

## *Supplementary Material*

### **Crystal structure, quantum chemical insights, and molecular docking studies Naryl-2-(*N*-disubstituted) acetamide compounds: potential inhibitors for neurodegenerative enzymes.**

**Lorena Camargo-Ayala<sup>1,\*</sup>, Mauricio Bedoya<sup>2,3</sup>, Luis Prent-Peñaloza<sup>4</sup>, Efraín Polo-Cuadrado<sup>1</sup>, Edison Osorio<sup>5</sup>, Iván Brito<sup>6</sup>, Gerzon E. Delgado<sup>6,7</sup>, Wendy González<sup>8,9</sup> and Margarita Gutierrez<sup>2,\*</sup>.**

<sup>1</sup> Laboratorio Síntesis Orgánica y Actividad Biológica (LSO-Act-Bio), Instituto de Química de Recursos Naturales, Universidad de Talca, Casilla 747, Talca 3460000, Chile.

<sup>2</sup> Centro de Investigación de Estudios Avanzados del Maule (CIEAM), Vicerrectoría de Investigación y Postgrado, Universidad Católica del Maule, Talca 3466706, Chile.

<sup>3</sup> Laboratorio de Bioinformática y Química Computacional (LBQC), Departamento de Medicina Traslacional, Facultad de Medicina, Universidad Católica del Maule, Talca 3466706, Chile.

<sup>4</sup> Departamento de Ciencias Químicas, Facultad de Ciencias Exactas, Universidad Andrés Bello, Quillota 980, Viña del Mar, Chile.

<sup>5</sup> Facultad de Ciencias Naturales y Matemáticas, Universidad de Ibagué, Carrera 22 Calle 67, Ibagué 730001, Colombia

<sup>6</sup> Departamento de Química, Facultad de Ciencias Básicas, Universidad de Antofagasta, Avda., Universidad de Antofagasta, Campus Coloso, Antofagasta 02800, Chile.

<sup>7</sup> Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida 5101, Venezuela.

<sup>8</sup> Centro de Bioinformática y Simulaciones Moleculares (CBSM), Universidad de Talca, Casilla 747, Talca 3460000, Chile.

<sup>9</sup> Facultad de Ingeniería and Millennium Nucleus of Ion Channels-Associated Diseases (MiNICAD), Universidad de Talca, 3460000 Talca, Chile.

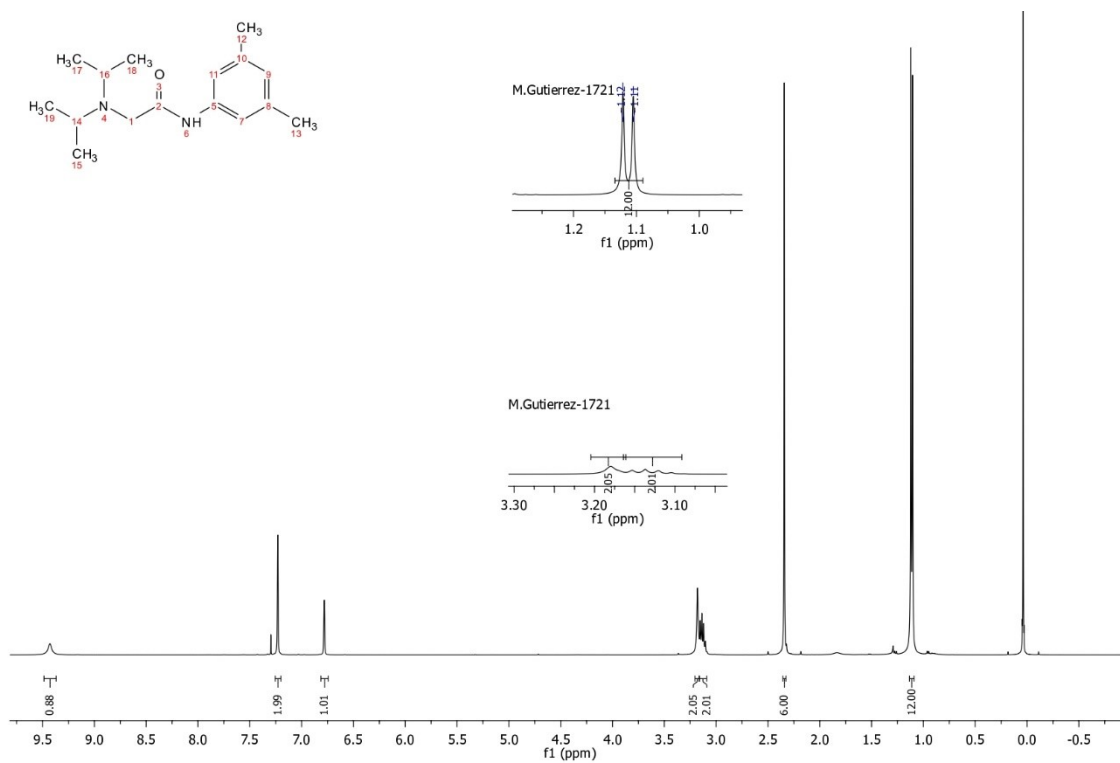
**\*Correspondence:**

Margarita Gutiérrez  
([mgutierrez@utalca.cl](mailto:mgutierrez@utalca.cl))

Lorena Camargo-Ayala  
([loreca17@gmail.com](mailto:loreca17@gmail.com))

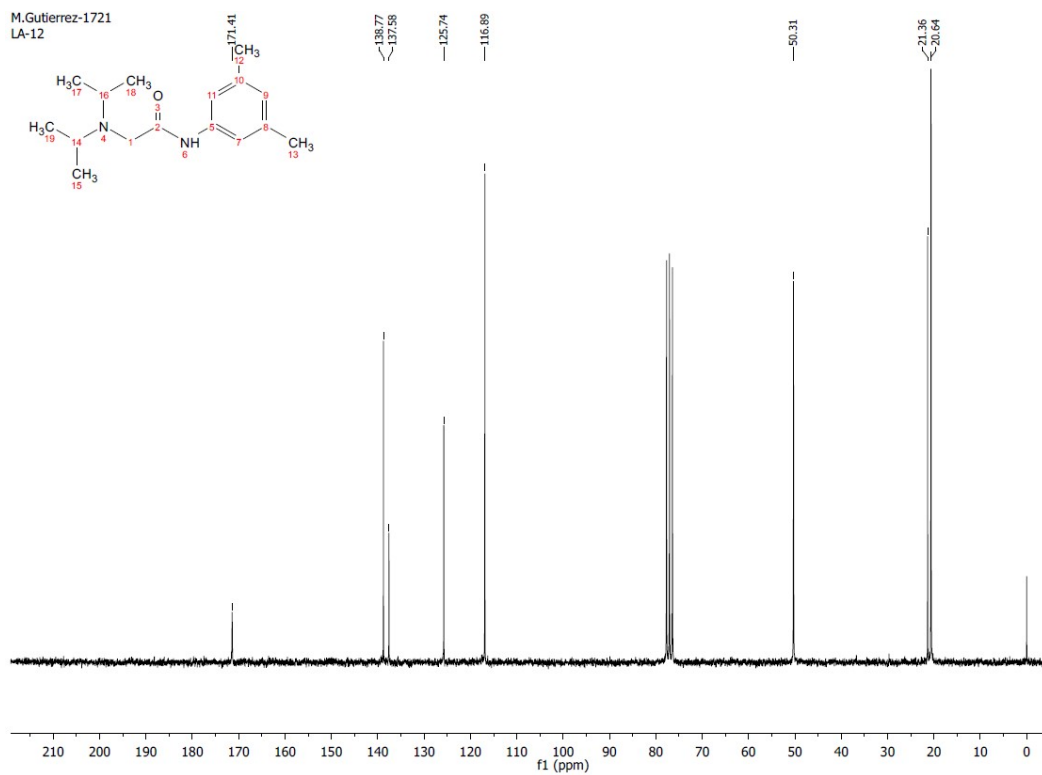
# 1 Supplementary Data

## 1.1 Characterization data

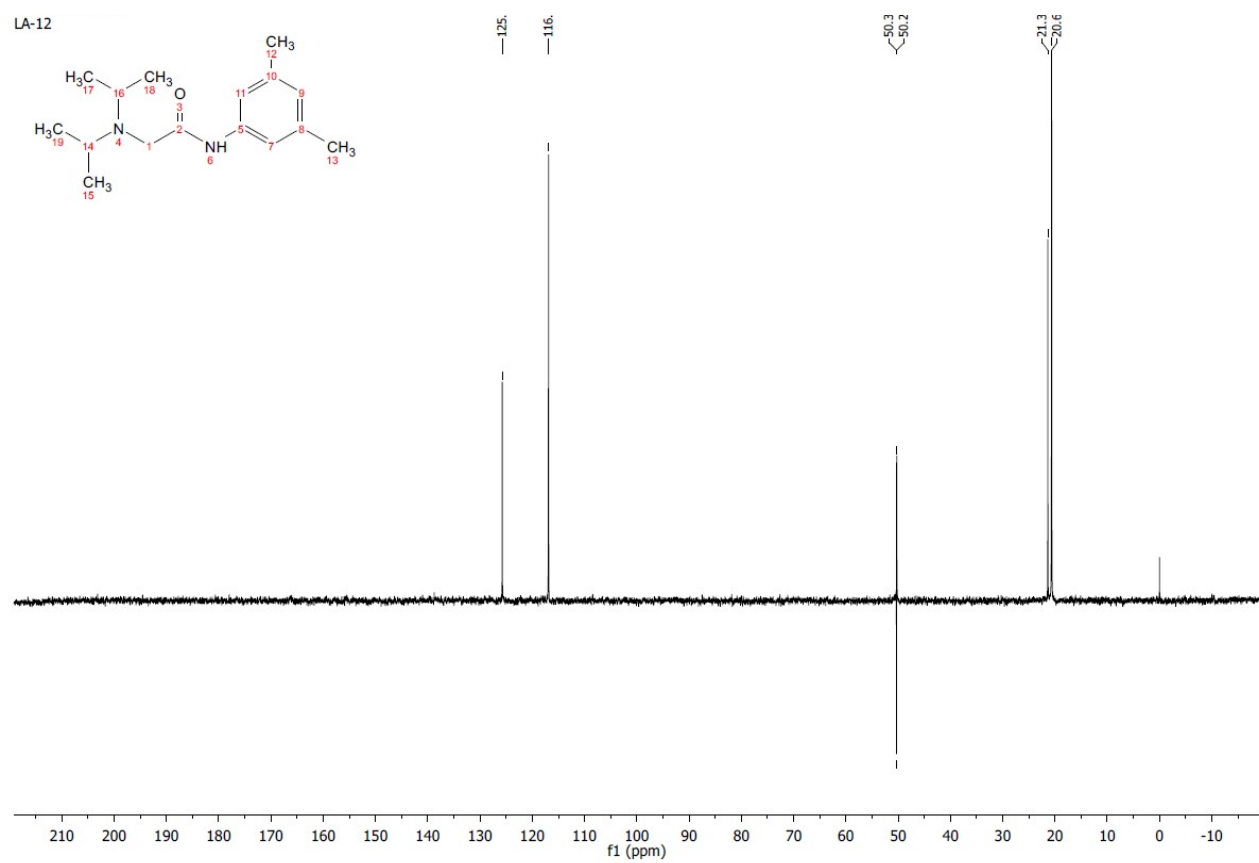


**Fig S 1.**  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ) of 2-(diisopropylamino)-*N*-(3,5-dimethylphenyl)acetamide (5a)

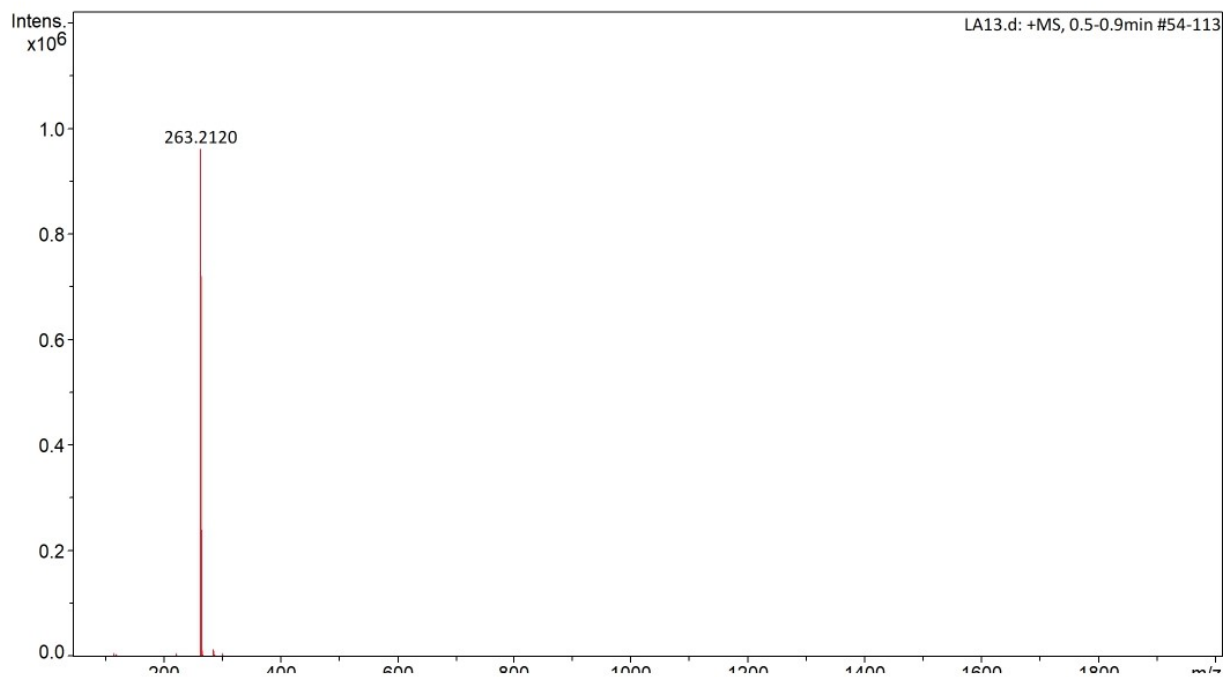
M.Gutierrez-1721  
LA-12



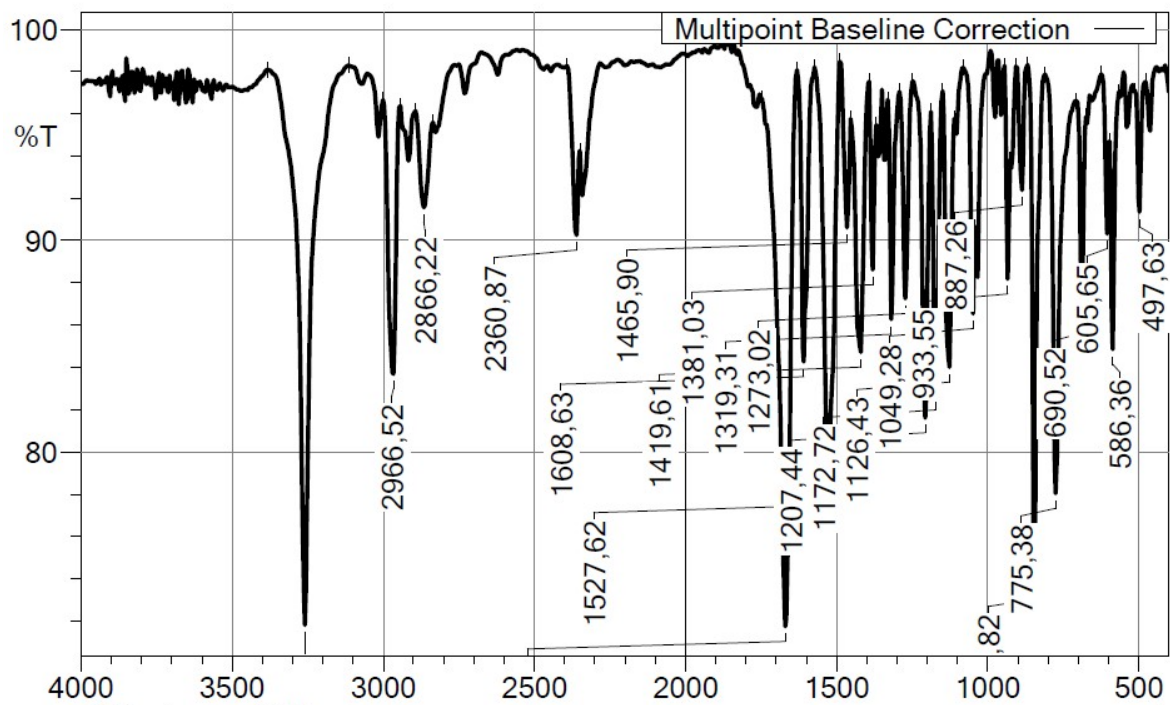
**Fig S 2.** <sup>13</sup>C- NMR (100 MHz, CDCl<sub>3</sub>) of 2-(diisopropylamino)-*N*-(3,5-dimethylphenyl)acetamide (5a)



**Fig S 3.** DEPT-135 (CDCl<sub>3</sub>) of 2-(diisopropylamino)-*N*-(3,5-dimethylphenyl)acetamide (5a)



**Fig S 4.** HRMS (ESI, m/z) of 2-(diisopropylamino)-*N*-(3,5-dimethylphenyl)acetamide (5a)



**Fig S 5.** IR of of 2-(diisopropylamino)-*N*-(3,5-dimethylphenyl)acetamide (5a)

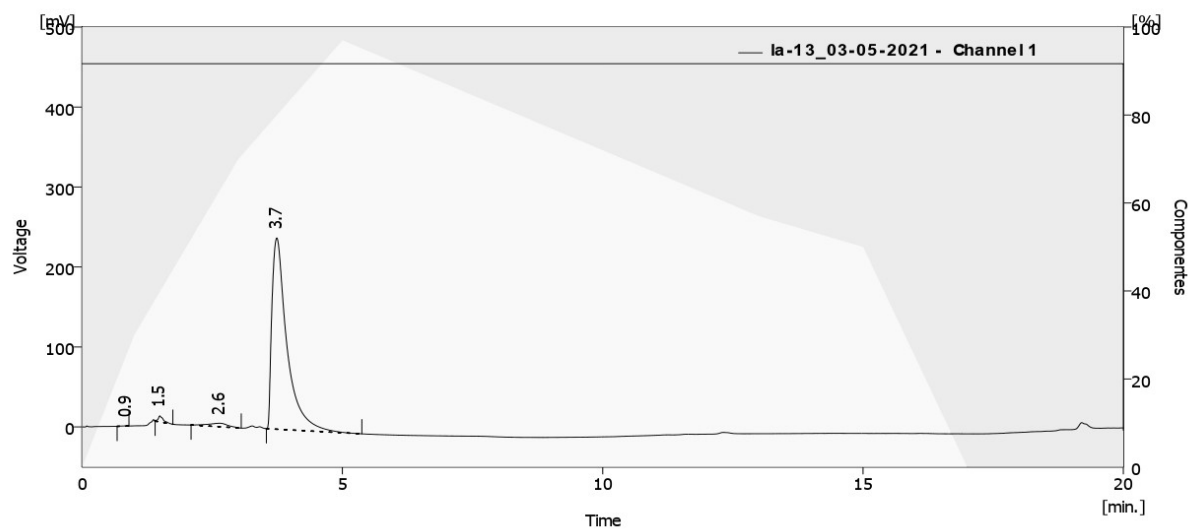
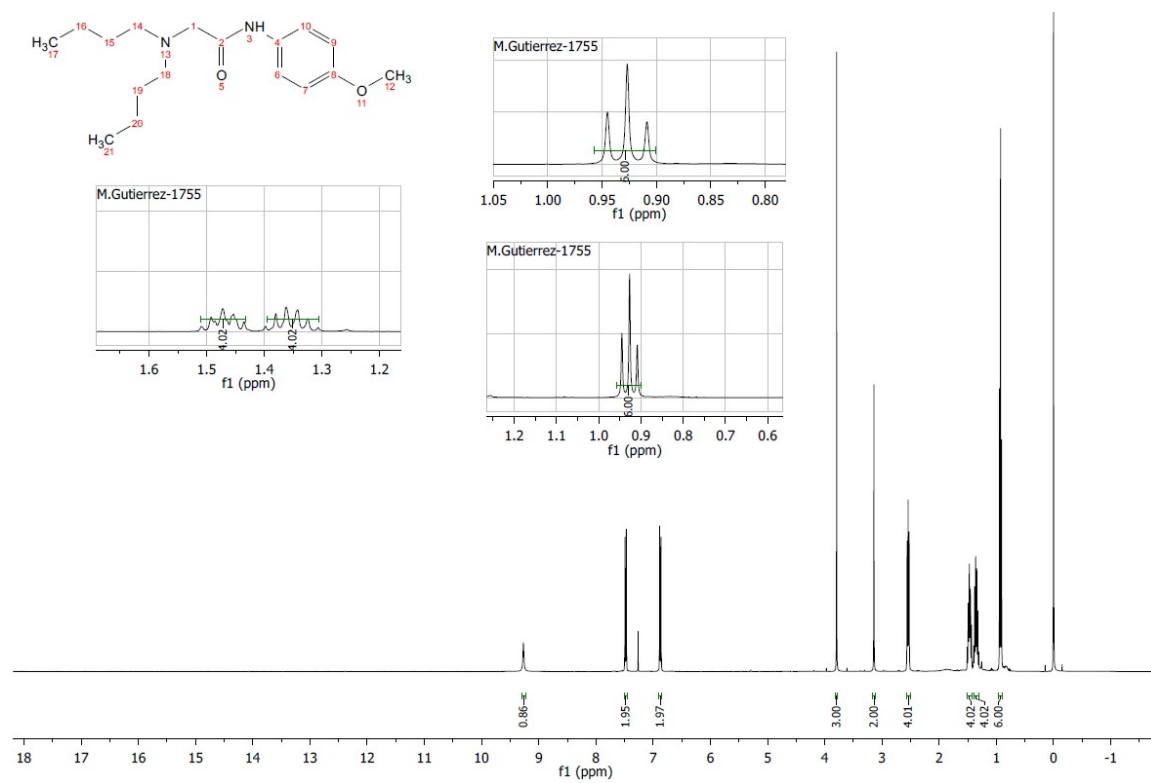


Tabla de resultados (Sin cal. - la-13\_03-05-2021 - Channel 1)

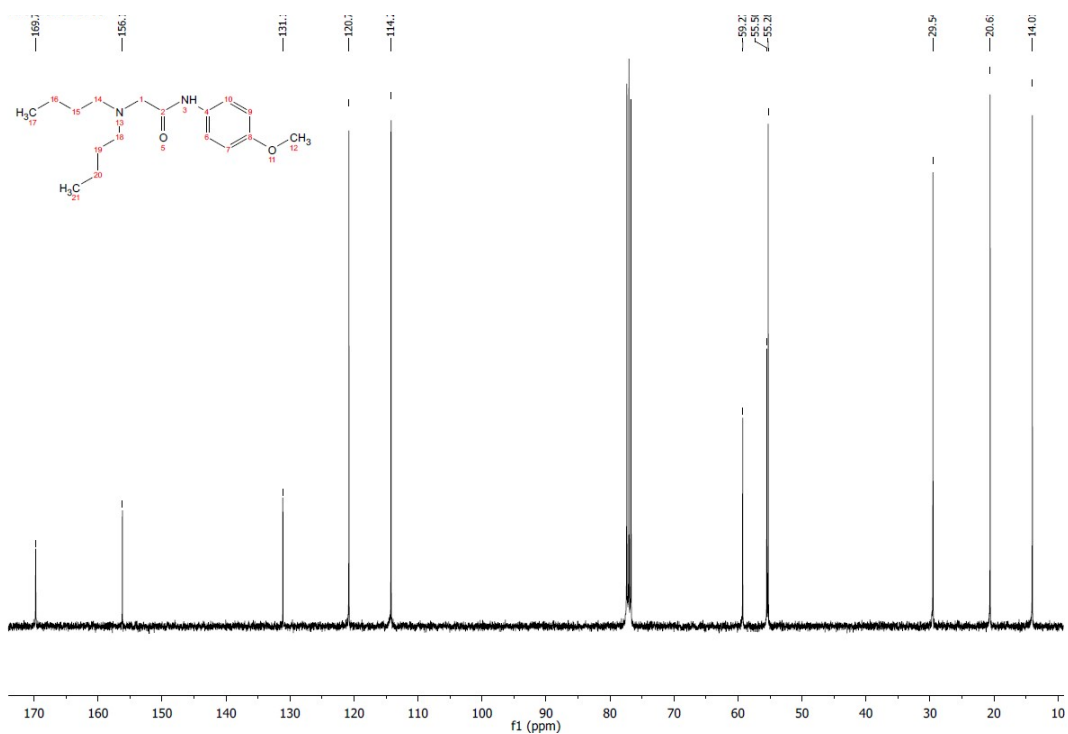
	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	0.857	2.681	0.226	0.1	0.1	0.12	1000	
2	1.493	52.462	7.620	1.1	3.0	0.09	654	
3	2.637	115.516	4.425	2.3	1.8	0.63	647	
4	3.740	4804.234	239.256	96.6	95.1	0.28	935	
	Total	4974.893	251.528	100.0	100.0			

**Fig S 6.** HPLC of 2-(diisopropylamino)-N-(3,5-dimethylphenyl)acetamide (5a)

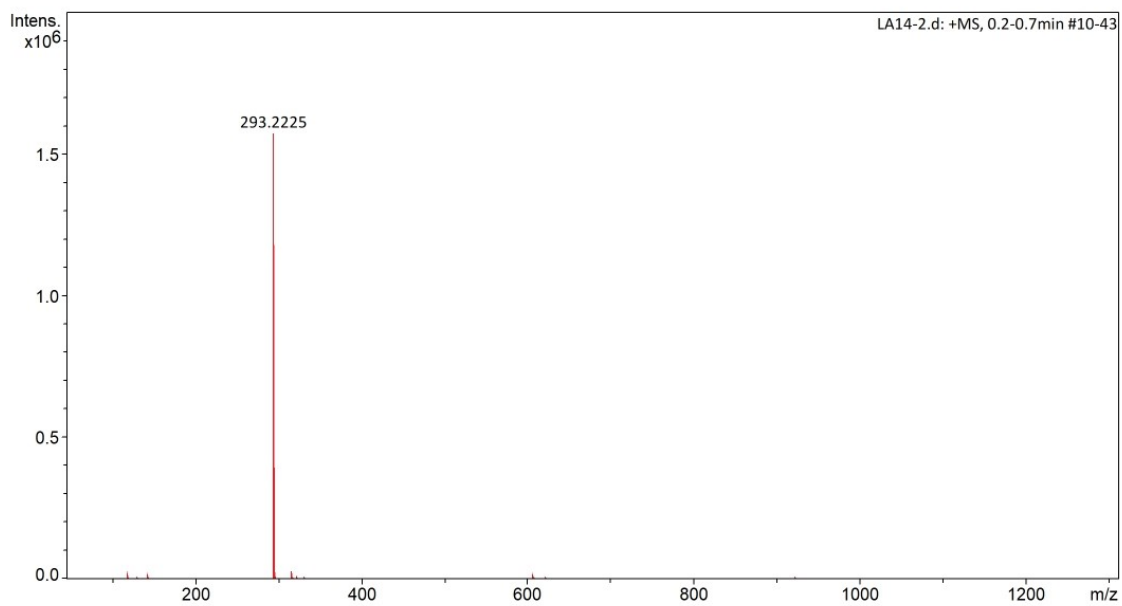


**Fig S 7.** <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) of 2-(dibutylamino)-*N*-(4-methoxyphenyl)acetamide (5b)

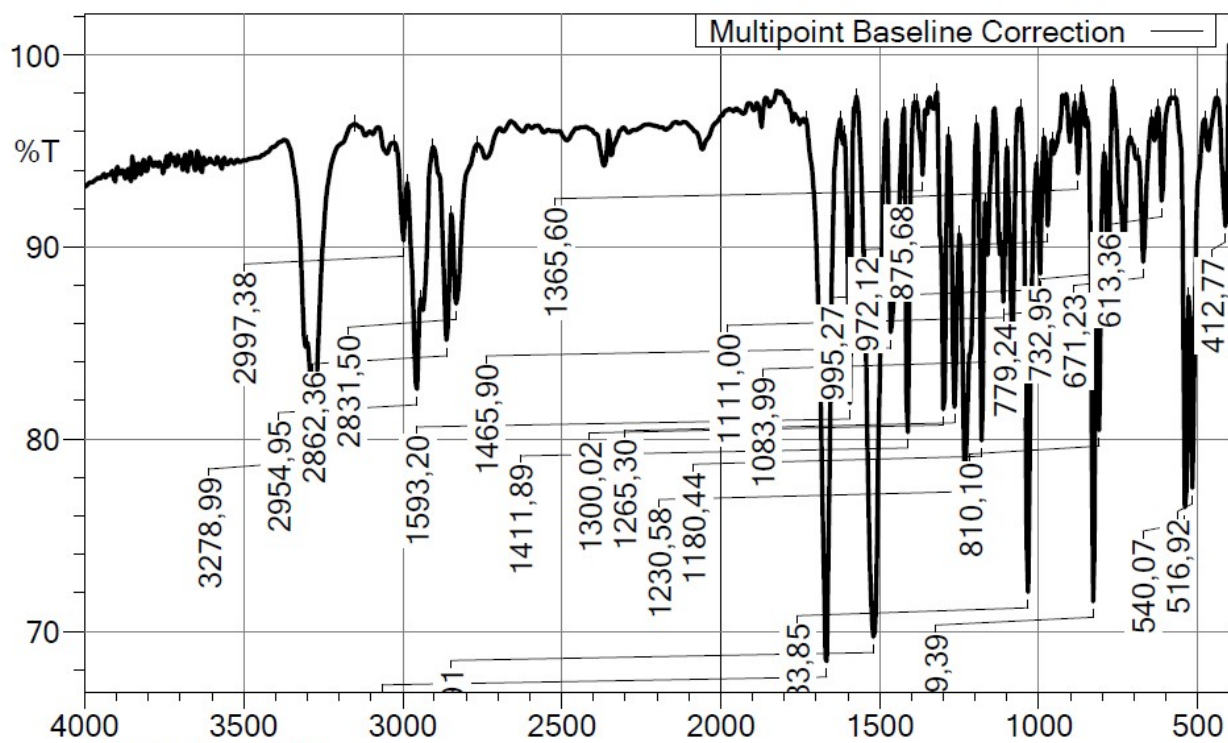




**Fig S 8.** <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>) of 2-(dibutylamino)-*N*-(4-methoxyphenyl)acetamide (5b)



**Fig S 9.** HRMS (ESI, m/z) of 2-(dibutylamino)-*N*-(4-methoxyphenyl)acetamide (5b)



**Fig S 10.** IR of 2-(dibutylamino)-*N*-(4-methoxyphenyl)acetamide (5b)

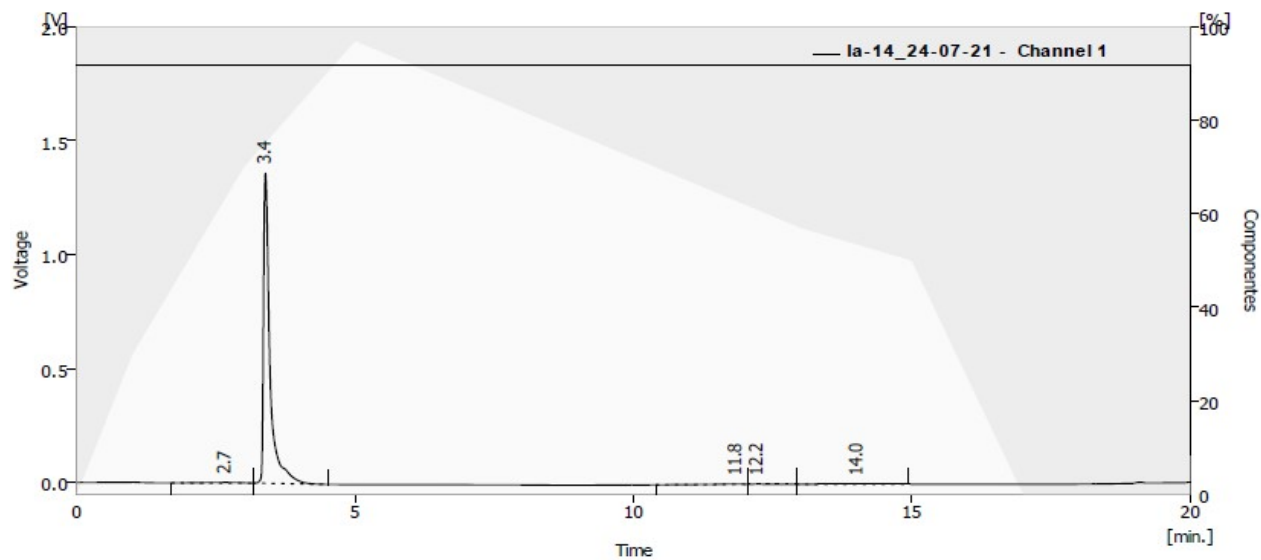
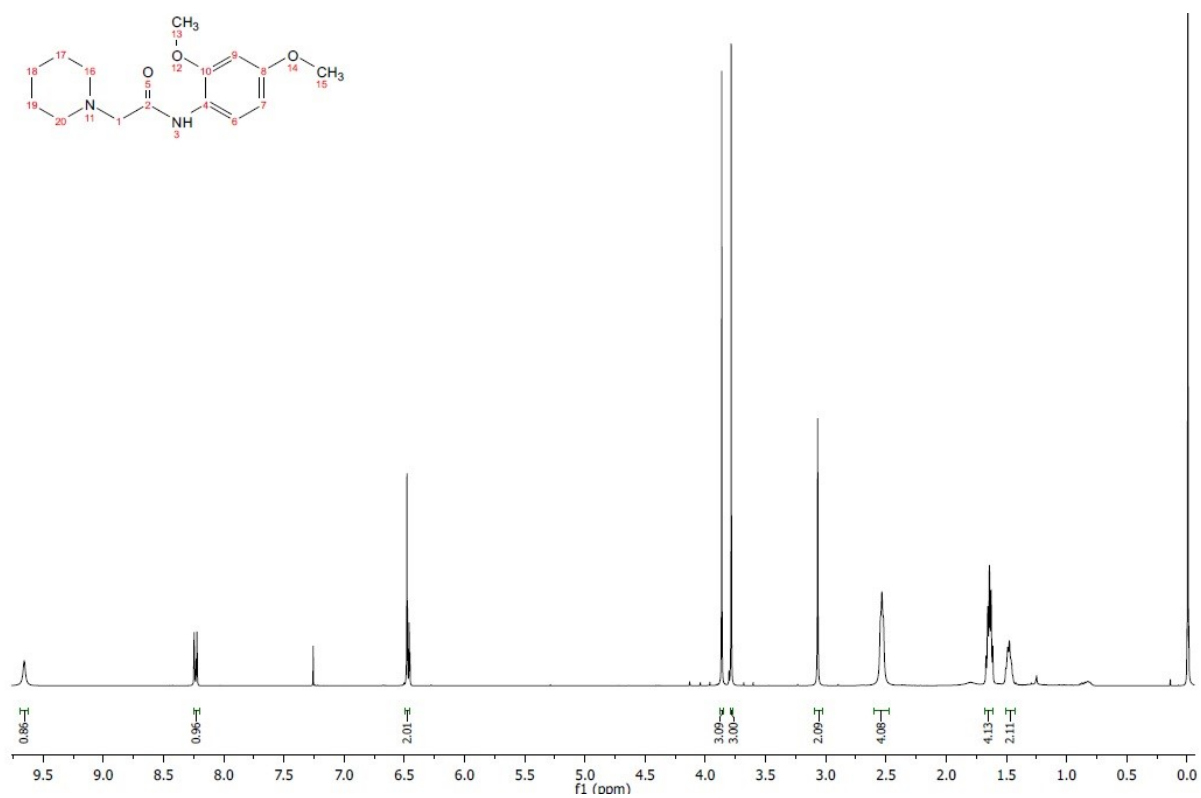


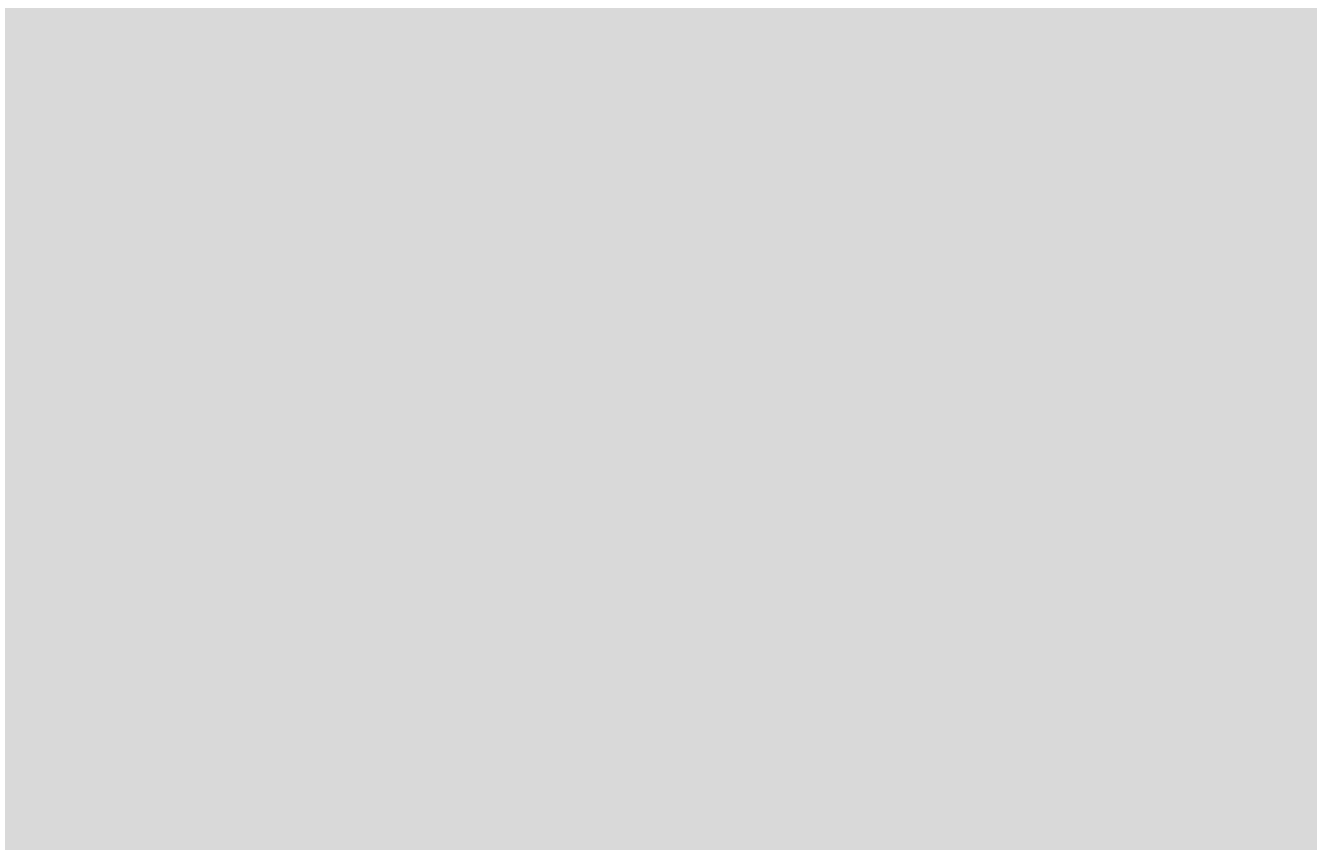
Tabla de resultados (Sin cal. - la-14\_24-07-21 - Channel 1)

	Tiempo de retenc. [min]	Area [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	2.673	123.030	2.473	1.1	0.2	0.87	683	
2	3.393	11128.945	1360.230	98.2	99.6	0.10	512	
3	11.843	53.257	1.543	0.5	0.1	0.38	1000	
4	12.227	13.285	0.658	0.1	0.0	0.27	1000	
5	14.020	17.816	0.275	0.2	0.0	0.86	1000	
	Total	11336.333	1365.180	100.0	100.0			

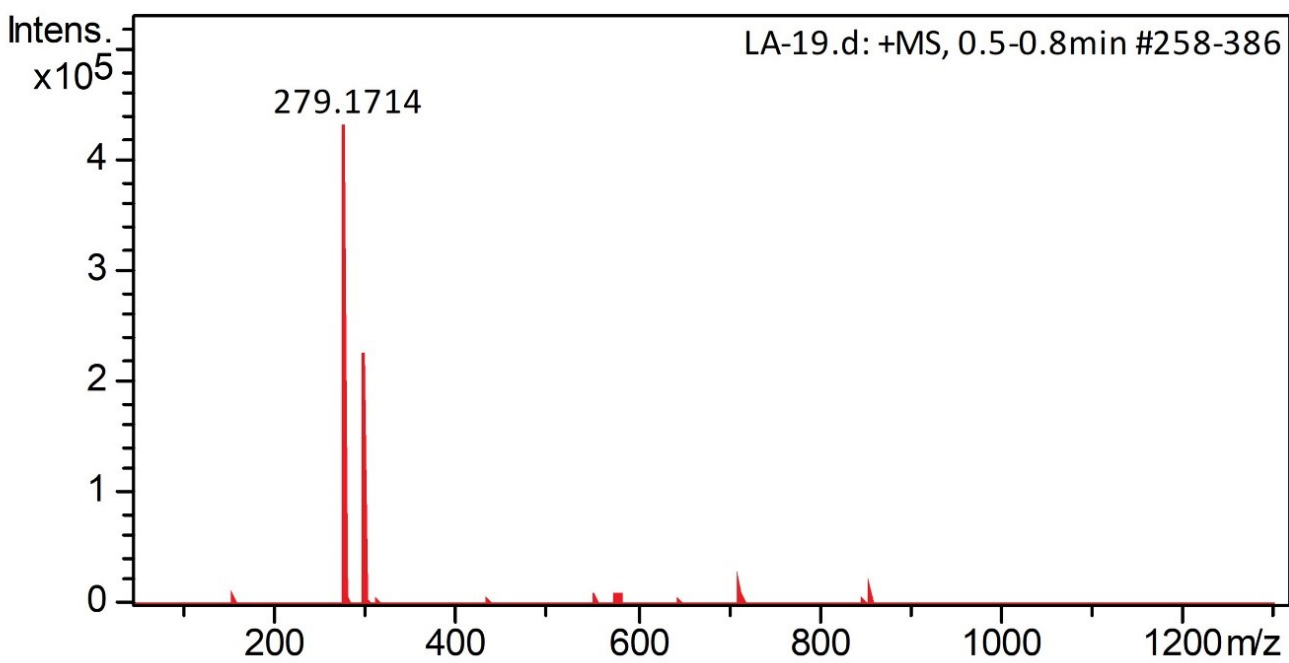
**Fig S 11.** HPLC of 2-(dibutylamino)-N-(4-methoxyphenyl)acetamide (5b)



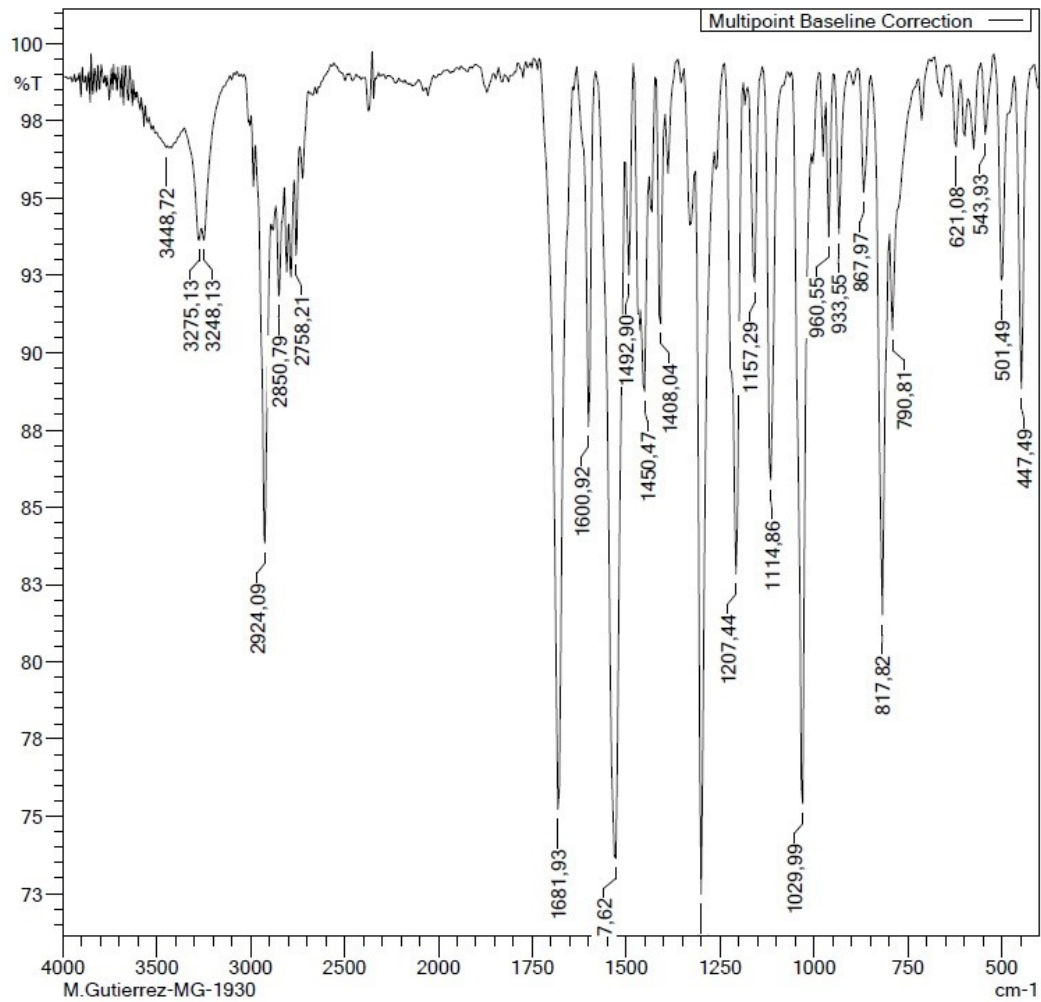
**Fig S 12.** <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) of *N*-(2,4-dimethoxyphenyl)-2-(piperidin-1-yl)acetamide (5c)



**Fig S 13.**  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ) of *N*-(2,4-dimethoxyphenyl)-2-(piperidin-1-yl)acetamide (5c)



**Fig S 14.** HRMS (ESI, m/z) of *N*-(2,4-dimethoxyphenyl)-2-(piperidin-1-yl)acetamide (5c)



**Fig S 15.** HPLC of *N*-(2,4-dimethoxyphenyl)-2-(piperidin-1-yl)acetamide (5c)



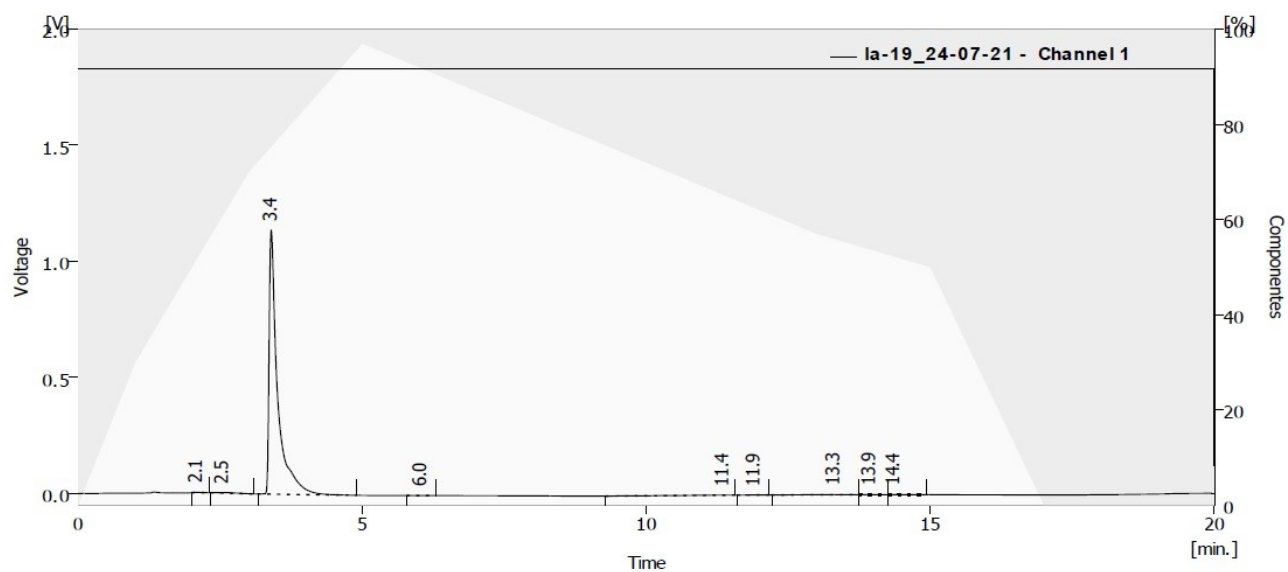
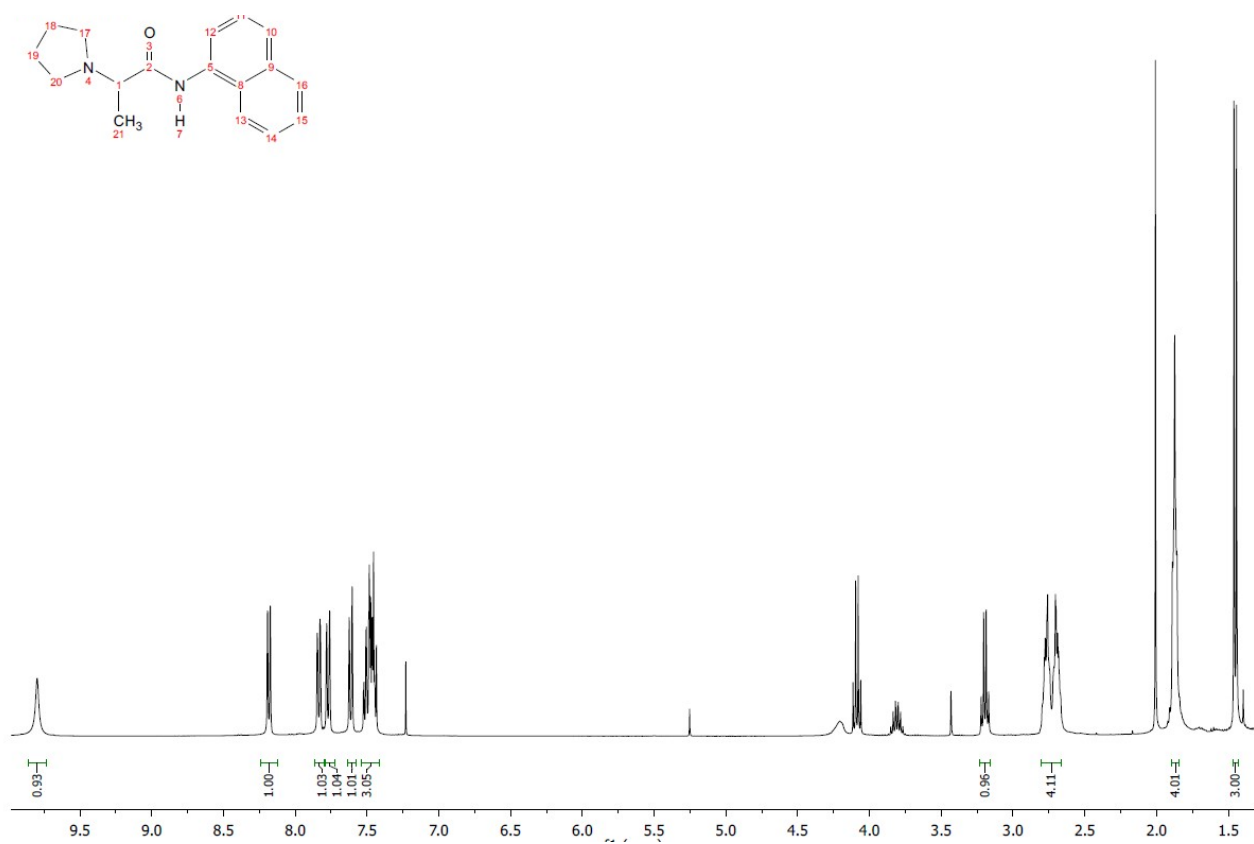


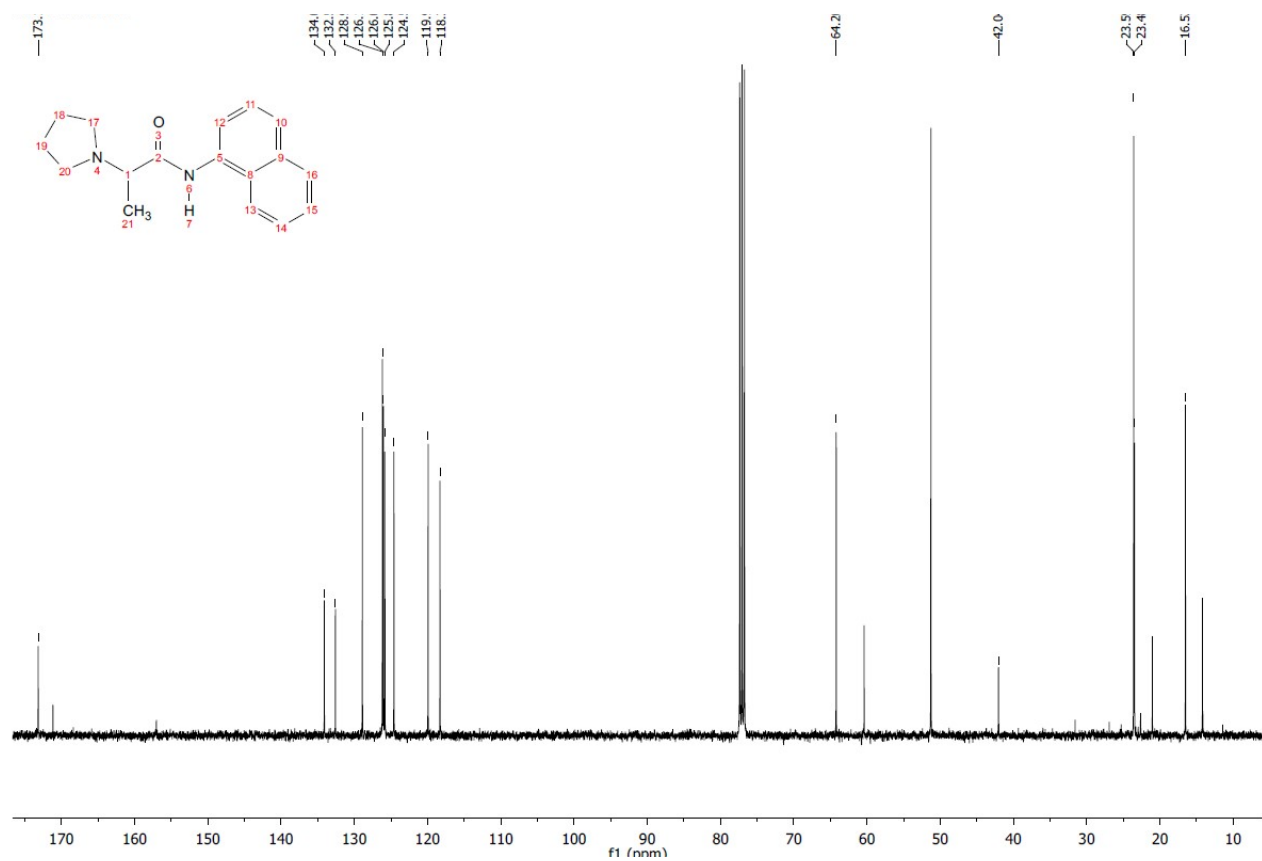
Tabla de resultados (Sin cal. - la-19\_24-07-21 - Channel 1)

	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	2.083	13.268	1.212	0.1	0.1	0.17	991	
2	2.543	61.638	2.217	0.5	0.2	0.38	755	
3	3.400	11813.634	1137.463	98.2	99.3	0.13	583	
4	6.030	9.851	0.596	0.1	0.1	0.30	995	
5	11.353	56.946	0.678	0.5	0.1	0.39	1000	
6	11.900	11.168	0.634	0.1	0.1	0.40	1000	
7	13.303	41.922	1.010	0.3	0.1	0.52	1000	
8	13.933	14.267	0.877	0.1	0.1	0.27	1000	
9	14.360	5.358	0.292	0.0	0.0	0.28	1000	
	Total	12028.053	1144.978	100.0	100.0			

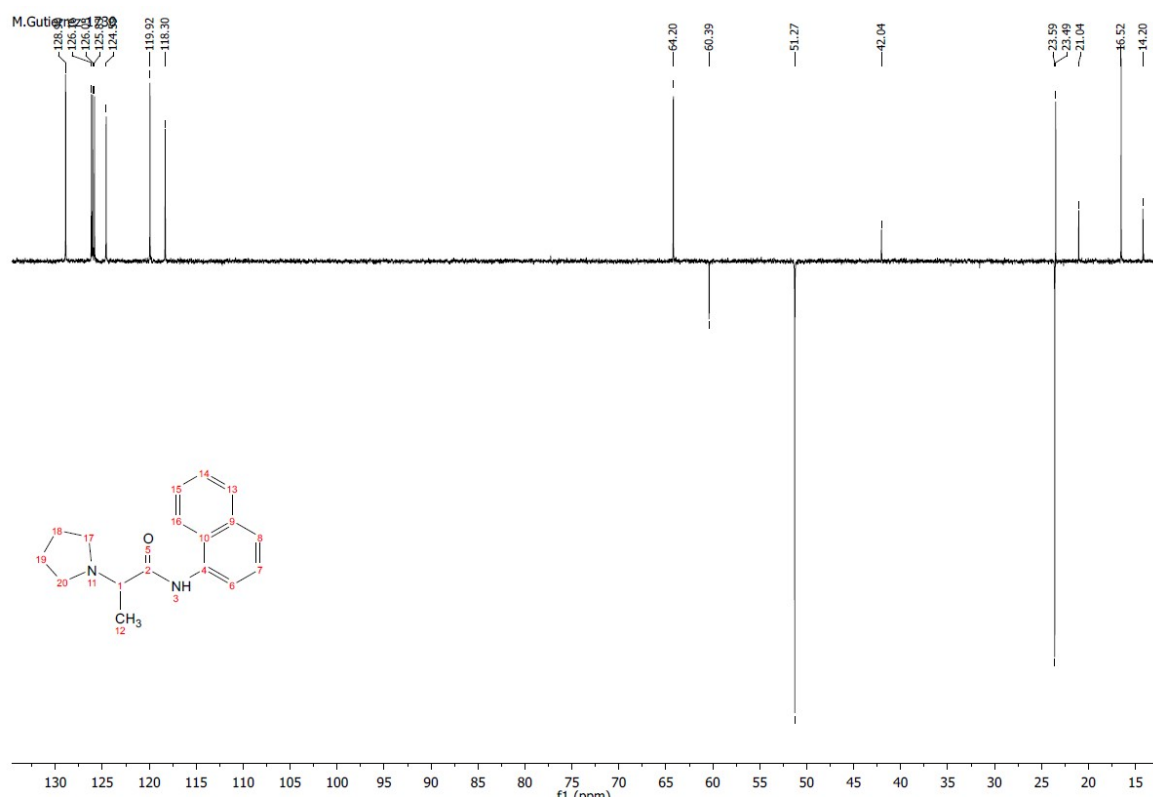
Fig S 16. HPLC of *N*-(2,4-dimethoxyphenyl)-2-(piperidin-1-yl)acetamide (5c)



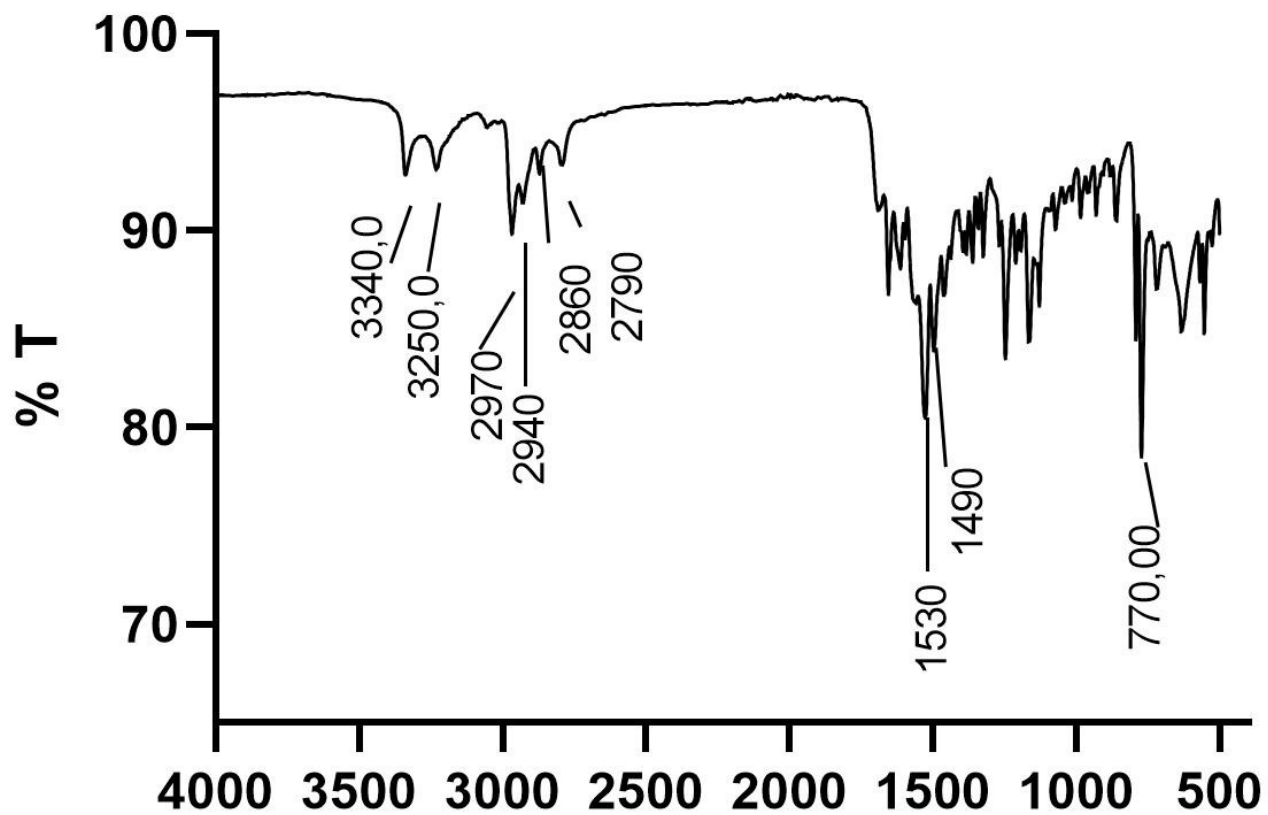
**Fig S 17.** <sup>1</sup>H- NMR (400 MHz, CDCl<sub>3</sub>) of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propanamide (5d)



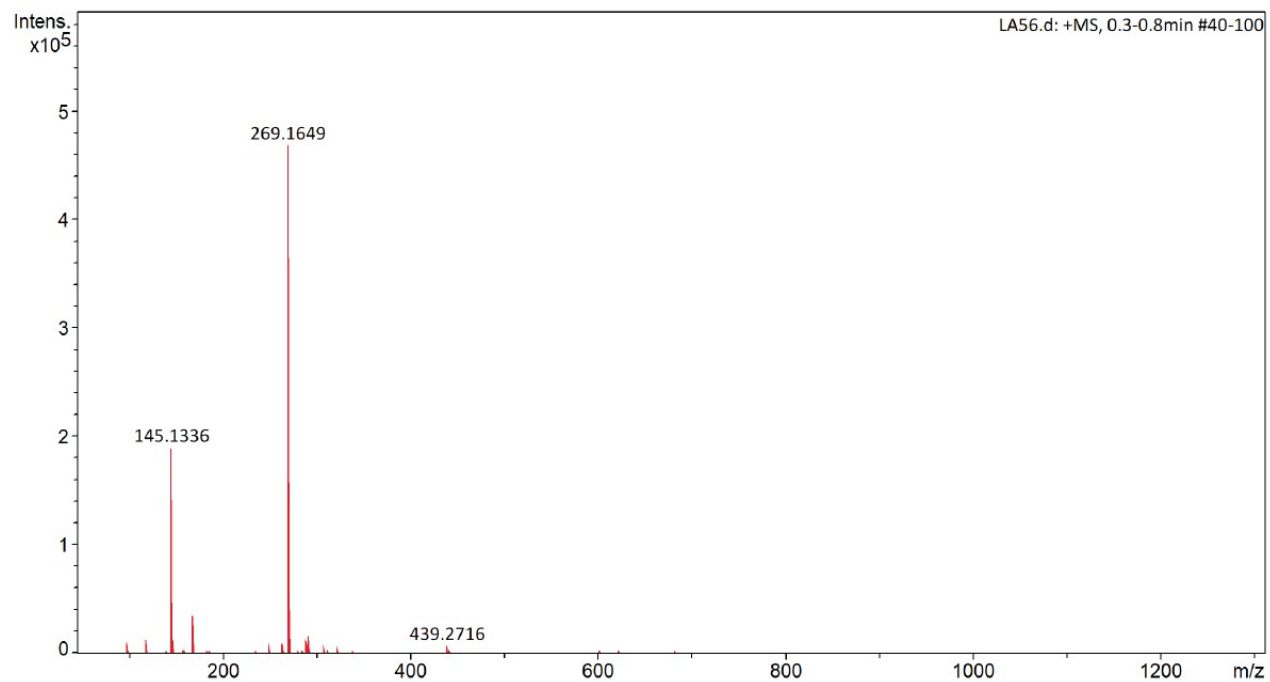
**Fig S 18.** <sup>13</sup>C- NMR (100 MHz, CDCl<sub>3</sub>) of of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propanamide (5d)



**Fig S 19.** DEPT-135 of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propanamide (5d)



**Fig S 20.** IR of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propanamide (5d)



**Fig S 21.** HRMS (ESI, m/z) of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propanamide (5d)

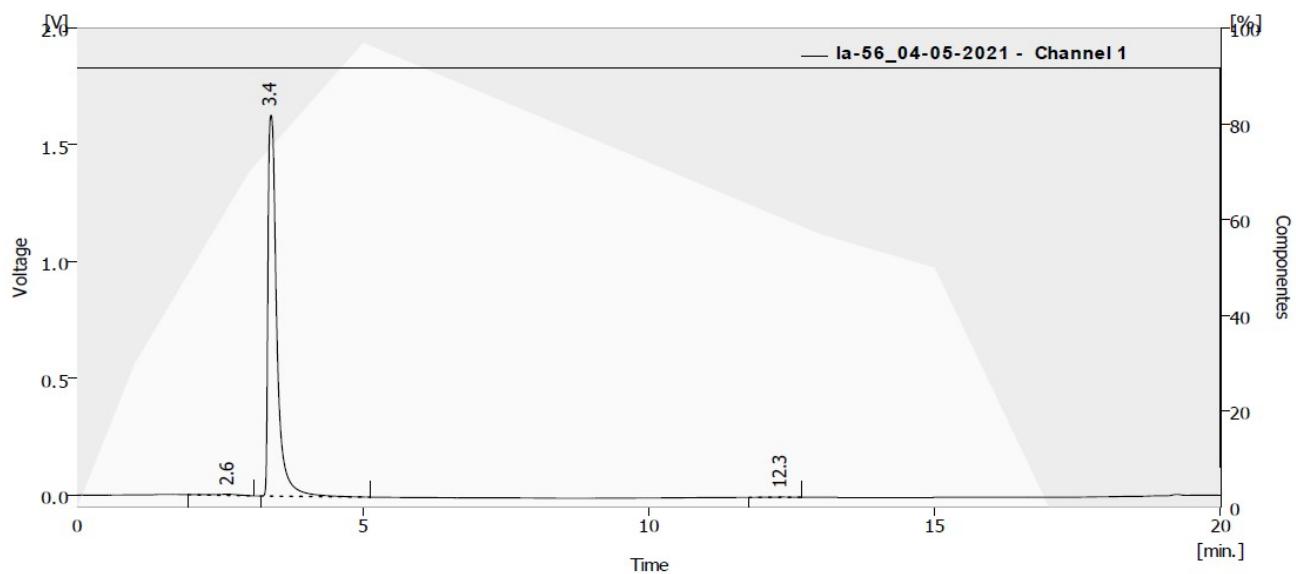


Tabla de resultados (Sin cal. - la-56\_04-05-2021 - Channel 1)

	Tiempo de retenc [min]	Área [mV.s]	Altura [mV]	Area [%]	Altura [%]	A05 [min]	PDA Peak Purity	Nombre Compuesto
1	2.640	154.070	4.755	0.9	0.3	0.88	776	
2	3.390	17513.720	1630.825	99.0	99.6	0.15	402	
3	12.313	22.616	1.368	0.1	0.1	0.20	998	
	Total	17690.407	1636.947	100.0	100.0			

Fig S 22. HPLC of *N*-(naphthalen-1-yl)-2-(pyrrolidin-1-yl)propenamide (5d)