

**Electronic Supplementary Information (ESI) for**  
**Synthesis, antimicrobial activity and molecular simulation of thiourea derivatives containing**  
**6-carboalkoxybenzo[d]thiazole and D-glucose moieties**

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### 1. General procedure for the synthesis of alkyl 2-aminobenzo[d]thiazole-6-carboxylates (2a-i)

2-Aminobenzo[d]thiazole-6-carboxylic esters (**2a-i**) were prepared from 4-aminobenzoic acid (**1a-i**) and appropriate alcohols by modifying literature synthetic procedure.[1, 2] To a solution of appropriate ester 4-aminobenzoates (**2a-i**, 0.1 mol) in glacial acetic acid (100 mL), ammonium thiocyanate (0.2 mol, 15.2 g) was added with stirring in ice bath. The reaction mixture was cooled to 5°C, and a solution of bromine (4.8 mL, 0.093 mol) in acetic acid (25 mL) was added dropwise with stirring. A yellow suspension was appeared. The reaction mixture was then stirred at room temperature for 30 min more. The yellow precipitates were filtered and dissolved in cold water (100 mL). The obtained solution was neutralized using 25% ammonia solution to pH 8. The product was filtered, washed by cold water, and crystallized from 96% ethanol to afford the titled 2-aminobenzo[d]thiazoles **3a-i** that were displayed as follows.

#### *Methyl 2-aminobenzo[d]thiazole-6-carboxylate (3a)*

Pale-yellow crystals from methyl *p*-aminobenzoate (**2a**, 0.1 mol, 15.1 g). Yield: 11.6 g (56%); M.p.: 192–193°C, ref. [3]:193°C.

#### *Ethyl 2-aminobenzo[d]thiazole-6-carboxylate (3b)*

Pale-yellow crystals from ethyl *p*-aminobenzoate (**2b**, 0.1 mol, 16.5 g). Yield: 11 g (50%); M.p.: 243–245°C, ref. [3]: 244–245°C.

#### *Propyl 2-aminobenzo[d]thiazole-6-carboxylate (3c)*

Pale-yellow crystals from *n*-propyl *p*-aminobenzoate (**2c**, 0.1 mol, 17.9 g). Yield: 17.5 g (74%); M.p.: 208–209°C, ref. [3]: 209°C.

#### *Isopropyl 2-aminobenzo[d]thiazole-6-carboxylate (3d)*

Pale-yellow crystals from isopropyl *p*-aminobenzoate (**2d**, 0.1 mol, 17.9 g). Yield: 16. g (68%); M.p.: 206–208°C, ref. [3]: 208°C.

#### *Butyl 2-aminobenzo[d]thiazole-6-carboxylate (3e)*

Pale-yellow crystals from *n*-butyl *p*-aminobenzoate (**2e**, 0.1 mol, 19.3 g). Yield: 16.5 g (66%); M.p.: 205–206°C, ref. [3]: 206°C.

#### *Isobutyl 2-aminobenzo[d]thiazole-6-carboxylate (3f)*

Pale-yellow crystals from isobutyl *p*-aminobenzoate (**2f**, 0.1 mol, 19.3 g). Yield: 17.0 g (68%); M.p.: 187–188°C.

#### *Pentyl 2-aminobenzo[d]thiazole-6-carboxylate (3g)*

Pale-yellow crystals from *n*-pentyl *p*-aminobenzoate (**2g**, 0.1 mol, 20.7 g). Yield: 19.0 g (72%); M.p.: 190–192°C.

*Isopentyl 2-aminobenzo[d]thiazole-6-carboxylate (3h)*

Pale-yellow crystals from isopentyl *p*-aminobenzoate (**2h**, 0.1 mol, 20.7 g). Yield: 18.5 g (70%); M.p.: 188–189°C.

*Octyl 2-aminobenzo[d]thiazole-6-carboxylate (3i)*

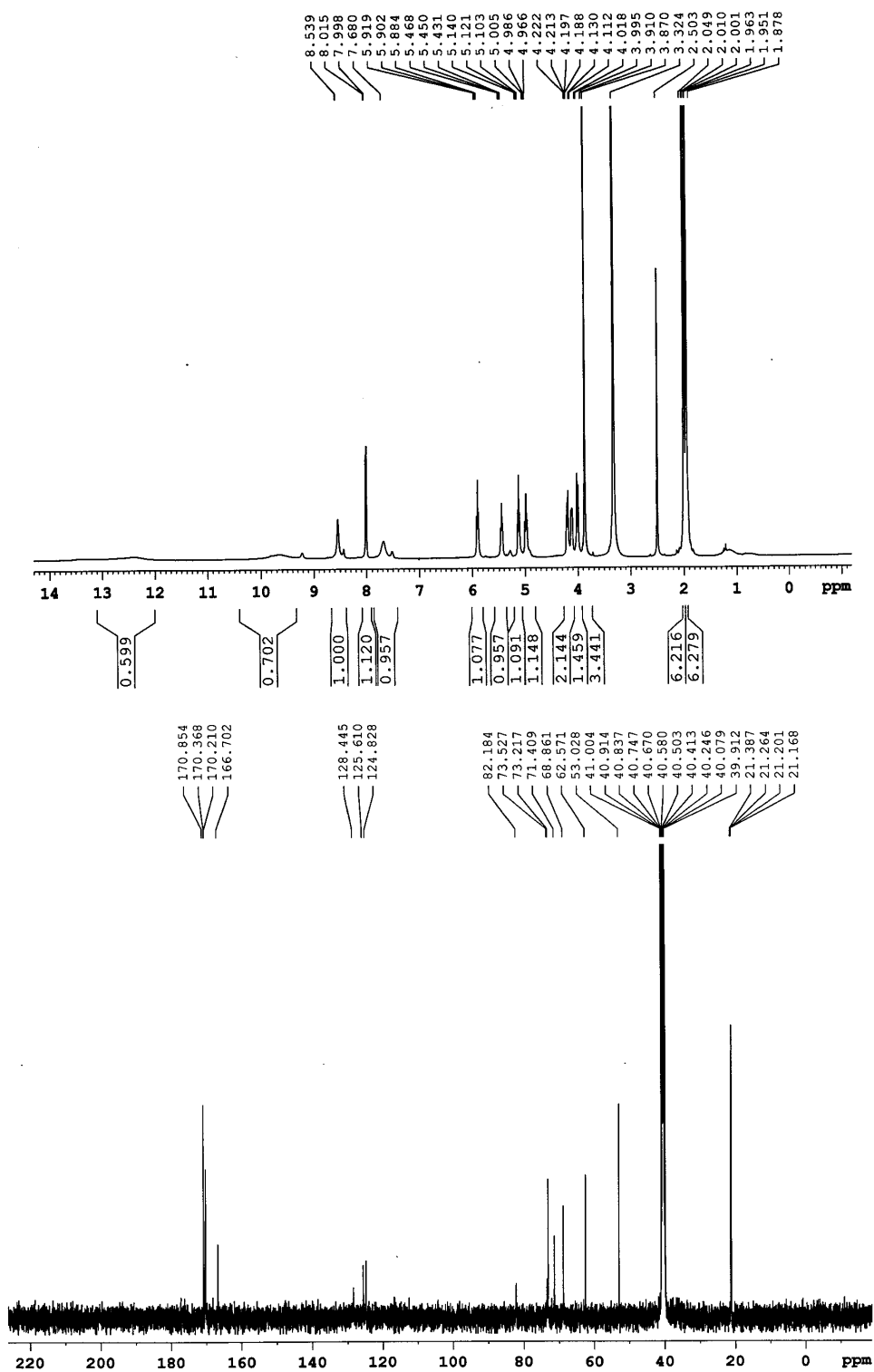
Pale-yellow crystals from octyl *p*-aminobenzoate (**2i**, 0.1 mol, 20.7 g). Yield: 15.9 g (52%); M.p.: 160–162°C.

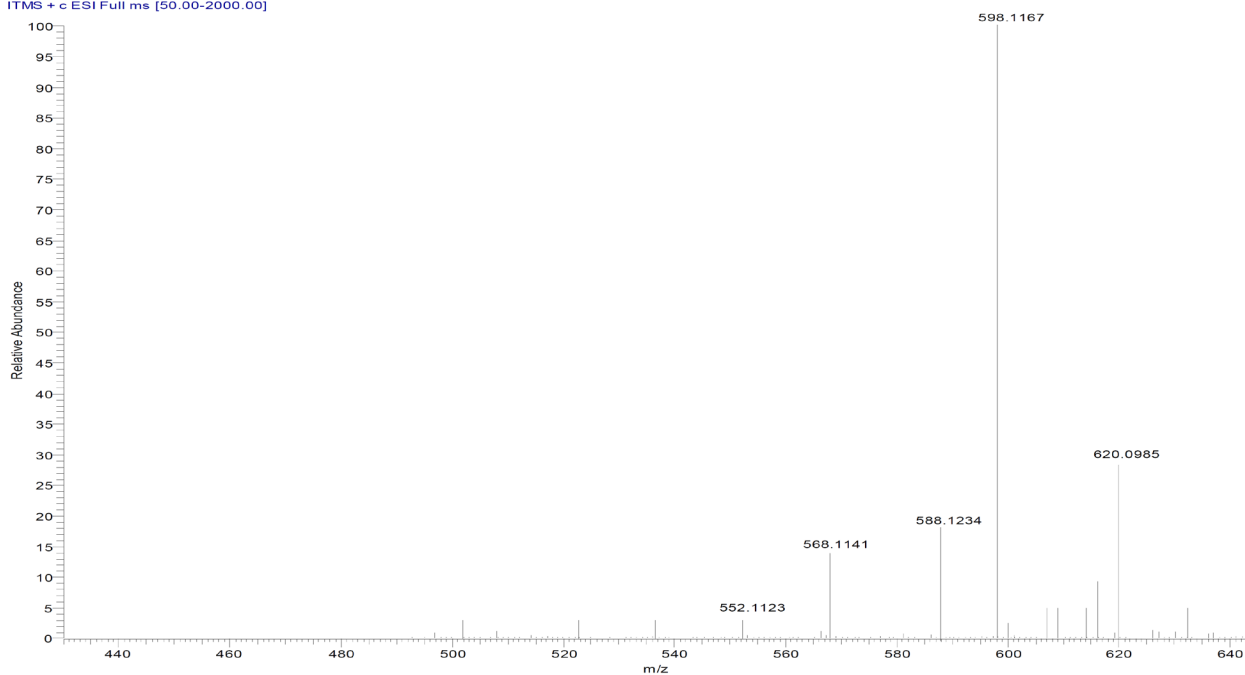
References

- [1] M. Durcik, Ž. Toplak, N. Zidar, J. Ilaš, A. Zega, D. Kikelj, L.P. Mašič, T. Tomašič, Efficient Synthesis of Hydroxy-Substituted 2-Aminobenzo[d]thiazole-6-carboxylic Acid Derivatives as New Building Blocks in Drug Discovery, *ACS Omega* 5(14) (2020) 8305-8311.
- [2] R.V. Patel, S.W. Park, Catalytic N-formylation for synthesis of 6-substituted-2-benzothiazolylimino-5-piperazinyl-4-thiazolidinone antimicrobial agents, *Res. Chem. Intermed.* 41(8) (2015) 5599-5609.
- [3] S.S. Naim, S.K. Singh, S. Sharma, *ChemInform Abstract: Studies in Antiparasitic Agents. Part 17. Synthesis of 2-Acylamino-6- substituted-benzothiazoles as Potential Anthelmintic Agents*, *ChemInform* 22(31) (1991).

## 2. NMR and MS of thioureas 4a-i

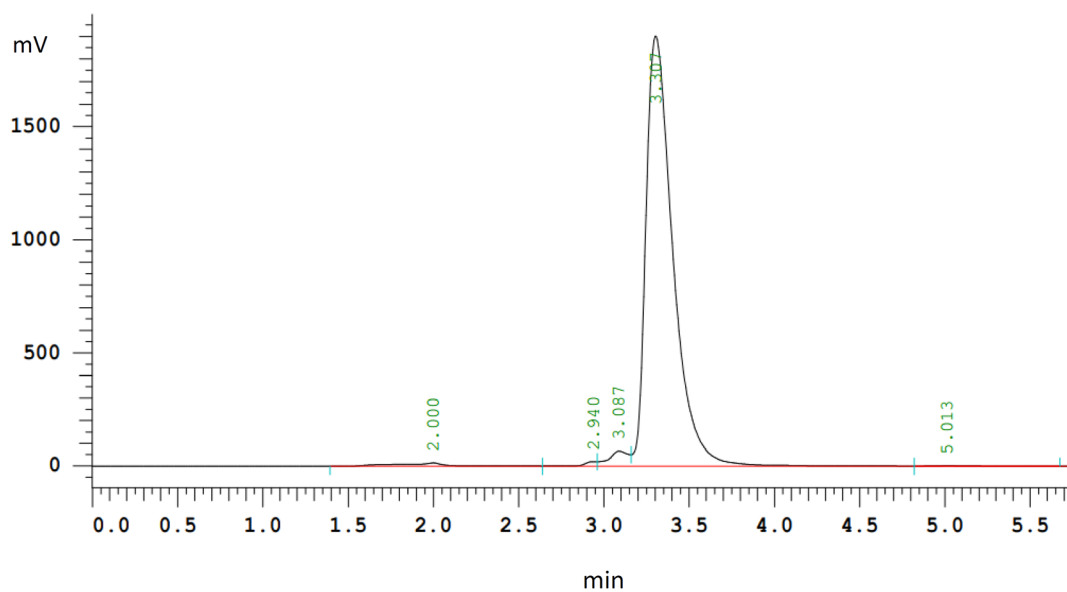
*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carbomethoxybenzo[d]thiazole-2-yl)thiourea*  
(4a)



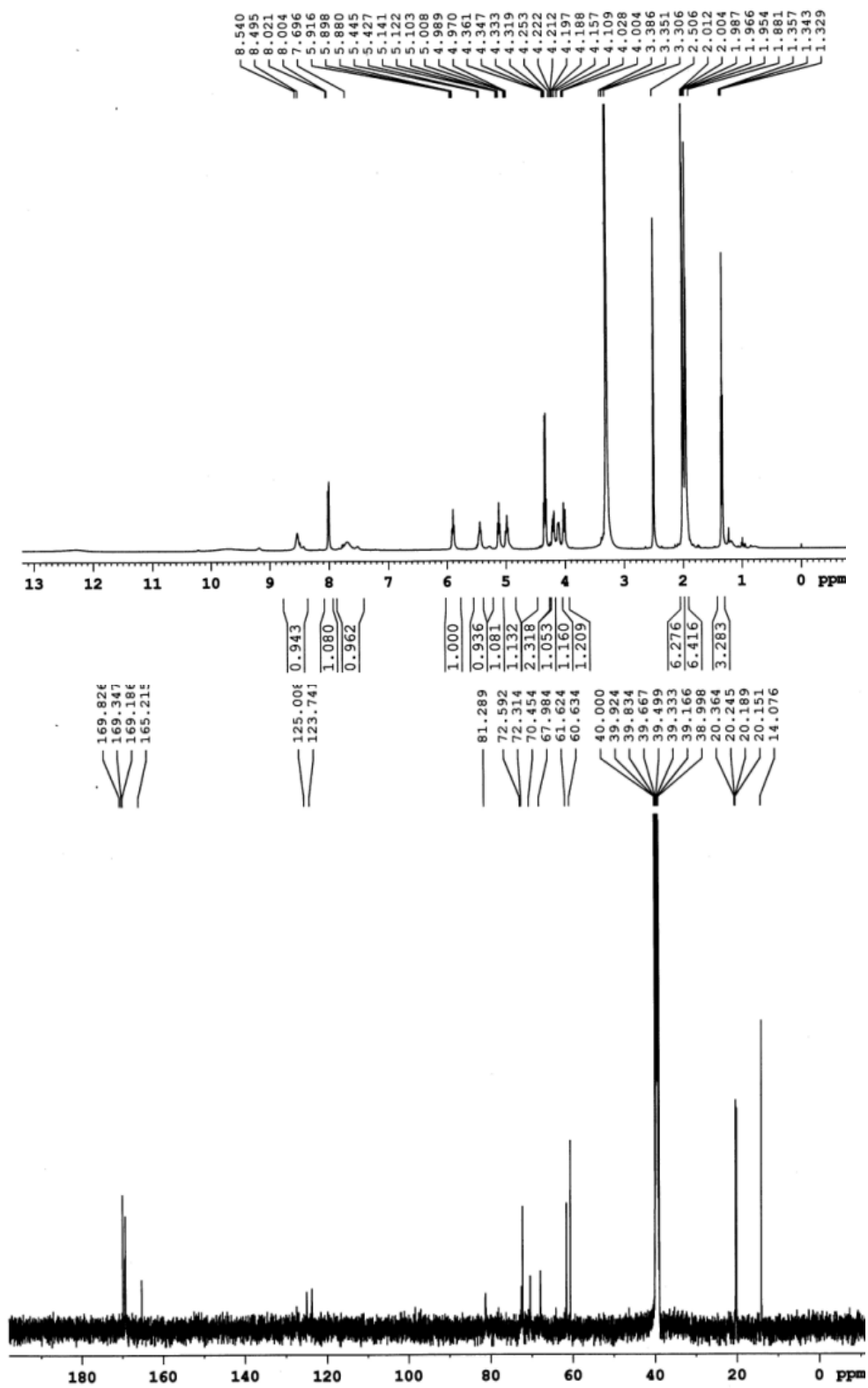


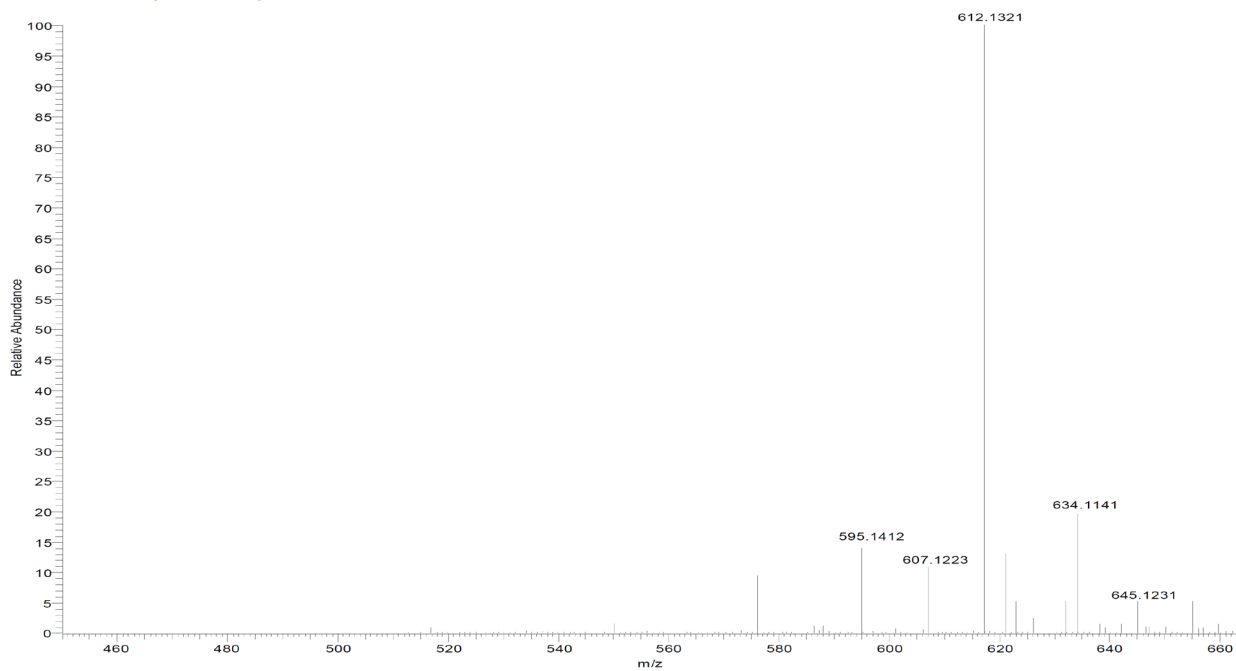
## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	2.000	302963	1.384	BV
2	2.940	102967	0.470	VV
3	3.087	520051	2.421	VV
4	3.307	20931637	95.623	VV
5	5.013	22165	0.101	TBB
		21889783	100.00	



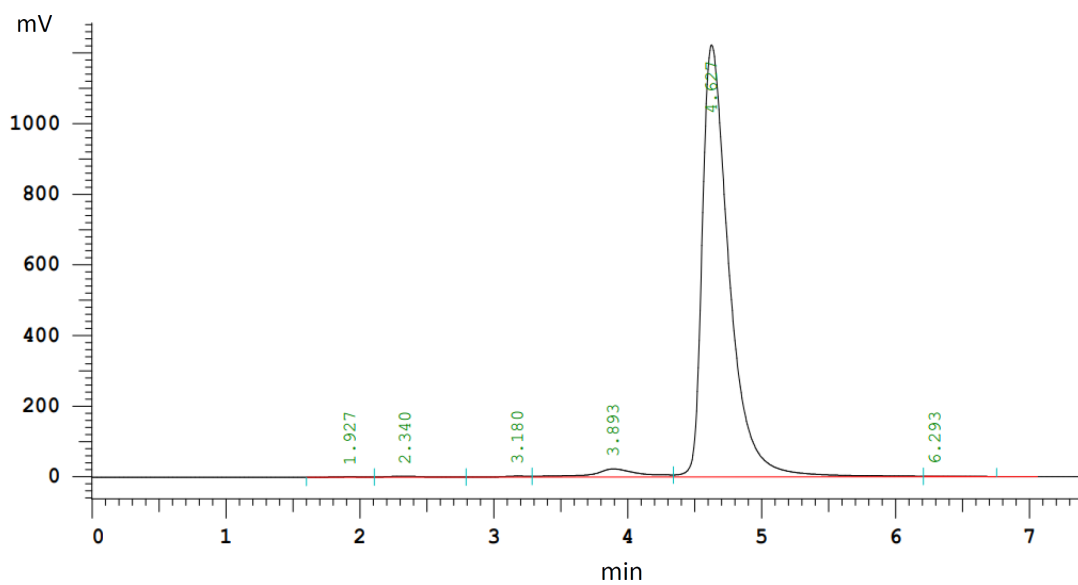
*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carboethoxybenzo[d]thiazole-2-yl)thiourea*  
(4b)



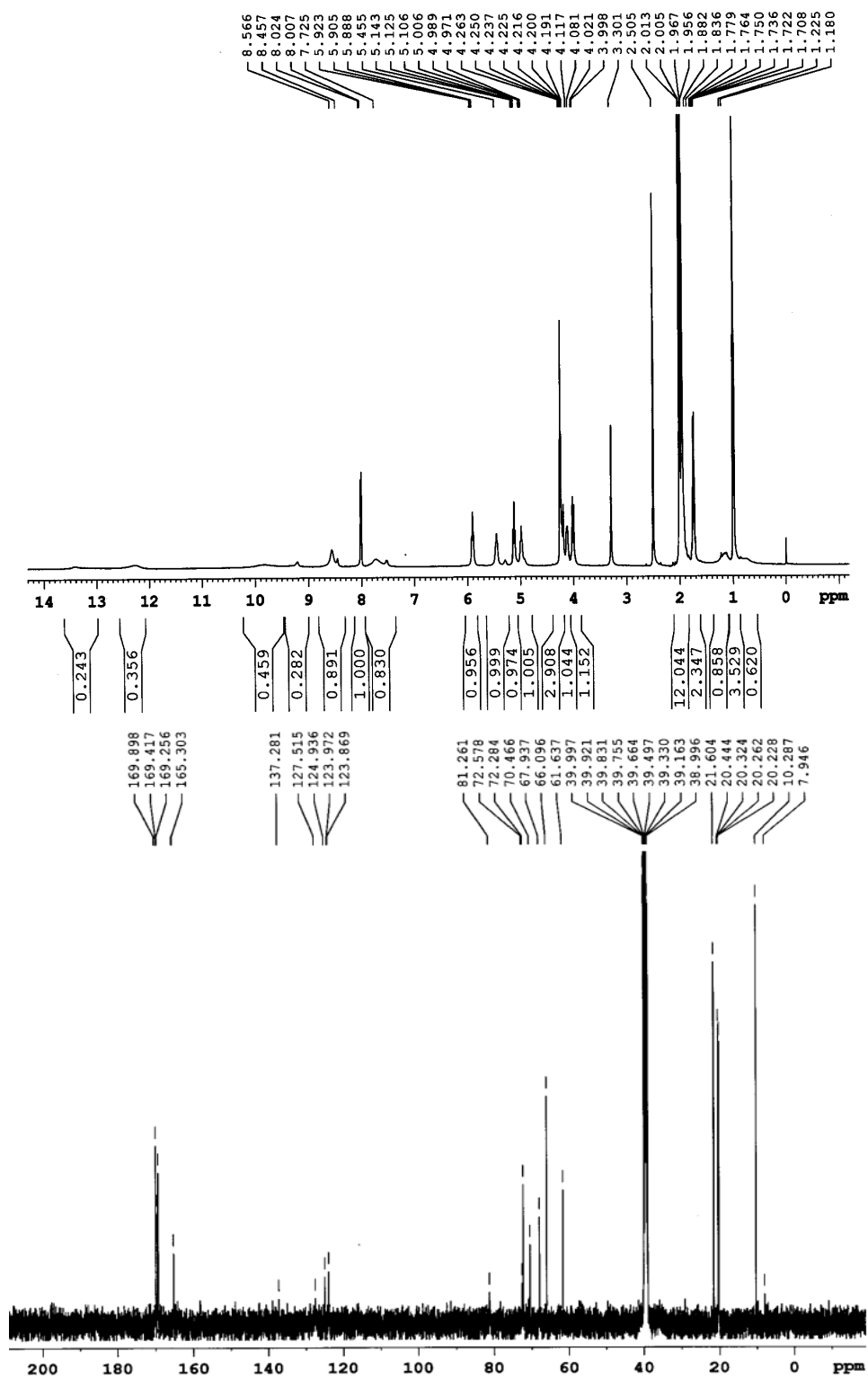


## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	1.927	25856	0.145	BV
2	2.340	56014	0.314	VV
3	3.180	41491	0.232	VV
4	3.893	564929	3.163	VV
5	4.627	17168353	96.126	VV
6	6.293	3631	0.020	TBB
		17860274	100.00	

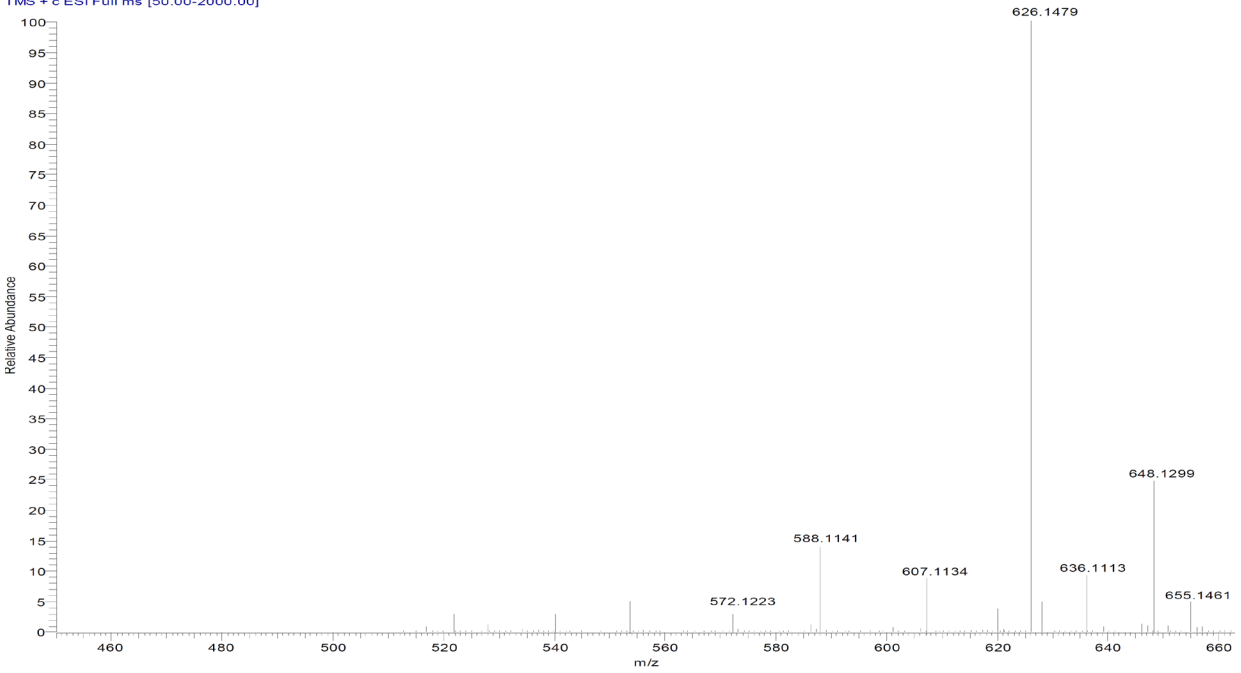


1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carbopropoxybenzo[d]thiazole-2-yl)thiourea  
(4c)



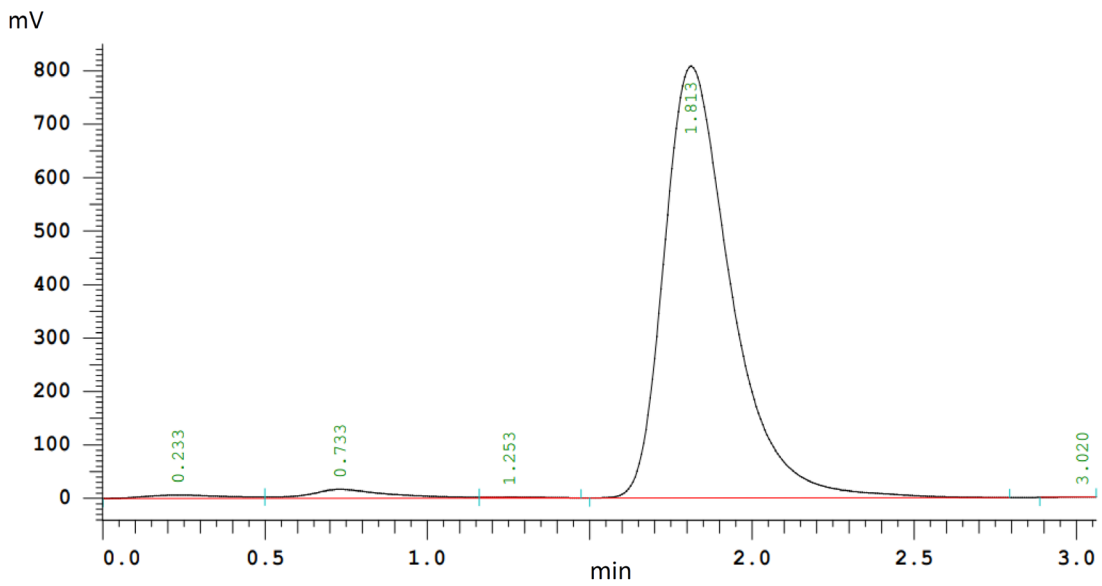


200509150922 #10 (1).4.02 (V.V) NELIOPES D.  
TMS + c ESI Full ms (50.00-2000.00)

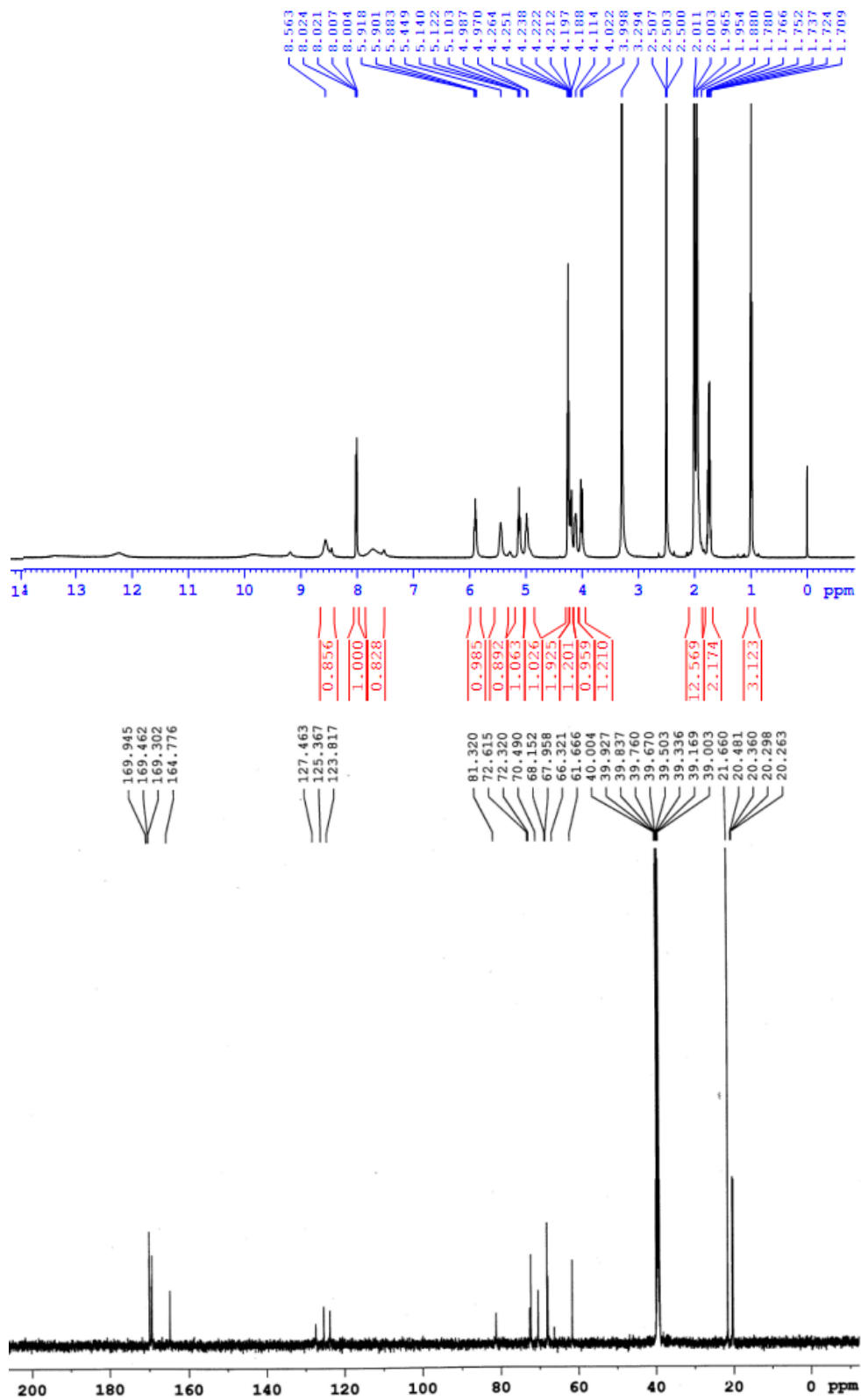


## HPLC

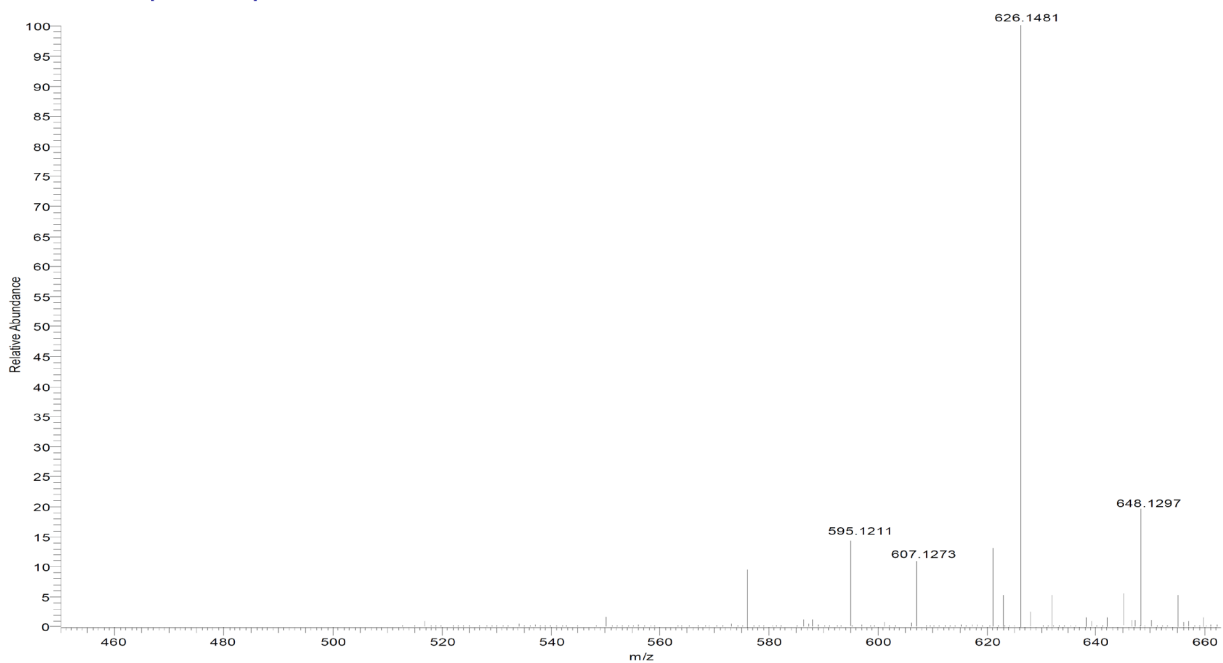
No.	RT	Area (%)	Concentration (%)	BC
1	0.233	117269	0.979	BV
2	0.733	310345	2.590	VV
3	1.253	6941	0.058	VB
4	1.813	11543559	96.355	TBB
5	3.020	2091	0.017	BB
		11980205	100.00	



*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carboisopropoxybenzo[d]thiazole-2-yl)thiourea (4d)*

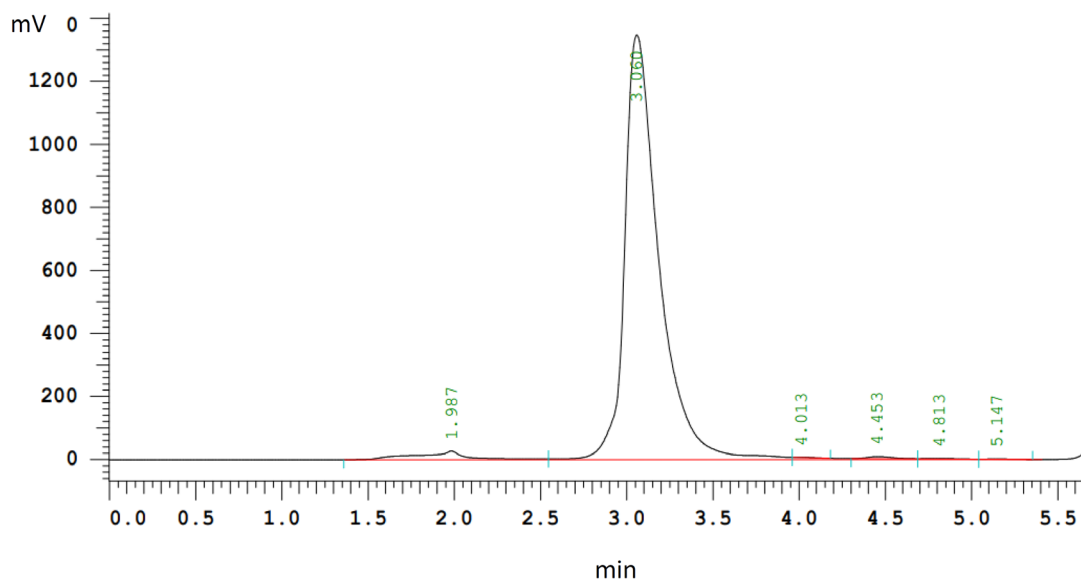


TTMS + c ESI Full ms [50.00-2000.00]

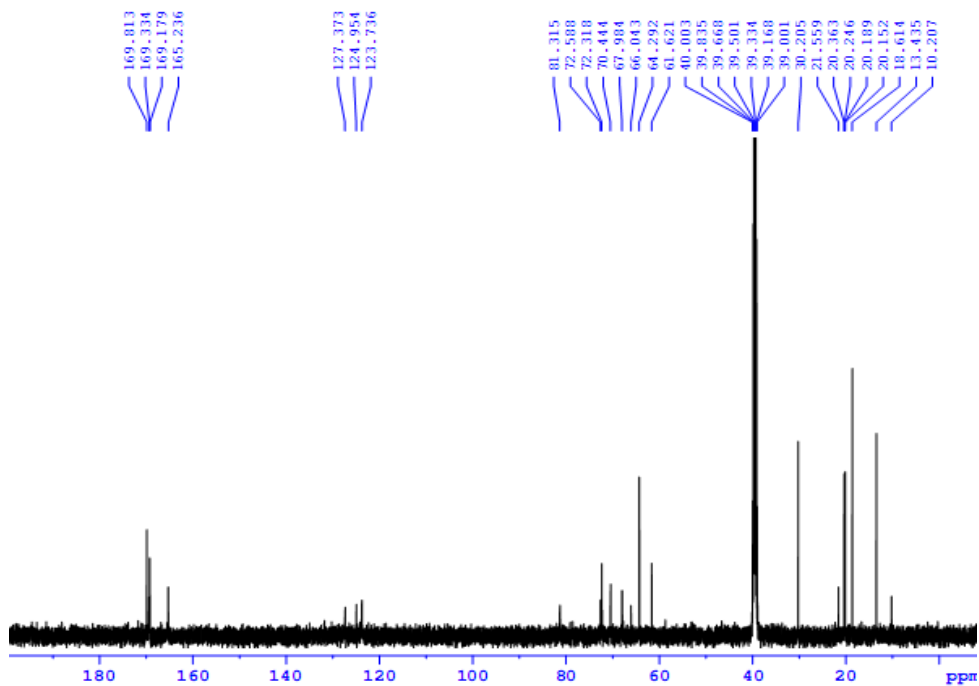
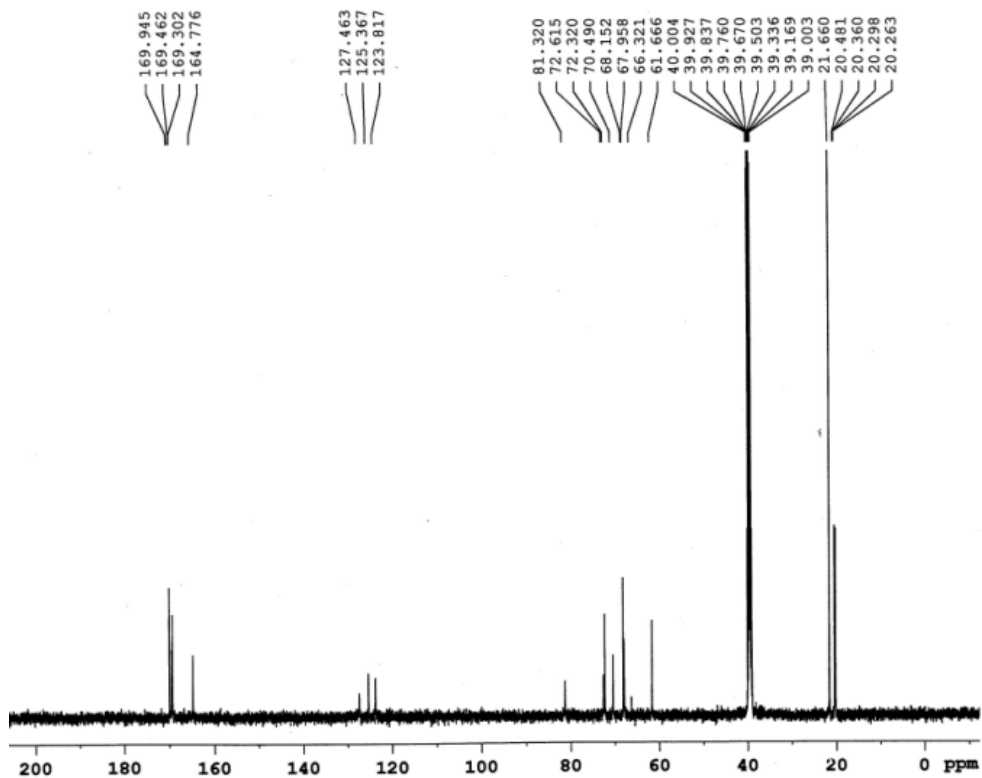


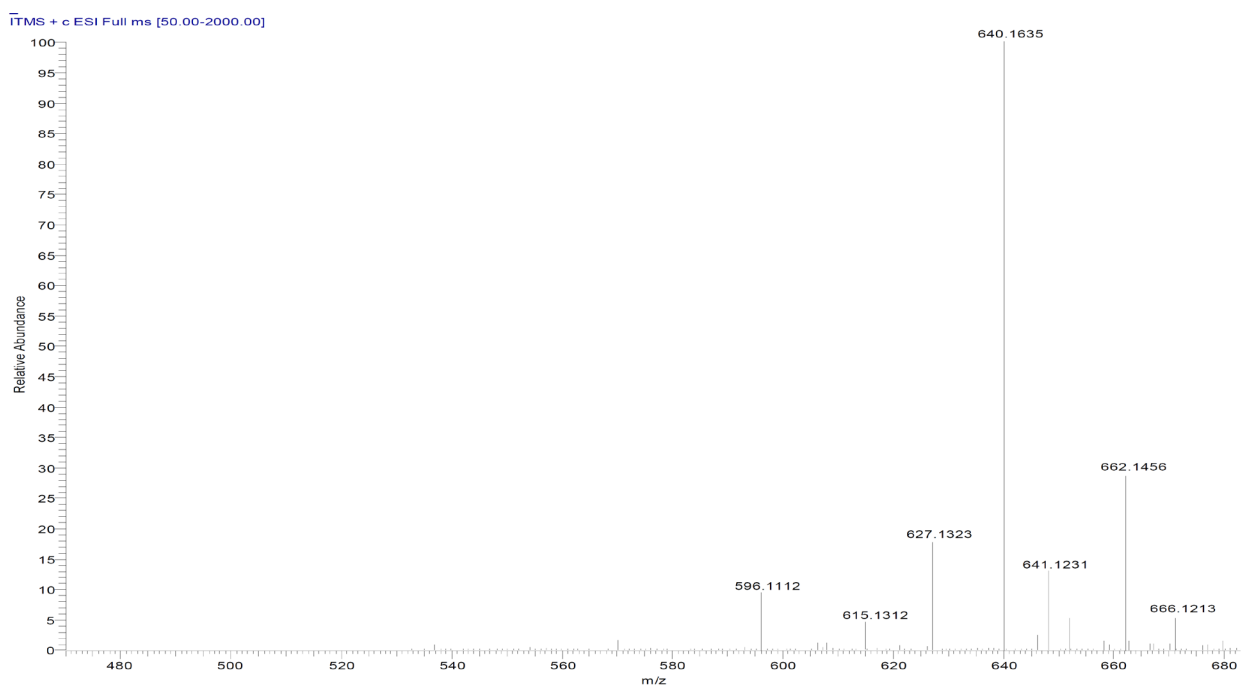
## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	1.987	579340	2.964	BV
2	3.060	18864396	96.529	VV
3	4.013	8213	0.042	TBB
4	4.453	65138	0.333	TBV
5	4.813	16684	0.085	TVV
6	5.147	8858	0.045	TVB
		19542647	100.00	



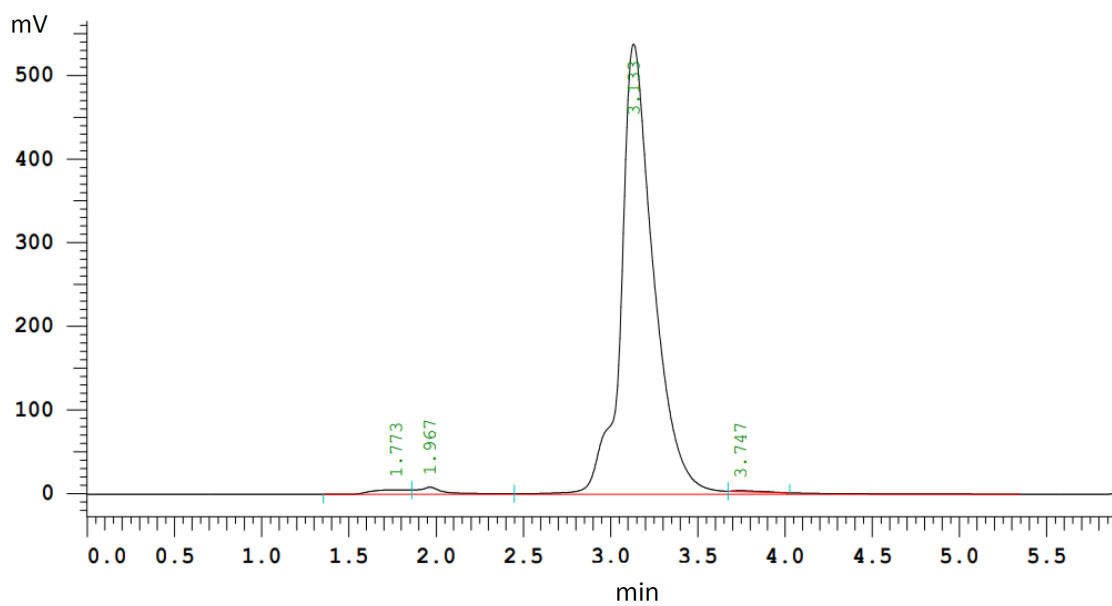
*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carbobutoxybenzo[d]thiazole-2-yl)thiourea*  
(4e)



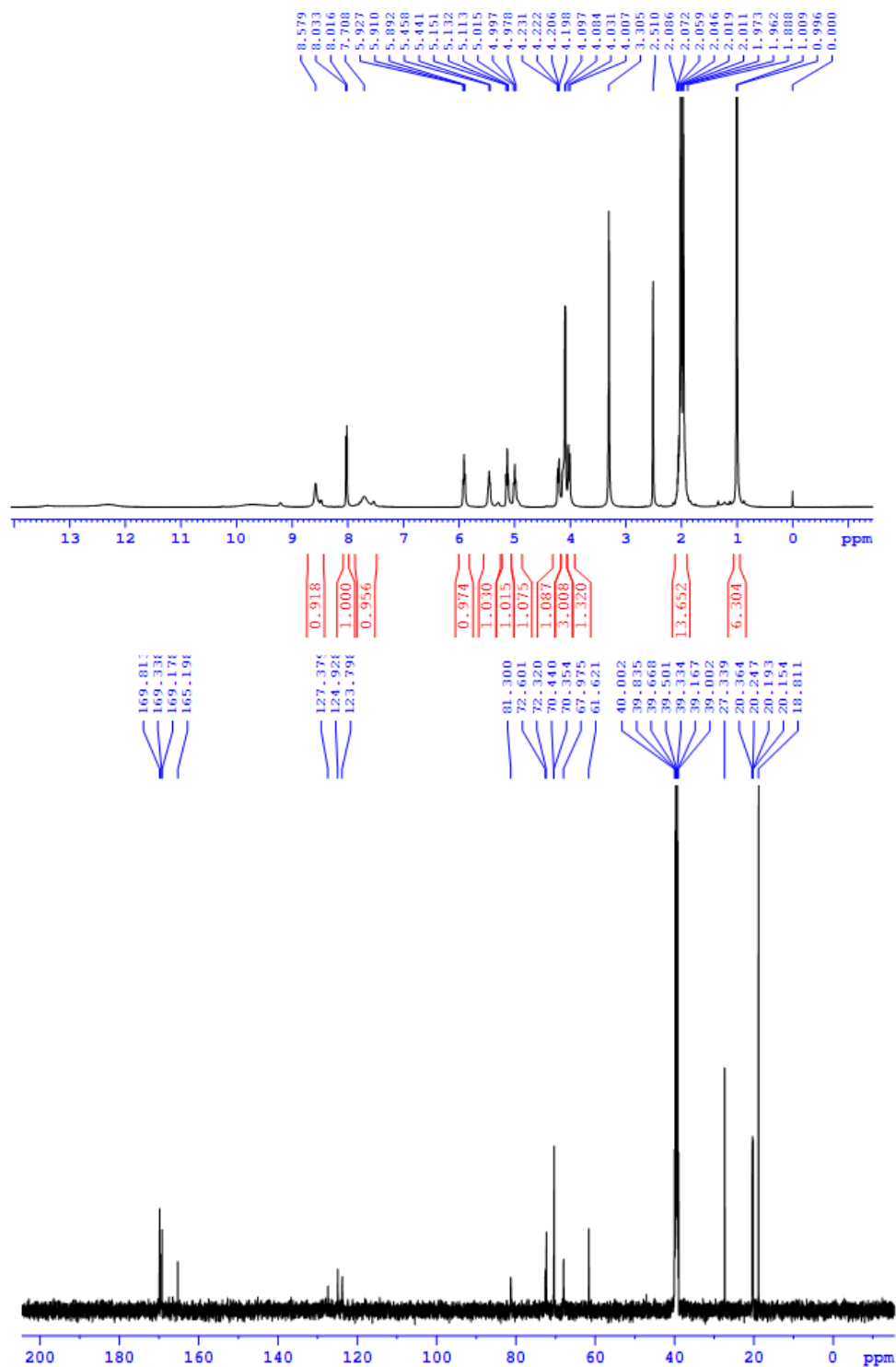


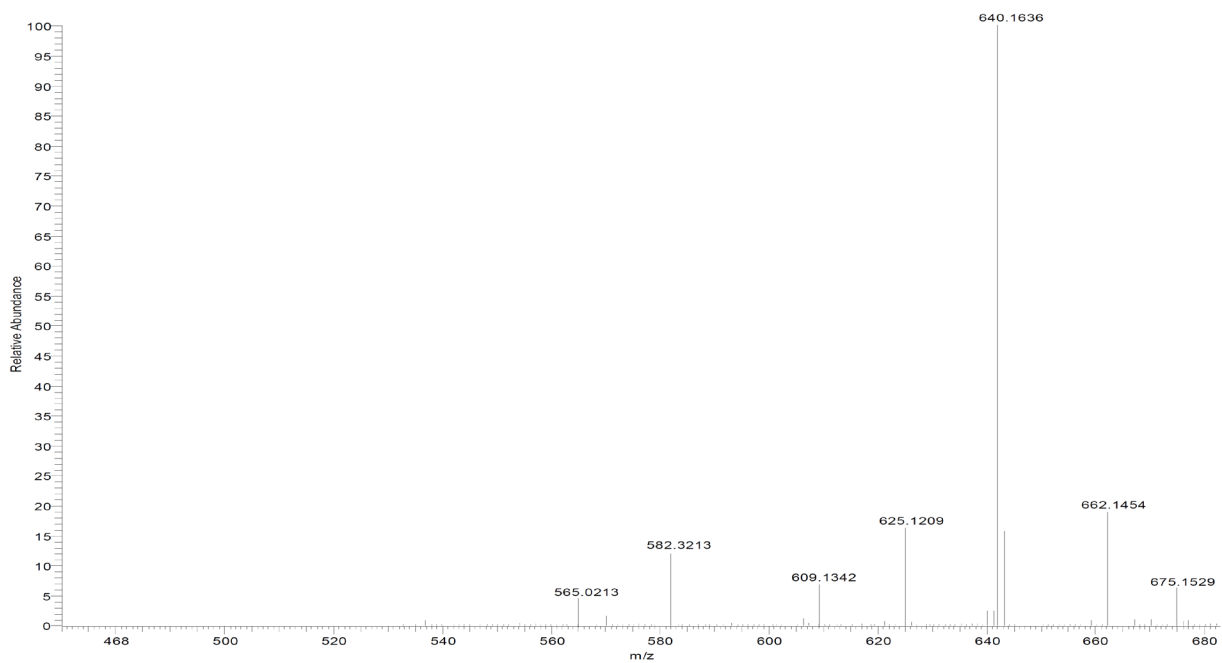
## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	1.773	80402	1.102	BV
2	1.967	98089	1.345	VV
3	3.133	7101267	97.364	VV
4	3.747	137930	0.189	TBB
			100.00	



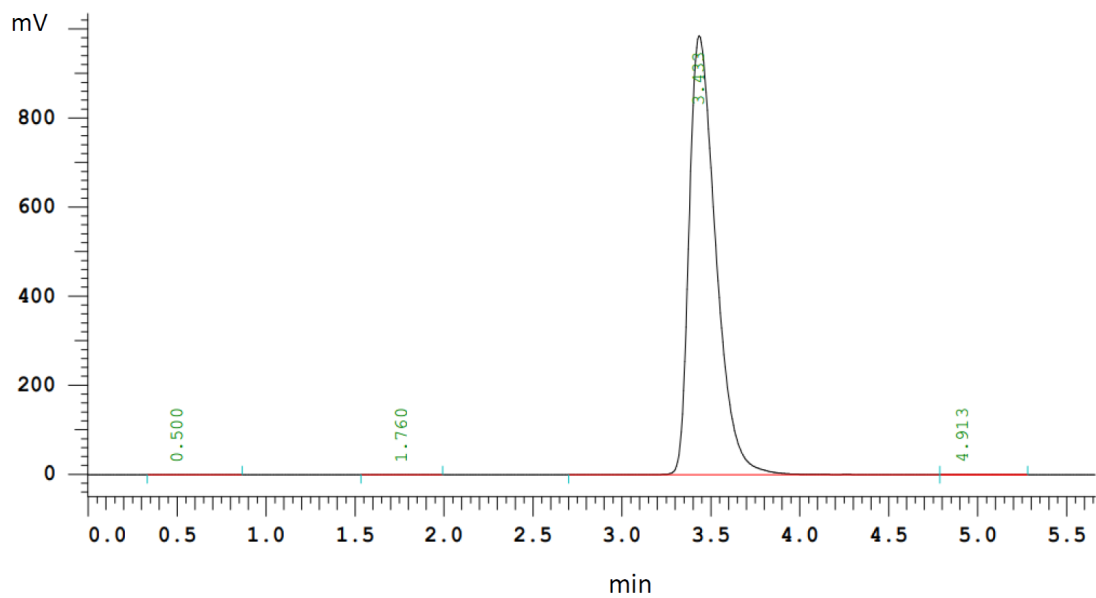
*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carboisobutoxybenzo[d]thiazole-2-yl)thiourea*  
(4f)



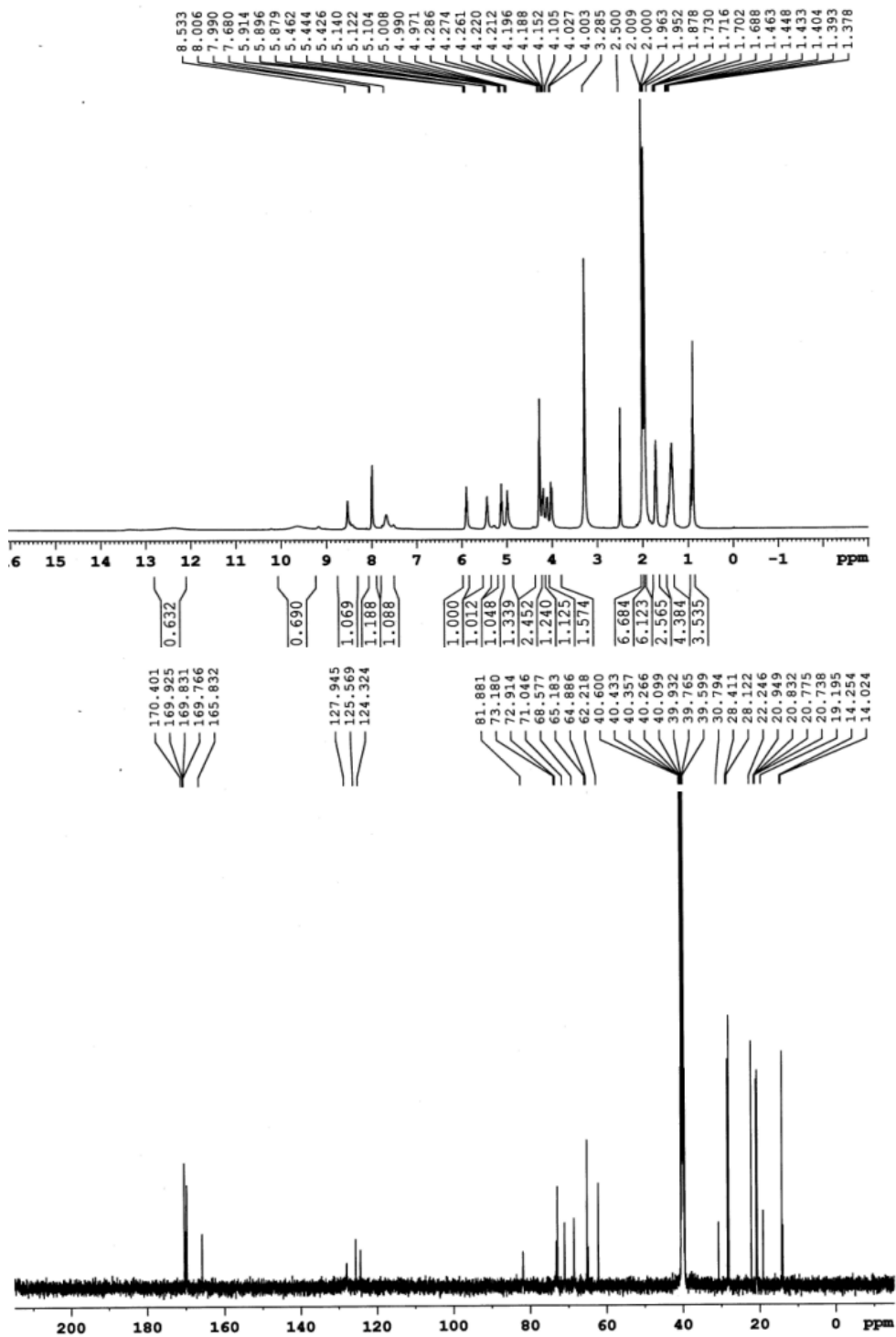


## HPLC

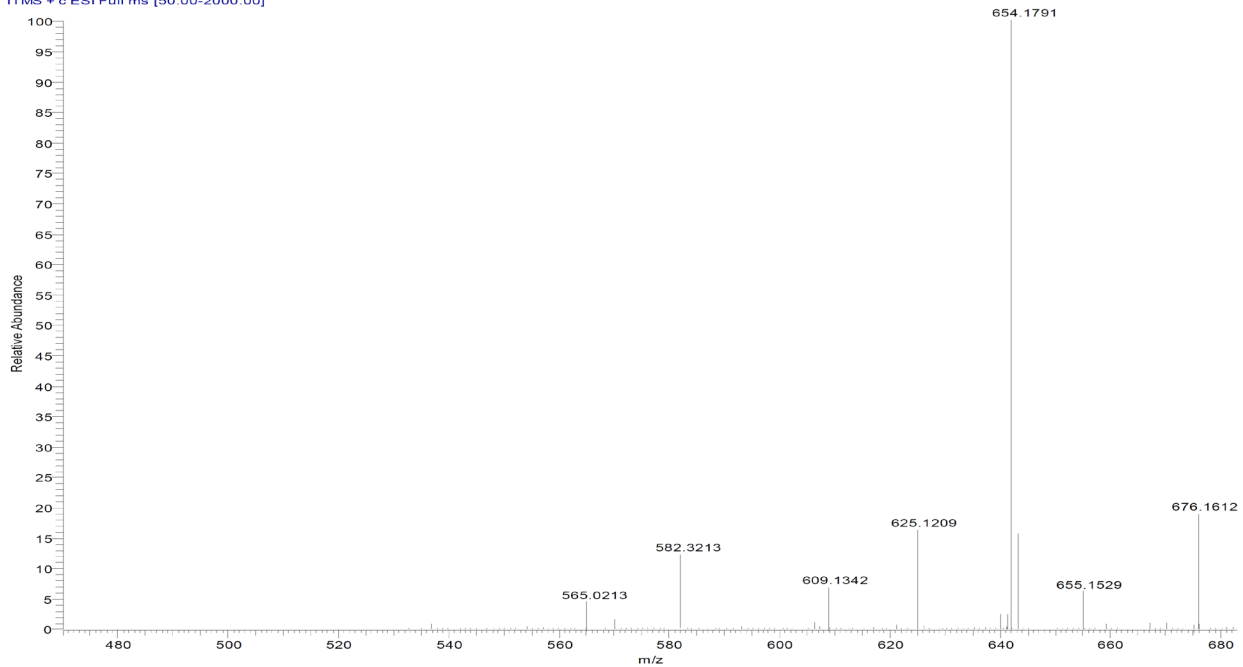
No.	RT	Area (%)	Concentration (%)	BC
1	0.500	826	0.008	BB
2	1.760	812	0.008	BB
3	3.433	10267216	99.973	BB
4	4.913	1126	0.011	TBB
		10269980	100.00	



1-(2,3,4,6-Tetra-O-acetyl- $\beta$ -D-glucopyranosyl)-3-(6-carbopentoxybenzo[d]thiazole-2-yl)thiourea  
(4g)

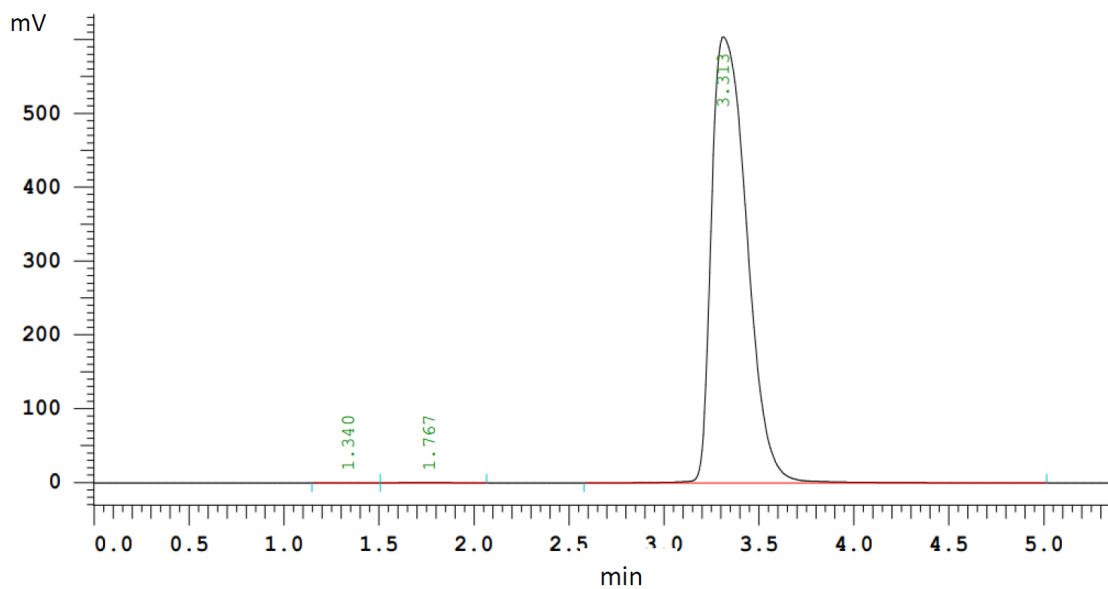




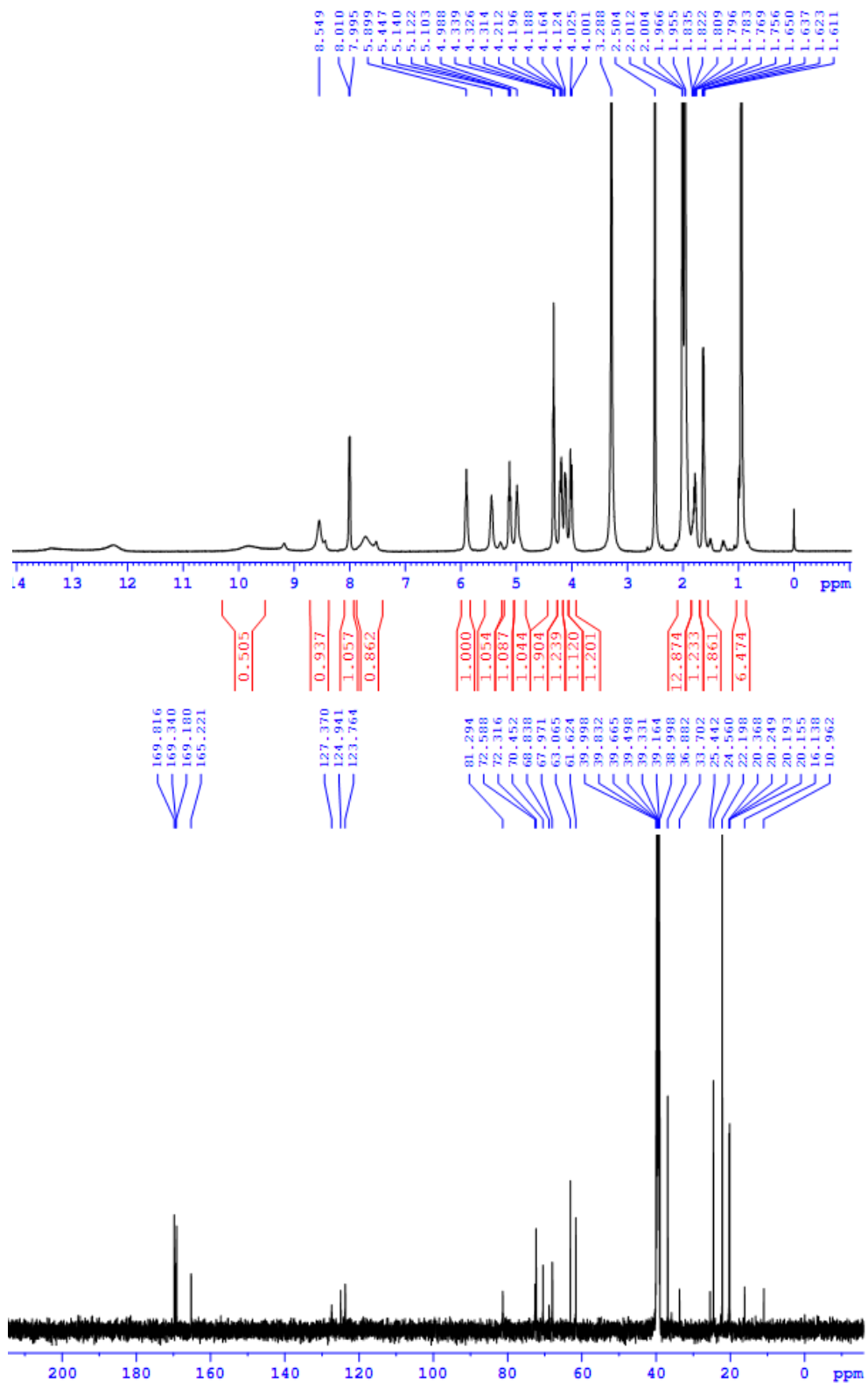


## HPLC

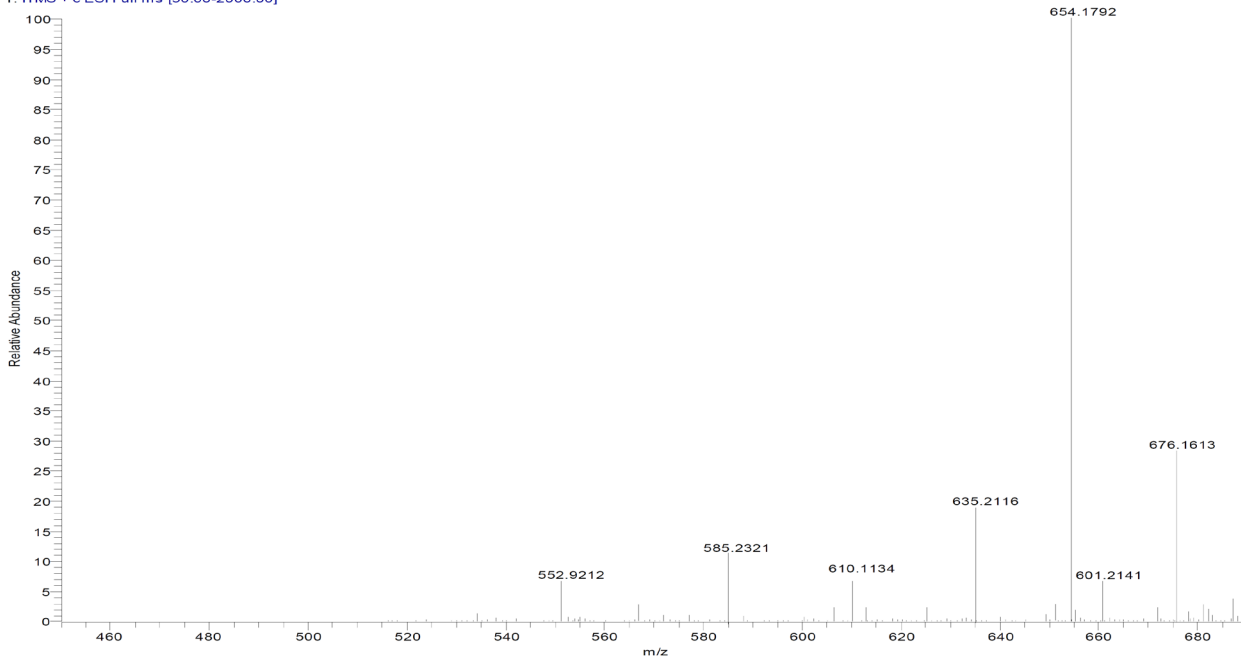
No.	RT	Area (%)	Concentration (%)	BC
1	1.340	1964	0.025	BB
2	1.767	9615	0.123	BB
3	3.313	7817217	99.852	BB
		7828796	100.00	



*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carboisopentybenzo[d]thiazole-2-yl)thiourea (4h)*

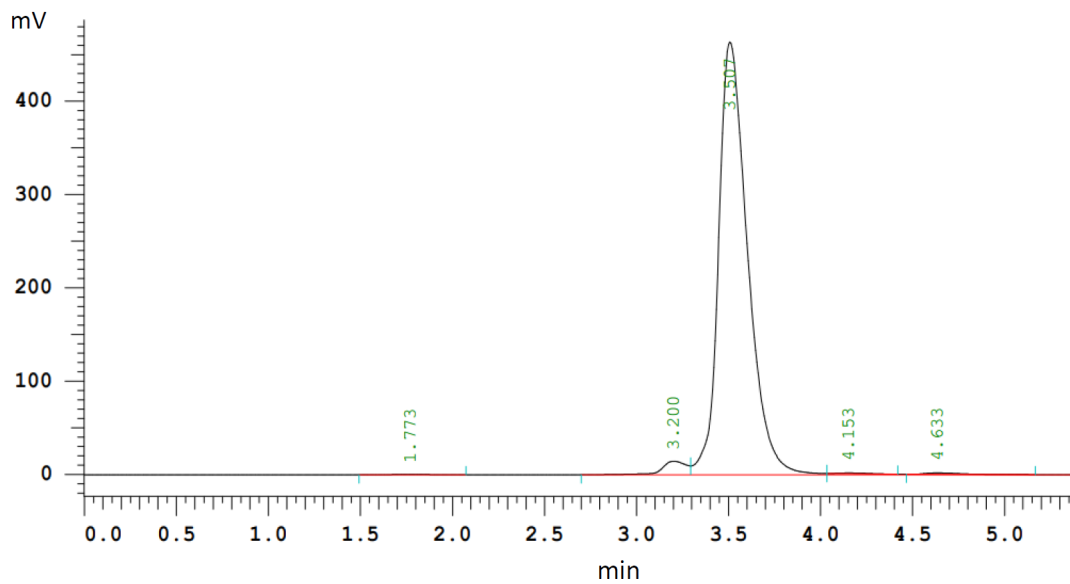


T: ITMS + c ESI Full ms [50.00-2000.00]

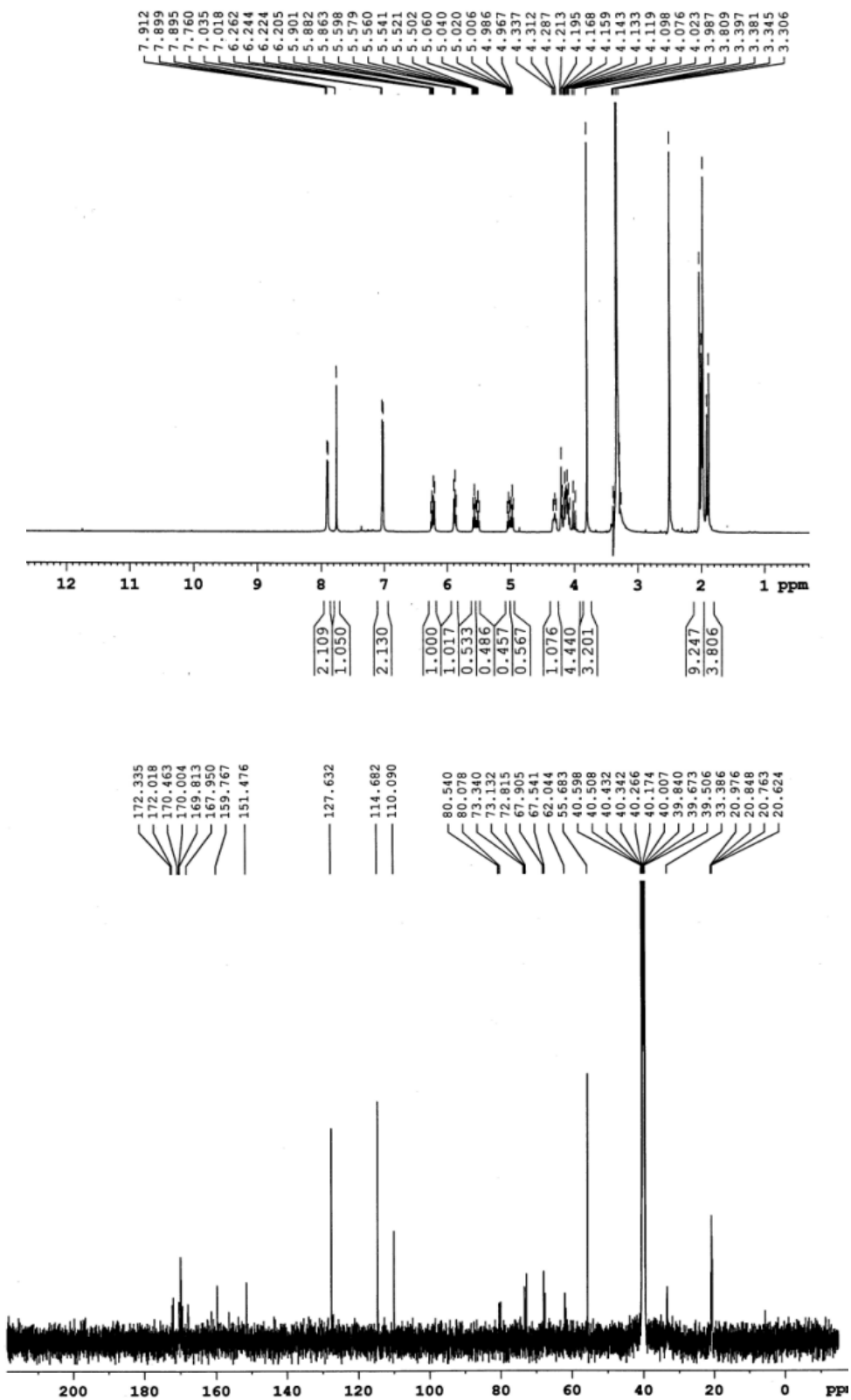


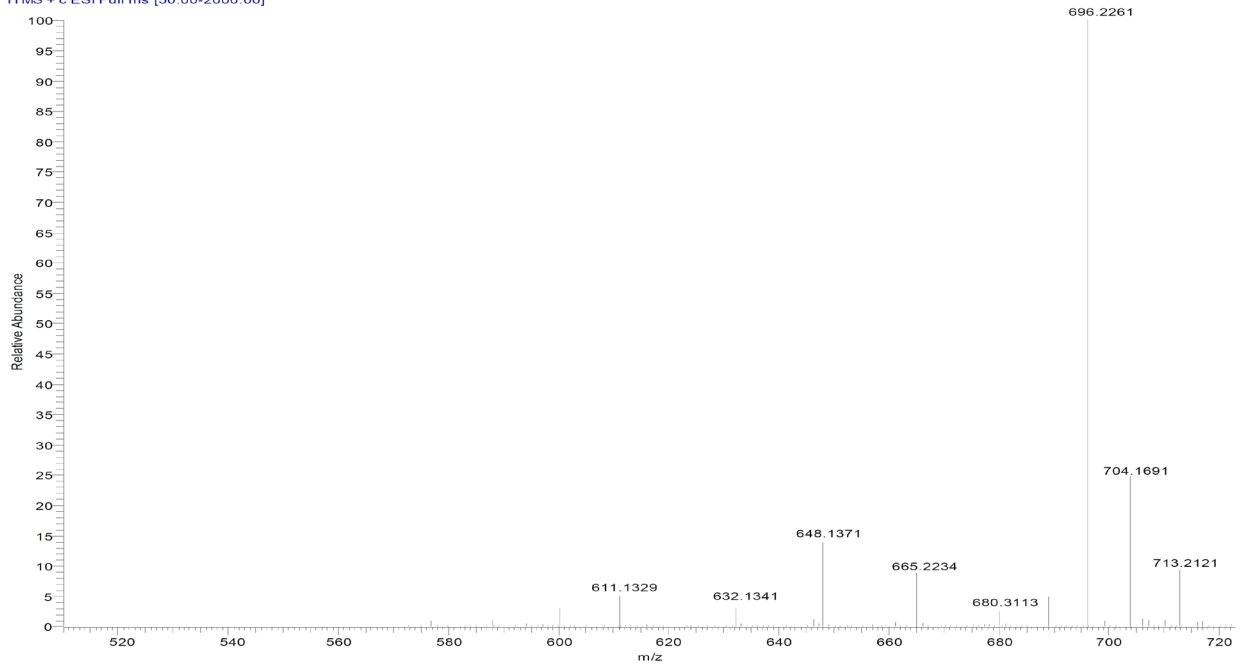
## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	1.773	5537	0.105	BB
2	3.200	131857	2.494	BV
3	3.507	5119190	96.807	VV
4	4.153	10559	0.200	TBB
5	4.633	20880	0.395	TBB
			100.00	



*1-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-3-(6-carbooctyloxybenzo[d]thiazole-2-yl)thiourea*  
**(4i)**





## HPLC

No.	RT	Area (%)	Concentration (%)	BC
1	1.727	139498	0.681	BV
2	1.967	198369	0.968	VV
3	3.127	20094728	98.101	VV
4	3.753	51104	0.249	TBB
			100.00	

