

## DISCUSSION

This chapter discusses the adopted synthetic procedures to achieve the target compounds. The present thesis comprises four synthetic schemes:

### Scheme 1:

- 2-(Benzylsulfanyl)-4-hydrazinyl-6-methylpyrimidine **4**
- *N'*-[2-(Benzylsulfanyl)-6-methylpyrimidin-4-yl]-4-substituted benzene-sulfonohydrazides **5a,b**

### Scheme 2:

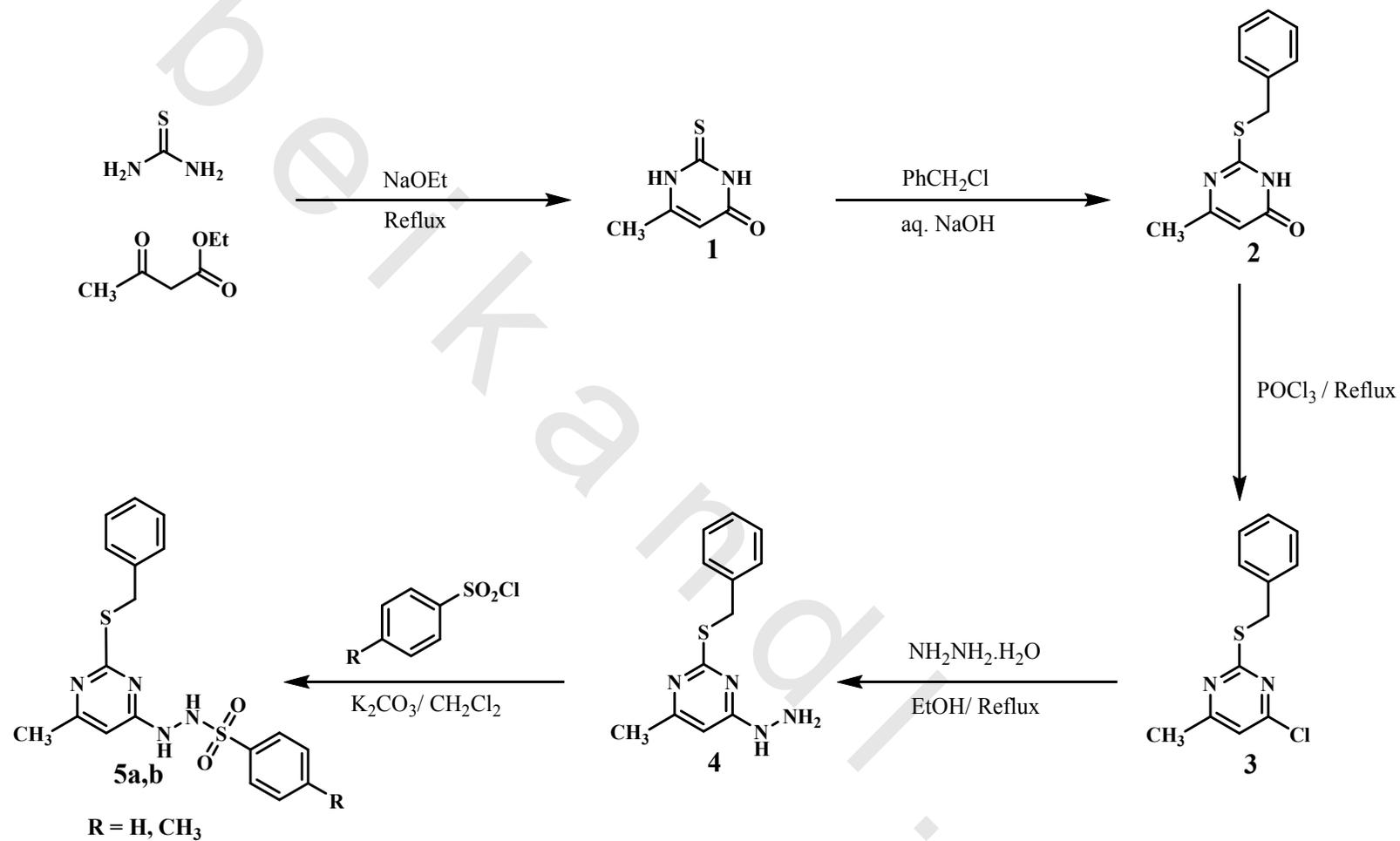
- 4-[2-(4-Substituted benzylidene)hydrazinyl]-2-(benzylsulfanyl)-6-methylpyrimidines **6a-c**
- 3-(4-Substituted phenyl)-5-(benzylsulfanyl)-8-bromo-7-methyl-[1,2,4]triazolo[4,3-*c*]-pyrimidines **7a-c**
- 1-[3-(4-Substituted phenyl)-5-(Benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]-pyrimidin-2(3*H*)-yl]ethanones **8a-c**
- 5-(Benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]pyrimidine-3-thiol **9**
- 3-Substituted sulfanyl-5-(benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]pyrimidines **10a,b**
- 2-{{5-(Benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]pyrimidin-3-yl}sulfanyl}-1-phenylethanone **11**

### Scheme 3:

- 2-[2-(Benzylsulfanyl)-6-methylpyrimidin-4-yl]-*N*-allyl (or phenyl)hydrazine-1-carbothioamides **12a,b**
- 4-(4-Substituted phenyl)-2-{{2-[2-(benzylsulfanyl)-6-methylpyrimidin-4-yl]hydrazono}-3-allyl (or phenyl)-2,3-dihydrothiazoles **13a-f**
- 5-(Benzylsulfanyl)-7-methyl-*N*-phenyl-[1,2,4]triazolo[4,3-*c*]pyrimidin-3-amine **14**

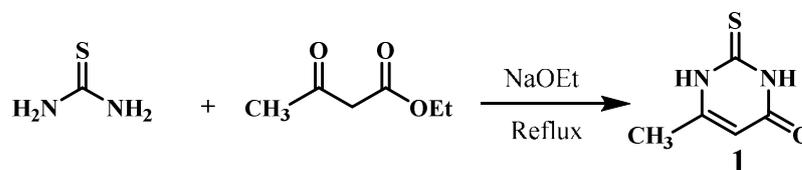
### Scheme 4:

- 2-[(4-Chloro-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone **16**
- 2-[(4-Chloro-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone oxime **17**
- 2-[(4-Hydrazinyl-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone oxime **18**
- 2-{{2-[(4-Methyl-6-oxo-1,6-dihydropyrimidin-2-yl)sulfanyl]-1-phenylethylidene}-*N*-phenylhydrazine-1-carbothioamide **19**



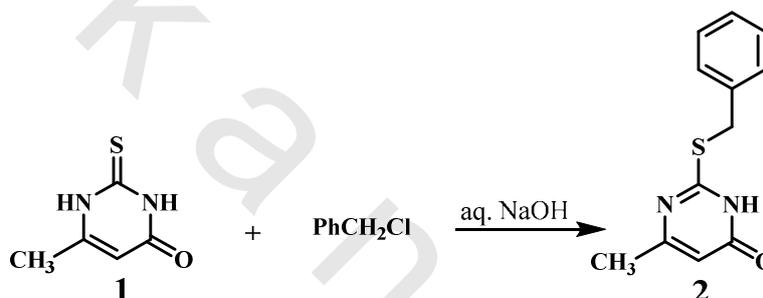
Scheme 1

## Scheme 1

6-Methyl-2-thioxo-2,3-dihydropyrimidin-4(1H)-one, **1**

In the present investigation, the pyrimidinone **1** was prepared by heating under reflux a mixture of thiourea and ethyl acetoacetate in presence of sodium ethoxide followed by acidification with hydrochloric acid adopting the reaction conditions described in the reported procedure.<sup>(99)</sup>

IR spectrum showed stretching absorption bands characteristic for NH, C=O and N-C=S functional groups at their expected frequencies.

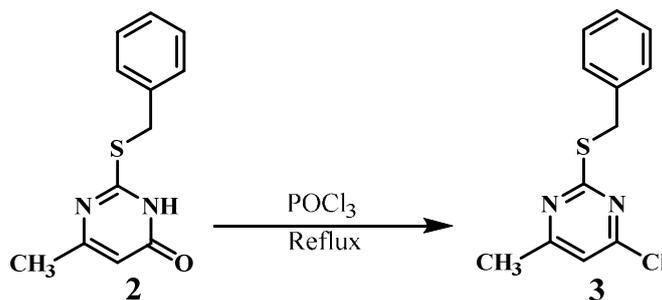
2-(Benzylsulfanyl)-6-methylpyrimidin-4(3H)-one, **2**

Several methods were reported for the alkylation of thiols including stirring at room temperature with alkyl halide in aqueous sodium hydroxide,<sup>(100,101)</sup> or in ethanolic sodium ethoxide.<sup>(102)</sup> Also, alkylation was performed by heating under reflux a mixture of thiol, alkyl halide and sodium hydroxide in ethanol<sup>(102)</sup> or THF.<sup>(103)</sup> The use of dry acetone containing anhydrous  $K_2CO_3$ ,<sup>(104-106)</sup> ethanolic sodium methoxide<sup>(107)</sup> and ethanol containing anhydrous sodium acetate<sup>(108)</sup> were also reported. Some authors reported that alkylation could proceed without base either by fusion<sup>(102)</sup> or reflux in high boiling solvent such as DMF.<sup>(106)</sup>

In the present investigation, compound **2** was prepared by adapting the reported procedure<sup>(109)</sup> by stirring mixture of the pyrimidinone **1** with benzyl chloride in presence of aqueous sodium hydroxide at room temperature.

IR spectrum showed stretching absorption bands corresponding to NH, C=O, C=N and C-S-C groups at their expected frequencies.

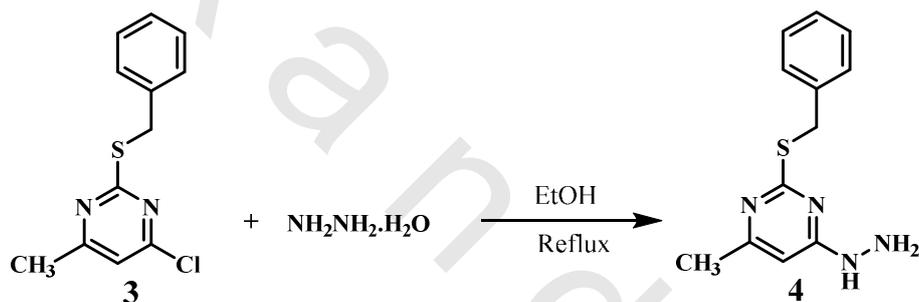
### 2-(Benzylsulfanyl)-4-chloro-6-methylpyrimidine, 3



It has been reported that chlorination of substituted pyrimidinones could be achieved using either phosphorous oxychloride<sup>(109,110)</sup> or phosphorous pentachloride.<sup>(111)</sup>

In the present investigation, the chloropyrimidine 3 was prepared by heating under reflux a mixture of compound 2 and phosphorous oxychloride. The reaction mixture was cooled to room temperature then poured over crushed ice and the oil obtained was extracted as described in the reported procedure.<sup>(109)</sup>

### 2-(Benzylsulfanyl)-4-hydrazinyl-6-methylpyrimidine, 4



The title compound was prepared by heating under reflux a mixture of compound 3 and hydrazine hydrate 99% in absolute ethanol adopting the reaction conditions described for the synthesis of related compounds.<sup>(112)</sup>

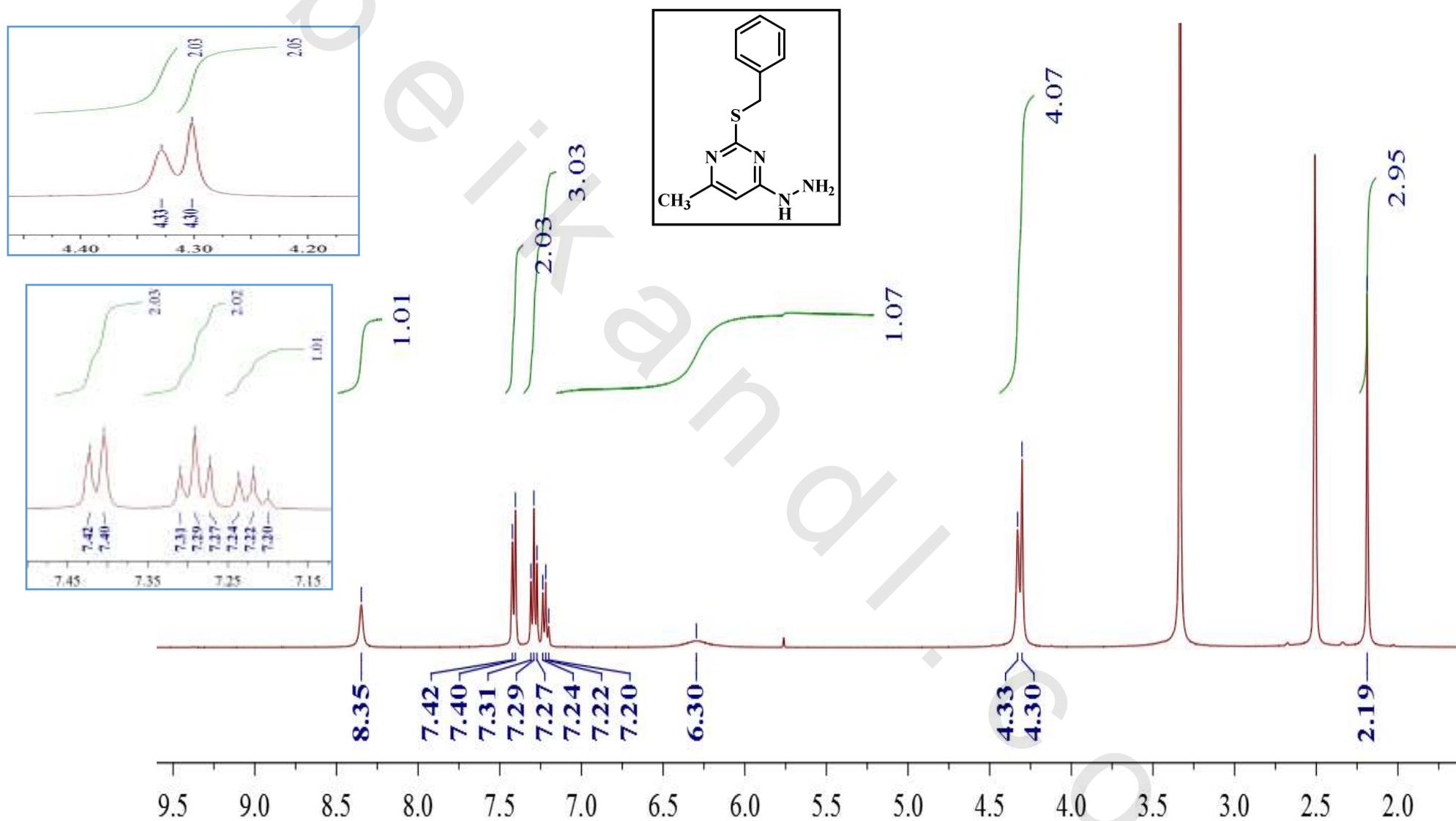
It is worthy to mention that nucleophilic displacements of sulfanyl groups were reported in analogous reactions.<sup>(99,113)</sup>

**IR** spectrum showed stretching absorption bands characteristic for NH and NH<sub>2</sub> functions besides the expected stretching absorption bands corresponding to C=N and C-S-C groups.

**<sup>1</sup>H-NMR** spectrum (Figure 1) showed two D<sub>2</sub>O-exchangeable signals assigned for the two shielded NH<sub>2</sub> protons and one deshielded NH proton. A downfield signal, assigned for pyrimidine C<sub>5</sub>-H, and 5 downfield aromatic protons, assigned for the phenyl ring, were also identified. In addition, two upfield signals assigned for the shielded C<sub>6</sub>-CH<sub>3</sub> and S-CH<sub>2</sub> protons were resonated at their expected chemical shifts.

**<sup>13</sup>C-NMR** spectrum (Figure 2) showed signals assigned for pyrimidine and phenyl carbons in addition to signals assigned for CH<sub>3</sub> and S-CH<sub>2</sub> carbons.

**HRMS** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 247.687 corresponding to C<sub>12</sub>H<sub>15</sub>N<sub>4</sub>S.

Figure 1:  $^1\text{H-NMR}$  spectrum of compound 4

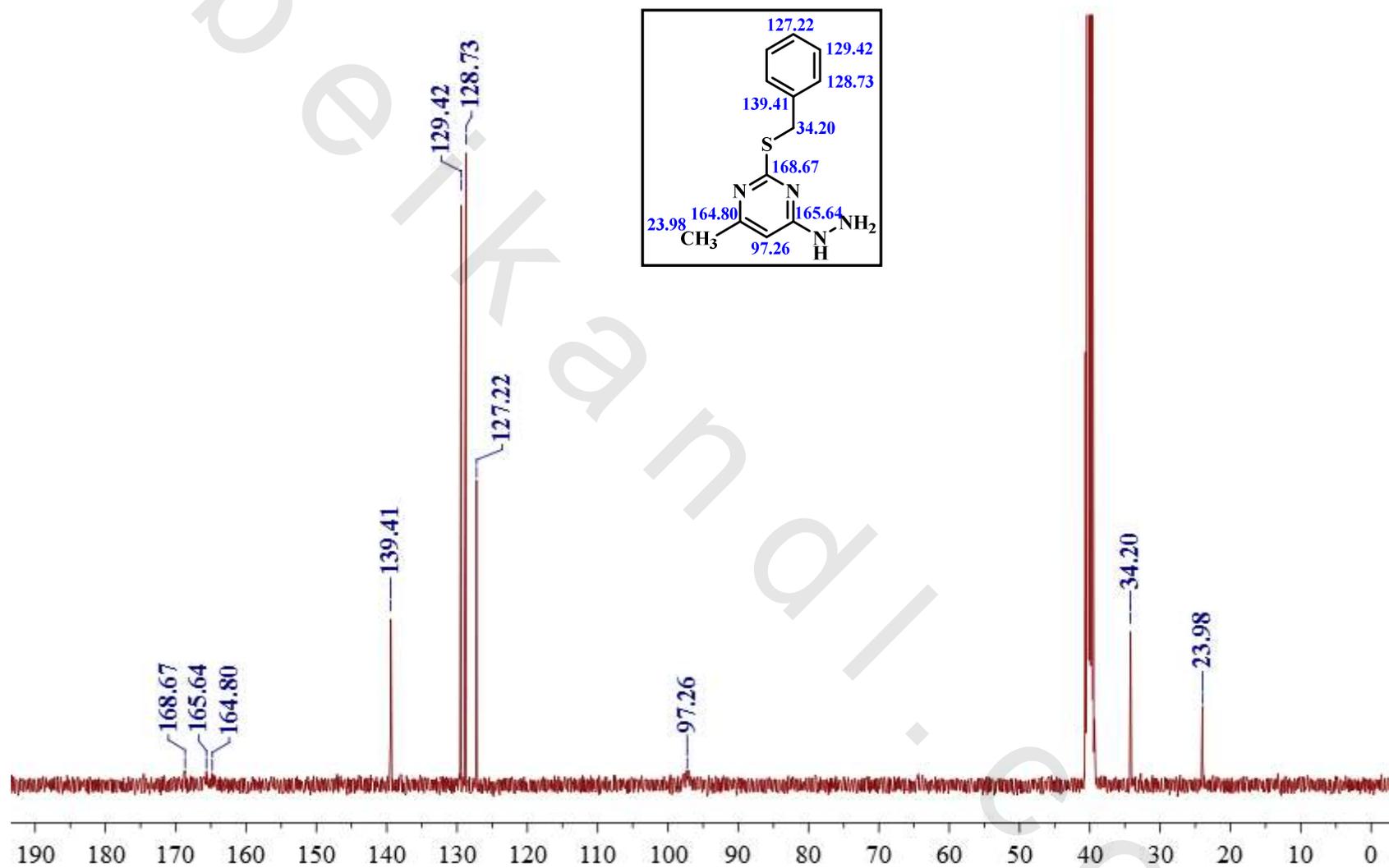
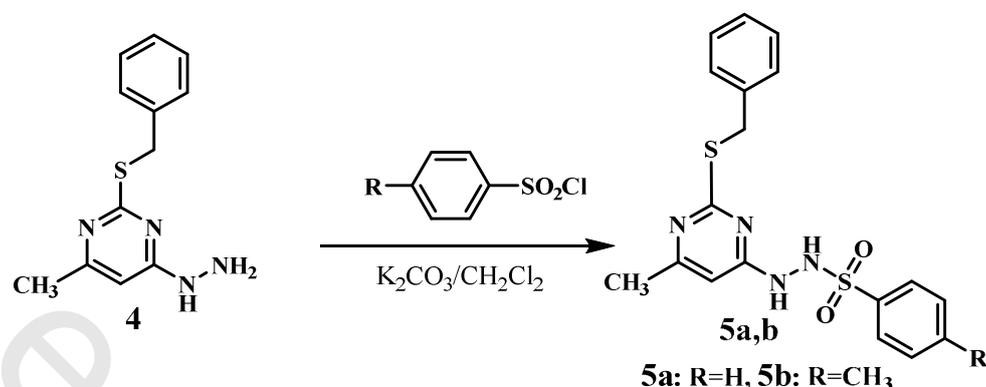


Figure 2:  $^{13}\text{C}$ -NMR spectrum of compound 4

***N'*-[2-(Benzylsulfanyl)-6-methylpyrimidin-4-yl]-4-substituted benzene-sulfonohydrazides, 5a,b**



In general, hydrazine compounds are known to react readily with arylsulfonyl chlorides under basic conditions.<sup>(114,115)</sup> Among reported methods, stirring the reactants in dry pyridine at room temperature<sup>(114)</sup> as well as heating under reflux in dry solvents, e.g. benzene, containing catalytic amount of triethylamine<sup>(115)</sup> were extensively documented.

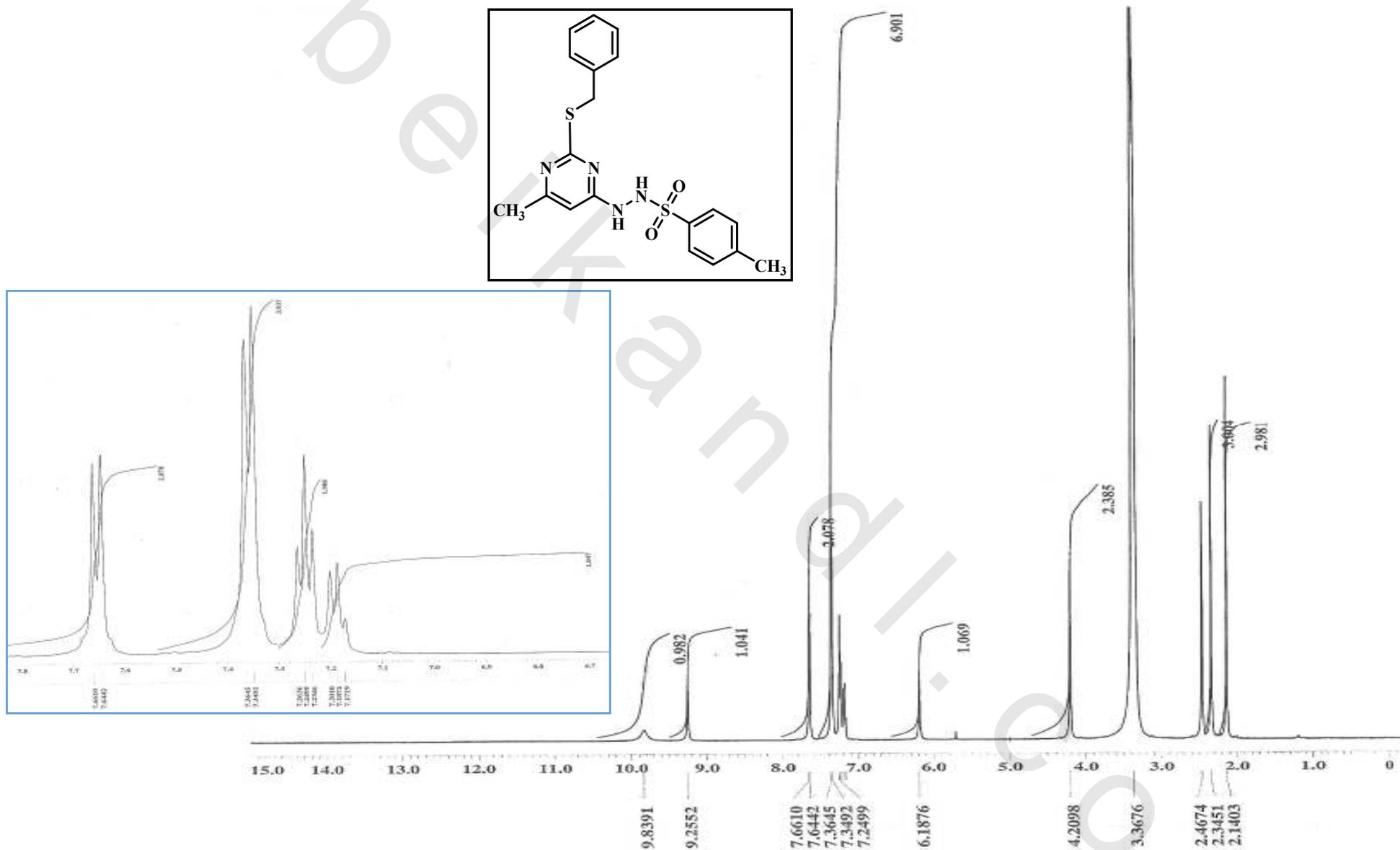
The synthesis of the title compounds was achieved by adapting the reaction conditions reported for the preparation of related compounds<sup>(116)</sup> by stirring mixture of the hydrazino derivative **4**, the suitable arylsulfonyl chloride and anhydrous potassium carbonate in methylene chloride at room temperature followed by solvent removal and addition of water.

**IR** spectra of compounds **5a,b** showed characteristic stretching absorption band for NH group as well as strong asymmetric and symmetric stretching bands assigned for SO<sub>2</sub> moiety in addition to the characteristic stretching absorption bands due to C=N and C-S-C functions at their expected frequencies.

**<sup>1</sup>H-NMR** spectra of compounds **5a,b** revealed the characteristic two consecutive D<sub>2</sub>O-exchangeable downfield signals assigned for the two NH protons, besides signals assigned for the aromatic and CH<sub>3</sub> protons at their expected chemical shifts. The **<sup>1</sup>H-NMR** spectrum of compound **5b** is shown in figure 3.

**<sup>13</sup>C-NMR** spectrum of compound **5b** (Figure 4) showed signals assigned for pyrimidine, benzyl and tolyl carbons at their expected chemical shifts.

**HRMS** of compound **5b** (Figure 5) showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 401.084 corresponding to C<sub>19</sub>H<sub>21</sub>N<sub>4</sub>O<sub>2</sub>S<sub>2</sub>.

Figure 3: <sup>1</sup>H-NMR spectrum of compound 5b

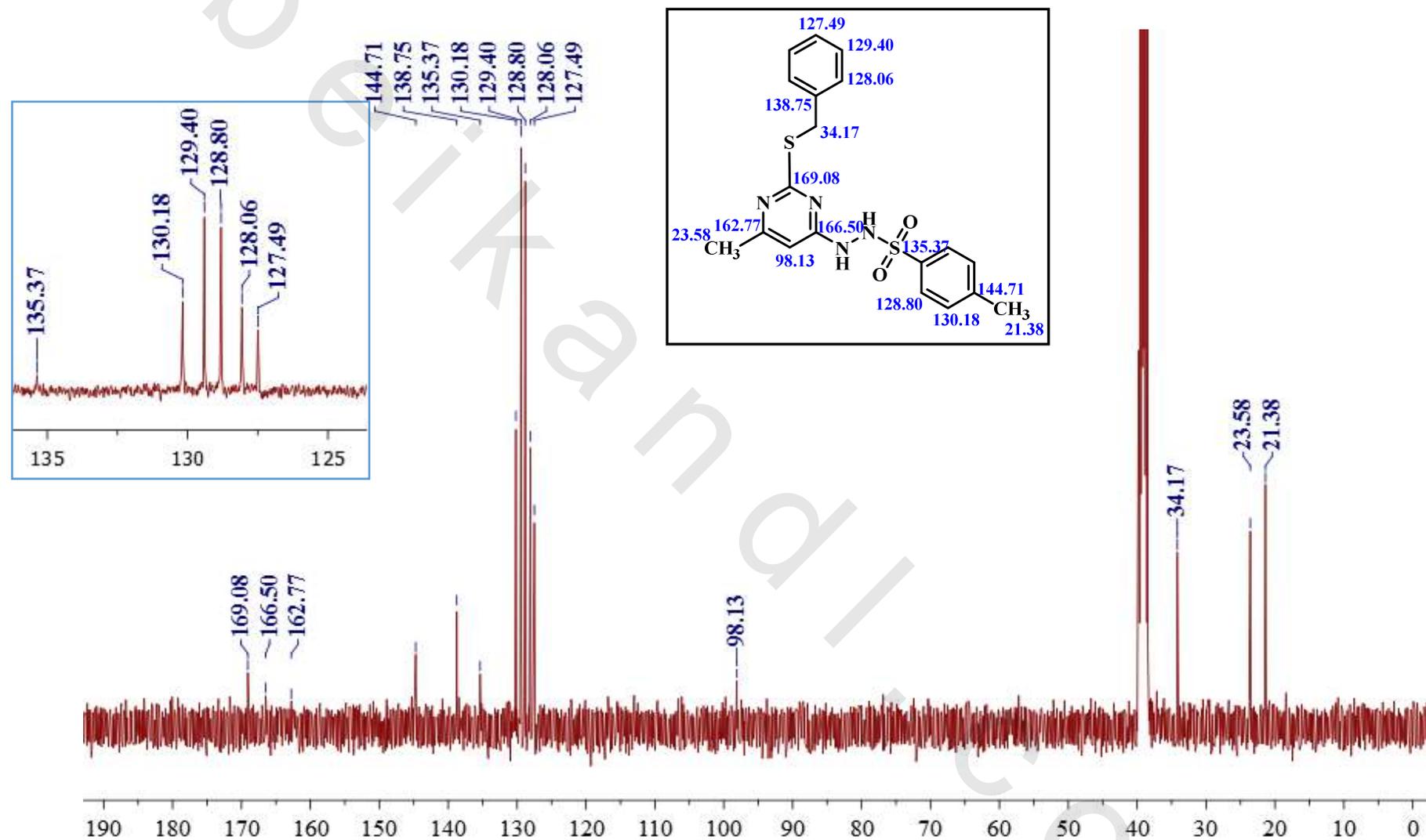


Figure 4:  $^{13}\text{C}$ -NMR spectrum of compound 5b

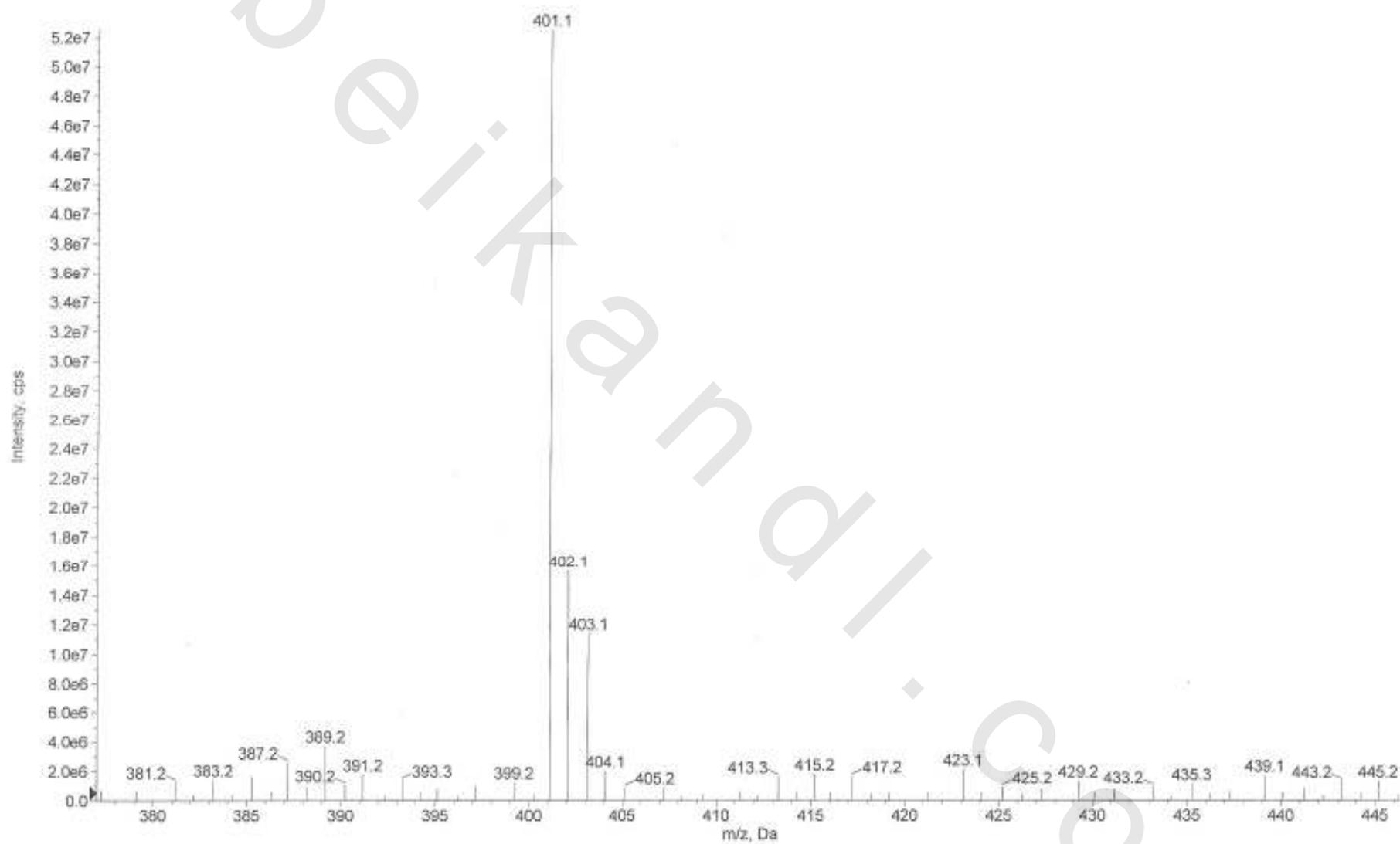
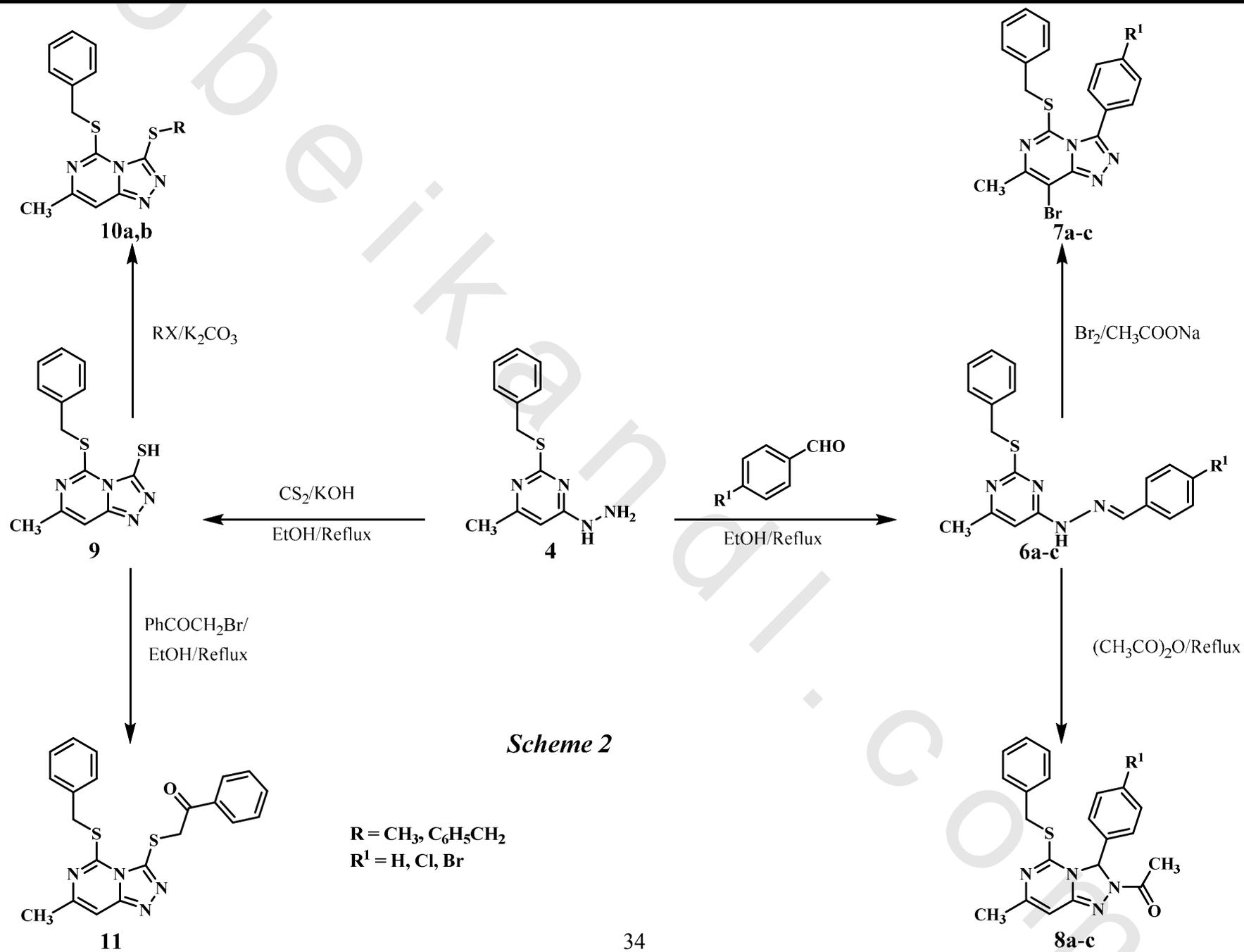


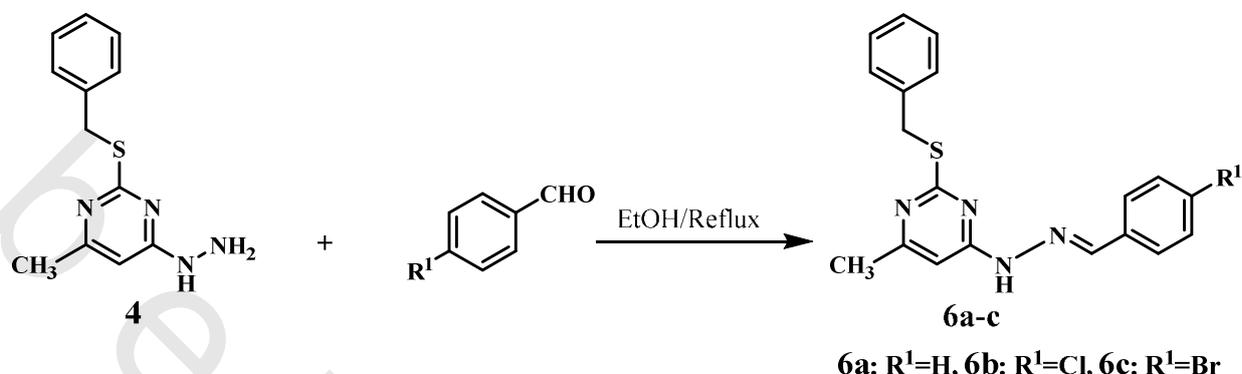
Figure 5: HRMS of compound 5b



Scheme 2

## Scheme 2

## 4-[2-(4-Substituted benzylidene)hydrazinyl]-2-(benzylsulfanyl)-6-methylpyrimidines, 6a-c



It has been reported that hydrazines condense with the appropriate carbonyl compounds under neutral,<sup>(117)</sup> acidic<sup>(118)</sup> or alkaline<sup>(119)</sup> conditions utilizing different solvents either at room temperature,<sup>(117)</sup> under reflux<sup>(120,121)</sup> or microwave irradiation.<sup>(122)</sup> Alternatively, hydrazones were also prepared by fusion.<sup>(123)</sup>

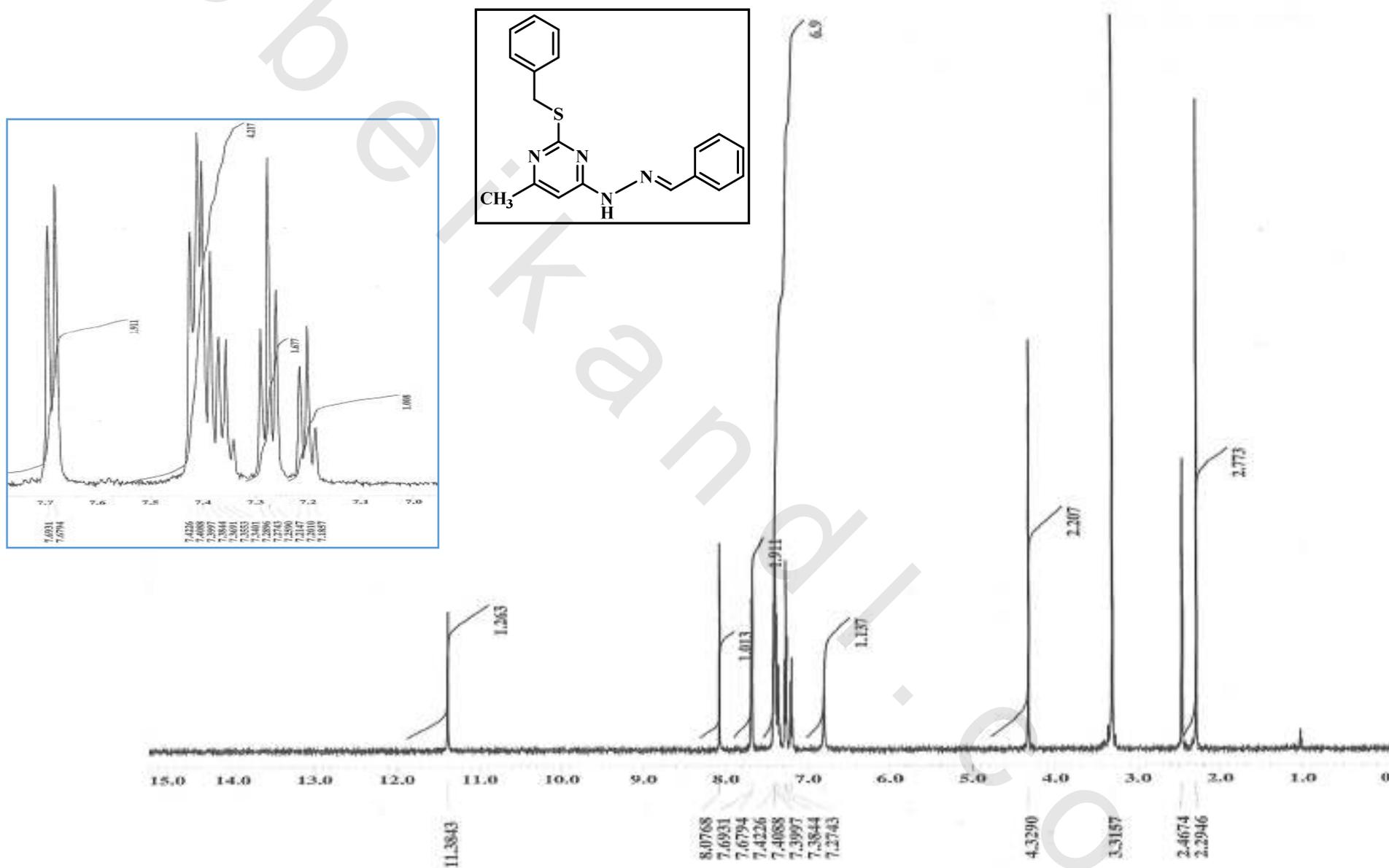
In the present investigation, condensing equimolar amounts of the hydrazino derivative **4** with the appropriate aromatic aldehydes in refluxing ethanol in accordance to a conventional reported procedure<sup>(121)</sup> afforded the corresponding hydrazones **6a-c**.

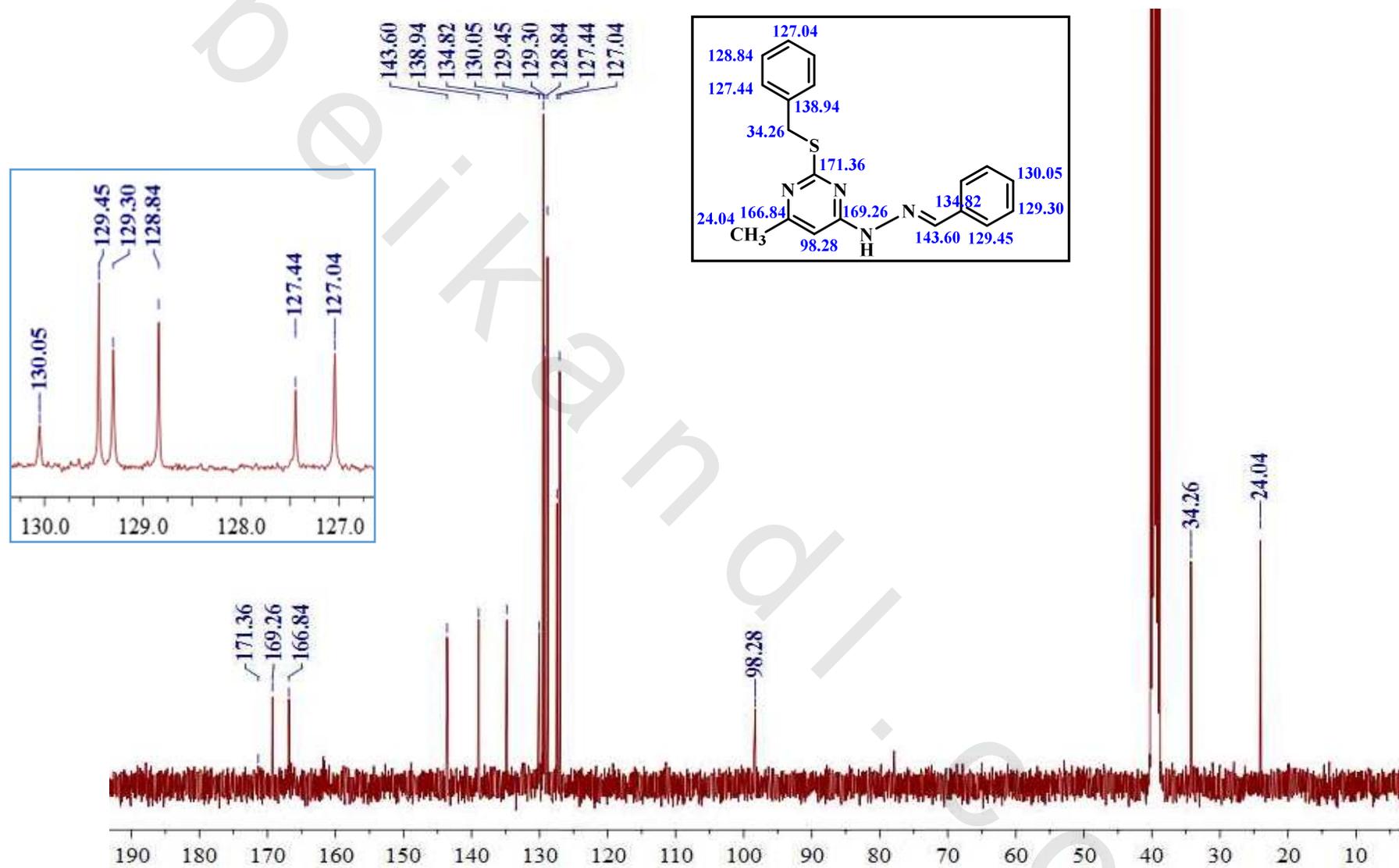
**IR** spectra of compounds **6a-c** lacked stretching absorption bands characteristic for NH<sub>2</sub> of the hydrazine moiety present in their precursor. In addition, usual absorption bands due to NH, C=N and C-S-C were well detected at their expected frequencies.

<sup>1</sup>H-NMR spectra of compounds **6a-c** revealed the disappearance of upfield D<sub>2</sub>O-exchangeable signal assigned for NH<sub>2</sub> protons present in their precursor. In addition, signals for other protons appeared at their expected chemical shifts. The <sup>1</sup>H-NMR spectrum of compound **6a** is shown in figure 6.

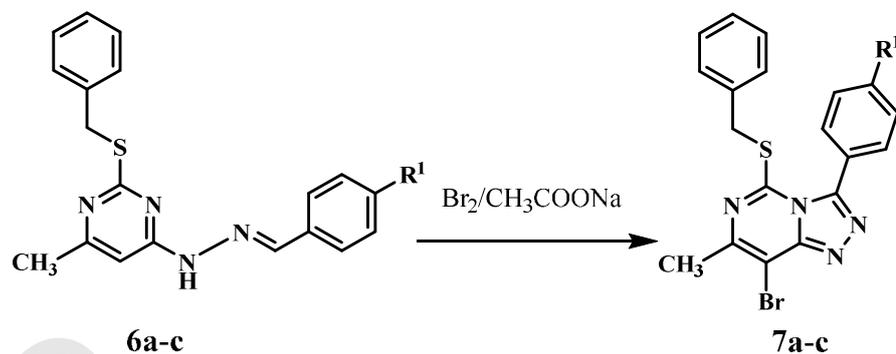
<sup>13</sup>C-NMR spectrum of compound **6a** (Figure 7) showed signals assigned for pyrimidine and two phenyl carbons. In addition, signals for other carbons were detected at their expected chemical shifts.

**HRMS** of compound **6a** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 335.069 corresponding to C<sub>19</sub>H<sub>19</sub>N<sub>4</sub>S. **HRMS** of compound **6b** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 368.893 corresponding to C<sub>19</sub>H<sub>18</sub>ClN<sub>4</sub>S. **HRMS** of compound **6c** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 412.727 corresponding to C<sub>19</sub>H<sub>18</sub>BrN<sub>4</sub>S.

Figure 6: <sup>1</sup>H-NMR spectrum of compound 6a

Figure 7:  $^{13}\text{C}$ -NMR spectrum of compound 6a

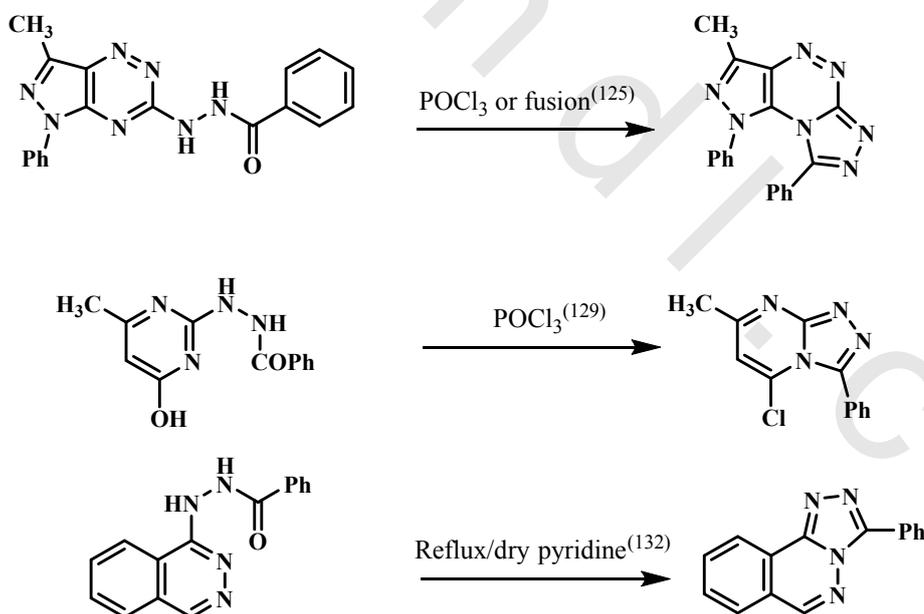
### 3-(4-Substituted phenyl)-5-(benzylsulfanyl)-8-bromo-7-methyl-[1,2,4]-triazolo[4,3-c]pyrimidines, 7a-c



**7a:** R<sup>1</sup>=H, **7b:** R<sup>1</sup>=Cl, **7c:** R<sup>1</sup>=Br

It has been reported that aryltriazoloheterocycles have been prepared through dehydrogenation of the arylidenehydrazino intermediates by heating in a high b.p. solvent such as DMSO<sup>(124)</sup> or heating in SOCl<sub>2</sub>.<sup>(125)</sup> Oxidative cyclization of the arylidenehydrazino intermediates could be also achieved using bromine in glacial acetic acid,<sup>(105,126,127)</sup> bromine in chloroform containing sodium bicarbonate,<sup>(128)</sup> or lead tetra-acetate in benzene or acetic acid.<sup>(129,130)</sup>

Furthermore, aryltriazoloheterocycles could be obtained via the dehydration of benzoylhydrazinoheterocycles by fusion at 240-245 °C,<sup>(125)</sup> treatment with phosphorous oxychloride either alone<sup>(129)</sup> or in xylene<sup>(125,131)</sup> or heating in dry pyridine.<sup>(132)</sup>



In addition, reaction of hydrazinoheterocycles with aldehydes either by fusion at 100 °C<sup>(133)</sup> or in presence of refluxing glacial acetic acid<sup>(104)</sup> could directly result in aryltriazoloheterocycles.

In the present investigation, the title compounds were prepared from the corresponding arylidenehydrazino derivatives **6a-c** using bromine and sodium acetate in glacial acetic acid adopting the reaction conditions described for the synthesis of related compounds.<sup>(127,130)</sup>

Interestingly, electrophilic bromination of triazolopyrimidine at position 8 occurred and was verified by Beilstein test for halogens,  $^1\text{H-NMR}$  and EIMS. The postulated mechanism of compounds **7a-c** formation is illustrated in figure 8.

**IR** spectra of compounds **7a-c** lacked stretching absorption band characteristic for NH function present in their precursors. In addition, stretching absorption bands corresponding to C=N and C-S-C were revealed at their expected frequencies.

$^1\text{H-NMR}$  spectra of compounds **7a-c** revealed the disappearance of the three signals assigned for NH, N=CH and triazolopyrimidine C<sub>8</sub>-H protons present in their precursors. In addition, signals for other protons were well identified at their expected chemical shifts. The  $^1\text{H-NMR}$  spectrum of compound **7b** is shown in figure 9.

$^{13}\text{C-NMR}$  spectrum of compound **7a** (Figure 10) showed signals assigned for the triazolopyrimidine carbons. Moreover, signals for other carbons were detected at their expected chemical shifts.

**EIMS** of compound **7a** (Figure 11) showed molecular ion peak at  $m/z$  412 ( $M^{+}+2$ ), corresponding to  $\text{C}_{19}\text{H}_{15}^{81}\text{BrN}_4\text{S}$ . The base peak was at  $m/z$  83. **EIMS** of compound **7b** (Figure 12) showed molecular ion peak at  $m/z$  448 ( $M^{+}+4$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{81}\text{Br}^{37}\text{ClN}_4\text{S}$ , 446 ( $M^{+}+2$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{79}\text{Br}^{37}\text{ClN}_4\text{S}$  or  $\text{C}_{19}\text{H}_{14}^{81}\text{Br}^{35}\text{ClN}_4\text{S}$  and at  $m/z$  444 ( $M^{+}$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{79}\text{Br}^{35}\text{ClN}_4\text{S}$ . The base peak was at  $m/z$  159. **EIMS** of compound **7c** showed molecular ion peak at  $m/z$  492 ( $M^{+}+4$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{81}\text{Br}^{81}\text{BrN}_4\text{S}$ , 490 ( $M^{+}+2$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{79}\text{Br}^{81}\text{BrN}_4\text{S}$  and at  $m/z$  488 ( $M^{+}$ ), corresponding to  $\text{C}_{19}\text{H}_{14}^{79}\text{Br}^{79}\text{BrN}_4\text{S}$ . The base peak was at  $m/z$  91.

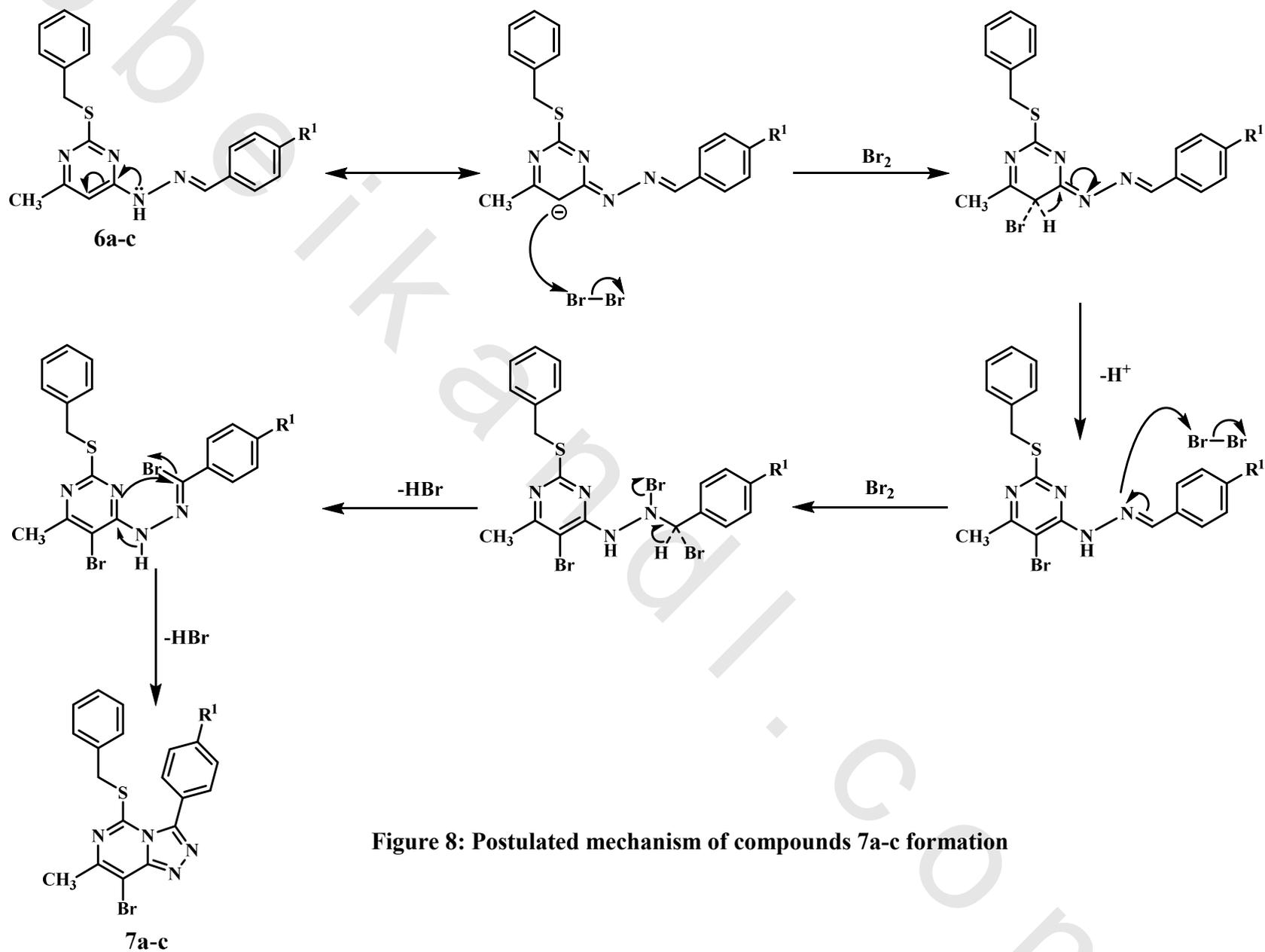


Figure 8: Postulated mechanism of compounds 7a-c formation

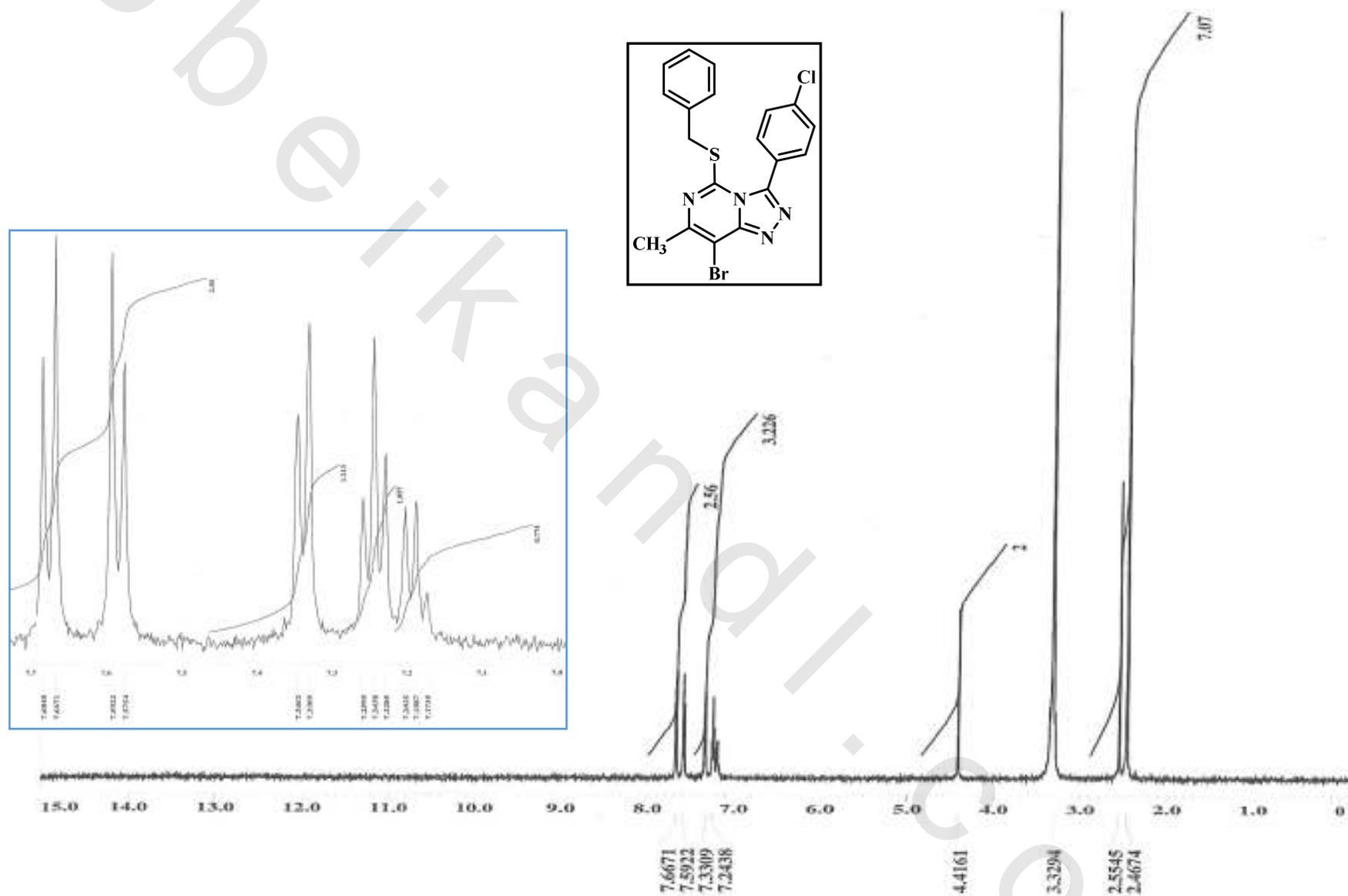
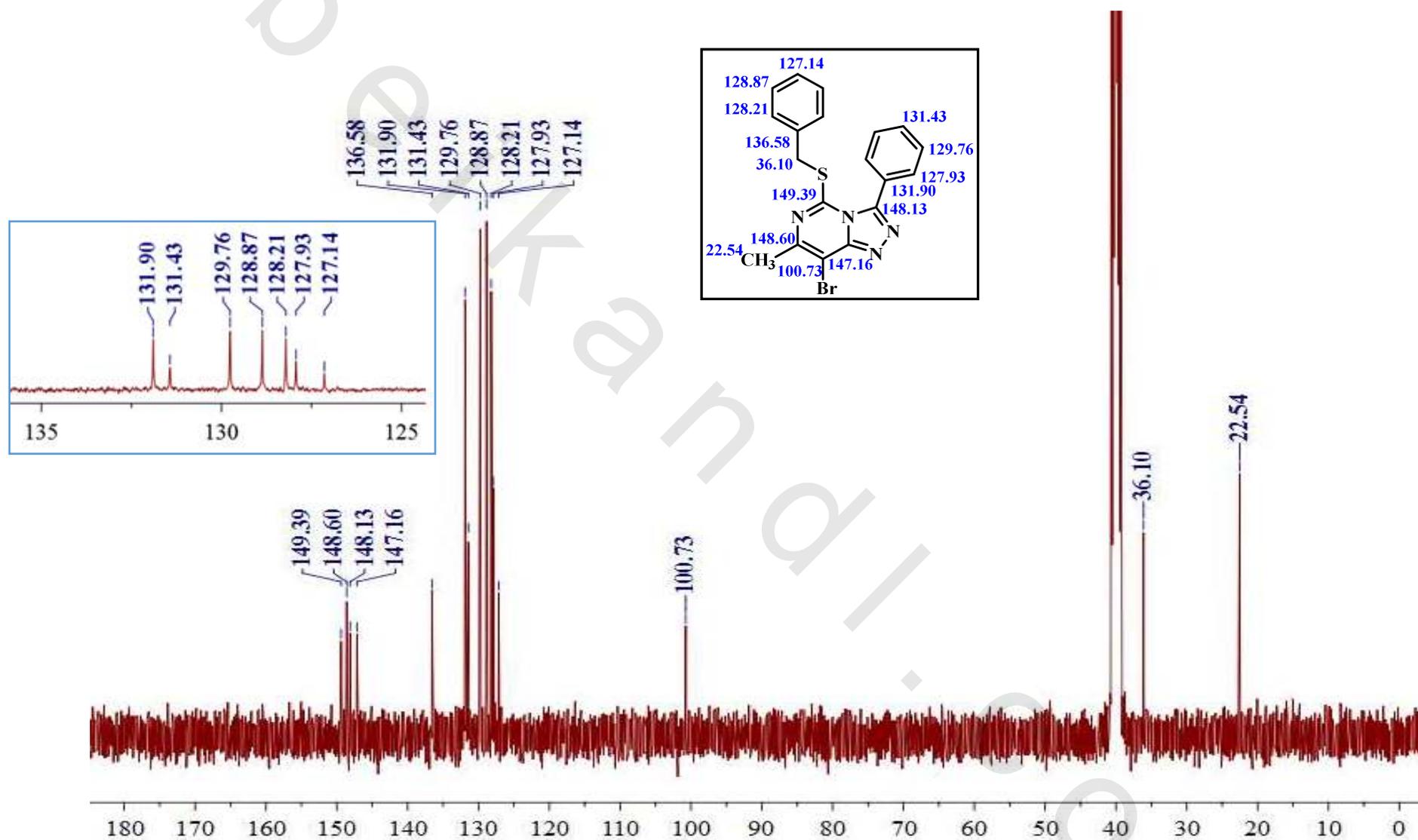


Figure 9: <sup>1</sup>H-NMR spectrum of compound 7b

Figure 10:  $^{13}\text{C}$ -NMR spectrum of compound 7a

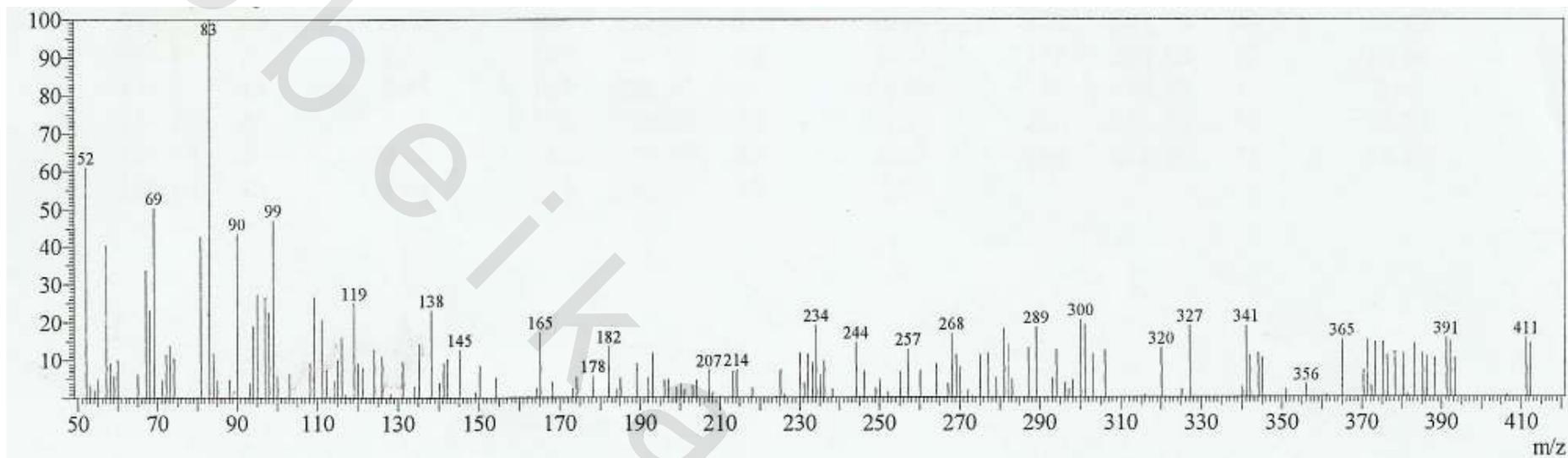


Figure 11: EIMS of compound 7a

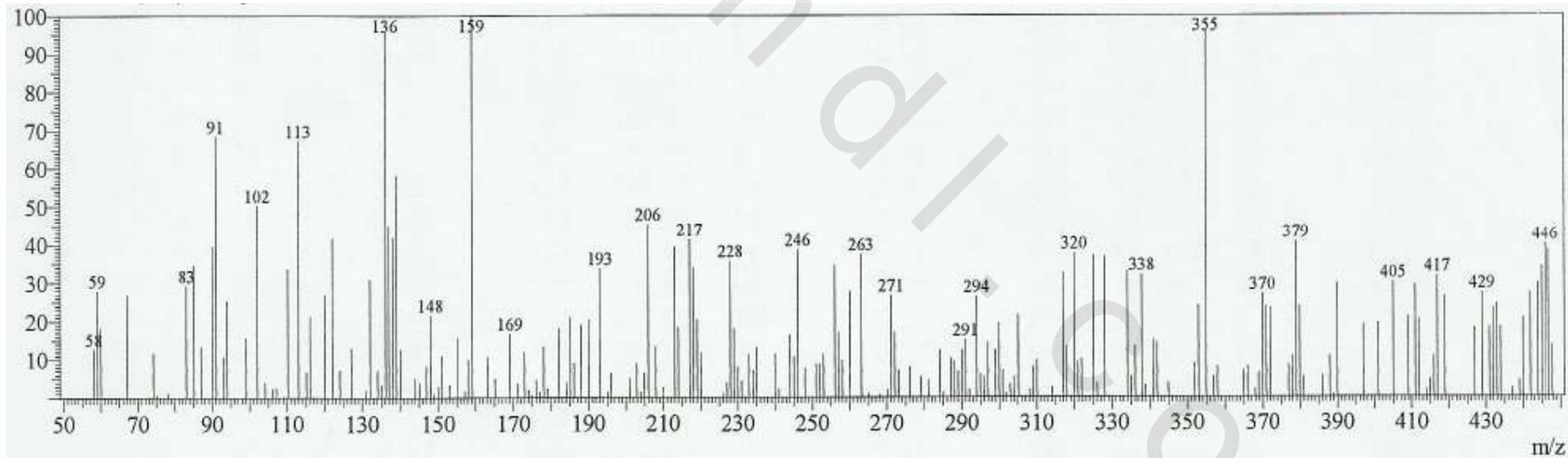
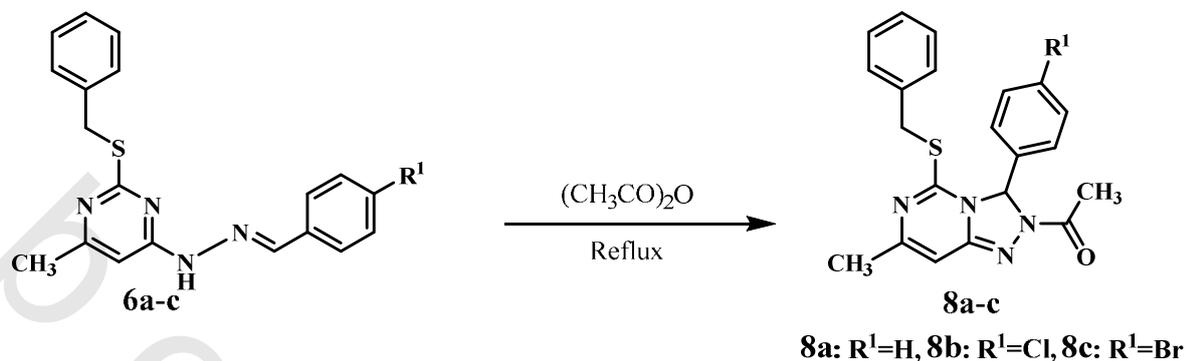


Figure 12: EIMS of compound 7b

**1-[5-(Benzylsulfanyl)-3-(4-substituted phenyl)-7-methyl-[1,2,4]triazolo-[4,3-c]pyrimidin-2(3H)-yl]ethanones, 8a-c**



In accordance to the reported reaction conditions adopted for the synthesis of analogous compounds,<sup>(134)</sup> the target compounds **8a-c** were obtained by refluxing a mixture of the appropriate arylidenehydrazino derivatives **6a-c** and acetic anhydride.

**IR** spectra for compounds **8a-c** lacked stretching absorption band characteristic for NH function present in their precursors and displayed stretching absorption band characteristic for C=O group in addition to the usual stretching absorption bands due to C=N and C-S-C at their expected frequencies.

**<sup>1</sup>H-NMR** spectra of compounds **8a-c** revealed the disappearance of the two signals assigned for NH and N=CH protons present in their precursors and the appearance of an upfield signal assigned for CO-CH<sub>3</sub> protons. Other protons signals characteristic for the molecule were detected at their expected chemical shifts. The <sup>1</sup>H-NMR spectrum of compound **8c** is shown in figure 13.

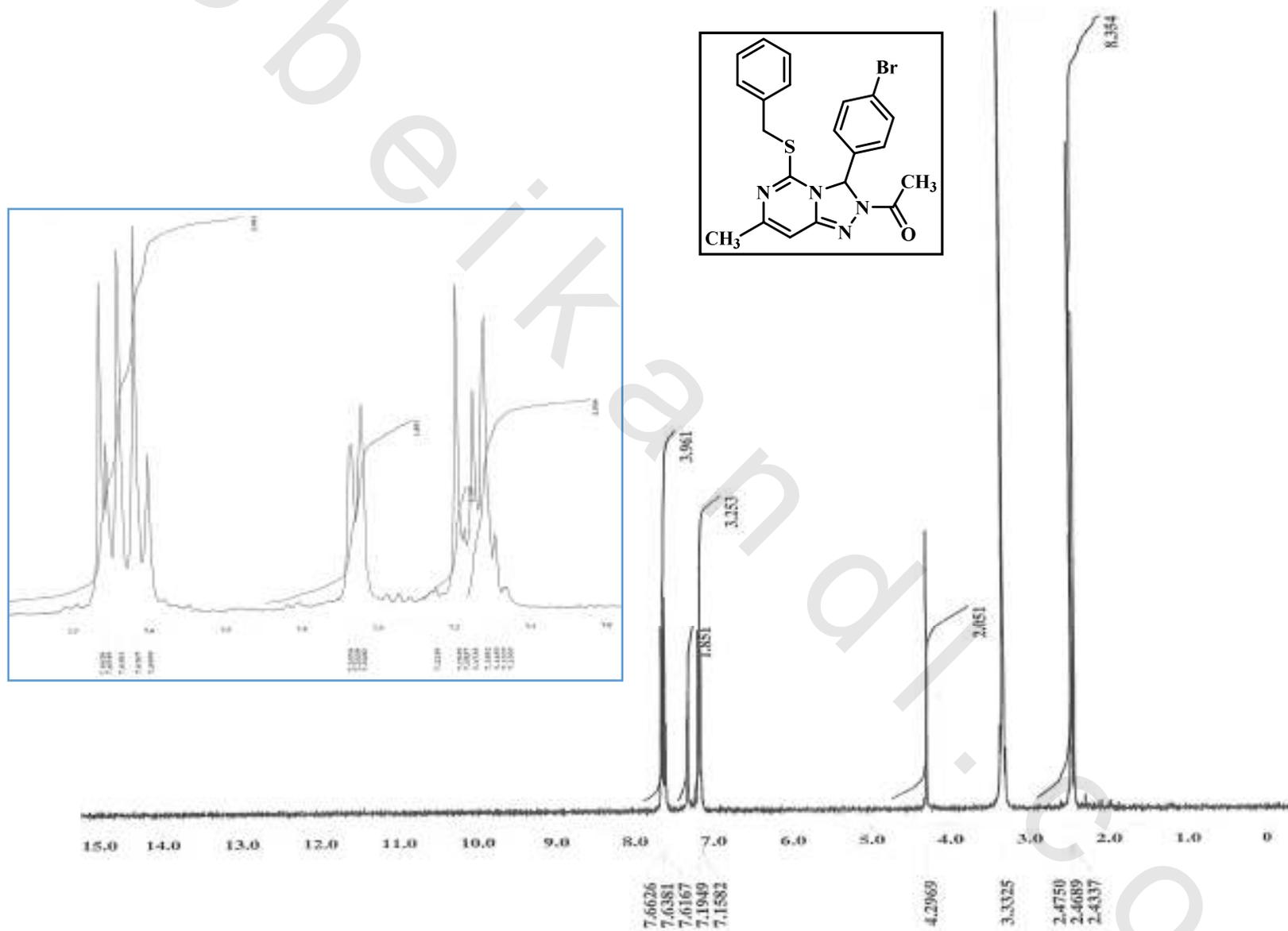
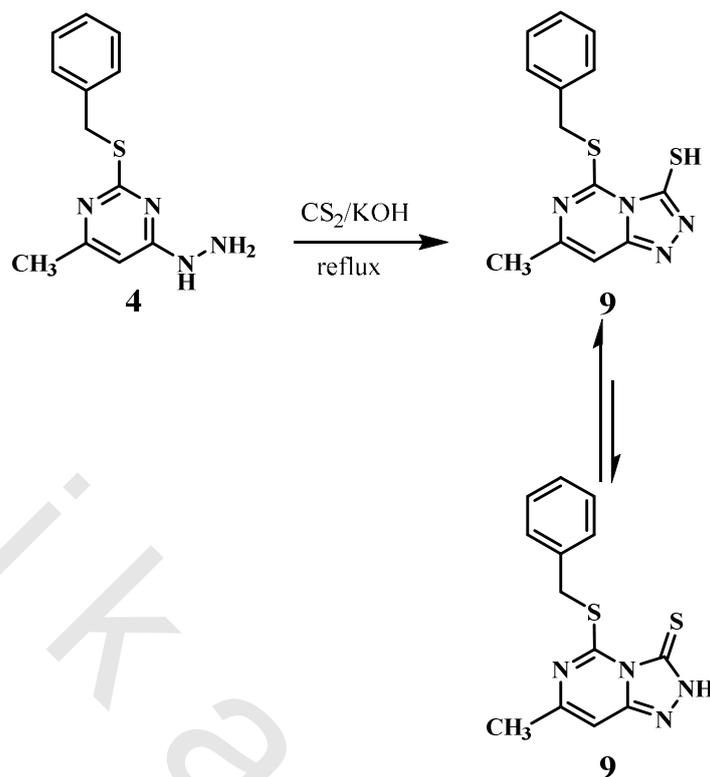


Figure 13: <sup>1</sup>H-NMR spectrum of compound 8c

5-(Benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]pyrimidine-3-thiol, **9**

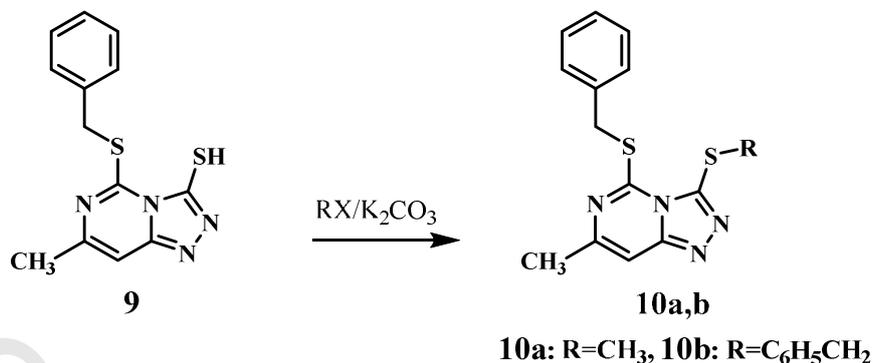
It was reported that mercaptotriazoloheterocycles were prepared by treatment of hydrazinoheterocycles with carbon disulphide only,<sup>(104)</sup> carbon disulphide and KOH<sup>(105,135)</sup> or carbon disulphide and pyridine.<sup>(136-138)</sup>

In the present work, the title compound was obtained by refluxing **4** with carbon disulphide in ethanolic KOH, followed by acidification to pH 5 adopting the reaction conditions described for the synthesis of analogous compounds.<sup>(135)</sup>

**IR** spectrum showed stretching absorption bands characteristic for both NH and SH functions indicating that compound **9** existed as thione-thiol tautomers. In addition, usual stretching absorption bands corresponding to C=N and C-S-C functions appeared at their expected frequencies.

<sup>1</sup>**H-NMR** spectrum lacked the D<sub>2</sub>O-exchangeable signal assigned for hydrazino NH<sub>2</sub> present in the precursor. In addition, a deshielded D<sub>2</sub>O-exchangeable signal assigned for SH proton. Signals for other protons were identified at their expected chemical shifts.

**HRMS** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 289.060 corresponding to C<sub>13</sub>H<sub>13</sub>N<sub>4</sub>S<sub>2</sub>.

**3-Substituted sulfanyl-5-(benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-c]-pyrimidines, 10a,b**

The title compounds **10a,b** were prepared by adopting the reaction conditions described for the synthesis of related compounds<sup>(139)</sup> by stirring **9** with either methyl iodide or benzyl chloride in dry DMF containing K<sub>2</sub>CO<sub>3</sub> at room temperature.

**IR** spectra of compounds **10a,b** lacked stretching absorption bands characteristic for SH function present in their precursor while revealed usual absorption bands characteristic for C=N and C-S-C groups at their expected frequencies.

**<sup>1</sup>H-NMR** spectra of compounds **10a,b** lacked the downfield D<sub>2</sub>O-exchangeable signal assigned for SH proton present in their precursor. In addition, signals for other protons were well identified at their expected chemical shifts. The <sup>1</sup>H-NMR spectrum of compound **10a** is shown in figure 14.

**<sup>13</sup>C-NMR** spectrum of compound **10b** (Figure 15) showed signals characteristic for CH<sub>3</sub> and two CH<sub>2</sub> carbons. In addition, signals for triazolopyrimidine and two phenyl carbons were detected at their expected chemical shifts.

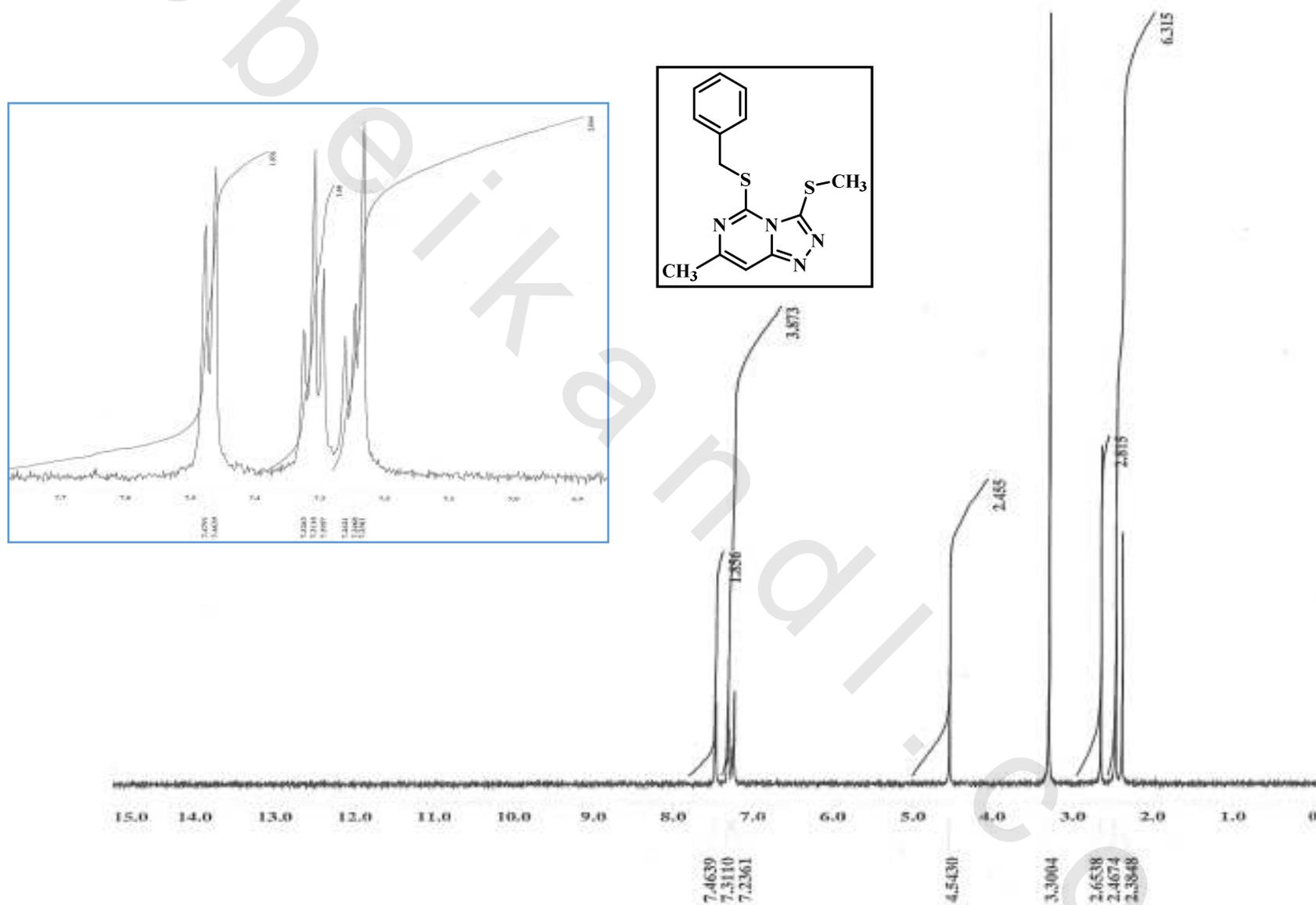
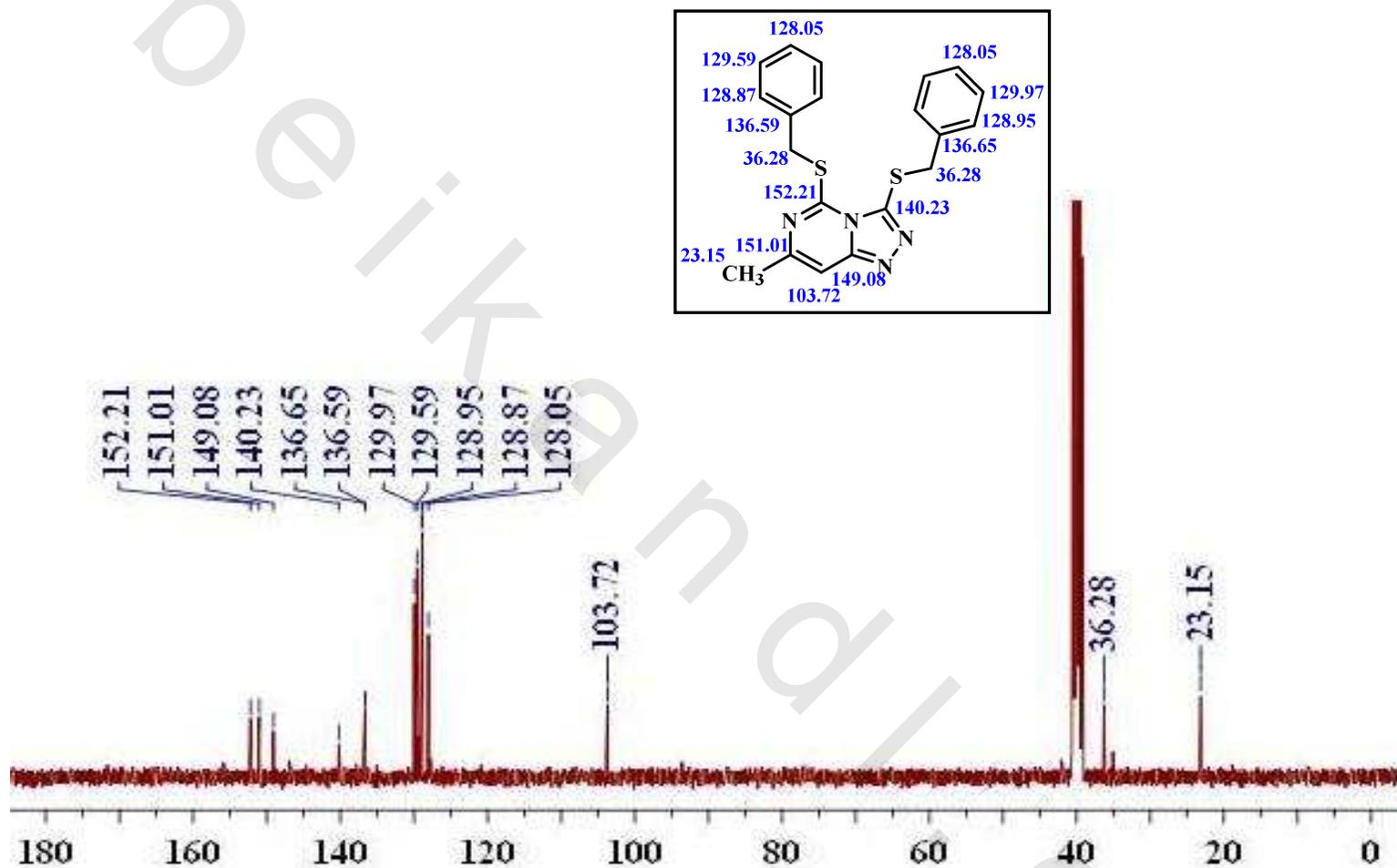
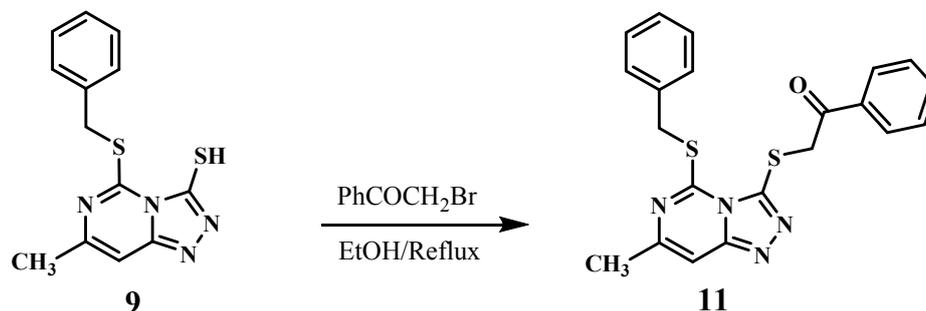


Figure 14: <sup>1</sup>H-NMR spectrum of compound 10a

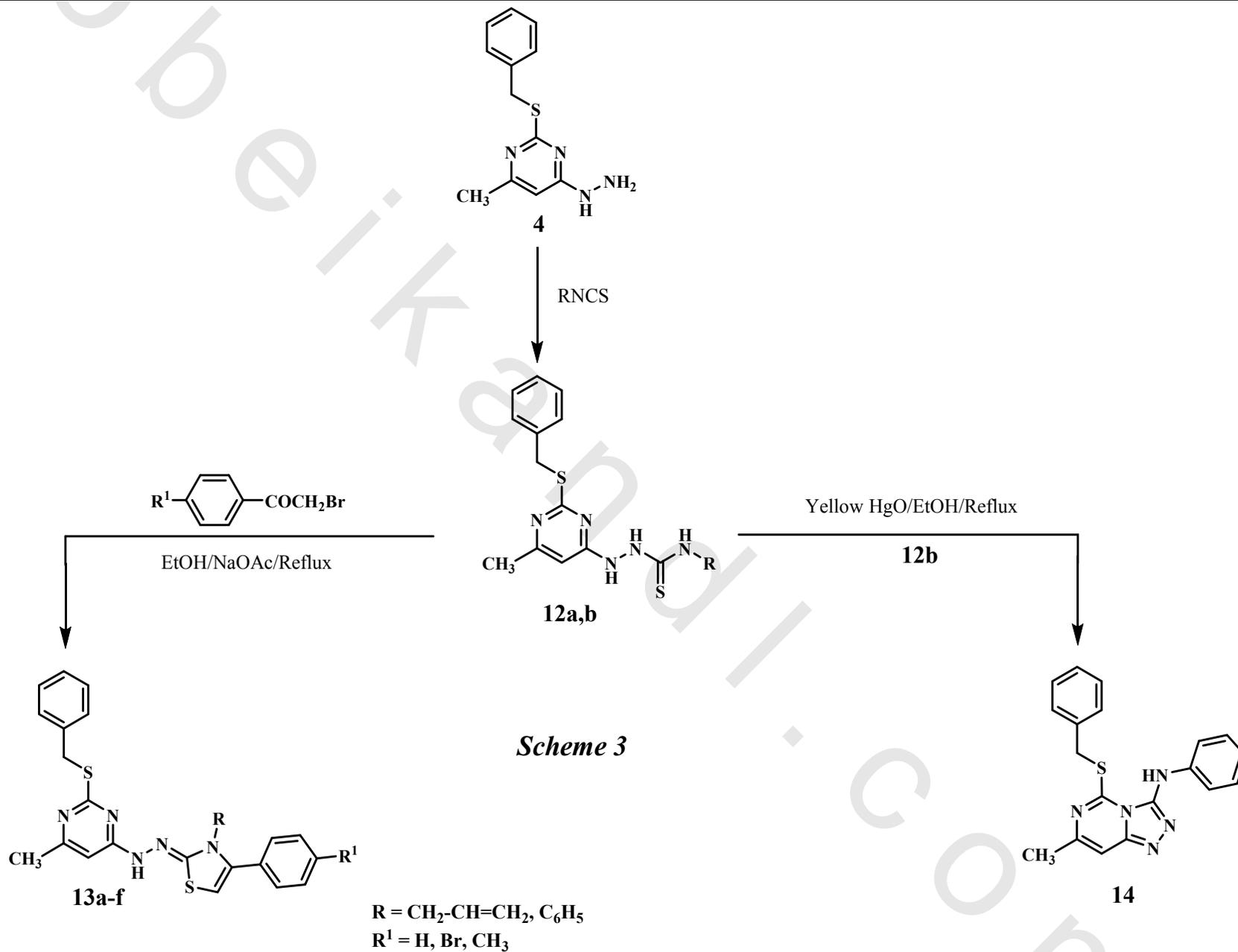
Figure 15:  $^{13}\text{C}$ -NMR spectrum of compound 10b

**2-{{5-(Benzylsulfanyl)-7-methyl-[1,2,4]triazolo[4,3-*c*]pyrimidin-3-yl}-sulfanyl}-1-phenylethanone, 11**

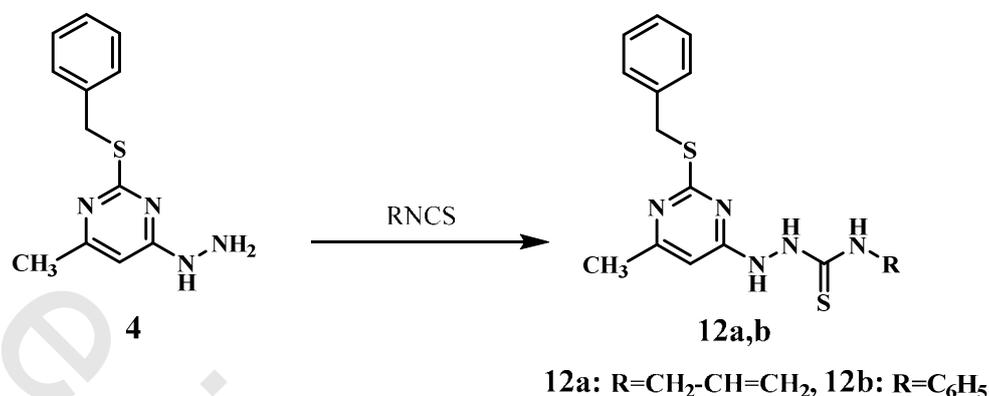
The title compound was prepared by following the reaction conditions described for the synthesis of analogous compounds<sup>(128)</sup> by refluxing **9** with phenacyl bromide in absolute ethanol.

**IR** spectrum showed stretching absorption bands characteristic for C=O, C=N and C-S-C functions at their expected frequencies.

**<sup>1</sup>H-NMR** spectrum lacked the downfield D<sub>2</sub>O-exchangeable signal assigned for SH proton present in the precursor while showed three upfield signals assigned for CH<sub>3</sub> and the two CH<sub>2</sub> protons. In addition, signals for other protons were identified at their expected chemical shifts.



## Scheme 3

2-[2-(Benzylsulfanyl)-6-methylpyrimidin-4-yl]-*N*-allyl (or phenyl) hydrazine-1-carbothioamides, **12a,b**

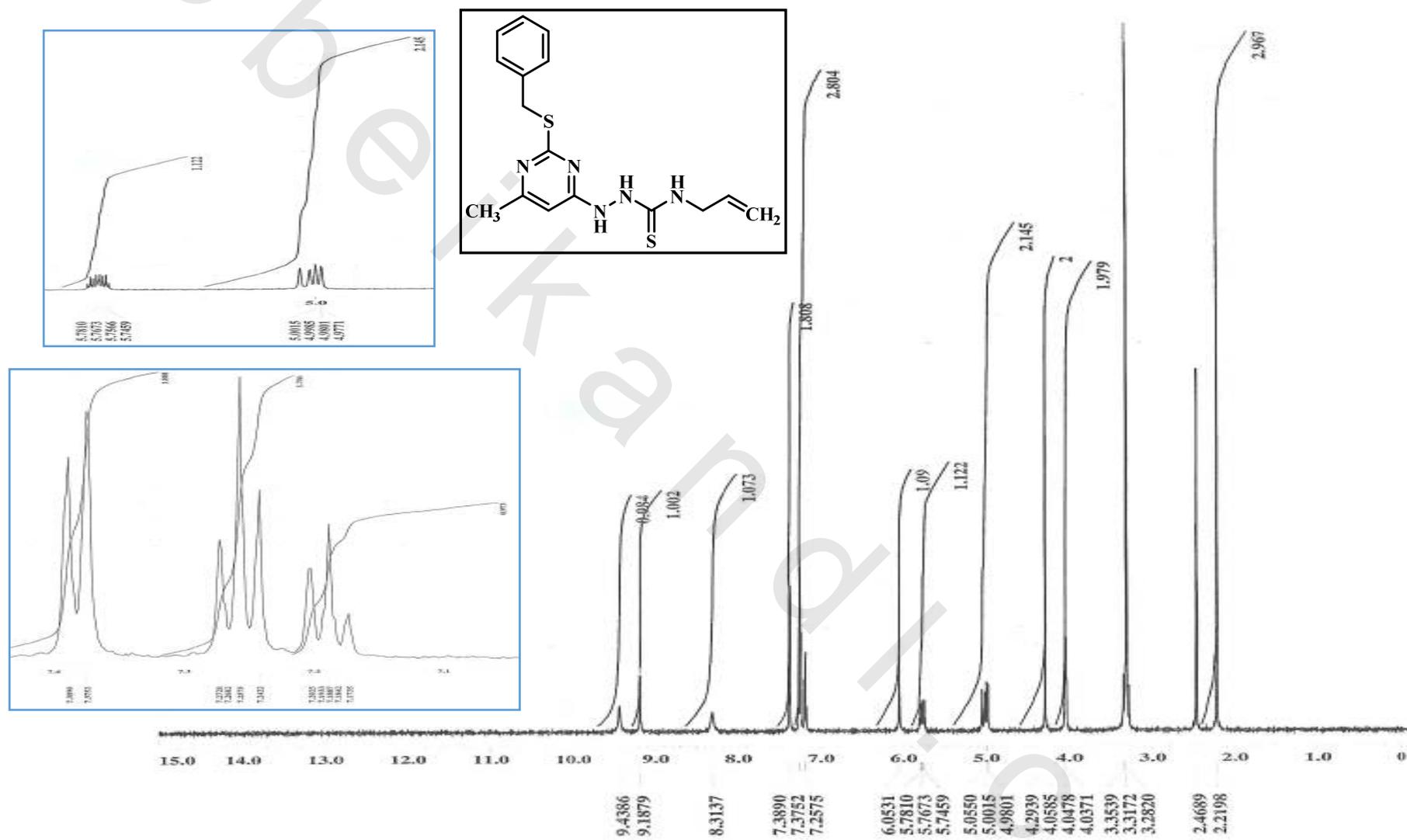
It has been reported that hydrazine derivatives react readily with substituted isothiocyanates under neutral<sup>(140-142)</sup> or basic<sup>(143,144)</sup> conditions either at room temperature<sup>(144)</sup> or under reflux.<sup>(140,141)</sup>

In the present investigation, the title compounds **12a,b** were prepared by applying the reaction conditions described for the synthesis of analogous compounds<sup>(142)</sup> by stirring a mixture of the hydrazino derivative **4** with the appropriate isothiocyanate in ethanol at room temperature.

**IR** spectra of compounds **12a,b** showed stretching absorption bands characteristic for N-C=S function, in addition to stretching absorption bands characteristic for NH, C=N and C-S-C groups.

**<sup>1</sup>H-NMR** spectra of compounds **12a,b** showed 3 downfield D<sub>2</sub>O-exchangeable signals assigned for NHHCSNH protons. Signals for other protons were identified at their expected chemical shifts. In addition, <sup>1</sup>H-NMR spectrum for **12a** (Figure 16) showed signals corresponding to the allyl protons.

**<sup>13</sup>C-NMR** spectrum of compound **12a** (Figure 17) revealed signals characteristic for CH<sub>3</sub> and allyl carbons. In addition, signals for pyrimidine and benzyl carbons were detected at their expected chemical shifts.

Figure 16: <sup>1</sup>H-NMR spectrum of compound 12a

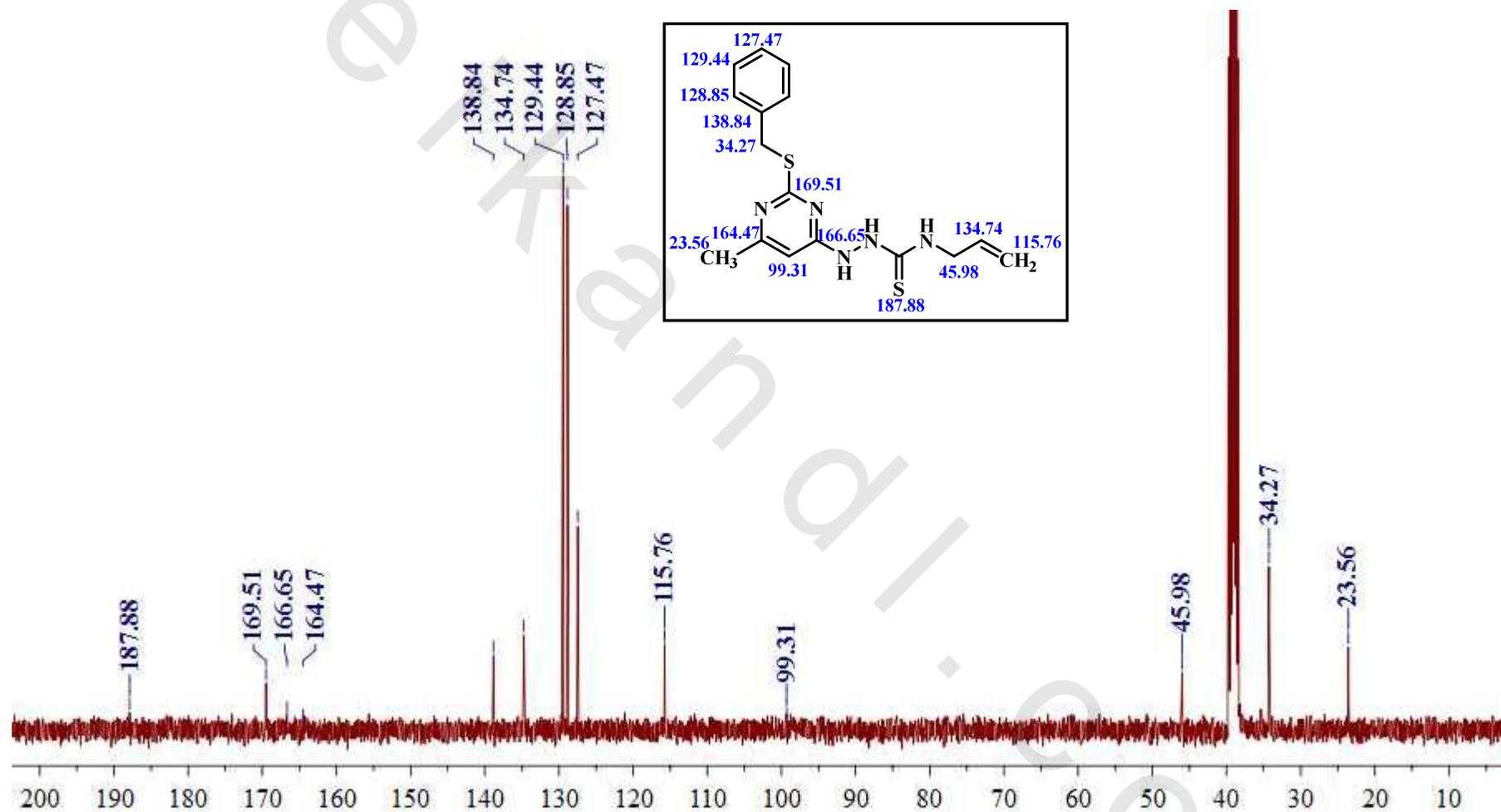
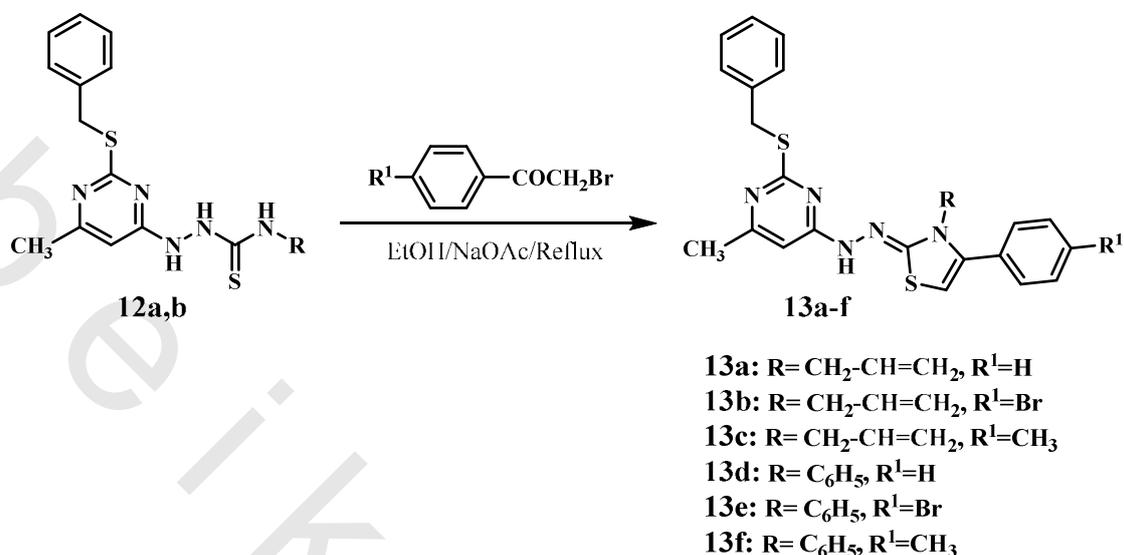


Figure 17:  $^{13}\text{C}$ -NMR spectrum of compound 12a

#### 4-(4-Substituted phenyl)-2-{2-[2-(benzylsulfanyl)-6-methylpyrimidin-4-yl]hydrazono}-3-allyl (or phenyl)-2,3-dihydrothiazoles, **13a-f**



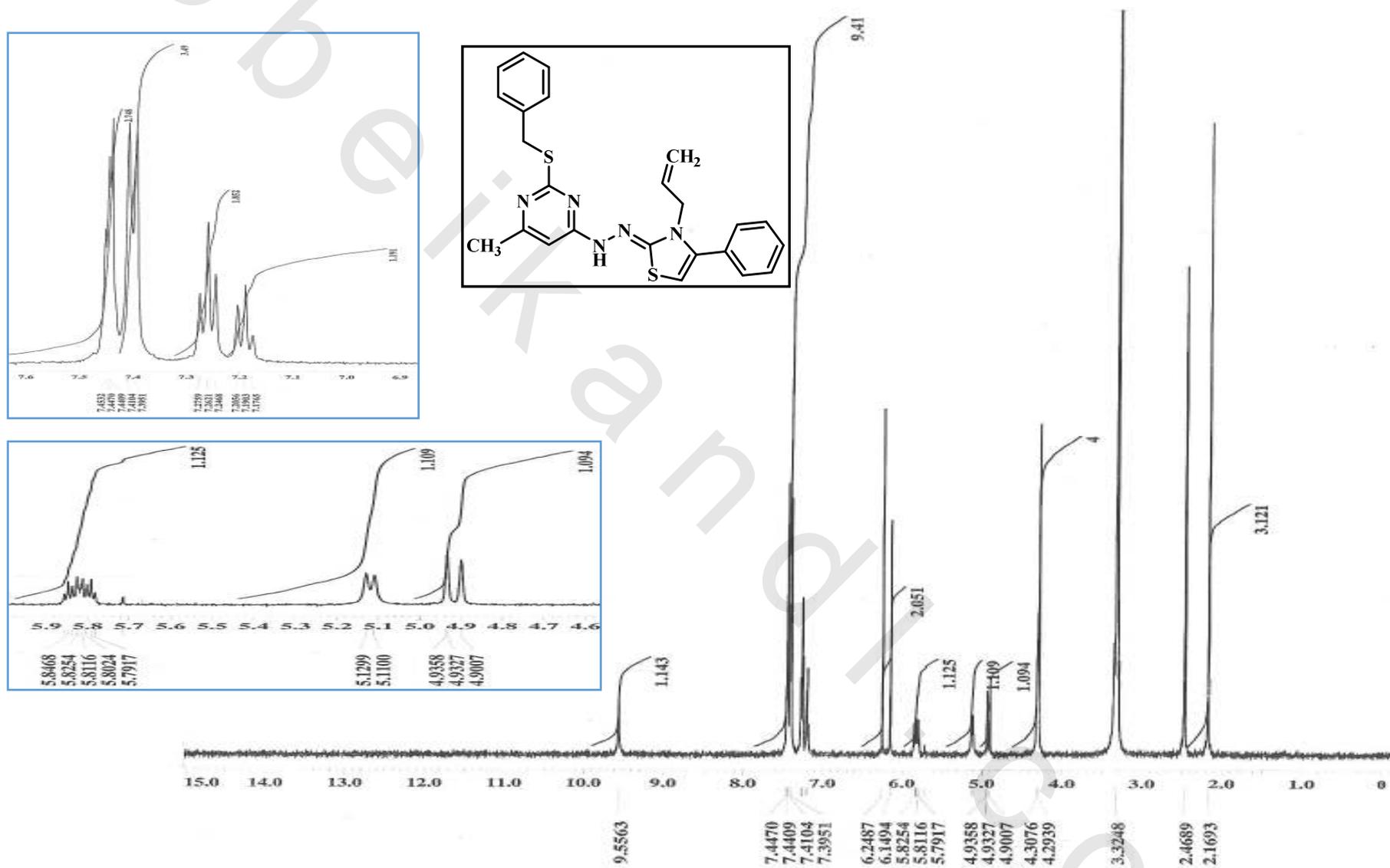
Thiazoline derivatives were reported to be prepared by cyclocondensation of thioureas,<sup>(145)</sup> thiosemicarbazides<sup>(146,147)</sup> or thiosemicarbazones<sup>(148,149)</sup> with phenacyl bromides.

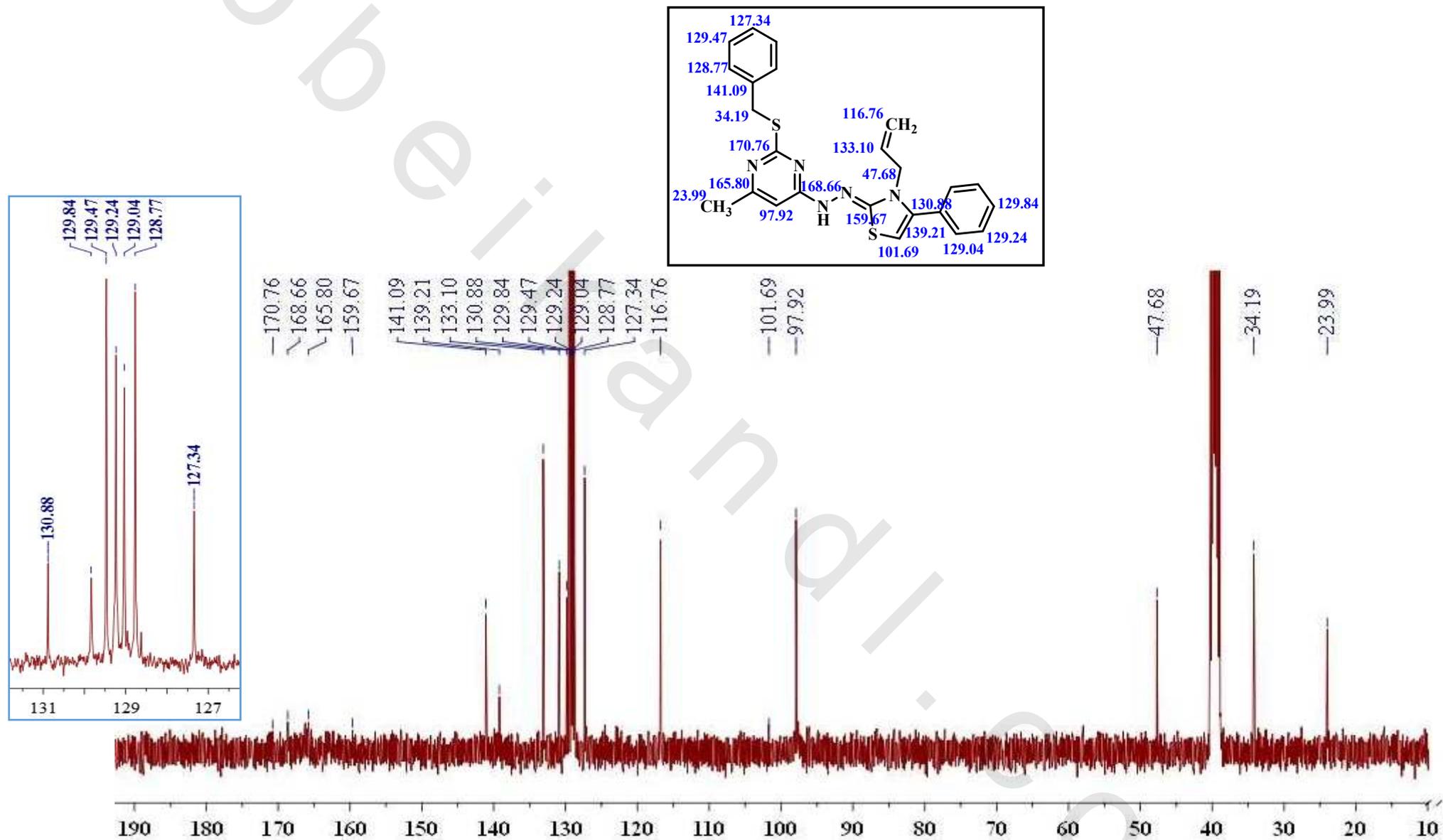
In the present study, the title compounds **13a-f** were prepared following the reaction conditions described for the synthesis of related compounds<sup>(150)</sup> by refluxing a mixture of the appropriate thiosemicarbazide and the selected 4-substituted phenacyl bromide in presence of anhydrous sodium acetate in absolute ethanol.

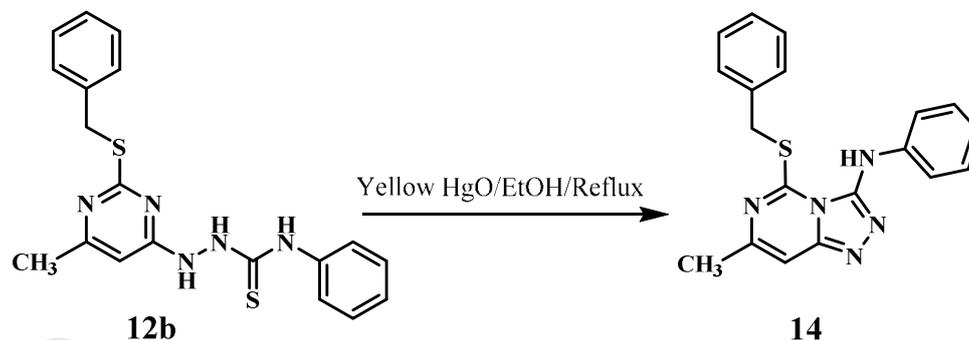
**IR** spectra of compounds **13a-f** showed stretching absorption bands characteristic for NH, C=N and C-S-C functions.

**<sup>1</sup>H-NMR** spectra of compounds **13a-f** lacked the two D<sub>2</sub>O-exchangeable signals assigned for NHCSNH protons present in their precursors while revealed the downfield signal assigned for thiazole C<sub>5</sub>-H proton. Signals assigned for aromatic, CH<sub>3</sub> and CH<sub>2</sub> protons were detected at their expected chemical shifts. In addition, <sup>1</sup>H-NMR spectra for **13a-c** showed signals corresponding to the allyl protons. The <sup>1</sup>H-NMR spectrum of compound **13a** is shown in figure 18.

**<sup>13</sup>C-NMR** spectrum of compound **13a** (Figure 19) showed signals assigned for thiazole carbons. Moreover, signals assigned for CH<sub>3</sub>, CH<sub>2</sub> and allyl carbons were detected at their expected chemical shifts. Pyrimidine and two phenyl carbons were also detected at their expected chemical shifts.

Figure 18: <sup>1</sup>H-NMR spectrum of compound 13a

Figure 19:  $^{13}\text{C}$ -NMR spectrum of compound 13a

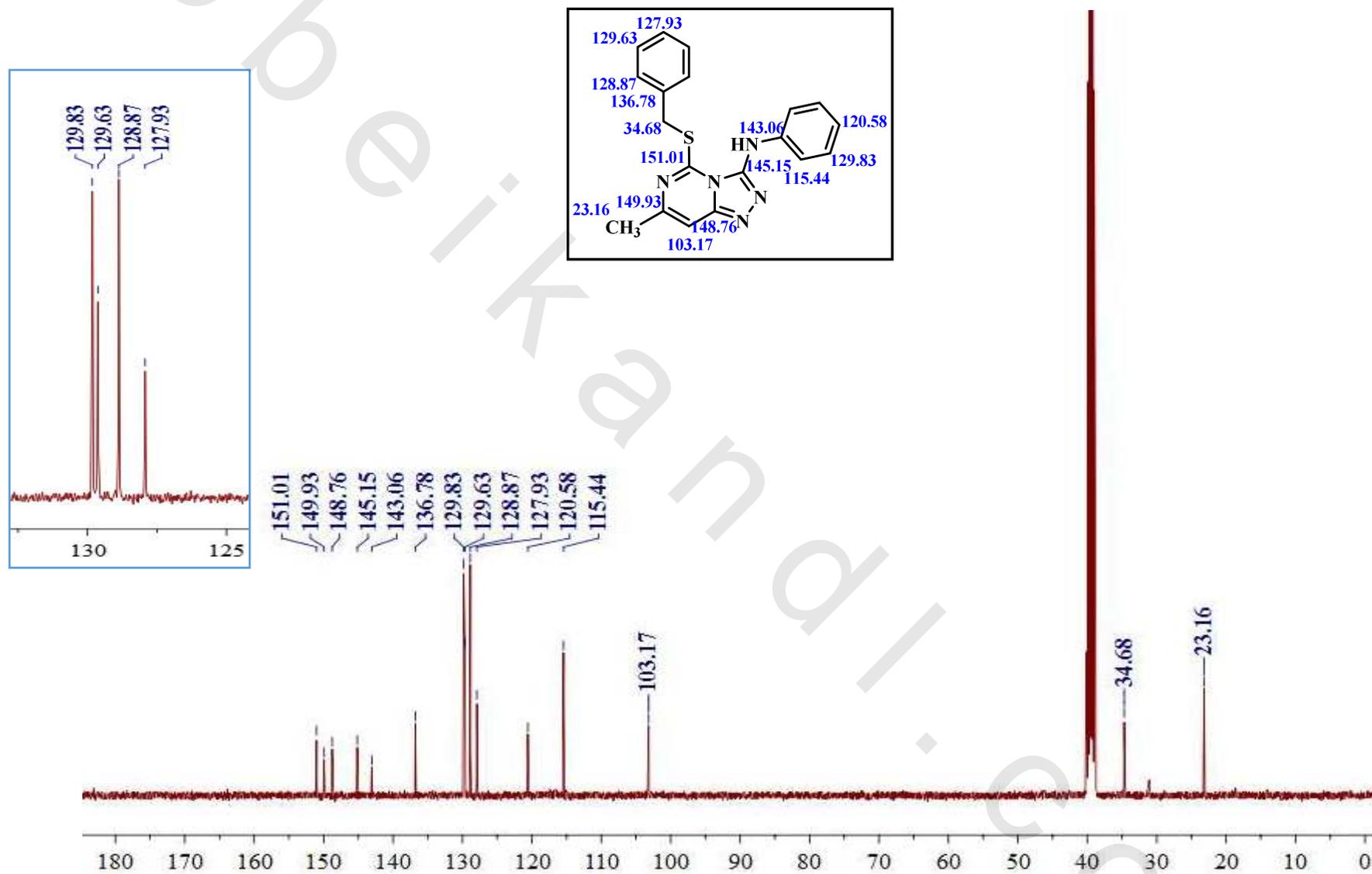
**5-(Benzylsulfanyl)-7-methyl-N-phenyl-[1,2,4]triazolo[4,3-c]pyrimidin-3-amine, 14**

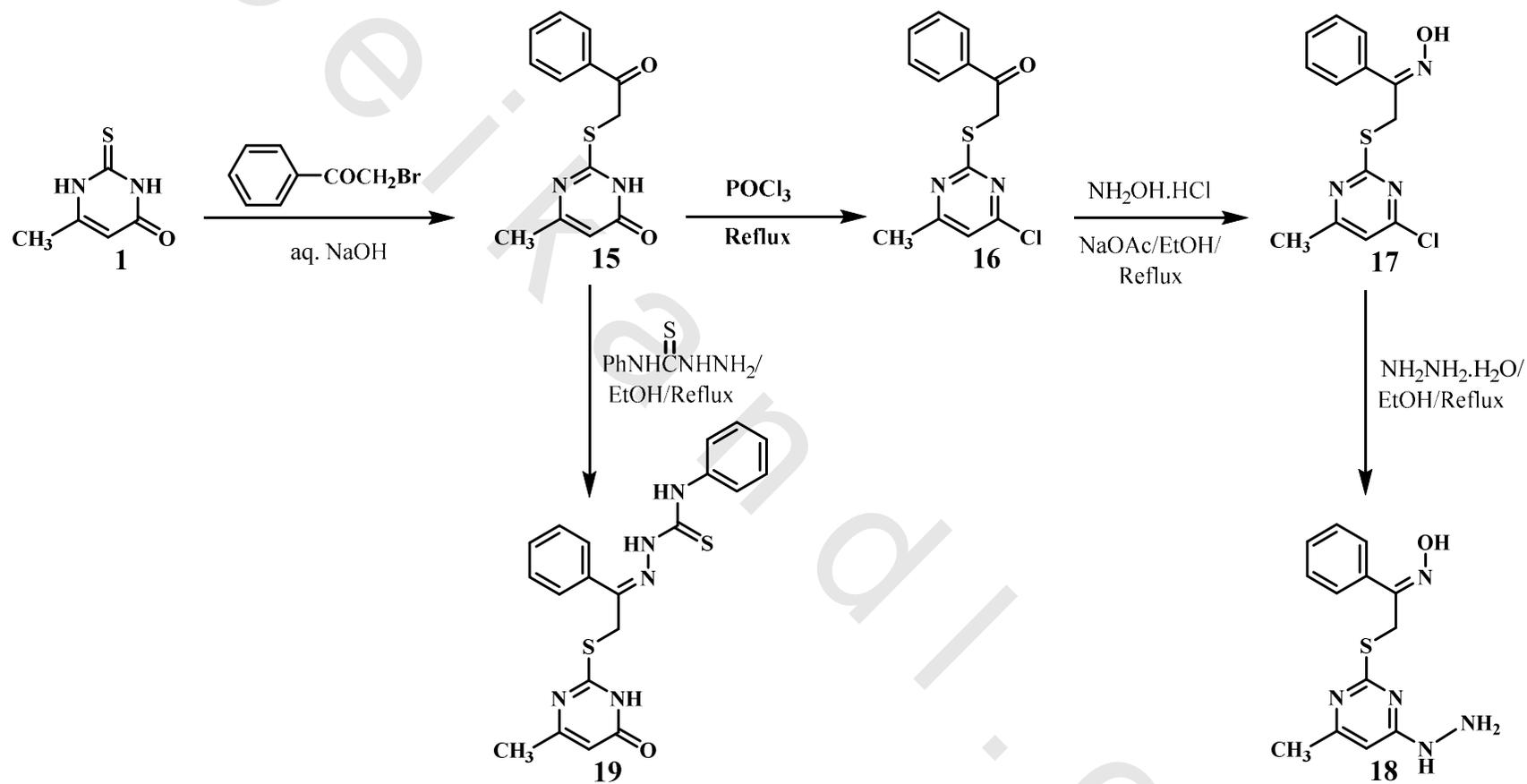
In accordance to the reported reaction conditions applied for the synthesis of analogous derivatives,<sup>(151)</sup> the title compound was prepared by reacting the thiosemicarbazide **12b** with freshly prepared yellow mercuric oxide in absolute ethanol.

**IR** spectrum showed stretching absorption bands characteristic for NH, C=N and C-S-C functions.

**<sup>1</sup>H-NMR** spectrum lacked the two D<sub>2</sub>O-exchangeable signals assigned for NHNHCS protons present in the precursor. Signals assigned for CH<sub>3</sub>, CH<sub>2</sub> and aromatic protons were detected at their expected chemical shifts.

**<sup>13</sup>C-NMR** spectrum (Figure 20) showed signals assigned for the triazolopyrimidine carbons. In addition, signals for CH<sub>3</sub>, CH<sub>2</sub> and two phenyl carbons were detected at their expected chemical shifts.

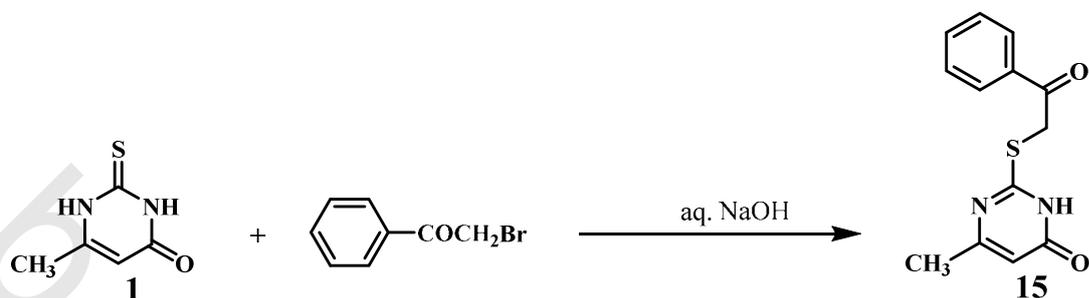
Figure 20:  $^{13}\text{C}$ -NMR spectrum of compound 14



Scheme 4

## Scheme 4

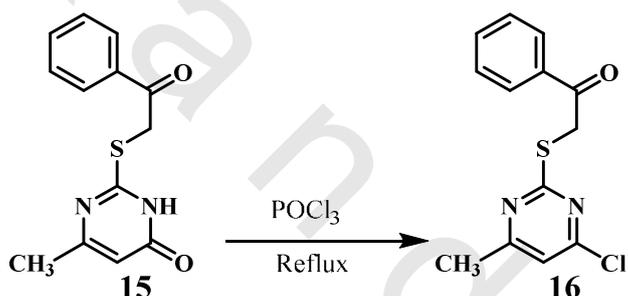
## 6-Methyl-2-[(2-oxo-2-phenylethyl)sulfanyl]pyrimidin-4(3H)-one, 15



The title compound was prepared by adapting the reported procedure<sup>(152)</sup> by stirring a mixture of the pyrimidinone **1** with phenacyl bromide in presence of aqueous sodium hydroxide at room temperature.

IR spectrum showed stretching absorption bands characteristics for NH, C=O, C=N and C-S-C groups at their expected frequencies.

## 2-[(4-Chloro-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone, 16

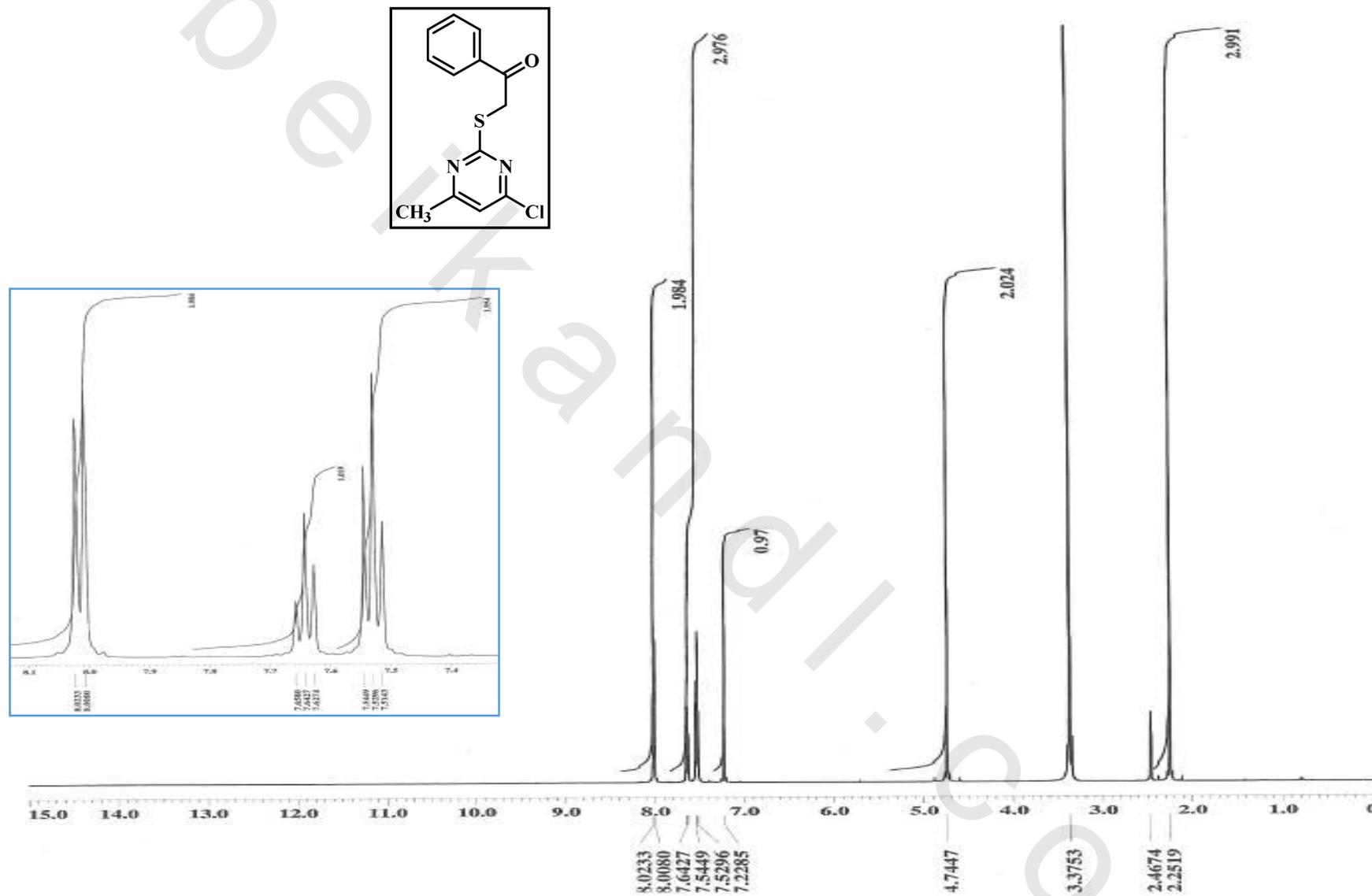


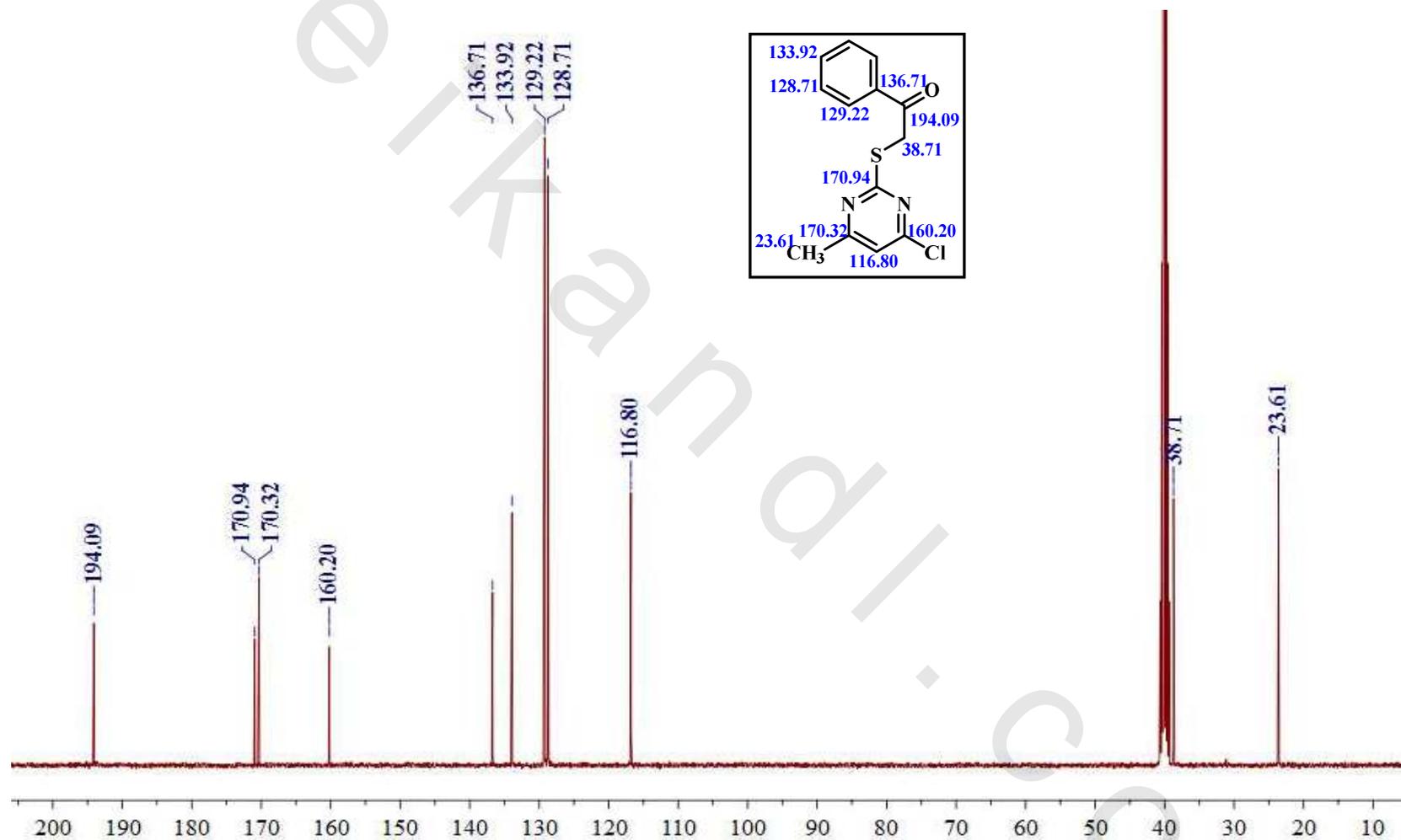
In accordance to the reported reaction conditions adopted for the synthesis of related derivatives,<sup>(109)</sup> the title compound was prepared by heating under reflux a mixture of compound **15** and phosphorous oxychloride. The reaction mixture was cooled to room temperature then poured over crushed ice.

IR spectrum showed stretching absorption bands characteristic for C=O, C=N and C-S-C functions at their expected frequencies.

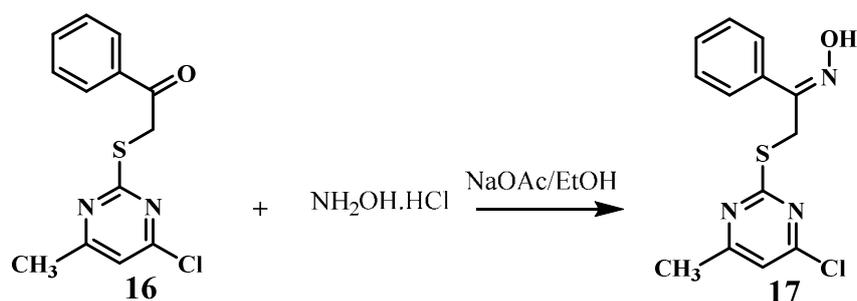
<sup>1</sup>H-NMR spectrum (Figure 21) revealed signals assigned for CH<sub>3</sub>, CH<sub>2</sub> and aromatic protons at their expected chemical shifts.

<sup>13</sup>C-NMR spectrum (Figure 22) showed signals characteristic for CH<sub>3</sub>, CH<sub>2</sub> and C=O carbons. In addition, signals for pyrimidine and phenyl carbons were detected at their expected chemical shifts.

Figure 21:  $^1\text{H-NMR}$  spectrum of compound 16

Figure 22:  $^{13}\text{C}$ -NMR spectrum of compound 16

## 2-[4-Chloro-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone oxime, 17



Several methods were reported for ketoxime formation. The classic method is based on the reaction of ketones with hydroxylamine hydrochloride in the presence of aqueous NaOH,<sup>(153)</sup> NaOAc–aqueous *n*-PrOH,<sup>(154)</sup> NaOAc–aqueous ethanol<sup>(155)</sup> or aqueous Na<sub>2</sub>CO<sub>3</sub>.<sup>(156)</sup>

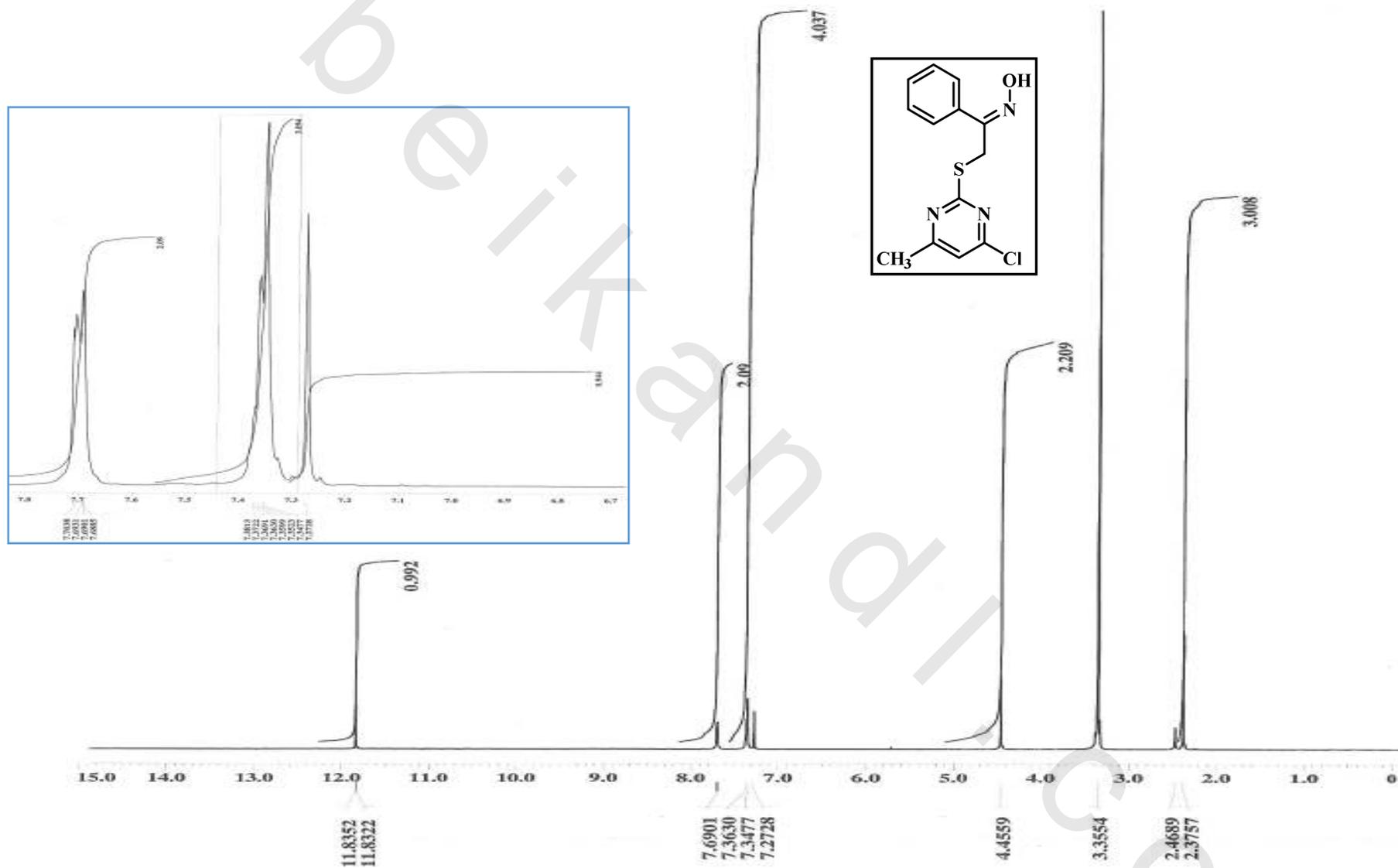
Saikia *et al.*<sup>(157)</sup> has reported a new method for oxime synthesis based on grinding ketones with NH<sub>2</sub>OH.HCl under solvent-free condition in presence of Bi<sub>2</sub>O<sub>3</sub> as catalyst at room temperature.

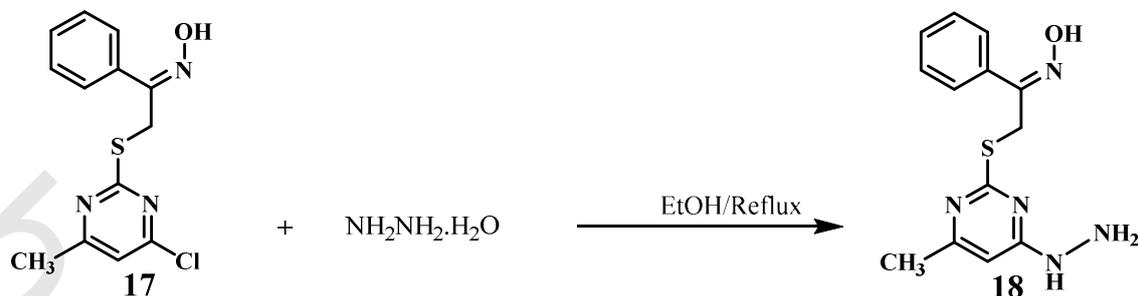
In the present study, the title compound was prepared by adopting the reaction conditions described for the synthesis of similar compounds<sup>(155)</sup> by refluxing the ketone **16** and NH<sub>2</sub>OH.HCl in presence of anhydrous NaOAc in absolute ethanol.

**IR** spectrum showed stretching absorption bands characteristic for OH group while lacked stretching absorption band characteristic for C=O function. In addition, stretching absorption bands corresponding to C=N and C-S-C groups were identified at their expected frequencies.

**<sup>1</sup>H-NMR** spectrum (Figure 23) revealed a downfield D<sub>2</sub>O-exchangeable signal, assigned for OH proton. In addition, signals assigned for CH<sub>3</sub>, CH<sub>2</sub> and aromatic protons were identified at their expected chemical shifts.

**<sup>13</sup>C-NMR** spectrum showed signals characteristic for C=N-OH and CH<sub>3</sub> carbons. In addition, signals for other carbons were detected at their expected chemical shifts.

Figure 23: <sup>1</sup>H-NMR spectrum of compound 17

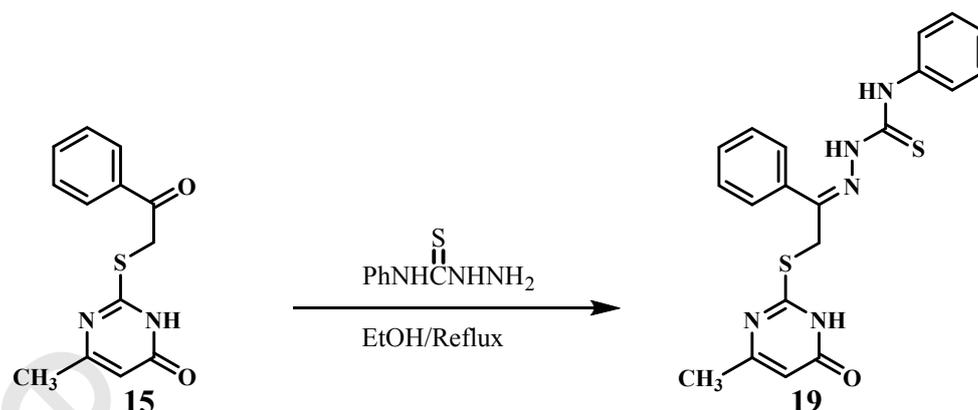
**2-[(4-Hydrazinyl-6-methylpyrimidin-2-yl)sulfanyl]-1-phenylethanone oxime, 18**

The title compound was prepared following the reaction conditions reported for the synthesis of analogous compounds<sup>(112)</sup> by heating under reflux a mixture of the oxime **17** and hydrazine hydrate 99% in absolute ethanol.

**IR** spectrum showed stretching absorption bands characteristic for NH and NH<sub>2</sub> functions besides the expected stretching absorption bands corresponding to OH, C=N and C-S-C functions.

**<sup>1</sup>H-NMR** spectrum showed three D<sub>2</sub>O-exchangeable signals, assigned for two shielded NH<sub>2</sub> protons, and two deshielded signals, assigned for NH and OH protons. In addition, signals assigned for aromatic, CH<sub>3</sub> and CH<sub>2</sub> protons were identified at their expected chemical shifts.

**HRMS** showed the molecular ion peak (M+1)<sup>+</sup> at *m/z* 290.051 corresponding to C<sub>13</sub>H<sub>16</sub>N<sub>5</sub>OS

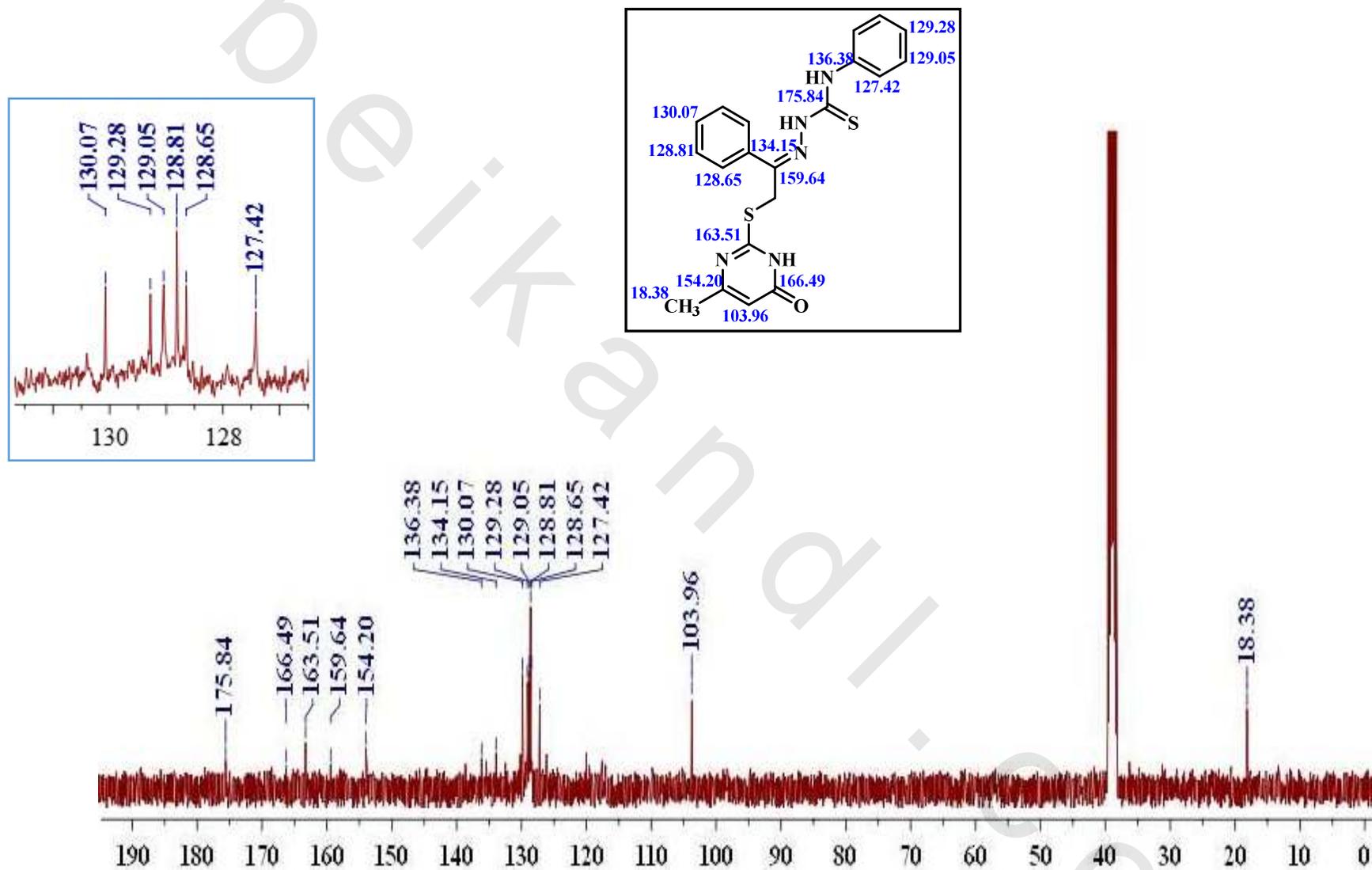
**2-{2-[(4-Methyl-6-oxo-1,6-dihydropyrimidin-2-yl)sulfanyl]-1-phenylethylidene}-N-phenylhydrazine-1-carbothioamide, 19**

This compound was prepared by applying the reaction conditions reported for the synthesis of related compounds<sup>(158)</sup> by heating under reflux a mixture of the ketone **15** and phenyl thiosemicarbazide in absolute ethanol.

**IR** spectrum showed stretching absorption bands characteristic for N-C=S function besides the expected stretching absorption bands corresponding to NH, C=O, C=N and C-S-C groups.

**<sup>1</sup>H-NMR** spectrum showed 3 downfield D<sub>2</sub>O-exchangeable signals assigned for NHCSNH besides pyrimidine NH protons. In addition, signals assigned for aromatic, CH<sub>3</sub> and CH<sub>2</sub> protons were identified at their expected chemical shifts.

**<sup>13</sup>C-NMR** spectrum (Figure 24) showed signals characteristic for CH<sub>3</sub>, C=O and C=S carbons. In addition, signals for other carbons were detected at their expected chemical shifts.

Figure 24:  $^{13}\text{C}$ -NMR spectrum of compound 19