Chapter IV

Facile synthesis of sulfone-bearing indoles and related heterocycles via a sequential formal vinylic substitution and intramolecular Heck coupling reaction

4.1. Introduction

Indoles constitute one of the most abundant and important nitrogen heterocycles with a wide range of applications. The indole motif is present at the core of numerous natural products, drug molecules and agrochemicals.[1] A majority among the numerous structurally diverse, naturally occurring indole derivatives possess important pharmacological activites.[2] For example, vasoconstrictor hormone serotonin is an important monoamine neurotransmitter and reserpine is an indole-alkaloid used for the treatment of high blood pressure (Figure 1). Additionally, a variety of biological (such as cytotoxic, antiviral, antimicrobial, antiparasitic and anti-inflammatory) activities are exhibited by indole ring-bearing marine natural products.[3]

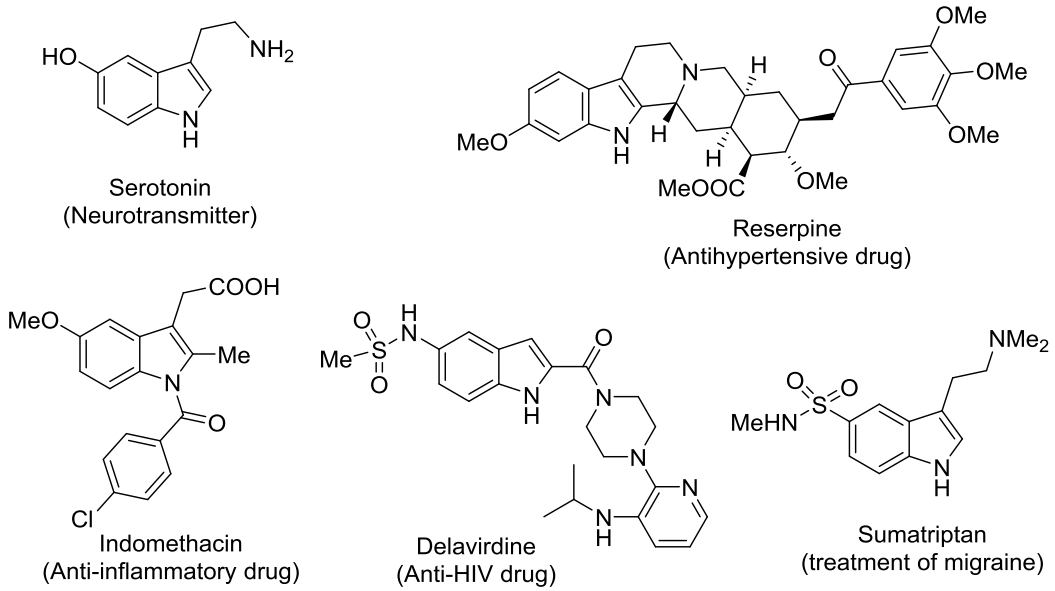


Figure 1: Some important biologically active natural and synthetic indole derivatives

Figure 1 shows some natural and synthetic indole derivatives that are bioactive or marketed as drugs. Indomethacin, for example, is a non-steroidal anti-inflammatory drug that works by inhibiting COX,[4] delavirdine is used for the treatment of human immunodeficiency virus type-1 (HIV-1),[5] and sumatriptan, (sold under the brand name imitrex) is a serotonin receptor agonist used for the treatment of migraine.[6]

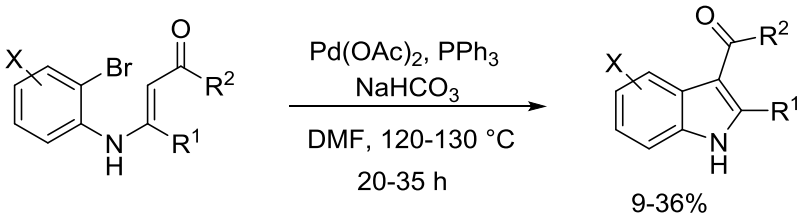
Owing to their importance and widespread applications, a variety of methods have been developed for indole synthesis. The most notable among them, Fischer indole synthesis introduced in 1883 constitutes one of the most powerful and popular method for indole synthesis.[7] In addition, other important classical methods include Madelung cyclisation of N-acyl-*o*-toluidines, Leimhruber-Batcho synthesis from *o*-nitrotoluene, Bischler-Möhlau synthesis from α-bromoacetophenone and aniline, Gassman indole synthesis and Bartoli synthesis.[8] Modern methods such as metal-catalyzed cyclization reactions of *o*-haloanilino enamines,[9] N-allyl-*o*-halo anilines,[10] *o*-halo-N-propargyl anilides,[11] *o*-vinyl anilines,[12] and *o*-allyl anilines[13] also afford convenient and efficient access to indoles.

The work described in this chapter focuses on a strategy for synthesis of indoles from *o*-haloanilino enamine derivatives *via* intramolecular Heck reaction (presented later in detail). In order to put the results in proper perspective, a brief overview of reported methods of indole construction from *o*-haloanilino enamines is presented below.

4.2. Synthesis of indoles from o-haloanilino enamines

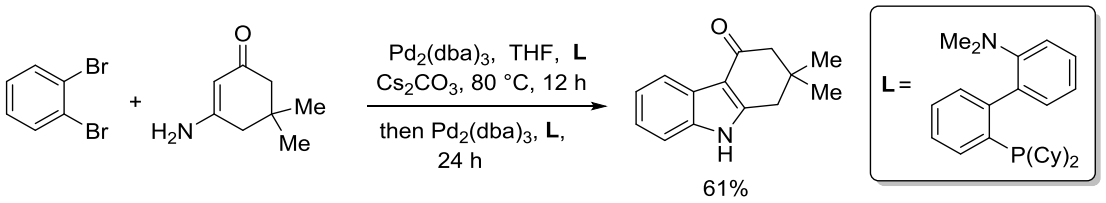
Kobayashi and co-workers reported in 1980 that *o*-haloaniline enamines conjugated to a carbonyl group can be converted to indole derivatives via intramolecular Heck reaction.

The enaminones were typically generated via the condensation of *o*-bromoaniline with 1,3-dicarbonyl compounds and the Pd-catalyzed Heck-cyclisation was carried out at high temperatures in DMF (Scheme 1).



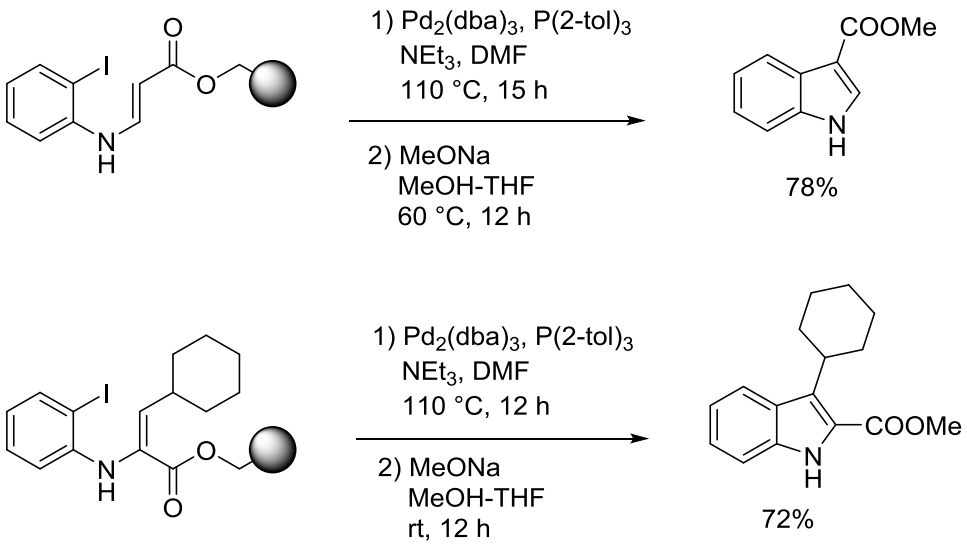
Scheme 1: Synthesis of indole derivatives via intramolecular Heck cyclisation

A domino Buchwald- Hartwig-Heck cyclisation for synthesis of 2,3-disubstituted indole derivatives has been reported. In this reaction, *o*-halo-enaminones generated by Buchwald-Hartwig coupling of vinylogous amides and dihaloarenes undergo an in situ Heck cyclization reaction to furnish indole derivatives (Scheme 2).



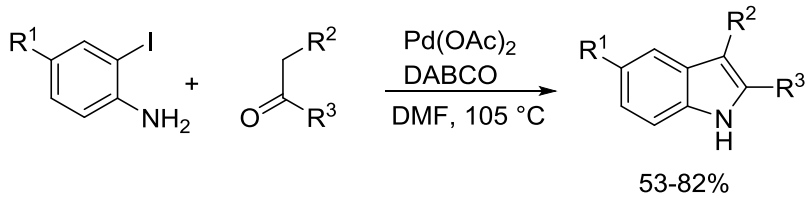
Scheme 2: Domino reaction for construction of 2,3-substituted indole derivatives

Haloanilino enamines conjugated to an ester group were also employed in study for preparation of indole derivatives. Kondo and co-workers developed a solid-phase synthesis of indole-3-carboxylates using similar substrates. Thus, the palladium-catalyzed cyclisation of immobilized enaminoesters followed by transesterification afforded indole-3-carboxylate derivatives as depicted in Scheme 3.



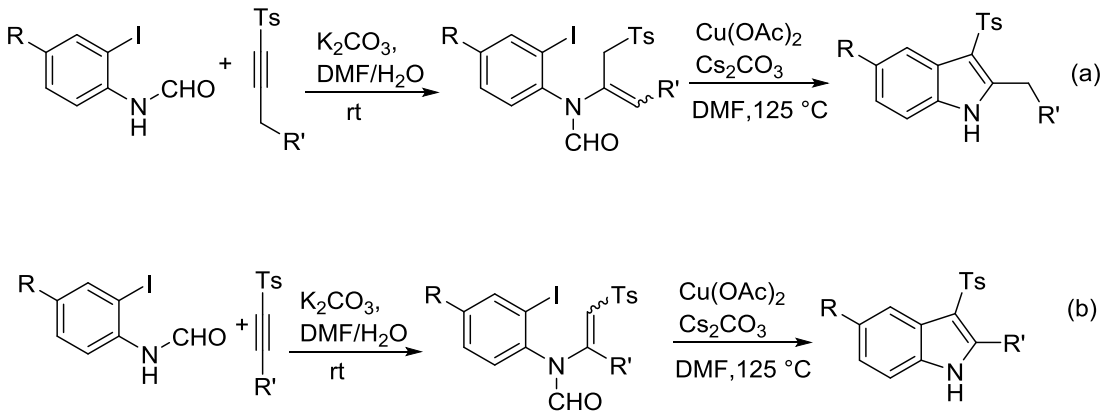
Scheme 3: Synthesis of indole-3-carboxylate and indole-2-carboxylate from o-iodoanilino enaminoesters

An efficient method for synthesis of indoles via annulation reaction between 2-iodoanilines and ketones was developed by Chen and co-workers. The reaction involved the generation of o-iodoanilino enamine followed by intramolecular Heck cyclisation to afford the corresponding indole derivative (Scheme 4).



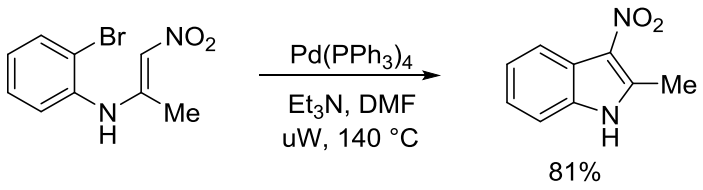
Scheme 4: Generation of enamine and subsequent Heck-cyclisation to afford indoles

The conjugate addition of o-iodoaniline derivatives to acetylenic sulfones containing γ-hydrogen afforded inseparable mixture of isomeric enamines (Scheme 5a). Similarly, terminal acetylenic sulfones reacted to afford enamines conjugated with sulfonyl group (Scheme 5b). Both classes of enamine derivatives underwent copper-catalyzed intramolecular coupling reaction to afford substituted 3-sulfonyl indole derivatives (Scheme 5).



Scheme 5: Cu-catalyzed synthesis of 3-sulfonyl indole derivatives

Kurth and co-workers have reported a microwave assisted construction of 3-nitroindoles from o-bromoanilino enamines via Pd-catalyzed intramolecular Heck-coupling reaction (Scheme 6).



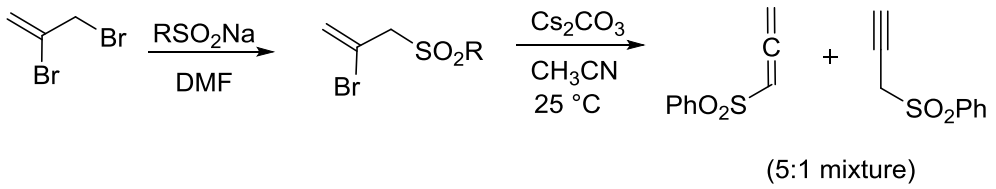
Scheme 6: Microwave assisted synthesis of 3-nitroindoles

4.3. Background to the present work

Allenyl sulfones are versatile building blocks in organic synthesis, however their potential remains largely underexploited.[14] Recent investigations form our laboratory have revealed novel reactivity patterns of allenyl sulfones and related specie for construction of various carbocycles and heterocycles. A short overview of these investigations that are particularly relevant for the work described in this chapter is given below.

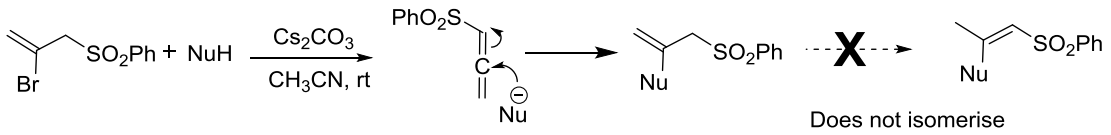
A key observation in this regard was that 2-bromoallyl sulfones could be transformed to allenyl sulfones by Cs_2CO_3 promoted dehydrohalogenation.[15] The 2-bromoallyl

sulfones are in turn, easily prepared from commercially available 2,3-dibromopropene and arylsulfinate salts (Scheme 7).



Scheme 7: Preparation of allenyl sulfone from 2-bromoallyl sulfone

Interestingly, isolation of the allenyl sulfone was not essential for its subsequent transformations. It was found that a variety of suitable nucleophiles underwent conjugate addition to *in-situ* generated allenyl sulfone and afforded functionalized allyl sulfones (Scheme 8). However, the overall reaction may be viewed as formal vinyl displacement reaction of 2-bromo allylsulfones.

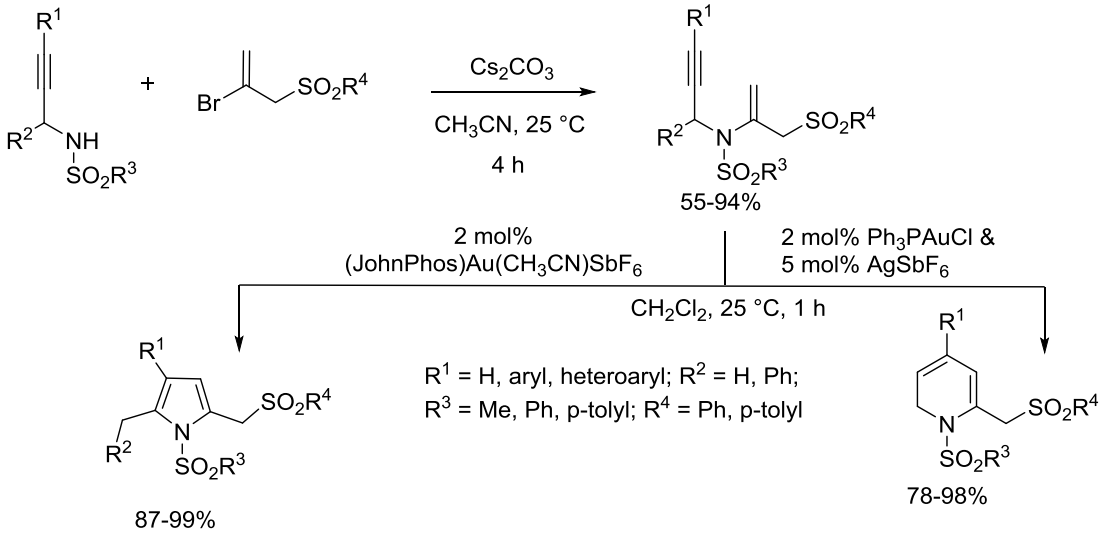


Scheme 8: Addition of nucleophile to in-situ generated allenyl sulfone

It may be noted that the double bond in the Michael adduct (Scheme 8) is not-conjugated to the sulfonyl group, despite being generated under basic conditions. This is presumably due to the well-known propensity of vinyl sulfones to undergo base-catalyzed isomerisation to produce allyl sulfones.[16] This feature allows for the development of further reactions of this reactive terminal alkene unit.

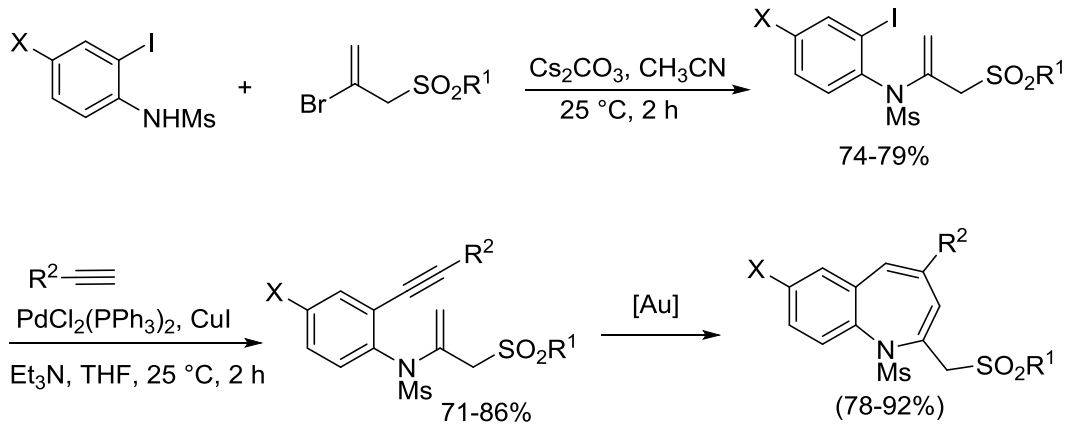
For example, the reaction of propargyl sulfonamides with 2-bromoallyl sulfone generated N-propargyl-N-vinyl sulfonamide adduct (aza-enynes) via the intermediacy

of allenyl sulfone. Subsequent gold-catalyzed cycloisomerisation of these aza-enynes proceeded in divergent pathways depending upon the choice of catalysts to afford substituted pyrroles or dihydropyridines (Scheme 9).[17] Echavarren's gold catalyst promoted the formation of pyrrole derivatives whereas a combination of gold and silver catalysts effected the formation of dihydropyridine derivatives.



Scheme 9: Conjugate addition of propargyl sulfonamide to allenyl sulfone and subsequent catalytic divergent cycloisomerisation

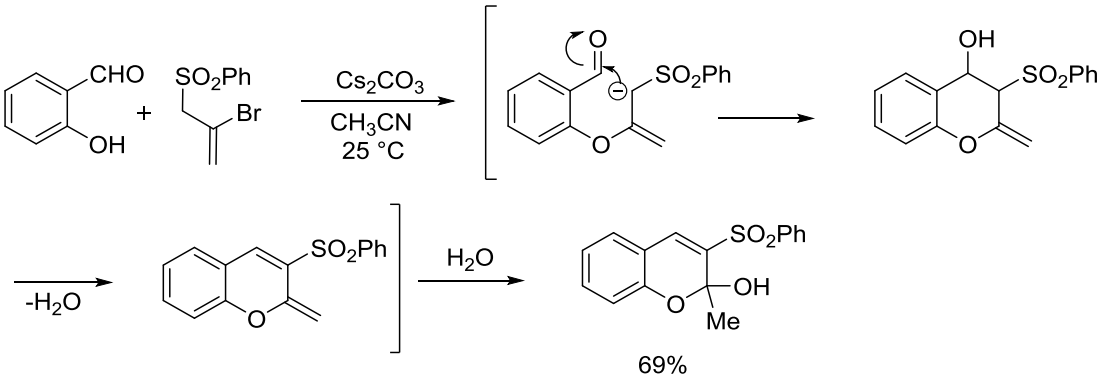
Other nitrogen heterocyclic compounds could also be produced by varying the position of alkyne unit or by incorporating extra carbon atoms in sulfonamide component. The formal vinylic displacement of bromo allylsulfone by 2-iodoaniline derivative, followed by Sonogashira coupling afforded an assortment of 3-aza-1,6-enynes. The regioselective cycloisomerization of latter catalyzed by a Au(I)-catalyst generated benzo-1-azepine derivatives (Scheme 10).[18]



R^1 = Ph, p-tolyl; R^2 = aryl, TMS; X = H, Cl;[Au] = $[JohnPhosAu(CH_3CN)]SbF_6$

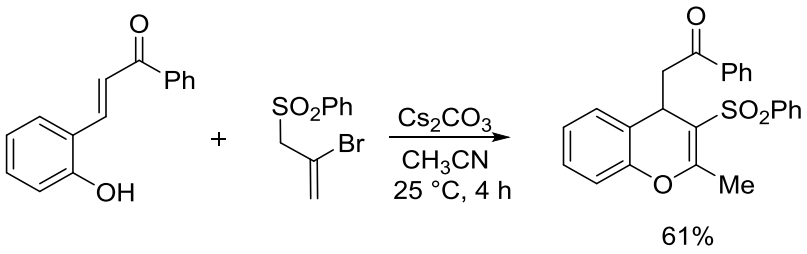
Scheme 10: Addition of o-iodoaniline derivative to allenyl sulfone and catalytic cycloisomerisation of 3-aza-1,6-enyne system

Similarly, oxygen nucleophiles such as phenols also underwent conjugate addition to allenyl sulfones. The cesium carbonate mediated cyclocondensation reaction of salicylaldehyde and 2-bromoallyl sulfone afforded 3-sulfonylchromene derivatives (Scheme 11).[15]



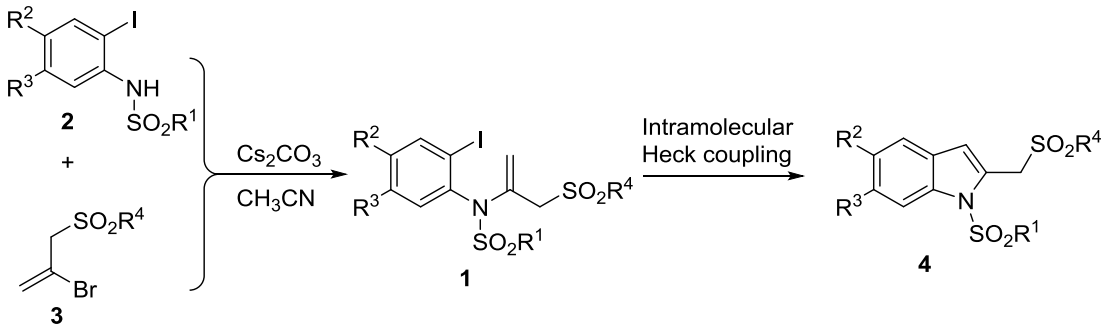
Scheme 11: Base promoted reaction of salicylaldehyde and allenyl sulfone

Additionally, the reaction of o-hydroxy chalcone and 2-bromoallyl sulfone furnished 3-sulfonyl-4*H*-chromene derivatives (Scheme 12). The base mediated reaction proceeds *via* oxa-Michael-Michael addition and isomerisation sequence.[19]



Scheme 12: Reaction of o-hydroxy chalcone with allenyl sulfone

It is clear from the foregoing discussion that the formal vinylic substitution reaction of allyl bromosulfones provides access to enamine-like and enol ether like products in a convenient manner. We surmised that these reactive product classes may further be elaborated to construct important heterocyclic derivatives. Therefore, we undertook investigations with a view to further explore synthetic utility of allenyl sulfones for the synthesis of sulfone containing heterocyclic compound *viz*., indole. It was envisaged that N-vinyl-o-halo sulfonamide/o-iodoanilino enamine **1** could be generated via the reaction of N-sulfonyl-o-iodoaniline **2** and 2-bromoallyl sulfone **3**. Subsequent intramolecular Heck coupling reaction was expected to lead to functionalized indole derivatives (Scheme 13).

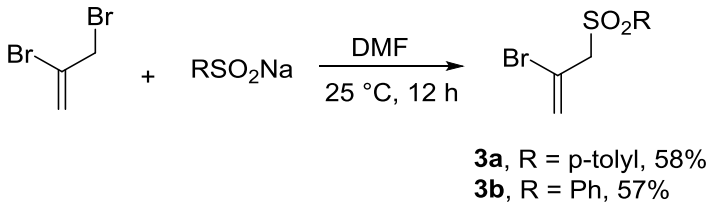


Scheme 13: Preparation and proposed reaction of N-vinyl-o-halo sulfonamide

4.4 Results and discussion

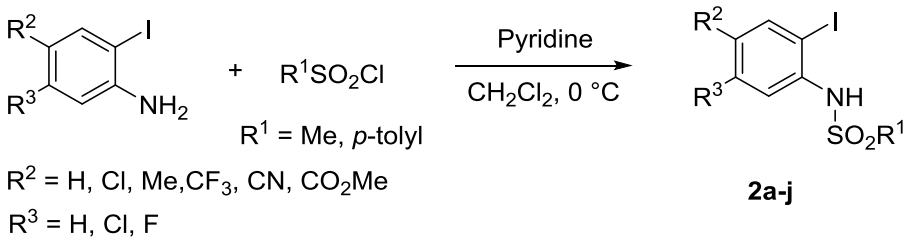
The proposed reaction sequence required access to 2-bromoallyl sulfones **3**. They were conveniently prepared as per the reported protocol starting from commercially available

1,3-dibromopropene.[15] A straightforward nucleophilic displacement reaction of the bromide in 2, 3-dibromopropene with arylsulfinate salts afforded the 2-bromoallyl sulfones **3a-b** in good yields (Scheme 14).



Scheme 14: Preparation of 2-bromoallyl sulfones **3a-b**

The required N-sulfonyl-o-iodoaniline derivatives **2** were then generated from the sulfonylation of corresponding anilines (Scheme 15). The sulfonamides **2a-j** were characterized by comparison of their physical and spectroscopic data with reported values.

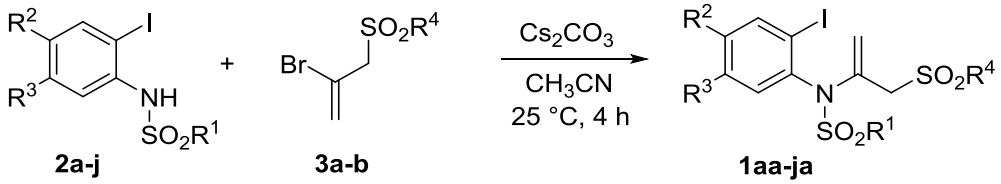


Scheme 15: Preparation of sulfonamides **2a-j**

The N-vinyl-o-halo sulfonamide precursors **(1aa-1ja)** were then prepared from 2-bromoallyl sulfones **(3a-b)** and N-sulfonyl-o-halo aniline **(2a-j)** *via* the formal vinylic substitution reaction. All the substrates reacted smoothly under the previously optimized conditions[17] to afford the corresponding N-vinyl-o-halo sulfonamides **1** in very good to high yields (Table 1). The products were characterized by standard spectroscopic analysis. The salient spectroscopic features of a representative product **1aa** are described below.

In ^{1}H NMR of **1aa**, two mutually coupled doublet signals at δ 5.53 (d, J = 1.2Hz, 1H) and δ 5.29 (d, J = 1.2Hz, 1H) were visible which were assigned to the terminal alkene protons. An AB quartet centered at δ 3.84 corresponded to the methylene unit adjacent to the sulfonyl group. Normally, this CH_2 group is expected to appear as a singlet. The fact that they appear as an AB quartet indicates that they form a very similar diastereotopic pair. A plausible reason for this could be the slow pyramidal inversion of sulfonamide nitrogen. In the ^{13}CNMR spectrum, this methylene resonated at δ 59.7. In addition, the peaks at δ 118.9 and 102.3 confirmed the presence of the alkene carbons. Other spectroscopic data were also in agreement with the structure **1aa** (see experimental section for details).

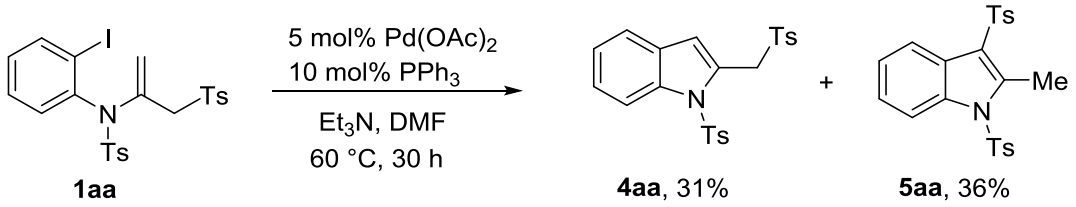
Table 1: Synthesis of N-vinyl-o-iodo sulfonamide *via* vinylic displacement reaction of 2-bromoallyl sulfones[a]



Entry	N-vinyl-o-iodo sulfonamide **(2)**	Bromoallyl sulfones **(3)**	Product (**1**)	Yield (%)[b]
1	**2a**, R^1 = p-tolyl; $R^2 = R^3$ = H	**3a**, R^4 = p-tolyl	**1aa**	79
2	**2a**	**3b**, R^4 = Ph	**1ab**	81
3	**2b**, R^1 = p-tolyl; R^2 = H, R^3 = Cl	**3a**, R^4 = p-tolyl	**1ba**	83
4	**2c**, R^1 = p-tolyl; R^2 = Cl, R^3 = H	**3a**, R^4 = p-tolyl	**1ca**	78
5	**2d**, R^1 = p-tolyl, $R^2 = CH_3$, R^3 = H	**3a**, R^4 = p-tolyl	**1da**	76
6	**2d**	**3b**, R^4 = Ph	**1db**	74
7	**2e**, R^1 = p-tolyl; R^2 = H, R^3 = F	**3a**, R^4 = p-tolyl	**1ea**	71
8	**2f**, $R^1 = CH_3$; $R^2 = R^3$ = H	**3a**, R^4 = p-tolyl	**1fa**	72
9	**2g**, $R^1 = CH_3$; R^2 = H, R^3 = Cl	**3b,** R^4 = Ph	**1gb**	78
10	**2h**, $R^1 = CH_3$; $R^2 = CF_3$, R^3 = H	**3b,** R^4 = Ph	**1hb**	68
11	**2i**, $R^1 = CH_3$; R^2 = CN, R_3 = H	**3a**, R^4 = p-tolyl	**1ia**	63
12	**2j**, $R^1 = CH_3$; $R^2 = CO_2Me$, R^3 = H	**3a**, R^4 = p-tolyl	**1ja**	69

[a]Reaction conditions: **2a-j** (1mmol), **3a-b** (1.5 mmol), Cs_2CO_3 (2.5mmol), acetonitrile (10 ml), 4h, 25 ˚C.
[b]Yields of products isolated after column chromatography

Following the synthesis of the precursors **1**, the conditions for implementing the proposed intramolecular Heck reaction were explored. To test our hypothesis, substrate **1aa** was subjected to the standard reaction conditions of intramolecular Heck coupling reaction.[20] A reaction was observed when **1aa** was treated with catalytic palladium acetate, triphenylphosphine and triethylamine in DMF at 60 °C. After standard work-up and chromatographic purification, two easily separable products were isolated from the reaction mixture (Scheme 16). They were identified as isomeric indoles **4aa** and **5aa** based on spectroscopic analysis.



Scheme 16: Intramolecular Heck coupling reaction of **1aa**

In ^{1}H NMR spectrum of **4aa** a singlet at δ 6.89 corresponding to one proton was assigned to the hydrogen at 3-position of indole. The singlet at δ 5.03 (2H) indicated the presence of methylene group in the product. Singlet resonances at δ 2.42 and δ 2.29 corresponding to three hydrogens each indicated that both the tosyl groups were intact. In the ^{13}C NMR spectrum, the signal at δ 55.1 confirmed the presence of the methylene unit. DEPT-135 spectrum of **4aa** confirmed that the signal at δ 55.1 is indeed a methylene group. Analysis of the mass spectrum clearly indicated that the iodine has been lost. Based on these observations, **4aa** was identified as the expected product of Heck coupling reaction, N-tosyl-2-tosylmethylindole. The isolated yield of **4aa** corresponded to a paltry 31%.

On the other hand, the ^{1}H NMR spectrum of the major product **5aa** showed three single resonances of three protons each at δ 2.97, 2.37 and 2.36. While the last two of these

singlets were clearly arising from the tosyl groups, the one at δ 2.97 indicated that a methyl group is present elsewhere in the molecule. The absence of any CH_2 resonance pointed to the fact that the double bond in **1aa** may have isomerised prior to the Heck coupling reaction. The signal at δ 13.1 in the ^{13}C NMR spectrum (methyl group) also supported this suggestion. DEPT-135 spectrum also showed that there are no methylene units in **5aa**. Based on all these **5aa** was assigned the structure 3-methyl-1,2-ditosylindole as depicted in Scheme 15. It may be noted that this product was obtained in 36% yield.

It may be recalled here that the base-mediated isomerisation of vinyl sulfones to allyl sulfones (and vice versa) is well documented. Therefore, it is reasonable to assume that the substrate **1aa** underwent isomerisation to the corresponding vinyl sulfonamide under the conditions of the Heck reaction. It is presumable that the coupling of the vinyl sulfone is more facile under these conditions.

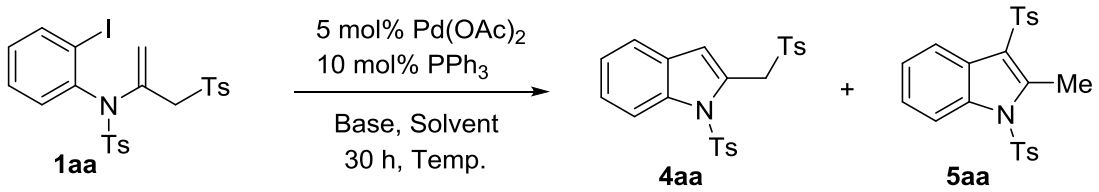
Although two products were formed in the Heck coupling reaction, their chromatographic separation was rather straightforward However, the Heck coupling reaction was further investigated with a view to improve the selectivity. The results of this optimization study are summarized in Table 2.

Initially, the effect of increasing the amount of base was explored. When reaction was tested with 3 equivalents of triethylamine, the yield of product **5aa** increased to 43% along with a reduction of the yield of **4aa** to 26% (entry 2). Increase in reaction temperature to 80 ˚C improved the selectivity for **5aa** (64%) over **4aa** (16%) further (entry 3). Indoles **4aa** and **5aa** were formed in lower yields (23% and 18 % respectively) when the reaction was carried out at 40˚C (entry 4). Interestingly, selective formation of indole derivative **5aa** was observed when either K_2CO_3 or Cs_2CO_3 was used as the base in DMF at 80 ˚C. Formation of monosubstituted indole **4aa** was not at all detected;

however, the isolated yields of **5aa** were only moderate under these conditions (46% and 52%; entries 5 and 6). The use of sodium bicarbonate as a base did not help in improving the yield or selectivity (entry 7). The performance of DBU as a base was also not satisfactory (entry 8). Similar results were obtained when the coupling reaction was carried out in acetonitrile in presence of various bases (entries 9-12).

Based on these results, the combination of $Pd(OAc)_2$, PPh_3 and Et_3N in DMF at 80 ˚C was selected as the optimum conditions for further investigations. It may be noted that the use of cesium carbonate in DMF afforded a single product (**5aa**) selectively. However, column chromatography was necessary in either case for the separation of products. Therefore, the reaction condition that afforded a higher yield and an additional product (without any added effort for separation) was selected for scope exploration.

Table 2: Optimisation of reaction conditions for intramolecular Heck coupling of **1aa**[a]

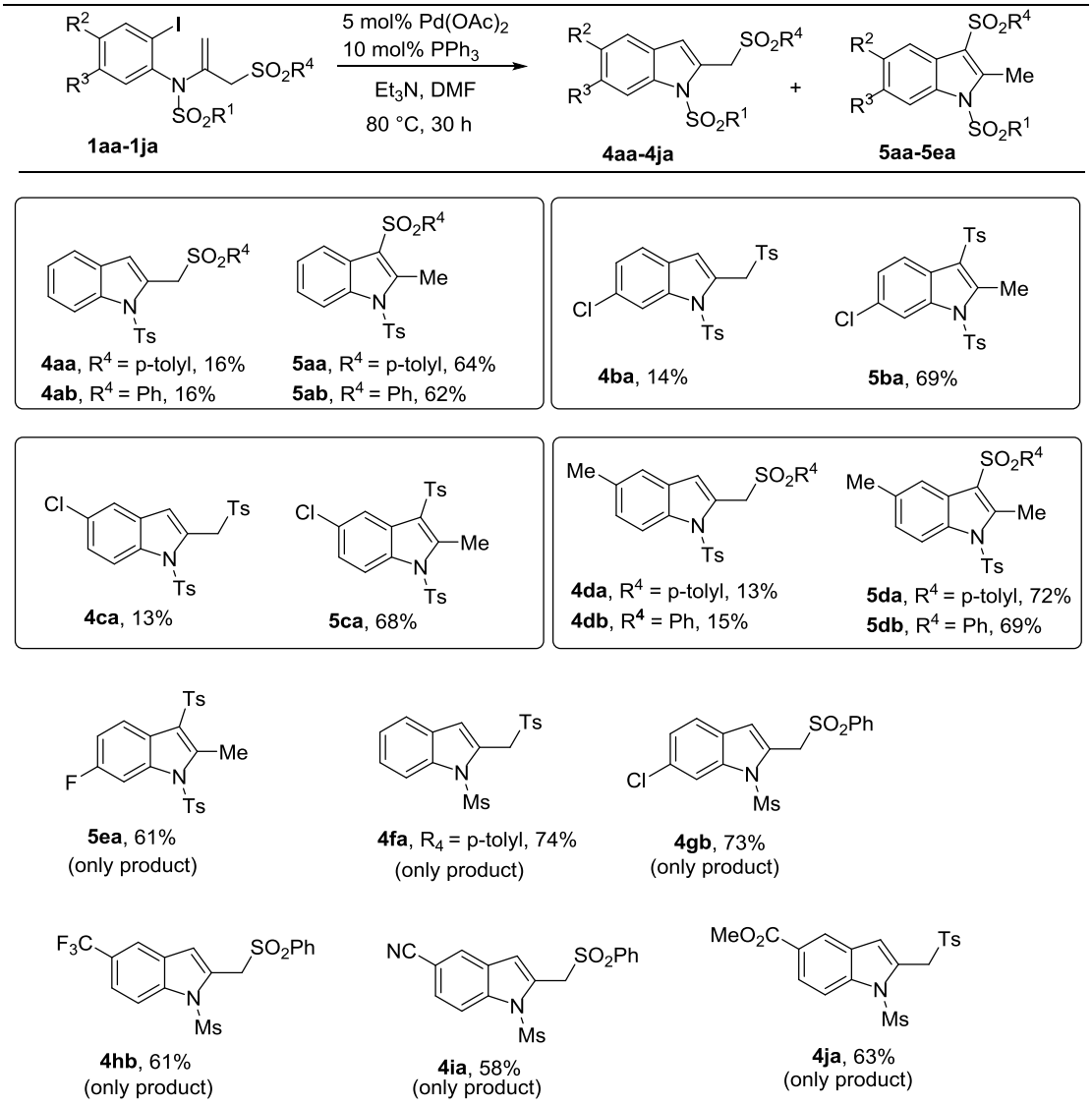


Entry	Solvent	Base	Temp.(˚C)	Yield of **4aa** (%)[b]	Yield of **5aa** (%)[b]
1[c]	DMF	Et_3N	60	31	36
2	DMF	Et_3N	60	26	43
3	**DMF**	**Et_3N**	**80**	**16**	**64**
4	DMF	Et_3N	40	23	18
5	DMF	K_2CO_3	80	-	46
6	**DMF**	**Cs_2CO_3**	**80**	**-**	**52**
7	DMF	$NaHCO_3$	80	19	31
8	DMF	DBU	80	Traces	23
9	MeCN	Et_3N	80	21	56
10	MeCN	Cs_2CO_3	80	18	41
11	MeCN	$NaHCO_3$	80	14	26
12	MeCN	K_2CO_3	80	15	37

[a]Reaction conditions: **1aa** (0.2mmol), $Pd(OAc)_2$ (5mol%), PPh_3 (10mol%), Et_3N (3 equiv), DMF (2ml). [b]Isolated yields of products. [c]2equiv of Et_3N was used.

As the method appeared suitable for the generation of two isomeric indoles from readily available precursors, its scope and generality were examined. Thus, the N-vinyl-o-halo sulfonamides **1aa-1ja** were subjected to the optimized conditions of the Heck coupling reaction. All of these substrates reacted smoothly to afford the indole derivatives **4** and **5**. The results are summarized in Table 3.

Table 3: Substrate scope of coupling reaction[a]



[a]Reaction conditions: **1aa-1ja** (0.4 mmol), $Pd(OAc)_2$ (5mol%), PPh_3 (10mol%), Et_3N (1.2 mmol), DMF (4ml).

The investigations revealed some very interesting features of this transformation. The most notable observation was that the reaction outcome is heavily dependent on the N-

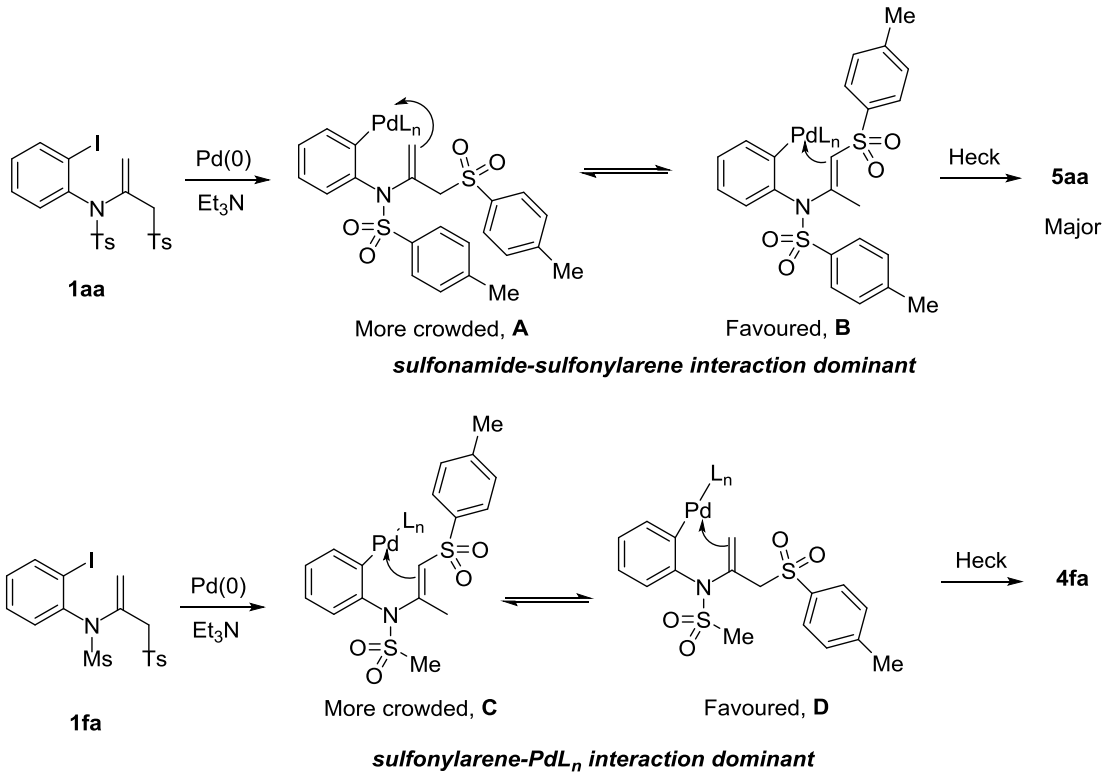
sulfonyl substituent. Substrates endowed with tosyl unit on the nitrogen (**1aa-1db**) generally reacted to afford both the indole products. The 2,3-disubstituted indoles **5aa-5db** were the major products in these cases. Minor amounts of corresponding 2-sulfonylmethyl indoles **4aa-4db** were also isolated in these reactions. Fluorine-bearing sulfonamide **1ea**, however, afforded a single product, the 2,3-disubstituted indole **5ea** in 61% yield.

Interestingly, all the substrates having N-methanesulfonyl groups (**1fa-1ja**) reacted under identical conditions to afford only the 2-sulfonylmethyl indoles **4fa-4ja** in good to high yields. In addition, the reaction showed a good level of functional group tolerance. Indole derivatives having halogens (Cl and F), trifluorormethyl, cyano and ester groups could be produced from corresponding precursors without trouble.

From the results depicted in table 3, it may be surmised that that it is possible to selectively access either of the indole derivatives (**4** or **5**) via this protocol. If the desired target is the 2-sulfonylmethyl indole **4**, the synthetic sequence may be initiated with N-mesylation of the iodoanilines **2**. On the other hand, 2,3-disubstituted indoles **5** may be selectively produced by using the N-tosyl derivatives.

The observed regioselectivity of Heck cyclisation presumably has steric origins. The organopalladium intermediate generated after oxidative addition of Pd(0) to **1aa** for example, may exist as two isomeric alkenes **A** and **B**. These isomeric alkenes can interact with palladium via either the α-sulfonyl or the γ-sulfonyl end. As both the sulfonyl groups (on nitrogen and carbon) are large in this case, the sterically favoured

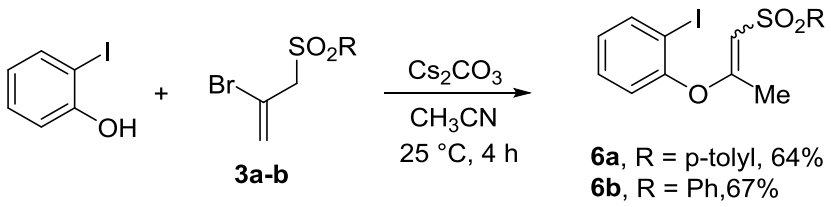
mode of cyclization may involve the reaction of the the α-sulfonyl end of the alkene **B**. This eventually leads to the formation of 2,3-substituted indole **5aa**. On the other hand, when the N-sulfonyl group is relatively smaller, as in the case of **1fa**, the major steric interaction becomes the one between N-sufonyl and the PdL_n unit. Therefore, out of the two depicted cyclisation intermediates **C** and **D**, the latter would be of less energy. It is clear that Heck cyclization via **D** would lead to the formation of the 3-substituted indole **4fa** (Scheme 17).



Scheme 17: Rationalisation of regioselectivity of Heck cyclisation based on minimisation of steric interactions

The successful development of the above-described indole synthesis method inspired further investigations to expand its scope towards the construction of other heterocyclic derivatives. It was conceivable that an analogous route starting from 2-iodophenols may

culminate in the generation of substituted benzofurans. In order to explore this possibility, the Cs_2CO_3-mediated reactions of 2-iodophenol and 2-bromoallyl sulfones **3a-b** were undertaken. It may be noted here that phenols have previously been successfully employed in similar formal vinylic substitution reactions developed in our laboratory (Scheme 11-12).[15,19] The reactions of o-iodophenol and **3a**-b, however, did not furnish the expected allyl sulfone products. Instead, the more substituted alkenes (vinyl sulfones) **6a-b** were obtained after standard workup and column chromatographic separation (Scheme 18).

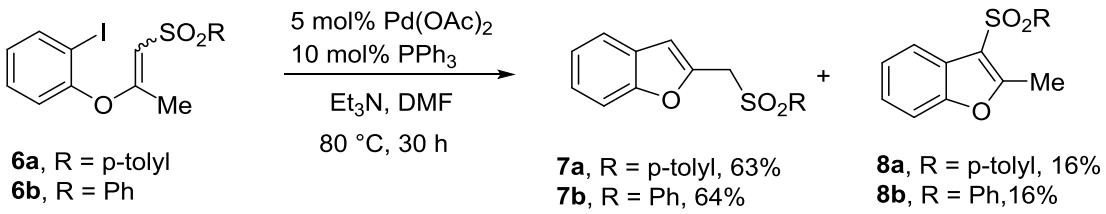


Scheme 18: Base-mediated reaction of 2-iodophenol and allylbromo sulfones **3a-b**

The products were identified via standard spectroscopic analysis. For example, the singlet absorptions at δ 5.96 (s, 1H) and 1.77 (s, 3H) in the ^{1}H NMR spectrum of **6b** clearly indicated the formation of the trisubstituted olefin unit. The stereochemistry of the double bond was not assigned at this stage as it was irrelevant in view of the planned intramolecular Heck reaction.

The two enol ethers **6a-b** were then subjected to the optimized conditions for the intramolecular Heck coupling reaction. In both the cases, two isomeric benzofurans were obtained after work-up and column chromatographic separation of the reaction mixtures. Spectroscopic analysis of the separated products revealed that the 2-

sulfonylmethyl benzofurans **7a-b** were the major product in both the cases. The 2,3-disubstituted benzofurans **8a-b** were isolated in lesser amounts (Scheme 19). It is notable that benzofurans constitute an important class of heterocycles owing to their widespread presence in nature, bioactive molecules and functional materials.[21]



6a, R = p-tolyl
6b, R = Ph

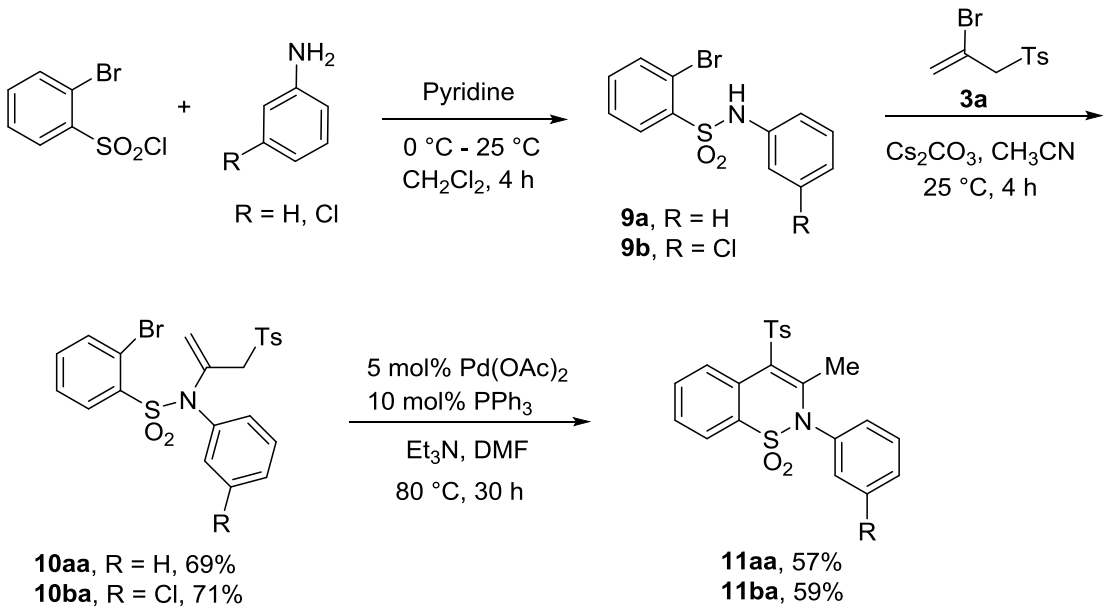
7a, R = p-tolyl, 63%
7b, R = Ph, 64%

8a, R = p-tolyl, 16%
8b, R = Ph,16%

Scheme 19: Intramolecular Heck reactions of 1-iodo-2-vinyloxy derivatives **6a-b**

It is intriguing that the regioselectivity of the benzofuran formation is opposite to that observed for the indole formation. Further studies may be required to gain an in-depth understanding of the factors that control the regioselectivity of these reactions.

The sequence of formal vinylic substitution-Heck coupling was also applicable to the construction of novel benzosultam derivatives. The sulfonamides **9a-b**[22] endowed with a bromine atom at the ortho-position was prepared from commercially available 2-bromobenzenesulfonyl chloride as shown in Scheme 19. The formal vinylic substitution reaction of the sulfonamides **9a-b** and 2-bromoallyl sulfone **3a** proceeded smoothly to afford the expected N-vinyl sulfonamides **10a-b** in good yields. The latter were then subjected to the previously established conditions of intramolecular Heck reaction. Disubstituted benzosultam derivatives were selectively formed in moderate yields after workup and chromatographic separation of the reaction mixture (Scheme 20). The products were characterised on the basis of standard spectroscopic analysis.



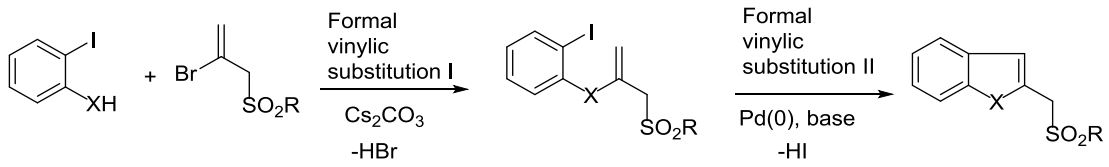
Scheme 20: Synthesis of benzosultam derivatives *via* formal vinylic substitution-Heck coupling sequence

The Heck cyclization afforded only single products in both the cases. The selectivity was similar to the one observed in N-tosyl indole formations. It may be presumed that the presence of the rather bulky N-sulfonylaryl group is responsible for the observed selectivity as seen in the case of N-tosyl indole formation (see Scheme 16). Incidentally, benzosultam derivatives are known to possess important biological activities, hence constitute much sought after synthetic targets.

4.5. Conclusion

In conclusion, a new strategy for synthesis of various important heterocyclic compounds, *viz*., indoles, benzofurans and benzosultams, has been developed. The sequence, in fact, involves two formal vinylic substitutions. The first one is mediated by cesium carbonate wherein the bromide of bromoallyl sulfone is displaced by either a nitrogen or oxygen nucleophile (sulfonamide or phenol). The second vinylic

substitution is an intramolecular Heck cyclization where in the aryl halide is substituted by the pendant alkene (Scheme 20).



Scheme 20: The method as a combination of two sequential vinylic substitutions

The intramolecular Heck coupling reaction exhibited interesting regioselective preferences. Both 2-sulfonylmethyl indoles and 2,3-disubstituted indoles could be selectively produced by choosing the right N-sulfonyl group. The vinylic substitution reaction of o-iodophenol and subsequent Heck cyclization showed selectivity that was different from corresponding aza analogues. A convenient synthesis of novel benzosultam derivatives were also developed using the same protocol. The heterocyclic motifs produced by this method are well known pharmacophores and valuable synthetic targets. Therefore, it is presumable that this method may find applications in the synthesis of designed molecules for development of therapeutics.

4.6. Experimental section

General information

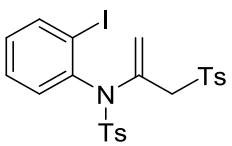
All ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ solvent at ambient temperature, chemical shift δ are given in ppm on a scale downfield from TMS, and the coupling constant *J* are in Hz. The signal patterns are indicated as follows: s, Singlet; d, doublet; t, triplet; dd, doublet of doublet; m, multiplet; brs = broad). FTIR spectra were recorded as neat. Melting points were recorded on an electrothermal apparatus and are uncorrected. All the reagents and solvents were used

without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Column chromatography was carried out using silica gel (60-120 mesh and 100- 200 mesh) packed in glass columns. All reactions were performed in oven-dried glassware with magnetic stirring. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm) and staining by $KMnO_4$. High-resolution mass spectra were recorded with q-TOF electrospray mass spectrometer. All purchased chemicals were used as received.

Synthesis of sulfonamide: General procedure

To a solution of the N-sulfonyl-o-iodo aniline **2** (1.0 mmol) and 2-bromoallyl sulfone **3** (1.5 mmol) in acetonitrile (10 mL), cesium carbonate (2.5 mmol) was added at room temperature and stirred the mixture for 4 hours. After completion of reaction, solvent was removed on a rotavapor and deionized water (20 mL) was added. The solution was extracted with ethyl acetate (3 X 15 mL). The combined organic extracts was washed with brine, dried over anhydrous sodium sulfate and concentrated on a rotavapor. Column chromatography of the residue on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure products.

Spectroscopic data for N-vinyl-o-iodo sulfonamides 1a-j



1aa, N-(2-iodophenyl)-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 448.29 mg, 79%

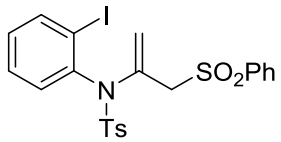
Melting point: 131-133 ˚C

IR (KBr) υ_{max}: 2922, 1620, 1595, 1460, 1346, 1311, 1157, 655, 586

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0, 1.2Hz, 1H), 7.72 (d, *J* = 8.4Hz, 2H), 7.56 (d, *J* = 8.4Hz, 2H), 7.34-7.21 (m, 4H), 7.22 (d, *J* = 8.0Hz, 2H), 7.05 (ddd, *J* = 8.0, 6.9, 2.2Hz, 1H), 5.53 (d, *J* = 1.2Hz, 1H), 5.29 (d, *J* = 1.2Hz, 1H), 3.84 (AB q, *J* = 15.2Hz , 2H), 2.45 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 144.5, 140.9, 140.0, 136.1, 135.1, 133.5, 132.5, 130.5, 129.7, 129.6, 129.2, 128.9, 128.7, 118.9, 102.3, 59.7, 21.7

HRMS calcd for $C_{23}H_{22}INO_4S_2$ (M+H) 568.0114 ; found 568.0116



1ab, N-(2-iodophenyl)-4-methyl-N-(3-(phenylsulfonyl)prop-1-en-2-yl)benzene sulfonamide

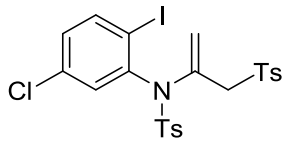
Colorless oil, 448.28 mg, 81%

IR (KBr) υ_{max}: 3062, 2924, 1591, 1496, 1315, 1153, 526

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0, 1.2Hz, 1H), 7.72–7.69 (m, 4H), 7.62-7.58 (m, 1H), 7.46 (t, *J* = 7.8Hz, 2H), 7.36–7.29 (m, 4H), 7.05 (ddd, *J* = 8.0, 6.8, 2.0Hz, 1H), 5.53, (d, *J* = 1.2Hz, 1H), 5.28 (d, *J* = 1.2Hz, 1H), 3.86 (AB q, *J* = 15.6Hz, 2H), 2.45 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.0, 139.9, 138.1, 136.1, 133.9, 133.3, 132.5, 130.6, 129.6, 129.2, 129.1, 128.9, 128.7, 118.8, 102.2, 59.7, 21.7

HRMS calcd for $C_{22}H_{20}INO_4S_2$ (M+H) 553.9957 ; found 553.9977



1ba, N-(5-chloro-2-iodophenyl)-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 499.57 mg, 83%

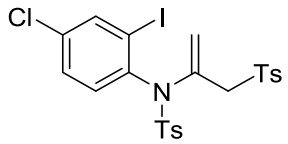
Melting point: 123-125 ˚C

IR (KBr) υ_{max}: 3244, 2924, 1620, 1595, 1448, 1309, 1157, 586, 516

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (t, J = 8.4Hz, 3H), 7.57 (d, J = 8.4Hz, 2H), 7.33 (d, J = 8.0Hz, 2H), 7.24 (d, J = 8.0Hz, 2H), 7.14 (d, J = 2.4Hz, 1H), 7.04 (dd, J = 8.4, 2.4Hz, 1H), 5.55 (d, J = 1.2Hz, 1H), 5.43 (d, J = 1.2Hz, 1H), 3.85 (AB q, J = 15.6Hz, 2H), 2.46 (s, 3H), 2.42 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.8, 141.3, 141.2, 135.7, 135.2, 134.9, 133.4, 132.2, 130.7, 129.8, 129.7, 128.9, 128.6, 119.7, 99.9, 59.9, 21.8, 21.7

HRMS calcd for $C_{23}H_{21}ClINO_4S_2$ (M+H) 601.9724; found 601.9737



1ca, N-(4-chloro-2-iodophenyl)-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 469.48 mg,78%

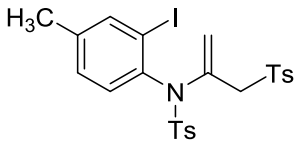
Melting point: 119-120 ˚C

IR (KBr) υ_{max}: 3091, 1597, 1577, 1463, 1334, 1163, 578

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 2.4Hz, 1H), 7.71 (d, J = 8.4Hz, 2H), 7.54 (d, J = 8.4Hz, 2H), 7.33–7.28 (m, 3H), 7.23-7.19 (m, 3H), 5.55 (d, J = 1.2Hz, 1H), 5.37 (d, J = 1.2Hz, 1H), 3.81 (s, 2H), 2.46 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.7, 140.2, 138.6, 135.9, 135.6, 134.9, 133.2, 132.7, 129.7, 129.6, 129.3, 128.9, 128.7, 120.0, 102.7, 59.6, 21.7

HRMS calcd for $C_{23}H_{21}ClINO_4S_2$ (M+H) 601.9724 ; found 601.9748



1da, N-(2-iodo-4-methylphenyl)-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 441.57 mg, 76%

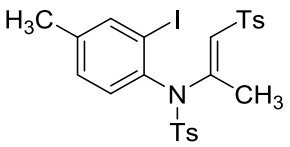
Melting point: 116-117 ˚C

IR (KBr) υ_{max}: 3041, 2924, 1624, 1595, 1477, 1319, 1159, 509

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4Hz, 2H), 7.64 (s, 1H), 7.55 (d, J = 8.0Hz, 2H), 7.31 (d, J = 8.0Hz, 2H), 7.22 (d, J = 8.4Hz, 2H), 7.16–7.10 (m, 2H), 5.52 (s, 1H), 5.25 (s, 1H), 3.82 (s, 2H), 2.45 (s, 3H), 2.42 (s, 3H), 2.31 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 144.4, 141.3, 141.1, 137.2, 136.2, 135.1, 133.5, 131.9, 130.0, 129.6, 129.5, 128.9, 128.7, 118.6, 102.0, 59.6, 21.7, 20.7

HRMS calcd for $C_{24}H_{24}INO_4S_2$ (M+H) 582.0270 ; found 582.0284



1da', (E)-N-(2-iodo-4-methylphenyl)-4-methyl-N-(1-tosylprop-1-en-2yl)benzene sulfonamide

White solid

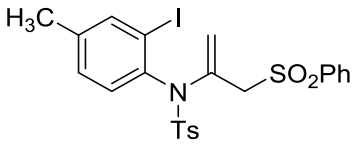
Melting point: 145-146 ˚C

IR (KBr) υ_{max}: 3035, 2922, 1581, 1473, 1365, 1292, 1130, 819, 661

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.68 (m, 4H), 7.27 (m, 4H), 7.20 (d, *J* = 8.4Hz, 1H), 7.14 (d, *J* = 8.0Hz, 1H), 6.09 (s, 1H), 2.43 (s, 3H), 2.42 (s, 3H), 2.34 (s, 3H), 2.18 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 145.2, 143.8, 141.8, 141.4, 139.9, 137.4, 136.2, 131.3, 130.0, 129.9, 129.7, 128.5, 127.0, 117.9, 101.7, 21.8, 21.7, 20.7, 17.3

HRMS calcd for $C_{24}H_{24}INO_4S_2$ (M+H) 582.0270 ; found 582.0271



1db,N-(2-iodo-4-methylphenyl)-4-methyl-N-(3-(phenylsulfonyl)prop-1-en-2-yl) benzenesulfonamide

Colorless oil, 419.29 mg, 74%

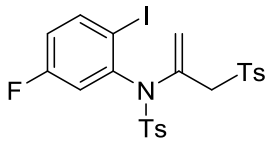
Melting point: 119-121 ˚C

IR (KBr) υ_{max}: 3040, 2922, 1620, 1585, 1440, 1307, 1153, 547

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.69 (m, 4H), 7.65 (d, *J* = 1.2Hz, 1H), 7.60 (t, *J* = 7.6Hz, 1H), 7.45 (t, *J* = 7.6Hz, 2H), 7.31 (d, *J* = 8.0Hz, 2H), 7.16 (d, *J* = 8.0Hz, 1H), 7.12 (d, *J* = 8.0, 1.6Hz, 1H), 5.52 (d, *J* = 1.2Hz, 1H), 5.24 (d, *J* = 1.2Hz, 1H), 3.85 (AB q, *J* = 15.2Hz, 2H), 2.45 (s, 3H), 2.31 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 141.4, 141.1, 138.1, 137.1, 136.2, 133.8, 133.4, 131.9, 130.0, 129.5, 129.0, 128.9, 128.8, 118.4, 101.9, 59.7, 21.7, 20.6

HRMS calcd for $C_{23}H_{22}INO_4S_2$ (M+H) 568.0114 ; found 568.0131



1ea, N-(5-fluoro-2-iodophenyl)-4-methyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 415.66 mg, 71%

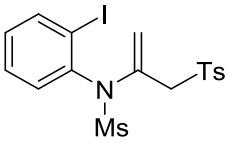
Melting point: 114-115 ˚C

IR (KBr) υ_{max}: 3099, 1589, 1460, 1354, 1292, 1159, 815, 580, 518

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 8.8, 6.0Hz, 1H), 7.73 (d, *J* = 8.4Hz, 2H), 7.57 (d, *J* = 8.4Hz, 2H), 7.33 (d, *J* = 8.0Hz, 2H), 7.24 (d, *J* = 8.0Hz, 2H), 6.99 (dd, *J* = 8.8, 3.2Hz, 1H), 6.85 (ddd, *J* = 8.8, 7.6, 3.2Hz, 1H), 5.53 (s, *J* = 1.6Hz, 1H), 5.35 (s, *J* = 1.6Hz, 1H), 3.84 (AB q, *J* = 15.6Hz, 2H), 2.46 (s, 3H), 2.42 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d), 144.9 (d), 141.4, 141.3 (d), 135.8, 135.1, 133.4, 129.8, 129.7, 128.9, 128.7, 119.8 (d), 119.3, 118.2 (d), 95.7 (d), 59.9, 21.8, 21.7

HRMS calcd for $C_{23}H_{21}FINO_4S_2$ (M+H) 586.0020 ; found 586.0026



1fa, N-(2-iodophenyl)-N-(3-tosylprop-1-en-2-yl)methanesulfonamide

White solid, 353.77 mg, 72%

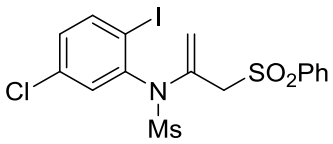
Melting point: 132-134 ˚C

IR (KBr) υ_{max}: 2922, 1629, 1595, 1462, 1334, 1309, 1286, 1147, 765, 516

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0Hz, 1H), 7.76 (d, *J* = 8.0Hz, 2H), 7.61 (d, *J* = 8.0Hz, 1H), 7.44 (t, *J* = 8.0Hz, 1H), 7.34 (d, *J* = 8.4Hz, 2H), 7.09 (t, *J* = 7.6Hz, 1H), 5.83 (s, 1H), 5.11 (s, 1H), 3.66 (AB q, *J* = 15.2Hz, 2H), 3.38 (s, 1H), 2.44 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 141.0, 139.6, 135.4, 132.7, 132.5, 130.8, 130.0, 129.6, 128.5, 116.9, 102.3, 59.7, 41.2, 21.7

HRMS calcd for $C_{17}H_{18}INO_4S_2$ (M+H) 491.9801; found 491.9811



1gb, N-(5-chloro-2-iodophenyl)-N-(3-(phenylsulfonyl)prop-1-en-2-yl)methane sulfonamide

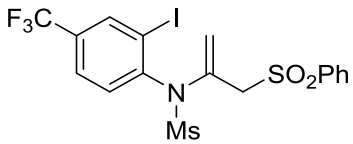
Pale yellow oil, 399.18 mg, 78%

Melting point: IR (KBr) υ_{max}: 2931, 1579, 1469, 1315, 1149, 746, 518

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.86 (m, 3H), 7.67 (t, J = 7.6Hz, 1H), 7.58–7.51 (m, 3H), 7.42-7.39 (m, 1H), 5.84 (s, 1H), 5.16 (s, 1H), 3.68 (AB q, J = 15.2Hz, 2H), 3.37 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 138.4, 138.3, 136.0, 134.3, 132.9, 132.4, 129.9, 129.5, 128.5, 117.5, 102.5, 59.6, 41.3

HRMS calcd for $C_{16}H_{15}ClINO_4S_2$ (M+H) 511.9255; found 511.9250



1hb, N-(2-iodo-4-(trifluoromethyl)phenyl)-N-(3-(phenylsulfonyl)prop-1-en-2 yl) methanesulfonamide

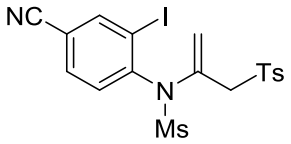
Reddish viscous oil, 370.82 mg, 68%

Melting point: IR (KBr) υ_{max}: 2933, 1600, 1446, 1315, 1126, 524

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.87 (d, J = 7.6Hz, 2H), 7.73–7.64 (m, 3H), 7.56 (t, J = 7.6Hz, 2H), 5.88 (s, 1H), 5.21 (s, 1H), 3.67 (AB q, J = 15.2Hz, 2H), 3.40 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.3, 137.9 (q), 134.4, 132.5 (q), 129.5, 128.4, 126.6, (q), 123.7, 121.0, 118.0, 102.3, 59.7, 41.5

HRMS calcd for $C_{17}H_{15}F_3INO_4S_2$ (M+H) 545.9518; found 545.9517



1 ia, N-(4-cyano-2-iodophenyl)-N-(3-tosylprop-1-en-2-yl)methanesulfonamide

Yellow solid, 325.31 mg, 63%

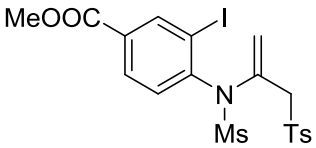
Melting point: 116-117 ˚C

IR (KBr) υ_{max}: 2924, 2233, 1629, 1595, 1469, 1315, 1149, 513

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.73-7.71 (m, 4H), 7.34 (d, J = 8.4Hz, 2H), 5.88 (s, 1H), 5.20 (s, 1H), 3.61 (AB q, J = 15.6Hz, 2H), 3.40 (s, 3H), 2.44 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 144.2, 144.0, 135.3, 133.0, 132.9, 132.1, 130.1, 128.4, 118.1, 116.2, 114.6, 102.6, 59.8, 41.5, 21.8

HRMS calcd for $C_{18}H_{17}IN_2O_4S_2$ (M+H) 516.9753; found 516.9764



1ja, methyl 3-iodo-4-(N-(3-tosylprop-1-en-2-yl)methylsulfonamido)benzoate

Pale yellow solid, 379.08 mg, 69%

Melting point: 132-134 ˚C

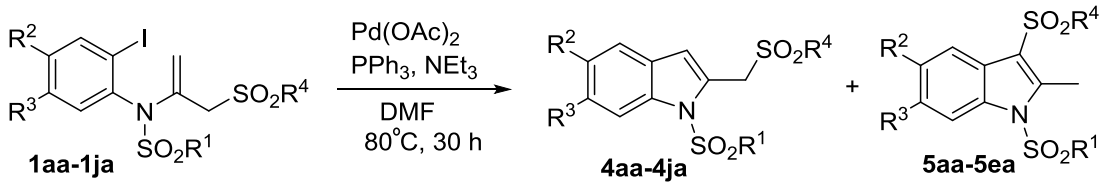
IR (KBr) υ_{max}: 2927, 1639, 1593, 1429, 1340, 1149, 509

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.08 (dt, J = 8.4, 1.6Hz, 1H), 7.74 (d, J = 8.0Hz, 2H), 7.66 (dd, J = 8.4, 1.6Hz, 1H), 7.34 (d, J = 8.0Hz, 2H), 5.88 (s, 1H), 5.20 (s, 1H), 3.94 (s, 3H), 3.65 (AB q, J = 15.6Hz, 2H), 3.41 (s, 3H), 2.44 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 145.4, 143.7, 142.0, 135.4, 132.3, 132.2, 132.1, 130.6, 130.0, 128.4, 117.6, 101.9, 59.7, 52.8, 21.7

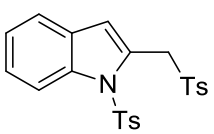
HRMS calcd for $C_{19}H_{20}INO_6S_2$ (M+H) 549.9856; found 549.9858

General procedure for indole synthesis



A mixture of N-vinyl-o-iodosulfonamide **1** (0.4mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%) and triethylamine (1.2 mmol) in DMF (4 ml) was stirred at 80 ˚C for 30 h. Upon completion of reaction, the reaction mixture was diluted with saturated NH_4Cl and product was extracted with ethyl acetate (3×15 ml). The combined organic layer was washed with brine, dried over sodium sulfate and concentrated at rotavapour under reduced pressure. The residue was subjected to column charomatography on silica gel using petroleum ether-ethyl acetate as eluent to afford analytically pure sample of the product.

Spectroscopic data for products



4aa, 1-tosyl-2-(tosylmethyl)-1H-indole

White solid, 28.13 mg, 16%

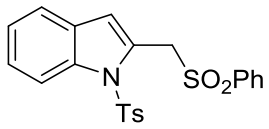
Melting point: 139-140 ˚C

IR (KBr) υ_{max}: 2935, 1593, 1490, 1446, 1367, 1309, 1147, 813, 651

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4Hz, 1H), 7.66 (d, *J* = 8.0Hz, 2H), 7.55 (d, *J* = 8.0Hz, 2H), 7.48 (d, *J* = 7.6Hz, 1H), 7.30–7.20 (m, 4H), 7.14 (d, *J* = 8.4Hz, 2H), 6.89 (s, 1H), 5.03 (s, 2H), 2.42 (s, 3H), 2.29 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 145.1, 137.3, 135.4, 135.1, 129.9, 129.7, 129.2, 128.8, 127.6, 126.5, 125.4, 124.1, 121.3, 116.1, 115.2, 55.1, 21.8, 21.6

HRMS calcd for $C_{23}H_{21}NO_4S_2$ (M+H) 440.0991; found 440.0990



4ab, 2-((phenylsulfonyl)methyl)-1-tosyl-1H-indole

White solid, 27.23 mg, 16%

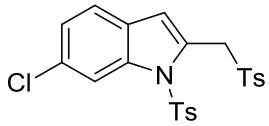
Melting point: 118-119 ˚C

IR (KBr) υ_{max}: 3014, 2947, 1565, 1448, 1361, 1300, 1145, 736, 538

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4Hz, 1H), 7.78 (d, *J* = 8.0Hz, 2H), 7.64 (t, *J* = 7.6Hz, 1H), 7.54 (d, *J* = 8.4Hz, 2H), 7.49–7.45 (m, 3H), 7.30–7.22 (m, 2H), 7.13 (d, *J* = 8.4Hz, 2H), 6.90 (s, 1H), 5.05 (s, 2H), 2.29 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 138.3, 137.3, 135.0, 134.1, 129.9, 129.2, 129.1, 128.8, 127.4, 126.5, 125.5, 124.1, 121.3, 116.3, 115.2, 55.2, 21.6

HRMS calcd for $C_{22}H_{19}NO_4S_2$ (M+H) 426.0834 ; found 426.0838



4ba, 6-chloro-1-tosyl-2-(tosylmethyl)-1H-indole

White solid, 26.54 mg, 14%

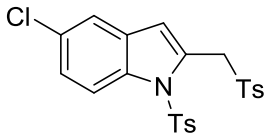
Melting point: 127-129 ˚C

IR (KBr) υ_{max}: 3107, 2924, 1563, 1452, 1369, 1317, 1153, 536

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 1.6Hz, 1H), 7.65 (d, *J* = 8.4Hz, 2H), 7.56 (d, *J* = 8.4Hz, 2H), 7.40 (d, *J* = 8.4Hz, 1H), 7.28 (d, *J* = 8.0Hz, 2H), 7.22 (dd, *J* = 8.4, 2.0Hz, 1H), 7.18 (d, *J* = 8.0Hz, 2H), 6.88 (s, 1H), 4.99 (s, 2H), 2.44 (s, 3H), 2.32 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.3, 137.6, 135.3, 134.9, 131.5, 130.0, 129.8, 128.7, 128.3, 127.6, 126.5, 124.8, 122.0, 115.4, 115.3, 55.0, 21.8, 21.6

HRMS calcd for $C_{23}H_{20}ClNO_4S_2$ (M+H) 474.0601; found 474.0610



4ca, 5-chloro-1-tosyl-2-(tosylmethyl)-1H-indole

White solid, 24.65 mg, 13%

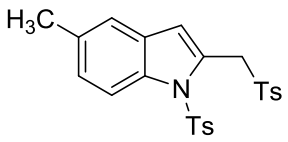
Melting point: 135-136 ˚C

IR (KBr) υ_{max}: 2922, 1595, 1442, 1371, 1317, 1155, 715, 536

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.8Hz, 1H), 7.65 (d, *J* = 8.4Hz, 2H), 7.53 (d, *J* = 8.0HZ, 2H), 7.44 (d, *J* = 2.0Hz, 1H), 7.27 (d, *J* = 8.0Hz, 2H), 7.23 (dd, *J* = 8.8, 2.0HZ, 1H), 7.15 (d, *J* = 8.4Hz, 2H), 6.81 (s, 1H), 5.00 (s, 2H), 2.42 (s, 3H), 2.30 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 145.3, 135.6, 135.3, 134.9, 130.3, 130.0, 129.9, 129.8, 129.2, 128.8, 126.5, 125.7, 120.8, 116.2, 115.1, 55.0, 21.8, 21.6

HRMS calcd for $C_{23}H_{20}ClNO_4S_2$ (M+H) 474.0601; found 474.0616



4da, 5-methyl-1-tosyl-2-(tosylmethyl)-1H-indole

White solid, 23.58 mg, 13%

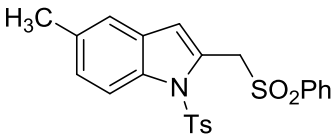
Melting point: 120-122 ˚C

IR (KBr) υ_{max}: 3035, 2922, 1581, 1435, 1365, 1292, 1130, 661

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4Hz, 1H), 7.66 (d, J = 8.0Hz, 2H), 7.53 (d, J = 8.0Hz, 2H), 7.27 (d, J = 8.0Hz, 2H), 7.14–7.09 (m, 3H), 6.83 (s, 3H), 5.02 (s, 2H), 2.43(s, 3H), 2.39 (s, 3H), 2.30 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 135.6, 135.4, 135.1, 133.8, 129.8, 129.7, 129.4, 128.8, 127.6, 126.9, 126.5, 121.1, 116.0, 114.9, 55.2, 21.8, 21.6, 21.2

HRMS calcd for $C_{24}H_{23}NO_4S_2$ (M+H) 454.1147 ; found 454.1149



4db, 5-methyl-2-((phenylsulfonyl)methyl)-1-tosyl-1H-indole

White solid, 26.37 mg, 15%

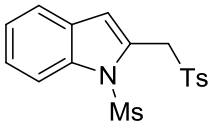
Melting point: 117-118 ˚C

IR (KBr) υ_{max}: 3010, 2941, 1585, 1450, 1359, 1298, 1170, 738, 578

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.8Hz, 1H), 7.77 (dd, J = 8.4, 1.2Hz, 2H), 7.66-7.11 (m, 1H), 7.52–7.45 (m, 4H), 7.25 (s, 1H), 7.13-7.09 (m, 3H), 6.83 (s, 1H), 5.03 (s, 2H), 2.38 (s, 3H), 2.29 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 138.2, 135.6, 135.0, 134.0, 133.8, 129.8, 129.4, 129.0, 128.9, 127.4, 127.0, 126.4, 121.1, 116.2, 114.9, 55.2, 21.6, 21.1

HRMS calcd for $C_{23}H_{21}NO_4S_2$ (M+H) 440.0991; found 440.1004



4fa, 1-(methylsulfonyl)-2-(tosylmethyl)-1H-indole

White solid, 107.58 mg, 74%

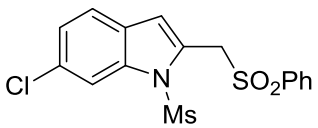
Melting point:

IR (KBr) υ_{max}: 3014, 2926, 1565, 1446, 1355, 1309, 1151, 536

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4Hz, 1H), 7.79 (d, J = 8.0Hz, 2H), 7.56 (d, J = 7.6Hz, 1H), 7.37–7.34 (m, 3H), 7.30 (d, J = 7.6Hz, 1H), 6.65 (s, 1H), 4.97 (s, 2H), 3.42 (s, 3H), 2.46 (, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 147.0, 135.9, 130.0, 128.5, 126.7, 125.6, 123.8, 121.5, 114.4, 114.0, 54.8, 41.2, 21.8

HRMS calcd for $C_{17}H_{17}NO_4S_2$ (M+H) 364.0678; found 364.0681



4gb, 6-chloro-1-(methylsulfonyl)-2-((phenylsulfonyl)methyl)-1H-indole

White solid, 112.09 mg, 73%

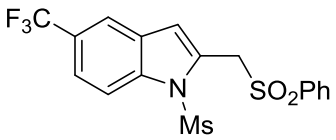
Melting point: 186-187 ˚C

IR (KBr) υ_{max}: 2953, 1583, 1444, 1361, 1309, 1161, 543

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6Hz, 2H), 7.87 (d, J = 8.8Hz, 1H), 7.70 (t, J = 7.6Hz, 1H), 7.59 (t, J = 7.6Hz, 2H), 7.53 (s, 1H), 7.34 (dd, J = 7.2, 1.6Hz, 1H), 6.58 (s, 1H), 4.98 (s, 2H), 3.43 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 135.3, 134.4, 129.7, 129.6, 129.5, 128.5, 127.9, 125.9, 121.0, 115.1, 113.7, 54.6, 41.5

HRMS calcd for $C_{16}H_{14}ClNO_4S_2$ (M+H) 384.0132; found 384.0149



4hb, 1-(methylsulfonyl)-2-((phenylsulfonyl)methyl)-5-(trifluoromethyl)-1H-indole

White solid, 101.85 mg, 61%

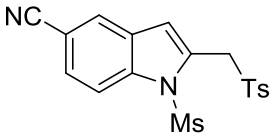
Melting point: 204-205 ˚C

IR (KBr) υ_{max}: 3008, 2953, 1620, 1448, 1356, 1313, 1159, 542

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.8Hz, 1H), 7.93 (d, J = 8.4Hz, 2H), 7.86 (d, J = 0.8Hz, 1H), 7.73–7.69 (m, 1H), 7.63-7.58 (m, 3H), 6.71 (s, 1H), 5.02 (s, 2H), 3.49 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.4, 134.4, 129.5, 128.6, 128.5, 128.1, 126.2 (q), 123.0, 122.3(q), 119.0(q), 114.5, 114.2, 54.6, 41.8

HRMS calcd for $C_{17}H_{14}F_3NO_4S_2$ (M+H) 418.0395; found 418.0415



4ia, 1-(methylsulfonyl)-2-(tosylmethyl)-1H-indole-5-carbonitrile

White solid, 90.12 mg, 58%

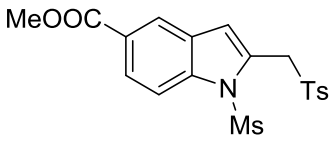
Melting point: 180-181 ˚C

IR (KBr) υ_{max}: 3020, 2926, 2223, 1595, 1456, 1363, 1303, 1138, 509

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4Hz, 1H), 7.91 (d, J = 1.6Hz, 1H), 7.80 (d, J = 8.0Hz, 2H), 7.63 (dd, J = 8.4, 1.6Hz, 1H), 7.39 (d, J = 8.0Hz, 2H), 6.69 (s, 1H), 4.98 (s, 2H), 3.53 (s, 3H), 2.48 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 138.6, 135.5, 130.2, 129.4, 128.5, 128.4, 128.3, 126.3, 119.0, 115.0, 113.5, 107.6, 54.6, 42.0, 21.8

HRMS calcd for $C_{18}H_{16}N_2O_4S_2$ (M+H) 389.0630; found 389.0631



4ja, methyl 1-(methylsulfonyl)-2-(tosylmethyl)-1H-indole-5-carboxylate

White solid, 106.21 mg, 63%

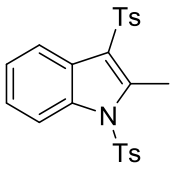
Melting point: 178-179 ˚C

IR (KBr) υ_{max}: 3014, 2958, 1716, 1606, 1438, 1354, 1136, 538

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.08 (d, J = 8.8Hz, 1H), 7.99 (d, J = 8.8Hz, 1H), 7.80 (d, J = 7.6Hz, 2H), 7.39 (d, J = 7.6Hz, 2H), 6.68 (s, 1H), 4.99 (s, 2H), 3.95 (s, 3H), 3.51 (s, 3H), 2.48 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 145.5, 139.4, 135.6, 130.1, 128.5, 128.3, 128.2, 126.6, 125.9, 123.7, 114.5, 113.8, 54.7, 52.3, 41.7, 21.8

HRMS calcd for $C_{19}H_{19}NO_6S_2$ (M+H) 422.0733; found 422.0749



5aa, 2-methyl-1,3-ditosyl-1H-indole

White solid, 112.52 mg, 64%

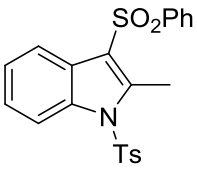
Melting point: 176-178 ˚C

IR (KBr) υ_{max}: 2922, 1593, 1543, 1442, 1371, 1153, 715, 534

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.19 (m, 1H), 8.11-8.09 (m, 1H), 7.80 (d, *J* = 8.0Hz, 2H), 7.69 m(d, *J* = 8.4Hz, 2H), 7.34-7.31 (m, 2H), 7.25 (d, *J* = 8.0Hz, 4H), 2.97 (s, 3H), 2.37 (s, 3H), 2.36 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 144.2, 142.3, 139.8, 135.6, 135.4, 130.3, 129.9, 126.7, 126.5, 125.5, 125.4, 124.8, 120.4, 119.9, 114.4, 21.7, 21.6, 13.1

HRMS calcd for $C_{23}H_{21}NO_4S_2$ (M+H) 440.0991 ; found 440.1000



5ab, 2-methyl-3-(phenylsulfonyl)-1-tosyl-1H-indole

White solid, 105.53 mg, 62%

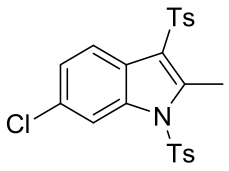
Melting point: 164-165 ˚C

IR (KBr) υ_{max}: 3057, 1544, 1442, 1373, 1313, 1182, 700, 542

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.8Hz, 1H), 8.11 (d, *J* = 8.8Hz, 1H), 7.92 (d, *J* = 7.6Hz, 2H), 7.69 (d, *J* = 8.0Hz, 2H), 7.54 (t, *J* = 7.2Hz, 1H), 7.47 (t, *J* = 7.6Hz, 1H), 7.37–7.31 (m, 2H), 7.26 (d, *J* = 7.6Hz, 2H), 2.98 (s, 3H), 2.38 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.1, 142.7, 142.6, 135.6, 135.4, 133.2, 130.4, 129.3, 126.7, 126.4, 125.6, 125.4, 124.9, 120.4, 119.5, 114.5, 21.7, 13.1

HRMS calcd for $C_{22}H_{19}NO_4S_2$ (M+H) 426.0834; found 426.0838



5ba, 6-chloro-2-methyl-1,3-ditosyl-1H-indole

White solid, 130.82 mg, 69%

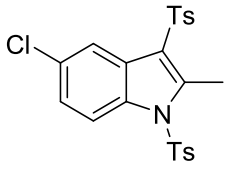
Melting point: 194-196 ˚C

IR (KBr) υ_{max}: 2922, 1544, 1417, 1373, 1311, 1151, 761, 535

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 1.6Hz, 1H), 8.02 (d, J = 8.8Hz, 1H), 7.77 (d, J = 8.4Hz, 2H), 7.68 (d, J = 8.4Hz, 2H), 7.31–7.24 (m, 5H), 2.92 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 144.4, 142.8, 139.5, 135.9, 135.1, 131.7, 130.5, 130.0, 126.7, 126.5, 125.5, 124.0, 121.2, 119.8, 114.6, 21.8, 21.6, 13.1

HRMS calcd for $C_{23}H_{20}ClNO_4S_2$ (M+H) 474.0601; found 474.0608



5ca, 5-chloro-2-methyl-1,3-ditosyl-1H-indole

White solid, 128.92 mg, 68%

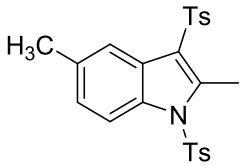
Melting point: 188-189 ˚C

IR (KBr) υ_{max}: 2924, 1541, 1436, 1373, 1315, 1149, 759, 532

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.8Hz, 1H), 8.11 (d, J = 2.0Hz, 1H), 7.78 (d, J = 8.4Hz, 2H), 7.66 (d, J = 8.4Hz, 2H), 7.31–7.25 (m, 5H), 2.93 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 144.5, 143.5, 139.5, 135.1, 134.0, 130.8, 130.4, 130.0, 126.7, 126.5, 125.8, 120.0, 119.5, 115.5, 21.7, 21.6, 13.2

HRMS calcd for $C_{23}H_{20}ClNO_4S_2$ (M+H) 474.0601; found 474.0617



5da, 2,5-dimethyl-1,3-ditosyl-1H-indole

White solid, 130.62 mg, 72%

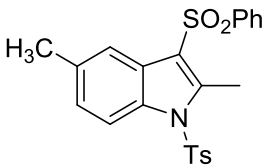
Melting point: 191-193 ˚C

IR (KBr) υ_{max}: 2924, 1591, 1544, 1456, 1369, 1315, 1145, 677, 534

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.8Hz, 1H), 7.89 (d, J = 1.6Hz, 1H), 7.79 (d, J = 8.4Hz, 2H), 7.66 (d, J = 8.4Hz, 2H), 7.25–7.22 (m, 4H), 7.15 (dd, J = 8.8, 1.6Hz, 1H), 2.94 (s, 3H), 2.43 (s, 3H), 2.36 (s, 6H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 144.1, 142.3, 139.8, 135.4, 134.6, 133.8, 130.3, 129.9, 126.9, 126.6, 126.4, 125.6, 120.1, 119.6, 114.1, 21.7, 21.6, 21.5, 13.1

HRMS calcd for $C_{24}H_{23}NO_4S_2$ (M+H) 454.1147; found 454.1147



5db, 2,5-dimethyl-3-(phenylsulfonyl)-1-tosyl-1H-indole

White solid, 121.31 mg, 69%

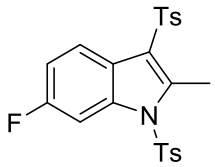
Melting point: 172-173 ˚C

IR (KBr) υ_{max}: 2924, 1593, 1544, 1444, 1373, 1313, 1147, 678, 538

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4Hz, 1H), 7.92-7.89 (m, 3H), 7.67 (d, J = 8.4Hz, 2H), 7.55-7.51 (m, 1H), 7.48–7.44 (m, 2H), 7.24 (d, J = 8.0Hz, 2H), 7.16 (dd, J = 8.8, 1.6Hz, 1H), 2.94 (s, 3H), 2.43 (s, 3H), 2.37 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 142.7, 142.6, 135.4, 134.7, 133.8, 133.2, 130.3, 129.2, 127.0, 126.6, 126.4, 125.6, 120.1, 119.2, 114.1, 21.7, 21.5, 13.1

HRMS calcd for $C_{23}H_{21}NO_4S_2$ (M+H) 440.0991; found 440.1005



5ea, 6-fluoro-2-methyl-1,3-ditosyl-1H-indole

White solid, 111.64 mg, 61%

Melting point: 187-188 ˚C

IR (KBr) υ_{max}: 2922, 1591, 1546, 1483, 1373, 1317, 1149, 806, 532

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.8, 5.6Hz, 1H), 7.96 (dd, J = 10.4, 2.0Hz, 1H), 7.78 (d, J = 8.0Hz, 2H), 7.69 (d, J = 8.0Hz, 2H), 7.27 (t, J = 8.4Hz, 4H), 7.09 (td, J = 8.8, 2.0Hz, 1H), 2.93 (s, 3H), 2.39 (s, 3H). 2.36 (s, 3H)

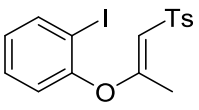
^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1 (d), 146.4, 144.4, 142.6 (d), 139.6, 135.8 (d), 135.1, 130.5, 130.0, 126.7, 126.5, 121.7, 121.4 (d), 119.7, 113.2 (d), 102.0 (d), 21.7, 21.6, 13.1

HRMS calcd for $C_{23}H_{20}FNO_4S_2$ (M+H) 458.0897; found 458.0921

Synthesis of 1-iodo-2-vinyloxy benzene derivative 6

To a solution of the 2-iodophenol (1.0 mmol) and 2-bromoallyl sulfone **3** (1.5 mmol) in acetonitrile (10 mL) cesium carbonate (2.5 mmol) was added at room temperature and stirred the mixture for 4 hours. After completion of reaction, solvent was removed on a rotavapor and deionized water (20 mL) was added. The solution was extracted with ethyl acetate (3 X 15 mL). The combined organic extracts was washed with brine, dried over anhydrous sodium sulfate and concentrated on a rotavapor. Column chromatography of the residue on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure products.

Spectroscopic data



6a, (E)-1-iodo-2-((1-tosylprop-1-en-2-yl)oxy)benzene

White solid, 265.12 mg, 64%

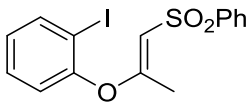
Melting point: 136-137 ˚C

IR (KBr) υ_{max}: 3068, 1627, 1462, 1284, 1130, 757

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4Hz, 2H), 7.76 (dd, J = 8.0, 1.6Hz, 1H), 7.30–7.25 (m, 3H), 6.92–6.88 (m, 1H), 6.85 (dd, J = 8.0, 1.2Hz, 1H), 5.95 (d, J = 0.8Hz, 1H), 2.39 (s, 3H), 1.75 (d, J = 0.8Hz, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 153.5, 143.8, 139.8, 139.5, 129.8, 129.4, 128.3, 127.1, 121.0, 113.7, 89.4, 21.6, 19.1

HRMS calcd for $C_{16}H_{15}IO_3S$ (M+H) 414.9866; found 414.9887



6b, (E)-1-iodo-2-((1-(phenylsulfonyl)prop-1-en-2-yl)oxy)benzene

White solid, 268.15 mg, 67%

Melting point: 122-123 ˚C

IR (KBr) υ_{max}: 3070, 2924, 1627, 1458, 1436, 1286, 1126, 752, 567

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.6Hz, 2H), 7.76 (d, *J* = 8.0Hz, 1H), 7.57–7.54 (m, 1H), 7.48 (t, *J* = 7.2Hz, 2H), 7.29 (t, *J* = 7.6Hz, 1H), 6.92 (t, *J* = 7.6Hz, 1H), 6.84 (d, *J* = 8.0Hz, 1H), 5.96 (s, 1H), 1.77 (s, 3H)

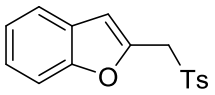
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.4, 142.4, 139.8, 132.9, 129.8, 128.8, 128.3, 127.3, 121.2, 113.0, 89.5, 19.2

HRMS calcd for $C_{15}H_{13}IO_3S$ (M+H) 400.9709; found 400.9711

Procedure for synthesis of benzofuran derivatives

A mixture of 1-iodo-2-vinyloxy benzene **6** (0.4mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%) and triethylamine (1.2 mmol) in DMF (4 ml) was stirred at 80 ˚C for 30 h. Upon completion of reaction, the reaction mixture was diluted with saturated NH_4Cl and product was extracted with ethyl acetate (3×15 ml). The combined organic layer was washed with brine, dried over sodium sulfate and concentrated at rotavapour under reduced pressure. The residue was subjected to column charomatography on silica gel using petroleum ether-ethyl acetate as eluent to afford analytically pure sample of the product.

Spectroscopic data



7a, 2-(tosylmethyl)benzofuran

White solid, 72.16 mg, 63%

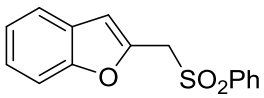
Melting point: 196-197 ˚C

IR (KBr) υ_{max}: 2987, 1591, 1448, 1303, 1286, 1145, 719, 520

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.4Hz, 2H), 7.53–7.51 (m, 1H), 7.37–7.35 (m, 1H), 7.29–7.27 (m, 3H), 7.22 (td, J = 7.6, 1.2Hz, 1H), 6.67 (d, J = 0.8Hz, 1H), 4.53 (s, 2H), 2.43 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 145.3, 145.2, 135.3, 129.8, 128.6, 128.0, 125.0, 123.1, 121.3, 111.3, 108.9, 56.5, 21.7

HRMS calcd for $C_{16}H_{14}O_3S$ (M+H) 287.0743; found 287.0746



7b, 2-((phenylsulfonyl)methyl)benzofuran

White solid, 69.71 mg, 64%

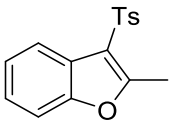
Melting point: 162-163 ˚C

IR (KBr) υ_{max}: 2880, 1581, 1448, 1305, 1141, 735, 569

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0Hz, 2H), 7.63 (t, J = 7.6Hz, 1H), 7.52–7.45 (m, 3H), 7.33 (d, J = 8.0Hz, 1H), 7.24–7.19 (m, 2H), 6.63 (s, 2H), 4.54 (s, 2H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 145.1, 138.2, 134.1, 129.2, 128.6, 127.9, 125.0, 123.2, 121.3, 111.3, 109.0, 56.5

HRMS calcd for $C_{15}H_{12}O_3S$ (M+H) 273.0586; found 273.0589



8a, 2-methyl-3-tosylbenzofuran

White solid, 18.32 mg, 16%

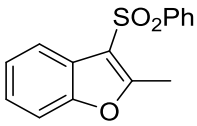
Melting point: 122-123 ˚C

IR (KBr) υ_{max}: 2922, 1583, 1446, 1296, 1143, 758, 580

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.85 (m, 3H), 7.42-7.39 (m, 1H), 7.31–7.28 (m, 4H), 2.80 (s, 3H), 2.38 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 153.2, 144.3, 139.7, 129.9, 126.7, 125.2, 124.4, 124.3, 120.3, 118.2, 111.2, 21.6, 13.6

HRMS calcd for $C_{16}H_{14}O_3S$ (M+H) 287.0743; found 287.0740



8b, 2-methyl-3-(phenylsulfonyl)benzofuran

White solid, 17.42 mg, 16%

Melting point: 106-107 ˚C

IR (KBr) υ_{max}: 3064, 2920, 1577, 1444, 1309, 1149, 750, 545

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4Hz, 2H), 7.88–7.86 (m, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.50 (t, J = 7.6 HZ, 2H), 7.42–7.39 (m, 1H), 7.31–7.28 (m, 2H), 2.80 (s, 3H)

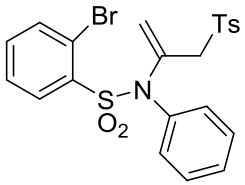
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 153.3, 142.5, 133.3, 129.3, 126.7, 125.3, 124.5, 124.4, 120.3, 117.9, 111.3, 13.7

HRMS calcd for $C_{15}H_{12}O_3S$ (M+H) 273.0586; found 273.0589

Procedure for synthesis 2-bromo-N-vinyl benzenesulfonamide 10

To a solution of the 2-bromobenzenesulfonamide **9** (1.0 mmol) and 2-bromoallyl sulfone **3** (1.5 mmol) in acetonitrile (10 mL) cesium carbonate (2.5 mmol) was added at room temperature and stirred the mixture for 4 hours. After completion of reaction, solvent was removed on a rotavapor and deionized water (20 mL) was added. The solution was extracted with ethyl acetate (3 X 15 mL). The combined organic extracts was washed with brine, dried over anhydrous sodium sulfate and concentrated on a rotavapor. Column chromatography of the residue on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure products.

Spectroscopic data



10aa, 2-bromo-N-phenyl-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 349.43 mg, 69%

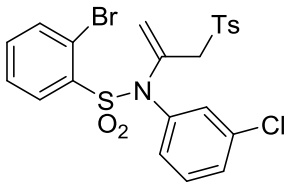
Melting point: 144-145 ˚C

IR (KBr) υ_{max}: 3062, 2924, 1593, 1489, 1448, 1317, 1149, 689, 513

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.2, 2.4Hz, 1H), 7.70 (dd, J = 7.6, 1.6Hz, 1H), 7.58 (d, J = 8.4Hz, 2H), 7.37–7.33 (m, 2H), 7.23–7.19 (m, 7H), 5.38 (s, 1H), 5.37 (s, 1H), 4.06 (s, 2H), 2.41 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 138.0, 137.9, 135.8, 135.4, 135.1, 134.3, 133.4, 130.0, 129.9, 129.8, 129.6, 129.2, 128.6, 128.5, 127.5, 121.0, 120.0, 60.5, 21.7

HRMS calcd for $C_{22}H_{20}BrNO_4S_2$ (M+H) 506.0095; found 506.0093



10ba, 2-bromo-N-(3-chlorophenyl)-N-(3-tosylprop-1-en-2-yl)benzenesulfonamide

White solid, 384.01 mg, 71%

Melting point: 151-152 ˚C

IR (KBr) υ_{max}: 3089, 2924, 1585, 1471, 1317, 1083, 684. 514

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, J = 6.8, 2.4Hz, 1H), 7.73 (d, J = 6.8Hz, 1H), 7.58 (d, J = 8.0Hz, 2H), 7.40 (t, J = 4.4Hz, 2H), 7.26–7.23 (m, 3H), 7.17–7.13 (m, 3H), 5.50 (s, 1H), 5.35 (s, 1H), 4.08 (s, 2H), 2.43 (s, 3H)

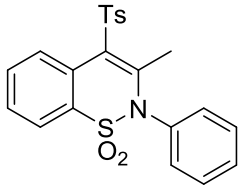
^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 139.1, 137.5, 135.9, 135.2, 134.9, 134.6, 134.5, 133.4, 130.0, 129.8, 129.3, 128.6, 128.4, 127.63, 127.61, 121.6, 120.9, 60.5, 21.8

HRMS calcd for $C_{22}H_{19}BrClNO_4S_2$ (M+H) 539.9706; found 539.9700

Procedure for synthesis of benzosultam derivative 11

A mixture of 2-bromo-N-vinylbenzenesulfonamide **10** (0.4mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%) and triethylamine (1.2 mmol) in DMF (4 ml) was stirred at 80 ˚C for 30 h. Upon completion of reaction, the reaction mixture was diluted with saturated NH_4Cl and product was extracted with ethyl acetate (3×15 ml). The combined organic layer was washed with brine, dried over sodium sulfate and concentrated at rotavapour under reduced pressure. The residue was subjected to column charomatography on silica gel using petroleum ether-ethyl acetate as eluent to afford analytically pure sample of the product.

Spectroscopic data



11aa, 3-methyl-2-phenyl-4-tosyl-2H-benzo[e][1,2]thiazine 1,1-dioxide

White solid, 97.01 mg, 57%

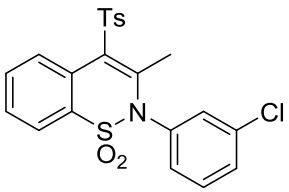
Melting point: 168-169 ˚C

IR (KBr) υ_{max}: 3064, 2924, 1570, 1541, 1492, 1346, 1282, 1139, 1083, 665. 565

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 8.4Hz, 1H), 7.74 (d, J = 8.0Hz, 3H), 7.59 (t, J = 4.0Hz, 1H), 7.47 (d, J = 7.6Hz, 1H), 7.44–7.39 (m, 3H), 7.24 (d, J = 8.0Hz, 2H), 7.14–7.12 (m, 2H), 2.41 (s, 3H), 2.35 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 144.2, 139.0, 134.9, 132.3, 132.2, 129.8, 129.7, 129.6, 128.8, 128.3, 127.6, 126.9, 123.1, 122.0, 21.6, 20.7

HRMS calcd for $C_{22}H_{19}NO_4S_2$ (M+H) 426.0834; found 426.0833



11ba, 2-(3-chlorophenyl)-3-methyl-4-tosyl-2H-benzo[e][1,2]thiazine 1,1-dioxide

White solid, 108.55 mg, 59%

Melting point: 184-185 ˚C

IR (KBr) υ_{max}: 2960, 1571, 1546, 1469, 1357, 1284, 1143, 1083, 671. 565

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.4Hz, 1H), 7.72 (d, J = 8.4Hz, 3H), 7.61–7.57 (m, 1H), 7.46 (td, J = 8.0, 0.8Hz, 1H), 7.38 (dt, J = 8.0, 1.6Hz, 1H), 7.32 (t, J = 8.0Hz, 1H), 7.23 (d, J = 8.0Hz, 2H), 7.11 (t, J = 2.0Hz, 1H), 7.05–7.02 (m, 1H), 2.41 (s, 3H), 2.34 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 144.3, 138.7, 135.9, 135.3, 132.4, 130.5, 129.8, 129.7, 129.4, 128.8, 128.6, 127.8, 127.0, 124.0, 122.1, 21.6, 20.7

HRMS calcd for $C_{22}H_{18}ClNO_4S_2$ (M+H) 460.0444; found 460.0436

4.7. References

1. (a) Ishikura, M.; Yamada, K. *Nat. Prod. Rep*. **2009**, *26*, 803. (b) Kaushik, N. K.; Kaushik, N.; Attri, P.; Kumar, N.; Kim, C. H.; Verma, A. K.; Choi, E. H. *Molecules* **2013**, *18*, 6620. (c) Andreani, A.; Rambaldi, M. *J. Hetrocyclic. Chem.* **1988**, *25*, 1519.

2. (a) Crooke, S. T.; Bradner, W. T. *Cancer Treatment Reviews* **1976**, *3*, 121. (b) Berger, M.; Gray, J. A.; Roth, B. L. *Annu. Rev. Med*. **2009**. *60*, 355. (c) Chen, F.-E.; Huang, J. *Chem. Rev*. **2005**, *105*, 4671.

3. Gul, W.; Hamann, M. T. *Life Sciences* **2005**, *78*, 442.

4. Blobaum, A. L.; Uddin, M. J.; Felts, A. S.; Crews, B. C.; Rouzer, C. A.; Marnett, L. J. *ACS Medicinal Chemistry Letters* **2013**, *4*, *5*, 486.

5. Tran, J. Q.; Gerber, J. G.; Kerr, B. M. *Clin Pharmacokinet* **2001**, *40*, 207.

6. Plosker, G. L.; McTavish, D. *Drugs* **1994**, *47*, 622.

7. (a) Hughes, D. L.; *Org. Prep. Proced. Int.* **1993**, *25*, 607. (b) Robinson, B.; *Chem. Rev.* **1963**, *63*, 373.

8. (a) Gribble, G. W.; *J. Chem. Soc. Perkin. Trans*. **2000**, *1*, 1045. (b) Taber, B. F.; Tirunahari, P. K. *Tetrahedron* **2011**, *67*, 7195.

9. (a) Iida, H.; Yuasa, Y.; Kibayashi, C. *J. Org. Chem.* **1980,** *45*, 2938. (b) Edmonson, S. D.; Mastracchio, A.; Parmee, E. R. *Org. Lett.* **2000,** *2*, 1109. (c) Yamazaki, K.; Nakamura, Y.; Kondo, Y. *J. Org. Chem.* **2003**, *68*, 6011. (d) Chen, C.; Lieberman, D. R.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1997**, *62*, 2676. (e) Gao, D.; Parvez, M.; Back, T. G. *Chem. Eur. J*. **2010**, *16*, 14281. (f) Nguyen, H. H.; Kurth, M. J. *Org. Lett*. **2013**, *15*, 362.

10. (a) Zhang, H.-C.; Maryanoff, B. E. *J. Org. Chem*. **1997**, *62*, 1804. (b) Yun, W.; Mohan, R. *Tetrahedron Lett*. **1996**, *37*, 7189.

11. Brown, D.; Gribb, R.; Sridharan, V.; Tambyrajah, V.; Thornton-Pett, M. *Tetrahedron* **1998**, *54*, 2595.

12. Wu, M.; Yan. R. *Synlett* **2017**, *28*, 729.

13. Nallagonda, R.; Rehan, M.; Ghorai, P. *Org. Lett.* **2014,** *16*, 4786.

14. Yadav D.; Meon, R.S. *Org. Biomol. Chem.* **2020**, *18*, 365.

15. Kumar, A.; Thadkapally, S.; Menon, R. S. *J. Org. Chem*. **2015**, *80*, 11048.

16. (a) Hirata, T.; Sasada, Y.; Ohtani, T.; .Asada, T.; Kinoshita, H.; Senda, H.; Inomata, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 75. (b) Inomata, K.; Hirata, T.; Suhara, H.; Kinoshita, H.; Kotake, H.; Senda, H. *Chem. Lett.* **1988**, 2009.

17. Undeela, S.; Thadkapally, S.; Nanubolu, J. B.; Singarapu, K. K.; Menon, R. S. *Chem. Commun.* **2015**, *51*, 13748.

18. Undeela, S.; Ravikumar, G.; Nanubolu, J. B.; Singarapu, K. K.; Menon, R. S. *Chem. Commun.* **2016**, *52*, 4824.

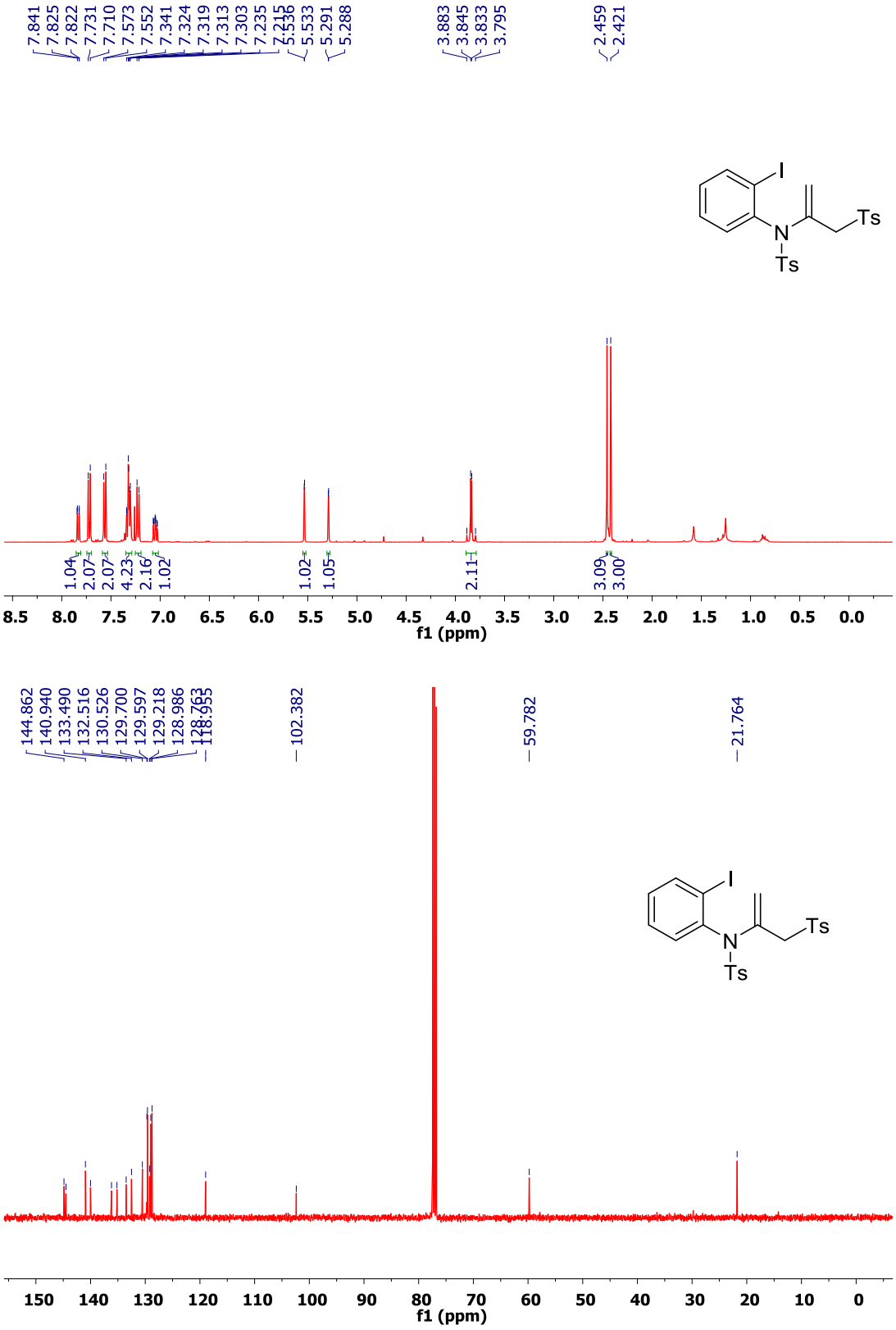
19. Thadkapally, S.; Kunjachan, A. C.; Menon, R. S. *Beilstein J. Org. Chem.* **2016,** *12*, 16.

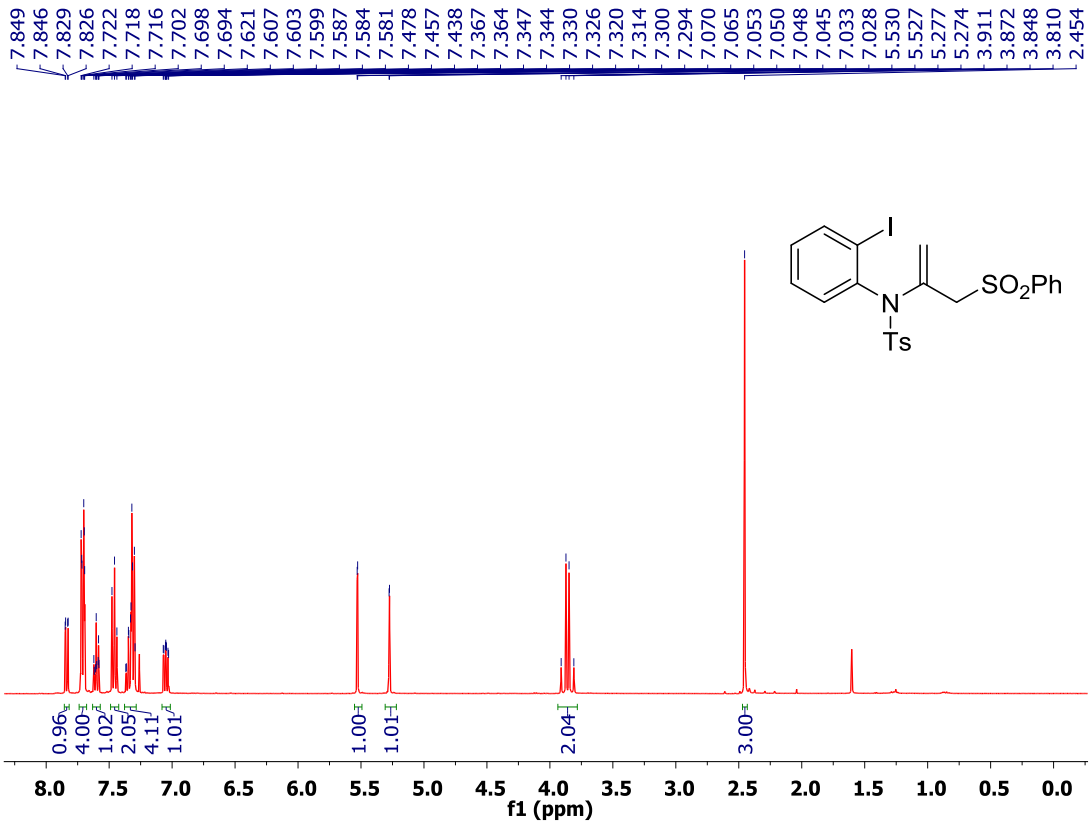
20. Gibson, S. E.; Middleton, R. J. *Contemp. Org. Synth.* **1996**, *3*, 447.

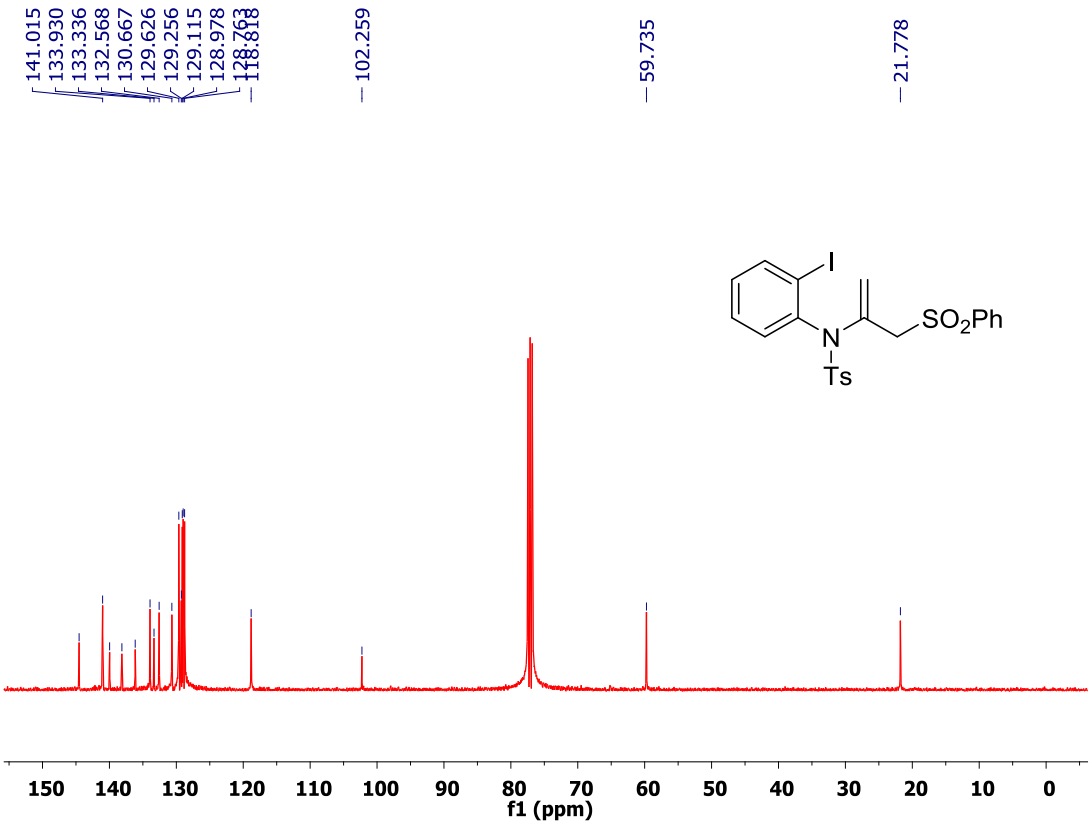
21. (a) Miao, Yu-H.; Hu, Yu-H,; Yang, J.; Liu, T.; Sun, J.; Wang, X-J. *RSC Adv.* **2019**, *9*, 27510. (b) Khanam, H.; Shamsuzzaman. *Eur. J. of Med.Chem.***2015**, *97*, 483.

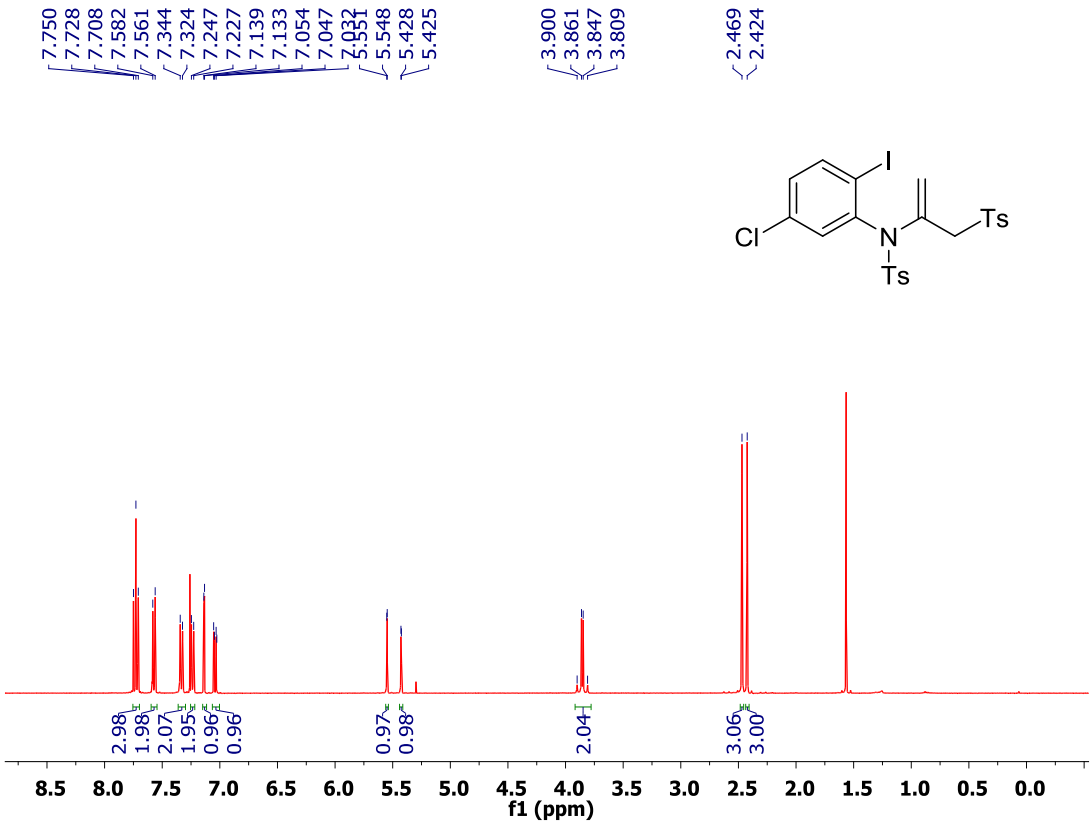
22. S. Debnath, S. Mondal, S. *J. Org. Chem*. **2015**, *80*, 3940.

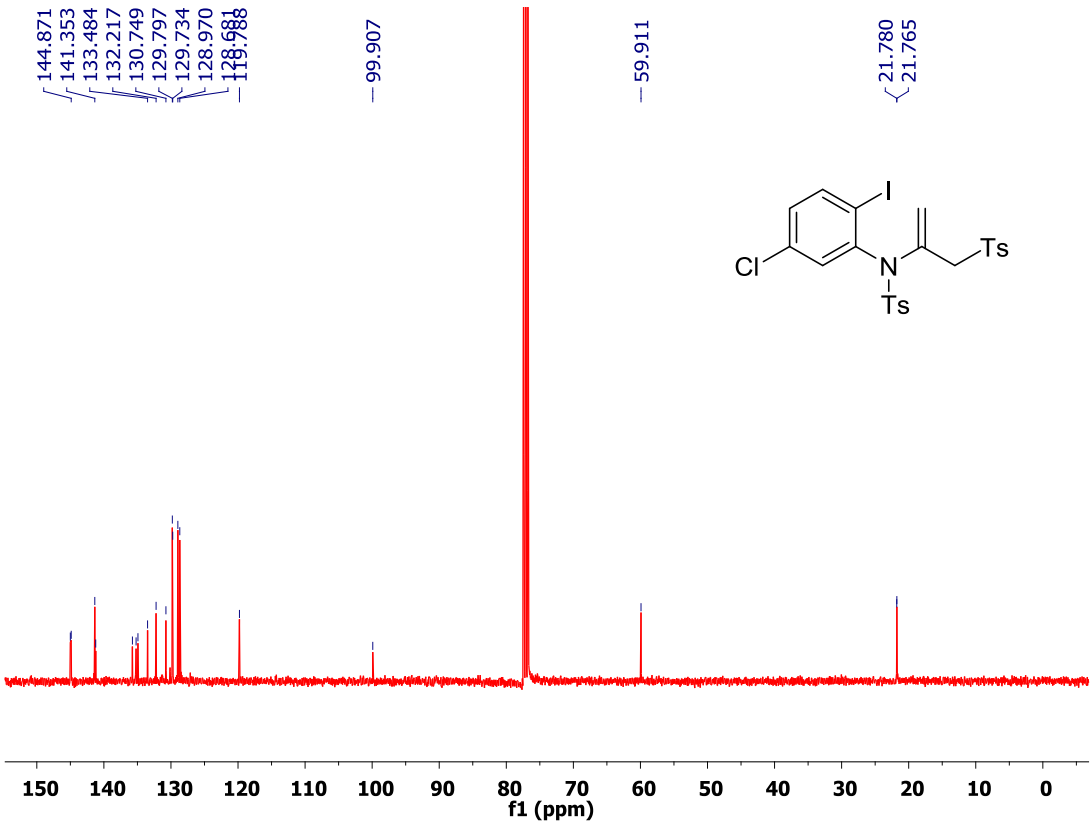
4.8. NMR spectra of new compounds [^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$)]

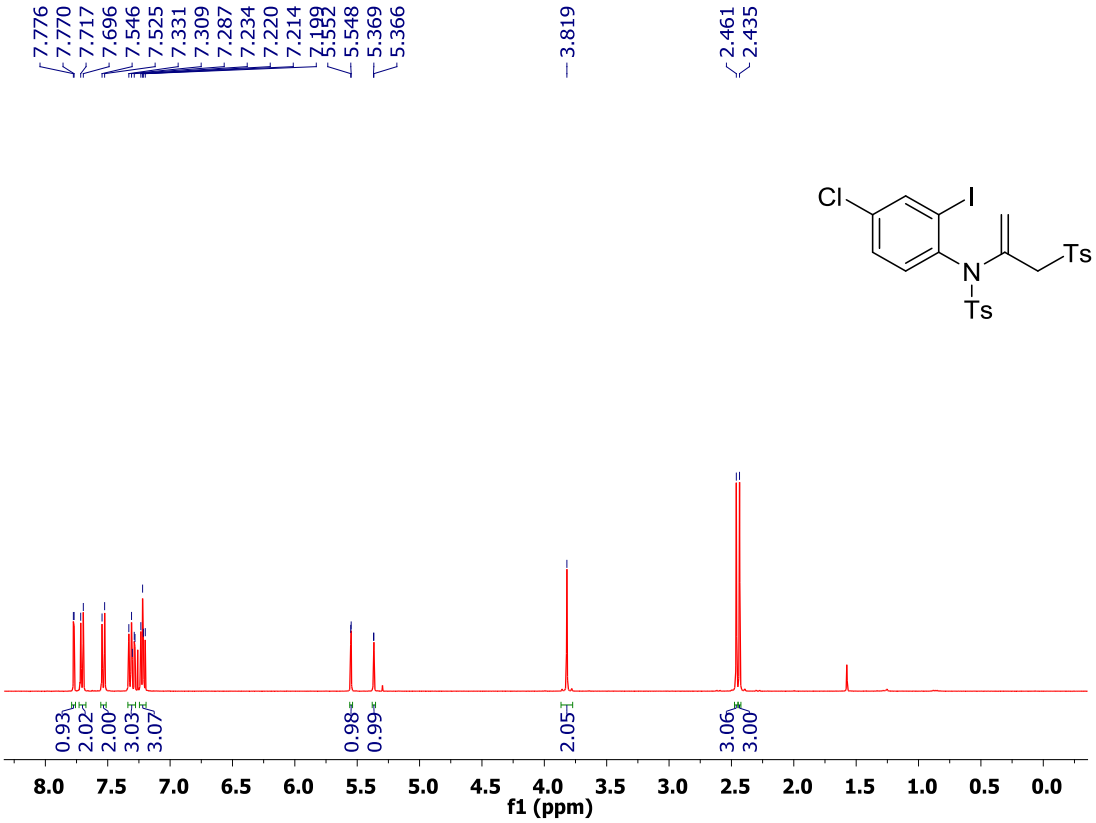


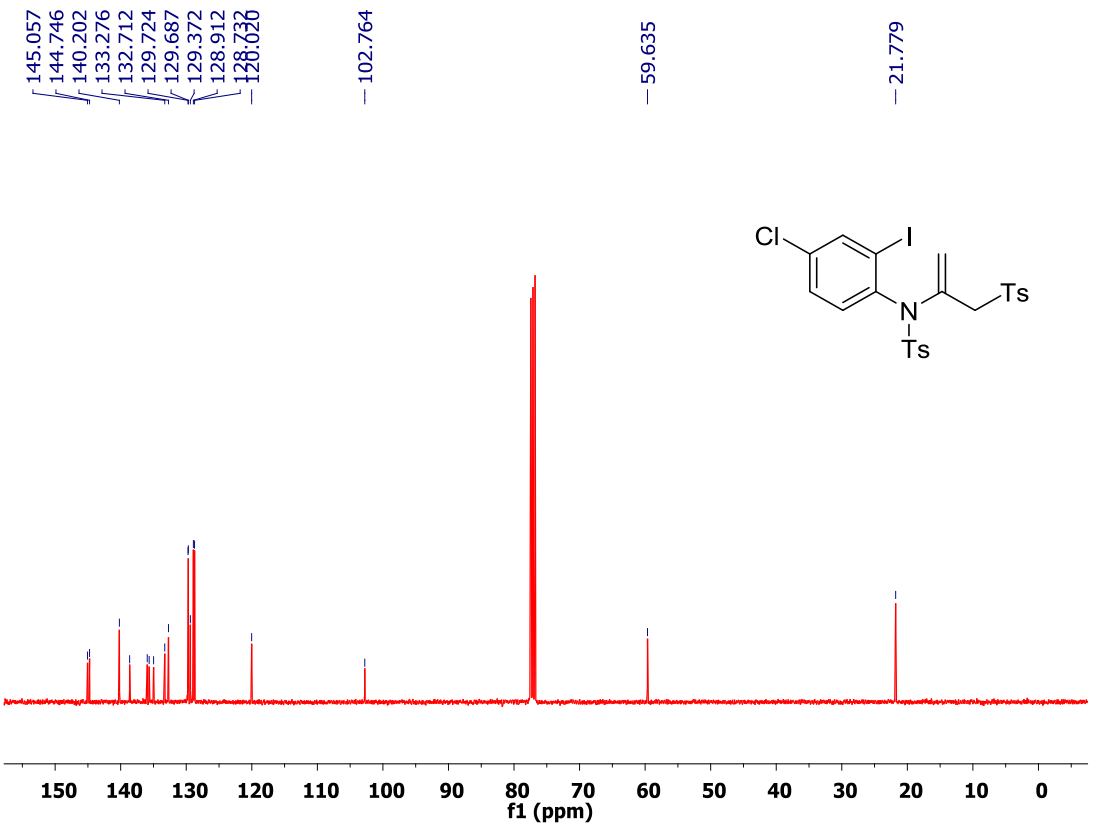

7.849
7.846
7.829
7.826
7.722
7.718
7.716
7.702
7.698
7.694
7.621
7.607
7.603
7.599
7.587
7.584
7.581
7.478
7.457
7.438
7.367
7.364
7.347
7.344
7.330
7.326
7.320
7.314
7.300
7.294
7.070
7.065
7.053
7.050
7.048
7.045
7.033
7.028
5.530
5.527
5.277
5.274
3.911
3.872
3.848
3.810
2.454
I
SO2Ph
N
Ts
0.96
4.00
1.02
2.05
4.11
1.01
1.00
1.01
2.04
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

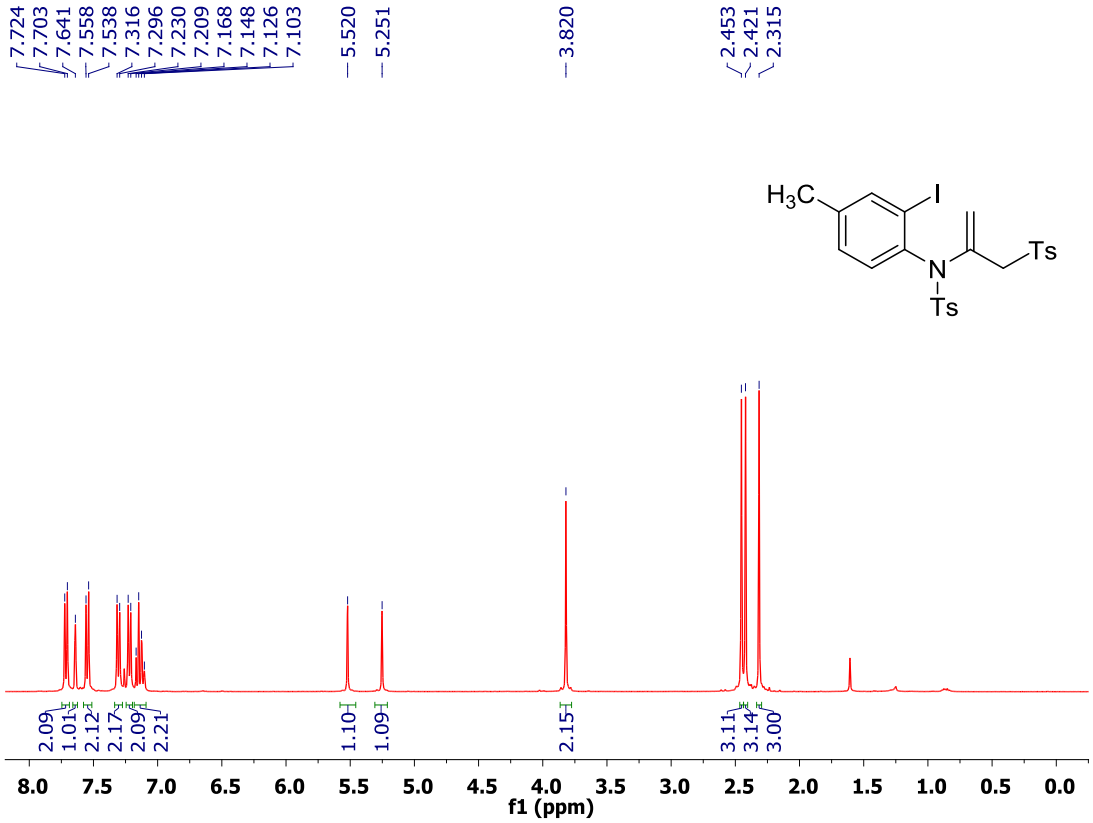

141.015
133.930
133.336
132.568
130.667
129.626
129.256
129.115
128.978
128.763
128.618
102.259
59.735
21.778
I
SO2Ph
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

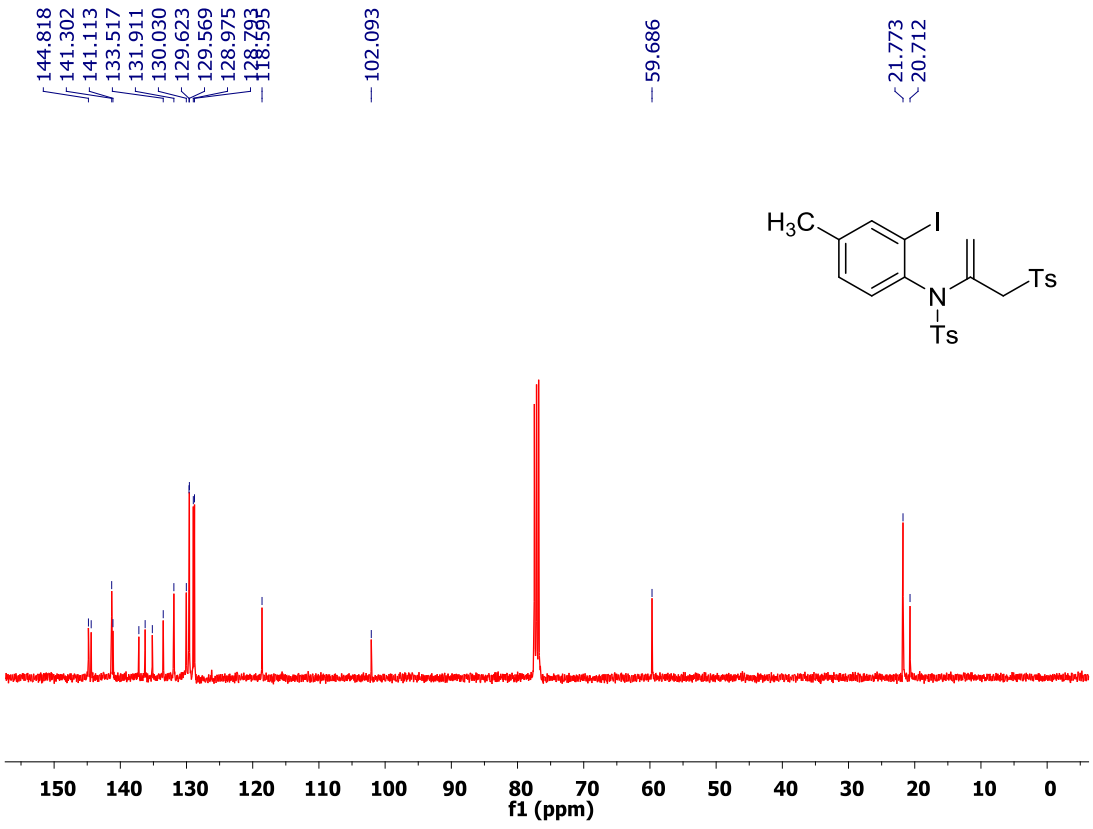

7.750
7.728
7.708
7.582
7.561
7.344
7.324
7.247
7.227
7.139
7.133
7.054
7.047
5.548
5.428
5.425
3.900
3.861
3.847
3.809
2.469
2.424
I
Cl
N
Ts
Ts
2.98
1.98
2.07
1.95
0.96
0.96
0.97
0.98
2.04
3.06
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

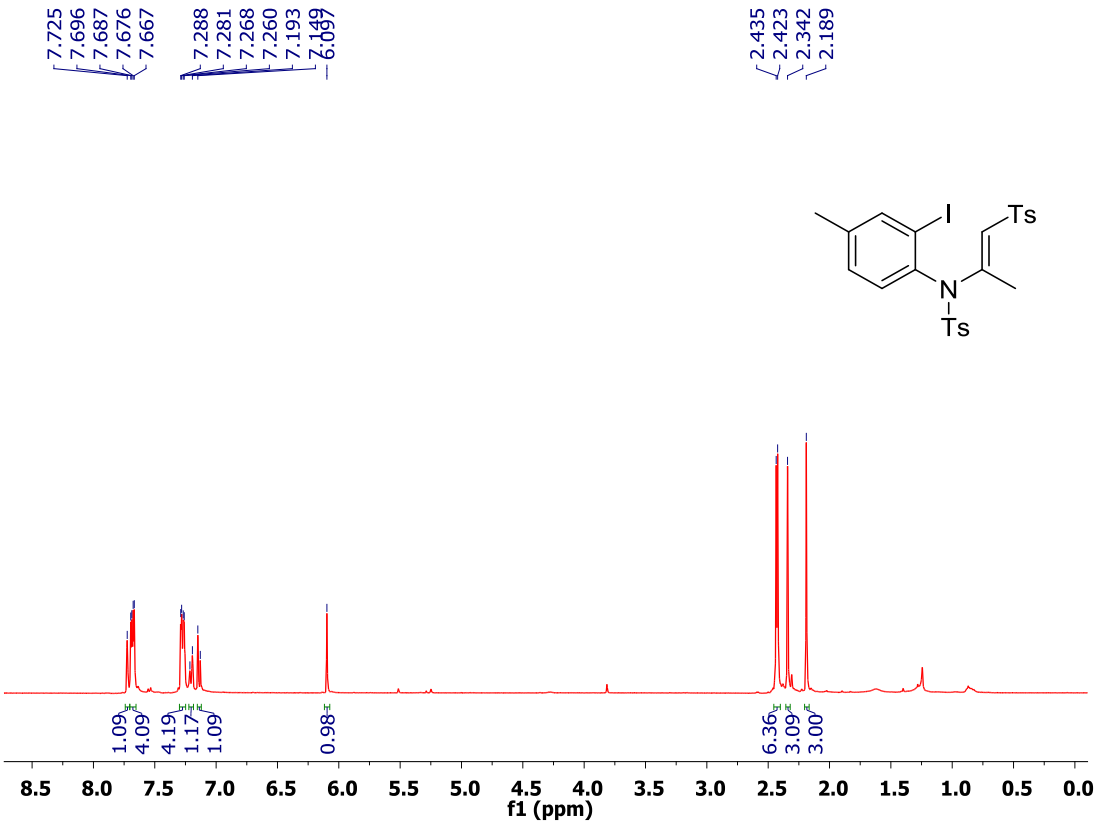

144.871
141.353
133.484
132.217
130.749
129.797
129.734
128.970
99.907
59.911
21.780
21.765
I
Cl
N
Ts
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

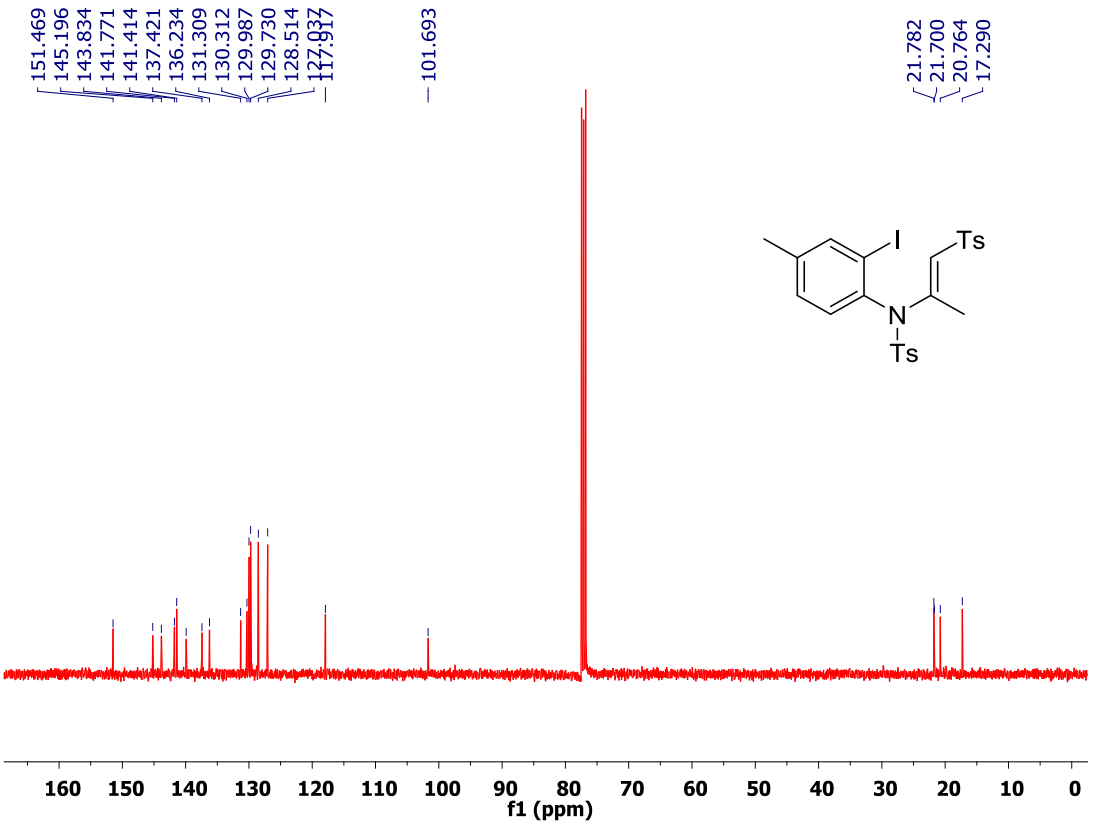

7.776
7.770
7.717
7.696
7.546
7.525
7.331
7.309
7.287
7.234
7.220
7.214
7.199
7.192
5.548
5.369
5.366
3.819
2.461
2.435
Cl
I
Ts
N
Ts
0.93
2.02
2.00
3.03
3.07
0.98
0.99
2.05
3.06
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

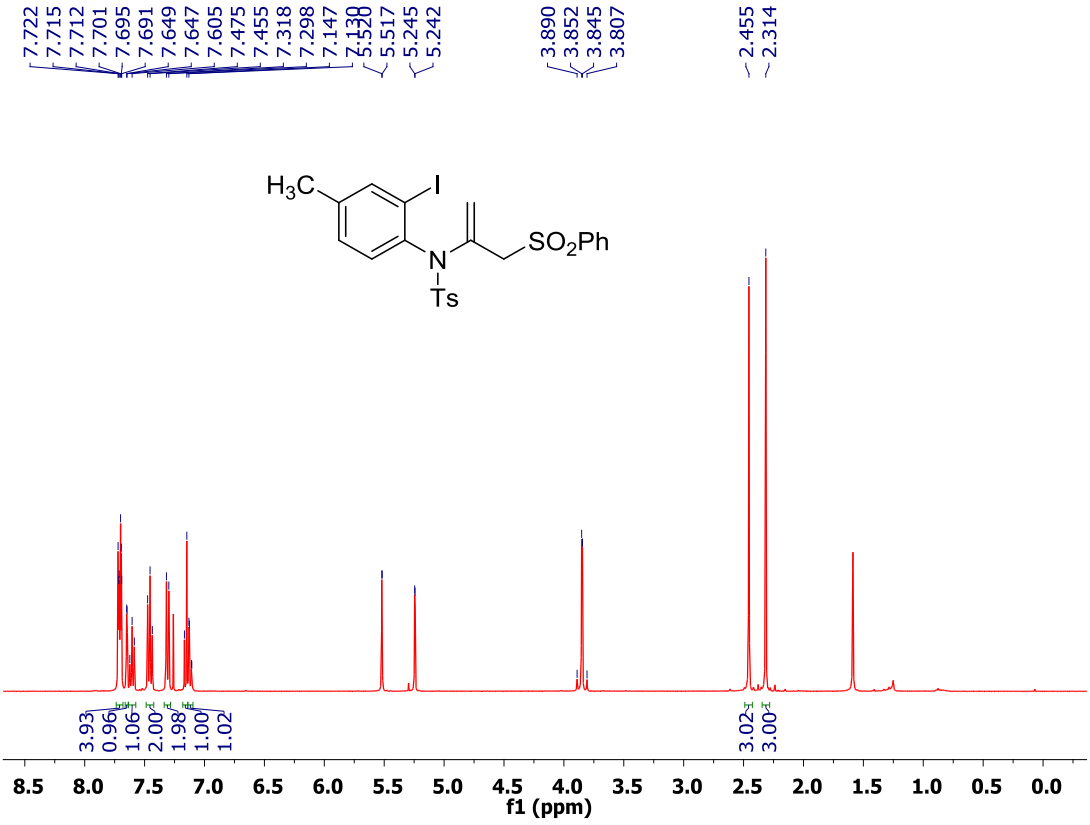

145.057
144.746
140.202
133.276
132.712
129.724
129.687
129.372
128.912
128.632
128.020
102.764
59.635
21.779
Cl
I
Ts
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

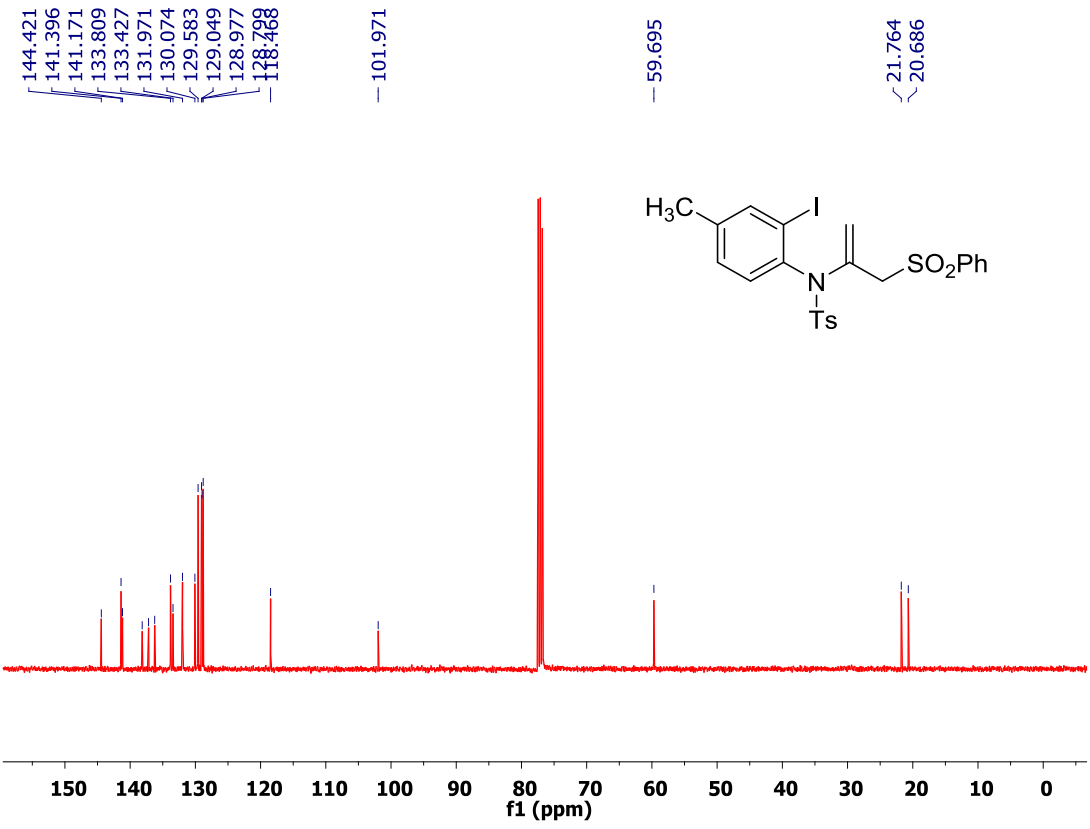

7.724
7.703
7.641
7.558
7.538
7.316
7.296
7.230
7.209
7.168
7.148
7.126
7.103
5.520
5.251
3.820
2.453
2.421
2.315
H3C
I
Ts
N
Ts
2.09
1.01
2.12
2.17
2.09
2.21
1.10
1.09
2.15
3.11
3.14
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

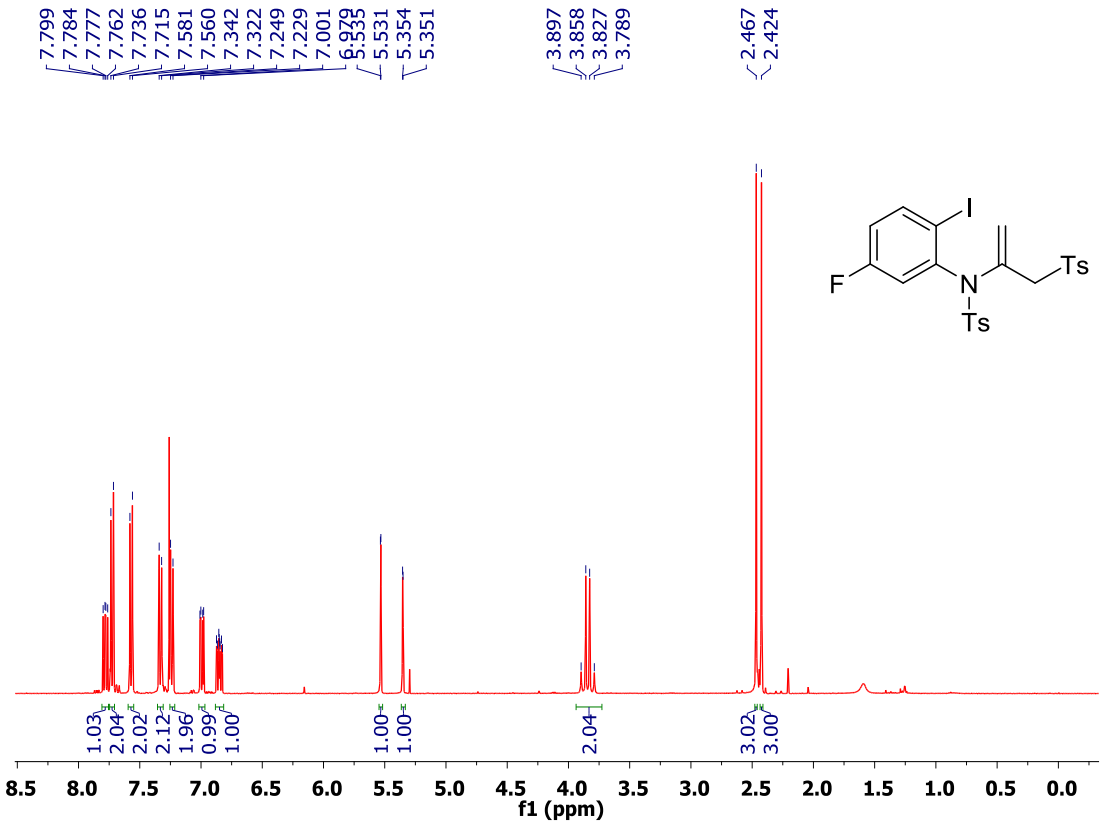

144.818
141.302
141.113
133.517
131.911
130.030
129.623
129.569
128.975
128.793
128.595
118.595
102.093
59.686
21.773
20.712
H3C
I
Ts
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

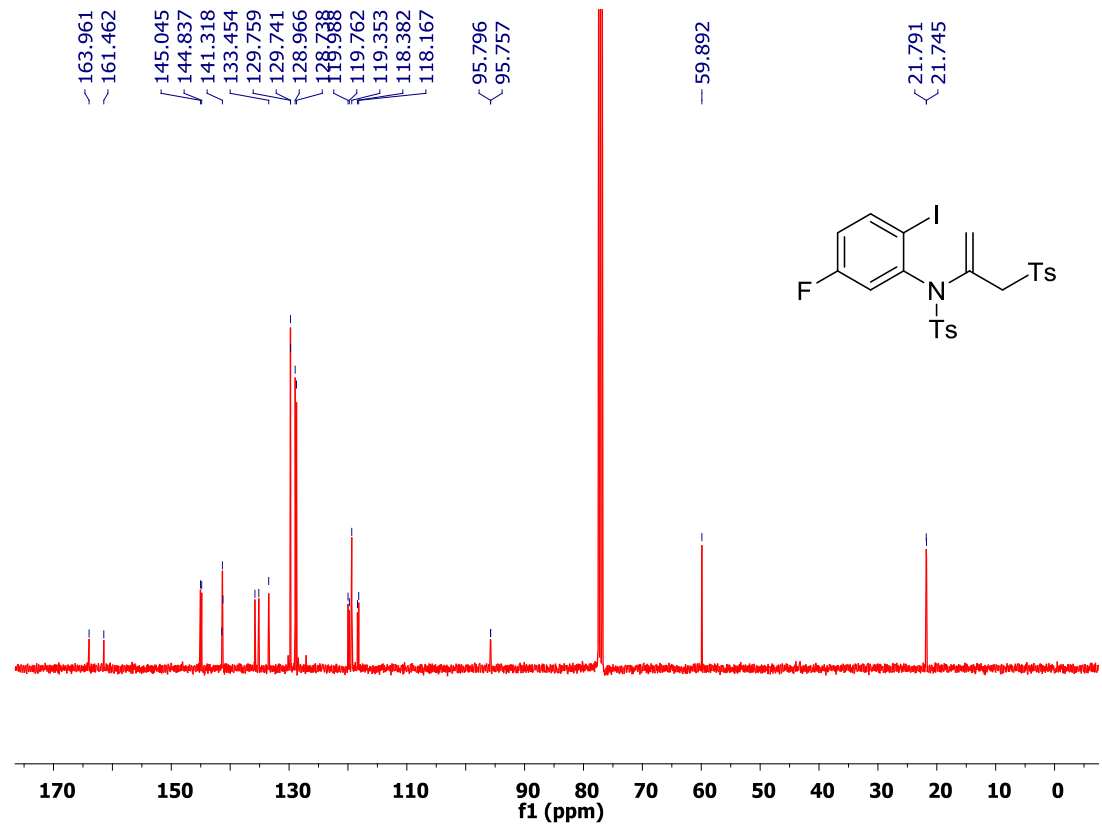

7.725
7.696
7.687
7.676
7.667
7.288
7.281
7.268
7.260
7.193
7.149
6.097
2.435
2.423
2.342
2.189
I
Ts
N
Ts
1.09
4.09
4.19
1.17
1.09
0.98
6.36
3.09
3.00
f1 (ppm)

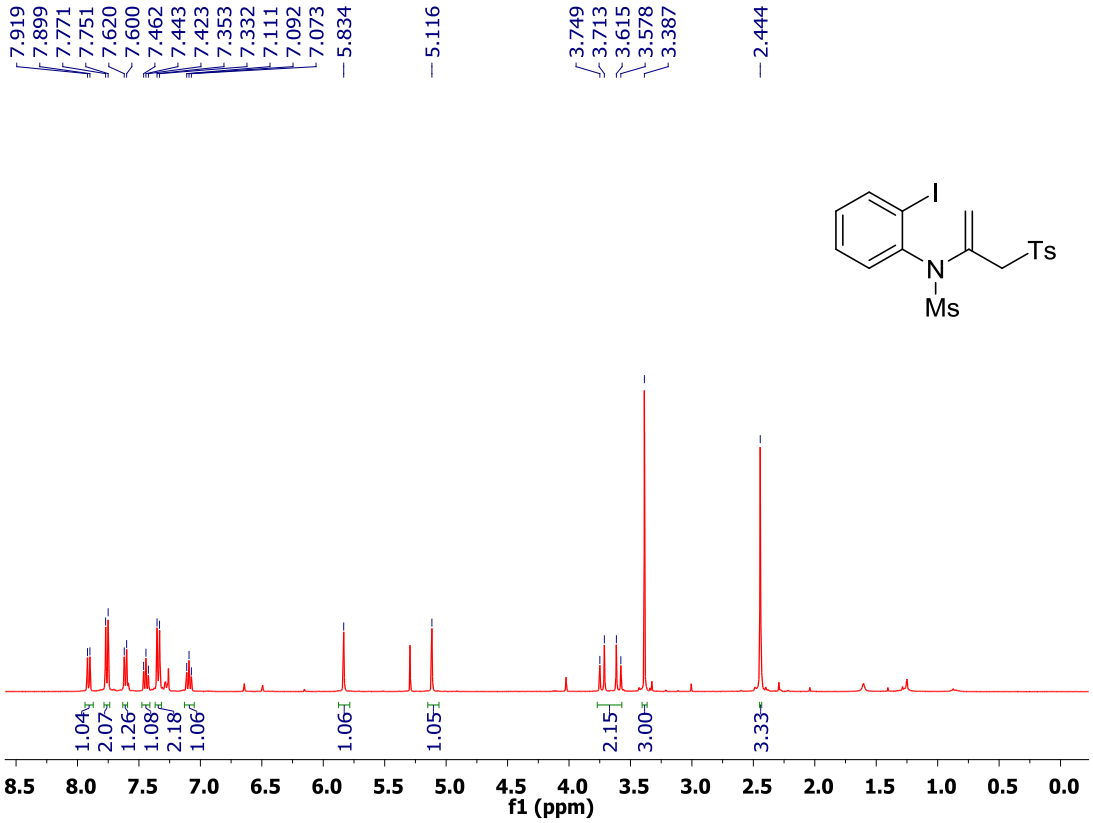

151.469
145.196
143.834
141.771
141.414
137.421
136.234
131.309
130.312
129.987
129.730
128.514
127.037
117.917
101.693
21.782
21.700
20.764
17.290
I
Ts
N
Ts
f1 (ppm)

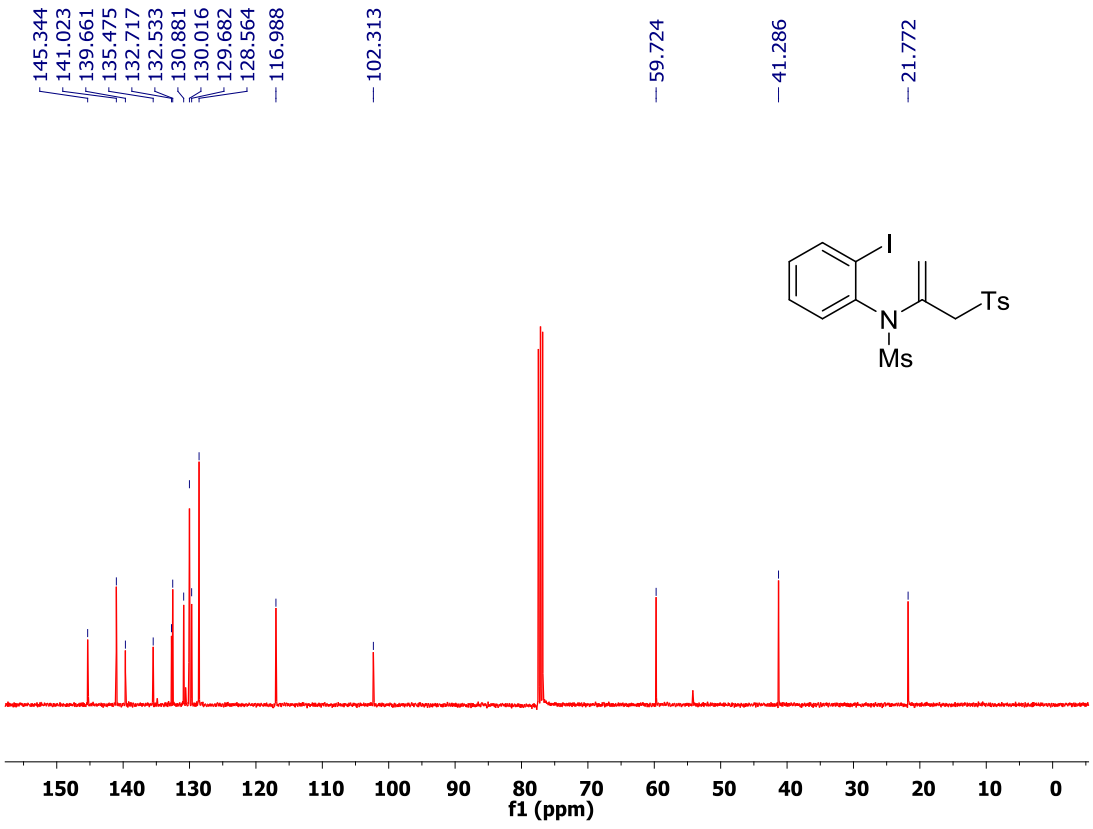

7.722
7.715
7.712
7.701
7.695
7.691
7.649
7.647
7.605
7.475
7.455
7.318
7.298
7.147
7.130
5.520
5.517
5.245
5.242
3.890
3.852
3.845
3.807
2.455
2.314
H3C
I
SO2Ph
N
Ts
3.93
0.96
1.06
2.00
1.98
1.00
1.02
3.02
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

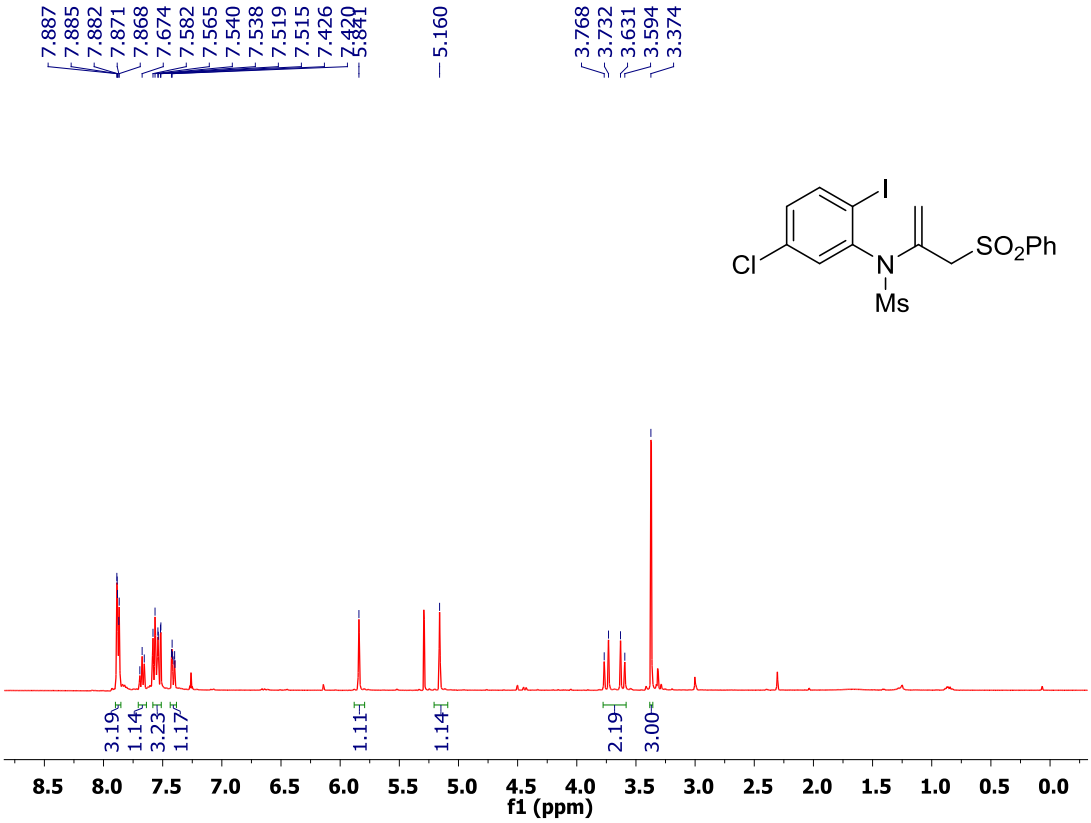

144.421
141.396
141.171
133.809
133.427
131.971
130.074
129.583
129.049
128.977
128.799
128.468
101.971
59.695
21.764
20.686
H3C
I
SO2Ph
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

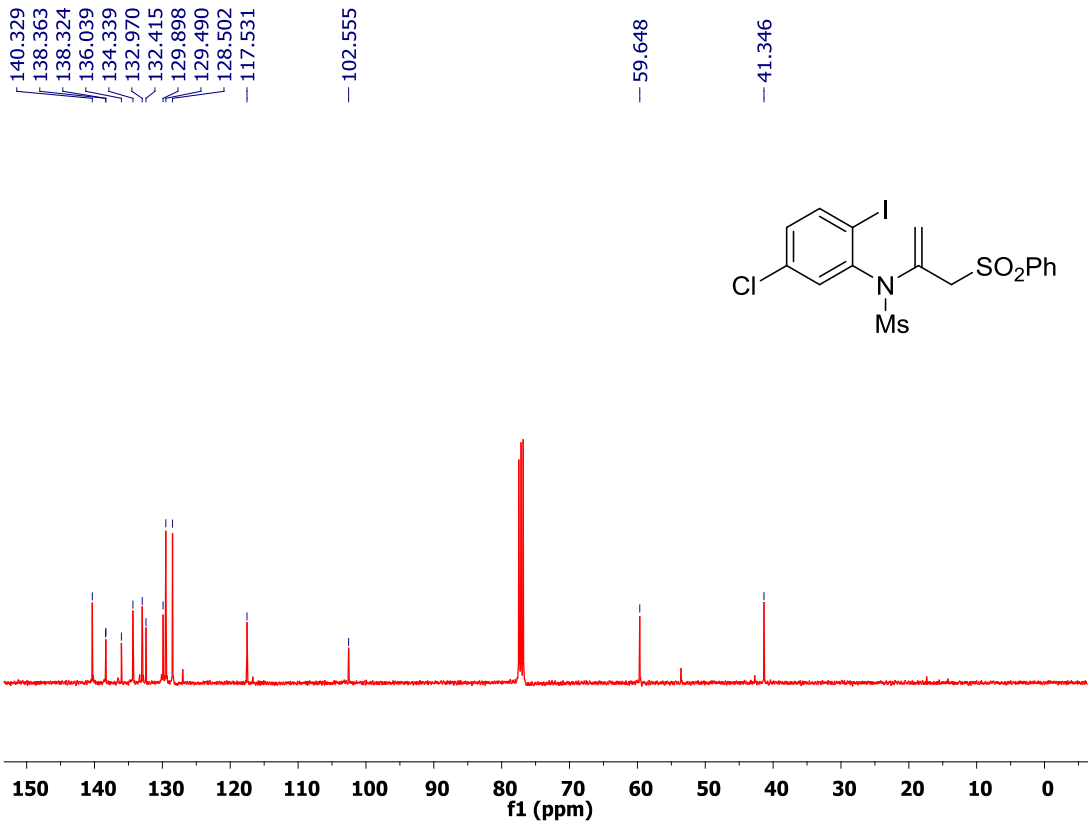

7.799
7.784
7.777
7.762
7.736
7.715
7.581
7.560
7.342
7.322
7.249
7.229
7.001
6.979
6.935
5.531
5.354
5.351
3.897
3.858
3.827
3.789
2.467
2.424
I
F
N
Ts
Ts
1.03
2.04
2.02
2.12
1.96
0.99
1.00
1.00
1.00
2.04
3.02
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


163.961
161.462
145.045
144.837
141.318
133.454
129.759
129.741
128.966
119.762
119.353
118.382
118.167
95.796
95.757
59.892
21.791
21.745
I
F
N
Ts
Ts
170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

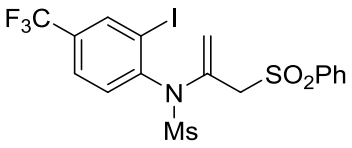

7.919
7.899
7.771
7.751
7.620
7.600
7.462
7.443
7.423
7.353
7.332
7.111
7.092
7.073
5.834
5.116
3.749
3.713
3.615
3.578
3.387
2.444
I
Ts
N
Ms
1.04
2.07
1.26
1.08
2.18
1.06
1.06
1.05
2.15
3.00
3.33
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

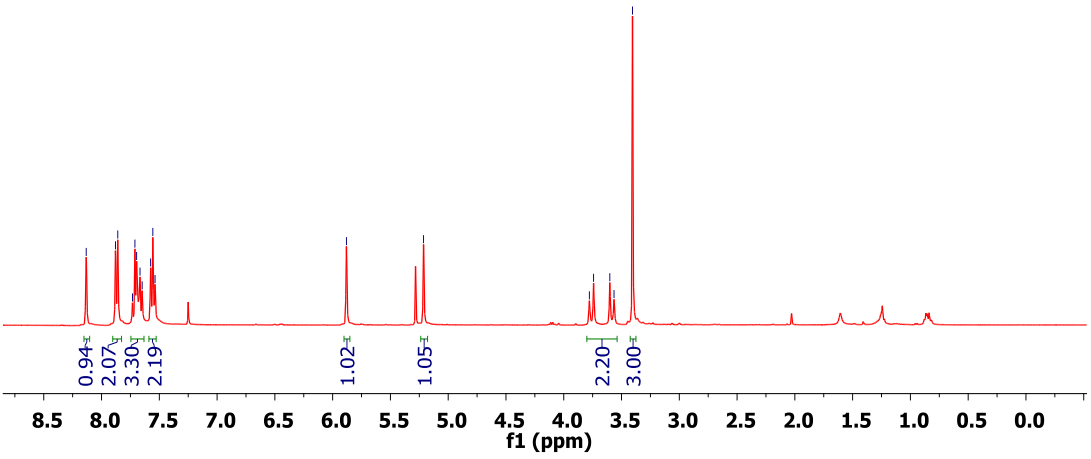

145.344
141.023
139.661
135.475
132.717
132.533
130.881
130.016
129.682
128.564
116.988
102.313
59.724
41.286
21.772
I
Ts
N
Ms
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.887
7.885
7.882
7.871
7.868
7.674
7.582
7.565
7.540
7.538
7.519
7.515
7.426
7.420
7.411
5.160
3.768
3.732
3.631
3.594
3.374
I
Cl
N
Ms
SO2Ph
3.19
1.14
3.23
1.17
1.11
1.14
2.19
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

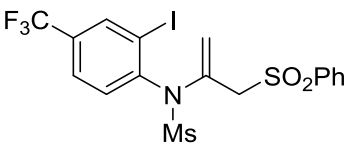

140.329
138.363
138.324
136.039
134.339
132.970
132.415
129.898
129.490
128.502
117.531
102.555
59.648
41.346
I
Cl
N
Ms
SO2Ph
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

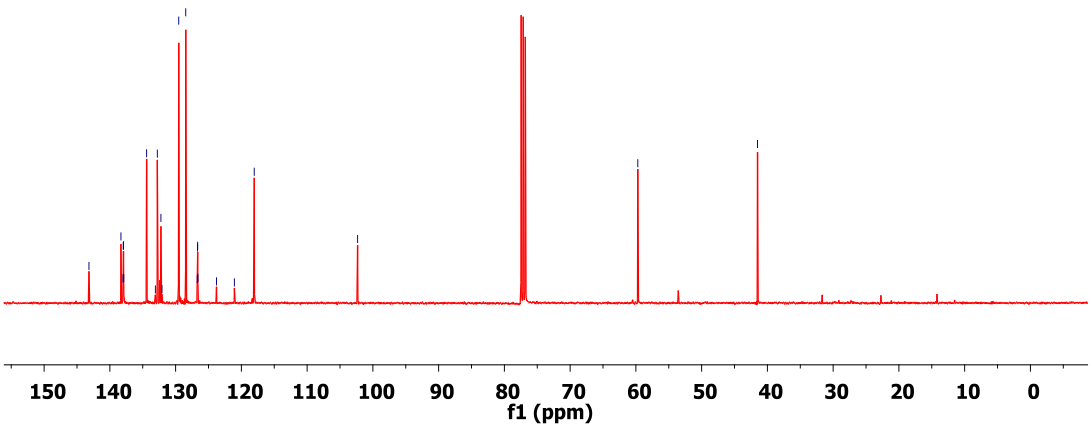

8.133
7.879
7.860
7.732
7.711
7.696
7.667
7.648
7.575
7.556
7.537
5.881
5.213
3.778
3.742
3.601
3.565
3.405

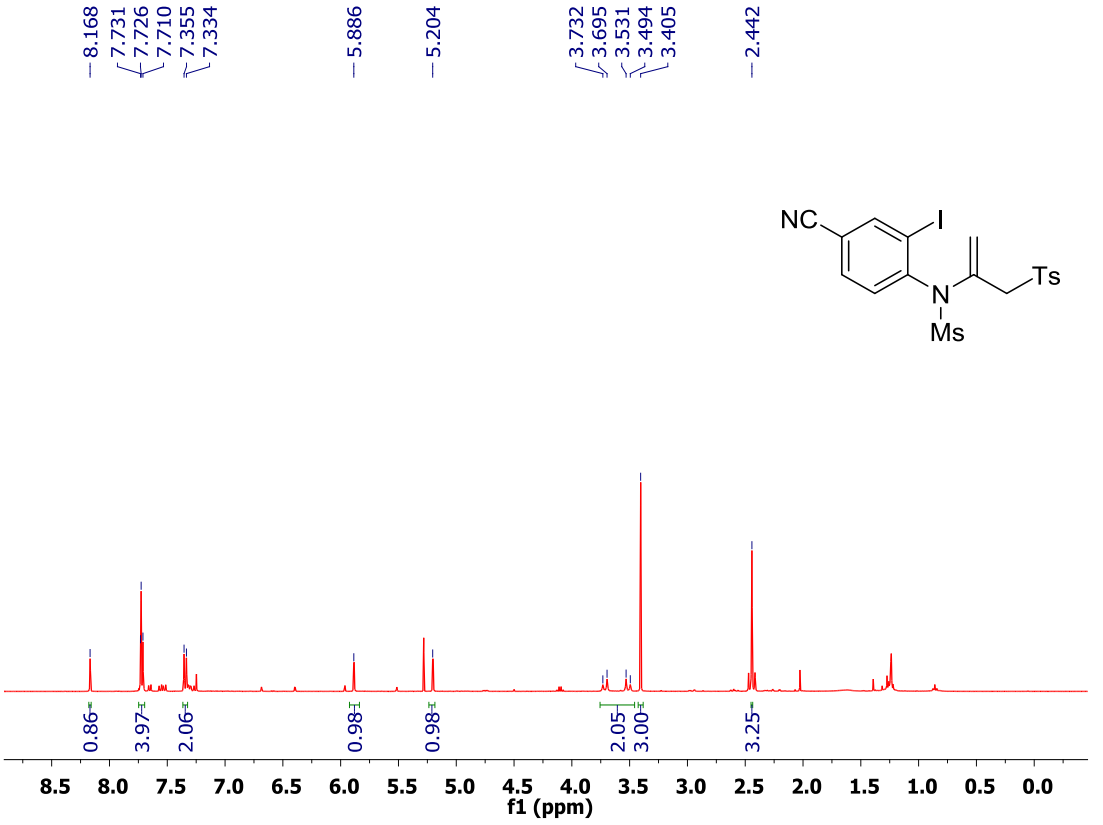

F3C
I
SO2Ph
N
Ms

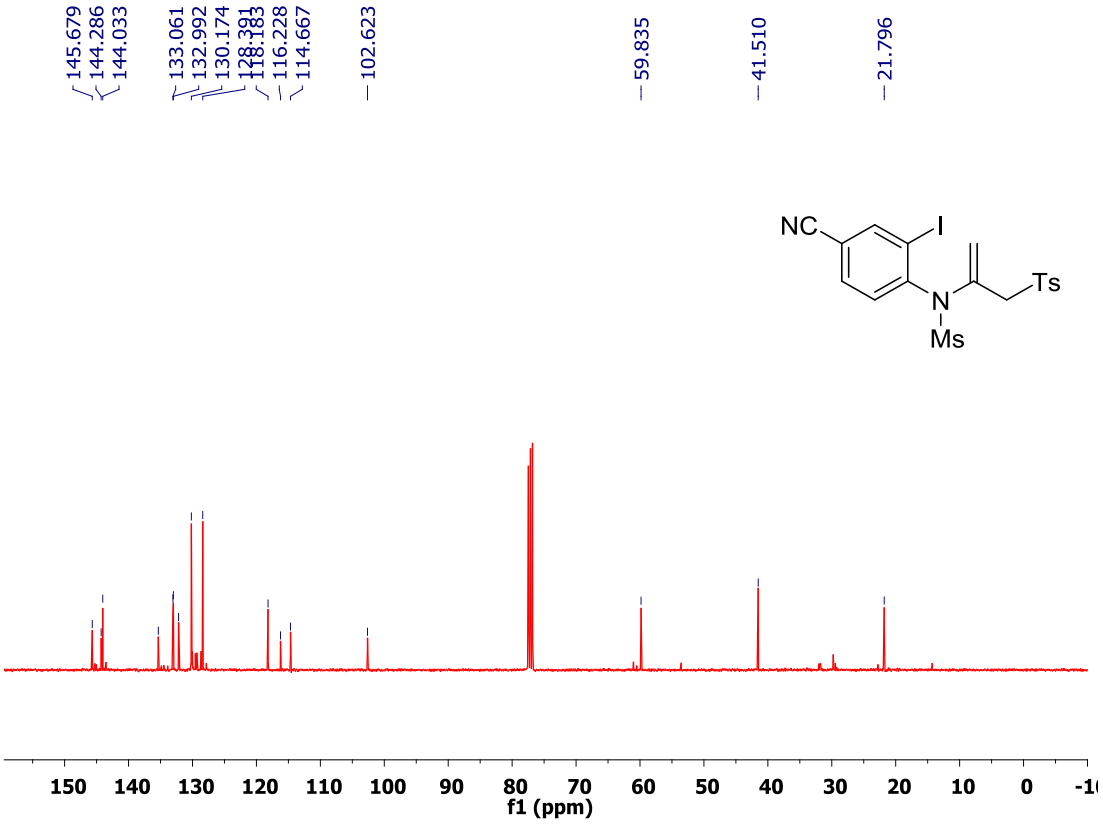

0.94
2.07
3.30
2.19
1.02
1.05
2.20
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

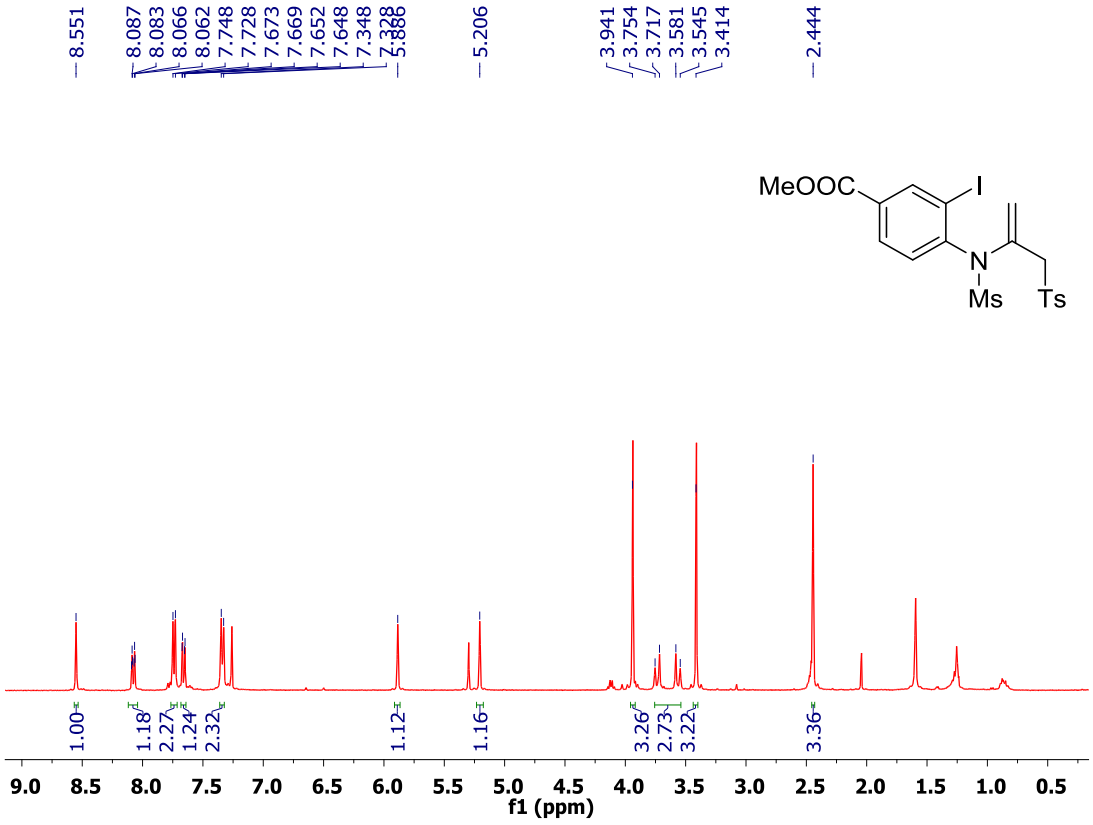

143.178
138.315
137.964
137.926
137.889
134.409
132.780
132.235
129.524
128.460
126.677
126.643
126.609
118.041
102.322
59.709
41.502

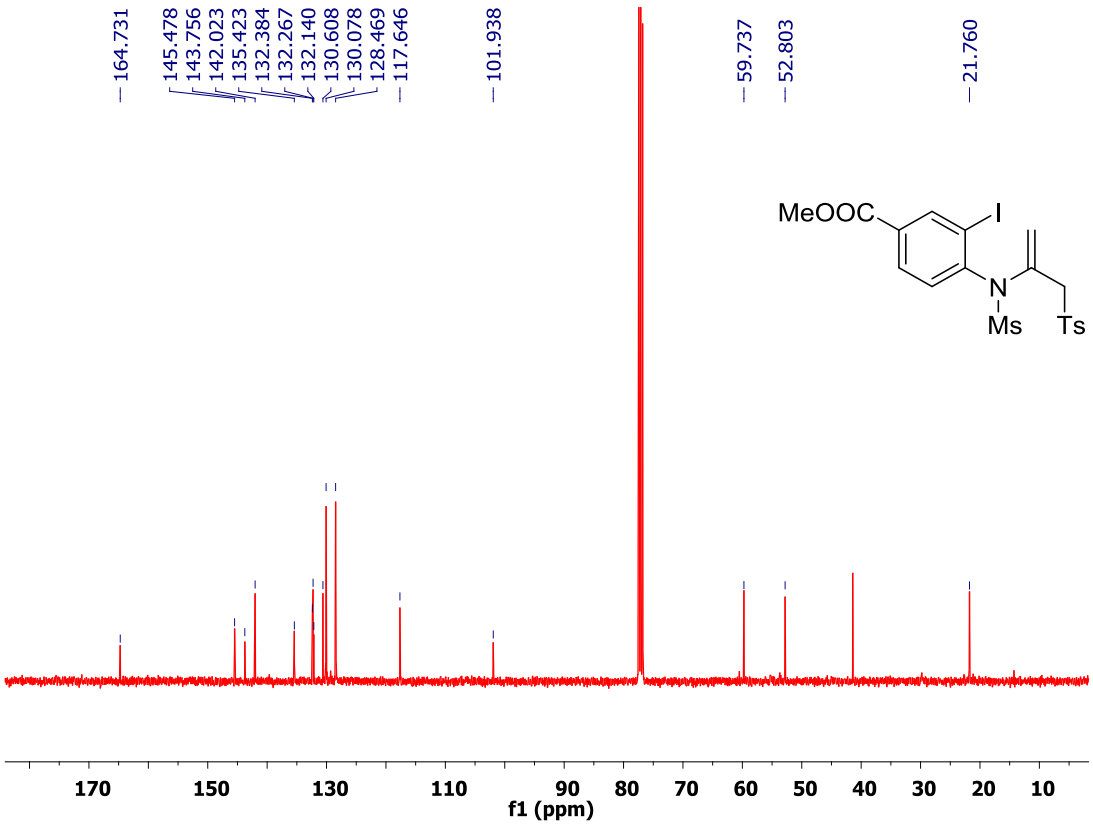

F3C
I
SO2Ph
N
Ms

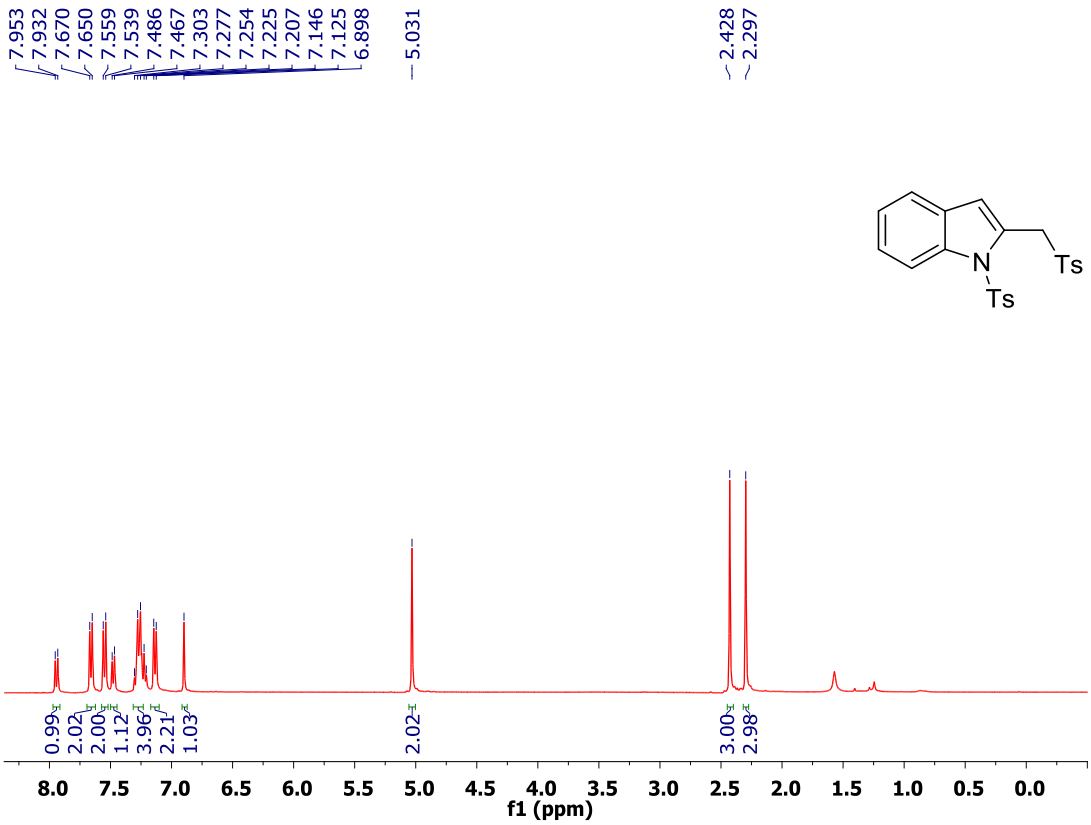

150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

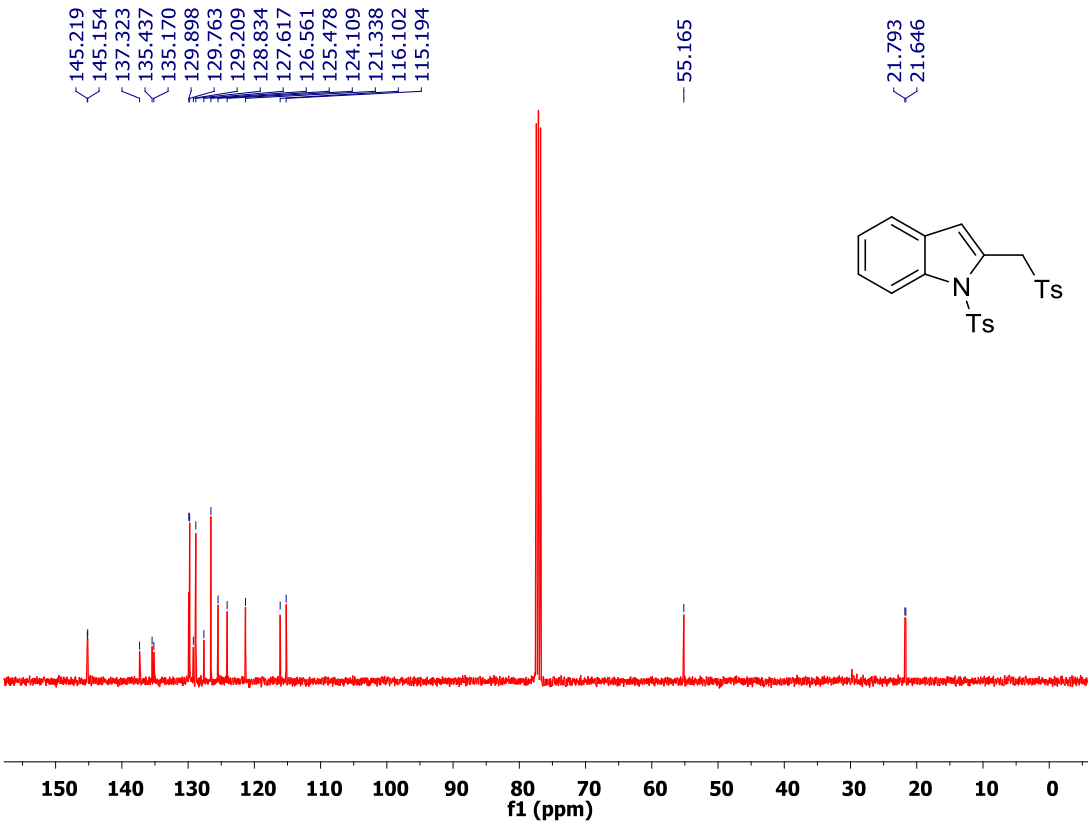

8.168
7.731
7.726
7.710
7.355
7.334
5.886
5.204
3.732
3.695
3.531
3.494
3.405
2.442
NC
I
Ts
N
Ms
0.86
3.97
2.06
0.98
0.98
2.05
3.00
3.25
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


145.679
144.286
144.033
133.061
132.992
130.174
128.391
118.183
116.228
114.667
102.623
59.835
41.510
21.796
NC
I
Ts
N
Ms
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

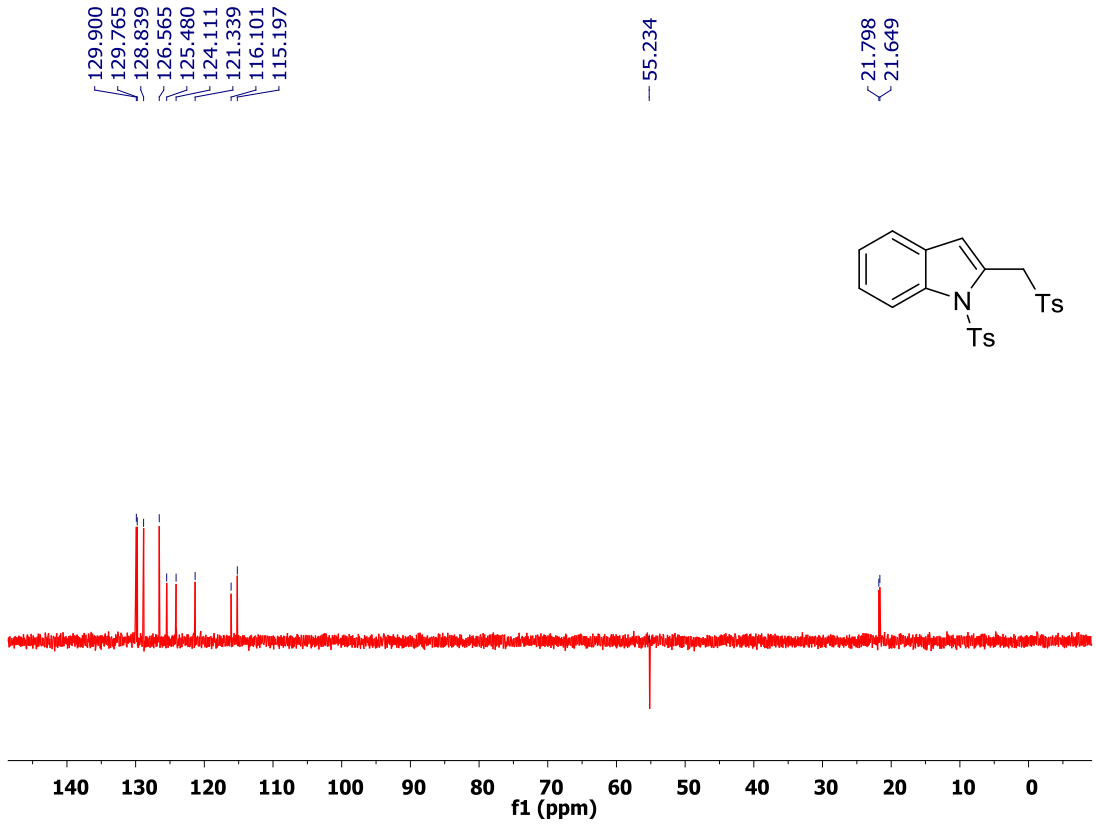

8.551
8.087
8.083
8.066
8.062
7.748
7.728
7.673
7.669
7.652
7.648
7.348
5.206
3.941
3.754
3.717
3.581
3.545
3.414
2.444
MeOOC
I
N
Ms
Ts
1.00
1.18
2.27
1.24
2.32
1.12
1.16
3.26
2.73
3.22
3.36
f1 (ppm)

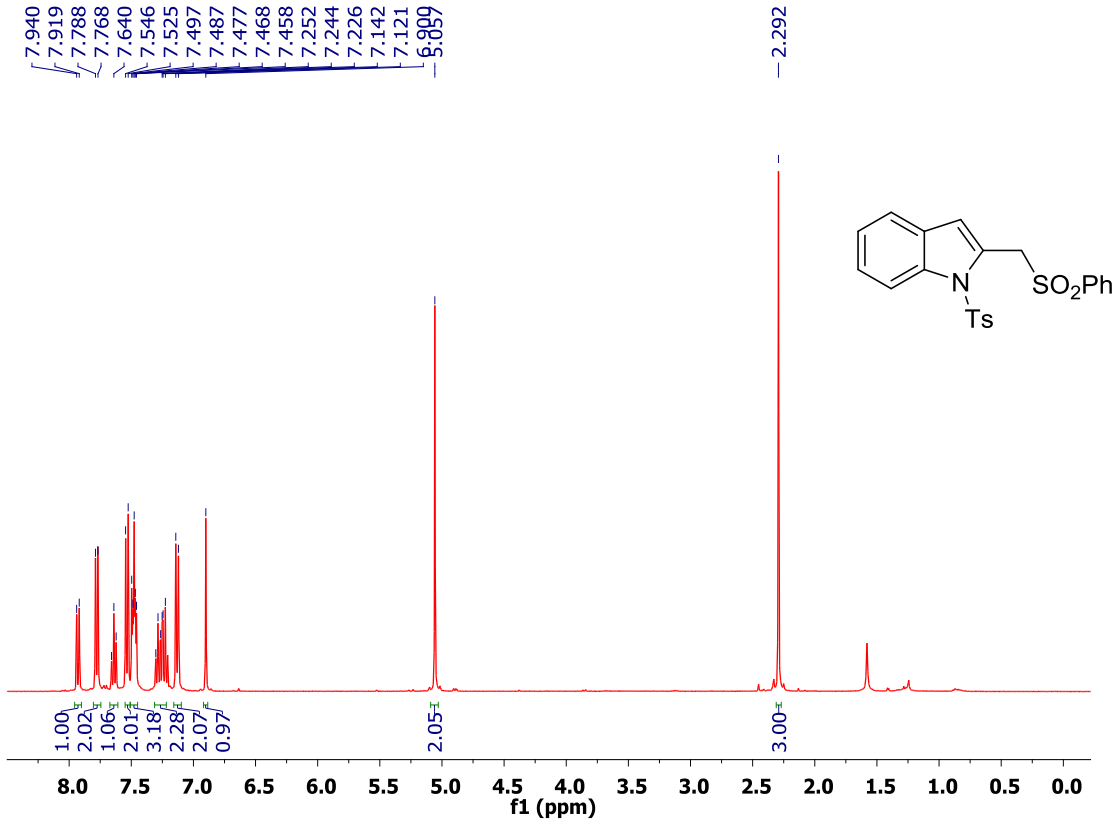

164.731
145.478
143.756
142.023
135.423
132.384
132.267
132.140
130.608
130.078
128.469
117.646
101.938
59.737
52.803
21.760
MeOOC
I
N
Ms
Ts
f1 (ppm)

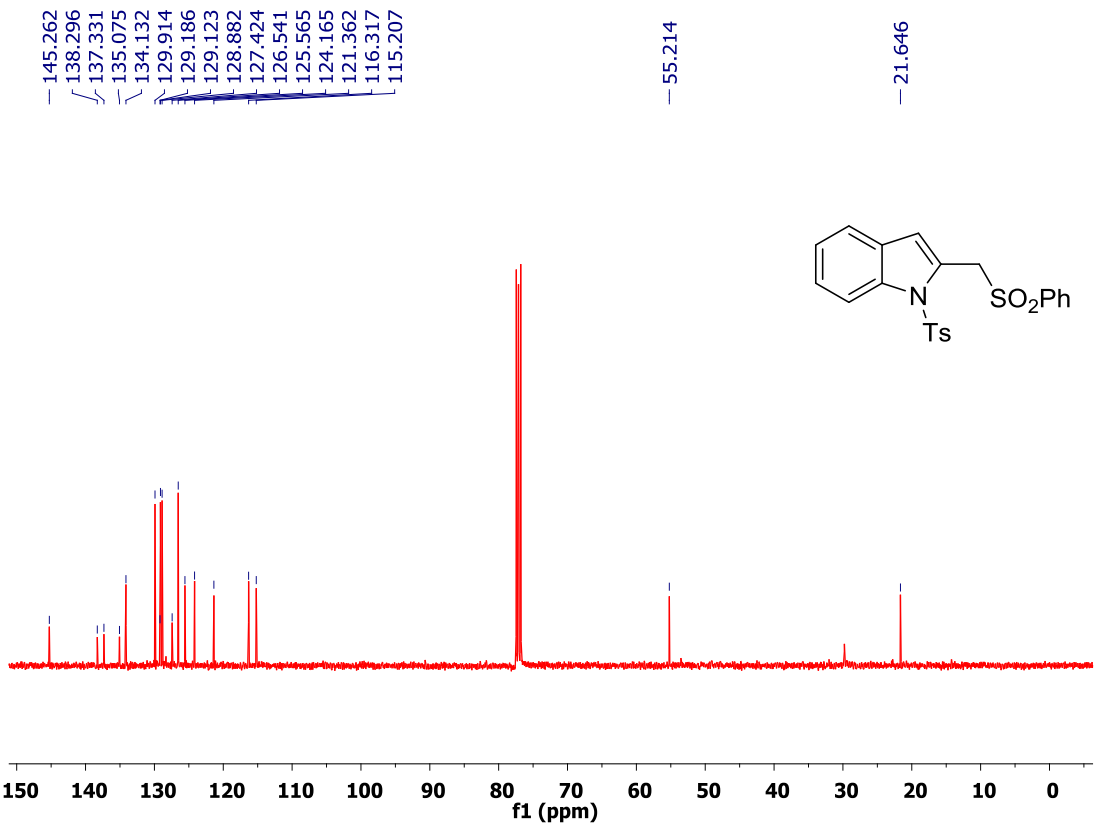

7.953
7.932
7.670
7.650
7.559
7.539
7.486
7.467
7.303
7.277
7.254
7.225
7.207
7.146
7.125
6.898
5.031
2.428
2.297
N
Ts
Ts
0.99
2.02
2.00
1.12
3.96
2.21
1.03
2.02
3.00
2.98
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

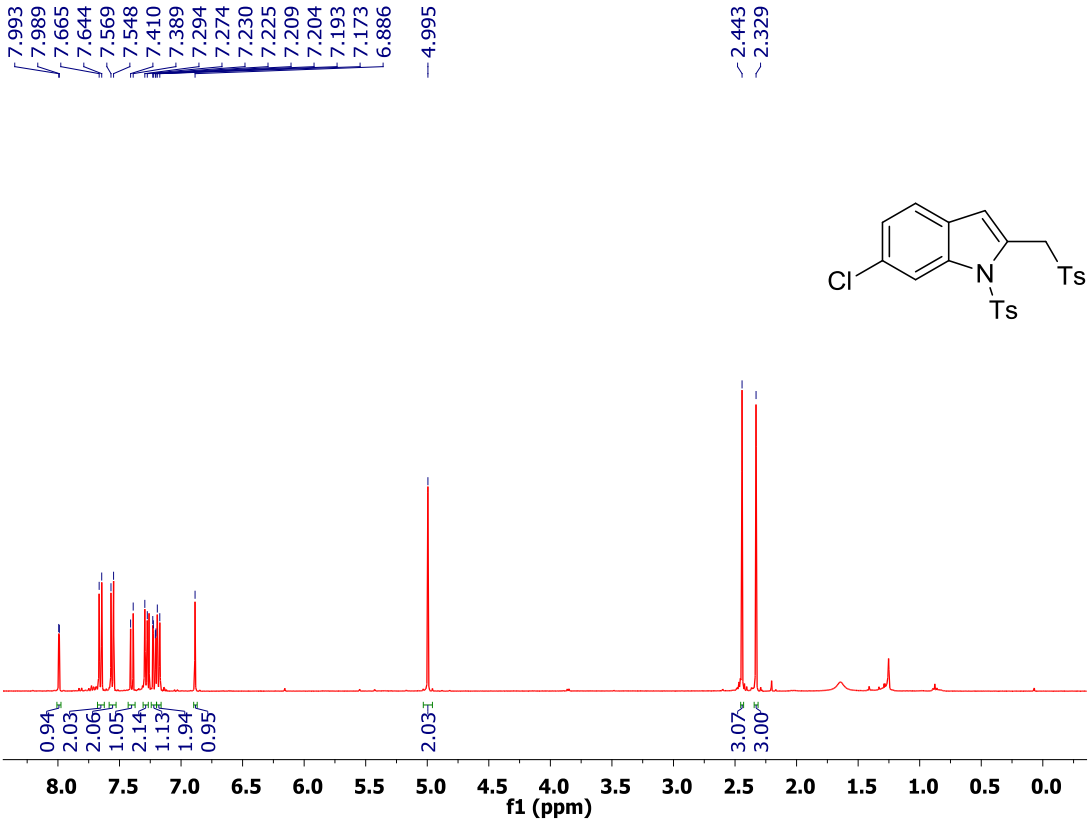

145.219
145.154
137.323
135.437
135.170
129.898
129.763
129.209
128.834
127.617
126.561
125.478
124.109
121.338
116.102
115.194
55.165
21.793
21.646
N
Ts
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

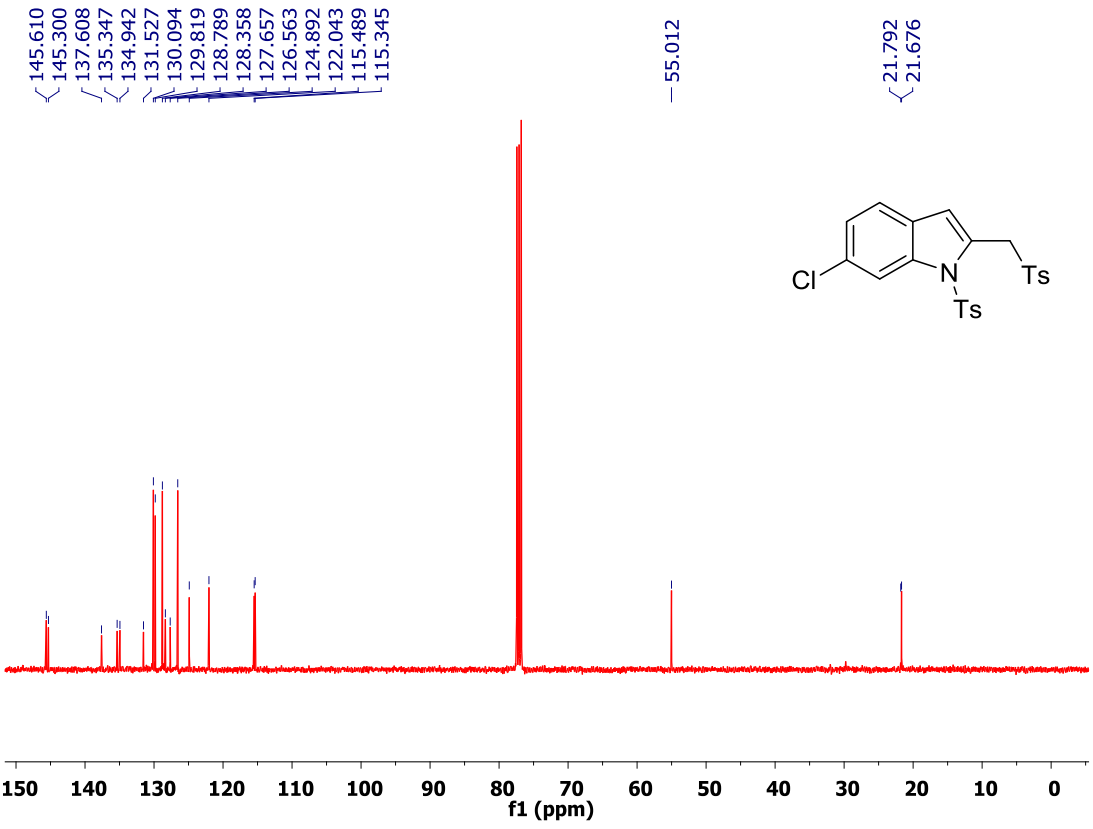
DEPT-135

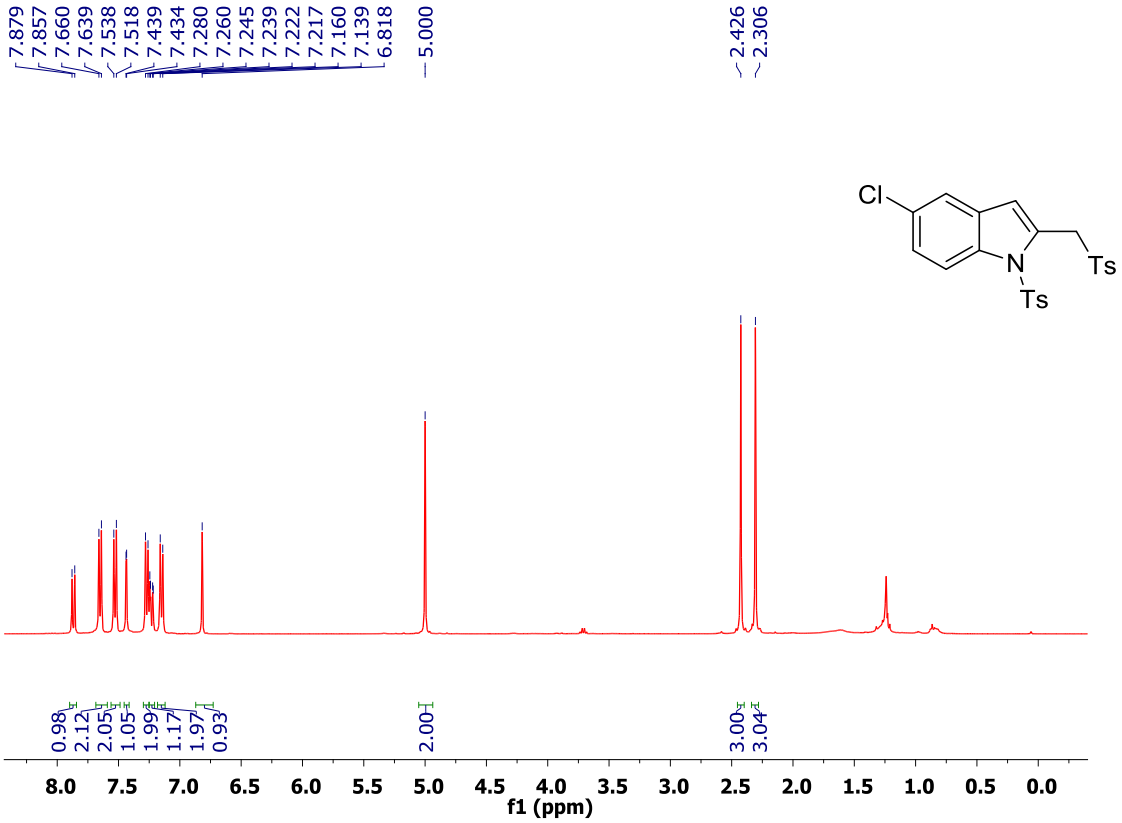

129.900
129.765
128.839
126.565
125.480
124.111
121.339
116.101
115.197
55.234
21.798
21.649
N
Ts
Ts
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

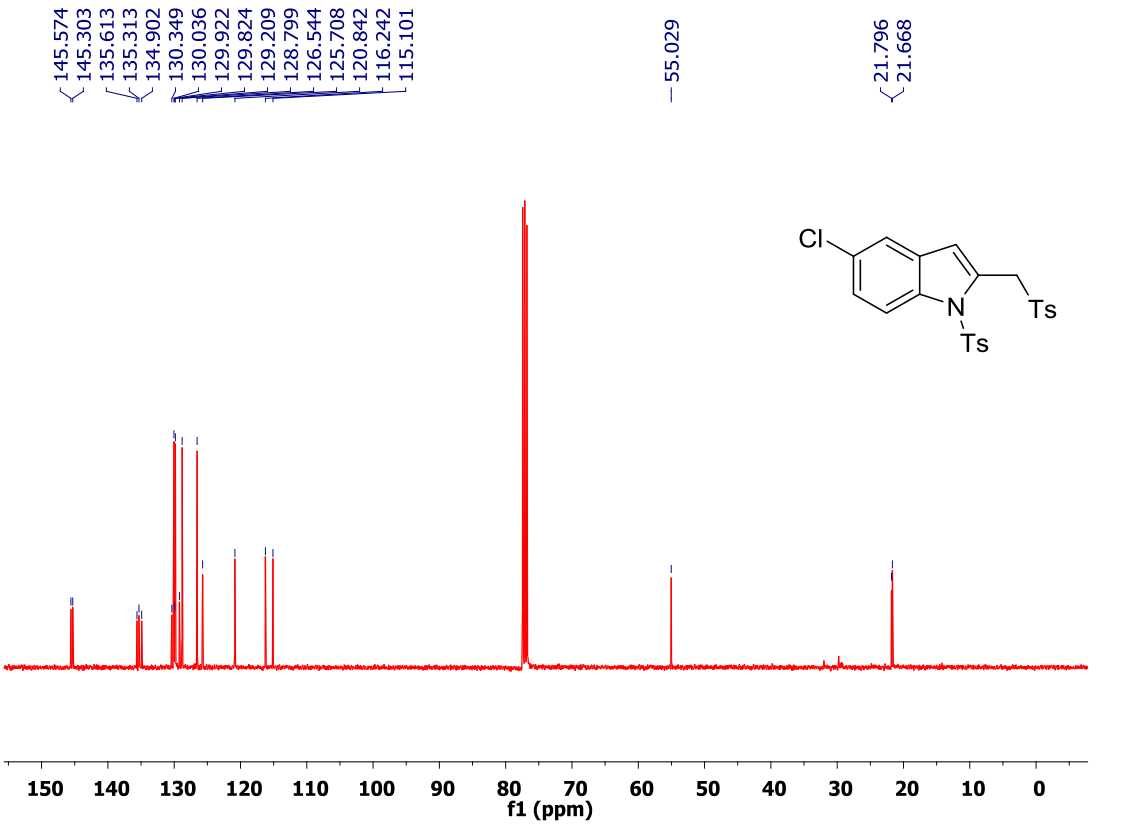

7.940
7.919
7.788
7.768
7.640
7.546
7.525
7.497
7.487
7.477
7.468
7.458
7.252
7.244
7.226
7.142
7.121
6.899
5.057
2.292
1.00
2.02
1.06
2.01
3.18
2.28
2.07
0.97
2.05
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
N
Ts
SO2Ph

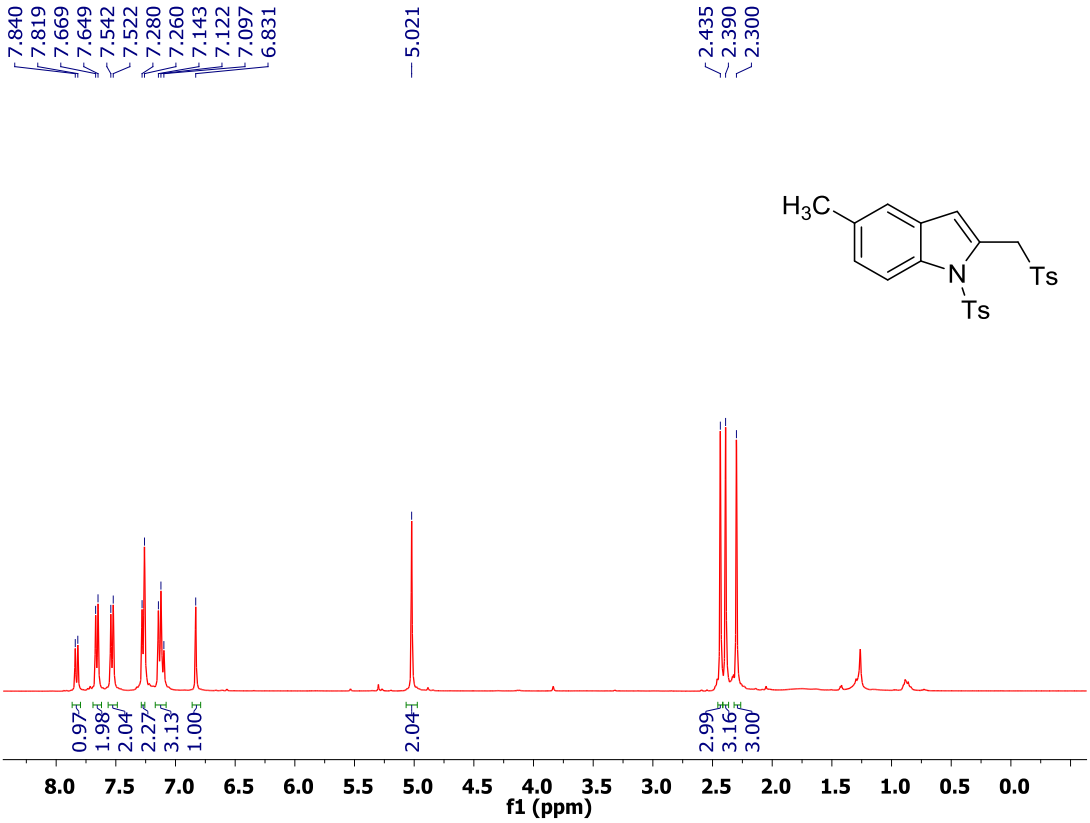

145.262
138.296
137.331
135.075
134.132
129.914
129.186
129.123
128.882
127.424
126.541
125.565
124.165
121.362
116.317
115.207
55.214
21.646
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
N
Ts
SO2Ph

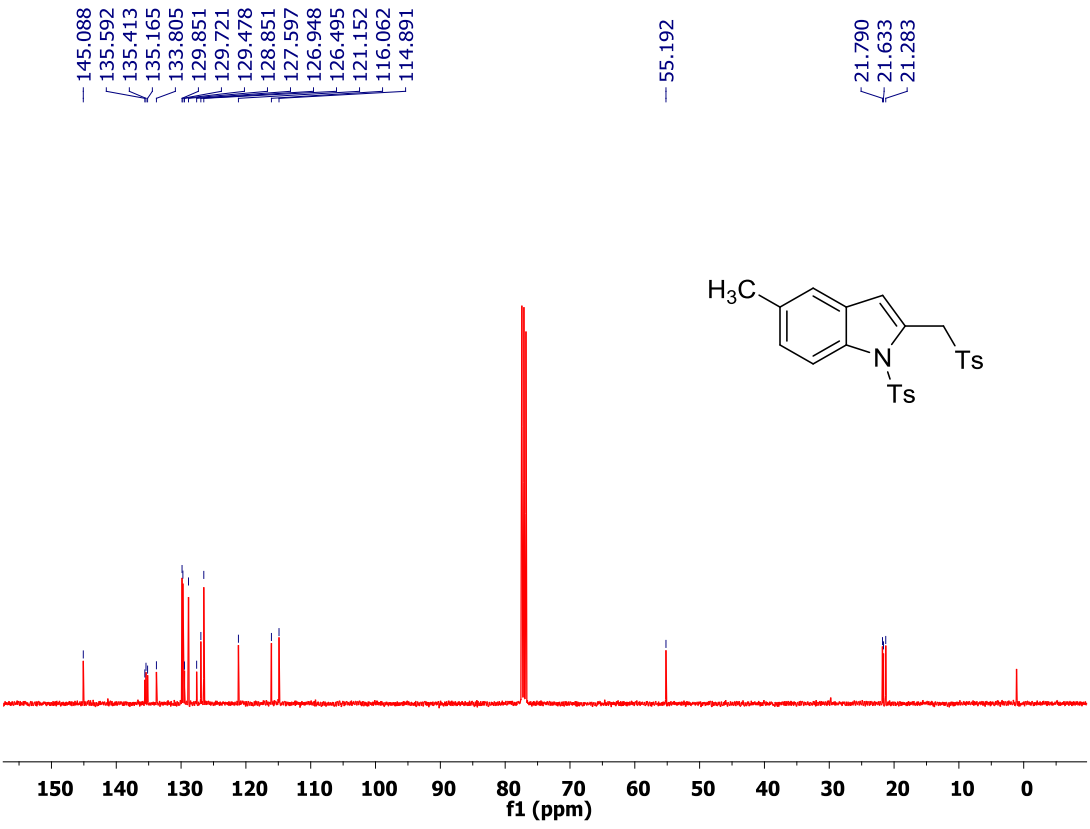

7.993
7.989
7.665
7.644
7.569
7.548
7.410
7.389
7.294
7.274
7.230
7.225
7.209
7.204
7.193
7.173
6.886
4.995
2.443
2.329
Cl
N
Ts
Ts
0.94
2.03
2.06
1.05
2.14
1.13
1.94
0.95
2.03
3.07
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

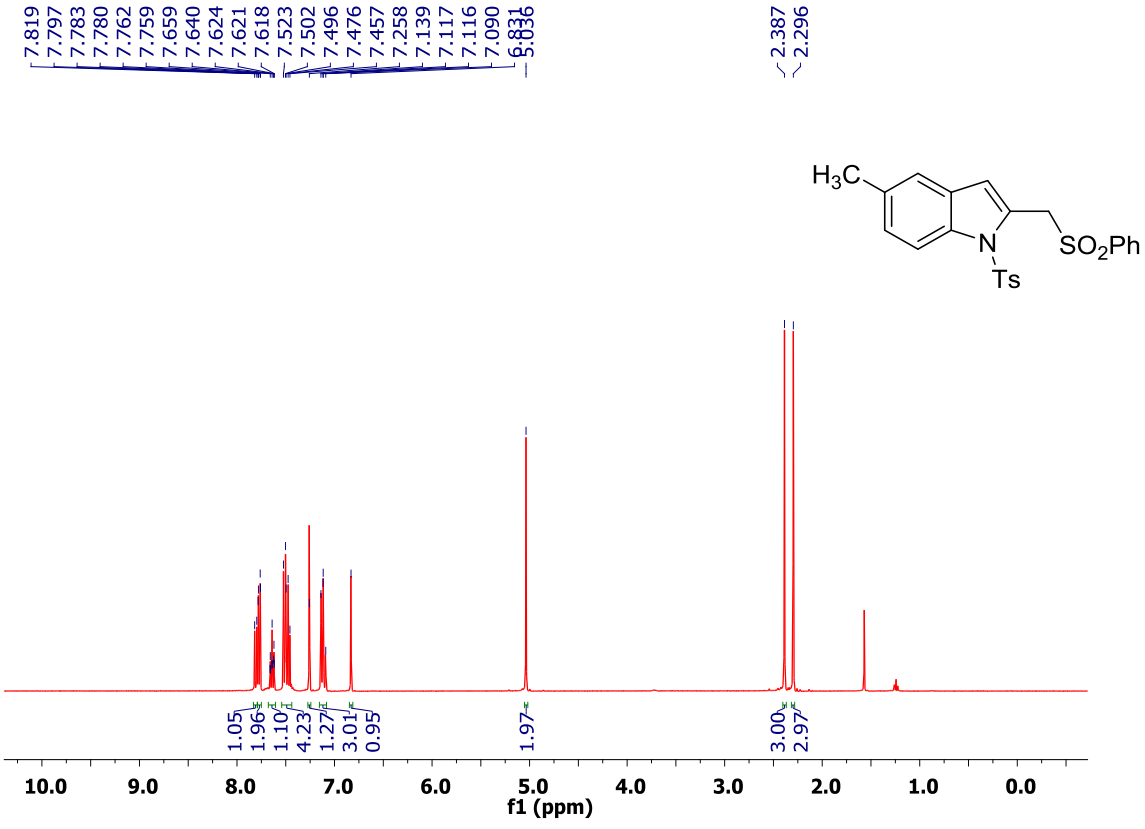

145.610
145.300
137.608
135.347
134.942
131.527
130.094
129.819
128.789
128.358
127.657
126.563
124.892
122.043
115.489
115.345
55.012
21.792
21.676
Cl
N
Ts
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

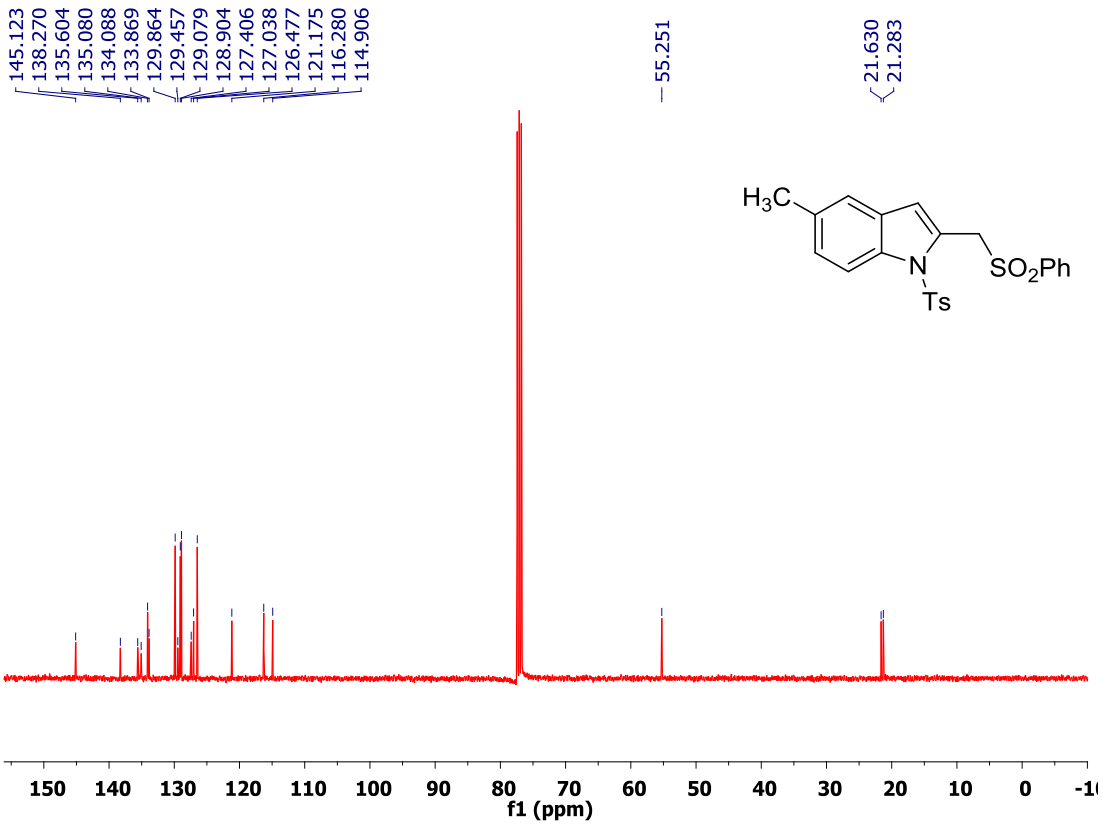

7.879
7.857
7.660
7.639
7.538
7.518
7.439
7.434
7.280
7.260
7.245
7.239
7.222
7.217
7.160
7.139
6.818
5.000
2.426
2.306
Cl
N
Ts
Ts
0.98
2.12
2.05
1.05
1.99
1.17
1.97
0.93
2.00
3.00
3.04
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

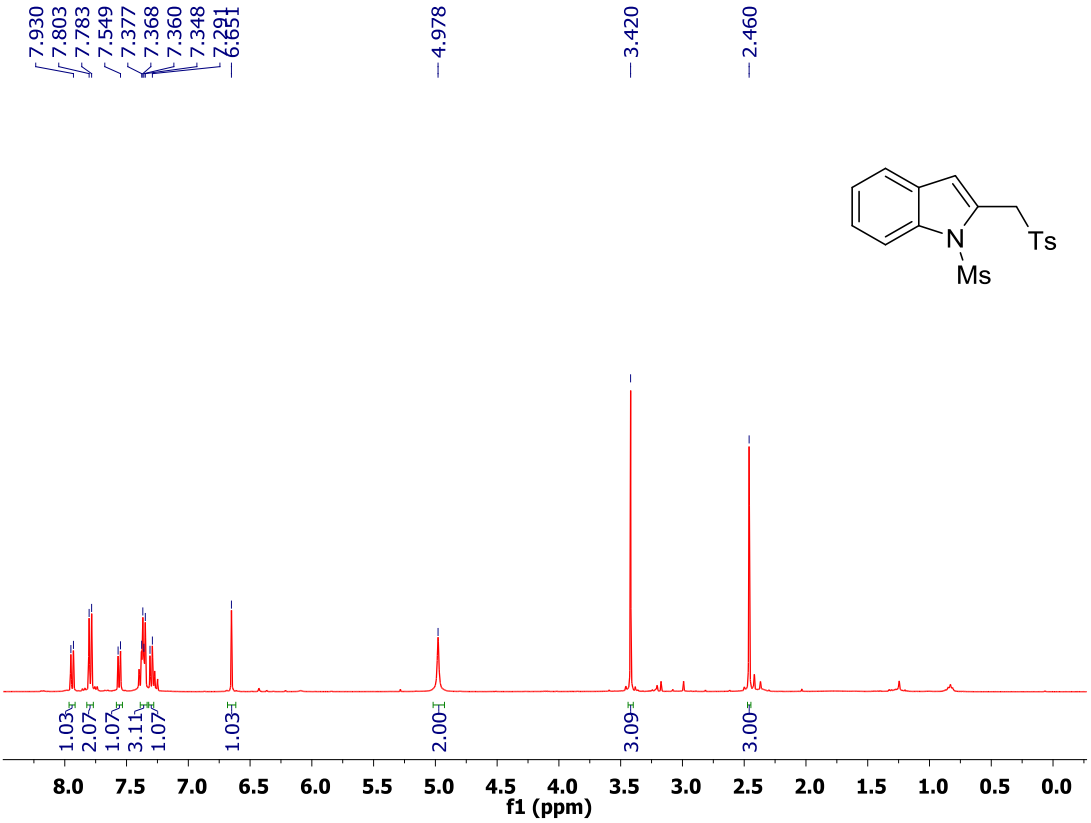

145.574
145.303
135.613
135.313
134.902
130.349
130.036
129.922
129.824
129.209
128.799
126.544
125.708
120.842
116.242
115.101
55.029
21.796
21.668
Cl
N
Ts
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

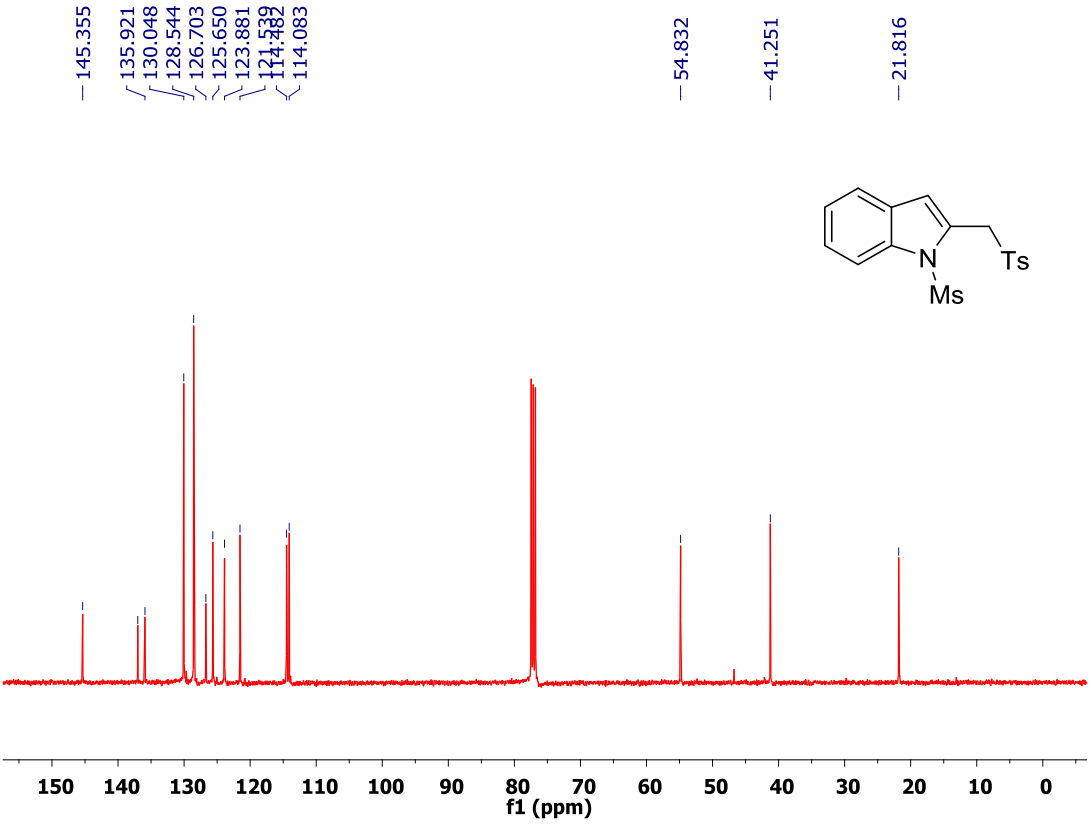

7.840
7.819
7.669
7.649
7.542
7.522
7.280
7.260
7.143
7.122
7.097
6.831
5.021
2.435
2.390
2.300
H3C
N
Ts
Ts
0.97
1.98
2.04
2.27
3.13
1.00
2.04
2.99
3.16
3.00
f1 (ppm)

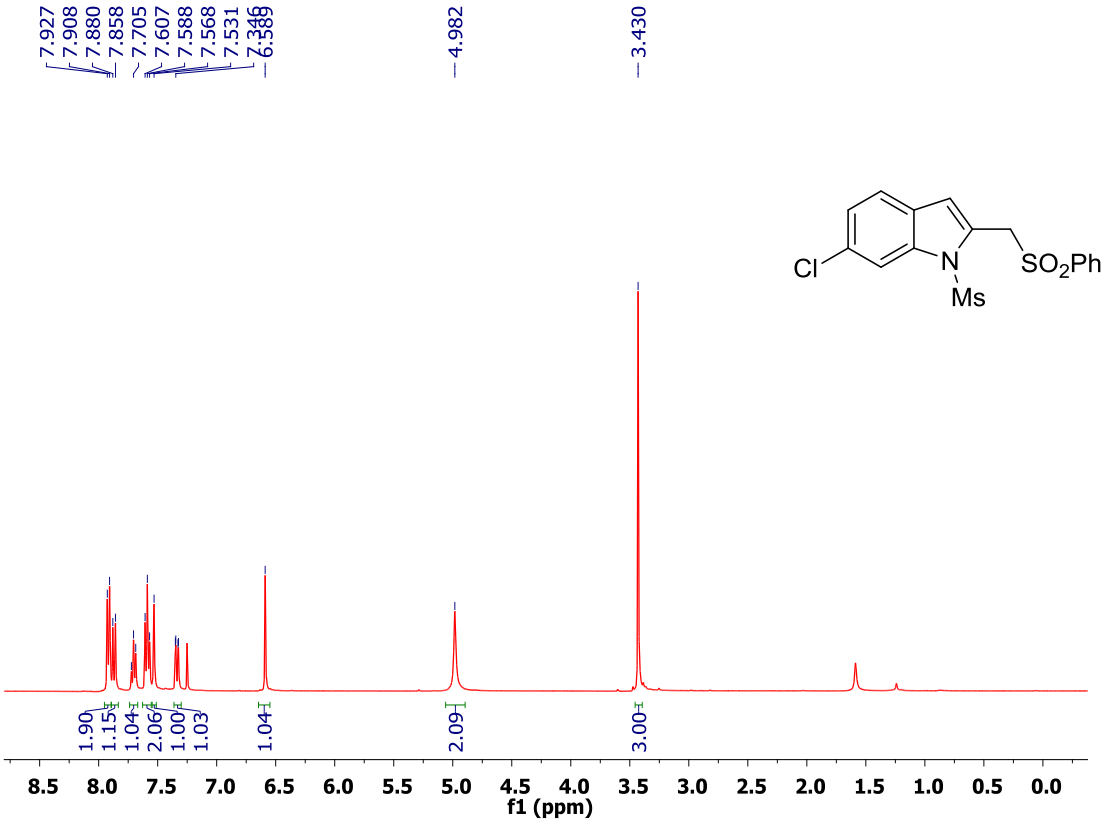

145.088
135.592
135.413
135.165
133.805
129.851
129.721
129.478
128.851
127.597
126.948
126.495
121.152
116.062
114.891
55.192
21.790
21.633
21.283
H3C
N
Ts
Ts
f1 (ppm)

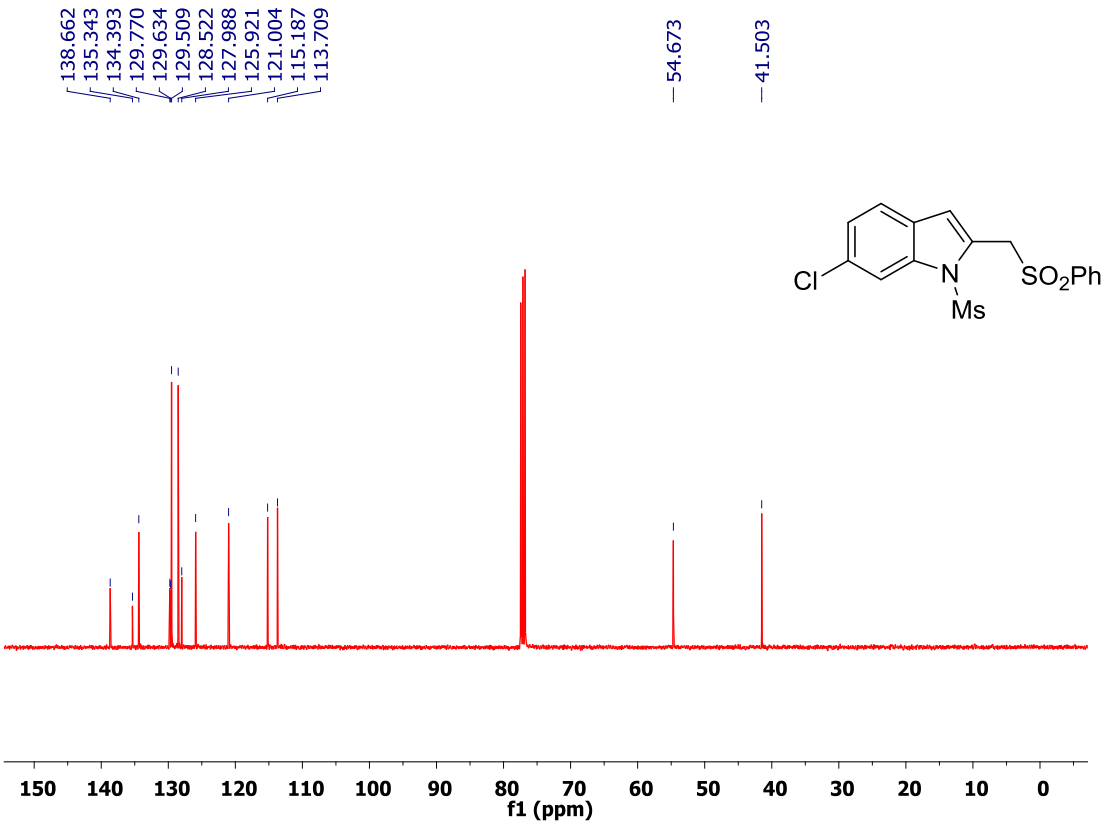

7.819
7.797
7.783
7.780
7.762
7.759
7.659
7.640
7.624
7.621
7.618
7.523
7.502
7.496
7.476
7.457
7.258
7.139
7.117
7.116
7.090
6.831
6.830
2.387
2.296
H3C
N
Ts
SO2Ph
1.05
1.96
1.10
4.23
1.27
3.01
0.95
1.97
3.00
2.97
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

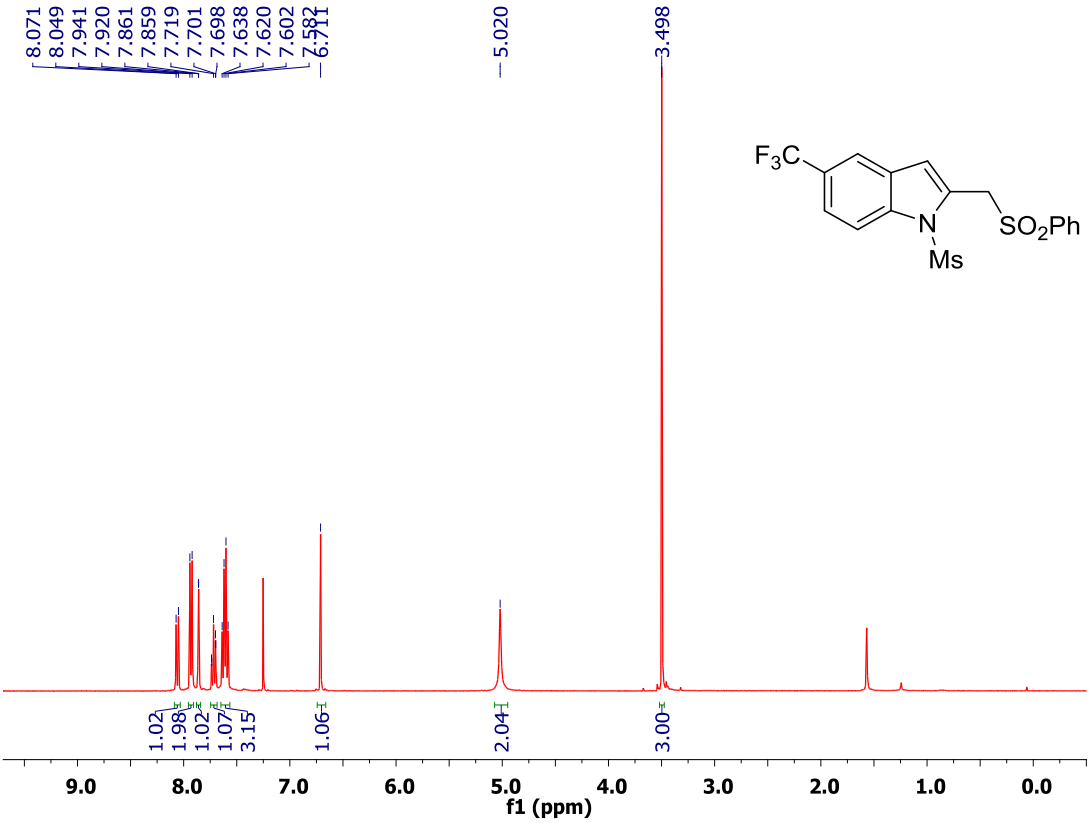

145.123
138.270
135.604
135.080
134.088
133.869
129.864
129.457
129.079
128.904
127.406
127.038
126.477
121.175
116.280
114.906
55.251
21.630
21.283
H3C
N
Ts
SO2Ph
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

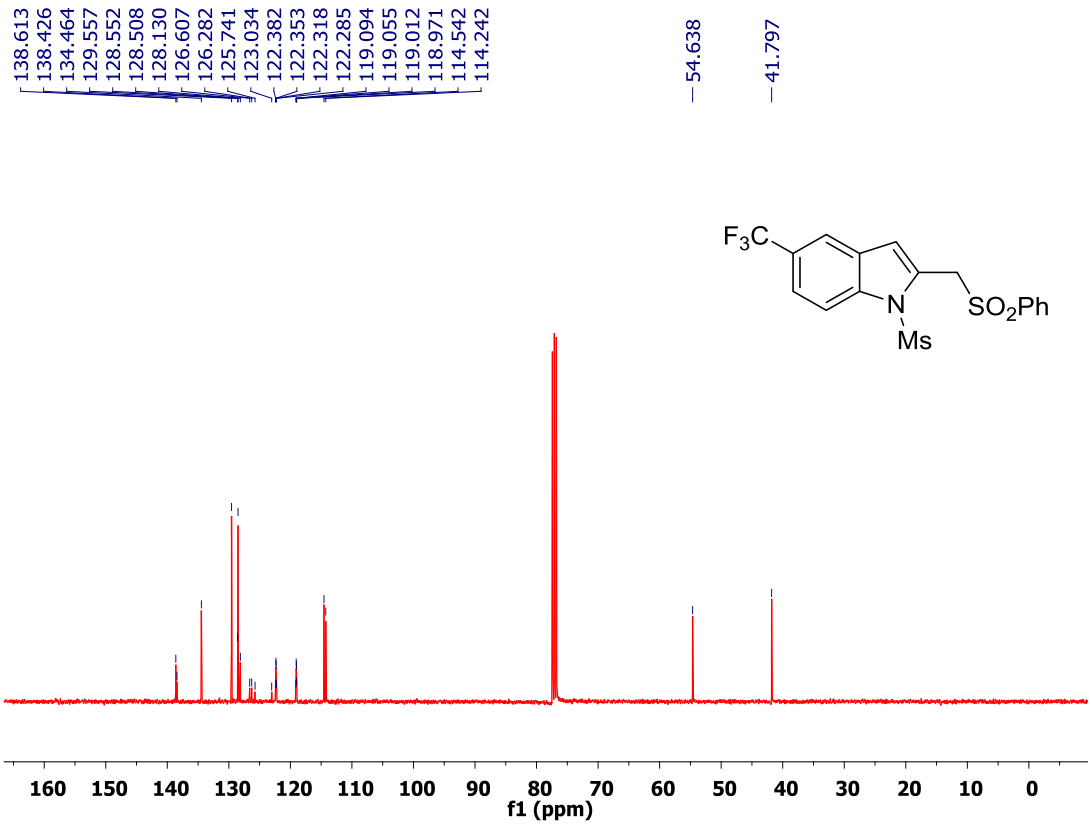

7.930
7.803
7.783
7.549
7.377
7.368
7.360
7.348
7.291
6.651
4.978
3.420
2.460
Ts
N
Ms
1.03
2.07
1.07
3.11
1.07
1.03
2.00
3.09
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

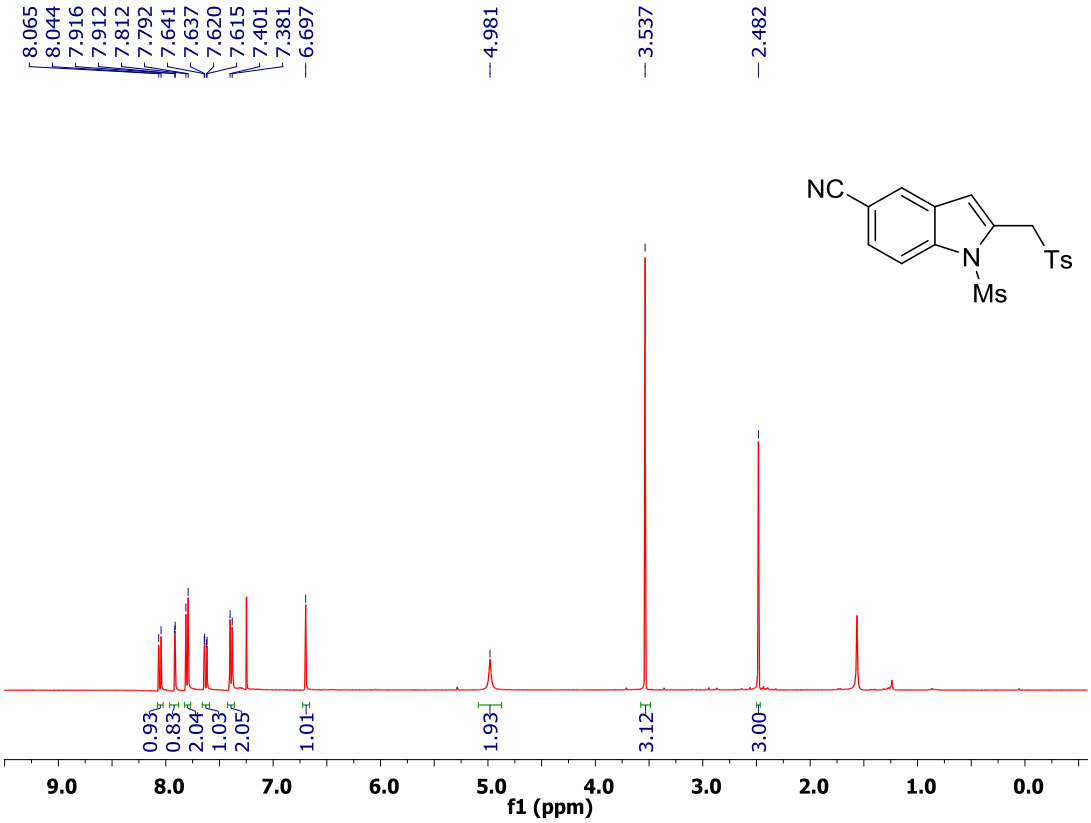

145.355
135.921
130.048
128.544
126.703
125.650
123.881
121.539
114.782
114.083
54.832
41.251
21.816
Ts
N
Ms
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

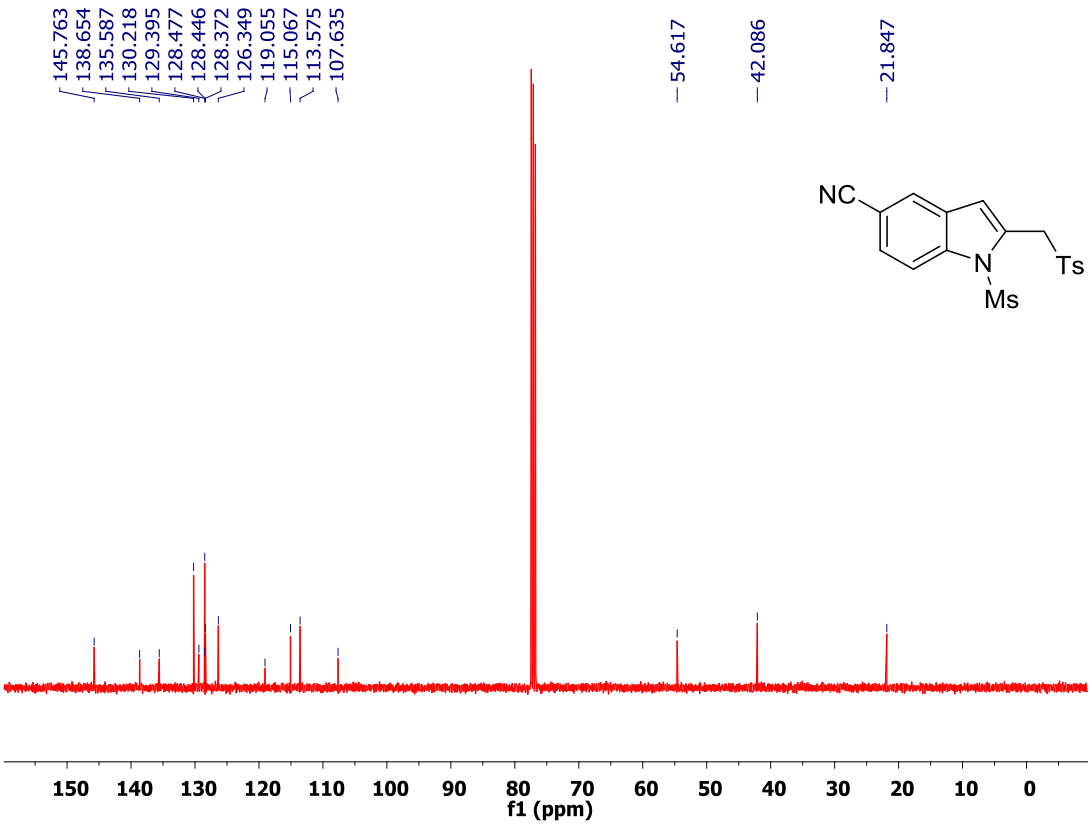

7.927
7.908
7.880
7.858
7.705
7.607
7.588
7.568
7.531
7.346
6.589
4.982
3.430
Cl
N
Ms
SO2Ph
1.90
1.15
1.04
2.06
1.00
1.03
1.04
2.09
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

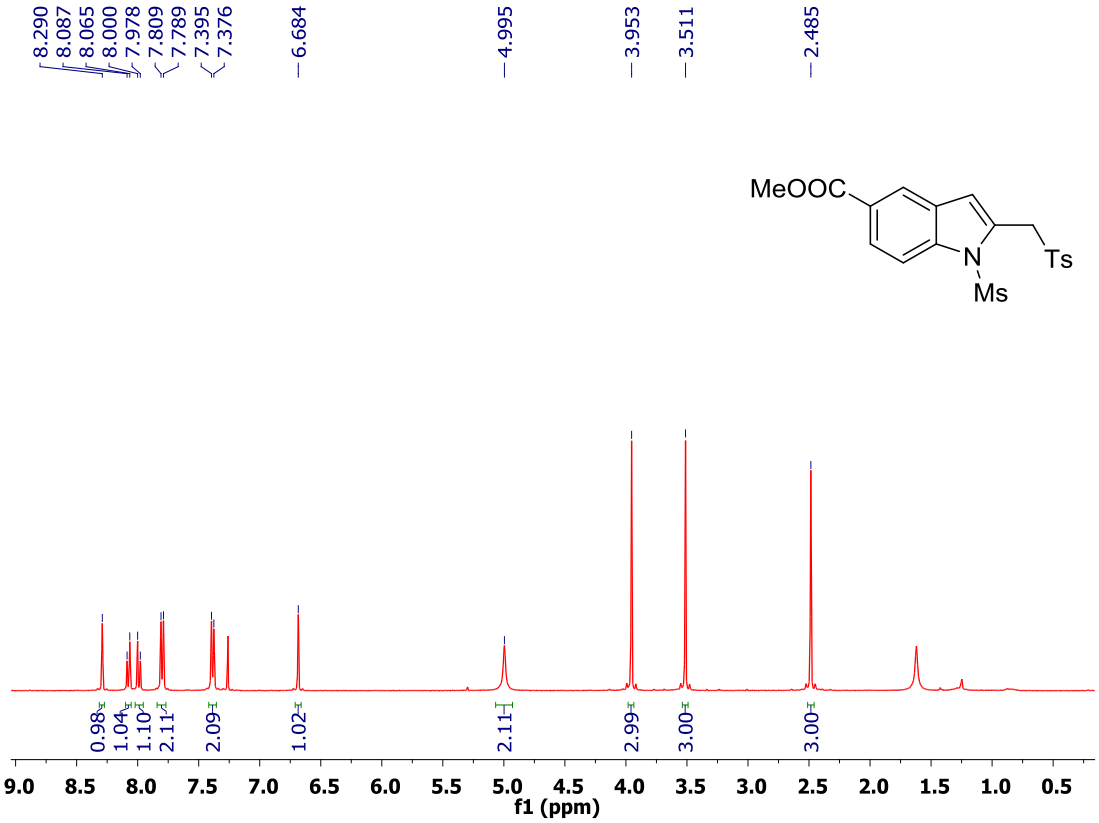

138.662
135.343
134.393
129.770
129.634
129.509
128.522
127.988
125.921
121.004
115.187
113.709
54.673
41.503
Cl
N
Ms
SO2Ph
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

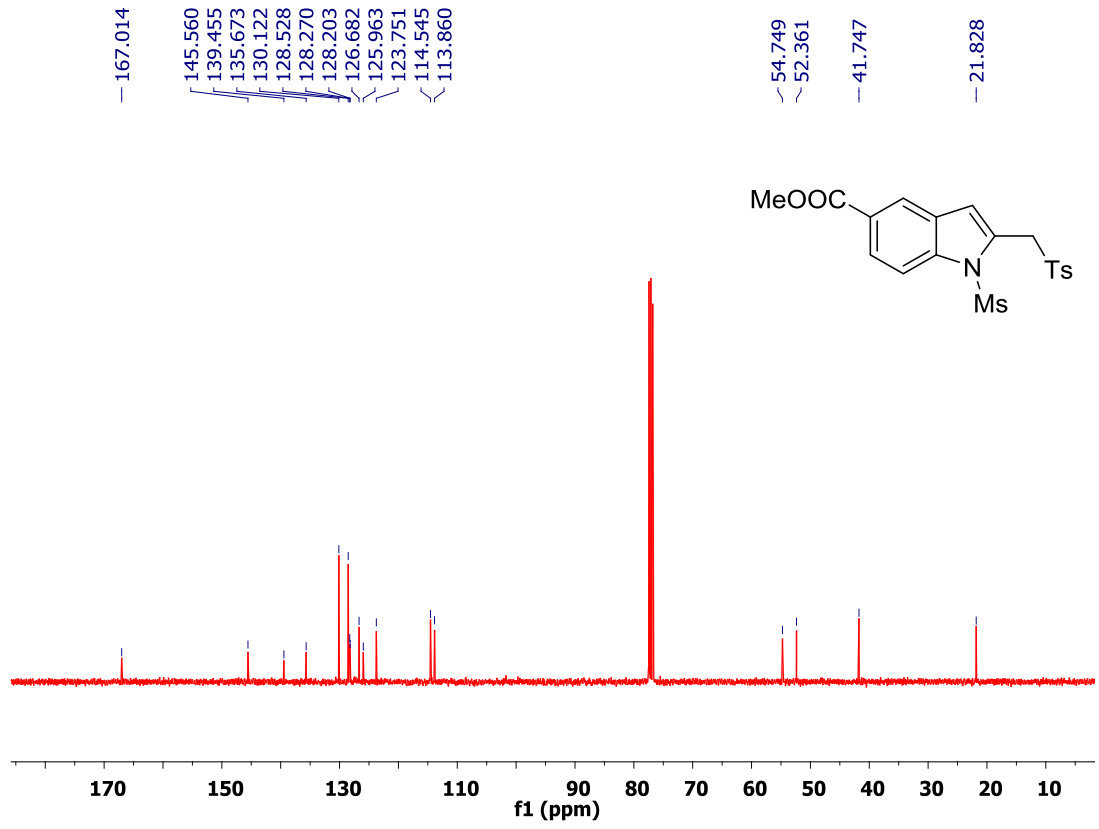

8.071
8.049
7.941
7.920
7.861
7.859
7.719
7.701
7.698
7.638
7.620
7.602
7.582
7.581
6.711
5.020
3.498
F3C
N
Ms
SO2Ph
1.02
1.98
1.02
1.07
3.15
1.06
2.04
3.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

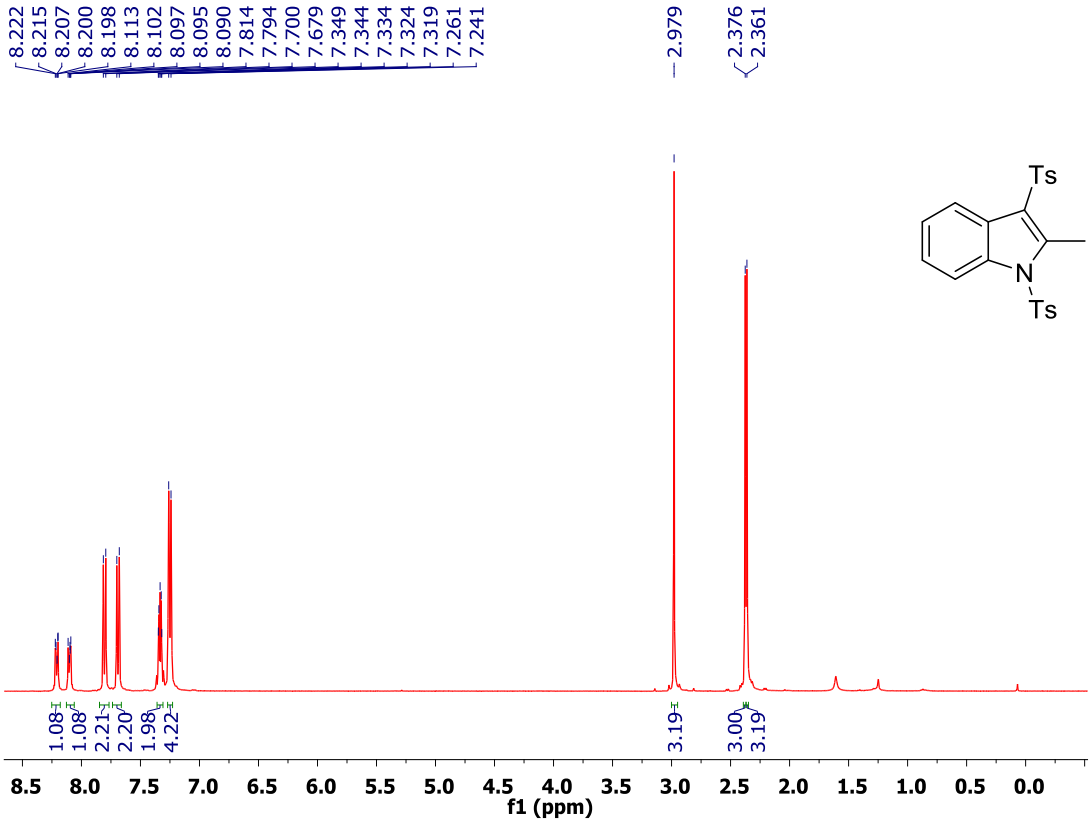

138.613
138.426
134.464
129.557
128.552
128.508
128.130
126.607
126.282
125.741
123.034
122.382
122.353
122.318
122.285
119.094
119.055
119.012
118.971
114.542
114.242
54.638
41.797
F3C
N
Ms
SO2Ph
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

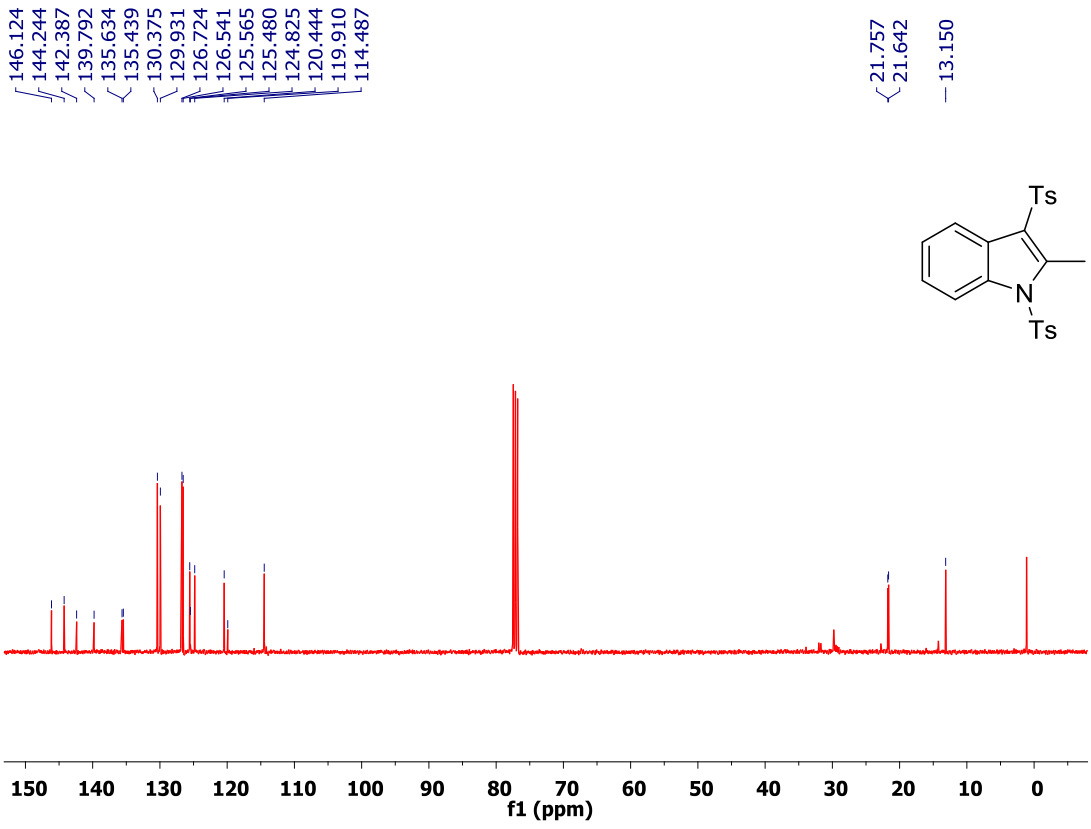

8.065
8.044
7.916
7.912
7.812
7.792
7.641
7.637
7.620
7.615
7.401
7.381
6.697
4.981
3.537
2.482
NC
N
Ts
Ms
0.93
0.83
2.04
1.03
2.05
1.01
1.93
3.12
3.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


145.763
138.654
135.587
130.218
129.395
128.477
128.446
128.372
126.349
119.055
115.067
113.575
107.635
54.617
42.086
21.847
NC
N
Ts
Ms
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

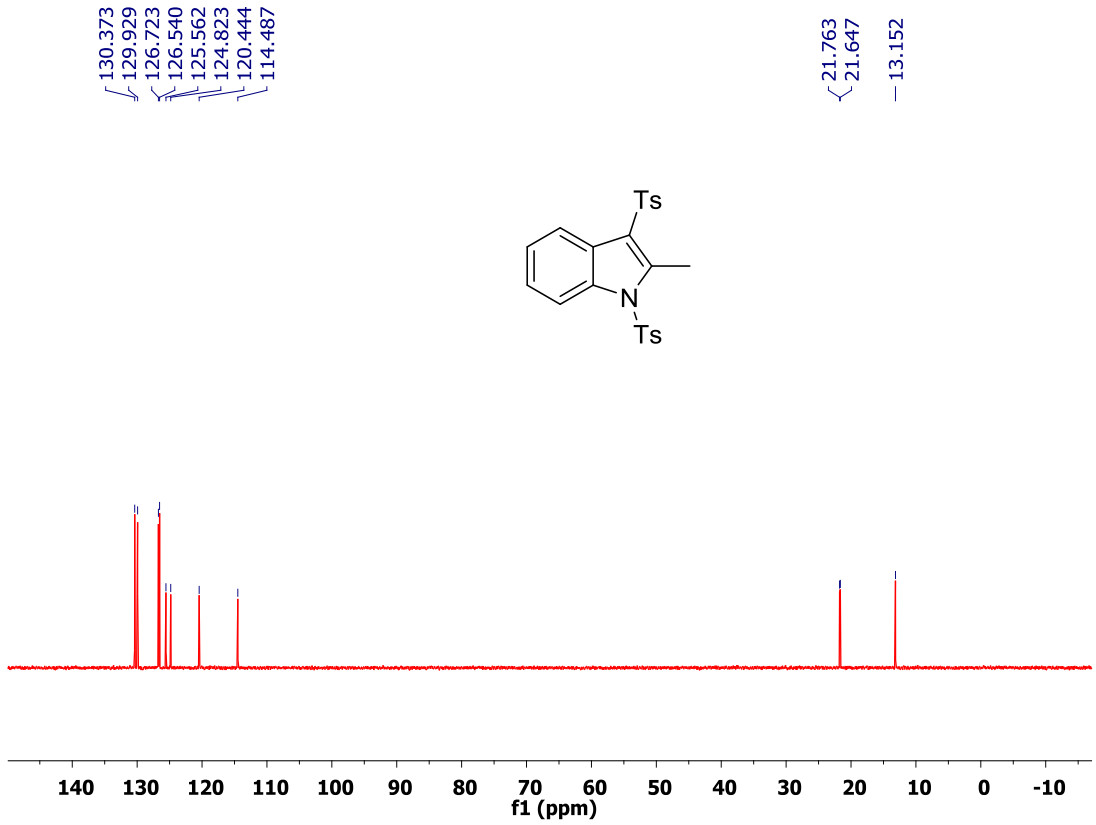

8.290
8.087
8.065
8.000
7.978
7.809
7.789
7.395
7.376
6.684
4.995
3.953
3.511
2.485
MeOOC
N
Ts
Ms
0.98
1.04
1.10
2.11
2.09
1.02
2.11
2.99
3.00
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

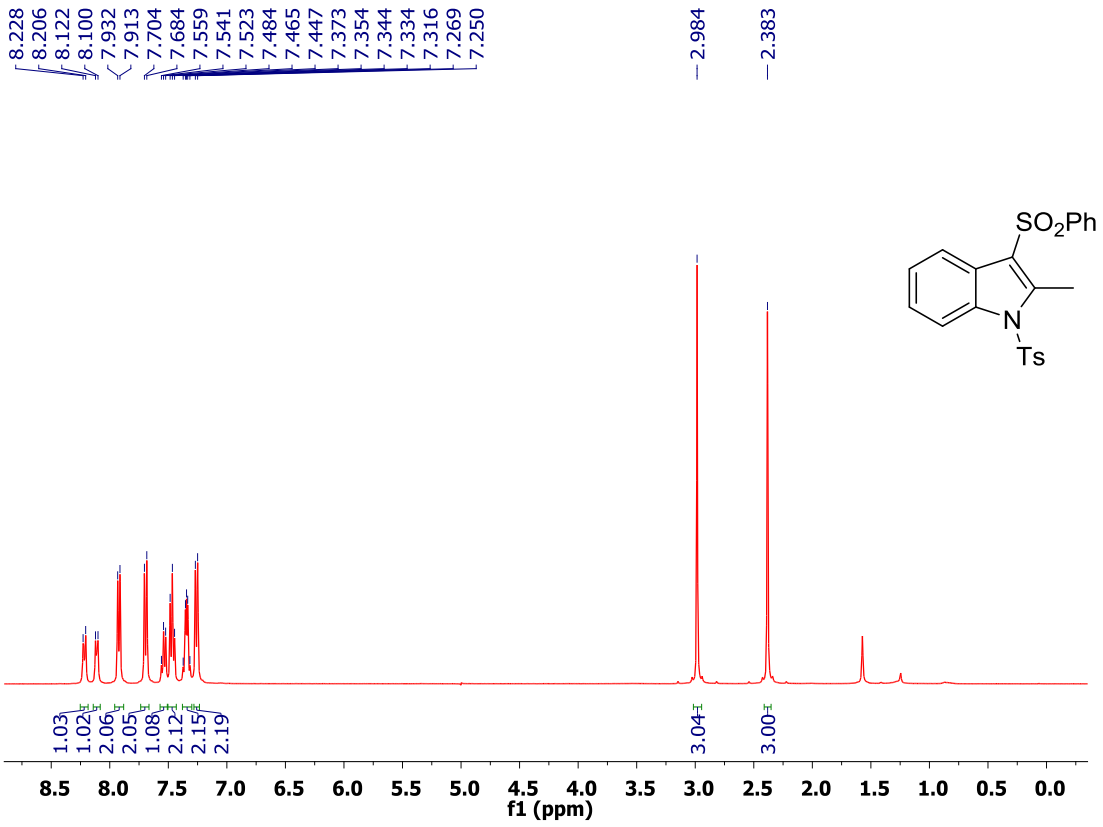

167.014
145.560
139.455
135.673
130.122
128.528
128.270
128.203
126.682
125.963
123.751
114.545
113.860
54.749
52.361
41.747
21.828
MeOOC
N
Ts
Ms
170 150 130 110 90 80 70 60 50 40 30 20 10
f1 (ppm)

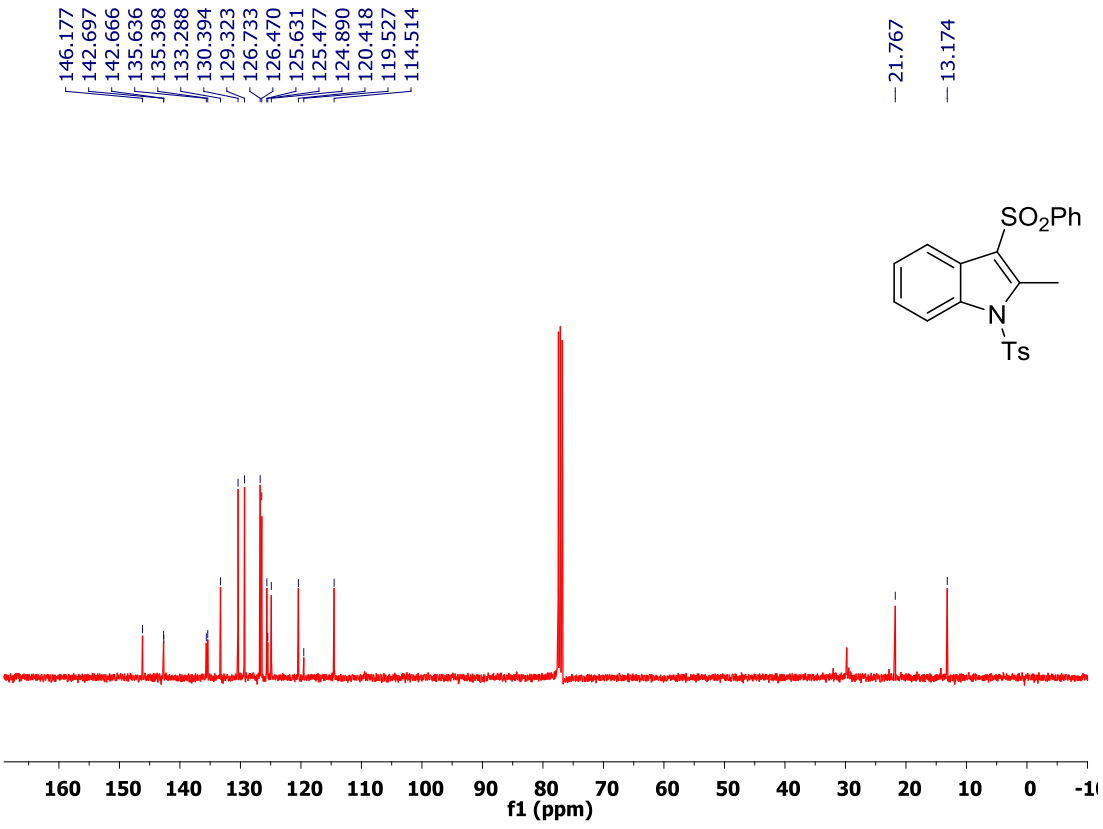

8.222
8.215
8.207
8.200
8.198
8.113
8.102
8.097
8.095
8.090
7.814
7.794
7.700
7.679
7.349
7.344
7.334
7.324
7.319
7.261
7.241
2.979
2.376
2.361
Ts
N
Ts
1.08
1.08
2.21
2.20
1.98
4.22
3.19
3.00
3.19
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

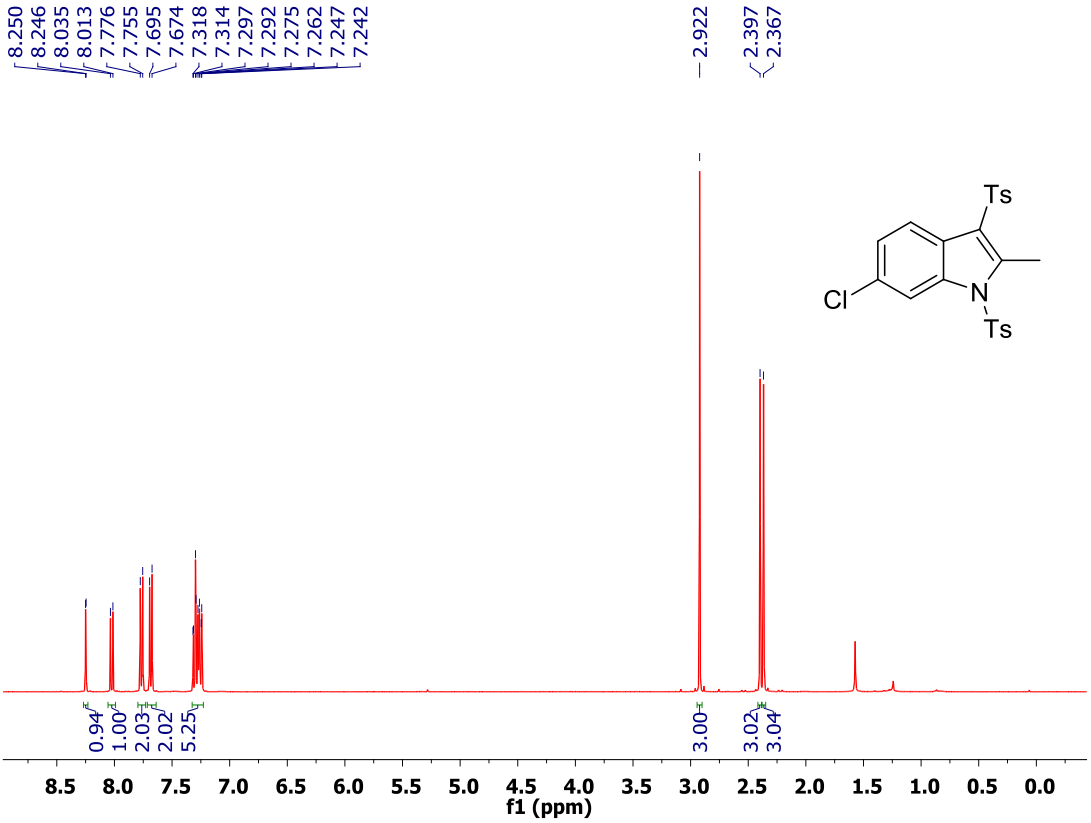

146.124
144.244
142.387
139.792
135.634
135.439
130.375
129.931
126.724
126.541
125.565
125.480
124.825
120.444
119.910
114.487
21.757
21.642
13.150
Ts
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

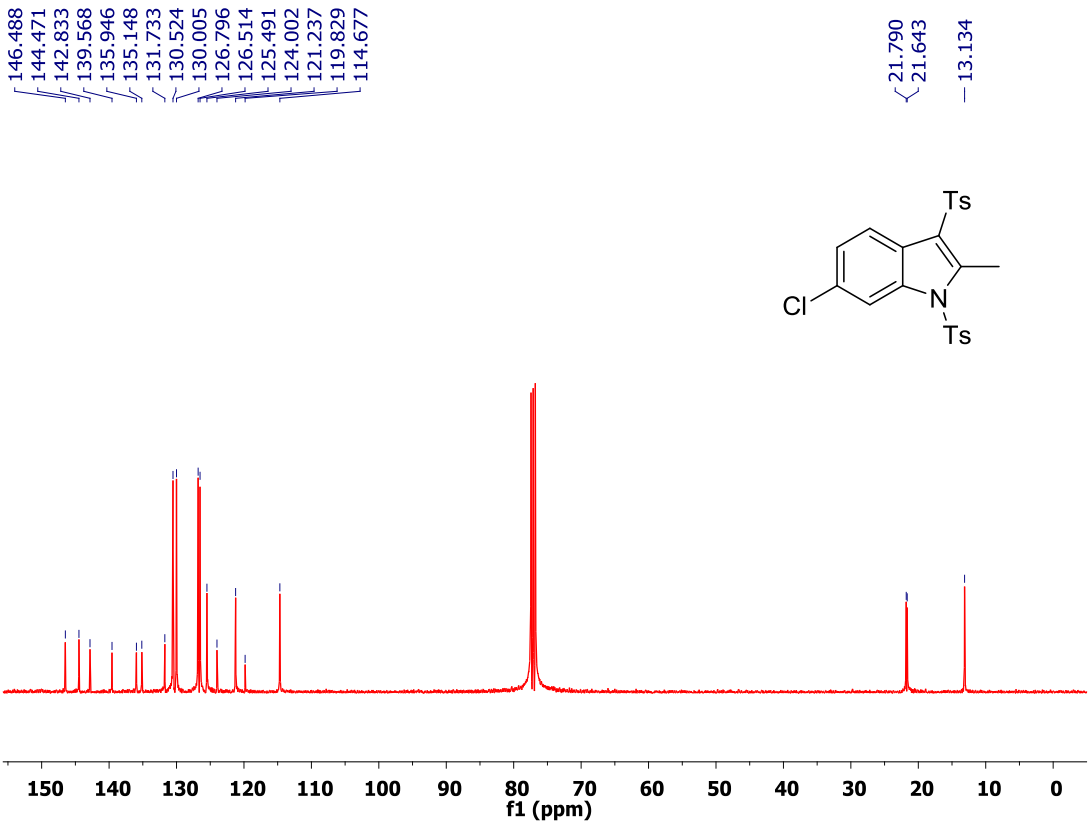
DEPT-135

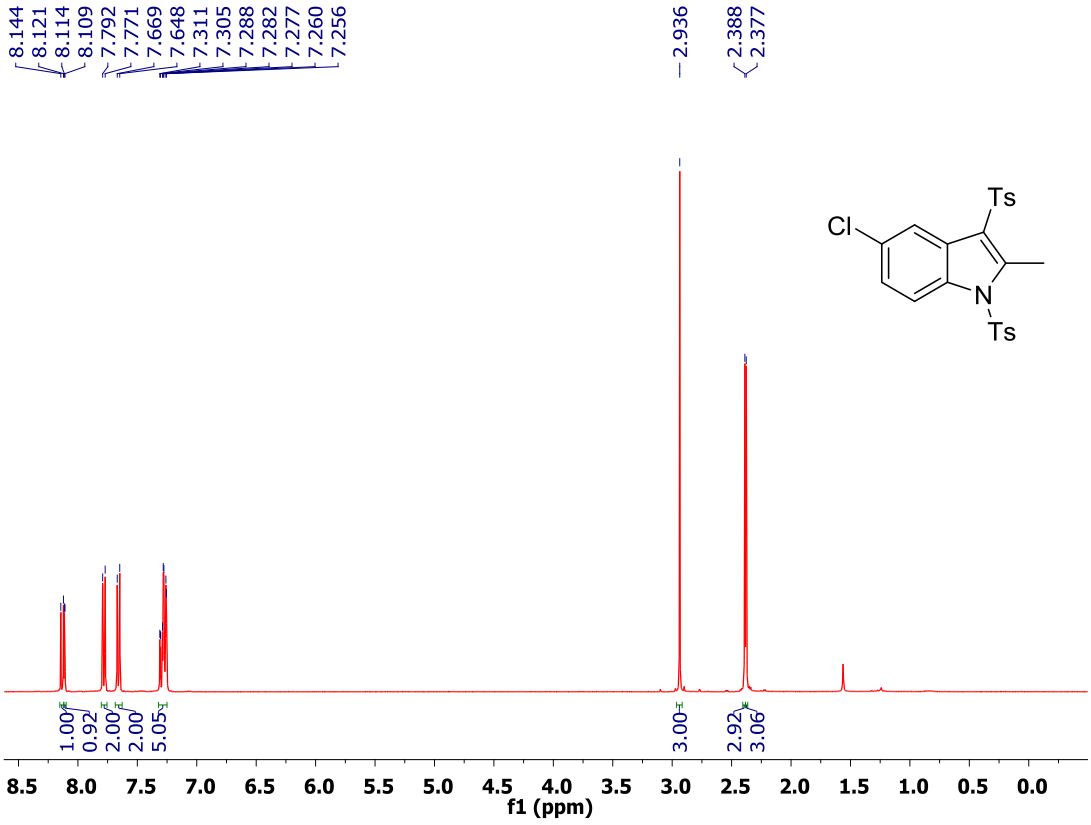

130.373
129.929
126.723
126.540
125.562
124.823
120.444
114.487
21.763
21.647
13.152
Ts
N
Ts
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

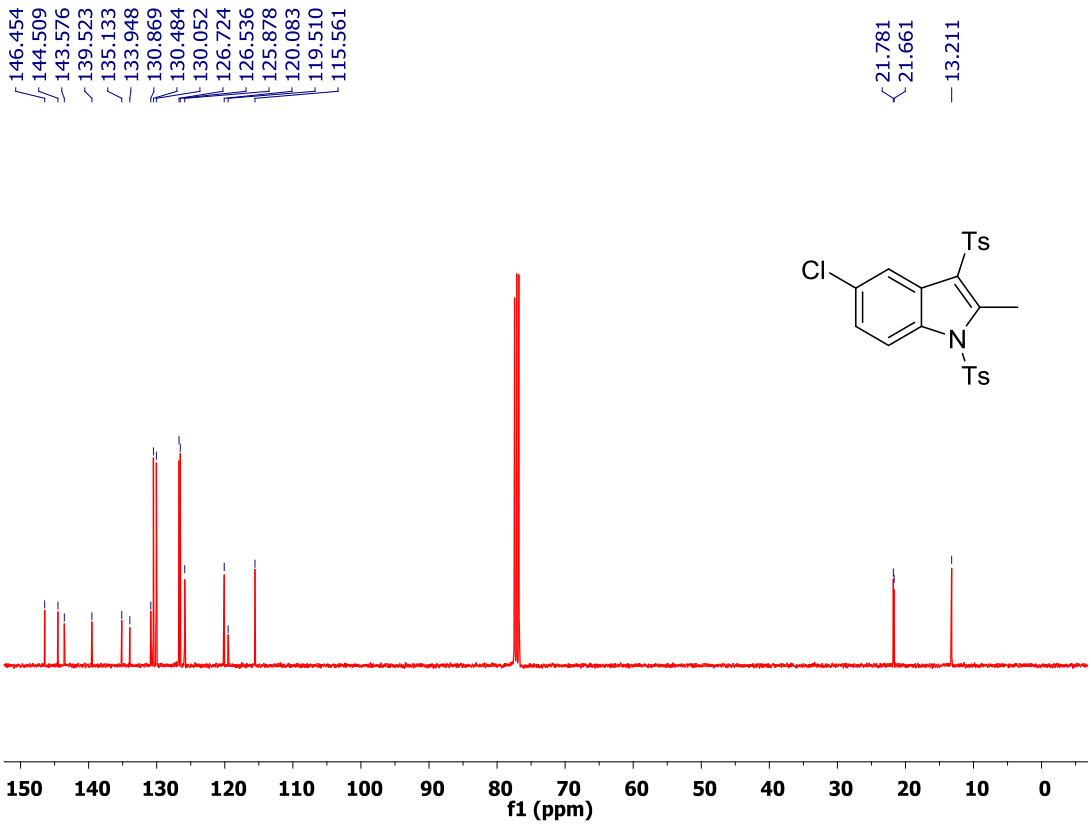

8.228
8.206
8.122
8.100
7.932
7.913
7.704
7.684
7.559
7.541
7.523
7.484
7.465
7.447
7.373
7.354
7.344
7.334
7.316
7.269
7.250
2.984
2.383
SO2Ph
N
Ts
1.03
1.02
2.06
2.05
1.08
2.12
2.15
2.19
3.04
3.00
f1 (ppm)

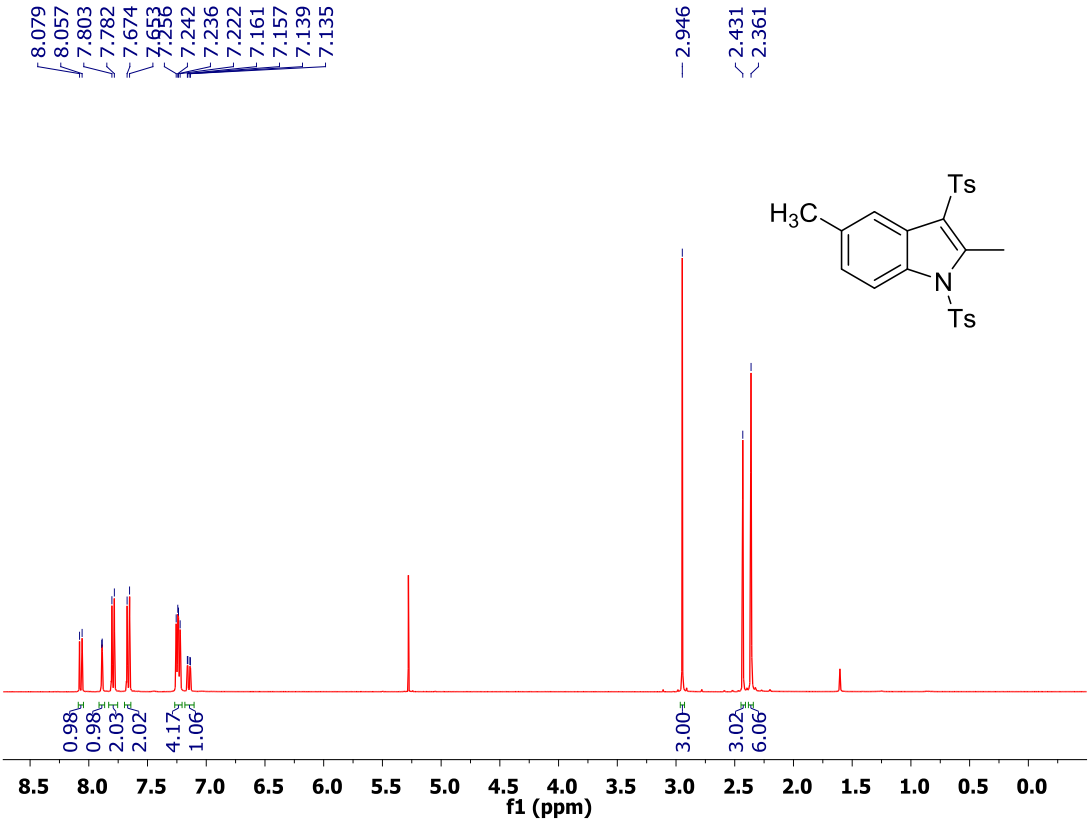

146.177
142.697
142.666
135.636
135.398
133.288
130.394
129.323
126.733
126.470
125.631
125.477
124.890
120.418
119.527
114.514
21.767
13.174
SO2Ph
N
Ts
f1 (ppm)

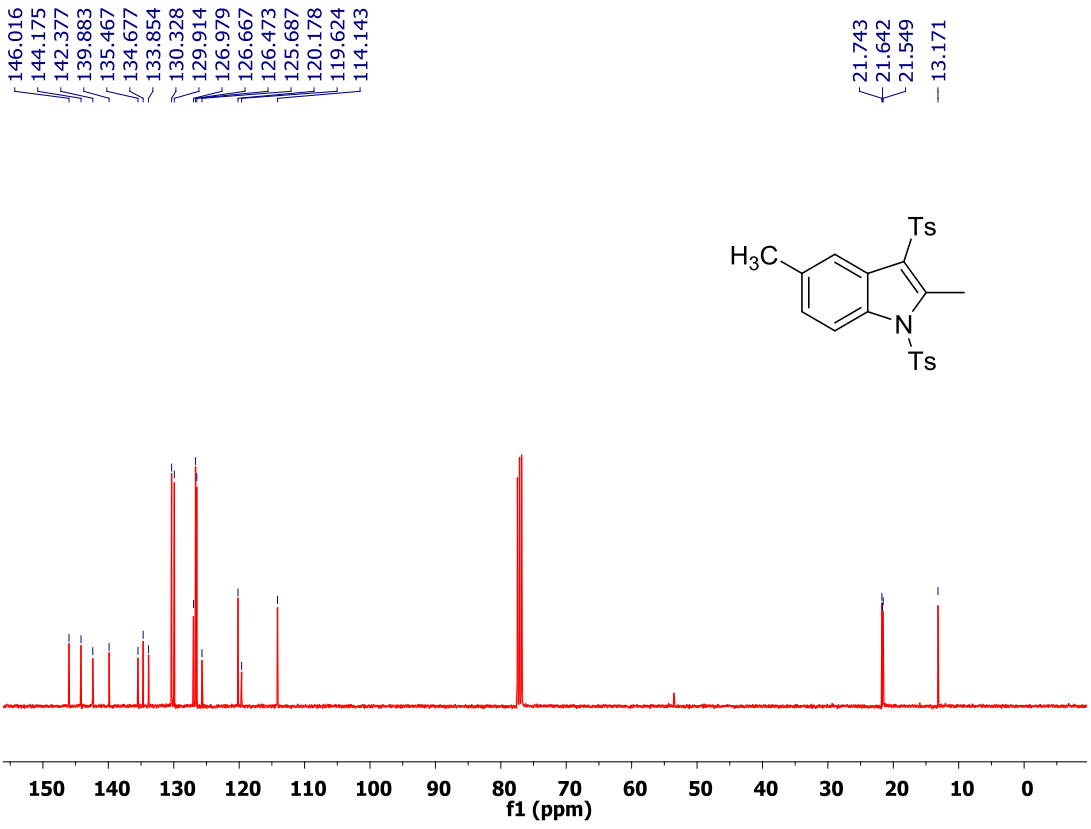

8.250
8.246
8.035
8.013
7.776
7.755
7.695
7.674
7.318
7.314
7.297
7.292
7.275
7.262
7.247
7.242
2.922
2.397
2.367
Ts
Cl
N
Ts
0.94
1.00
2.03
2.02
5.25
3.00
3.02
3.04
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

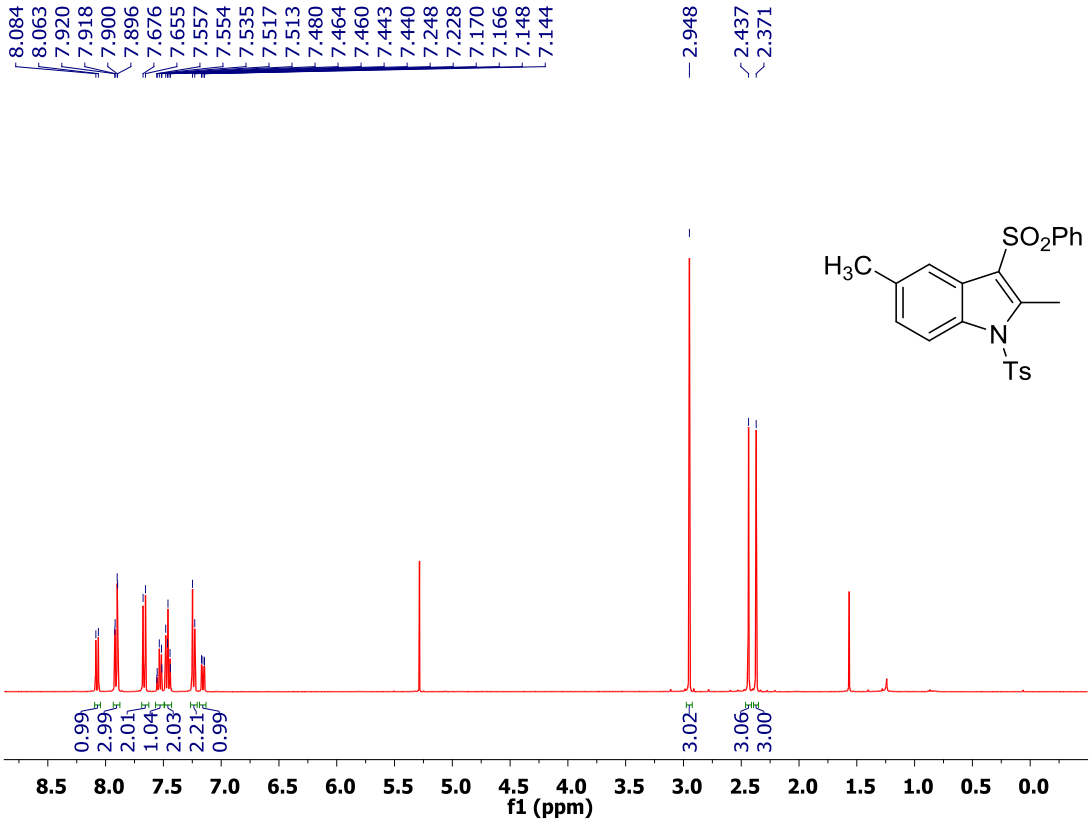

146.488
144.471
142.833
139.568
135.946
135.148
131.733
130.524
130.005
126.796
126.514
125.491
124.002
121.237
119.829
114.677
21.790
21.643
13.134
Ts
Cl
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

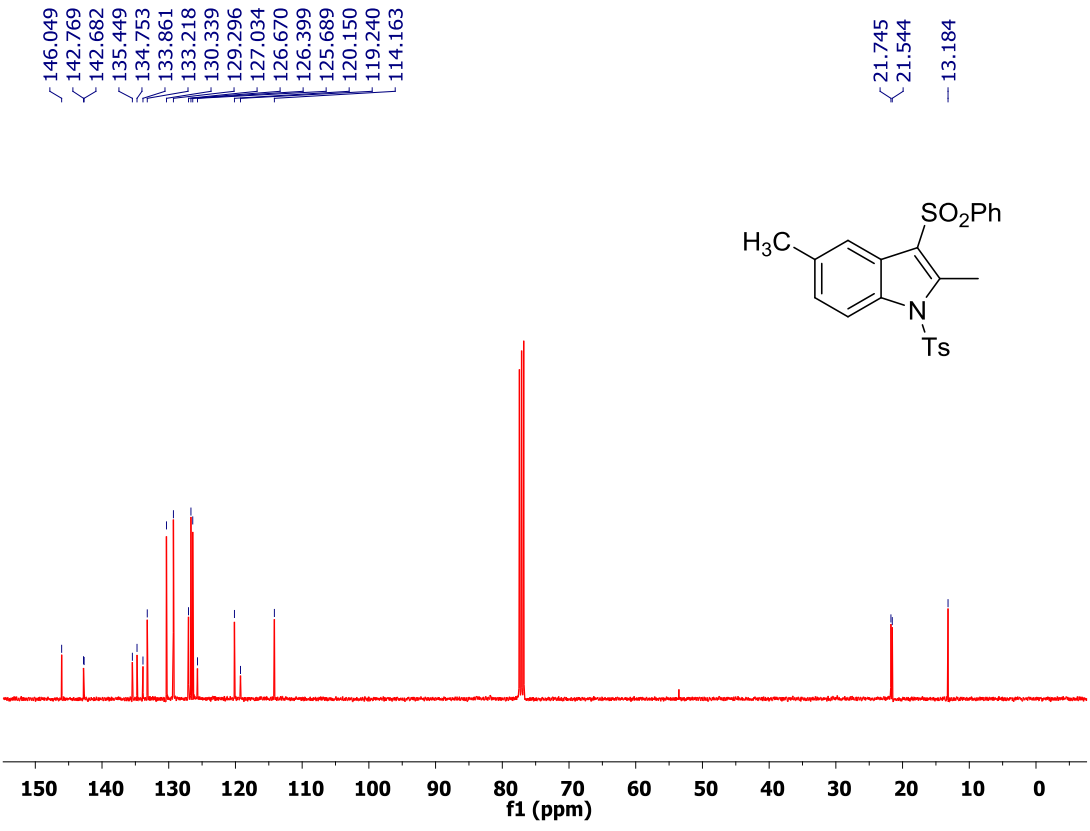

8.144
8.121
8.114
8.109
7.792
7.771
7.669
7.648
7.311
7.305
7.288
7.282
7.277
7.260
7.256
2.936
2.388
2.377
Cl
Ts
N
Ts
1.00
0.92
2.00
2.00
5.05
3.00
2.92
3.06
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

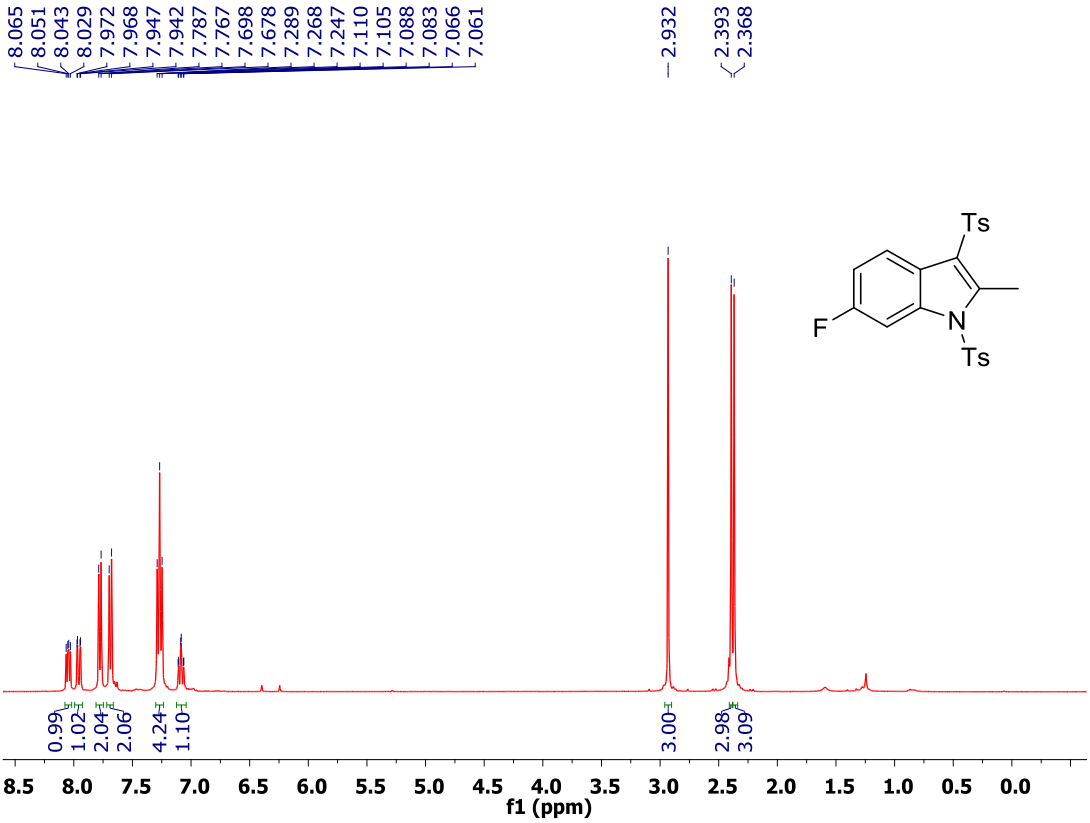

146.454
144.509
143.576
139.523
135.133
133.948
130.869
130.484
130.052
126.724
126.536
125.878
120.083
119.510
115.561
21.781
21.661
13.211
Cl
Ts
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

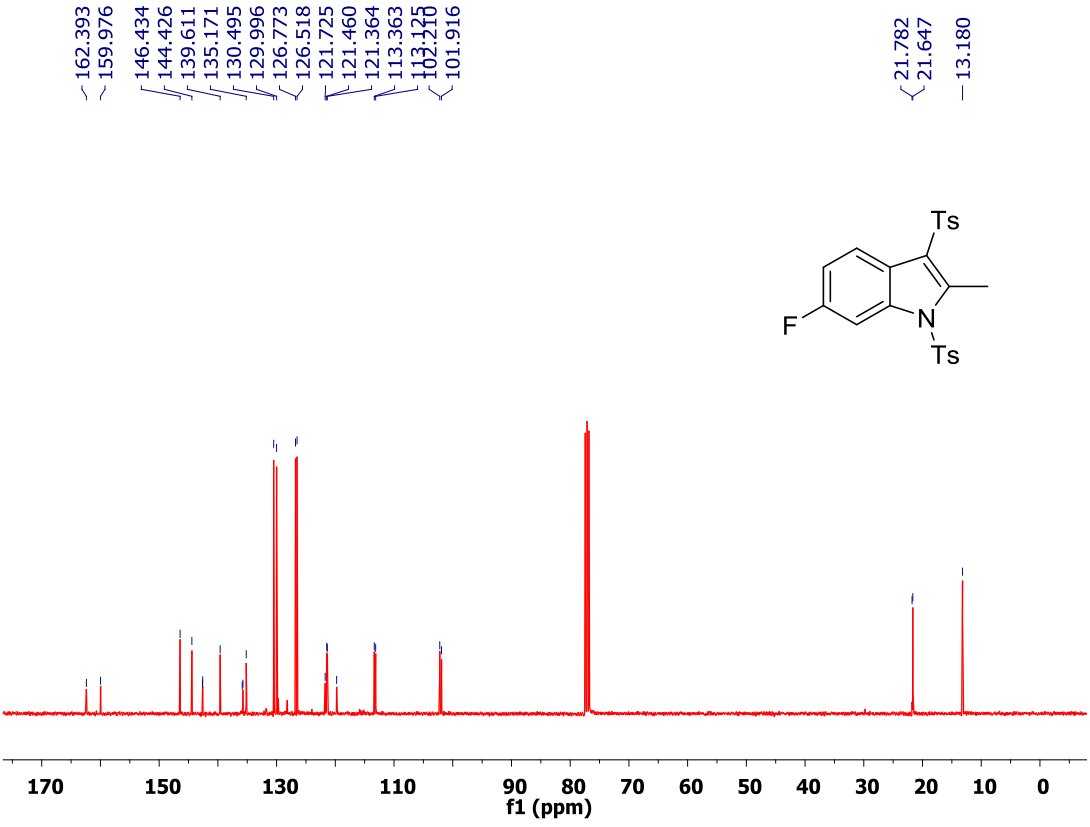

8.079
8.057
7.803
7.782
7.674
7.653
7.255
7.242
7.236
7.222
7.161
7.157
7.139
7.135
2.946
2.431
2.361
Ts
H3C
N
Ts
0.98
0.98
2.03
2.02
4.17
1.06
3.00
3.02
6.06
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

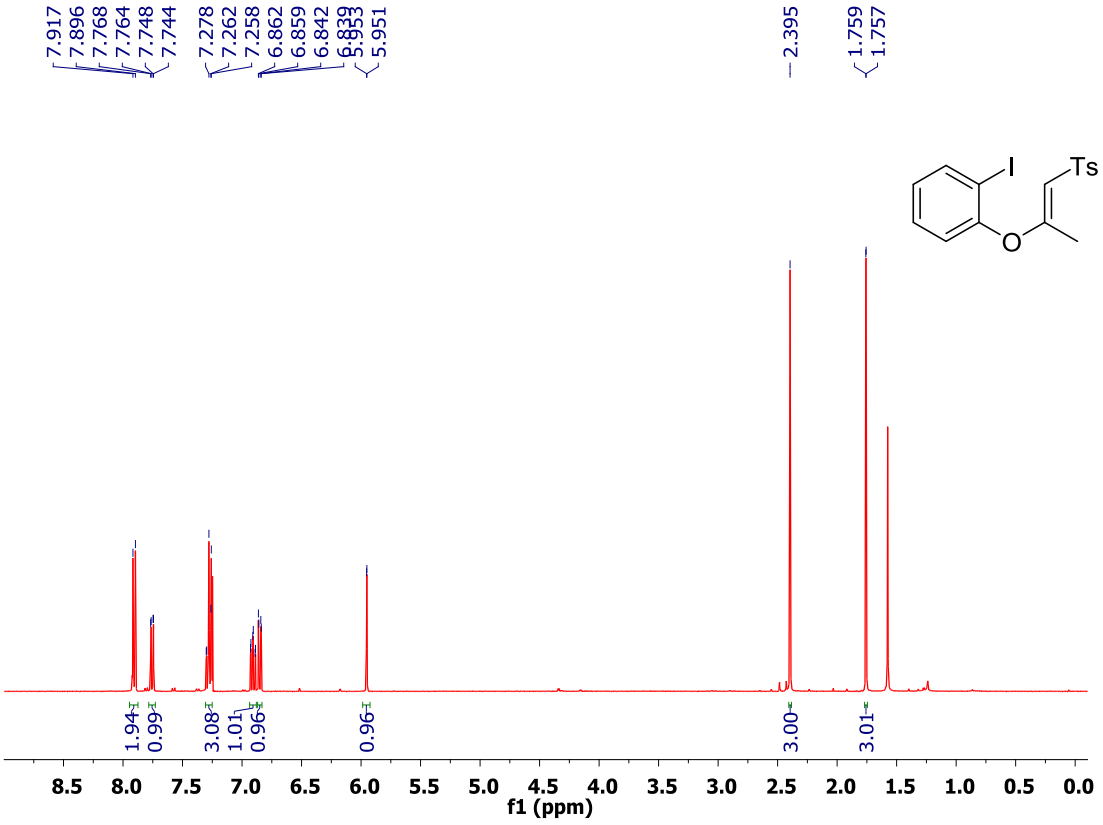

146.016
144.175
142.377
139.883
135.467
134.677
133.854
130.328
129.914
126.979
126.667
126.473
125.687
120.178
119.624
114.143
21.743
21.642
21.549
13.171
Ts
H3C
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

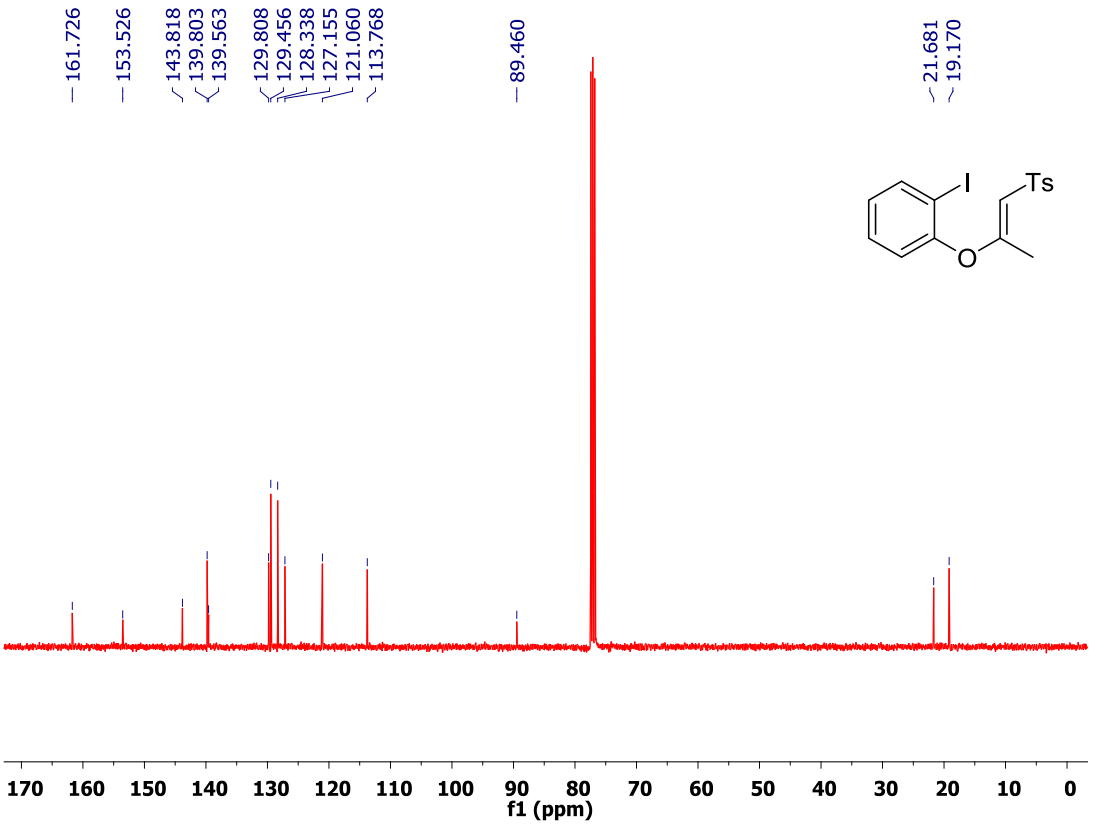

8.084
8.063
7.920
7.918
7.900
7.896
7.676
7.655
7.557
7.554
7.535
7.517
7.513
7.480
7.464
7.460
7.443
7.440
7.248
7.228
7.170
7.166
7.148
7.144
2.948
2.437
2.371
SO2Ph
H3C
N
Ts
0.99
2.99
2.01
1.04
2.03
2.21
0.99
3.02
3.06
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

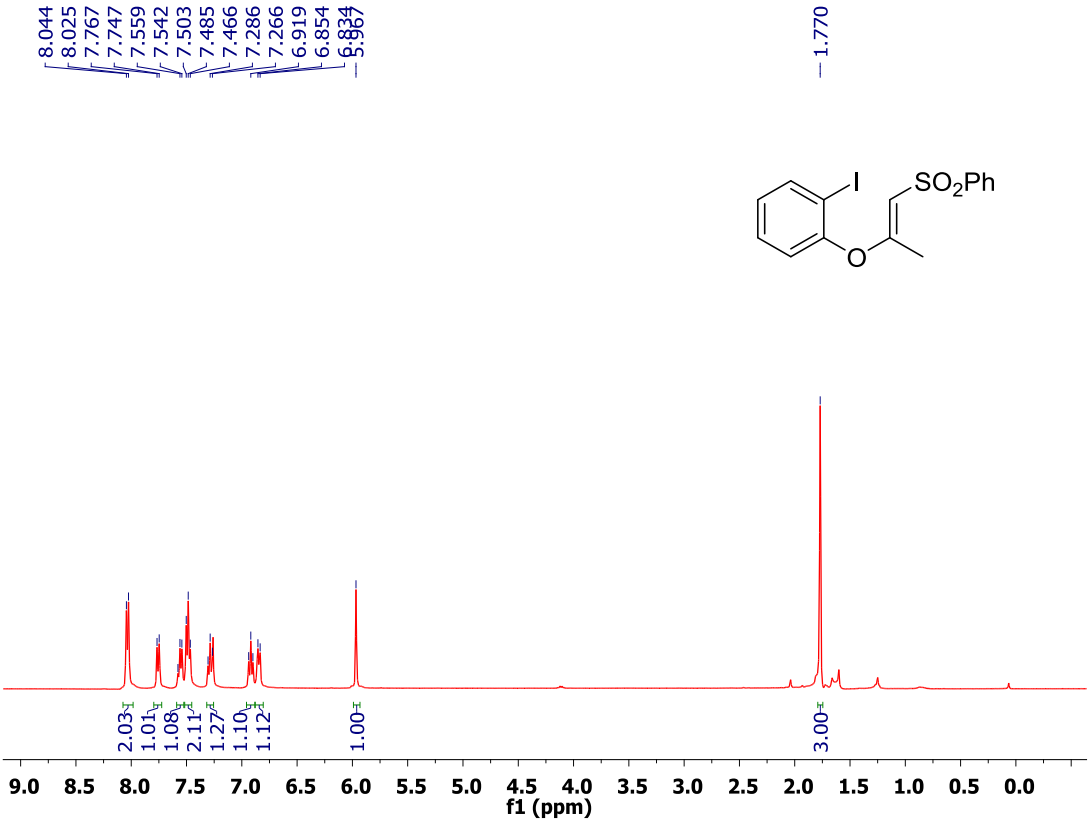

146.049
142.769
142.682
135.449
134.753
133.861
133.218
130.339
129.296
127.034
126.670
126.399
125.689
120.150
119.240
114.163
21.745
21.544
13.184
SO2Ph
H3C
N
Ts
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

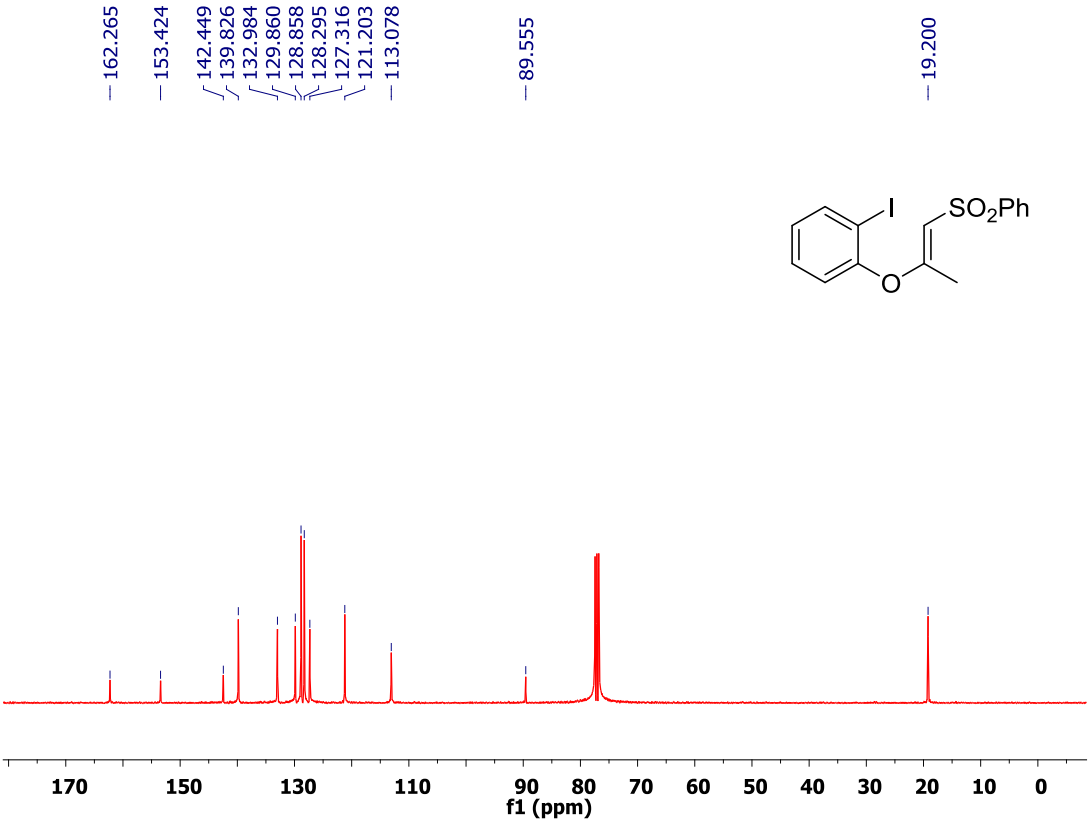

8.065
8.051
8.043
8.029
7.972
7.968
7.947
7.942
7.787
7.767
7.698
7.678
7.289
7.268
7.247
7.110
7.105
7.088
7.083
7.066
7.061
2.932
2.393
2.368
Ts
F
N
Ts
0.99
1.02
2.04
2.06
4.24
1.10
3.00
2.98
3.09
f1 (ppm)

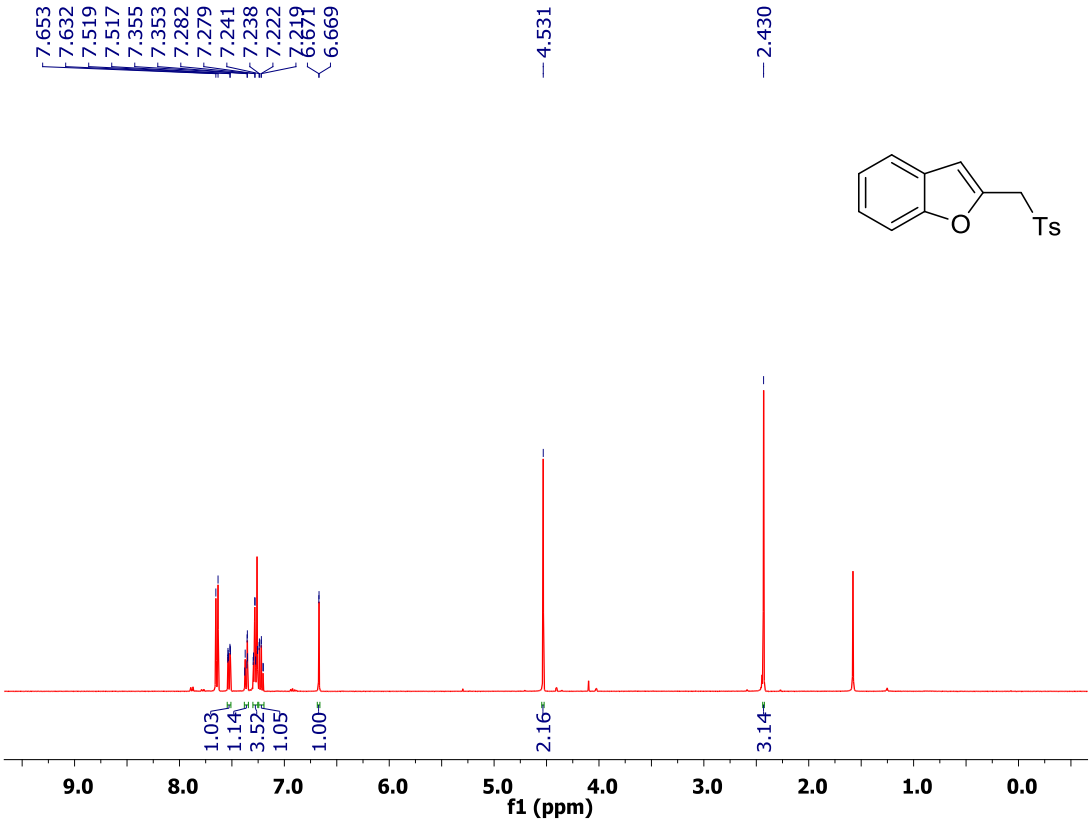

162.393
159.976
146.434
144.426
139.611
135.171
130.495
129.996
126.773
126.518
121.725
121.460
121.364
113.363
113.125
102.210
101.916
21.782
21.647
13.180
Ts
F
N
Ts
f1 (ppm)

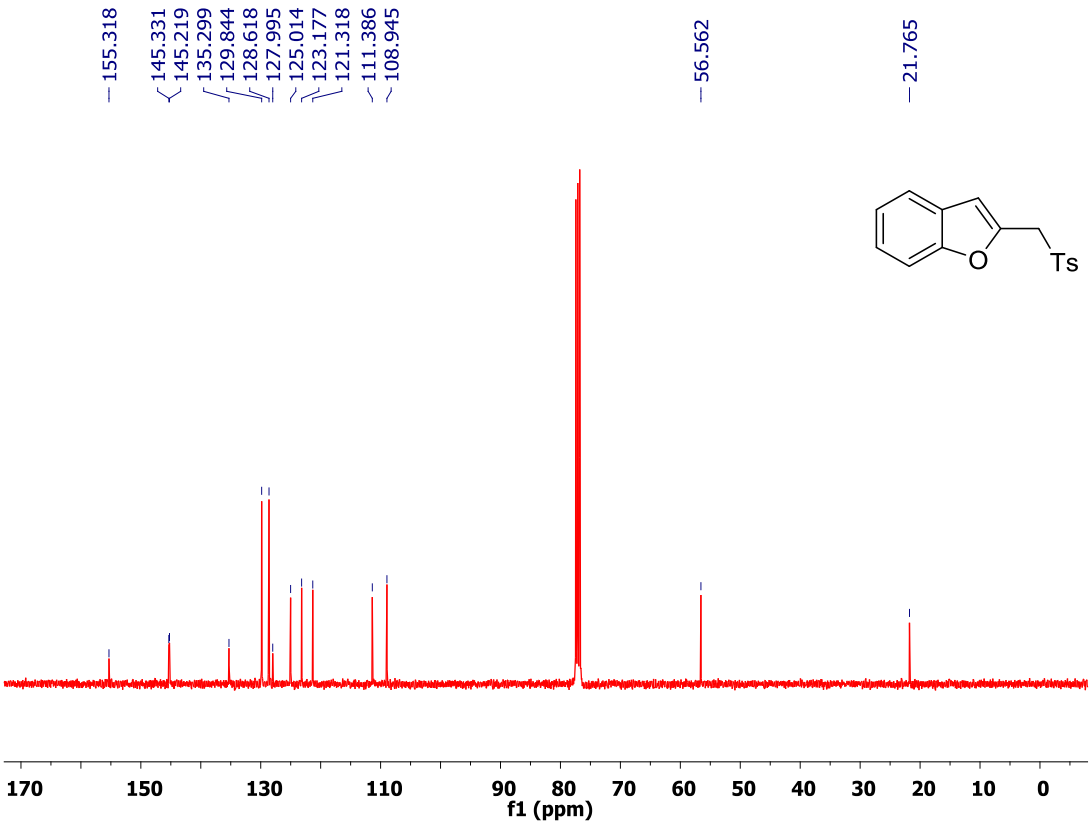

7.917
7.896
7.768
7.764
7.748
7.744
7.278
7.262
7.258
6.862
6.859
6.842
5.951
2.395
1.759
1.757
I
Ts
O
1.94
0.99
3.08
1.01
0.96
0.96
3.00
3.01
f1 (ppm)

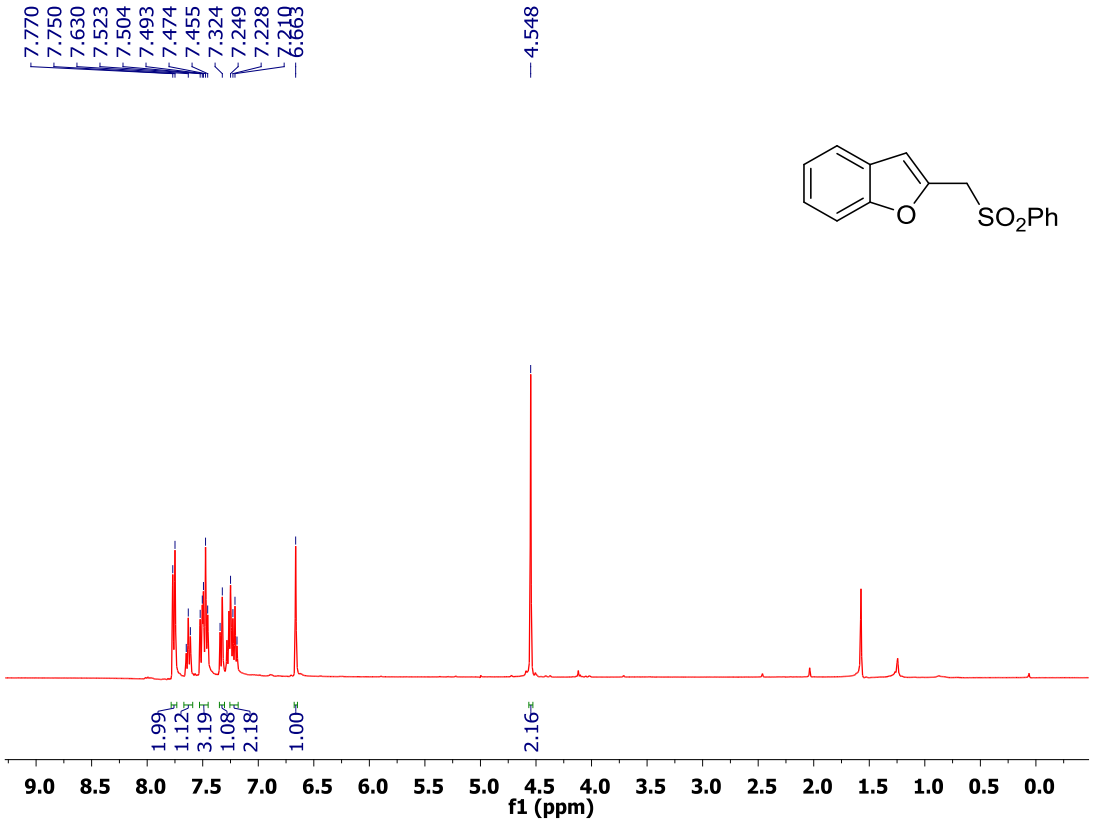

161.726
153.526
143.818
139.803
139.563
129.808
129.456
128.338
127.155
121.060
113.768
89.460
21.681
19.170
I
Ts
O
f1 (ppm)

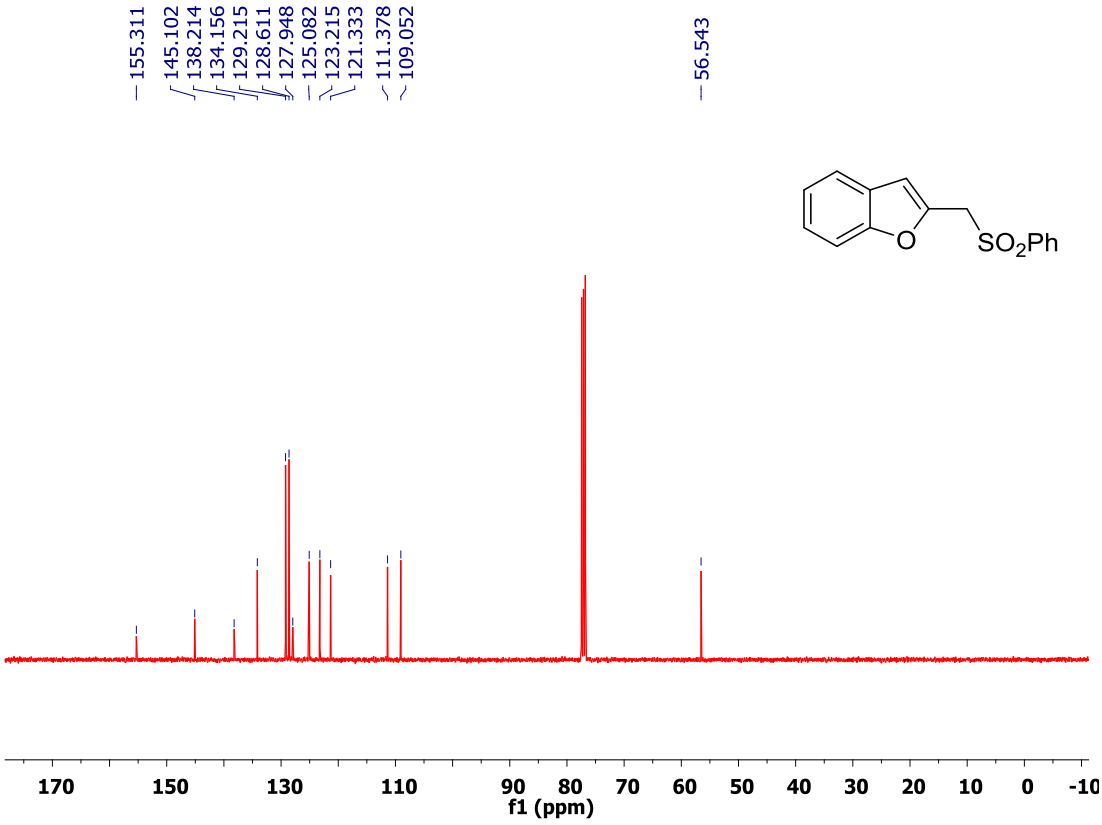

8.044
8.025
7.767
7.747
7.559
7.542
7.503
7.485
7.466
7.286
7.266
6.919
6.854
6.834
5.967
1.770
I
SO2Ph
O
2.03
1.01
1.08
2.11
1.27
1.10
1.12
1.00
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

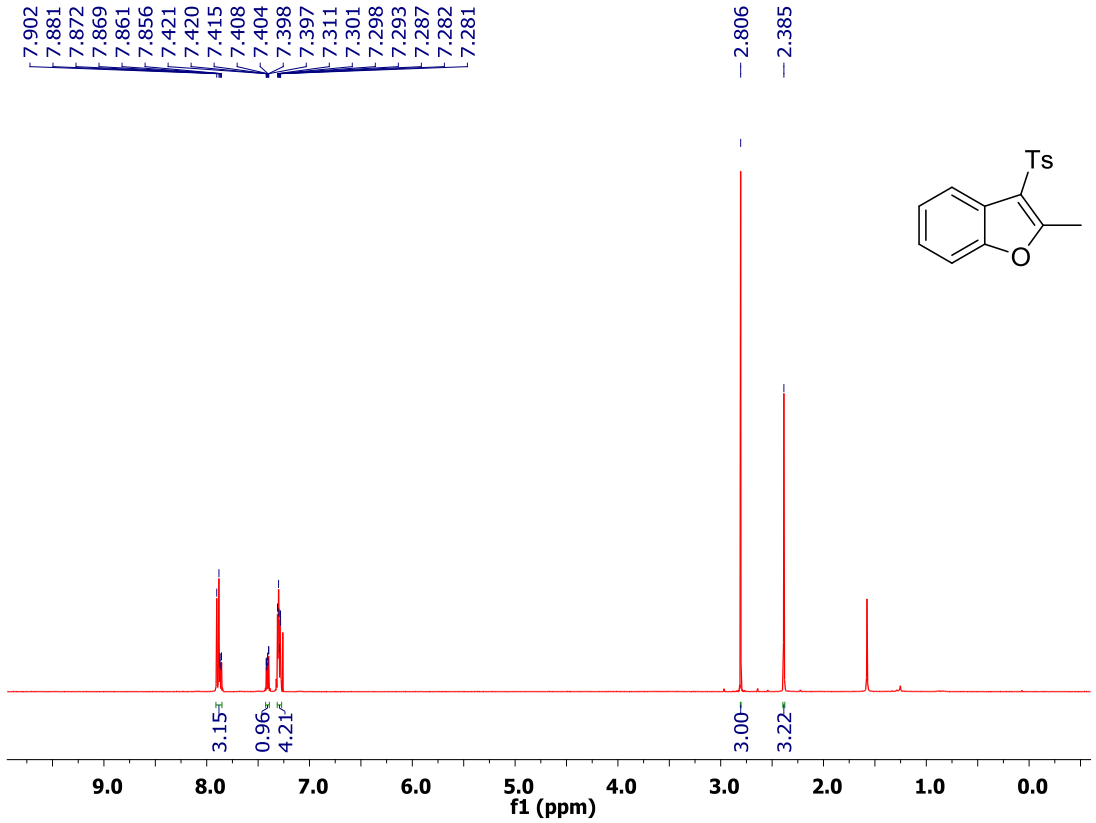

162.265
153.424
142.449
139.826
132.984
129.860
128.858
128.295
127.316
121.203
113.078
89.555
19.200
I
SO2Ph
O
170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

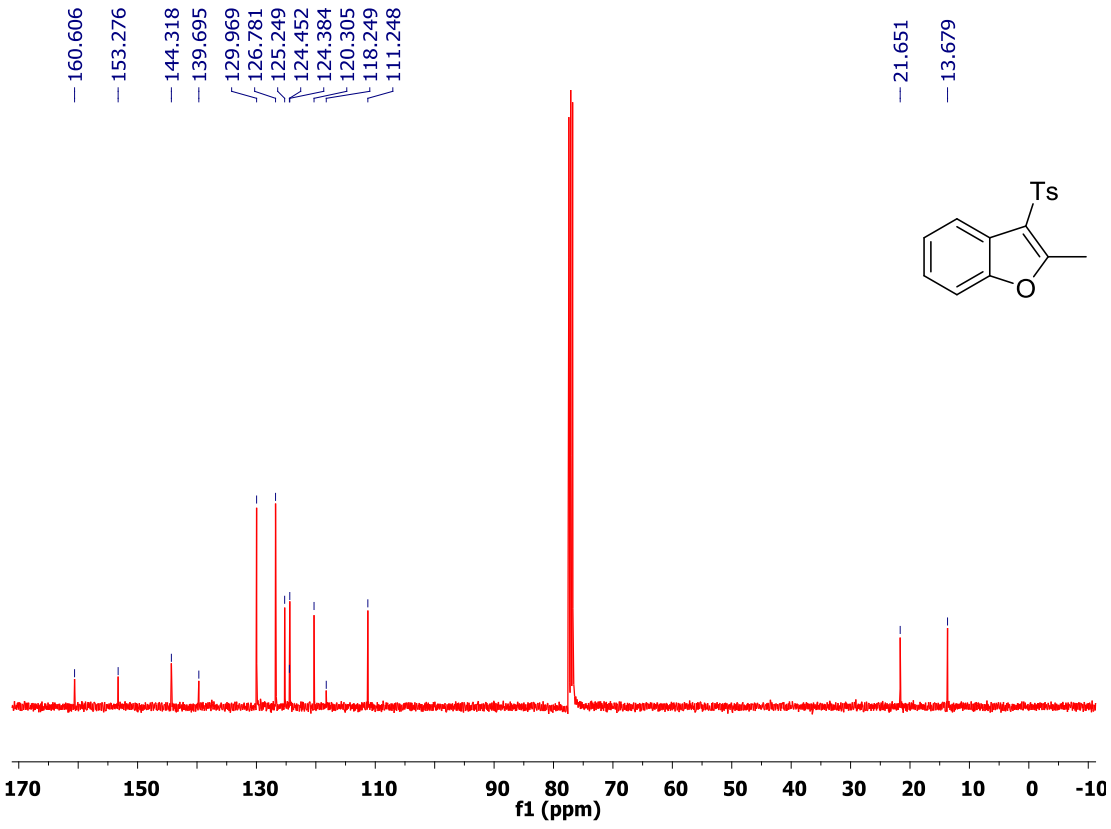

7.653
7.632
7.519
7.517
7.355
7.353
7.282
7.279
7.241
7.238
7.222
7.219
6.671
6.669
4.531
2.430
O
Ts
1.03
1.14
3.52
1.05
1.00
2.16
3.14
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

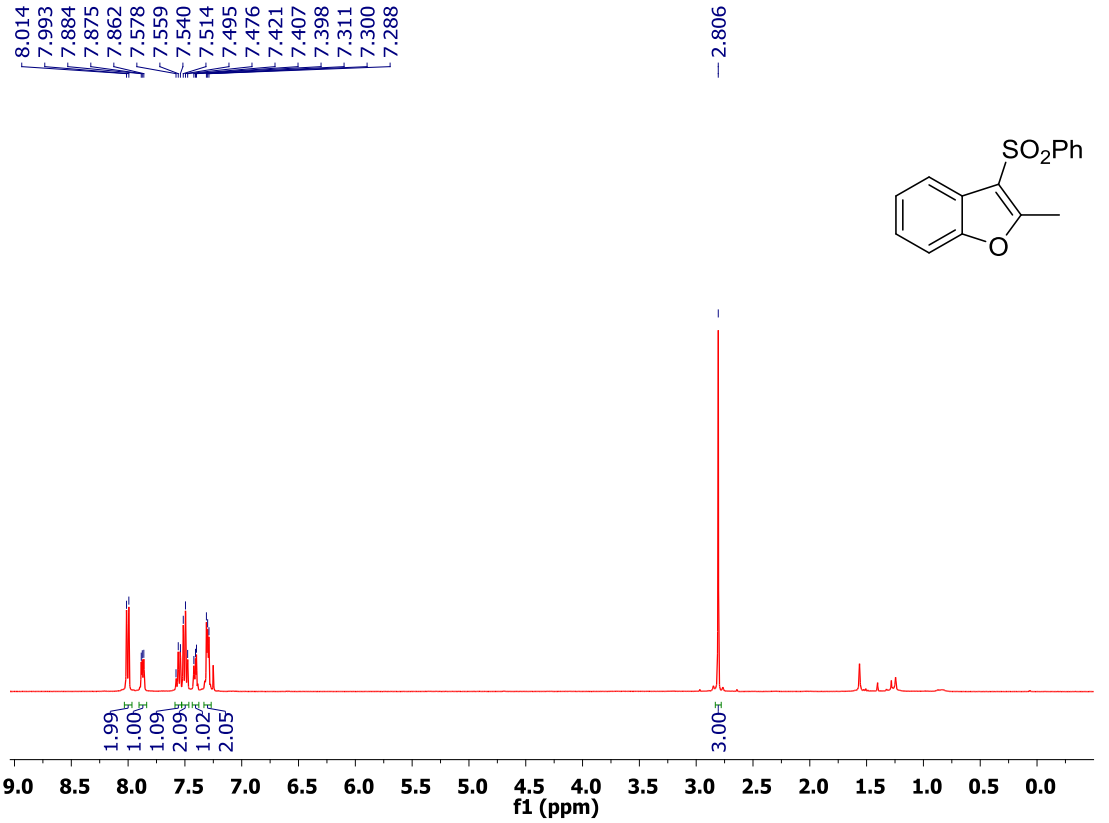

155.318
145.331
145.219
135.299
129.844
128.618
127.995
125.014
123.177
121.318
111.386
108.945
56.562
21.765
O
Ts
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

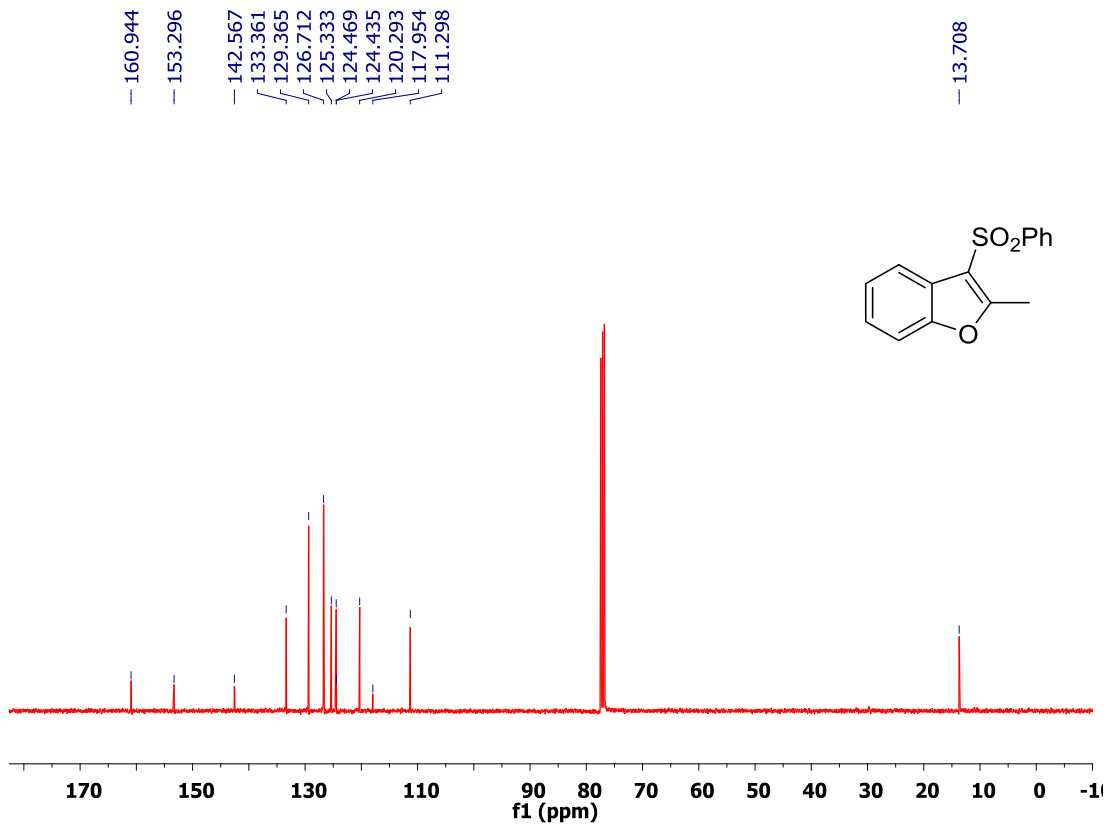

7.770
7.750
7.630
7.523
7.504
7.493
7.474
7.455
7.324
7.249
7.228
6.663
4.548
O
SO2Ph
1.99
1.12
3.19
1.08
2.18
1.00
2.16
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

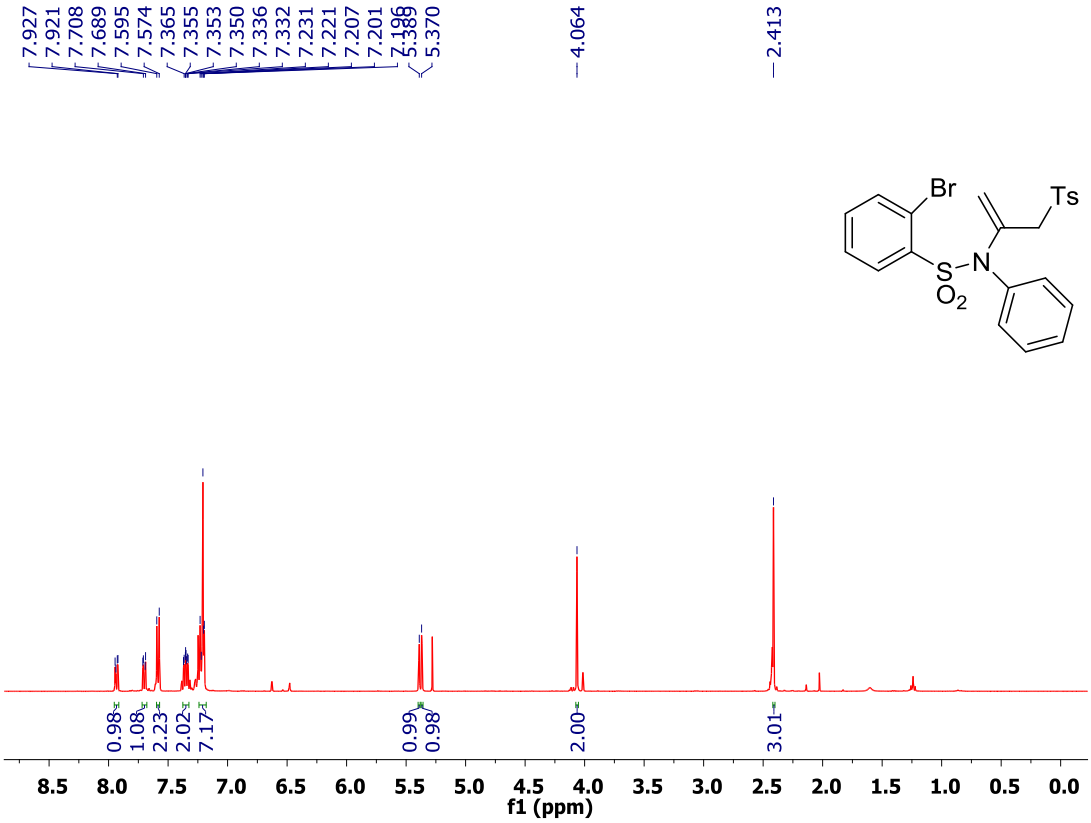

155.311
145.102
138.214
134.156
129.215
128.611
127.948
125.082
123.215
121.333
111.378
109.052
56.543
O
SO2Ph
170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

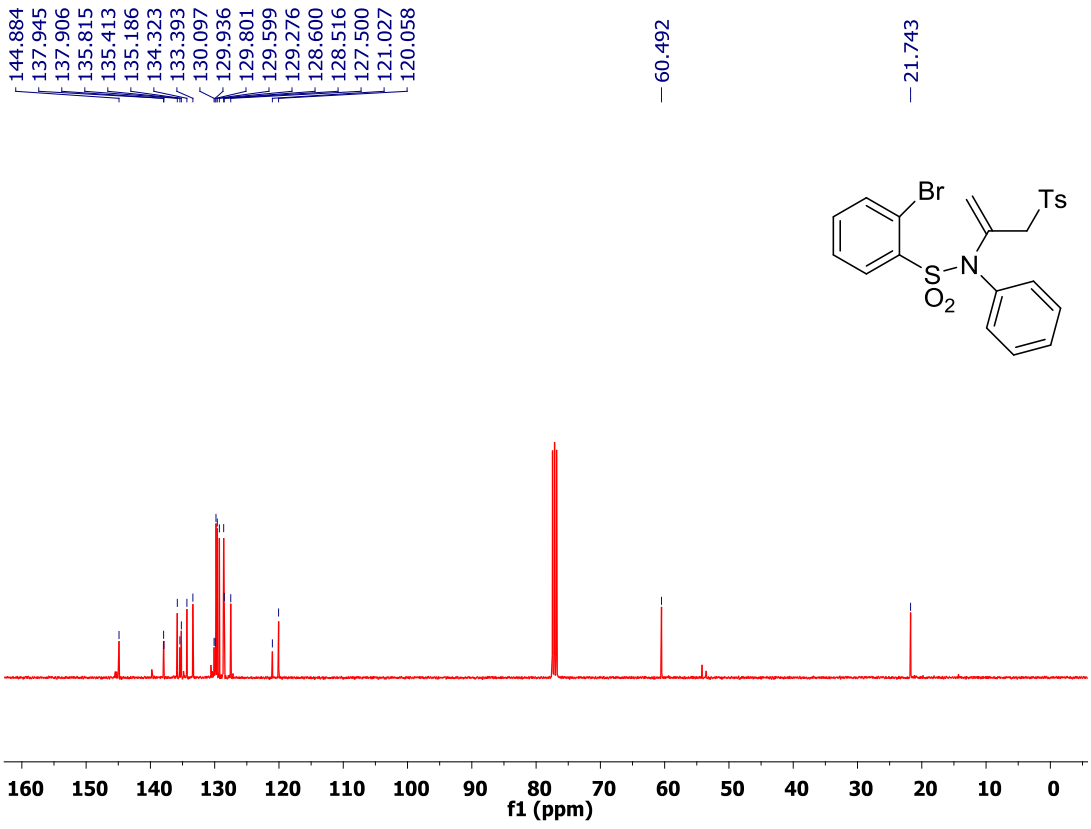

7.902
7.881
7.872
7.869
7.861
7.856
7.421
7.420
7.415
7.408
7.404
7.398
7.397
7.311
7.301
7.298
7.293
7.287
7.282
7.281
2.806
2.385
Ts
O
3.15
0.96
4.21
3.00
3.22
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

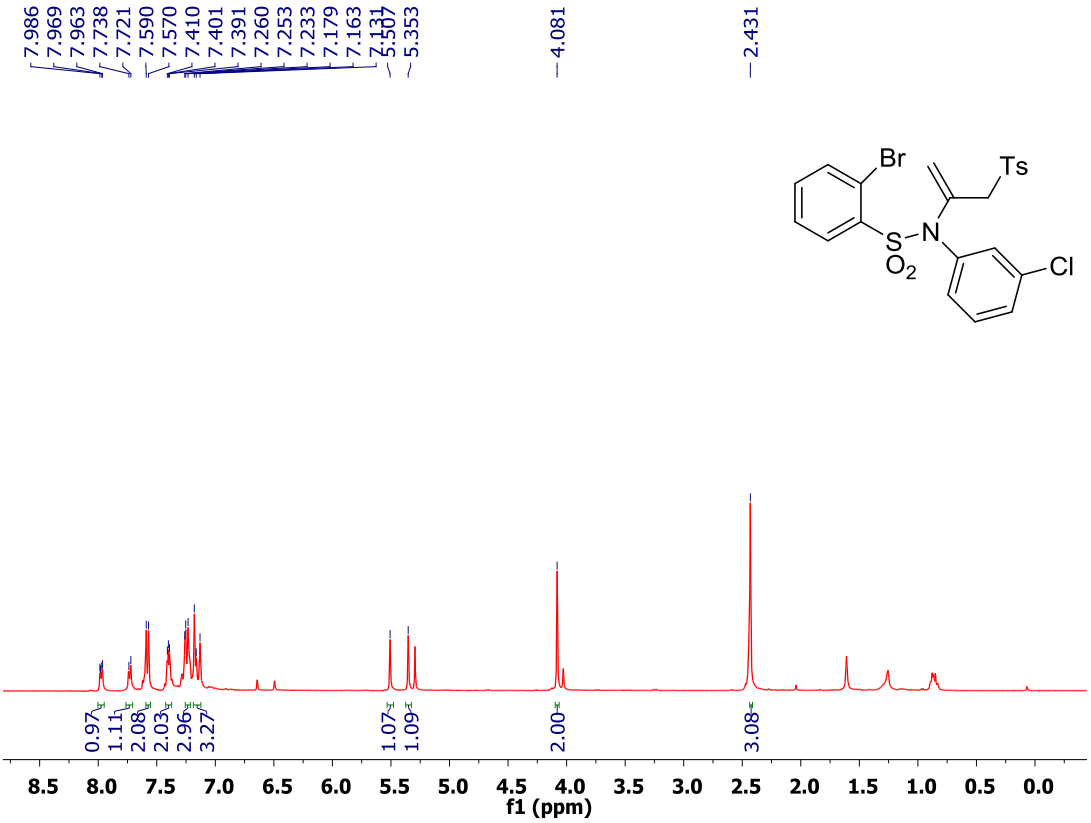

160.606
153.276
144.318
139.695
129.969
126.781
125.249
124.452
124.384
120.305
118.249
111.248
21.651
13.679
Ts
O
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

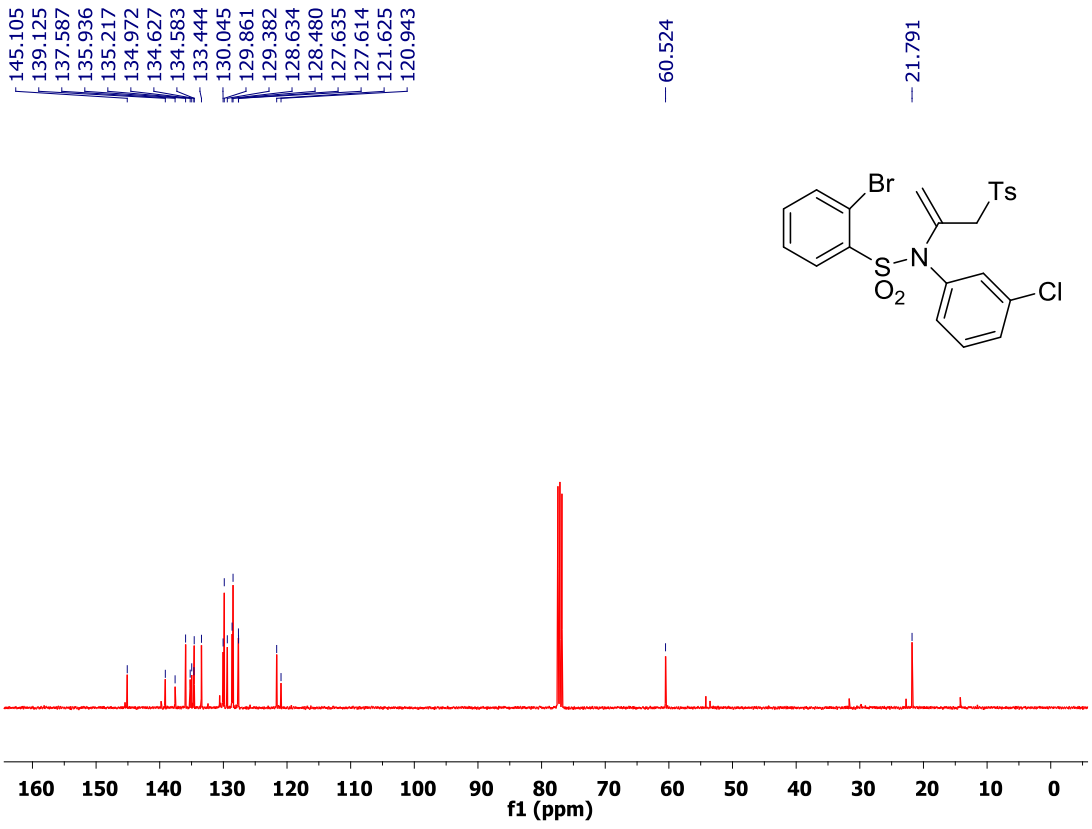

8.014
7.993
7.884
7.875
7.862
7.578
7.559
7.540
7.514
7.495
7.476
7.421
7.407
7.398
7.311
7.300
7.288
2.806
SO2Ph
O
1.99
1.00
1.09
2.09
1.02
2.05
3.00
f1 (ppm)

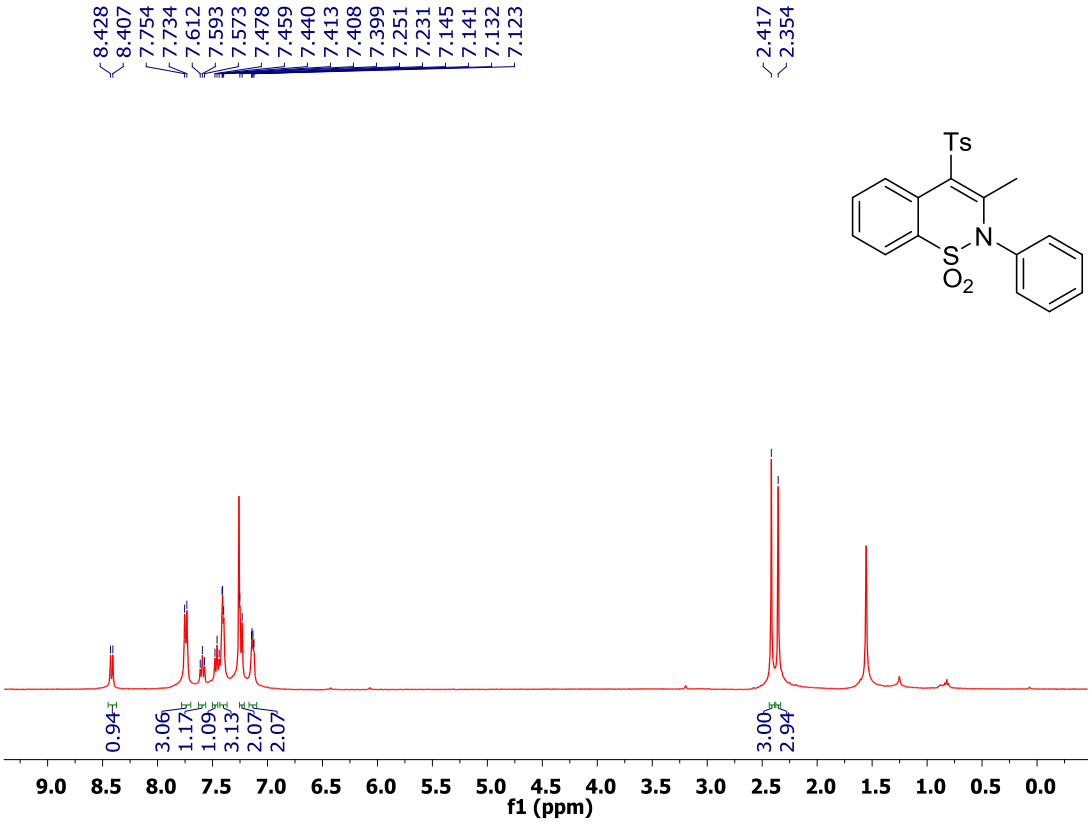

160.944
153.296
142.567
133.361
129.365
126.712
125.333
124.469
124.435
120.293
117.954
111.298
13.708
SO2Ph
O
f1 (ppm)

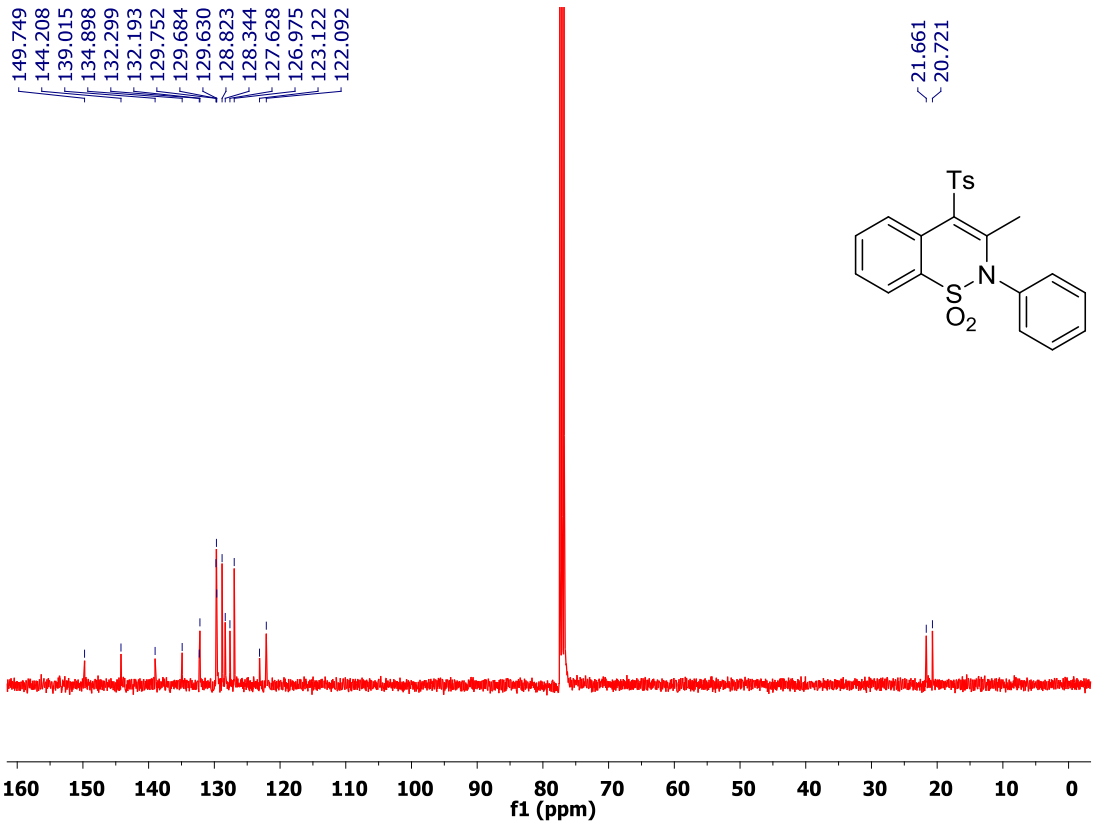

7.927
7.921
7.708
7.689
7.595
7.574
7.365
7.355
7.353
7.350
7.336
7.332
7.231
7.221
7.207
7.201
5.389
5.370
4.064
2.413
Br
Ts
S
N
O2
0.98
1.08
2.23
2.02
7.17
0.99
0.98
2.00
3.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

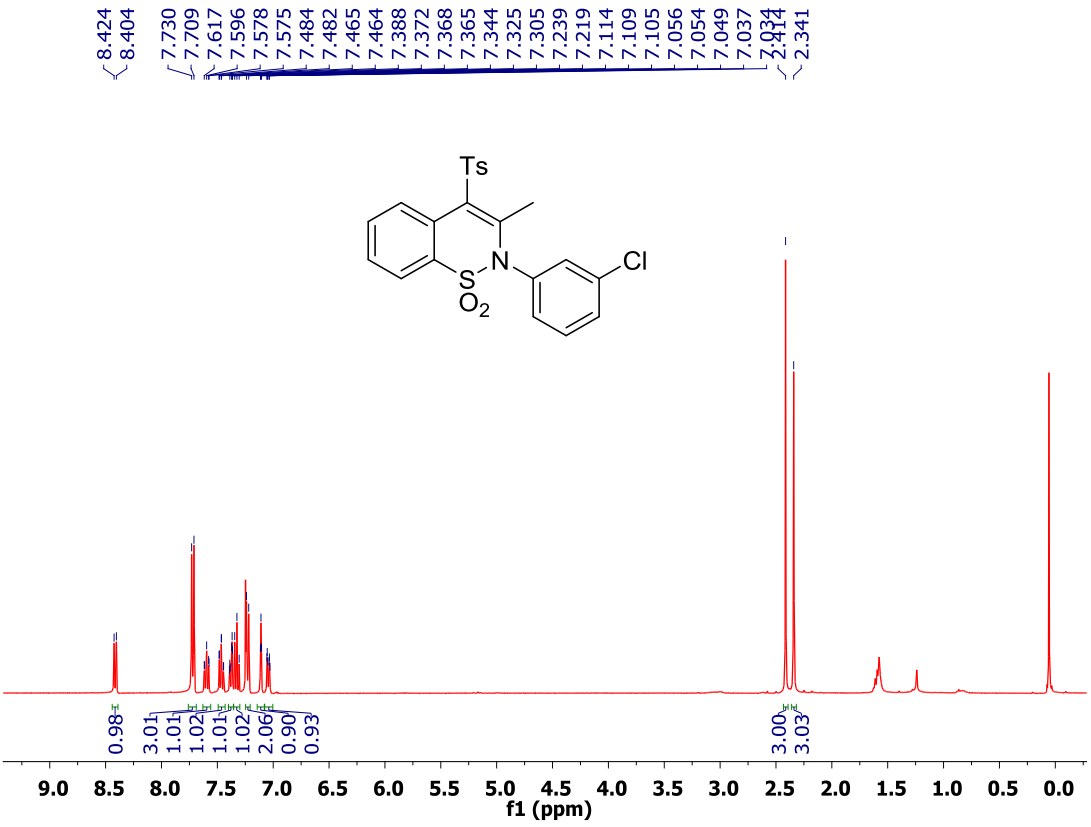

144.884
137.945
137.906
135.815
135.413
135.186
134.323
133.393
130.097
129.936
129.801
129.599
129.276
128.600
128.516
127.500
121.027
120.058
60.492
21.743
Br
Ts
S
N
O2
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

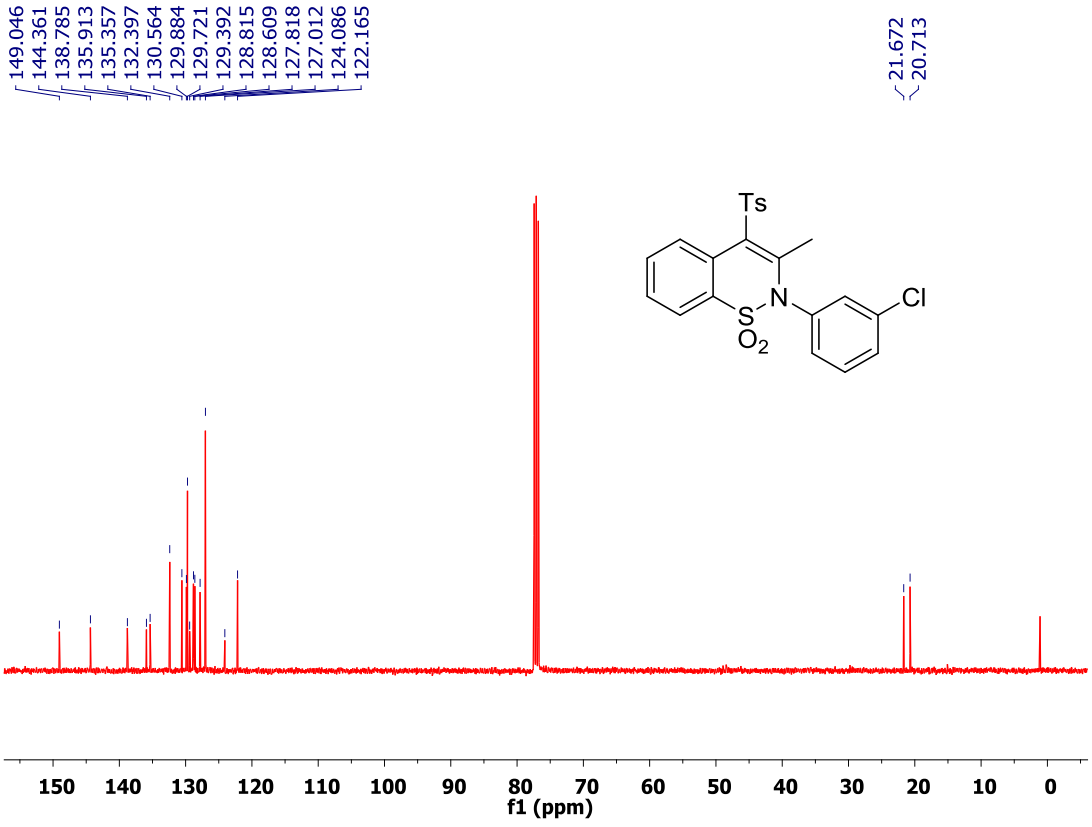

7.986
7.969
7.963
7.738
7.721
7.590
7.570
7.410
7.401
7.391
7.260
7.253
7.233
7.179
7.163
7.131
5.507
5.353
4.081
2.431
Br
Ts
S
N
O2
Cl
0.97
1.11
2.08
2.03
2.96
3.27
1.07
1.09
2.00
3.08
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


145.105
139.125
137.587
135.936
135.217
134.972
134.627
134.583
133.444
130.045
129.861
129.382
128.634
128.480
127.635
127.614
121.625
120.943
60.524
21.791
Br
Ts
S
N
O2
Cl
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.428
8.407
7.754
7.734
7.612
7.593
7.573
7.478
7.459
7.440
7.413
7.408
7.399
7.251
7.231
7.145
7.141
7.132
7.123
2.417
2.354
Ts
N
S
O2
0.94
3.06
1.17
1.09
3.13
2.07
2.07
3.00
2.94
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


149.749
144.208
139.015
134.898
132.299
132.193
129.752
129.684
129.630
128.823
128.344
127.628
126.975
123.122
122.092
21.661
20.721
Ts
N
S
O2
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.424
8.404
7.730
7.709
7.617
7.596
7.578
7.575
7.484
7.482
7.465
7.464
7.388
7.372
7.368
7.365
7.344
7.325
7.305
7.239
7.219
7.114
7.109
7.105
7.056
7.054
7.049
7.037
2.414
2.341
Ts
N
S
O2
Cl
0.98
3.01
1.01
1.02
1.01
1.02
2.06
0.90
0.93
3.00
3.03
f1 (ppm)


149.046
144.361
138.785
135.913
135.357
132.397
130.564
129.884
129.721
129.392
128.815
128.609
127.818
127.012
124.086
122.165
21.672
20.713
Ts
N
S
O2
Cl
f1 (ppm)