Supplementary Material

Development of α-acyloxycarboxamides targeting *Leishmania amazonensis* parasite

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Spectroscopic analysis of cinnamic acid derivatives

Figure 1. Infrared (ATR - FTIR) spectrum of ethyl cinnamate (**3a**).

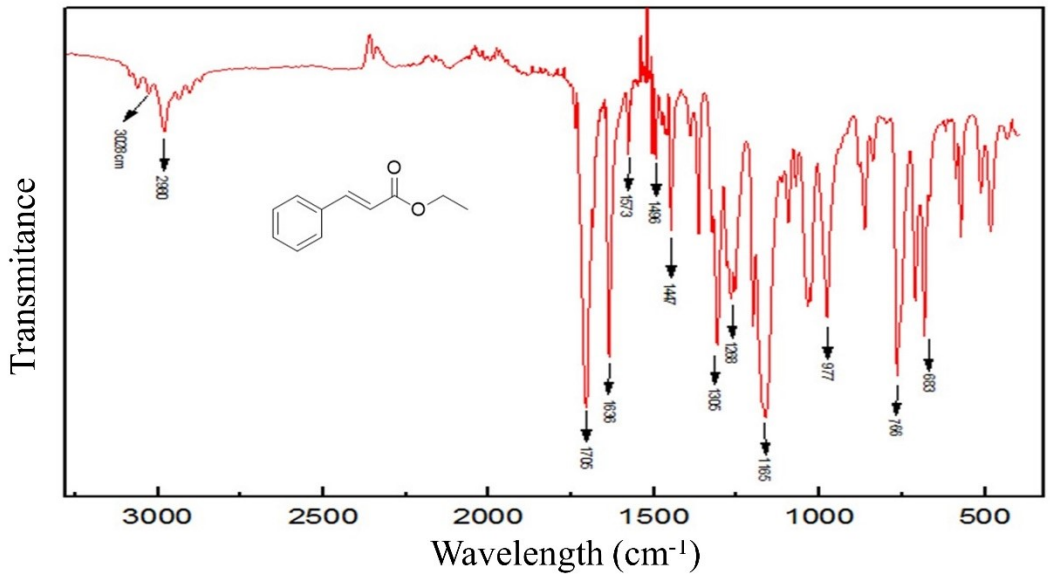

Figure 2. ^{1}H NMR spectrum of ethyl cinnamate (400 MHz, $CDCl_3$) (**3a**)

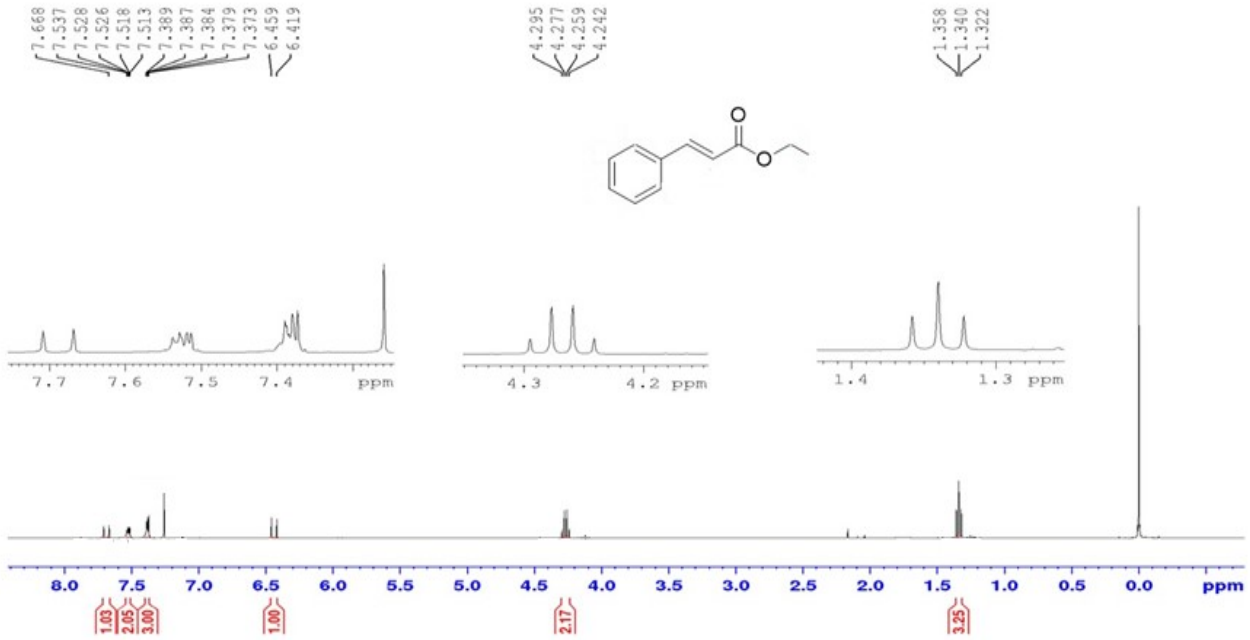

Figure 3. ^{13}C NMR spectrum of ethyl cinnamate (100 MHz, $CDCl_3$) (**3a**).

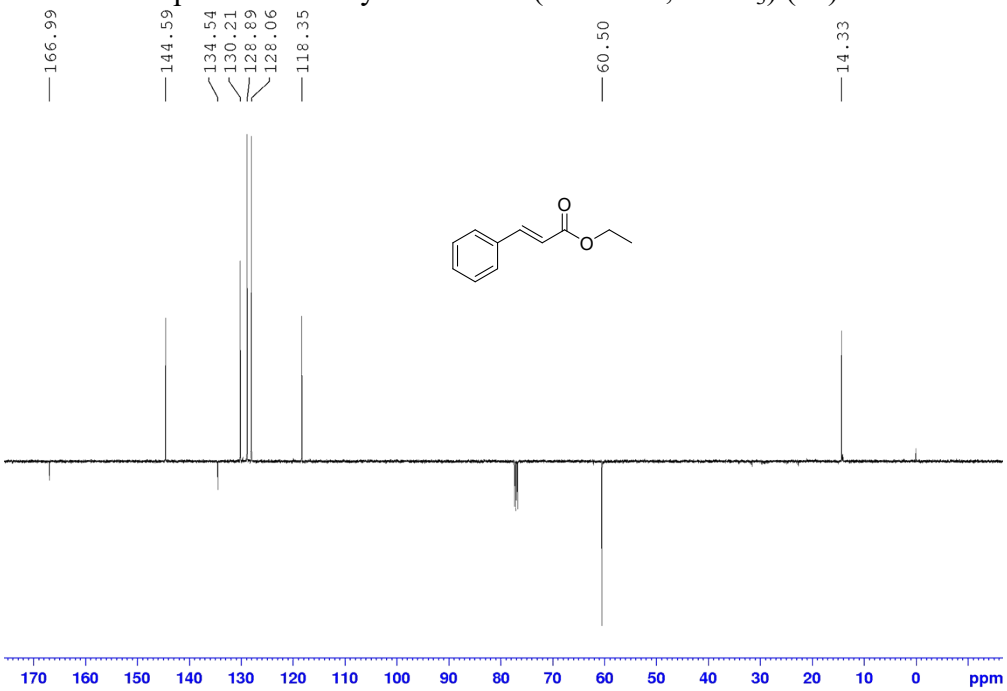

Figure 4. ^{1}H NMR spectrum of ethyl *o*-phenylcinnamate (600 MHz, $CDCl_3$) (**3b**).

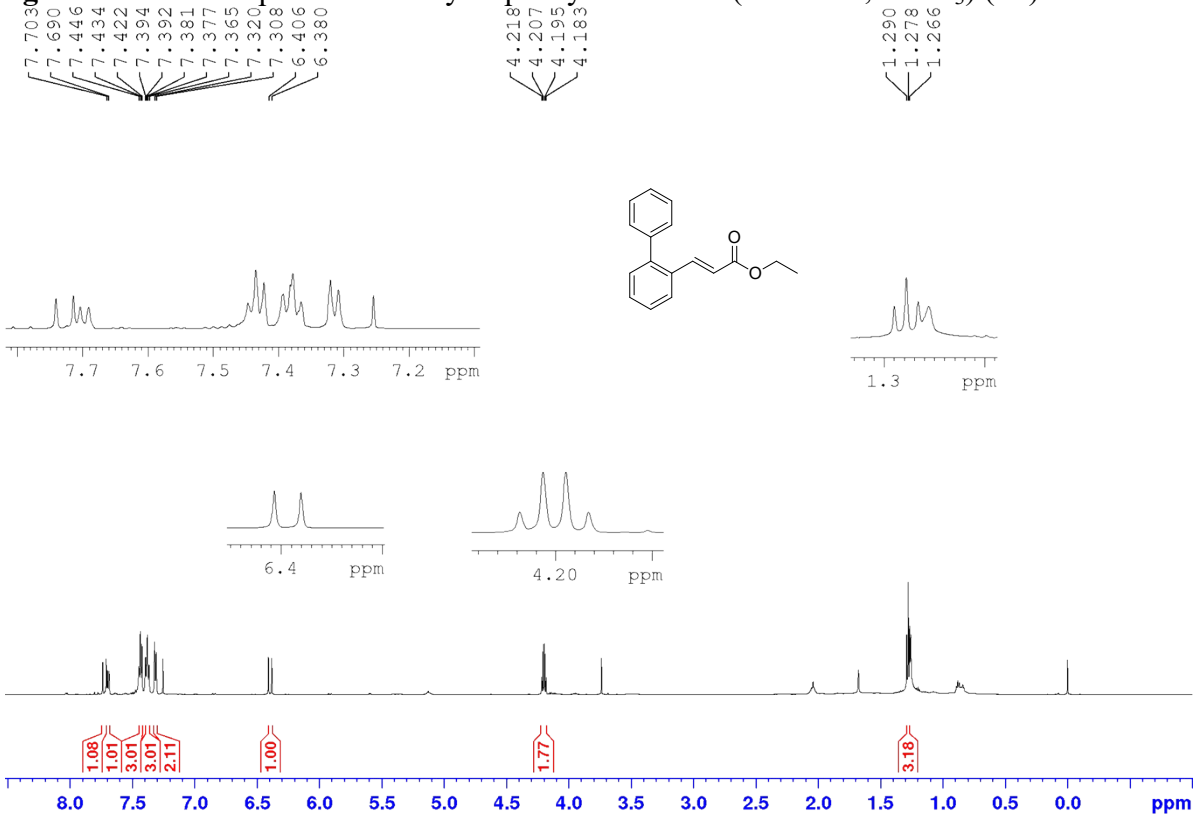

Figure 5. ^{1}H NMR spectrum of ethyl *p*-*t*-butylcinnamate (600 MHz, $CDCl_3$) (**3c**).

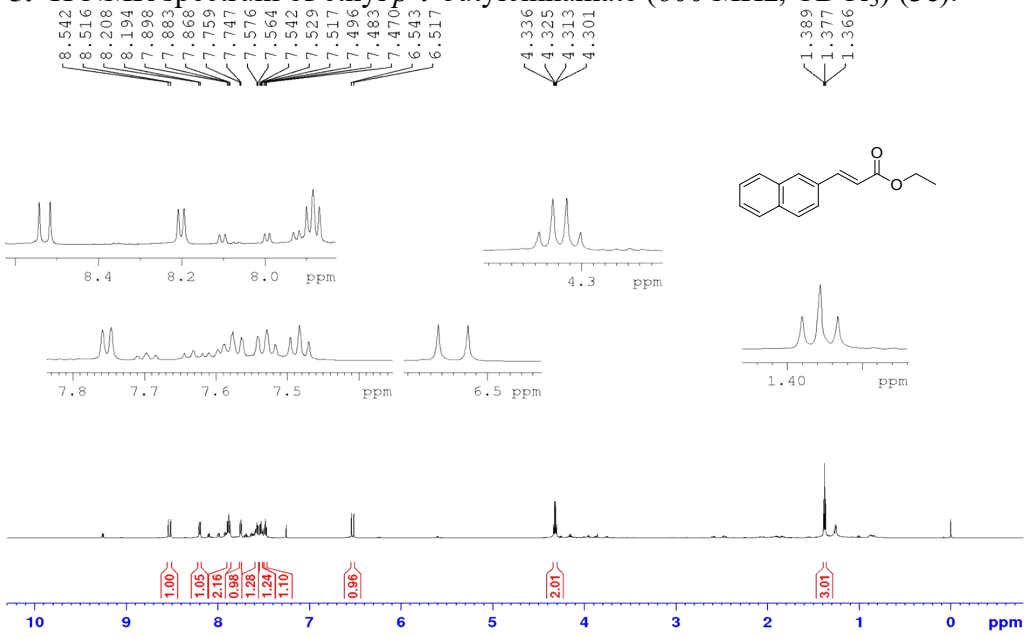

Figure 6. Infrared (ATR - FTIR) spectrum of ethyl *p*-chlorocinnamate (**3d**).

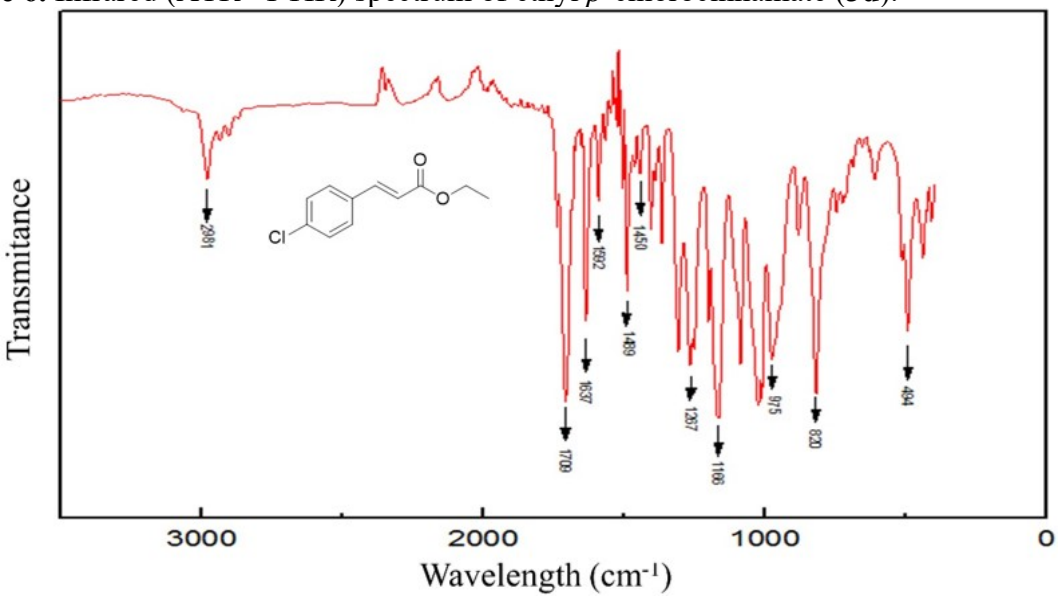

Figure 7. ^{1}H NMR spectrum of ethyl *p*-chlorocinnamate (400 MHz, $CDCl_3$) (**3d**).

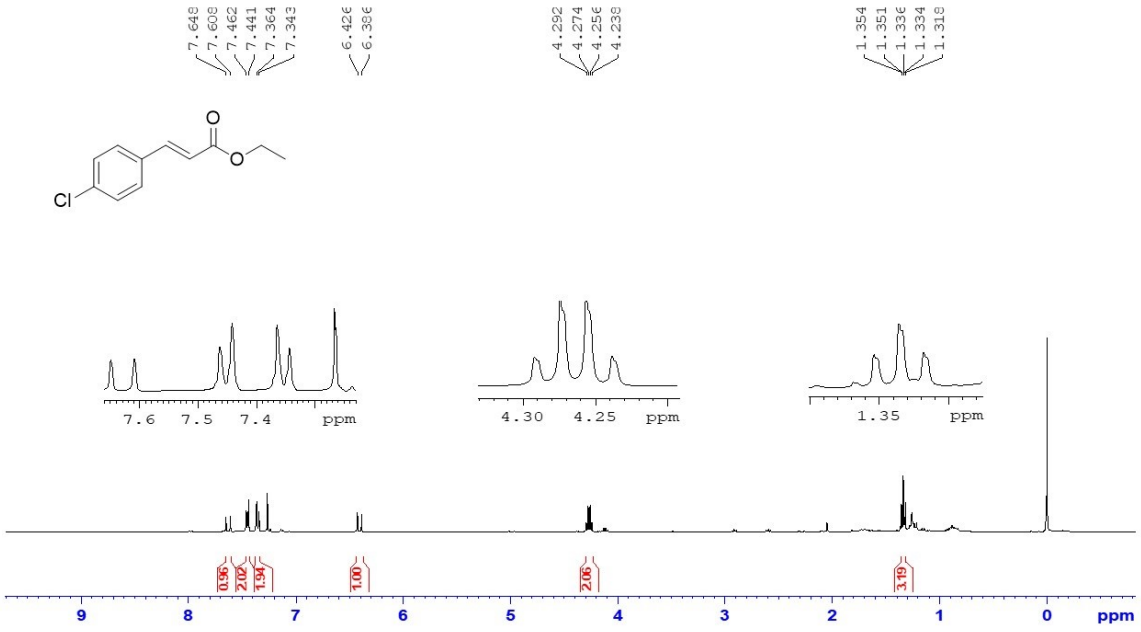

Figure 8. ^{13}C NMR spectrum of ethyl *p*-chlorocinnamate (100 MHz, $CDCl_3$) (**3d**).

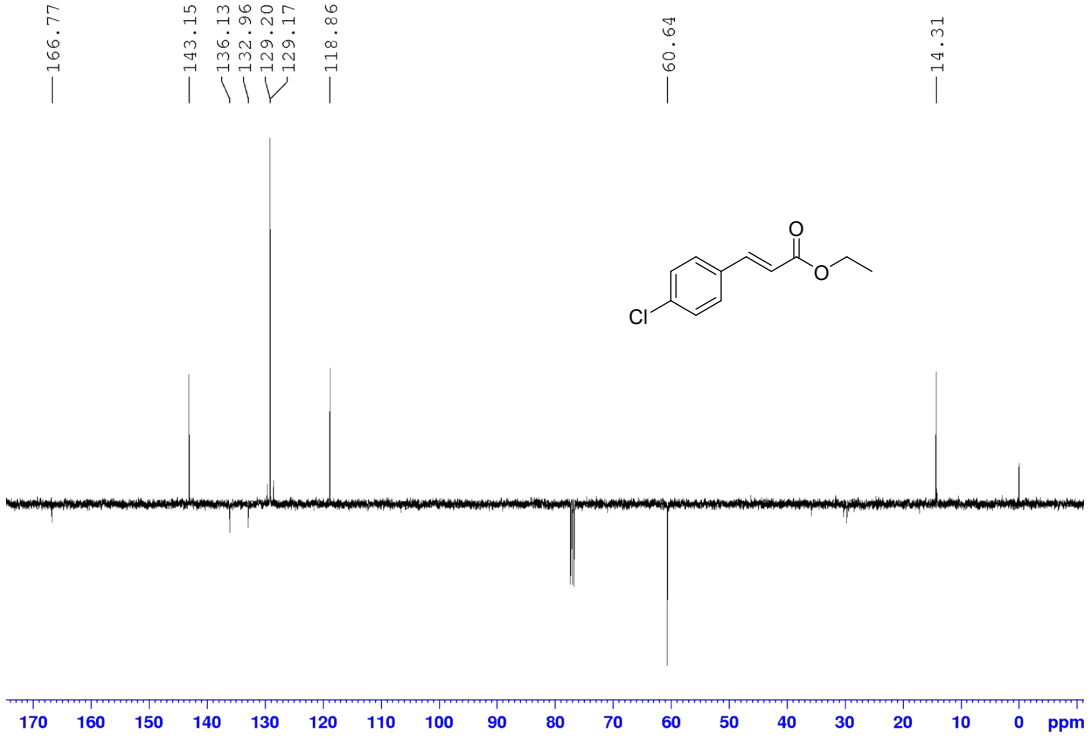

Figure 9. ^{1}H NMR spectrum of ethyl *p*-trifluoromethoxycinnamate (400 MHz, $CDCl_3$) (**3e**).

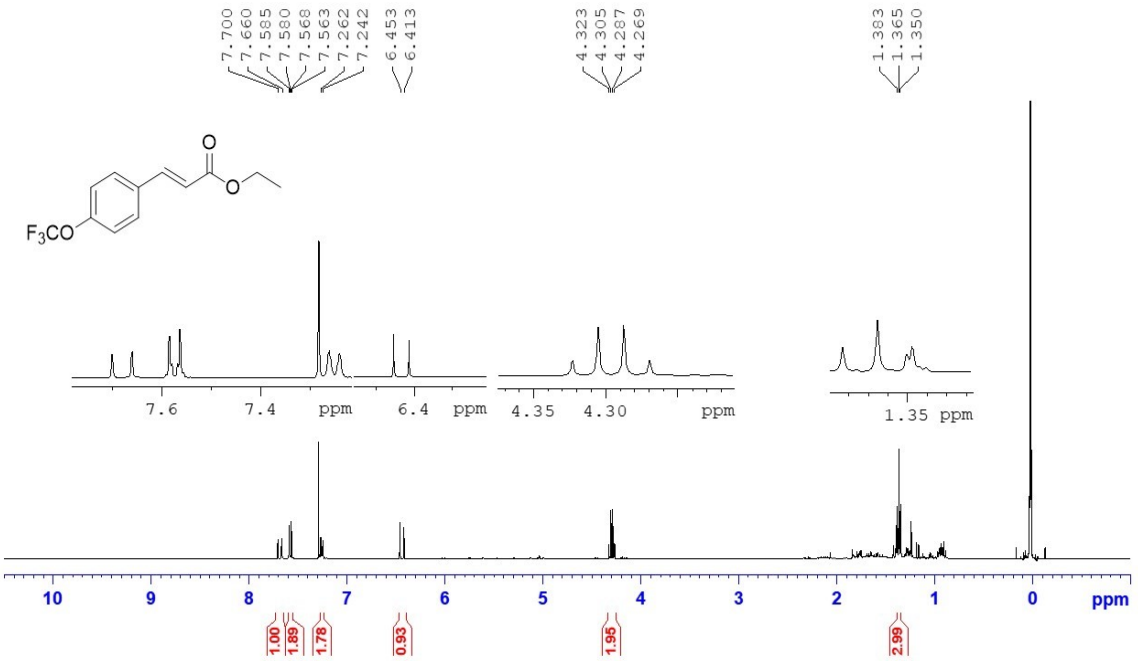

Figure 10. ^{13}C NMR spectrum of ethyl *p*-trifluoromethoxycinnamate (100 MHz, $CDCl_3$) (**3e**).

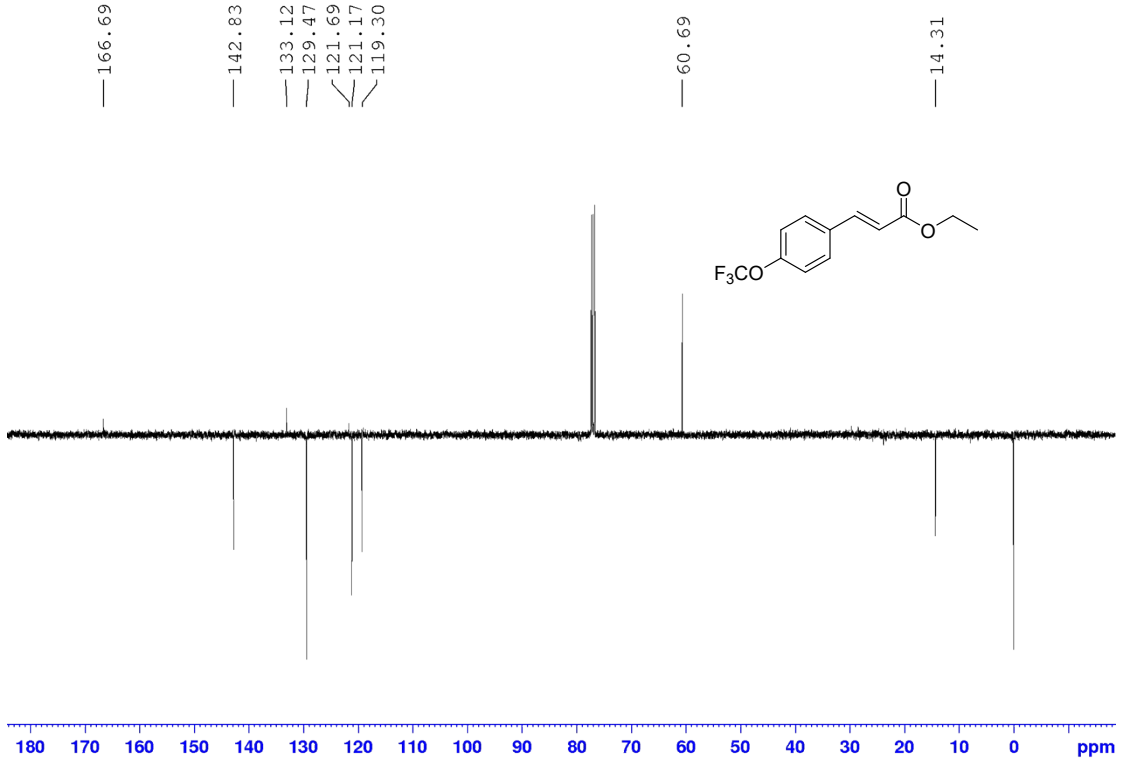

Figure 11. Infrared (ATR - FTIR) spectrum of Cinnamic acid (**4a**).

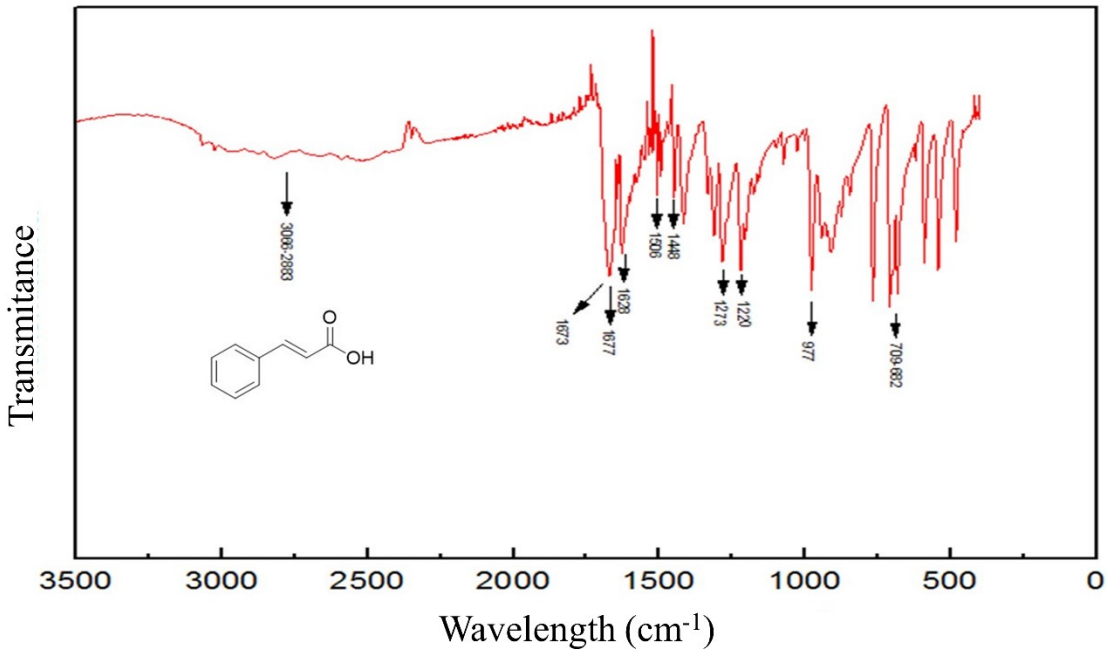

Figure 12. ^{1}H NMR spectrum of cinnamic acid (**4a**) (600 MHz; $CDCl_3$).

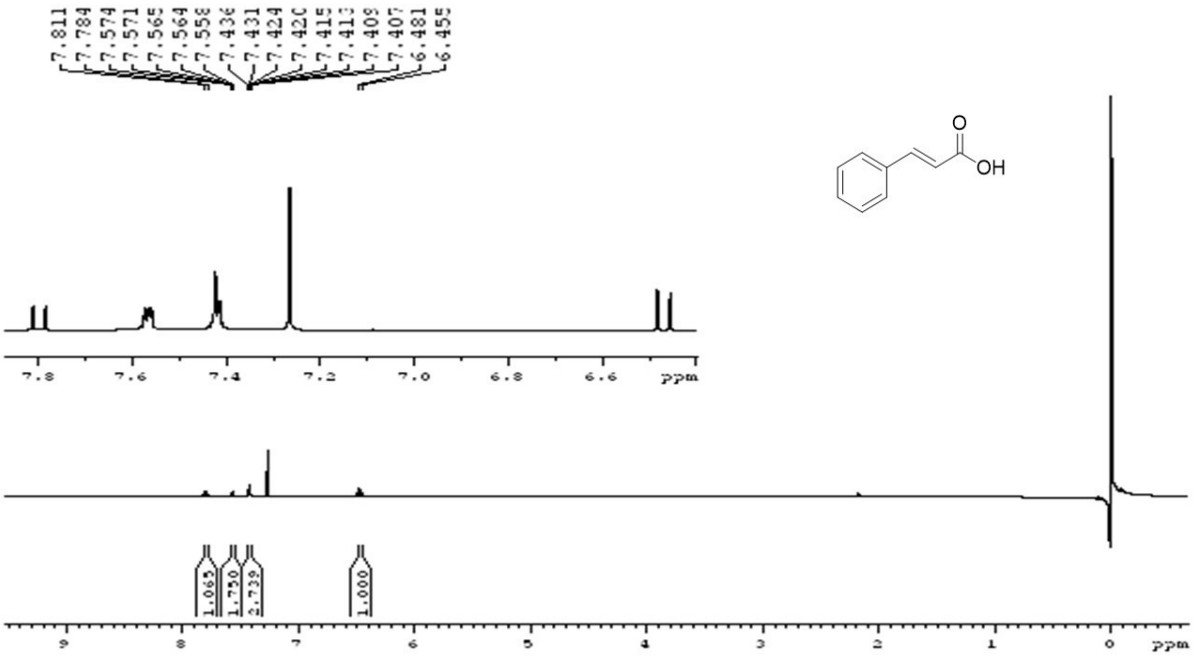

Figure 13. ^{13}C NMR spectrum of cinnamic acid (**4a**) (100 MHz; $CDCl_3$).

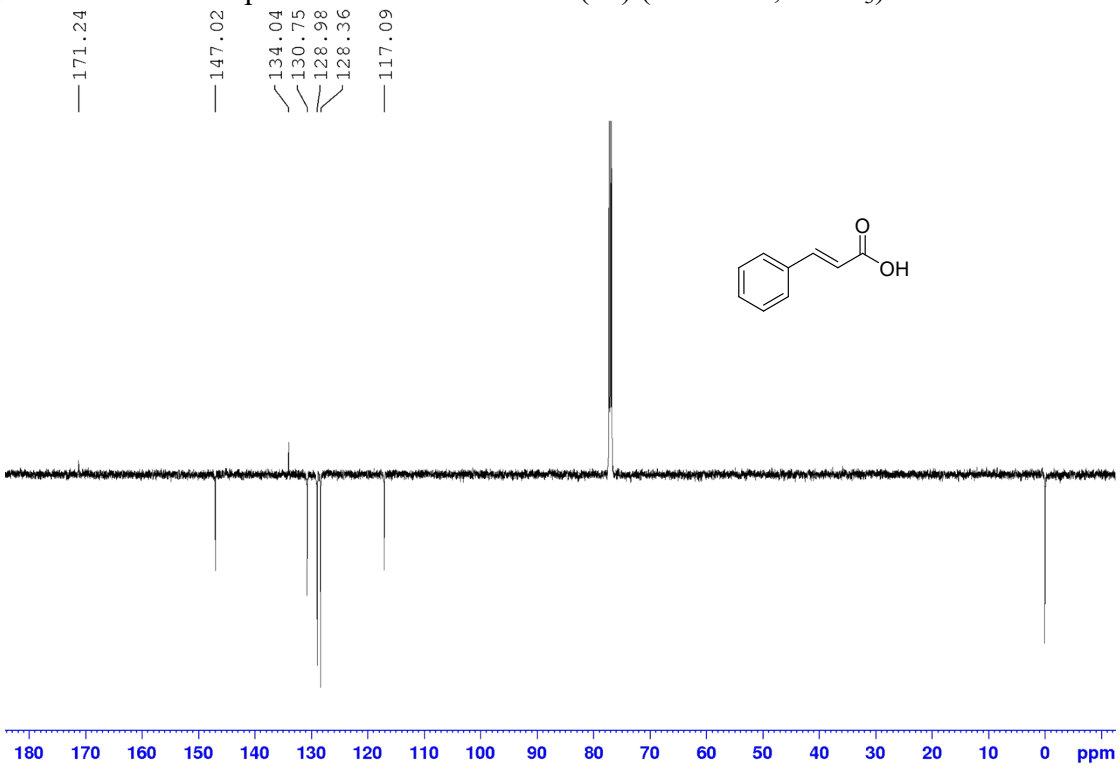

Figure 14. ^{1}H NMR spectrum of *o*-phenylcinnamate acid (**4b**) (600 MHz; $CDCl_3/CD_3OD$).

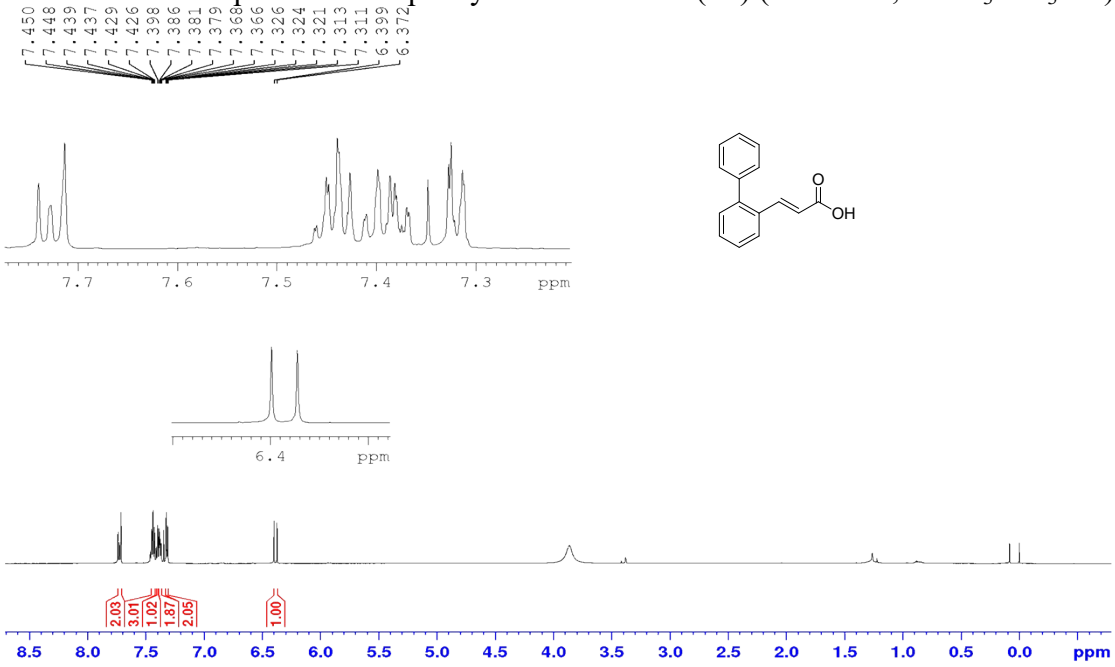

Figure 15. ^{13}C NMR spectrum of *o*-phenylcinnamate acid (**4b**) (150 MHz; $CDCl_3/CD_3OD$).

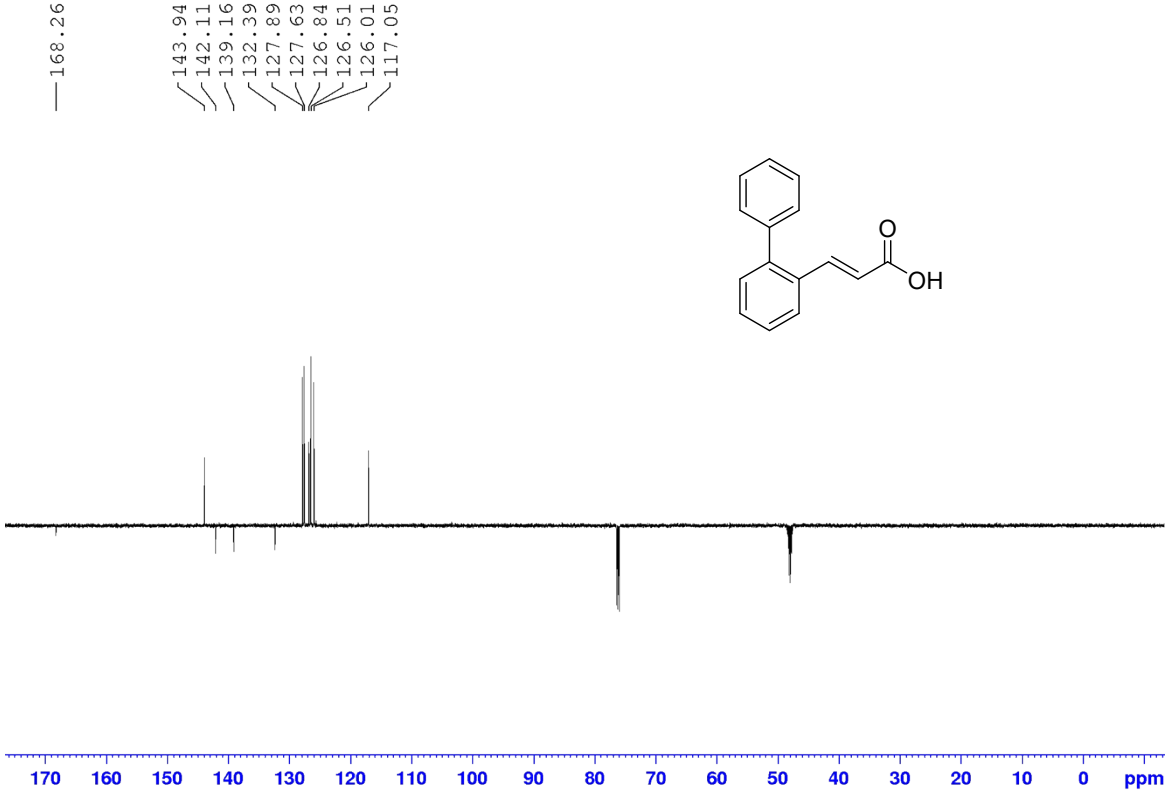

Figure 16. [1]H NMR spectrum of (*E*) – 3 – (naphthalen – 2 – yl) acrylic acid (**4c**) (600 MHz; DMSO-*d6*).

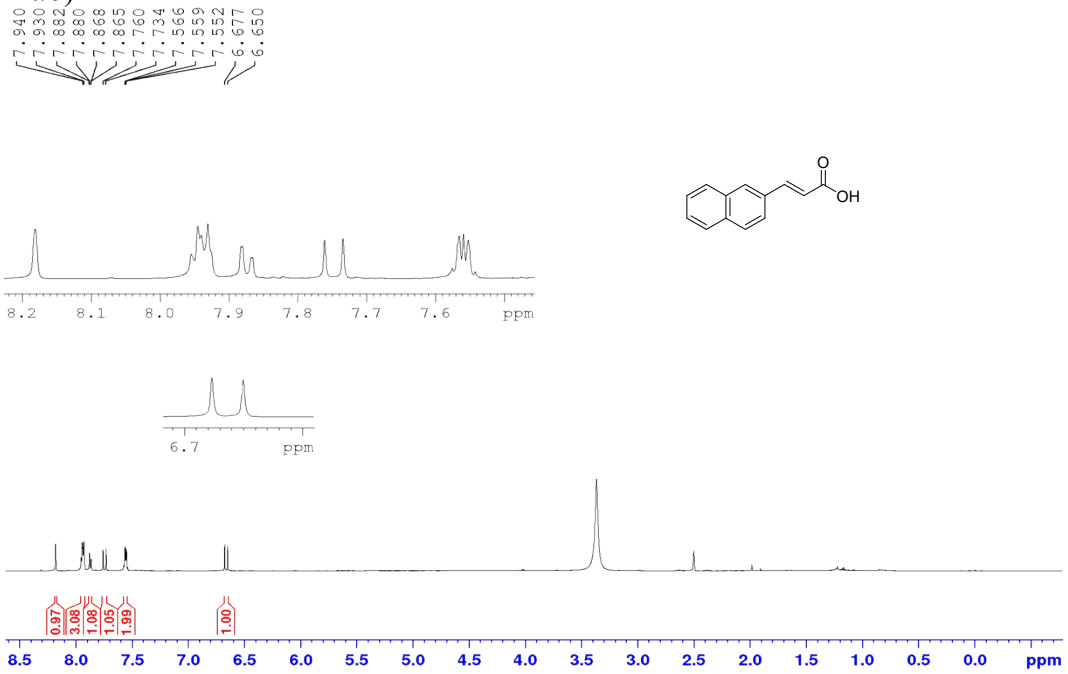

Figure 17. [1]H NMR spectrum of *p*-chlorocinnamic acid (**4d**) (600 MHz; DMSO-*d6*).

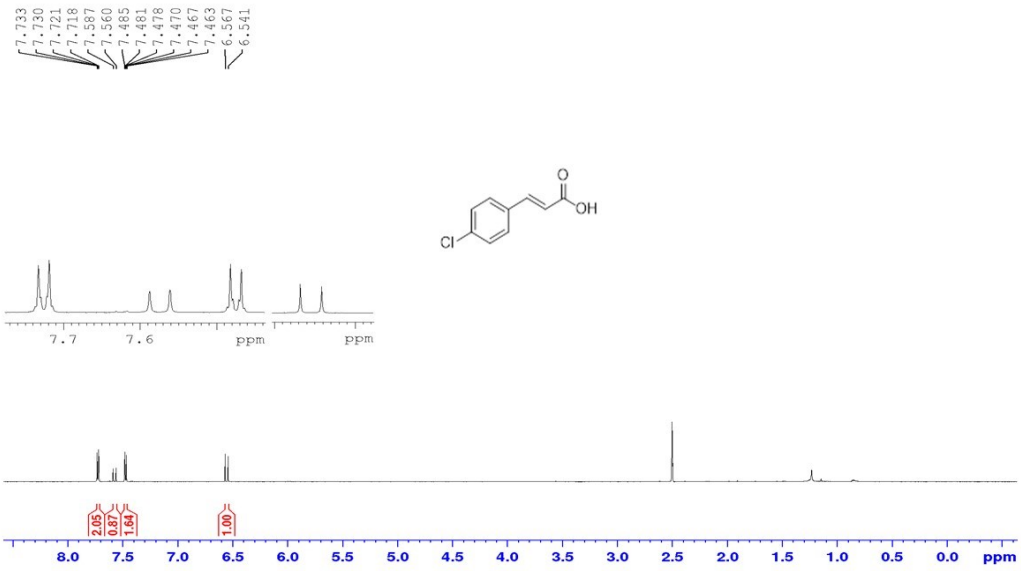

Figure 18. ^{13}C NMR spectrum of *p*-chlorocinnamic acid (**4d**) (150 MHz; DMSO-*d6*).

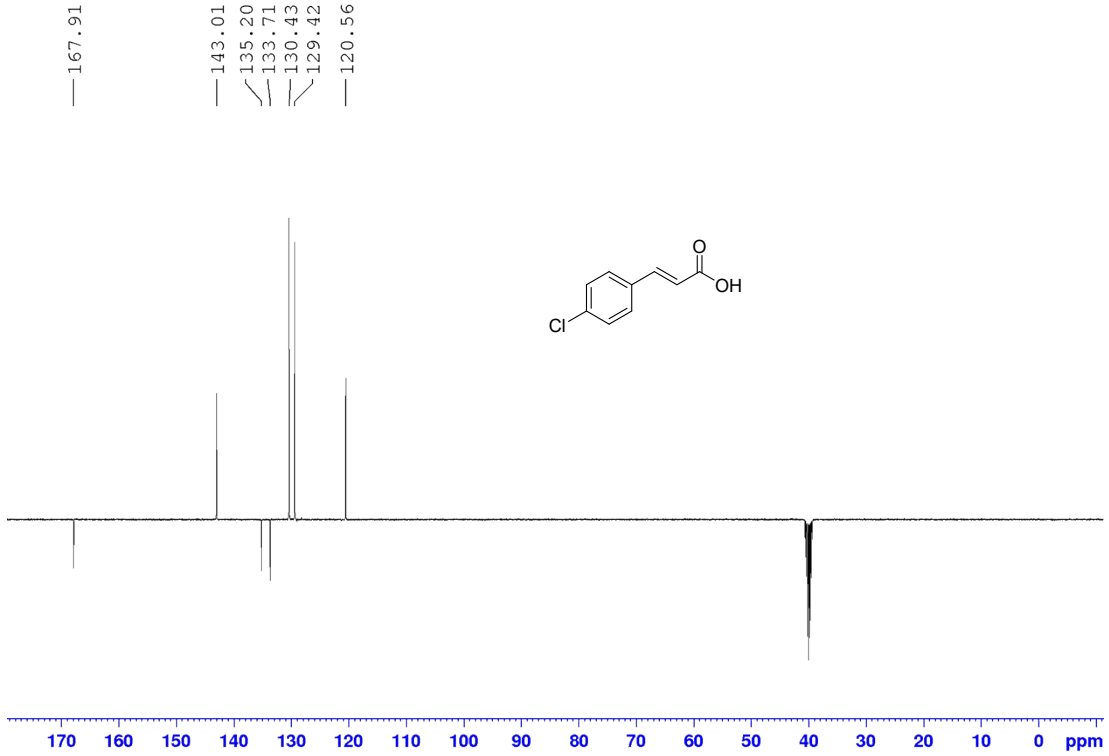

Figure 19. ^{1}H NMR spectrum of *p*-trifluoromethoxycinnamic acid (**4e**) (600 MHz; DMSO-*d6*).

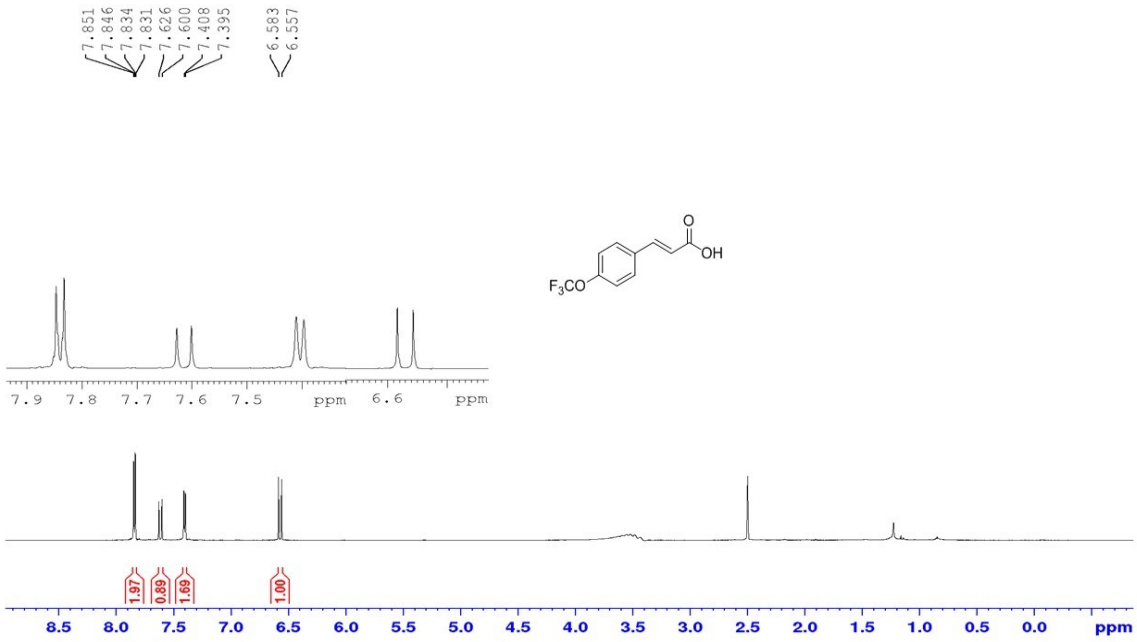

Figure 20. ^{13}C NMR spectrum of *p*-trifluoromethoxycinnamic acid (**4e**) (150 MHz; $CDCl_3$/ DMSO-*d6*).

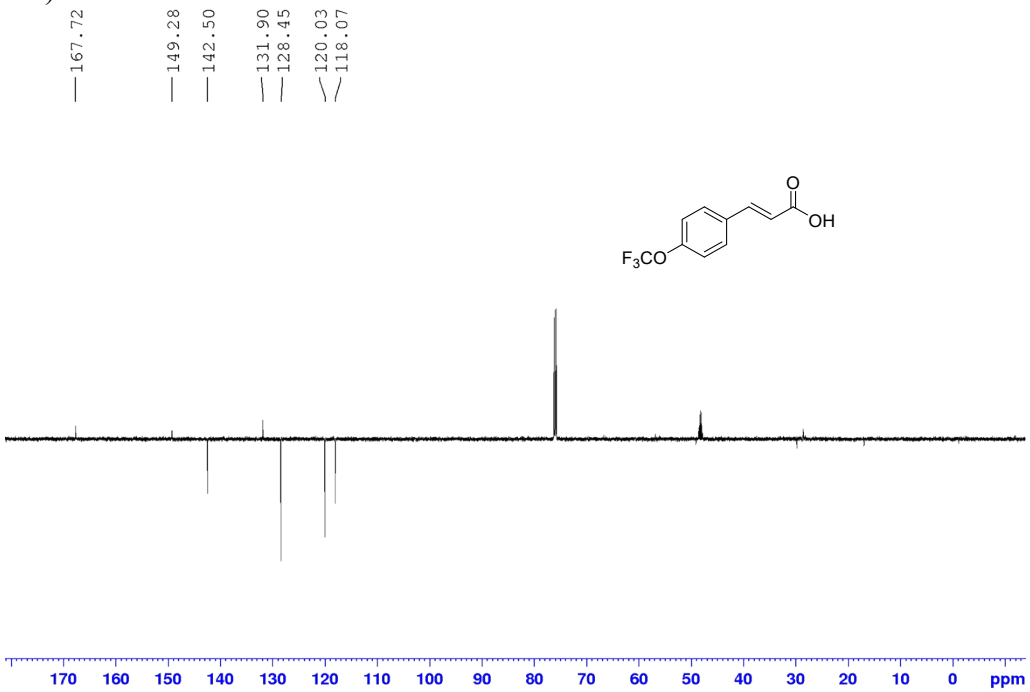

Figure 21. Infrared (ATR - FTIR) spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7a$_1$**).

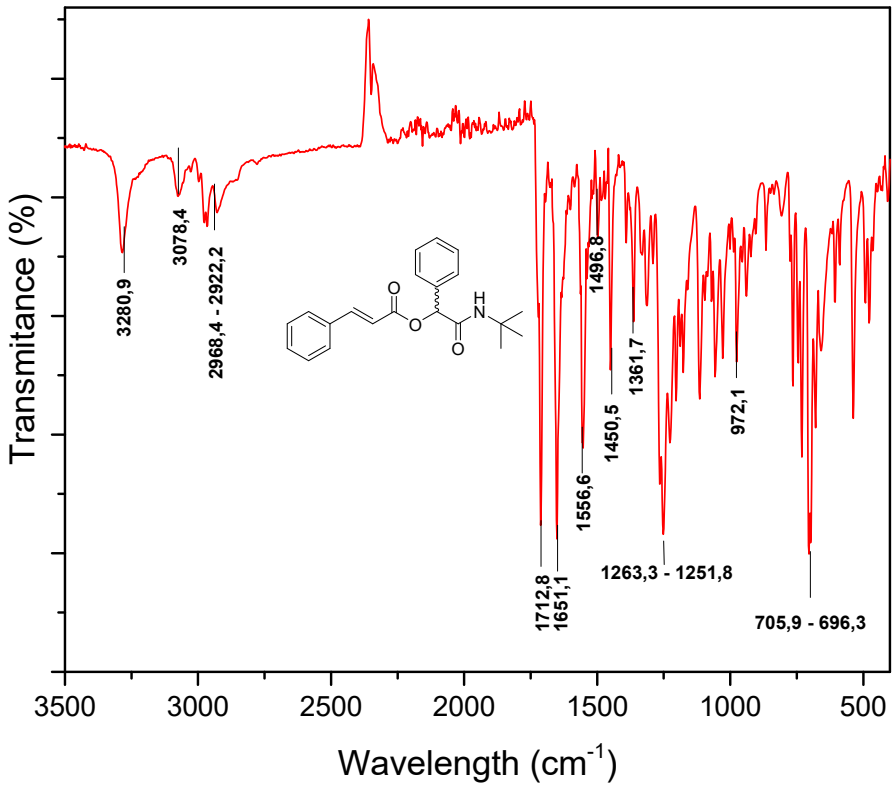

Figure 22. ^{1}H NMR spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7a$_1$**) (600 MHz; $CDCl_3$).

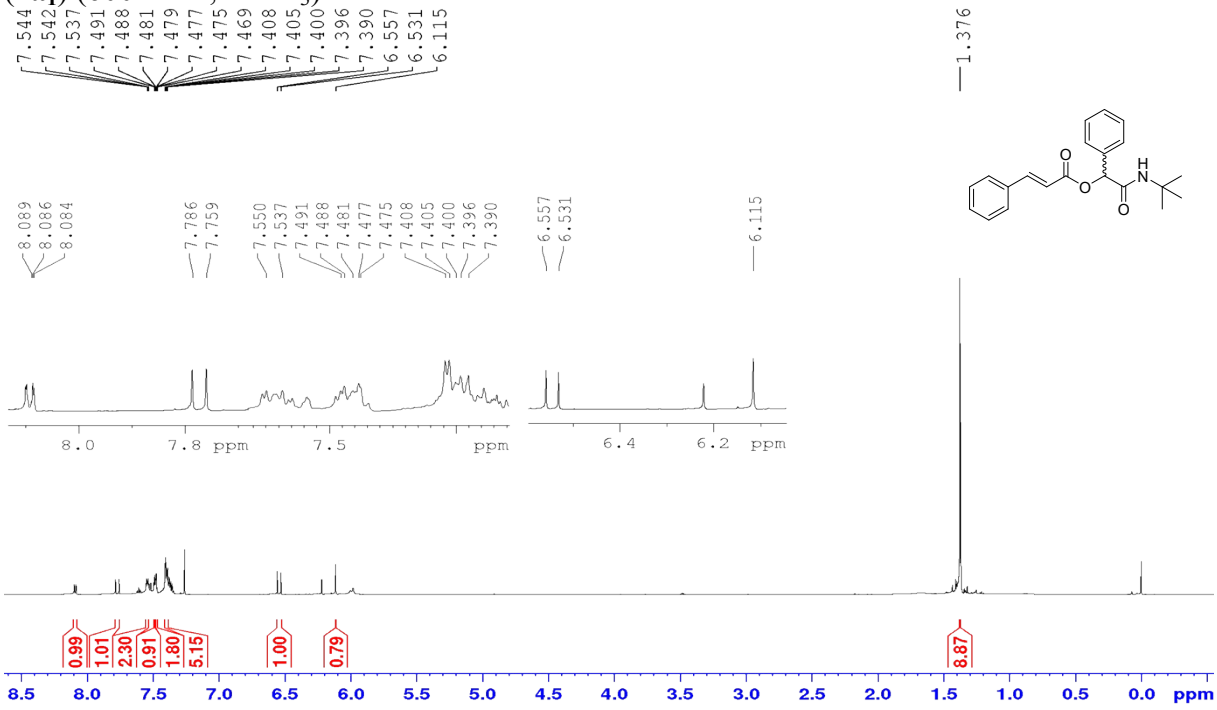

Figure 23. ^{13}C NMR spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7a$_1$**) (150 MHz; $CDCl_3$).

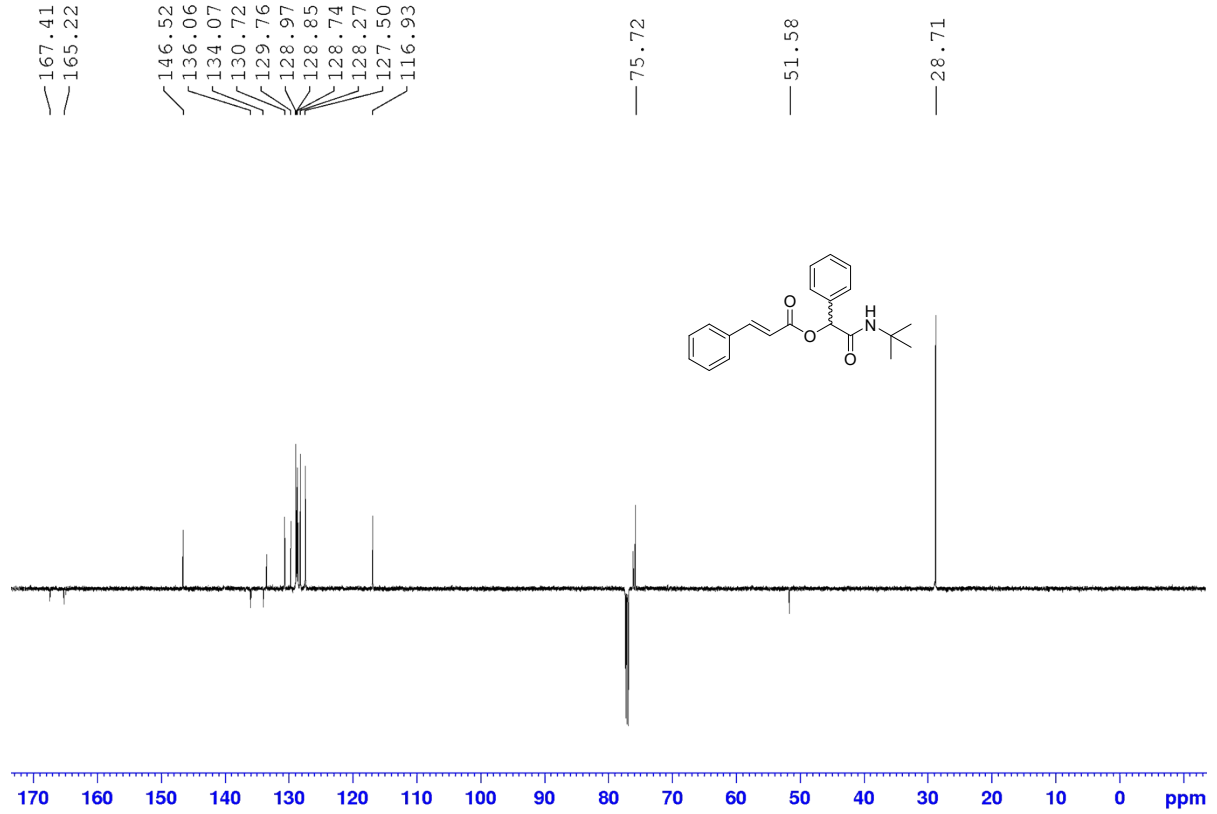

Figure 24. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7a$_1$**).

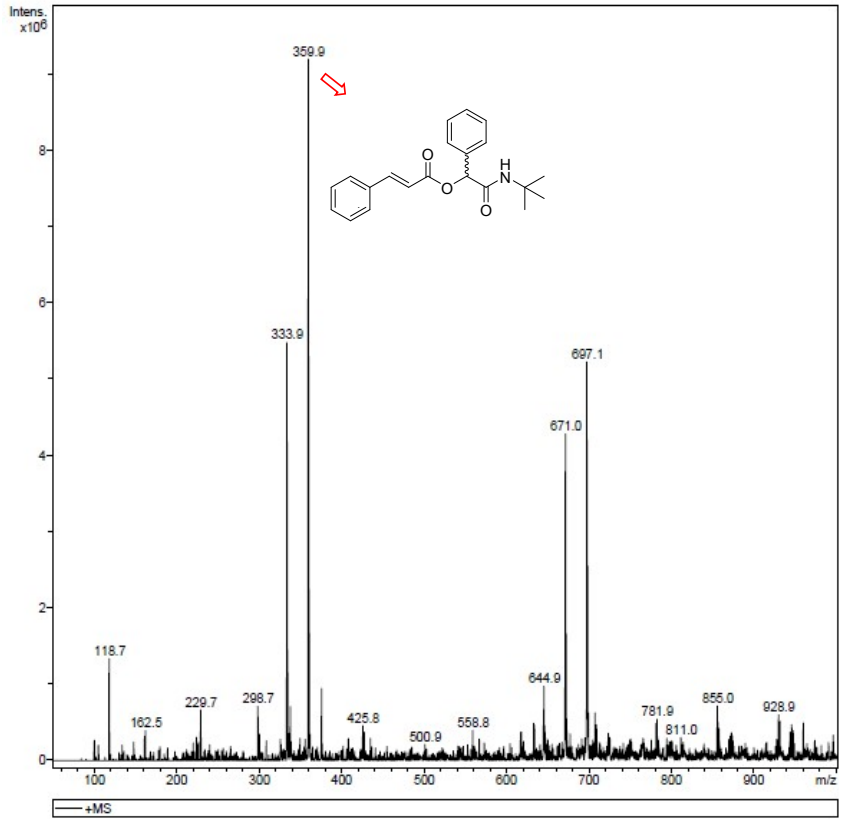

Figure 25. Infrared (ATR - FTIR) spectrum of 2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl cinnamate (**7a2**).

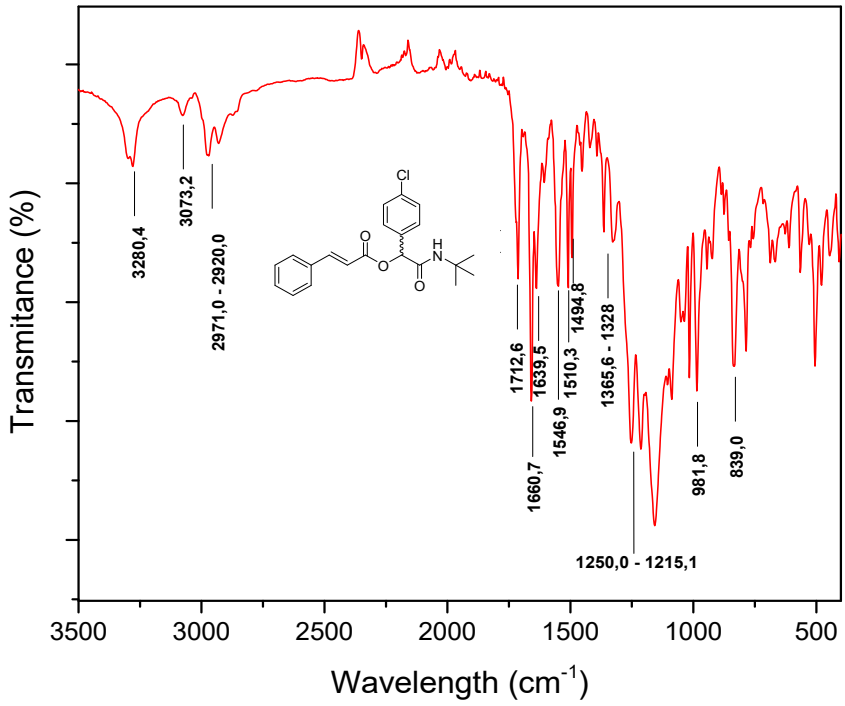

Figure 26. ^{1}H NMR spectrum of 2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl cinnamate (**7a2**) (600 MHz; $CDCl_3$).

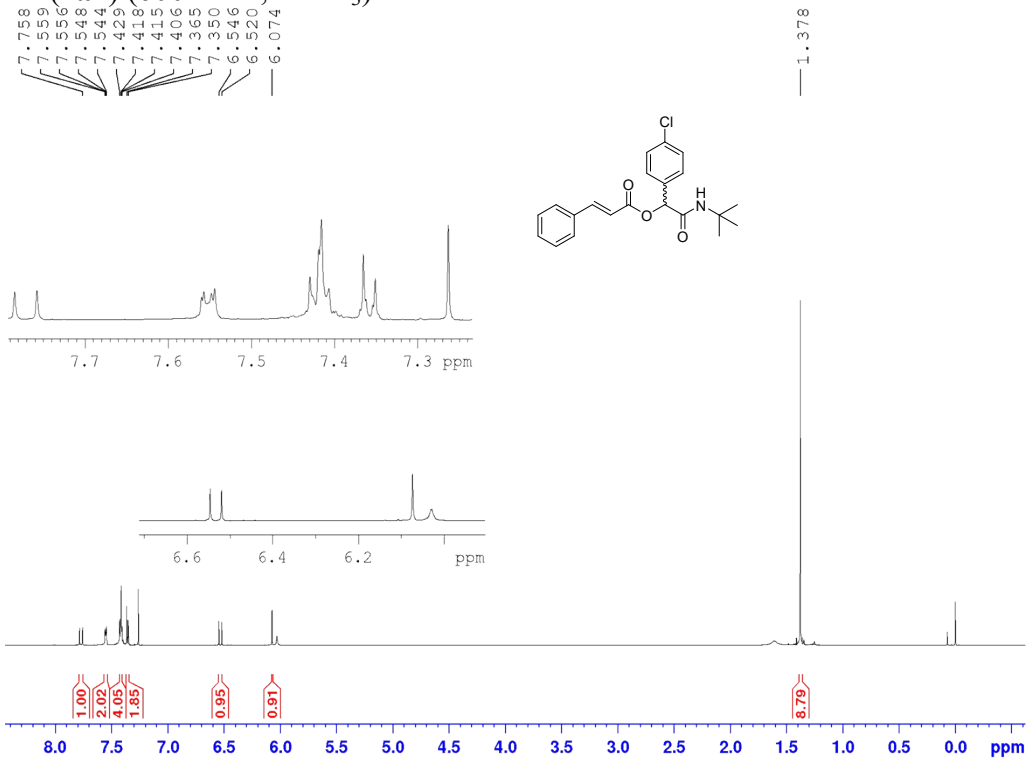

Figure 27. ^{13}C NMR spectrum of 2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl cinnamate (**7a2**) (150 MHz; $CDCl_3$).

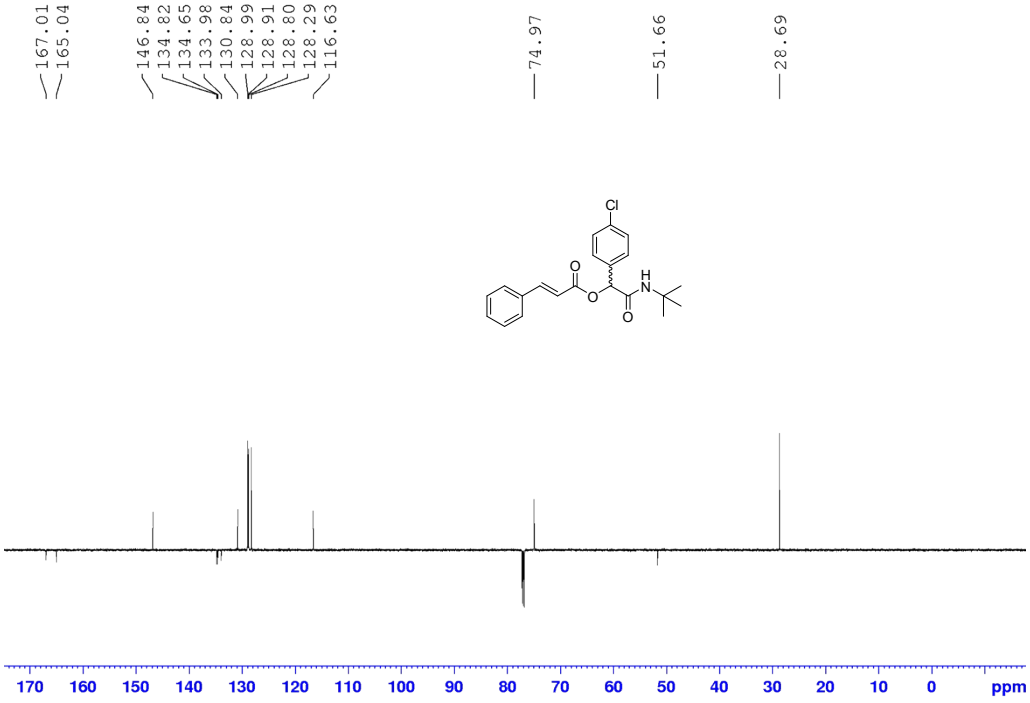

Figure 28. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7a$_2$**).

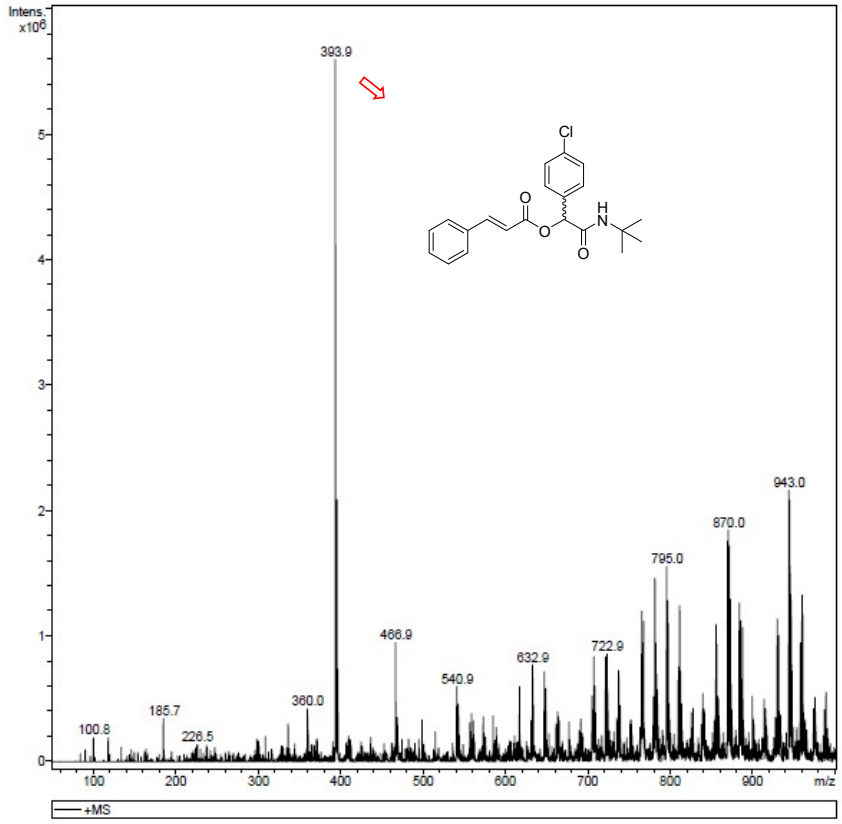

Figure 29. Infrared (ATR - FTIR) spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2-yl)acrylate (**7b$_1$**).

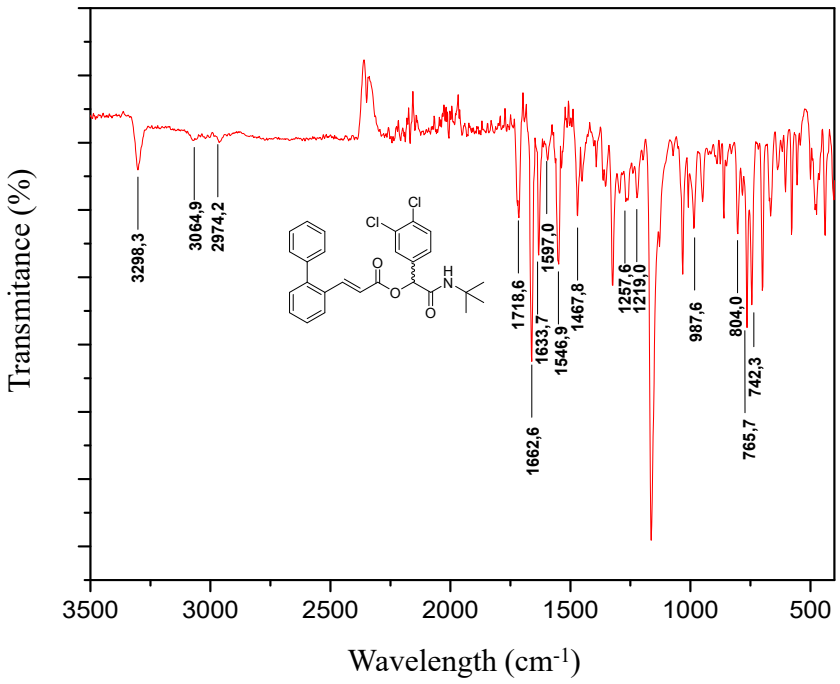

Figure 30. [1]H NMR spectrum of *E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2-yl)acrylate (**7b$_1$**) (600 MHz; $CDCl_3$).

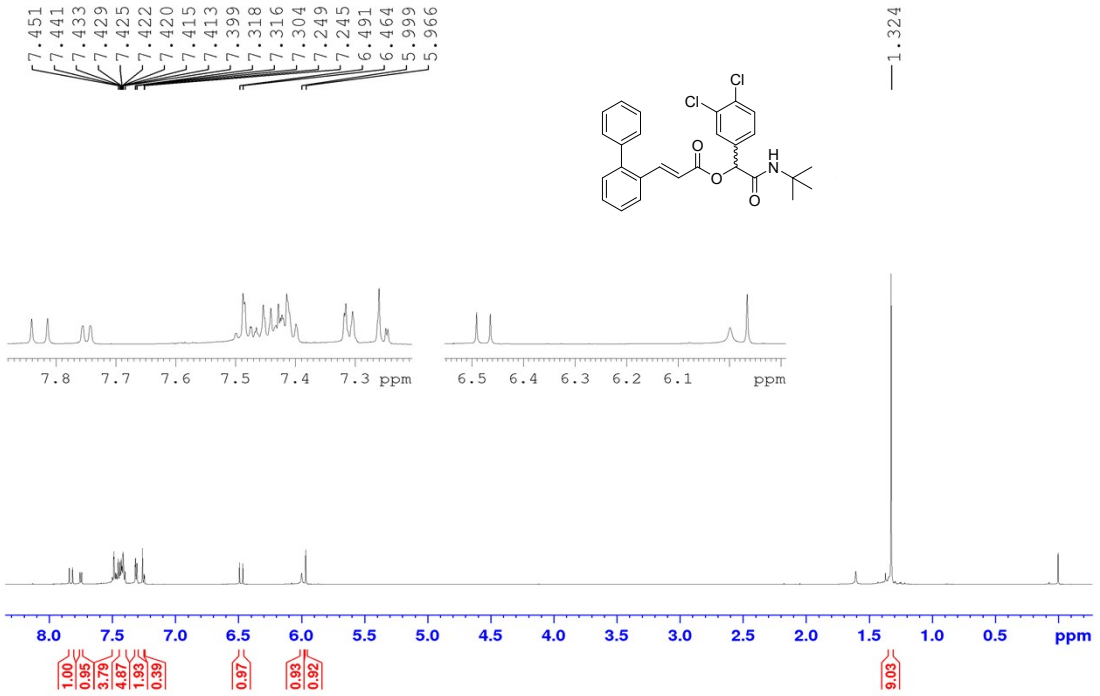

Figure 31. [13]C NMR spectrum of *E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2-yl)acrylate (**7b$_1$**) (150 MHz; $CDCl_3$).

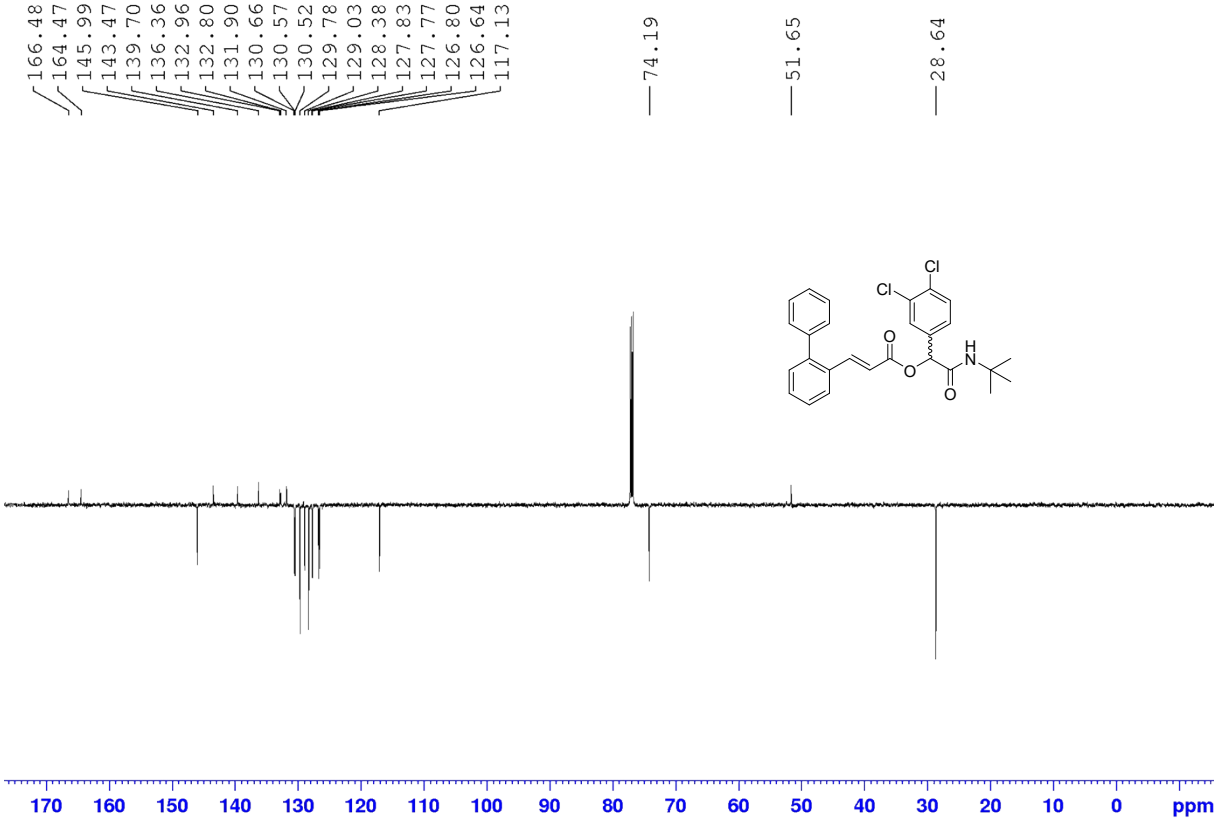

Figure 32. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of 2 – (*tert*-Butylamino) – 2 – oxo – 1 – phenylethyl cinnamate (**7b$_1$**).

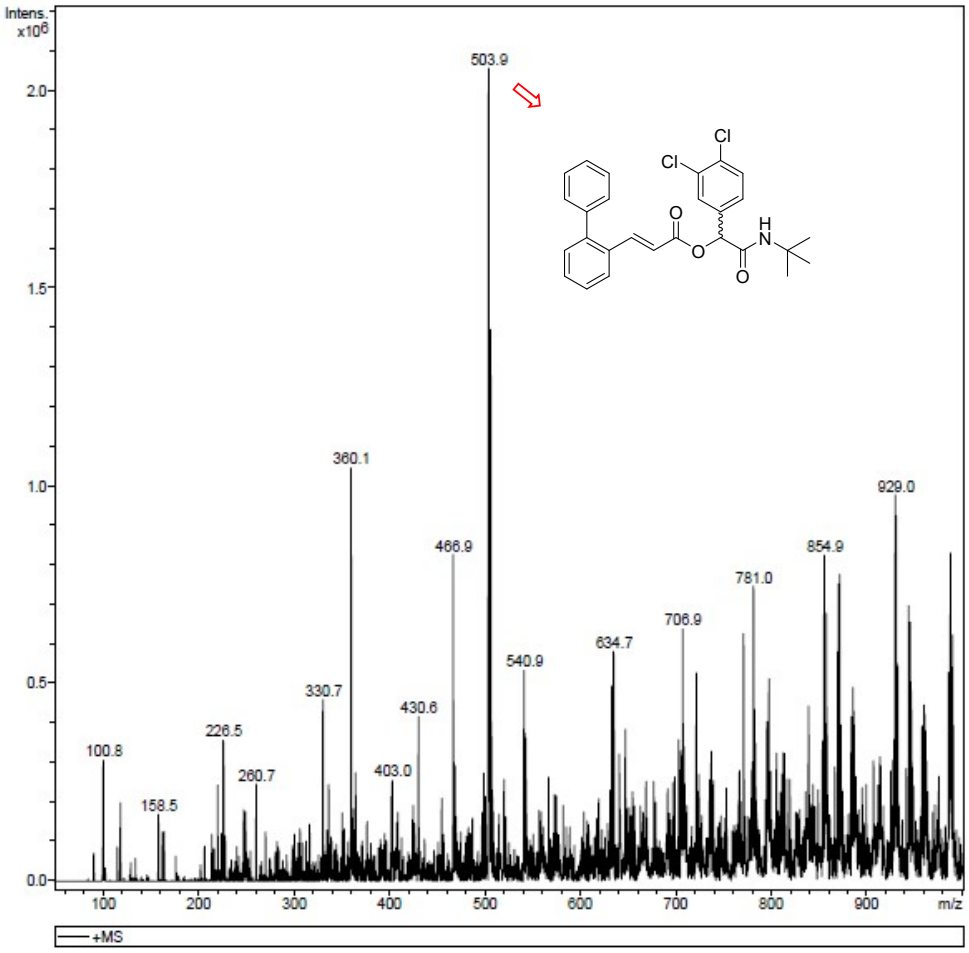

Figure 33. Infrared (ATR - FTIR) spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dimethoxyphenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2- yl)acrylate (**7b$_2$**).

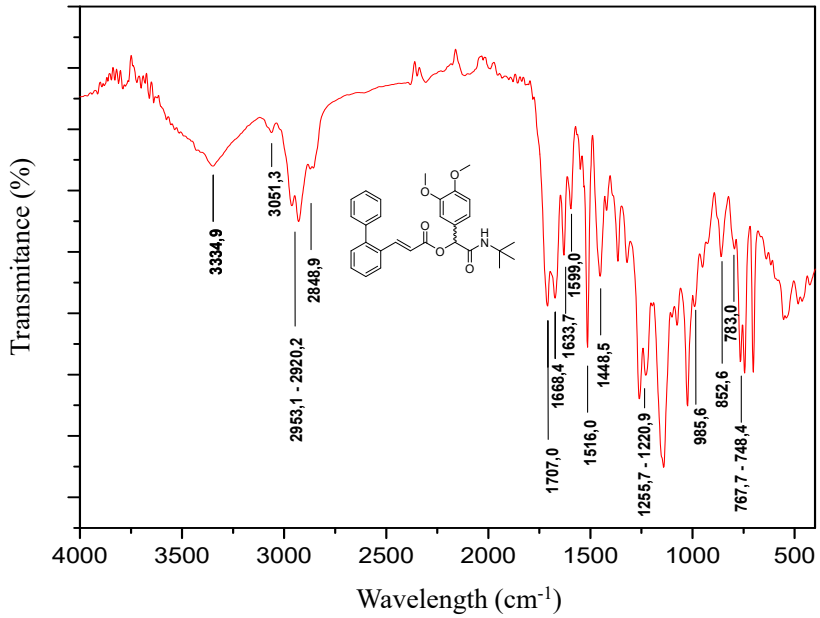

Figure 34. [1]H NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4- dimethoxyphenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2- yl)acrylate (**7b$_2$**) (600 MHz; $CDCl_3$).

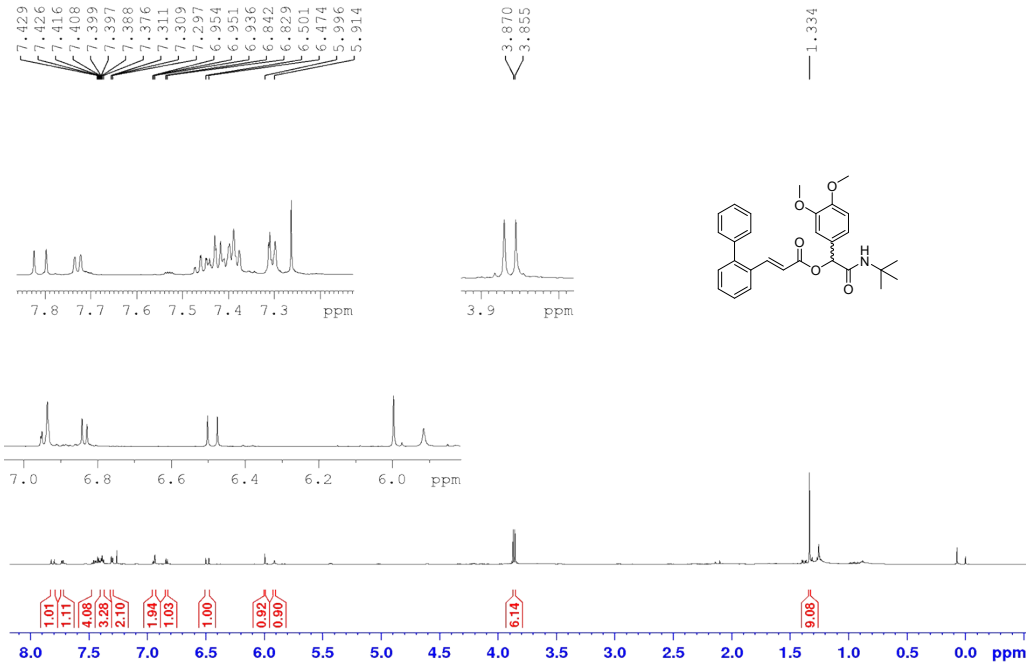

Figure 35. [13]C NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4- dimethoxyphenyl)-2-oxoethyl 3-([1,1'-biphenyl]-2- yl)acrylate (**7b$_2$**) (150 MHz; $CDCl_3$).

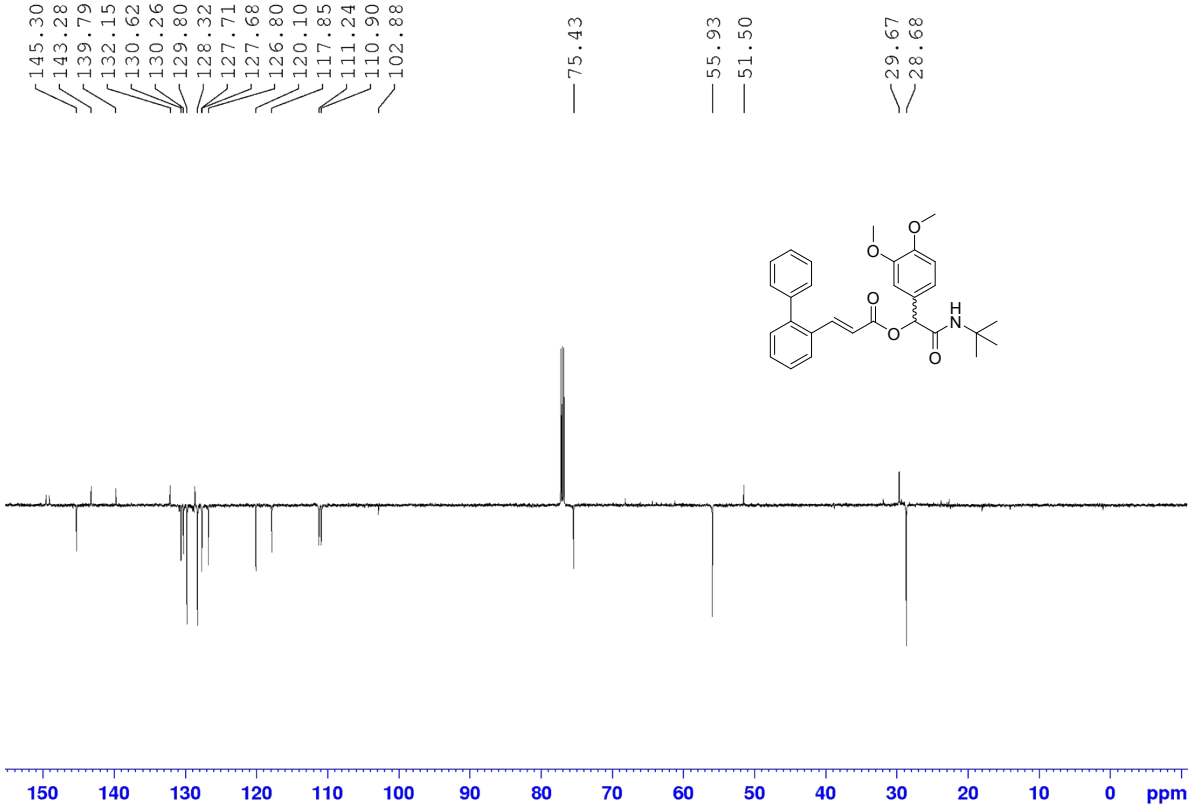

Figure 36. Infrared (ATR - FTIR) spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-(naphthalen-2-yl)acrylate (**7cb1**).

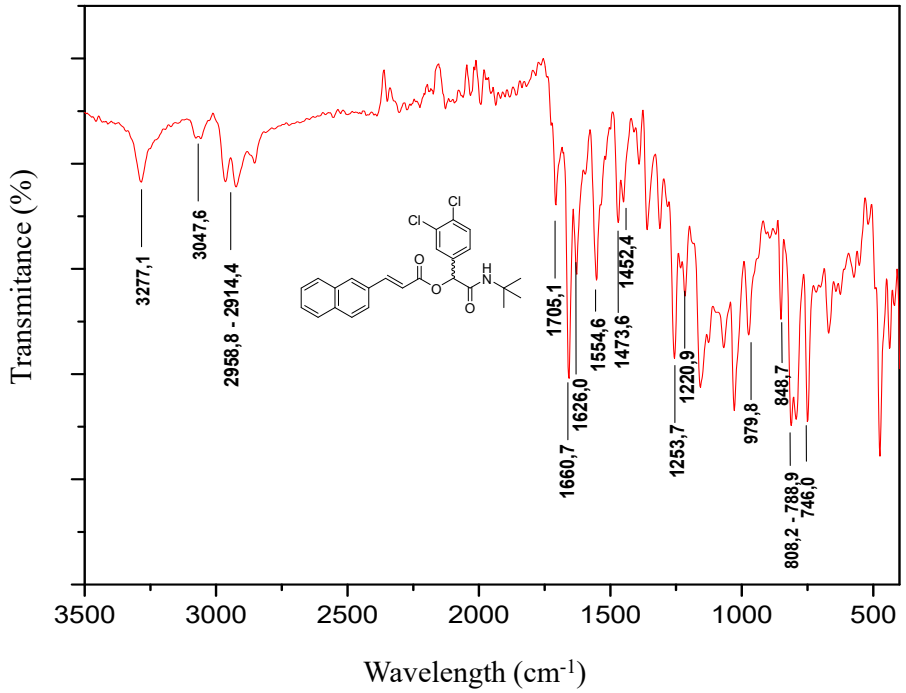

Figure 37. ^{1}H NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-(naphthalen-2-yl)acrylate (**7cb1**) (600 MHz; $CDCl_3$).

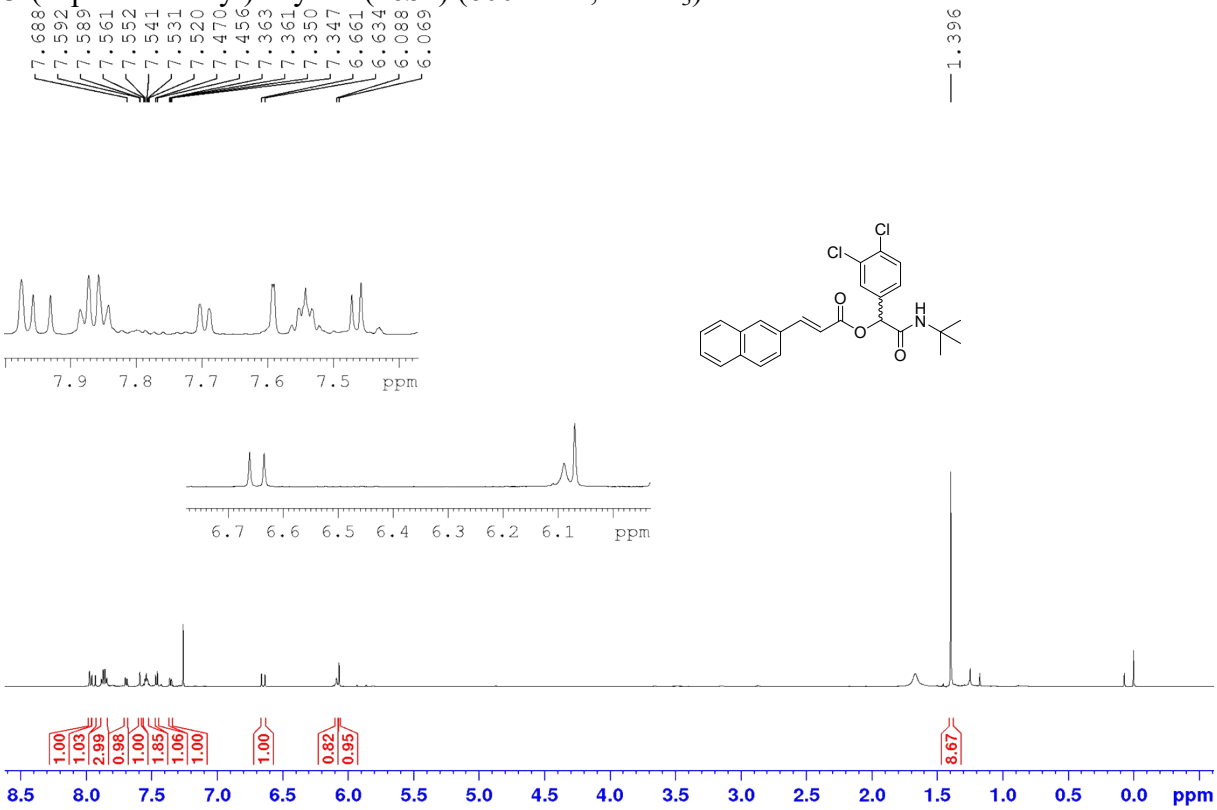

Figure 38. ^{13}C NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-(naphthalen-2-yl)acrylate (**7cb1**) (150 MHz; $CDCl_3$).

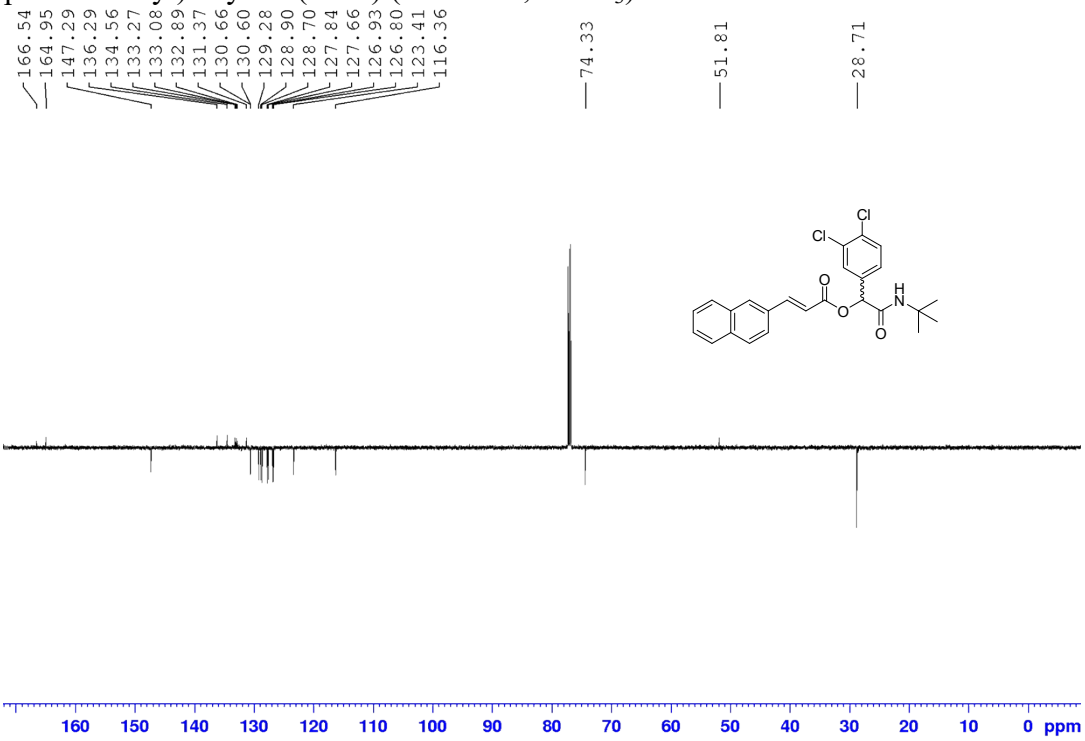

Figure 39. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4-dichlorophenyl)-2-oxoethyl 3-(naphthalen-2-yl)acrylate (**7cb1**).

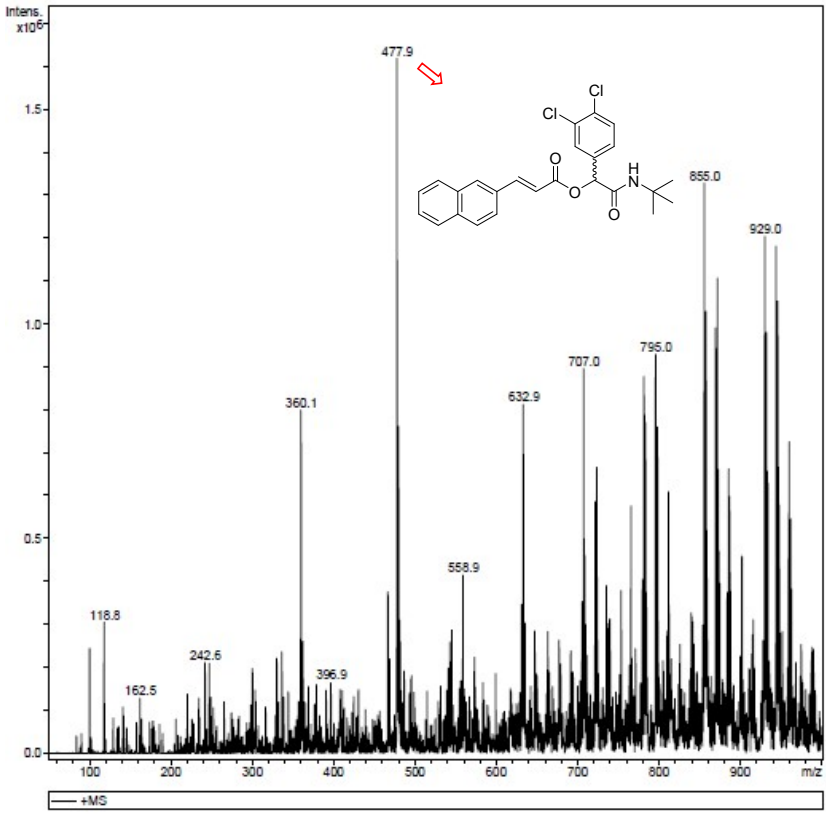

Figure 40. Infrared (ATR - FTIR) spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4dichlorophenyl)-2 oxoethyl 3-(4-chlorophenyl)acrylate (**7db$_1$**).

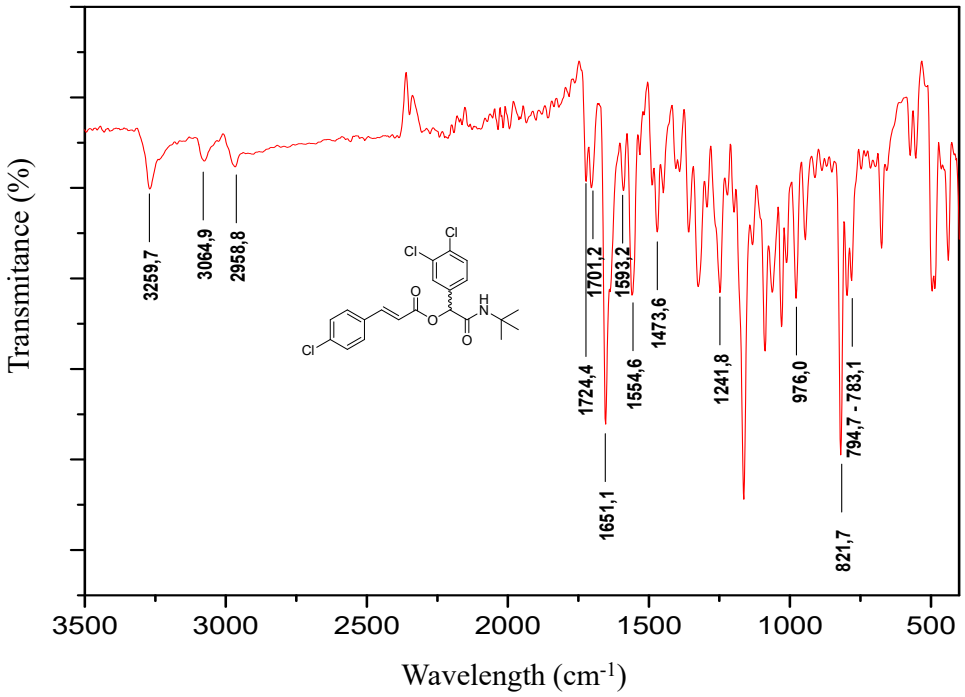

Figure 41. ^{1}H NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4dichlorophenyl)-2 oxoethyl 3-(4-chlorophenyl)acrylate (**7db$_1$**). (600 MHz; $CDCl_3$).

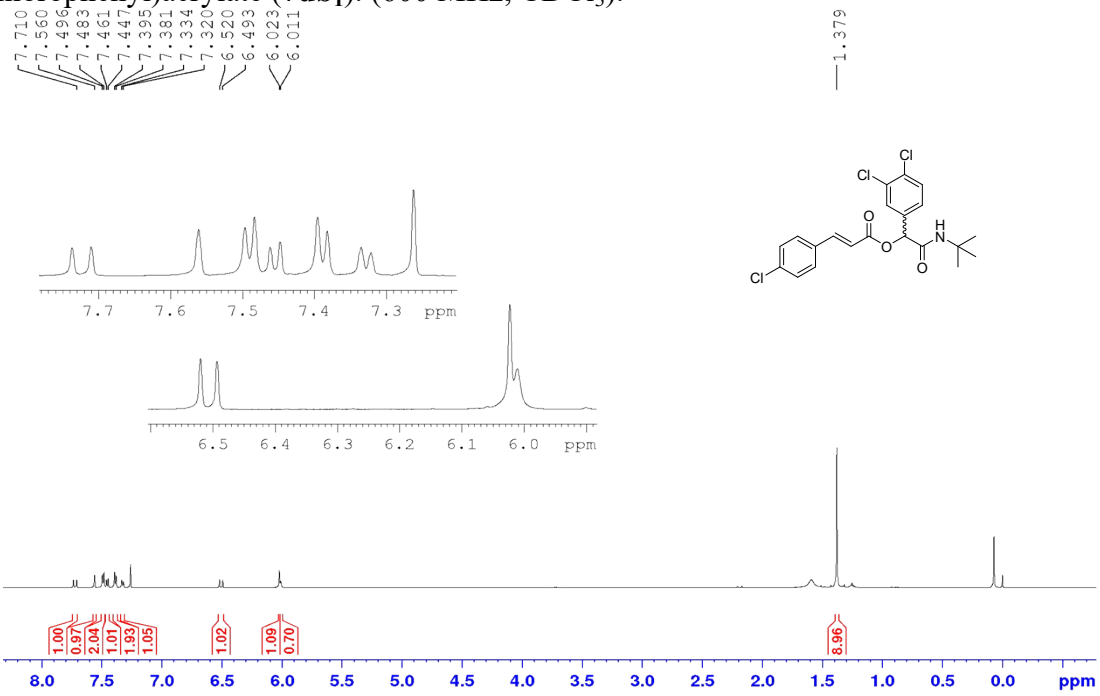

Figure 42. ^{13}C NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4dichlorophenyl)-2 oxoethyl 3-(4-chlorophenyl)acrylate (**7db$_1$**) (150 MHz; $CDCl_3$).

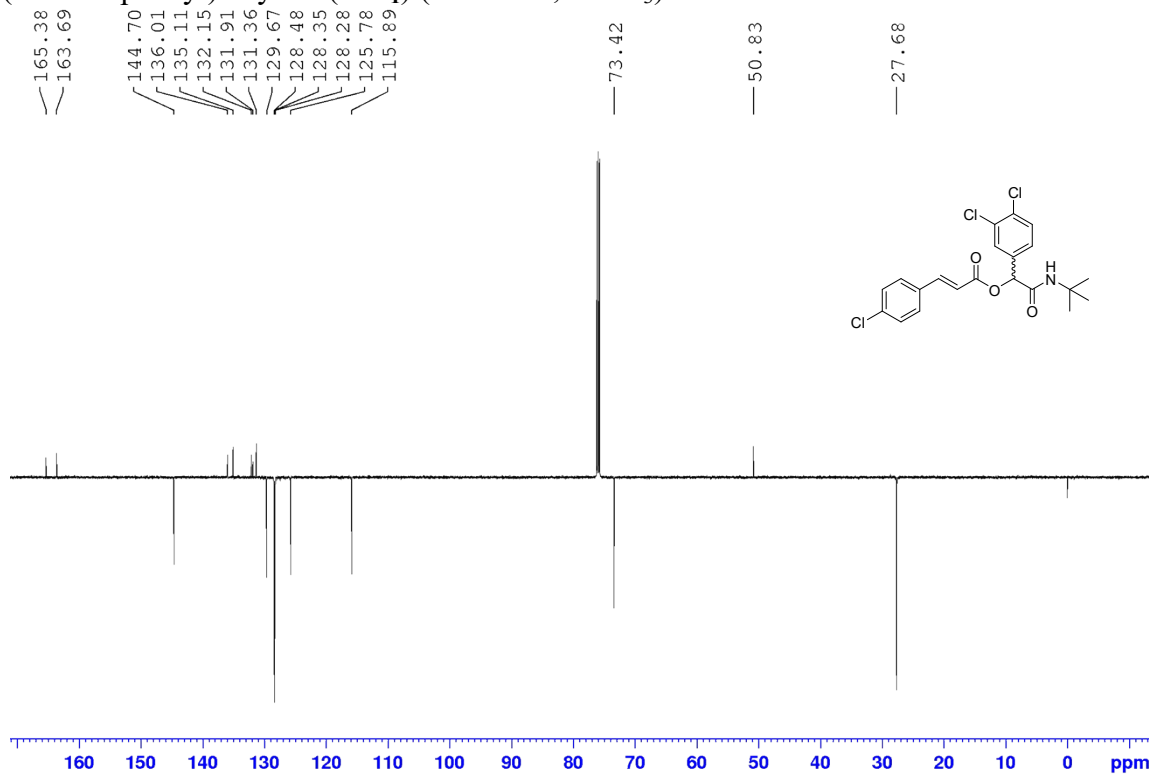

Figure 43. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of (*E*)-2-(*tert*-Butylamino)-1-(3,4dichlorophenyl)-2 oxoethyl 3-(4-chlorophenyl)acrylate (**7db$_1$**).

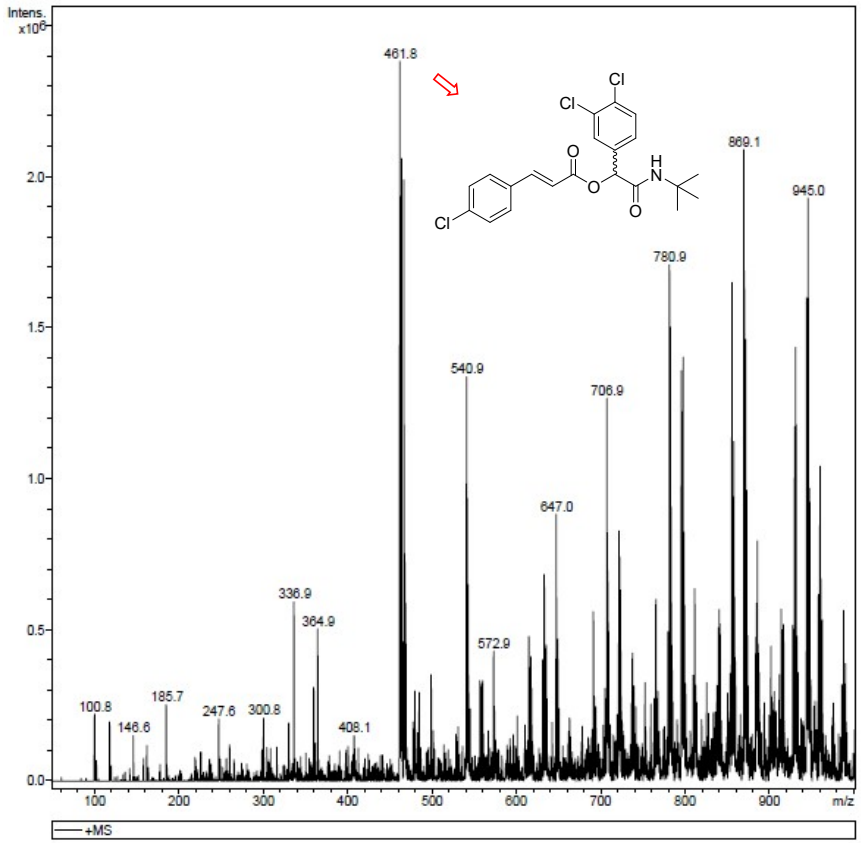

Figure 44. Infrared (ATR - FTIR) spectrum of (*E*)-2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2 oxoethyl 3-(4-(trifluoromethoxy) phenyl)acrylate (**7ea2**).

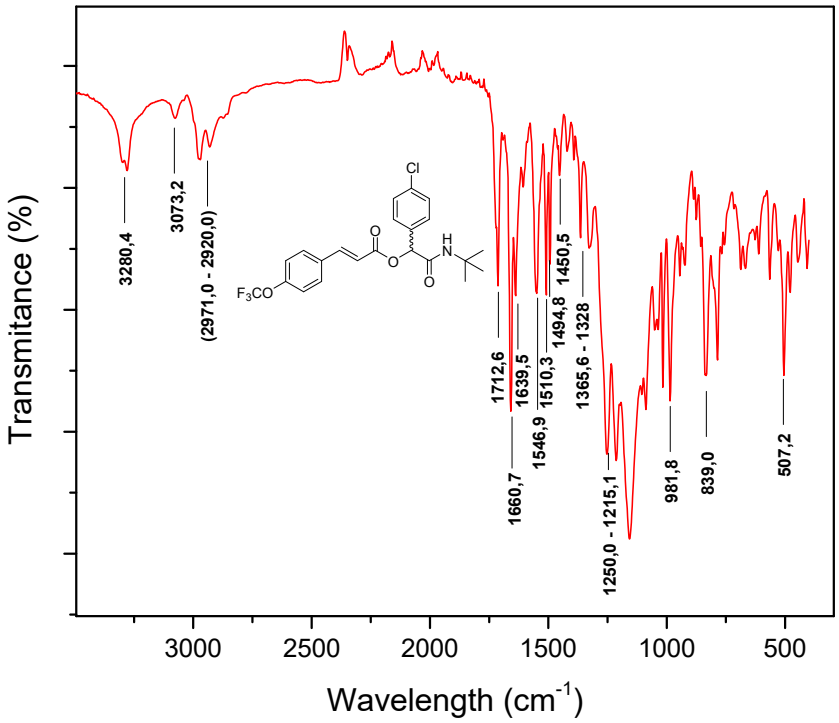

Figure 45. ^{1}H NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2 oxoethyl 3-(4-(trifluoromethoxy) phenyl)acrylate (**7ea2**) (600 MHz; $CDCl_3$).

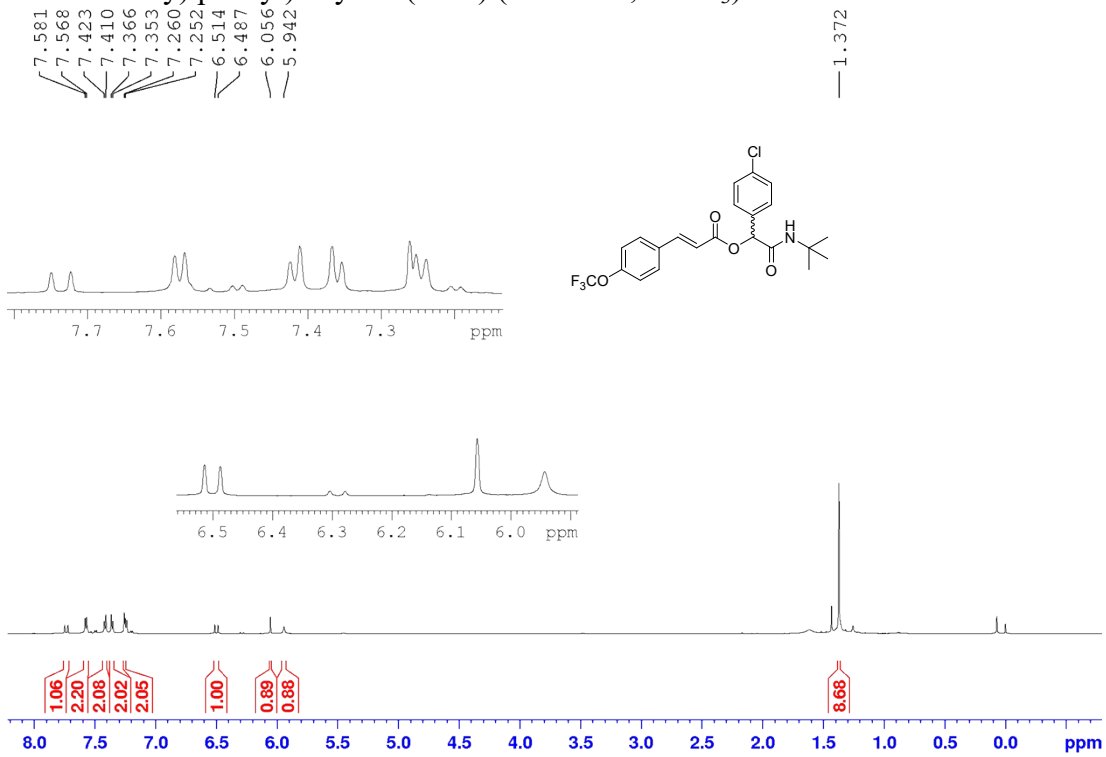

Figure 46. ^{13}C NMR spectrum of (*E*)-2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2 oxoethyl 3-(4-(trifluoromethoxy) phenyl)acrylate (**7ea2**) (150 MHz; $CDCl_3$).

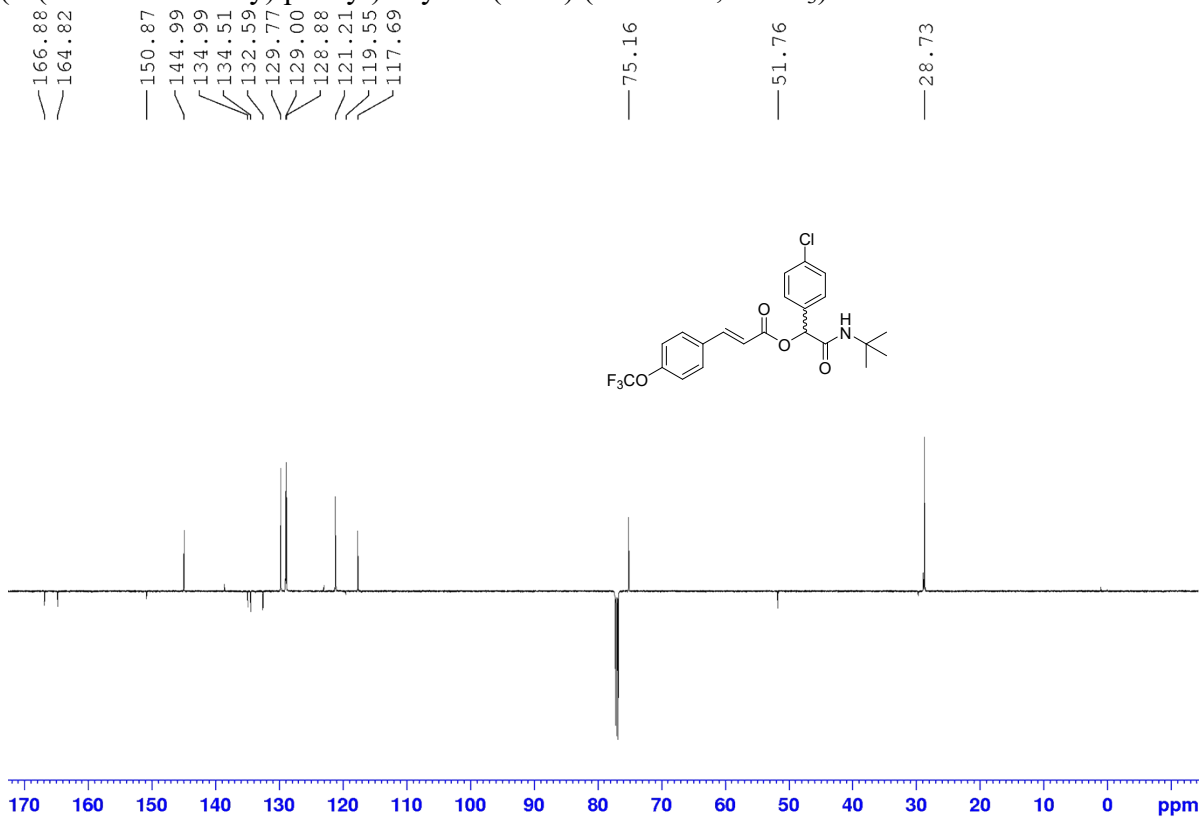

Figure 47. ESI-TOF (*m/z*) - $[M+Na]^+$ spectrum of (*E*)-2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2 oxoethyl 3-(4-(trifluoromethoxy) phenyl)acrylate (**7ea2**).

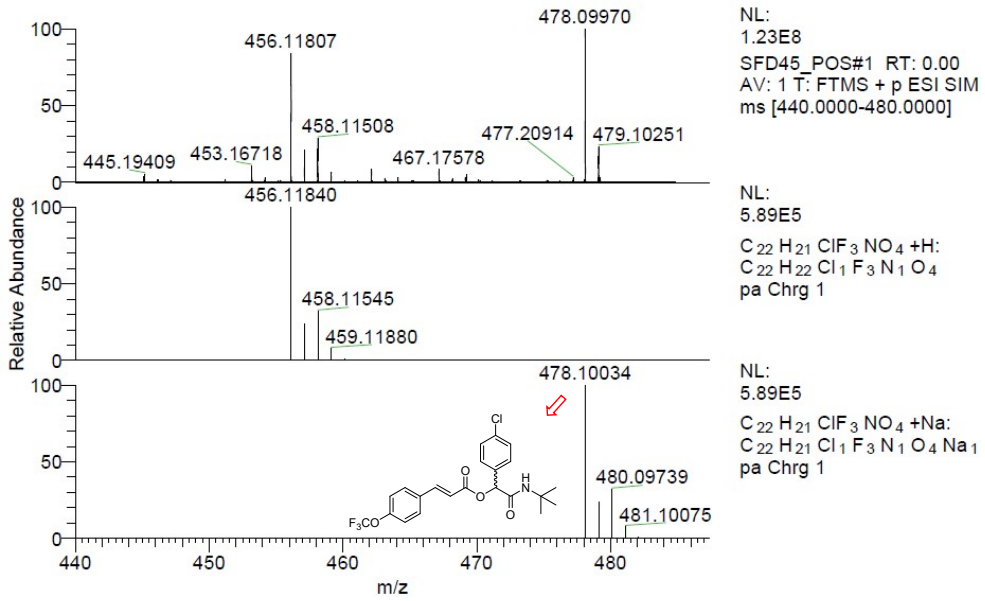

Table 1. Results of the virtual screening of biological targets present in *Leishmania* of compound 7a1 based on reverse docking.

Key targets	Target name (gene)	UniProt code	Description	Free energy of binding (kcal/mol)
O93874_COCLU	17HSDcl	93874	17beta-hydroxysteroid dehydrogenase	**-7.361**
Q8ILP4_PLAF7		Q8ILP4	Pantothenate quinase, putative	**-7.873**
ACER2_HUMAN	ACER2	Q5QJU3	Alkaline ceramidase 2	**-8.099**
STXA_SHIDY	stxA	Q9FBI2	Subunit A of Shiga toxin	**-8.597**
PPAP_HUMAN	ACP3	P15309	Prostatic acid phosphatase	**-7.480**
AMD_HUMAN	PAM	P19021	Peptidyl-glycine alpha-amidant monooxygenase	**-7.667**
CA2D1_RAT	Cacna2d1	P54290	Alpha-2/delta-1 subunit of the voltage-dependent calcium channel	**-7.200**
AK1BA_HUMAN	AKR1B10	60218	Aldo-keto reductase family 1 member B10	**-7.622**
MALX3_YEAST	IMA1	P53051	Oligo-1,6-glucosidase IMA1	**-8.044**
KCNQ2_MOUSE	Kcnq2	Q9Z351	Subfamily of voltage-gated potassium channels, KQT member 2	**-7.923**
CACB1_RAT	Cacnb1	P54283	Beta-1 subunit of the voltage-dependent L-type calcium channel	**-7.412**
VMAT2_HUMAN	SLC18A2	Q05940	Synaptic vesicular amine transporter	**-8.525**
RBBP9_HUMAN	RBBP9	75884	Serine hydrolase RBBP9	**-8.246**
A0A060INS8_CAPHI	CTSH	A0A060INS8	Cathepsin H	**-8.179**
CP24A_HUMAN	CYP24A1	Q07973	1,25-dihydroxyvitamin D(3) 24-hydroxylase, mitochondrial	**-7.758**
MMP1_HUMAN	MMP1	P03956	Interstitial collagenase	**-7.697**
MMP9_HUMAN	MMP9	P14780	Matrix metalloproteinase-9	**-7.399**
CP27B_MOUSE	Cyp27b1	35084	25-hydroxyvitamin D-1 alpha-hydroxylase, mitochondrial	**-8.381**
MMP2_HUMAN	MMP2	P08253	72 kDa type IV collagenase	**-8.155**
C3TDZ2_ECOLX	fabH	C3TDZ2	3-oxoacyl-[acyl-transporter protein] synthase 3	**-8.287**
AMPL_PIG	LAP3	P28839	Cytosol aminopeptidase	**-8.608**

Key targets	Target name (gene)	Code in UniProt	Description	Free energy of binding (kcal/mol)
NR1H4_HUMAN	NR1H4	Q96RI1	Bile acid receptor	**-7.217**
Q94F81_MAIZE	hda106	Q94F81	Histone deacetylase type HD2 HDA106	**-7.971**
HDAC7_HUMAN	HDAC7	Q8WUI4	Histone deacetylase 7	**-7.538**
CAC1B_RAT	Cacna1b	Q02294	Alpha-1B subunit of the voltage-dependent N-type calcium channel	**-7.312**
H9B8T9_CAPHI	CTSB	H9B8T9	Cathepsin B	**-7.014**
Q72874_9HIV1	pol	-	Pol polyprotein	**-8.120**
Q7ZJM1_9HIV1	pol	-	Integrase	**-7.560**
LPXC_PSEAE	lpxC	P47205	UDP-3-O-acyl-N-acetylglucosamine deacetylase	**-7.380**
DHB3_RAT	Hsd17b3	54939	Testosterone 17-beta-desidrogenase 3	**-7.298**
TLR4_MOUSE	Tlr4	Q9QUK6	Receiver type Toll 4	**-7.661**
PSA_HUMAN	NPEPPS	P55786	Puromycin-sensitive aminopeptidase	**-8.284**
AK1C4_HUMAN	AKR1C4	P17516	Aldo-keto reductase family 1 member C4	**-7.959**
HDAC5_HUMAN	HDAC5	Q9UQL6	Histone deacetylase 5	**-7.100**
S12A2_HUMAN	SLC12A2	P55011	Solute carrier family 12 member 2	**-7.700**
TTHY_HUMAN	TTR	P02766	Transthyretin	**-7.617**
FOS_HUMAN	FOS	P01100	Proto-oncogene c-Fos	**-7.153**
KCNQ3_HUMAN	KCNQ3	43525	Subfamily of voltage-gated potassium channels, KQT member 3	**-7.800**
GABT_RAT	Abat	P50554	mitochondrial 4-aminobutyrate aminotransferase	**-7.134**
ALDR_HUMAN	AKR1B1	P15121	Aldo-keto reductase family 1 member B1	**-7.059**
AGP1_YEAST	AGP1	P25376	General amino acid permease AGP1	**-7.937**
HDAC1_MOUSE	Hdac1	9106	Histone deacetylase 1	**-7.104**
P96830_MYCTO		P96830	Protein containing TYR_PHOSPHATASE_2 domain	**-8.293**
CAH13_MOUSE	Ca13	Q9D6N1	Carbonic anhydrase 13	**-8.732**

Table 1. *Continued.*

Key targets	Target name (gene)	Code in UniProt	Description	Free energy of binding (kcal/mol)
HDAC9_HUMAN	HDAC9	Q9UKV0	Histone deacetylase 9	**-7.790**
	PDB: 2JK6		Trypanothione reductase	**-8.092**
	-		Pantothenate quinase, putative	**-7.200**
	3UIB		Protein Kinase A	**-7.865**
	PDB: 4JZX		Ceramide sintase	**-8.180**
	PDB: 4C7H		N-myristoyltransferase	**-8.980**
	PDB: 5OEY		Frutose-1,6-bisphosphatase	**-7.510**
	-		Secreted acid phosphatase	**-8.208**
	-		Serine hydrolase	**-7.784**
	Homology		Aspartyl aminopeptidase	**-7.989**
	Homology		Aldehyde dehydrogenase	**-8.281**
	Homology		Mitochondrial	**-7.708**
			Kinetoplastids (KMP-11)	**-7.999**
			Glycoprotein – gp46/M-2	**-7.767**
	Leishmanolysin (GP63)		Glycoproteins - gp63	**-7.681**