Design, Synthesis and Bioactivity Evaluation of Novel Isoxazole-Amide Derivatives Containing an Acylhydrazone Moiety as New Active Antiviral Agents

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Table S1. The preliminary in vivo antiviral activities against TMV and CMV of the target compounds **7a–7v** at 500 mg/L.

Compounds	TMV			CMV		
	Curative activity (%)	Protection activity (%)	Inactivation activity (%)	Curative activity (%)	Protection activity (%)	Inactivation activity (%)
7a	48.5 ± 3.0	54.2 ± 3.1	85.6 ± 1.7	38.4 ± 1.2	47.6 ± 1.3	69.9 ± 1.5
7b	40.8 ± 2.1	46.5 ± 5.0	83.4 ± 2.1	33.6 ± 1.4	44.7 ± 1.8	65.8 ± 1.7
7c	39.4 ± 1.3	59.4 ± 2.2	87.7 ± 2.3	37.9 ± 1.9	54.6 ± 2.1	72.6 ± 2.4
7d	62.9 ± 1.2	67.2 ± 3.0	93.6 ± 3.3	56.7 ± 2.1	63.8 ± 2.5	91.4 ± 2.6
7e	28.2 ± 3.1	39.8 ± 2.1	55.1 ± 2.9	14.4 ± 1.3	24.6 ± 1.5	42.3 ± 1.2
7f	36.7 ± 1.4	50.2 ± 4.2	78.8 ± 1.6	33.5 ± 1.6	43.6 ± 2.3	76.9 ± 2.1
7g	35.6 ± 2.2	42.4 ± 1.7	74.7 ± 1.8	30.7 ± 1.8	40.5 ± 1.4	70.8 ± 1.9
7h	64.5 ± 1.2	69.6 ± 2.6	94.1 ± 1.2	58.8 ± 2.2	65.4 ± 2.5	92.0 ± 2.6
7i	50.4 ± 1.2	58.2 ± 2.3	86.4 ± 1.9	47.3 ± 1.6	54.7 ± 2.1	80.7 ± 1.8
7j	55.4 ± 1.3	65.3 ± 1.1	92.6 ± 3.2	51.6 ± 1.7	57.5 ± 1.6	81.8 ± 2.7
7k	47.5 ± 1.1	56.4 ± 2.3	85.5 ± 3.7	48.3 ± 1.5	54.8 ± 2.2	78.4 ± 2.6
7l	43.9 ± 4.2	60.4 ± 4.1	89.4 ± 3.3	41.6 ± 1.8	56.2 ± 2.4	75.8 ± 2.3
7m	65.1 ± 2.2	69.7 ± 1.0	95.3 ± 2.6	58.6 ± 2.5	64.4 ± 1.7	92.8 ± 2.8
7n	36.5 ± 1.0	43.6 ± 1.2	67.5 ± 1.8	26.5 ± 1.1	34.8 ± 1.4	52.9 ± 1.3
7o	42.2 ± 4.5	56.3 ± 1.5	84.2 ± 2.1	39.6 ± 2.2	49.7 ± 1.6	75.8 ± 2.5
7p	40.9 ± 4.1	49.4 ± 1.0	78.2 ± 1.4	36.2 ± 2.0	44.8 ± 1.4	69.9 ± 1.8
7q	67.0 ± 2.3	72.7 ± 2.2	96.3 ± 1.5	60.8 ± 2.7	67.8 ± 2.9	93.8 ± 1.9
7r	56.7 ± 2.1	64.3 ± 2.3	93.3 ± 3.1	57.9 ± 2.5	63.6 ± 2.4	91.9 ± 2.8
7s	52.3 ± 1.6	60.3 ± 4.1	89.1 ± 1.3	47.7 ± 1.8	52.2 ± 2.3	80.6 ± 1.5
7t	68.8 ± 2.5	74.8 ± 2.6	96.9 ± 2.9	65.9 ± 2.8	70.2 ± 2.5	94.6 ± 2.4
7u	40.5 ± 2.2	57.4 ± 2.0	76.9 ± 1.2	36.2 ± 2.1	48.9 ± 2.2	68.7 ± 2.3
7v	37.2 ± 3.1	42.5 ± 3.0	67.7 ± 2.8	31.4 ± 1.2	38.6 ± 1.4	62.0 ± 2.5
NNM	55.6 ± 1.6	63.8 ± 2.9	92.5 ± 1.3	54.7 ± 3.4	62.6 ± 2.5	91.0 ± 3.0

Table S2. The EC_{50} values of the target compounds **7a–7v** against TMV in vivo.

Compounds	EC_{50} (mg/L)		
	Curative activity	Protection activity	Inactivation activity
7a	358.5 ± 3.4	256.5 ± 3.4	97.8 ± 1.6
7b	395.8 ± 3.1	324.7 ± 3.2	132.8 ± 1.9
7c	356.8 ± 3.2	288.6 ± 2.8	105.6 ± 1.8
7d	238.9 ± 1.9	187.2 ± 2.4	46.7 ± 1.2
7e	536.3 ± 3.7	429.8 ± 2.9	245.1 ± 2.3
7f	370.7 ± 3.5	290.7 ± 3.8	148.9 ± 2.6
7g	395.6 ± 3.2	322.6 ± 2.2	171.5 ± 2.1
7h	195.5 ± 2.3	172.6 ± 2.8	43.1 ± 1.5
7i	516.7 ± 3.2	345.2 ± 2.6	86.4 ± 1.2
7j	291.4 ± 3.1	232.3 ± 2.6	52.9 ± 1.5
7k	364.5 ± 3.5	276.8 ± 2.9	118.7 ± 1.7
7l	336.8 ± 4.7	249.4 ± 4.5	95.8 ± 1.6
7m	189.9 ± 2.5	176.5 ± 2.5	44.5 ± 1.5
7n	487.6 ± 4.8	361.7 ± 2.7	228.5 ± 2.3
7o	368.6 ± 4.3	280.3 ± 3.3	123.7 ± 2.6
7p	385.6 ± 4.1	299.8 ± 3.2	146.8 ± 2.5
7q	179.6 ± 3.5	169.2 ± 2.9	36.9 ± 1.8
7r	266.8 ± 2.9	199.4 ± 3.5	42.7 ± 1.6
7s	332.3 ± 3.2	296.5 ± 3.5	80.6 ± 1.4
7t	168.5 ± 1.9	157.6 ± 2.1	33.7 ± 1.7

7u	417.8 ± 2.8	377.1 ± 2.3	172.4 ± 3.6
7v	448.9 ± 3.7	421.6 ± 3.5	197.7 ± 3.8
NNM	286.4 ± 2.2	198.2 ± 2.1	46.3 ± 1.9

Table S3. The EC_{50} values of the target compounds **7a–7v** against CMV in vivo.

Compounds	EC_{50} (mg/L)		
	Curative activity	Protection activity	Inactivation activity
7a	365.2 ± 3.6	338.6 ± 3.2	114.5 ± 1.9
7b	378.2 ± 3.8	357.7 ± 3.5	138.2 ± 2.3
7c	387.6 ± 3.6	347.4 ± 2.8	147.8 ± 2.3
7d	276.5 ± 2.4	247.8 ± 2.9	57.3 ± 1.9
7e	547.6 ± 3.5	528.2 ± 2.6	318.6 ± 2.9
7f	412.6 ± 3.8	389.3 ± 3.6	193.6 ± 2.9
7g	428.9 ± 3.8	406.4 ± 2.9	223.5 ± 3.2
7h	226.4 ± 3.5	215.8 ± 2.5	53.7 ± 1.8
7i	361.2 ± 3.5	328.7 ± 2.9	108.7 ± 1.3
7j	338.7 ± 3.4	288.9 ± 3.5	93.8 ± 1.8
7k	355.5 ± 3.9	319.6 ± 2.5	105.4 ± 1.9
7l	358.8 ± 4.2	331.5 ± 3.6	129.6 ± 1.8
7m	248.5 ± 3.6	198.3 ± 3.2	51.8 ± 1.4
7n	519.9 ± 4.7	488.3 ± 4.5	287.8 ± 2.9
7o	395.4 ± 3.7	379.8 ± 3.4	169.2 ± 2.9
7p	407.4 ± 4.2	389.4 ± 3.6	192.3 ± 2.8
7q	227.3 ± 3.2	179.7 ± 2.5	47.6 ± 1.9
7r	268.5 ± 2.6	236.9 ± 3.2	56.4 ± 1.4
7s	353.7 ± 3.5	342.7 ± 3.6	89.4 ± 1.3
7t	197.9 ± 2.8	168.4 ± 2.8	45.8 ± 1.2
7u	438.9 ± 3.6	422.8 ± 2.9	226.8 ± 3.9
7v	456.7 ± 3.9	438.9 ± 3.9	234.6 ± 3.6
NNM	297.3 ± 1.4	263.4 ± 2.5	62.8 ± 1.8

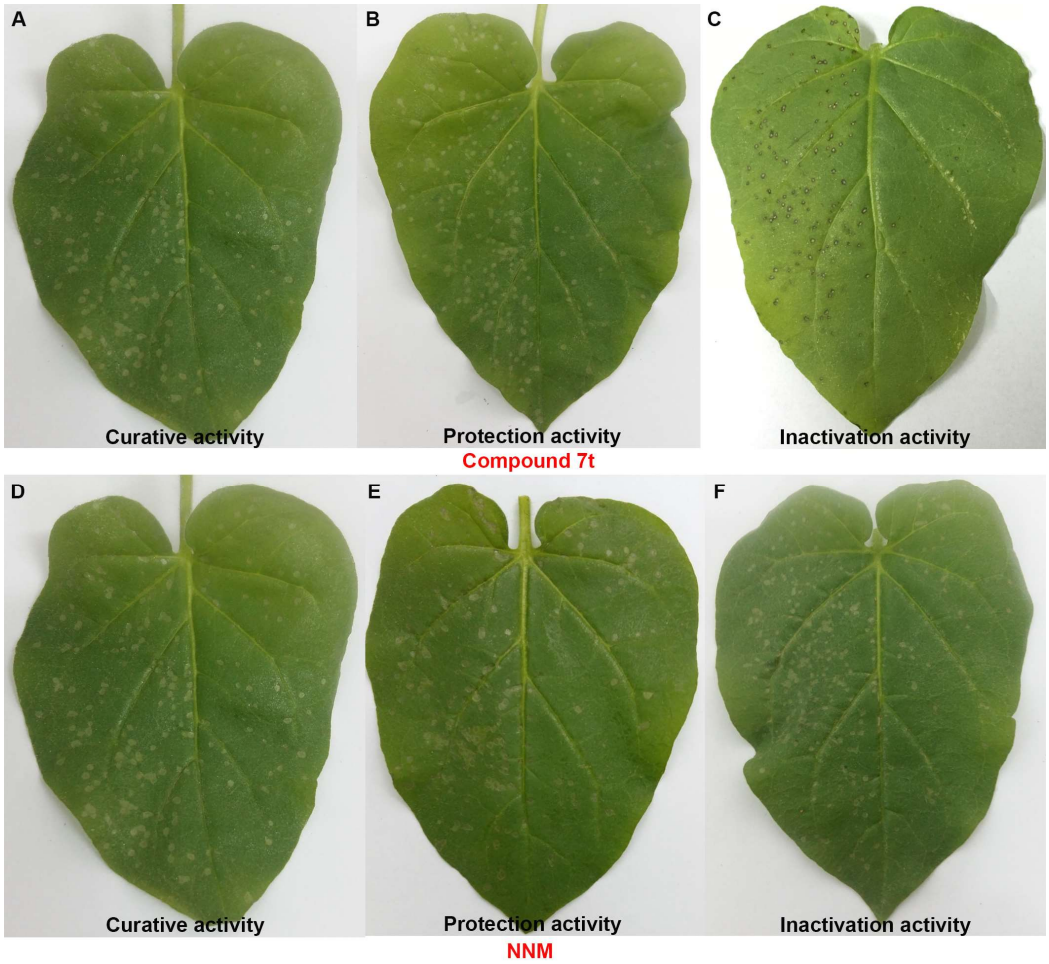


Figure S1. The antiviral activity of compound **7t** against TMV at 500 mg/L. Left: smeared with solvent; Right: smeared with compound **7t** or NNM.

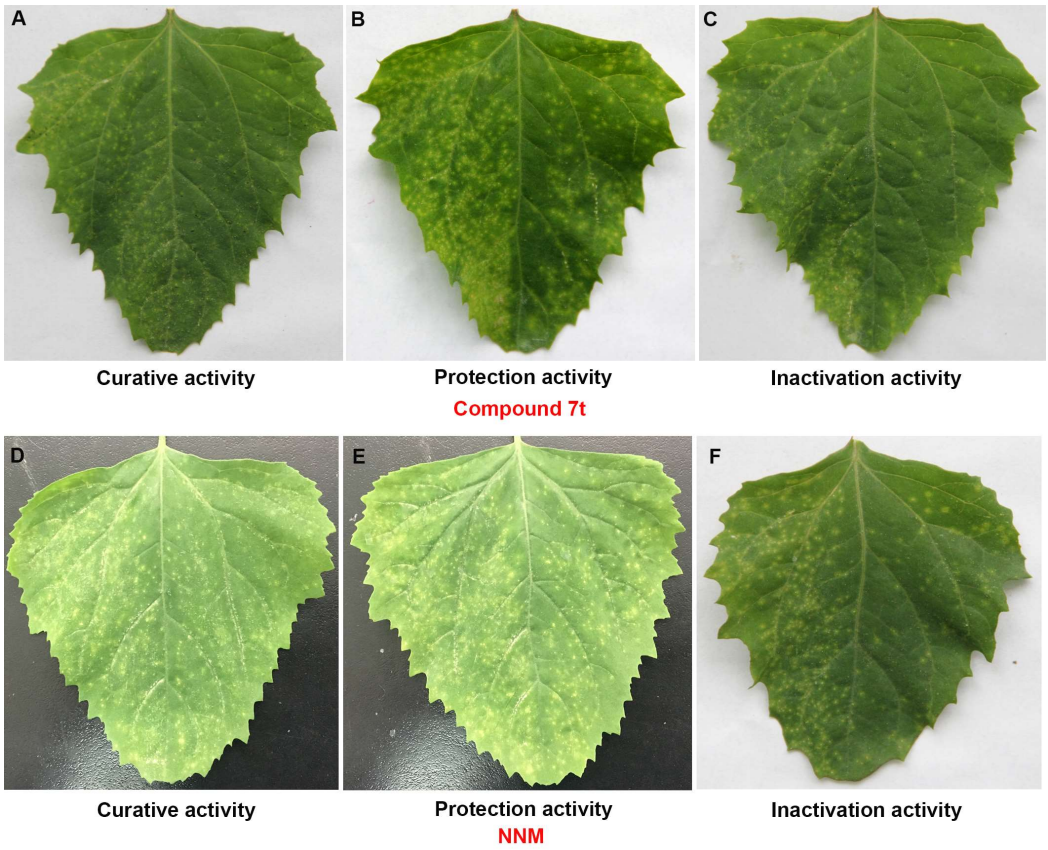
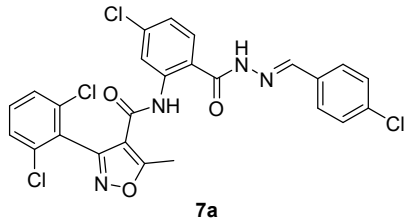
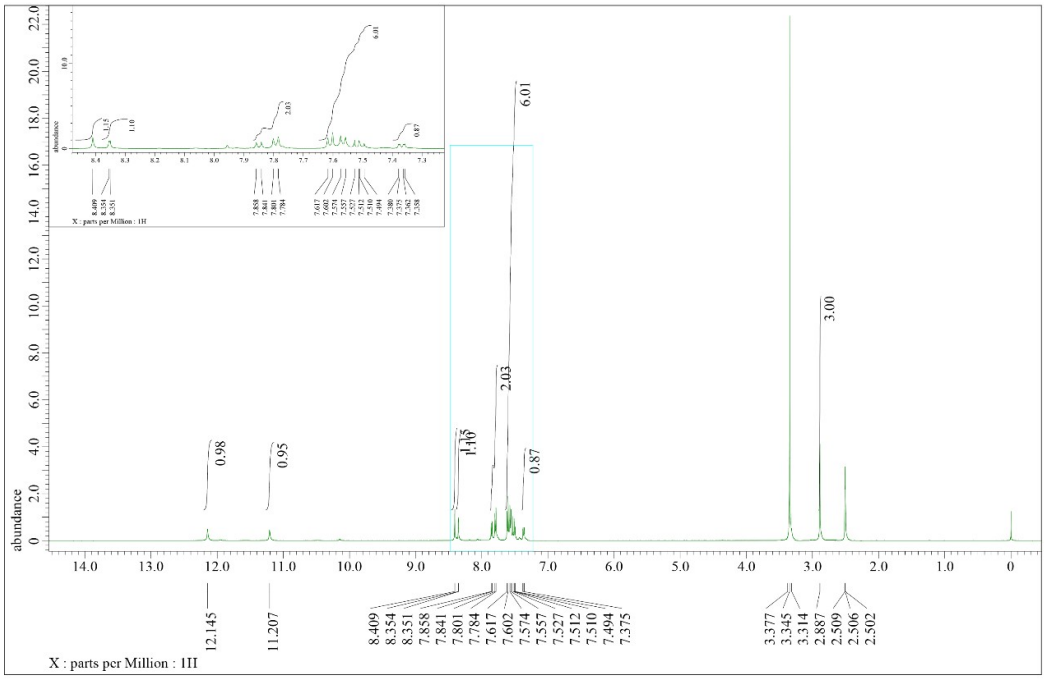


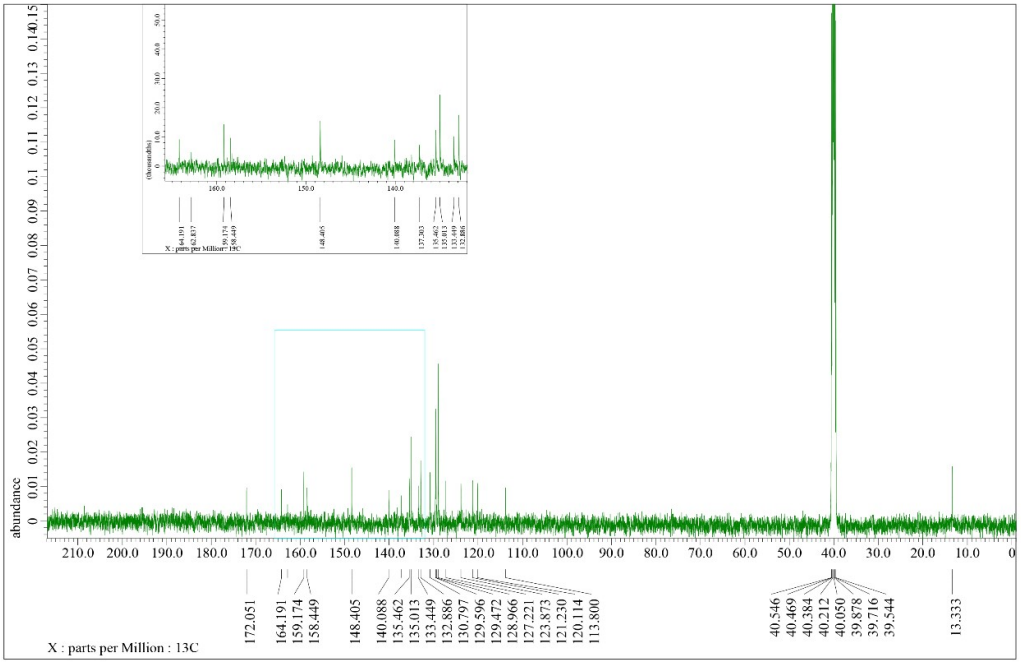
Figure S2. The antiviral activity of compound **7t** against CMV at 500 mg/L. Left: smeared with solvent; Right: smeared with compound **7t** or NNM.



7a



^{1}H NMR of Compound 7a



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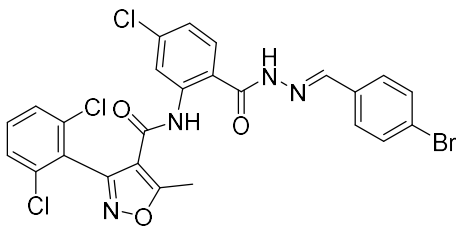
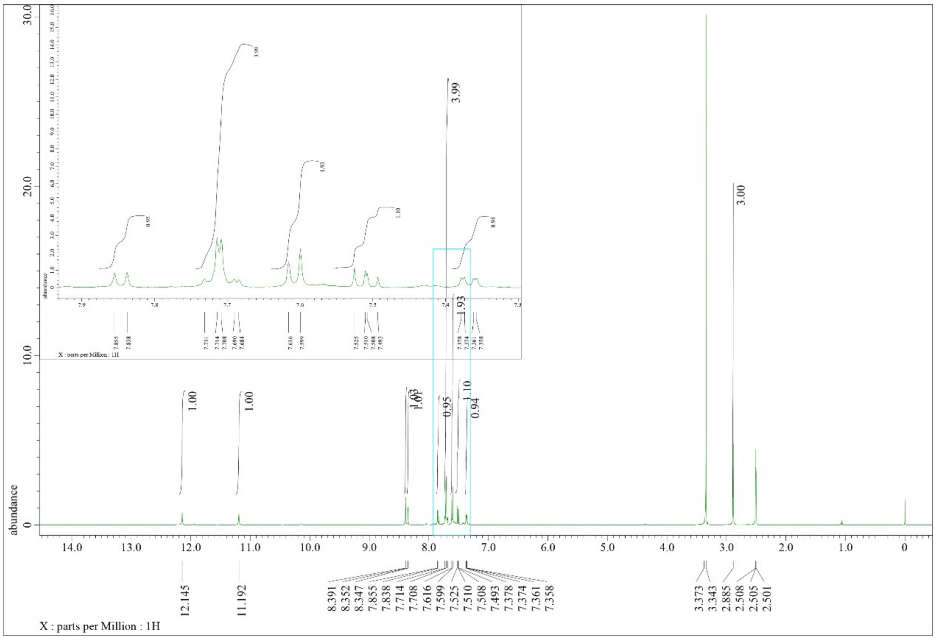


4b



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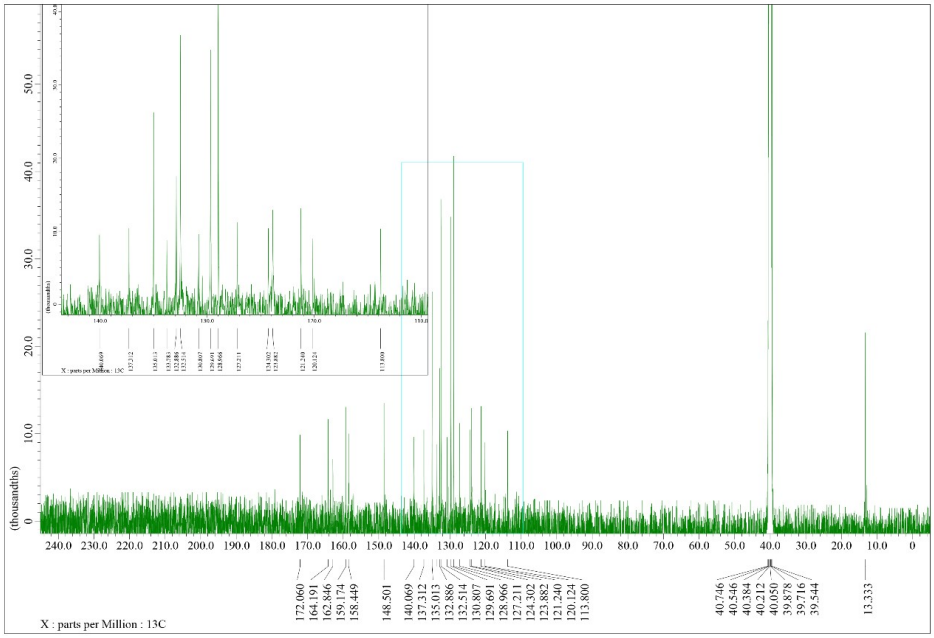

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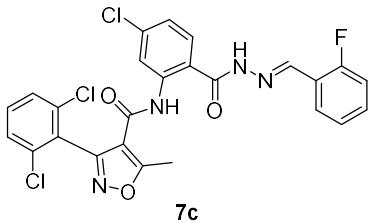

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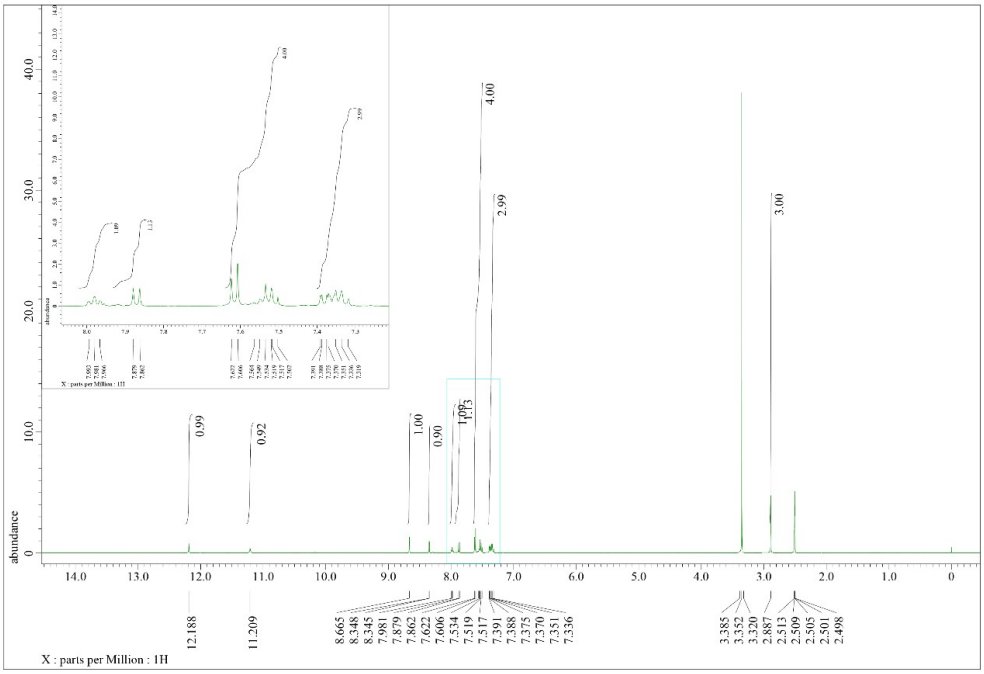

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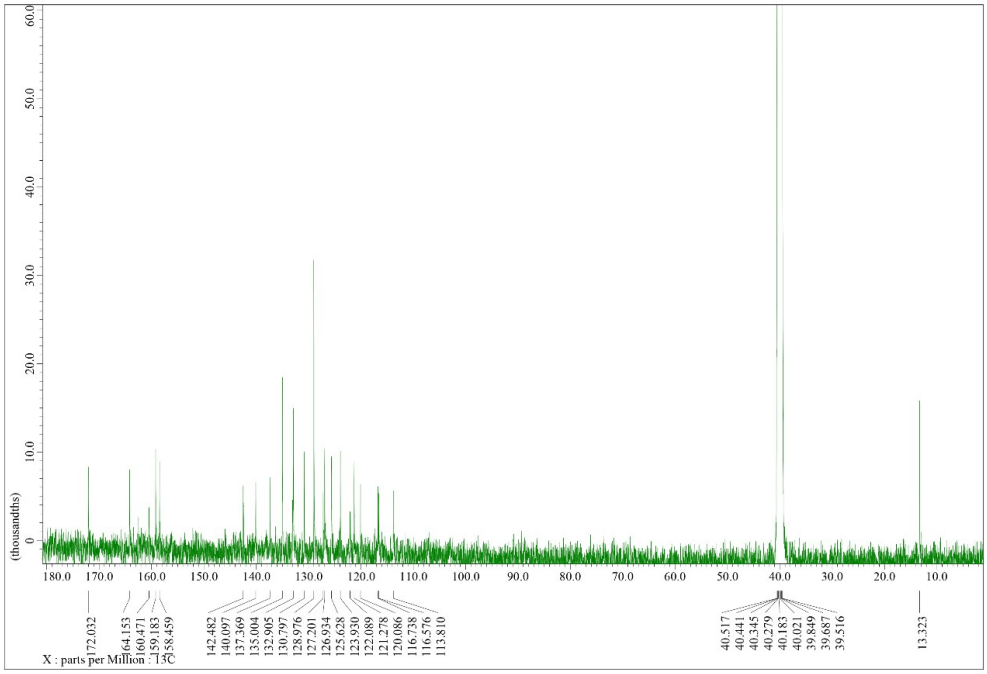

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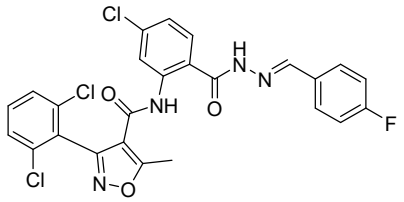

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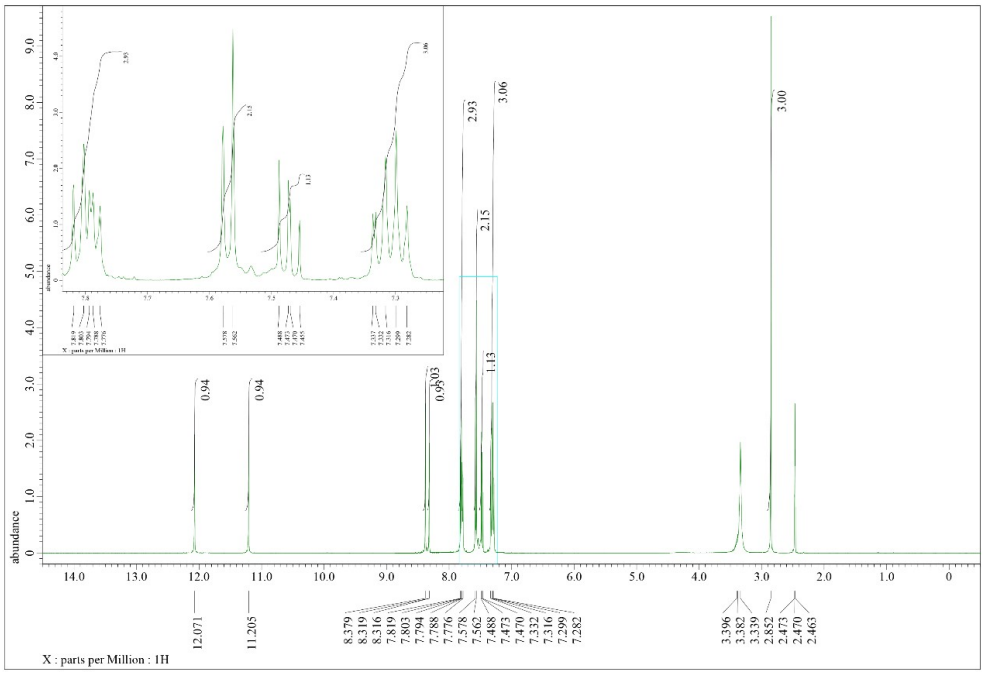

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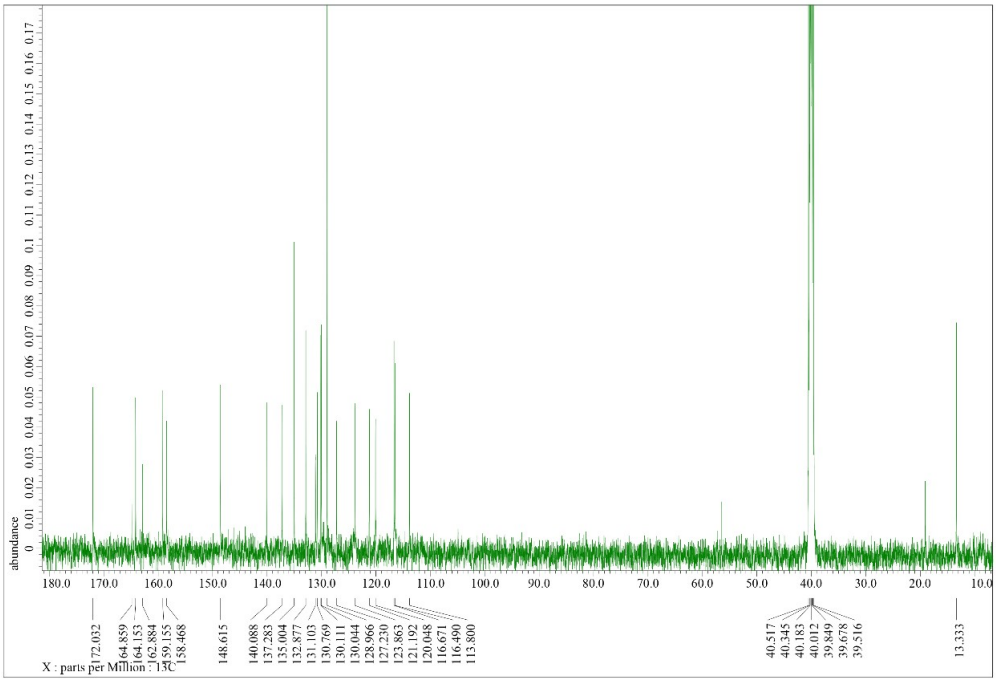

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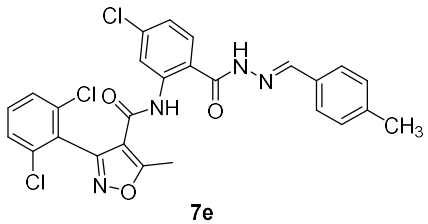

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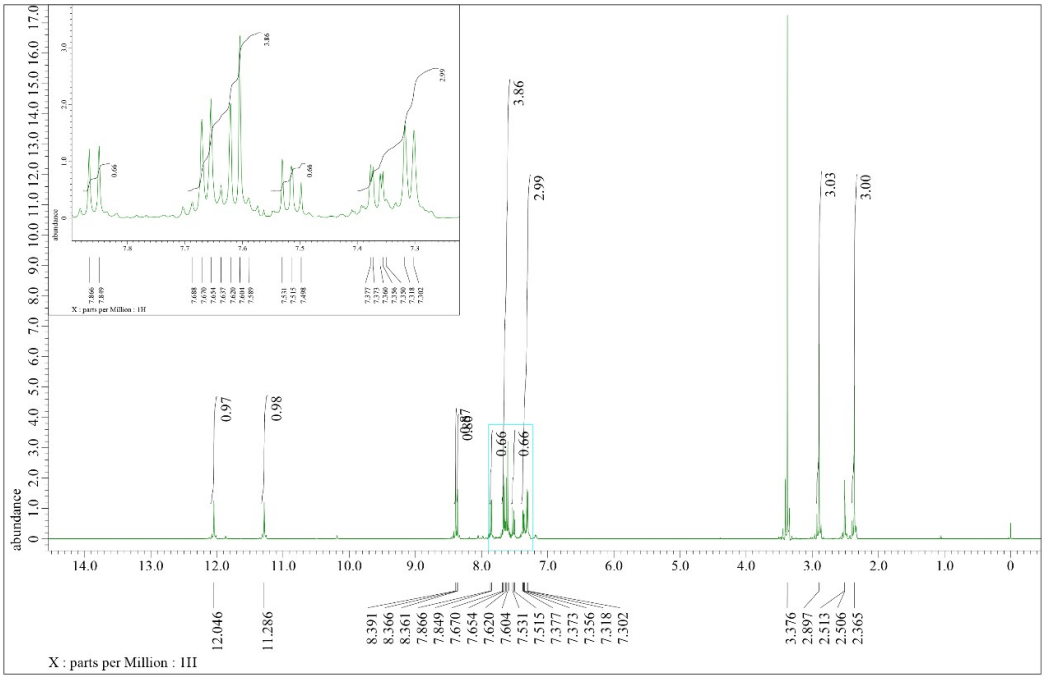

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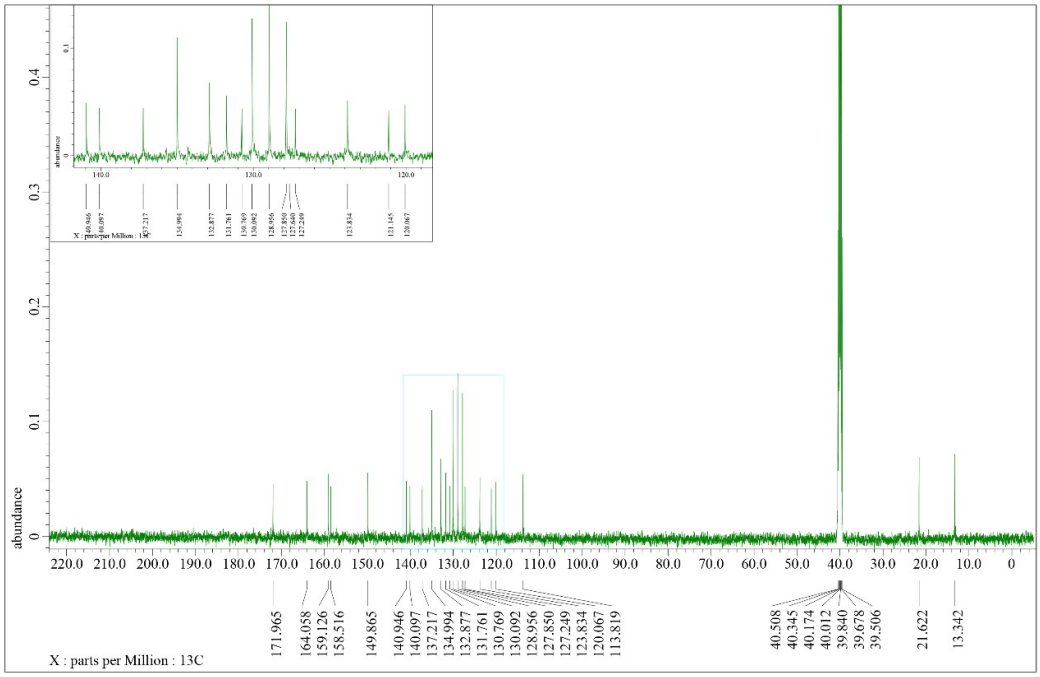

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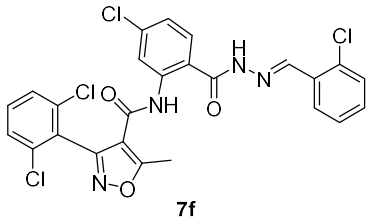

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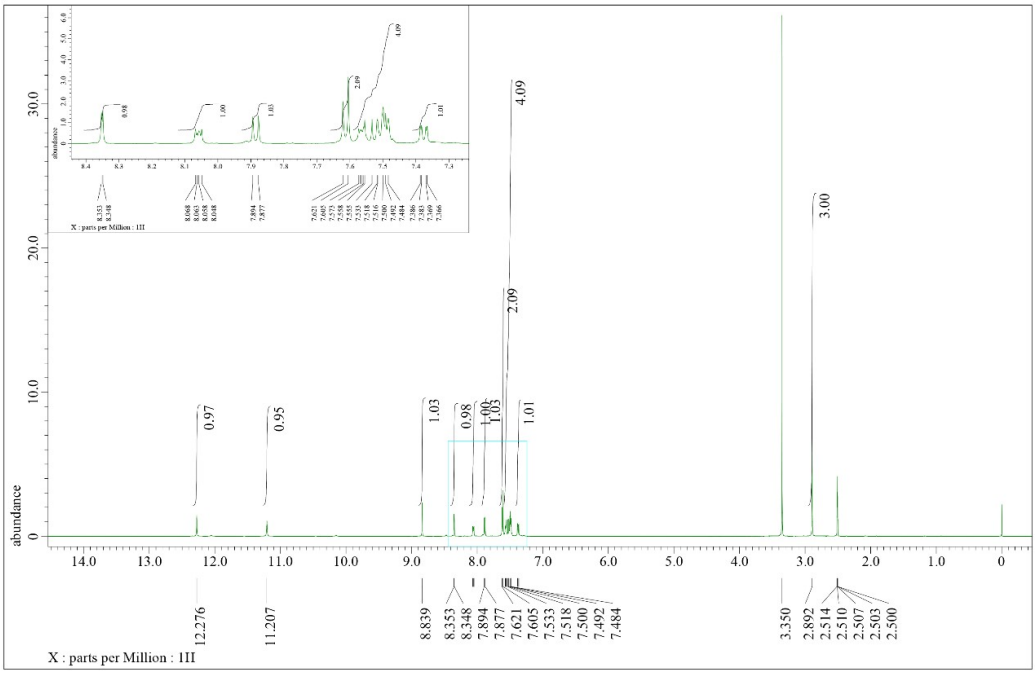

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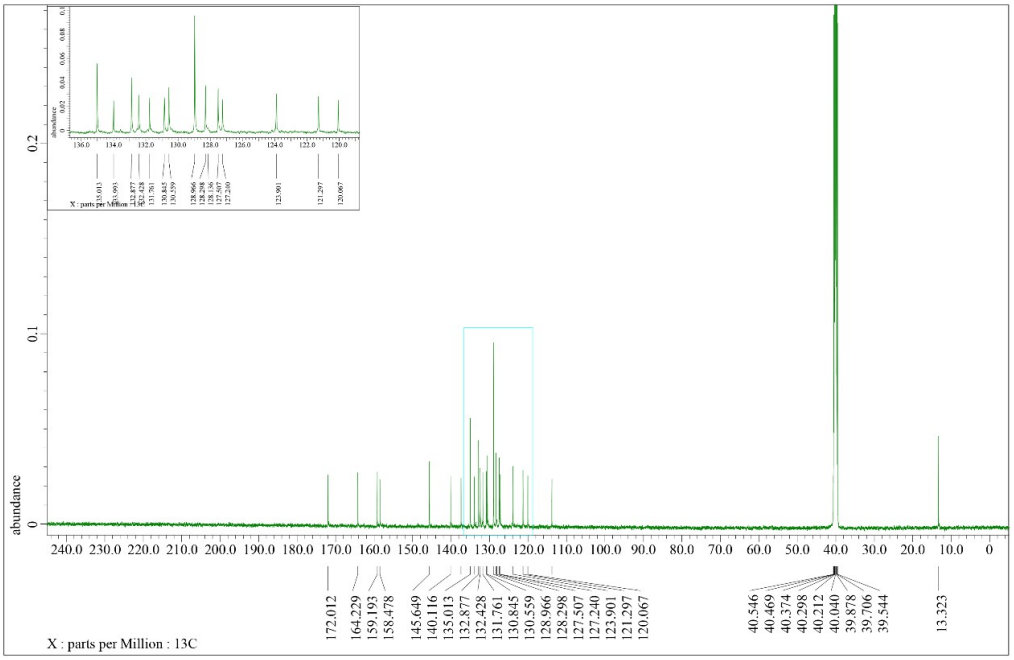

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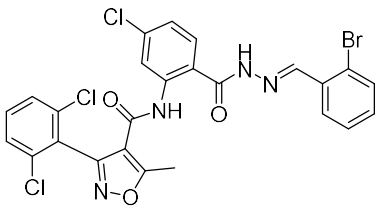

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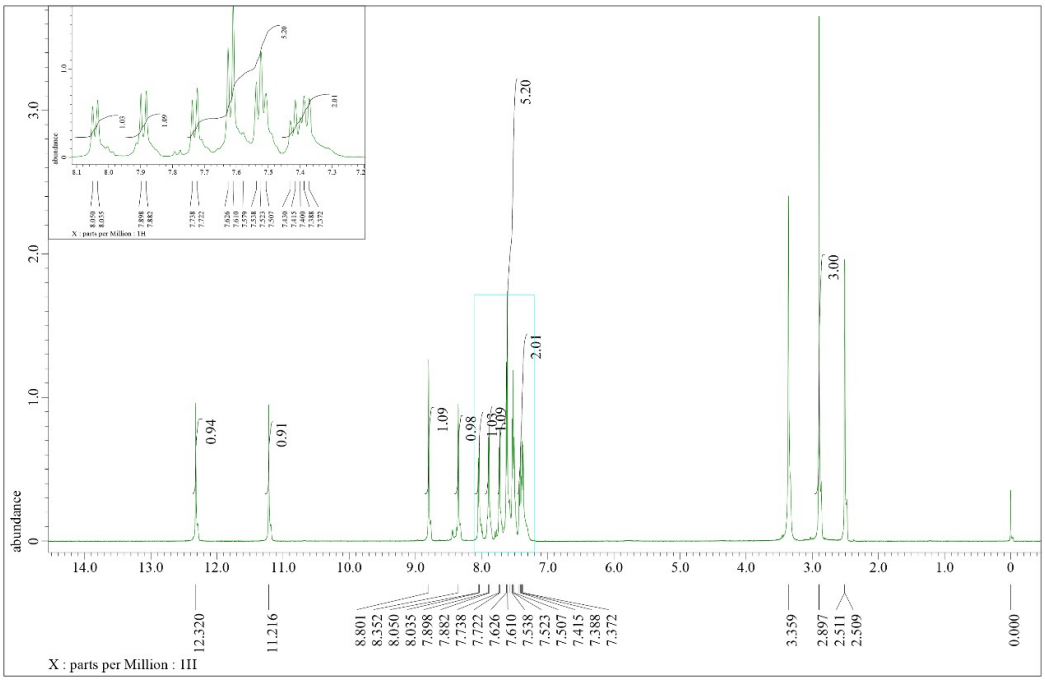

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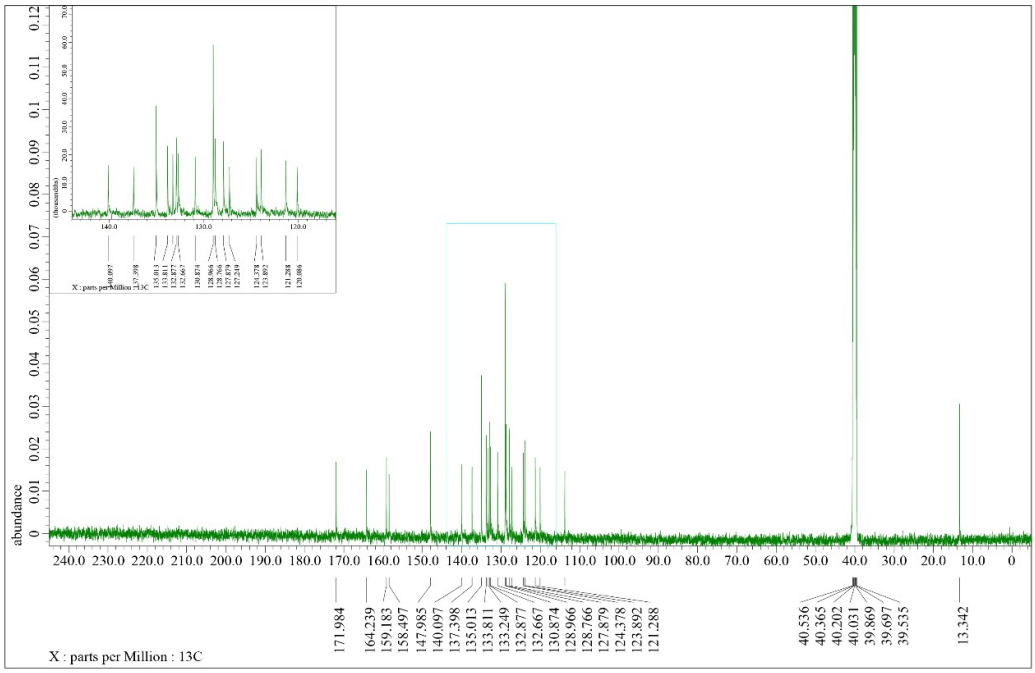

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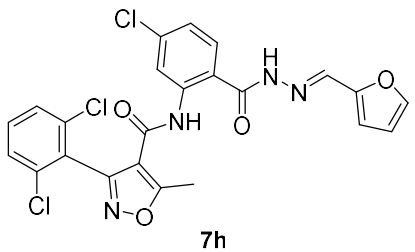

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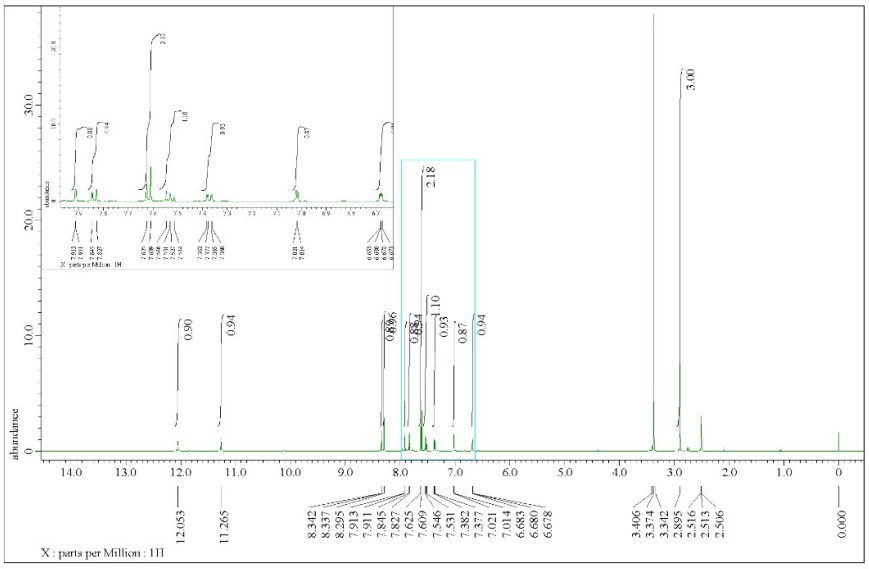

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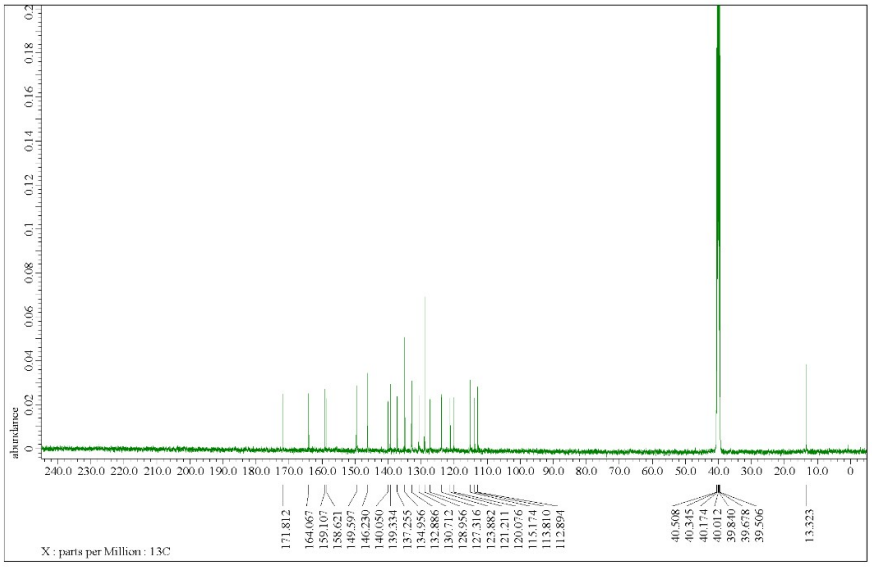

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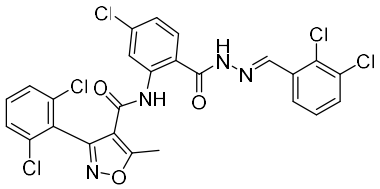

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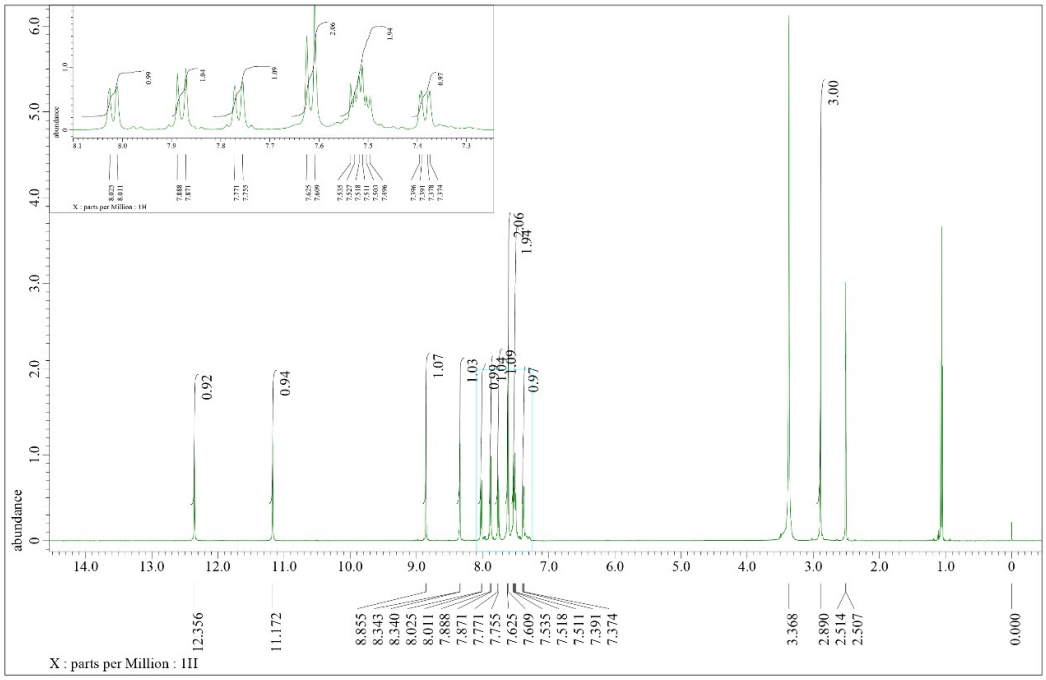

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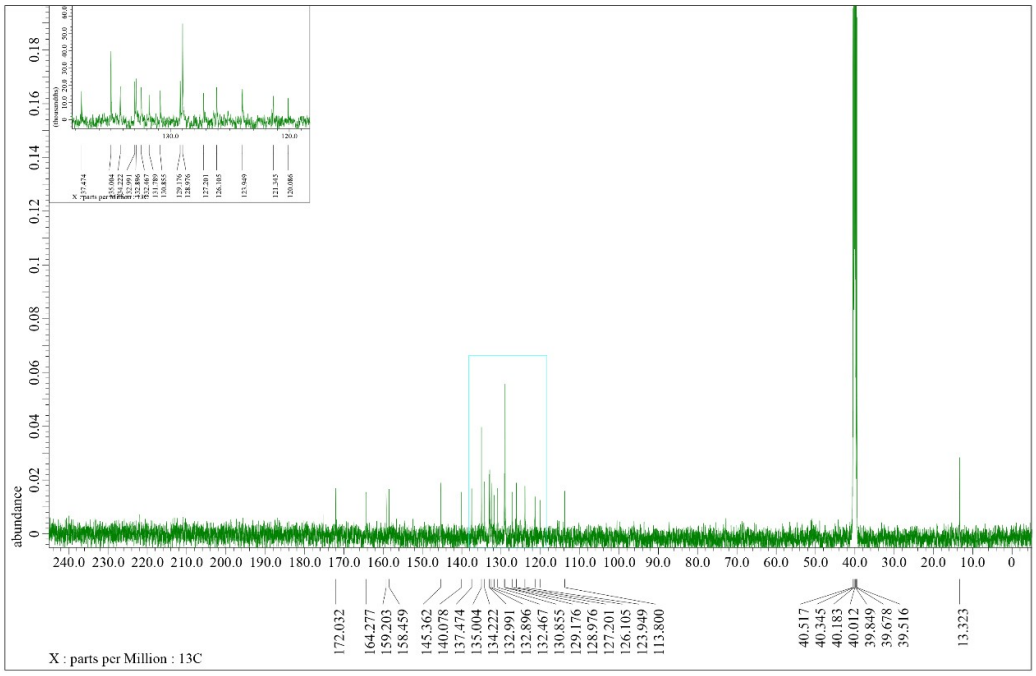

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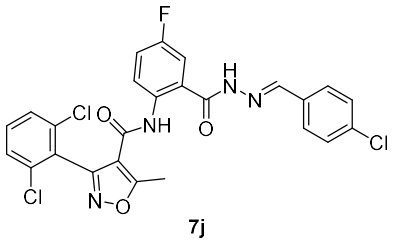

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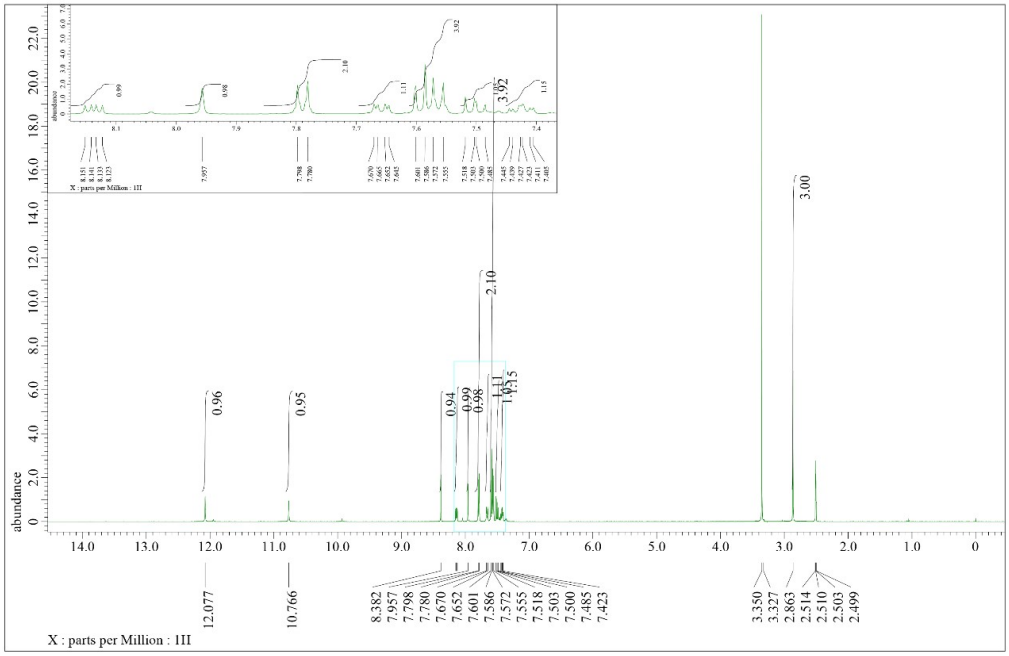

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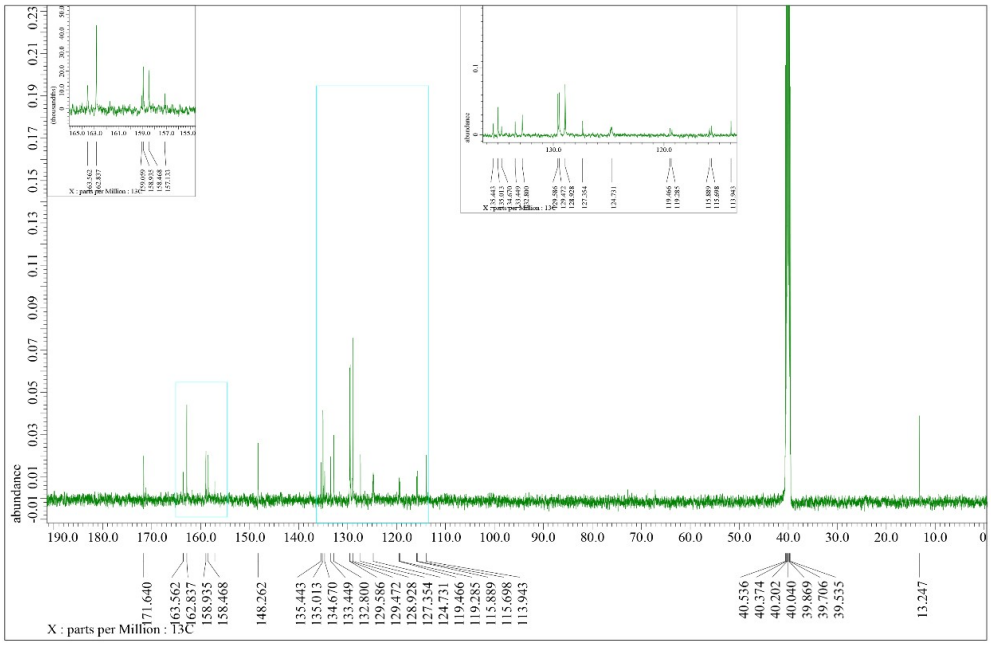

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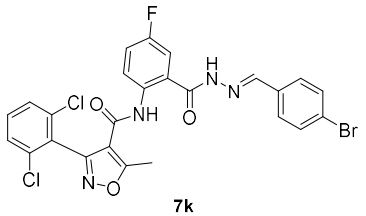
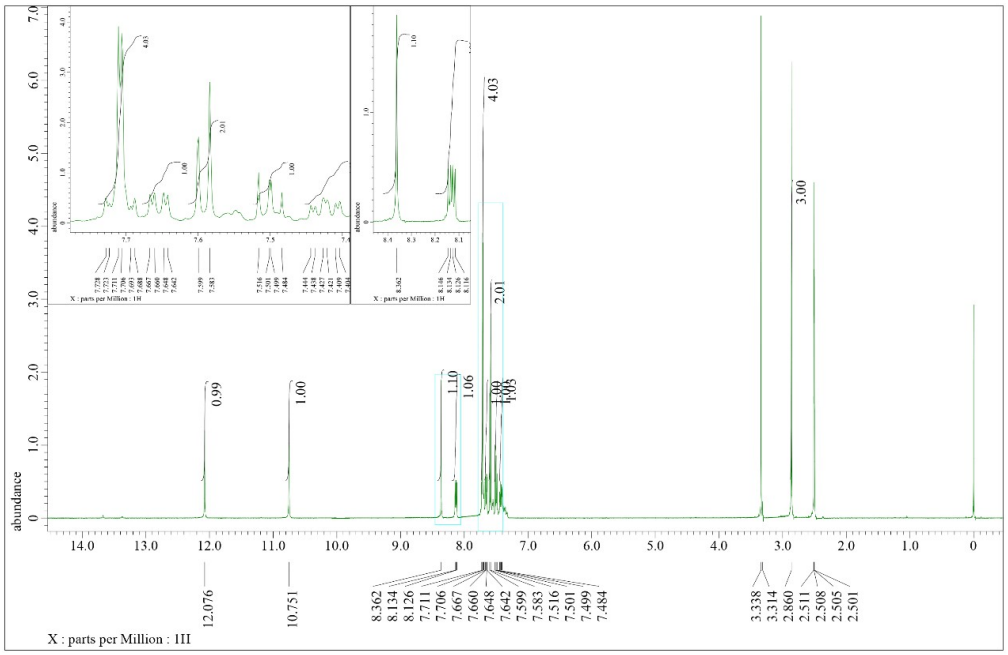


7k



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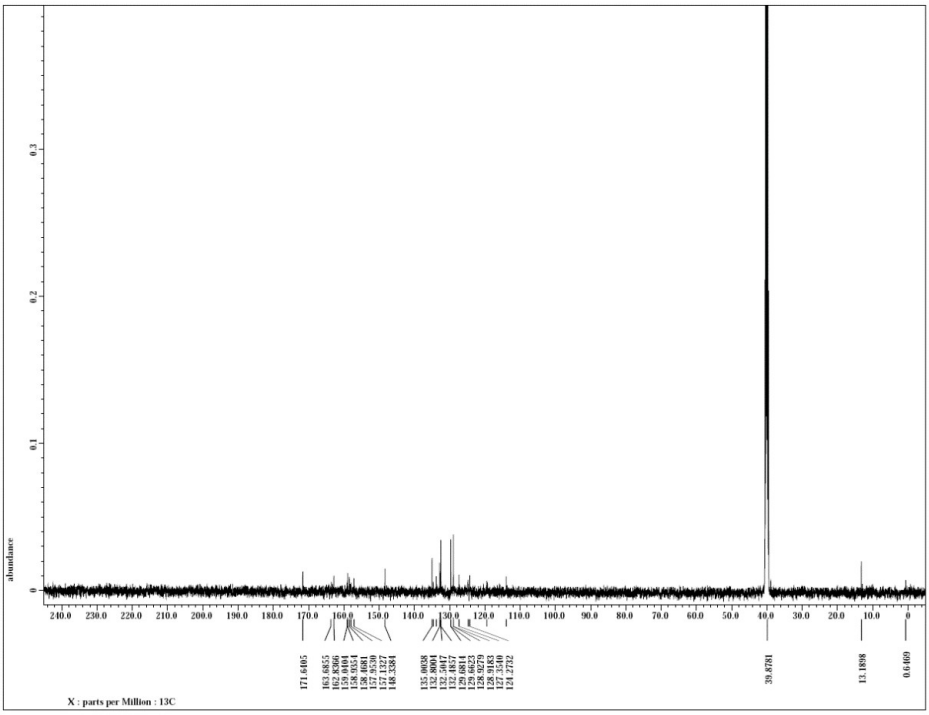

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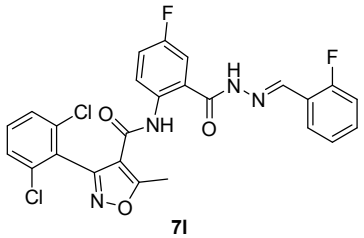
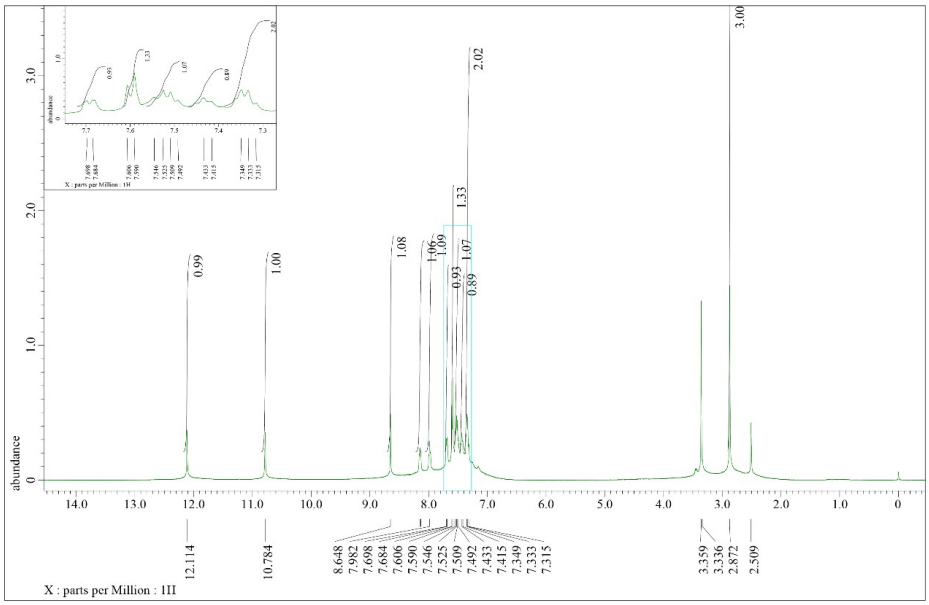


7l



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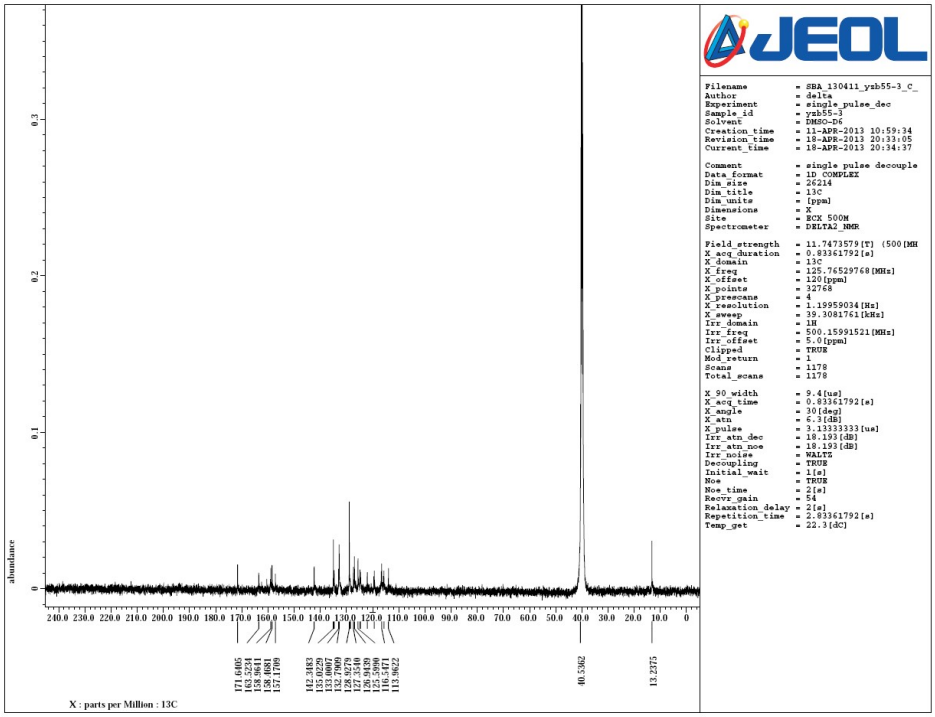

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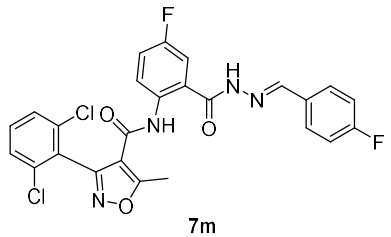
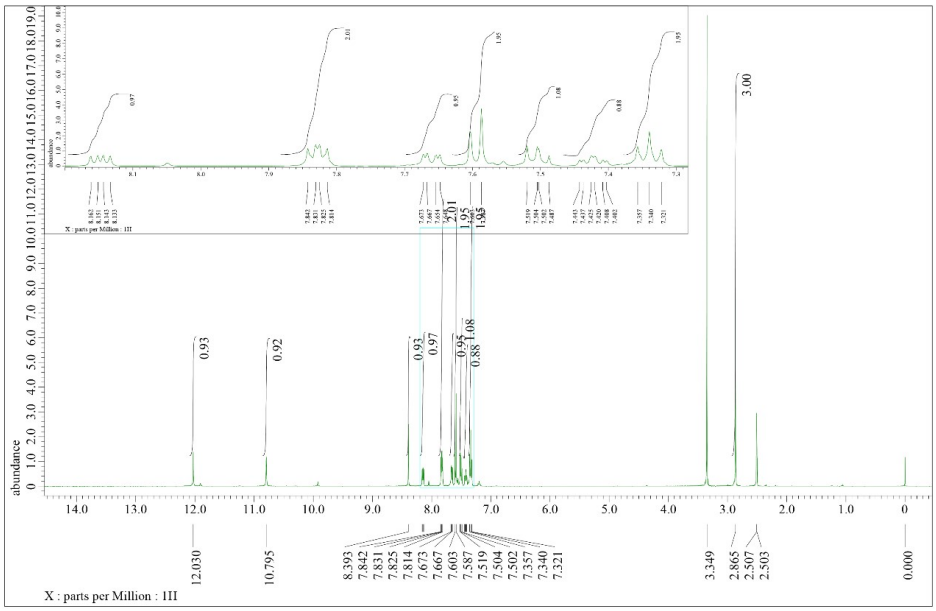
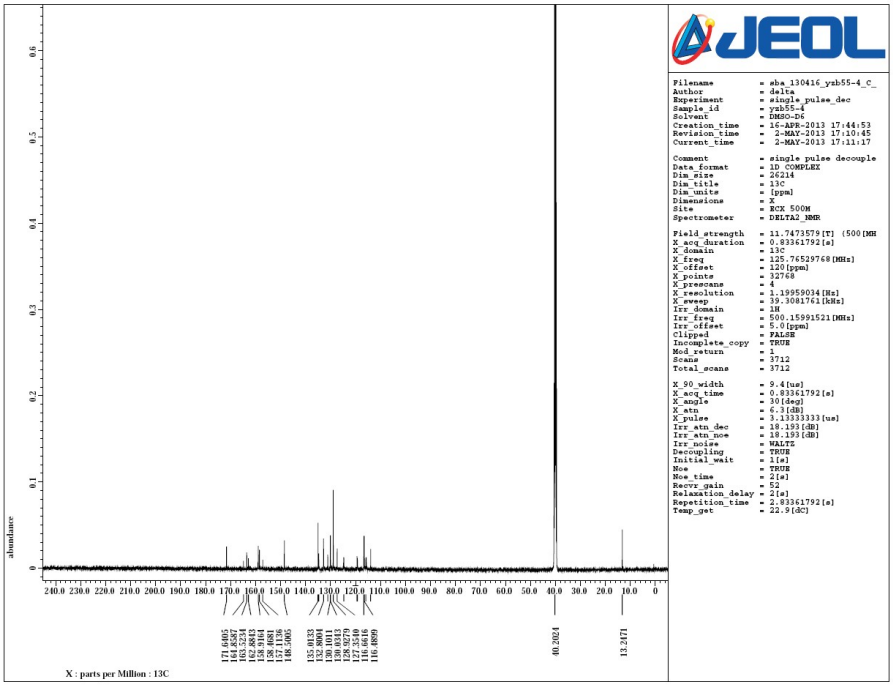


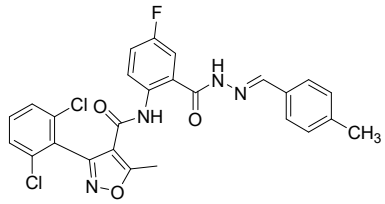
7m



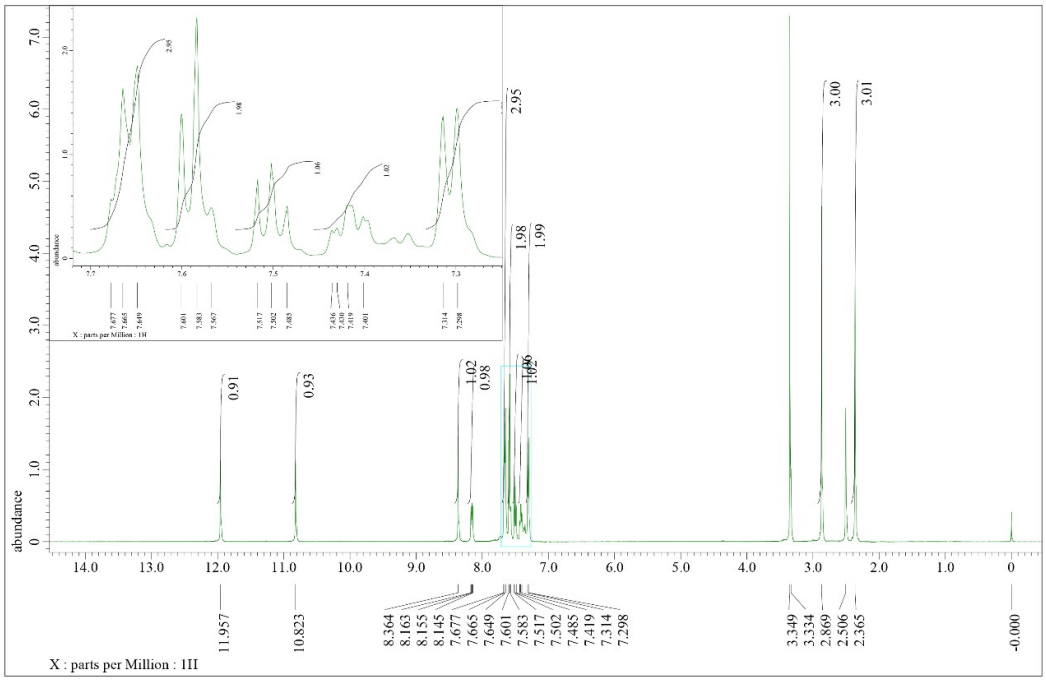
^{1}H NMR of Compound 7m



^{13}C NMR of Compound 7m



7n



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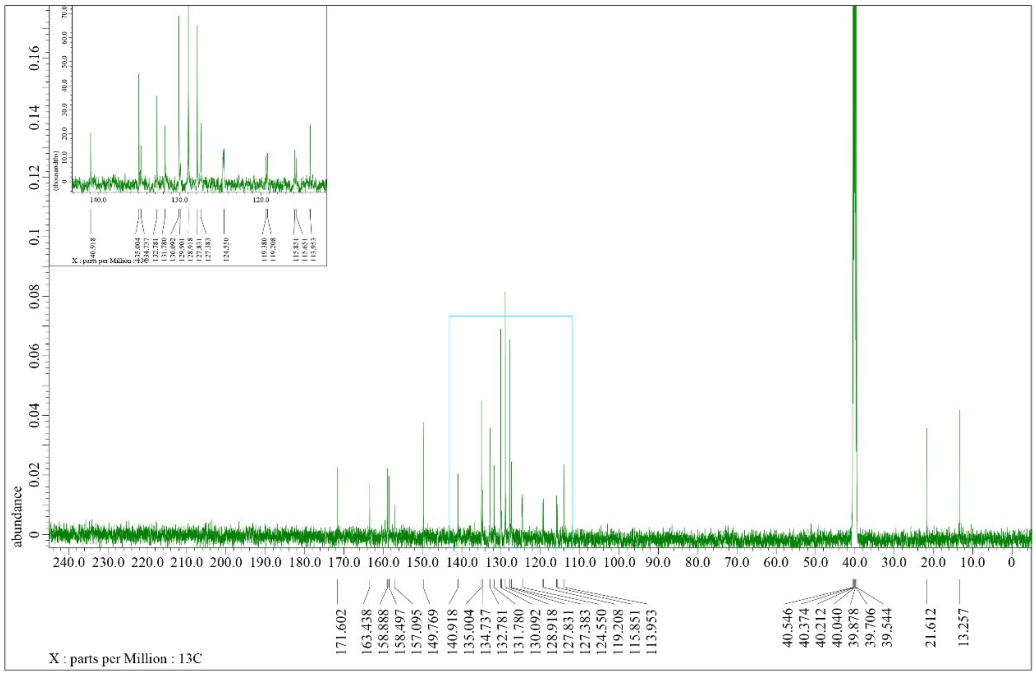

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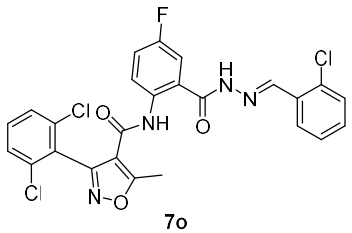
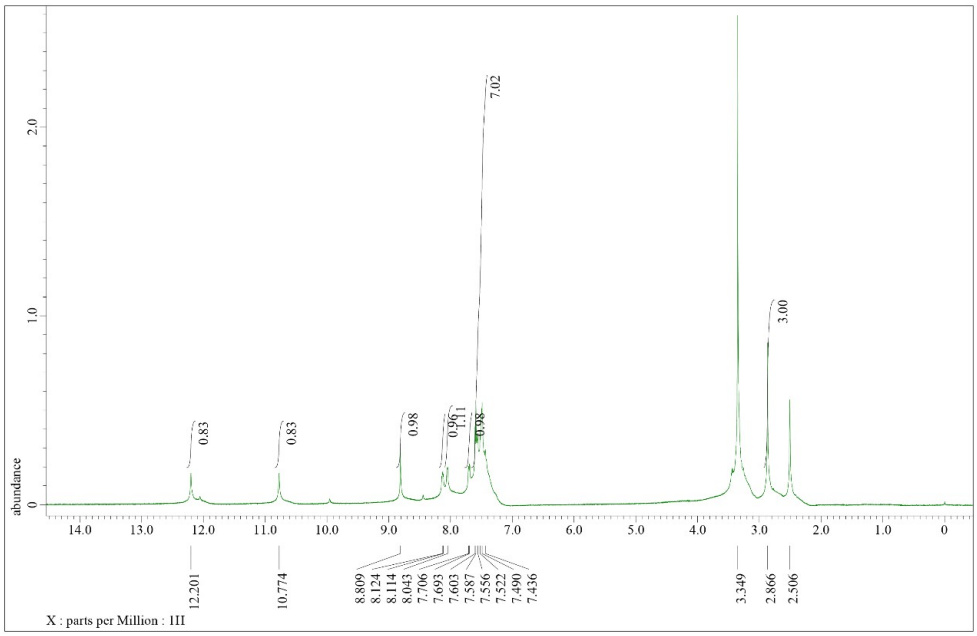
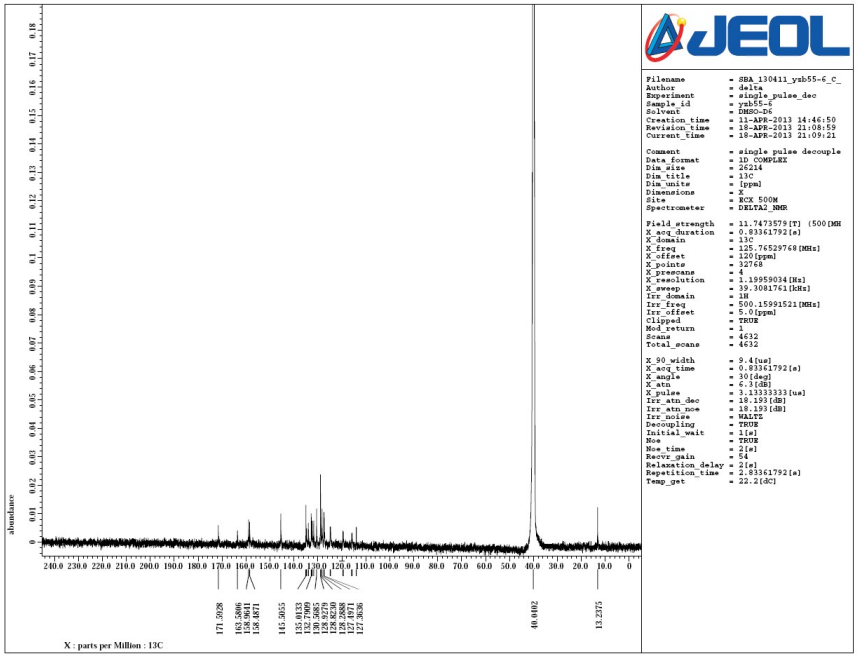


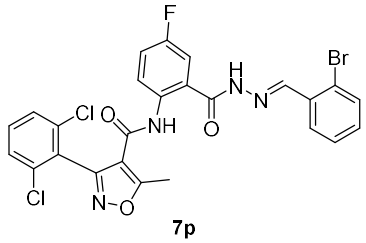
7o



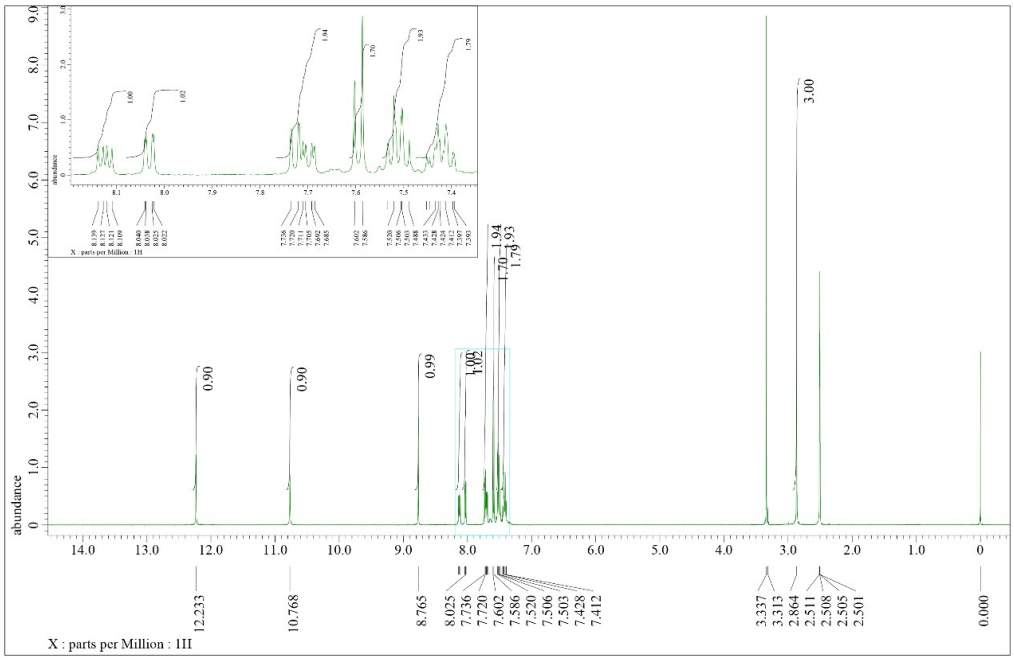
^{1}H NMR of Compound7o



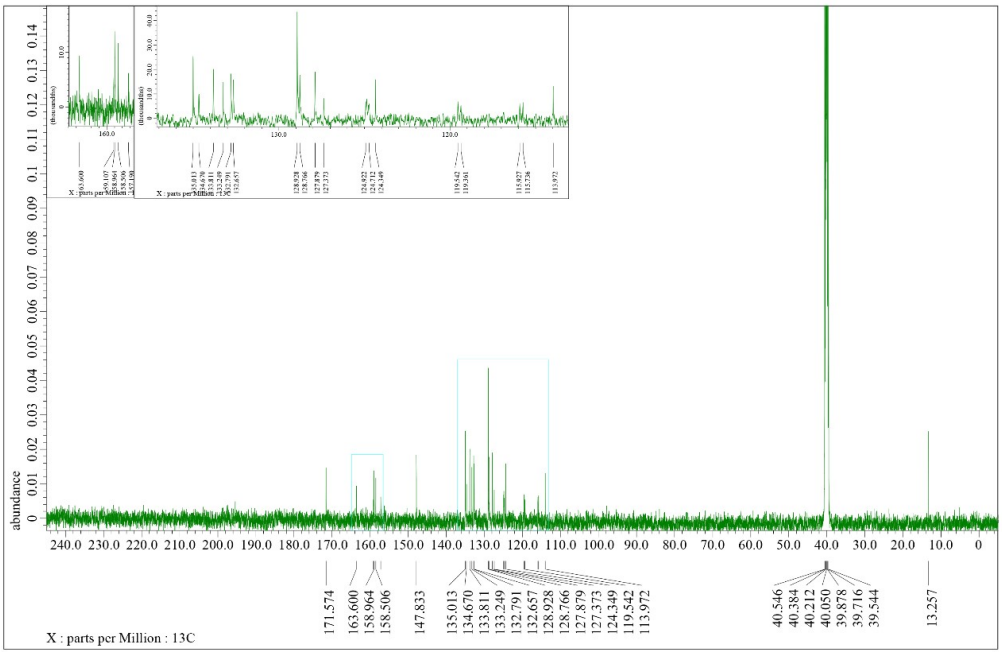
^{13}C NMR of Compound 7o



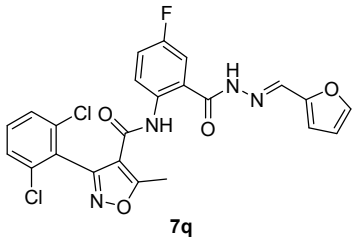
7p



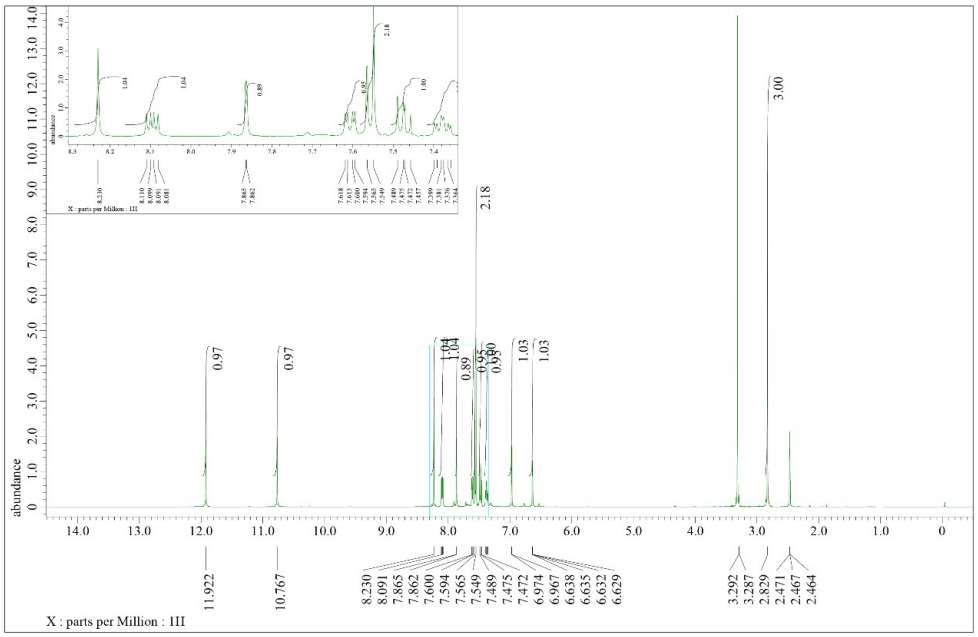
^{1}H NMR of Compound 7p



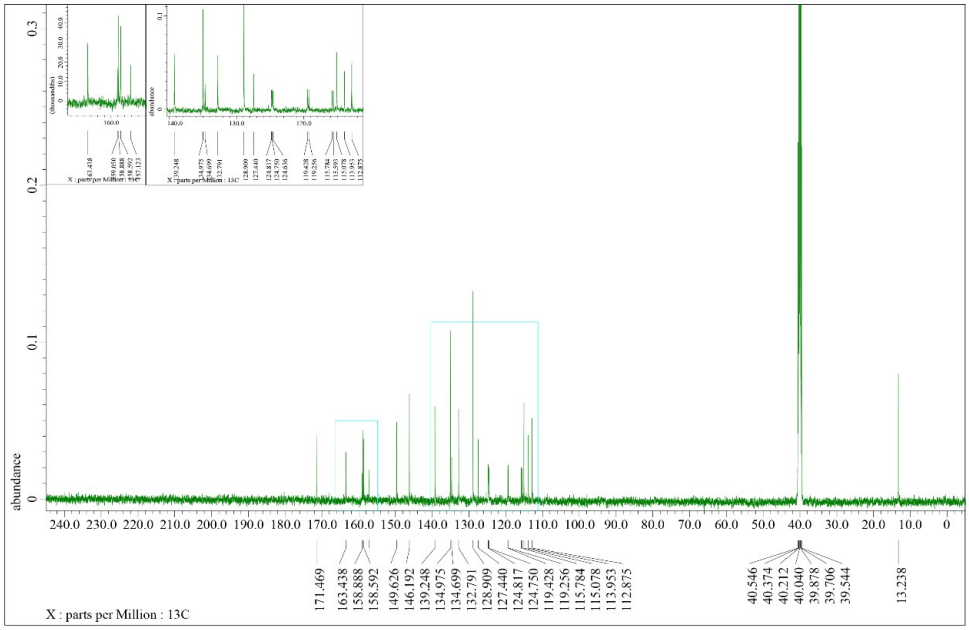
^{13}C NMR of Compound 7p



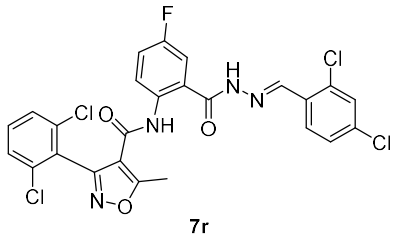
7q



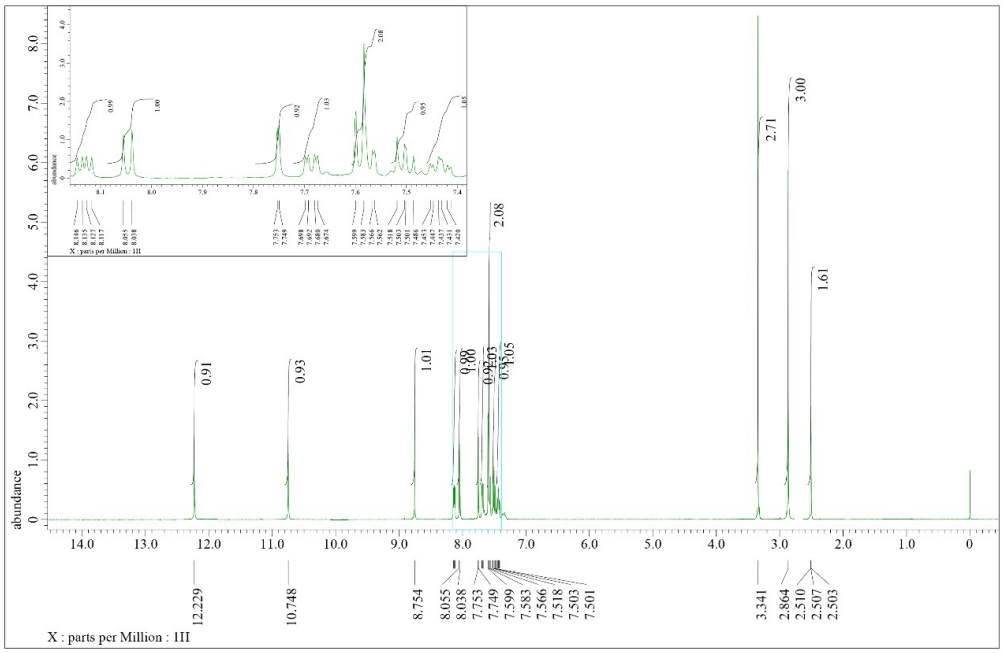
^{1}H NMR of Compound 7q



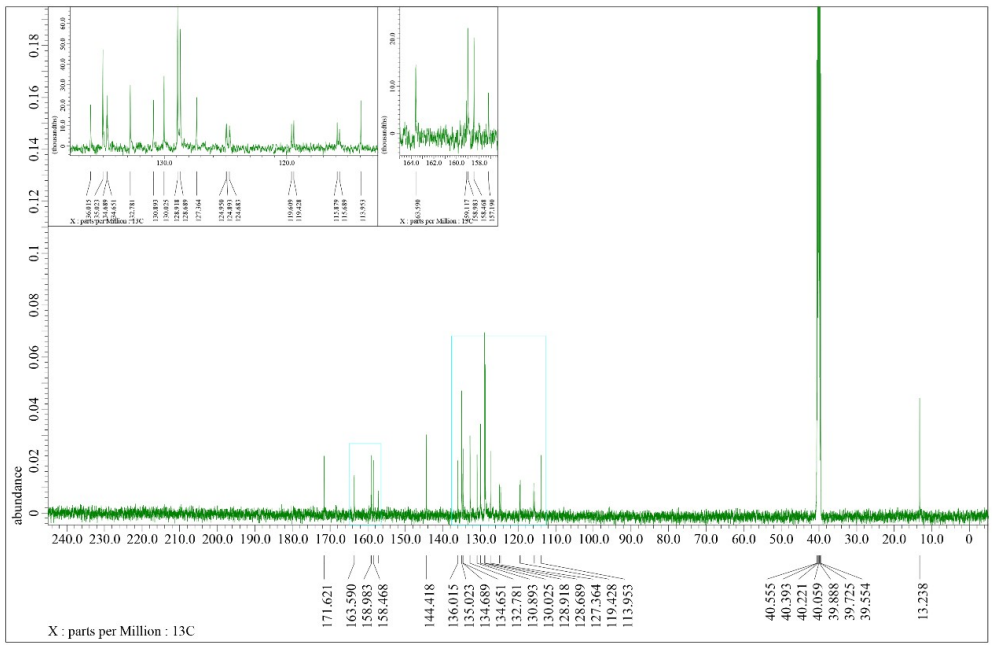
^{13}C NMR of Compound 7q



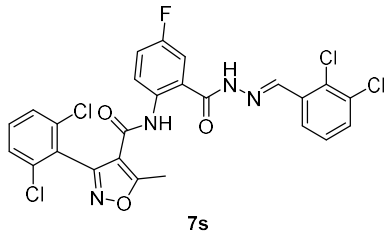
7r



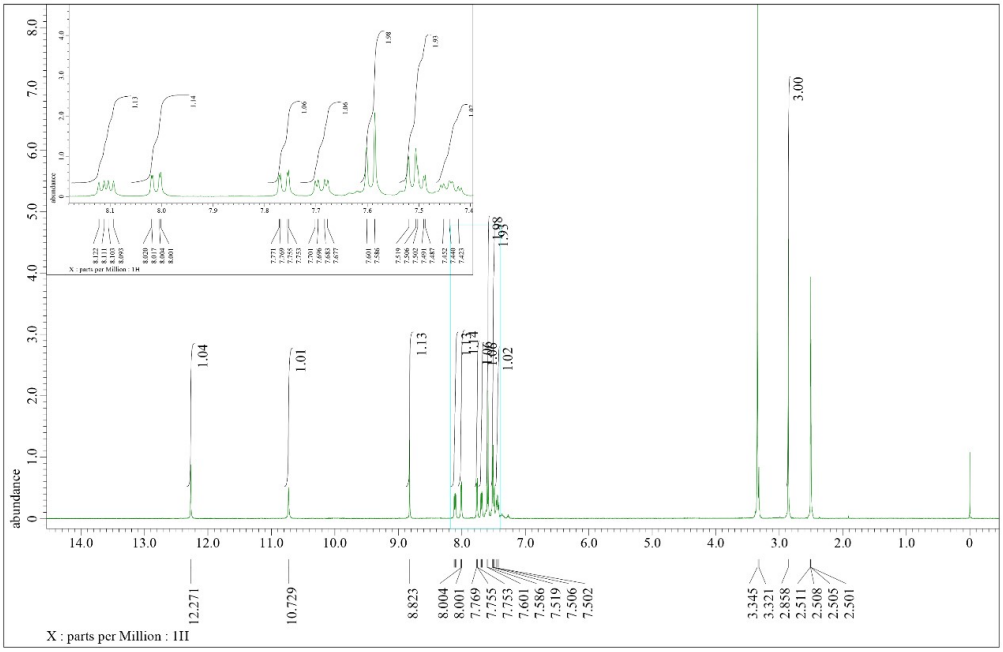
^{1}H NMR of Compound 7r



^{13}C NMR of Compound 7r



7s



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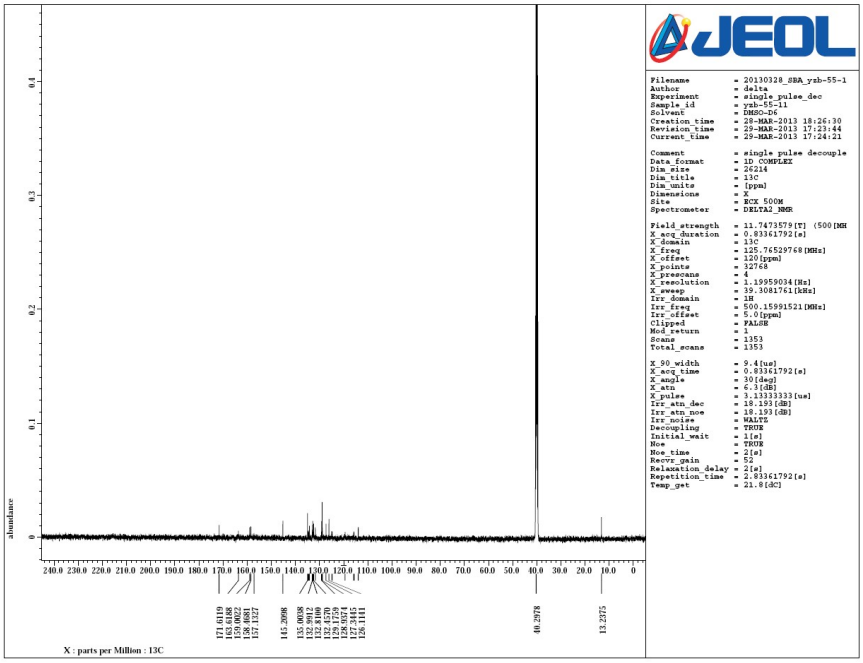

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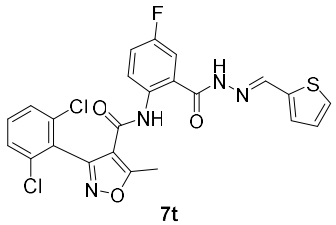
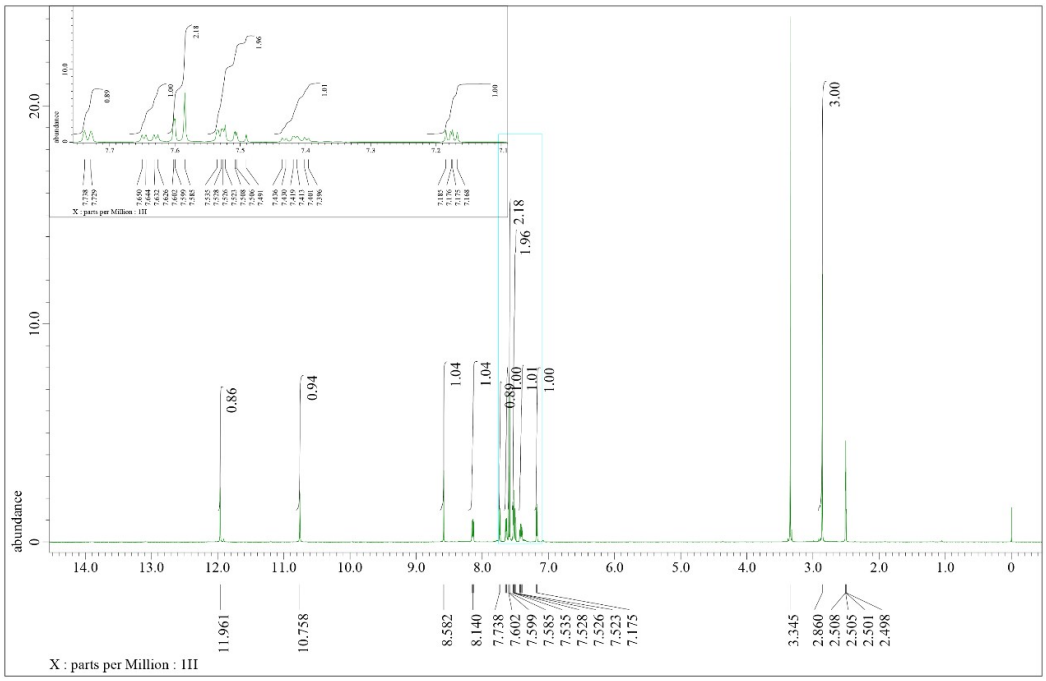
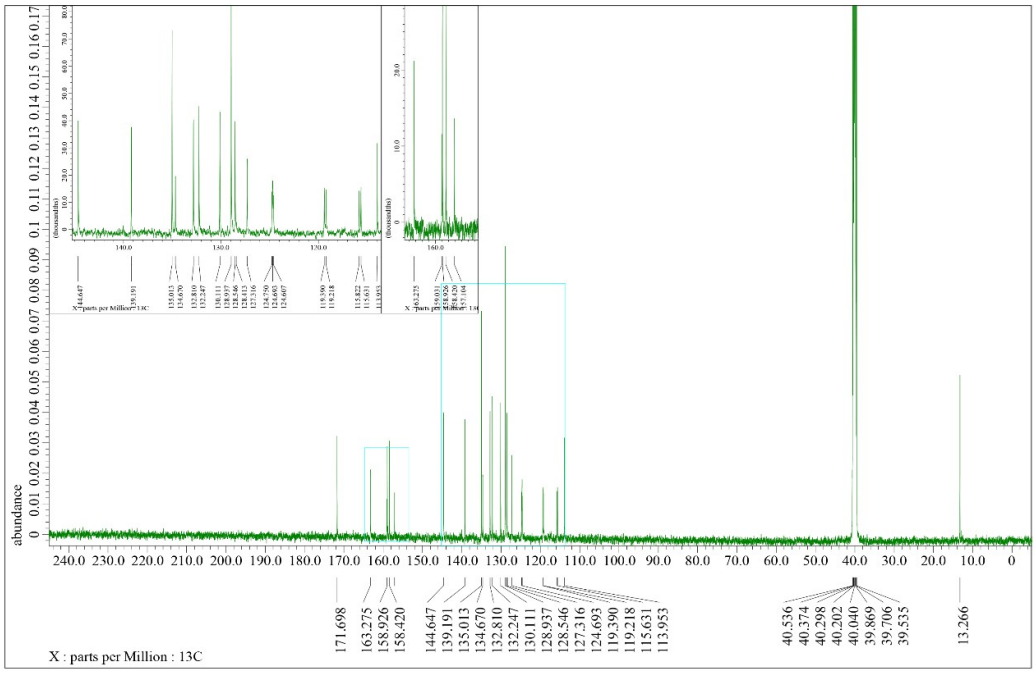


7t



^{1}H NMR of Compound 7t



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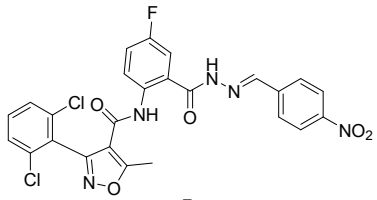
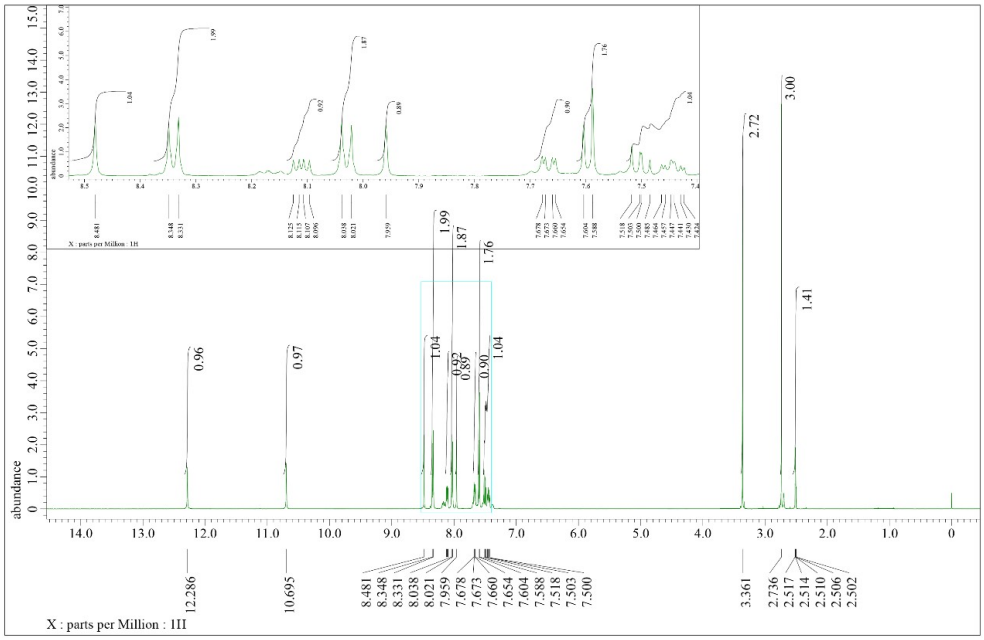


7u



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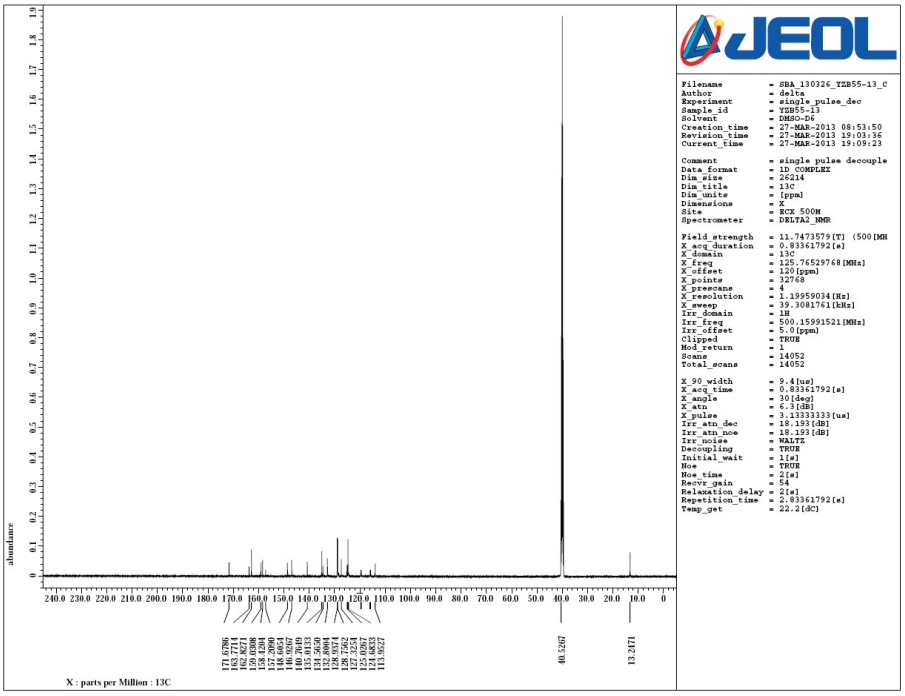

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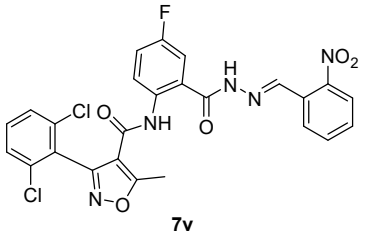
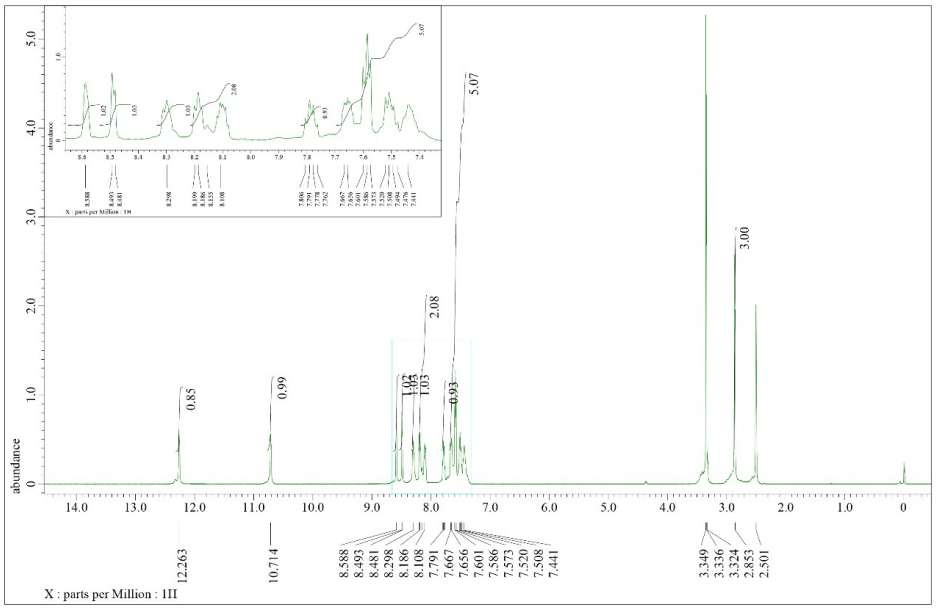
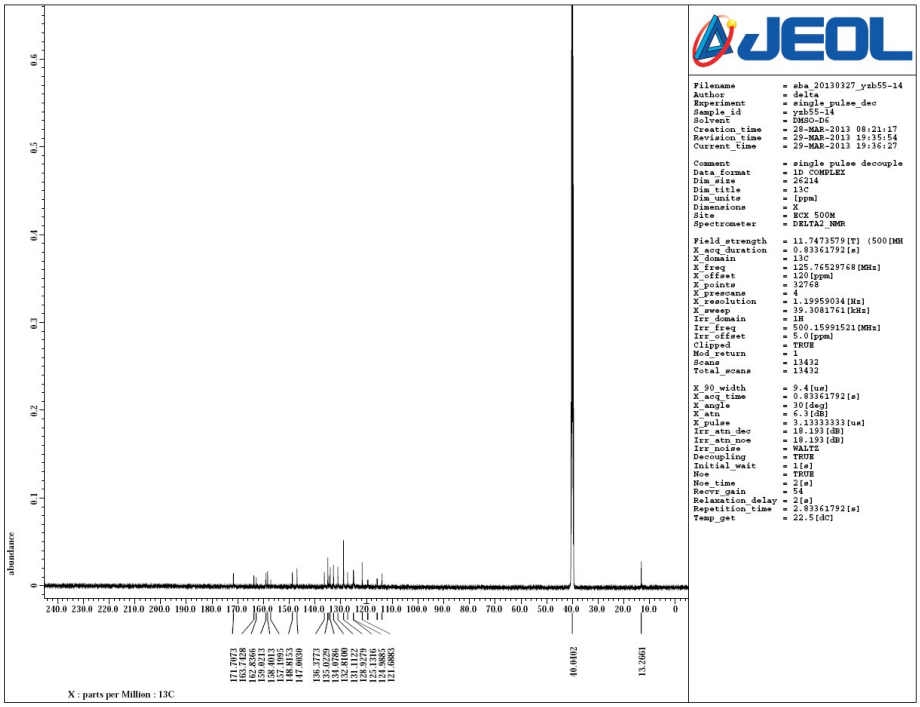


7v



^{1}H NMR of Compound 7v



^{13}C NMR of Compound 7v