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# Graphical Abstract

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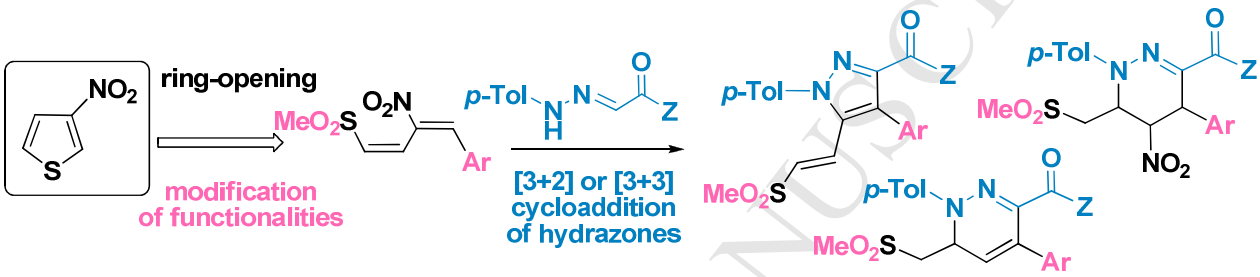

# Synthesis of Poly-functionalized Pyrazoles and Pyridazines from Nitrobutadienes: an Interesting Dichotomy of Practical Relevance

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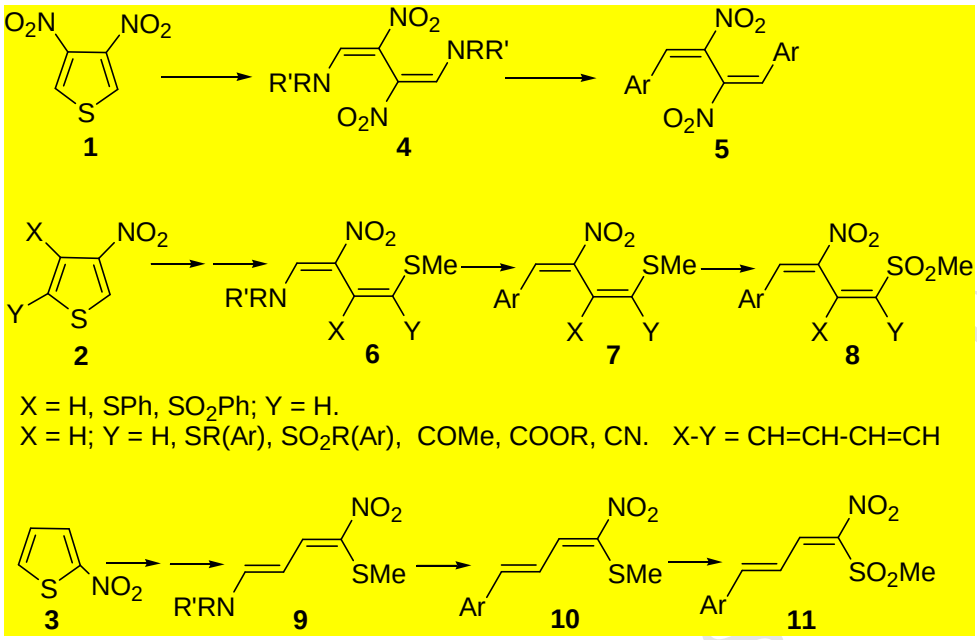
**Abstract**. The initial ring-opening of 3-nitrothiophene and further structural modifications lead to nitrobutadienic building-blocks whose synthetic usefulness in the field of heterocycles has been widely demonstrated. As a further example, the Michael addition of a hydrazone anion to the nitrovinyl moiety of nitrobutadienes generates 1,2-diazaheterocycles as the final result of an overall MIRC process. Depending on the nature of the substituents on the Michael-type acceptor and on the hydrazono nucleophile, an interesting dichotomy is observed, that leads to either 5-member or 6-member N-heterocycles with complete selectivity. The results obtained appear to be both of mechanistic and synthetic interest *e.g.* in the field of heterocycles endowed with potential pharmacological/biological activity.

*Keywords*: Nitrogen heterocycles / Michael additions / nitrobutadienes / pyrazoles / pyridazines.

## 1. Introduction

The synthesis of N-heterocycles is a goal of utmost importance in organic, bioorganic and pharmaceutical chemistry,[1] and the intermediacy of conjugated nitrodienes has been recently reviewed.[2] In this field, over the last two decades our research group has provided a valuable contribution thanks to the versatility of building-blocks such as **4**-**11** (Scheme 1). Such poly-functionalized units, most conveniently obtainable from the initial ring-opening of suitably-substituted nitrothiophenes with secondary amines,[3-5] followed by modifications of the original functionalities so as to meet specific requirements, both structural and electronic (Scheme 1), exhibit a multi-faceted behaviour:[6] this obviously encompasses the well-known reactivity of *e.g.* nitrovinyl, nitroenaminic, sulfonylvinyl systems.[7] Accordingly, the nitrobutadienes reported in Scheme 1 have provided sulfur, oxygen and/or nitrogen atoms for the construction of a number of different heterocycles in an overall ring-opening/ring-closing protocol characterized by a high atom economy.[8]

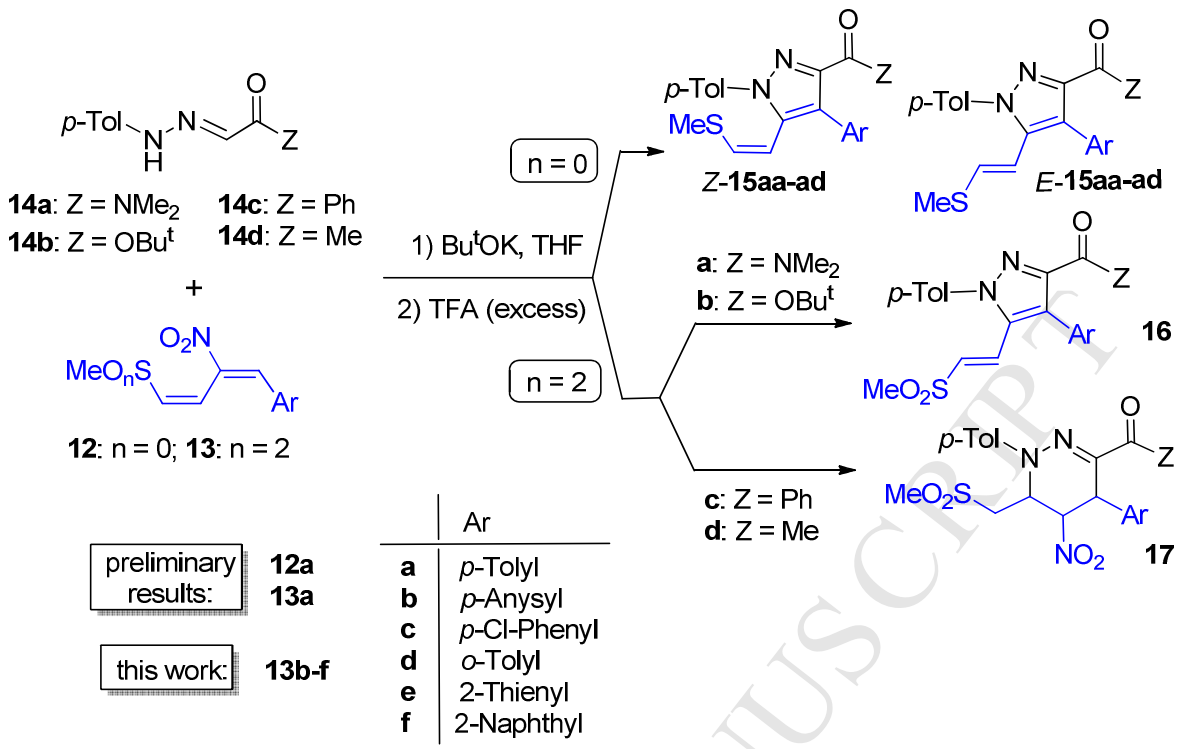



**Scheme 1**. Nitrobutadienic building-blocks from the initial ring-opening of nitrothiophenes **1-3**.

More recently, the construction of poly-functionalized heterocycles has been successfully performed by means of an initial Michael-type addition onto the nitrovinylic moiety of nitrobutadienes,[8a,d-h] a synthetic approach sometimes indicated as a Michael addition Induced Ring Closure (MIRC) process.[9]

In this line, preliminary results[10] on the reaction between the model nitrobutadienes **12a** and **13a** (Scheme 1, Ar = *p*-Tol, X = Y = H in **7** and **8**, respectively), purposely chosen in order to provide two significantly different electronic distribution patterns on the diene moiety, and the anions of hydrazones **14a-d**, have enlightened the possibility to apply the initial Michael-type addition strategy also to the preparation of heterocycles containing two adjacent nitrogen atoms (cf. Scheme 2). Actually, with the exception of some pyrazolines,[6b] similar structures were still lacking in our expanding "pool" although pyrazoles, in particular, surely represent appealing targets: the wide range of biological and pharmacological activities displayed by such molecules (among which: anti-hyperglycemic, anti-inflammatory, anti-obesity, or antitumoral[11]) accounts for the impressive amount of literature which continuously deals with relevant synthetic or applicative aspects.[12]

On the grounds of the preliminary results, it seemed therefore worthwhile to fully investigate the behaviour of nitrobutadienes **13** in order to better define the scope of the access to highly-functionalized pyrazoles or pyridazines such as **16** or **17**, respectively, and also to gain more information on the origin of the dichotomic behaviour that generates different N-heterocyclic structures. Relevant results are reported hereinafter.




**Scheme 2**. Pyrazoles **15** and **16**, and tetrahydropyridazines **17** from the reaction between **12a** and **13a-g** with the anions of α-oxohydrazones **14a-d**. Data for **12a** and **13a** are from a preliminary communication.[10]

## 2. Results and discussion

### *Dichotomic behaviour of nitrosulfonylbutadienes 13*

As shown in Scheme 2, the behavior of nitrobutadienes **12a** and **13a** towards the anions (generated with Bu$^t$OK) of hydrazones **14a-d** in THF at -78 °C turns out to be markedly different. On one side, sulfide **12a** effectively builds-up a pyrazole nucleus independently of the nature of Z in the employed hydrazone, with a partial inversion of the exocyclic C=C double-bond configuration.[10]

Much more interestingly, depending on the nature of Z, sulfone **13a** produces two different heterocycles. The latter reaction was therefore considered to deserve a deeper insight and was first of all extended to other substrates with different Ar moieties. The results obtained by treatment of nitrobutadienes **13b-f** with the α-oxohydrazones **14a-d** (Scheme 2, Tables 1 and 2) cleanly line-up with the preliminary ones for the model *p*-tolyl derivative **13a**: whichever the nature of Ar, hydrazones **14a**,**b** (Z = $NMe_2$ and OBu$^t$, respectively) exclusively furnish the tetra-substituted pyrazoles **16** (Table 1), while **14c**,**d** (Z = Ph and Me, respectively) exclusively lead to the likewise

fully-substituted tetrahydropyridazines **17** (Table 2). Interestingly enough, not even traces of pyridazine derivatives have ever been observed for similar reactions on sulfide **12a**.[10]

**Table 1**. Tetra-substituted pyrazoles **16** from the reaction of Scheme 2.[a]

| Entry | Substrate | Ar in 13 | Hydrazone | Z in 14 | Pyrazole 16 (Yields %)[b] |
|---|---|---|---|---|---|
| 1 | **13a** | *p*-Tolyl | **14a** | $NMe_2$ | **16aa** (98%)[c] |
| 2 | " | " | **14b** | $OBu^t$ | **16ab** (50%)[c] |
| 3 | **13b** | *p*-Anisyl | **14a** | $NMe_2$ | **16ba** (54%) |
| 4 | " | " | **14b** | $OBu^t$ | **16bb** (63%) |
| 5 | **13c** | *p*-Cl-Phenyl | **14a** | $NMe_2$ | **16ca** (50%) |
| 6 | " | " | **14b** | $OBu^t$ | **16cb** (71%) |
| 7 | **13d**[d] | *o*-Tolyl | **14a** | $NMe_2$ | **16da** (74%; 88:12)[e] |
| 8 | **13e**[d] | 2-Thienyl | **14a** | $NMe_2$ | **16ea** (93%) |
| 9 | **13f** | 2-Naphthyl | **14a** | $NMe_2$ | *f* |

[a] Reaction conditions (if not otherwise stated): *i)* **14** (1 equiv with respect to **13**), $Bu^tOK$ (1 equiv) in THF/Ar, -78 °C, 30'; *ii)* **13** (0.1 M in THF), 1-2 h; *iii)* TFA (5 equiv), -78 °C (2h) to rt, overnight. [b] Yields of chromatographically pure products. [c] Data from ref. 10. [d] Quenching with 20 equiv of TFA. [e] *Z:E* ratio, as judged by $^1H$ NMR analysis. [f] Complex final mixture.

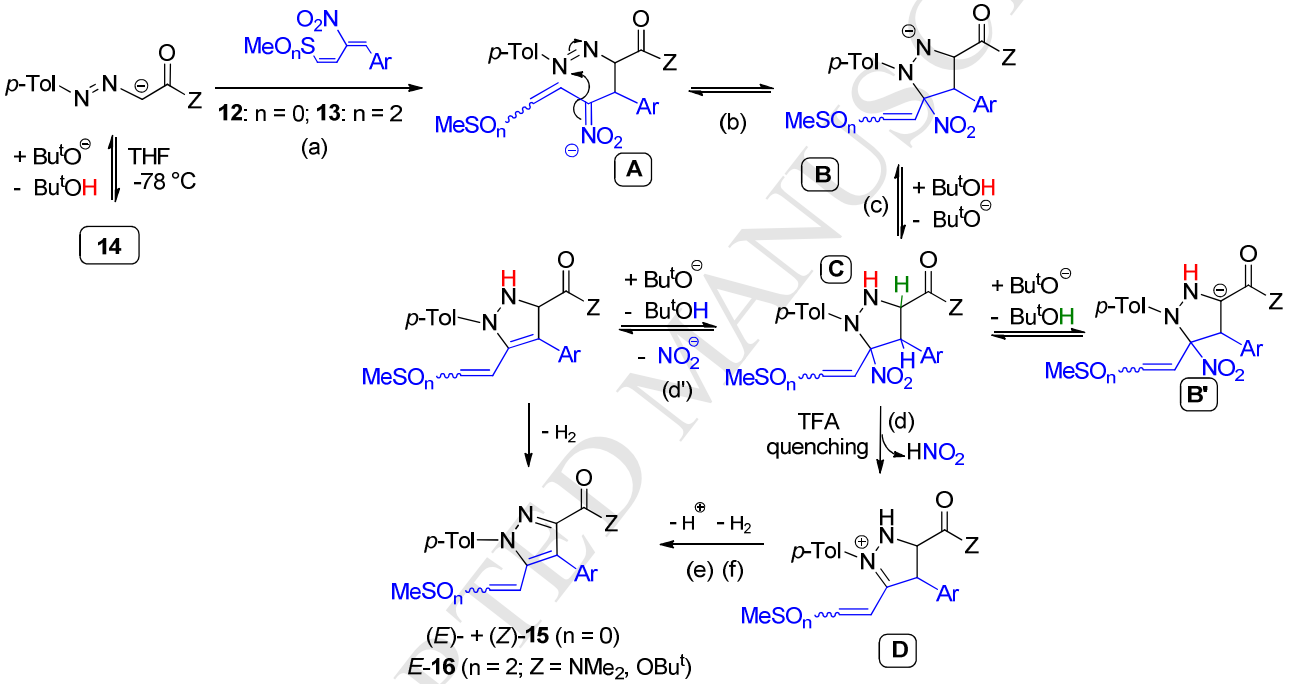
**Table 2**. Tetra-substituted tetrahydropyridazines **17** from the reaction of Scheme 2.[a]

| Entry | Substrate | Ar in 13 | Hydrazone | Z in 14 | Pyridazine 17 (Yields %)[b] |
|---|---|---|---|---|---|
| 1 | **13a** | *p*-Tolyl | **14c** | Ph | **17ac** (98%)[c] |
| 2 | " | " | **14d** | Me | **17ad** (98%)[c] |
| 3 | **13b** | *p*-Anisyl | **14c** | Ph | **17bc** (75%) |
| 4 | " | " | **14d** | Me | **17bd** (90%) |
| 5 | **13c** | *p*-Cl-Phenyl | **14c** | Ph | **17cc** (75%) |
| 6 | " | " | **14d** | Me | **17cd** (75%) |
| 7 | **13d** | *o*-Tolyl | **14c** | Ph | **17dc** (68%) |
| 8 | " | " | **14d** | Me | **17dd** (69%) |
| 9 | **13f** | 2-Naphthyl | **14c** | Ph | *d* |
| 10 | " | " | **14d** | Me | **17fd** (98%) |

[a] Reaction conditions: *i)* **14** (1 equiv with respect to **13**), $Bu^tOK$ (1 equiv) in THF/Ar, 0 °C, 30'; *ii)* **13** (0.1 M in THF), 0.5-1 h; *iii)* TFA (5 equiv), 0 °C to rt, 1 h. [b] Yields of chromatographically pure products. [c] Data from ref. 10. [d] Complex final mixture.

As far as tetrahydropyridazines **17** are concerned, we noticed that a considerable yield improvement could be obtained by performing both deprotonation of **14** and addition of **13** at 0 °C, concomitantly reducing the time for quenching to 1 h. Yields reported in Table 2 are those obtained in such optimized conditions.

As outlined in the preliminary communication,[10] a reasonable mechanistic pathway to the pyrazole nucleus can be envisaged as depicted in Scheme 3, whereby a Michael-type addition of the hydrazone anion to the nitrovinyl moiety of **12** or **13** (step *a*) is followed by the intramolecular attack of the resulting nitronate **A** onto the diazo group (step *b*),[13] which exploits the driving force represented by intramolecularity.




**Scheme 3.** Proposed mechanism for the formation of pyrazoles **15** and **16**.

From pyrazolidine **C**, aromatization could in principle be achieved via base-catalyzed β-elimination of nitrous acid (step *d'*), followed by oxidation: the latter presumably accomplishable, in the absence of external added oxidants, by the cleaved nitrite anion itself, as already verified in previous different instances.[8a] Nonetheless, in such conditions, the process proves to be quite sluggish, leading to partial decomposition and to a meagre overall balance.

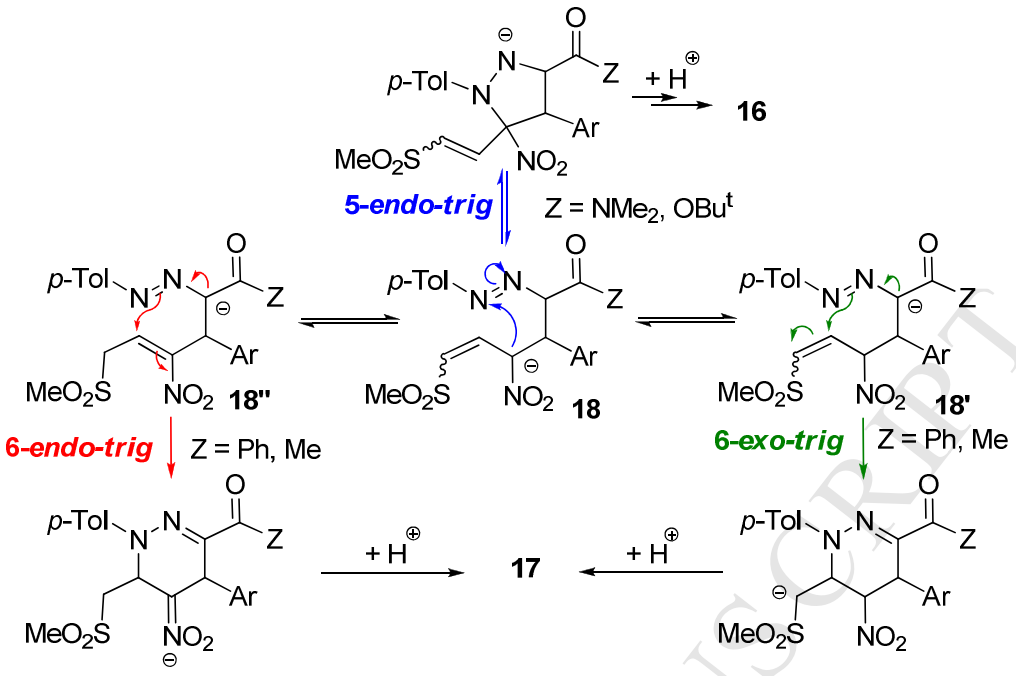
On the other hand, acidic quenching (excess TFA) after disappearance of substrate, effectively drives the reaction to completion favouring[13a] the elimination of nitrous acid (step *d*) by protonation of the nitro group; deprotonation and oxidation (by nitrous acid: see above) of the resulting iminium cation (**D**) (steps *e* and *f*) lead to the final pyrazole derivative. The quantitative

protonation of the pyrazolidine anion (**B**, or possibly **B'**) should also lead to a more efficient result, minimizing alternative, decomposition pathways.

The observed configurational scrambling at the exocyclic double bond, only partial in the case of **15a**,[10] but complete in the case of **16** (with the exception of **16da**: Table 1, entry 7), may be rationalized considering that the intermediate open-chain nitronate **A** may delocalize the negative charge onto the adjacent double bond: a delocalization which is expected to be more important for sulfones **13** than for sulfides **12**. It should also be considered that the closure of the pyrazolidine nucleus is probably a slow step, due to the low electrophilic character of the diazo group: thus the anion could be allowed to equilibrate according to the relevant stability of the two stereoisomers, and much more so for the sulfones which, thanks to effective charge delocalization, should experience a longer lifetime in the reaction conditions. The preference for the *E* configuration shown by **16** is predictably due to steric reasons, and steric factors most likely play a role in determining the only partial isomerization in the case of the hindered *o*-methylphenyl derivative (**16da**).

The most intriguing aspect of the system under study is surely the dichotomic behaviour (Scheme 2) displayed by sulfones **13**, as mirrored by the complete chemoselectivity observed in dependence of the nature of Z in the COZ moiety of the hydrazone employed: the anions of the α-hydrazonoamide **14a** and of the α-hydrazonoester **14b** giving pyrazoles **16** in good yields, while the anions of α-hydrazonoketones **14c** and **14d** leading to tetrahydropyridazines **17** (Scheme 2), almost exclusively as single diastereoisomers out of the three possible ones (for configurational attribution see further in the text).

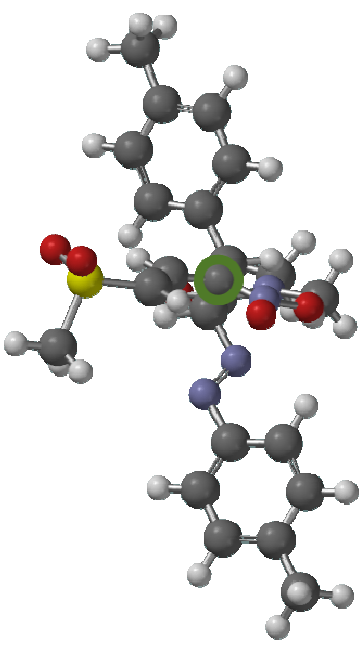
In order to explain such a dichotomy, we considered (Scheme 4) that the nitronate **18** (i. e. nitronate **A** of Scheme 3, with n = 2), should be particularly stabilized by charge-delocalization on both the nitro group, and the sulfonylvinyl moiety (see also above in the text). Such an occurrence reasonably allows the anion a longer lifetime, so that, as an alternative to the expected unfavoured 5-*endo*-*trig* cyclization to pyrazole, it could also equilibrate with **18'** or **18''** (Scheme 4) by transfer of the negative charge to the position adjacent to the COZ moiety. The new anion (**18''** being most likely the preferred structure, on the grounds of the alleged higher stability of a nitrovinyl with respect to a sulfonylvinyl moiety [8d,e,g,h]) seems to have definitely more chance to exist when the carbonyl involved is that of a ketone, rather than that of an amide or of an ester, due to the higher ability of the former to contribute to the stabilization of an adjacent negative charge.



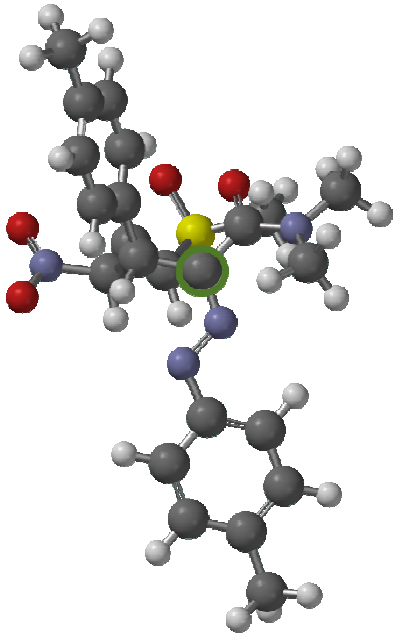

**Scheme 4.** The proposed rationale behind the dichotomic behavior of nitrobutadienes **13a-e**.

On the tautomerized **18''** (or **18'**) anion, an electronically-inverted cyclization process becomes possible, whereby a nucleophilic hydrazone anion couples with an electrophilic nitrovinyl (or sulfonylvinyl) moiety, easily providing a six-membered ring: thus, 6-*endo-trig* or, possibly, 6-*exo-trig* cyclization routes are in principle recognizable, leading to the same final outcome **17**.

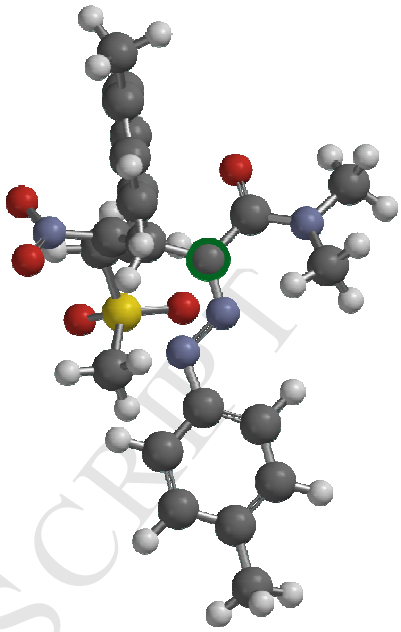
To confirm our hypothesis, we carried out quantum-mechanical calculations[14] on the carbanionic intermediates **18**, **18'** and **18''** for the model amide (**aa**) and methyl ketone (**ad**) derivatives. As shown in Chart 1, for the ketone derivatives there is no substantial difference among the relative stabilities of the three tautomeric anions, and therefore in the acidities of the corresponding conjugated acids. However, in the case of the amide **18aa** is significantly more stable than the other ones: this brings the acidity of the hydrogen in α to the nitro group to be considerably higher (more than 4 units of p$K_a$[15]) than that of the hydrogen in α to the amido group.



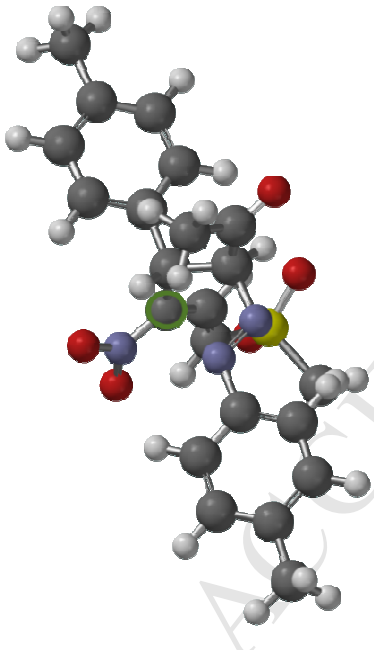
**18aa:** Reference



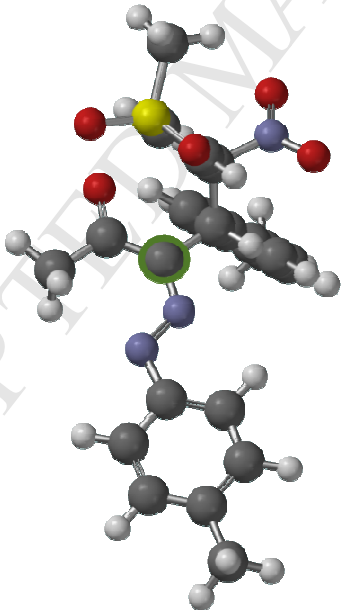
**18'aa:** ΔE = + 15.7 kJ/mol
Δp$K_a$ = + 4.24



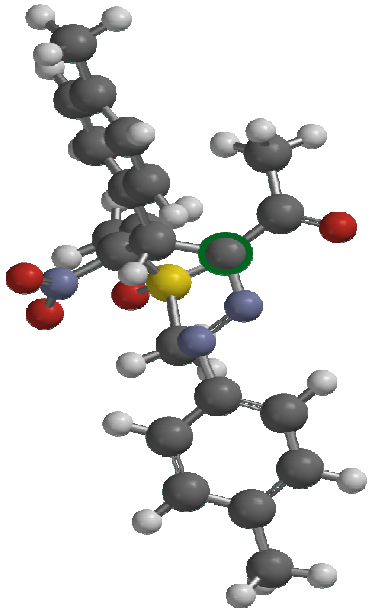
**18''aa:** ΔE = + 15.1 kJ/mol
Δp$K_a$ = + 4.08



**18ad:** Reference



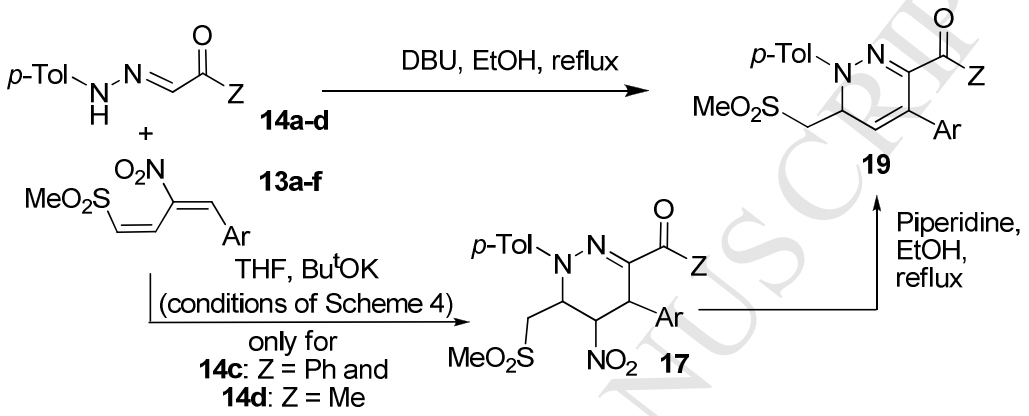
**18'ad:** ΔE = - 0.2 kJ/mol
Δp$K_a$ = - 0.05



**18''ad:** ΔE = - 0.4 kJ/mol
Δp$K_a$ = - 0.11

**Chart 1**. Results of the geometry optimization and energy minimization on **18aa**, **18'aa** and **18''aa** and on **18ad**, **18'ad** and **18''ad**.

In line with the proposed rationale, it is reasonable that the competition between the two pathways may be affected by the choice of the reaction medium and, as the formation of a tetrahydropyridazine needs an efficient proton transfer, a protic solvent would conceivably direct the reaction towards **17**, accelerating the proton transfer from **18** to **18'** or **18''**. Interestingly, the treatment of an equimolar **13** + **14** mixture with DBU (1 equiv) in refluxing ethanol effectively leads to the dihydropyridazino ring of **19**, independent of the nature of COZ (Scheme 5 and Table 3).




**Scheme 5**. Dihydro- and tetrahydro-pyridazines **19** and **17** from reactions of **13** and 1**4**.

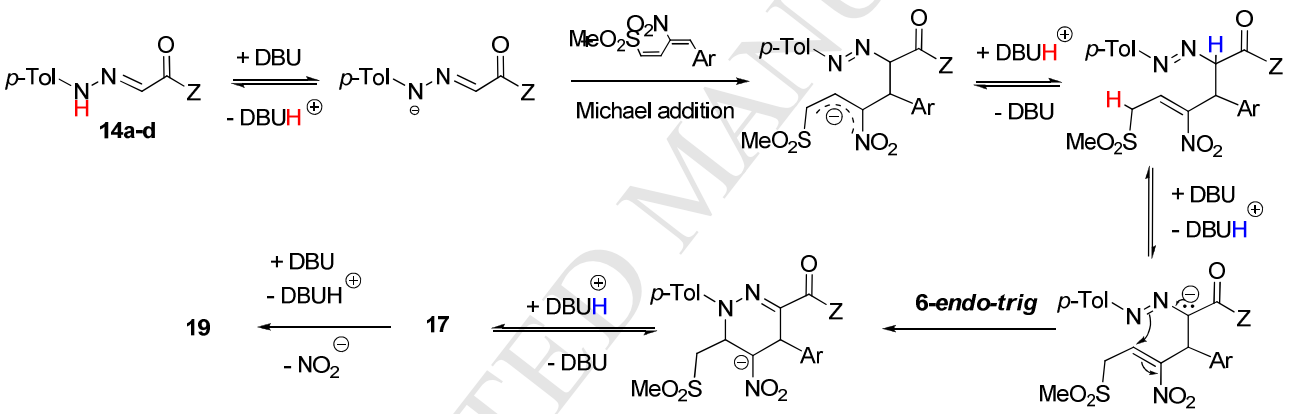
**Table 3**. Dihydropyridazines **19** from the reaction of **13** and **14** with DBU in EtOH (Scheme 5).[a]

| Entry | Substrate | Ar in 13 | Hydrazone | Z in 14 | Dihydropyridazines (Yields %)[b] |
|---|---|---|---|---|---|
| 1 | **13a** | *p*-Tolyl | **14a** | $NMe_2$ | **19aa** (71%) |
| 2 | " | " | **14b** | $OBu^t$ | **19ab** (80%) |
| 3 | " | " | **14c** | Ph | **19ac** (72%) |
| 4 | " | " | **14d** | Me | **19ad** (81%) |
| 5 | **13b** | *p*-Anisyl | **14a** | $NMe_2$ | **19ba** (52%) |
| 6 | " | " | **14b** | $OBu^t$ | **19bb** (87%) |
| 7 | " | " | **14c** | Ph | **19bc** (99%) |
| 8 | " | " | **14d** | Me | **19bd** (84%) |
| 9 | **13c** | *p*-Cl-Phenyl | **14a** | $NMe_2$ | **19ca** (70%) |
| 10 | " | " | **14b** | $OBu^t$ | **19cb** (88%) |
| 11 | " | " | **14c** | Ph | **19cc** (78%) |
| 12 | " | " | **14d** | Me | **19cd** (95%) |
| 13 | **13f** | 2-Naphthyl | **14a** | $NMe_2$ | **19fa** (63%) |
| 14 | " | " | **14c** | Ph | **19fc** (68%) |
| 15 | " | " | **14d** | Me | **19fd** (68%) |

[a] Reaction conditions: **13** (50 mg), **14** (1 equiv), DBU (1 equiv) in EtOH (3 mL), reflux, 1h; aqueous quenching.
[b] Yields of isolated products.

The most likely precursor of **19** is represented by the tetrahydropyridazine **17**, which would undergo β-elimination of $HNO_2$ in the basic medium to afford the final conjugated azadiene. To confirm this very last point, we have successfully verified the feasibility of $HNO_2$ elimination from **17ac** and **17ad** to obtain **19ac** and **19ad** by means of an alternative two-step route: the use of piperidine in refluxing ethanol leading to an almost quantitative smooth conversion in both cases (see Scheme 5).

For the formation of dihydropyridazines **19**, the sequence of Scheme 6 can be envisaged, in which the base guarantees, whatever the nature of Z, the proton exchange that eventually leads to the 6-*endo-trig* cyclization and $HNO_2$ elimination; note that, overall, only one equivalent of base is required to drive the reaction to completion.

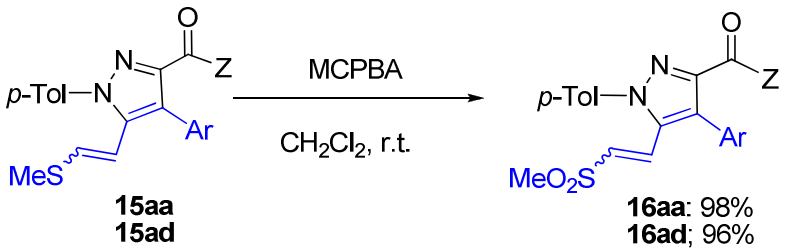



**Scheme 6**. DBU-assisted proton-transfers in ethanol at reflux.

This methodology also gives the 6-membered pyridazine system when the COZ is an amide or an ester function, so bypassing the obstacle represented by the dichotomic behavior described in Scheme 2.

On the other hand, it should be noted that the other drawback, i.e. the failure to obtain pyrazoles when COZ in **14** is a ketonic moiety (Z = alkyl, aryl), is in turn very easily bypassed, insofar as pyrazoles **16** can be obtained (although as diastereomeric mixtures) by oxidation of the methylthio substituent in **15**, typically employing MCPBA in dichloromethane (Scheme 7).

Successful oxidation tests have been carried out on the diastereomeric mixtures isolated from the reaction of Scheme 2:[10] almost quantitative yields are coupled with a complete stereospecificity, the *Z* / *E* ratio of sulfides being recovered unaltered in the corresponding sulfones.

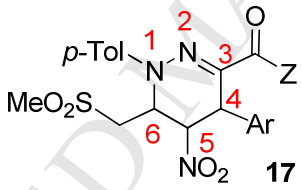



**Scheme 7**. Sulfonylvinylpyrazoles **16** obtained by oxidation of the corresponding sulfides **15**.

***Relative Configuration attribution for tetrahydropyridazines 17***

As already stated above, tetrahydropyridazines **17** are obtained as a single racemic diastereoisomer out of the possible four. The relative configurations can be assigned based on the $^1$H NMR coupling constants ($J_{(4H\text{-}5H)}$ and $J_{(5H\text{-}6H)}$). The available data (collected in Table 4) show that, when changing COZ from benzoyl to acetyl, chemical shifts and/or coupling constants inherent to protons 4-H, 5-H, 6-H in the heterocyclic ring undergo some significant variations.

**Table 4**. $^1$H NMR spectroscopic data[a] for the tetrahydropyridazine ring protons of the racemic **17**.




| 17 | COZ | Ar | $\delta$(4-H)[b] | $\delta$(5-H)[c] | $\delta$(6-H)[d] | $J_{(4H\text{-}5H)}$ | $J_{(5H\text{-}6H)}$ |
|---|---|---|---|---|---|---|---|
| **17ac** | Benzoyl | *p*-Tolyl | 4.97 | 5.35 | 5.45 | 9.9 | 4.0 |
| **17bc** | " | *p*-Anisyl | 4.95 | 5.35 | 5.44 | 9.6 | 4.2 |
| **17cc** | " | *p*-Cl-Phenyl | 4.97 | 5.33 | 5.47 | 9.9 | 3.9 |
| **17dc** | " | *o*-Tolyl | 5.19 | 5.43 (2H, m) | | 9.0 | no det. |
| **17ad** | Acetyl | *p*-Tolyl | 4.73 | 5.28 | 5.13 | 7.7 | 3.9 |
| **17bd** | " | *p*-Anisyl | 4.72 | 5.28 | 5.13 | 7.5 | 3.9 |
| **17cd** | " | *p*-Cl-Phenyl | 4.73 | 5.25 | 5.18 | 8.1 | 3.9 |
| **17dd** | " | *o*-Tolyl | 4.93 | 5.35 | 5.10 | 6.8 | 3.9 |
| **17fd** | " | 2-Naphthyl | 4.93 | 5.42 | 5.26 | 8.1 | 3.9 |

[a] Chemical shifts $\delta$ in ppm from internal TMS, coupling constants *J* in Hz, solvent $CDCl_3$. No long-range coupling was detected at 300 MHz. [b] Doublet. [c] Doublet of doublets. [d] Doublet of partially overlapped triplets (apparent quadruplet).

In particular, as far as the coupling constants are concerned, while the $J_{(4H\text{-}5H)}$ values seem definitely to correspond to a *trans* axial-axial coupling for COPh derivatives ($J_{(4H\text{-}5H)}$ = 9.0-9.9),

some doubts arise for COMe ones; on the other hand, $J_{(5H\text{-}6H)}$ definitely seem in agreement with a *cis* relationship for both *series* of compounds. The doubt about the relative stereochemistry at C-4 and C-5 in the acetyl derivatives was definitely solved by the X-ray structural analysis of **17bd** (Figure 1) as a representative model system for the series.

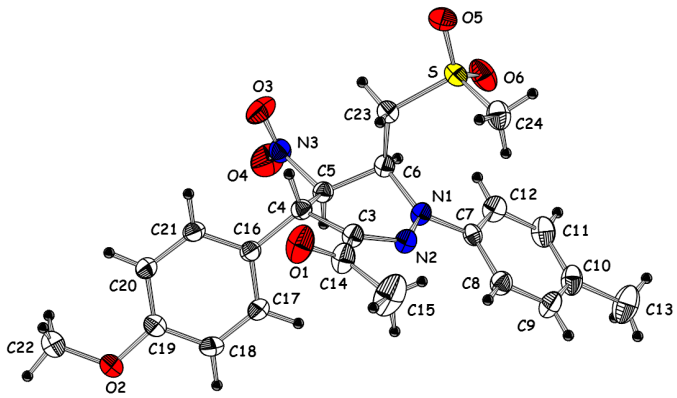



**Figure 1**. Ortep of **17bd**.

## Conclusions

The biological/pharmacological interest in N-heterocyclic structures fosters a continuous approach to new synthetic pathways overcoming limitations and/or drawbacks of known protocols. The results herein insert a further tile into the overgrowing patchwork of N-heterocycle synthesis by means of the exploitation of powerful building-blocks such as poly-functionalized conjugated nitrobutadienes.

The most remarkable feature is surely represented by the dichotomic behaviour of Scheme 2, whereby the nature of the final heterocycle is tuned by the Z substituent and by the resulting acidifying power of the acetyl (COZ) moiety onto the α-hydrogen atom of intermediate **18**: this is rationalized in Scheme 4 and substantiated by the quanto-mechanical results reported in Chart 1.

On the other hand, the two “drawbacks” envisaged from the dichotomy of Scheme 2 can be both overcome as far as a) by modifying the reaction conditions, the diazine nucleus can be effectively attained independently on the nature of Z (Scheme 5), while b) pyrazoles “prohibited” by the use of **13** as substrates can be in turn easily prepared when starting from the corresponding sulfides **12** and performing a final, almost quantitative MeS to $MeSO_2$ stereospecific oxidation (Scheme 7).

Overall, we feel that the results herein represent a significant upgrade in the field of the synthesis of diversely functionalized N-heterocycles of possible biological/pharmacological interest.

## Experimental Section

**Materials and methods:** $^{1}$H NMR and $^{13}$C NMR spectra were recorded with a Varian Mercury 300 Plus spectrometer, at 300 and 75 MHz, respectively; chemical shifts (TMS as internal reference) are reported as $\delta$ values (ppm). Gas chromatography - mass spectrometry (GC-MS) was performed on HP 5890/5971 (EI 70 eV) system equipped with a HP-1 MS capillary column (12 m x 0.2 mm i.d x 0.33 μm). High-resolution mass spectra (HRMS) were obtained with an Agilent MSD TOF mass spectrometer, and recorded in positive ion mode with an electrospray (ESI) source. Melting points were determined with a Büchi 535 apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrum 65 FT-IR and wave numbers are reported in $cm^{-1}$. Petroleum ether and light petroleum refer to the fractions with bp 40-60 °C and 80-100 °C, respectively. Silica gel 230-400 mesh was used for column chromatography, all solvents being distilled before use. Tetrahydrofuran (THF) was purified by standard methods and distilled over potassium benzophenone ketyl before use. All other commercially available reagents were used as received.

Compounds **13a-f**,[16] **14a-d**[17]and **15aa-ad**[10] have been already described.

***Reactions of sulfones* 13a-f *with the anions of hydrazones* 14a,b *at -78 °C***

In a flask, the appropriate hydrazone **14** (0.2 mmol, 1 equiv *vs*. the nitrobutadiene **13**) was dissolved in THF (2.2 mL) under Ar and magnetic stirring; the temperature was brought to -78 °C and a 1M solution of Bu$^{t}$OK (1 equiv) was added. After 30 min, a THF solution of the appropriate nitrobutadiene (0.2 mmol in 2.2 mL) was added, and the reaction mixture kept at - 78 °C for 1-2 h. TFA (5 equiv) was then added, and the mixture maintained at – 78 °C under magnetic stirring for 2 h, and finally allowed to reach room temperature overnight. The mixture was then poured into water and extracted with ethyl acetate. The organic phases were dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure. The obtained crude was purified by chromatography on a silica gel column, using petroleum ether/ethyl acetate mixtures as eluent.

***Reactions of sulfones* 13a-f *with the anions of hydrazones* 14c,d *at 0 °C***

A modification of the methodology described above was employed wherein the temperature was maintained at 0 °C throughout, and allowed to reach 25 °C within 1 h after quenching with TFA.

***(E)*-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16aa)**.[10] Beige solid, mp 193-194 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1639 (s), 1512 (m), 1386 (m), 1311 (m), 1306 (m), 1292 (s), 1137 (s), 1126 (s), 1107 (m). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (3H, s), 2.44 (3H, s), 2.80 (3H, s), 2.90 (3H, s), 2.99 (3H, s), 6.31 (1H, d, *J* 15.6 Hz), 7.23-7.30 (4H, m), 7.34 (4H, app. s), 7.43 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 21.5, 35.1, 38.6, 43.0, 125.0, 125.9, 127.6, 128.9, 129.5, 130.0, 130.4, 132.6, 136.1, 138.5, 139.9, 146.8,

164.2. GC-MS: *m/z* 423(34) [$M^+$], 366(21), 344(19), 299(99), 287(24), 273(100), 256(36), 242(16), 212(10), 164(10), 142(30), 128(21), 115(14), 106(12), 91(51), 77(16), 72(71), 65(52). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_3S$ 424.1689, found 424.1684.

***tert*-Butyl (*E*)-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxylate (16ab)**.[10] Orange solid, mp 144-145 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.34 (9H, s), 2.42 (3H, s), 2.44 (3H, s), 2.75 (3H, s), 6.12 (1H, d, *J* 15.7 Hz), 7.18 (2H, d, *J* 8.4 Hz), 7.26 (2H, d, *J* 7.8 Hz), 7.29-7.37 (5H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 21.5, 28.0, 42.9, 82.1, 126.0, 127.4, 128.7, 129.4, 129.5, 129.7, 130.4, 134.1, 135.9, 138.3, 140.2, 143.8, 161.0 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{29}N_2O_4S$ 453.1843, found 453.1847.

***(E)*-4-(4-Methoxyphenyl)-*N*,*N*-dimethyl-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ba)**. Colourless solid, mp 168-169 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.80 (3H, s), 2.91 (3H, s), 3.00 (3H, s), 3.85 (3H, s), 6.32 (1H, d, *J* 15.6 Hz), 6.98 (2H, d, *J* 8.7 Hz), 7.30-7.35 (6H, m), 7.43 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 35.1, 38.7, 43.0, 55.4, 114.7, 122.7, 124.7, 125.9, 126.0, 128.8, 129.5, 130.4, 130.9, 132.6, 132.6, 136.2, 140.0, 159.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_4S$ 440.1639, found 440.1634.

***tert*-Butyl (*E*)-4-(4-methoxyphenyl)-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxylate (16bb)**. Colourless solid, mp 197-198 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1715 (s), 1611 (w), 1517 (w), 1500 (m), 1461 (w), 1367 (w), 1321 (w), 1310 (w), 1298 (s), 1246 (m), 1213 (m), 1175 (w), 1155 (s), 1138 (s), 1126 (s), 1047 (w), 1026 (w), 1016 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.36 (9H, s), 2.45 (3H, s), 2.77 (3H, s), 3.87 (3H, s), 6.14 (1H, d, *J* 15.6 Hz), 7.00 (2H, d, *J* 8.4 Hz), 7.23 (2H, d, *J* 8.4 Hz), 7.31-7.36 (5H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 28.0, 42.9, 55.5, 82.1, 114.3, 123.8, 126.0, 127.0, 128.7, 129.4, 130.4, 131.1, 134.1, 135.9, 140.2, 143.9, 159.7, 161.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{29}N_2O_5S$ 469.1792, found 469.1798.

***(E)*-4-(4-Chlorophenyl)-*N*,*N*-dimethyl-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ca)**. Red solid, mp 107-110 °C (taken-up with petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1633 (m), 1511 (m), 1385 (w), 1305 (m), 1130 (s), 1090 (m), 1004 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.81 (3H, s), 2.97 (3H, s), 3.01 (3H, s), 6.27 (1H, dd, *J* 15.9 Hz), 7.32-7.46 (9H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 35.3, 38.7, 42.9, 123.9, 125.9, 129.2, 129.1, 129.5, 129.5, 130.5, 131.1, 132.8, 134.8, 136.0, 140.2, 146.6, 163.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{23}ClN_3O_3S$ 444.1143, found 444.1140.

***tert*-Butyl (*E*)-4-(4-chlorophenyl)-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxylate (16cb)**. Yellow solid, mp 151-152 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1726 (m), 1489 (w), 1370 (m), 1320 (w), 1314 (w), 1295 (m), 1217 (m), 1158 (m), 1139 (s), 1130 (s), 1104 (m), 1092 (m), 1020 (w), 1004 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.35 (9H, s), 2.45 (3H, s), 2.78 (3H, s), 6.10 (1H, d, *J* 15.6 Hz), 7.25 – 7.37 (7H, m), 7.46 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 28.0, 42.9, 82.4, 125.9, 126.0, 129.1, 129.1, 129.2, 130.4, 131.4, 134.1, 134.7, 135.8, 140.4, 143.7, 160.7 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{24}H_{26}ClN_2O_4S$ 473.1296, found 473.1292.

***(Z)*-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-4-*o*-tolyl-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16da)**. Yellow solid.$^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.92 (3H, s), 2.25 (3H, s), 2.41 (3H, s), 3.01 (3H, s), 3.12 (3H, s), 6.34 (1H, d, *J* 11.6 Hz), 6.90 (1H, d, *J* 11.6 Hz), 7.13- 7.31 (6H, m), 7.42 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.2, 21.3, 35.3, 39.0, 40.9, 123.7, 125.0, 125.9, 128.3, 130.0, 130.6, 130.7, 131.2, 131.2, 132.9, 133.4, 136.9, 137.9, 138.7, 146.3, 164.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_3S$ 424.1689, found 424.1683.

***(E)*-*N*,*N*-Dimethyl-5-(2-(methylsulfonyl)vinyl)-4-(2-thienyl)-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ea)**. Pale green solid, mp 167-168 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1633 (s), 1513 (m), 1384 (w), 1315 (w), 1292 (s), 1260 (w), 1138 (s), 1114 (m), 1043 (w), 1017 (w). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.83 (3H, s), 2.99 (3H, s), 3.04 (3H, s), 6.39 (1H, d, *J* 15.6 Hz), 7.12 (1H, dd, *J* 5.1 and 3.5 Hz), 7.16 (1H, dd, *J* 3.5 and 1.3 Hz), 7.33 (4H, s), 7.43 (1H, dd, *J* 5.1 and 1.3 Hz), 7.49 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 35.2, 38.8, 42.9, 117.7, 125.8, 127.7, 128.1, 128.9, 128.9, 130.0, 130.5, 130.5, 133.6, 136.0, 140.2, 147.2, 163.7. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{20}H_{22}N_3O_3S_2$ 416.1097, found 416.1095.

**[6-(Methylsulfonylmethyl)-5-nitro-1,4-di-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl) methanone (17ac)**.[10] Yellow solid, mp 121-123 °C (ethanol). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.26 (3H, s), 2.34 (3H, s), 2.73 (3H, s), 3.31-3.44 (2H, m), 4.96 (1H, d, *J* 9.8 Hz), 5.35 (1H, dd, *J* 9.7 and 4.0 Hz), 5.45 (1H, app. q), 7.10 (2H, d, *J* 8.1 Hz), 7.17 (2H, d, *J* 8.1 Hz), 7.21 (2H, d, *J* 8.7 Hz), 7.31 (2H, d, *J* 8.7 Hz), 7.38-7.47 (2H, m), 7.50-7.57 (1H, m), 7.93-7.97 (2H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 21.2, 40.3, 42.6, 49.9, 52.1, 86.2, 118.1, 128.0, 128.2, 130.3, 130.5, 130.5, 132.7, 132.9, 134.6, 136.4, 138.5, 141.3, 142.8, 189.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_5S$ 506.1744, found 506.1749.

**1-[6-(Methylsulfonylmethyl)-5-nitro-1,4-di-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17ad)**.[10] Yellow solid, mp 79-80 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1675 (m), 1556 (s), 1511 (s), 1360 (m), 1303 (s), 1260 (m), 1163 (m), 1135 (s), 1089 (w). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.30 (3H, s), 2.38 (6H, s), 2.77 (3H, s), 3.28 (1H, dd, *J* 14.8 and 5.7 Hz), 3.39 (1H, dd, *J* 14.8 and 5.0 Hz), 4.73 (1H, d, *J* 7.6 Hz), 5.14 (1H, app. q), 5.28 (1H, dd, *J* 7.6 and 3.9 Hz), 7.02 (2H, d, *J* 8.1 Hz), 7.13 (2H, d, *J* 7.8 Hz), 7.26 (2H, d, *J* 8.1 Hz), 7.36 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 21.3, 25.0, 39.5, 42.6, 49.3, 51.8, 85.5, 120.0, 127.6, 130.3, 130.4, 133.8, 135.6, 138.3, 141.3, 142.1, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_5S$ 444.1588, found 444.1585.

**[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17bc)**. Yellow solid, mp 160-161 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1641 (m), 1560 (s), 1511 (s), 1302 (s), 1270 (m), 1251 (m), 1185 (m), 1175 (m), 1149 (s), 1137 (m), 1120 (s), 1025 (m). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.73 (3H, s), 3.28-3.48 (2H, m), 3.73 (3H, s), 4.95 (1H, d, *J* 9.6 Hz), 5.35 (1H, dd, *J* 9.6 and 4.2 Hz), 5.44 (1H, dd, *J* 9.6 and 5.4 Hz), 6.82 (2H, d, *J* 8.7 Hz), 7.18-7.23 (4H, m), 7.30 (2H, d, *J* 8.7 Hz), 7.40-7.46 (2H, m), 7.52-7.57 (1H, m), 7.95 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 39.9, 42.5, 50.0, 52.1, 55.4,

86.2, 115.1, 118.1, 127.6, 128.2, 129.2, 130.4, 130.5, 132.7, 134.6, 136.4, 141.3, 142.9, 159.6, 189.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_6S$ 522.1693, found 522.1692.

**1-[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17bd)**. Yellow solid, mp 165-166 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.38 (6H, s), 2.78 (3H, s), 3.27 (1H, dd, *J* 15.0 and 6.3 Hz), 3.40 (1H, dd, *J* 15.0 and 5.1 Hz), 3.77 (3H, s), 4.72 (1H, d, *J* 7.5 Hz), 5.14 (1H, app. q), 5.28 (1H, dd, *J* 7.5 and 3.9 Hz), 6.85 (2H, d, *J* 9.0 Hz), 7.06 (2H, d, *J* 8.7 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.37 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.0, 39.1, 42.6, 49.7, 51.8, 55.4, 85.5, 115.0, 120.0, 128.7, 128.9, 130.4, 135.6, 141.3, 142.1, 159.6, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_6S$ 460.1537, found 460.1532.

**[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17cc)**. Brown solid, mp 104-106 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1646 (m), 1158 (s), 1511 (s), 1491 (m), 1340 (m), 1304 (s), 1262 (m), 1197 (m), 1168 (m), 1132 (s), 1117 (s), 1092 (s), 1054 (m), 1015 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 2.34 (3H, s), 2.73 (3H, s), 3.27-3.44 (2H, m), 4.97 (1H, d, *J* 9.9 Hz), 5.33 (1H, dd, *J* 9.9 and 3.9 Hz), 5.47 (1H, app. q), 7.14-7.36 (8H, m), 7.38-7.50 (2H, m), 7.51-7.61 (1H, m), 7.94 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 40.1, 42.6, 49.9, 52.1, 85.9, 118.1, 128.3, 129.5, 129.9, 130.5, 130.5, 132.9, 134.6, 134.7, 134.9, 136.2, 141.1, 141.9, 188.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{25}ClN_3O_5S$ 526.1198, found 526.1192.

**1-[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17cd)**. Orange solid, mp 101-102 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1672 (m), 1558 (m), 1511 (m), 1492 (m), 1361 (m), 1303 (s), 1161 (m), 1135 (s), 1091 (s), 1063 (m), 1044 (m), 1014 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (6H, s), 2.78 (3H, s), 3.27 (1H, dd, *J* 14.8 and 5.9 Hz), 3.37 (1H, dd, *J* 14.8 and 5.1), 4.73 (1H, d, *J* 8.1 Hz), 5.18 (1H, app. q), 5.25 (1H, dd, *J* 8.1 and 3.9 Hz), 7.10 (2H, d, *J* 8.4 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.31 (2H, d, *J* 8.4 Hz), 7.37 (2H, d, *J* 8.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.0, 39.3, 42.6, 49.4, 51.8, 85.3, 119.8, 129.2, 129.8, 130.5, 134.5, 135.5, 135. 8, 141.1, 141.4, 195.0. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{21}H_{23}ClN_3O_5S$ 464.1041, found 464.1046.

**[6-(Methylsulfonylmethyl)-5-nitro-4-*o*-tolyl-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17dc)**. Yellow solid, mp 155-156 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.68 (3H, s), 2.73 (3H, s), 3.36 (1H, dd, *J* 15.0 and 5.1 Hz), 3.45 (1H, dd, *J* 15.0 and 5.1 Hz), 5.19 (1H, d, *J* 9.0 Hz), 5.36-5.50 (2H, m), 6.98 (1H, d, *J* 7.1 Hz), 7.04-7.17 (2H, m), 7.17-7.27 (3H, m), 7.31 (2H, d, *J* 8.6 Hz), 7.36-7.46 (2H, m), 7.48-7.58 (1H, m), 7.91 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 19.6, 20.9, 37.0, 42.5, 49.9, 52.1, 85.6, 118.5, 126.4, 127.0, 128.1, 128.5, 130.5, 132.0, 132.6, 134.4, 134.8, 136.4, 138.0, 141.3, 143.2, 189.1 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_5S$ 506.1744, found 506.1740.

**1-[6-(Methylsulfonylmethyl)-5-nitro-4-*o*-tolyl-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17dd)**. Pale pink solid, mp 211- 212 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1668 (m), 1560 (s), 1507 (m), 1359 (m), 1321 (m), 1300 (s), 1266 (m), 1242 (m), 1187 (m), 1169 (s), 1145 (m),

1125 (s), 1096 (m), 1039 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.39 (3H, s), 2.58 (3H, s), 2.77 (3H, s), 3.29 (1H, dd, *J* 14.4 and 6.6 Hz), 3.44 (1H, dd, *J* 14.7 and 4.8 Hz), 4.93 (1H, d, *J* 6.6 Hz), 5.10 (1H, br q), 5.35 (1H, dd, *J* 6.9 and 3.9 Hz), 6.77 (1H, d, *J* 7.5 Hz), 7.08-7.24 (3H, m), 7.28 (2H, d, *J* 8.7 Hz), 7.37 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 19.6, 21.0, 24.9, 36.6, 42.6, 49.1, 51.9, 84.3, 120.6, 126.5, 126.9, 128.5, 130.4, 131.9, 135.2, 135.8, 137.3, 141.3, 142.2, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_5S$ 444.1588, found 444.1591.

**1-[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl] ethanone (17fd)**. Yellow solid, mp 118-120 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1675 (m), 1555 (s), 1509 (s), 1359 (m), 1303 (s), 1257 (m), 1164 (m), 1129 (s), 1088 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.40 (3H, s), 2.41 (3H, s), 2.77 (3H, s), 3.32 (1H, dd, *J* 14.7 and 6.0 Hz), 3.42 (1H, dd, *J* 14.7 and 5.1 Hz), 4.93 (1H, d, *J* 8.1 Hz), 5.25 (1H, app. q), 5.42 (1H, dd, *J* 8.1 and 4.2 Hz), 7.27-7.31 (3H, m), 7.41 (2H, d, *J* 8.4 Hz), 7.45-7.51 (2H, m), 7.58 (1H, s), 7.75-7.85 (3H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.1, 40.0, 42.6, 49.5, 51.8, 85.5, 119.7, 125.1, 126.7, 126.8, 127.2, 127.9, 128.0, 129.7, 130.5, 133.1, 133.5, 134.2, 135.6, 141.2, 142.0, 195.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{26}N_3O_5S$ 480.1588, found 480.1585.

***Reactions of nitrobutadienes* 13a-c,f *with hydrazones* 14a-d *and DBU in ethanol***

In a flask, the appropriate nitrobutadiene **13** (50.0 mg) and hydrazone **14** (1 equiv) were dissolved in EtOH (3 mL) and DBU was added (1 equiv) under magnetic stirring. The mixture was then warmed to reflux for 1 h, and when completed (as verified by TLC), diluted with ethyl acetate and washed with water. The organic phase was dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure. The obtained crude was purified by chromatography on a silica gel column, using petroleum ether/ethyl acetate mixtures as eluent.

***N,N*-Dimethyl-6-(methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19aa)**.[10] Orange solid, mp 138-139 °C (dichloromethane/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1621 (s), 1508 (s), 1287 (s), 1166 (m), 1126 (s), 1082 (s), 1060 (m), 1036 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.34 (3H, s), 2.95 (3H, s), 2.97 (3H, s), 3.18 (3H, s), 3.23 (1H, dd, *J* 2.6 and 13.4 Hz), 3.66 (1H, dd, *J* 9.8 and 13.4 Hz), 5.72 (1H, ddd, *J* 2.7, 7.2 and 9.9 Hz), 6.24 (1H, d, *J* 6.9 Hz), 7.14 (4H, app. s), 7.18 (2H, d, *J* 8.4 Hz), 7.32 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.7, 21.4, 35.2, 38.8, 43.2, 47.3, 54.4, 115.6, 121.0, 127.1, 129.5, 130.3, 132.1, 132.7, 133.1, 138.5, 141.5, 142.0, 165.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{28}N_3O_3S$ 426.1846, found 426.1850.

***tert*-Butyl 6-(methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19ab)**.[10] Yellow solid, mp 86-88 °C (diethyl ether/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1710 (m), 1509 (m), 1367 (w), 1297 (m), 1272 (m), 1255 (m), 1168 (s), 1110 (s), 1036 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.30 (9H, s), 2.34 (3H, s), 2.36 (3H, s), 2.99 (3H, s), 3.21 (1H, dd, *J* 13.4 and 2.9 Hz), 3.56 (1H, dd, *J* 13.4 and 9.9 Hz), 5.77 (1H, ddd, *J* 9.9, 7.2 and 2.9 Hz), 6.02 (1H, d, *J* 7.2 Hz), 7.08-7.17 (4H, m), 7.20 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 21.3, 27.8, 43.2 47.8, 54.3, 81.9, 116.2, 119.2, 127.5, 128.9, 130.2, 132.8, 133.6, 135.0, 138.0, 138.9, 141.1, 162.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{31}N_2O_4S$ 455.1999, found 455.1993.

**[6-(Methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl)methanone (19ac)**.[10] Yellow solid, mp 189-190 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1647 (m), 1527 (w), 1507 (m), 1319 (w), 1309 (w), 1296 (m), 1285 (m), 1270 (w), 1248 (w), 1201 (m), 1186 (m), 1177 (m), 1149 (m), 1137 (s), 1055 (w), 1031 (w), 1015 (w), 1011 (w).$^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.31 (3H, s), 2.33 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.3 and 2.5 Hz), 3.61 (1H, dd, *J* 13.2 and 10.0 Hz), 5.84 (1H, ddd, *J* 9.5, 7.3 and 2.1 Hz), 6.25 (1H, d, *J* 7.1 Hz), 7.10 (4H, app. s), 7.19 (2H, d, *J* 8.4 Hz), 7.32 (2H, d, *J* 8.6 Hz), 7.52 (2H, app. t), 7.62 (1H, app. t), 8.11 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 21.4, 43.3, 47.6, 54.8, 116.1, 120.5, 127.3, 128.3, 129.3, 130.4, 130.8, 132.8, 133.2, 133.8, 133.8, 137.0, 138.1, 141.0, 143. 7, 189.4. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{27}N_2O_3S$ 459.1737, found 459.1733.

**1-[6-(Methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19ad)**.[10] Yellow solid, mp 136-137 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1668 (s), 1511 (m), 1487 (m), 1370 (m), 1310 (m), 1293 (s), 1285 (m), 1250 (m), 1196 (s), 1191 (s), 1180 (s), 1139 (s), 1112 (m), 1096 (m), 1036 (w), 1021 (w).$^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.37 (3H, s), 2.54 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.2 and 2.7 Hz), 3.51 (1H, dd, *J* 13.2 and 9.9 Hz), 5.78 (1H, ddd, *J* 9.9, 7.2 and 2.7 Hz), 6.05 (1H, d, *J* 7.2 Hz), 7.03 (2H, d, *J* 8.0 Hz), 7.13 (2H, d, *J* 8.0 Hz), 7.25 (2H, d, *J* 8.4 Hz), 7.45 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 21.4, 26.0, 43.4, 47.9, 54.6, 116.4, 120.1, 127.5, 129.0, 130.5, 132.7, 134.4, 134.6, 137.8, 140.8, 143.4, 194.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}N_2O_3S$ 397.1580, found 397.1576.

**4-(4-Methoxyphenyl)-*N*,*N*-dimethyl-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine -3-carboxamide (19ba)**. Yellow solid, mp 103-104 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1631 (m), 1609 (m), 1509 (s), 1291 (s), 1245 (s), 1170 (s), 1126 (s), 1083 (m), 1024 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.94 (3H, s), 2.97 (3H, s), 3.15 (3H, s), 3.24 (1H, dd, *J* 13.5 and 2.7 Hz), 3.63 (1H, dd, *J* 13.5 and 9.6 Hz), 3.81 (3H, s), 5.72 (1H, ddd, *J* 9.6, 7.2 and 2.7 Hz), 6.21 (1H, d, *J* 7.2 Hz), 6.86 (2H, d, *J* 8.7 Hz), 7.13-7.24 (4H, m), 7.32 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.2, 38.8, 43.3, 47.3, 54.4, 55.4, 114.2, 115.6, 120.5, 128.4, 128.5, 130.3, 131.7, 132.7, 141.5, 142.0, 159.9, 165.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{28}N_3O_4S$ 442.1795, found 442.1799.

***tert*-Butyl 4-(4-methoxyphenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19bb)**. Yellow solid, mp 78-80 °C (toluene/petroleum ether). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.31 (9H, s), 2.34 (3H, s), 2.98 (3H, s), 3.21 (1H, dd, *J* 13.2 and 2.4 Hz), 3.55 (1H, dd, *J* 13.2 and 9.6 Hz), 3.82 (3H, s), 5.76 (1H, ddd, *J* 9.6, 7.5 and 2.6 Hz), 6.00 (1H, d, *J* 7.2 Hz), 6.87 (2H, d, *J* 8.4 Hz), 7.15 (2H, d, *J* 8.6 Hz), 7.20 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.5 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 27.9, 43.3, 47.8, 54.3, 55.5, 82.0, 113.7, 116.2, 118.8, 128.9, 130.3, 130.3, 132.4, 133.6, 139.0, 141.1, 159.6, 162.6. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{31}N_2O_5S$ 471.1948, found 471.1943.

**[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-1-(*p*-tolyl)-1,6-dihydropyridazin-3-yl] (phenyl)methanone (19bc)**. Yellow solid, mp 105-106 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1607 (m), 1597 (m), 1508 (s), 1291 (s), 1247 (s), 1174 (s), 1155 (s), 1131 (s), 1073 (w), 1026 (m). $^1$H NMR

($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.2 and 2.5 Hz), 3.60 (1H, dd, *J* 13.2 and 10.0 Hz), 3.77 (3H, s), 5.83 (1H, ddd, *J* 9.8, 7.2 and 2.5 Hz), 6.22 (1H, d, *J* 7.2 Hz), 6.82 (2H, d, *J* 8.7 Hz), 7.11-7.21 (4H, m), 7.32 (2H, d, *J* 8.7 Hz), 7.48-7.57 (2H, m), 7.58-7.66 (1H, m), 8.07-8.13 (2H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 43.4, 47.7, 54.9, 55.4, 114.1, 116.2, 120.0, 128.4, 128.7, 129.1, 130.5, 130.8, 132.8, 132.9, 133.8, 137.0, 141.0, 143.7, 159.7, 189.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{27}N_2O_4S$ 475.1686, found 475.1680.

**1-[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl] ethanone (19bd)**. Yellow solid, mp 194-195 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1663 (s), 1609 (w), 1513 (s), 1489 (m), 1368 (m), 1338 (w), 1294 (s), 1241 (s), 1173 (s), 1144 (s), 1131 (s), 1085 (m), 1066 (m), 1031 (m), 1023 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.37 (3H, s), 2.54 (3H, s), 2.97 (3H, s), 3.19 (1H, d, *J* 13.2 and 2.4 Hz), 3.50 (1H, dd, *J* 13.2 and 9.9 Hz), 3.81 (3H, s), 5.77 (1H, ddd, *J* 9.9, 7.5 and 2.7 Hz), 6.02 (1H, d, *J* 6.9 Hz), 6.86 (2H, d, *J* 8.7 Hz), 7.07 (2H, d, *J* 8.7 Hz), 7.25 (2H, d, *J* 8.7 Hz), 7.45 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 26.0, 43.4, 48.0, 54.6, 55.4, 113.7, 116.4, 119.7, 128.8, 129.9, 130.5, 132.3, 134.4, 140.9, 143.3, 159.5, 194.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}N_2O_4S$ 413.1530, found 413.1526.

**4-(4-Chlorophenyl)-*N*,*N*-dimethyl-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19ca)**. Yellow solid, mp 85-86 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1638 (m), 1506 (m), 1403 (m), 1295 (m), 1203 (m), 1172 (m), 1128 (m), 1090 (s), 1040 (m), 1013 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.96 (3H, s), 2.98 (3H, s), 3.13 – 3.29 (4H, m), 3.66 (1H, dd, *J* 13.2 and 9.9 Hz), 5.75 (1H, app. t), 6.26 (1H, d, *J* 7.2 Hz), 7.13-7.23 (4H, m), 7.28-7.36 (4H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.3, 38.9, 43.2, 47.2, 54.3, 115.7, 122.0, 128.6, 129.0, 130.4, 131.3, 133.0, 134.7, 141.2, 141.4, 165.4 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}ClN_3O_3S$ 446.1300, found 446.1305.

***tert*-Butyl 4-(4-chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19cb)**. Yellow solid, mp 100-101 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1700 (m), 1493 (m), 1319 (m), 1297 (m), 1281 (m), 1268 (m), 1257 (m), 1170 (m), 1133 (s), 1121 (s), 1092 (m), 1073 (m), 1042 (m), 1015 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.31 (9H, s), 2.34 (3H, s), 2.98 (3H, s), 3.21 (1H, dd, *J* 13.2 and 2.7 Hz), 3.56 (1H, dd, *J* 13.2 and 9.9 Hz), 5.80 (1H, ddd, *J* 9.9, 7.2 and 2.7 Hz), 6.03 (1H, d, *J* 7.2 Hz), 7.16 (2H, d, *J* 8.4 Hz), 7.21 (2H, d, *J* 8.4 Hz), 7.32 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 27.9, 43.2, 47.7, 54.2, 82.2, 116.3, 120.0, 128.5, 129.1, 130.3, 131.9, 134.0, 134.0, 136.6, 138.0, 141.0, 162.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{24}H_{28}ClN_2O_4S$ 475.1453, found 475.1454.

**[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl) methanone (19cc)**. Yellow solid, mp 202-203 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1660 (m), 1649 (m), 1505 (m), 1447 (w), 1286 (s), 1263 (w), 1252 (m), 1234 (w), 1174 (s), 1156 (m), 1144 (s), 1131 (s), 1091 (m), 1066 (m), 1012 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.96 (3H, s), 3.19 (1H, dd, *J* 13.0 and 2.5 Hz), 3.61 (1H, dd, *J* 13.0 and 10.1 Hz), 5.86 (1H, ddd, *J* 9.9, 7.2 and 2.5 Hz), 6.25 (1H, d, *J* 7.1 Hz), 7.15 (2H, d, *J* 8.5 Hz), 7.19 (2H, d, *J* 8.8 Hz), 7.26 (2H, d, *J* 8.5 Hz), 7.32 (2H, d, *J* 8.7 Hz), 7.47-7.52 (2H, m), 7.56-7.72 (1H, m), 8.08 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 43.2, 47.5, 54.7, 116.2, 121.5, 128.4, 128.7, 128.7, 128.8, 130.5,

130.7, 132.2, 132.9, 134.1, 135.4, 136.9, 140.8, 142.9, 189.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{24}ClN_2O_3S$ 479.1191, found 479.1187.

**1-[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19cd)**. Yellow solid, mp 201-202 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1666 (s), 1511 (m), 1485 (s), 1402 (m), 1370 (m), 1335 (m), 1304 (m), 1291 (s), 1280 (s), 1253 (m), 1242 (m), 1188 (s), 1178 (s), 1138 (s), 1094 (s), 1017 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.38 (3H, s), 2.53 (3H, s), 2.97 (3H, s), 3.20 (1H, dd, *J* 12.9 and 2.4 Hz), 3.51 (1H, dd, *J* 12.9 and 9.9 Hz), 5.81 (1H, ddd, *J* 9.9, 7.2 and 2.6 Hz), 6.06 (1H, d, *J* 7.1 Hz), 7.08 (2H, d, *J* 8.4 Hz), 7.22-7.33 (4H, m), 7.45 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 25.8, 43.3, 47.9, 54.5, 116.4, 121.1, 128.4, 129.0, 130.5, 131.7, 133.9, 134.6, 136.2, 140.7, 142.6, 194.7. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{21}H_{22}ClN_2O_3S$ 417.1034, found 417.1030.

***N*,*N*-Dimethyl-6-(methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19fa)**. Yellow solid, mp 185-186 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1644 (m), 1623 (s), 1611 (m), 1503 (s), 1412 (m), 1404 (m), 1304 (s), 1296 (s), 1269 (m), 1246 (m), 1199 (), 1174 (m), 1140 (s), 1126 (s), 1080 (s), 1061 (m), 1046 (m), 1032 (s), 1013 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.94 (3H, s), 2.98 (3H, s), 3.20 (3H, s), 3.28 (1H, dd, *J* 13.2 and 2.4 Hz), 3.71 (1H, dd, *J* 13.2 and 9.6 Hz), 5.79 (1H, ddd, *J* 9.6, 7.2 and 2.4 Hz), 6.38 (1H, d, *J* 6.9 Hz), 7.20 (2H, d, *J* 8.4 Hz), 7.36 (3H, app. d), 7.44-7.52 (2H, m), 7.73-7.87 (4H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.2, 38.8, 43.2, 47.4, 54.5, 115.7, 121.9, 125.0, 126.5, 127.8, 128.4, 128.4, 130.3, 132.3, 132.8, 133.2, 133.4, 133.5, 141.5, 142.0, 165.7 (two couples of isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{28}N_3O_3S$ 462.1846, found 462.1841.

**[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl) methanone (19fc)**. Yellow solid, mp 196-197 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1644 (s), 1597 (m), 1506 (s), 1320 (m), 1294 (s), 1280 (m), 1267 (m), 1259 (m), 1194 (m), 1174 (m), 1154 (m), 1142 (m), 1132 (s), 1126 (s), 1055 (m), 1040 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.98 (3H, s), 3.22 (1H, dd, *J* 13.1 and 2.5 Hz), 3.66 (1H, dd, *J* 13.2 and 10.0 Hz), 5.90 (1H, ddd, *J* 9.9, 7.2 and 2.5 Hz), 6.38 (1H, d, *J* 7.1 Hz), 7.21 (2H, d, *J* 8.4 Hz), 7.23-7.28 (1H, m), 7.37 (2H, d, *J* 8.7 Hz), 7.40-7.46 (2H, m), 7.47-7.58 (2H, m), 7.61-7.69 (1H, m), 7.72 (1H, d, *J* 8.5 Hz), 7.75-7.81 (3H, m), 8.13 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 43.2, 47.6, 54.9, 116.2, 121.5, 125.5, 126.3, 126.4, 126.5, 127.8, 128.1, 128.3, 128.3, 130.5, 130.7, 132.8, 133.0, 133.2, 133.3, 133.9, 134.4, 137.0, 140.9, 143.5, 189.3. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{30}H_{27}N_2O_3S$ 494.1664, found 494.1661.

**1-[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19fd)**. Yellow solid, mp 219-220 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1672 (s), 1507 (s), 1367 (m), 1321 (w), 1304 (s), 1295 (s), 1202 (s), 1180 (s), 1141 (s), 1128 (s), 1083 (m), 1031 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (3H, s), 2.57 (3H, s), 3.00 (3H, s), 3.23 (1H, dd, *J* 13.2 and 2.6 Hz), 3.58 (1H, dd, *J* 13.2 and 9.9 Hz), 5.84 (1H, ddd, *J* 9.9, 7.5 and 2.6 Hz), 6.18 (1H, d, *J* 7.1 H), 7.16 (1H, dd, *J* 8.4 and 1.8 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.41-7.52 (4H, m), 7.69 (1H, s), 7.76 (1H, d, *J* 8.5 Hz), 7.79-7.86 (2H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 25.9, 43.4, 48.0, 54.7, 116.5, 121.0, 126.0, 126.2, 126.3, 127.5, 127.8, 128.2, 130.5, 130.5, 132.8, 133.0, 133.3,

135.0, 135.4, 140.8, 143.2, 194.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{25}N_2O_3S$ 433.1580, found 433.1583.

***Reactions of tetrahydropyridazines* 17ac *and* 17ad *to dihydropyridazines* 19ac *and* 19ad**

In a flask, the appropriate diazine **17** (0.60 mmol) dissolved in EtOH (2 mL) was added with piperidine (2 drops) and warmed to reflux for 1 h under magnetic stirring. After verifying the end of reaction by TLC, the mixture was then diluted with ethyl acetate, washed with water and dried over $Na_2SO_4$. Filtration and removal of the solvent under reduced pressure allowed to obtain the crude product **19**, almost pure at the $^1$H-NMR analysis (quantitative yields).

***Oxidation reactions of sulfides* 15aa *and* 15ac *to sulfones* 16aa *and* 16ac**

In a flask, the appropriate sulfide **15** (50.0 mg, prepared as described in ref. 8) dissolved in $CH_2Cl_2$ (5 mL) was added with MCPBA (77%, 2.2 equiv) under magnetic stirring. The end of the reaction was verified by TLC. The final mixture was diluted with $CH_2Cl_2$, washed with $NaHSO_3$ 5% in water, then with $Na_2CO_3$ saturated solution and finally with water. The organic phase was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The obtained crude was almost pure (as a diastereomeric *Z:E* mixture) at the $^1$H-NMR analysis (quantitative yields).

**(*E*)** and **(*Z*)-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16aa)**. Yellow solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.02 (3H *Z*, s), 2.36 (3H *Z*, s), 2.40 (3H *E* + 3H *Z*, s), 2.45 (3H *E*, s), 2.81 (3H *E*, s), 2.91 (3H *E*, s), 2.96 (3H *Z*, s), 3.00 (3H *E*, s), 3.05 (3H *Z*, s), 6.32 (1H *E*, d, *J* 15.6 Hz), 6.47 (1H *Z*, d, *J* 11.7 Hz), 7.06 (1H *Z*, d, *J* 11.4 Hz), 7.15-7.38 (8H *E* + 8H *Z*, d, *J* 8.1 Hz), 7.44 (1H *E*, d, *J* 15.6 Hz).

**(*E*)** and **(*Z*)-1-{5-[2-(Methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazol-3-yl}ethanone (16ad)**. Beige solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.98 (3H *Z*, s), 2.37 (3H *Z*, s), 2.42 (3H Z + 3H *E*, s), 2.47 (3H *E*, s), 2.57 (3H *E*, s), 2.62 (3H *Z*, s), 2.76 (3H *E*, s), 6.15 (1H *E*, d, *J* 15.6 Hz), 6.39 (1H *Z*, d, *J* 11.4 Hz), 6.95 (1H *Z*, d, *J* 11.4 Hz), 7.16 – 7.37 (5H *E* + 6H *Z*, m), 7.37 (4H, *E*, s), 7.44 (2H *Z*, d, *J* 8.4 Hz).

A few milligrams of the *E* compound could be isolated. Beige solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.42 (3H, s), 2.47 (3H, s), 2.56 (3H, s), 2.76 (3H, s), 6.15 (1H, d, *J* 15.6 Hz), 7.21 (2H, d, *J* 8.3 Hz), 7.27 (2H, d, *J* 8.0 Hz), 7.33 (1H, d, *J* 15.7 Hz) 7.37 ( 4H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.3, 21.4, 27.9, 42.8, 125.7, 126.5, 127.9, 129.1, 129.5, 129.6, 130.4, 134.4, 135.8, 138.4, 140.2, 148.1, 193.6 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{23}N_2O_3S$ 395.1424, found 395.1427.

***Crystal data for compound 17bd***

$C_{22}H_{25}N_3O_6S$, M = 459.5, light yellow-coloured crystal with truncated pyramid shape, and maximum dimensions 0.40 × 0.40 × 0.2 mm. Monoclinic, space group $P2_1/c$, $a$ = 8.927(1) Å, $b$ = 22.430(4) Å, $c$ = 11.713(2) Å, β = 101.72(1) Å, $V$ = 2296.4(6) Å$^3$, $Z$ = 4, F(000) = 968, $d_{calc}$ = 1.329 g/cm$^3$, μ (MoKα) = 0.18 mm$^{-1}$. Crystals were grown from ethanol.

Intensity data were collected at 295 K on a Bruker-Nonius MACH3 diffractometer (graphite monochromated Mo Kα radiation): $\omega$-$\theta$ scans, scan width 1.05°, minimum speed 0.97° min$^{-1}$, $\theta_{max}$ =

28°; 6009 total measured reflections, 5518 independent reflections of which 2954 with $F_o > 4\,\sigma(F_o)$; the structure was solved with the SIR*2014* program,[18] by applying Direct Methods procedures. The initial Fourier map showed 26 peaks which were attributed to the proper atomic species (non-hydrogen atoms), in agreement with the expected chemical formula. This partial model was then refined by means of full-matrix least squares cycles using the SHELXL program,[19] and completed with the additional peaks taken from the difference Fourier map. After some cycles of anisotropic refinement of the heavier atoms, all hydrogen atoms were also obtained in subsequent difference Fourier maps. Their coordinates and isotropic displacement parameters ($U_{iso}$) could be freely refined, except for two methyl groups (C13 and C15), which showed large anisotropic displacement parameters. In this case, the H atoms were restrained in idealized positions (AFIX 137 instruction) with the corresponding $U_{iso}$ value constrained to 1.2 times the $U_{eq}$ of the bonded C atom.
The final agreement indices are: *R*1= 0.057, over 2954 reflections with $F_o > 4\sigma\ F_o$, and *wR*2 = 0.133, for 367 refined parameters and 5518 reflections, mean shift/e.s.d = 0.003, Goodness of fit *S* = 0.973, $\Delta\rho_{min}$ = -0.23 eÅ$^{-3}$, $\Delta\rho_{max}$ = +0.20 eÅ$^{-3}$.

Figure 1 shows the ortep diagram of the molecule with atom numbering. Bond distances and bond angles are in the normal range if compared with tabulated values for similar compounds and no notably short intermolecular contact is found. In accordance with the general classification of puckering in six-membered rings,[20] the central ring formed by N1, N2, C3, C4, C5, C6 exhibits an envelope (or half-boat) conformation, being the C6 atom out of the mean plane defined by the other five atoms (distance C6-plane ≅ 0.7 Å). The substituents to the asymmetric carbon atoms of the central ring (C4, C5, C6) are arranged in the crystal in *trans-cis* conformation.
As no H atoms are directly bound to the more electronegative elements N, O, S, only hydrogen bonds of C-H…O type can be established between the molecules. Although these interactions are quite numerous in this structure (11 different contacts), they are rather weak, as attested by the donor…acceptor distances (C….O), whose values are well greater than (only in two cases, slightly lower than) the sum of the van der Waals radii.

Crystallographic data (CIF file, FCF file) for the structure in this paper have been deposited with the Cambridge Crystallographic Data centre as supplementary publication numbers CCDC-1403698. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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**Supplementary Data**

Spectroscopic data; copies of the $^{1}$H and $^{13}$C NMR spectra for all compounds; details of the computational studies; crystallographic materials for compound **17bd**.

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15. p$K_a$ = ΔE / 2.303 RT; at -78 °C (the temperature at which the reaction was performed): 2.303 RT = 2.303 * 8.314 J $K^{-1}$ $mol^{-1}$ * 195 K = 3.7 kJ/mol.
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# Synthesis of Poly-Functionalized Pyrazoles and Pyridazines from Nitrobutadienes: an Interesting Dichotomy of Practical Relevance

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## Supplementary Data

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# Experimental Section

**Materials and methods:** $^{1}$H NMR and $^{13}$C NMR spectra were recorded with a Varian Mercury 300 Plus spectrometer, at 300 and 75 MHz, respectively; chemical shifts (TMS as internal reference) are reported as $\delta$ values (ppm). High-resolution mass spectra (HRMS) were obtained with an Agilent MSD TOF mass spectrometer, and recorded in positive ion mode with an electrospray (ESI) source. Melting points were determined with a Büchi 535 apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrum 65 FT-IR and wave numbers are reported in cm$^{-1}$. Petroleum ether and light petroleum refer to the fractions with bp 40-60 °C and 80-100 °C, respectively. Silica gel 230-400 mesh was used for column chromatography, all solvents being distilled before use. Tetrahydrofuran (THF) was purified by standard methods and distilled over potassium benzophenone ketyl before use. All other commercially available reagents were used as received.

Compounds **13a-g**,[1] **14a-d**,[2] and **15aa-ad**[3] have been already described.

***Reactions of sulfones* 13a-f *with the anions of hydrazones* 14a,b *at -78 °C***

In a flask, the appropriate hydrazone **14** (0.2 mmol, 1 equiv *vs*. the nitrobutadiene **13**) was dissolved in THF (2.2 mL) under Ar and magnetic stirring; the temperature was brought to -78 °C and a 1M solution of Bu$^{t}$OK (1 equiv) was added. After 30 min, a THF solution of the appropriate nitrobutadiene (0.2 mmol in 2.2 mL) was added, and the reaction mixture kept at - 78 °C for 1-2 h. TFA (5 equiv) was then added, and the mixture maintained at -78 °C under magnetic stirring for 2 h, and finally allowed to reach room temperature overnight. The mixture was then poured into water and extracted with ethyl acetate. The organic phases were dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure. The obtained crude was purified by chromatography on a silica gel column, using petroleum ether/ethyl acetate mixtures as eluent.

***Reactions of sulfones* 13a-f *with the anions of hydrazones* 14c,d *at 0 °C***

A modification of the methodology described above was employed wherein the temperature was maintained at 0 °C throughout, and allowed to reach 25 °C within 1 h after quenching with TFA.

***(E)*-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16aa)**.[3] Beige solid, mp 193-194 °C (ethanol). IR (ATR): $\tilde{\nu}$ (cm$^{-1}$) 1639 (s), 1512 (m), 1386 (m), 1311 (m), 1306 (m), 1292 (s), 1137 (s), 1126 (s), 1107 (m). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (3H, s), 2.44 (3H, s), 2.80 (3H, s), 2.90 (3H, s), 2.99 (3H, s), 6.31 (1H, d, *J* 15.6 Hz), 7.23-7.30 (4H, m), 7.34 (4H, app. s), 7.43 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 21.4, 21.5, 35.1, 38.6, 43.0, 125.0, 125.9, 127.6, 128.9, 129.5, 130.0, 130.4, 132.6, 136.1, 138.5, 139.9, 146.8, 164.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_3S$ 424.1689, found 424.1684.

***tert*-Butyl (*E*)-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxilate (16ab)**.[3] Orange solid, mp 144-145 °C (ethanol). $^{1}$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.34 (9H, s), 2.42 (3H, s), 2.44 (3H, s), 2.75 (3H, s), 6.12 (1H, d, *J* 15.7 Hz), 7.18 (2H, d, *J* 8.4 Hz), 7.26 (2H, d, *J* 7.8 Hz), 7.29-7.37 (5H, m). $^{13}$C NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 21.4, 21.5, 28.0, 42.9, 82.1, 126.0,

127.4, 128.7, 129.4, 129.5, 129.7, 130.4, 134.1, 135.9, 138.3, 140.2, 143.8, 161.0 (two carbons are accidentally isochronous). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{29}N_2O_4S$ 453.1843, found 453.1847.

***(E)*-4-(4-Methoxyphenyl)-*N,N*-dimethyl-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ba)**. Colourless solid, mp 168-169 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.80 (3H, s), 2.91 (3H, s), 3.00 (3H, s), 3.85 (3H, s), 6.32 (1H, d, *J* 15.6 Hz), 6.98 (2H, d, *J* 8.7 Hz), 7.30-7.35 (6H, m), 7.43 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 35.1, 38.7, 43.0, 55.4, 114.7, 122.7, 124.7, 125.9, 126.0, 128.8, 129.5, 130.4, 130.9, 132.6, 132.6, 136.2, 140.0, 159.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_4S$ 440.1639, found 440.1634.

***tert*-Butyl *(E)*-4-(4-methoxyphenyl)-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxylate (16bb)**. Colourless solid, mp 197-198 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1715 (s), 1611 (w), 1517 (w), 1500 (m), 1461 (w), 1367 (w), 1321 (w), 1310 (w), 1298 (s), 1246 (m), 1213 (m), 1175 (w), 1155 (s), 1138 (s), 1126 (s), 1047 (w), 1026 (w), 1016 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.36 (9H, s), 2.45 (3H, s), 2.77 (3H, s), 3.87 (3H, s), 6.14 (1H, d, *J* 15.6 Hz), 7.00 (2H, d, *J* 8.4 Hz), 7.23 (2H, d, *J* 8.4 Hz), 7.31- 7.36 (5H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 28.0, 42.9, 55.5, 82.1, 114.3, 123.8, 126.0, 127.0, 128.7, 129.4, 130.4, 131.1, 134.1, 135.9, 140.2, 143.9, 159.7, 161.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{29}N_2O_5S$ 469.1792, found 469.1798.

***(E)*-4-(4-Chlorophenyl)-*N,N*-dimethyl-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ca)**. Red solid, mp 107-110 °C (taken-up with petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1633 (m), 1511 (m), 1385 (w), 1305 (m), 1130 (s), 1090 (m), 1004 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.81 (3H, s), 2.97 (3H, s), 3.01 (3H, s), 6.27 (1H, dd, *J* 15.9 Hz), 7.32-7.46 (9H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) 21.4, 35.3, 38.7, 42.9, 123.9, 125.9, 129.2, 129.1, 129.5, 129.5, 130.5, 131.1, 132.8, 134.8, 136.0, 140.2, 146.6, 163.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{23}ClN_3O_3S$ 444.1143, found 444.1140.

***tert*-Butyl *(E)*-4-(4-chlorophenyl)-5-[2-(methylsulfonyl)vinyl]-1-*p*-tolyl-1*H*-pyrazole-3-carboxylate (16cb)**. Yellow solid, mp 151-152 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1726 (m), 1489 (w), 1370 (m), 1320 (w), 1314 (w), 1295 (m), 1217 (m), 1158 (m), 1139 (s), 1130 (s), 1104 (m), 1092 (m), 1020 (w), 1004 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.35 (9H, s), 2.45 (3H, s), 2.78 (3H, s), 6.10 (1H, d, *J* 15.6 Hz), 7.25- 7.37 (7H, m), 7.46 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 28.0, 42.9, 82.4, 125.9, 126.0, 129.1, 129.1, 129.2, 130.4, 131.4, 134.1, 134.7, 135.8, 140.4, 143.7, 160.7 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{24}H_{26}ClN_2O_4S$ 473.1296, found 473.1292.

***(Z)*-*N,N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-4-*o*-tolyl-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16da)**. Yellow solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.92 (3H, s), 2.25 (3H, s), 2.41 (3H, s), 3.01 (3H, s), 3.12 (3H, s), 6.34 (1H, d, *J* 11.6 Hz), 6.90 (1H, d, *J* 11.6 Hz), 7.13 – 7.31 (6H, m), 7.42 (2H, d, *J* 8.4 Hz). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.2, 21.3, 35.3, 39.0, 40.9, 123.7, 125.0, 125.9, 128.3, 130.0, 130.6, 130.7, 131.2, 131.2, 132.9, 133.4, 136.9, 137.9, 138.7, 146.3, 164.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{26}N_3O_3S$ 424.1689, found 424.1683.

***(E)*-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-4-(2-thienyl)-1-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16ea)**. Pale green solid, mp 167-168 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1633 (s), 1513 (m), 1384 (w), 1315 (w), 1292 (s), 1260 (w), 1138 (s), 1114 (m), 1043 (w), 1017 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.45 (3H, s), 2.83 (3H, s), 2.99 (3H, s), 3.04 (3H, s), 6.39 (1H, d, *J* 15.6 Hz), 7.12 (1H, dd, *J* 5.1 and 3.5 Hz), 7.16 (1H, dd, *J* 3.5 and 1.3 Hz), 7.33 (4H, s), 7.43 (1H, dd, *J* 5.1 and 1.3 Hz), 7.49 (1H, d, *J* 15.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.4, 35.2, 38.8, 42.9, 117.7, 125.8, 127.7, 128.1, 128.86, 128.9, 130.0, 130.5, 130.5, 133.6, 136.0, 140.2, 147.2, 163.7. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{20}H_{22}N_3O_3S_2$ 416.1097, found 416.1095.

**[6-(Methylsulfonylmethyl)-5-nitro-1,4-di-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17ac)**.[3] Yellow solid, mp 121-123 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.26 (3H, s), 2.34 (3H, s), 2.73 (3H, s), 3.31 – 3.44 (2H, m), 4.96 (1H, d, *J* 9.8 Hz), 5.35 (1H, dd, *J* 9.7 and 4.0 Hz), 5.45 (1H, app. q), 7.10 (2H, d, *J* 8.1 Hz), 7.17 (2H, d, *J* 8.1 Hz), 7.21 (2H, d, *J* 8.7 Hz), 7.31 (2H, d, *J* 8.7 Hz), 7.38 - 7.47 (2H, m), 7.50 - 7.57 (1H, m), 7.93 - 7.97 (2H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 21.2, 40.3, 42.6, 50.0, 52.1, 86.2, 118.1, 128.0, 128.2, 130.3, 130.5, 130.5, 132.7, 132.9, 134.6, 136.4, 138.5, 141.3, 142.8, 189.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_5S$ 506.1744, found 506.1749.

**1-[6-(Methylsulfonylmethyl)-5-nitro-1,4-di-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17ad)**.[3] Yellow solid, mp 79-80 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1675 (m), 1556 (s), 1511 (s), 1360 (m), 1303 (s), 1260 (m), 1163 (m), 1135 (s), 1089 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.30 (3H, s), 2.38 (6H, s), 2.77 (3H, s), 3.28 (1H, dd, *J* 14.8 and 5.7 Hz), 3.39 (1H, dd, *J* 14.8 and 5.0 Hz), 4.73 (1H, d, *J* 7.6 Hz), 5.14 (1H, app. q), 5.28 (1H, dd, *J* 7.6 and 3.9 Hz), 7.02 (2H, d, *J* 8.1 Hz), 7.13 (2H, d, *J* 7.8 Hz), 7.26 (2H, d, *J* 8.1 Hz), 7.36 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 21.3, 25.0, 39.5, 42.6, 49.3, 51.8, 85.5, 120.0, 127.6, 130.3, 130.4, 133.8, 135.6, 138.3, 141.3, 142.1, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_5S$ 444.1588, found 444.1585.

**[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17bc)**. Yellow solid, mp 160-161 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1641 (m), 1560 (s), 1511 (s), 1302 (s), 1270 (m), 1251 (m), 1185 (m), 1175 (m), 1149 (s), 1137 (m), 1120 (s), 1025 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.73 (3H, s), 3.28 – 3.48 (2H, m), 3.73 (3H, s), 4.95 (1H, d, *J* 9.6 Hz), 5.35 (1H, dd, *J* 9.6 and 4.2 Hz), 5.44 (1H, dd, *J* 9.6 and 5.4 Hz), 6.82 (2H, d, *J* 8.7 Hz), 7.18-7.23 (4H, m), 7.30 (2H, d, *J* 8.7 Hz), 7.40-7.46 (2H, m), 7.52-7.57 (1H, m), 7.95 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 39.9, 42.5, 50.0, 52.1, 55.4, 86.2, 115.1, 118.1, 127.6, 128.2, 129.2, 130.4, 130.5, 132.7, 134.6, 136.4, 141.3, 142.9, 159.6, 189.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_6S$ 522.1693, found 522.1692.

**1-[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17bd)**. Yellow solid, mp 165-166 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.38 (6H, s), 2.78 (3H, s), 3.27 (1H, dd, *J* 15.0 and 6.3 Hz), 3.40 (1H, dd, *J* 15.0 and 5.1 Hz), 3.77 (3H, s), 4.72 (1H, d, *J* 7.5 Hz), 5.14 (1H, app. q), 5.28 (1H, dd, *J* 7.5 and 3.9 Hz), 6.85 (2H, d, *J* 9.0 Hz), 7.06 (2H, d, *J* 8.7 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.37 (2H, d, *J* 8.7

Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.0, 39.1, 42.6, 49.3, 51. 8, 55.4, 85.5, 115.0, 120.0, 128.7, 128.9, 130.4, 135.6, 141.3, 142.1, 159.6, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_6S$ 460.1537, found 460.1532.

**[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17cc)**. Brown solid, mp 104-106 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1646 (m), 1158 (s), 1511 (s), 1491 (m), 1340 (m), 1304 (s), 1262 (m), 1197 (m), 1168 (m), 1132 (s), 1117 (s), 1092 (s), 1054 (m), 1015 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.73 (3H, s), 3.27-3.44 (2H, m), 4.97 (1H, d, *J* 9.9 Hz), 5.33 (1H, dd, *J* 9.9 and 3.9 Hz), 5.47 (1H, app. q), 7.14-7.36 (8H, m), 7.38-7.50 (2H, m), 7.51-7.61 (1H, m), 7.94 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 40.1, 42.6, 49.9, 52.1, 85.9, 118.1, 128.3, 129.5, 129.9, 130.5, 130.5, 132.9, 134.6, 134.7, 134.9, 136.2, 141.1, 141.9, 188.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{25}ClN_3O_5S$ 526.1198, found 526.1192.

**1-[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17cd)**. Orange solid, mp 101-102 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1672 (m), 1558 (m), 1511 (m), 1492 (m), 1361 (m), 1303 (s), 1161 (m), 1135 (s), 1091 (s), 1063 (m), 1044 (m), 1014 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (6H, s), 2.78 (3H, s), 3.27 (1H, dd, *J* 14.8 and 5.9 Hz), 3.37 (1H, dd, *J* 14.8 and 5.1), 4.73 (1H, d, *J* 8.1 Hz), 5.18 (1H, app. q), 5.25 (1H, dd, *J* 8.1 and 3.9 Hz), 7.10 (2H, d, *J* 8.4 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.31 (2H, d, *J* 8.4 Hz), 7.37 (2H, d, *J* 8.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.0, 39.3, 42.6, 49.4, 51.8, 85.3, 119.8, 129.2, 129.8, 130.5, 134.5, 135.5, 135.8, 141.1, 141.4, 195.0. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{21}H_{23}ClN_3O_5S$ 464.1041, found 464.1046.

**[6-(Methylsulfonylmethyl)-5-nitro-4-*o*-tolyl-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl](phenyl)methanone (17dc)**. Yellow solid, mp 155-156 °C (ethanol). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.68 (3H, s), 2.73 (3H, s), 3.36 (1H, dd, *J* 15.0 and 5.1 Hz), 3.45 (1H, dd, *J* 15.0 and 5.1 Hz), 5.19 (1H, d, *J* 9.0 Hz), 5.36- 5.50 (2H, m), 6.98 (1H, d, *J* 7.1 Hz), 7.04-7.17 (2H, m), 7.17-7.27 (3H, m), 7.31 (2H, d, *J* 8.6 Hz), 7.36- 7.46 (2H, m), 7.48- 7.58 (1H, m), 7.91 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 19.6, 20.9, 37.0, 42.5, 49.9, 52.1, 85.6, 118.5, 126.4, 127.0, 128.1, 128.5, 130.5, 132.0, 132.6, 134.4, 134.8, 136.4, 138.0, 141.3, 143.2, 189.1 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{28}N_3O_5S$ 506.1744, found 506.1740.

**1-[6-(Methylsulfonylmethyl)-5-nitro-4-*o*-tolyl-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl]ethanone (17dd).** Pale pink solid, mp 211-212 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1668 (m), 1560 (s), 1507 (m), 1359 (m), 1321 (m), 1300 (s), 1266 (m), 1242 (m), 1187 (m), 1169 (s), 1145 (m), 1125 (s), 1096 (m), 1039 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.39 (3H, s), 2.58 (3H, s), 2.77 (3H, s), 3.29 (1H, dd, *J* 14.4 and 6.6 Hz), 3.44 (1H, dd, *J* 14.7 and 4.8 Hz), 4.93 (1H, d, *J* 6.6 Hz), 5.10 (1H, br q), 5.35 (1H, dd, *J* 6.9 and 3.9 Hz), 6.77 (1H, d, *J* 7.5 Hz), 7.08 – 7.24 (3H, m), 7.28 (2H, d, *J* 8.7 Hz), 7.37 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 19.6, 21.0, 24.9, 36.6, 42.6, 49.1, 51.9, 84.3, 120.6, 126.5, 126.9, 128.5, 130.4, 131.9, 135.2, 135.8, 137.3, 141.3, 142.2, 195.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{26}N_3O_5S$ 444.1588, found 444.1591.

**1-[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-5-nitro-1-*p*-tolyl-1,4,5,6-tetrahydropyridazin-3-yl] ethanone (17fd).** Yellow solid, mp 118-120 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1675 (m), 1555 (s), 1509 (s), 1359 (m), 1303 (s), 1257 (m), 1164 (m), 1129 (s), 1088 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.40 (3H, s), 2.41 (3H, s), 2.77 (3H, s), 3.32 (1H, dd, *J* 14.7 and 6.0 Hz), 3.42 (1H, dd, *J* 14.7 and 5.1 Hz), 4.93 (1H, d, *J* 8.1 Hz), 5.25 (1H, app. q), 5.42 (1H, dd, *J* 8.1 and 4.2 Hz), 7.27-7.31 (3H, m), 7.41 (2H, d, *J* 8.4 Hz), 7.45-7.51 (2H, m), 7.58 (1H, s), 7.75-7.85 (3H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.0, 25.1, 40.0, 42.6, 49.5, 51.8, 85.5, 119.7, 125.1, 126.7, 126.8, 127.2, 127.9, 128.0, 129.7, 130.5, 133.1, 133.5, 134.2, 135.6, 141.2, 142.0, 195.1. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{26}N_3O_5S$ 480.1588, found 480.1585.

***Reactions of nitrobutadienes* 13a-c,f *with hydrazones* 14a-d *and DBU in ethanol***

In a flask, the appropriate nitrobutadiene **13** (50.0 mg) and hydrazone **14** (1 equiv) were dissolved in EtOH (3 mL) and DBU (1 equiv) was added under magnetic stirring. The mixture was then warmed to reflux for 1 h, and if completed (as verified by TLC), diluted with ethyl acetate and washed with water. The organic phase was dried over $Na_2SO_4$, filtered and the solvent removed under reduced pressure. The obtained crude was purified by chromatography on a silica gel column, using petroleum ether/ethyl acetate mixtures as eluent.

***N,N*-Dimethyl-6-(methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19aa)**.[3] Orange solid, mp 138-139 °C (dichloromethane/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1621 (s), 1508 (s), 1287 (s), 1166 (m), 1126 (s), 1082 (s), 1060 (m), 1036 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.34 (3H, s), 2.95 (3H, s), 2.97 (3H, s), 3.18 (3H, s), 3.23 (1H, dd, *J* 13.4 and 2.6 Hz), 3.66 (1H, dd, *J* 13.4 and 9.8 Hz), 5.72 (1H, ddd, *J* 9.9, 7.2 and 2.7 Hz), 6.24 (1H, d, *J* 6.9 Hz), 7.14 (4H, app. s), 7.18 (2H, d, *J* 8.4 Hz), 7.32 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75MHz): δ 20.7, 21.4, 35.2, 38.8, 43.2, 47.3, 54.4, 115.6, 121.0, 127.1, 129.5, 130.3, 132.1, 132.7, 133.1, 138.5, 141.5, 142.0, 165.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{28}N_3O_3S$ 426.1846, found 426.1850.

***tert*-Butyl 6-(methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19ab)**.[3] Yellow solid, mp 86-88 °C (diethyl ether/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1710 (m), 1509 (m), 1367 (w), 1297 (m), 1272 (m), 1255 (m), 1168 (s), 1110 (s), 1036 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.30 (9H, s), 2.34 (3H, s), 2.36 (3H, s), 2.99 (3H, s), 3.21 (1H, dd, *J* 13.4 and 2.9 Hz), 3.56 (1H, dd, *J* 13.4 and 9.9 Hz), 5.77 (1H, ddd, *J* 9.9, 7.2 and 2.9 Hz), 6.02 (1H, d, *J* 7.2 Hz), 7.08-7.17 (4H, m), 7.20 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.6 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 21.3, 27.8, 43.2, 47.8, 54.3, 81.9, 116.2, 119.2, 127.5, 128.9, 130.2, 132.8, 133.6, 135.0, 137.8, 138.9, 141.1, 162.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{31}N_2O_4S$ 455.1999, found 455.1993.

**[6-(Methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl)methanone (19ac)**.[3] Yellow solid, mp 189-190 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1647 (m), 1527 (w), 1507 (m), 1319 (w), 1309 (w), 1296 (m), 1285 (m), 1270 (w), 1248 (w), 1201 (m), 1186 (m), 1177 (m), 1149 (m), 1137 (s), 1055 (w), 1031 (w), 1015 (w), 1011 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.31 (3H, s), 2.33 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.3 and 2.5 Hz), 3.61 (1H, dd, *J* 13.2 and 10.0 Hz), 5.84 (1H, ddd, *J* 9.5, 7.3 and 2.1 Hz), 6.25 (1H, d, *J* 7.1 Hz), 7.10 (4H, app. s), 7.19 (2H, d, *J*

8.4 Hz), 7.32 (2H, d, *J* 8.6 Hz), 7.52 (2H, app. t), 7.62 (1H, app. t), 8.11 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 21.4, 43.3, 47.6, 54.8, 116.1, 120.5, 127.3, 128.3, 129.3, 130.4, 130.8, 132.8, 133.2, 133.8, 133.8, 137.0, 138.1, 141.0, 143.7, 189.4. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{27}N_2O_3S$ 459.1737, found 459.1733.

**1-[6-(Methylsulfonylmethyl)-1,4-di-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19ad)**.[3] Yellow solid, mp 136-137 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1668 (s), 1511 (m), 1487 (m), 1370 (m), 1310 (m), 1293 (s), 1285 (m), 1250 (m), 1196 (s), 1191 (s), 1180 (s), 1139 (s), 1112 (m), 1096 (m), 1036 (w), 1021 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.35 (3H, s), 2.37 (3H, s), 2.54 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.2 and 2.7 Hz), 3.51 (1H, dd, *J* 13.2 and 9.9 Hz), 5.78 (1H, ddd, *J* 9.9, 7.2 and 2.7 Hz), 6.05 (1H, d, *J* 7.2 Hz), 7.03 (2H, d, *J* 8.0 Hz), 7.13 (2H, d, *J* 8.0 Hz), 7.25 (2H, d, *J* 8.4 Hz), 7.45 (2H, d, *J* 8.4 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 21.4, 26.0, 43.4, 47.9, 54.6, 116.4, 120.1, 127.5, 129.0, 130.5, 132.7, 134.4, 134.6, 137.8, 140.8, 143.4, 194.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}N_2O_3S$ 397.1580, found 397.1576.

**4-(4-Methoxyphenyl)-*N*,*N*-dimethyl-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine -3-carboxamide (19ba)**. Yellow solid, mp 103-104 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1631 (m), 1609 (m), 1509 (s), 1291 (s), 1245 (s), 1170 (s), 1126 (s), 1083 (m), 1024 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.94 (3H, s), 2.97 (3H, s), 3.15 (3H, s), 3.24 (1H, dd, *J* 13.5 and 2.7 Hz), 3.63 (1H, dd, *J* 13.5 and 9.6 Hz), 3.81 (3H, s), 5.72 (1H, ddd, *J* 9.6, 7.2 and 2.7 Hz), 6.21 (1H, d, *J* 7.2 Hz), 6.86 (2H, d, *J* 8.7 Hz), 7.13- 7.24 (4H, m), 7.32 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.2, 38.8, 43.3, 47.3, 54.4, 55.4, 114.2, 115.6, 120.5, 128.4, 128.5, 130.3, 131.7, 132.7, 141.5, 142.0, 159.9, 165.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{23}H_{28}N_3O_4S$ 442.1795, found 442.1799.

***tert*-Butyl 4-(4-methoxyphenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19bb)**. Yellow solid, mp 78-80 °C (toluene/petroleum ether). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.31 (9H, s), 2.34 (3H, s), 2.98 (3H, s), 3.21 (1H, dd, *J* 13.2 and 2.4 Hz), 3.55 (1H, dd, *J* 13.2 and 9.6 Hz), 3.82 (3H, s), 5.76 (1H, ddd, *J* 9.6, 7.5 and 2.6 Hz), 6.00 (1H, d, *J* 7.2 Hz), 6.87 (2H, d, *J* 8.4 Hz), 7.15 (2H, d, *J* 8.6 Hz), 7.20 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.5 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 27.9, 43.3, 47.8, 54.3, 55.5, 82.0, 113.7, 116.2, 118.8, 128.9, 130.3, 130.3, 132.4, 133.6, 139.0, 141.1, 159.6, 162.6. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{31}N_2O_5S$ 471.1948, found 471.1943.

**[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl] (phenyl)methanone (19bc)**. Yellow solid, mp 105-106 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1607 (m), 1597 (m), 1508 (s), 1291 (s), 1247 (s), 1174 (s), 1155 (s), 1131 (s), 1073 (w), 1026 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.98 (3H, s), 3.19 (1H, dd, *J* 13.2 and 2.5 Hz), 3.60 (1H, dd, *J* 13.2 and 10.0 Hz), 3.77 (3H, s), 5.83 (1H, ddd, *J* 9.8, 7.2 and 2.5 Hz), 6.22 (1H, d, *J* 7.2 Hz), 6.82 (2H, d, *J* 8.7 Hz), 7.11-7.21 (4H, m), 7.32 (2H, d, *J* 8.7 Hz), 7.48-7.57 (2H, m), 7.58-7.66 (1H, m), 8.07-8.13 (2H, m) . $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 43.4, 47.7, 54.9, 55.4, 114.1, 116.2, 120.0, 128.4, 128.7, 129.1, 130.5, 130.8, 132.8, 132.9, 133.8, 137.0, 141.0, 143.7, 159.7, 189.5. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{27}H_{27}N_2O_4S$ 475.1686, found 475.1680.

**1-[4-(4-Methoxyphenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19bd)**. Yellow solid, mp 194-195 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1663 (s), 1609 (w), 1513 (s), 1489 (m), 1368 (m), 1338 (w), 1294 (s), 1241 (s), 1173 (s), 1144 (s), 1131 (s), 1085 (m), 1066 (m), 1031 (m), 1023 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.37 (3H, s), 2.54 (3H, s), 2.97 (3H, s), 3.19 (1H, d, *J* 13.2 and 2.4 Hz), 3.50 (1H, dd, *J* 13.2 and 9.9 Hz), 3.81 (3H, s), 5.77 (1H, ddd, *J* 9.9, 7.5 and 2.7 Hz), 6.02 (1H, d, *J* 6.9 Hz), 6.86 (2H, d, *J* 8.7 Hz), 7.07 (2H, d, *J* 8.7 Hz), 7.25 (2H, d, *J* 8.7 Hz), 7.45 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 26.0, 43.4, 48.0, 54.6, 55.4, 113.7, 116.4, 119.7, 128.8, 129.9, 130.5, 132.3, 134.4, 140.9, 143.3, 159.5, 194.9. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}N_2O_4S$ 413.1530, found 413.1526.

**4-(4-Chlorophenyl)-*N*,*N*-dimethyl-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19ca)**. Yellow solid, mp 85-86 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1638 (m), 1506 (m), 1403 (m), 1295 (m), 1203 (m), 1172 (m), 1128 (m), 1090 (s), 1040 (m), 1013 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.96 (3H, s), 2.98 (3H, s), 3.13 – 3.29 (4H, m), 3.66 (1H, dd, *J* 13.2 and 9.9 Hz), 5.75 (1H, app. t), 6.26 (1H, d, *J* 7.2 Hz), 7.13-7.23 (4H, m), 7.28-7.36 (4H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.3, 38.9, 43.2, 47.2, 54.3, 115.7, 122.0, 128.6, 129.0, 130.4, 131.3, 133.0, 134.7, 141.2, 141.4, 165.4 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{25}ClN_3O_3S$ 446.1300, found 446.1305.

***tert*-Butyl 4-(4-chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxylate (19cb)**. Yellow solid, mp 100-101 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1700 (m), 1493 (m), 1319 (m), 1297 (m), 1281 (m), 1268 (m), 1257 (m), 1170 (m), 1133 (s), 1121 (s), 1092 (m), 1073 (m), 1042 (m), 1015 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.31 (9H, s), 2.34 (3H, s), 2.98 (3H, s), 3.21 (1H, dd, *J* 13.2 and 2.7 Hz), 3.56 (1H, dd, *J* 13.2 and 9.9 Hz), 5.80 (1H, ddd, *J* 9.9, 7.2 and 2.7 Hz), 6.03 (1H, d, *J* 7.2 Hz), 7.16 (2H, d, *J* 8.4 Hz), 7.21 (2H, d, *J* 8.4 Hz), 7.32 (2H, d, *J* 8.4 Hz), 7.43 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 27.9, 43.2, 47.7, 54.2, 82.2, 116.3, 120.0, 128.5, 129.1, 130.3, 131.9, 134.0, 134.0, 136.6, 138.0, 141.0, 162.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{24}H_{28}ClN_2O_4S$ 475.1453, found 475.1454.

**[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl) methanone (19cc)**. Yellow solid, mp 202-203 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1660 (m), 1649 (m), 1505 (m), 1447 (w), 1286 (s), 1263 (w), 1252 (m), 1234 (w), 1174 (s), 1156 (m), 1144 (s), 1131 (s), 1091 (m), 1066 (m), 1012 (w). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.33 (3H, s), 2.96 (3H, s), 3.19 (1H, dd, *J* 13.0 and 2.5 Hz), 3.61 (1H, dd, *J* 13.0 and 10.1 Hz), 5.86 (1H, ddd, *J* 9.9, 7.2 and 2.5 Hz), 6.25 (1H, d, *J* 7.1 Hz), 7.15 (2H, d, *J* 8.5 Hz), 7.19 (2H, d, *J* 8.8 Hz), 7.26 (2H, d, *J* 8.5 Hz), 7.32 (2H, d, *J* 8.7 Hz), 7.47-7.52 (2H, m), 7.56-7.72 (1H, m), 8.08 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 43.2, 47.5, 54.7, 116.2, 121.5, 128.4, 128.7, 128.7, 128.8, 130.5, 130.7, 132.2, 132.9, 134.1, 135.4, 136.9, 140.8, 142.9, 189.2. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{24}ClN_2O_3S$ 479.1191, found 479.1187.

**1-[4-(4-Chlorophenyl)-6-(methylsulfonylmethyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19cd)**. Yellow solid, mp 201-202 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1666 (s), 1511 (m), 1485 (s), 1402 (m), 1370 (m), 1335 (m), 1304 (m), 1291 (s), 1280 (s), 1253 (m), 1242 (m), 1188 (s), 1178 (s), 1138 (s), 1094 (s), 1017 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.38 (3H, s), 2.53 (3H, s), 2.97

(3H, s), 3.20 (1H, dd, *J* 12.9 and 2.4 Hz), 3.51 (1H, dd, *J* 12.9 and 9.9 Hz), 5.81 (1H, ddd, *J* 9.9, 7.2 and 2.6 Hz), 6.06 (1H, d, *J* 7.1 Hz), 7.08 (2H, d, *J* 8.4 Hz), 7.22-7.33 (4H, m), 7.45 (2H, d, *J* 8.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 25.8, 43.3, 47.9, 54.5, 116.4, 121.1, 128.4, 129.0, 130.5, 131.7, 133.9, 134.6, 136.2, 140.7, 142.6, 194.7. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{21}H_{22}ClN_2O_3S$ 417.1034, found 417.1030.

***N,N*-Dimethyl-6-(methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazine-3-carboxamide (19fa)**. Yellow solid, mp 185-186 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1644 (m), 1623 (s), 1611 (m), 1503 (s), 1412 (m), 1404 (m), 1304 (s), 1296 (s), 1269 (m), 1246 (m), 1199 (), 1174 (m), 1140 (s), 1126 (s), 1080 (s), 1061 (m), 1046 (m), 1032 (s), 1013 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.94 (3H, s), 2.98 (3H, s), 3.20 (3H, s), 3.28 (1H, dd, *J* 13.2 and 2.4 Hz), 3.71 (1H, dd, *J* 13.2 and 9.6 Hz), 5.79 (1H, ddd, *J* 9.6, 7.2 and 2.4 Hz), 6.38 (1H, d, *J* 6.9 Hz), 7.20 (2H, d, *J* 8.4 Hz), 7.36 (3H, app. d), 7.44-7.52 (2H, m), 7.73-7.87 (4H, m). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.8, 35.2, 38.8, 43.2, 47.4, 54.5, 115.7, 121.9, 125.0, 126.5, 127.8, 128.4, 128.4, 130.3, 132.3, 132.8, 133.2, 133.4, 133.5, 141.5, 142.0, 165.7 (two couples of isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{26}H_{28}N_3O_3S$ 462.1846, found 462.1841.

**[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl](phenyl) methanone (19fc)**. Yellow solid, mp 196-197 °C (ethanol). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1644 (s), 1597 (m), 1506 (s), 1320 (m), 1294 (s), 1280 (m), 1267 (m), 1259 (m), 1194 (m), 1174 (m), 1154 (m), 1142 (m), 1132 (s), 1126 (s), 1055 (m), 1040 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.34 (3H, s), 2.98 (3H, s), 3.22 (1H, dd, *J* 13.1 and 2.5 Hz), 3.66 (1H, dd, *J* 13.2 and 10.0 Hz), 5.90 (1H, ddd, *J* 9.9, 7.2 and 2.5 Hz), 6.38 (1H, d, *J* 7.1 Hz), 7.21 (2H, d, *J* 8.4 Hz), 7.23-7.28 (1H, m), 7.37 (2H, d, *J* 8.7 Hz), 7.40-7.46 (2H, m), 7.47-7.58 (2H, m), 7.61-7.69 (1H, m), 7.72 (1H, d, *J* 8.5 Hz), 7.75-7.81 (3H, m), 8.13 (2H, app. d). $^{13}$C NMR ($CDCl_3$, 75 MHz) δ 20.8, 43.2, 47.6, 54.9, 116.2, 121.5, 125.5, 126.3, 126.4, 126.5, 127.8, 128.1, 128.3, 128.3, 130.5, 130.7, 132.8, 133.0, 133.2, 133.3, 133.9, 134.4, 137.0, 140.9, 143.5, 189.3. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{30}H_{27}N_2O_3S$ 494.1664, found 494.1661.

**1-[6-(Methylsulfonylmethyl)-4-(2-naphthyl)-1-*p*-tolyl-1,6-dihydropyridazin-3-yl]ethanone (19fd)**. Yellow solid, mp 219-220 °C (toluene/petroleum ether). IR (ATR): $\tilde{\nu}$ ($cm^{-1}$) 1672 (s), 1507 (s), 1367 (m), 1321 (w), 1304 (s), 1295 (s), 1202 (s), 1180 (s), 1141 (s), 1128 (s), 1083 (m), 1031 (m). $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.39 (3H, s), 2.57 (3H, s), 3.00 (3H, s), 3.23 (1H, dd, *J* 13.2 and 2.6 Hz), 3.58 (1H, dd, *J* 13.2 and 9.9 Hz), 5.84 (1H, ddd, *J* 9.9, 7.5 and 2.6 Hz), 6.18 (1H, d, *J* 7.1 H), 7.16 (1H, dd, *J* 8.4 and 1.8 Hz), 7.27 (2H, d, *J* 8.4 Hz), 7.41-7.52 (4H, m), 7.69 (1H, s), 7.76 (1H, d, *J* 8.5 Hz), 7.79-7.86 (2H, m). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 20.9, 25.9, 43.4, 48.0, 54.7, 116.5, 121.0, 126.0, 126.2, 126.3, 127.5, 127.8, 128.2, 130.5, 130.5, 132.8, 133.0, 133.3, 134.5, 135.4, 140.8, 143.2, 194.8. HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{25}H_{25}N_2O_3S$ 433.1580, found 433.1583.

***Reactions of tetrahydropyridazines* 17ac *and* 17ad *to dihydropyridazines* 19ac *and* 19ad**

In a flask, the appropriate tetrahydropyridazine **17** (0.60 mmol) dissolved in EtOH (2 mL) was added with piperidine (2 drops) and warmed to reflux for 1 h under magnetic stirring. After

verifying the end of reaction by TLC, the mixture was then diluted with ethyl acetate, washed with water and dried over $Na_2SO_4$. Filtration and removal of the solvent under reduced pressure allowed to obtain the crude product **19**, almost pure at the $^1$H-NMR analysis (quantitative yields).

***Oxidation of sulfides* 15aa *and* 15ac *to sulfones* 16aa *and* 16ac**

In a flask, the appropriate sulfide **15** (50.0 mg; prepared as described in ref. 3) dissolved in $CH_2Cl_2$ (5 mL) was added with MCPBA (77%, 2.2 mol equiv.) under magnetic stirring. The end of the reaction was verified by TLC. The final mixture was diluted with $CH_2Cl_2$, washed with $NaHSO_3$ 5% in water, then with $Na_2CO_3$ saturated solution and finally with water. The organic phase was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The obtained crude was almost pure (as a diastereomeric *Z*:*E* mixture) at the $^1$H-NMR analysis (quantitative yields).

**(*E*)** and **(*Z*)-*N*,*N*-Dimethyl-5-[2-(methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazole-3-carboxamide (16aa)**. Yellow solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.02 (3H *Z*, s), 2.36 (3H *Z*, s), 2.40 (3H *E* + 3H *Z*, s), 2.45 (3H *E*, s), 2.81 (3H *E*, s), 2.91 (3H *E*, s), 2.96 (3H *Z*, s), 3.00 (3H *E*, s), 3.05 (3H *Z*, s), 6.32 (1H *E*, d, *J* 15.6 Hz), 6.47 (1H *Z*, d, *J* 11.7 Hz), 7.06 (1H *Z*, d, *J* 11.4 Hz), 7.15 – 7.38 (8H *E* + 8H *Z*, d, *J* 8.1 Hz), 7.44 (1H *E*, d, *J* 15.6 Hz).

**(*E*)** and **(*Z*)-1-{5-[2-(Methylsulfonyl)vinyl]-1,4-di-*p*-tolyl-1*H*-pyrazol-3-yl}ethanone (16ad)**. Beige solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 1.98 (3H *Z*, s), 2.37 (3H *Z*, s), 2.42 (3H Z + 3H *E*, s), 2.47 (3H *E*, s), 2.57 (3H *E*, s), 2.62 (3H *Z*, s), 2.76 (3H *E*, s), 6.15 (1H *E*, d, *J* 15.6 Hz), 6.39 (1H *Z*, d, *J* 11.4 Hz), 6.95 (1H *Z*, d, *J* 11.4 Hz), 7.16 – 7.37 (5H *E* + 6H *Z*, m), 7.37 (4H, *E*, s), 7.44 (2H *Z*, d, *J* 8.4 Hz).

A few milligrams of the *E* isomer could be isolated. Beige solid. $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ (ppm) 2.42 (3H, s), 2.47 (3H, s), 2.56 (3H, s), 2.76 (3H, s), 6.15 (1H, d, *J* 15.6 Hz), 7.21 (2H, d, *J* 8.3 Hz), 7.27 (2H, d, *J* 8.0 Hz), 7.33 (1H, d, *J* 15.7 Hz) 7.37 ( 4H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (ppm) 21.3, 21.4, 27.9, 42.8, 125.7, 126.5, 127.9, 129.1, 129.5, 129.6, 130.4, 134.4, 135.8, 138.4, 140.2, 148.1, 193.6 (two isochronous carbons). HRMS (ESI) *m/z* calcd $[M + H]^+$ $C_{22}H_{23}N_2O_3S$ 395.1424, found 395.1427.

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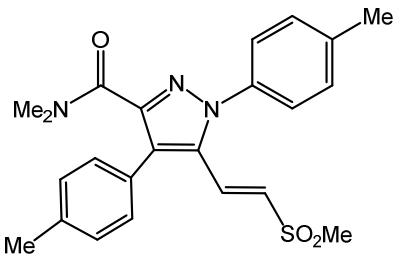
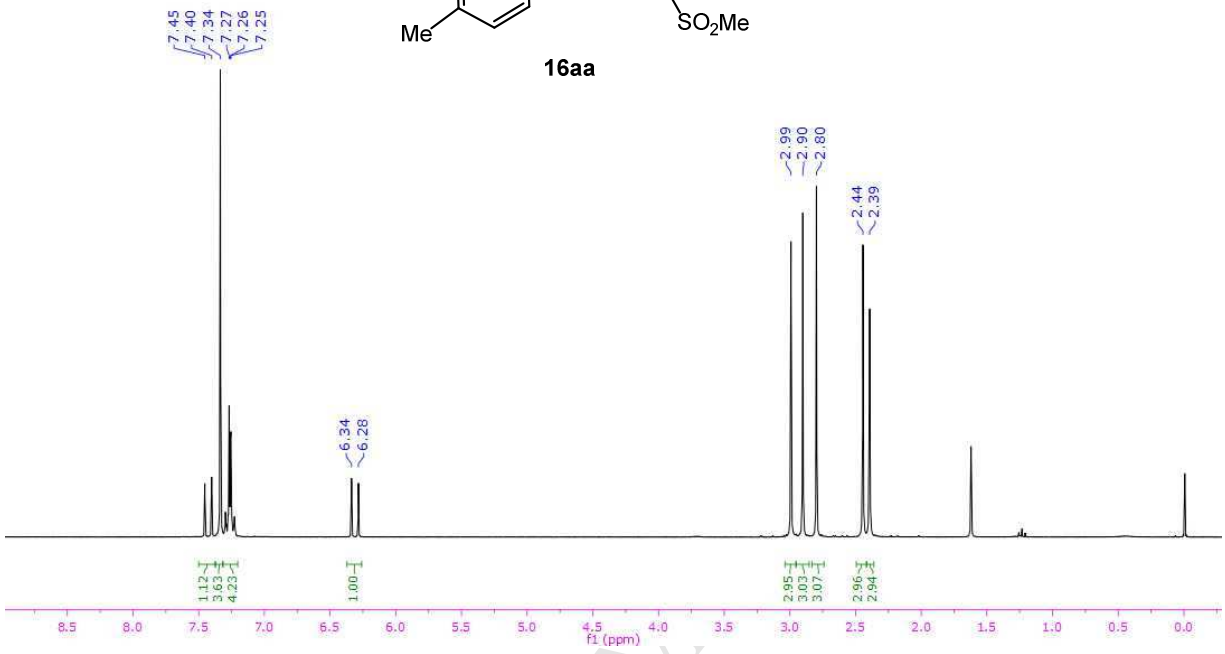
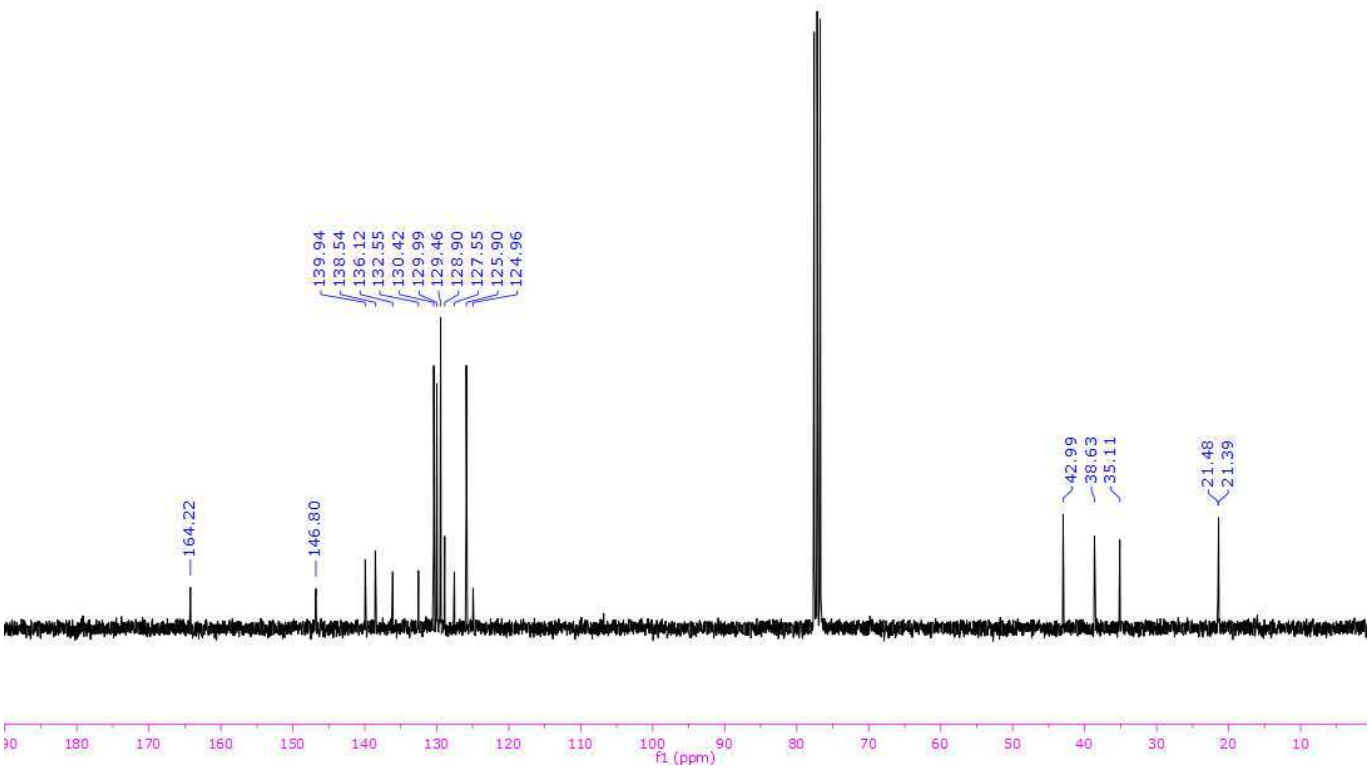
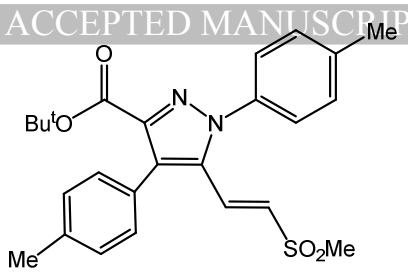
**$^1$H and $^{13}$C NMR Spectra**




**16aa**

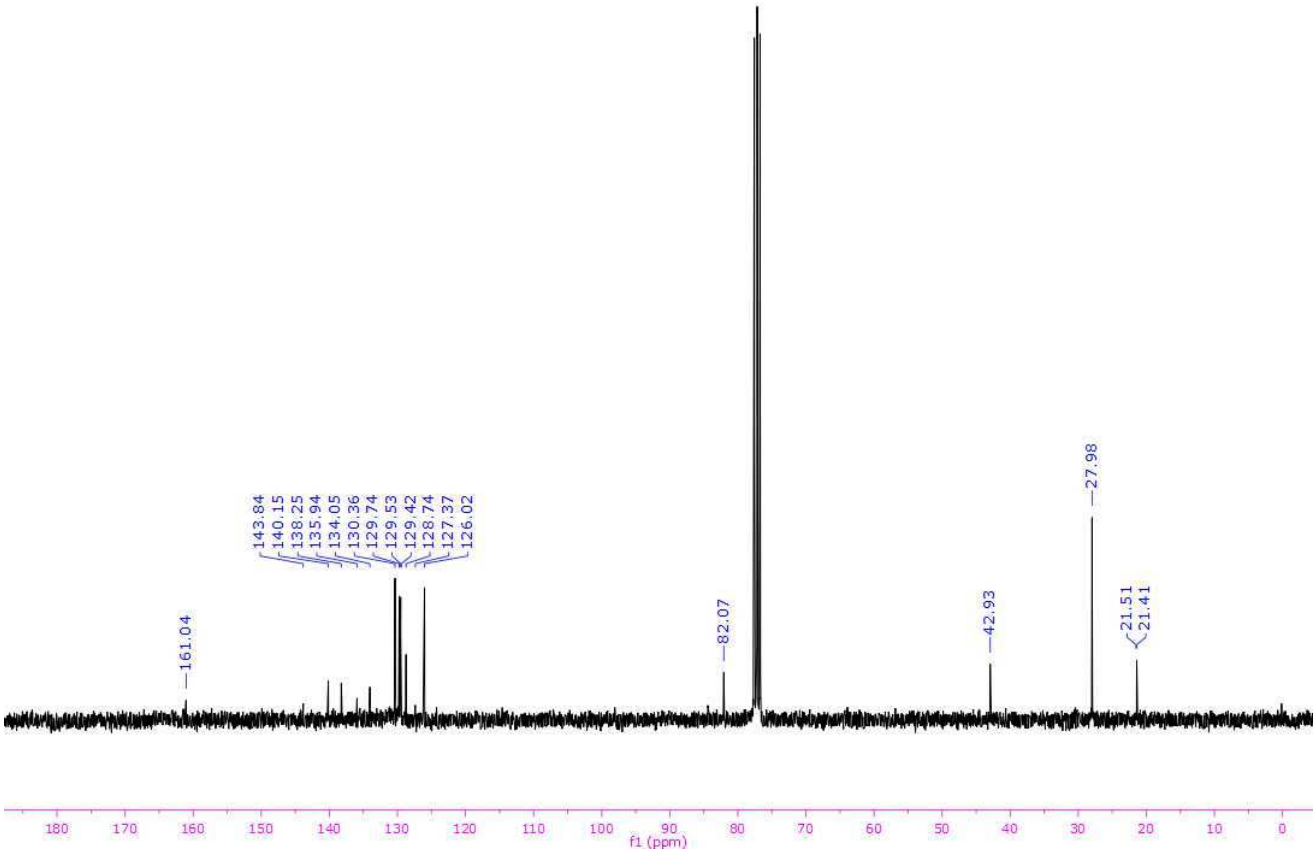


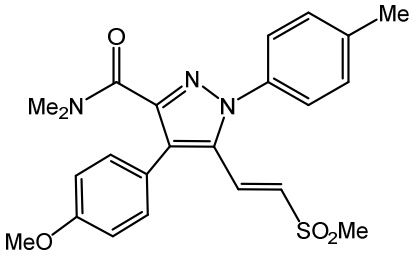





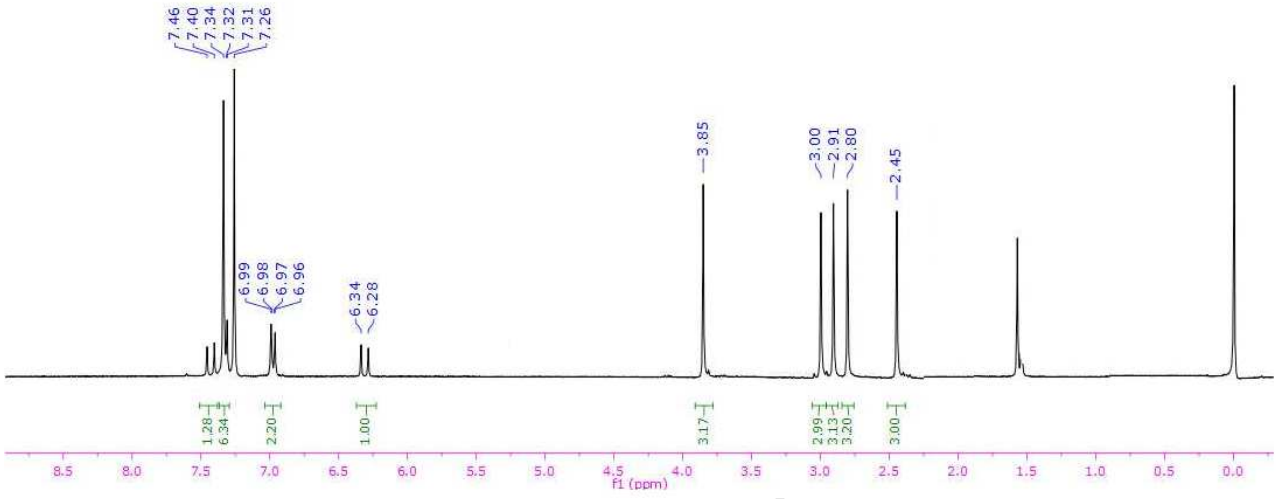

**16ab**

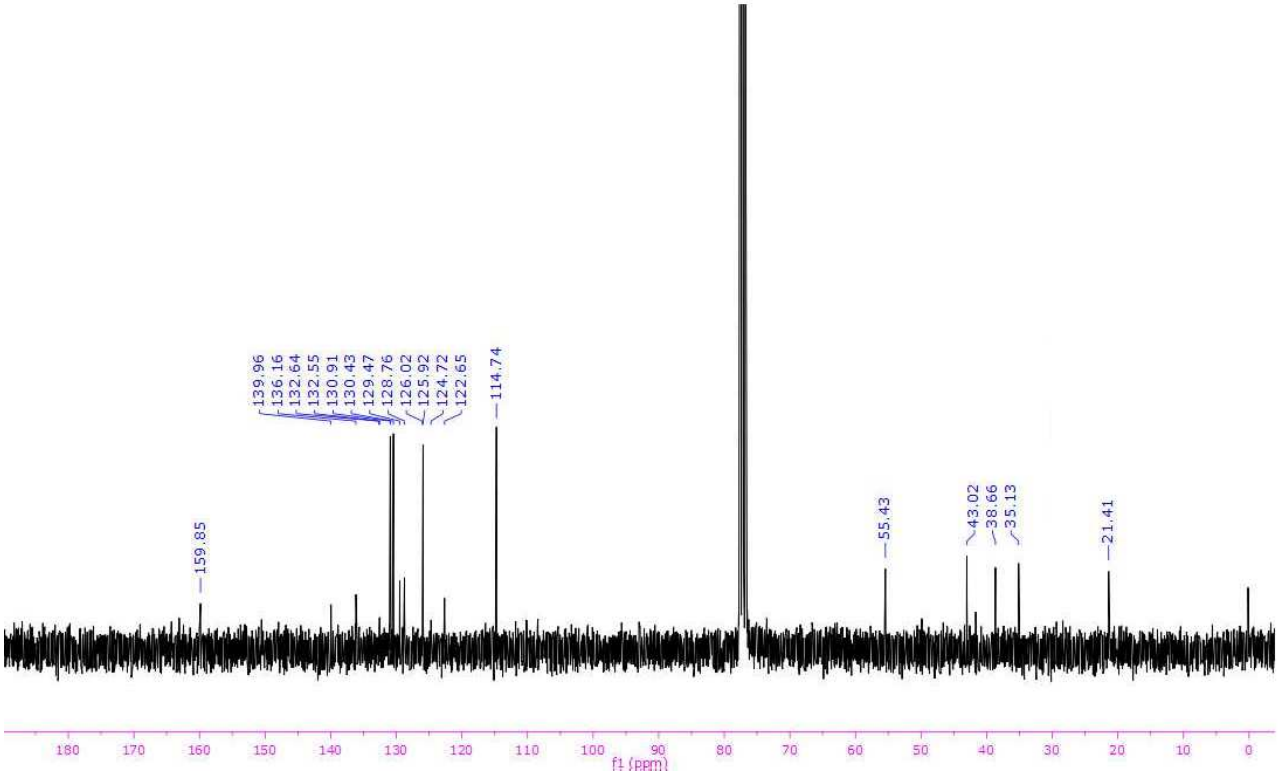


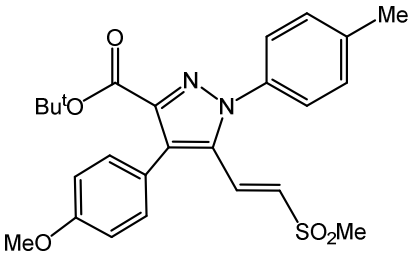






**16ba**

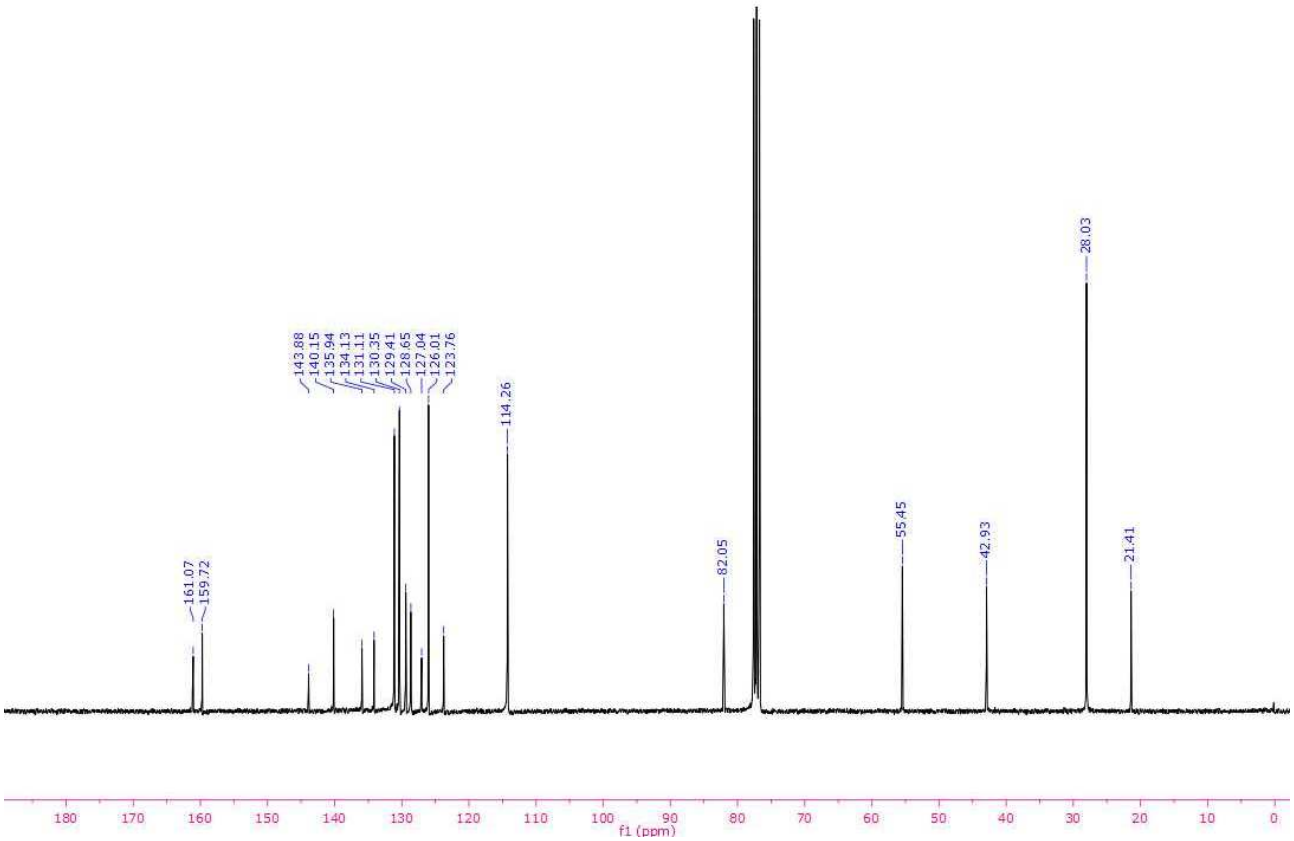


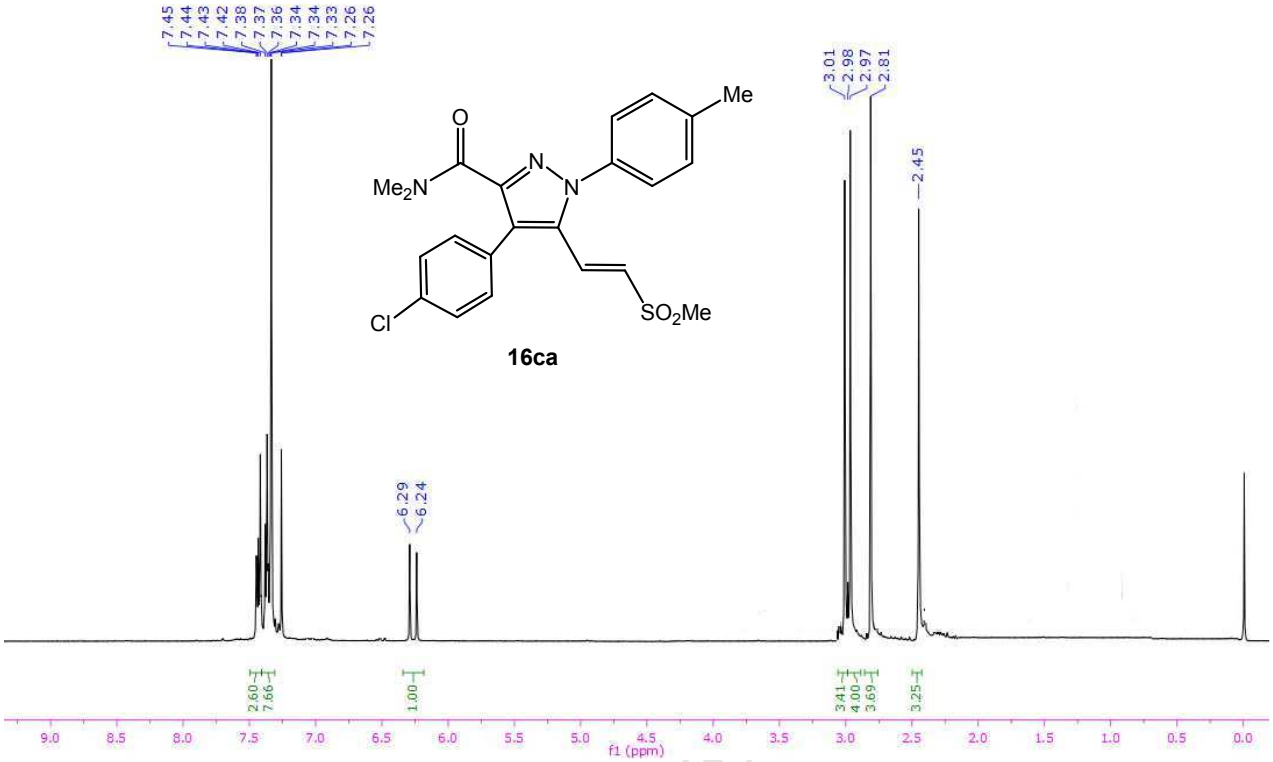



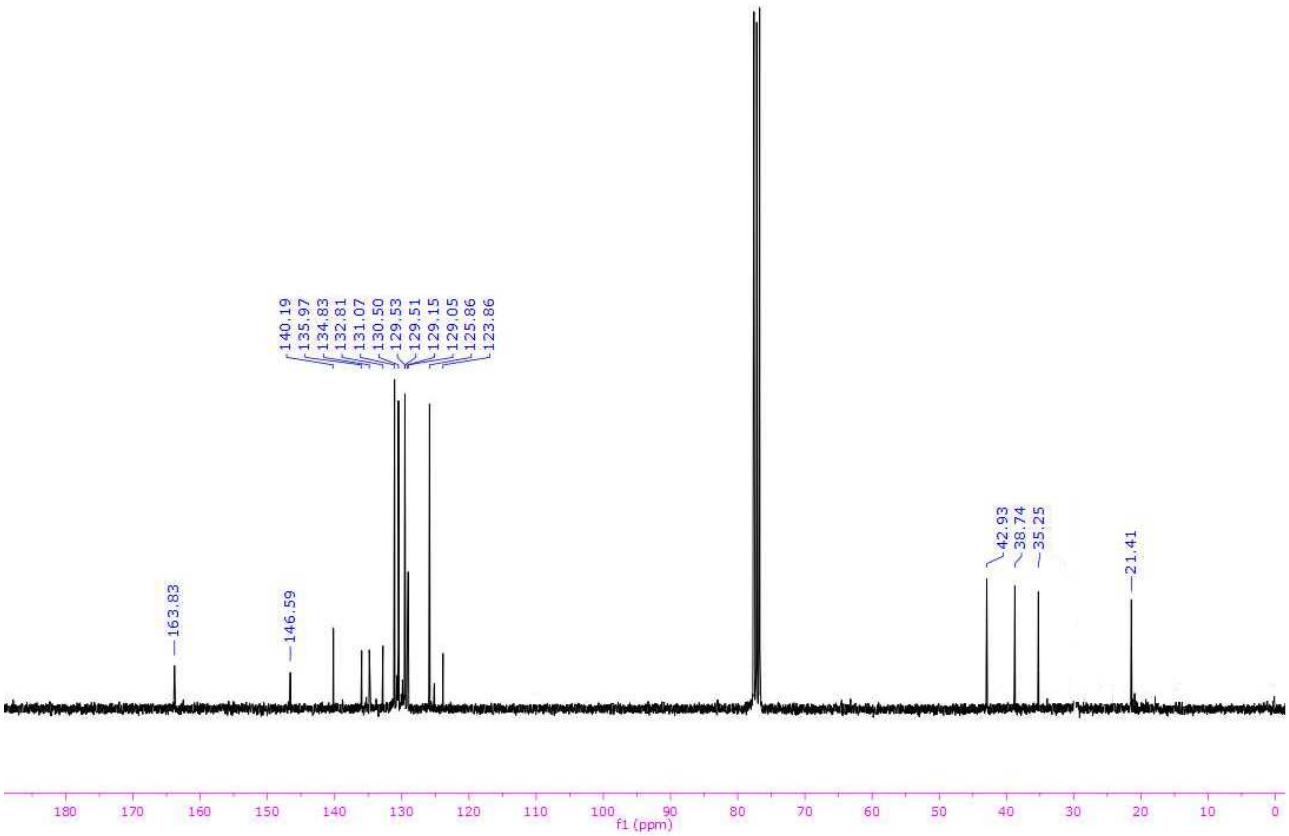


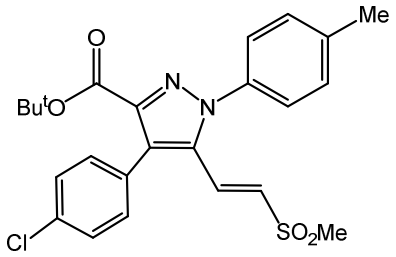

**16bb**



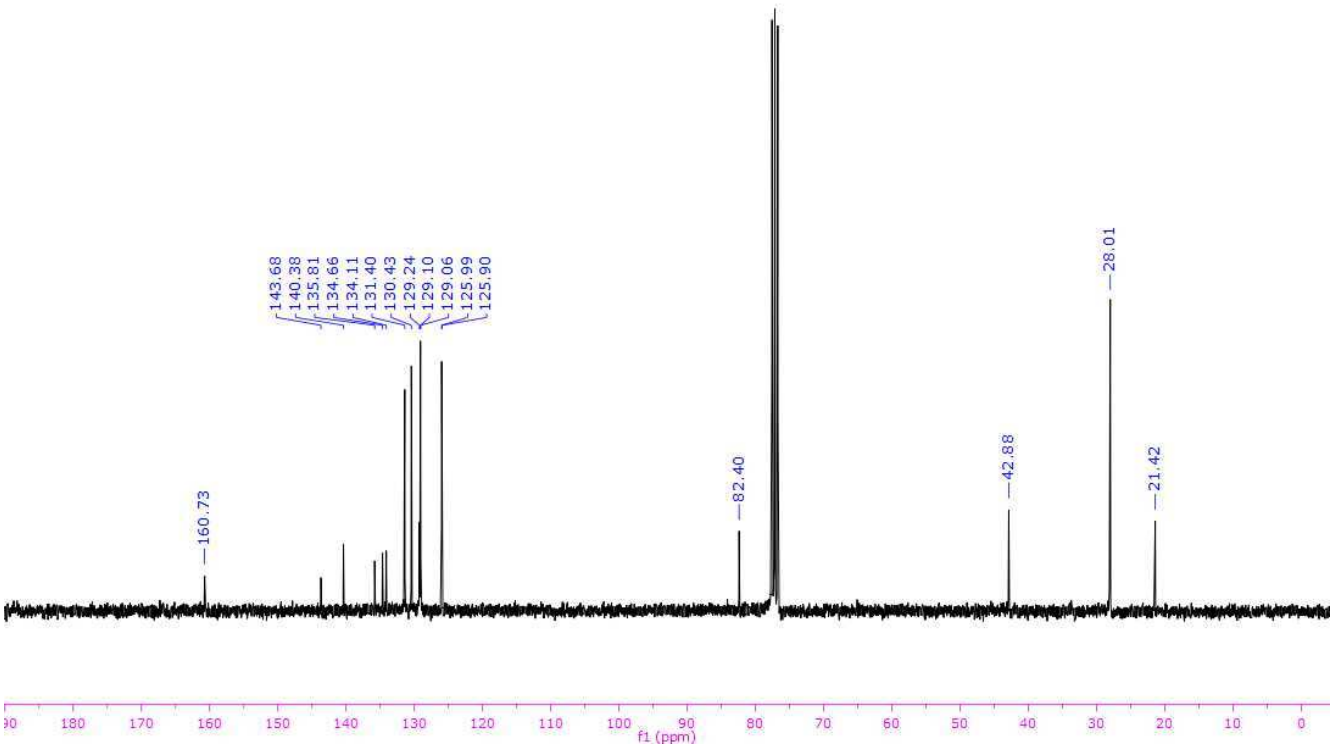


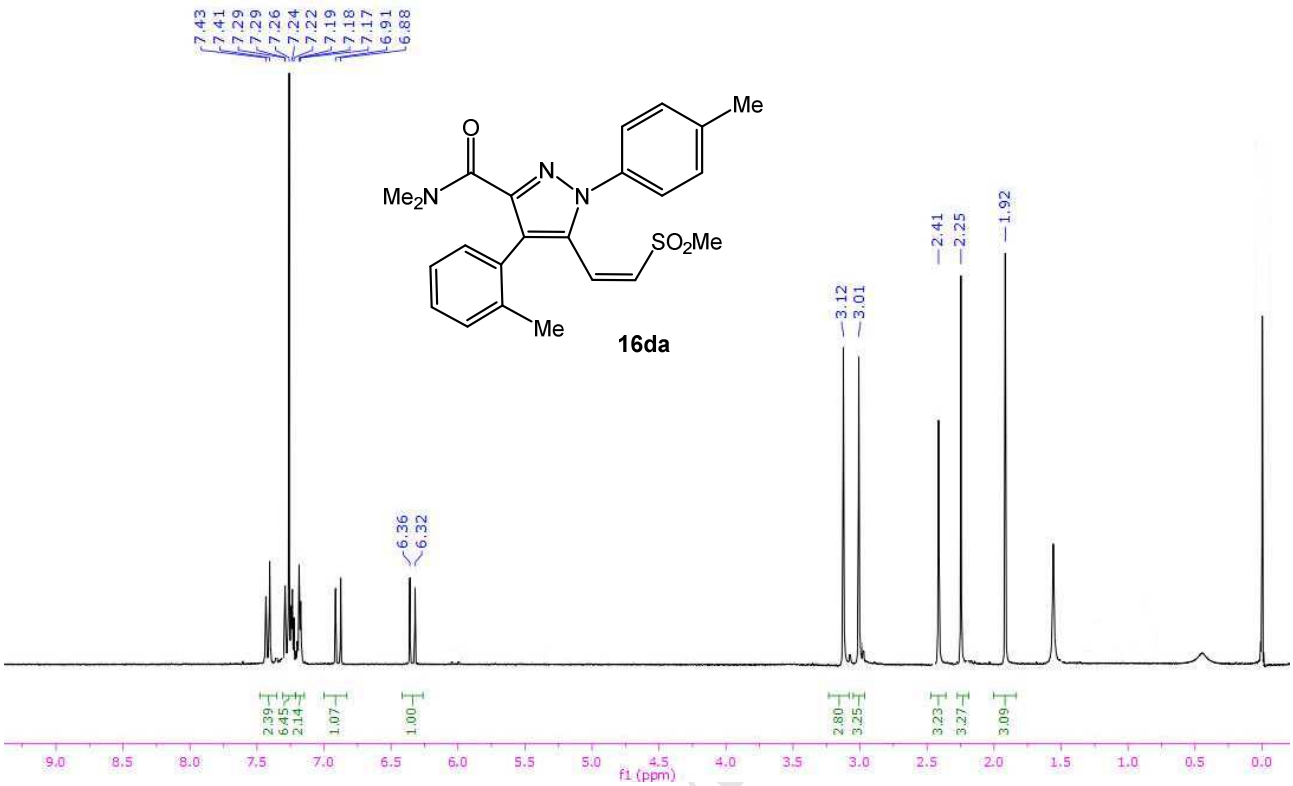



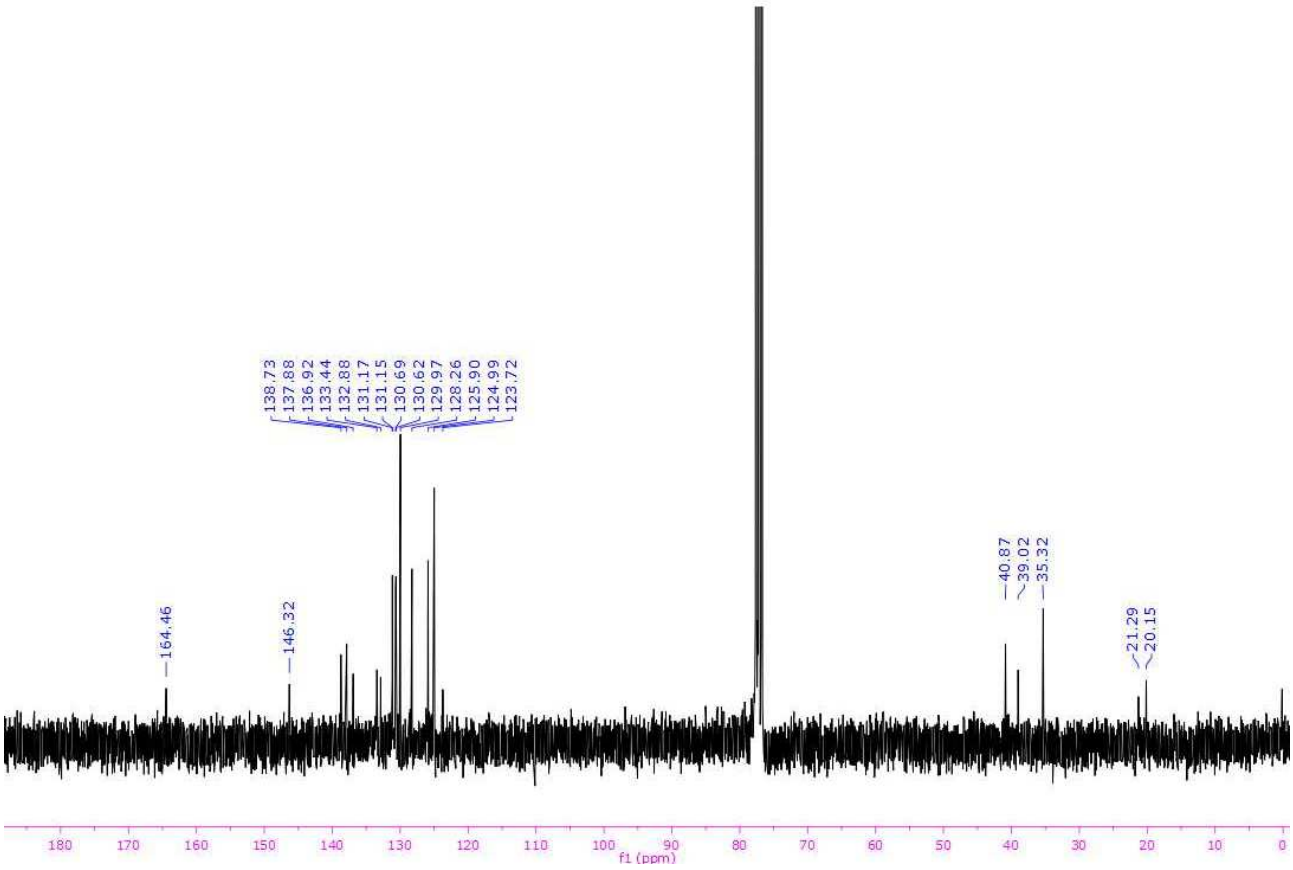


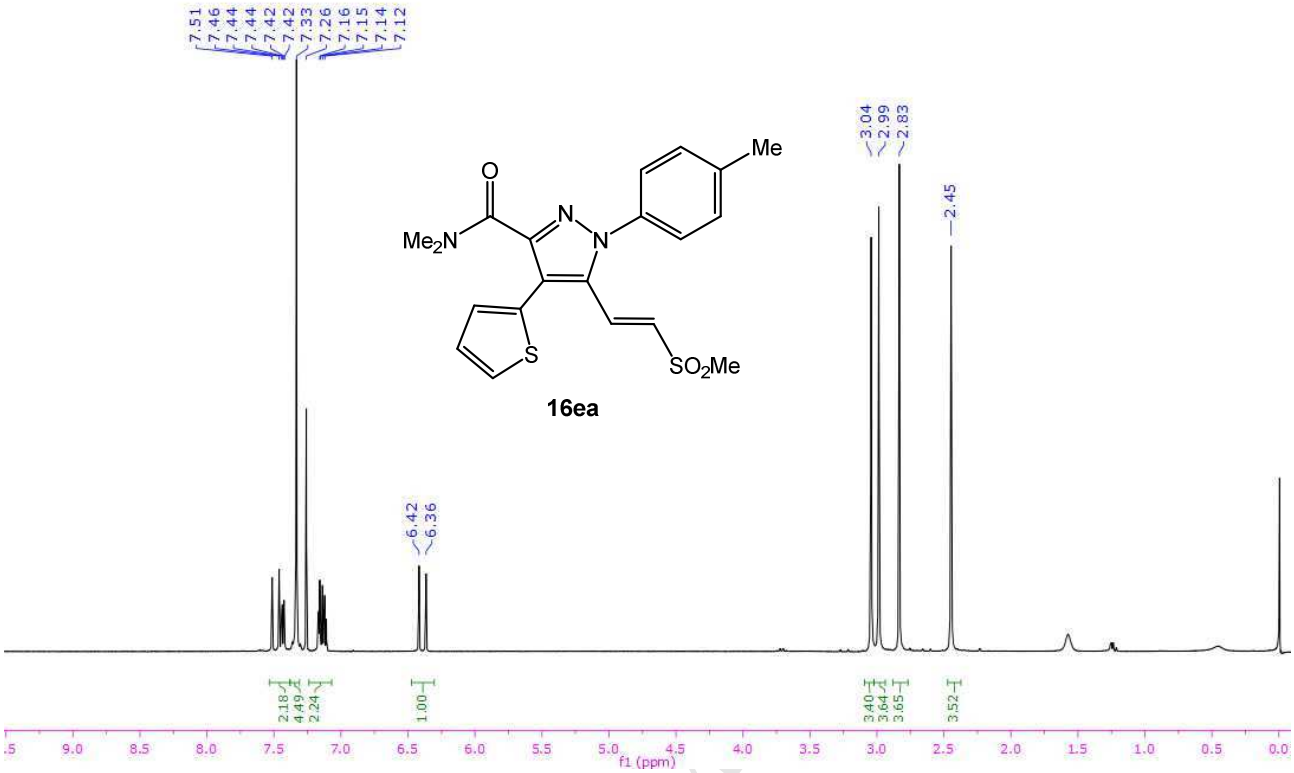

**16cb**

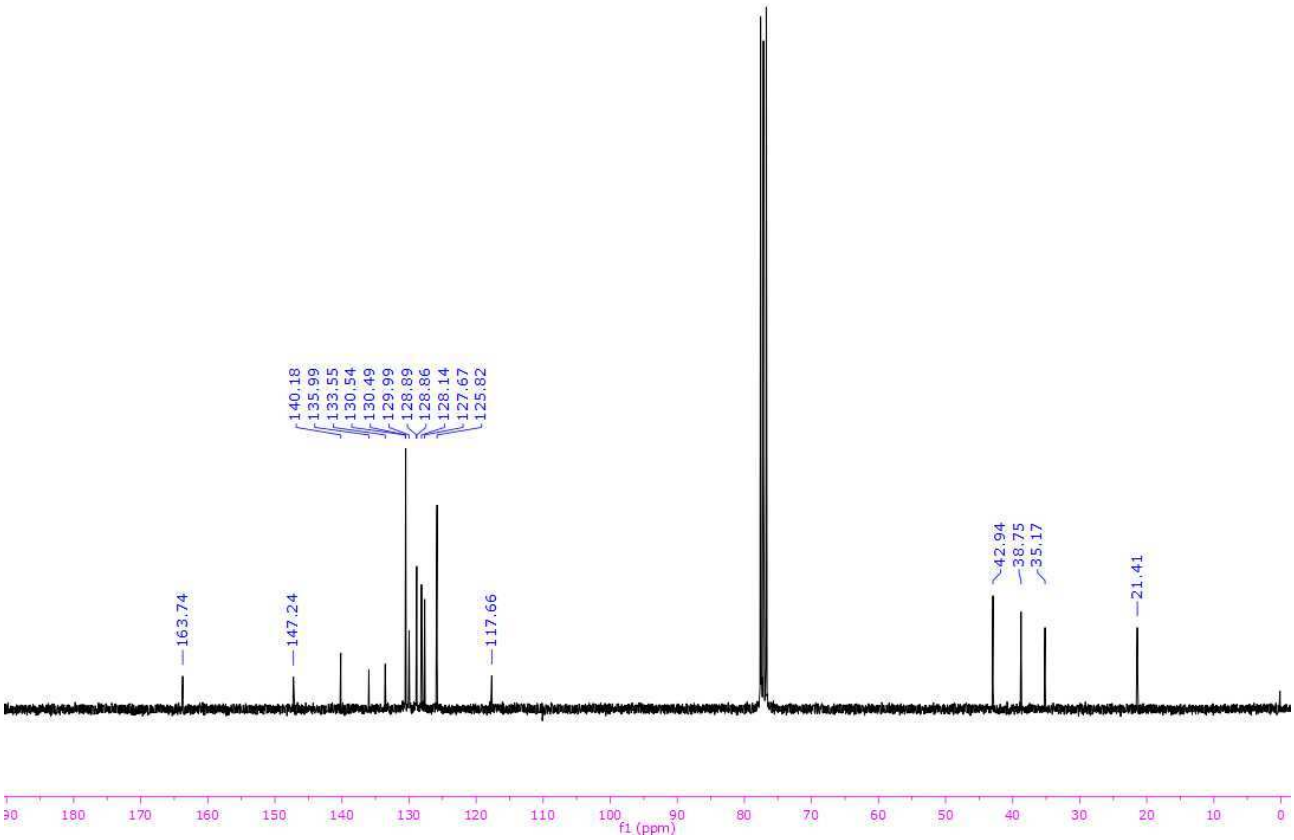


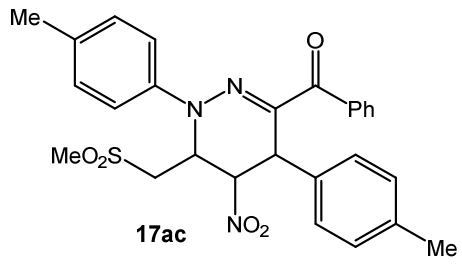





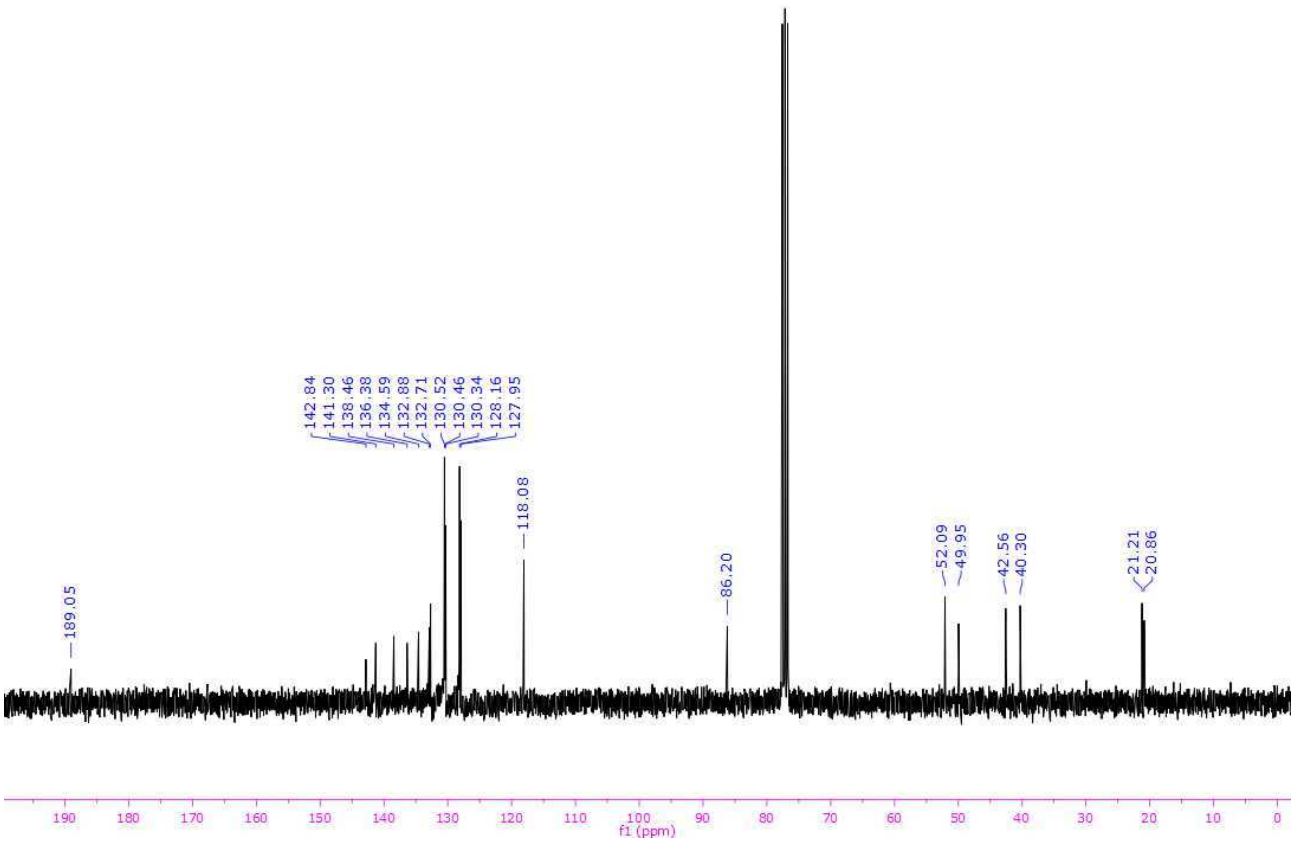


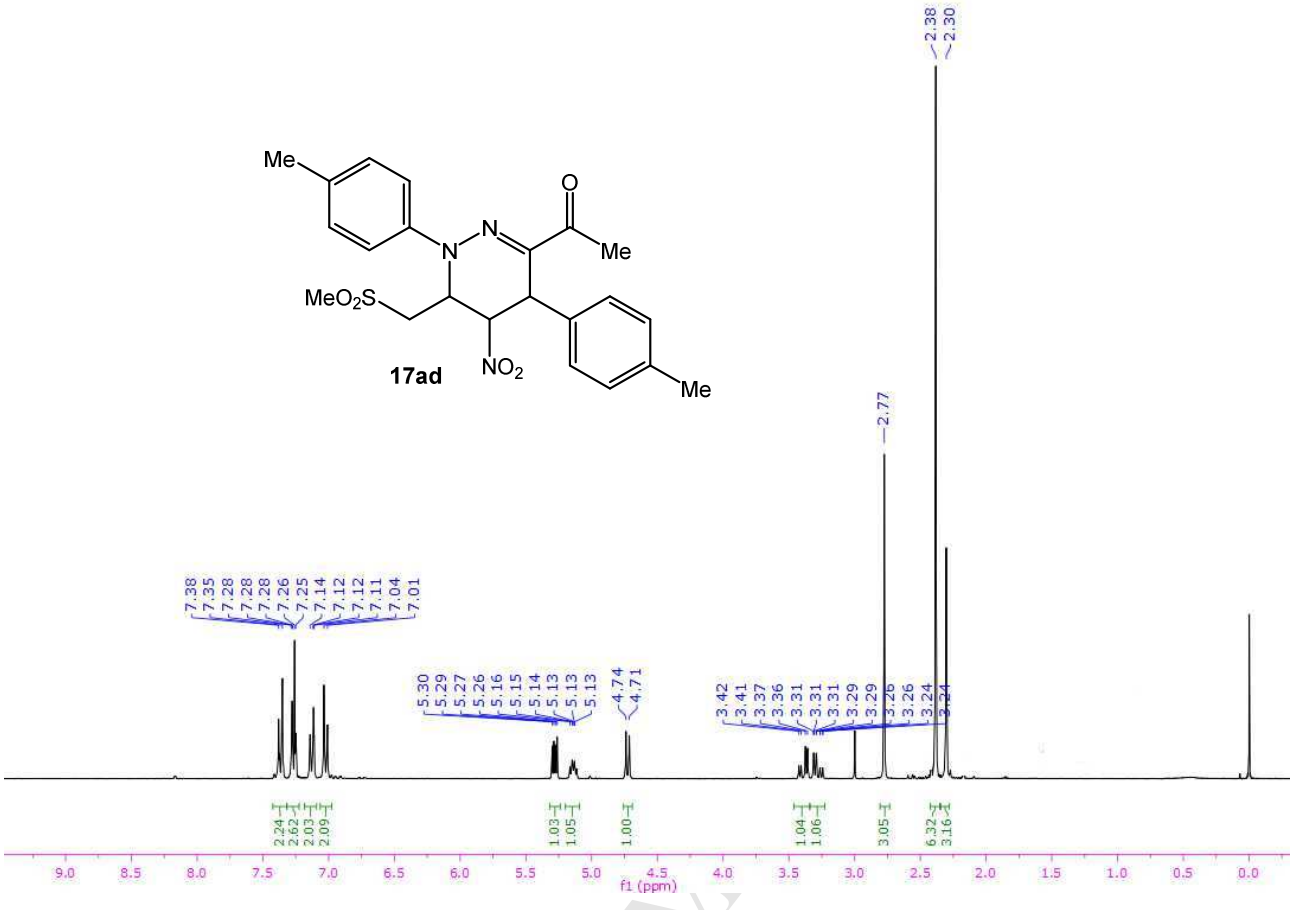



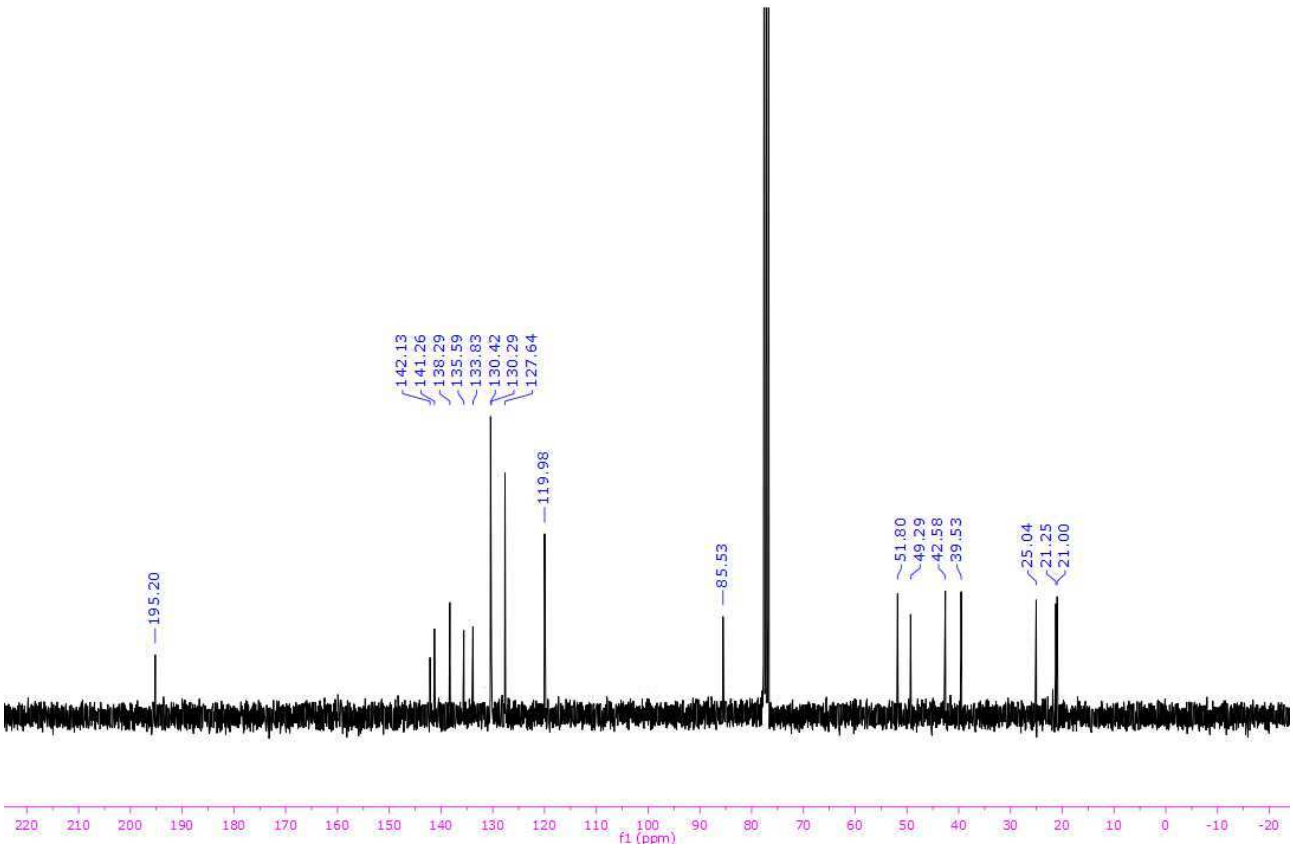


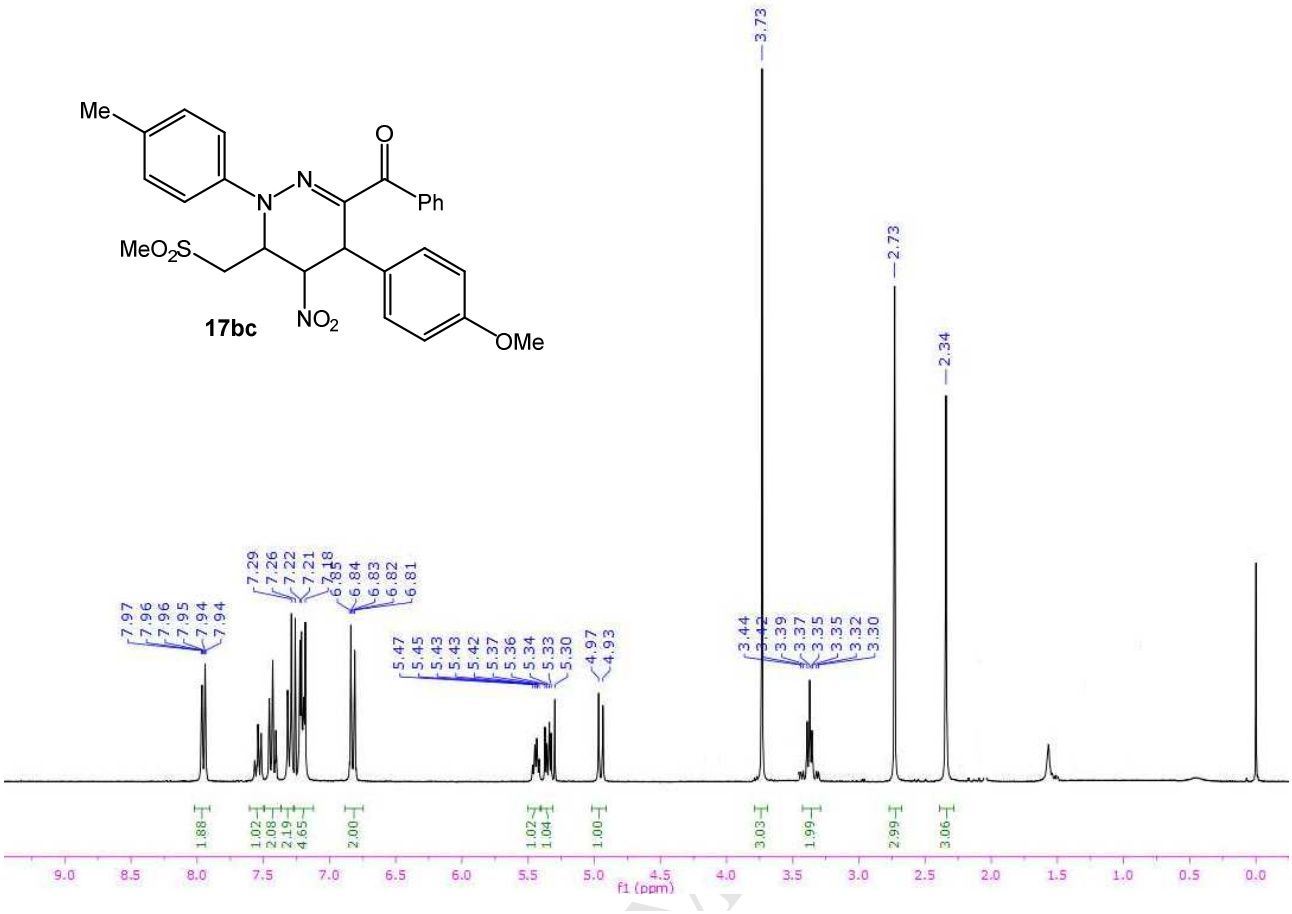

17ac

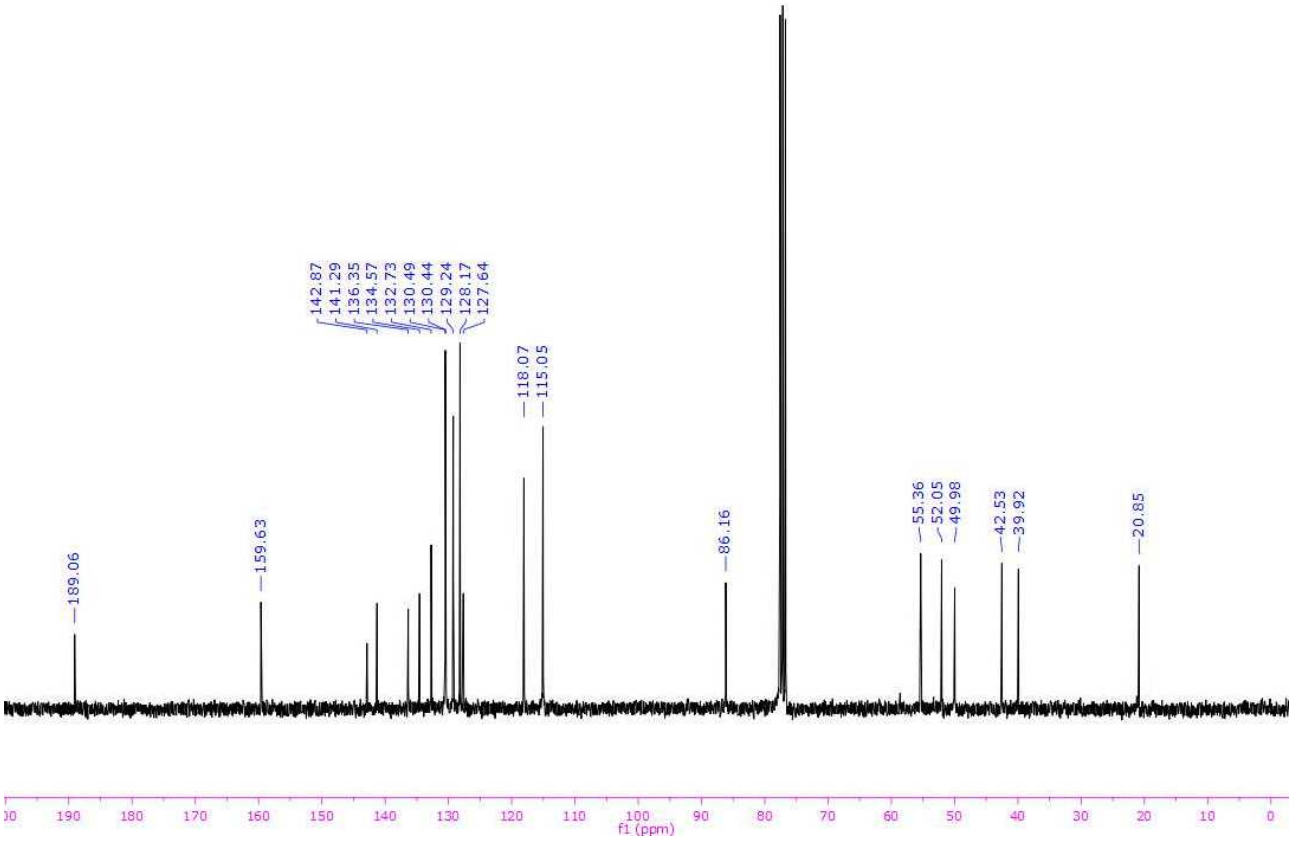


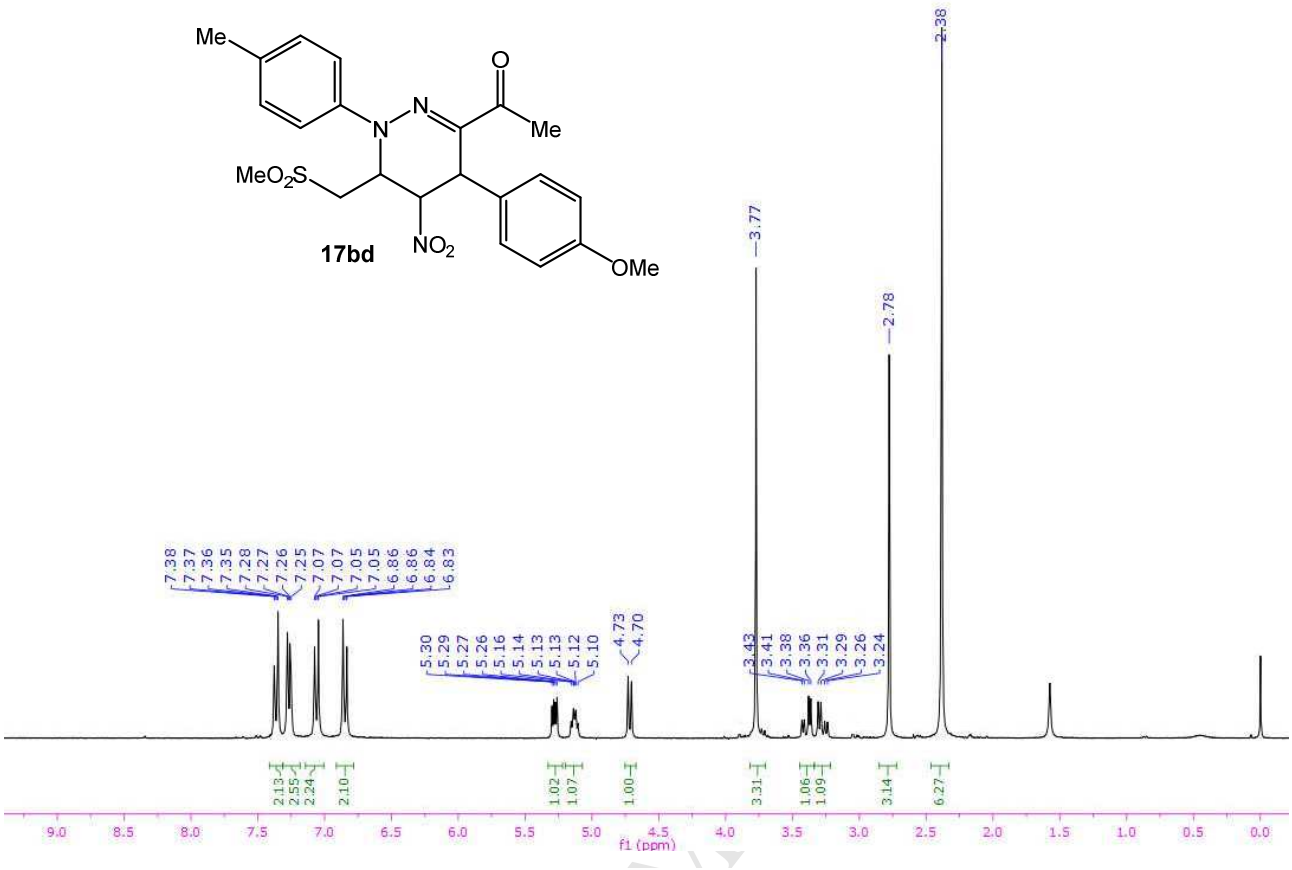



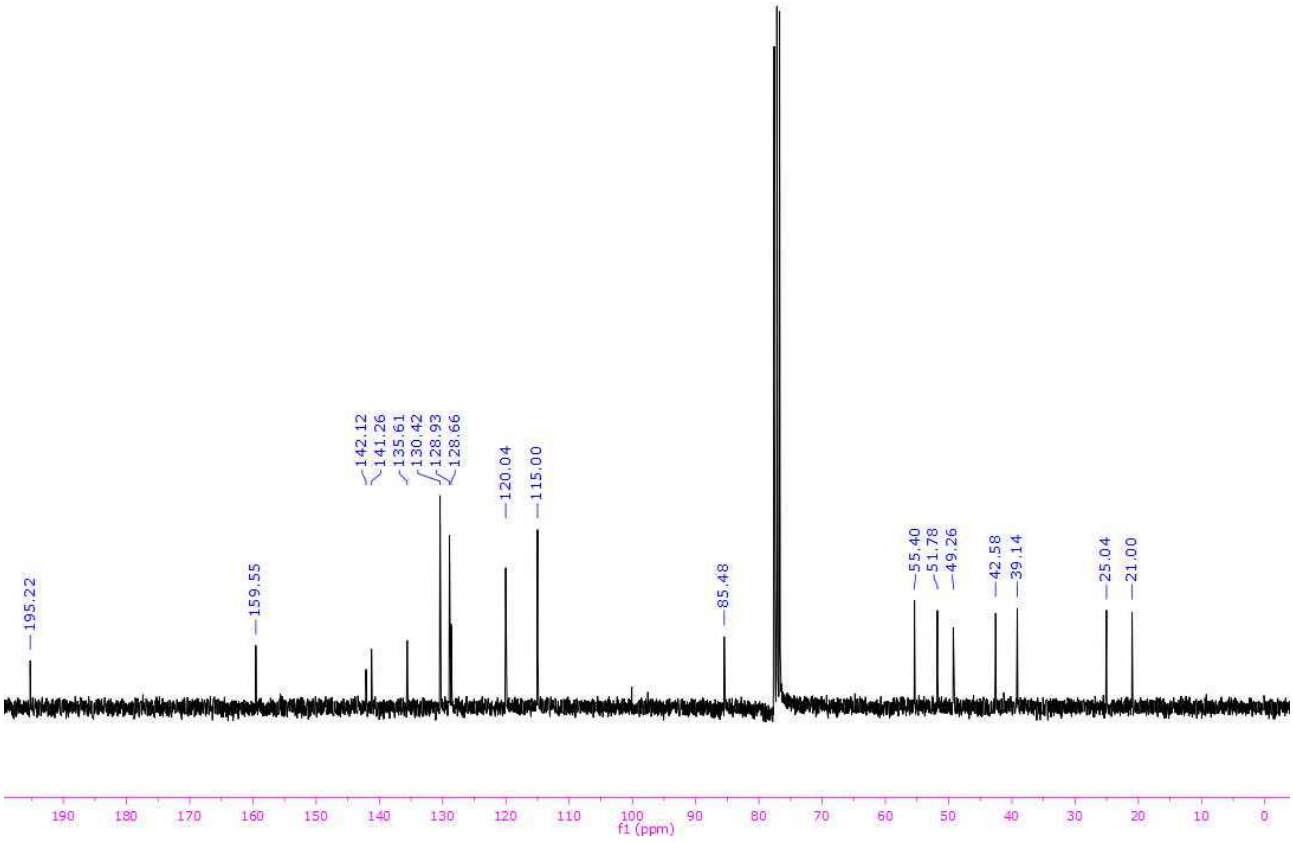


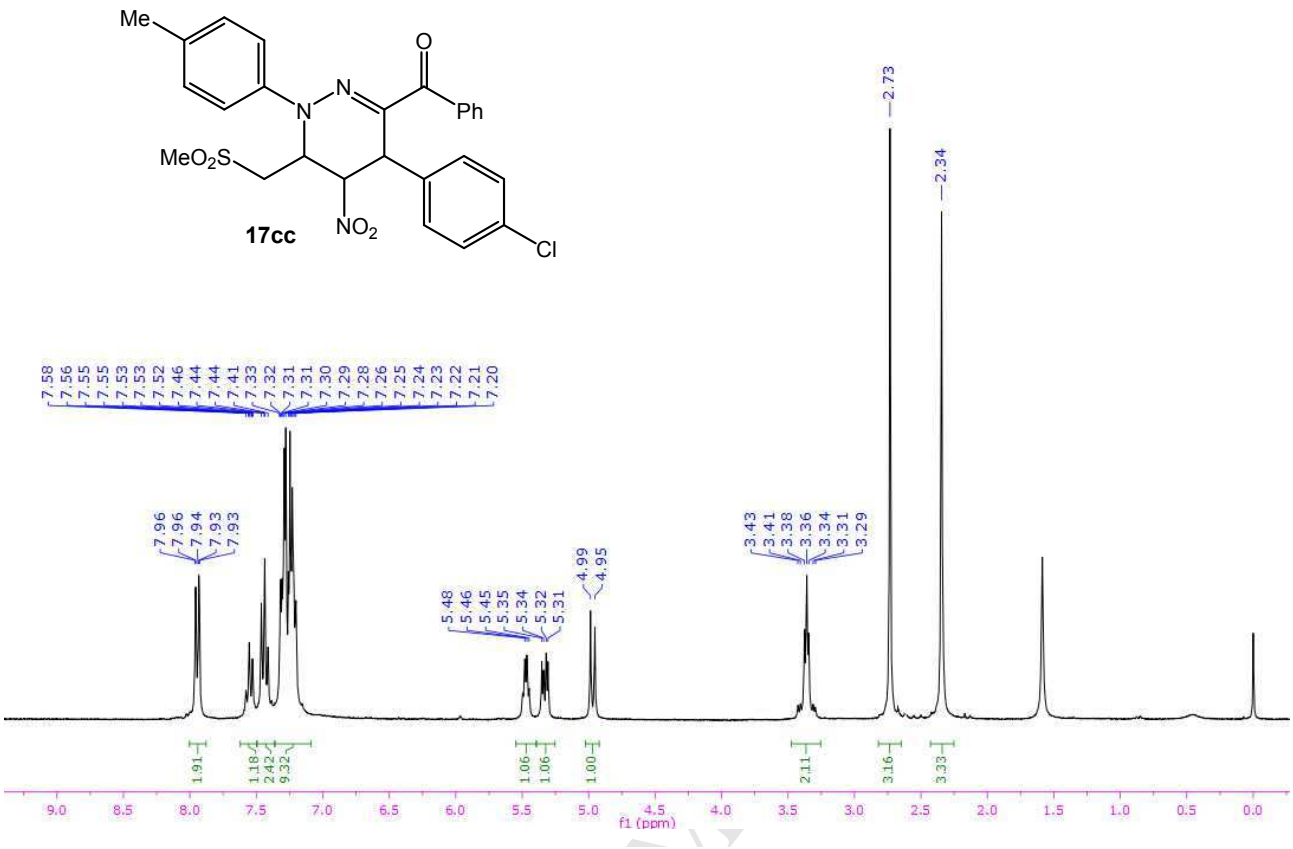



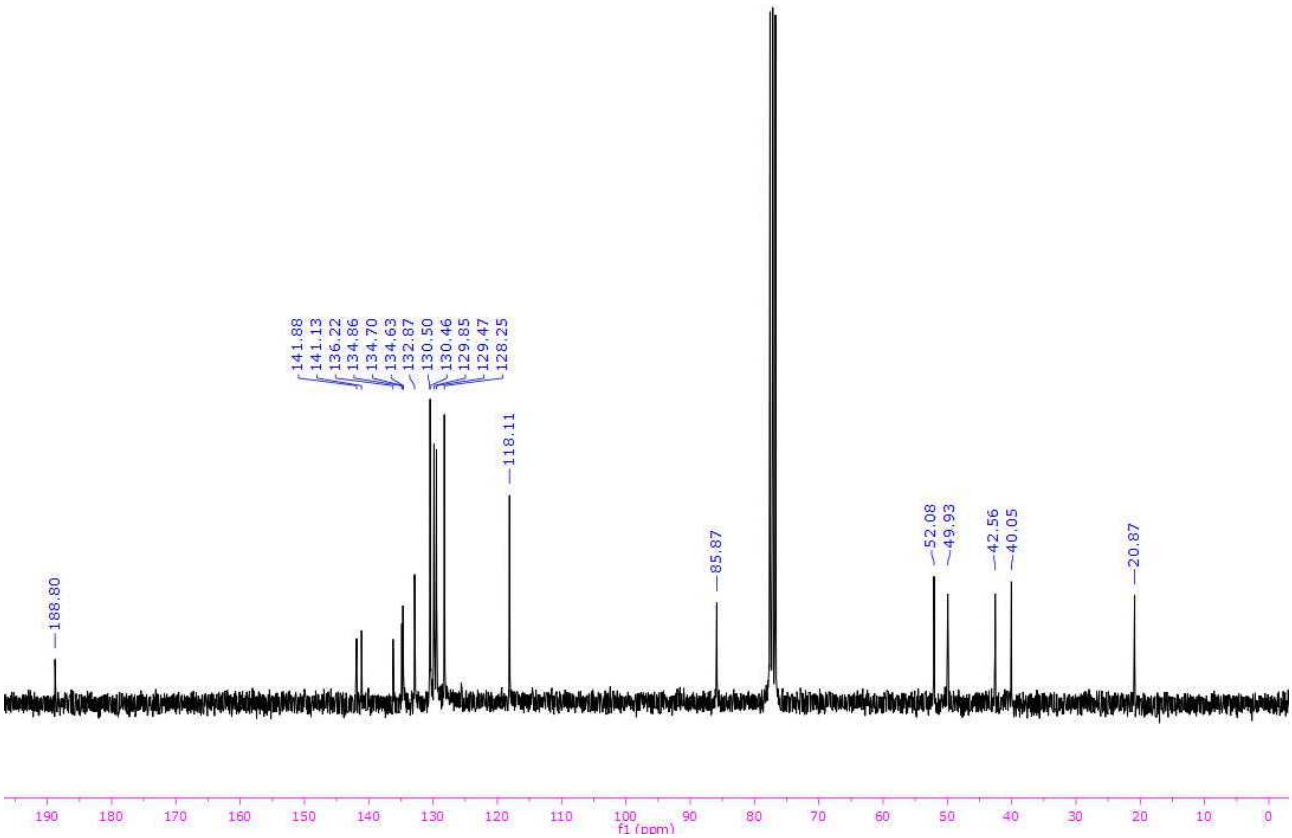


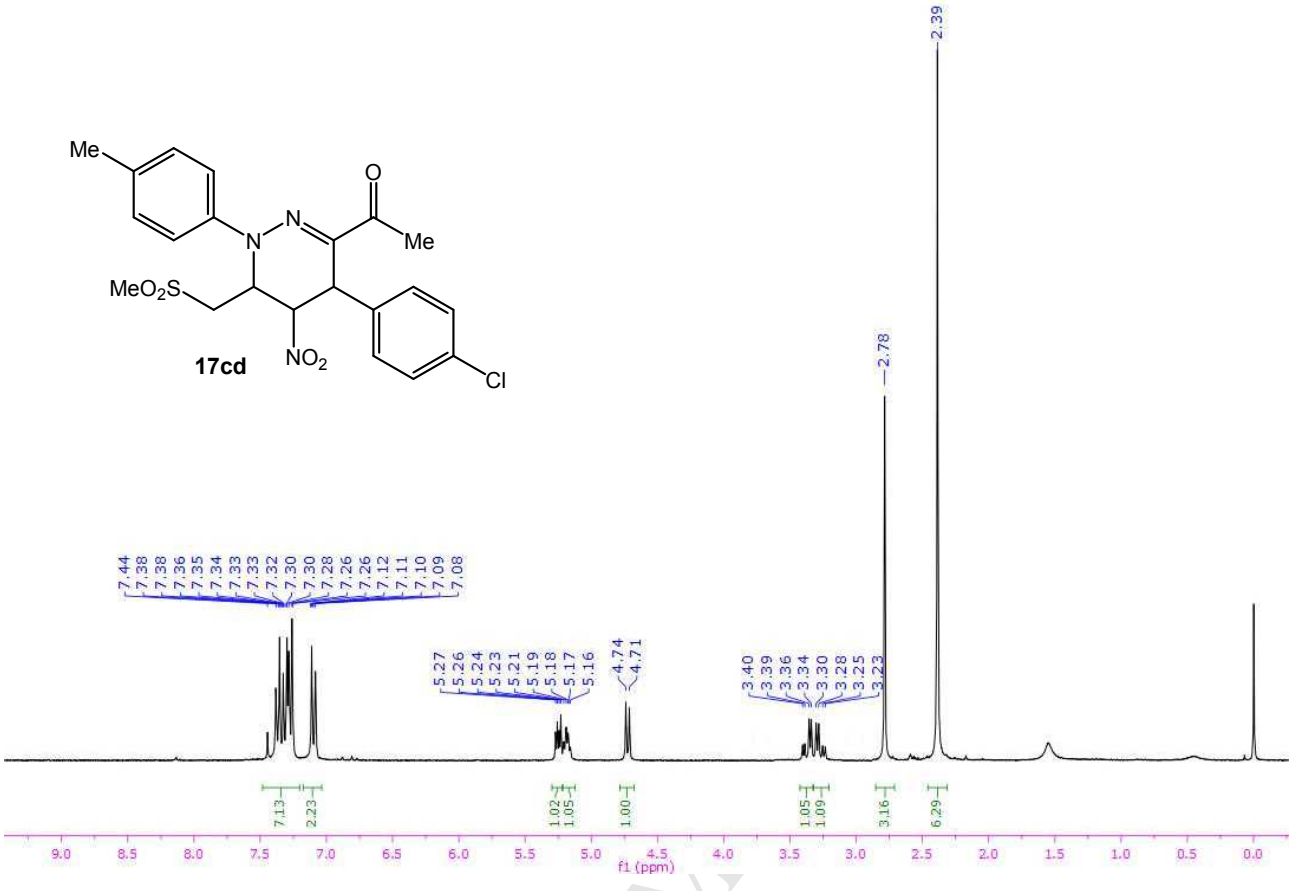



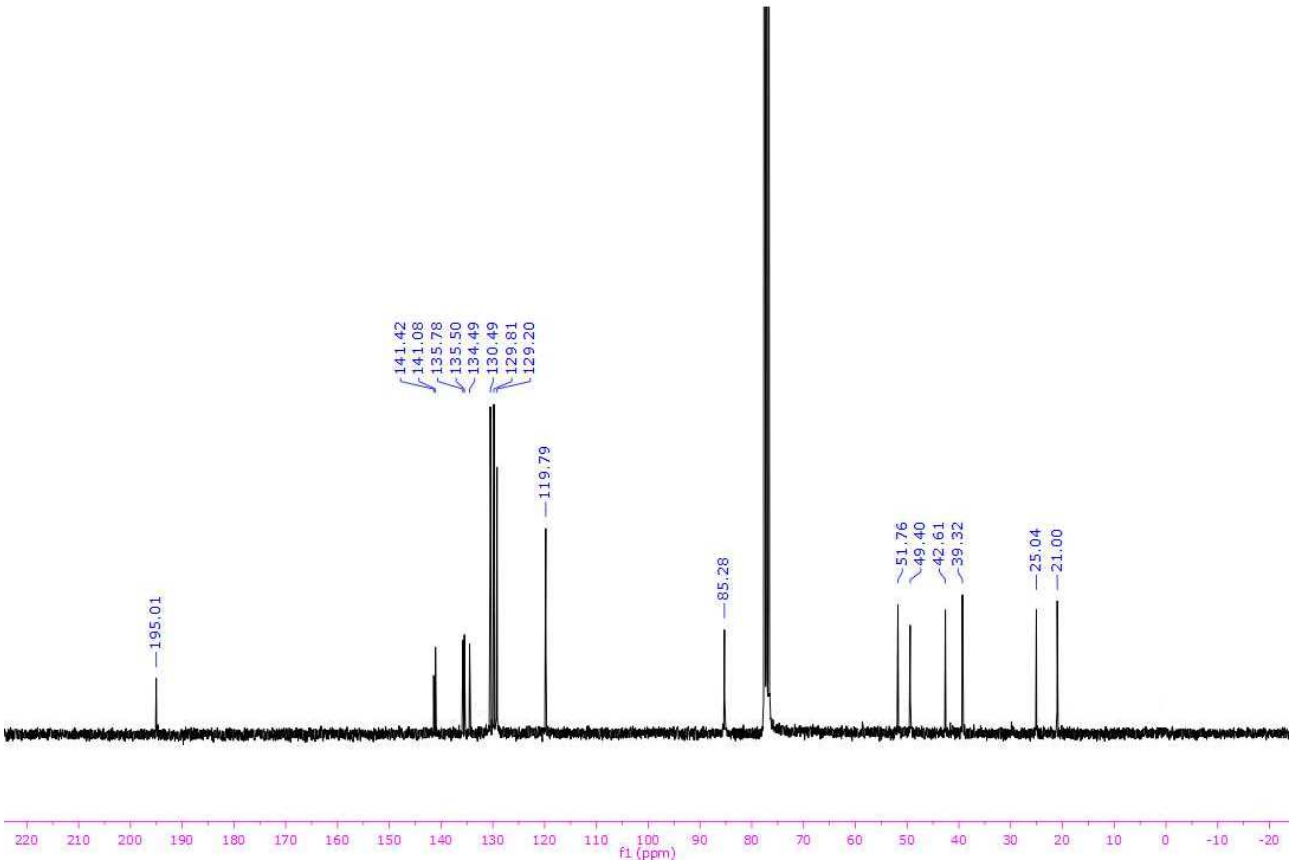


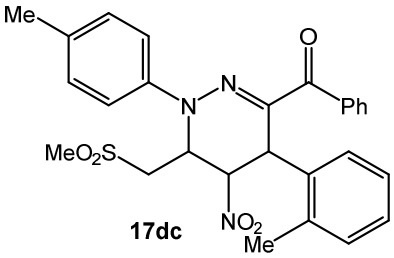





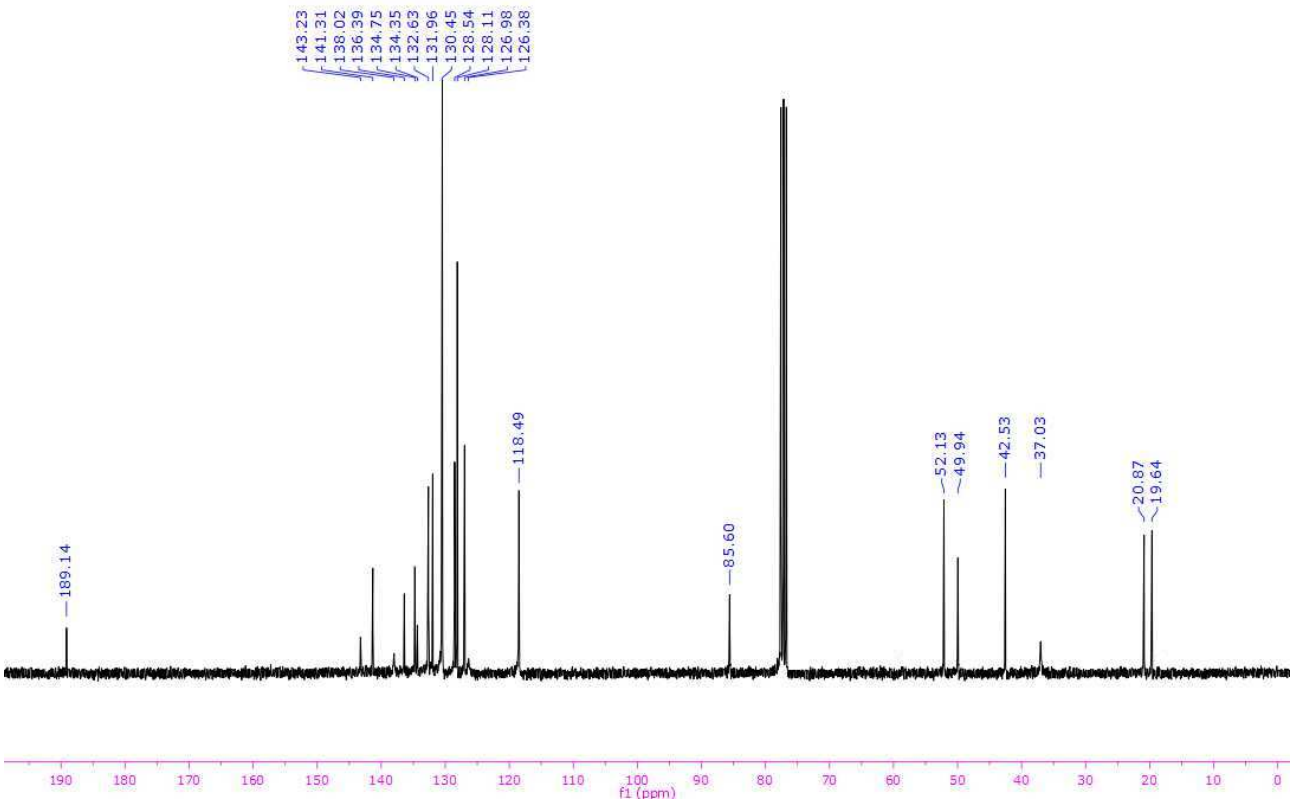


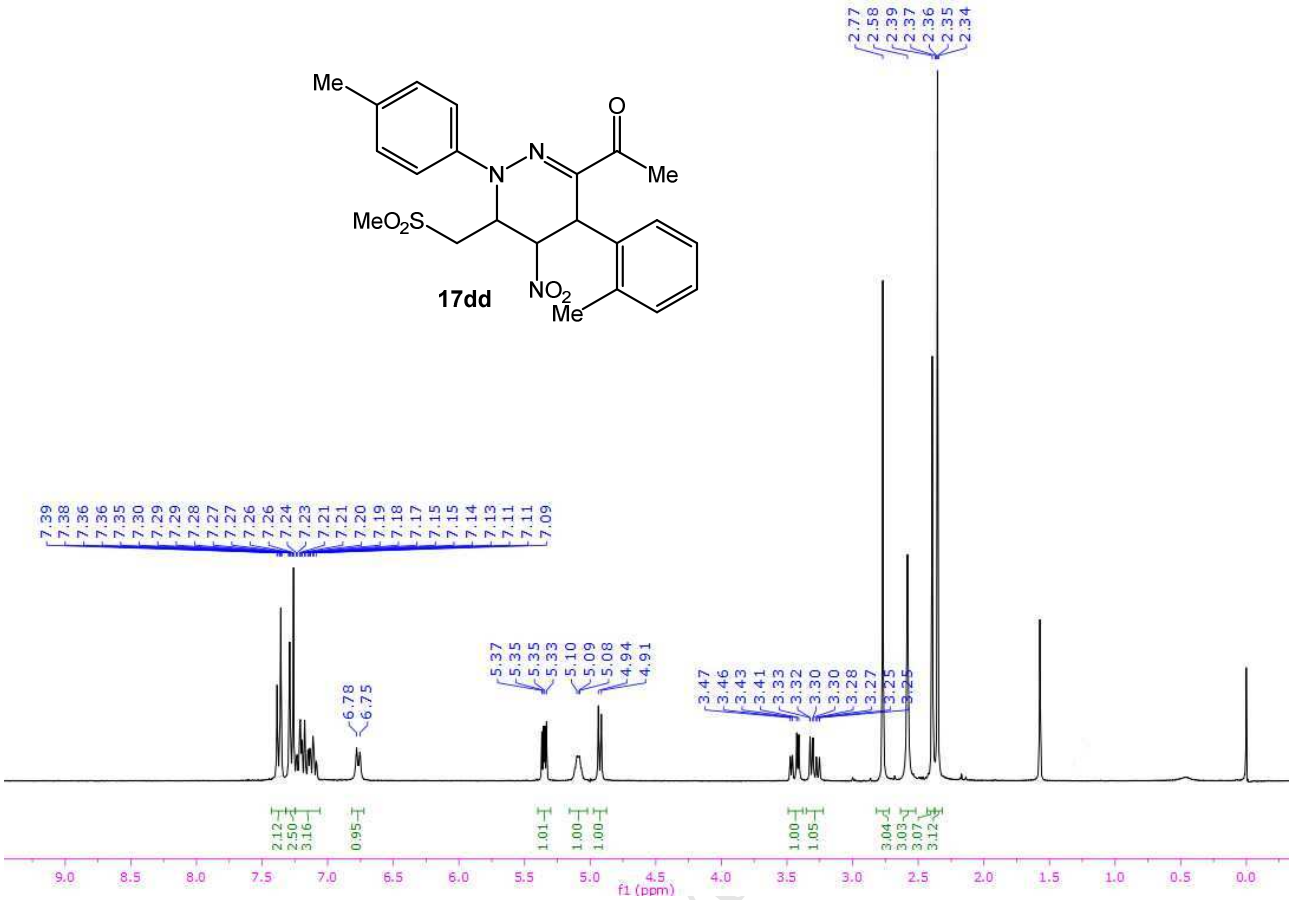



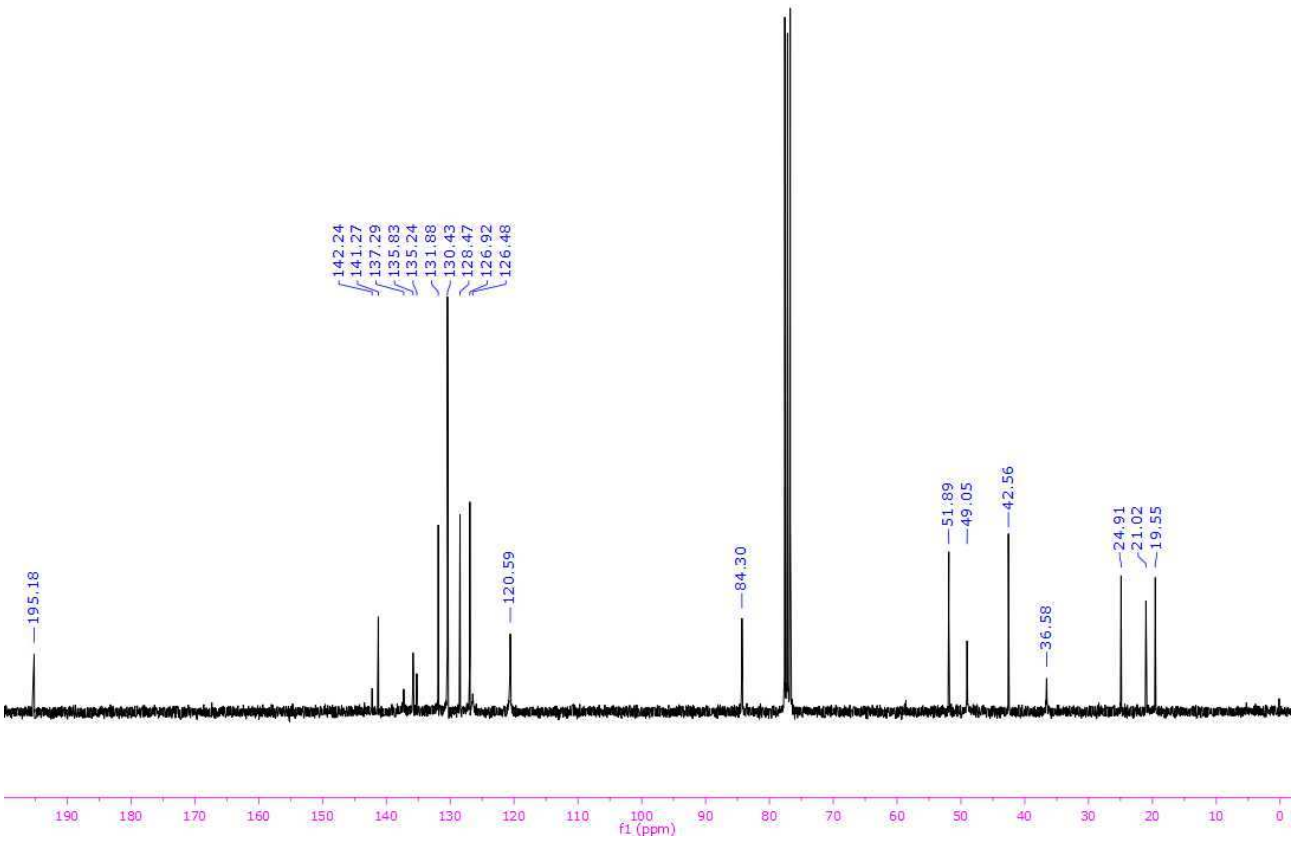


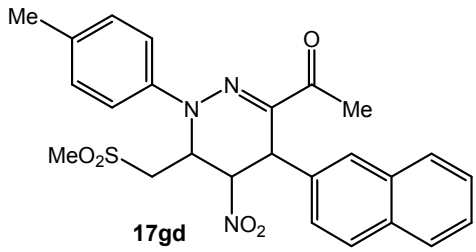

**17dc**





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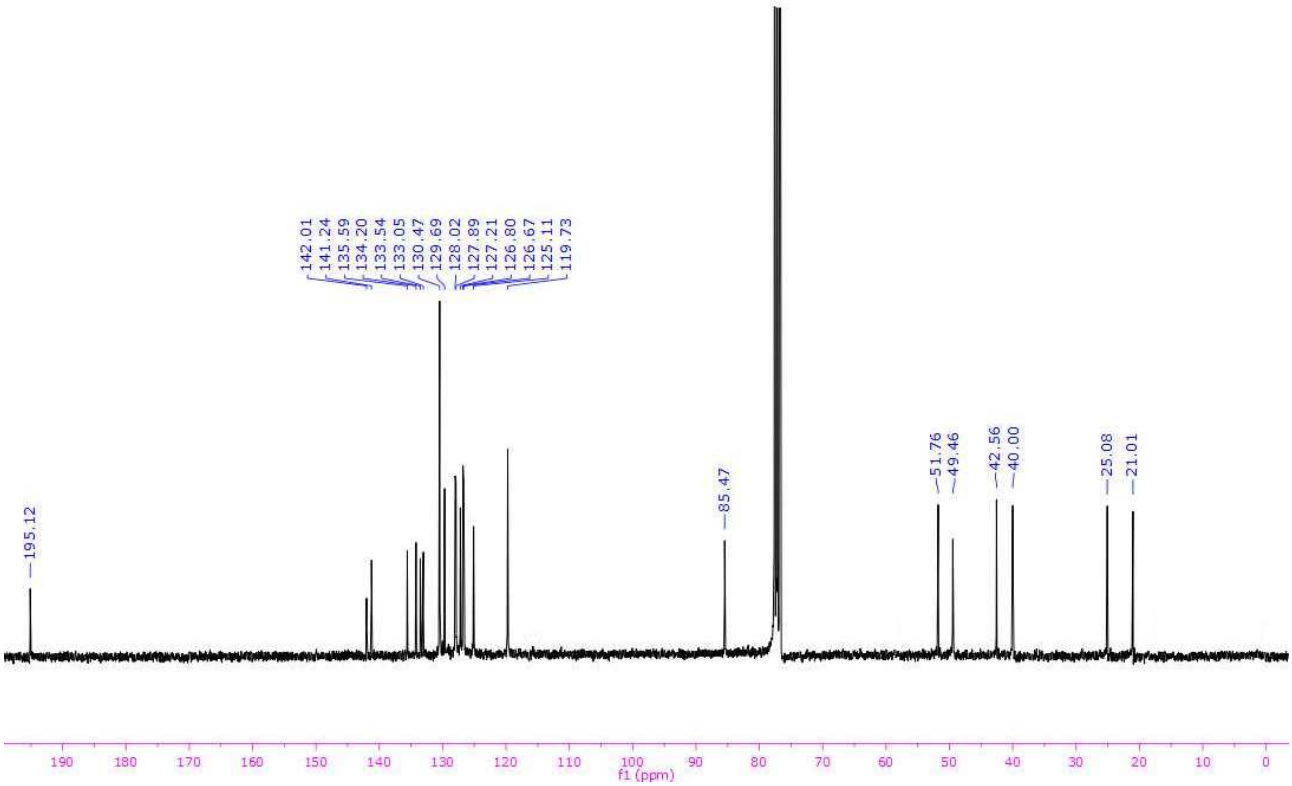
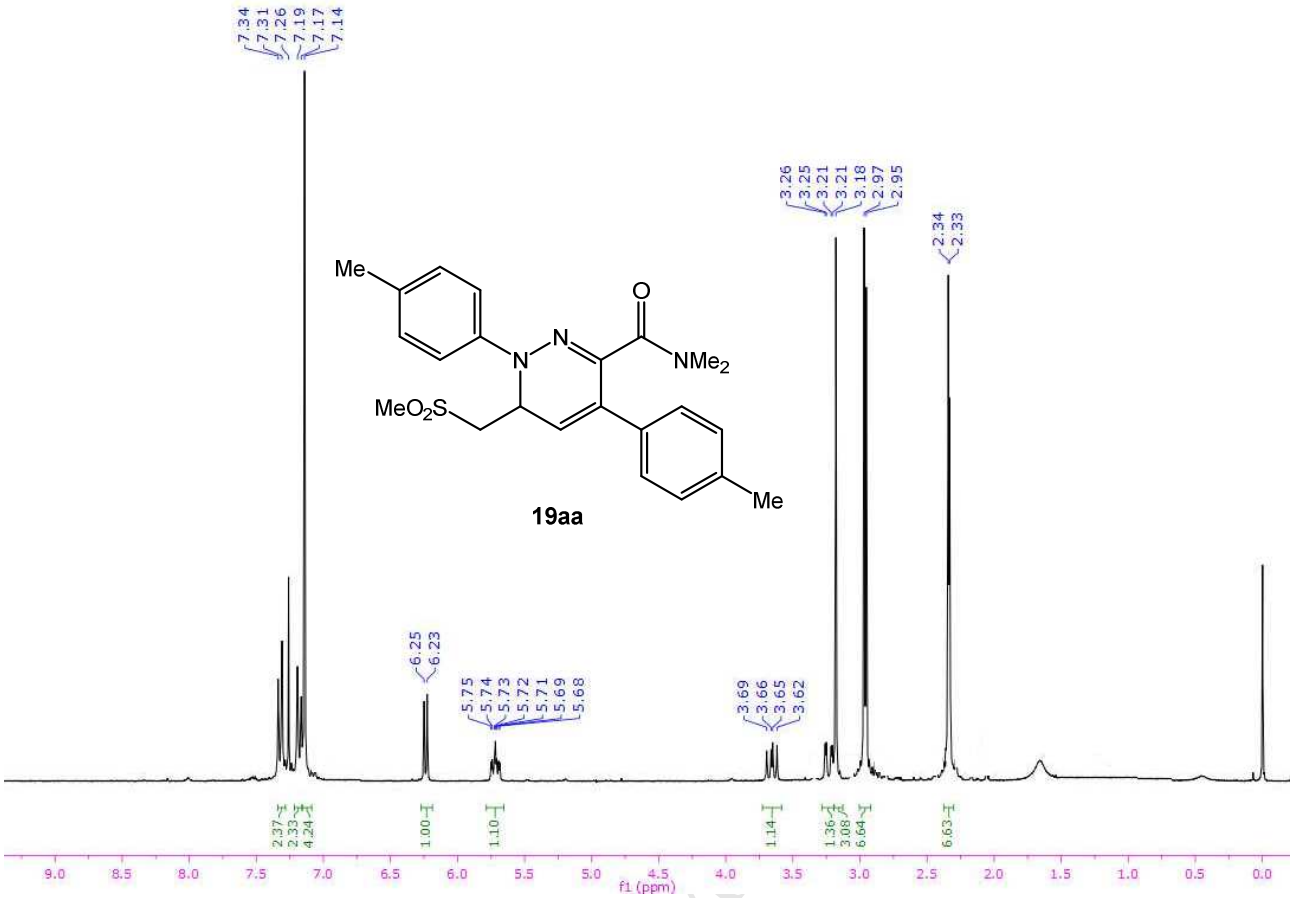
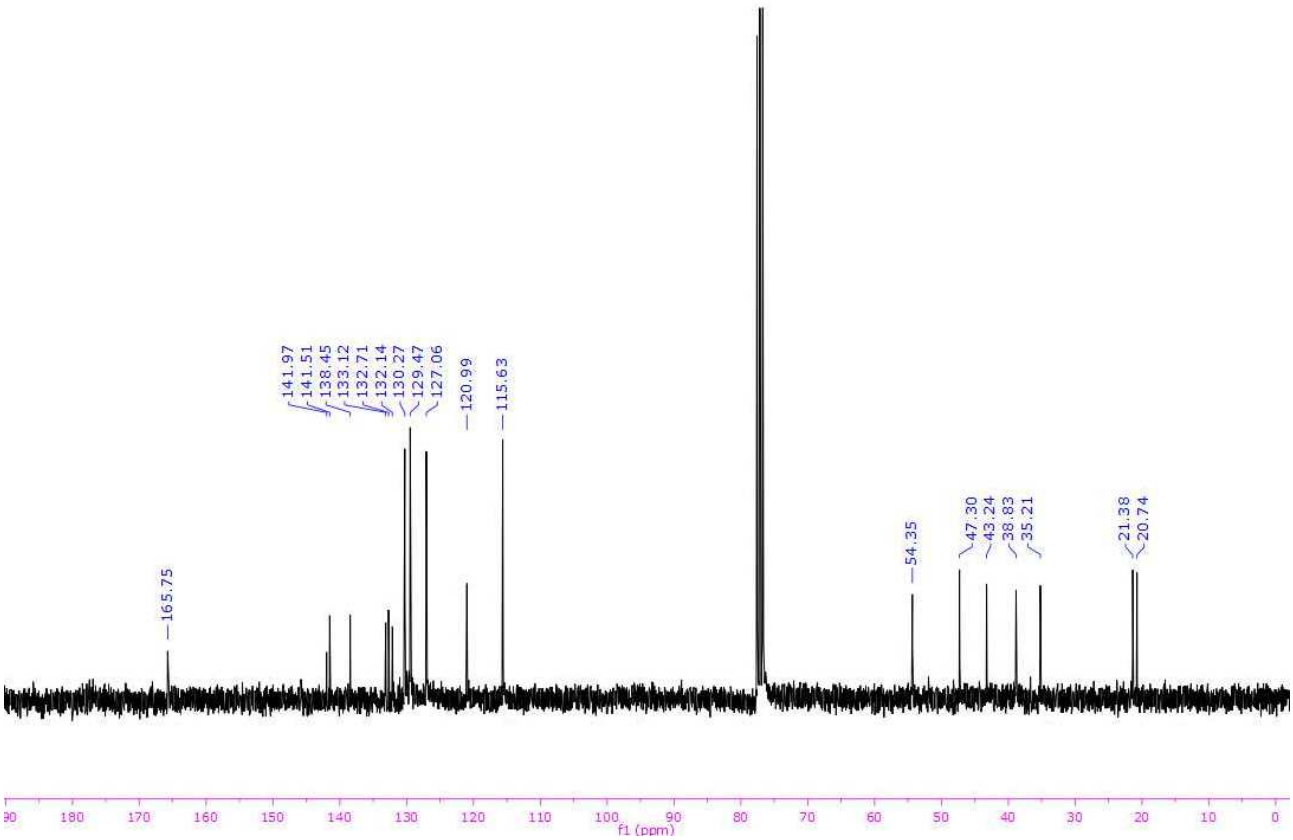
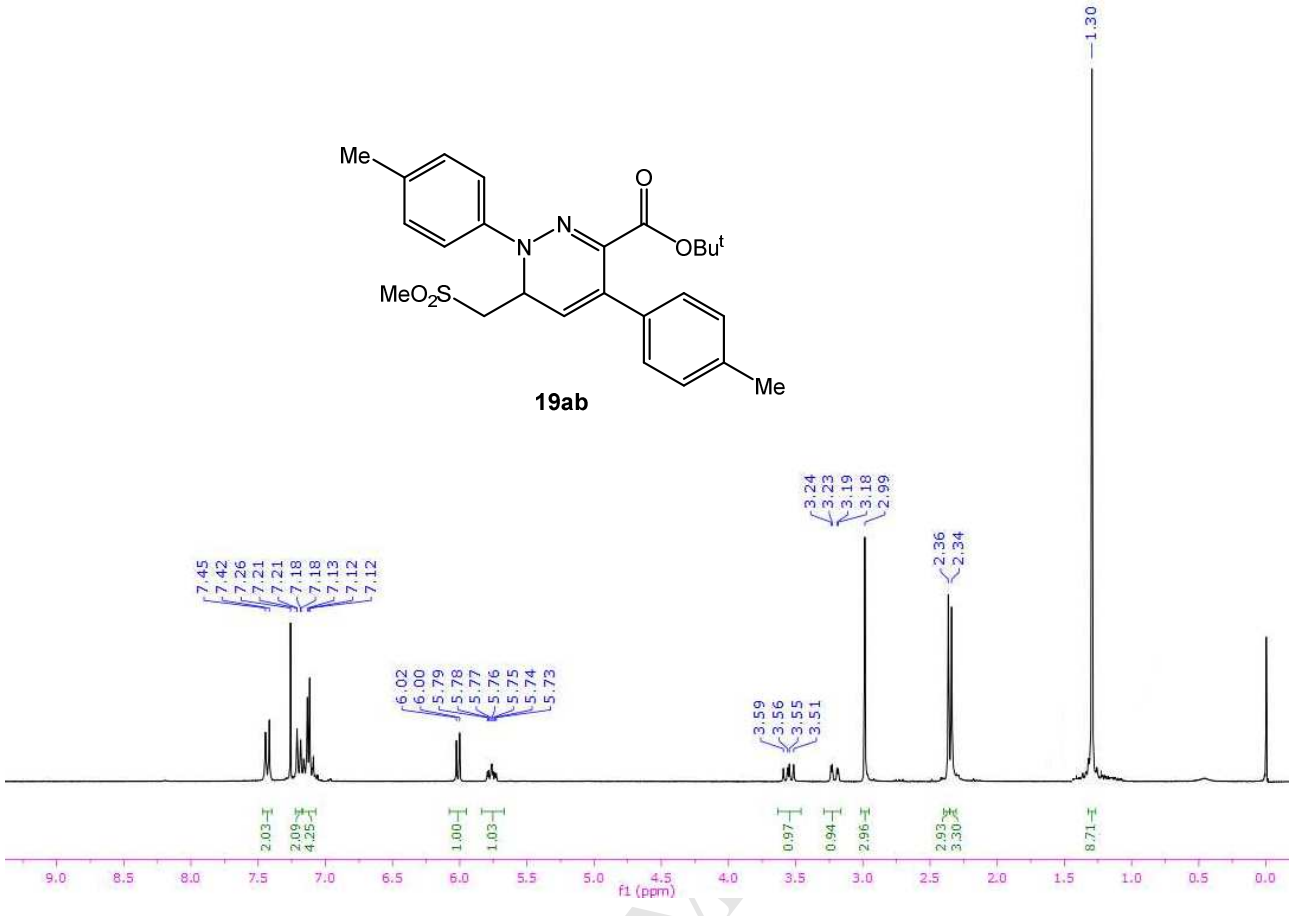
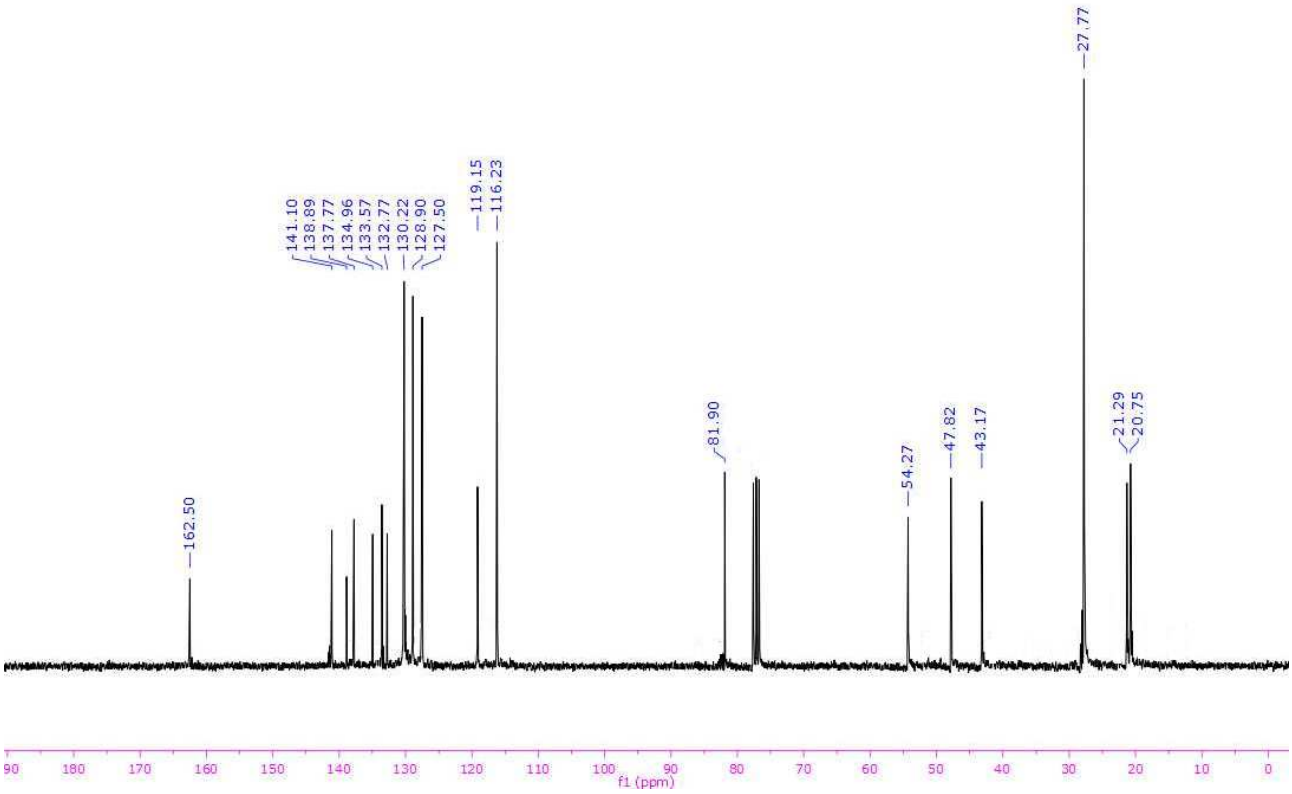
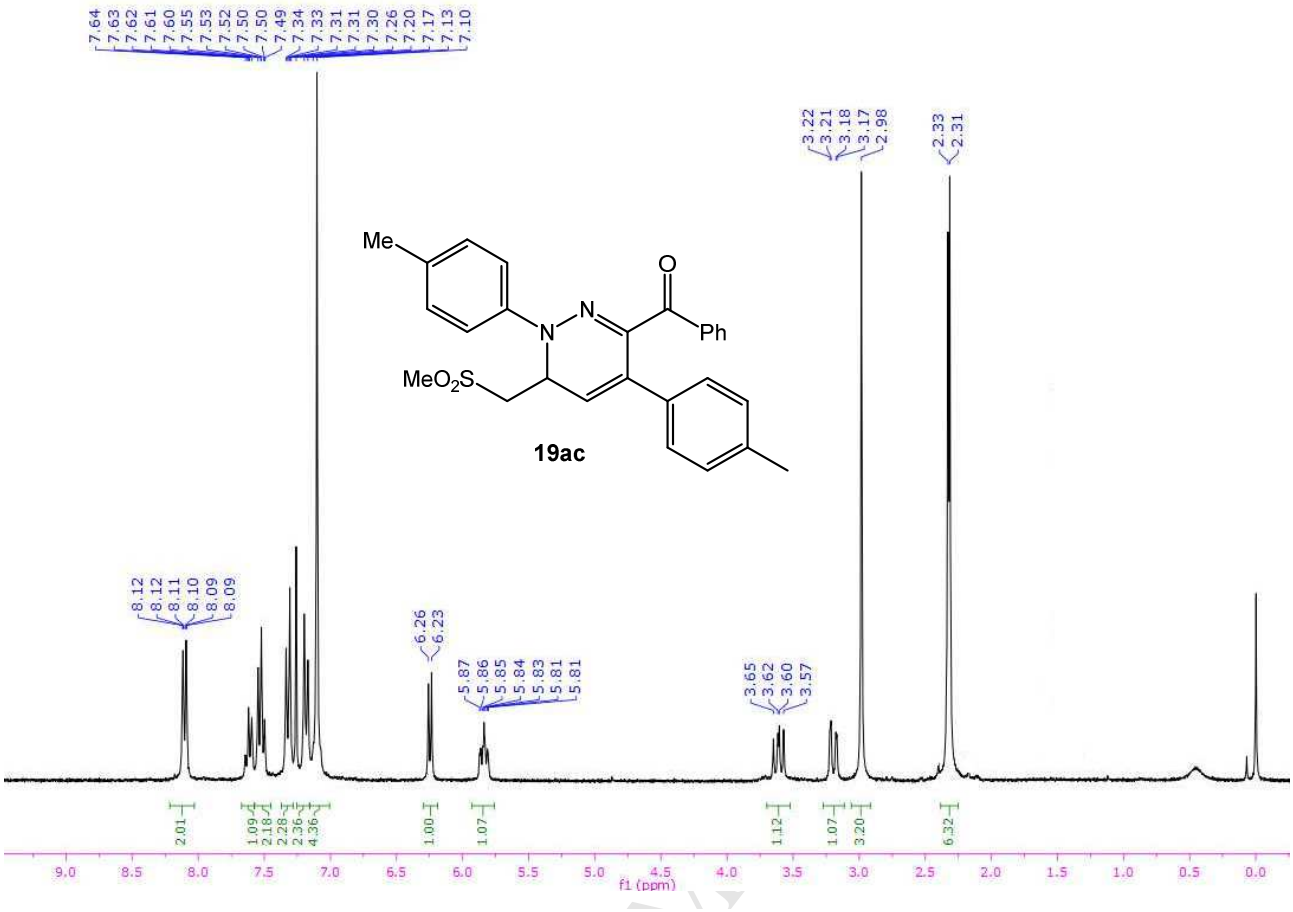


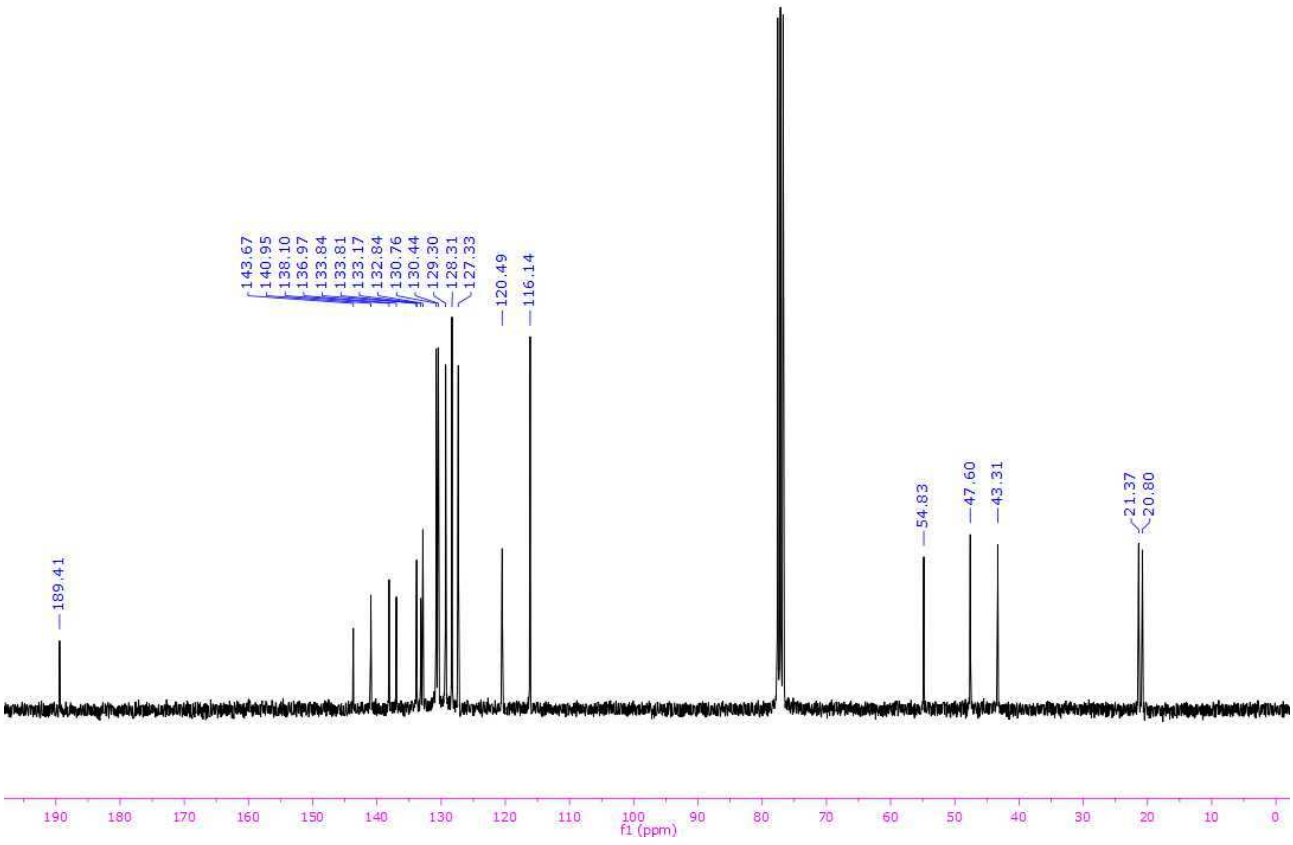


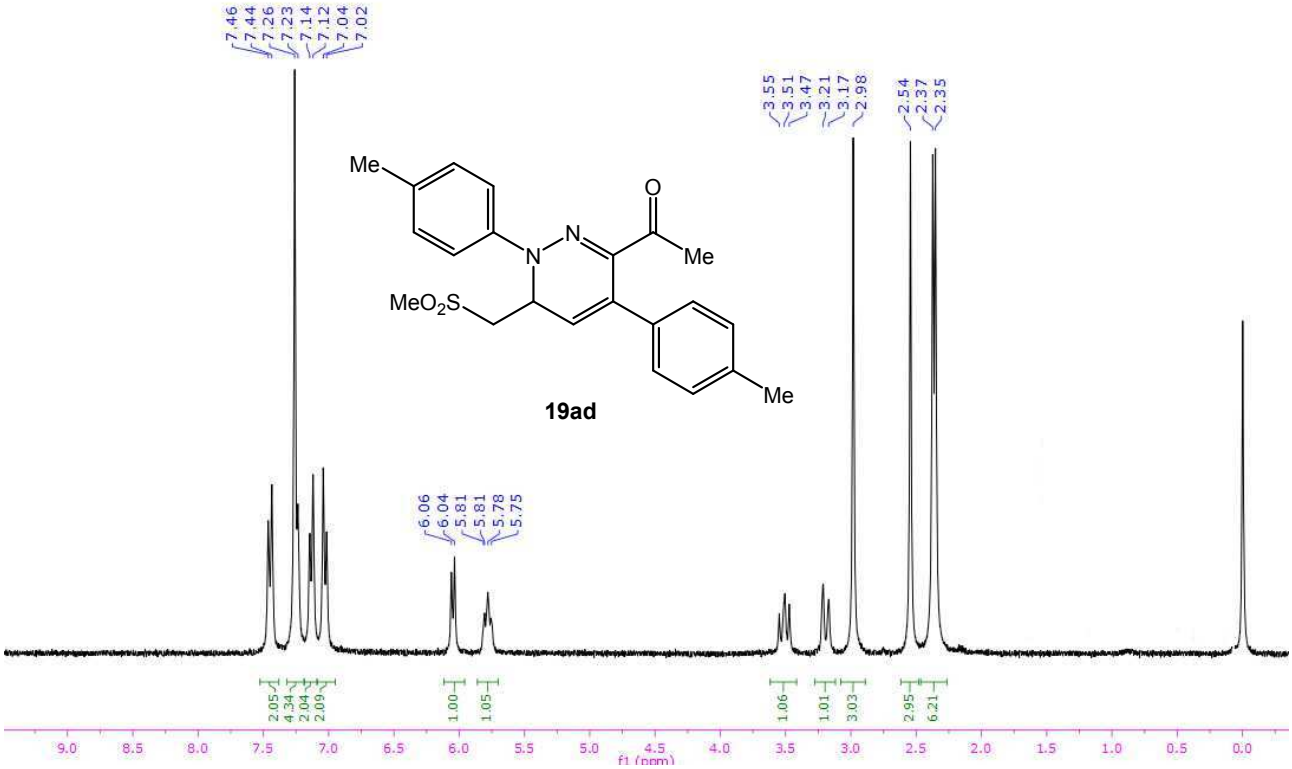



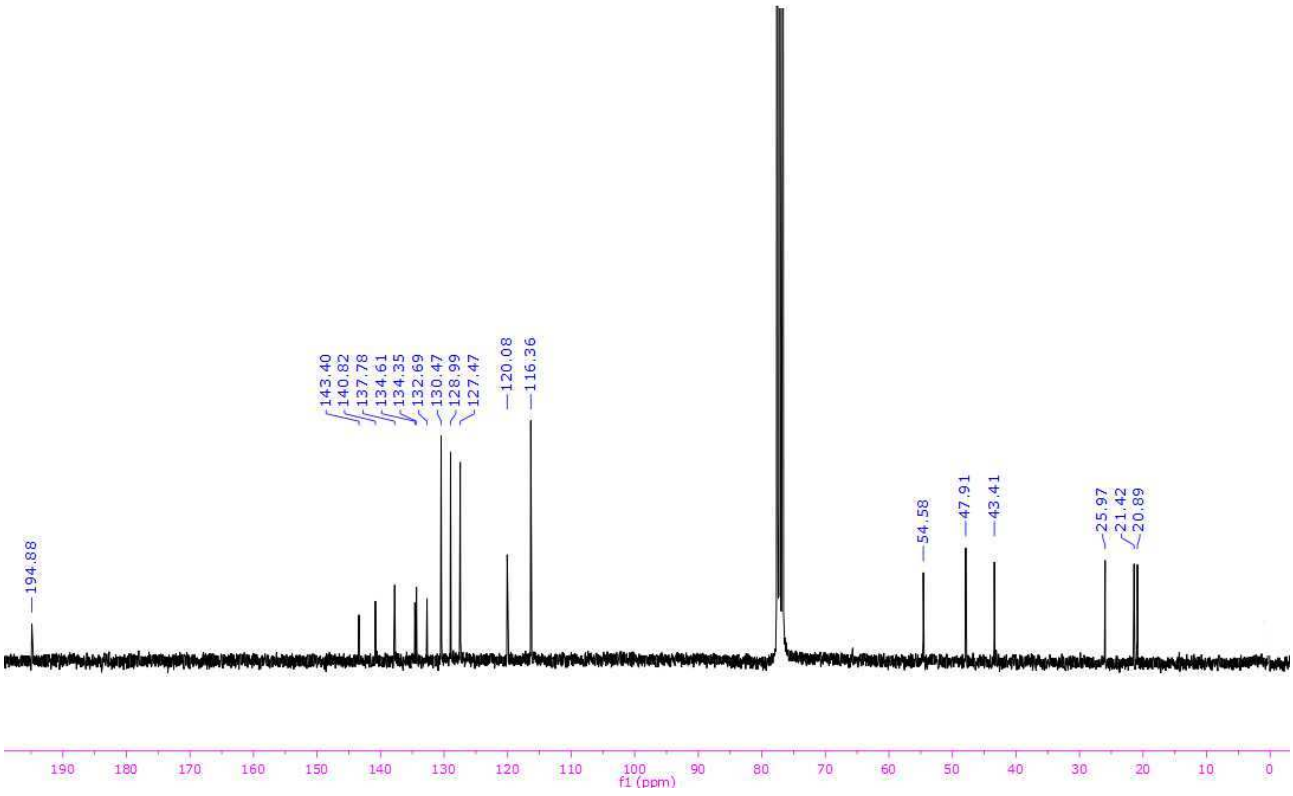


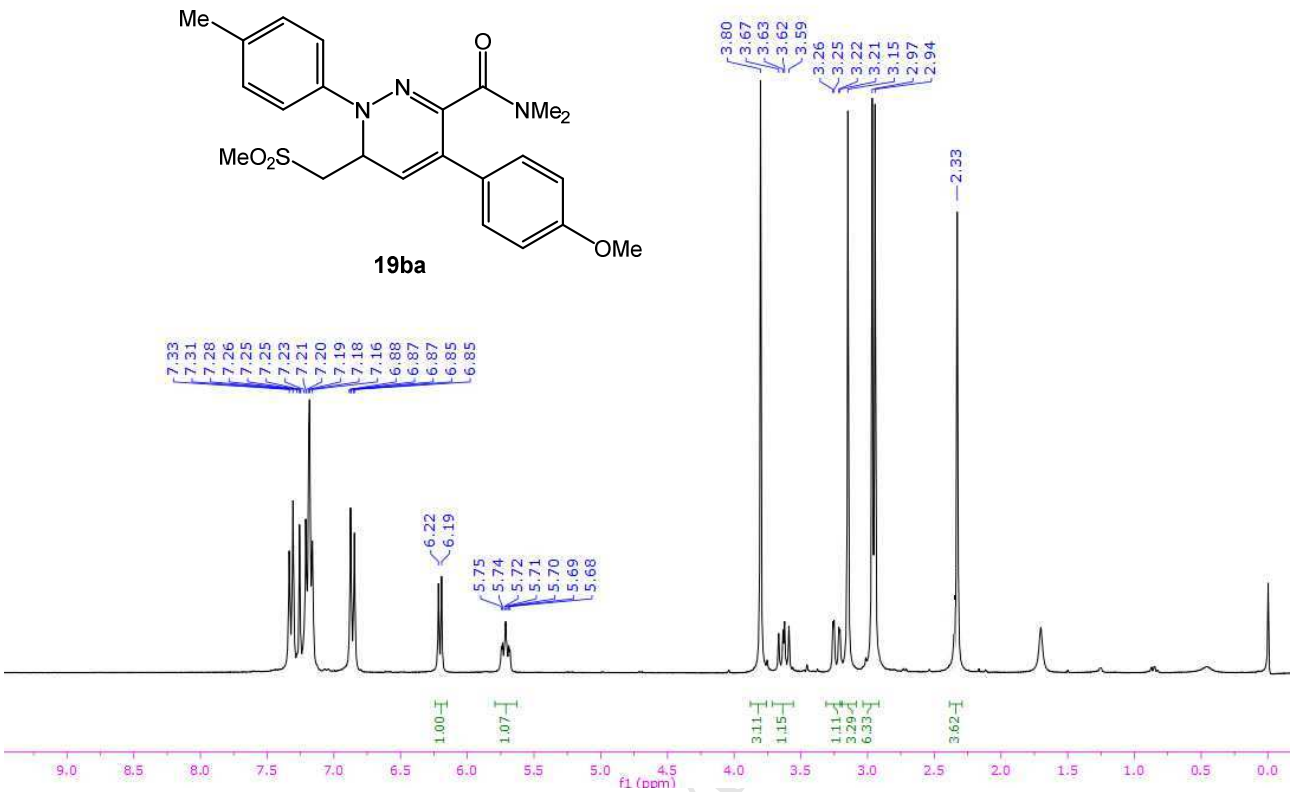



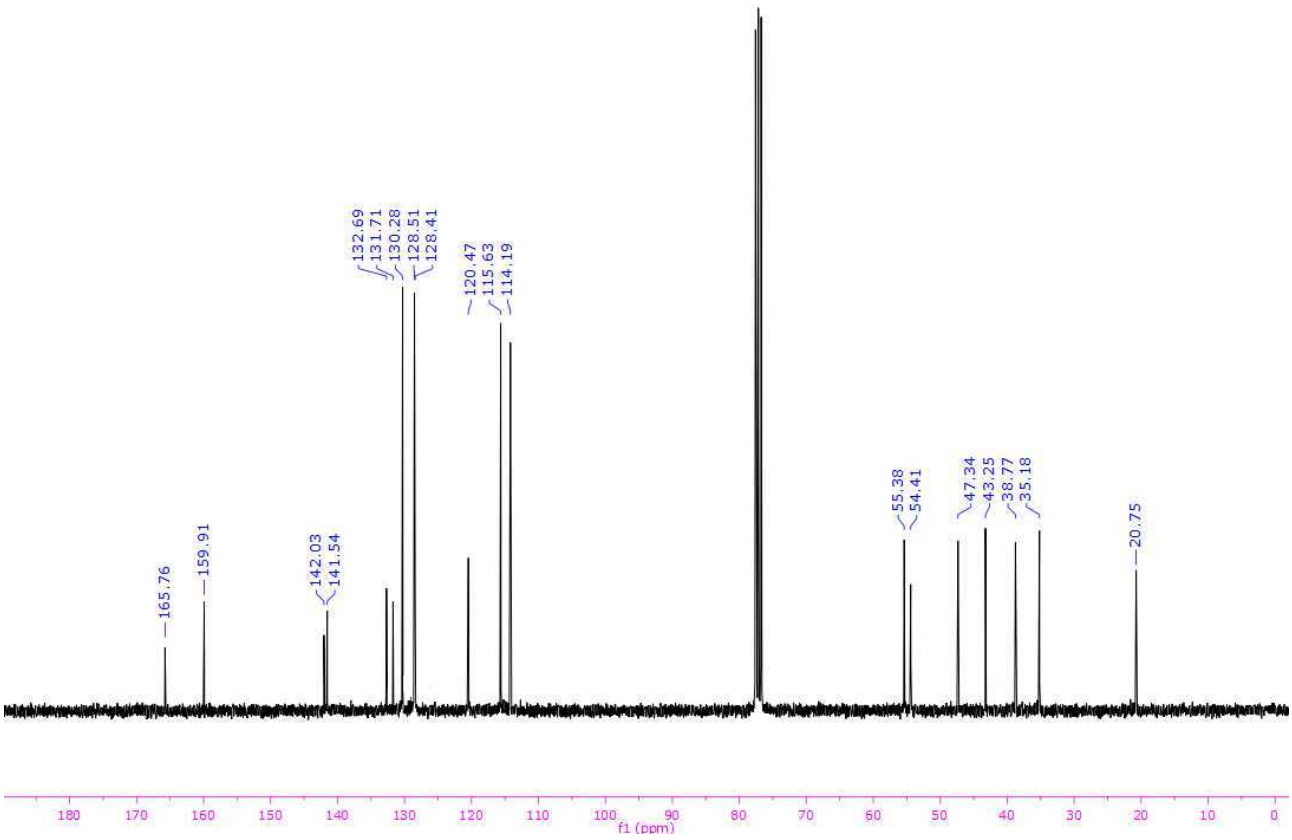


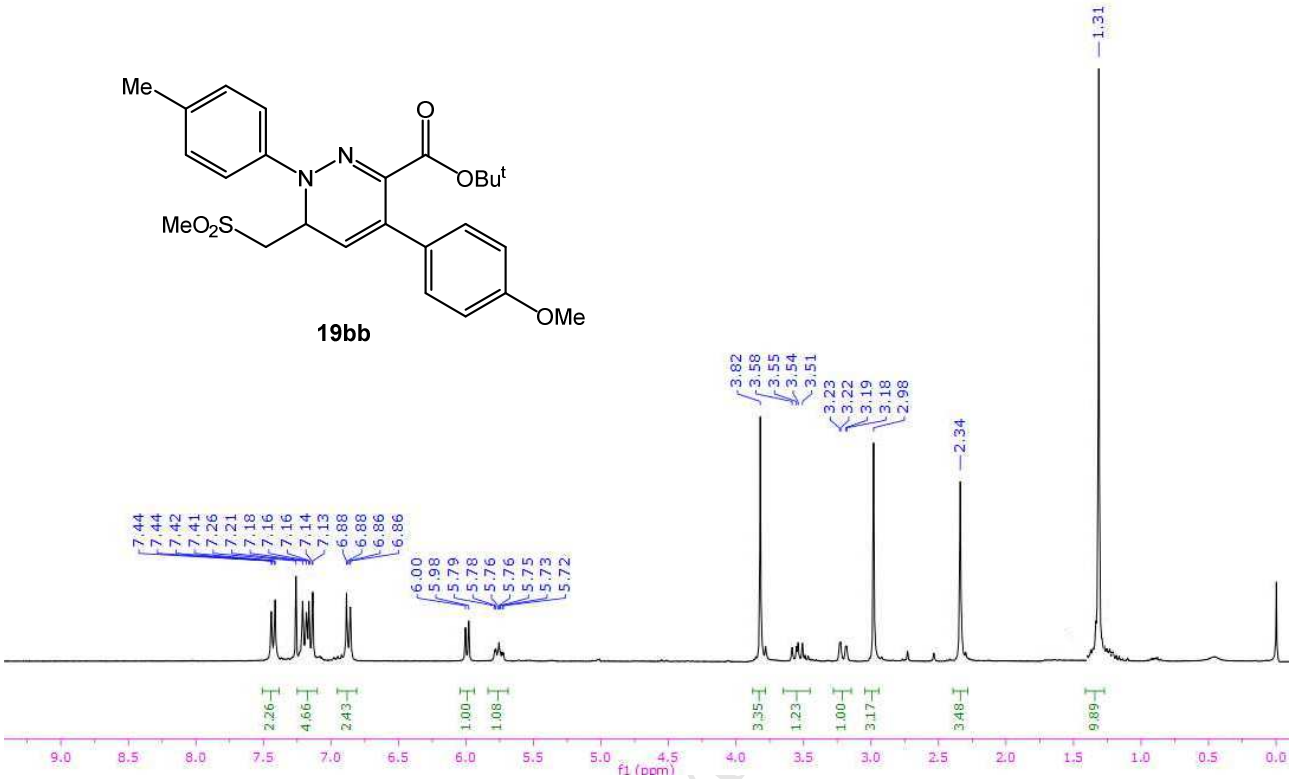



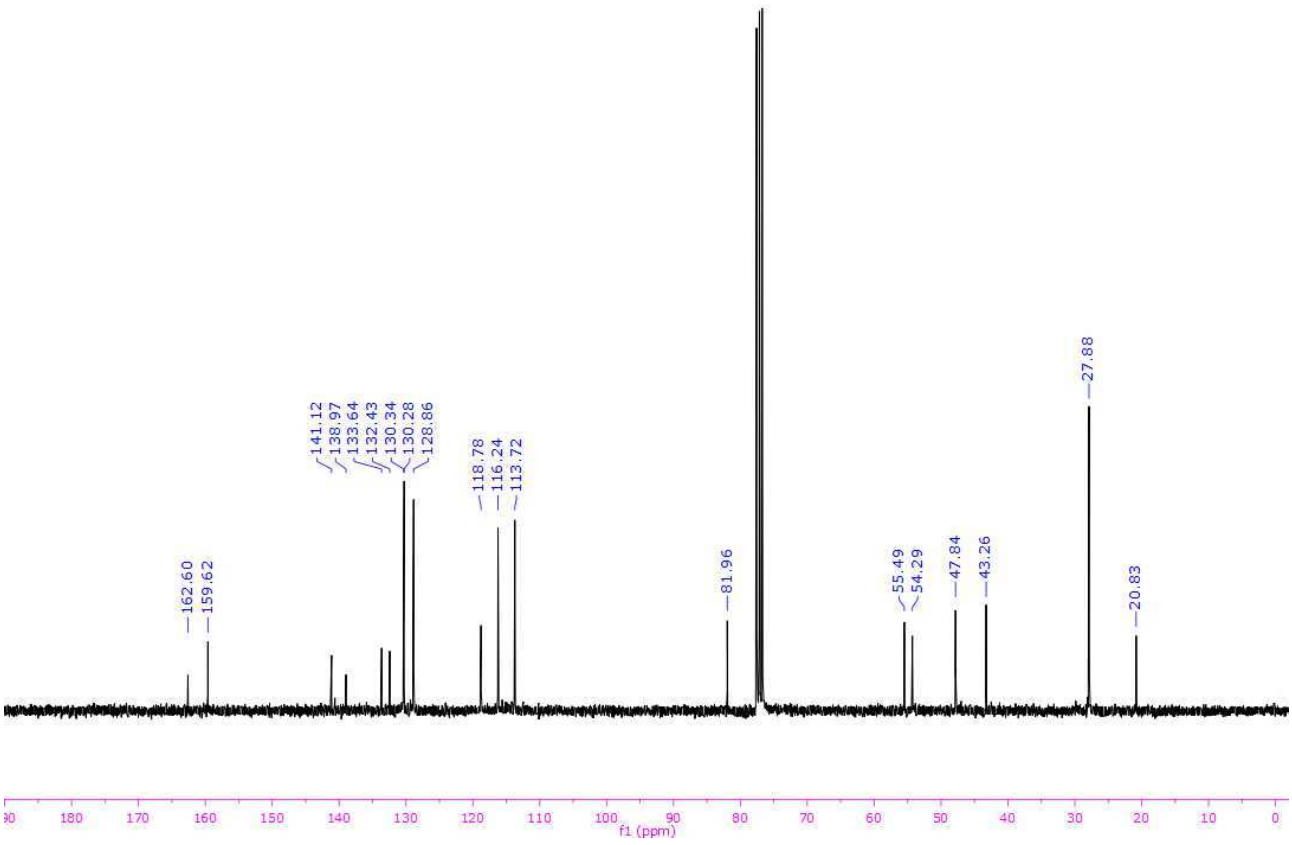


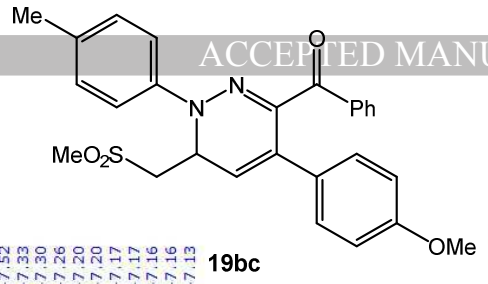





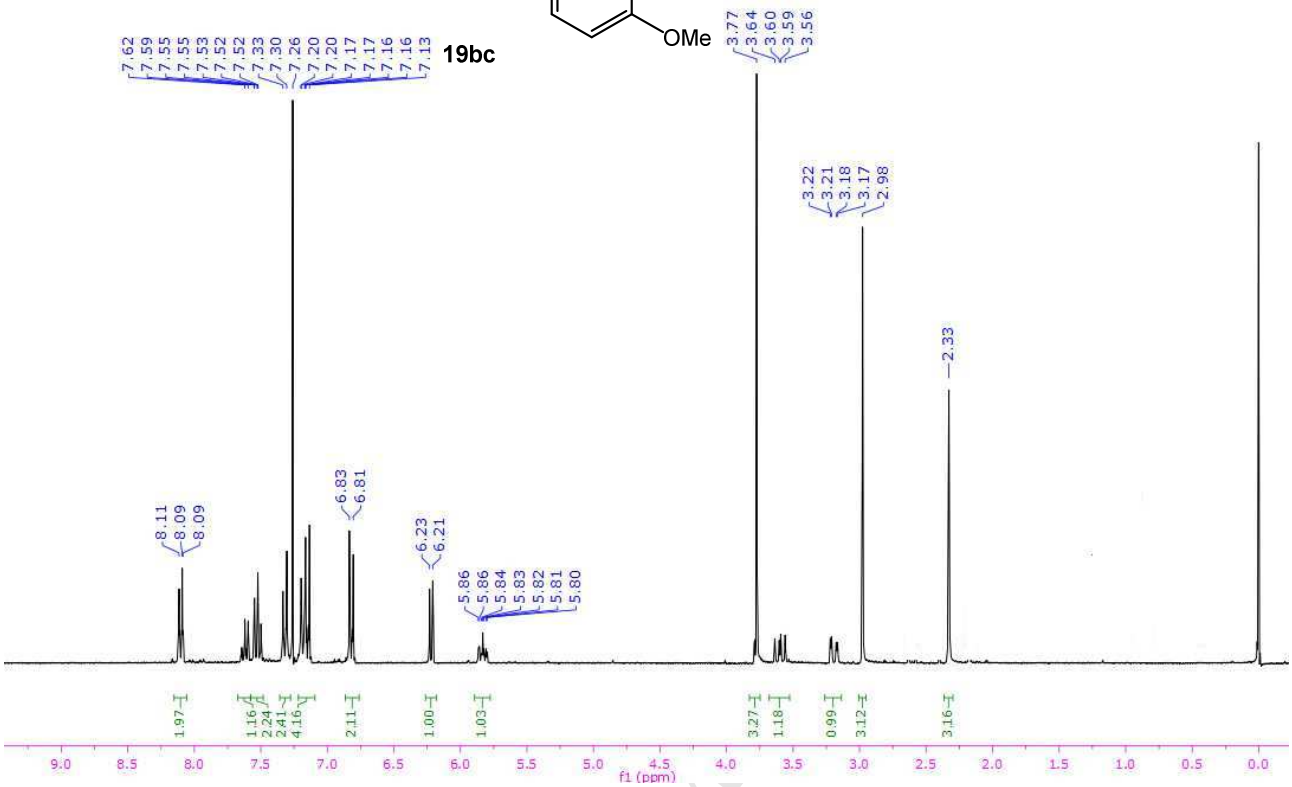



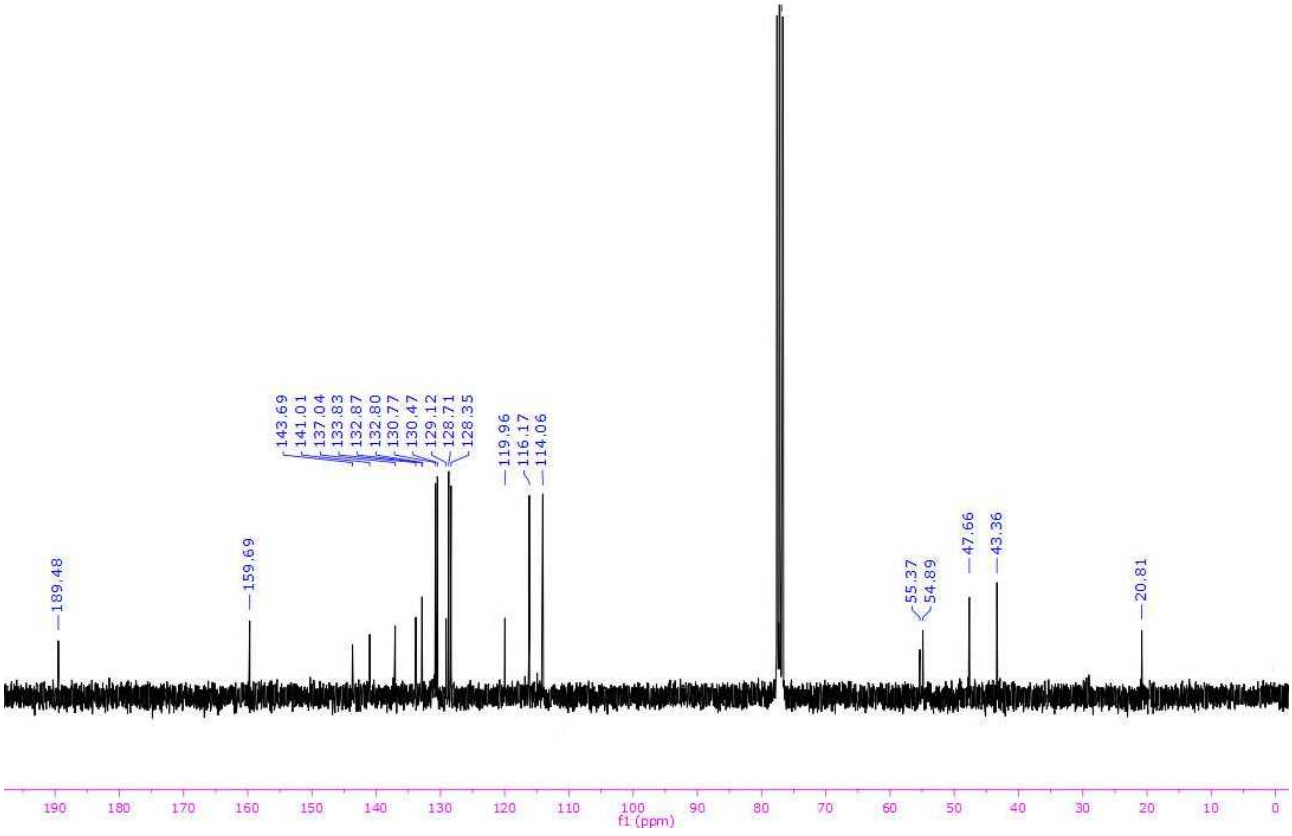


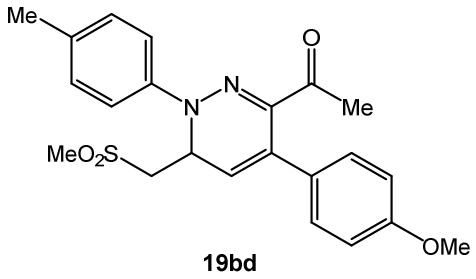






**19bc**

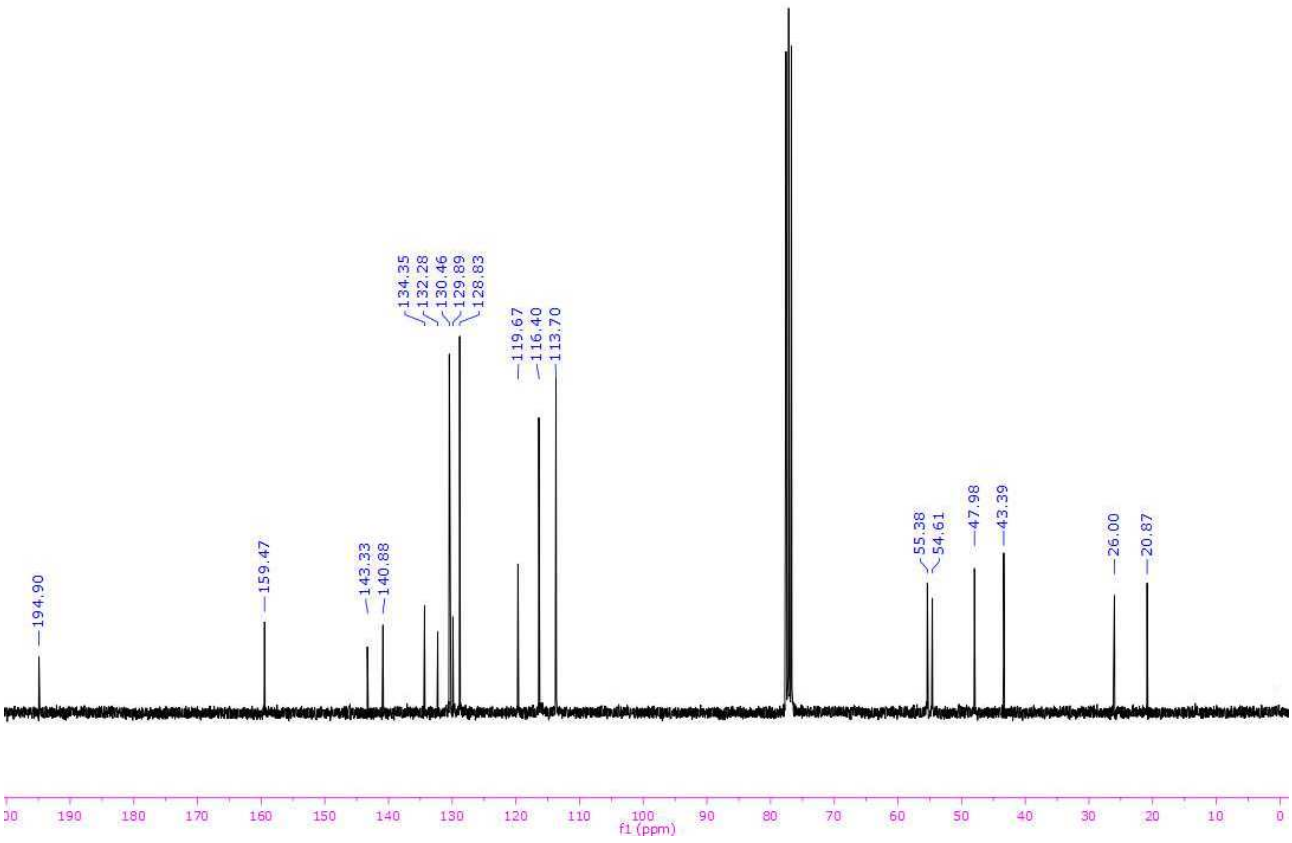


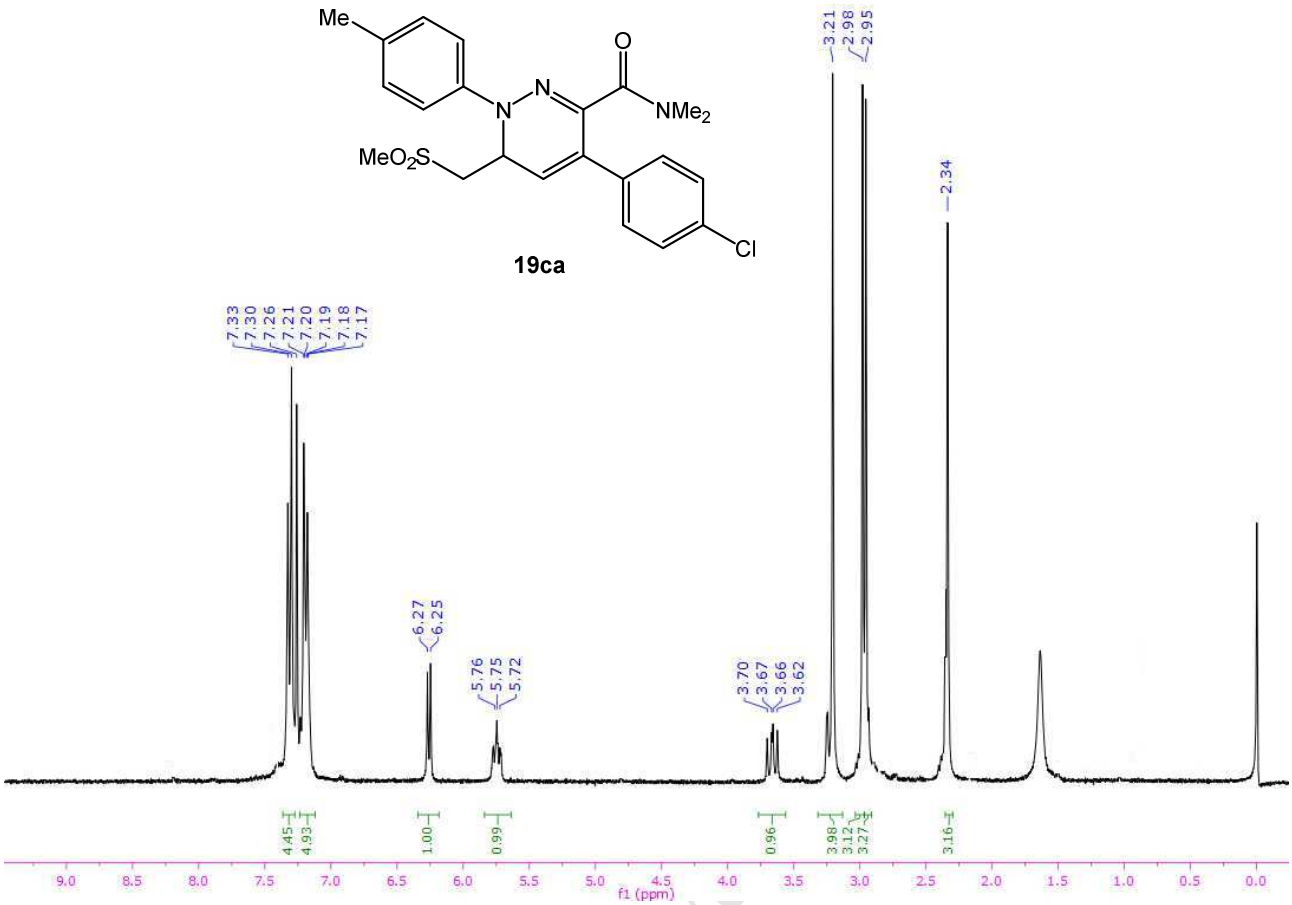



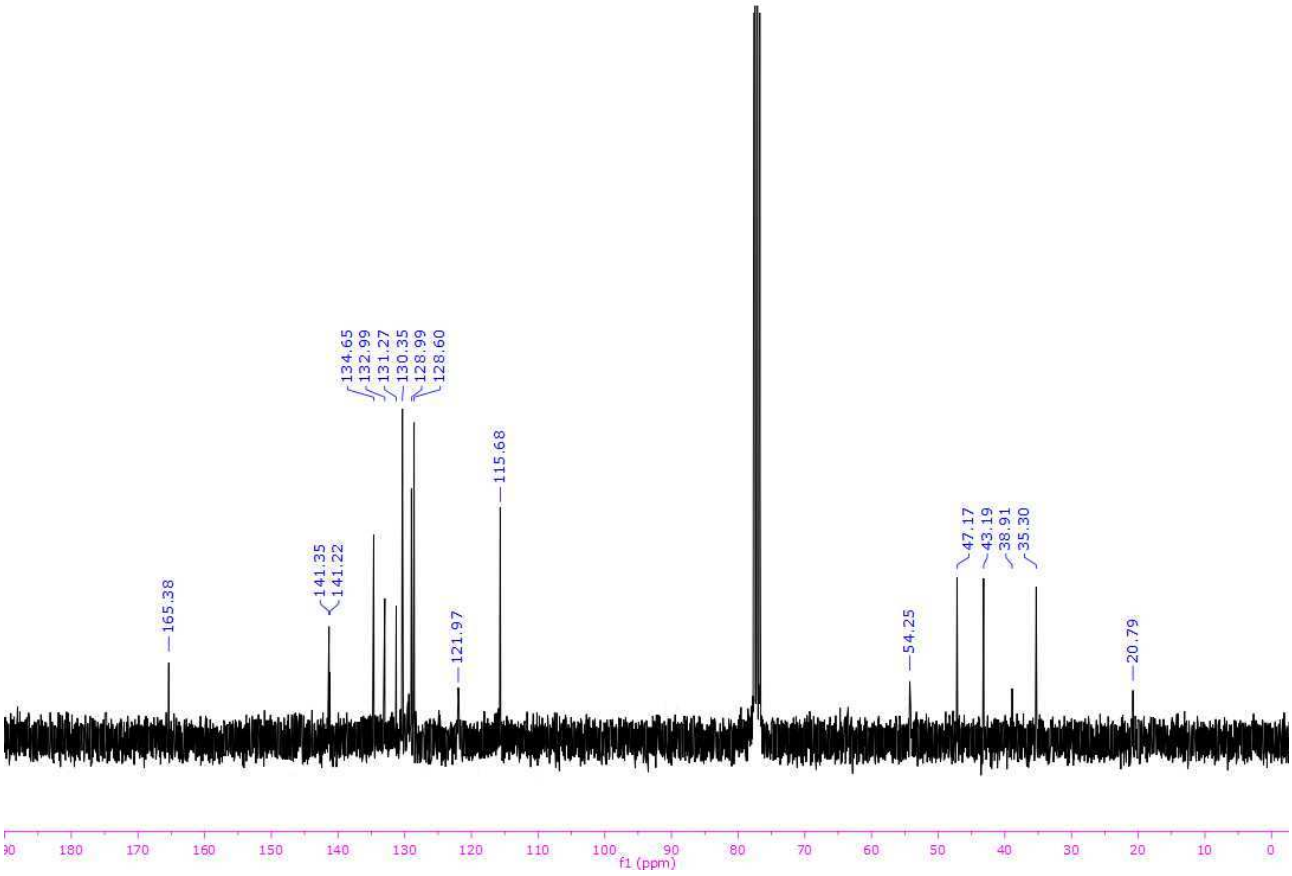


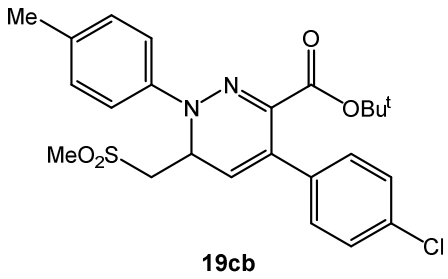

**19bd**





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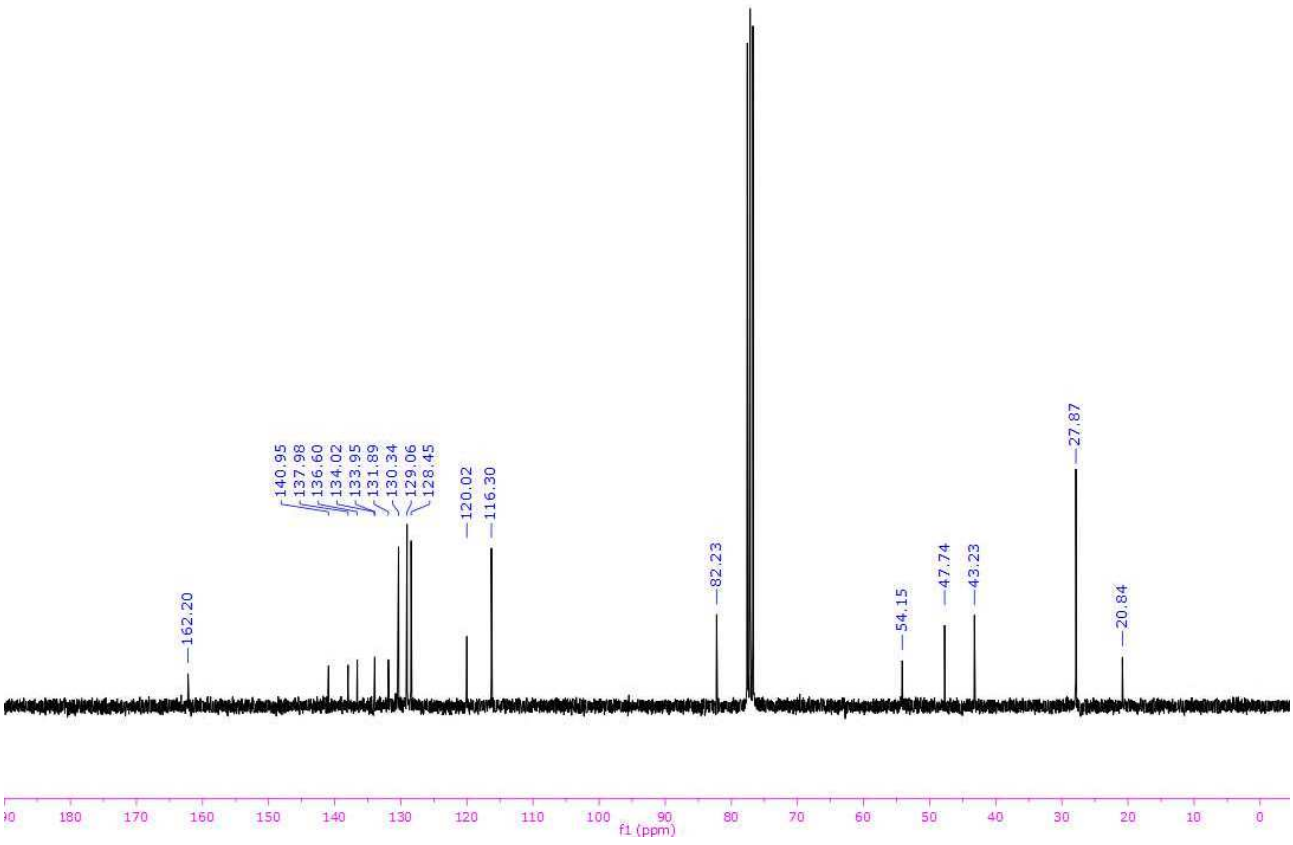
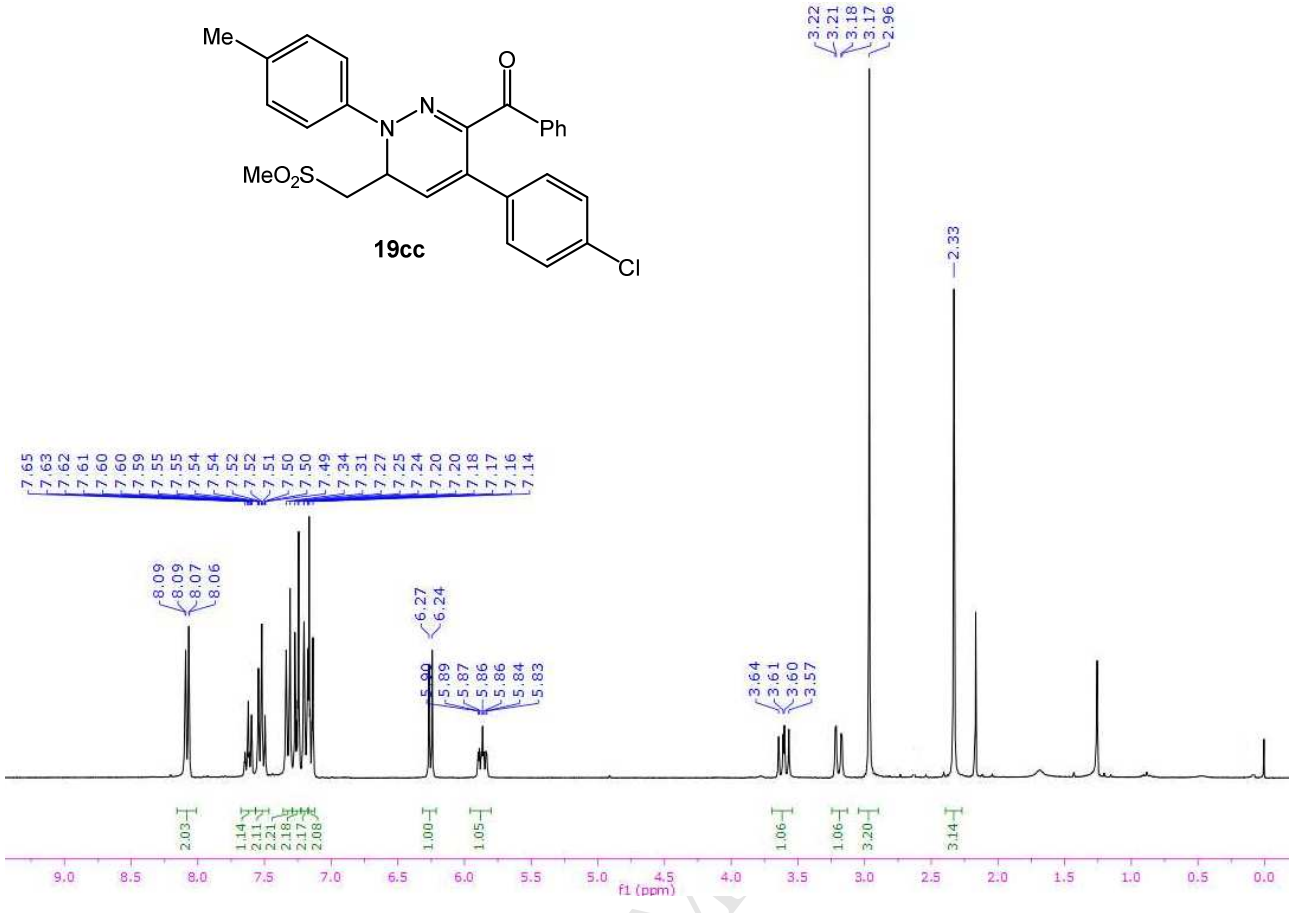
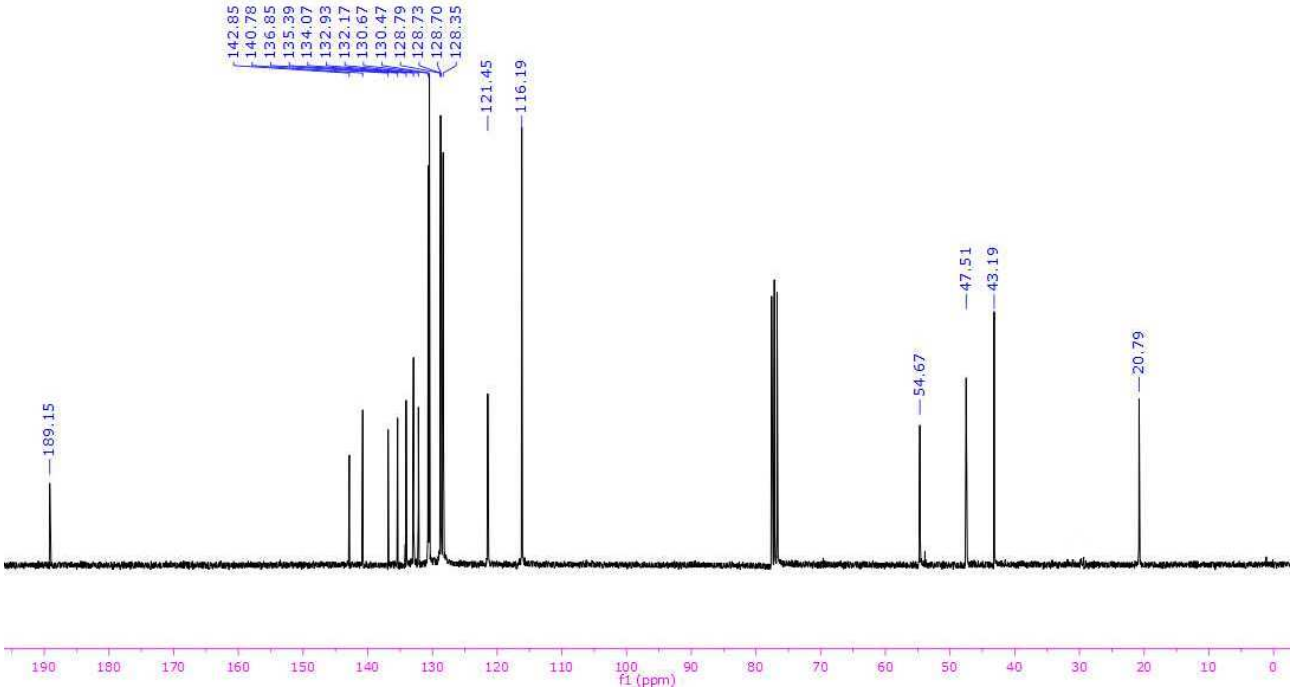
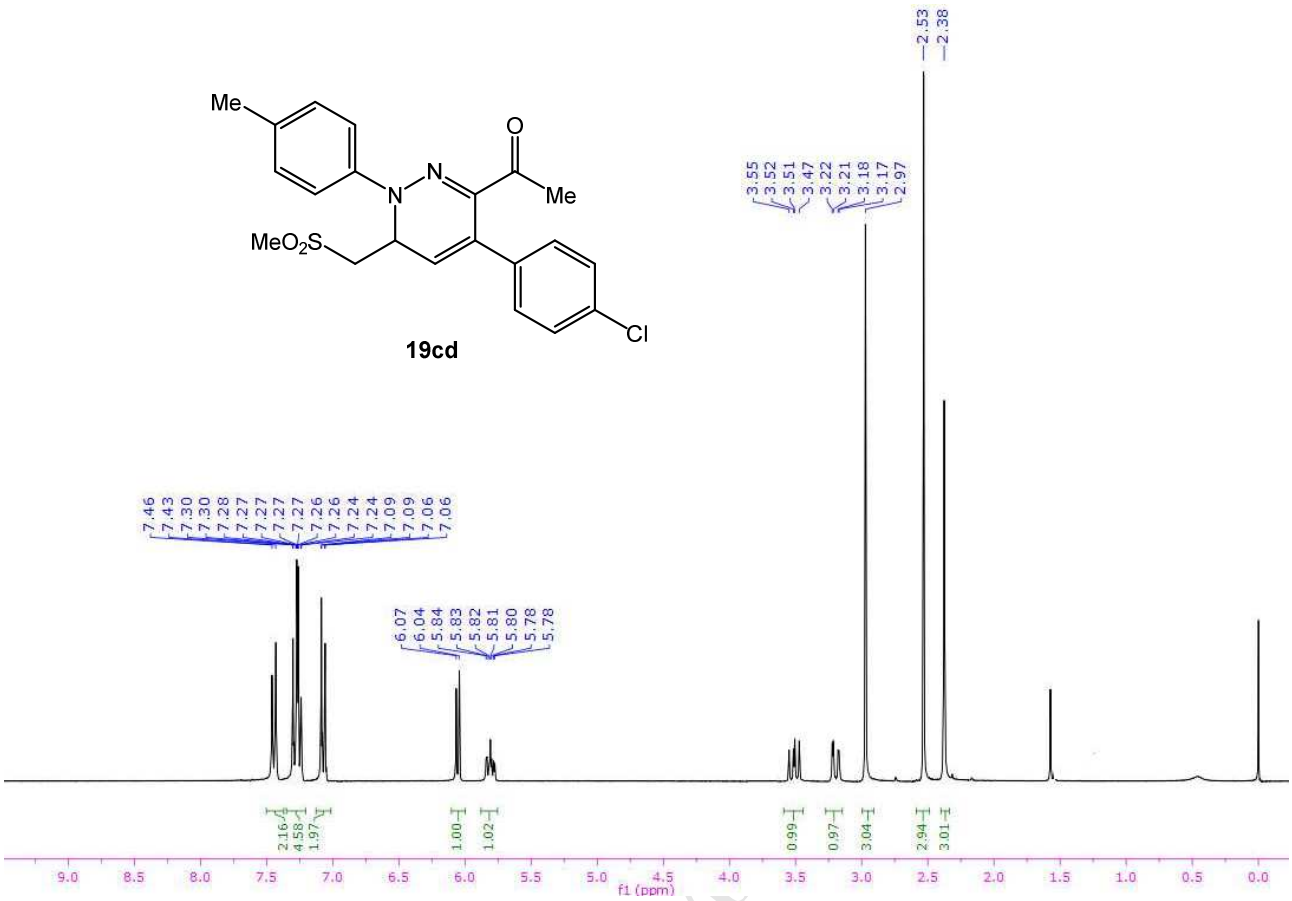
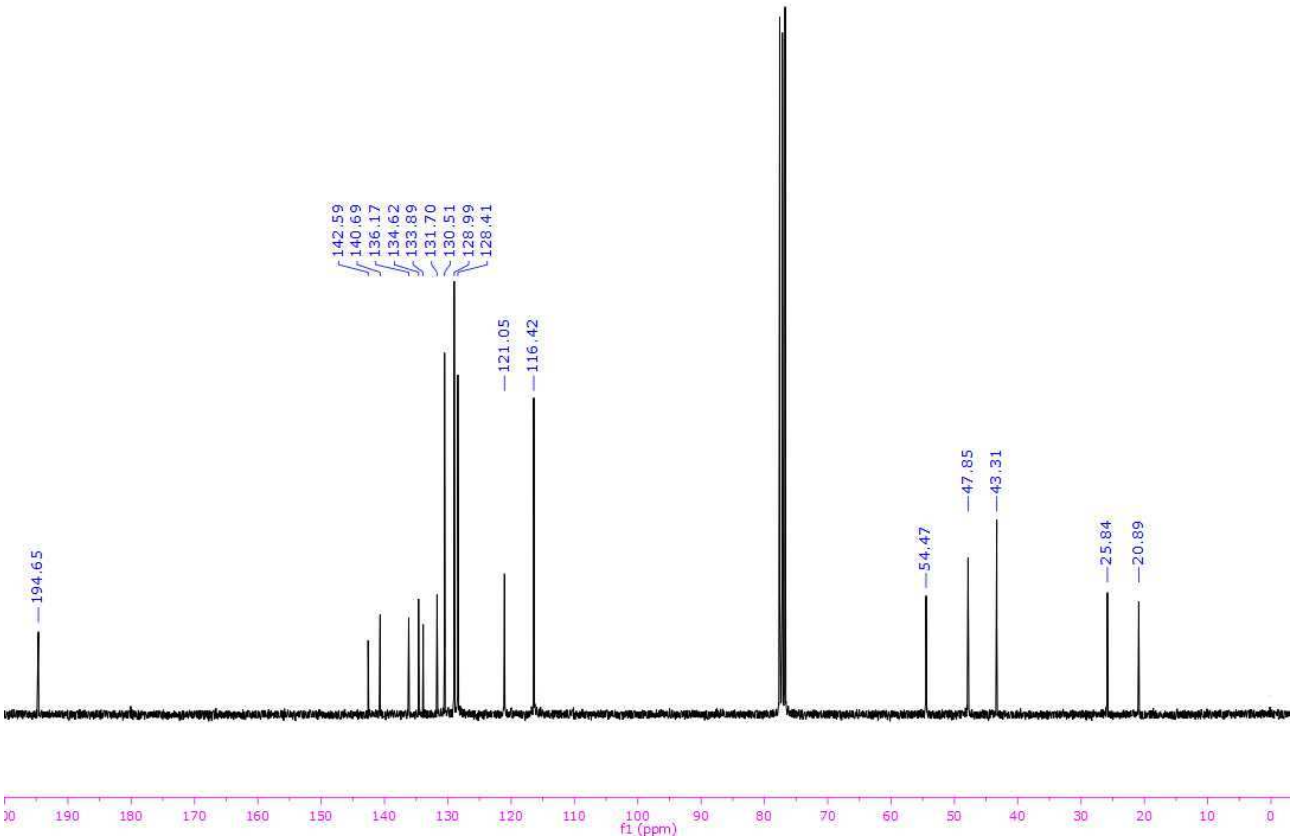
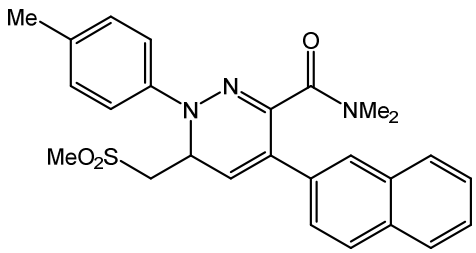




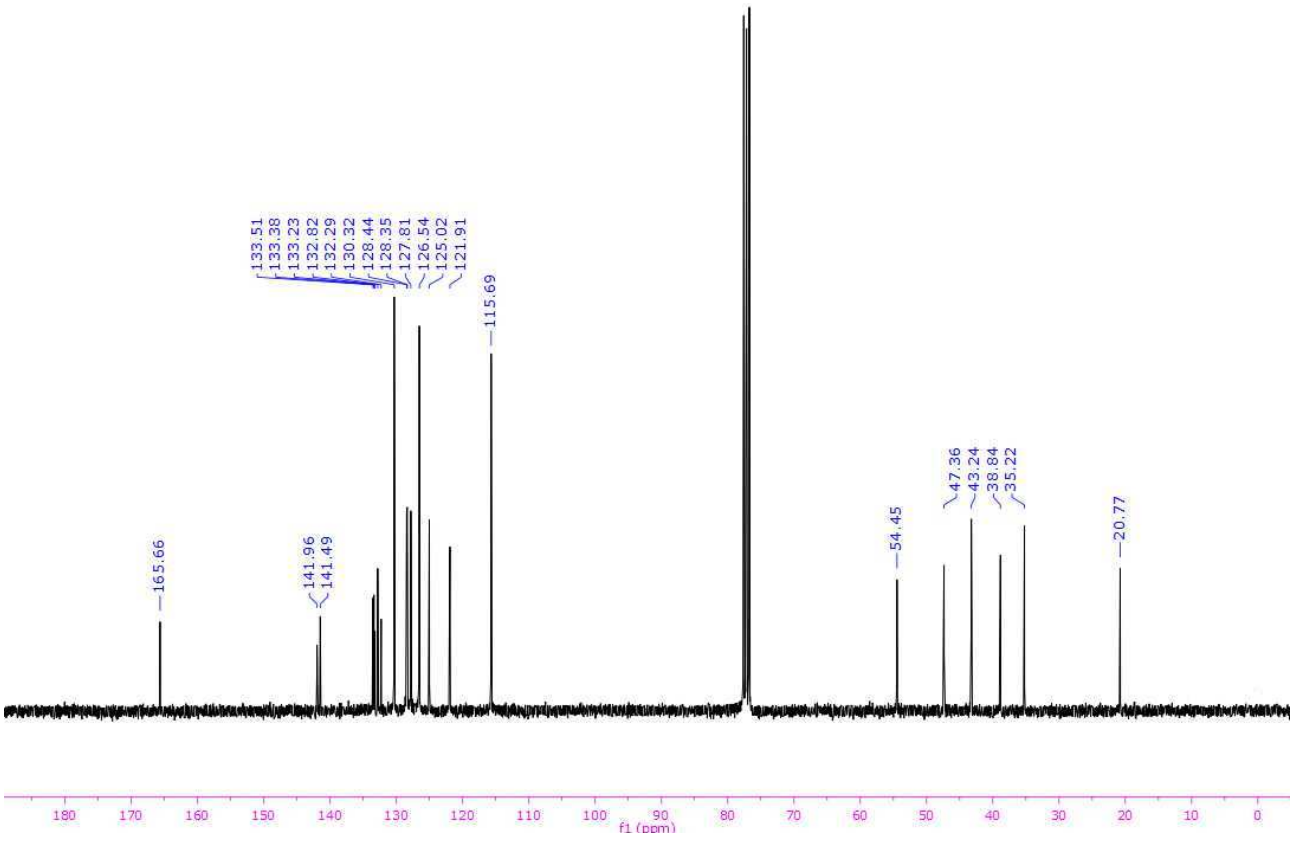


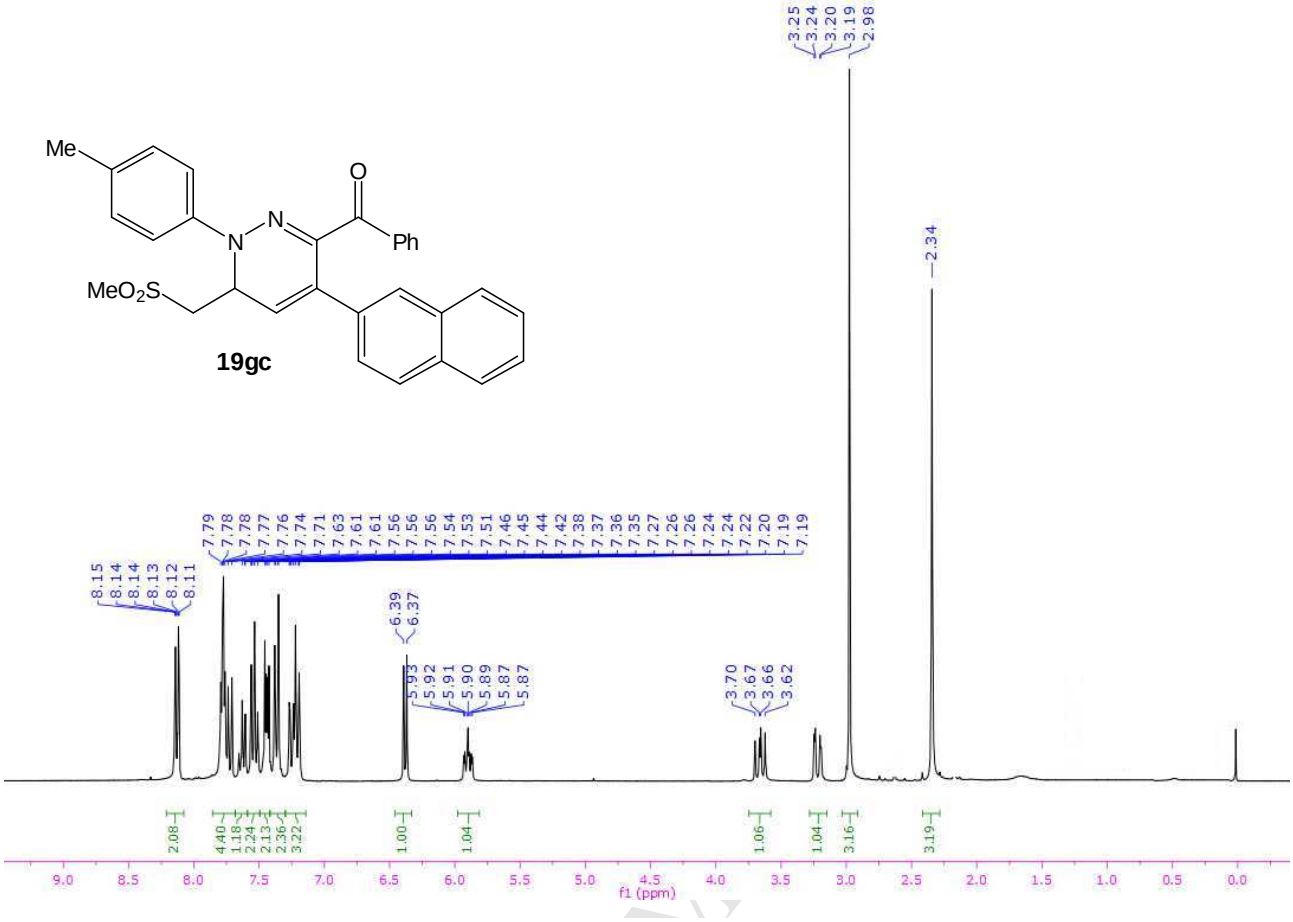



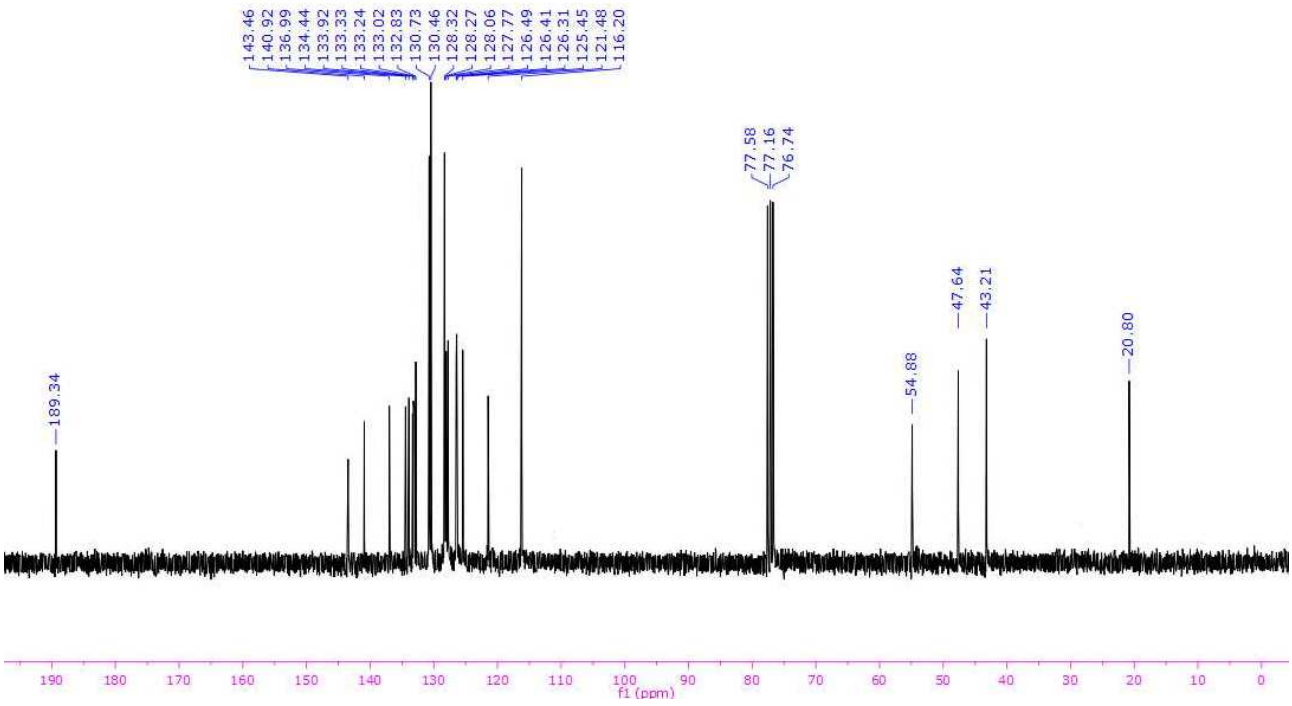


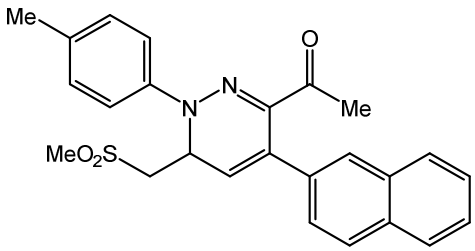

**19ga**



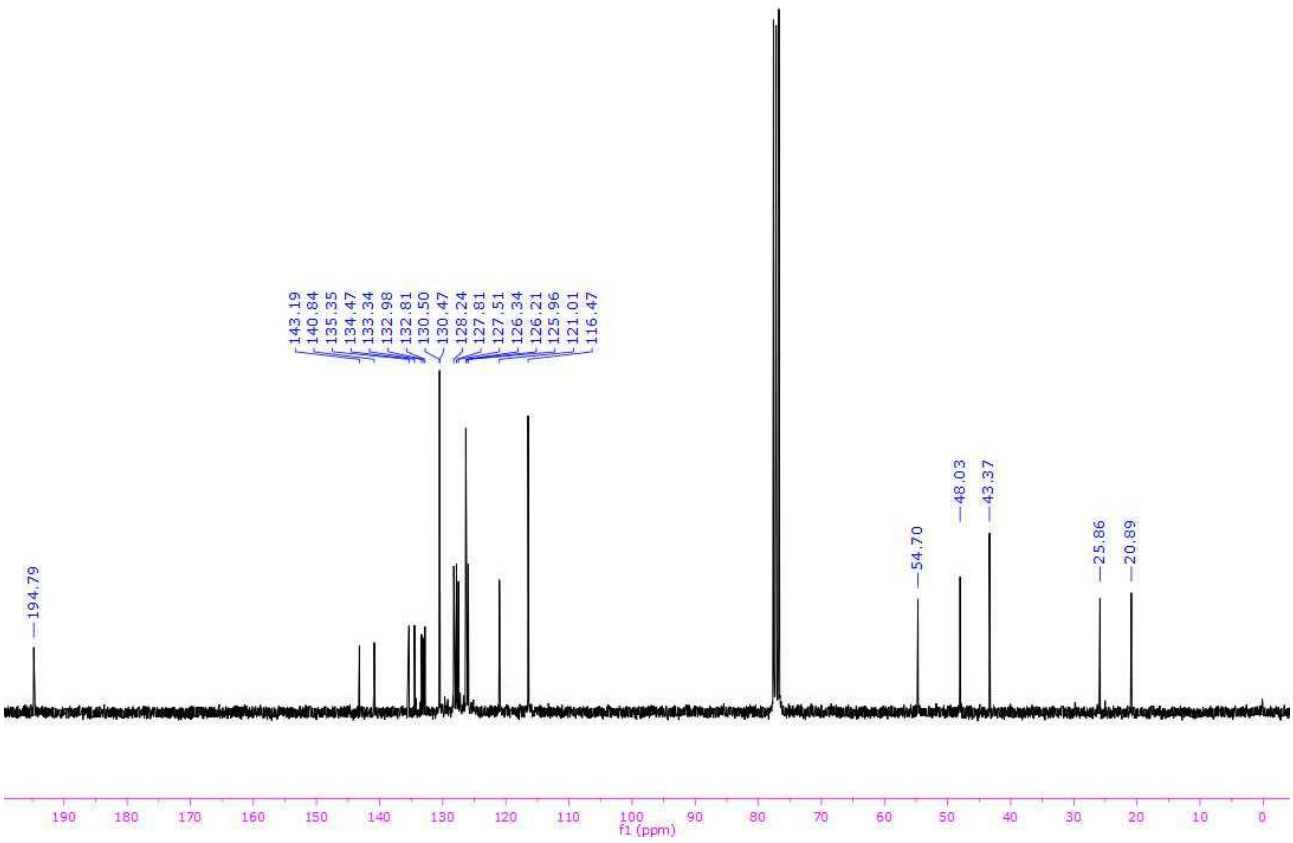


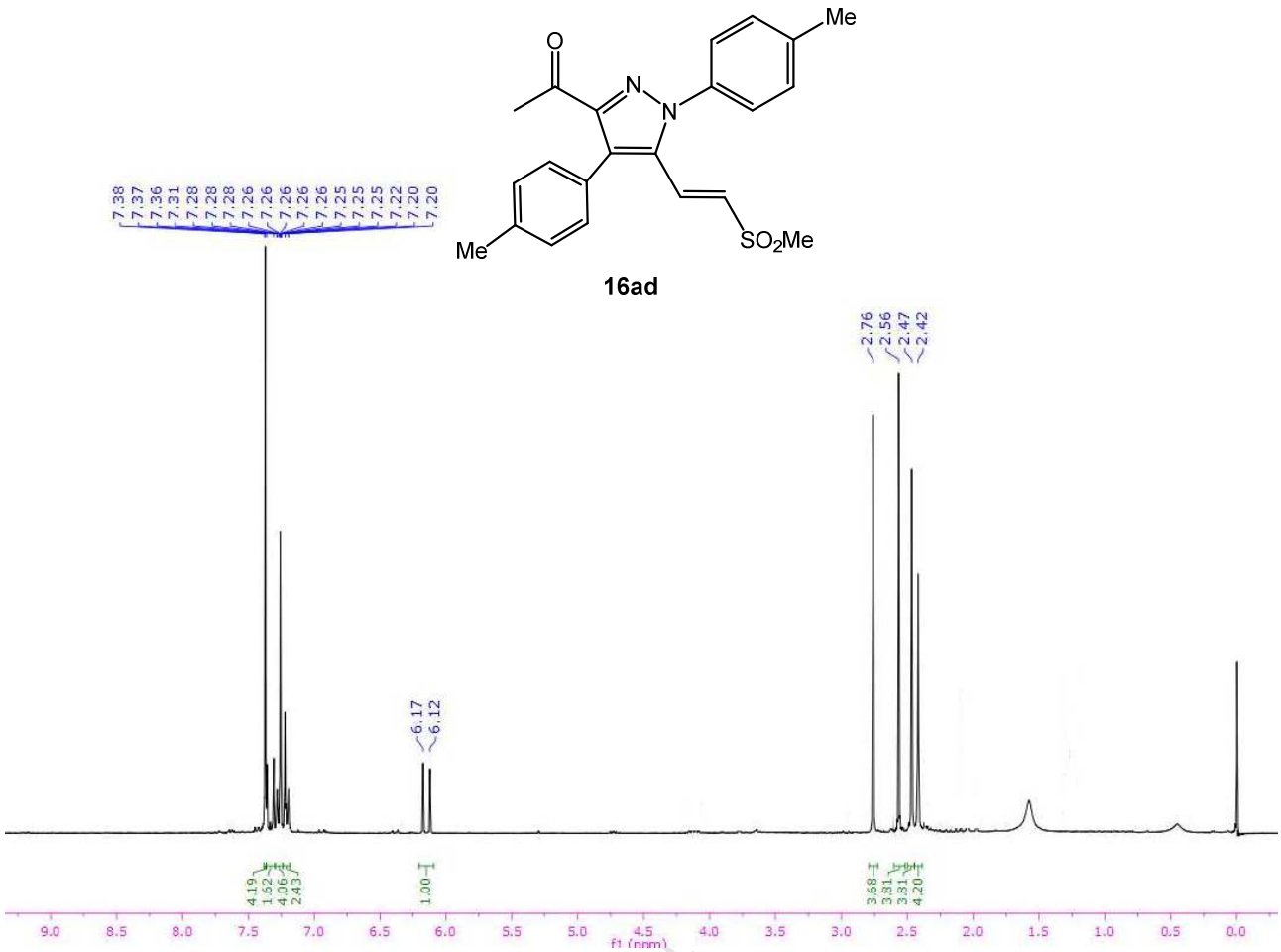





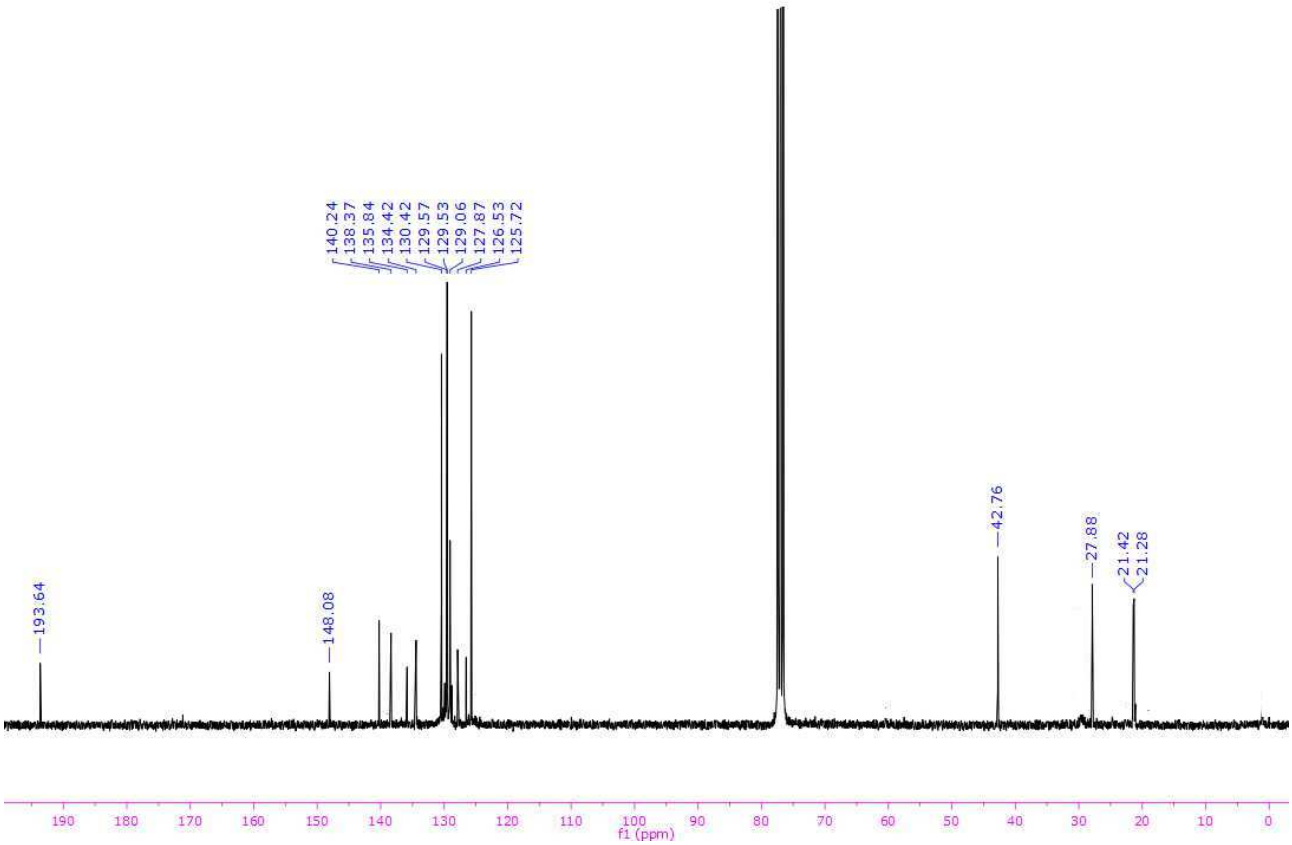

**19gd**






**16ad**



**Calculations on 18, 18′ and 18′′**

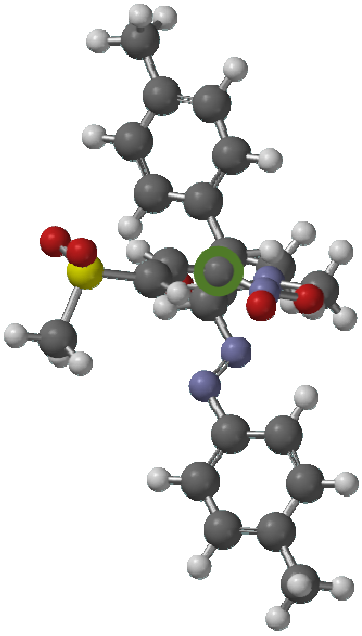
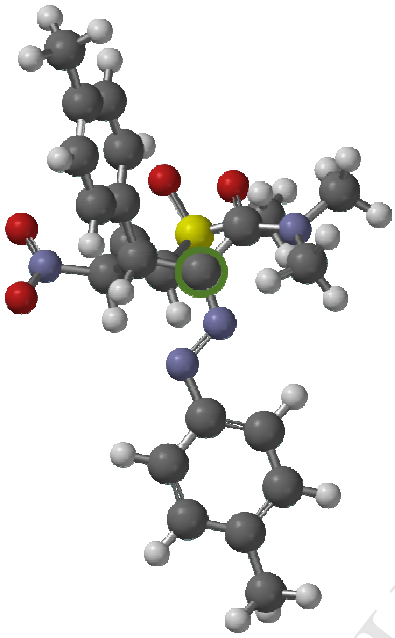
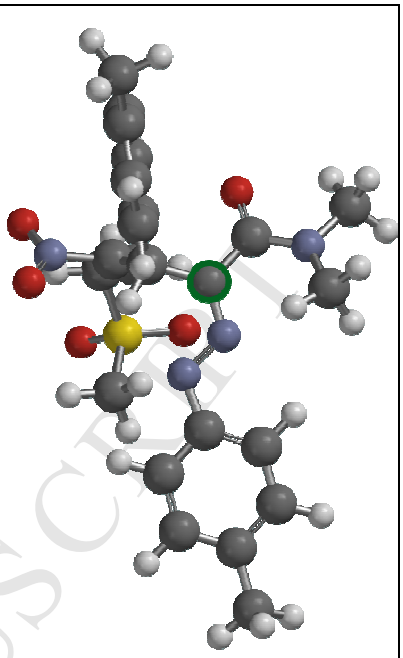
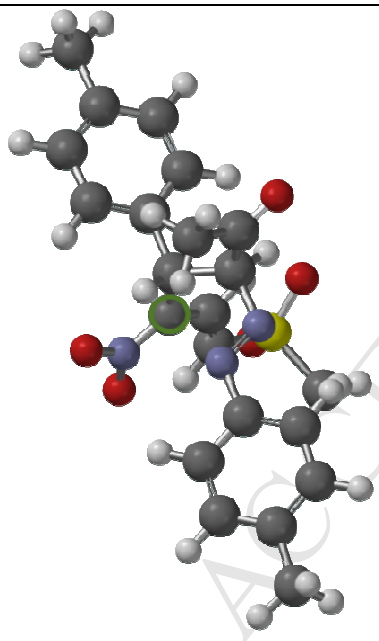
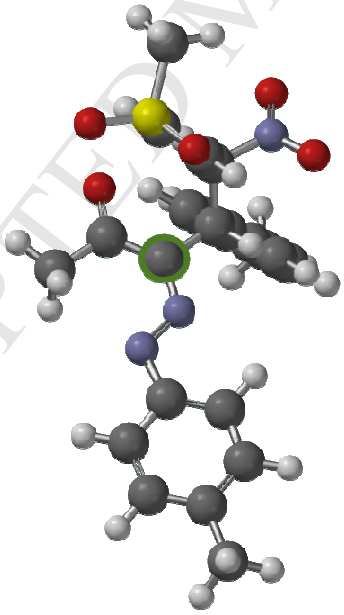
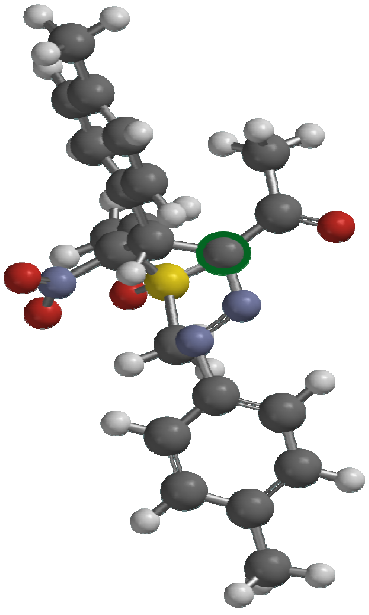
| | | |
|---|---|---|
|  **18aa:** Reference |  **18′aa:** ΔE = +15.7 kJ/mol<br>Δp$K_a$ = +4.24 |  **18′′aa:** ΔE = +15.1 kJ/mol<br>Δp$K_a$ = +4.08 |
|  **18ad:** Reference |  **18′ad:** ΔE = -0.2 kJ/mol<br>Δp$K_a$ = -0.05 |  **18′′ad:** ΔE = -0.4 kJ/mol<br>Δp$K_a$ = -0.11 |

**Chart 1.** Results of the geometry optimization and energy minimization on **18aa**, **18′aa** and **18′′aa** and on **18ad**, **18′ad** and **18′′ad**.

To confirm our idea about the reason of the observed dichotomy, we set off quanto-mechanical calculations[4] on the intermediates **18**, **18′** and **18″** for the model amide (**aa**) and ketone (**ad**) derivatives. As Shown on Chart 1, while for the ketone derivatives there is no sensible difference in the relative stability of the three intermediates, and therefore in the acidity of the conjugated acids, in the case of the amide, the intermediate **18aa** is significantly more stable than the other ones, and this brings the acidity of the hydrogen in alpha to the nitro group to be considerably higher (more than 4 units of p*K*a[5]) than the acidity of the hydrogen in alpha to the carboxylic group.

**X ray Crystallographic study on 17bd**

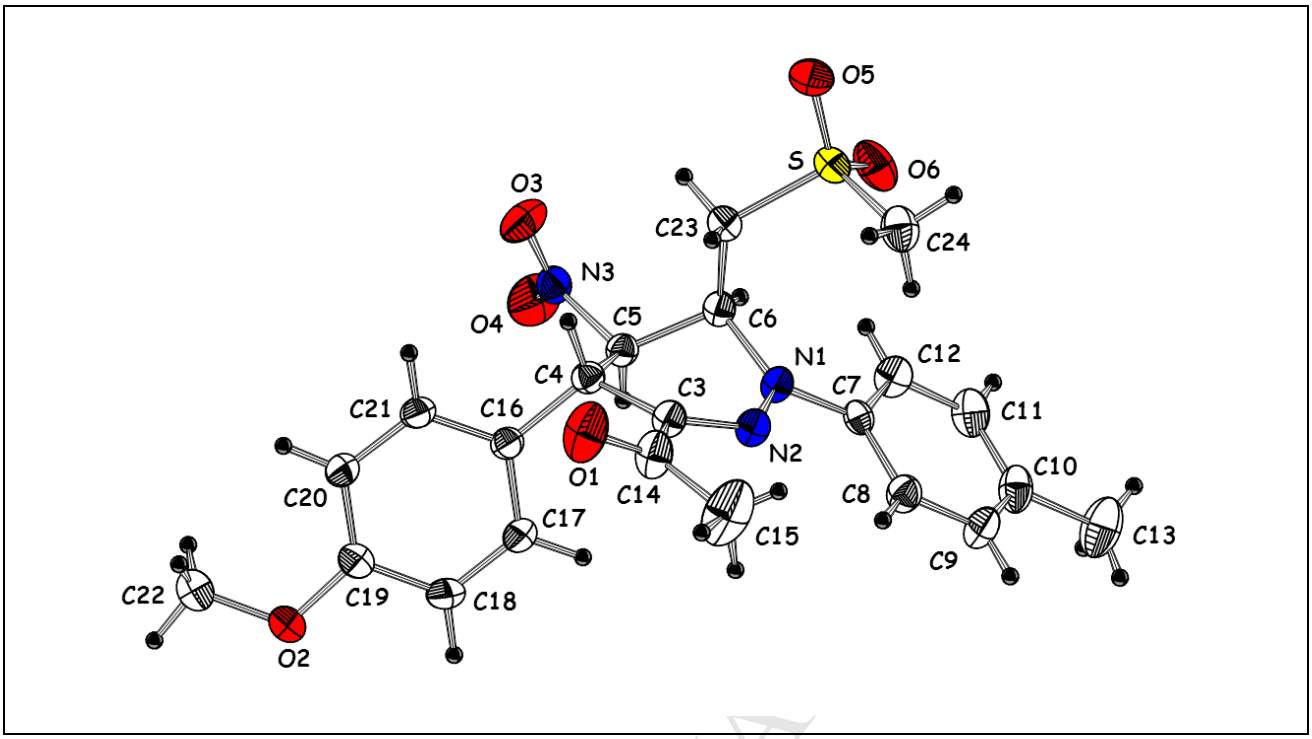
$C_{22}H_{25}N_3O_6S$, M = 459.5, light yellow-coloured crystal with truncated pyramid shape, and maximum dimensions 0.40 × 0.40 × 0.2 mm. Monoclinic, space group $P2_1/c$, $a$ = 8.927(1) Å, $b$ = 22.430(4) Å, $c$ = 11.713(2) Å, β = 101.72(1) Å, $V$ = 2296.4(6) Å$^3$, $Z$ = 4, F(000) = 968, $d_{calc}$ = 1.329 g/cm$^3$, μ (MoKα) = 0.18 mm$^{-1}$. Crystals were grown from ethanol.

Intensity data were collected at 295 K on a Bruker-Nonius MACH3 diffractometer (graphite monochromated Mo Kα radiation): $\omega$-$\theta$ scans, scan width 1.05°, minimum speed 0.97° min$^{-1}$, $\theta_{max}$ = 28°; 6009 total measured reflections, 5518 independent reflections of which 2954 with $F_o > 4\,\sigma(F_o)$; the structure was solved with the SIR*2014* program,[6] by applying Direct Methods procedures. The initial Fourier map showed 26 peaks which were attributed to the proper atomic species (non-hydrogen atoms), in agreement with the expected chemical formula. This partial model was then refined by means of full-matrix least squares cycles using the SHELXL program,[7] and completed with the additional peaks taken from the difference Fourier map. After some cycles of anisotropic refinement of the heavier atoms, all hydrogen atoms were also obtained in subsequent difference Fourier maps. Their coordinates and isotropic displacement parameters ($U_{iso}$) could be freely refined, except for two methyl groups (C13 and C15), which showed large anisotropic displacement parameters. In this case, the H atoms were restrained in idealized positions (AFIX 137 instruction) with the corresponding $U_{iso}$ value constrained to 1.2 times the $U_{eq}$ of the bonded C atom.
The final agreement indices are: $R1$= 0.057, over 2954 reflections with $F_o > 4\sigma\ F_o$, and $wR2$ = 0.133, for 367 refined parameters and 5518 reflections, mean shift/e.s.d = 0.003, Goodness of fit $S$ = 0.973, $\Delta\rho_{min}$ = -0.23 eÅ$^{-3}$, $\Delta\rho_{max}$ = +0.20 eÅ$^{-3}$.

Figure 1 shows the ortep diagram of the molecule with atom numbering. Bond distances and bond angles are in the normal range if compared with tabulated values for similar compounds and no notably short intermolecular contact is found. In accordance with the general classification of puckering in six-membered rings,[8] the central ring formed by N1, N2, C3, C4, C5, C6 exhibits an envelope (or half-boat) conformation, being the C6 atom out of the mean plane defined by the other five atoms (distance C6-plane ≅ 0.7 Å). The substituents to the asymmetric carbon atoms of the central ring (C4, C5, C6) are arranged in the crystal in trans-cis conformation.
As no H atoms are directly bound to the more electronegative elements N, O, S, only hydrogen bonds of C-H…O type can be established between the molecules. Although these interactions are quite numerous in this structure (11 different contacts), they are rather weak, as attested by the donor…acceptor distances (C….O), whose values are well greater than (only in two cases, slightly lower than) the sum of the van der Waals radii.

Crystallographic data (CIF file, FCF file) for the structure in this paper have been deposited with the Cambridge Crystallographic Data centre as supplementary publication numbers CCDC-1403698 Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 IEZ, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk]

**Ortep of 17bd**



## References and Notes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2. Dell'Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. *Tetrahedron* **1996**, *52*, 5889–5898; Dell'Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. *Tetrahedron* **1994**, *50*, 11239–11248; Dell'Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. *Tetrahedron* **1993**, *49*, 235–242.
3. Bianchi, L.; Carloni-Garaventa, A.; Maccagno, M.; Petrillo, G.; Scapolla, C.; Tavani, C. *Tetrahedron Lett.* **2012**, *53*, 6394–6400.
4. DFT/B3LYP/6-311++G**/SM8(THF) calculation have been performed.
5. $pK_a = \Delta E / 2.303\ RT$ ; at -78°C (the temperature at which the reaction was performed): $2.303\ RT = 2.303 * 8.314\ J\ K^{-1}\ mol^{-1} * 195\ K = 3.7\ kJ/mol$.
6. ***SIR*2014**. http://wwwba.ic.cnr.it/content/sir2011-v10; Burla, M. C.; Caliandro, R.; Carrozzini, B.; Cascarano, G. L.; Giacovazzo, C.; Mallamo, M.; Mazzone, A.; Polidori, G. **2014**, In preparation.
7. Sheldrick, G. M. *Acta Crystallogr.* A64, **2008**, 112-122.
8. Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354-1358.