Synthesis of Dibenzothiazines via a Palladium Catalyzed Cyclization of Aromatic Sulfoximines with Benzynes

A thesis submitted towards partial fulfillment of the requirements of BS-MS Dual Degree Program

By

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Certificate

This is to certify that this dissertation entitled ***"Synthesis of Dibenzothiazines via a Palladium Catalyzed Cyclization of Aromatic Sulfoximines with Benzynes"*** towards the partial fulfillment of BS-MS dual degree program at Indian Institute of Science Education and Research, Pune represents original research carried out by **Arjun Vijeta** at IISER Pune under the supervision of "Dr. Masilamani Jeganmohan, Associate professor, IISER Pune, Department of Chemistry" during the academic year 2015-2016.

Date: 27.04.2016

Place: Pune

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Declaration

I hereby declare that the matter embodied in the report entitled ***"Synthesis of Dibenzothiazines via a Palladium Catalyzed Cyclization of Aromatic Sulfoximines with Benzynes"*** are the results of the investigations carried out by me at the Department of Chemistry, Indian Institute of Science Education and Research (IISER), Pune, under the supervision of **Dr. Masilamani Jeganmohan** and the same has not been submitted elsewhere for any other degree.

Date: 27/04/2016 **Arjun Vijeta**

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1. Abstract

Aromatic heterocyclic rings are the backbone of various natural products and biologically active compounds. And, these compounds are made up of carbon-carbon or carbon-heteroatom bonds. Transition metal catalysed reactions are one of the efficient ways to construct these bonds. Annulation via chelation-assisted C-H bond activation is a most effective pathway in the synthesis of heterocyclic compounds since the synthesis of tri-heterocyclic rings is still limited in the literature. Here we reported the formation of a tri-heterocyclic ring, dibenzothiazines through the cyclisation of phenyl sulfoximine into benzyne ring in the presence of $Pd(OAc)_2$, $K_2S_2O_8$ and Pivalic acid at 110 ^oC.

2. Introduction

2.1 General aspects

Most of the biologically active compounds, natural products, pharmaceutical compounds, agricultural products and materials are made of framework with various carbon-carbon and carbon-heteroatom bonds. To develop the efficient as well as an eco-friendly method to construct carbon-carbon and carbon-heteroatom bonds has always been a great challenge for the synthetic organic chemists. An earlier approach to construct these bonds required a number of steps, careful handling and also have a threat to the environment. Late 1900s discovery of coupling reactions such as Stille coupling, Negishi coupling, Suzuki coupling, Heck reaction, Sonagashira coupling has shown great potential for the construction of carbon-carbon and carbon-heteroatom bonds. These coupling reactions are commonly used in the organic synthesis of natural products and other vital molecules. The great achievements of these coupling reactions have made Royal Swedish Academy of Sciences to award the Nobel Prize in Chemistry to Richard Heck, Ei-chi Negishi and Akira Suzuki for developing palladium-catalyzed carbon-carbon bond formation reactions in 2010. These coupling reactions have been widely used to synthesize heterocyclic rings in order to prepare natural products, biologically active compounds and other vital compounds.

2.2 Heterocyclic rings

Heterocyclic rings are cyclic structures which contain atoms with different kind of elements. Heterocyclic compounds may be inorganic or organic. Organic heterocycles contain at least one carbon atom and atoms of other elements such as N, O, S, P and Halogens[1]. Organic heterocycles are further classified into two types: *aliphatic heterocycles* and *aromatic heterocycles.* The aliphatic heterocycles size varies from 3-7 atoms in the ring; these compounds are cyclic analogues of amine, ester, thioether, ether, ketone and amide[2]. The aromatic heterocyclic compounds are cyclic rings which obey Huckel rules. The utmost common aromatic heterocyclic compounds found in nature are either bicyclic or tricyclic rings. Heterocyclic rings are present in wide numbers of natural products, vitamins, drugs such as antibiotic, antifungal, antidepressant, anti-HIV, antibacterial etc. as well as other biological molecules which are present in our bodies such as Nucleic acids and Nucleotides (Fig. 1).

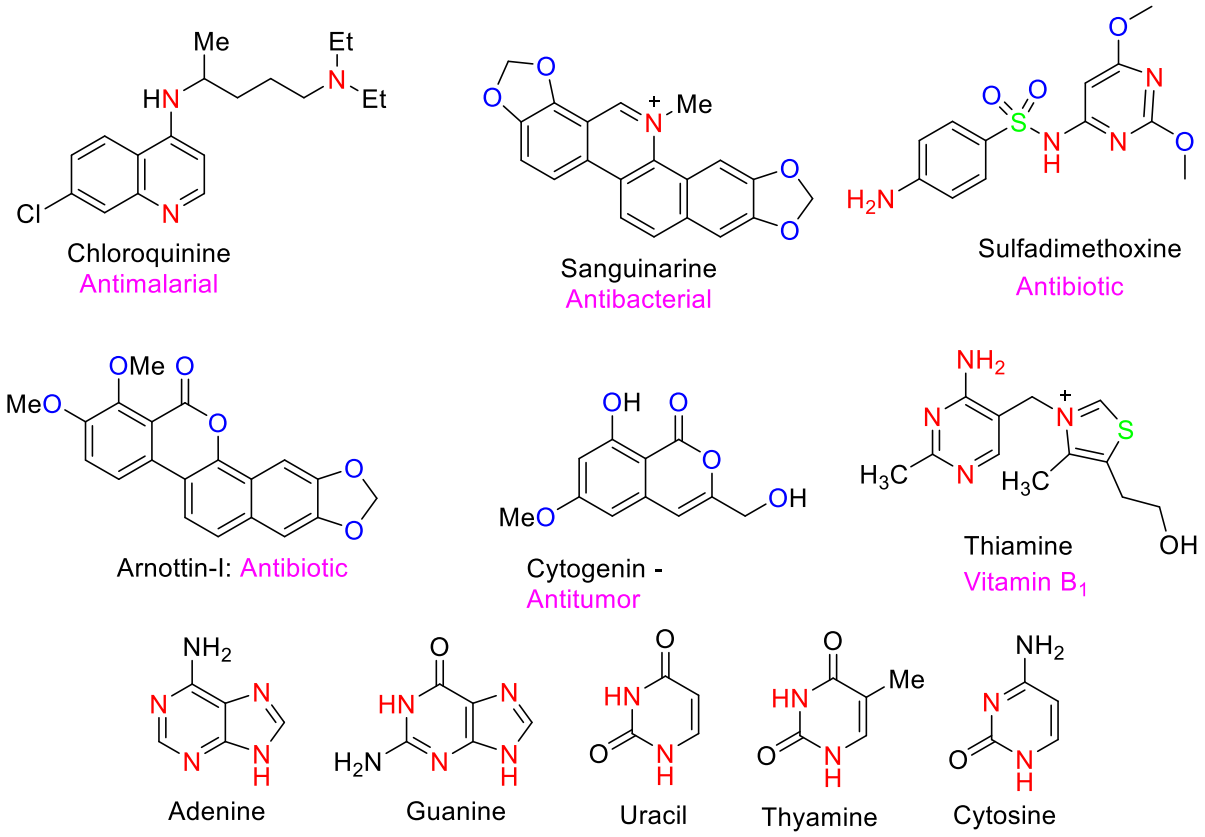


Figure 1: Representative biologically active heterocycle compounds

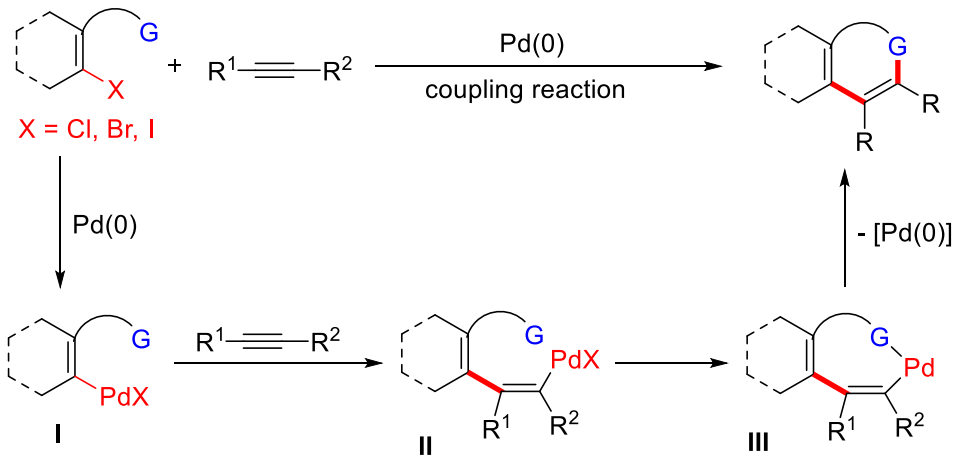
2.3 Synthesis of aromatic Heterocyclic rings

Synthesis of aromatic heterocyclic compounds has always been challenge for synthetic organic chemist. The appropriate way to synthesize any vital compounds containing heterocyclic rings are step by step synthesis. The earlier approach to synthesize any molecules using simple basic organic reaction used to be time-consuming due to numerous steps, atom uneconomical and harsh conditions. However, the recent finding of methodologies based on transition metal catalysed reactions have overcome these synthetic obstacles. Our interest is to synthesize heterocyclic rings using transition metal catalysed reactions.

2.3.1 Approaches to synthesize bicyclic ring using metal-catalysed reaction

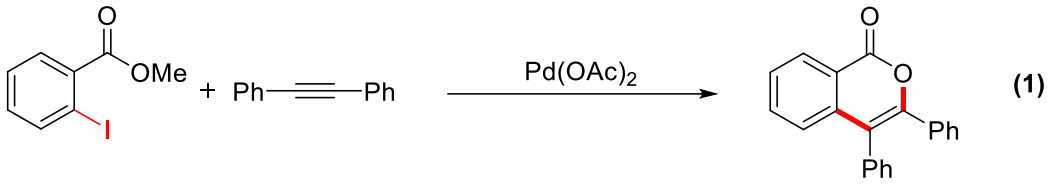
After the discovery of Heck cross-coupling reaction, the metal-catalysed reactions are well explored for the synthesis of heterocyclic rings. These cross-coupling reactions have also been used to synthesize bicyclic rings by cyclisation of halogen pre-functionalised aromatic organic molecules into carbon-carbon π-components. The reaction involves steps such as oxidative insertion, syn insertion and reductive insertion (Scheme 1). Various metals such as palladium, nickel, cobalt, rhodium etc. have been widely explored for this method.

Scheme 1: Mechanism of cross-coupling reaction



Among all the established methods from different metals, a palladium-catalysed cross-coupling reaction having one partner as *ortho*-iodoaromatic derivatives have been found

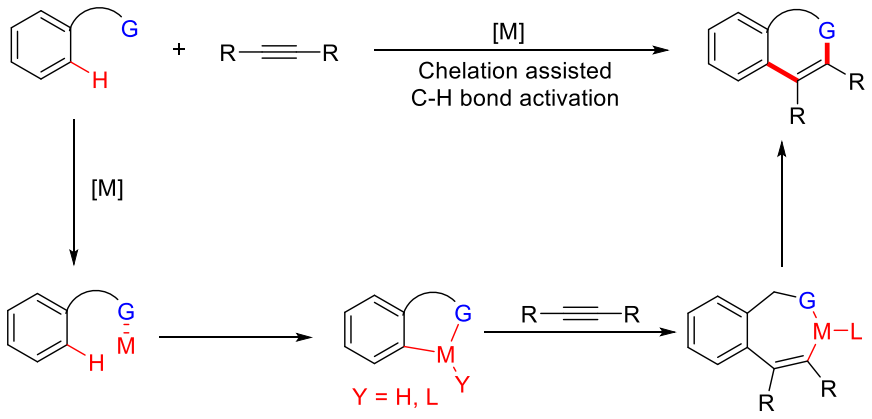
to be the most efficient. And, this methodology has been applied to the synthesis of various bicyclic aromatic rings such as indoles, isoquinoline, isocoumarin, benzothiazines, benzofurans and benzofuran.[3a-b] It is worth highlighting the Heck work on the synthesis of isocoumarin derivatives via cross-coupling pathway (eq. 1).[4]



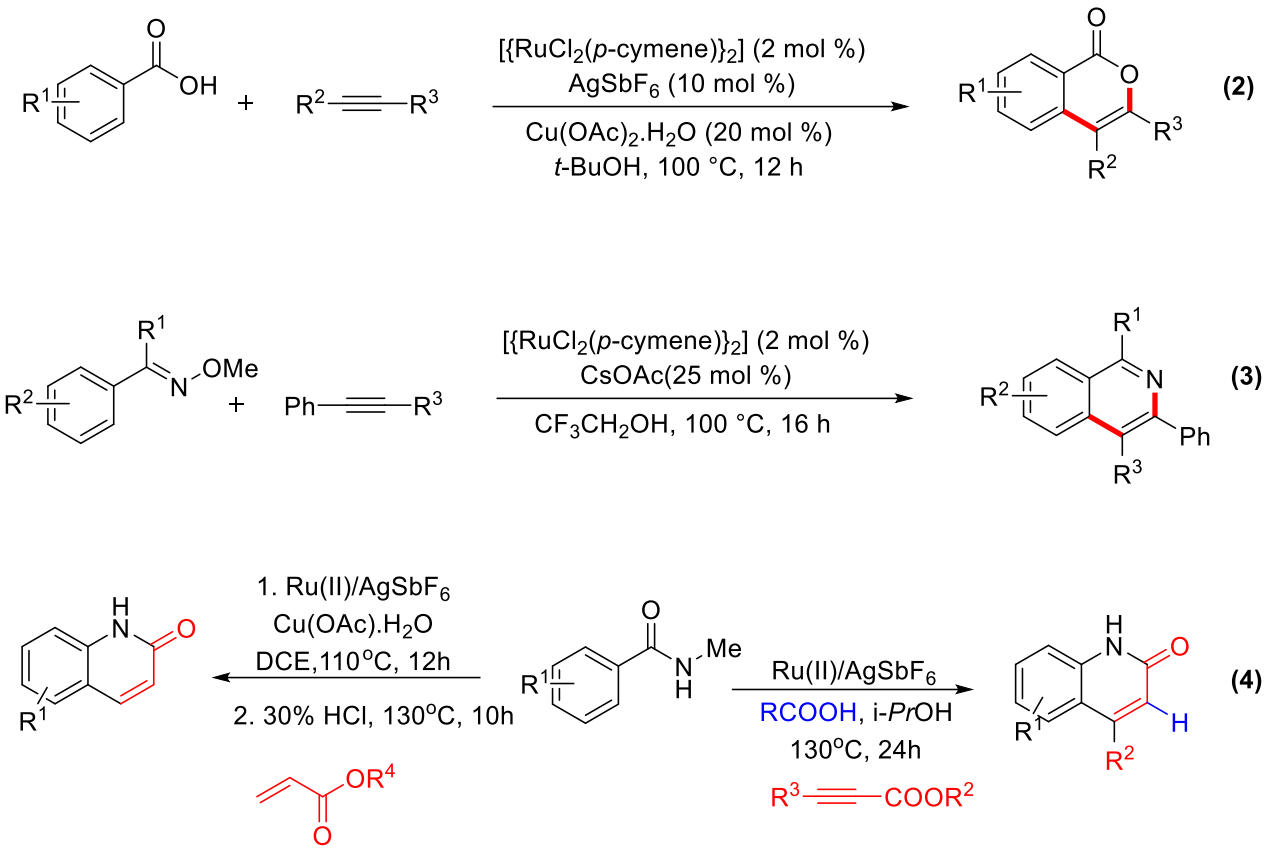
(1)

Although the cross-coupling reactions are efficient, they require pre-functionalised coupling partners, especially *ortho* halide substituted in order to activate the *ortho* carbon and the synthesis or availability of pre-functionalised required starting material become an issue for the cross-coupling reaction. Then in 1993, Murai reported a new methodology to construct carbon-carbon bond using metal catalysed chelation-assisted C-H bond activation of aromatic rings.[5] In this method, generally it requires a lone pair aided hetero atom like nitrogen, oxygen or sulphur containing directing groups on aromatic ring such that the directing group can chelate with metal (Scheme 2).

Scheme 2: Mechanism for chelation-assisted C-H bond activation.



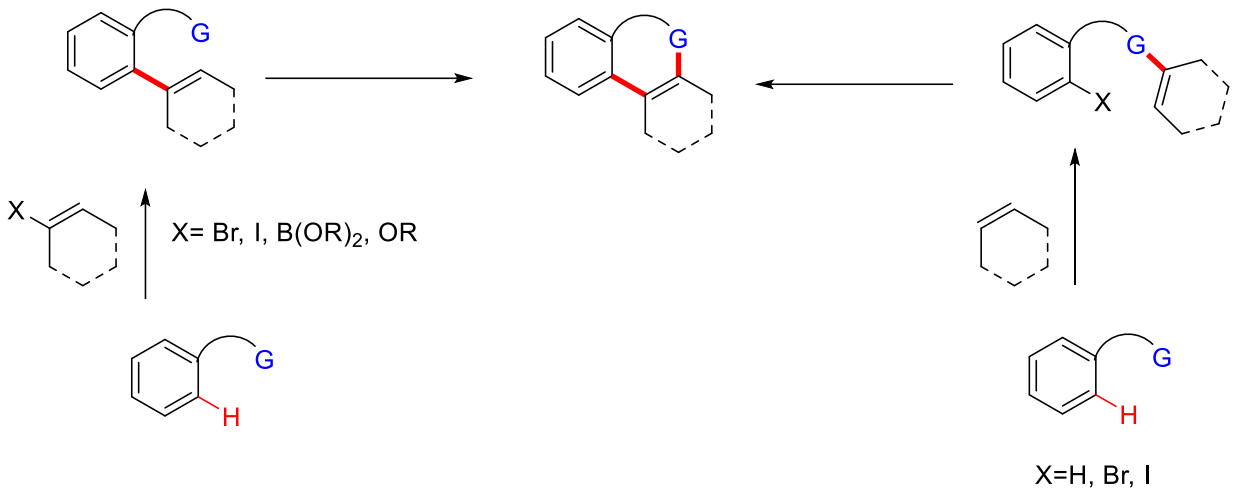
Concept tossed by Murai has now been well explored with palladium, nickel, rhodium, ruthenium etc. and has been used for the synthesis of various bicyclic rings.[6] It is worth mentioning our group's efforts in developing synthesis approach for the preparation of isocoumarin, 1-haloisoquinolines, 2-quinolinone and isoquinolone using [{$RuCl_2$(*p*-cymene)}$_2$] catalyst via chelation-assisted C-H bond activation(eq. 2-4).[7a-d]



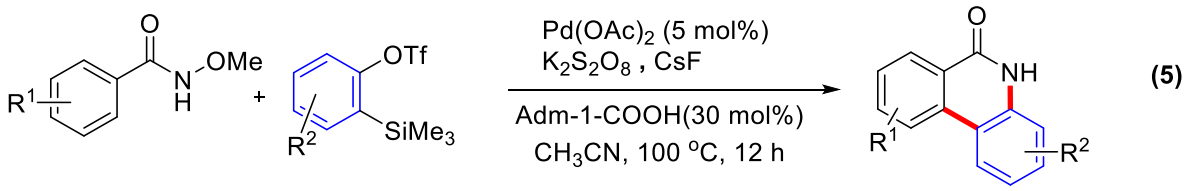
2.3.2 Approaches to synthesize tricyclic ring using Metal catalysed reaction

Generally, the synthesis of tricyclic rings using transition metal catalysed reaction occurs in two steps. The most common one is the formation of *ortho*-arylation of the arene either by cross-coupling reaction or transition metal chelation assisted by C-H bond activation followed by annulation with the heteroatom of the directing group.[8] Another approach is arylation to the heteroatom of the directing group on the aromatic ring followed by annulation via dehydrogenative or dehydrohalogenation coupling.[8] These two pathways have been used to synthesize various tricyclic rings such as dibenzofuran, carbazole, Phenanthridone, benzochromenone, etc.

Scheme 3: General pathway to prepare tricyclic rings



Recently, our group developed a new approach to synthesize tricyclic ring by performing insertion of *insitu* generated benzyne between the heteroatom of directing groups and *ortho* position of aromatic rings via chelation-assisted C-H bond activation. This concept has been applied for the synthesis of Phenanthridones (eq. 5).[9]

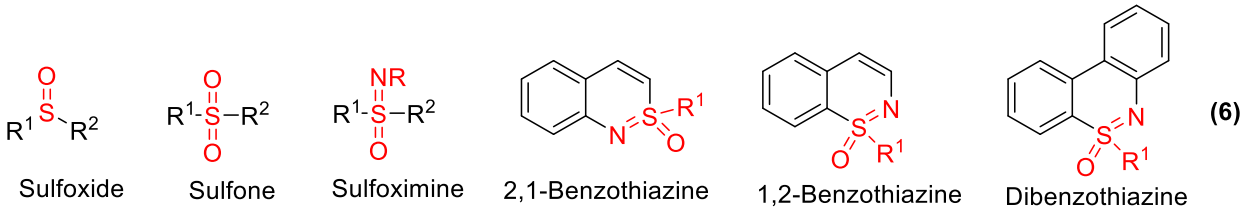


From the literature, it has been found that synthesis of nitrogen and oxygen based hetero aromatic ring are well explored whereas report on sulphur based hetero aromatic ring are still limited even when sulphur are found in many natural products and biologically active compound. We decided to design and develop new methodologies for the synthesis of hetero aromatic rings of sulphur compounds.

2.4 Sulfoximines

Sulphur as stereogenic atom consisting compounds have broad application in medicinal chemistry.[10] Sulfoxides and sulfones are among such classes of compounds which are

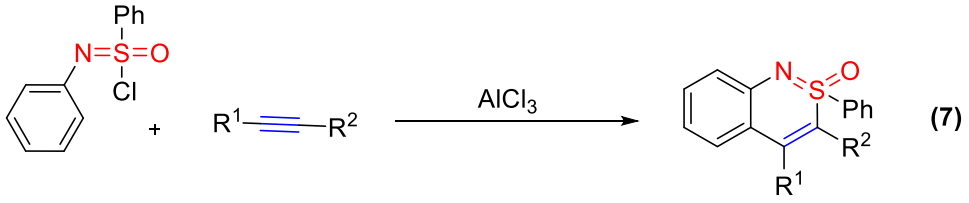
well explored in drug discovery due to their potential biological activities. In addition, a similar analogy is found in several naturally occurring compounds (eq 6).[11] But sulfoximines, the monoaza analogues of sulfones, have negligible exploration in medicinal chemistry. However, the recent finding of a sulfoximine derivative "BAY 1000394" as a potent pan-CDK inhibitor and its current phase I clinical trial for cancer therapy has insisted on exploring this functional group in drug discovery.[12] Apart from medicinal chemistry, sulfoximines can have astonishing future in asymmetric synthesis and agricultural industries.[13]



(6)

2.4.1 Development in Sulfoximine synthesis

In the literature, there are various reports for the synthesis of linear sulfoximines.[14] But the methods for preparation of cyclic sulfoximines is limited in the literature. Synthesis challenges of the cyclic sulfoximine have motivated the synthetic chemists to develop new synthetic approach towards these molecules. In 1987, Harmata's group reported the synthesis of bicyclic sulfoximine derivative 2,1-benzothiazine by Lewis acid mediated reaction of N-aryl sulfonimidoyl chlorides with alkynes (eq. 7).[15]



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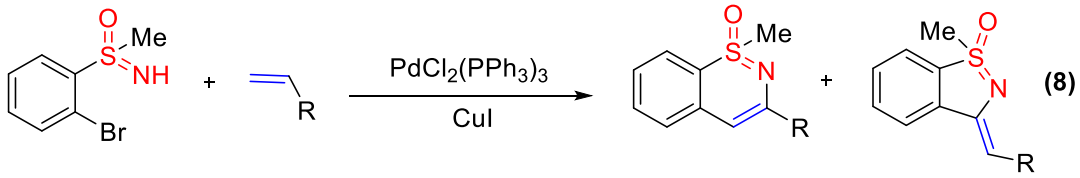
Later, in 2005 same group reported the cross-coupling of 2-bromophenyl substituted sulfoximines with terminal alkynes followed by cyclisation in the presence of palladium and copper catalysts afforded 1,2-benzothiazines and 1,2-benzoisothiazines (eq. 8).[16]



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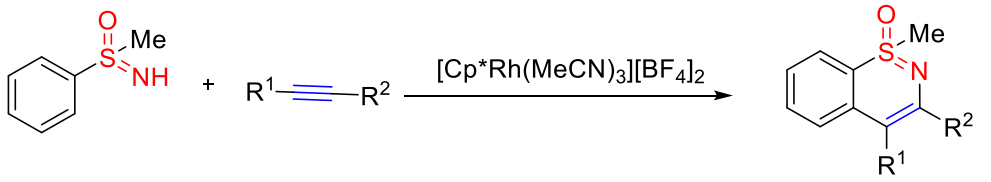
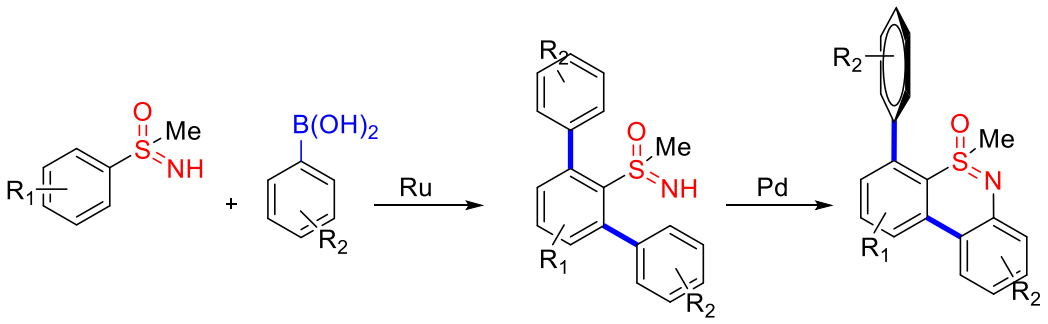
Very recently, Bolm's group reported the synthesis of bicyclic 1,2-benzothiazine derivatives via a chelation-assisted rhodium-catalyzed oxidative cyclization of phenyl sulfoximines with alkynes (eq. 9). [17]



(9)

Inspired by discoveries on the synthesis of bicyclic sulfoximine rings, we decided to develop methodologies for the preparation of tricyclic sulfoximine rings. Recently we synthesised tricyclic dibenzothiazines in two steps where the first step was a ruthenium-catalyzed *ortho* arylation of phenyl sulfoximines with aromatic boronic acids followed by intramolecular cyclization in the presence of palladium catalyst (eq. 10).[18]



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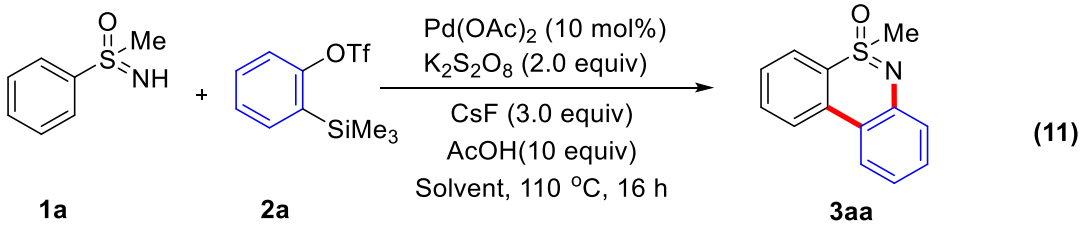
Stimulated with our recent finding, we approached to a new method to synthesis tricyclic dibenzothiazines in one step through a Pd-catalyzed oxidative cyclization of insitu generated benzyne with phenyl sulfoximine.

3. Result and Discussion:

Our main focus was to synthesize dibenzothiazines in one step. Initially, we tried our previous reported condition for the cyclisation of phenyl sulfoximine with benzyne precursor in the presence of [{$RuCl_2$(*p*-cymene)}$_2$], $AgSbF_6$ and Ag_2O in THF at 100^oC for 12 h along with CsF for the insitu generation of benzyne. In the reaction, exclusively *N*-arylation of sulfoximine was observed. Next, we decided to change the catalytic system from [{$RuCl_2$(*p*-cymene)}$_2$] to $Pd(OAc)_2$, as the reported literature suggest benzyne works efficiently for cyclisation in the presence of a Pd catalyst. We examined the cyclization reaction of **1a** with **2a** in the presence of $Pd(OAc)_2$ (10 mol%), acetic acid (10.0 equiv.) and CsF in CH_3CN. Here we observed, 60% *N*-Arylation **4aa** and 18% cyclised product **3aa**. To suppress the formation of *N*-Arylation **4aa**, we further optimised the reaction conditions by varying the parameters.

Initially, we examined our reaction using various protic and aprotic solvents such as THF, DME, DCE, methanol, toluene, acetonitrile, DMSO, DMF and water (Table 1). Among these, THF, methanol, toluene, DMF and water found to be ineffective for the cyclisation reaction (entries 2-6). However, in the case of DCE reaction occurred but cyclised product was not obtained (entry 1). Acetonitrile was found to be most effective among these, but the yield of cyclised product was very less (entry 7). Therefore to make this reaction productive we looked to other parameters.



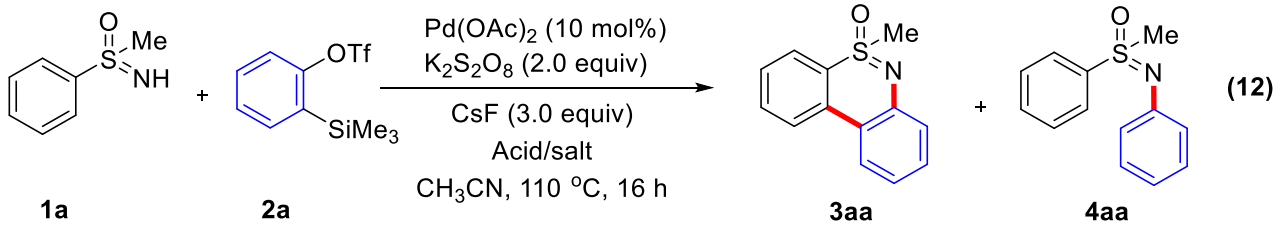
1a **2a** **3aa** **(11)**

Table 1- Cyclisation of 1a with 2a in different solvents to give 3aa.

S.no	Solvent (mL)	Yield of product 3aa (%)
1	DCE	_
2	THF	No reaction

3	Methanol	No reaction
4	Toluene	No reaction
5	DMF	No reaction
6	Water	No reaction
7	1,4-dioxane	10
8	Acetonitrile	18
9	DMSO	Trace

In the case of a palladium catalyst, an organic acid is needed to activate the C-H bond of substituted aromatics. Therefore, we examined different equivalence of acetic acid on the yield of **3aa**, but it was observed ineffective. Then, we tested various acid/salts possessing different steric as well as electronic effects such as pivalic acid, adam-1-COOH, mesitylene acid, benzoic acid, *p*-toluic acid and cesium pivalate (Table 2). Adam-1-COOH and mesitylene acid were found to be ineffective for the reaction (entries 3-4). Whereas, in the case of *P*-toluic acid and benzoic acid, the formation of *N*-arylation product **4aa** was observed along with traces of **3aa** (entries 5-6). Interestingly, 37% cyclised product **3aa** was observed along with 34% **4aa** formation in the case of pivalic acid (entry 2) and also Cesium pivalate yielded 20% **3aa** and 25% **4aa** (entry 7).



1a **2a** **3aa** **4aa** **(12)**

Table 2- Cyclisation of 1a with 2a in different additives to give 3aa.

S.no	Acid/salt (equiv)	Yield of product **3aa***(%)	Yield of product **4aa***(%)
1	No additive	_	75
2	Pivalic acid (3 equiv)	37	34

3	Adm-1-COOH (1 equiv)	_	_
4	Mesitylene acid (1equiv)	_	78
5	Benzoic acid (1 equiv)	Trace	75
6	p-tolylic acid(1 equiv)	Trace	70
7	Cesium Pivalate(1equiv)	20	25

* The mentioned yield are GC yields.

The effectiveness of pivalic acid in the formation of cyclic product **3aa**, provoked us to further investigate the effect of its concentration on **3aa** yield (Table 3). Initially, we added 3 equivalent of pivalic acid to the reaction mixture and observed 34% yield of **3aa** (entry 2) along with 34% *N*-arylation **4aa.** Surprisingly, when we used 5.0 equivalent of pivalic acid, an exclusive formation of cyclised product **3aa** in yield of 75% (entry 3) was observed. There was no further increment in yield by increasing the amount of pivalic acid (entry 4-5).

Table 3- Cyclisation of 1a with 2a in different concentration of pivalic acids to give 3aa.

S.no	Pivalic acid (equiv)	Yield of product **3aa***(%)	Yield of product **4aa***(%)
1	1	20	60
2	3	37	34
3	5	75	_
4	8	25	30
5	10	_	Trace

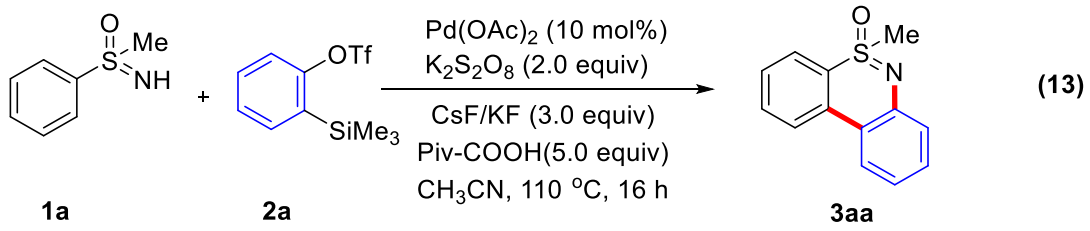
* The mentioned yield are GC yields.

Since the formation of *N*-arylation was observed in most of the trial reactions. We needed to control the formation of insitu benzyne generation basically we need a slow benzyne generation in this reaction. So, we tried various fluorinating agents in order to make the *insitu* benzyne generation faster or slower. In the case of CsF, the cyclization worked well and also worked equally with KF/18-crown-6, providing product **3aa** in 69% yield (entries 6-7). Surprisingly, KF without 18-crown-6 also yielded product **3aa** in 70% (entry 5). It is expected that the pivalic acid might dissociate the fluoride ion from KF. Whereas NaF, TBAF, NH_4F and AgF were not effective for the reaction (entries 1-4).

Table 4- Cyclisation of 1a with 2a in different Fluorine source to give 3aa.

S.no	Fluorine source(equiv.)	Yield of product 3aa (%)
1	NaF	No reaction
2	TBAF	Trace
3	NH_4F	No reaction
4	AgF	No reaction
5	KF	70
6	KF/18-crown-6	69
7	CsF	68

In order to further improve the yield of reaction various oxidants were examined such as $K_2S_2O_8$, $(NH_4)_2S_2O_8$, $Cu(OAc)_2$, Ag_2O and $PhI(OAc)_2$. Among these $K_2S_2O_8$ worked well for the reaction and $(NH_4)_2S_2O_8$, Ag_2O and $PhI(OAc)_2$ were totally ineffective in cyclisation of **1a**. Whereas in $Cu(OAc)_2$ case, the cyclization product was observed in a less amount along with the more *N*-arylated product. We also examined different temperatures for the reaction, amongst which 110^oC was found to be most effective. Finally, we decided sulfoximine (**1a**) (1.0 equiv) with 2-trimethylsilylphenyl triflate (**2a**) (1.3 equiv) in the presence of $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2.0 equiv), CsF or KF (3 equiv) and pivalic acid (5.0 equiv) in CH_3CN is a best conditions for the cyclization reaction (eq. 13).

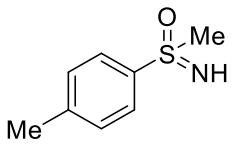
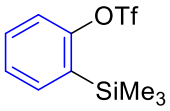
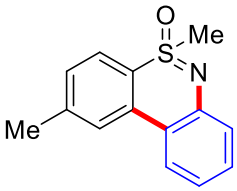
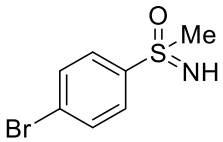
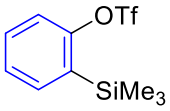
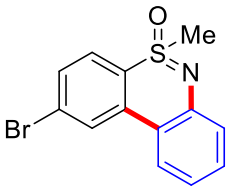
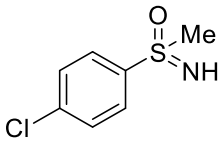
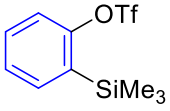
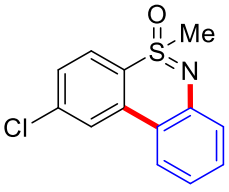


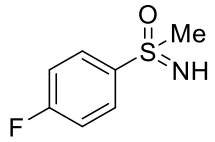
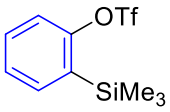
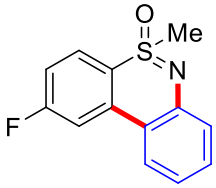
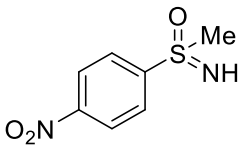
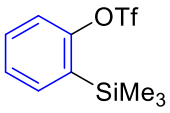
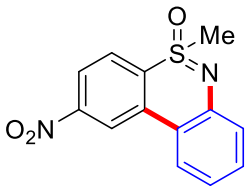
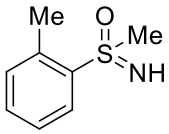
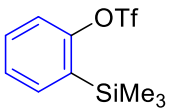
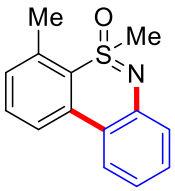
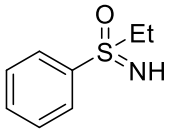
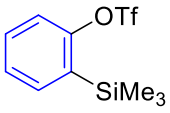
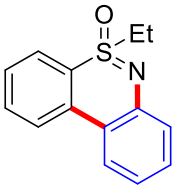
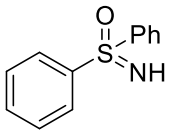
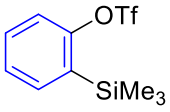
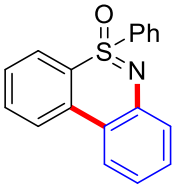
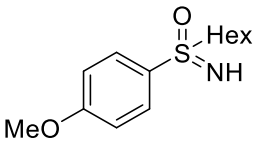
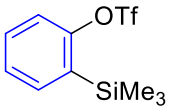
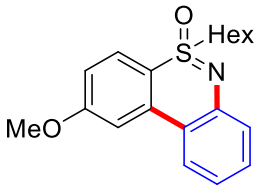
1a **2a** **3aa** **(13)**

The process of overcoming the formation of *N*-arylation by cyclisation in the reaction of sulfoximine **1a** with benzyne was captivating, and therefore we decided to explore the generality of the reaction. We started investigating our catalytic reaction with various sensitive functional groups such as Me, OMe, F, Br, NO_2. In all the cases, we found the reaction to be compatible (Table 5).

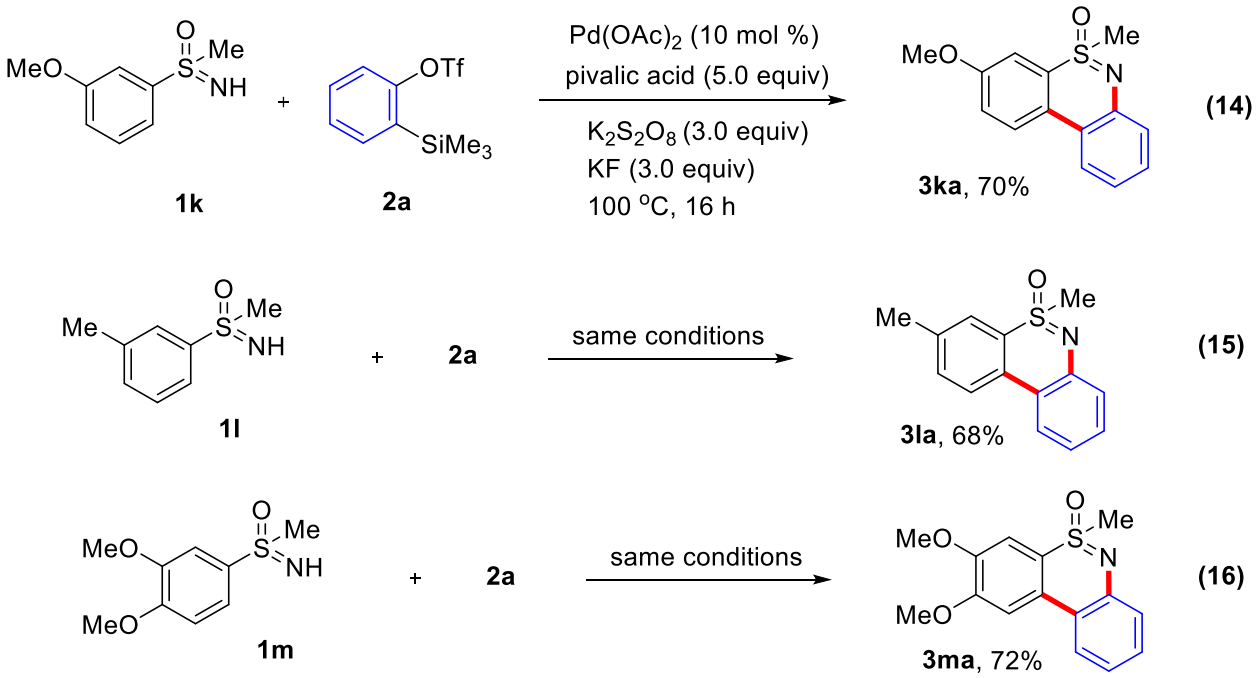
Treatment of methyl phenyl sulfoximine (**1b**) with benzyne precursor (**2a**) under optimised reaction condition gave exclusive dibenzothiazine product (**3ba**) in 68% yield (entry 1) and even sterically hindered *ortho* methyl substituted phenyl sulfoximine efficiently participated in the reaction giving substituted dibenzothiazine **3ga** in 62% yield (entry 6). In the case of sensitive groups which have an influence of electronic effect like nitro and halo groups- Br, Cl and F was minor, providing dibenzothiazine derivatives (**3ca-3fa**) in 61-68% yield(entries 2-5). Interestingly when *S*-methyl group was replaced by ethyl and Phenyl, the yield of resulting dibenzothiazine (**3ha-3ia**) was unaffected whereas increasing the chain length from methyl to hexyl on Sulphur affected the yield of product (**3ja**) (entries 7-9).

Table 5. Palladium-catalysed cyclisation of substituted Phenyl sulfoximines.

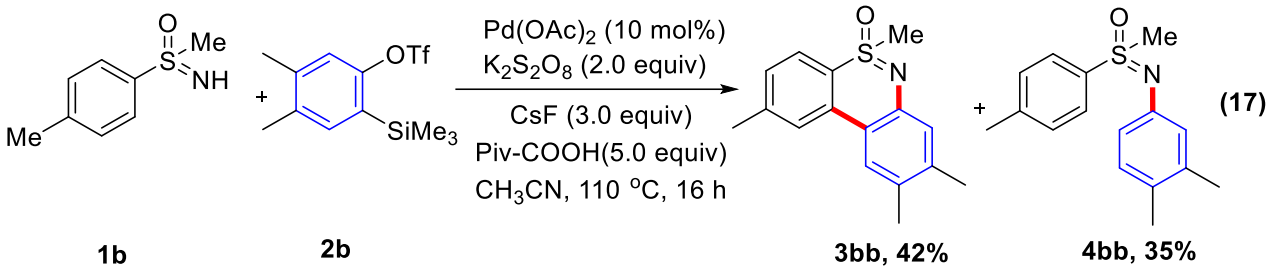
S.no	Sulfoximine (**1b-1j**)	Benzyne **2a**	Product(**3ab-3aj)**	Yield (%)
1	 **1b**		 **3ba**	68
2	 **1c**		 **3ca**	63
3	 **1d**		 **3da**	65

4	 **1e**		 **3ea**	68
5	 **1f**		 **3fa**	61
6	 **1g**		 **3ga**	62
7	 **1h**		 **3ha**	66
8	 **1i**		 **3ia**	63
9	 **1j**		 **3ja**	57

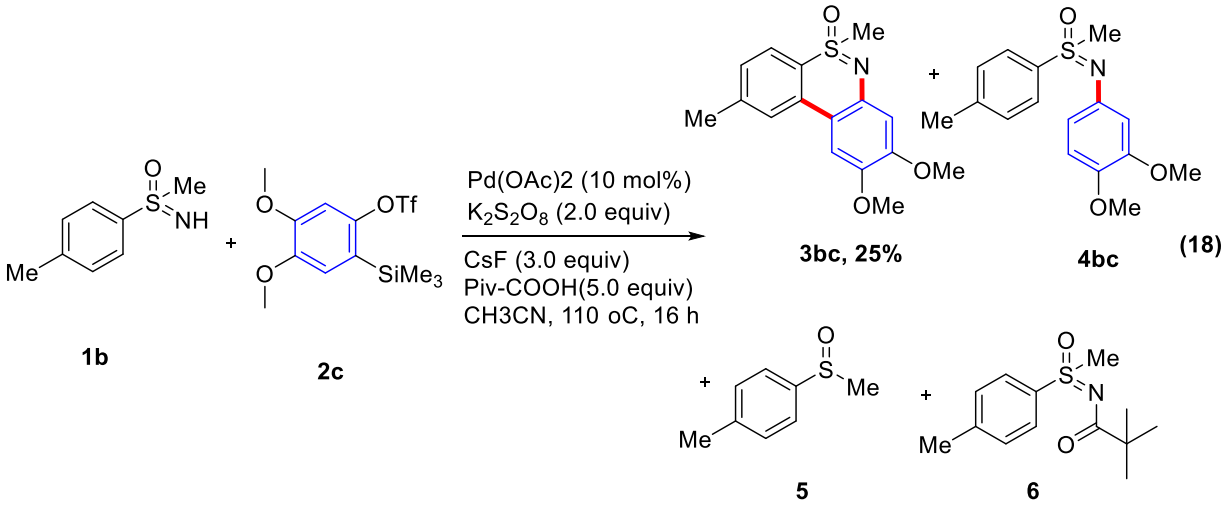
Our next investigation was on cyclisation reaction of unsymmetrical sulfoximines such as *meta* methoxy (**1k**), *meta* methyl (**1l**) and 3,4- dimethoxy(**1m**). In all the three cases, there are two positions for C-H bond activation (eq. 14-16). However, the cyclisation selectively happens at less steric centre and only one regioselective cyclised product (**3ka-3la**) was observed in 70%, 68% and 72% yield respectively.



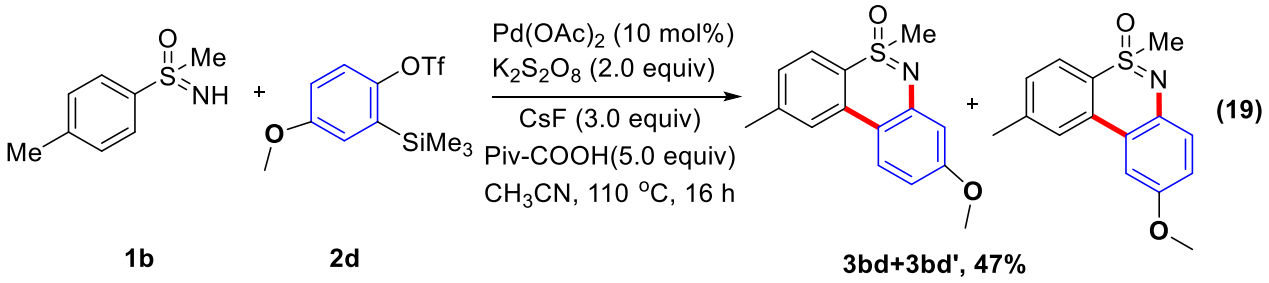
The scope of cyclisation was demonstrated over other substituted benzyne precursors. However, the reaction was not effective in these cases as that of in plane aryne precursor (**2a**) case. When we tried our optimised cyclisation reaction to 3,4 dimethyl aryne precursor (**2b**), it was observed only 42% substituted dibenzothiazine product (**3bb**) and along with it *N*-Arylation of substituted phenyl sulfoximine (**4bb**) in 35% (eq. 17). In order to improve the yield as well to supress the formation of *N*-Arylation, we again tried to optimise the reaction condition. We examined various acids such as adam-1-COOH, mesitylene acid, benzoic acid and p-toluic acid, but none of them was effective. Next, we tried different solvents such as THF, 1,4 dioxane and DMSO; also we investigated mixture of different solvents, among these CH_3CN:Dioxane in ratio of 8:1 was a bit more effective than only CH_3CN, but the formation of *N*-Arylation was not affected.



When we tried the cyclisation reaction with other substituted benzyne precursors, we observed that along with product (**3bc**) in 25% yield and *N*-Arylation (**4bc**) surprisingly two more by-products were formed; (1) *N*-acylation of sulfoximine **6** with pivalic acid and, (2) formation of sulfoxide **5** (eq. 18). To supress the formation of by-products when we decrease the concentration of pivalic acid to 3 or 1 equivalence, then the formation of *N*-arylation increased and only traces of product (**3bc**) was observed.

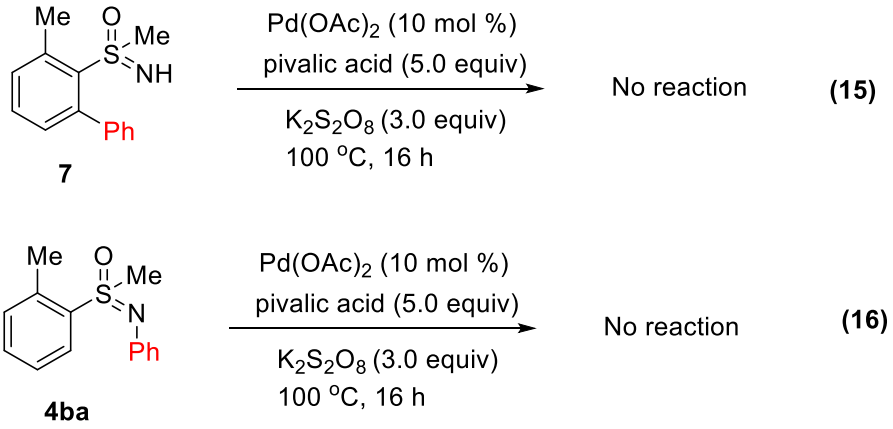


A similar trend was observed, when other benzyne precursors were treated with sulfoximine (**1b**). Next, we examined our cyclisation reaction for unsymmetrical benzyne precursor (**2d**) with substituted sulfoximine (**2b**). Here we didn't observe any selectivity for benzyne cyclisation and we got a mixture of dibenzothiazines (**3bd & 3bd'**) in 47% yield and *N*-Arylation with other by-products (eq. 19).



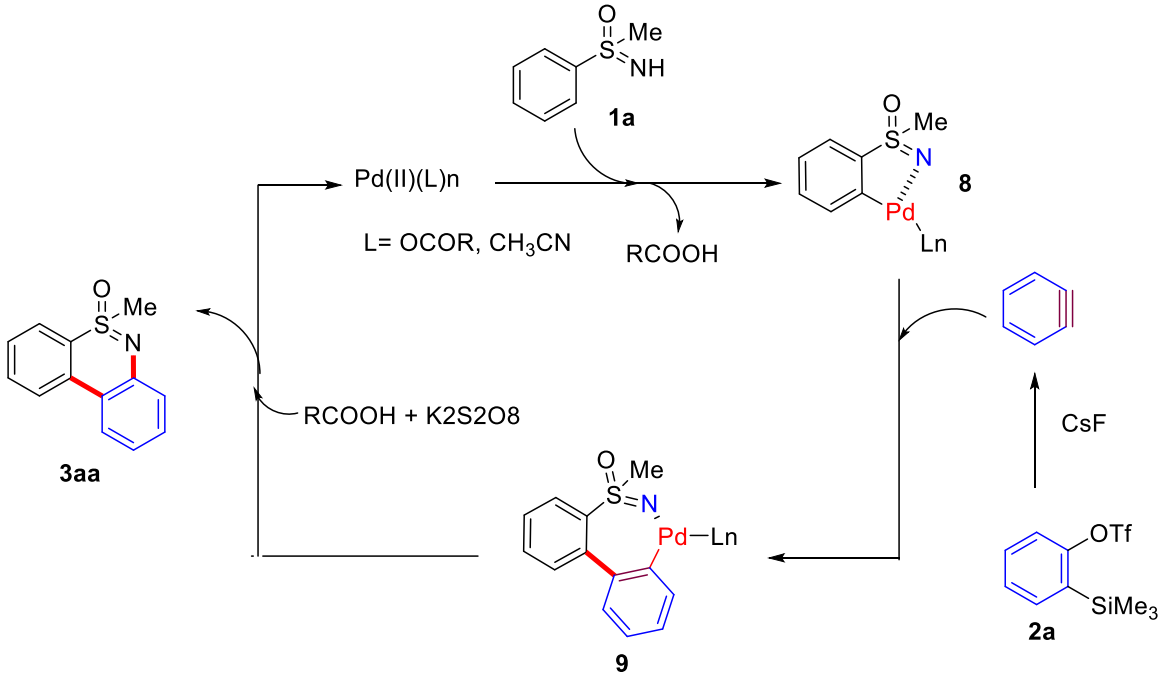
Finally, we did mechanistic studies to propose a mechanism for our cyclisation reaction. There were three possible pathway for this reaction to occur: 1) *ortho*-arylation of sulfoximine with benzyne forming product **7** followed by intramolecular C-N bond formation or, 2) *N*-arylation of sulfoximine with benzene yielding product **4ba** followed by intramolecular dehydrogenative aryl-aryl coupling or, 3) Insertion of benzyne into sulfoximine. To find plausible reaction mechanism, we did some reactions. To check 1st pathway, we prepared *ortho*-arylated sulfoximine **7** treated with $Pd(OAc)_2$, CsF and $K_2S_2O_8$ in CH_3CN at 110°C for 16 h (eq. 15). However, no cyclised product **3ga** was formed. To check the 2nd possibility, we treated the separately prepared N-Arylated sulfoximine **4ba** with $Pd(OAc)_2$, CsF and $K_2S_2O_8$ in CH_3CN at 110°C for 16 h (eq. 16), but no reaction occur in this case.

Scheme 2: Mechanistic studies.



The proposed mechanism for our cyclisation reaction is represented in **Scheme 3.** Coordination of the sulphoximine **1a** nitrogen to the palladium species followed by ortho-metalation provides a five-membered palladacycle intermediate **8**. Coordinative insertion of benzyne into intermediate **8** yields a seven-membered palladacycle intermediate **9**. Subsequent C–N bond formation and reductive elimination afford product **3a** and regenerate the active palladium species in the presence of RCOOH and $K_2S_2O_8$.

Scheme 3: Proposed mechanism.



4. Conclusion

We developed one step synthesis of substituted tricyclic dibenzothiazine via chelation-assisted palladium catalysed cyclisation of phenyl sulfoximine with Aryne. The reaction worked well with plane benzyne whereas in the case of other substituted benzyne different competing reactions occurred.

5. Experimental Section

5.1 General Information:

All the starting material preparation reactions were performed in an oven-dried round bottom flask and final transition metal catalysed reaction were done in a pressure tube. Commercial grade solvents were distilled prior to use. Column chromatography was performed using either 100-200 Mesh or 60-140 Mesh silica gel. Thin layer chromatography (TLC) was performed on silica gel plates. Visualization of spots on TLC plate was accomplished with short range UV light.

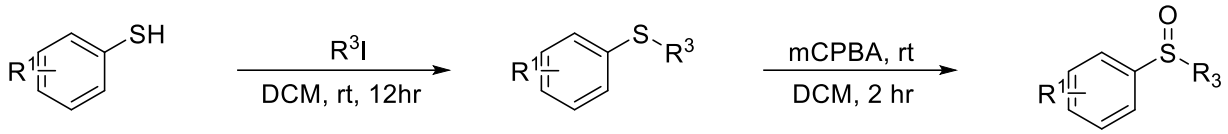
5.2 Procedure:

5.2.1 General preparation of dibenzothiazines derivatives by annulation of Phenyl sulfoximine into benzyne under palladium catalytic condition.

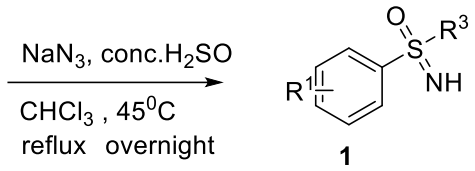
In a 15 mL pressure tube, Phenyl sulfoximine **1** (100 mg), $Pd(OAc)_2$ (10.0 mol %) and $K_2S_2O_8$ (2.0 equiv) were added. The tube was covered with septum and then evacuated and purged with nitrogen gas three times and CsF (3.0 equiv) was added inside the glove box. Then, acetonitrile (1.0 mL) and benzyne precursor **2** (1.3 equiv) were added in acetonitrile (2.0 mL) followed by pivalic acid (5.0 equiv) via syringes and the tube was evacuated and purged with nitrogen gas three times. After that, the a septum was taken out immediately and a screw cap was used to cover the tube and the reaction mixture was left for stirring at 110 °C for next 16 h. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2 and filtered through Celite belt, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexanes and ethyl acetate as eluent to give pure cyclised product **4**.

The isolated product is confirmed using H^1 and C^{13} NMR spectroscopy and mass spectrometry.

5.2.2 Preparation of sulfoximines:



R^1 = 4-F ,4-Br ,4-Cl ,4-NO_2 , 4-Me, 3-OMe, 3-Me , 2-Me R^3= Me, Et, Ph



1

Step1. Alkylation of substituted thiophenol: (only some sulfides)

A round bottom flask (100 ml) containing the substituted thiophenol (1 mmol), CH_2Cl_2 (20–25 ml) and K_2CO_3 (3 mmol) was stirred at 0 °C for 5 min. To this mixture, MeI or EtI was added. The reactions were stirred overnight at room temperature. The reaction mixtures were extracted with CH_2Cl_2 (3×50 ml), the solvent was dried over anhydrous Na_2SO_4 and was evaporated under vacuum. Purification by silica gel chromatography (hexane) resulted in 90–95% yield of sulfides.

Step 2.Oxidation of sulfides to sulfoxides:

A round bottom flask (100 ml) containing commercially available or prepared sulfides (1 mmol) dissolved in DCM (20 ml) was cooled to 0ºC, and mCPBA (2 eq.) in DCM was added slowly at 0 °C. The resulting mixture was allowed to stir at room temperature for 2 h. The mixture was washed with a saturated solution of NaHCO3 and were extracted with CH_2Cl_2 (3×50 ml), the solvent was dried over anhydrous Na_2SO_4 and was evaporated under vacuum. The product was purified by silica gel column chromatography to give 90% yield.

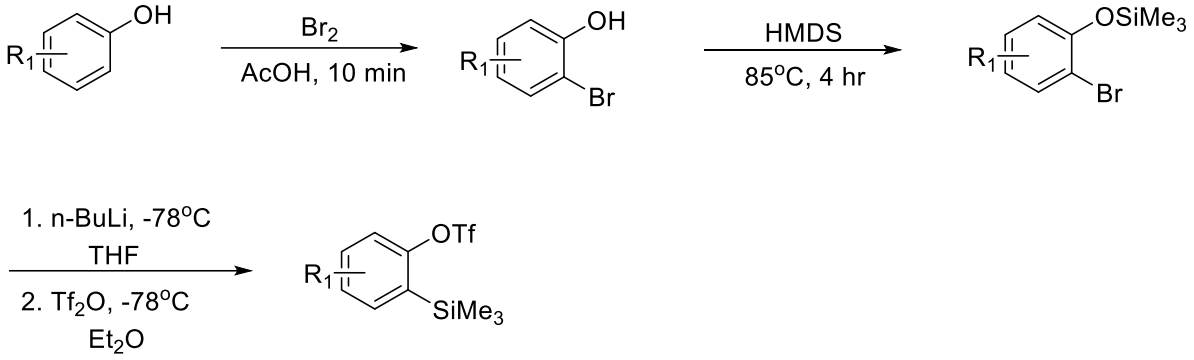
Step 3. Imination of sulfoxides:

A round bottom flask (100 ml) containing the sulfoxides (1 mmol), $CHCl_3$ (20–25 ml) and sodium azide (1.2 mmol) was stirred at 0 °C for 5 min. Concentrated sulphuric acid (~2.0 mL for 1.0 g of sulfoxide) was introduced over 5-10 minutes using dropping funnel

at 0 °C. The resulting mixture was slowly warmed up to 45 ^{o}C .The reaction was continued for an additional 12 h at 45 ^{o}C. In the reaction mixture ice-water was added to dilute remaining sulfuric acid. The organic layer was decanted and the aqueous layer was washed with minimum amount of $CHCl_3$. The aqueous layer was made slightly alkaline using 20% NaOH solution and extracted with $CHCl_3$ (3 × 5 mL, for 5 mmol sulfoxide). The combined organic extracts were dried over Na_2SO_4. The solvent was filtered and evaporated under reduced pressure. The crude residue was purified using column chromatography on silica gel to afford the desired sulfoximines **1** in good yields.

This procedure was not ineffective in the preparation of 3,4 dimethoxy phenyl methyl sulfoximine. However, the procedure reported by Carsten Bolm was helpful for the synthesis of 3,4 dimethoxy phenyl methyl sulfoximine.[19]

5.2.3 Preparation of Aryne Precursors



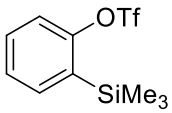
The required Aryne precursors were prepared by three steps.

Step 1: Preparation of substituted 2-bromopheonol: To a homogeneous solution of substituted phenol (1 mmol) in acetic acid at 0^{o}C, solution of Br_2 (0.9 mmol) in acetic acid was added dropwise and the reaction mixture was stirred for 10 min. Then the reaction mixture was poured on the ice and sodium thiosulphate solution was added to it. The organic layer was extracted with DCM and dried over Na_2SO_4. The solution was concentrated by evaporation under reduced pressure and finally obtained substituted 2-bromophenol.

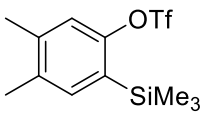
Step 2: Preparation of 2-bromophenoxytrimethylsilane: In 100 ml two necks R.B charged with 2-bromophenol (1 mmol), HMDS (1.5 mmol) was added under N_2 atmosphere and the reaction mixture was heated at 85^{o}C for 4 hours. The reaction mixture was concentrated by evaporation under reduced pressure to remove remaining of HMDS and obtained 2-bromophenoxytrimethylsilane in 90% yield.

Step 3: Preparation of 2-trimethylsilylphenyl triflate: To a solution of 2-bromophenoxytrimethylsilane (1 mmol) in THF at -78^{o}C, n-BuLi (1.3 mmol) was added dropwise and the mixture was stirred for 30 min. The temperature of reaction mixture was dropped to -100^{o}C and stopped stirring for 10 min. Then, the temperature was increased to -78^{o}C and diethyl ether was added to it. Subsequently, Tf_2O was added at -78^{o}C and stirred at same temperature for 30 min. The reaction mixture was brought to room temperature and aqueous solution was added. The organic layer was extracted in DCM and concentrated using rotary evaporation. The crude product was purified using column chromatography to yield 80% benzyne precursor.

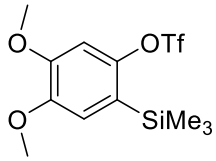
The above procedures were used to synthesis following benzyne precursor **2a-2g**:



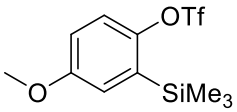
2a



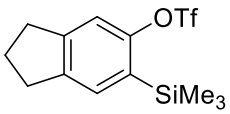
2b



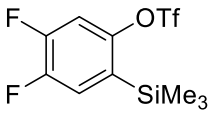
2c



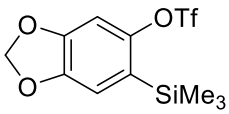
2d



2e



2f



2g

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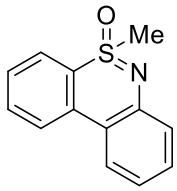
7. Appendix

Spectra Data of compounds.

5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3aa).

100 mg of **1a** was taken and 102 mg of product **3aa** was isolated (yield 69%).

Brown solid; eluent (20% ethyl acetate in hexanes).



^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.20 (d, J = 8.3 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 8.1 Hz, 1H), 7.09 (t, J = 8.2 Hz, 1H), 3.53 (s, 3H).

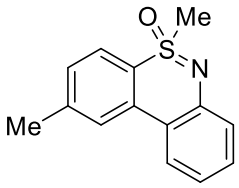
^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.8, 134.0, 132.9, 130.7, 127.9, 124.8, 124.8, 123.9, 123.5, 120.9, 117.4, 44.7**.**

HRMS (ESI): calc. for [($C_{13}H_{11}NOS$)H] (M+H) 230.0640, measured 230.0642

2,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide (3ba).

100 mg of **1b** was taken and 97.3 mg of product **3ba** was isolated (yield 68%).

Brown solid; eluent (15% ethyl acetate in hexanes).



^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.00 (d, *J* = 8.8 Hz, 1H), 7.99 (s, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.07 (t, *J* = 8.2 Hz, 1H), 3.50 (s, 3H), 2.55 (s, 3H).

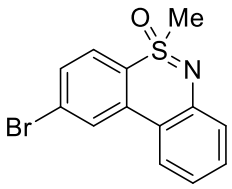
^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.7, 142.9, 134.0, 130.6, 129.0, 124.7, 124.0, 123.9, 123.4, 122.2, 120.7, 117.3, 44.9, 22.1.

HRMS (ESI): calc. for [($C_{14}H_{13}NOS$)H] (M+H) 244.0796, measured (not got yet) .

2-Bromo-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ca).

100 mg of **1c** was taken and 83.0 mg of product **3ca** was isolated (yield 63%).

Brown solid (shinning); eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.96 – 7.92 (m, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 9.8 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 7.0 Hz, 1H), 7.26 (d, *J* = 6.3 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 3.51 (s, 3H).

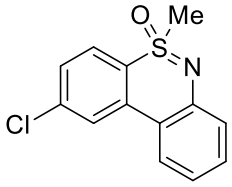
^{13}C NMR (CDCl$_3$, 100 MHz): δ 143.0, 135.8, 131.4, 130.9, 128.0, 126.9, 125.4, 125.0, 123.6, 123.3, 121.1, 116.3, 44.7.

HRMS (ESI): calc. for [($C_{13}H_{10}BrNOS$)H] (M+H) 307.9745, measured 307.9750.

2-Chloro-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3da)

100 mg of **1d** was taken and 90 mg of product **(3da)** was isolated (yield 65%).

Pale Pink solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 500 MHz): δ 8.17 (s, 1H), 7.94 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 6.3 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 3.52 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz): δ 143.1, 139.5, 135.8, 131.4, 128.1, 125.5, 125.0, 123.8, 123.6, 122.9, 121.1, 116.4, 44.8.

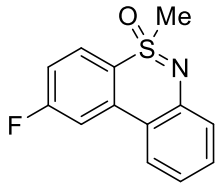
HRMS (ESI): calc. for [($C_{13}H_{10}ClNOS$)H] (M+H) 264.0250, measured 264.0249

.

2-Fluoro-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ea)

100 mg of **1e** was taken and 97.0 mg of product **3ea** was isolated (yield 68%).

White shinning solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 500 MHz): δ 8.35 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 6.6 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 3.51 (s, 3H).

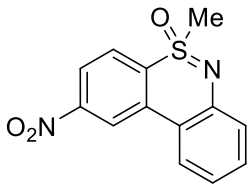
^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.4, 163.7, 143.1, 137.4, 137.4(F-Coupling), 131.5, 127.1, 127.0(F-Coupling), 124.9, 123.7, 121.0, 116.7, 116.2, 115.9(F-Coupling), 110.2, 110.0 (F-Coupling), 45.2.

HRMS (ESI): calc. for [($C_{13}H_{10}FNOS$)H] (M+H) 248.0545, measured 248.0551.

5-methyl-2-nitrodibenzo[c,e][1,2]thiazine 5-oxide (3fa).

100 mg of **1f** was taken and 83.5 mg of product **3fa** was isolated (yield 61%).

Yellow solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.08 (s, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 8.8 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.22 – 7.17 (m, 1H), 3.63 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.9, 135.6, 132.2, 130.9, 128.4, 125.4, 125.3, 123.9, 121.9, 121.8, 119.7, 116.7, 44.2.

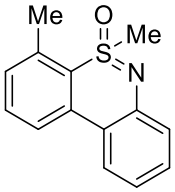
HRMS (ESI): calc. for [($C_{13}H_{10}N_2O_3S$)H] (M+H) 275.0490, measured 275.0499

.

4,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide (3ga).

100 mg of **1b** was taken and 88.8 mg of product **3ga** was isolated (yield 62%).

Colourless semisolid; eluent (35% ethyl acetate in hexanes).



^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08 (d, *J* = 8.0 Hz, 1 H), 7.96 (dd, *J* = 8.0, 4.0 Hz, 1 H), 7.63 (t, *J* = 8.0 Hz, 1 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.37 (t, *J* = 8.0 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.06 (t, *J* = 8.0 Hz, 1 H), 3.51 (s, 3 H), 2.85 (s, 3 H).

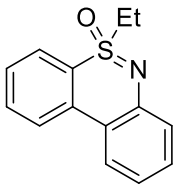
^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.2, 135.5, 135.2, 132.6, 131.2, 130.5, 124.6, 124.2, 123.9, 121.9, 120.6, 117.5, 47.8, 21.0.

HRMS (ESI): calc. for [($C_{14}H_{13}NOS$)H] (M+H) 244.0796, measured 244.0799.

5-Ethyldibenzo[c,e][1,2]thiazine 5-oxide (3ha).

100 mg of **1h** was taken and 94.8 mg of product **3ha** was isolated (yield 66%).

Dark brown; eluent (20% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.22 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 6.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 3.71 (dq, *J* = 14.5, 7.2 Hz, 1H), 3.56 (dq, *J* = 14.8, 7.4 Hz, 1H), 1.23 (t, *J* = 7.3 Hz, 3H).

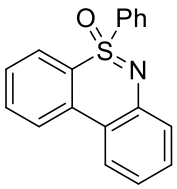
^{13}C NMR (CDCl$_3$, 100 MHz): δ 143.5, 135.2, 133.0, 130.7, 127.8, 124.9, 124.5, 123.8, 123.4, 121.7, 120.5, 116.7, 50.8, 8.6.

HRMS (ESI): calc. for [($C_{14}H_{13}NOS$)H] (M+H) 244.0796, measured 244.0799.

5-phenyldibenzo[c,e][1,2]thiazine 5-oxide (3ia)

100 mg of **1i** was taken and 84.5 mg of product **3ia** was isolated (yield 63%).

Dark brown solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.25 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 2H), 7.69-7.65 (m, 2H), 7.62 – 7.56 (m, 2H), 7.48 – 7.41 (m, 2H), 7.40 (d, *J* = 4.1 Hz, 2H), 7.17 (t, *J* = 8.3 Hz, 1H).

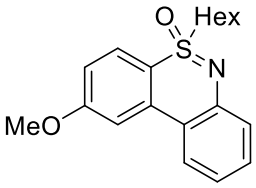
^{13}C NMR (CDCl$_3$, 100 MHz): δ 142.8, 139.2, 133.7, 132.3, 130.6, 129.6, 129.2, 127.7, 126.7, 125.8, 125.6, 125.5, 123.4, 121.1, 117.1**.**

HRMS (ESI): calc. for [($C_{18}H_{13}NOS$)H] (M+H) 292.0796, measured 292.0802.

5-Hexyl-2-methoxy dibenzo[c,e][1,2]thiazine 5-oxide (3ja).

100 mg of **1i** was taken and 73.5 mg of product **3ia** was isolated (yield 57%).

Dark brown solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.58 (d, *J* = 2.4 Hz, 1H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.23 (d, *J* = 9.4 Hz, 1H), 7.10 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.03 (t, *J* = 8.3 Hz, 1H), 3.98 (s, 3H), 3.56 (ddd, *J* = 14.4, 11.1, 5.0 Hz, 1H), 3.46 (ddd, *J* = 14.4, 11.0, 5.1 Hz, 1H), 1.75 – 1.64 (m, 1H), 1.54 – 1.41 (m, 1H), 1.40 – 1.28 (m, 3H), 1.24 – 1.16 (m, 5H), 0.82 (t, *J* = 6.9 Hz, 3H).

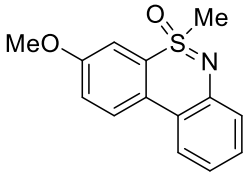
^{13}C NMR (CDCl$_3$, 100 MHz): δ 163.0, 144.2, 137.5, 130.8, 126.8, 124.9, 123.4, 120.1, 116.6, 115.4, 115.2, 106.7, 57.2, 55.7, 31.1, 27.7, 23.6, 22.3, 13.8.

HRMS (ESI): calc. for [($C_{19}H_{23}NO_2S$)H] (M+H) 330.1528, measured 330.1533

3-Methoxy-5-methyldibenzo[*c,e*][1,2]thiazine 5-oxide (3ka).

100 mg of **1i** was taken and 100.7 mg of product **3ia** was isolated (yield 70%).

Brick red solid; eluent (30% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 500 MHz): δ 8.05 (d, *J* = 9.3 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.28-7.25 (m, 3H), 7.21 – 7.16 (m, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 3.87 (s, 3H), 3.44 (s, 3H).

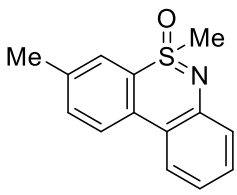
^{13}C NMR (CDCl$_3$, 100 MHz): δ 159.2, 141.7, 129.7, 127.1, 125.6, 125.4, 124.6, 122.9, 121.2, 120.8, 117.5, 106.5, 55.8, 44.7.

HRMS (ESI): calc. for [(C14H13NO_2S)H] (M+H) 260.0745, measured 260.0750

3,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide(3la).

100 mg of **1l** was taken and 97.0 mg of product **3la** was isolated (yield 68%).

Brick red solid; eluent (20% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 3.52 (s, 3H), 2.51 (s, 3H).

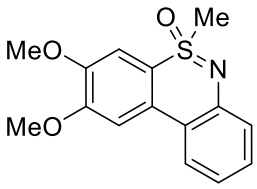
^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.4, 138.3, 134.2, 131.5, 130.3, 124.7, 124.6, 123.8, 123.7, 123.2, 120.8, 117.4, 44.8, 21.2.

HRMS (ESI): calc. for [($C_{14}H_{13}NOS$)H] (M+H) 244.0796, measured (not got yet).

2,3-Dimethoxy-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ma)

100 mg of **1m** was taken and 96.8 mg of product **3ma** was isolated (yield 72%).

Dark brown solid; eluent (40% ethyl acetate in hexanes).



^{1}H NMR ($CDCl_3$, 400 MHz):δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.53 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.27 (s, 1H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 4.08 (s, 3H), 4.01 (s, 3H), 3.47 (s, 3H).

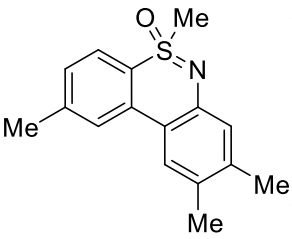
^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.3, 149.6, 142.5, 130.0, 129.2, 124.7, 122.8, 120.5, 117.0, 116.5, 105.2, 104.8, 56.4, 56.2, 45.8.

HRMS (ESI): calc. for [(C16H17NO$_3$S)H] (M+H) 290.0851, measured (not got yet).

2,5,8,9-tetramethyl dibenzo[c,e][1,2]thiazine 5-oxide (3bb).

100 mg of **1b** was taken and 67.0 mg of product **3bb** was isolated (yield 42%).

White solid; eluent (30% ethyl acetate in hexanes).



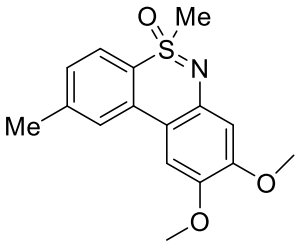
^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.73 (s, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.04 (s, 1H), 3.46 (s, 3H), 2.54 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.4, 140.9, 139.9, 134.2, 129.0, 128.4, 125.4, 124.0, 123.5, 122.0, 114.9, 44.9, 22.1, 19.9, 19.4.

HRMS (ESI): calc. for [($C_{16}H_{17}NOS$)H] (M+H) 272.1109, measured 272.1109.

8,9-Dimethoxy-2,5-dimethyl dibenzo[c,e][1,2]thiazine 5-oxide (3bc).

Brown solid; eluent (50% ethyl acetate in hexanes).

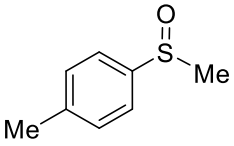


^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.80 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.39 (s, 1H), 7.31 (d, *J* = 8.9 Hz, 1H), 6.76 (s, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.50 (s, 3H), 2.53 (s, 3H).

(NMR has some impurities which is not isolable).

1-methyl-4-(methylsulfinyl)benzene (5).

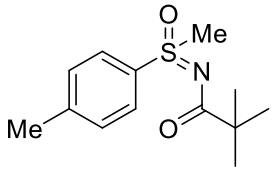
Yellow colour viscous liquid; eluent (45% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 2.70 (s, 3H), 2.41 (s, 3H).

N-(methyl(oxo)(p-tolyl)-sulfanylidene)pivalamide (6).

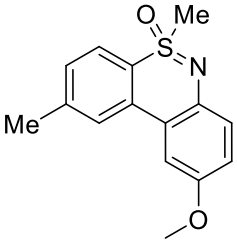
Brown colour solid; eluent (50% ethyl acetate in hexanes).



^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 3.29 (s, 3H), 2.44 (s, 3H), 1.22 (s, 9H).

9-methoxy-2,5-dimethyl-dibenzo[c,e][1,2]thiazine 5-oxide (3bd+3bd').

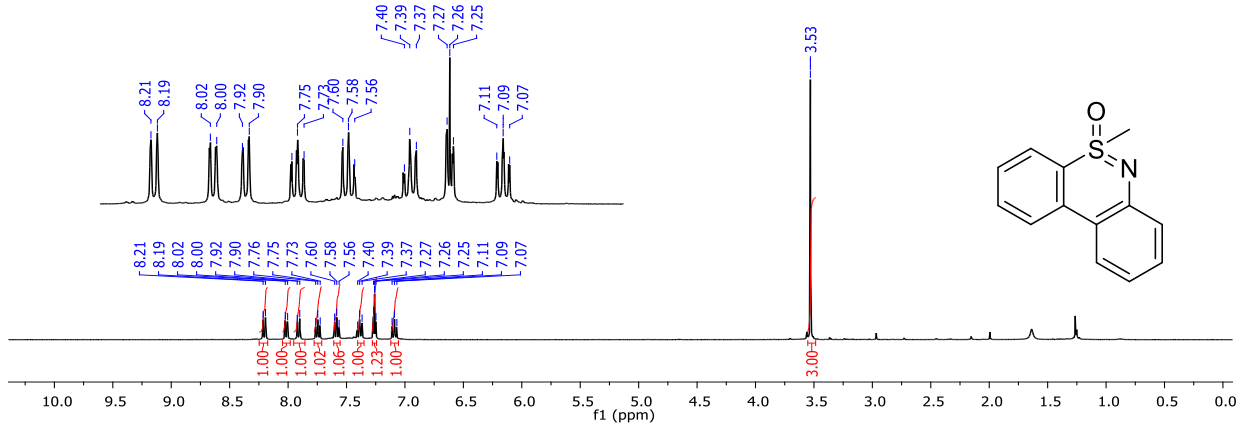
Brick red colour solid; eluent (40% ethyl acetate in hexanes).

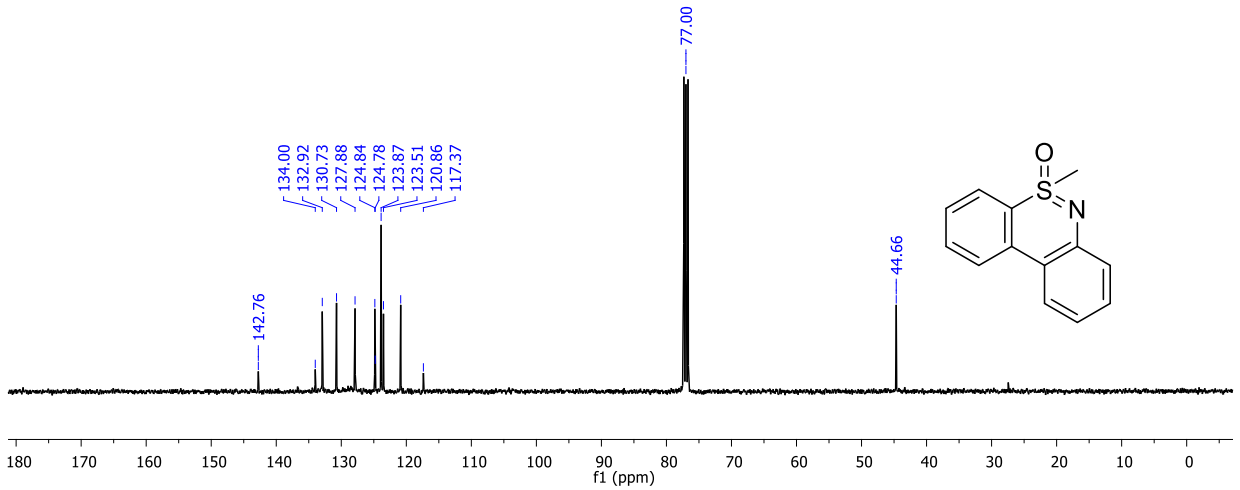


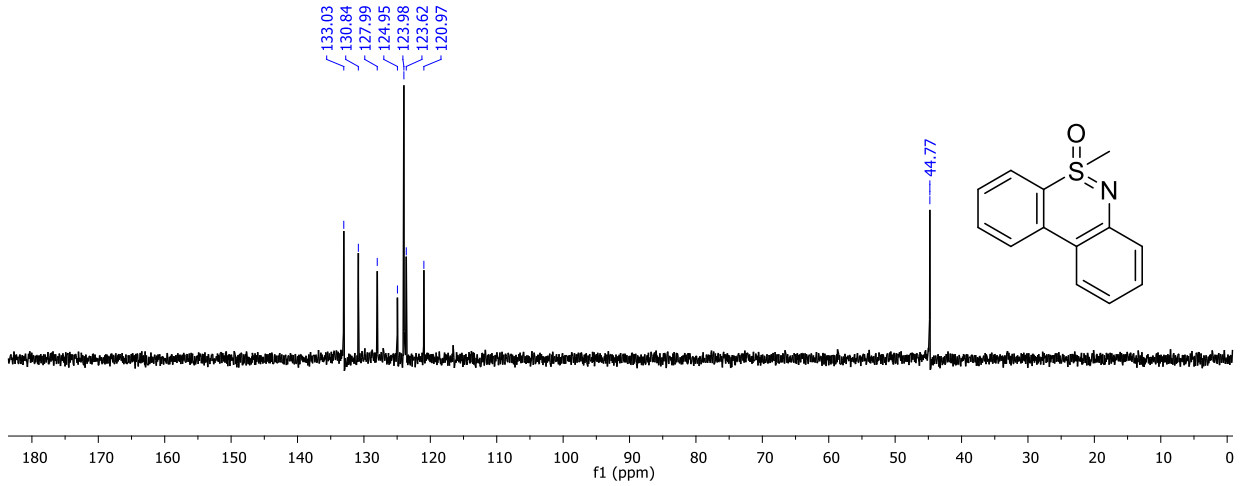
(Mixture of **3bd+3bd'** in the ratio of 1:0.7).

^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.94 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 8.9 Hz, 1H), 7.05 (s, 1H), 6.89 (d, *J* = 9.5 Hz, 1H), 3.47 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H).

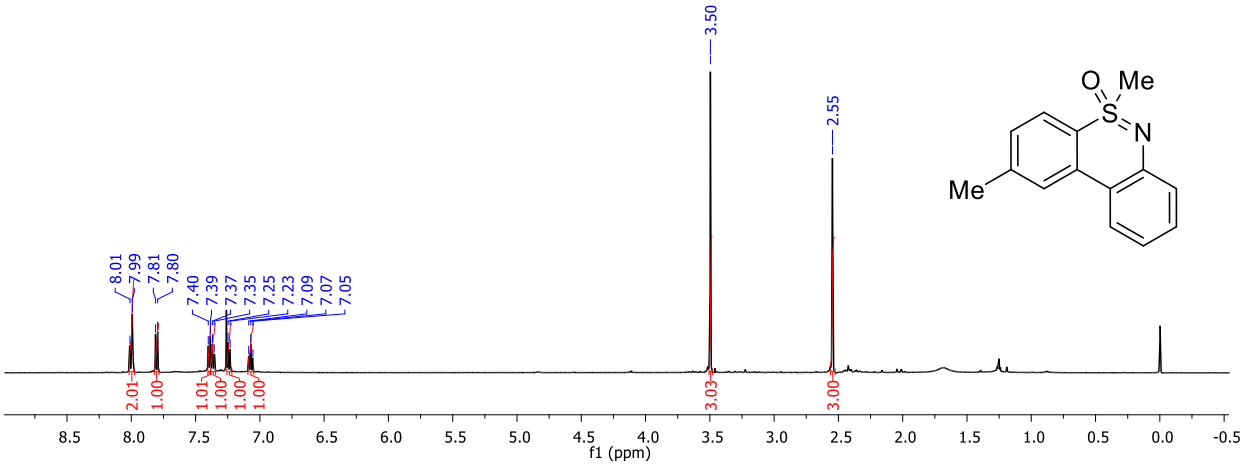
5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3aa).

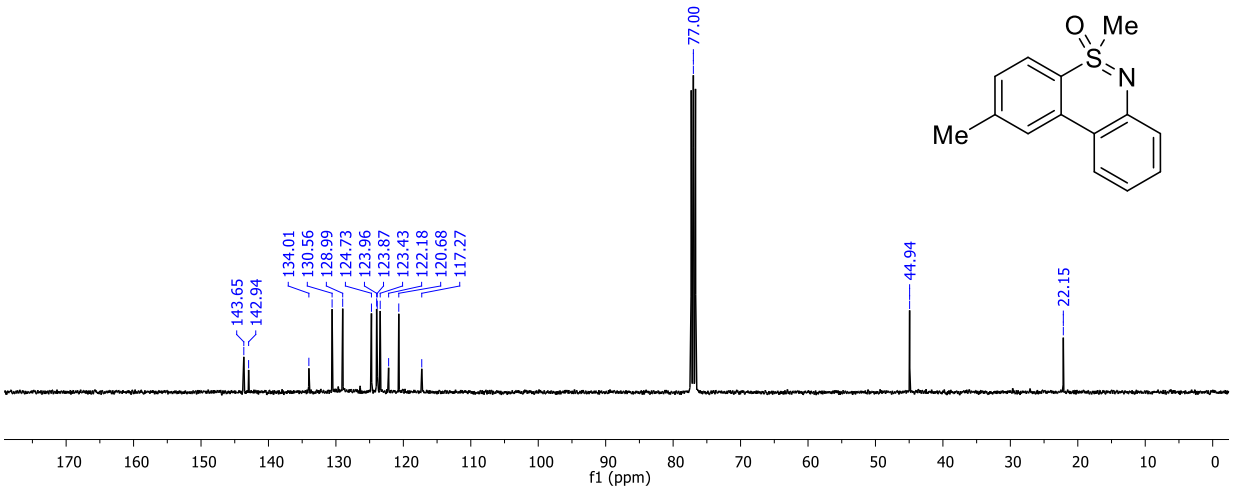


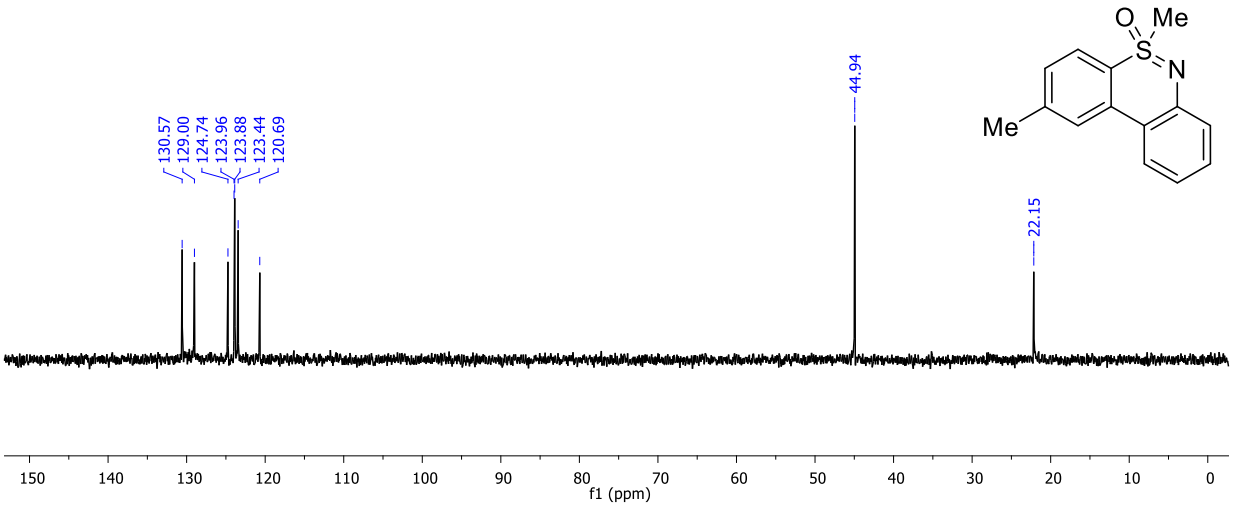




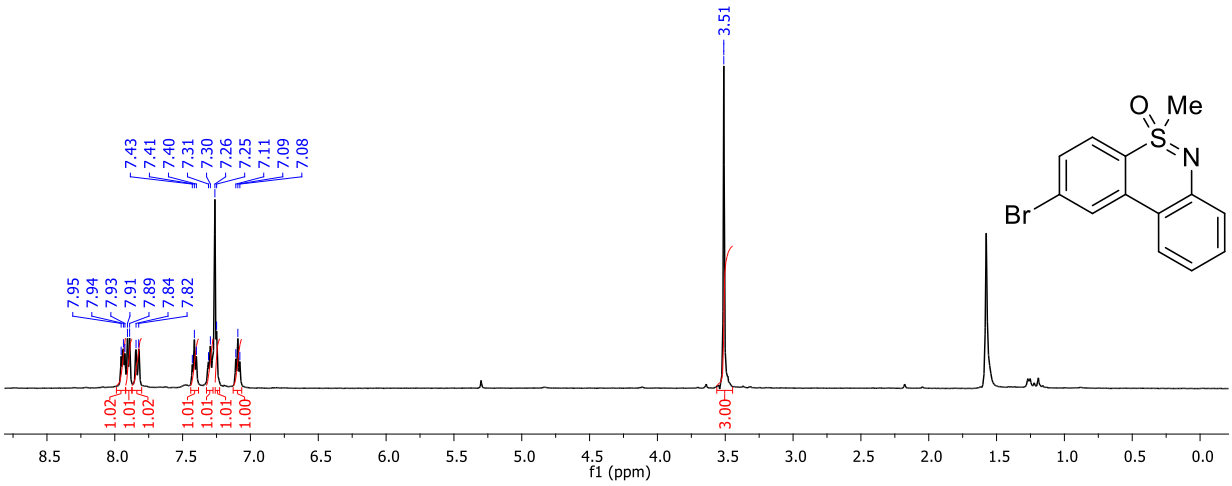
2,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide (3ba).

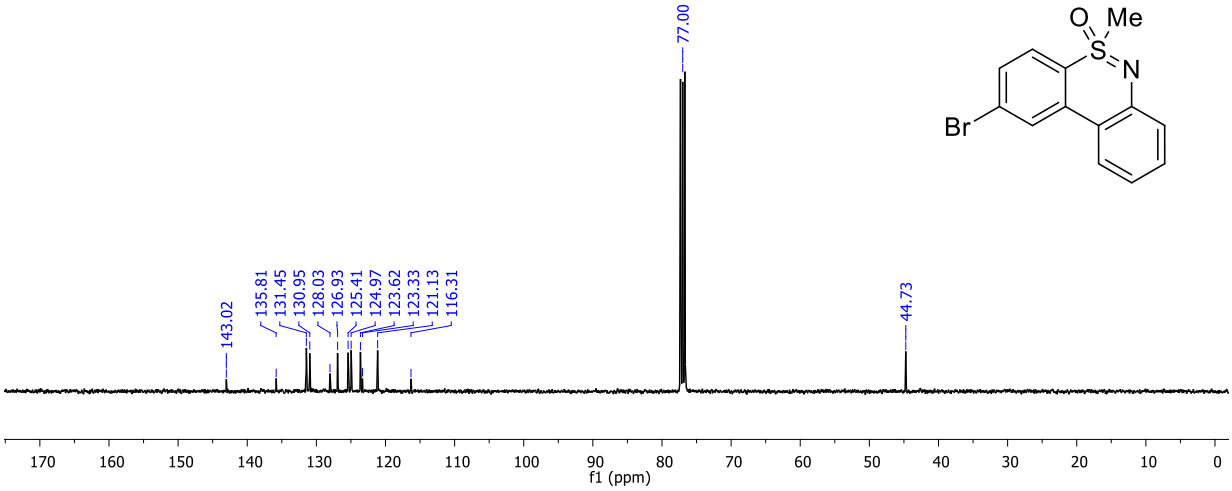


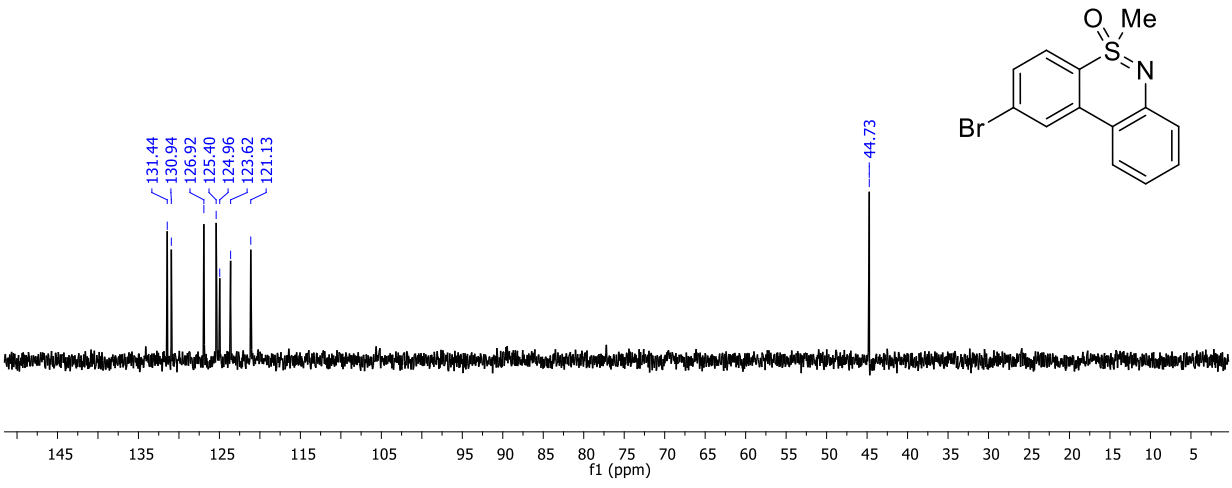




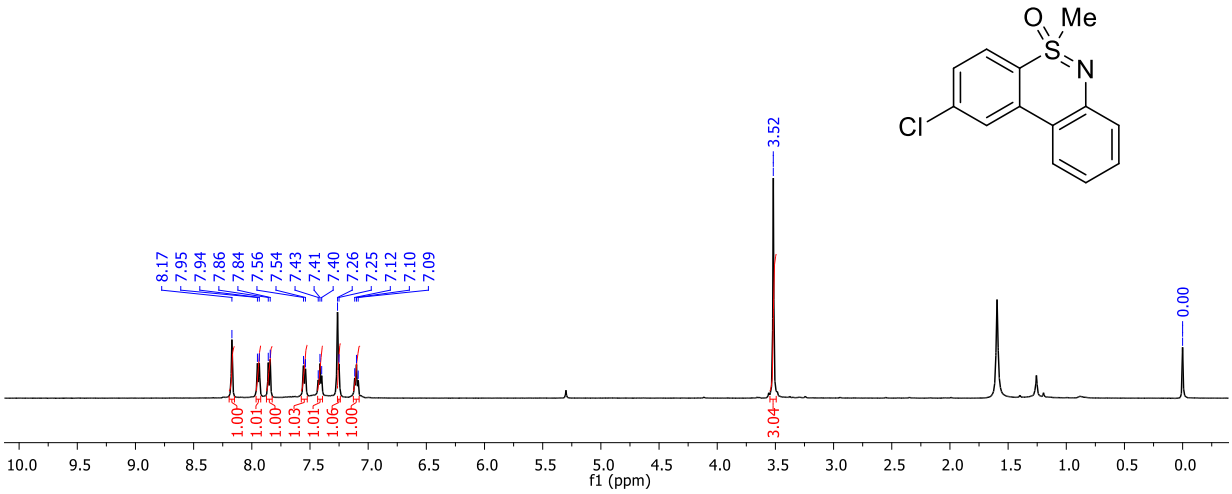
2-Bromo-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ca).

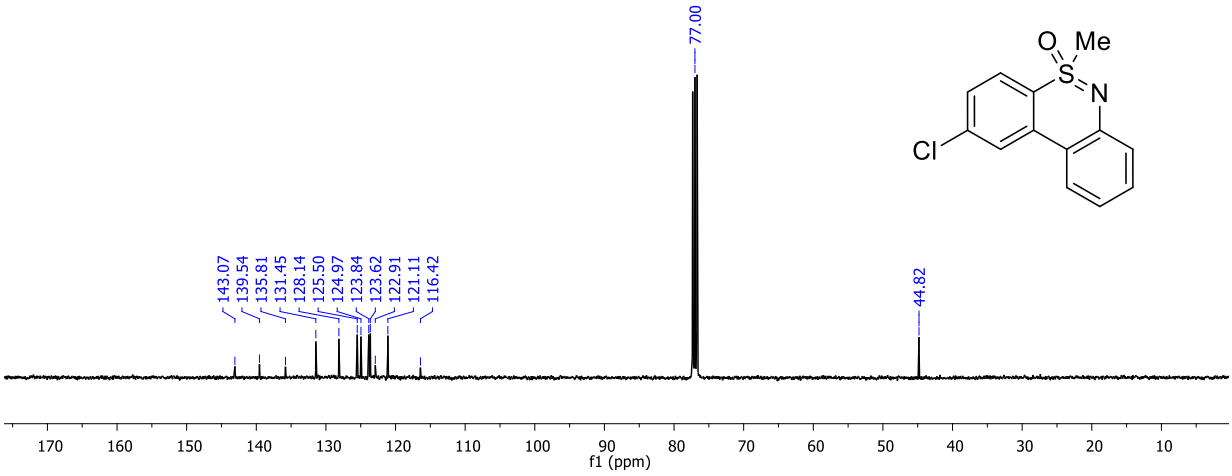


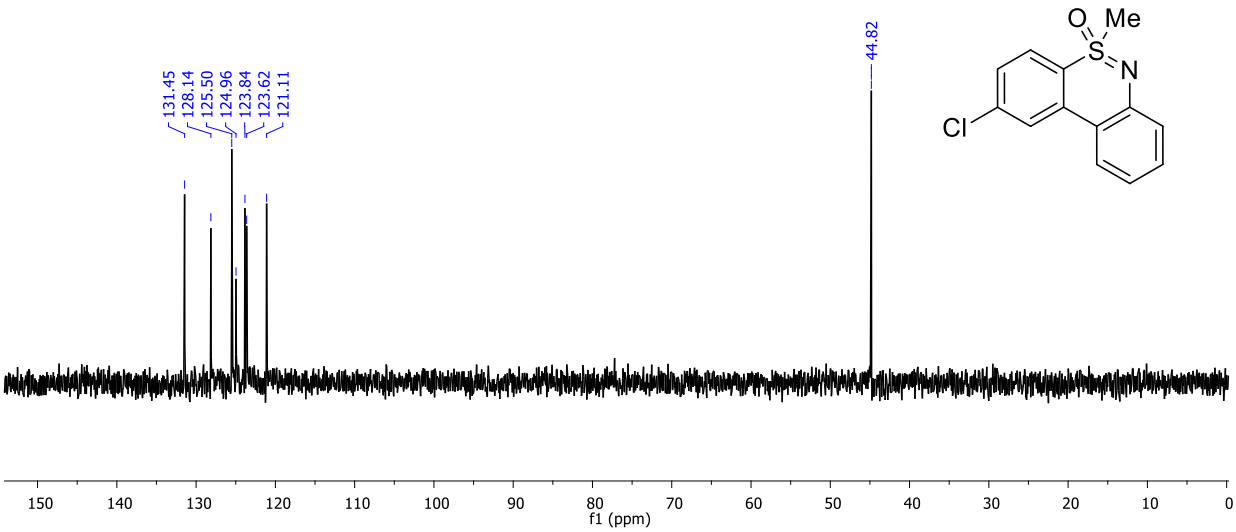




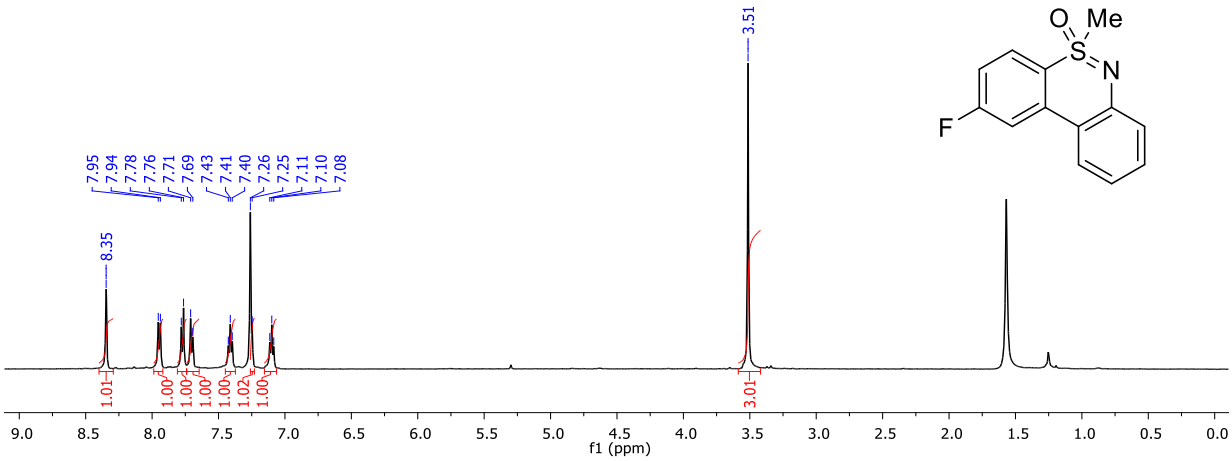
2-Chloro-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3da).

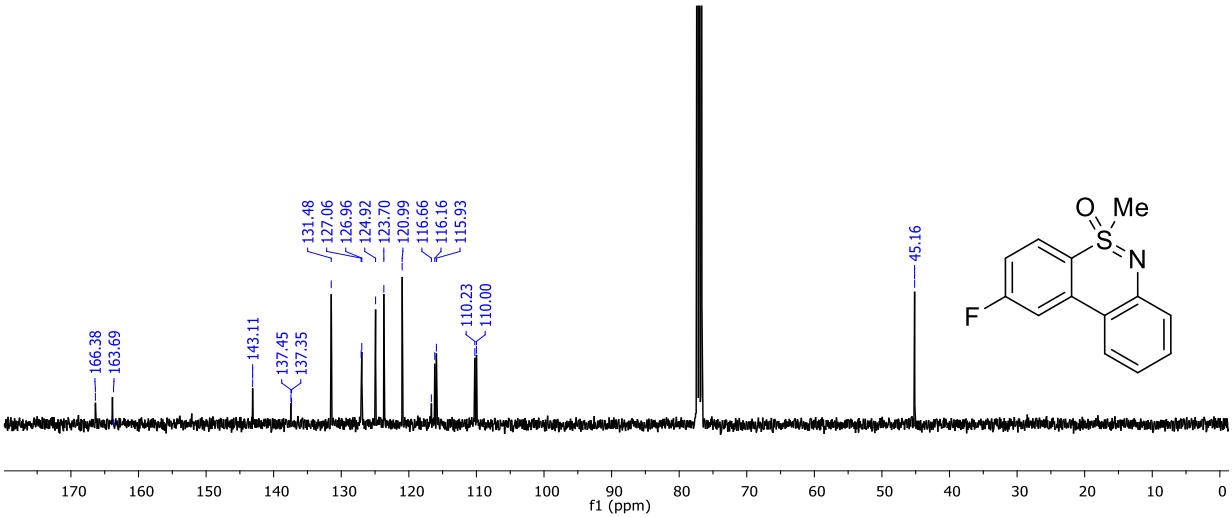


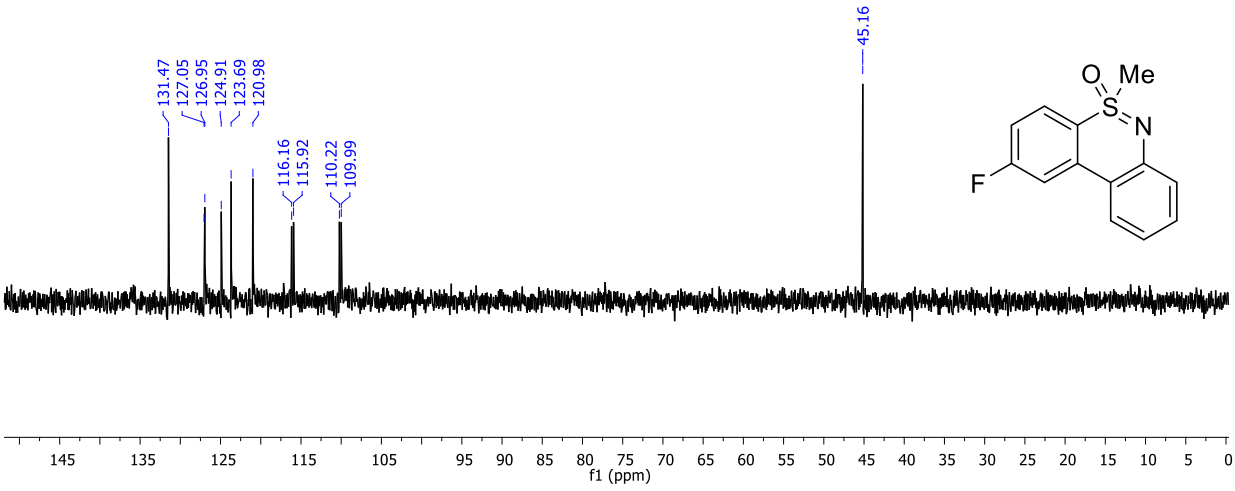




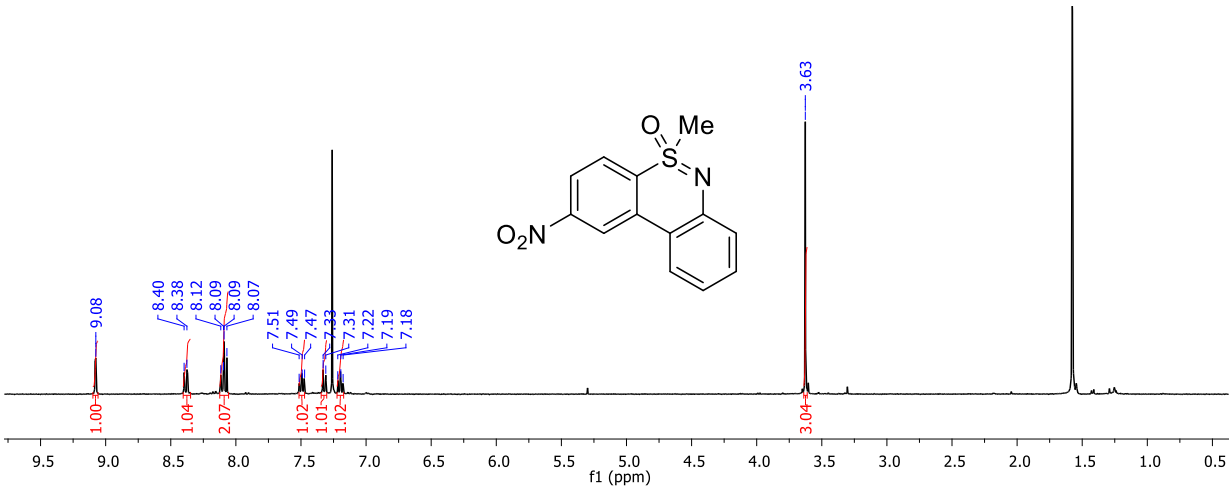
2-Fluoro-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ea).

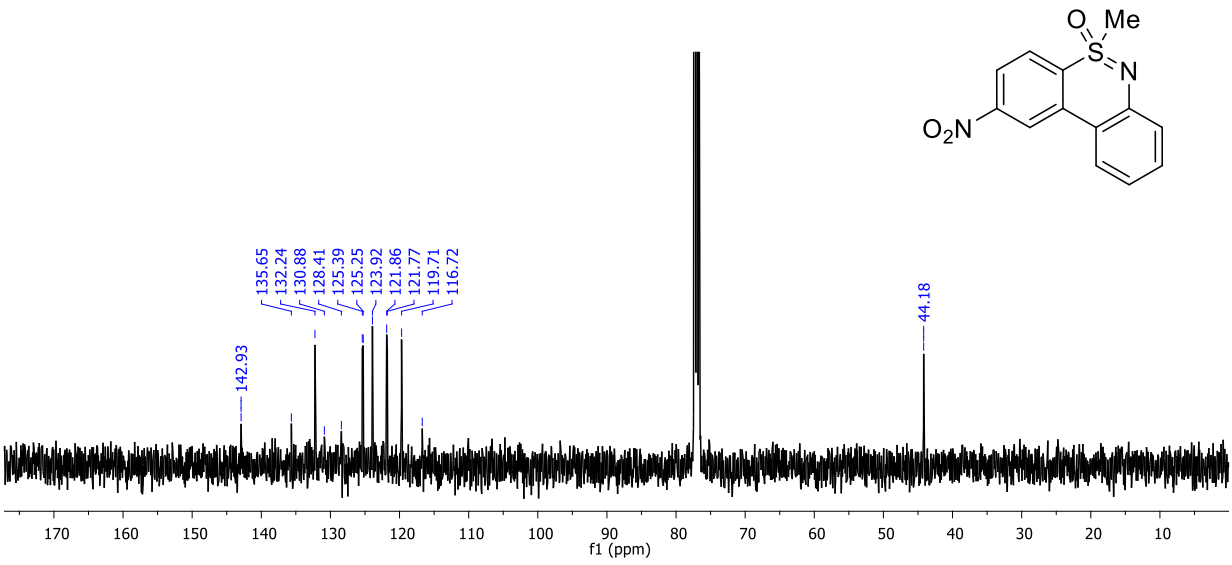




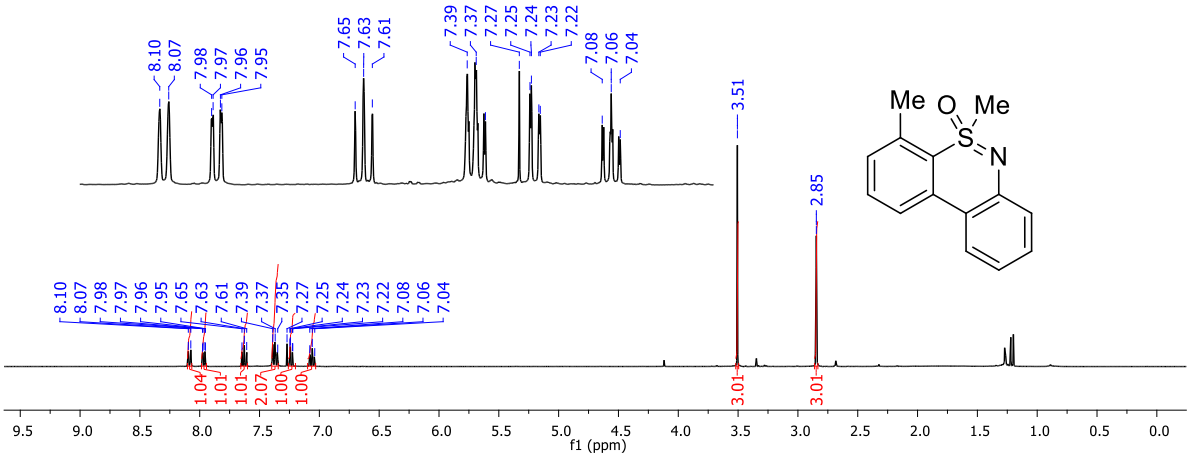


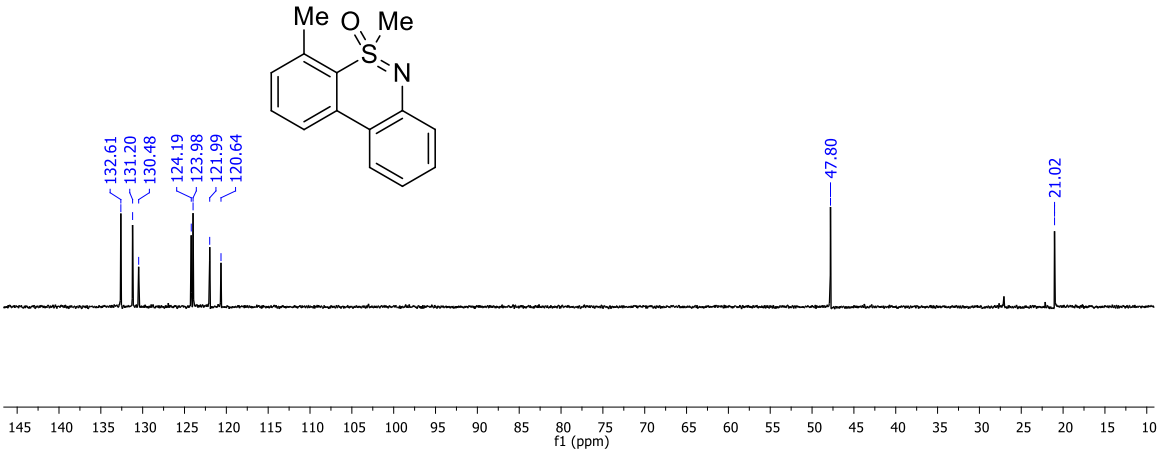
5-methyl-2-nitro-dibenzo[c,e][1,2]thiazine 5-oxide (3fa)

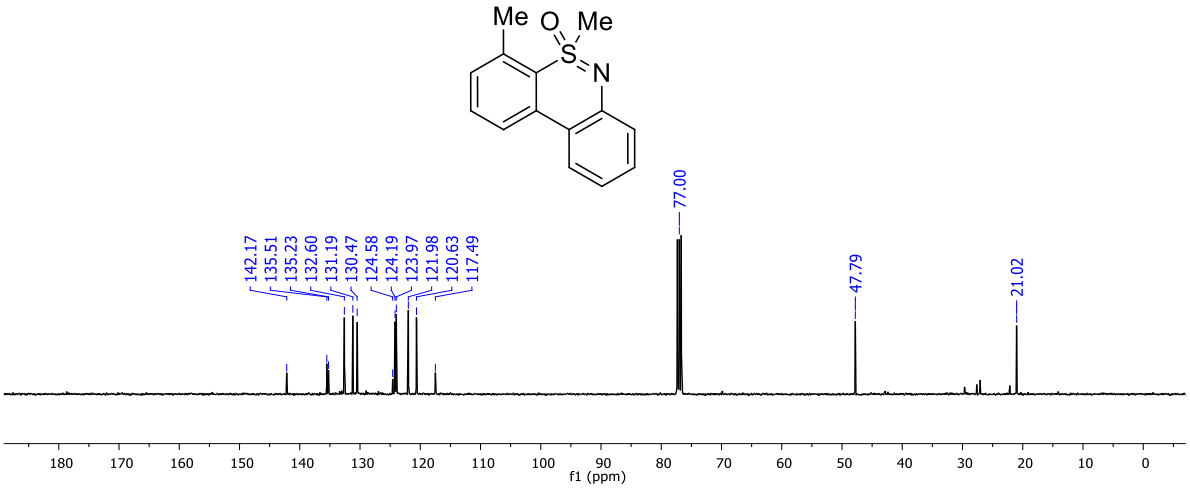




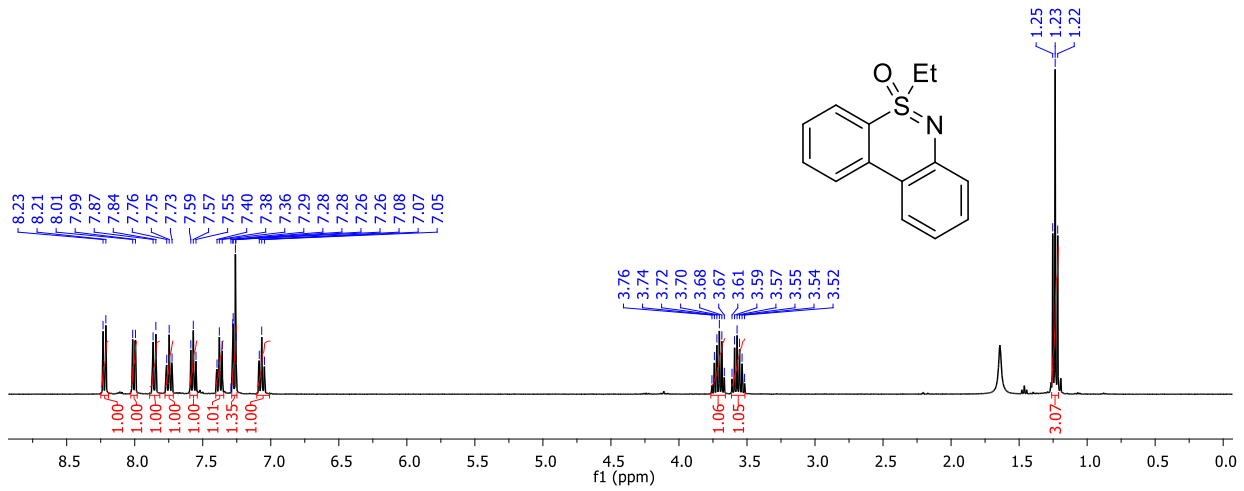
4,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide (3ga).

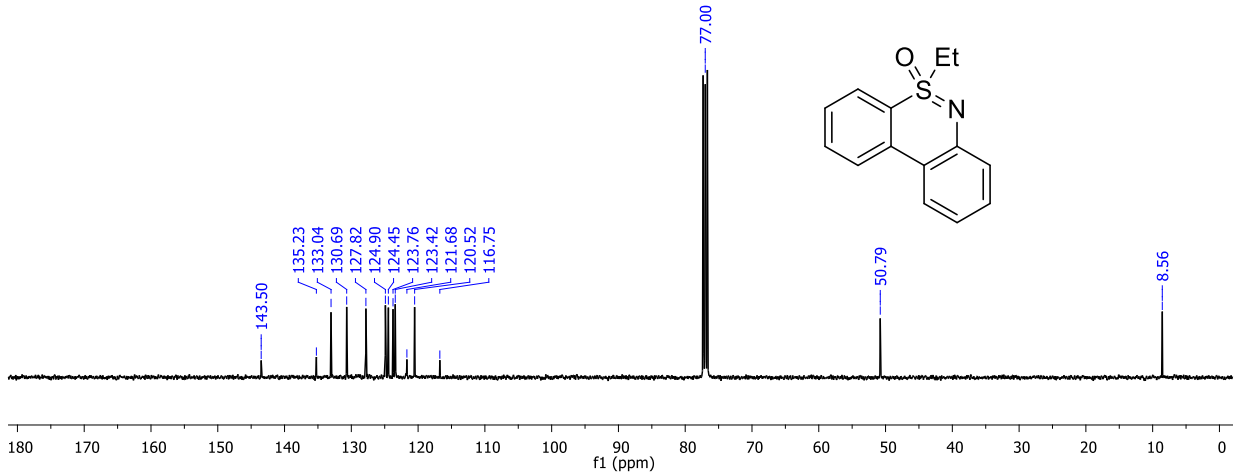


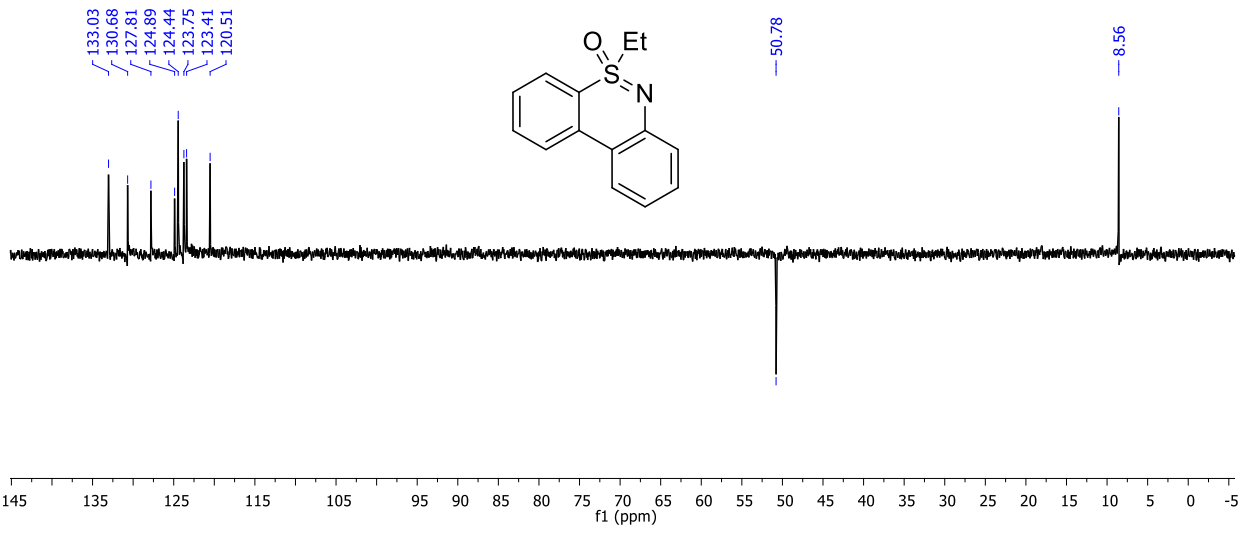




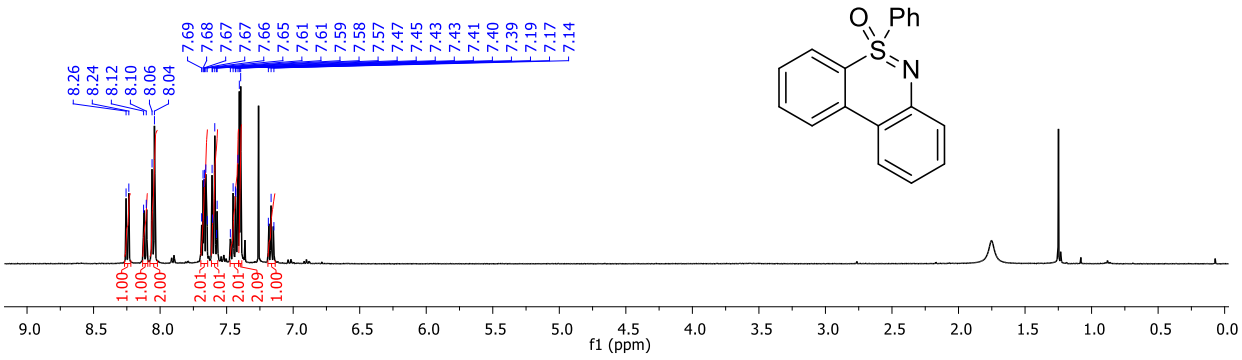
5-Ethyldibenzo[c,e][1,2]thiazine 5-oxide (3ha).

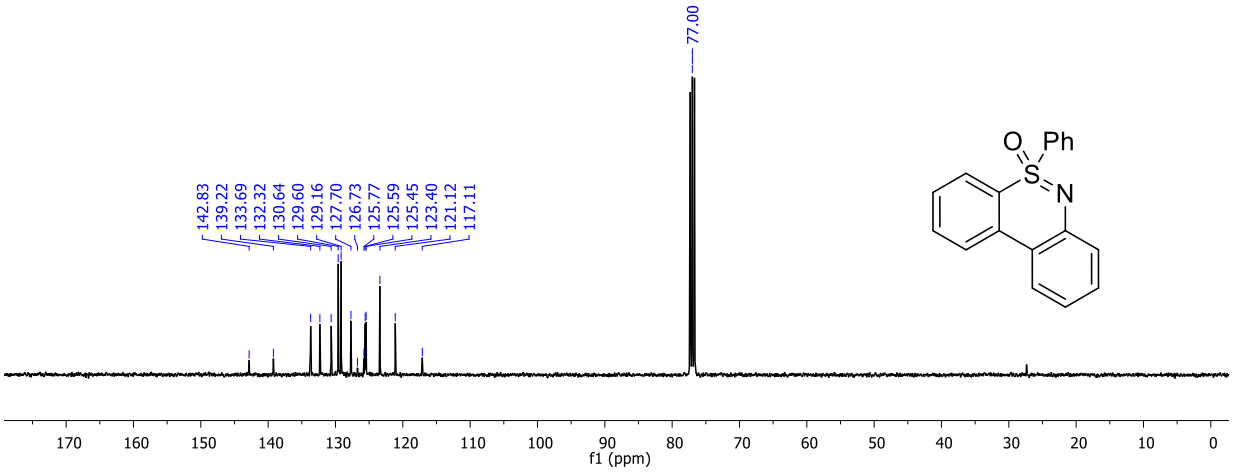


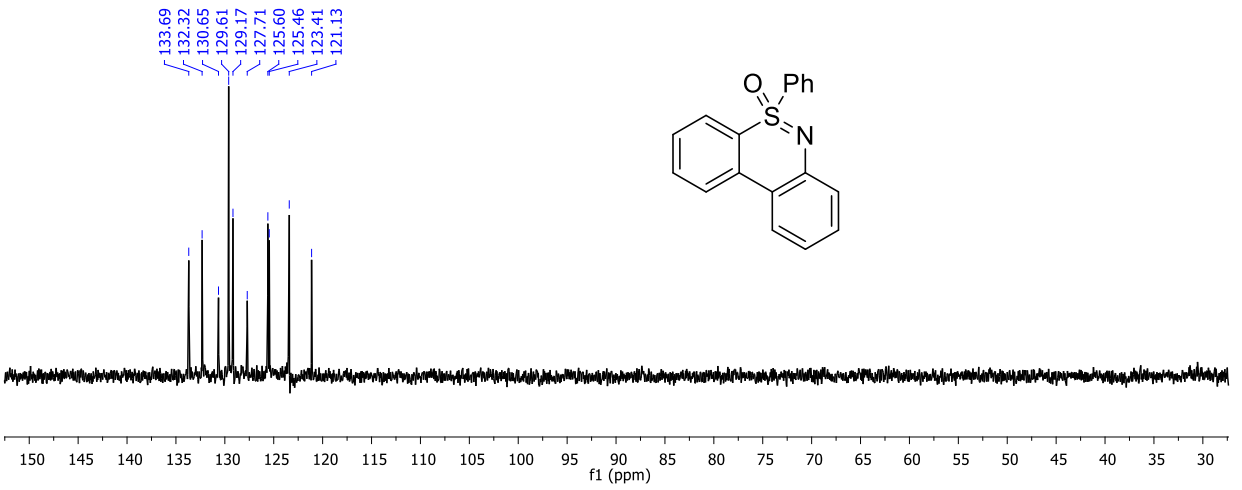




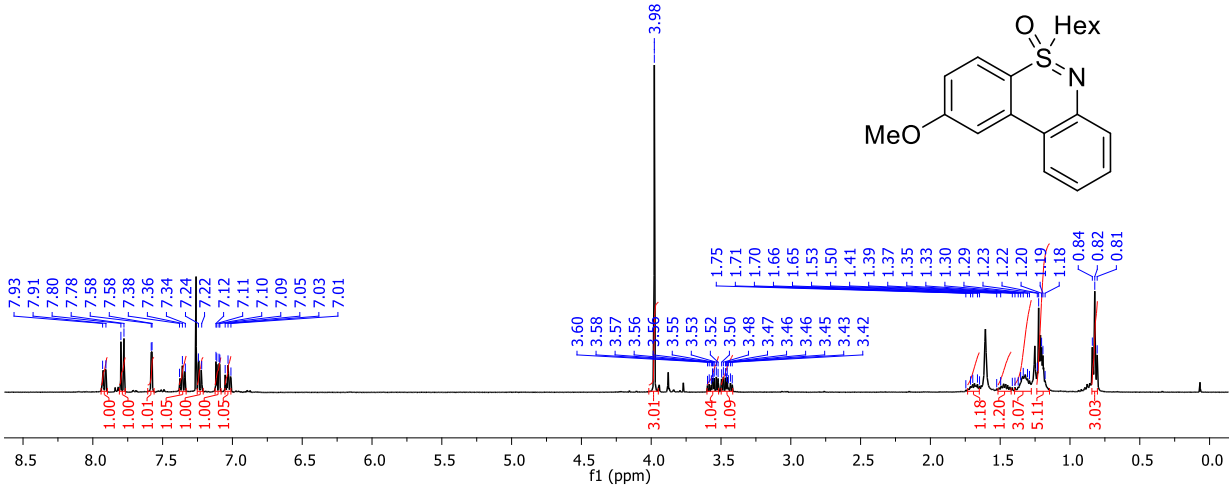
5-phenyldibenzo[c,e][1,2]thiazine 5-oxide (3ia).

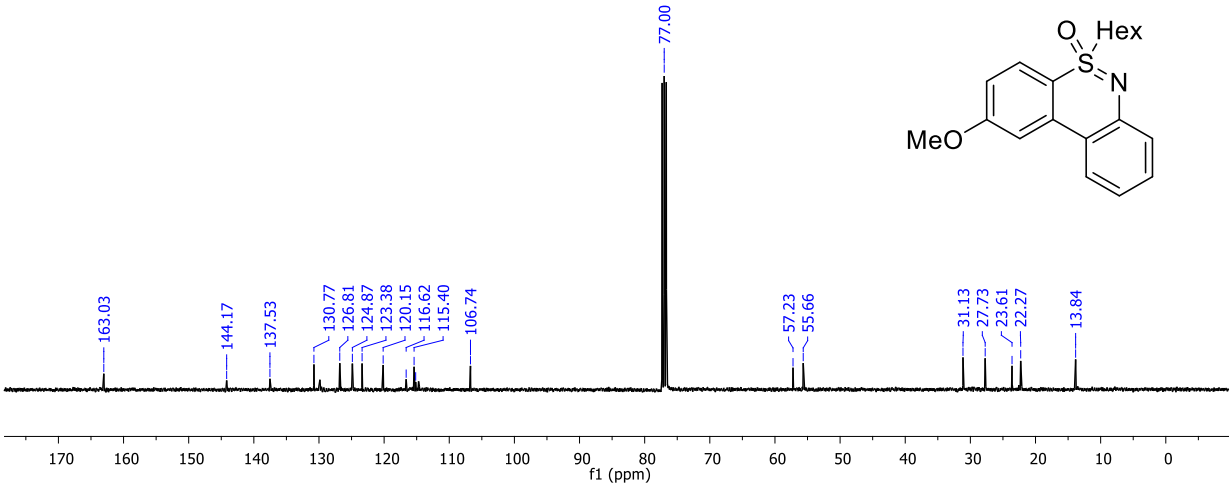


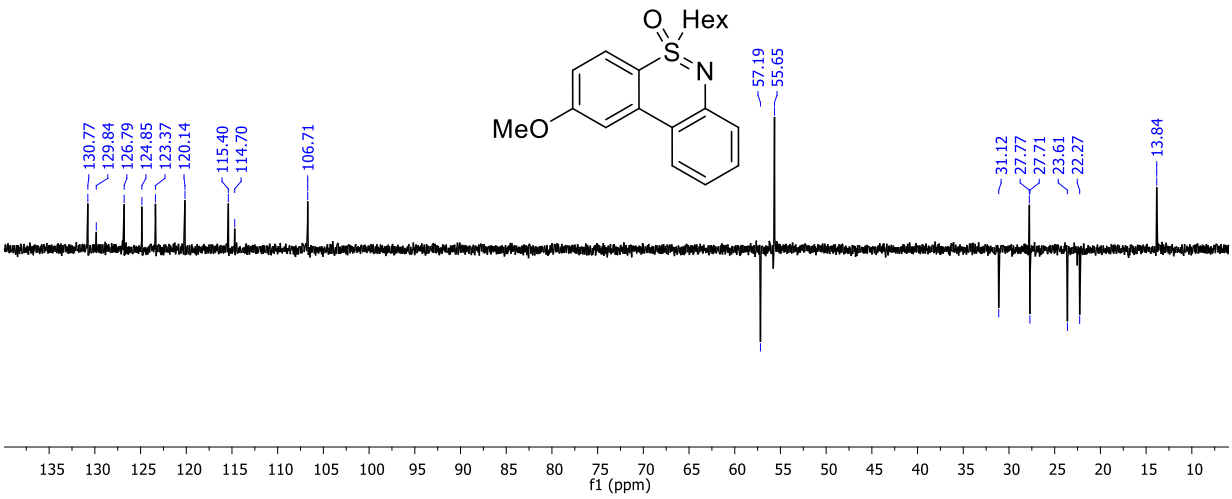




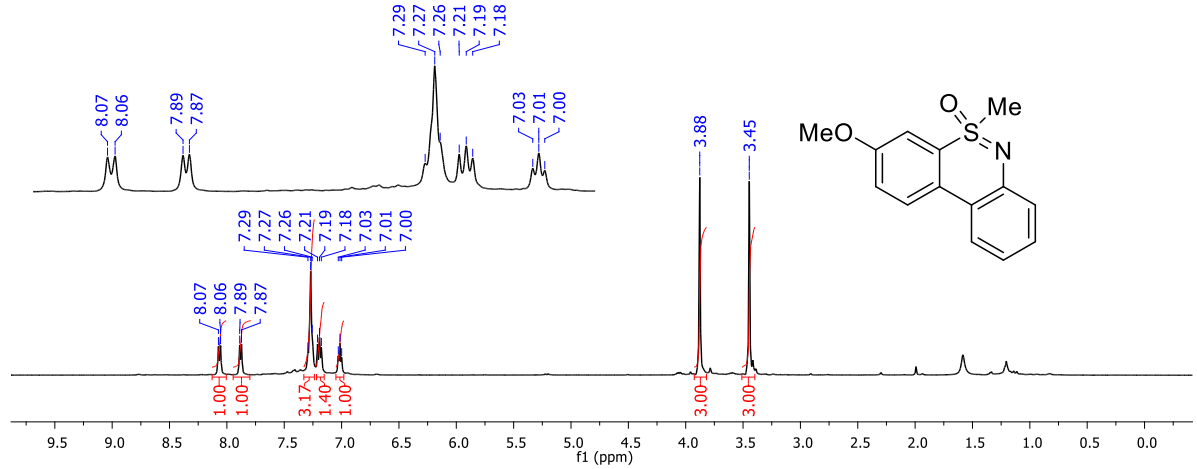
5-hexyl-2-methoxy dibenzo[c,e][1,2]thiazine 5-oxide (3ja).

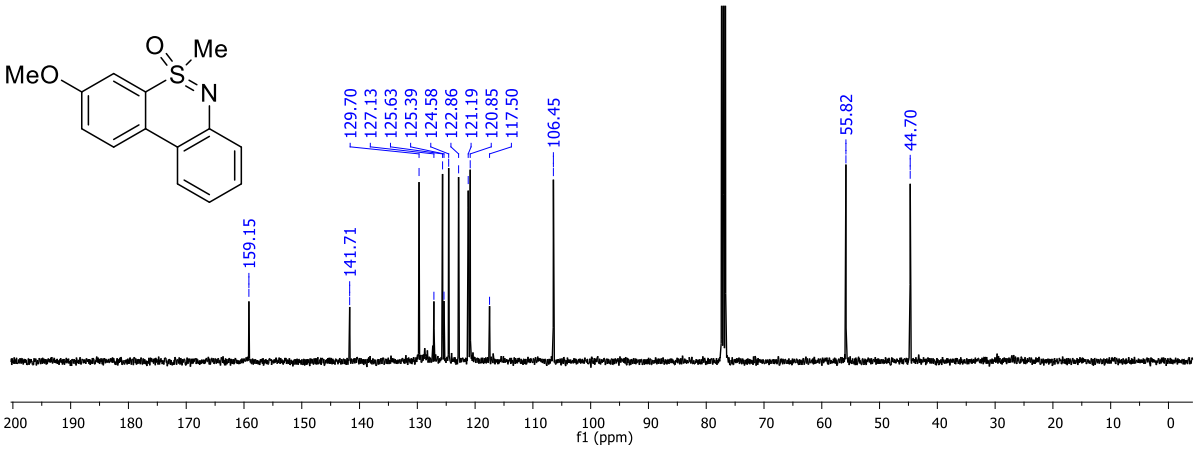


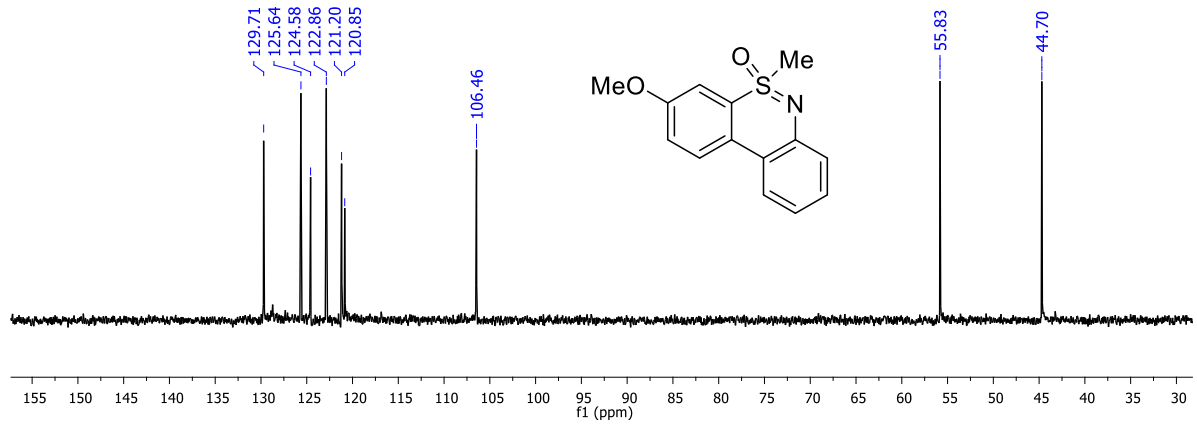




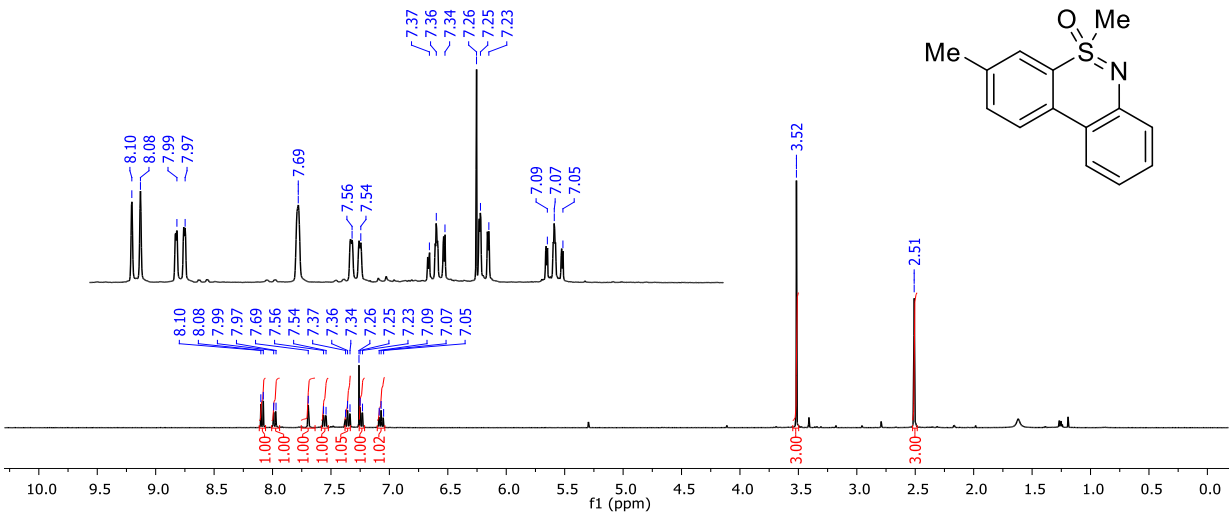
3-Methoxy-5-methyldibenzo[*c*,*e*][1,2]thiazine 5-oxide (3ka).

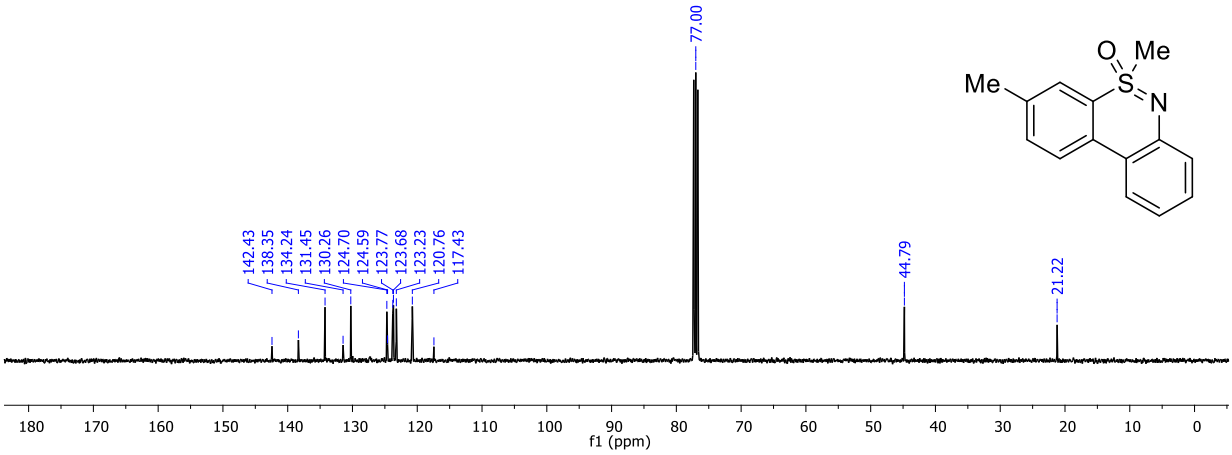


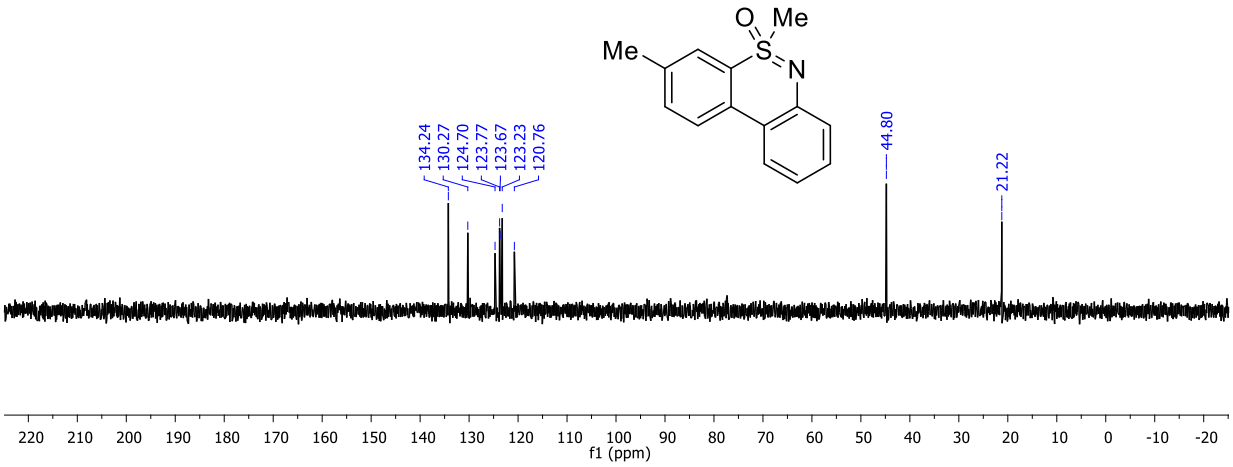




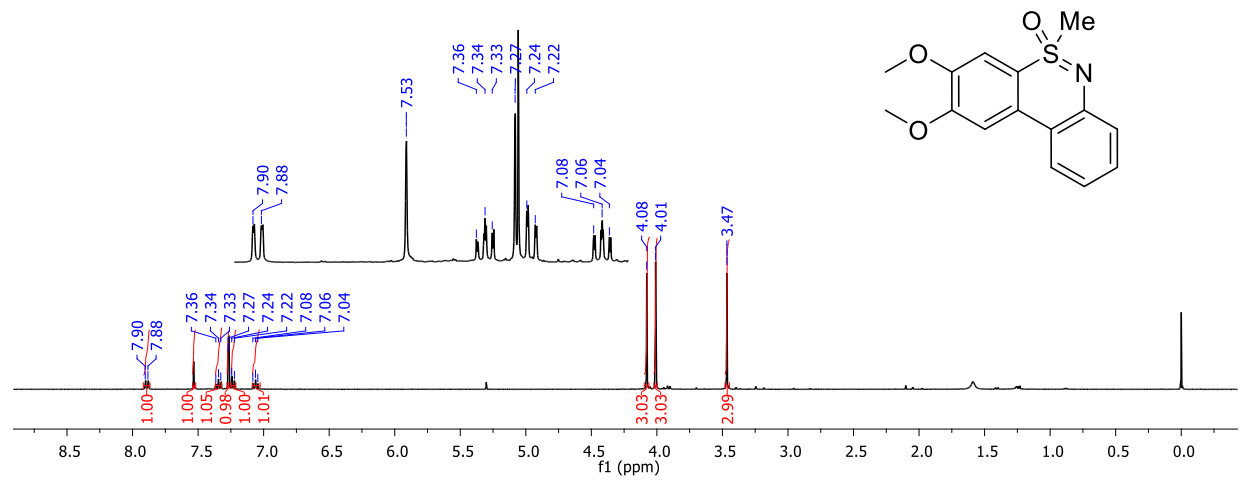
3,5-Dimethyldibenzo[c,e][1,2]thiazine 5-oxide (3la) .

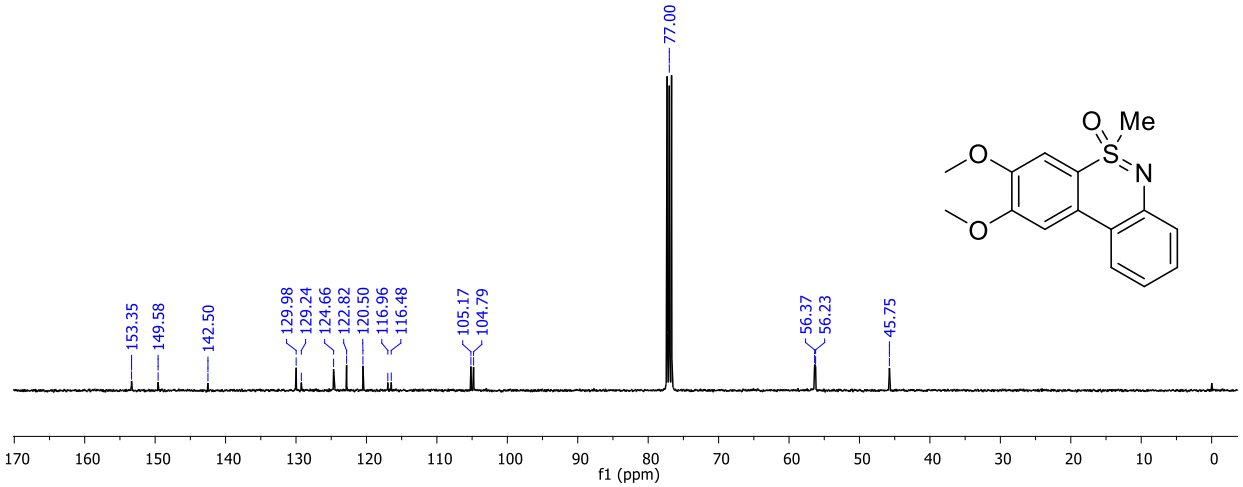


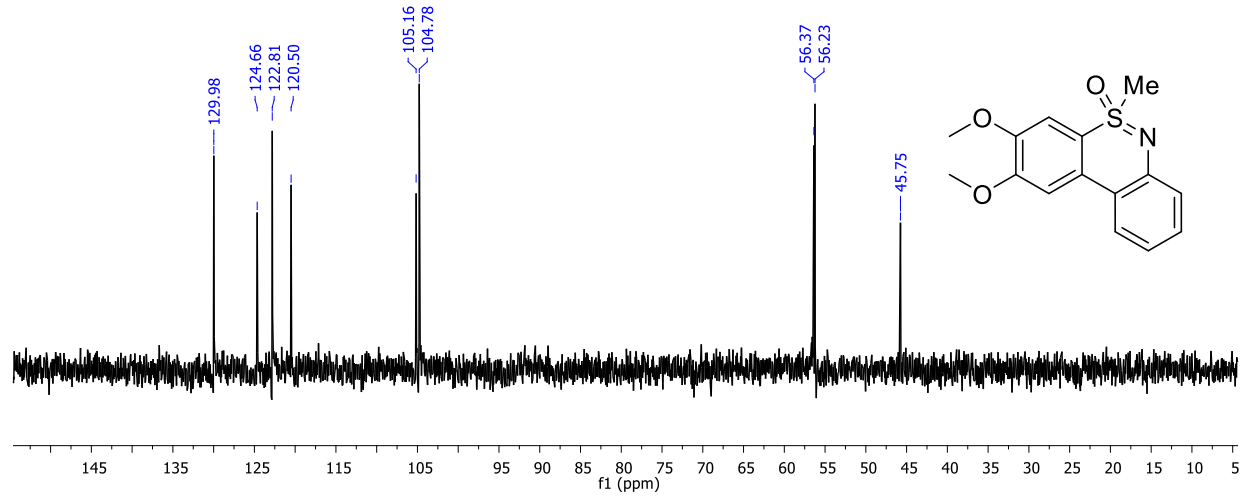




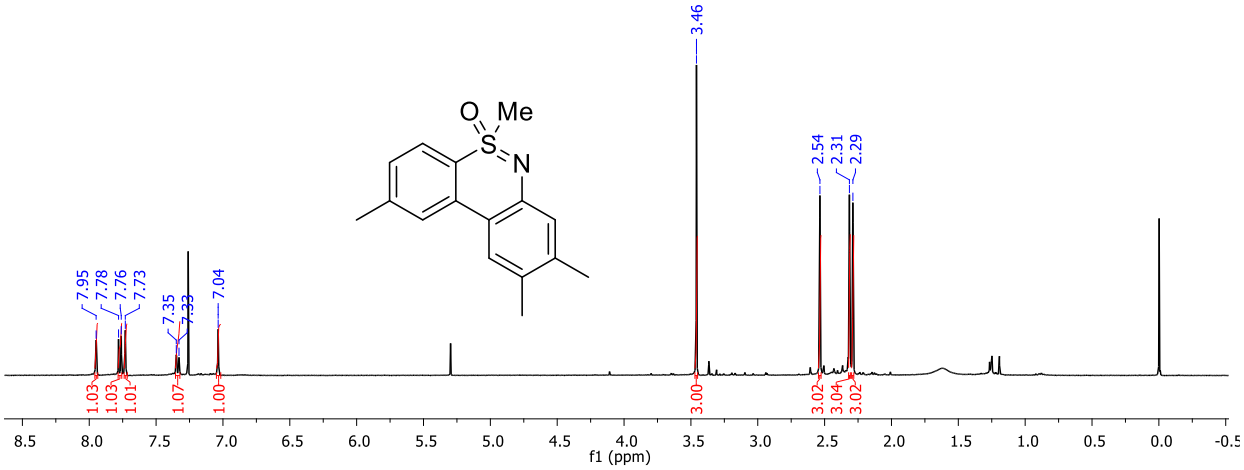
2,3-Dimethoxy-5-methyldibenzo[c,e][1,2]thiazine 5-oxide (3ma).

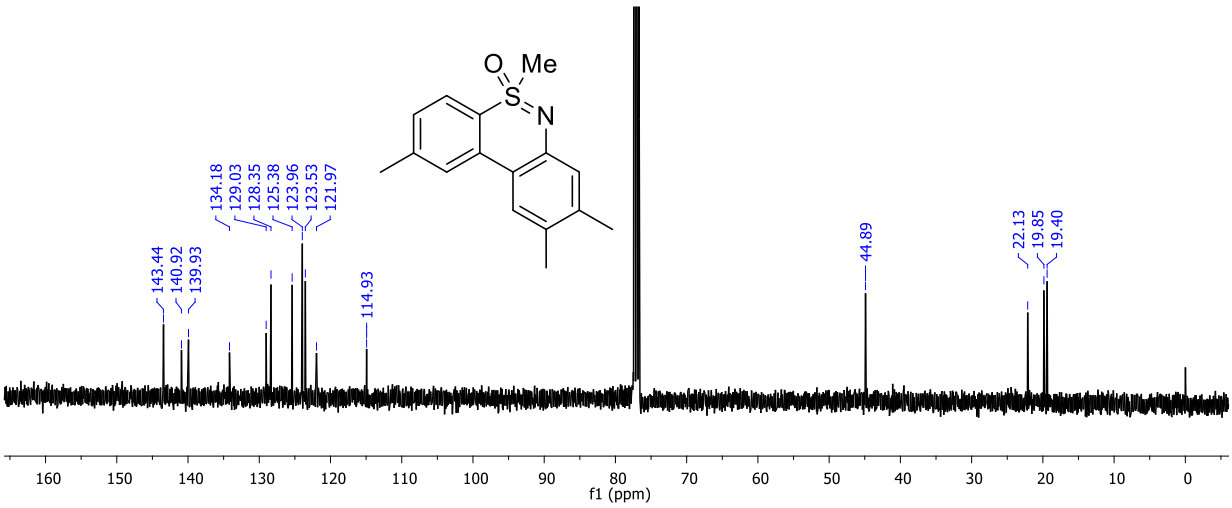


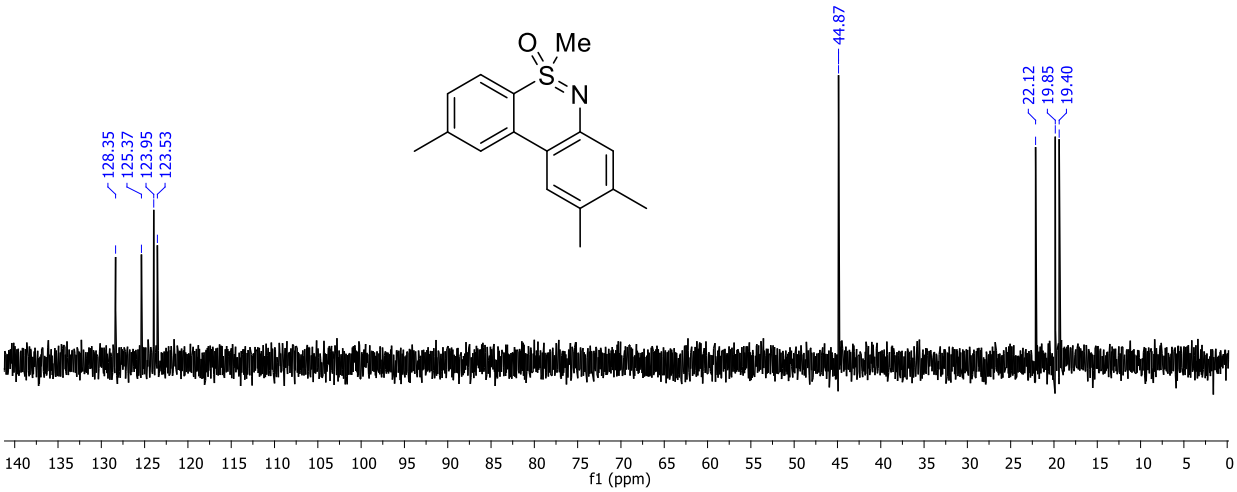




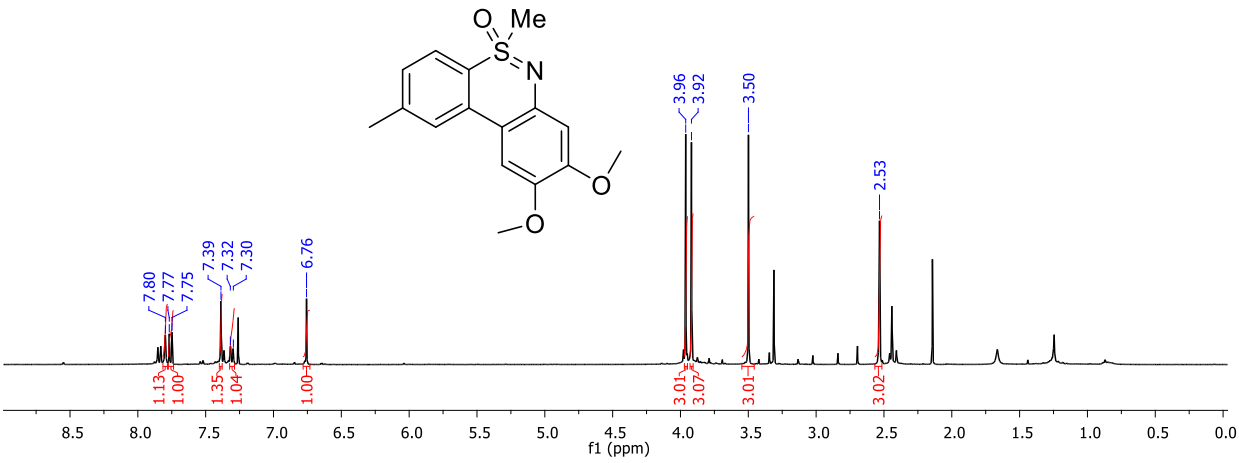
2,5,8,9-tetramethyl dibenzo[c,e][1,2]thiazine 5-oxide (3bb).



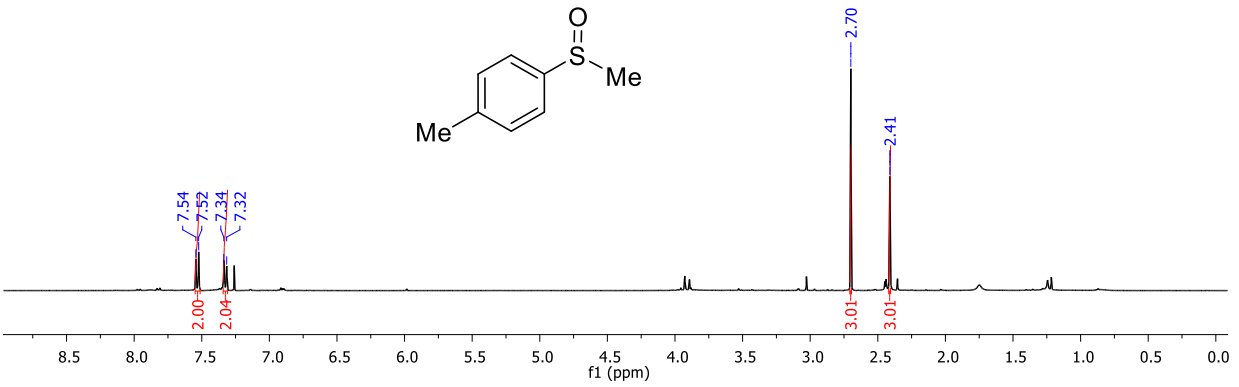




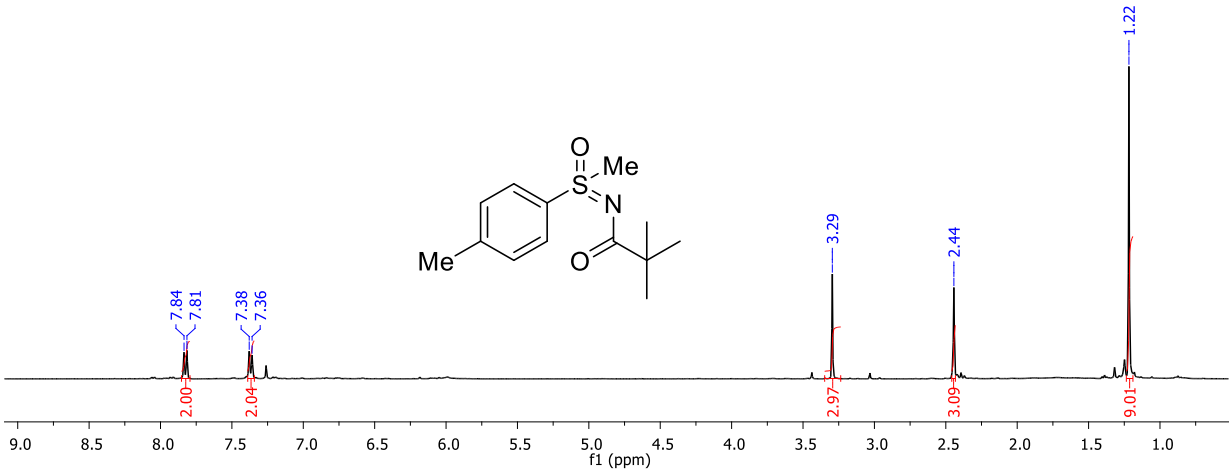
8,9-Dimethoxy-2,5-dimethyl dibenzo[c,e][1,2]thiazine 5-oxide (3bc).



1-methyl-4-(methylsulfinyl)benzene (5).



N-(methyl(oxo)(p-tolyl)-sulfanylidene)pivalamide (6).



9-methoxy-2,5-dimethyl-dibenzo[c,e][1,2]thiazine 5-oxide (3bd +3bd')