	1.07	1.06	1.04
H-7 _x	2.13	2.40	2.19	2.48
8-CH ₂	1.14	1.24	1.04	1.33
9-CH ₂	0.67	0.68	0.58	0.73
H-10	4.57	7.96	4.64	9.43
SO ₂ Me	2.85	2.68	2.84	-
-NH-	1.2-1.8		1.17	-
SO ₂ -NH-	-	4.94	-	-
N-Me	-	-	-	-
C ₉ -H	4.37	4.04	4.39	-
C ₁₀ -H	4.68	4.50	4.73	-
C ₁₁ -H	3.89	3.93	3.86	-
C ₁₂ -H	3.76	3.74	3.77	-

Carbon	7b (aminal)	7b (imine)	7c	Myrtenal
1	41.7	39.8	38.9	38.18
2	144.6	148.3	142.7	151.36
3	122.6	136.9	125.2	147.66
4	31.07	32.5	31.3	33.04
5	40.6	40.8	40.5	40.74
6	37.5	37.8	37.0	37.42
7	32.3	31.11	31.7	31.12
8	25.85	25.80	25.7	25.70
9	21.4	21.2	21.3	20.92
10	82.5	163.6	82.7	191.21
SO ₂ Me	37.7	40.9	37.7	-
N-Me	-	-	-	-
9'	48.0	51.5	47.8	-
10'	49.3	53.0	49.3	-
11'	64.2	54.5	63.8	-
12'	60.5	67.9	60.3	-

The NMR spectral data of **8b**, **8c**, **9d**, **9e**, **10d**, and **10e** also show about the same tendency.

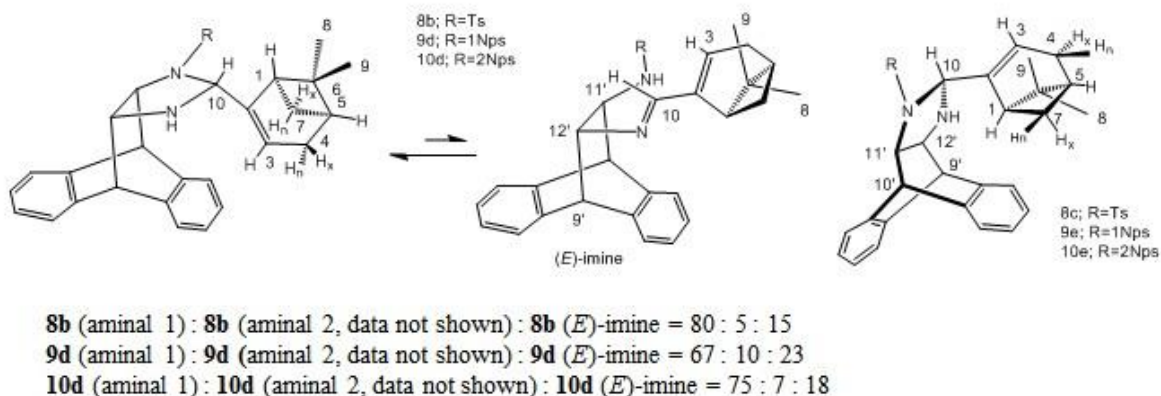
Table 6. Proton and carbon chemical shifts (δ in ppm) for myrtenal moieties and selected mother skeleton of **8b**, **8c**, **9d**, **9e**, **10d**, and **10e**.

Proton	8b (aminal)	8b (imine)	8c	9d (aminal)	9d (imine)	9e	10d (aminal)	10d (imine)	10e
H-1	0.98	2.58	0.87	1.24	2.61	0.82	1.02	2.58	0.88
H-3	5.22	6.01	5.50	5.07	6.05	5.53	5.24	5.85	5.56
H-4n	2.13	2.45	2.29	2.02*	2.38*	2.20	2.15	2.24	2.32
H-4x	2.13	2.45	2.07	1.95*	2.47*	2.05	2.09	2.37	2.09
H-5	1.95	2.14	1.93	1.91	2.22	1.88	1.95	2.12	1.94
H-7n	0.85	1.04	1.19	0.72	1.04	0.78	0.86	1.02	1.16
H-7x	2.08	2.39	2.19	2.08	2.39	2.01	2.09	2.38	2.18
8-CH ₃	1.15	1.27	1.03	1.18	1.27	0.99	1.16	1.27	1.04
9-CH ₃	0.77	0.78	0.56	0.73	0.71	0.53	0.792	0.787	0.56
H-10	4.25	7.58	4.13	4.66	7.83	4.69	4.36	4.51	4.23
-NH-	1.25		1.07	1.0-1.5		1.06	1.28		1.10
SO ₂ NH	-	5.42	-	-	5.54	-	-	5.52	-
SO ₂ Me	-	-	-	-	-	-	-	-	-
Me (Ts)	2.40	2.36	2.39	-	-	-	-	-	-
C ₉ -H	4.28	3.93	4.30	4.26	3.98	4.25	4.27	3.92	4.29
C ₁₀ -H	4.76	4.49	4.89	4.12	4.14	4.30	4.79	4.51	4.94
C ₁₁ -H	3.55	3.66	3.47	3.77	3.80	3.77	3.66	3.72	3.59
C ₁₂ -H	3.42	3.39	3.44	3.51	3.58	3.56	3.40	3.36	3.43

* exchangeable

Carbon	8b (aminal)	8b (imine)	8c	9d (aminal)	9d (imine)	9e	10d (aminal)	10d (imine)	10e
1	40.7	39.9	39.3	41.8	40.0	39.3	40.8	39.9	39.4
2	144.4	148.4	143.6	144.4	148.4	143.3	144.3	148.3	143.5
3	122.3	136.4	123.7	122.2	136.4	123.4	122.5	136.5	124.0
4	31.1	32.5	31.2	41.0	32.5	31.2	31.1	32.4	31.3
5	40.8	41.7	40.4	40.7	40.5	40.3	40.75	40.8	40.4
6	37.9	37.5	36.8	37.9	37.6	36.8	37.9	37.5	36.8
7	32.3	31.2	31.5	32.1	31.1	31.1	32.3	31.2	31.5
8	25.9	25.8	25.7	26.0	26.0	25.7	25.9	25.8	25.7
9	21.5	21.5	21.3	21.3	20.9	21.2	21.5	21.1	21.3
10	82.8	163.4	82.8	82.2	163.7	82.5	82.9	163.5	82.9
SO ₂ Me	-	-	-	-	-	-	-	-	-
Me (Ts)	21.5	21.1	21.5	-	-	-	-	-	-
C ₉	47.9	53.0	47.6	47.9	52.8	48.9	47.9	52.9	47.6
C ₁₀	49.7	51.1	49.6	49.0	50.0	47.6	49.6	51.1	49.7
C ₁₁	64.3	54.0	63.8	64.3	66.9	63.8	64.3	54.1	63.9
C ₁₂	60.2	67.0	60.3	60.6	54.3	60.5	60.2	67.0	60.4

Table 6. (continued)



Among the four sterically hindered products (**7b**, **8b**, **9d**, and **10d**), **8b** and **10d** are *o*-unsubstituted phenylsulfonyl (Ts and 2Nps) derivatives. I estimate that the (*E*)-imines of **8b**, **10d** may be hydrolyzed fast compared with sterically more hindered sulfonyl groups of **7b** and **9d**.

2.2.4 Separation mechanism of diastereomeric aminals on silica-gel TLC plates

The developing pattern of a pair of diastereomeric aminals on silica-gel TLC plates will be predicted by the following steps.

- 1) Determine the conformation of each diastereomeric aminal from chemical shifts, coupling constants, NOE etc. by NMR analyses.
- 2) Hydrogen bonds will occur predominantly between silica-gel particle (Si-OH) and the -SO₂- and -NH- sites of each aminal. As a result, the substrate adsorbs silica-gel particle at one side.

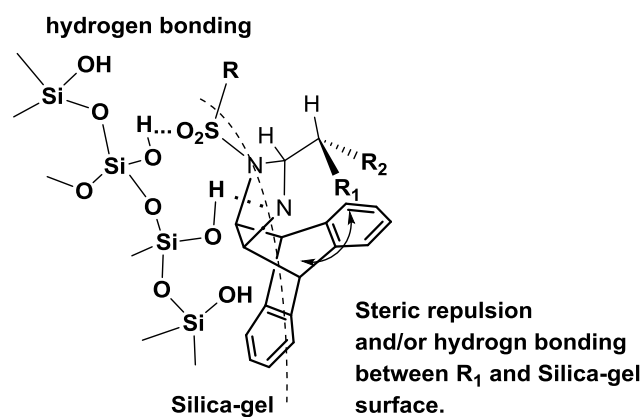


Fig. 9. A schematic view of the interaction of (12*R*)-RDA reagents with silica-gel stationary phase.

3) Consider the properties of parts of aldehyde moiety which are near to the silica-gel particle. Bulkiness and/or polarity of substituents affect the strength of interaction with the silica-gel particle. The substituents of aldehyde also interact with the $\text{-SO}_2\text{-}$ and -NH- sites of reagent. This process will be applied to α,β -unsaturated aldehydes and other types.

2.2.5. Configurational correlation model of RDA aminals

I submit here a configurational correlation model for the aminals from (12*R*)-mono-*N*-sulfonyl RDA reagents and α -disubstituted racemic aldehydes as shown in **Fig. 10**. The model can explain the chemical shift difference ($\Delta\delta$) of diastereomers, and predict the absolute configurations of separated aldehydes.

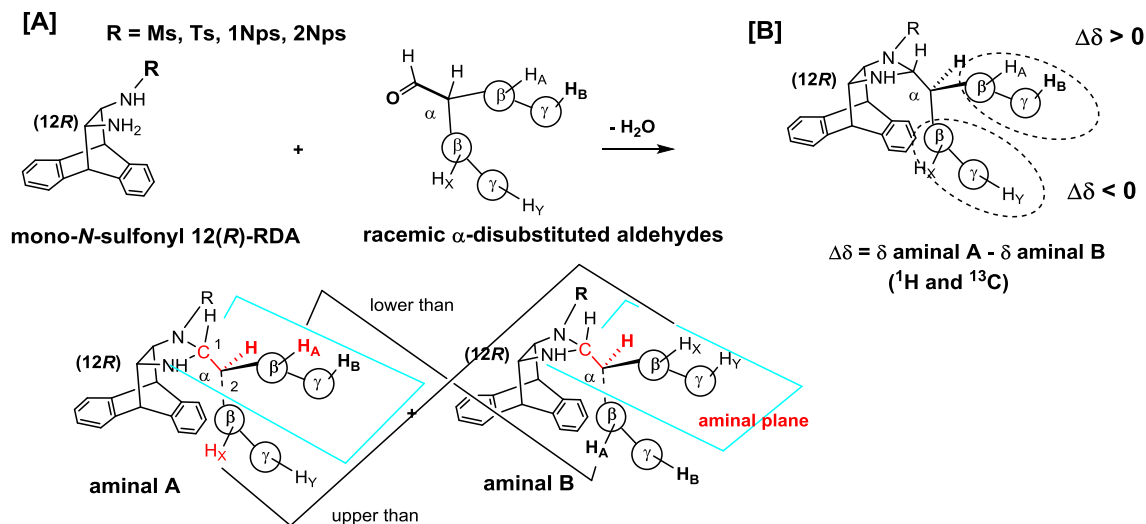


Fig. 10. (A) Configurational correlation model for the aminals from (12*R*)-mono-*N*-sulfonyl RDAs and α -disubstituted racemic aldehydes. (B) $\text{H}_{\text{A,B}}$ and $\text{H}_{\text{X,Y}}$ are on the far and near sides to the faced benzene ring of reagent in aminal A, respectively.

The idealized conformation of aminals from (12*R*)- mono-*N*-sulfonyl RDA reagents and racemic α -disubstituted aldehydes revealed as shown in **Fig. 10**.

1) The C_2 -methine proton of aldehyde moiety faces to the sulfonyl group.

- 2) The plane containing C₁, C₂-methine is named aminor plane for convenience.
 - 3) The H_X and H_Y protons of **aminol A** get close to one benzene ring of the reagent (under the aminor plane).
 - 4) Due to the diamagnetic effect of the benzene ring, the H_X and H_Y signals should appear upfield relative to those of the original aldehyde, and also the signals H_A and H_B of **aminol B** should appear upfield relative to those of **aminol A**.
 - 5) Therefore, when chemical shift difference is defined as $\Delta\delta$ (ppm) = $\delta_{\text{aminol A}} - \delta_{\text{aminol B}}$, if the signs are same to those shown in [B], the absolute configuration of aldehyde moieties in **aminol A** and **B** are same to those shown in [A].
 - 6) The chemical shifts of H_X and H_A are strongly affected.
 - 7) ¹³C NMR data is also available.
- NOE experiment for **aminols A** and **B** will support the above conclusion.

2.3. Preparation of chiral RDA reagents 7-10 from aminols with (-)-myrtenal S5

Chiral **7-10** were obtained by acidic methanolysis¹⁵⁾ of the corresponding aminols with **S5**. The sign and values of $[\alpha]_D$ of prepared chiral RDA reagents are as follows.

(12*R*)-**7**; $[\alpha]_D^{28} + 46.7$ (c 0.0296, CHCl₃), (12*S*)-**7**; $[\alpha]_D^{28} - 40.5$ (c 0.0292, CHCl₃) (12*R*)-**8**; $[\alpha]_D^{28} + 111$ (c 0.0203, CHCl₃), lit. $[\alpha]_D^{25} + 105.0$ (c 0.0329, CHCl₃)¹¹⁾

(12*S*)-**8**; $[\alpha]_D^{28} - 106$ (c 0.0260, CHCl₃)

(12*R*)-**9**; $[\alpha]_D^{26} + 94.7$ (c 0.0329, CHCl₃), (12*S*)-**9**; $[\alpha]_D^{27} - 89.9$ (c 0.032, CHCl₃)

(12*R*)-**10**; $[\alpha]_D^{24} + 80.8$ (c 0.0105, CHCl₃), (12*S*)-**10**; $[\alpha]_D^{23} - 78.8$ (c 0.0301, CHCl₃)

When overviewing the sign and values of $[\alpha]_D$ of them, the (12*R*)-reagents are plus sign and show bigger values than those of the corresponding (12*S*)-ones. Since the skeletons of RDA reagents and myrtenal are rigid, racemization of the skeletons will never occur. I estimated that the enantiomeric excess (ee) of the used (*R*)-(-)-myrtenal is less than 100%. The less sterically hindered diastereomeric aminols seem to be preferentially

formed through partial kinetic resolution, and some of hindered ones exist as several isomers in CDCl₃. I, therefore, measured the ee of enantiomers of RDA-Ms by chiral solvating method using an axially chiral carboxylic acid reagent; 2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acid (MNCB)¹⁶⁾. As a result, (12*R*)-RDA-Ms was 96% ee, and (12*S*)-RDA-Ms was 91% ee by this method as shown in **Fig. 11**.

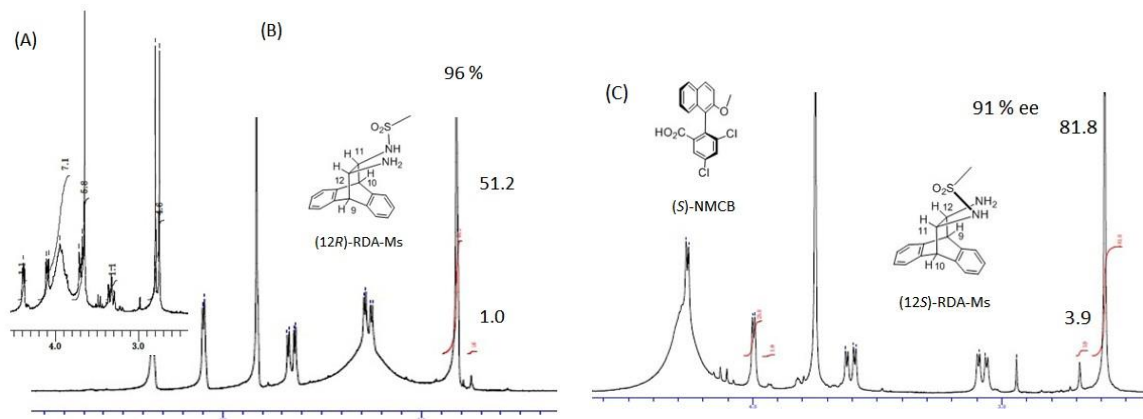


Fig. 11. Partial ¹H NMR spectra for **7** + (*S*)-MNCB (1eq.). (270 MHz, CDCl₃)

- (A) Racemic **7** + (*S*)-MNCB (1eq.),
- (B) (12*R*)-RDA-Ms **7** + (*S*)-MNCB (1eq.).
- (C) (12*S*)-RDA-Ms **7** + (*S*)-MNCB (1eq.).

2.4. Chiral stability of cyclic amins

Next, I examined the stability of amins from α-disubstituted aldehydes. Aminoal **10c**; *rel*-(12*R*)-**10**-(2*S*)-**S3**, in which the benzyl moiety of **S3** faces the benzene ring of **10**, was stable at rt for one month in the solid state. After refluxing in toluene for 2h, 30% of **10c** was epimerized to less hindered **10b**; *rel*-(12*R*)-**10**-(2*R*)-**S3**. The aminoal **10c** also epimerized to **10b** in 39% yield after stirring in AcOH/CHCl₃ (1:20) solution at rt for 12h. **10c**, however, was stable after stirring with MS3Å or MgSO₄ in CHCl₃ at rt for 24 h. Possible epimerization mechanism from **10c** to **10b** is shown in **Fig. 12**.

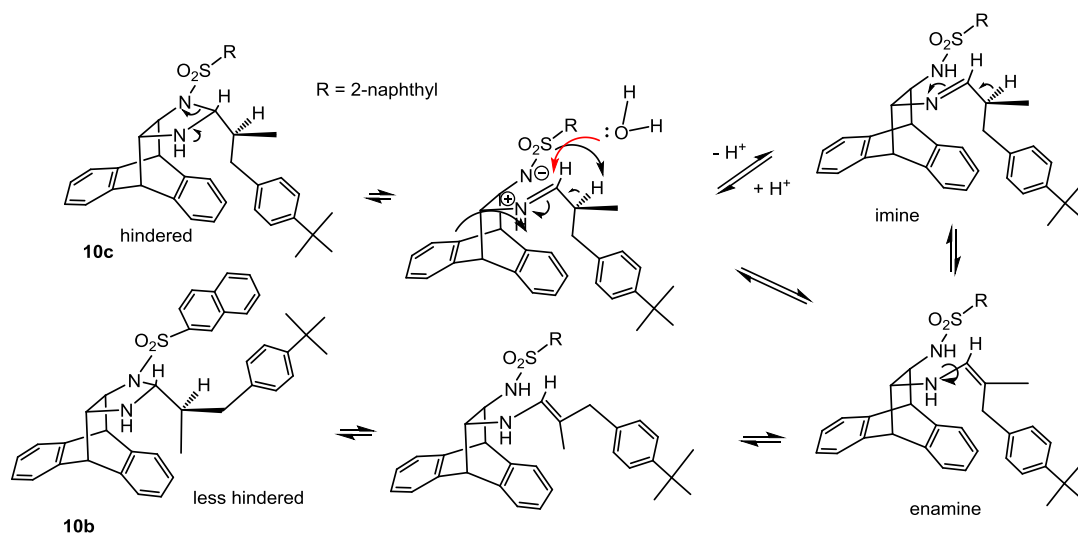


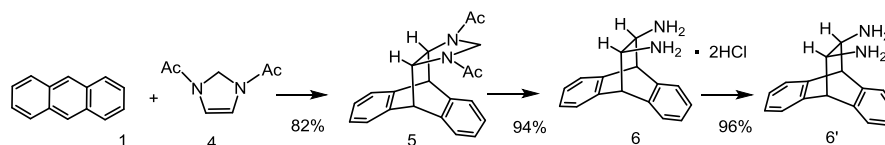
Fig. 12. Possible epimerization mechanism from **10c** to **10b**.

“Roofed” *cis*-diamine **6** was synthesized in a short step. The absolute configuration of reagent moiety in each aminal from **7-10** and (1*R*)-myrtenal **S5** could be determined by NMR analyses. The process for recovery of chiral aldehydes from chiral aminals still remains as a challenging theme.

CHAPTER 3

Conclusion

“Roofed” *cis*-diamine **6** and **6'** was synthesized in a short step.



The new method will be useful for determination of absolute configuration of chiral aldehydes and preparation of optical active aldehydes which can convert to the corresponding primary alcohols and carboxylic acids.

I submit here a configurational correlation model for the aminals from (12*R*)-mono-*N*-sulfonyl RDA reagents and α -disubstituted racemic aldehydes. The model can explain the chemical shift difference ($\Delta\delta$) of diastereomers, and predict the absolute configurations of aldehyde moieties.

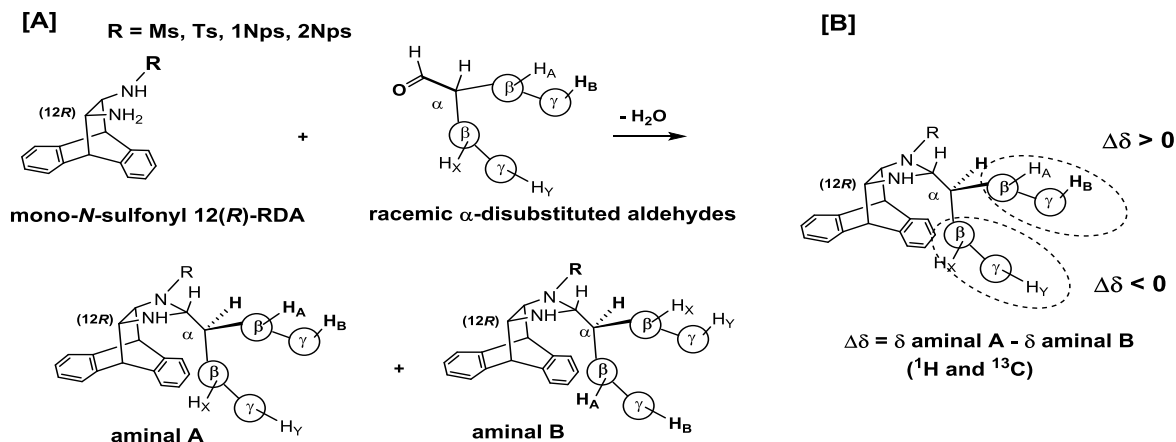


Fig. (A) Configurational correlation model for the aminals from (12*R*)-mono-*N*-sulfonyl RDAs and α -disubstituted racemic aldehydes. (B) $H_{A,B}$ and $H_{X,Y}$ are on the far and near sides to the faced benzene ring of reagent in aminal A, respectively.

Chapter 4.

Experimental Section

4.1. General Procedures

The solvent and reagents used were each a pure grade of the commercial product.

(1*R*)-(-)-Myrtenal (Aldrich, 21,824-3 02511JN, $[\alpha]_D^{22}$ -15° , neat) was used. Unless otherwise stated, they were used without purification. Melting points were determined on a Yanaco MP-S3 and uncorrected. Optical rotations were measured on a JASCO P-2200 instrument. NMR spectra were recorded on a JEOL JNM-EX270 or a Bruker AVANCE I [270 MHz/67.5 MHz or 500 MHz/126 MHz ($^1\text{H}/^{13}\text{C}$)] in CDCl_3 , using tetramethylsilane as an internal standard, unless otherwise stated. Mass spectra were obtained using JEOL AccuTOF JMS-T100GCv (FD-MS). Analytical TLC was performed on Merck Silica gel 60F254 (0.25 mm) on glass plates. Crude products were purified by column chromatography on Silica Gel 60 or 60N [Kanto (spherical) particle size: 40-50 μm].

Synthesis of **4**

I referred the reported reductive acetylation condition¹⁷. To a mixture of *N*-acetylimidazole (1.10 g, 10.0 mmol), acetic anhydride (2.85 mL, 30.0 mmol) in acetic acid (10 mL) was added sodium borohydride (0.57 g, 15.0 mmol) gradually at 0 $^\circ\text{C}$ under N_2 atmosphere. After the addition was complete, stirred for 10 min, then CH_3OH (10 mL) was added. The reaction mixture was concentrated under vacuum. The residue was directly applied to silica gel column chromatography (eluent: CHCl_3 : MeOH , 10:1) to give a white solid (1.44 g, 94%). Compound **4** exists as a mixture of three rotamers in $\text{DMSO}-d_6$.

The physicochemical properties of **4** coincided well with those of reported⁹).

Synthesis of **5**

I referred the reported Diels–Alder reaction condition¹⁸. *O*-Dichlorobenzene solution (20 mL) of **4** (3.14 g, 20.0 mmol), anthracene (4.46 g, 25.0 mmol), and *p*-hydroquinone (0.11 g, 1 mmol) was heated at reflux temp. under N₂ atmosphere for 15 h. The reaction mixture directly applied to silica gel column chromatography (eluent: CHCl₃:MeOH, 20:1→4:1) to give a white solid (5.52 g, 82%).

Mp 245.0–246.0 °C (EtOH-CH₂Cl₂).

FDMS (positive) *m/z* (rel. int. %) 332 (M⁺, 100), 178 (37), 154 (23). HRFDMS *m/z* [M]⁺ calcd. for C₂₁H₂₀N₂O₂, 332.15248; found, 332.15339.

Two rotamers of **6** exist in CDCl₃ (Asymmetric:symmetric = 2:1).

NMR δ_H (CDCl₃): Asymmetric; 7.1–7.45 (8H, m), 5.07 (1H, d, *J* = 3.3 Hz), 4.93 (1H, d, *J* = 7.5 Hz), 4.72 (1H, dd, *J* = 8.2, 3.3 Hz), 4.52 (1H, d, *J* = 3.3 Hz), 4.41 (1H, dd, *J* = 8.2, 3.3 Hz), 2.96 (1H, d, *J* = 7.5 Hz), 2.32 (3H, s), 1.87 (3H, s). Symmmetric; 7.1–7.45 (8H, m), 5.03 (2H, dd, *J* = 1.3, 1.3 Hz), 4.60 (2H, dd, *J* = 1.3, 1.3 Hz), 4.58 (1H, d, *J* = 5.3 Hz), 3.23 (1H, d, *J* = 5.3 Hz), 1.90 (6H, s); NMR δ_C (CDCl₃): 167.8, 167.4, 167.0, 139.8, 139.64, 139.57, 139.3, 137.9, 127.4, 127.2, 126.89, 126.86, 126.8, 125.7, 125.6, 125.4, 125.32, 125.26, 124.5, 63.9, 62.9, 61.24, 61.20, 60.1, 49.6, 46.3, 46.2, 22.53, 22.45, 21.6.

Synthesis of **6**

To a solution of MeOH (40 mL) and conc. HCl (20 mL) was added **5** (3.70 g, 111 mmol) in one portion, then heated at reflux temp. under N₂ atmosphere for 3 h. The reaction mixture was concentrated to dryness to give a white solid. The crude product was suspended in EtOAc and filtered to afford **6** (3.35 g, 97%). The ¹H and ¹³C NMR data for the salt of **6** were identical with those of reported⁸).

Synthesis of **6'**

To a suspension of **6** (0.92 g, 3.3 mmol) in CHCl₃ (10 mL) was added triethylamine (0.92 mL, 6.6 mmol) at rt under N₂ atmosphere, then the reaction mixture changed to a clear solution. The reaction mixture was stirred for 30 min to become a suspension again. The reaction mixture was concentrated under vacuum. The residue was directly applied to silica

gel column chromatography (eluent: CHCl₃:MeOH, 3:1) to give **6'** as a white solid (0.68 g, 96 %).

Mp 198.0-199.0 °C.

FDMS (positive) m/z (rel. int. %) 237 (M+H, 100), 178 (51).

HRFDMS m/z [M+H]⁺ calcd. for C₁₆H₁₇N₂, 237.13917; found, 237.13977.

NMR δ_H (CDCl₃): 7.30-7.35 (2H, m), 7.26-7.30 (2H, m), 7.15-7.20 (2H, m), 7.09-7.14 (2H, m), 4.16 (2H, br s), 3.26 (2H, br s), 1.09 (4H, br s); NMR δ_C (CDCl₃): 141.8, 139.6, 126.31, 126.25, 126.11, 123.97, 53.21, 51.91.

Preparation of amins from “roofed” *cis*-diamine **6'**.

Synthesis of **4a** and **4b**:

I referred the reported aminalization process¹⁴.

To solution of **4'** (50.0 mg, 0.21 mmol) in CHCl₃/MeOH (0.5 mL+ 0.2 mL) was added isobutyraldehyde (58 μl, 0.64 mmol) at rt under N₂ atmosphere. The reaction mixture was stirred for 8 h, then concentrated to dryness to give a white solid. The crude product was suspended in Et₂O and filtered to afford **4a** and **4b** [55.8 mg, 91%, **4a** (endo):**4b** (exo) = 4:1].

FDMS (positive) m/z (rel. int. %) 291 [M+H]⁺ (77), 247 (100), 178 (51). HRFDMS m/z [M+H]⁺ calcd. for C₂₀H₂₃N₂, 291.18612; found, 291.18634.

4a (endo)

NMR δ_H (CDCl₃): 7.1-7.35 (8H, m), 4.40 (2H, m), 3.49 (2H, m), 3.52 (1H, d, J = 5.2 Hz), 1.34 (1H, m), 0.64 (6H, d, J = 6.8 Hz); NMR δ_C (CDCl₃): 141.9, 139.8, 126.7 (x2), 126.3, 124.6, 82.0, 62.7, 48.5, 30.8, 17.9.

4b (exo)

NMR δ_H (CDCl₃): 7.1-7.35 (8H, m), 4.38 (2H, m), 3.69 (2H, m), 2.56 (1H, d, J = 7.5 Hz), 1.31 (1H, m), 0.75 (6H, d, J = 6.7 Hz); NMR δ_C (CDCl₃): 142.0, 140.2, 126.5, 126.2, 125.9, 124.4, 82.8, 62.6, 50.2, 33.2, 19.1.

Preparation of “roofed” *N*-monosulfonyl *cis*-diamines **7-10**

Synthesis of 7

To **6** (3.09 g, 0.01 mol) in CHCl_3 (30 mL) was added triethylamine (4.88 mL, 0.035 mol) at 0°C under N_2 atmosphere and stirred for 15 minutes. To the reaction mixture was added MsCl (1.11 g, 0.011 mol) in CHCl_3 (10 mL) slowly at 0°C and stirred for 1 h. The reaction mixture was concentrated under vacuum. The residue was directly applied to neutral silica gel column chromatography (eluent: CHCl_3 :MeOH, 10:1) to give **7** as a white solid (2.99 g, 95 %).

Mp 193.0 - 194.5°C .

FDMS (positive) m/z (rel. int. %) 315 $[\text{M}+\text{H}]^+$ (100), 178 (33), 136 (6).

HRFDMS m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$, 315.11566; found, 315.11672.

NMR δ_{H} (CDCl_3): 7.36-7.39 (1H, m), 7.27-7.35 (3H, m), 7.25 (1H, s), 7.17-7.22 (2H, m), 7.13-7.16 (2H, m), 4.49 (1H, d, $J = 2.7$ Hz), 4.20 (1H, d, $J = 2.9$ Hz), 3.66 (1H, dd, $J = 8.8$, 2.7 Hz), 3.46 (1H, dd, $J = 8.8$, 2.9 Hz), 2.96 (3H, s), 0.8-2.0 (br, NH_2); NMR δ_{C} (CDCl_3): 140.9, 140.6, 139.1, 138.7, 127.0, 126.8, 126.7, 126.62, 126.55, 126.1, 124.6, 124.2, 53.8, 52.6, 50.4, 50.2, 40.9.

Synthesis of 8

To **6** (1.95 g, 0.005 mol) in CHCl_3 (30 mL) was added triethylamine (2.44 mL, 0.0175 mol) at 0°C under N_2 atmosphere and stirred for 15 minutes. To the reaction mixture was added TsCl (1.11 g, 0.0055 mol) in CHCl_3 (10 mL) slowly at 0°C and stirred for 1 h. The reaction mixture was concentrated under vacuum. The residue was directly applied to neutral silica gel column chromatography (eluent: CHCl_3 :MeOH, 10:1) to give **8** as a white solid (1.89 g, 80%).

Mp 202.0 - 203.5°C .

FDMS (positive) m/z (rel. int. %) 391 $[\text{M}+\text{H}]^+$ (100), 212 (7), 178 (22).

HRFDMS m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{22}\text{N}_2\text{O}_2\text{S}$, 391.14640; found, 391.14802.

NMR δ_{H} (CDCl_3): 7.73 (2H, d, $J = 8.2$ Hz), 5.65 (1H, br), 4.34 (1H, d, $J = 2.6$ Hz), 4.13 (1H, d, $J = 2.6$ Hz), 3.41 (1H, dd, $J = 8.9$, 2.6 Hz), 3.22 (1H, dd, $J = 8.9$, 2.6 Hz), 2.42 (3H,

s), 0.7-1.7 (br, NH₂); NMR δ_C (CDCl₃): 143.2, 140.9, 140.7, 139.1, 138.6, 137.6, 129.7, 127.1, 126.9, 126.5, 126.4, 125.9, 124.5, 124.0, 53.3, 52.3, 49.90, 49.84, 21.5.

The ¹H and ¹³C NMR data for **8** were identical with those of reported¹¹).

Synthesis of **9**

To **6** (1.95 g, 0.005 mol) in CHCl₃ (30 mL) was added triethylamine (2.44 mL, 0.0175 mol) at 0°C under N₂ atmosphere and stirred for 15 minutes. To the reaction mixture was added 1NpsCl (1.25 g, 0.0055 mol) in CHCl₃ (10mL) slowly at 0°C and stirred for 1 h. The reaction mixture was concentrated under vacuum. The residue was directly applied to neutral silica gel column chromatography (eluent: CHCl₃:MeOH, 10:1) to give **9** as a white solid (1.89 g, 89%).

Mp 120.0-121.0 °C.

FDMS (positive) *m/z* (rel. int. %) 427 [M+H]⁺ (100), 248, 19), 178 (27).

HRFDMS *m/z* [M+H]⁺ calcd. for C₂₆H₂₂N₂O₂S, 427.14836; found, 427.14802.

NMR δ_H (CDCl₃): 8.56 (1H, m), 8.31 (1H, dd, *J* = 7.5, 1.3 Hz), 8.08 (1H, d, *J* = 8.3 Hz), 7.96 (1H, m), 7.54-7.63 (3H, m), 7.02-7.25 (4H, m), 6.81(1H, br d, *J* = 7.1 Hz), 5.5-6.5 (br, NH), 4.07 (1H, d, *J* = 2.9 Hz), 4.06 (1H, d, *J* = 2.7 Hz), 3.35 (1H, dd, *J* = 8.8, 2.7 Hz), 3.13 (1H, dd, *J* = (8.8, 2.9 Hz), 0.7-1.7 (br, NH₂); NMR δ_C (CDCl₃): 140.8, 140.7, 140.0, 138.6, 135.1, 134.3, 134.2, 129.7, 129.1, 128.15, 128.12, 126.9, 126.8, 126.7, 126.48, 126.45, 126.3, 125.8, 124.8, 124.4, 124.2, 124.1, 53.6, 52.1, 49.8, 49.6.

Synthesis of **10**

To **6** (1.95 g, 0.063 mol) in CHCl₃ (30 mL) was added triethylamine (3.08 mL, 2.44 g, 0.022 mol) at 0°C under N₂ atmosphere and stirred for 15 minutes. To the reaction mixture was added 2NpsCl (1.50 g, 0.0066 mol) in CHCl₃ (10mL) slowly at 0°C and stirred for 1 h. The reaction mixture was concentrated under vacuum. The residue was directly applied to neutral silica gel column chromatography (eluent: CHCl₃:MeOH, 10:1) to give **9** as a white solid (2.35 g, 87 %).

Mp 151.0-152.0 °C.

FDMS (positive) m/z (rel. int. %) 427 $[M+H]^+$ (100), 248 (11), 178 (33).

HRFDMS m/z $[M+H]^+$ calcd. for $C_{26}H_{22}N_2O_2S$, 427.14716; found, 427.14802.

NMR δ_H ($CDCl_3$): 8.44 (1H, d, $J = 1.4$ Hz) 7.95 (2H, br d, $J = 8.4$ Hz), 7.90 (1H, br d, $J = 8.0$ Hz), 7.80 (1H, dd, $J = 8.7, 1.8$ Hz), 7.58-7.65 (2H, m), 7.05-7.27 (8H, m), 5.5-6.5 (br, NH), 4.37 (1H, d, $J = 2.7$ Hz), 4.11 (1H, d, $J = 2.9$ Hz), 3.19 (1H, dd, $J = 8.8, 3.0$ Hz), 3.44 (1H, dd, $J = 8.8, 2.7$ Hz), 0.7-1.7 (br, NH_2); NMR δ_C ($CDCl_3$): 140.9, 140.7, 139.2, 138.7, 137.3, 134.8, 132.1, 129.5, 129.3, 128.8, 128.4, 127.9, 127.6, 126.95, 126.92, 126.54, 126.53, 126.4, 125.9, 124.5, 124.1, 122.4, 53.4, 52.3, 50.0, 49.9

Synthesis of **7a**

To **7** (120 mg, 0.38 mmol) in 2 mL CH_2Cl_2 was added isobutyraldehyde (70 μ L, 0.76 mmol, 2 eq) under N_2 atmosphere at r.t. and stirred for 1.5 hours. The reaction mixture was concentrated under vacuum. The residue was directly applied to neutral silica gel column chromatography (eluent: $CHCl_3$) to give compound **7a** as a white solid (135.9 mg, 97 %).

Mp 187.5-188.0 °C.

FDMS (positive) m/z (rel. int. %) 369 $[M+H]^+$ (98), 368 (65), 325 (100), 190 (54), 178 (60), 58 (70). HRFDMS m/z $[M+H]^+$ calcd. for $C_{21}H_{25}N_2O_2S$, 369.16367; found, 369.16466.

NMR δ_H ($CDCl_3$): 7.41-7.42 (1H, m), 7.29-7.35 (3H, m), 7.17-7.21 (2H, m), 7.11-7.15 (2H, m), 4.72 (1H, br s), 4.41 (1H, d, $J = 2.4$ Hz), 4.13 (1H, d, $J = 3.0$ Hz), 3.72-3.76 (2H, m), 2.83 (3H, s), 2.22 (1H, m), 1.50 (1H, br s), 0.82 (3H, d, $J = 7.1$ Hz), - 0.01 (3H, d, $J = 7.1$ Hz) ; NMR δ_C ($CDCl_3$): 141.3, 140.7, 139.9, 138.7, 127.4, 127.3, 126.8, 126.7, 126.6, 126.1, 125.2, 124.7, 84.2, 77.2, 64.9, 59.9, 49.4, 47.9, 36.2, 28.2, 19.5, 11.2

Synthesis of **8a**

A white solid (96 % yield), mp 190.0-190.5 °C.

FDMS (positive) m/z (rel. int. %) 445 $[M+H]^+$ (100), 444 (37), 266 (46), 178 (26), 58 (64).

HRFDMS m/z $[M+H]^+$ calcd. for $C_{27}H_{29}N_2O_2S$, 445.19497; found, 445.19351.

NMR δ_H ($CDCl_3$): 7.14-7.66 (14H, m), 4.84 (1H, m), 4.33 (1H, m), 3.49 (1H, m), 2.41 (4H, m), 1.55 (1H, m), 1.26 (1H, m), 0.80 (3H, d, $J = 7.1$ Hz), 0.03 (3H, d, $J = 7.1$ Hz); NMR δ_C

(CDCl₃): 143.9, 141.6, 140.9, 140.0, 138.7, 133.0, 129.8, 128.0, 127.6, 127.4, 126.7, 126.6, 126.5, 125.9, 125.1, 124.7, 84.2, 64.7, 59.7, 49.7, 47.8, 28.3, 21.5, 19.5, 11.4

Synthesis of **9a**

A white solid (96 % yield), mp 200.5-201.0 °C.

FDMS (positive) m/z (rel. int. %) 481 [M+H]⁺ (68), 480 (100), 437 (13), 302 (28), 178 (7).

HRFDMS m/z [M]⁺ calcd. for C₃₀H₂₈N₂O₂S, 480.18715; found, 480.18602.

NMR δ_H (CDCl₃): 8.93 (1H, d, J = 9.2 Hz), 7.98-8.28 (3H, m), 7.58-7.95 (3H, m), 7.05-7.25 (7H, m), 6.83 (1H, d, J = 6.9 Hz), 4.31 (1H, d, J = 3.6 Hz), 4.26 (1H, m), 4.01 (1H, d, J = 2.5 Hz), 3.66 (1H, dd, J = 8.4, 2.5 Hz), 3.47 (1H, m), 2.58 (1H, m), 1.25 (1H, br s), 0.81 (3H, d, J = 7.1 Hz), 0.02 (3H, d, J = 7.1 Hz); NMR δ_C (CDCl₃): 141.4, 140.7, 139.5, 138.8, 134.9, 134.3, 133.0, 130.7, 129.8, 128.7, 128.2, 127.3, 127.1, 126.6, 126.5, 126.5, 125.8, 125.4, 124.7, 124.6, 124.2, 84.3, 64.6, 60.1, 48.7, 47.7, 28.7, 19.6, 11.3

Synthesis of **10a**

A white solid (95 % yield), mp 199.0-200.0 °C.

FDMS (positive) m/z (rel. int. %) 481 [M+H]⁺ (66), 480 (41), 302 (46), 178 (36), 58 (73).

HRFDMS m/z [M+H]⁺ calcd. for C₃₀H₂₉N₂O₂S, 481.19497; found, 481.19372.

NMR δ_H (CDCl₃): 8.33 (1H, s), 7.92-7.98 (2H, m), 7.89 (1H, d, J = 8 Hz), 7.73-7.75 (1H, m), 7.58-7.65 (2H, m), 7.50 (1H, d, J = 7.2 Hz), 7.39 (1H, d, J = 7.2 Hz), 7.28 (1H, d, J = 6.9 Hz), 7.08-7.24 (6H, m), 4.88 (1H, d, J = 2.7 Hz), 4.32 (1H, d, J = 3.4 Hz), 3.84 (1H, br s), 3.62 (1H, dd, J = 8.7, 2.7 Hz), 3.37 (1H, br dd, J = 8.6, 3.4 Hz), 2.50 (1H, m), 1.2-1.35 (1H, br s), 0.81 (3H, d, J = 7.1 Hz), 0.05 (3H, d, J = 7.1 Hz); NMR δ_C (CDCl₃): 141.5, 140.9, 139.9, 138.7, 134.9, 133.2, 132.1, 129.3, 128.9, 127.9, 127.6, 127.6, 127.4, 126.8, 126.6, 126.6, 125.9, 125.1, 124.7, 123.2, 84.4, 64.8, 59.7, 49.7, 47.8, 28.4, 19.5, 11.4

Synthesis of **11a**

To **11** (40.2 mg, 0.010 mmol) in 2 mL CH₂Cl₂ was added isobutyraldehyde (5.0 μ L, 0.055 mmol) under N₂ atmosphere at r.t. and stirred for 1.5 hours. The reaction mixture was concentrated under vacuum to obtain **11a** as a colorless oil (47.5 mg, quant.).

Preparation of amins for Table 2.

Each of **7-10** and three equivalent amount of aldehydes **S1-S5** in CHCl₃ was stirred for 1 hour at rt. The reaction mixtures of **S5** were stirred overnight. Retention factor (*R_f*) were measured using different solvent combinations by using glass TLC plates (0.25 mm) of Merck Silica gel 60F254.

A; Hexane/EtOAc = 2:1, **B**; EtOAc, **C**; CHCl₃/MeOH = 3:1, **D**; Toluene/EtOAc = 20:1, **E**; Toluene/EtOAc = 10:1.

Spectral Data for **9b**, **9c**, **10b**, and **10c**

9b (aminal from *rel*-(12*R*)-9** and (2*R*)-**S1**)**

FDMS (positive) *m/z* (rel. int. %) 495 [M+H]⁺ (100), 494 (55), 437 (29), 316 (34), 178 (21). HRFDMS *m/z* [M]⁺ calcd. for C₃₁H₃₀N₂O₂S, 494.20280; found, 494.20312.

NMR δ_H (CDCl₃): 8.95 (1H, dd, *J* = 8.2, 1.0 Hz), 8.27 (1H, dd, *J* = 7.3, 1.2 Hz), 8.16 (1H, d, *J* = 8.2 Hz), 7.98 (1H, dd, *J* = 7.7, 1.8 Hz), 7.6-7.7 (3H, m), 7.0-7.3 (7H, m), 6.88 (1H, br d, *J* = 7.0 Hz), 4.34 (1H, br s), 4.32 (1H, d, *J* = 3.5 Hz), 4.07 (1H, d, *J* = 2.7 Hz), 3.67 (1H, dd, *J* = 8.6, 2.7 Hz), 3.47 (1H, br d, *J* = 8.6 Hz), 2.30 (1H, m), 1.25 (1H, m), 1.06 (1H, m), 0.82 (3H, t, *J* = 7.4 Hz), , - 0.01 (3H, d, *J* = 7.7 Hz); NMR δ_C (CDCl₃): 141.4, 140.7, 139.6, 138.8, 134.9, 134.3, 133.1, 130.7, 129.8, 128.9, 128.2, 127.3, 127.57, 127.11, 126.7, 126.6, 126.5, 125.9, 125.5, 124.72, 124.65, 124.2, 83.3, 64.4, 60.2, 48.8, 47.7, 35.6, 27.3, 12.2, 9.2.

9c (aminal from *rel*-(12*R*)-9** and (2*S*)-**S1**)**

FDMS (positive) *m/z* (rel. int. %) 495 [M+H]⁺ (100), 494 (44), 437 (27), 315 (30), 178 (19). HRFDMS *m/z* [M]⁺ calcd. for C₃₁H₃₀N₂O₂S, 494.20280; found, 494.20165.

major rotamer;

NMR δ_{H} (CDCl_3): 8.90 (1H, br d, $J = 7.9$ Hz), 8.28 (1H, dd, $J = 7.4, 1.2$ Hz), 8.16 (1H, d, $J = 8.2$ Hz), 7.98 (1H, dd, $J = 7.3, 2.3$ Hz), 7.0-7.7 (10H, m), 6.80 (1H, br d, $J = 8.2$ Hz), 4.32 (1H, br s), 4.31 (1H, d, $J = 3.6$ Hz), 4.02 (1H, d, $J = 2.7$ Hz), 3.77 (1H, dd, $J = 8.6, 2.7$ Hz), 3.51 (1H, br d, $J = 8.6$ Hz), 2.08 (1H, m), 0.79 (3H, d, $J = 7.1$ Hz), 0.52 (1H, m), 0.51 (3H, m), - 0.24 (1H, m); NMR δ_{C} (CDCl_3): 141.4, 140.7, 139.6, 138.8, 135.0, 134.3, 133.3, 130.7, 129.7, 128.9, 128.0, 127.2, 127.1, 126.9, 126.7, 126.6, 126.5, 125.9, 125.5, 124.7, 124.6, 124.2, 85.0, 646.4, 60.3, 48.7, 47.7, 35.9, 18.3, 16.3, 10.8.

10b (aminal from *rel*-(12*R*)-10 and (2*R*)-S3)

FDMS (positive) m/z (rel. int. %) 613 $[\text{M}+\text{H}]^+$ (87), 612 (100), 437 (29), 434 (33), 178 (15).
HRFDMS m/z $[\text{M}]^+$ calcd. for $\text{C}_{40}\text{H}_{40}\text{N}_2\text{O}_2\text{S}$, 612.28105; found, 612.28088.

NMR δ_{H} (CDCl_3): 8.19 (1H, br s), 7.0-7.9 (18H, m), 4.92 (1H, d, $J = 2.7$ Hz), 4.36 (1H, d, $J = 3.3$ Hz), 3.76 (1H, d, $J = 2.3$ Hz), 3.69 (1H, dd, $J = 8.6, 2.7$ Hz), 3.42 (1H, br dd, $J = 8.6, 3.3$ Hz), 2.81 (1H, m), 2.42 (1H, dd, $J = 13.8, 7.2$ Hz), 2.39 (1H, dd, $J = 13.8, 9.0$), 1.34 (9H, s), 0.15 (3H, d, $J = 6.8$ Hz); NMR δ_{C} (CDCl_3): 148.7, 141.5, 140.9, 140.0, 138.7, 137.1, 134.7, 132.5, 132.0, 129.4, 129.3, 129.0, 128.8, 128.7 (x2), 127.72, 127.67, 127.5, 126.7, 126.6, 126.5, 125.2 (x2), 125.1, 124.7, 123.2, 81.9, 64.6, 59.8, 49.7, 47.7, 39.9, 35.5, 34.4, 31.5 (x3), 10.2.

10c (aminal from *rel*-(12*R*)-10 and (2*S*)-S3)

FDMS (positive) m/z (rel. int. %) 613 ($\text{M}+\text{H}$, 87), 612 (100), 437 (29), 434 (32), 178 (12).
HRFDMS m/z $[\text{M}]^+$ calcd. for $\text{C}_{40}\text{H}_{40}\text{N}_2\text{O}_2\text{S}$, 612.28105; found, 612.28240.

NMR δ_{H} (CDCl_3): 8.36 (1H, br s), 6.9-8.00 (18H, m), 4.94 (1H, d, $J = 2.8$ Hz), 4.36 (1H, d, $J = 3.3$ Hz), 3.91 (1H, d, $J = 2.7$ Hz), 3.69 (1H, dd, $J = 8.6, 2.7$ Hz), 3.42 (1H, br dd, $J = 8.6, 3.3$ Hz), 2.59 (1H, m), 2.16 (br d, $J = 11.9$ Hz), 1.29 (9H, s), 0.88 (1H, dd, $J = 12.9, 11.9$), 0.71 (3H, d, $J = 7.1$ Hz); NMR δ_{C} (CDCl_3): 148.3, 141.5, 140.8, 139.9, 138.7, 137.6, 135.0, 133.2, 132.2, 129.4, 129.3, 128.7 (x2), 127.9, 127.66, 127.61, 127.58, 126.8, 126.62, 126.60, 126.0, 125.1, 124.9 (x2), 124.8, 123.2, 84.5, 64.9, 59.8, 49.8, 47.8, 35.9, 34.3, 31.41 (x3), 31.38, 16.4.

General procedure for preparation of amins from **7-10** with (1*R*)-(-)-myrtenal **S5**.

The amins **7b** and **7c** from racemic **7** and (1*R*)-(-)-myrtenal **S5**

To suspension of (1*R*)-(-)-myrtenal **S5** (70 mg, 0.466 mmol) and MS 3Å (100 mg) in CHCl₃ (1.5 mL) was added racemic **7** (109 mg, 0.347 mmol) at rt under N₂ atmosphere. The reaction mixture was stirred for 2 days, then concentrated to dryness. The residue was directly applied to silica gel column chromatography (eluent: hexane:EtOAc, 1:1) to give **7b** (59 mg, 38%) and **7c** (67 mg, 42 %) as white solids.

7b: [α]_D²⁷ – 7.10 (c 0.0155, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 447 [M+H]⁺ (48), 446 (100), 268 (10), 178 (6). HRFDMS *m/z* [M]⁺ calcd. for C₂₇H₃₀N₂O₂S, 446.20280; found, 446.20367.

7c: [α]_D²⁷ – 24.8 (c 0.0210, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 447 (M+H, 49), 446 (M, 100), 268 (12), 178 (6). HRFDMS *m/z* [M]⁺ calcd. for C₂₇H₃₀N₂O₂S, 446.20280; found, 446.20412. NMR δ_C (CDCl₃): 142.7, 141.1, 140.6, 140.1, 138.8, 127.3x2, 127.1, 126.8, 126.7, 125.9, 125.27, 125.23, 124.8, 40.5, 38.9, 37.7, 37.0, 31.7, 31.3, 25.7, 21.3.

8b: [α]_D²⁷ + 21.1 (c 0.0535, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 523 (M+H, 45), 522 (M, 100), 344 (15), 178 (8). HRFDMS *m/z* [M]⁺ calcd. for C₃₀H₃₄N₂O₂S, 522.23410; found, 522.233336. Major rotamer NMR δ_C (CDCl₃): 143.4, 143.8, 141.3, 140.7, 140.0, 138.6, 133.0, 129.6x2, 128.3x2, 127.4, 127.3, 126.7, 126.5, 126.0, 125.0, 124.7, 122.3, 82.8, 64.3, 60.2, 49.6, 47.9, 40.72, 40.63, 37.9, 32.3, 31.1, 25.9, 21.5, 21.4.

8c: [α]_D²⁷ – 48.1 (c 0.1036, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 523 (M+H, 45), 522 (M, 100), 344 (15), 178 (8). HRFDMS *m/z* [M]⁺ calcd. for C₃₀H₃₄N₂O₂S, 522.23410; found, 522.233336. Major amins NMR δ_C (CDCl₃): 143.7, 143.5, 141.3, 140.7, 140.0, 138.5, 132.7, 129.6x2, 128.1x2, 127.6, 127.3, 126.8, 126.7, 126.5, 125.6, 125.1, 124.6, 123.6, 82.7, 63.8, 60.3, 49.6, 47.6, 40.4, 39.3, 36.7, 37.0, 31.4, 31.23, 25.6, 21.5, 21.3.

The amins **9d** and **9e** from racemic **9** and (1*R*)-(-)-myrtenal **S5**

Racemic **9** (600 mg, 1.41 mmol) was added to suspension of (1*R*)-(-)-myrtenal **S5** 270 mg, 1.80 mmol) and MS 3 Å (500 mg) in CHCl₃ (5 mL) at rt under N₂ atmosphere. The reaction mixture was stirred for 3 days, then concentrated to dryness. The residue was directly applied to silica gel column chromatography (eluent: hexane:EtOAc, 2:1) to give **9d** (184 mg, 38%) and **9e** (306 mg, 39 %) as white solids.

9d: $[\alpha]_D^{26} + 13.9$ (*c* 0.0152, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 559 [M+H]⁺ (57), 558 (100), 380 (23), 178 (10). HRFDMS *m/z* [M]⁺ calcd for C₃₆H₃₄N₂O₂S 558.23410; found, 558.23353.

9e: $[\alpha]_D^{26} - 52.0$ (*c* 0.0235, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 559 (M+H, 58), 558 (100), 380 (17), 178 (8). HRFDMS *m/z* [M]⁺ calcd for C₃₆H₃₄N₂O₂S 558.23410; found, 558.23392.

The amina **10d** and **10e** from racemic **10** and (1*R*)-(-)-myrtenal **S5**

Racemic **10** (1.00 g, 2.34 mmol) was added to suspension of (1*R*)-(-)-myrtenal **S5** 528 mg, 3.52 mmol) and MS 3 Å (1.0 g) in CHCl₃ (10 mL) at rt under N₂ atmosphere. The reaction mixture was stirred for 3 days, then concentrated to dryness. The residue was directly applied to silica gel column chromatography (eluent: Toluene:EtOAc, 10:1) to give **9d** (80.0 mg, 6.0 %) and **9e** (626.6 mg, 47 %) as white solids.

10d: $[\alpha]_D^{28} + 5.3$ (*c* 0.0202, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 559 [M+H]⁺ (61), 558 (100), 380 (15), 178 (8). HRFDMS *m/z* [M]⁺ calcd for C₃₆H₃₄N₂O₂S 558.23410; found, 558.23566.

10e: $[\alpha]_D^{28} - 29.1$ (*c* 0.0211, CHCl₃); FDMS (positive) *m/z* (rel. int. %) 559 (M+H, 50), 558 (100), 380 (10), 178 (6). HRFDMS *m/z* [M]⁺ calcd for C₃₆H₃₄N₂O₂S 558.23410; found, 558.23494.

General procedure for preparation of chiral **7-10** by acidic methanolysis of the amina with (1*R*)-(-)-myrtenal **S5**

I referred the reported amination cleavage condition¹⁵.

(12*R*)-RDA-1Nps **9** from amination **9d**:

To 5% hydrogen chloride methanol solution (5 mL) was added amination **9d** (122.0 mg, 0.218 mmol) in one portion at rt under N₂ atmosphere. The reaction mixture was stirred for 8 h, then diluted with H₂O (5 mL). The reaction mixture was extracted with hexane (5 mL x 2), and the remaining layer was concentrated to dryness. The residue was dissolved in CHCl₃ (3 mL) and added with Et₃N (0.1 mL). After removal of solvent under vacuum, the residue was directly applied to silica gel column chromatography (eluent: CHCl₃:MeOH, 20:1) to give (12*R*)-**9** (90.0 mg, 97%) as a white amorphous powder. Myrtenal **S5** (29.0 mg, 88 %) was recovered from the hexane extract.

(12*R*)-**9**: $[\alpha]_D^{26} + 94.7$ (*c* 0.0329, CHCl₃)

Other chiral RDA reagents were obtained by the same cleavage reaction.

(12*R*)-RDA-Ms (12*R*)-**7**; $[\alpha]_D^{28} + 46.7$ (*c* 0.0296, CHCl₃) (98% yield)

(12*S*)-RDA-Ms (12*S*)-**7**; $[\alpha]_D^{27} - 89.9$ (*c* 0.032, CHCl₃) (quantitative)

(12*R*)-RDA-Ts (12*R*)-**8**; $[\alpha]_D^{28} + 111$ (*c* 0.0203, CHCl₃) (81% yield)

lit. $[\alpha]_D^{25} + 105.0$ (*c* 0.0329, CHCl₃)¹¹⁾

(12*S*)-RDA-Ts (12*S*)-**8**; $[\alpha]_D^{28} - 106$ (*c* 0.0260, CHCl₃) (77% yield)

(12*S*)-**9**: $[\alpha]_D^{27} - 89.9$ (*c* 0.032, CHCl₃)

(12*R*)-RDA-2Nps (12*R*)-**10**; $[\alpha]_D^{24} + 80.8$ (*c* 0.0105, CHCl₃)

(12*S*)-RDA-2Nps (12*S*)-**10**; $[\alpha]_D^{23} - 78.8$ (*c* 0.0301, CHCl₃) (63% yield)

Determination of enantiomeric purity of RDA reagents

The enantiomeric purity of RDA reagents was determined by using 2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acid (MNCB)¹⁶.

A chiral RDA reagent (0.01 mmol in CDCl₃) was measured ¹H NMR first, then (S)-MNCB (0.01 mmol) was added to the NMR sample and measured the mixed sample again.

Epimerization reaction from **10c** to **10b**.

Toluene solution (1.0 mL) of **10c** (5.2 mg) was heated at reflux temp. under N₂ atmosphere for 2 h. The reaction mixture was concentrated to dryness. The residue was directly measured by ¹H NMR in CDCl₃.

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APPENDIX TABLE OF CONTENT

- Fig. S1 ^1H and ^{13}C NMR spectra for **5** (500 MHz/126MHz, CDCl_3)
- Fig. S2 COSY (above) and NOESY (below) spectra for **5**. (500 MHz, CDCl_3)
- Fig. S3 HSQC (above) and HMBC (below) spectra for **5** (500 MHz/126MHz, CDCl_3)
- Fig. S4 ^1H NMR and ^{13}C spectra for **6'** (500 MHz/126MHz, CDCl_3)
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- Fig. S7 HSQC (above) and HMBC (below) spectra for **6a,b** (500 MHz/126MHz, CDCl_3)
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- Fig. S30 HSQC (above) and HMQC (below) spectra for **9b** (500 MHz/126MHz, CDCl_3)
- Fig. S31 ^1H and ^{13}C NMR spectra for **9c**. (500 MHz/126MHz, CDCl_3)

Fig. S32 COSY (above) and NOESY (below) spectra for **9c** (500 MHz, CDCl₃)

Fig. S33 HSQC (above) and HMQC (below) spectra for **9c** (500 MHz/126MHz, CDCl₃)

Fig. S34 Partial NOESY spectra for **9b** (up) and **9c** (down). (500 MHz, CDCl₃)

Fig. S35 ¹H NMR and ¹³C spectra for **10b**. (500 MHz/126MHz, CDCl₃)

Fig. S36 COSY (above) and NOESY (below) spectra for **10b** (500 MHz, CDCl₃)

Fig. S37 HSQC (above) and HMQC (below) spectra for **10b** (500 MHz/126MHz, CDCl₃)

Fig. S38 ¹H and ¹³C NMR spectra for **10c**. (500 MHz/126MHz, CDCl₃)

Fig. S39 COSY (above) and NOESY (below) spectra for **10c** (500 MHz, CDCl₃)

Fig. S40 HSQC (above) and HMQC (below) spectra for **10c** (500 MHz/126MHz, CDCl₃)

Fig. S41 ¹H NMR and ¹³C spectra for **7b**. (500 MHz/126MHz, CDCl₃)

Fig. S42 COSY (above) and NOESY (below) spectra for **7b** (500 MHz, CDCl₃)

Fig. S43 HSQC (above) and HMQC (below) spectra for **7b** (500 MHz/126MHz, CDCl₃)

Fig. S44 ¹H and ¹³C NMR spectra for **7c**. (500 MHz, CDCl₃)

Fig. S45 COSY (above) and NOESY (below) spectra for **7c**. (500 MHz, CDCl₃)

Fig. S46 HSQC (above) and HMQC (below) spectra for **7c** (500 MHz/126MHz, CDCl₃)

Fig. S47 ¹H NMR and ¹³C spectra for **8b**. (500 MHz/126MHz, CDCl₃)

Fig. S48 COSY (above) and NOESY (below) spectra for **8b**. (500 MHz, CDCl₃)

Fig. S49 HSQC (above) and HMQC (below) spectra for **8b** (500 MHz/126MHz, CDCl₃)

Fig. S50 ¹H NMR and ¹³C spectra for **8b**. (500 MHz/126MHz, CDCl₃)

Fig. S51 ¹H NMR and ¹³C spectra for **8c** (500 MHz/126MHz, CDCl₃)

Fig. S52 COSY (above) and NOESY (below) spectra for **8c** (500 MHz, CDCl₃)

Fig. S53 HSQC (above) and HMQC (below) spectra for **8c** (500 MHz/126MHz, CDCl₃)

Fig. S54 COSY (above) and NOESY (below) spectra for **9d** (500 MHz, CDCl₃)

Fig. S55 HSQC (above) and HMQC (below) spectra for **9d** (500 MHz/126MHz, CDCl₃)

Fig. S56 ¹H NMR and ¹³C spectra for **9c** (500 MHz/126MHz, CDCl₃)

Fig. S57 COSY (above) and NOESY (below) spectra for **9e** (500 MHz, CDCl₃)

Fig. S58 HSQC (above) and HMQC (below) spectra for **9e** (500 MHz/126MHz, CDCl₃)

Fig. S59 ¹H NMR and ¹³C spectra for **10d** (500 MHz/126MHz, CDCl₃)

Fig. S60 COSY (above) and NOESY (below) spectra for **10d** (500 MHz, CDCl₃)

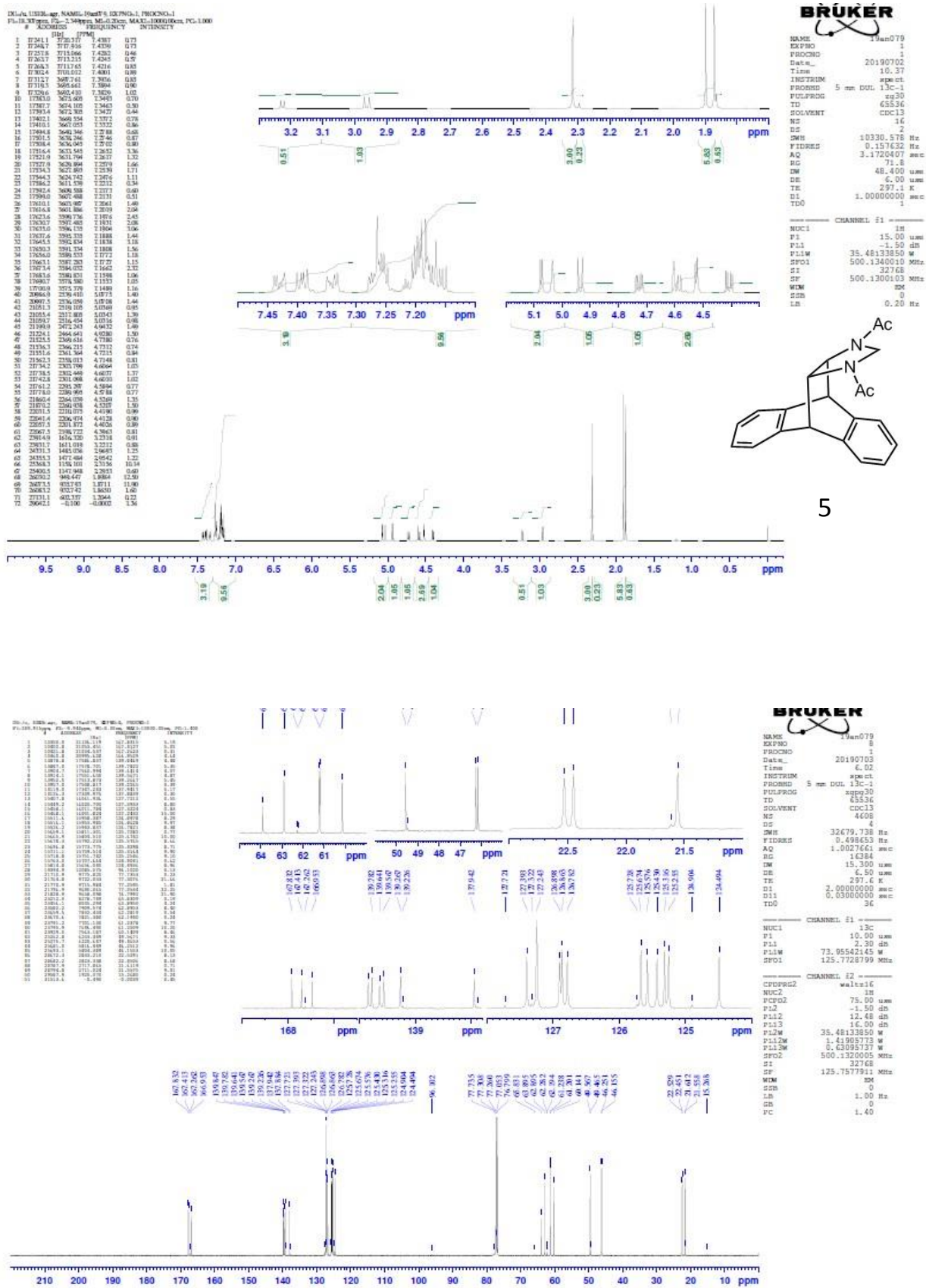
Fig. S61 HSQC (above) and HMQC (below) spectra for **10d** (500 MHz/126MHz, CDCl₃)

Fig. S62 ¹H NMR and ¹³C spectra for **10e** (500 MHz/126MHz, CDCl₃)

Fig. S63 COSY (above) and NOESY (below) spectra for **9e** (500 MHz, CDCl₃)

Fig. S64 HSQC (above) and HMQC (below) spectra for **9e** (500 MHz/126MHz, CDCl₃)

Appendix (Spectral data, table, and figures)



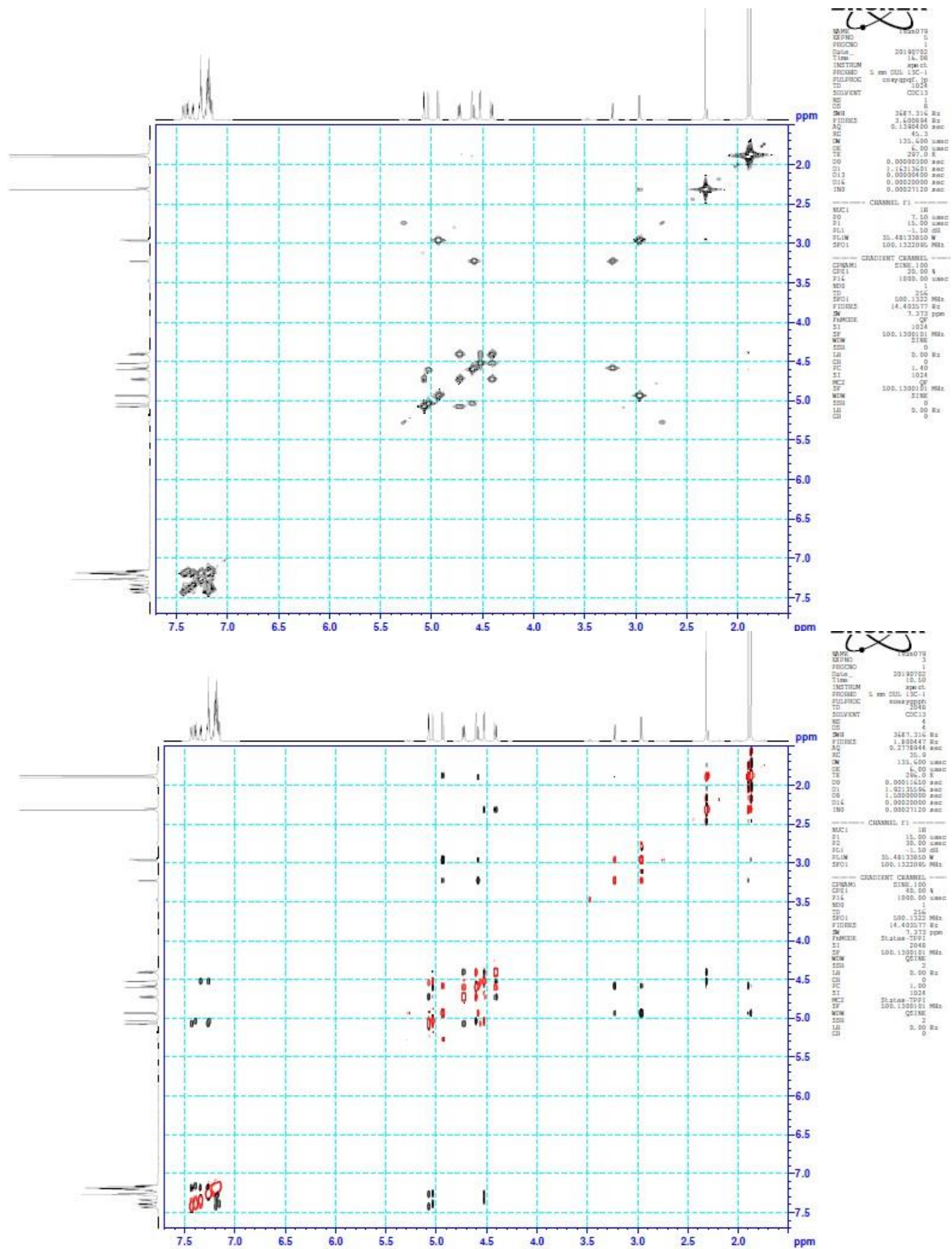


Fig. S2 COSY (above) and NOESY (below) spectra for **5**. (500 MHz, CDCl₃)

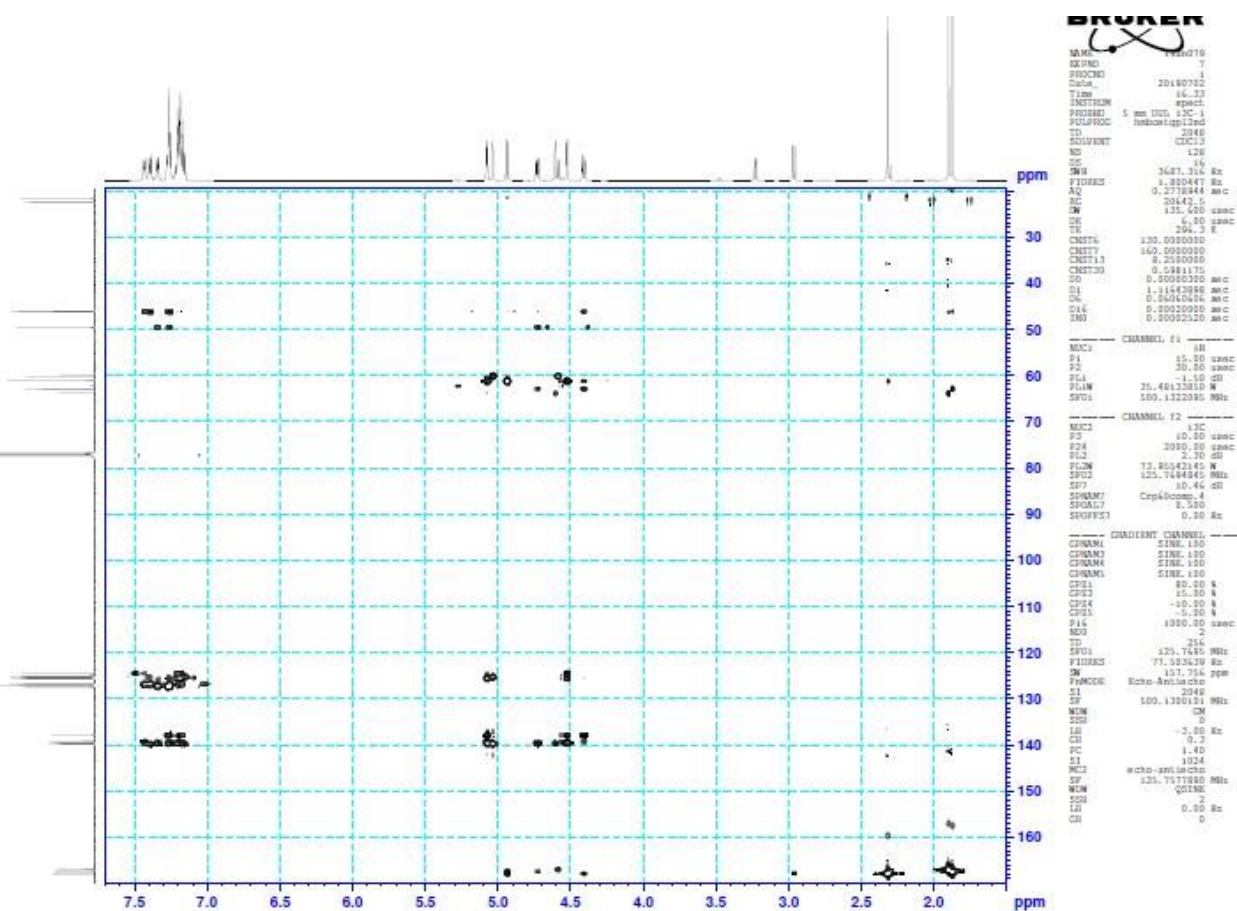
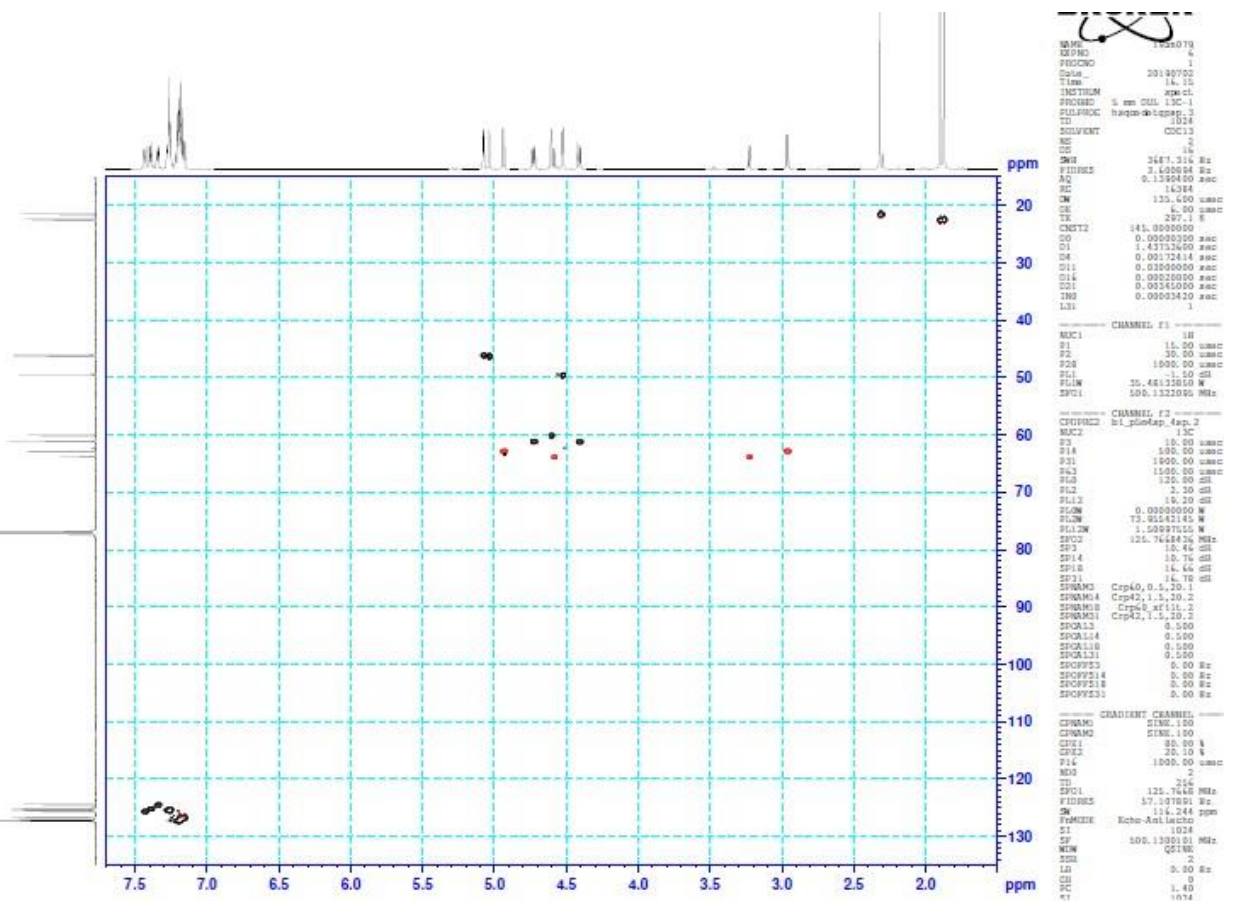


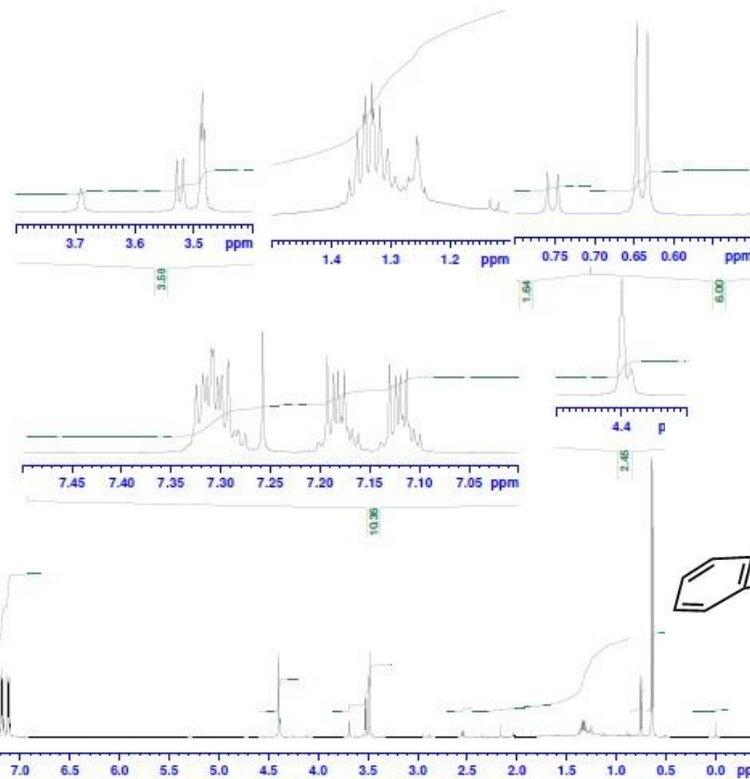
Fig. S3 HSQC (above) and HMBC (below) spectra for **5** (500 MHz/126MHz, CDCl₃)

1D 1H NMR (500 MHz, CDCl₃) of 6'

#	Chemical Shift (ppm)	Integration	Assignment
1	7.381	1.00	Aromatic
2	7.361	1.00	Aromatic
3	7.341	1.00	Aromatic
4	7.321	1.00	Aromatic
5	7.301	1.00	Aromatic
6	7.281	1.00	Aromatic
7	7.261	1.00	Aromatic
8	7.241	1.00	Aromatic
9	7.221	1.00	Aromatic
10	7.201	1.00	Aromatic
11	7.181	1.00	Aromatic
12	7.161	1.00	Aromatic
13	7.141	1.00	Aromatic
14	7.121	1.00	Aromatic
15	7.101	1.00	Aromatic
16	7.081	1.00	Aromatic
17	7.061	1.00	Aromatic
18	7.041	1.00	Aromatic
19	7.021	1.00	Aromatic
20	7.001	1.00	Aromatic
21	6.981	1.00	Aromatic
22	6.961	1.00	Aromatic
23	6.941	1.00	Aromatic
24	6.921	1.00	Aromatic
25	6.901	1.00	Aromatic
26	6.881	1.00	Aromatic
27	6.861	1.00	Aromatic
28	6.841	1.00	Aromatic
29	6.821	1.00	Aromatic
30	6.801	1.00	Aromatic
31	6.781	1.00	Aromatic
32	6.761	1.00	Aromatic
33	6.741	1.00	Aromatic
34	6.721	1.00	Aromatic
35	6.701	1.00	Aromatic
36	6.681	1.00	Aromatic
37	6.661	1.00	Aromatic
38	6.641	1.00	Aromatic
39	6.621	1.00	Aromatic
40	6.601	1.00	Aromatic
41	6.581	1.00	Aromatic
42	6.561	1.00	Aromatic
43	6.541	1.00	Aromatic
44	6.521	1.00	Aromatic
45	6.501	1.00	Aromatic
46	6.481	1.00	Aromatic
47	6.461	1.00	Aromatic
48	6.441	1.00	Aromatic
49	6.421	1.00	Aromatic
50	6.401	1.00	Aromatic
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52	6.361	1.00	Aromatic
53	6.341	1.00	Aromatic
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65	6.101	1.00	Aromatic
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68	6.041	1.00	Aromatic
69	6.021	1.00	Aromatic
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74	5.921	1.00	Aromatic
75	5.901	1.00	Aromatic
76	5.881	1.00	Aromatic
77	5.861	1.00	Aromatic
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81	5.781	1.00	Aromatic
82	5.761	1.00	Aromatic
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98	5.441	1.00	Aromatic
99	5.421	1.00	Aromatic
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143	4.541	1.00	Aromatic
144	4.521	1.00	Aromatic
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194	3.521	1.00	Aromatic
195	3.501	1.00	Aromatic
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197	3.461	1.00	Aromatic
198	3.441	1.00	Aromatic
199	3.421	1.00	Aromatic
200	3.401	1.00	Aromatic
201	3.381	1.00	Aromatic
202	3.361	1.00	Aromatic
203	3.341	1.00	Aromatic
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205	3.301	1.00	Aromatic
206	3.281	1.00	Aromatic
207	3.261	1.00	Aromatic
208	3.241	1.00	Aromatic
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211	3.181	1.00	Aromatic
212	3.161	1.00	Aromatic
213	3.141	1.00	Aromatic
214	3.121	1.00	Aromatic
215	3.101	1.00	Aromatic
216	3.081	1.00	Aromatic
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218	3.041	1.00	Aromatic
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222	2.961	1.00	Aromatic
223	2.941	1.00	Aromatic
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242	2.561	1.00	Aromatic
243	2.541	1.00	Aromatic
244	2.521	1.00	Aromatic
245	2.501	1.00	Aromatic
246	2.481	1.00	Aromatic
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248	2.441	1.00	Aromatic
249	2.421	1.00	Aromatic
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251	2.381	1.00	Aromatic
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253	2.341	1.00	Aromatic
254	2.321	1.00	Aromatic
255	2.301	1.00	Aromatic
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281	1.781	1.00	Aromatic
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284	1.721	1.00	Aromatic
285	1.701	1.00	Aromatic
286	1.681	1.00	Aromatic
287	1.661	1.00	Aromatic
288	1.641	1.00	Aromatic
289	1.621	1.00	Aromatic
290	1.601	1.00	Aromatic
291	1.581	1.00	Aromatic
292	1.561	1.00	Aromatic
293	1.541	1.00	Aromatic
294	1.521	1.00	Aromatic
295	1.501	1.00	Aromatic
296	1.481	1.00	Aromatic
297	1.461	1.00	Aromatic
298	1.441	1.00	Aromatic
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316	1.081	1.00	Aromatic
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319	1.021	1.00	Aromatic
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321	0.981	1.00	Aromatic
322	0.961	1.00	Aromatic
323	0.941	1.00	Aromatic
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325	0.901	1.00	Aromatic
326	0.881	1.00	A

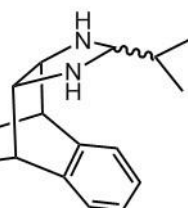
1H NMR (500 MHz, CDCl₃) of 6a,b

#	Chemical Shift (ppm)	Integration
1	7.381	0.28
2	7.361	0.28
3	7.341	0.28
4	7.321	0.28
5	7.301	0.28
6	7.281	0.28
7	7.261	0.28
8	7.241	0.28
9	7.221	0.28
10	7.201	0.28
11	7.181	0.28
12	7.161	0.28
13	7.141	0.28
14	7.121	0.28
15	7.101	0.28
16	7.081	0.28
17	7.061	0.28
18	7.041	0.28
19	7.021	0.28
20	7.001	0.28
21	6.981	0.28
22	6.961	0.28
23	6.941	0.28
24	6.921	0.28
25	6.901	0.28
26	6.881	0.28
27	6.861	0.28
28	6.841	0.28
29	6.821	0.28
30	6.801	0.28
31	6.781	0.28
32	6.761	0.28
33	6.741	0.28
34	6.721	0.28
35	6.701	0.28
36	6.681	0.28
37	6.661	0.28
38	6.641	0.28
39	6.621	0.28
40	6.601	0.28
41	6.581	0.28
42	6.561	0.28
43	6.541	0.28
44	6.521	0.28
45	6.501	0.28
46	6.481	0.28
47	6.461	0.28
48	6.441	0.28
49	6.421	0.28
50	6.401	0.28
51	6.381	0.28
52	6.361	0.28
53	6.341	0.28
54	6.321	0.28
55	6.301	0.28
56	6.281	0.28
57	6.261	0.28
58	6.241	0.28
59	6.221	0.28
60	6.201	0.28
61	6.181	0.28
62	6.161	0.28
63	6.141	0.28
64	6.121	0.28
65	6.101	0.28
66	6.081	0.28
67	6.061	0.28
68	6.041	0.28
69	6.021	0.28
70	6.001	0.28
71	5.981	0.28
72	5.961	0.28
73	5.941	0.28
74	5.921	0.28
75	5.901	0.28
76	5.881	0.28
77	5.861	0.28
78	5.841	0.28
79	5.821	0.28
80	5.801	0.28
81	5.781	0.28
82	5.761	0.28
83	5.741	0.28
84	5.721	0.28
85	5.701	0.28
86	5.681	0.28
87	5.661	0.28
88	5.641	0.28
89	5.621	0.28
90	5.601	0.28
91	5.581	0.28
92	5.561	0.28
93	5.541	0.28
94	5.521	0.28
95	5.501	0.28
96	5.481	0.28
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98	5.441	0.28
99	5.421	0.28
100	5.401	0.28



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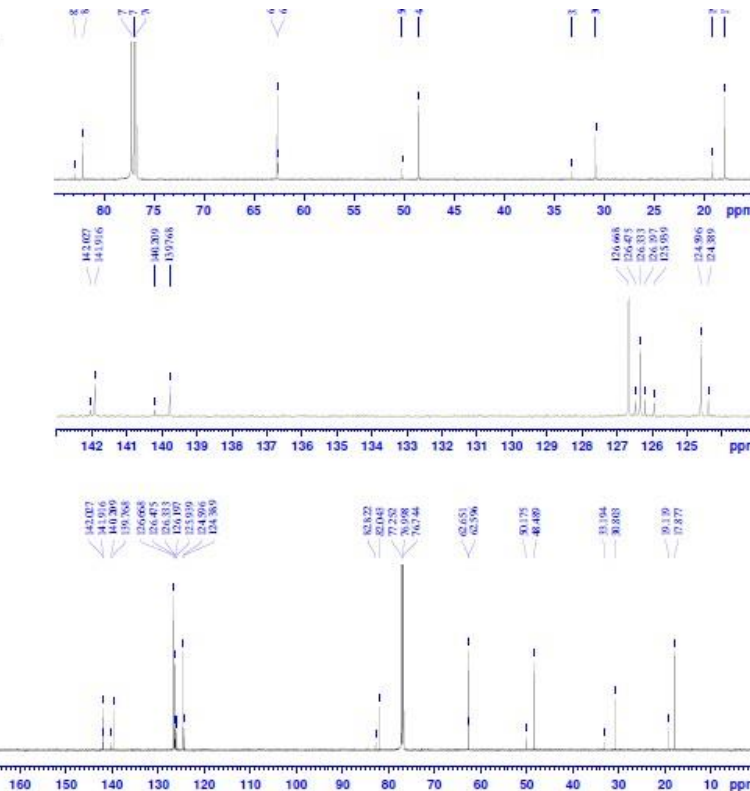
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PROCNO: 1
Date_: 20190701
Time: 11.14
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PULPROG: zgpg30
TD: 65536
SOLVENT: cdcl3
NS: 14
DS: 2
SWH: 10330.578 Hz
FIDRES: 0.157632 Hz
AQ: 3.1720407 sec
RG: 114
DM: 48.400 umm
DE: 6.00 umm
TE: 299.9 K
D1: 1.00000000 sec
TD0: 1



6a,b

13C NMR (126 MHz, CDCl₃) of 6a,b

#	Chemical Shift (ppm)	Integration
1	142.07	0.10
2	141.96	0.10
3	140.30	0.10
4	139.96	0.10
5	139.84	0.10
6	139.72	0.10
7	139.60	0.10
8	139.48	0.10
9	139.36	0.10
10	139.24	0.10
11	139.12	0.10
12	139.00	0.10
13	138.88	0.10
14	138.76	0.10
15	138.64	0.10
16	138.52	0.10
17	138.40	0.10
18	138.28	0.10
19	138.16	0.10
20	138.04	0.10
21	137.92	0.10
22	137.80	0.10
23	137.68	0.10
24	137.56	0.10
25	137.44	0.10
26	137.32	0.10
27	137.20	0.10
28	137.08	0.10
29	136.96	0.10
30	136.84	0.10
31	136.72	0.10
32	136.60	0.10
33	136.48	0.10
34	136.36	0.10
35	136.24	0.10
36	136.12	0.10
37	136.00	0.10
38	135.88	0.10
39	135.76	0.10
40	135.64	0.10
41	135.52	0.10
42	135.40	0.10
43	135.28	0.10
44	135.16	0.10
45	135.04	0.10
46	134.92	0.10
47	134.80	0.10
48	134.68	0.10
49	134.56	0.10
50	134.44	0.10
51	134.32	0.10
52	134.20	0.10
53	134.08	0.10
54	133.96	0.10
55	133.84	0.10
56	133.72	0.10
57	133.60	0.10
58	133.48	0.10
59	133.36	0.10
60	133.24	0.10
61	133.12	0.10
62	133.00	0.10
63	132.88	0.10
64	132.76	0.10
65	132.64	0.10
66	132.52	0.10
67	132.40	0.10
68	132.28	0.10
69	132.16	0.10
70	132.04	0.10
71	131.92	0.10
72	131.80	0.10
73	131.68	0.10
74	131.56	0.10
75	131.44	0.10
76	131.32	0.10
77	131.20	0.10
78	131.08	0.10
79	130.96	0.10
80	130.84	0.10
81	130.72	0.10
82	130.60	0.10
83	130.48	0.10
84	130.36	0.10
85	130.24	0.10
86	130.12	0.10
87	130.00	0.10
88	129.88	0.10
89	129.76	0.10
90	129.64	0.10
91	129.52	0.10
92	129.40	0.10
93	129.28	0.10
94	129.16	0.10
95	129.04	0.10
96	128.92	0.10
97	128.80	0.10
98	128.68	0.10
99	128.56	0.10
100	128.44	0.10



BRUKER

NAME: 6a,b
EXPNO: 1
PROCNO: 1
Date_: 20190702
Time: 6.54
INSTRUM: spect
PROBHD: 5 mm DUL 13C-1
PULPROG: zgpg30
TD: 65536
SOLVENT: cdcl3
NS: 14
DS: 2
SWH: 32679.738 Hz
FIDRES: 0.498653 Hz
AQ: 1.0027643 sec
RG: 14384
DM: 15.300 umm
DE: 6.50 umm
TE: 300.0 K
D1: 2.00000000 sec
D11: 0.03000000 sec
TD0: 24

CHANNEL F1
NUC1: 13C
P1: 10.00 umm
PL1: 2.30 dB
PL1W: 73.95542485 W
SFO1: 125.7728799 MHz

CHANNEL F2
CPDPRG2: waltz16
NUC2: 1H
PCPD2: 75.00 umm
PL2: -1.50 dB
PL12: 12.48 dB
PL13: 14.00 dB
PL2W: 35.48133850 W
PL12W: 1.41905773 W
PL13W: 0.43095737 W
SFO2: 500.1320005 MHz
S1: 32748
SF: 125.7577921 MHz
WDM: 0
SDB: 0
LB: 1.00 Hz
GB: 0
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Fig. S5 ¹H and ¹³C NMR spectra for 6a,b.(500 MHz/126MHz, CDCl₃)

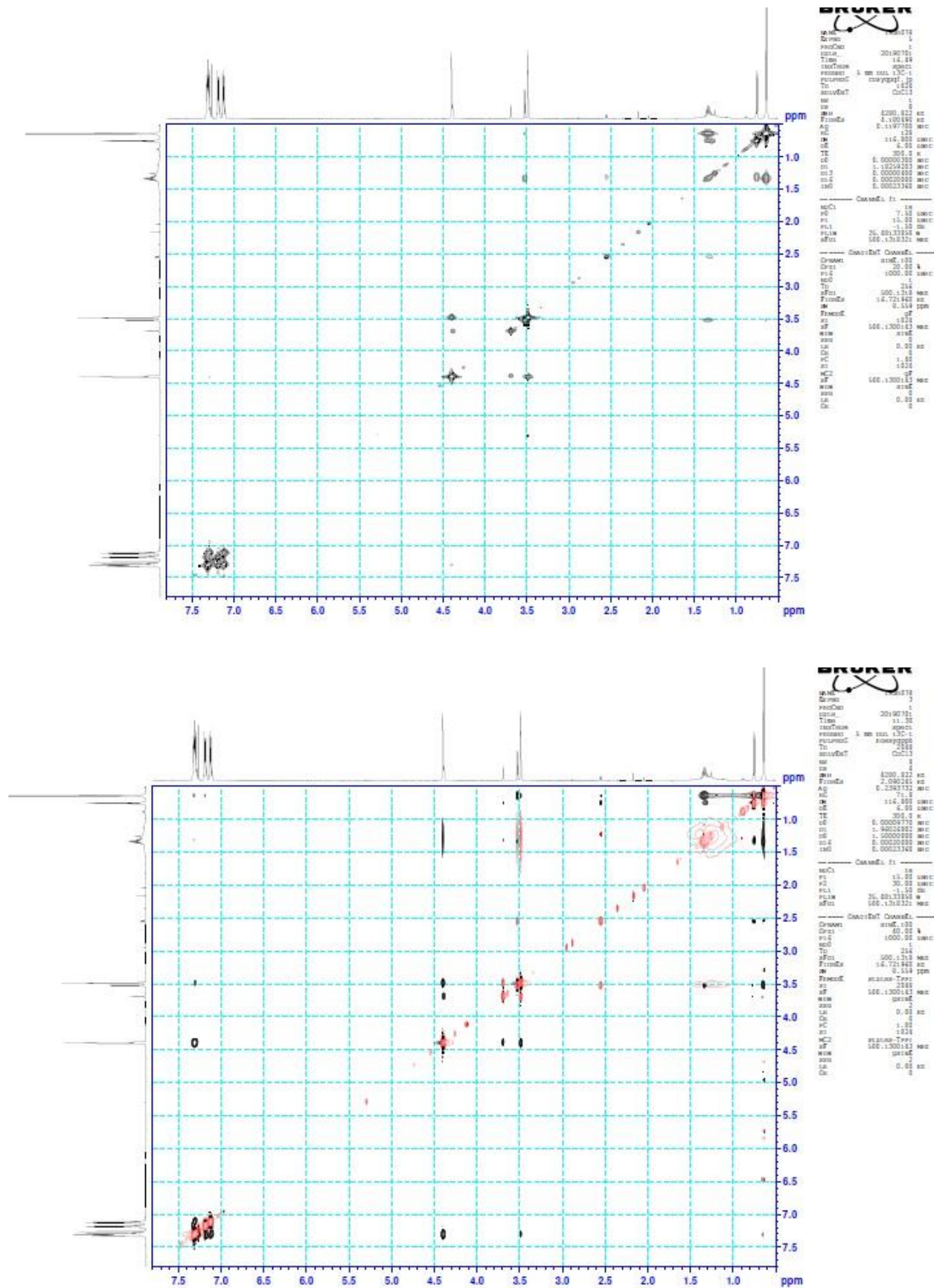
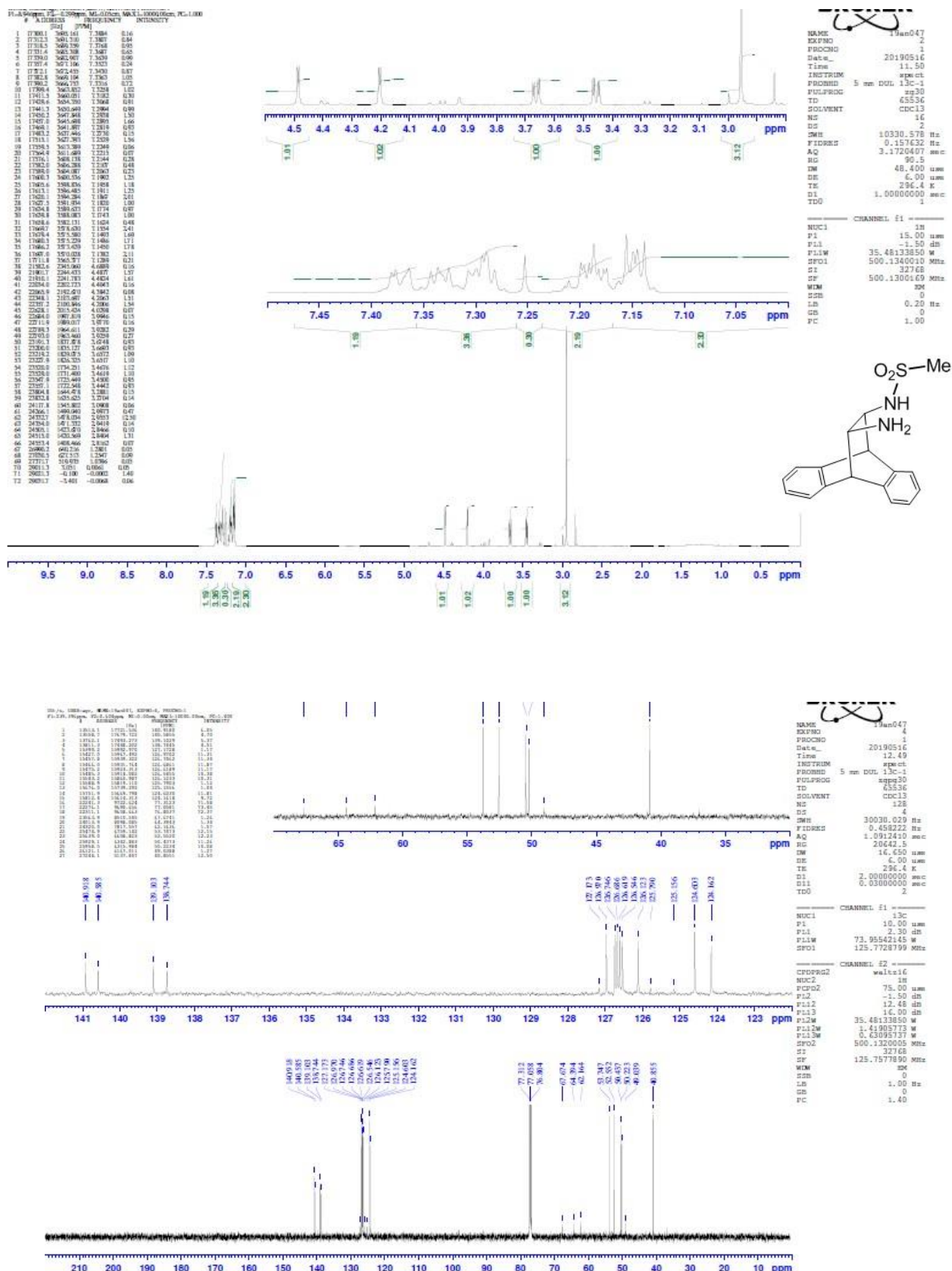


Fig. S6 COSY (above) and NOESY (below) spectra for **6a,b** (500 MHz, CDCl₃)



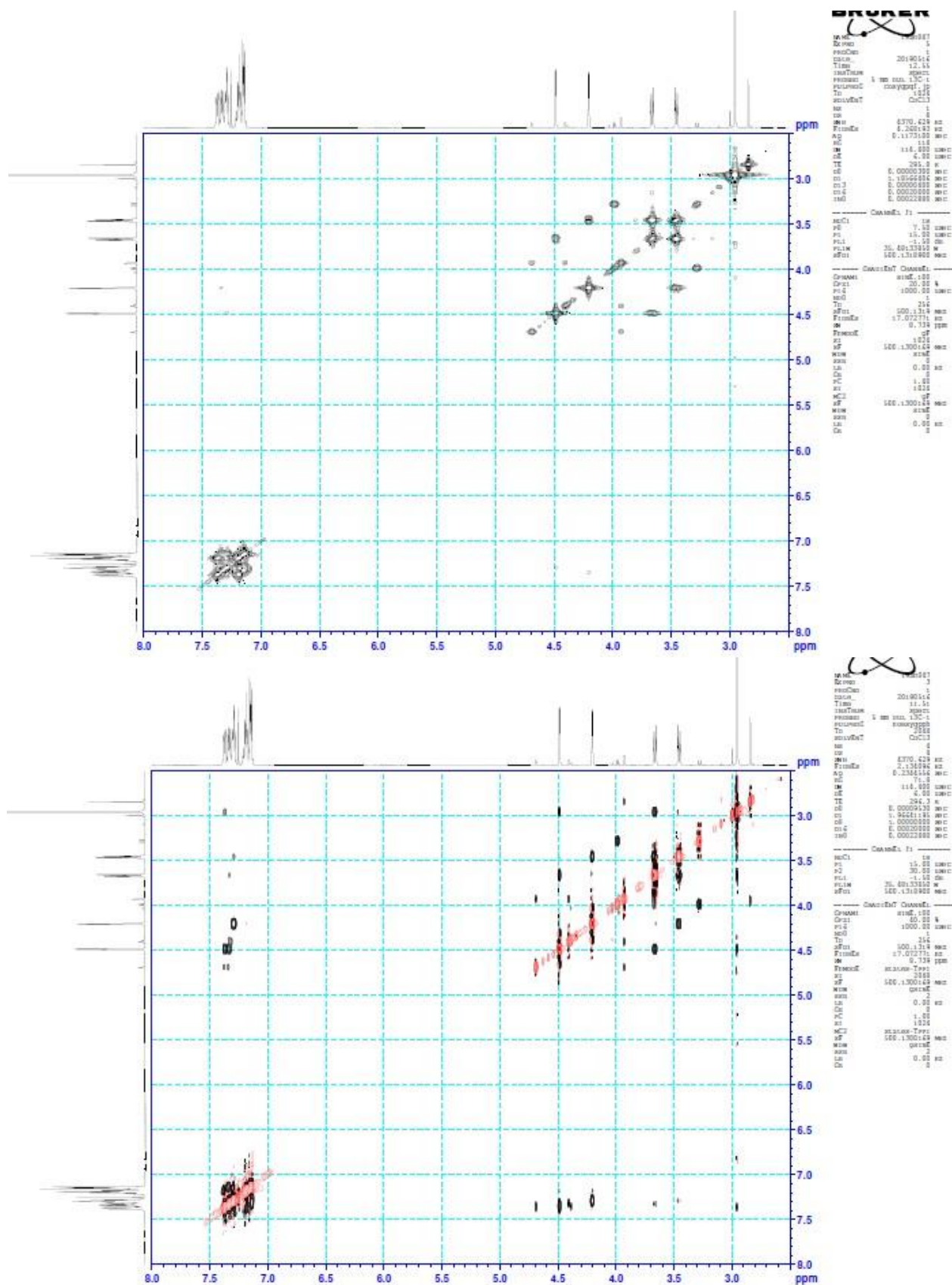


Fig. S9 COSY (above) and NOESY (below) spectra for **7** (500 MHz, CDCl₃)

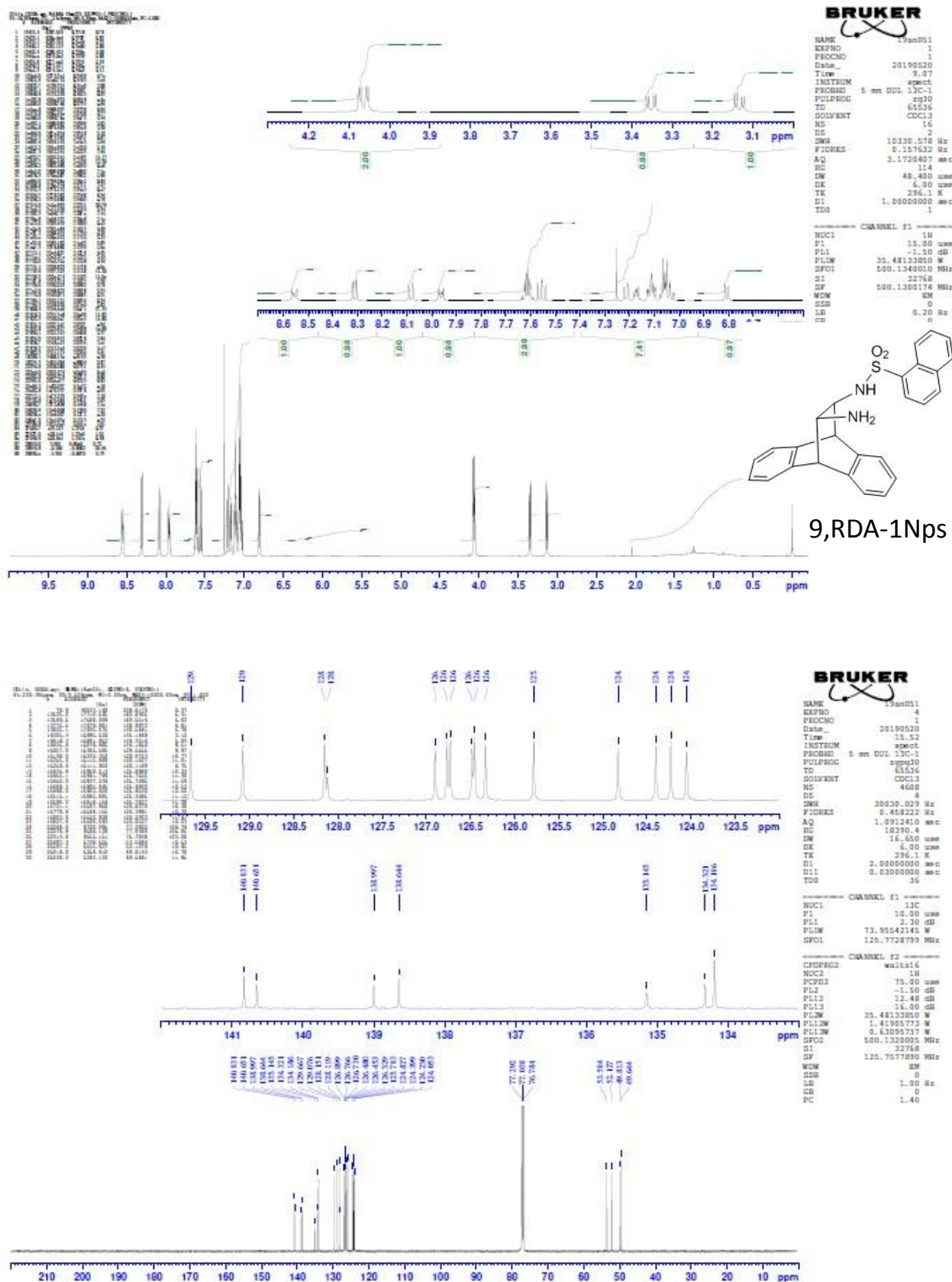


Fig. S12 ^1H and ^{13}C NMR spectra for **9**; RDA-1Nps. (500 MHz/126MHz, CDCl_3)

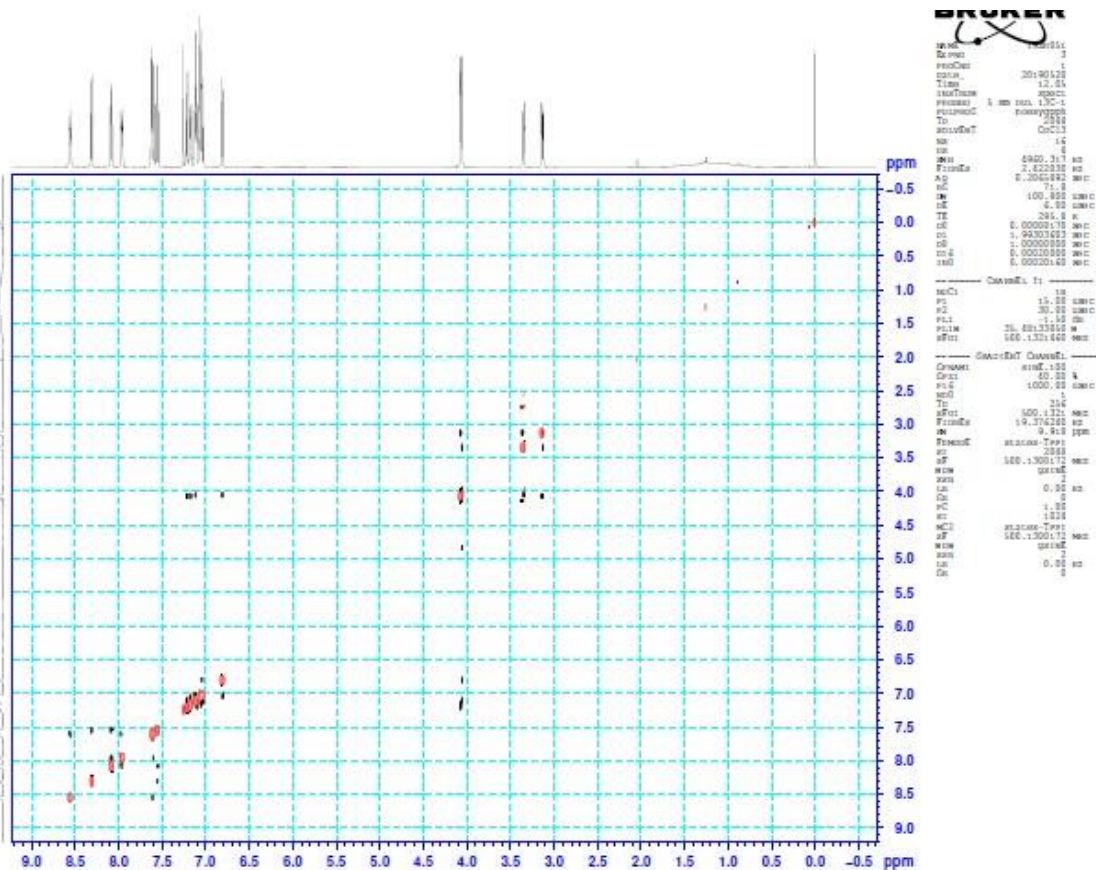


Fig. S13 COSY (above) and NOESY (below) spectra for **9** (500 MHz, CDCl₃)

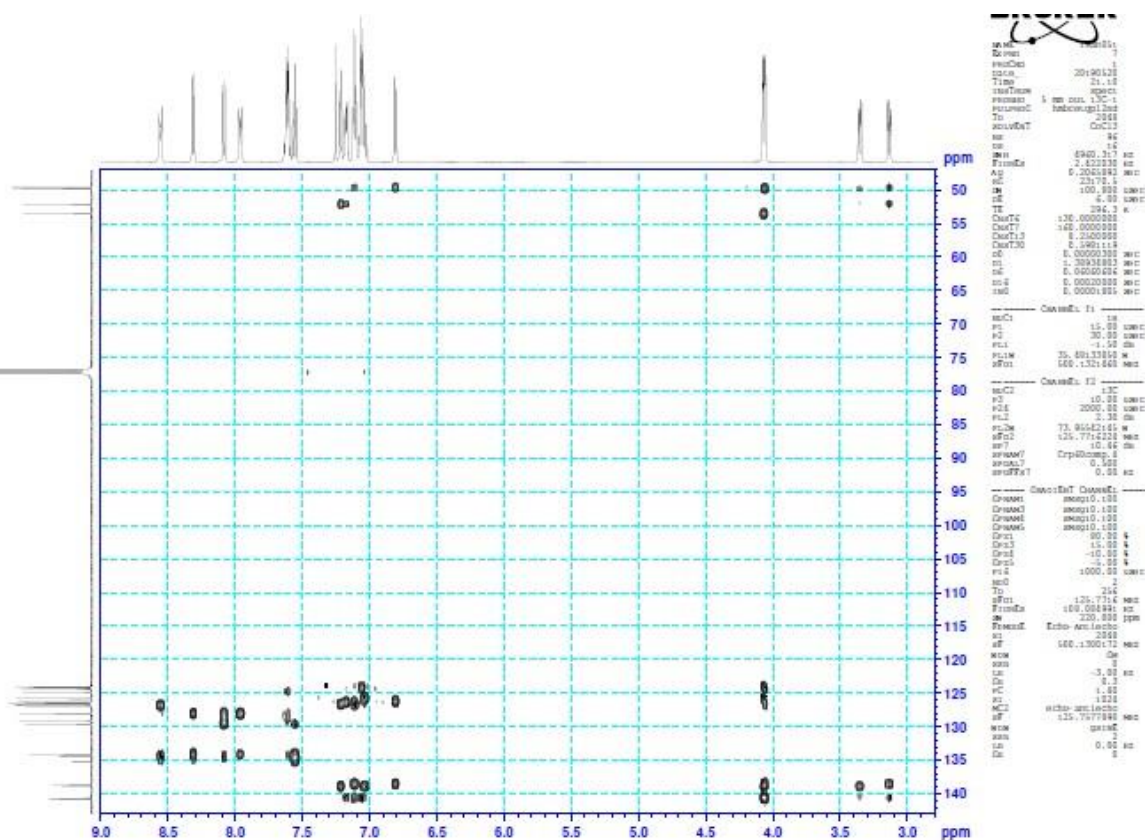
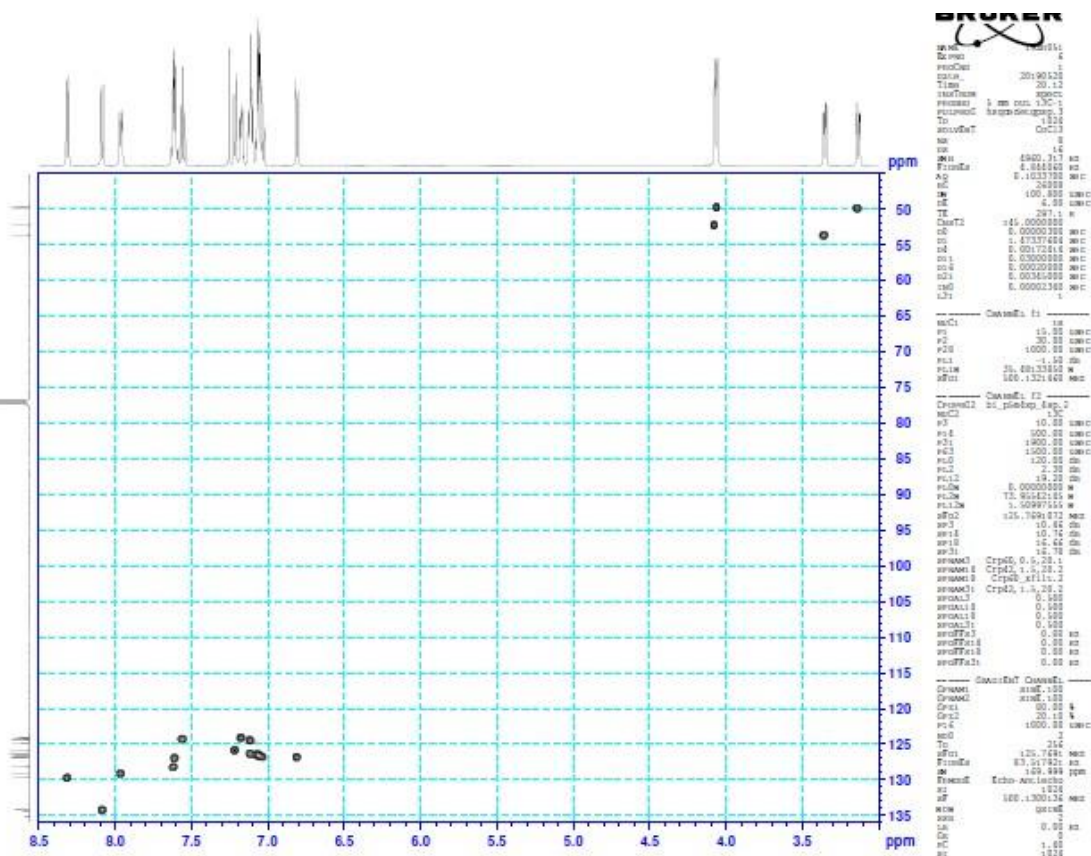
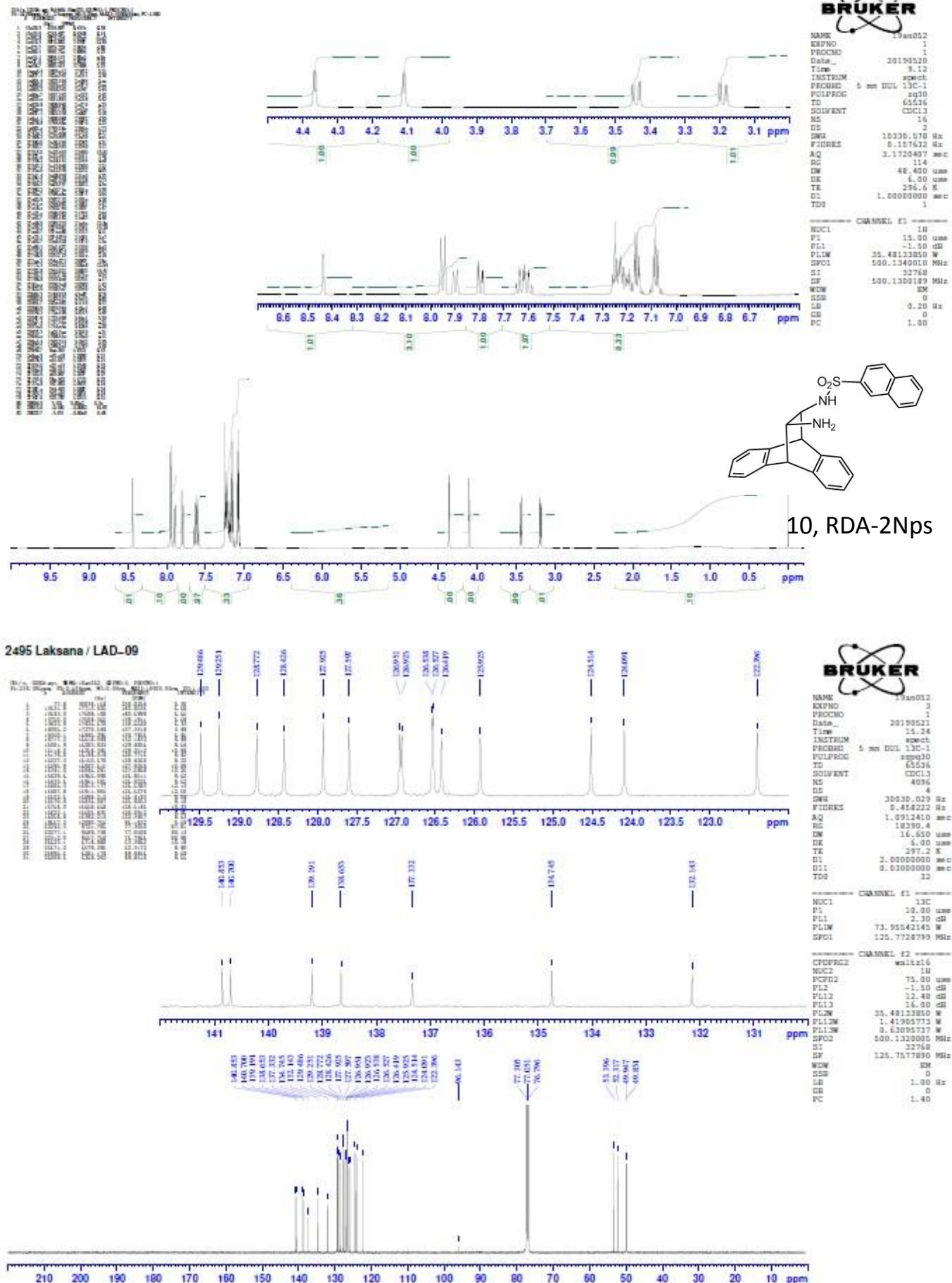


Fig. S14 HSQC (above) and HMBC (below) spectra for **9** (500 MHz/126MHz, CDCl₃)



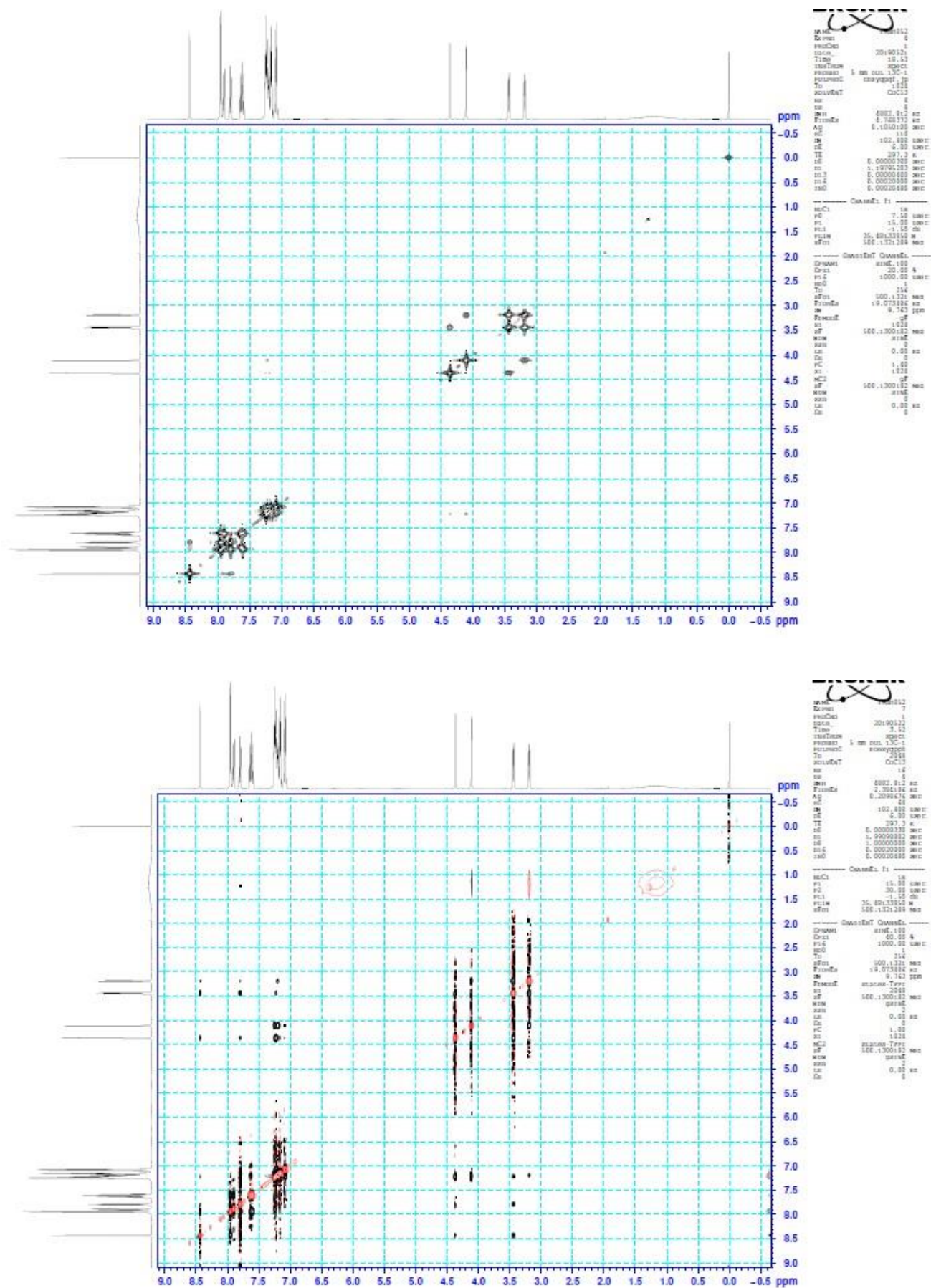


Fig. S16 COSY (above) and NOESY (below) spectra for **10** (500 MHz, CDCl₃)



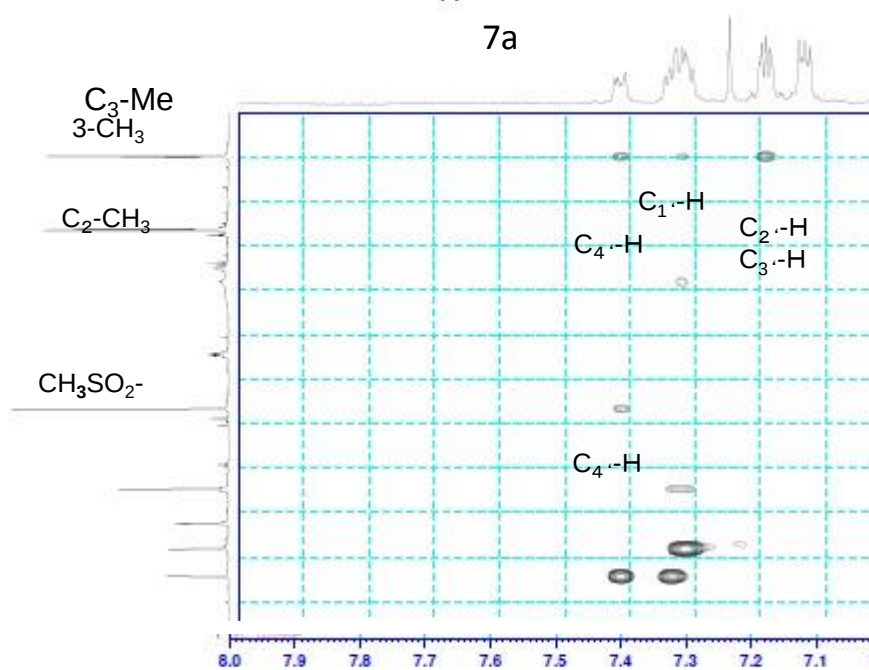
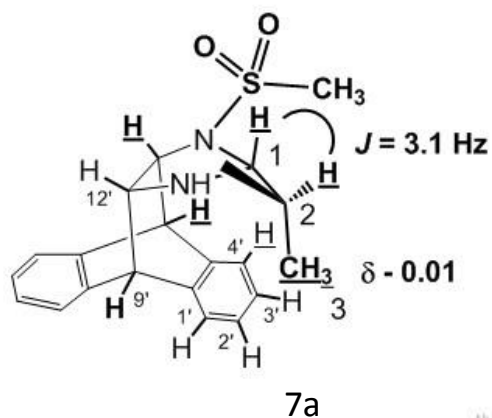
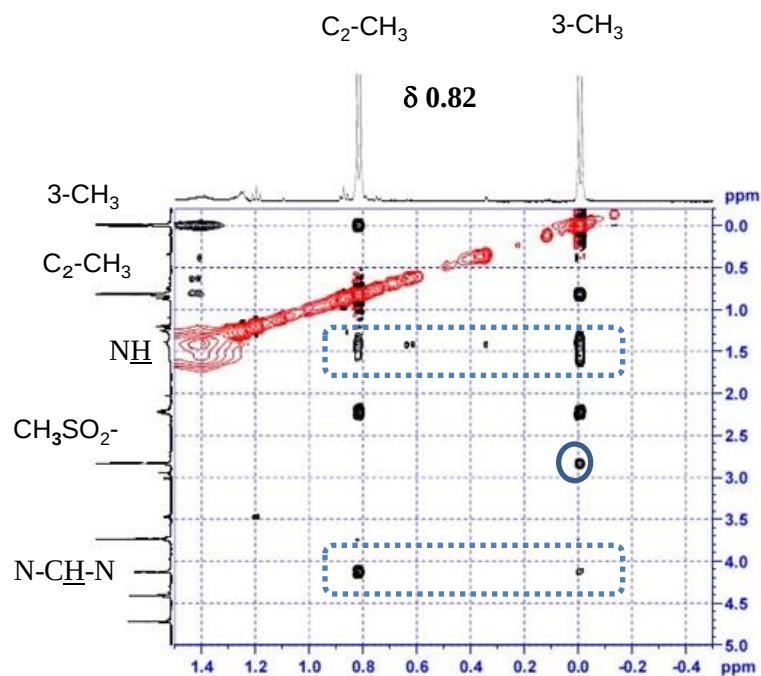


Fig. S21 Partial NOESY spectrum (500 MHz; CDCl₃) for **7a** and the conformation of **7a**.

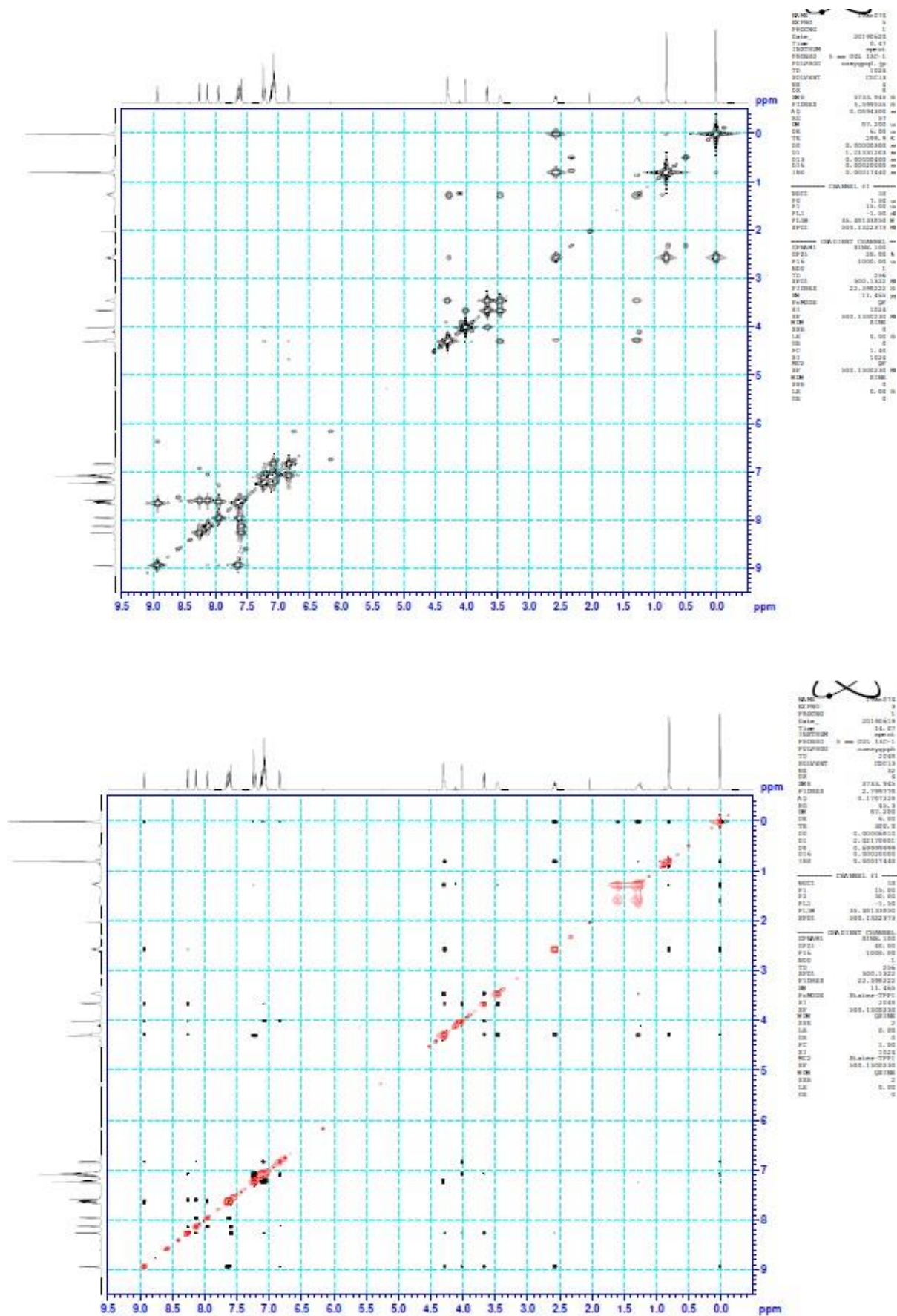


Fig. S23 COSY and NOESY spectra for **9a**. (500 MHz, CDCl_3)

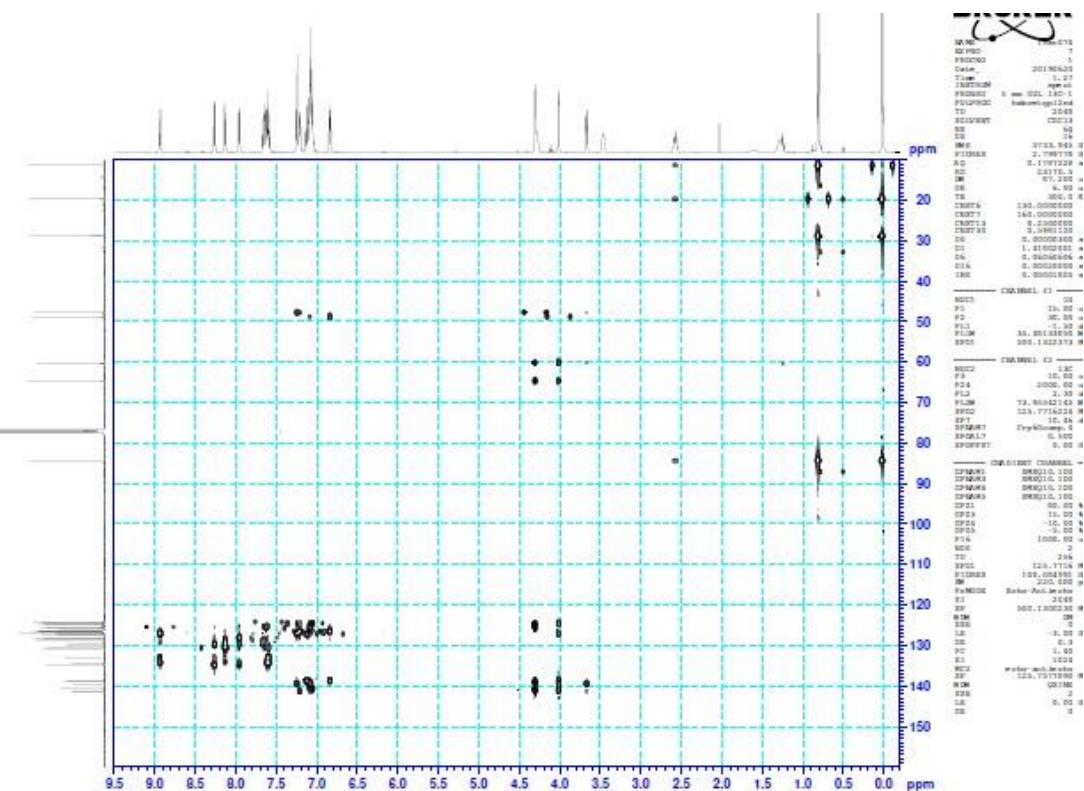
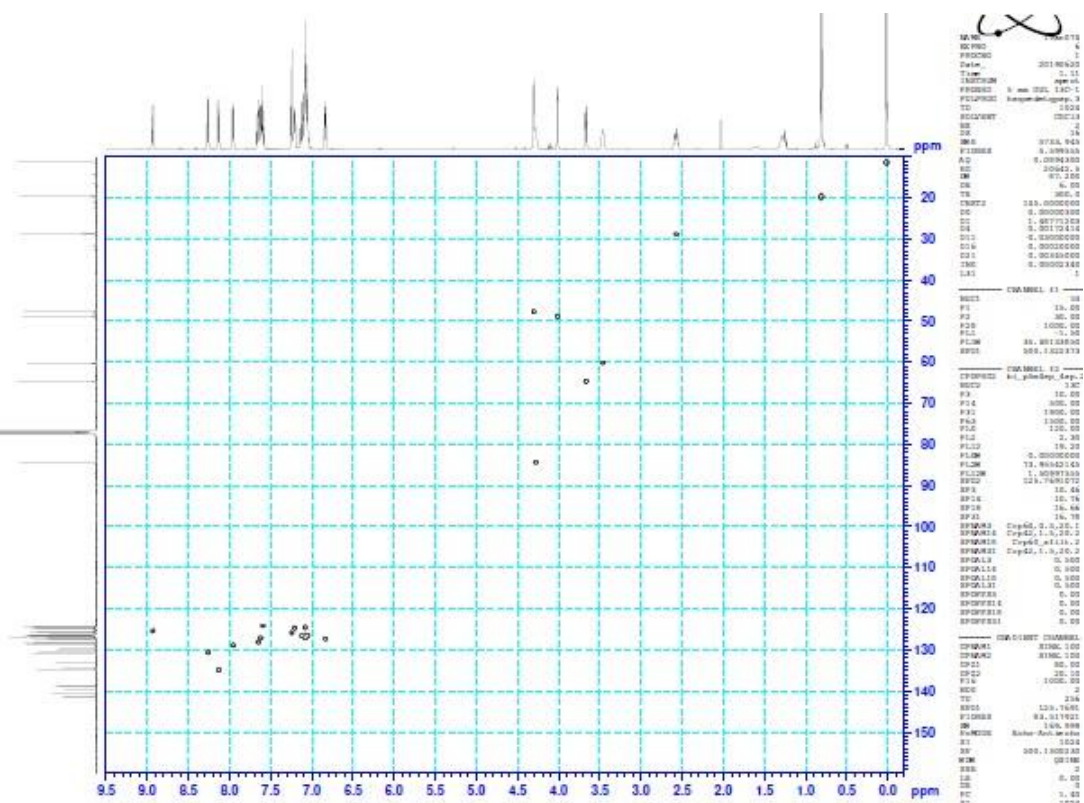


Fig. S24 HSQC and HMBC spectra for **9a**. (500 MHz/126MHz, CDCl₃)

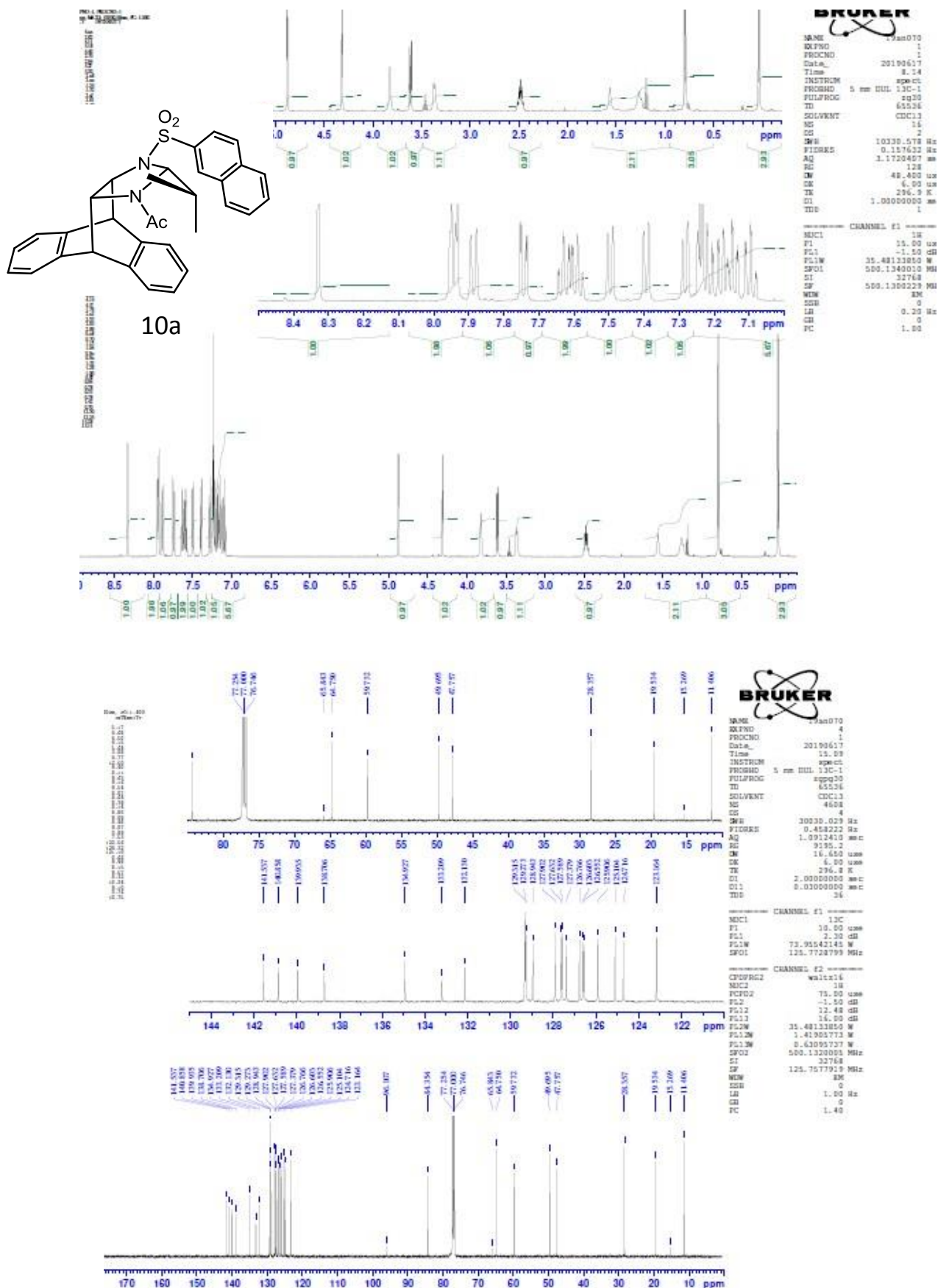


Fig. S25 ¹H and ¹³C NMR spectra for compound **10a**. (500 MHz/126MHz, CDCl₃)

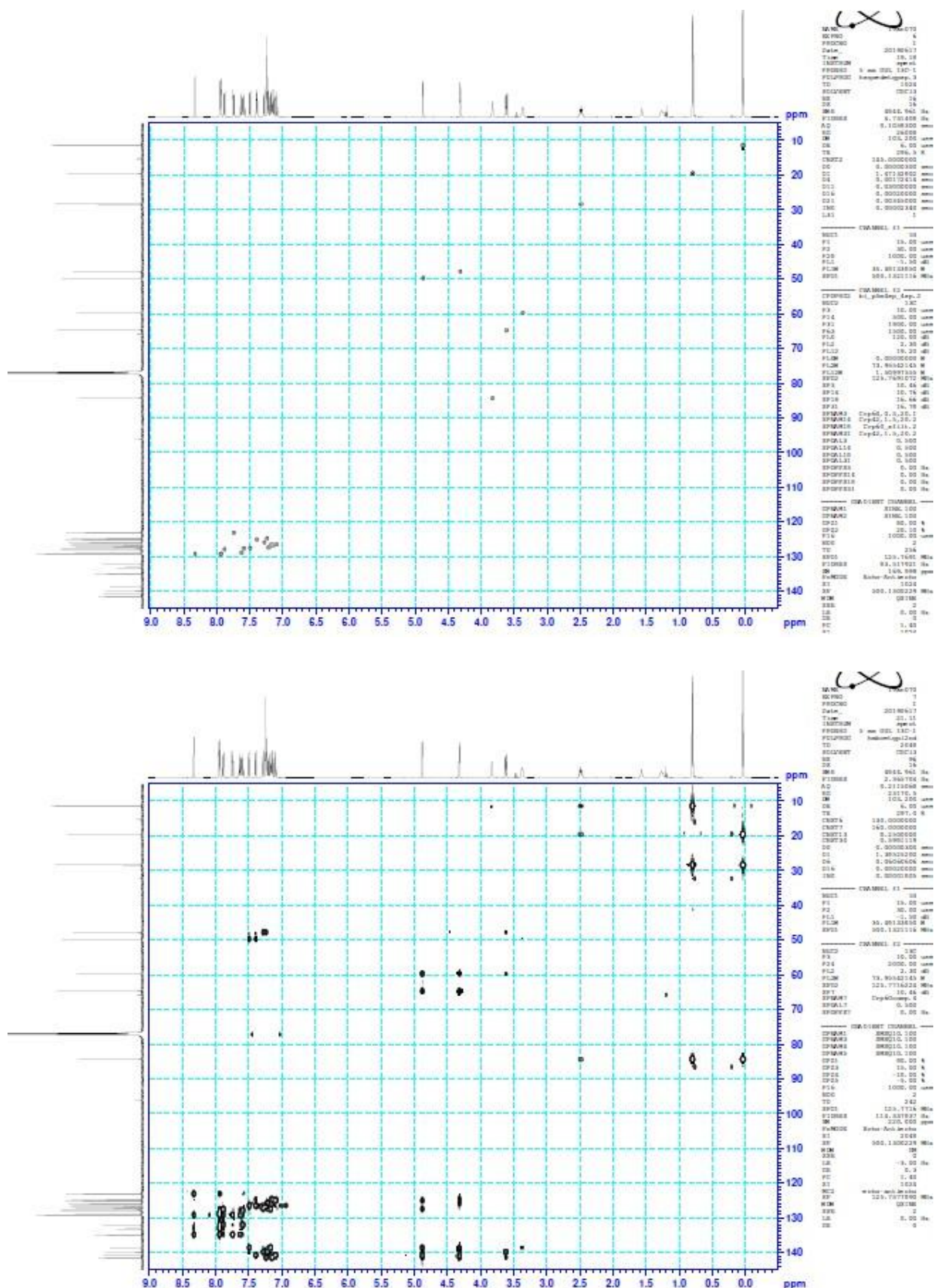


Fig. S27 HSQC (above) and HMQC (below) spectra for **10a**. (500 MHz/126MHz, CDCl₃)

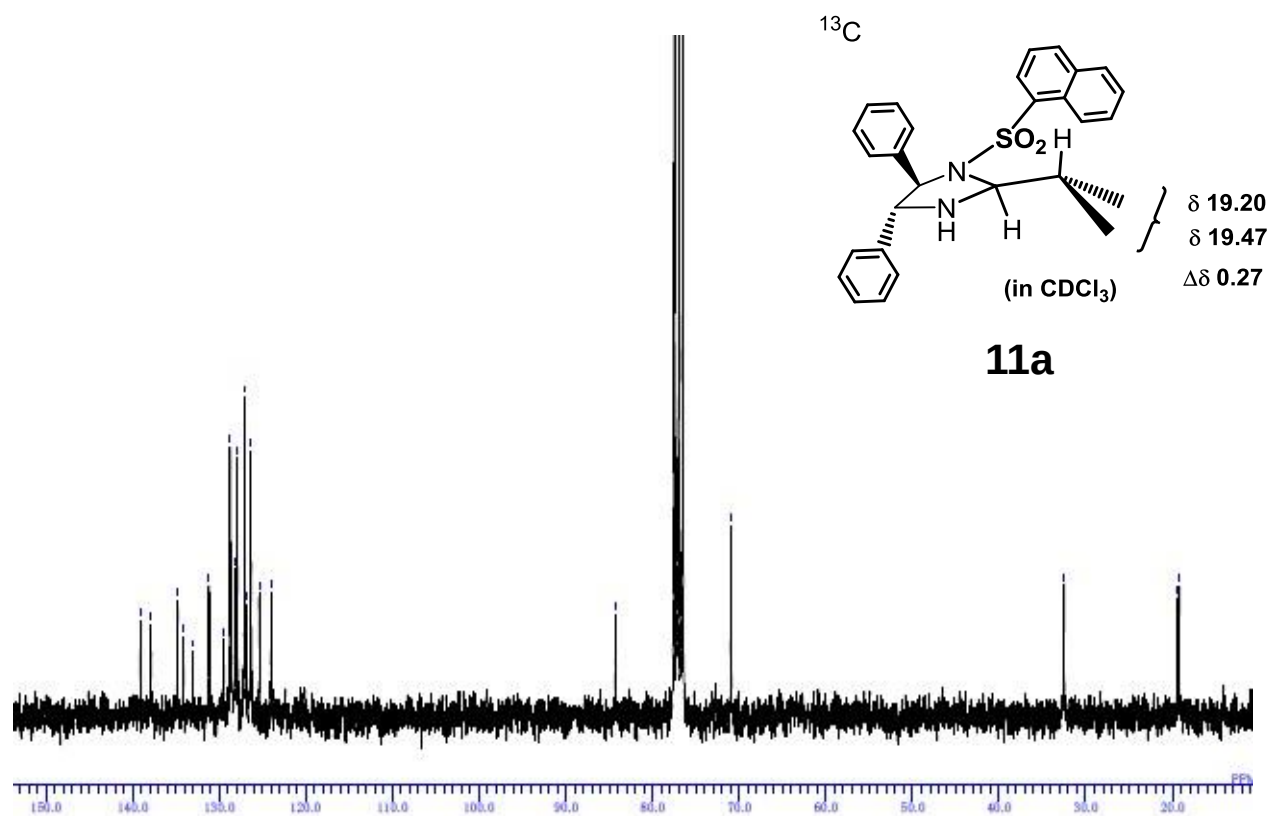
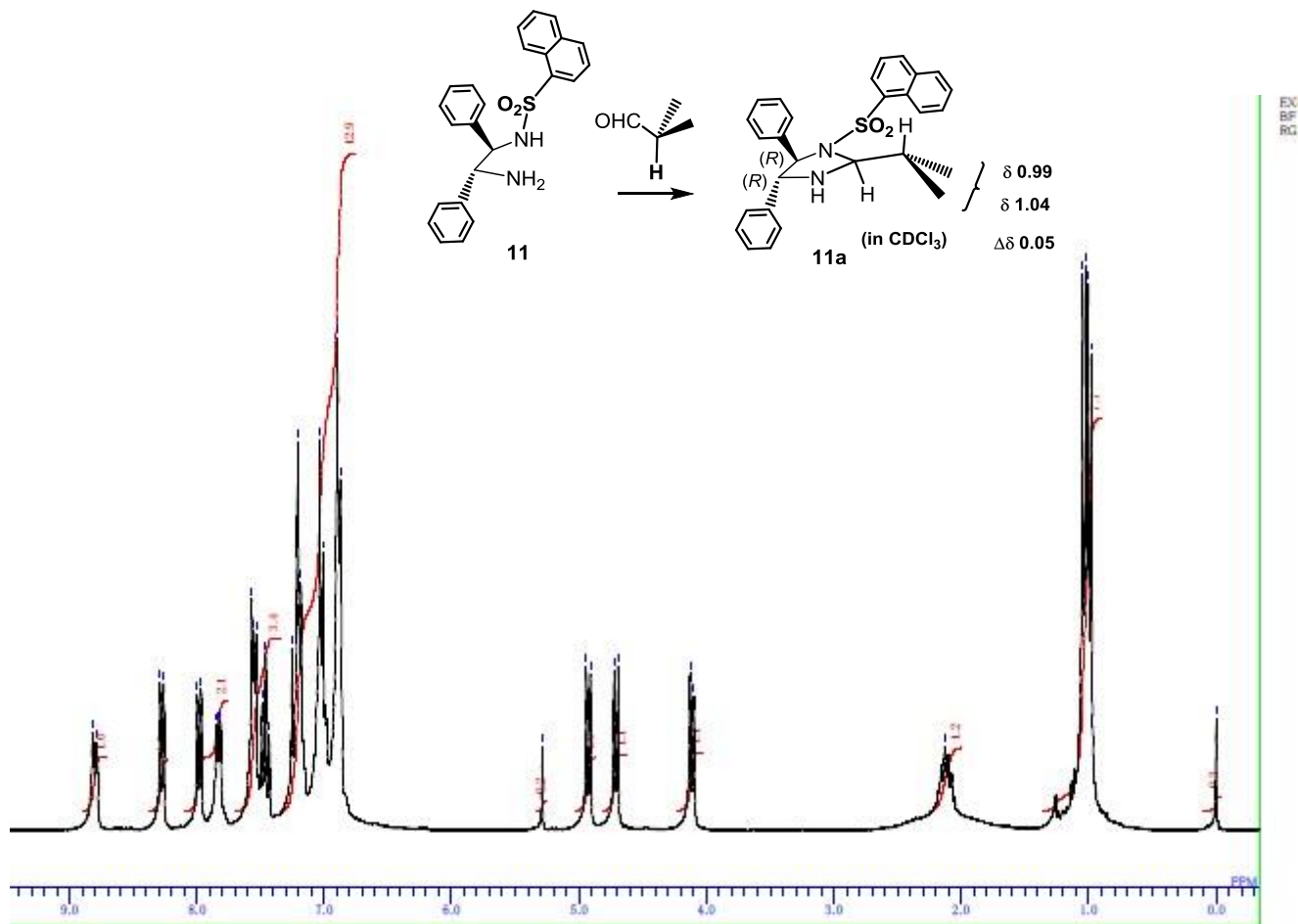


Fig. S28 ¹H NMR and ¹³C spectra for compound **11a** (270 MHz/67.5 MHz, CDCl₃)

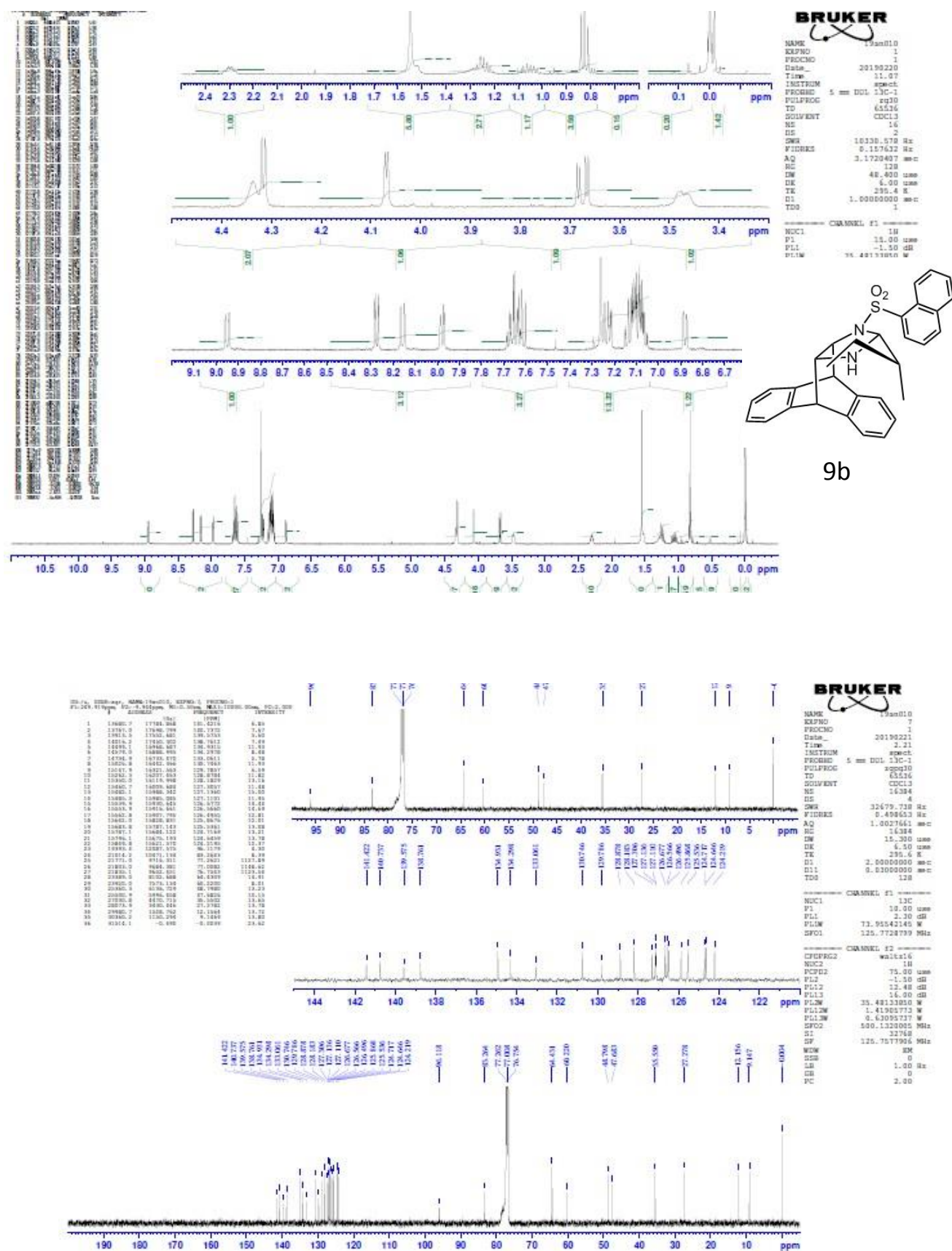


Fig. S29 ¹H and ¹³C NMR spectra for **9b**. (500 MHz/126MHz, CDCl₃)

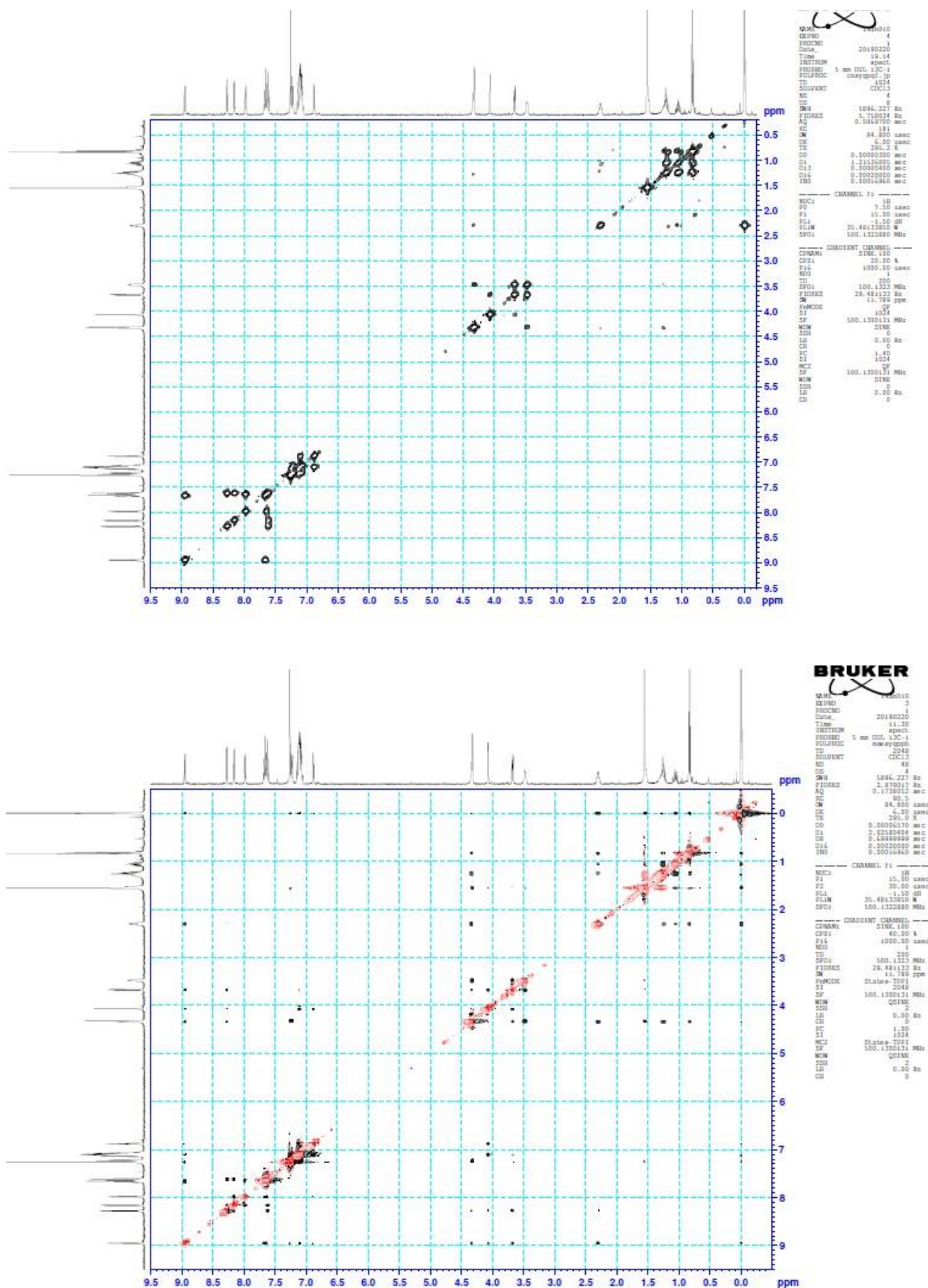


Fig. S30 COSY (above) and NOESY (below) spectra for **9b** (500 MHz, CDCl₃)

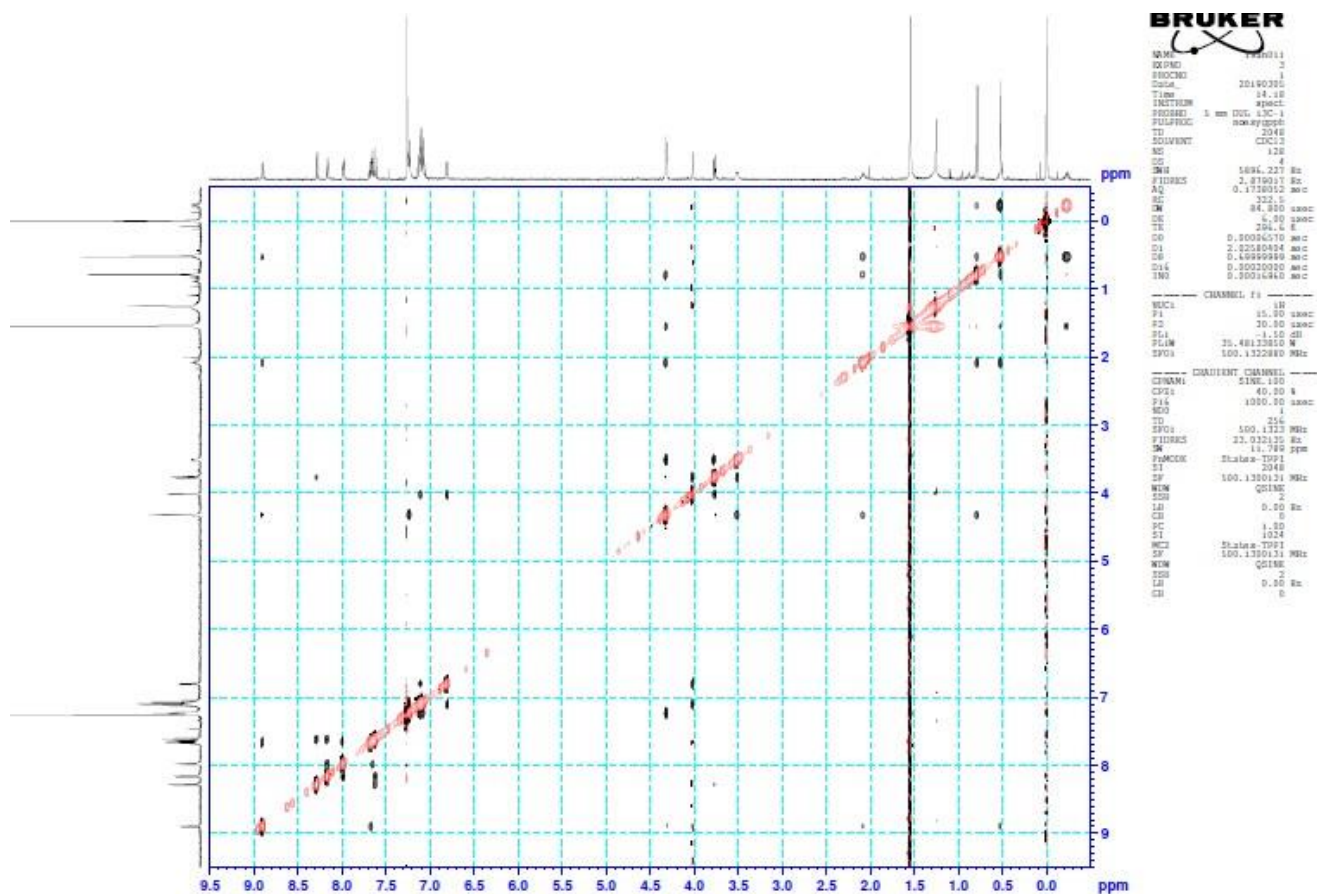
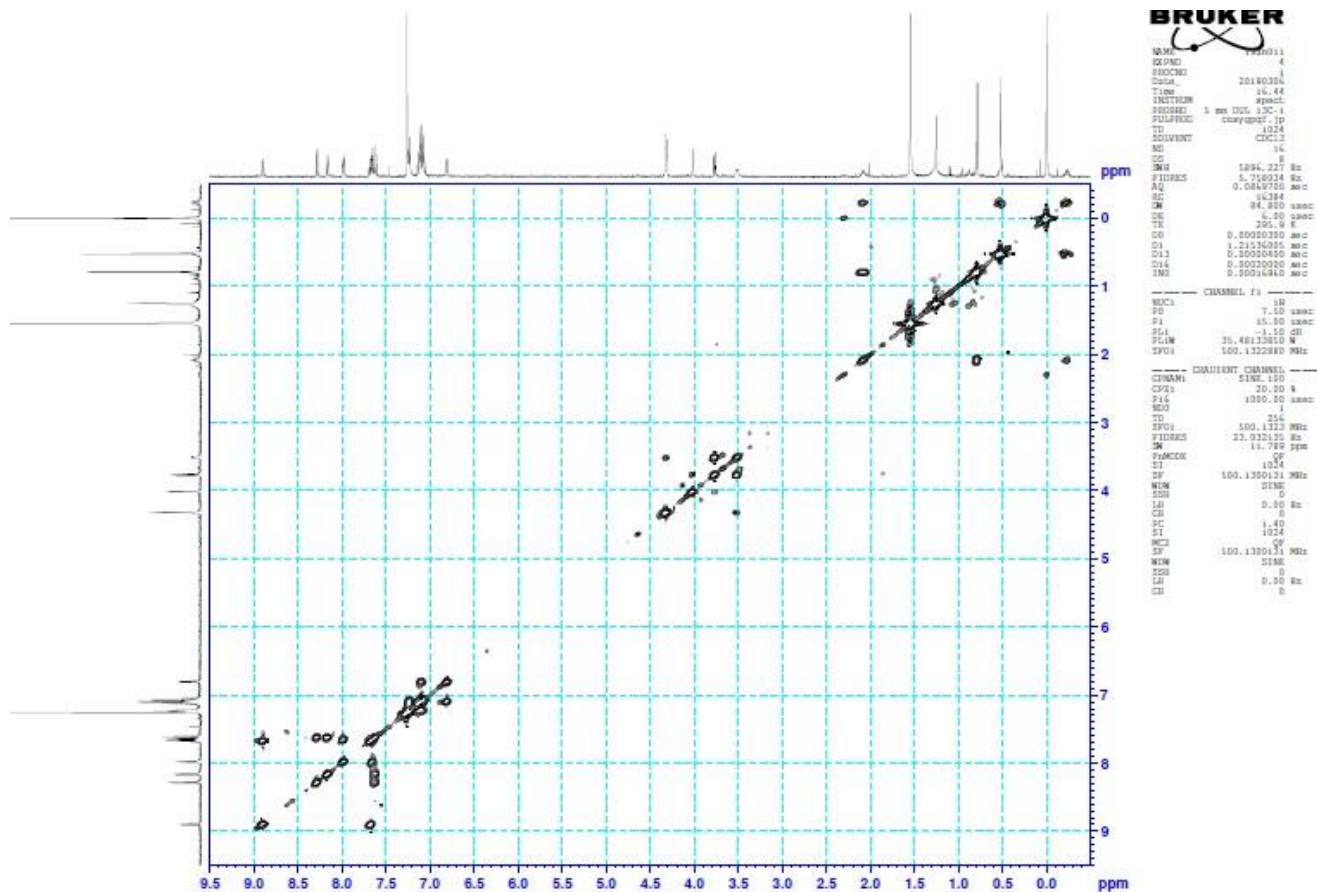


Fig. S33 COSY (above) and NOESY (below) spectra for **9c** (500 MHz, CDCl₃)

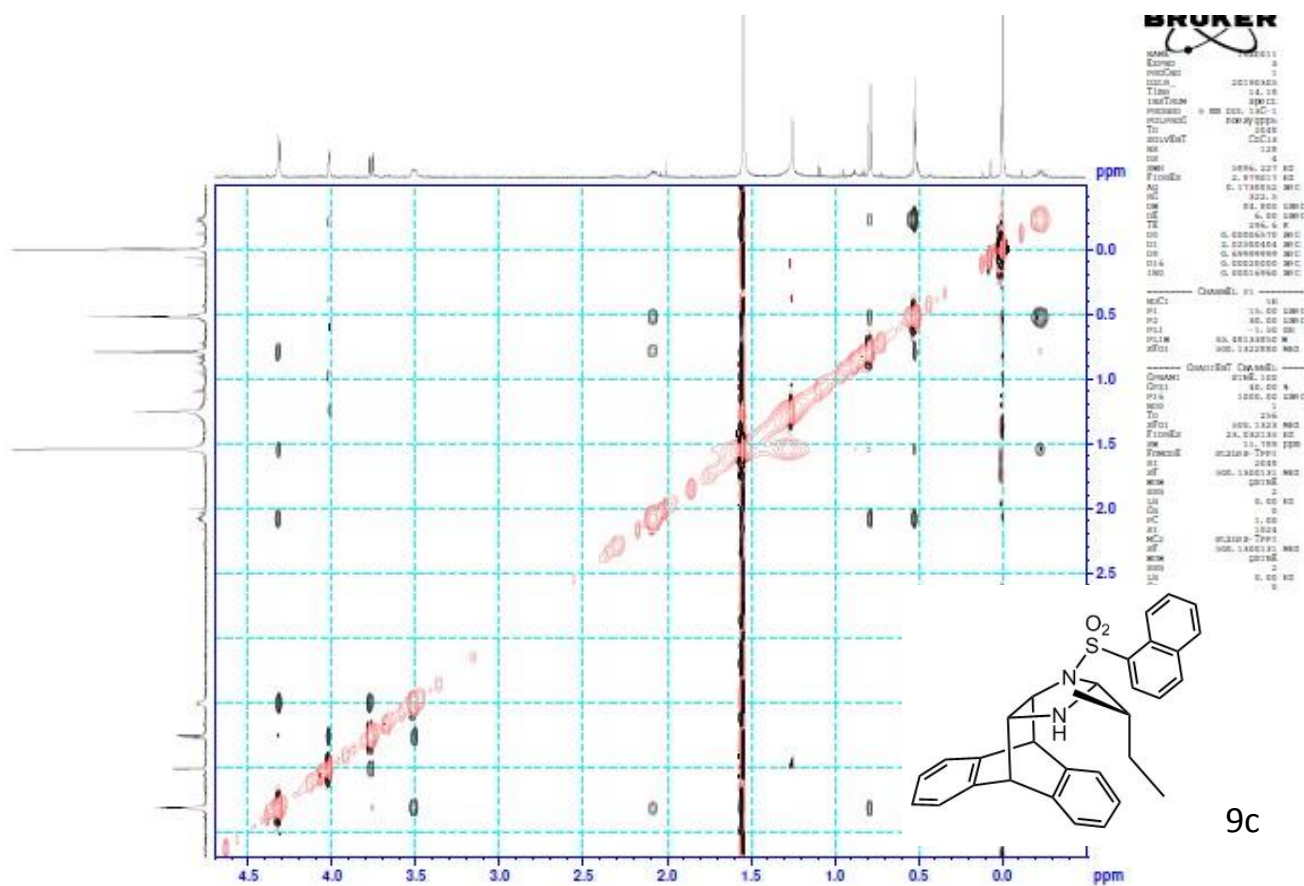
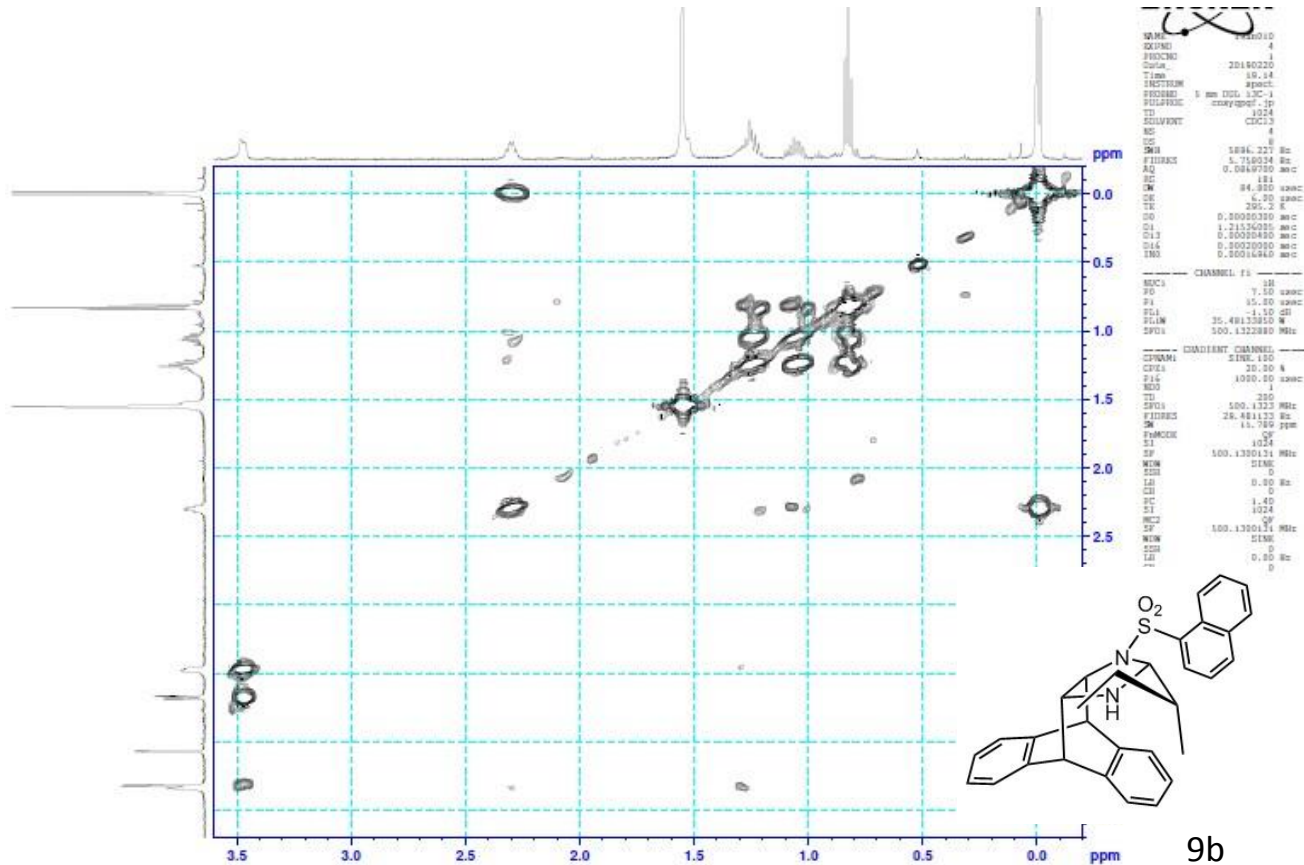


Fig. S35 Partial NOESY spectra for **9b** (up) and **9c** (down). (500 MHz, CDCl₃)

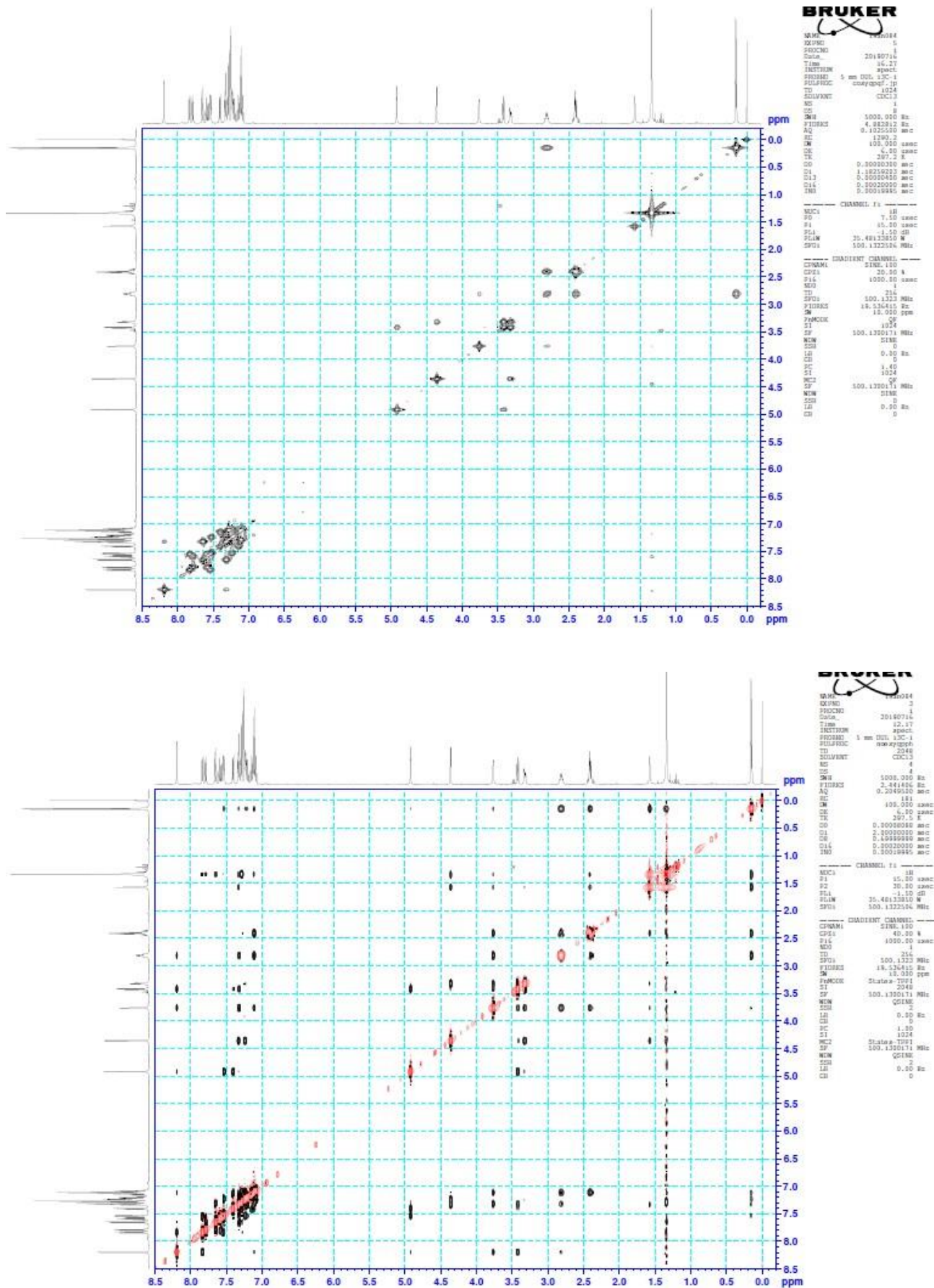


Fig. S37 COSY (above) and NOESY (below) spectra for **10b** (500 MHz, CDCl₃)

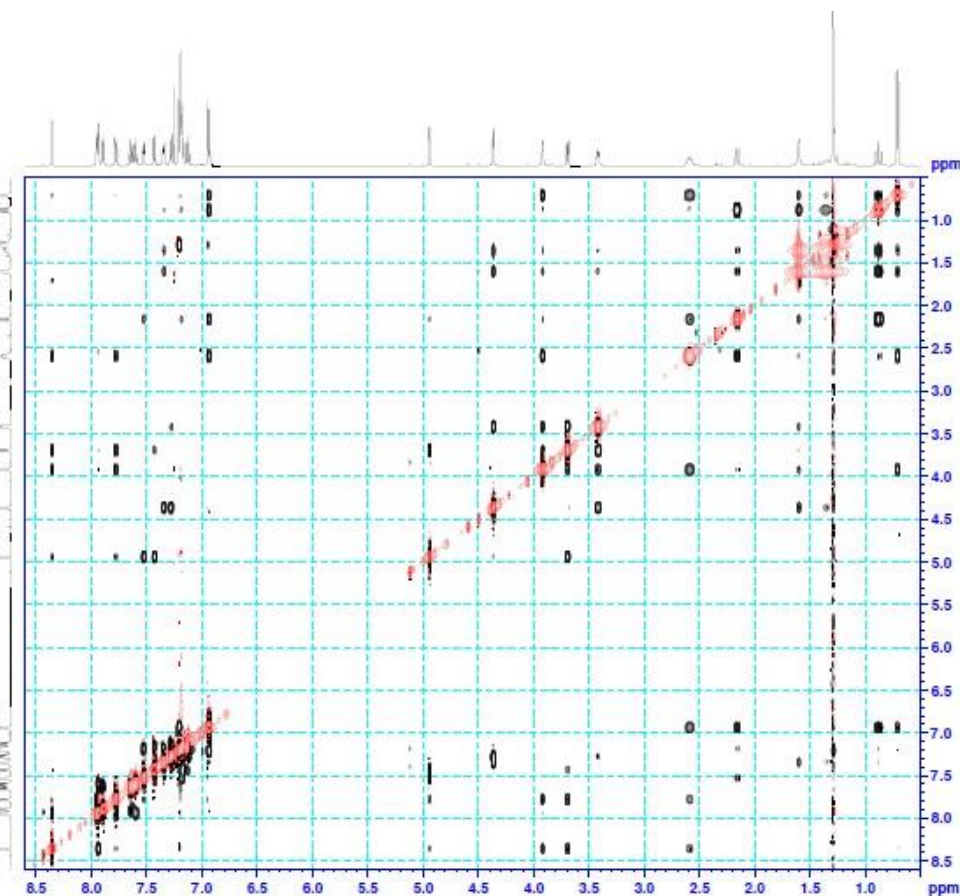
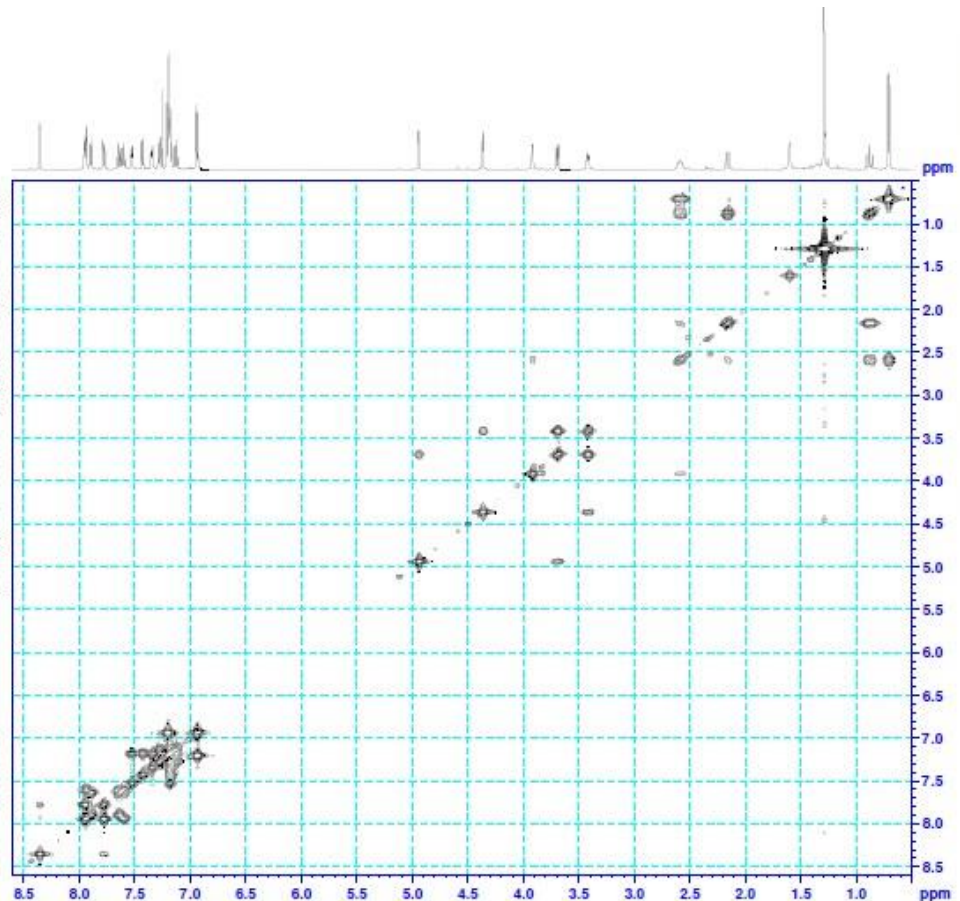


Fig. S40 COSY (above) and NOESY (below) spectra for **10c** (500 MHz, CDCl₃)

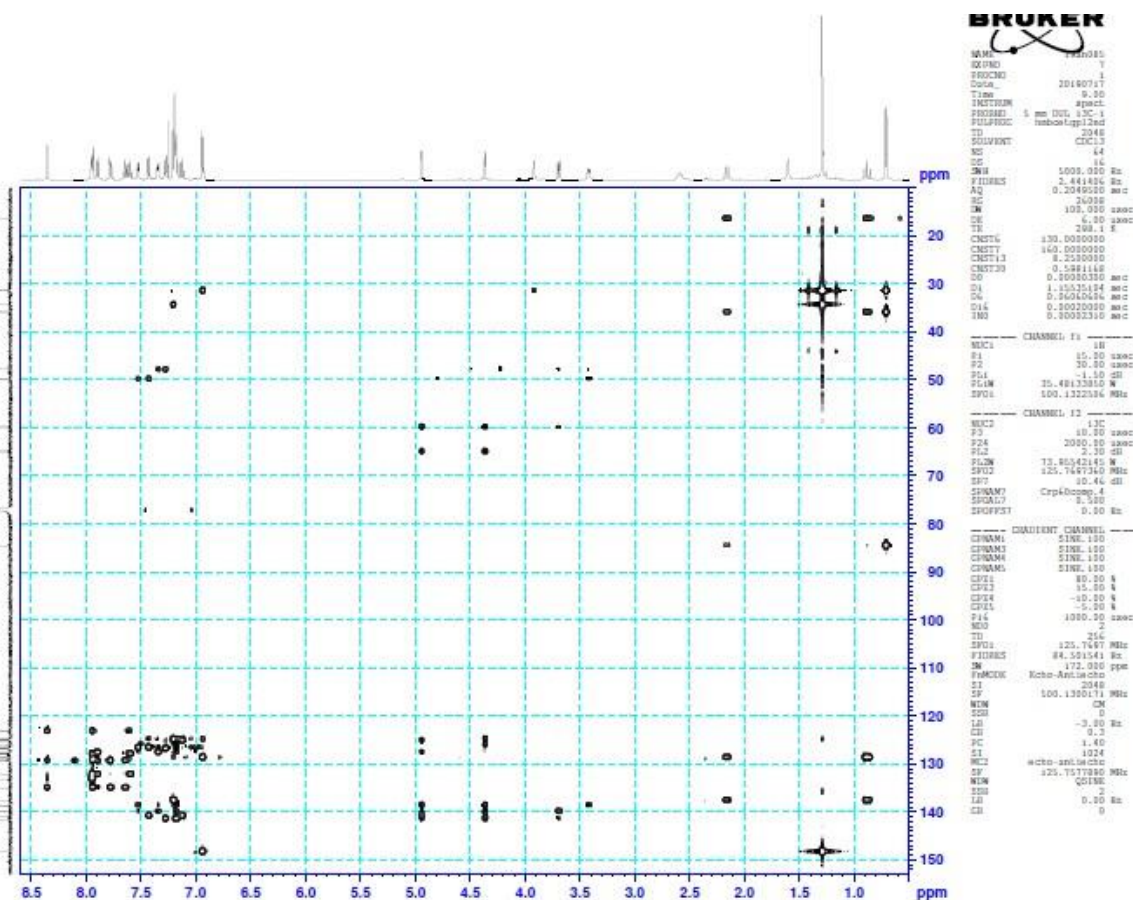
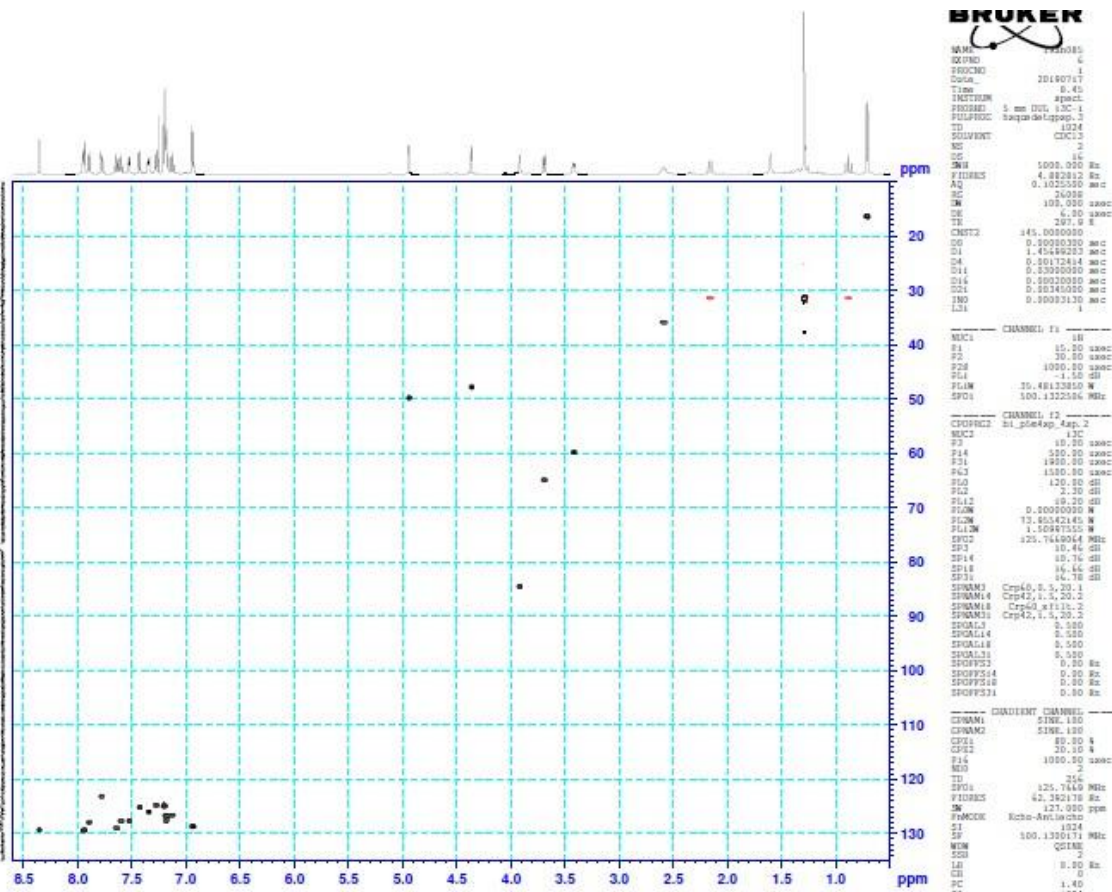


Fig. S41 HSQC (above) and HMQC (below) spectra for **10c** (500 MHz/126MHz, CDCl₃)

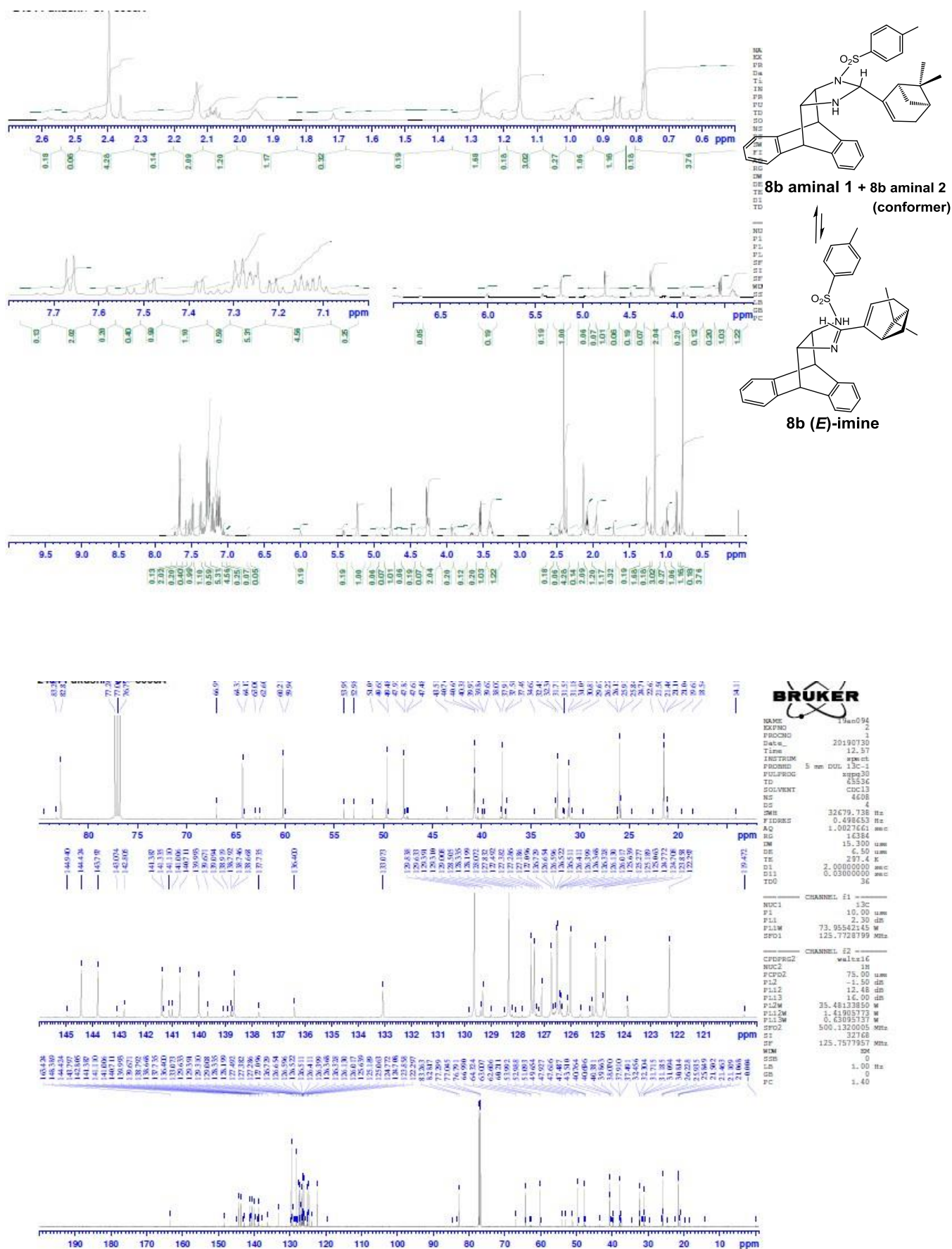


Fig. S48 ¹H NMR and ¹³C spectra for **8b**. (500 MHz/126MHz, CDCl₃)

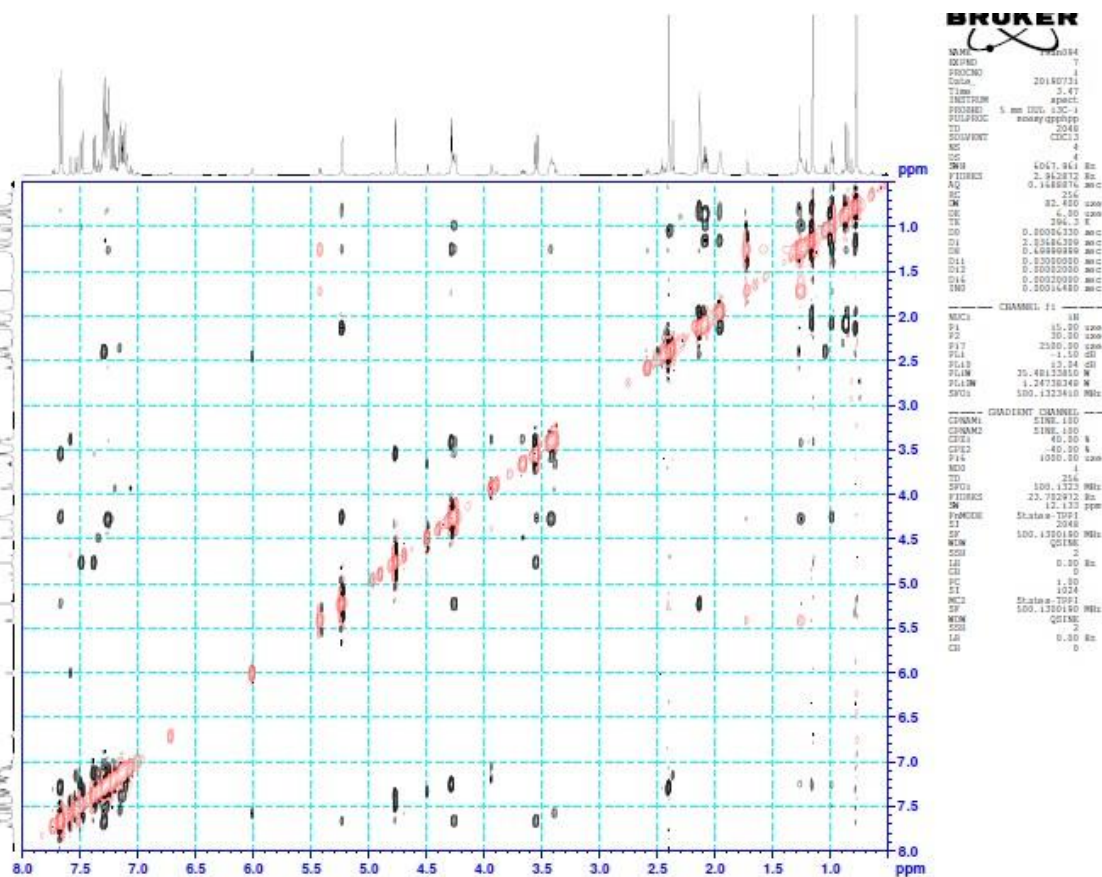
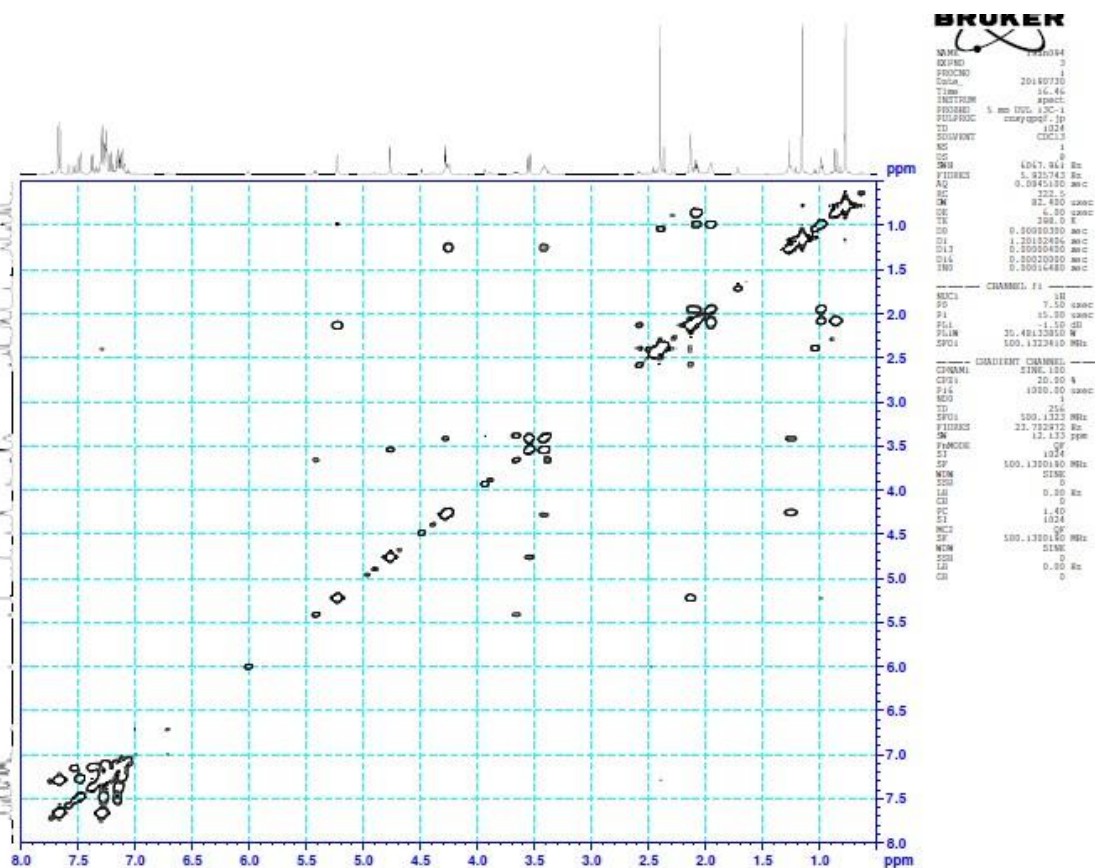


Fig. S49 COSY (above) and NOESY (below) spectra for **8b**. (500 MHz, CDCl₃)

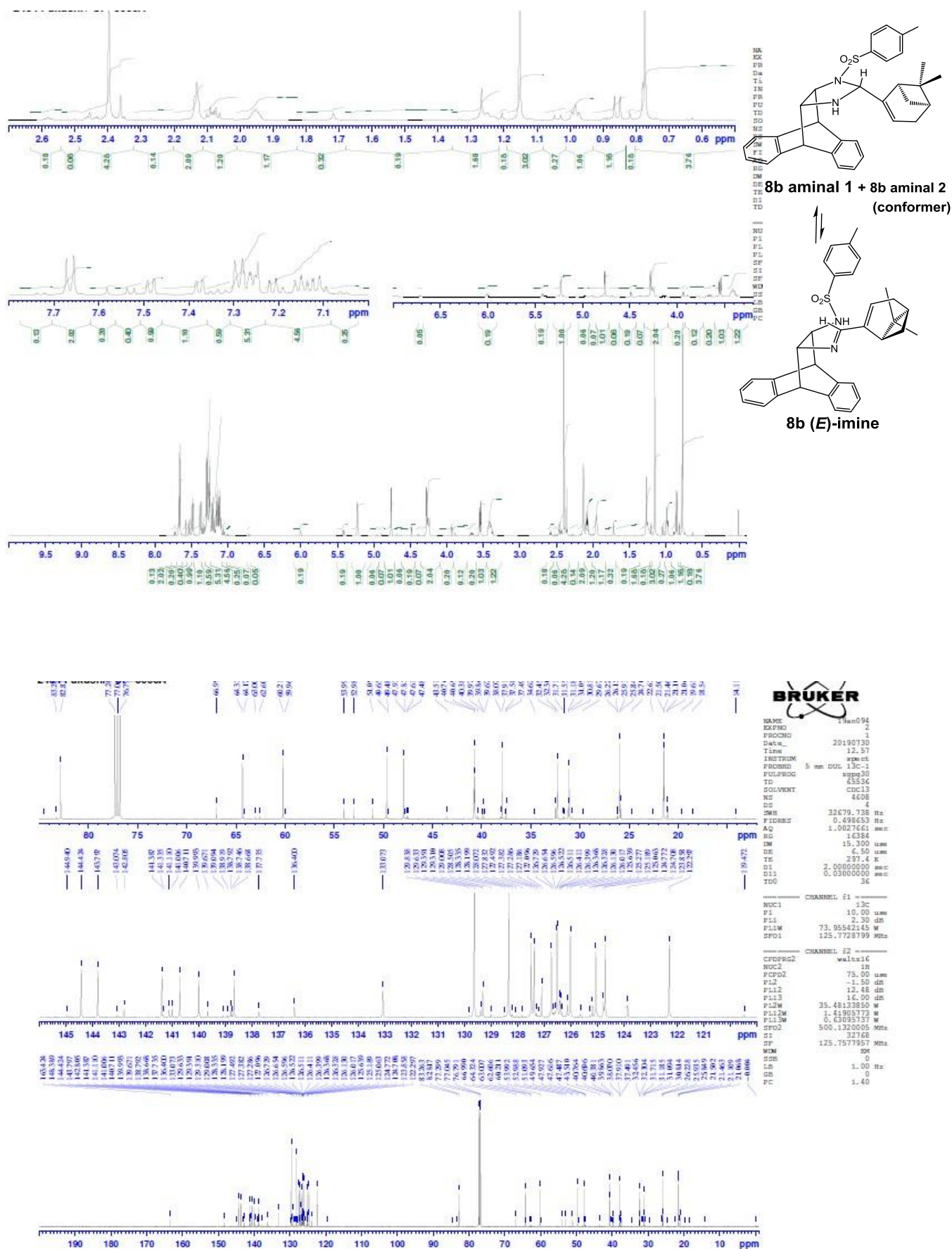


Fig. S51 ¹H NMR and ¹³C spectra for **8b**. (500 MHz/126MHz, CDCl₃)

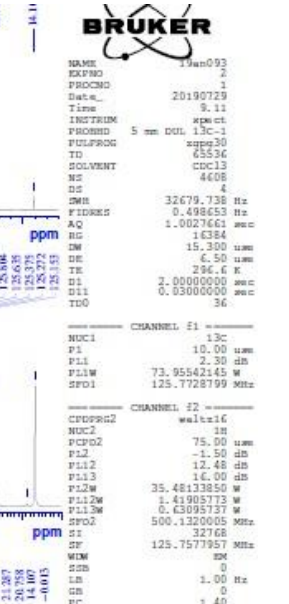
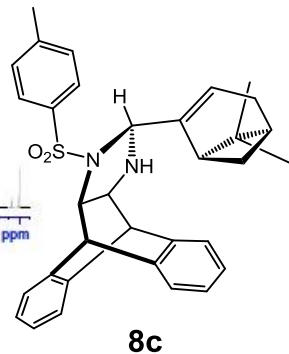


Fig. S52 ^1H NMR and ^{13}C spectra for **8c** (500 MHz/126MHz, CDCl_3)

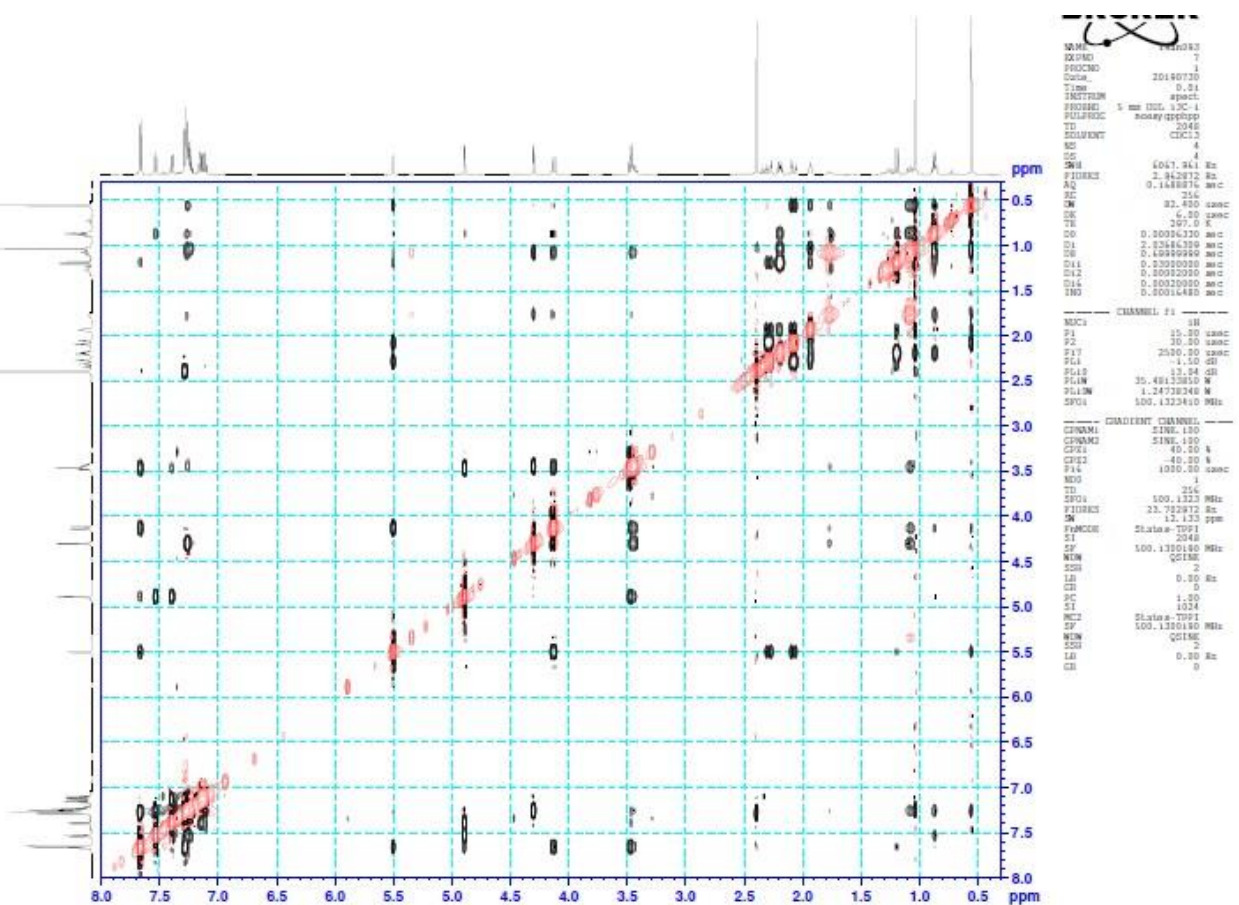
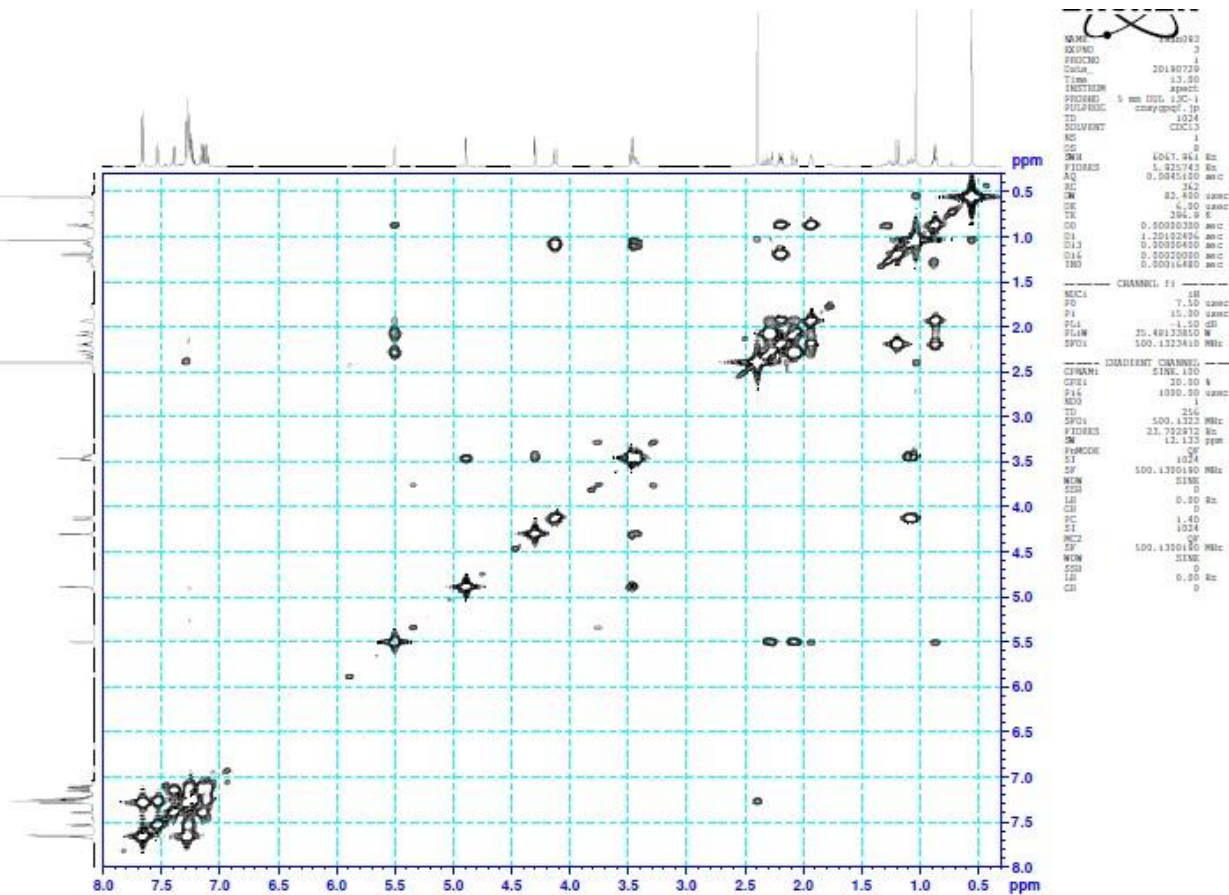


Fig. S53 COSY (above) and NOESY (below) spectra for **8c** (500 MHz, CDCl₃)

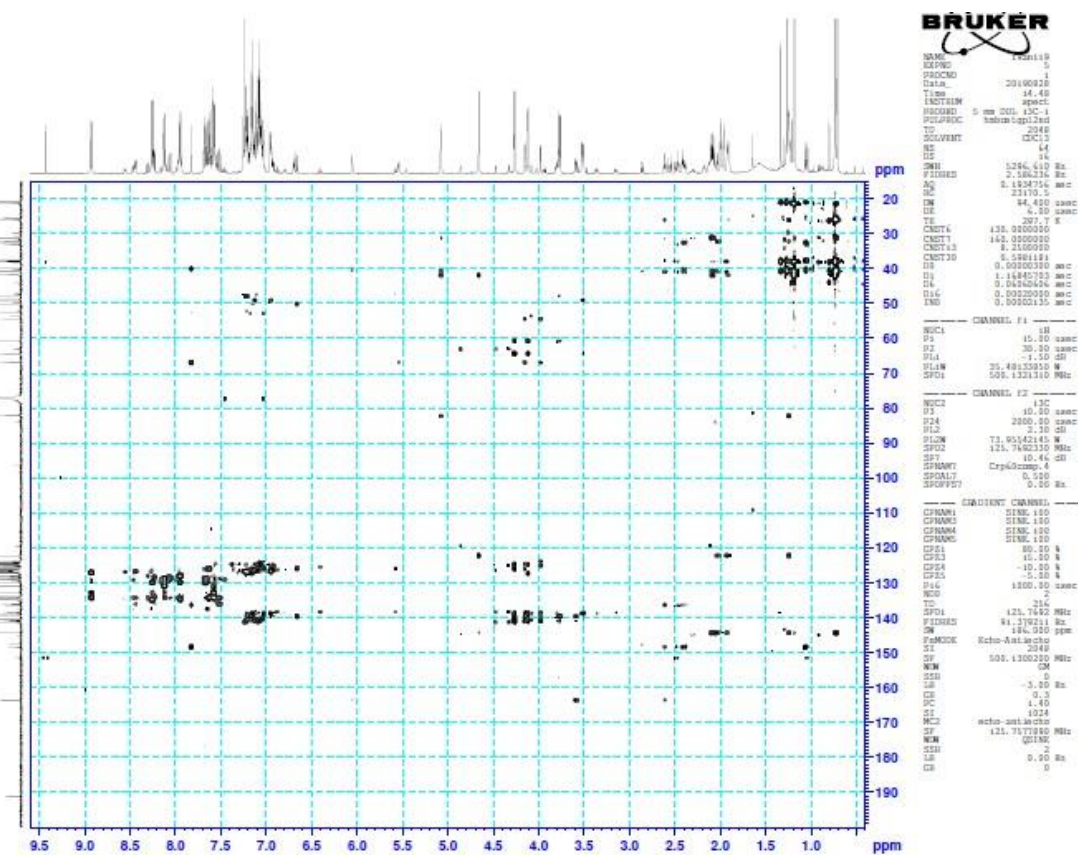


Fig. S56 HSQC (above) and HMQC (below) spectra for **9d** (500 MHz/126MHz, CDCl₃)

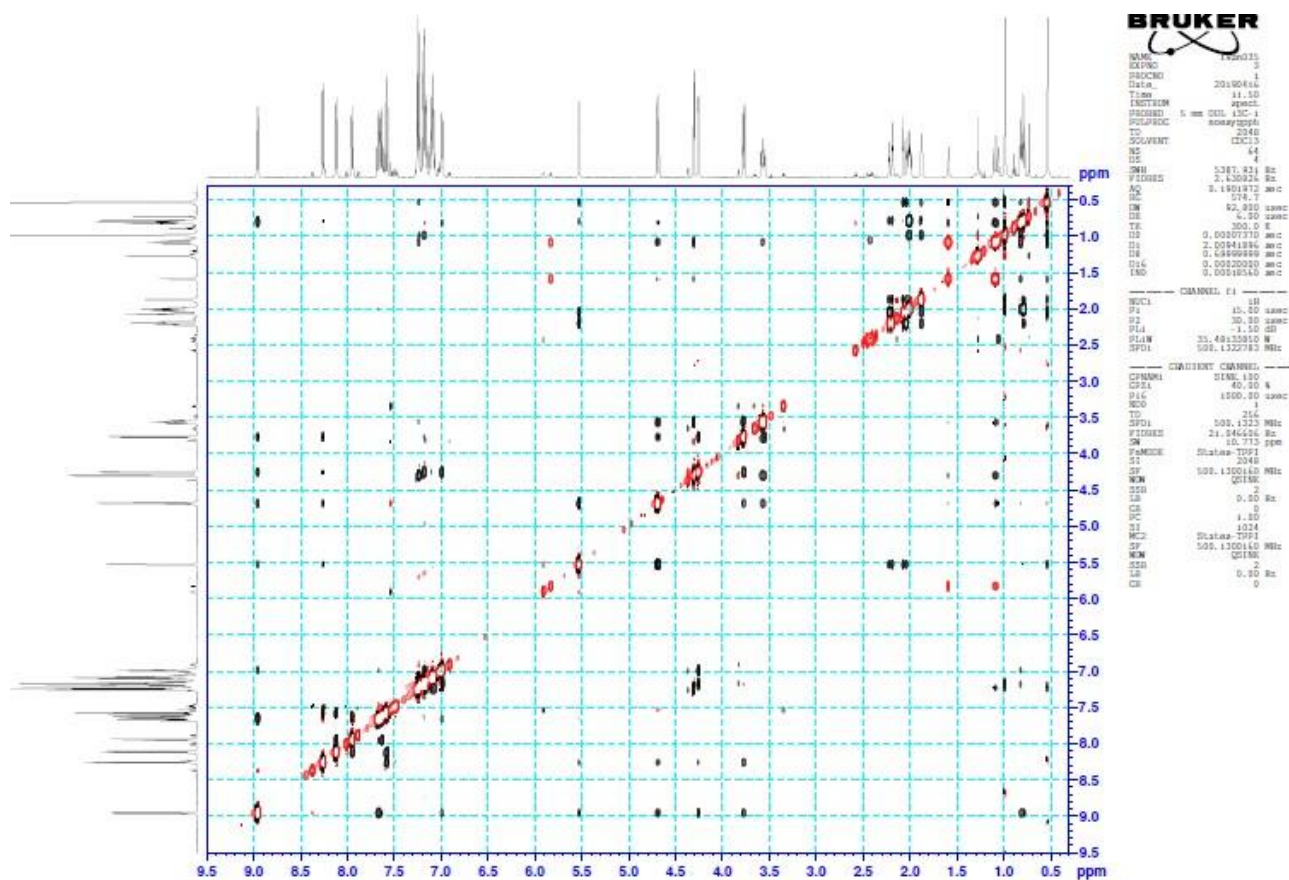
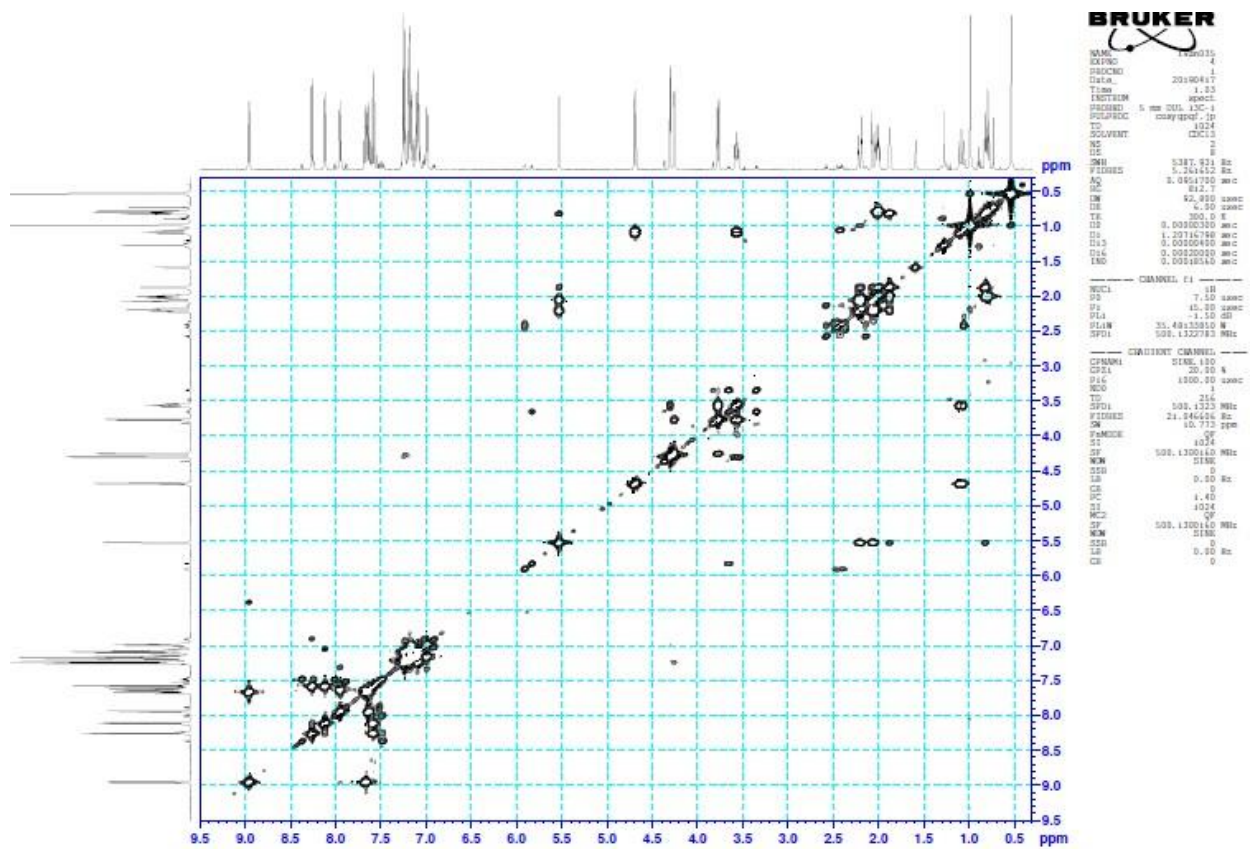


Fig. S58 COSY (above) and NOESY (below) spectra for **9e** (500 MHz, CDCl₃)

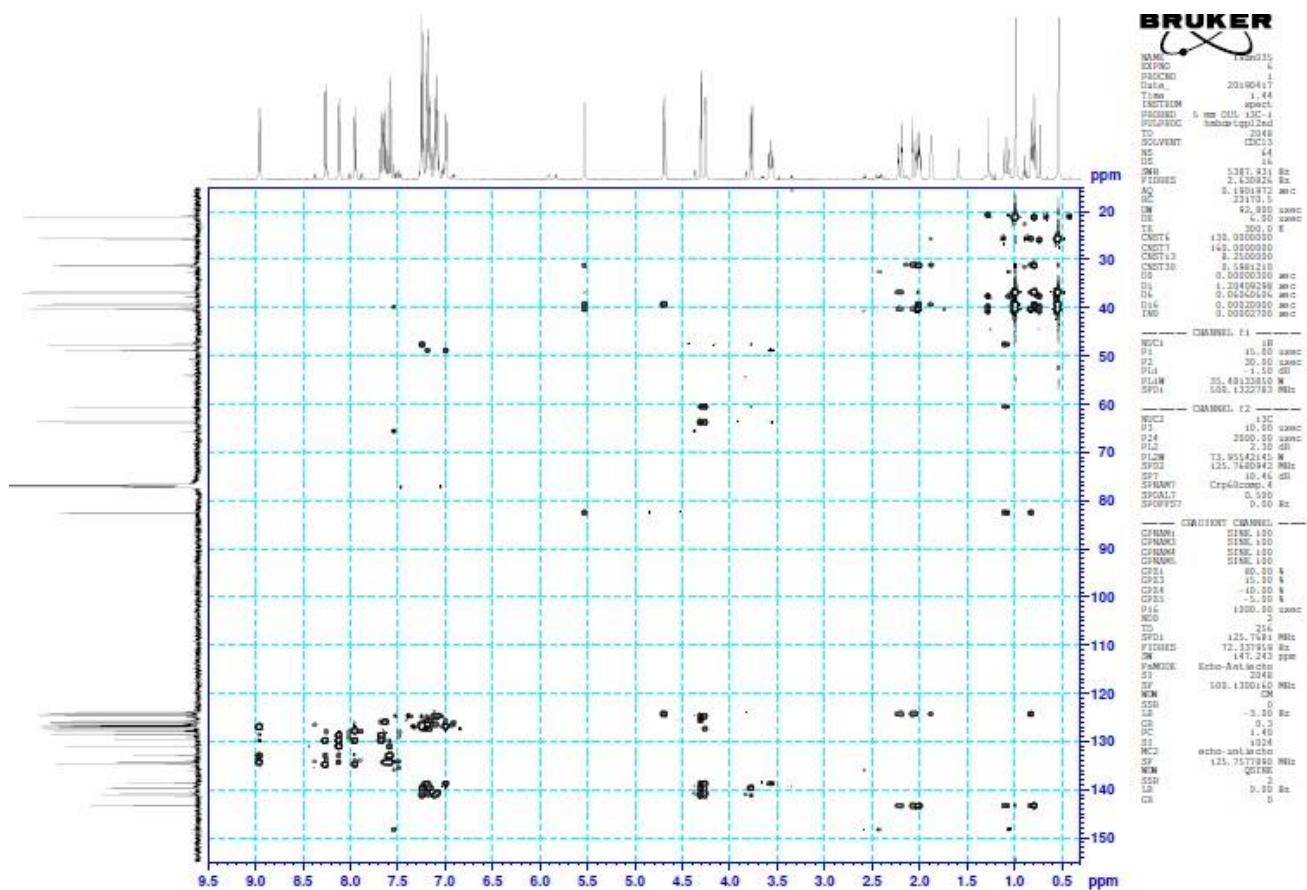
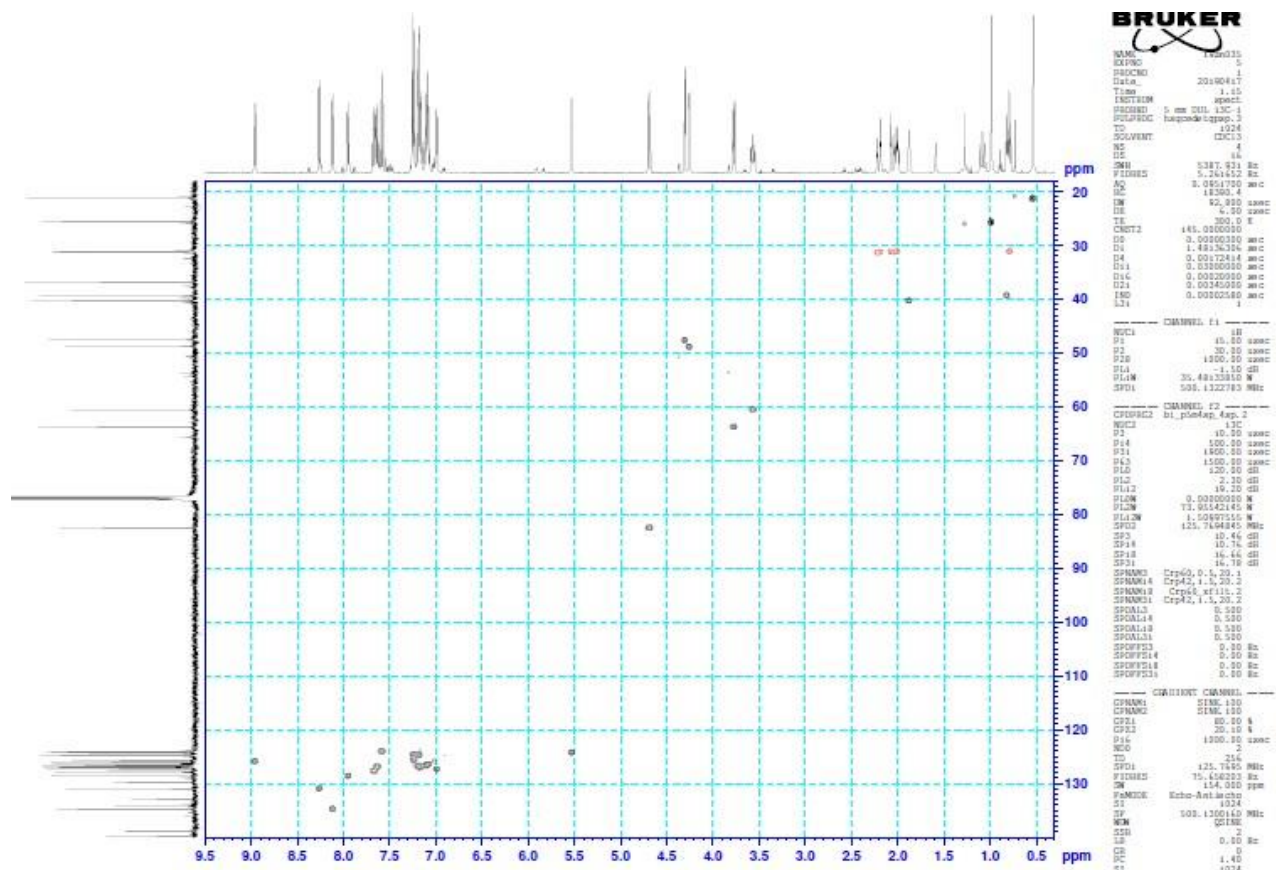


Fig. S59 HSQC (above) and HMQC (below) spectra for **9e** (500 MHz/126MHz, CDCl₃)

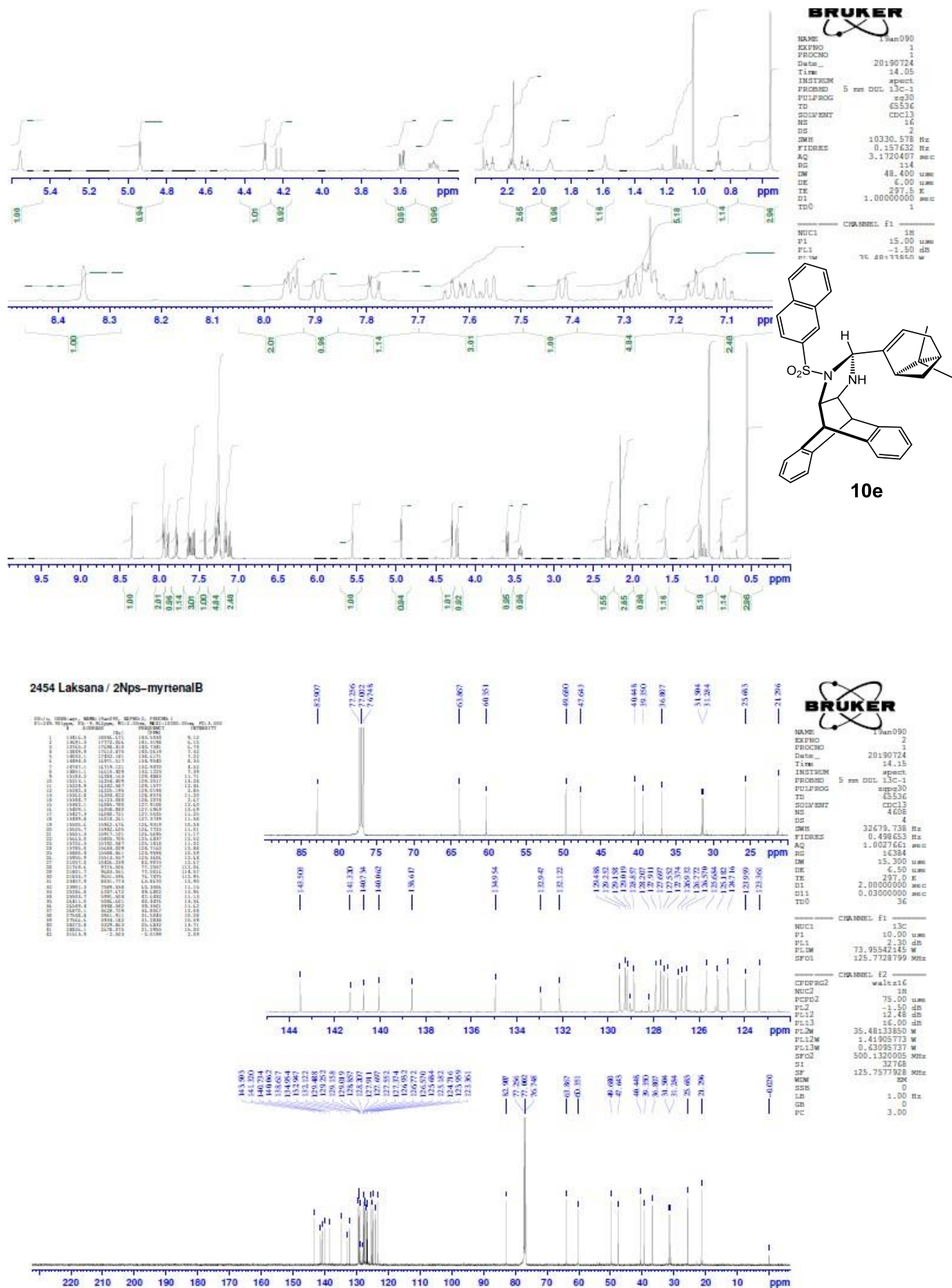


Fig. S63 ^1H NMR and ^{13}C spectra for **10e** (500 MHz/126MHz, CDCl_3)

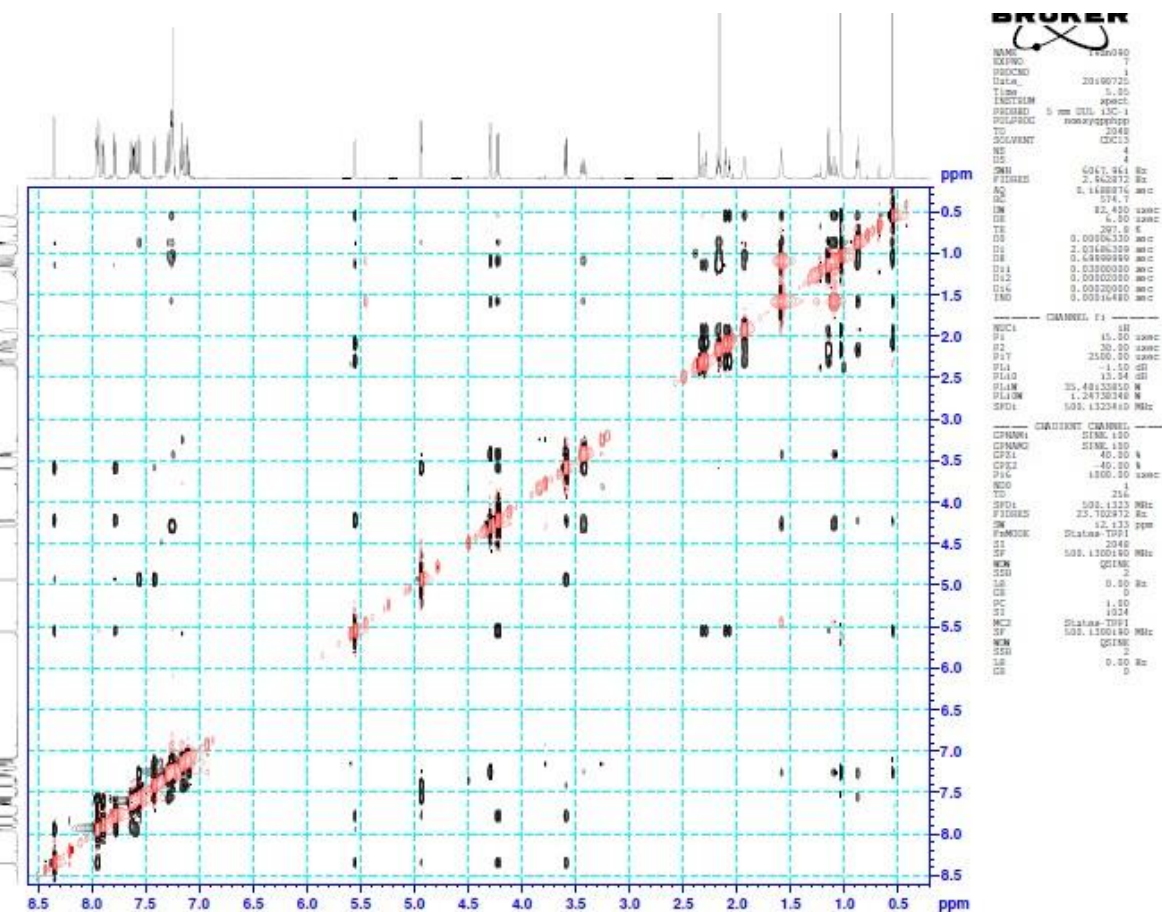
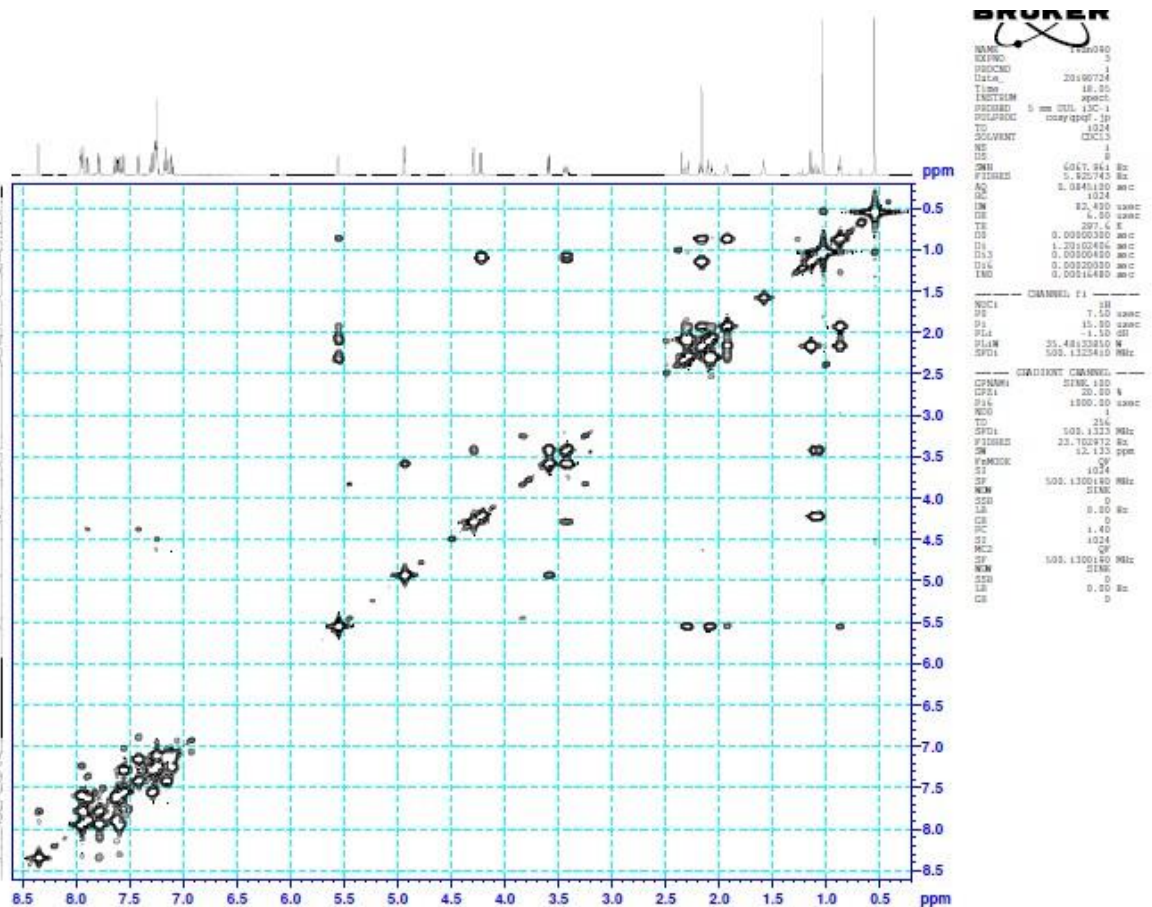


Fig. S64 COSY (above) and NOESY (below) spectra for **9e** (500 MHz, CDCl₃)

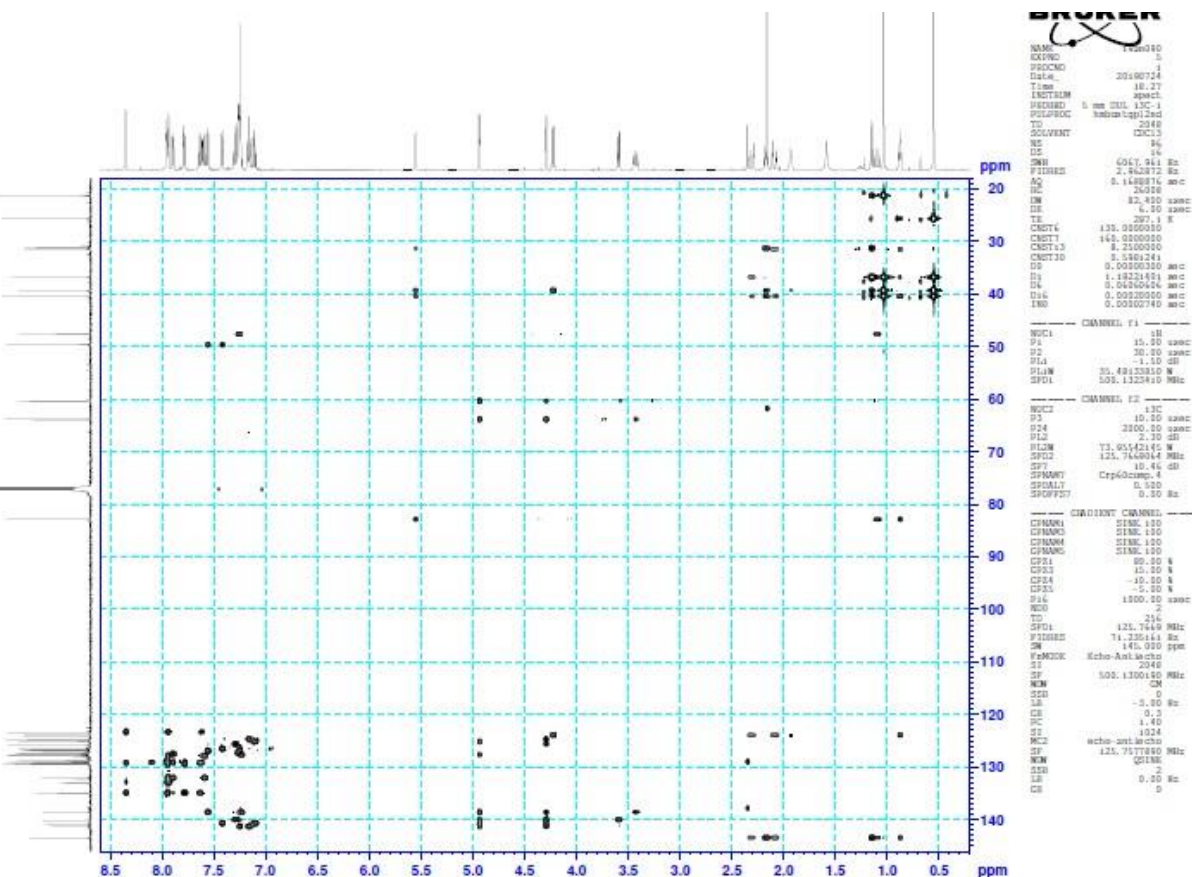
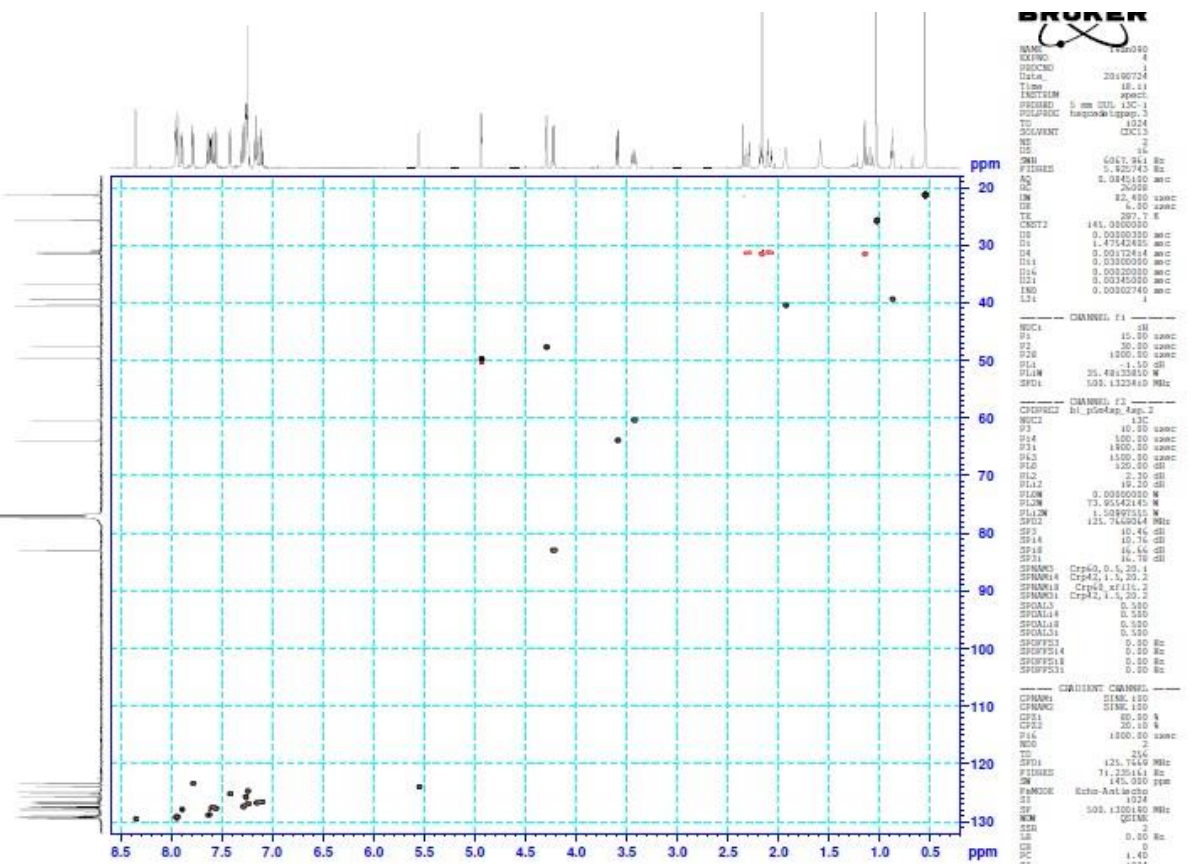


Fig. S65 HSQC (above) and HMQC (below) spectra for **9e** (500 MHz/126MHz, CDCl₃)