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Preparation,Characterization And Biological Activity Of Some New Amides From Thiazolidine-4-carboxylic Acid.

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الخلاصة

تضمنت الدراسة تحضير سلسلة من الامايد الجديده من تفاعل بعض الامينات الاروماتية مع حامض-5,5-ثنائي مثيل-2-فنيل الثايزولدين-4-كربوكسيل(A)،والذي تم تحضيره من تفاعل البنزالديهايد مع د.بنسلامين D-Penicillamine تحت ظروف طفيفة، من خلال تفاعل التخليق بين البنسلامين والبنزالديهايد تحت درجة حرارة الغرفة باستخدام الايثانول والماء كمذيب. وتتم حماية مجموعة الأمين في حلقة ثيازوليدين(A) عن طريق التفاعل مع أنهيدريد حامض الخليك ; والذي تم تحويله إلى مشتق 3- اسيتايل ثايزولدين(At) 3-acetyl-5,5-dimethyl-2-phenylthiazolidine-4- carboxylicacid .وتم الحصول على الأميدات المقابلة من تفاعل المركب (At) مع الأمينات المختلفة باستخدام DDC / HOBt كعوامل ازدواج ،تم تشخيص جميع المركبات المحضرة من خلال قياس درجة الانصهار وقياس أطياف تحت الاحمراء واطياف الكتلة واطياف الرنين النووي المغناطسي البروتوني. وأخيراً تم دراسة الفعالية البيولوجية.

Abstract:

A new series of amides from different aromatic amines and2-phenyl thiazolidine-4-carboxylic acid which were prepared from the reaction of benzaldehyde with D-penicillamine under slightly conditions, thiazolidine have been synthesized in one step by cyclization of penicillamine with benzaldehydes in ethanol and water at room temperature . The amine group in the thiazolidine ring is protected by reaction with the acetic anhydride ,which was converted to the corresponding 3-aceylthiazolidine derivative . Reaction of N-aceyl-protected carboxylic acids with different amines using DDC/HOBt gave corresponding amides ,The general synthesis of 2-phenyl-thiazolidine-4-carboxylic acid amides is shown in Scheme 1. All products were characterized and identified by FT.I.R and ^{1}H-NMR spectroscopy , and Finally a biological activity (antimicrobial) for the new prepared products were checked.

Keywords : D-penicillamine; thiazolidine ,carboxamide,Antimicrobial.

1-Introduction

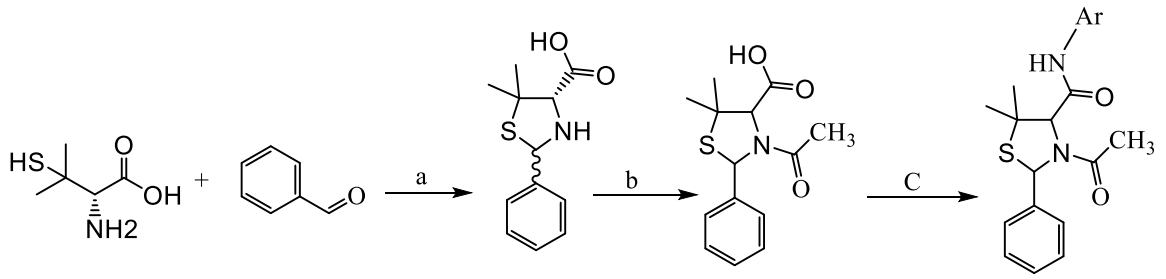
Thiazolidine is a family of heterocyclic compounds, It is one of the classes of heterocyclic 5-member saturated ring compounds that contain sulfur and nitrogen as heteroatom's in the 1 and 3 positions in the form of thioether and amines group, respectively [(1)]. Thiazolidine-4-carboxylic acid(TC) and 2-substituted are unnatural amino acid analogs of L-proline, One straightforward way to obtain it is by reacting α-aminothiols like (L-cysteine or D-pencillamine) with reactive carbonyls [(2)]. 2-arylthiazolidine carboxylic acids and derivatives are great interest in organic, bioorganic, natural product and medicinal chemistry. Thiazolidine amides are one of the most important (TC) derivatives as they have various biological activities like antimicrobials as in penicillins , cephalosporins, carbapenems, clavunalic acid, narcodicins and thienamicyn [(3)]; immunomodulators[(4)],antiviral drug [(5)], anti-diabetic agents[(6)], antihypertensive drugs[(7)], antifungal[(8)], antibactrial[(9)] ,anti HIV[(10)] , Potential treatments for neurodegenerative processes and memory loss[(11)], and potent cytotoxic agents for both prostate cancer and melanoma[(12)],In addition, these derivatives have been widely used as chiral ligands in several organometallic reactions[(13)]. Researchers have extensively explored thiazolidine amides, for their biological activities and organic catalytic applications. The concurrent effect of a thiazolidine ring and a functional group of amide in thiazolidine amide moieties, has always been found to be important scaffolds with many biological activities[(14)], therefore large number of these heterocyclics were synthesized by structure modifications in a series of compounds for the development of newer, multi-target drugs with broad spectrum bioactivity.In this work a series of 2-phenyl-thiazolidine-4-carboxylic acid amides has been synthesized, and biological evaluation .

2-Experimental:-

All chemical were supplied from merck, sigma and fluka chemicals companies.Uncorrected melting points were determined by using thermal scientific apparatus. Fourier transfrom infrared spectra were recorded using KBr discs on 8400s, shimadzu,Japan. Spectrophotometer and the measurement were done in chem.Dept ,Basrah university.^{1}H-nmr spectra were recorded at 400 MHz on Iran by using Bruker (400MHz) in a DMSO-*d*6 solution with tetramethylsilane as an internal standard. Mass spectra were recorded using the (El) Impact Electron technique at (70 ev) on Amirkabir University- Iran. Using an agilent mass 5975 spectrometer analyzer quadropole. Thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 plates (0.25 mm thick, art 1.05714.)

2-1. **Synthesis of 2-phenylthiazolidine-4-carboxylic acids(A):**

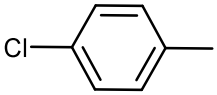
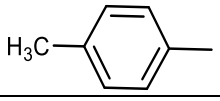
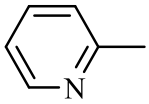
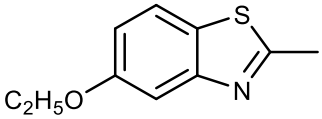
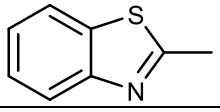
Compound(A) was is prepared from the condensation of D-penicillamine with a benzaldehyde . performing modifications in already reported method [15]. in excellent yields (Scheme 1).

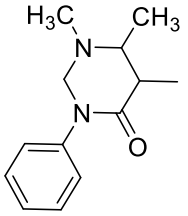
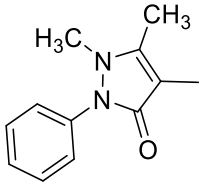
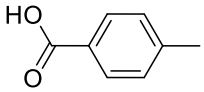
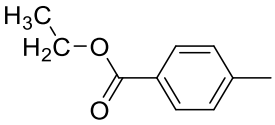
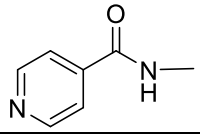
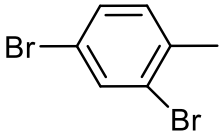
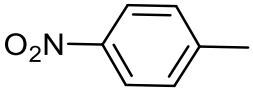
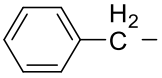


(a)Solvent ETOH :H_2O, stir . 24h (b):Na_2CO_3 6%, acetic anhydride (c):DCC,HOBT,DCM Stir 24h

Scheme 1: General method for the preparation of thiazolidine carboxylic acid derivative from penicillamine.

Table 1: Synthesis of 2-substituted thiazolidine carboxylic acid derivatives

Com.	Ar	m.p	Yield (%)	Structure& Molecular weight
b_1		159-160	69.3	$C_{20}H_{21}ClN_2O_2S$ M. Wt: 388.91
b_2		170-171	71	$C_{21}H_{24}N_2O_2S$ M .Wt: 368.50
b_3		179-180	52	$C_{19}H_{21}N_3O_2S$ M. Wt: 355.46
b_4		199-200	54.5	$C_{23}H_{25}N_3O_3S_2$ M. Wt: 455.59
b_5		198-200	76	$C_{21}H_{21}N_3O_2S_2$ M. Wt: 411.54

b_6		209-110dec	84	$C_{26}H_{32}N_4O_3S$ M Wt: 480.63
b_7		205-207dec	65	$C_{25}H_{28}N_4O_3S$ M.Wt: 464.58
b_8		168-170	63	$C_{21}H_{22}N_2O_4S$ MWt: 398.48
b_9		197-198	72	$C_{23}H_{26}N_2O_4S$ M.Wt: 426.53
b_{10}		138-139	72	$C_{20}H_{22}N_4O_3S$ M. Wt: 398.48
b_{11}		148-150	66	$C_{20}H_{20}Br_2N_2O_2S$ M. Wt: 512.26
b_{12}		116-119	62	$C_{20}H_{21}N_3O_4S$ M. Wt: 399.47
b_{13}		68-70	71	$C_{21}H_{24}N_2O_2S$ M. Wt: 368.50

2.2. Synthesis of 3-acetyl-5,5-dimethyl-2-phenylthiazolidine-4-carb- oxylic acid (At).[16]

The title compound were prepared from the corresponding 5,5-dimethyl-2-phenylthiazolidine-4-carboxylic acid (A1)acid according to literature procedure [16] With some modification. A solution containing thiazolidine (A1) (2.37 g, 10 mmole) in 6% aqueous Na_2CO_3 (25 ml) with cooled in ice- bath and stirred, Acetic anhydride (1 equivalent) is dropped to the solution over 2 min, After everything had been added the solution was stirred for a further 60 minutes, the reaction was followed by TLC. The crude mixture was filtered off and washed with a saturated solution of aqueous NaCl (15 ml) and extracted three times with CH_2Cl_2 (3× 15 ml). The organic phase was dried over Na_2SO4 and the solvent evaporated .At (2.01 g, 84.4%) as white crystals: mp 213–215. °C; IR _max (KBr) 3500, 2400-3400b,3050 ,2924, 1724,1624

,1494 ,1454 ,1415,1355, 1197, 732 cm^{-1}; The 1H NMR spectrum((400 MHz, (DMSO-*d6*)

2.3. Preparation of the mono amide of thiazolidine-4- carboxylic acid (b_1-b_{13}).[17]

Mono amide was prepared according to the literature procedure [17] with some modification. To a stirred solution of **3-**acetyl-5,5-dimethyl-2-phenylthiazolidine-4-carboxylic acid (2.8g 10mmol) DDC (1.25 equiv) and HOBt (1 equiv) in CH_2Cl_2 (25-50 mL) was stirred for 10 min. To this solution, appropriate amine (1 equiv) in 5ml CH_2Cl_2 was added over a period of 15 min .After the addition was completed the mixture stirred overnight, under an atmosphere of nitrogen, The white precipitate formed (dicyclohexylurea) was filtered of and the filtrate was diluted with CH_2Cl_2 (100-150 mL) and sequentially washed with water, sat $NaHCO_3$, a 5% citric acid solution (10ml) and brine and dried over Na_2SO_4.The solvent was evaporated and the residue was purified by silica gel column chromatograph (eluent ethylacetate:n-hexane 2:8).The physical properties and elemental analysis were registered and presented in Table 1:

3-acetyl-N-(4-chlorophenyl)-5,5-dimethyl-2-phenylthiazolidine-4-carboxamide(b_1)

Compound (b_1) was prepared from (At)(2.8g, 10 mmol) and 4-chloroaniline (1.3g, 10 mmol) according to the procedure described above. IR _max (KBr) 3290 ,3109 ,2931.8 ,1734,1703,1627.9,1541,1398; 1H NMR spectrum(400 MHz, (DMSO-*d6*):δ= 1.31 (3H, s), 1.62 (3H, s), 1.82 (3H, s), 5.29 (1H, s), 6.62(1H, s), 7.32-8.21 (9H, m ,ArH). EIMS (EI): m/z [M]+:(388.08m/z , 0.55%); Mwt=388.3

3-acetyl-5,5-dimethyl-2-phenyl-N-(p-tolyl)thiazolidine-4-carbox-amide(b_2)

Compound (b_1) was prepared from (At)(2.8g, 10 mmol) and 4- p-toluidine (1.07g, 10 mmol) according to the procedure described above. IR _max (KBr) 3100, 3045, 2931, 1734, 1624, 1494,1354; 1H NMR spectrum((400 MHz, (DMSO-d6)showed the presence of the two diastereoisomers (2S,4S) and (2R,4S) (ratio 38:62); Minor isomer: 1H NMR (400 MHz, (DMSO-*d6*):δ= δ= 1.32 (3H, s), 1.67 (3H, s), 2.29 (6H, s), 4.81 (1H, s), 6.37(1H, s), 7.18-8.0 (9H, m ,ArH). EIMS (EI,70ev): m/z [M]+:(368.5,m/z , 13.34%); Mwt=368.4

3-acetyl-5,5-dimethyl-2-phenyl-N-(pyridin-2-yl)thiazolidine-4-carboxamide(b_3)

Compound (b_3) was prepared from (At)(2.8g, 10 mmol) and pyridin-2-amine (0.94g, 10 mmol) according to the procedure described above. IR _max (KBr) 3199, 3064, 2976,1739, 1707, 1627, 1608,1340; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed : δ= 1.30 (3H, s), 1.60 (3H, s), 1.73 (3H, s), 4.53 (1H, s), 6.43(1H,

s), 7.30-7.80 (10H, m ,ArH). EIMS (EI,70ev): m/z [M]+:(355.46m/z , 0.86%); Mwt=355.4

3-acetyl-N-(6-ethoxybenzo[d]thiazol-2-yl)-5,5-dimethyl-2-phenyl thiazolidine-4-carboxamide(b_4)

Compound (b_4) was prepared from (At)(2.8g, 10 mmol) and 6-ethoxybenzo[d]thiazol-2-amine (1.94g, 10 mmol) according to the procedure described above. IR _max (KBr), 3226, 3059, 2966,1708.9,1664, 1631, 1593, 1566,1388,1228; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.32 (3H, s), 1.38 (3H, t), 1.66 (3H, s), 1.66 (3H, s), 4.10 (2H, q),4.99(1H, s), 6.41(1H, s), 7.08-7.98 (8H, m ,ArH). EIMS (EI,70ev): m/z [M]+:(455.59m/z , 9.60%); Mwt=455.32.

3-acetyl-N-(benzo[d]thiazol-2-yl)-5,5-dimethyl-2-phenylthiazolidin-e-4-carboxamide(b_5)

Compound (b_5) was prepared from (At)(2.8g, 10 mmol) and 5-amino-1,6-dimethyl-3-phenyltetrahydropyrimidin-4(1H)-one (1.5g , 10 mmol) according to the procedure described above. IR _max (KBr), 3062, 3028, 2968,1734,1624, 1519, 1354, 1207 cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*): δ= 1.39 (3H, s), 1.61 (3H, s), 1.67 (3H, s), 2.08 (3H, s), 3.09 (3H, s), 4.81 (1H, s),6.35(1H, s), 7.28-7.93 (10H, m ,ArH). EIMS (EI,70ev): m/z [M]+:(480.63m/z ,0.08%); Mwt=480.5.

3-acetyl-N-(1,6-dimethyl-4-oxo-3-phenylhexahydropyrimidin-5-yl)-5,5-dimethyl-2-phenylthiazolidine-4-carboxamide (b_6)

Compound (b_6) was prepared from (At)(2.8g, 10 mmol) and benzo[d]thiazol-2-amine (2.19g, 10 mmol) according to the procedure described above. IR _max (KBr), 3156, 3045,2976 , 1734, 1666.5, 1624, 1492,1334cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.33 (3H, s), 1.68 (3H, s), 1.69 (3H, s), 5.02 (1H, s),6.42(1H, s), 7.33-8.02 (9H, m ,ArH). EIMS (EI,70ev): m/z [M]+:(411.54m/z , 1.25%); Mwt=411.2.

3-acetyl-N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-5,5-dimethyl-2-phenylthiazolidine-4-carboxamide(b_7)

Compound (b_7) was prepared from (At)(2.8g, 10 mmol) and 4-aminoantipyrine (2.03g, 10 mmol) according to the procedure described above. IR _max (KBr), 3230, 3059,2972,1718 ,1629 ,1680,1558, 1458, 1394cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.31 (3H, s), 1.42 (3H, s), 1.64 (3H, s), 2.22 (3H, s), 3.09 (3H, s), 4.84 (1H, s),6.37(1H, s), 7. 3-8.0 (m, (10H,ArH), 9.37(1H, s). EIMS (EI,70ev): m/z [M]+:(464.58m/z ,0.06%); Mwt=464.32.

2-(3-acetyl-5,5-dimethyl-2-phenylthiazolidine-4-carboxamido)-5-carboxybenzene-1-ylium (b_8)

Compound (b_8) was prepared from (At)(2.8g, 10 mmol) and 4-aminobenzoic acid (1.37g, 10 mmol) according to the procedure described above, IR _max (KBr), 3200, 3148,3028, 2933 ,1734 ,1666, 1624, 1514,1375,1195cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.34 (3H, s), 1.60 (3H, s), 1.73 (3H, s), 4.53 (1H, s),6.43(1H, s), 7.02-7.82(9H,ArH). EIMS (EI,70ev): m/z [M]+:(397.47m/z ,0.86%); Mwt=397.4

ethyl 4-(3-acetyl-5,5-dimethyl-2-phenylthiazolidine-4-carboxamido)benzoate(b_9)

Compound (b_9) was prepared from (At)(2.8g, 10 mmol) and Ethyl 4-aminobenzoate (1.65g, 10 mmol) according to the procedure described above IR _max (KBr), 3298, 3062,2931, 1658,1543 ,1454, 1344, 1269cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.31 (3H, t), 1.61 (3H, s), 1.71 (3H, s), 1.82 (3H, s), 4.54 (2H, q),5.30(1H, s), 6.62(1H, s), 7.29-8.24(9H,ArH). EIMS (EI,70ev): m/z [M]+:(426.16m/z ,0.33%); Mwt=426.32

3-acetyl-N'-isonicotinoyl-5,5-dimethyl-2-phenylthiazolidine-4-carbohydrazide(b_{10})

Compound (b_{10}) was prepared from (At)(2.8g, 10 mmol) and isonicotinohydrazide (1.37g, 10 mmol) according to the procedure described above IR _max (KBr), 3498, 3062,2933, 1734,1666,1624 ,1595, 1460, 1336cm^{-1} 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.31 (3H, s), 1.64 (3H, s), 1.72 (3H, s), 4.77 (1H, s),6.40(1H, s), 7.29-8.24(9H,ArH) ,10.44(1H, s), 10.62(1H, s), EIMS (EI,70ev): m/z [M]+:(398.48m/z ,1.1%); Mwt=398.2

3-acetyl-N-(2,4-dibromophenyl)-5,5-dimethyl-2-phenylthiazolidine-4-carboxamide(b_{11})

Compound (b_{11}) was prepared from (At)(2.8g, 10 mmol) and 2,4-dibromo aniline (2.5g, 10 mmol) according to the procedure described above IR _max (KBr), 3098, 3052,2926, 1734,,1624 ,1494, 1415, 1355cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.31 (3H, s), 1.62 (3H, s), 1.82 (3H, s), 5.3 (1H, s),6.62(1H, s), 7.32-8.26 (3H,ArH). EIMS (EI,70ev): m/z [M]+:(512.26m/z ,0.28%); Mwt=512.32

3-acetyl-5,5-dimethyl-N-(4-nitrophenyl)-2-phenylthiazolidine-4-carboxamide(b_{12})

Compound (b_{12}) was prepared from (At)(2.8g, 10 mmol) and 4-nitroaniline (1.4g, 10 mmol) according to the procedure described above IR _max (KBr), 3375, 3052,2933, 1734,,1680 ,1658,1527, 1415, 1327cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed: δ= 1.56 (3H, s), 1.65 (3H, s), 1.93 (3H, s), 4.88 (1H, s),6.34(1H, s), 7.23-8.23 (9H,ArH). EIMS (EI,70ev): m/z [M]+:(399.47m/z ,0.13%); Mwt=399.32.

3-acetyl-N-benzyl-5,5-dimethyl-2-phenylthiazolidine-4-carboxami-de(b_{13})

Compound (b_{13}) was prepared from (At)(2.8g, 10 mmol) and phenyl methan amine (1.07 g, 10 mmol) according to the procedure described above IR _max (KBr), 3375, 3050,2970, 1734,,1624,1658,1527, 1415, 1327cm^{-1}; 1H NMR spectrum((400 MHz, (DMSO-*d6*)showed the presence of the two diastereoisomers (2S,4S) and (2R,4S) (ratio 38:62); Minor isomer: :δ= 1.27 (s, 3H), 1.54 (s, 3H), 3.53 (s, 1H), 5.62 (s, 1H), 6.91 (t, *J* = 7.7 Hz, 4H), 6.78 (dt, *J* = 15.9, 8.0 Hz, 3H), 6.71 (t, *J* = 8.0 Hz, 1H) (3H,ArH) ; Major isomer:: δ= 1.31 (3H, s), 1.62 (3H, s), 3.59 (1H, s),5.96(1H, s), 6.91 (t, *J* = 7.7 Hz, 4H), 6.78 (dt, *J* = 15.9, 8.0 Hz, 3H), 6.71 (t, *J* = 8.0 Hz, 1H) (3H,ArH). EIMS (EI,70ev): m/z [M]+:(297.4m/z ,37.65%); Mwt=297.32

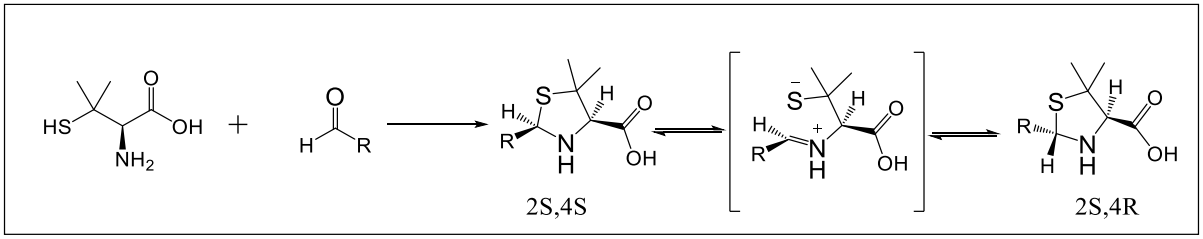
2-4. **Antimicrobial activity assay**

The diffusion Well Agar method (18) was followed to measure the biological effectiveness by activating the bacterial cell cultures used in the study. By using the cork drill and adding the prepared material whose biological efficacy is to be measured (0.1 ml) at a concentration of 200 parts per million, used solvent Dimethyl sulphoxalate (DMSO). The plates were incubated for 24 hours at a temperature of 37C◦.The antibacterial activity was evaluated by measuring the zone of inhibition (in mm) against test organisms compared with standard antibiotics such as ampicillin . Measurements were recorded at Basra University / College of Science / Department of Biology.

3-Results and discussion

Synthesis of the target compounds 2-phenylthiazolidine-4-carboxylic acid amide (b1-b15) wase achieved in three steps using inexpensive commercially available materials.The first step involved formation of Thiazolidine carboxylic acid (A1), were synthesized with good yields by condensing (S)-2-amino-3-mercapto-3-methylbutanoic acid with benzaldehyde (schem 1). The typical cyclization reaction was carried out in room temperatures in a water/ethanol mixture(75:25,v:v); after purification by recrystallization from aqueous ethanol; Pure thiazolidine was obtained (87%) yield ,Thus thiazolidine derivatives are obtained as diasteromeric mixtures, because cyclazation of D-penicillamine to build 2-substitution thiazolidine , gives rise to a new chiral center at C-2 position of the thiazolidine ring, affording a mixtures of two diasteroisomer; with respect to C2 (2S,4S) (2R,4S). In solution these

diastereoisomers interconvert through a mechanism involving opening of the thiazolidine ring [19](schem2). while the subsequent N-acylation of this mixture, as previously reported [15-17], occurred stereoselectively with the preferential formation of the cis stereoisomer.

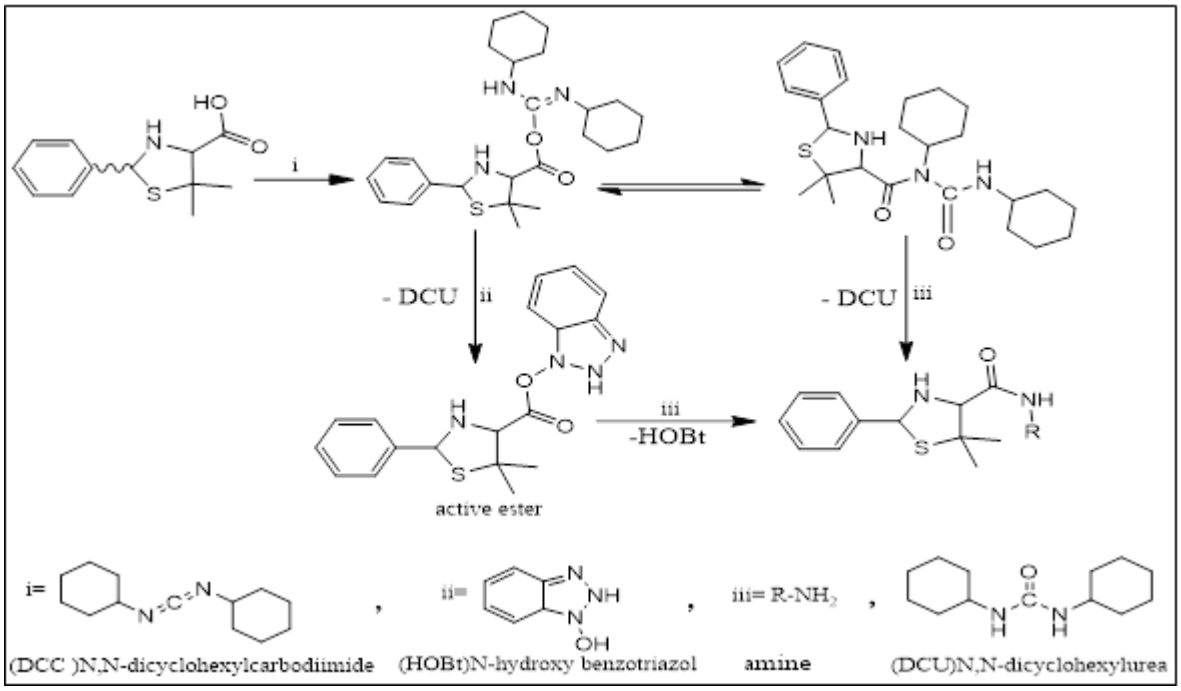


(schem2): Proposed isomerisation pathway for C-(2) isomers in thiazolidine

Second step involve protection of secondary amine group in thiazolidine ring To get the compound(At); by reacting the compound(A_1) with acetic anhydride in a base medium of sodium carbonate. Third step involve prepared Thiazolidine amides (b_1-b_{13}) are directly from various aliphatic, aromatic, and heterocyclic primary amines with corresponding N-acetyl thiazolidine -4- carboxylic acids(At) by in situ conversion of their carboxyl group to a more reactive group by coupling reagents, N,N-dicyclohexylcarbodiimide (DCC) has been used in this case as a coupling reagents; HOBt has also been used with a coupling agent to avoid unwanted side reactions, with dichloromethane(DCM) as a solvent (schem3).

(schem3). mechanism involve prepared Thiazolidine amides

The structure was checked by FT.IR and ^{1}H-NMR spectra, mass as shown in the figures(3-1)-(3-40). The FT.IR spectra of amide thiazolidine compound were detected by the disappear of the acid hydroxyl band (O-H strt) which appeared at 3500 cm^{-1}, and appearance of two band belonging to carbonyl group (C=O strt) of the primary and secondary amide in the range (1700-1734) cm^{-1} and (1624-1667) cm^{-1} Respectively. These facts confirmed the correct expected structure also it showed one a peak at (3200-3400)cm^{-1} which related to the (N-H) stretching band, and (1550-



1608) cm^{-1} Due to the bending band, also 1059 cm^{-1} peak for the (C-O strt). And finally a peak at 3000-3100 cm^{-1} for the aromatic (C-H str) and 2850-2999 for the aliphatic (C-H str). The ^{1}H-NMR spectra for The formation of the 2-phenylthiazolidine-4-carboxylic acid amide system were characterized by the emergence of two signals at 2.5 and 3.3 ppm attributable to the DMSO-*d6* solvent and to water. The most important characteristic of the NMR spectra of the prepared compounds is the emergence of a single signal at the range of (8.5 - 12.3)ppm attributable to the proton of the amide NH group , All the spectra generally appear identical and include two signal regions the aliphatic region in which the singlet signals (s, 3H) of the protons of the methyl group (α-CH3-5 , β-CH3-5 and CH_3-acetyl) proton appear in the range (1.3-3 1.3-3)ppm; and the protons of thiazolidine ring C-2 and C-4 showed singlet in the range (4.5-6.8)ppm, the aromatic region appears two multiple signals within the range of (6.9-8.6)ppm, MS(70 eV), of the studied compounds are characterized by the presence of a molecular ion peak that

appears at m / z corresponding to the molecular weight and a relatively low abundance (0.2-9.3%.) and a base peak at m/z(43,56,113,192).

A preliminary study was conducted that includes measuring the effectiveness of the prepared compounds against the growth of some microorganisms. Two types of biology were tested, one of which gave a positive detection of *staphylococcus* (+ ve) and the other gave a negative detection of the aforementioned dye *E-coli* (-ve) and used concentrations of each of the compounds under test They are (0.0002g / ml) in DMSO as solvent. Table (2) shows the results of the tests for thirteen compounds on the two mentioned types of microorganisms with the mentioned concentrations. The study showed clear effectiveness of compounds ((b_3,b_6,b_8,b_9 ,b_{12},b_{13}), especially their effect on the growth of the two types of microorganisms used, and there are other compounds (b_7,b_{11}) that showed effectiveness against *staphylococcus* (+ve) types of organisms used, such as compounds (b_1,b_4,b_5) As for the rest of the compounds, they did not show any significant activity towards the two, as in Table (2).

Table (2) shows the biological activity of some of the prepared compounds

Comp-	*staphylococcus* (+ve)	*E-coil* (-ve)
b_1	-	-
b_2	-	-
b_3	11	10
b_4	-	-
b_5	-	-
b_6	11	18
b_7	10	-
b_8	13	15
b_9	13	10
b_{10}	15	21
b_{11}	20	-
b_{12}	16	16
b_{13}	14	10

Conclusion

We have synthesized a series of amide thiazolidine derivatives. The cyclo-condensation reactions of thiazolidine occurred in high yields. The synthesized compounds were characterized by their physical constants ((melting point, molecular formula, molecular weight and solubility in different organic solvents), and their structures were evaluated using FT-IR, 1H-NMR and mass spectrometry

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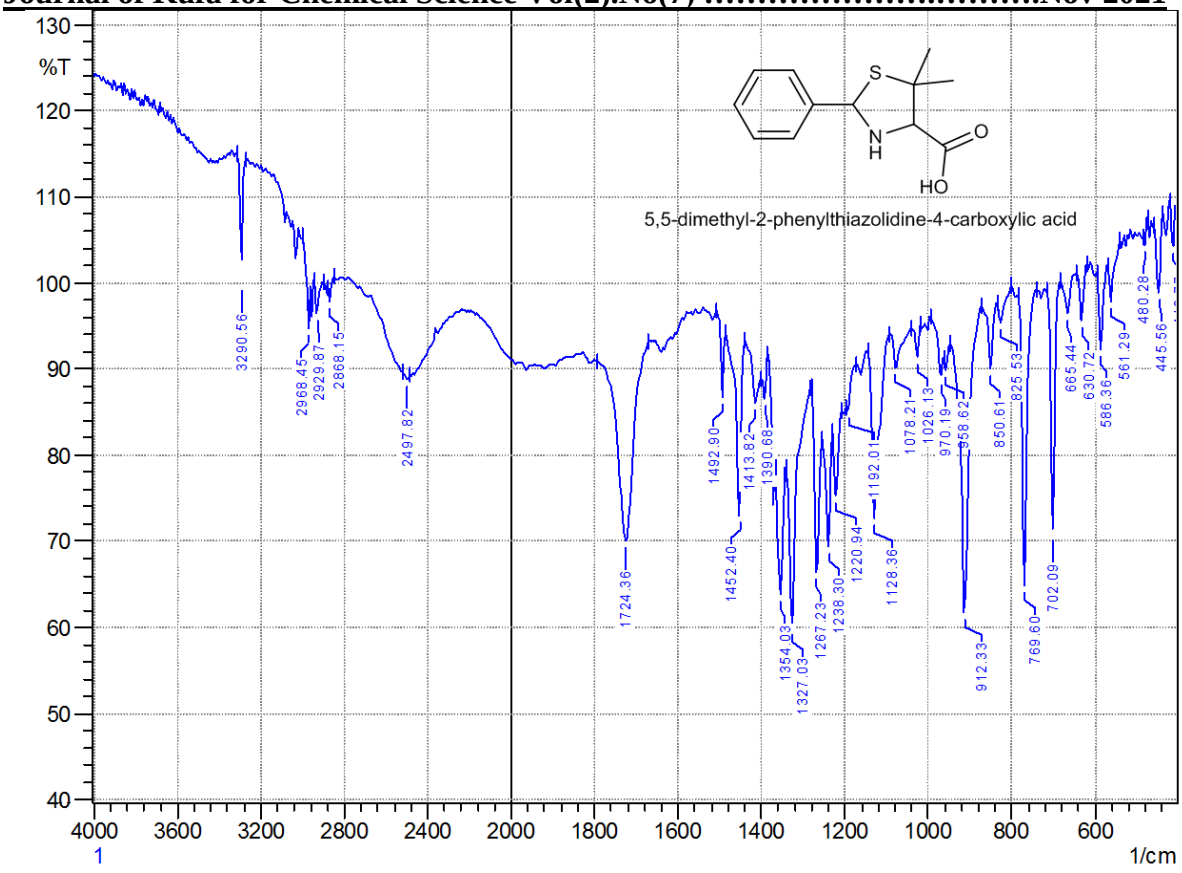
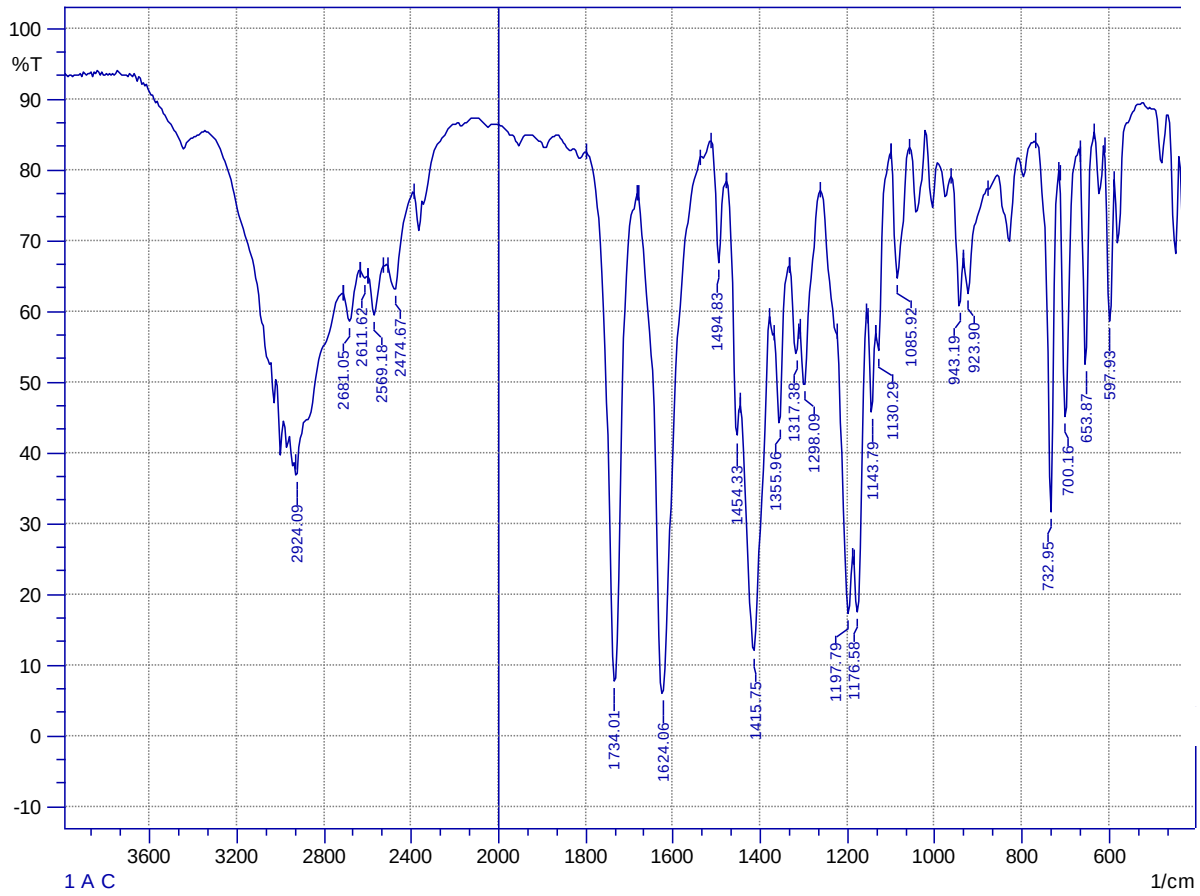


Figure 3–2 : FT-IR spectrum of compound [At]



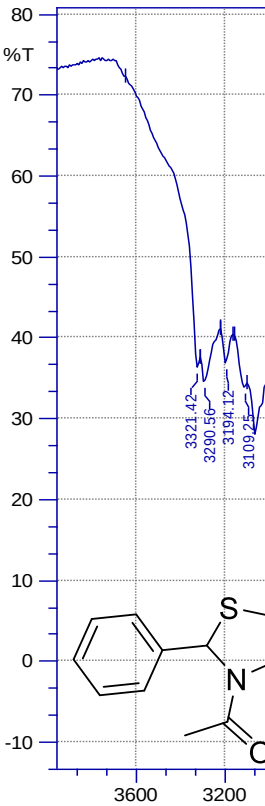


Figure 3–3 : FT-IR spectrum of compound [b_1]

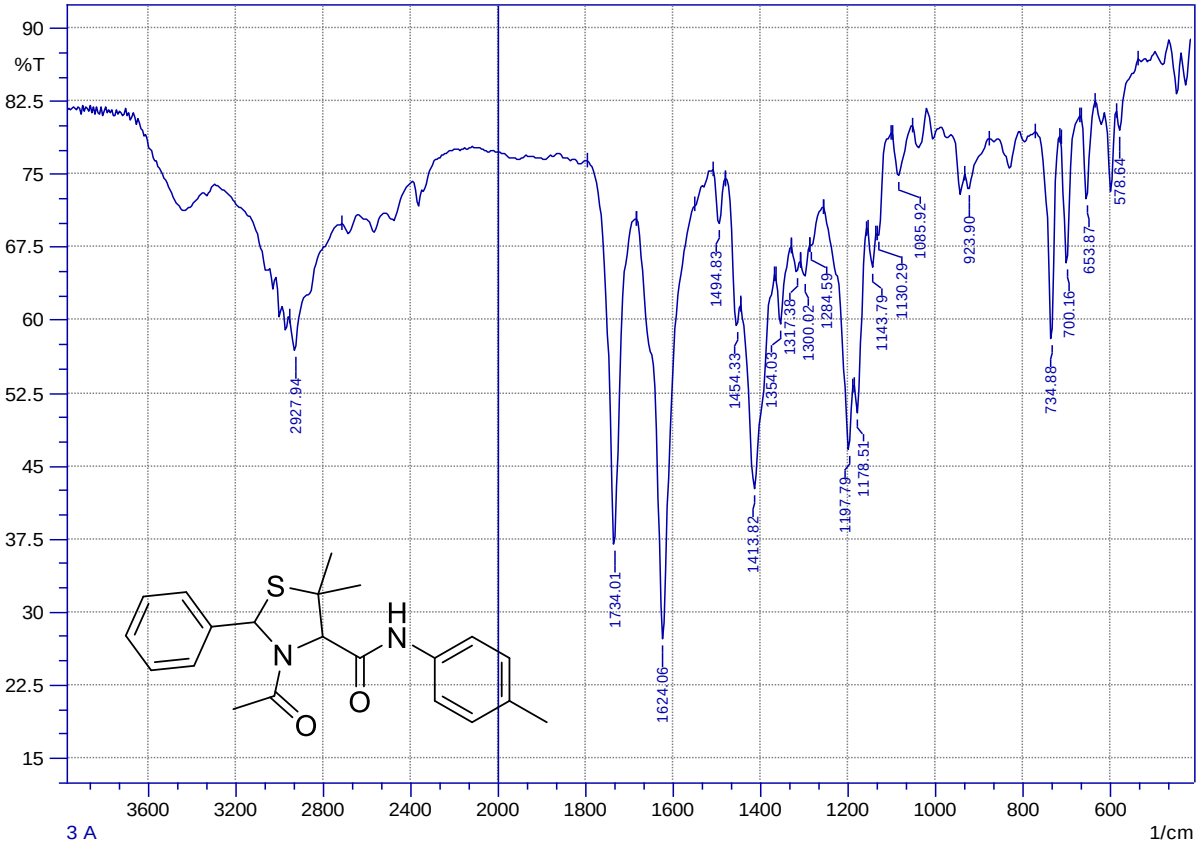


Figure 3–4 : FT-IR spectrum of compound [b_2]

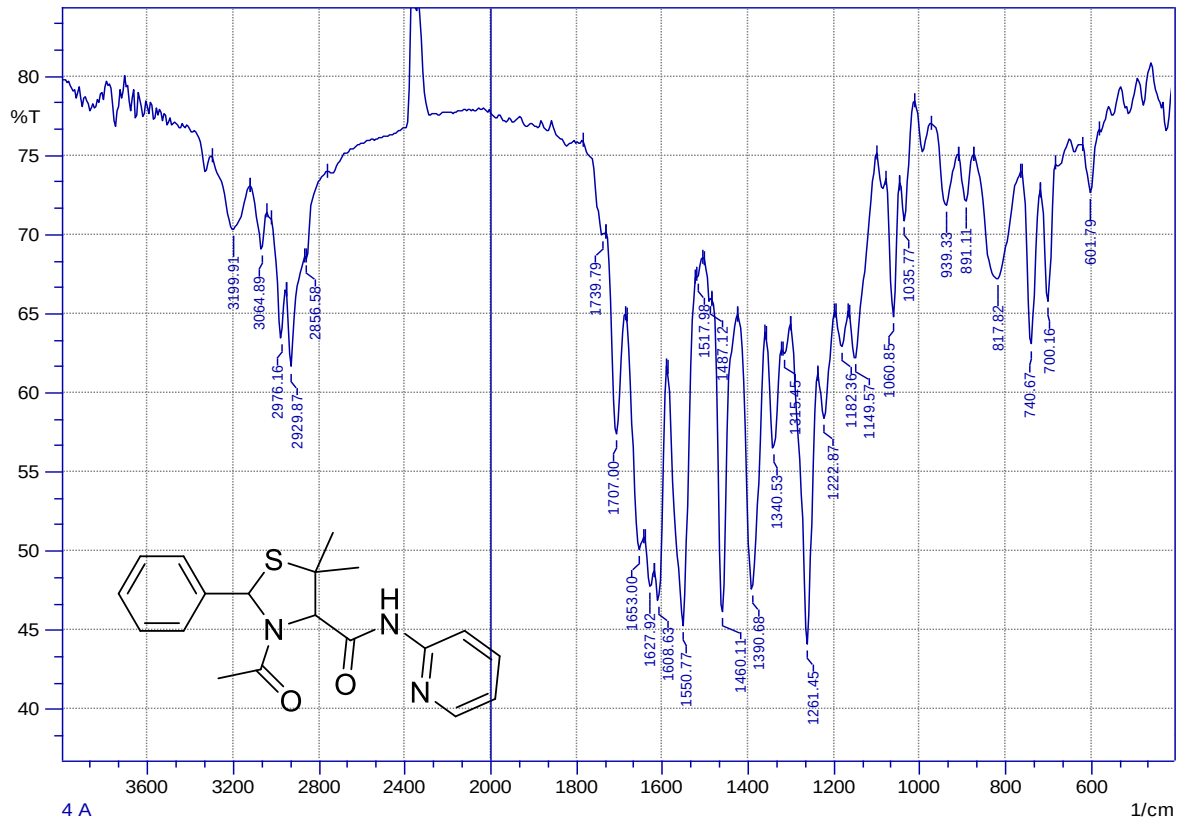


Figure 3–5 : FT-IR spectrum of compound [b_3]

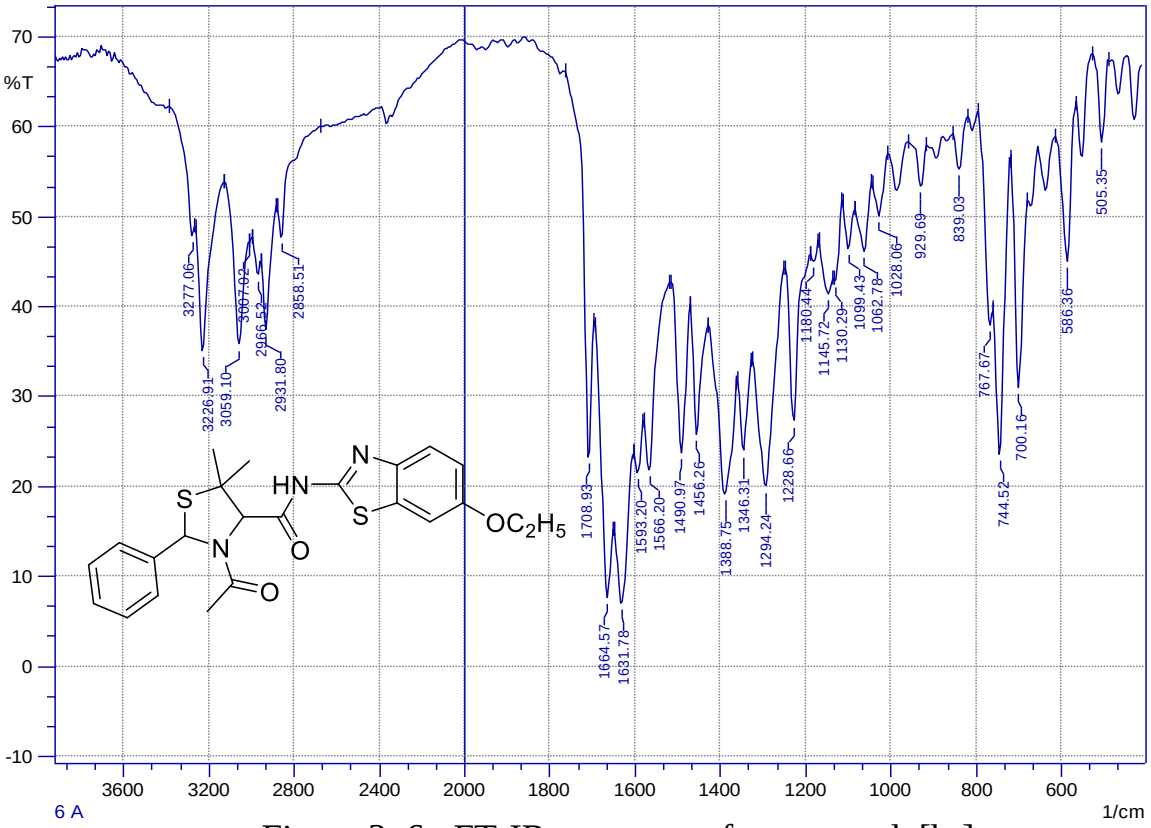


Figure 3–6 : FT-IR spectrum of compound [b_4]

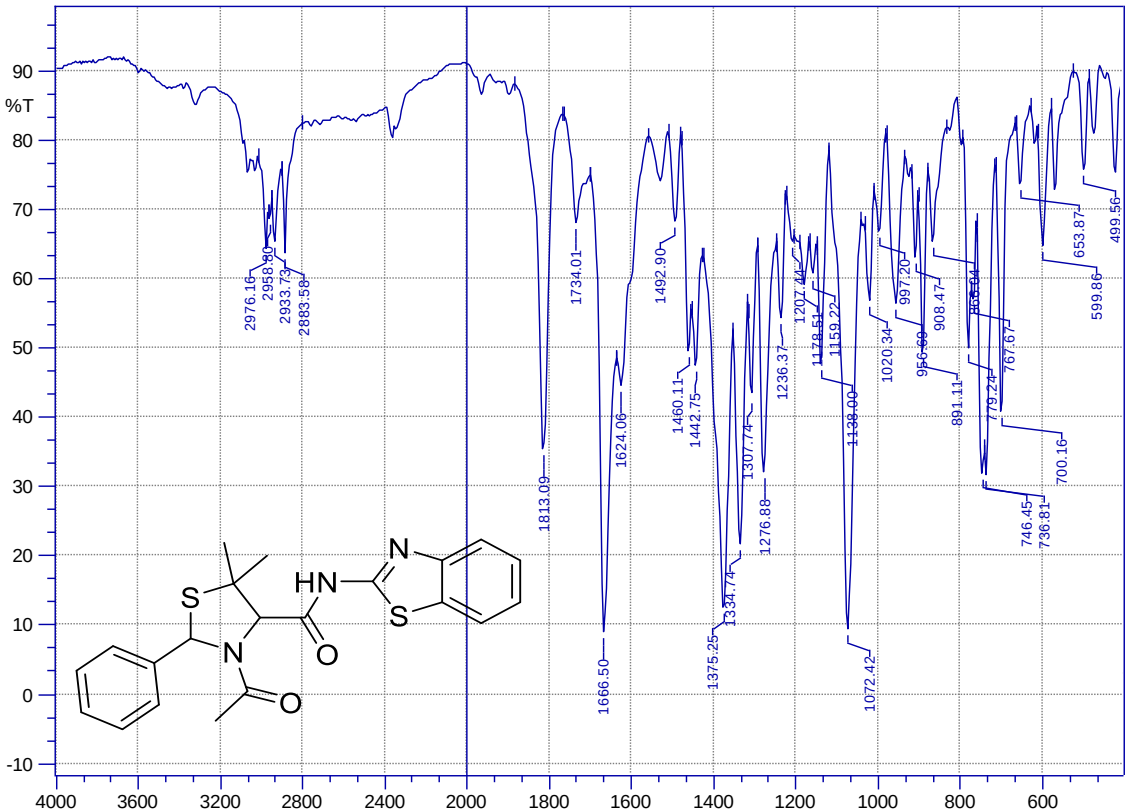
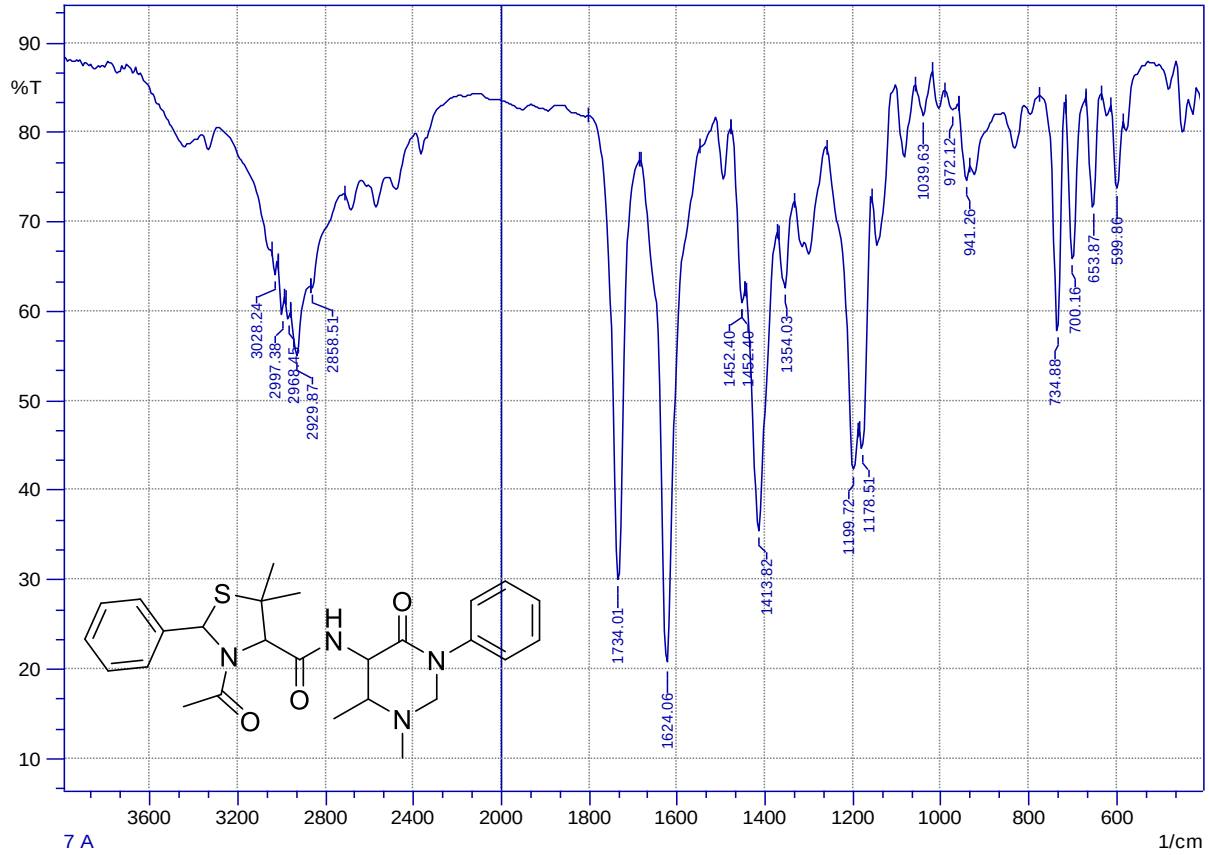


Figure 3–7 : FT-IR spectrum of compound [b_5]



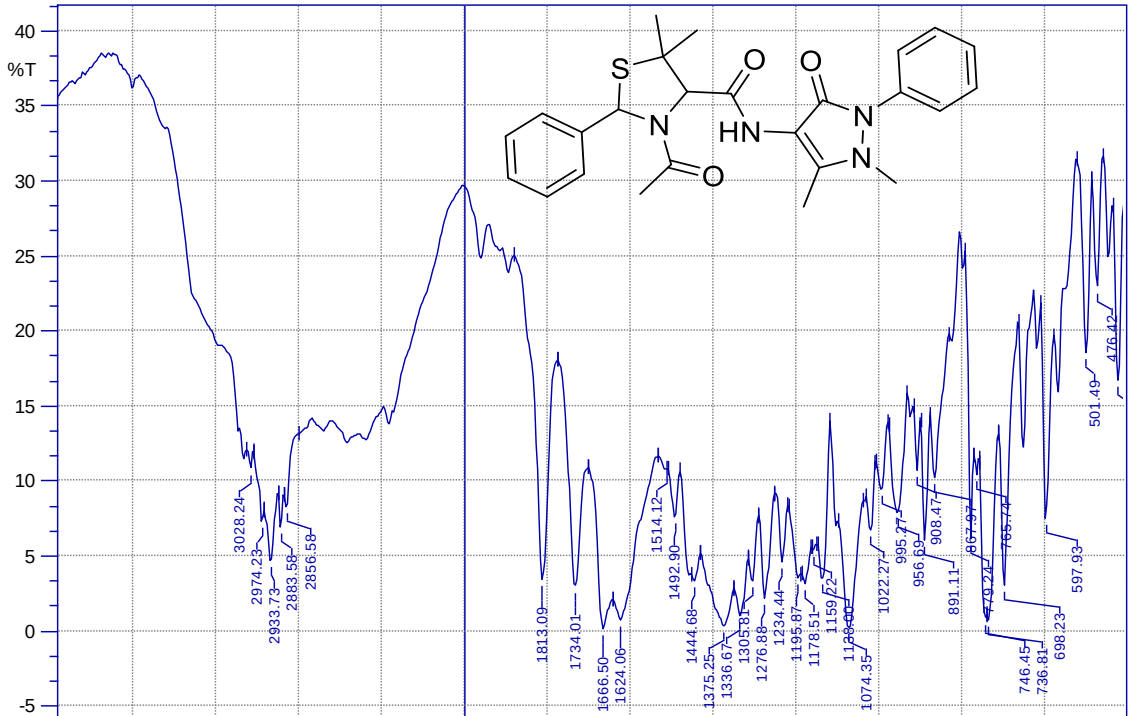
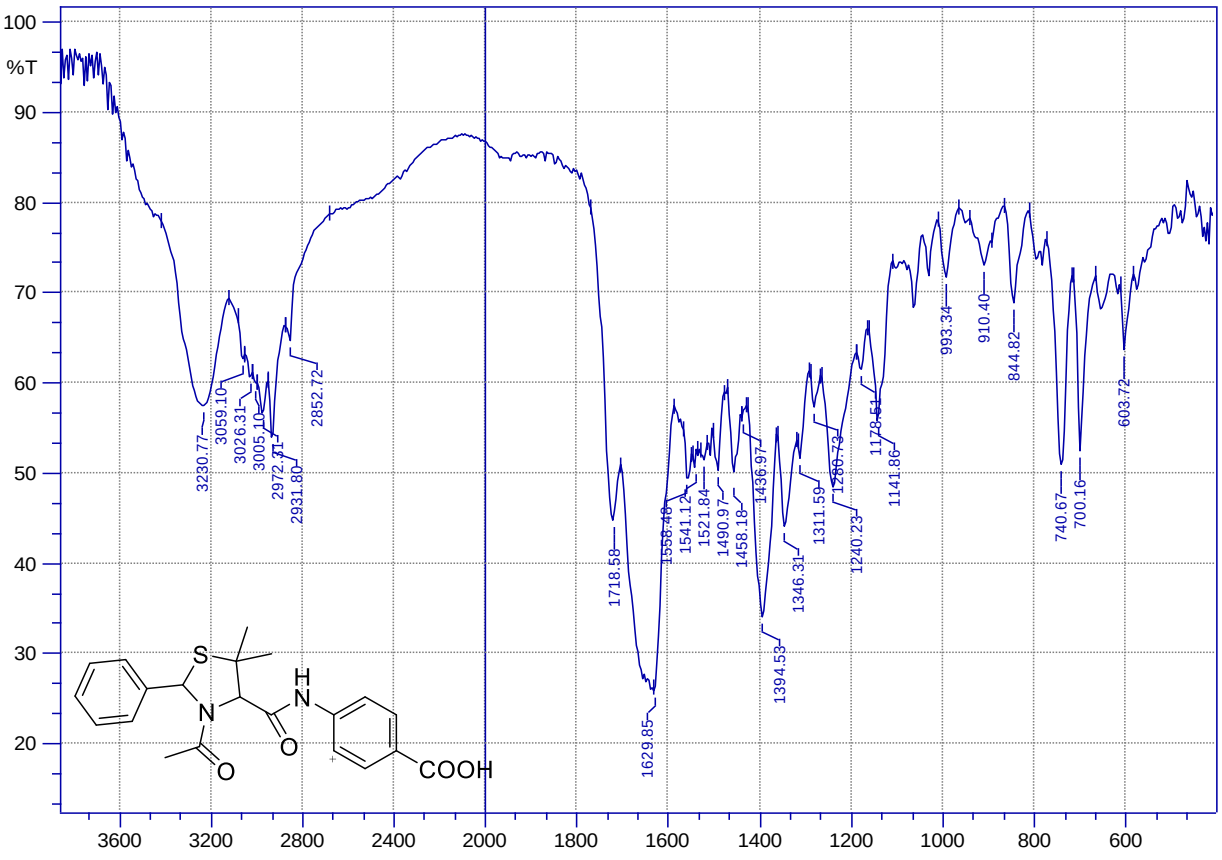
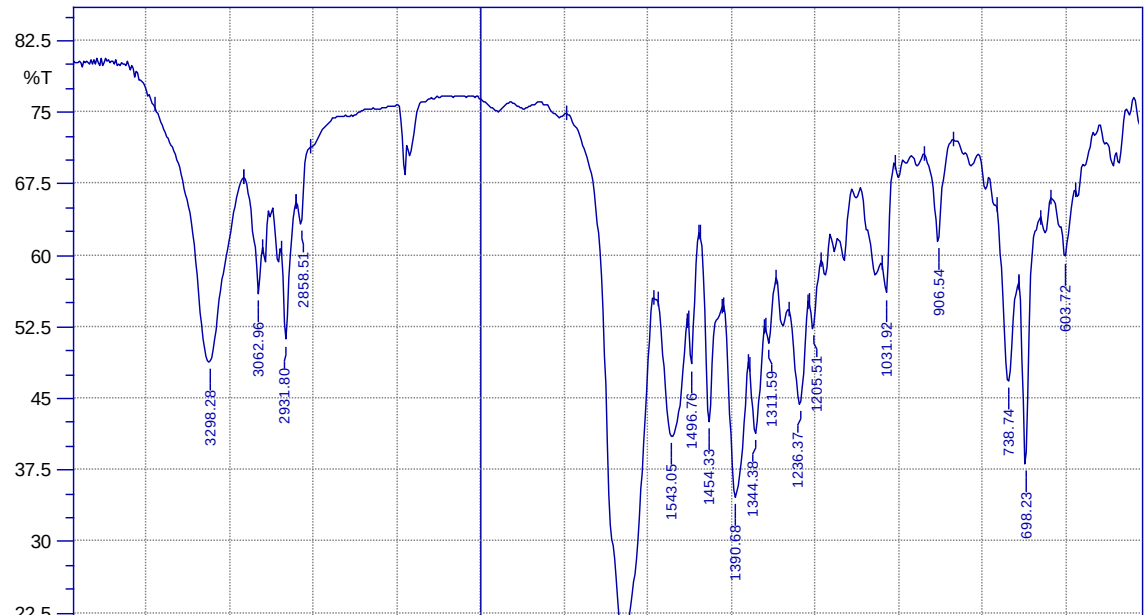


Figure 3–9 : FT-IR spectrum of compound [b_7]





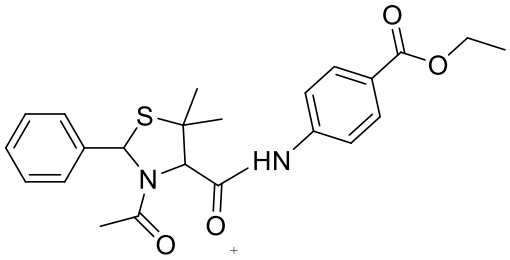


Figure 3–11 : FT-IR spectrum of compound [b_9]

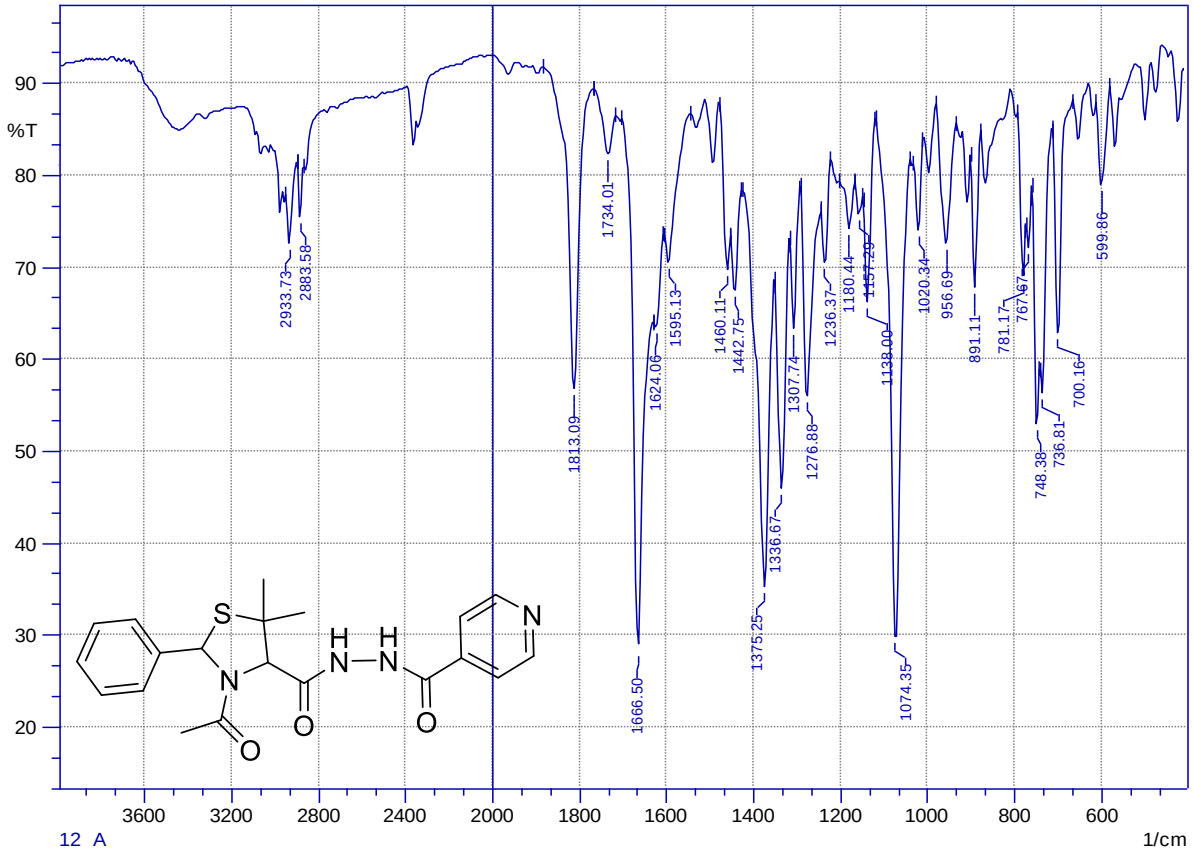
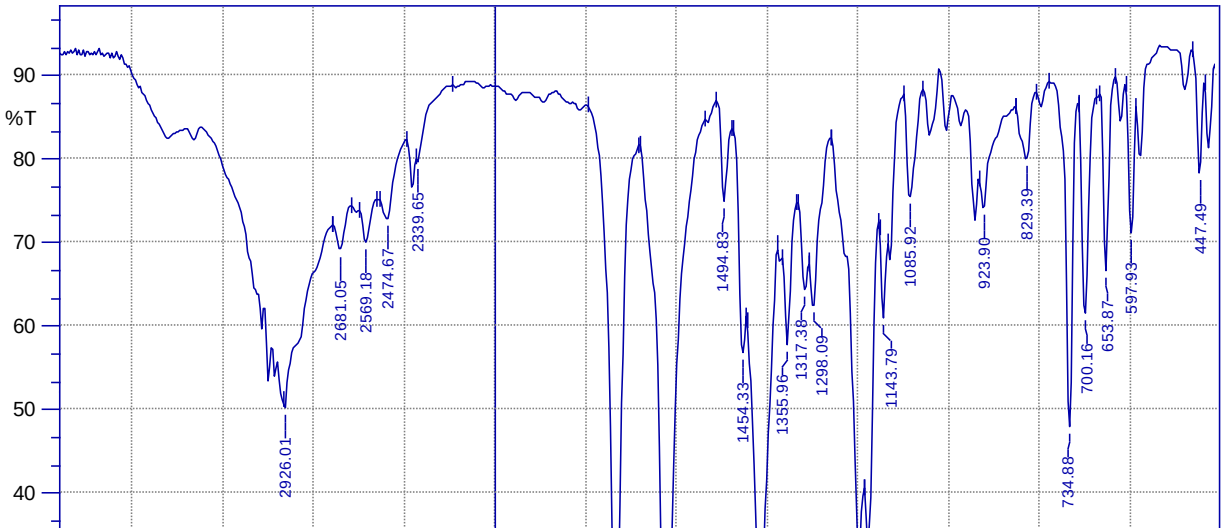


Figure 3–11 : FT-IR spectrum of compound [b_{10}]



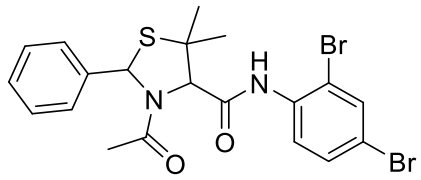
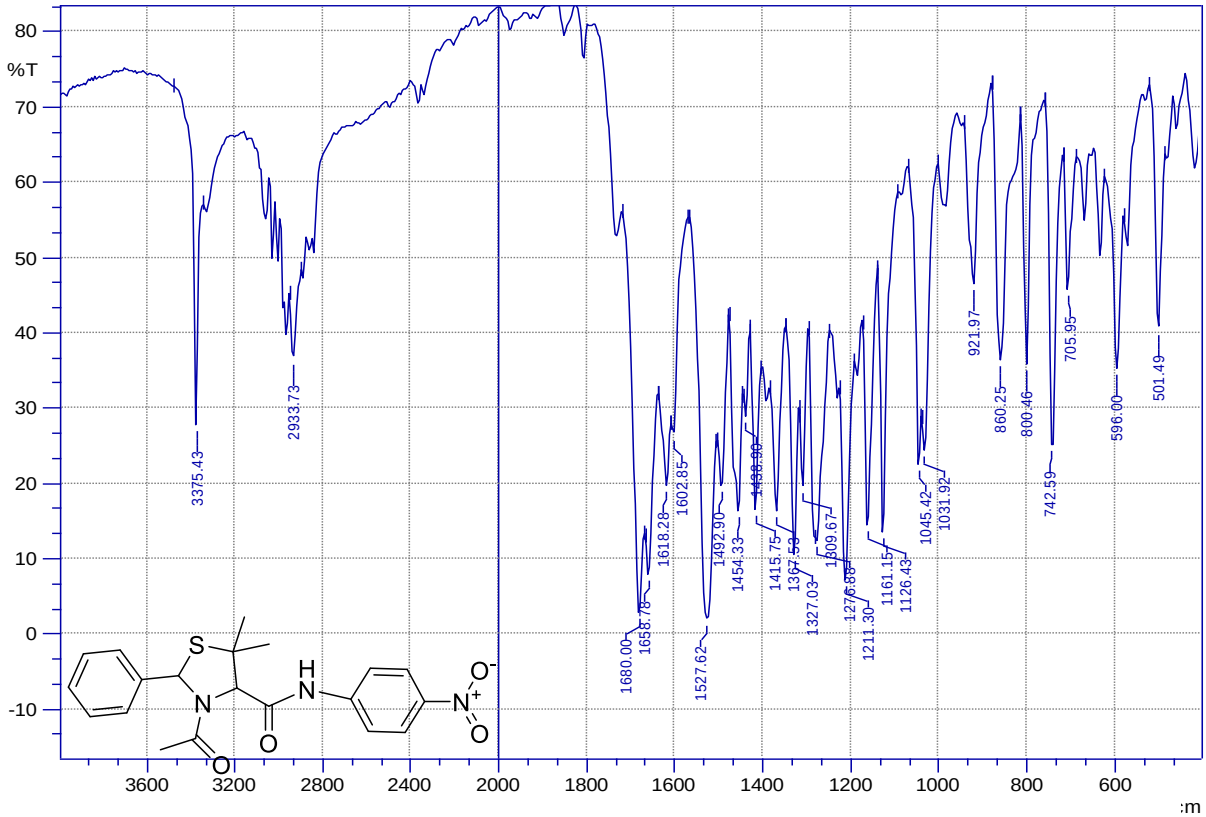
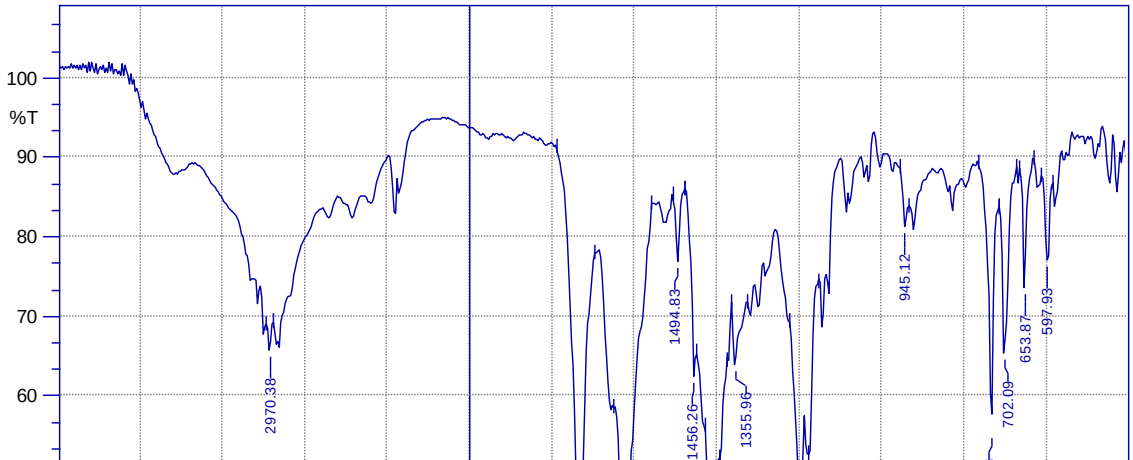


Figure 3–11 : FT-IR spectrum of compound [b_{11}]





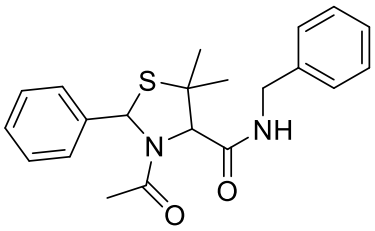


Figure 3–14 : FT-IR spectrum of compound [b_{13}]

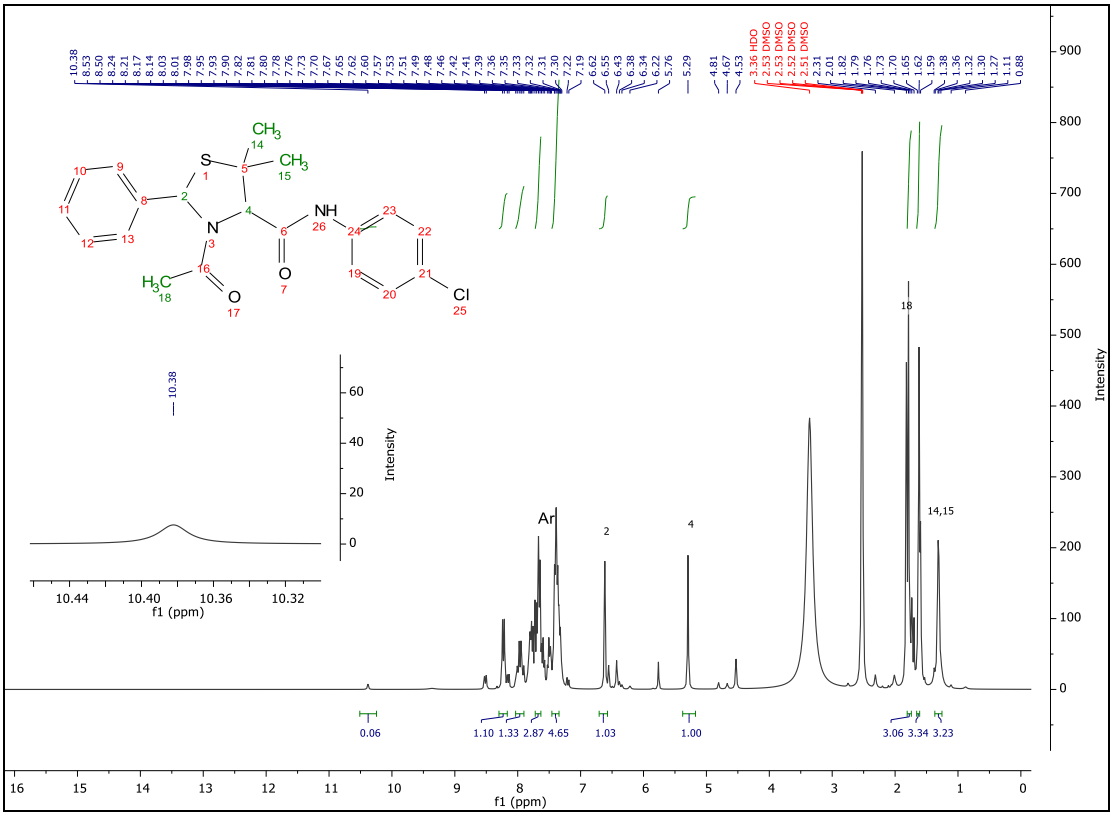


Figure 3–15 : ^{1}H-NMR spectrum of compound [b_1]

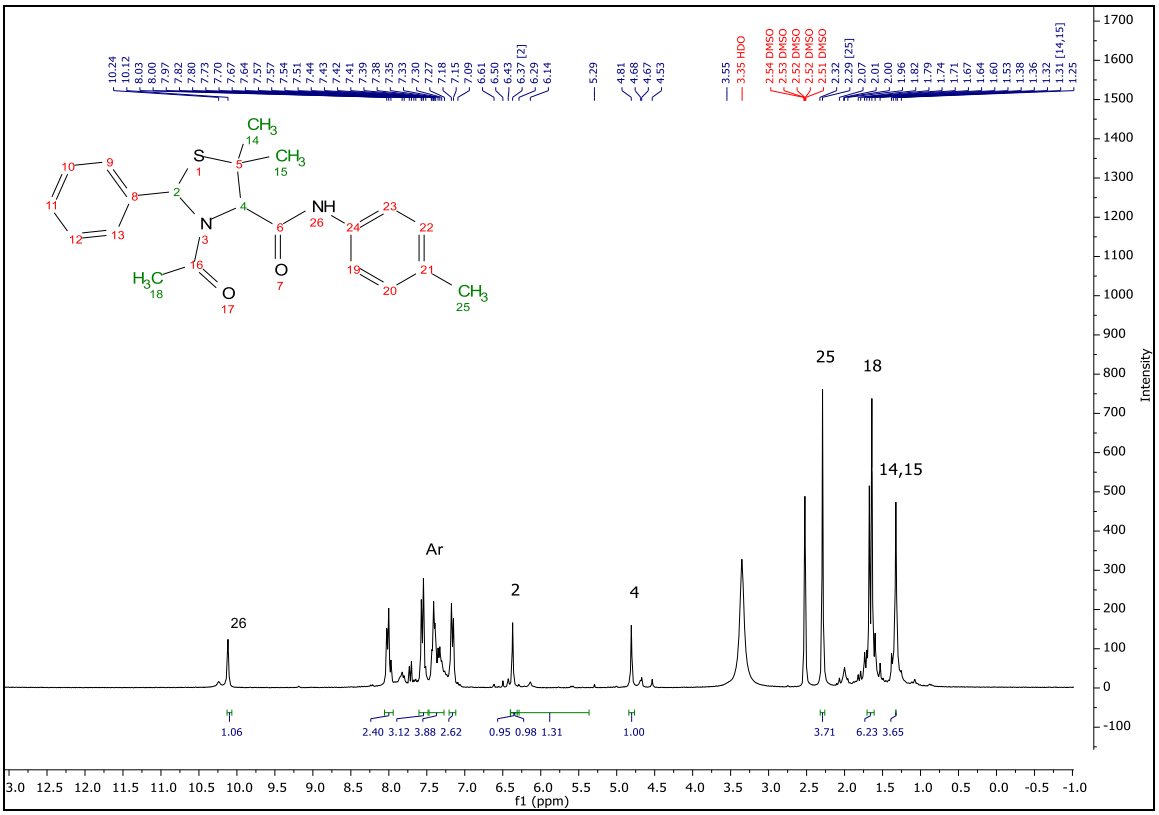


Figure 3–16 : ^{1}H-NMR spectrum of compound [b_2]

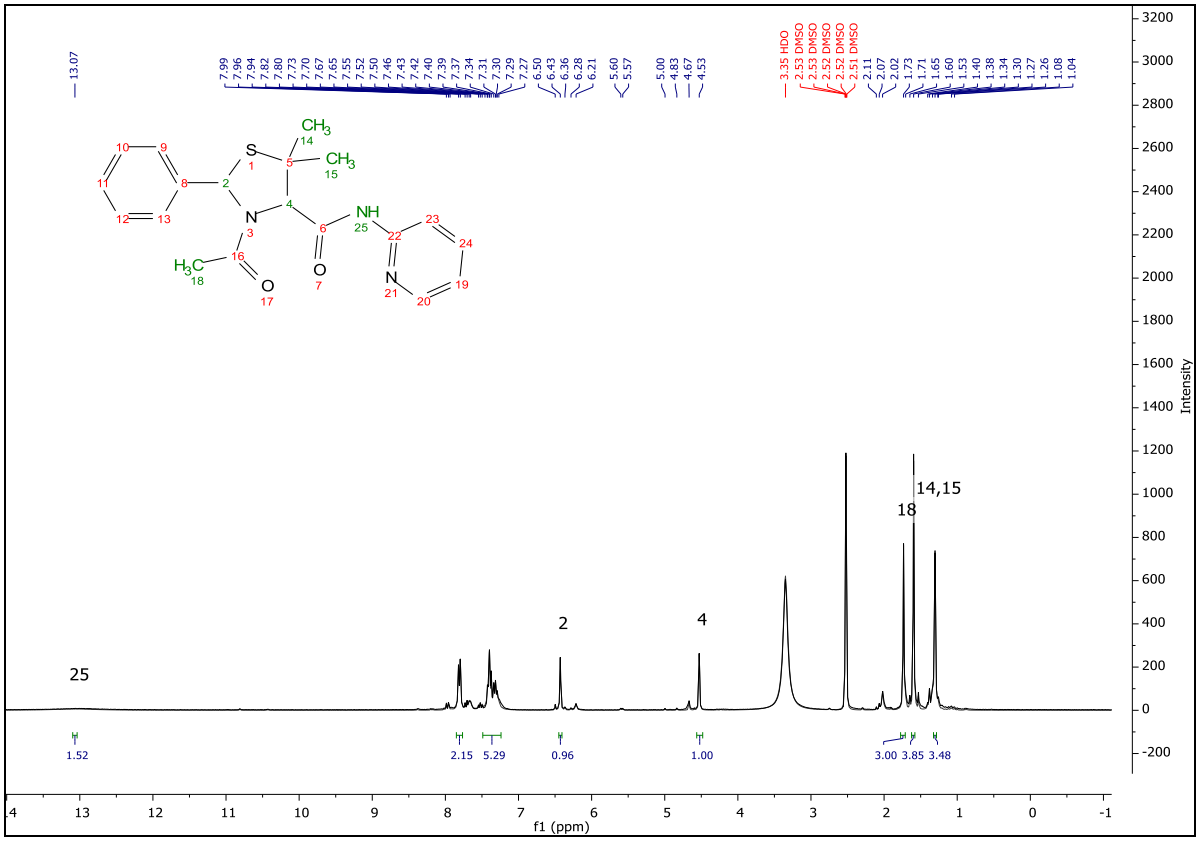


Figure 3–17 : $_1$H-NMR spectrum of compound [b_3]

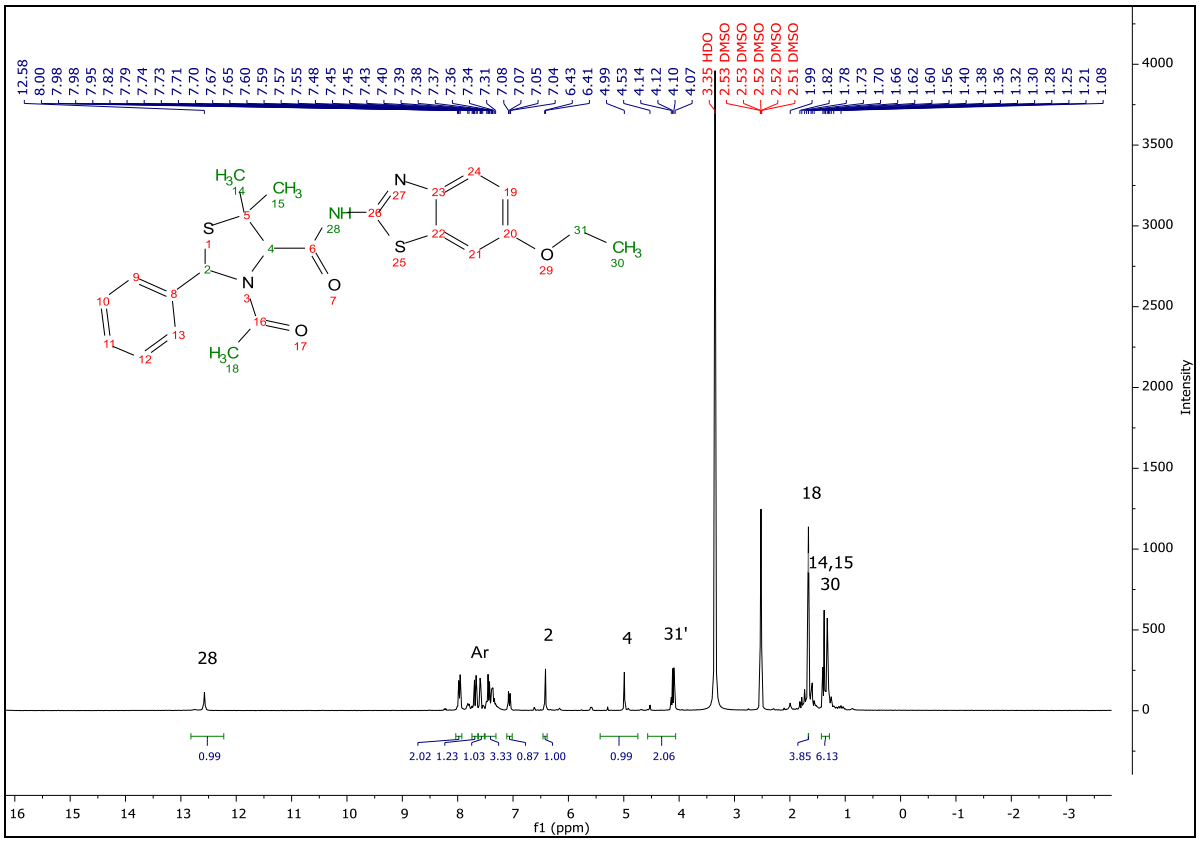


Figure 3–17 : $_1$H-NMR spectrum of compound [b_4]

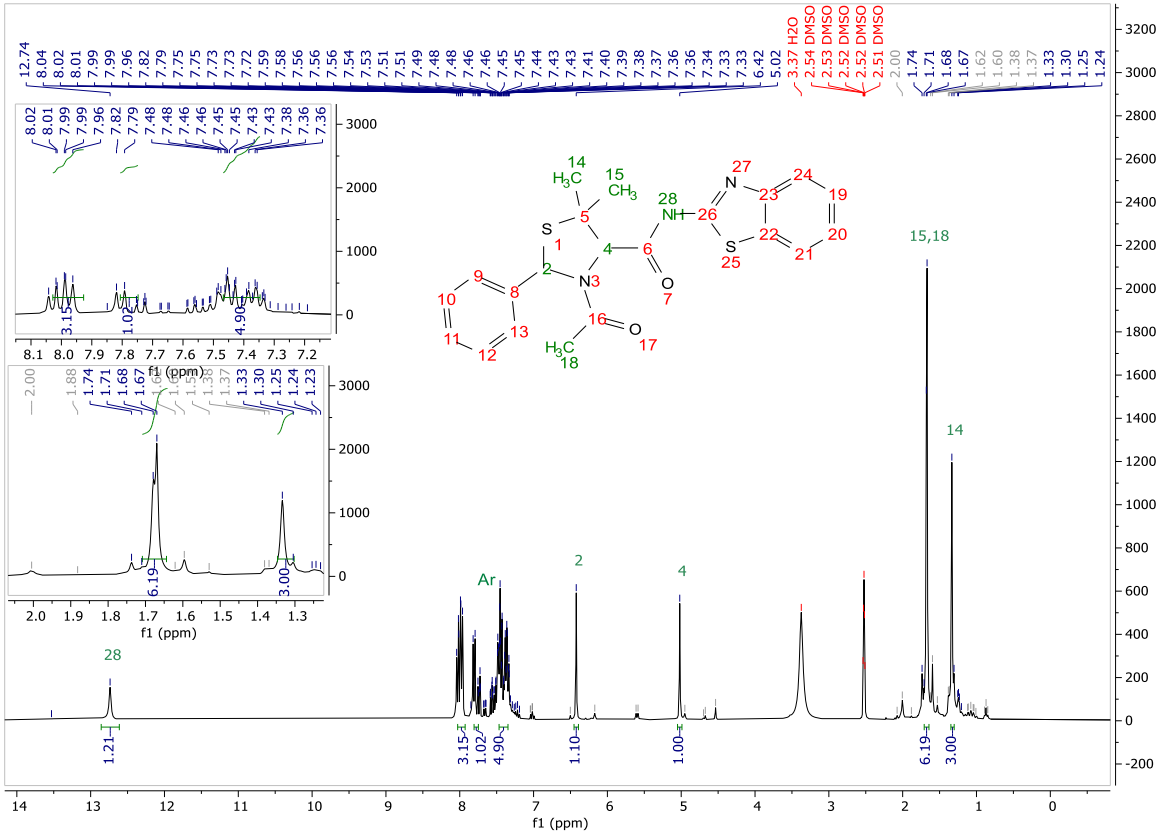


Figure 3–18 : $_1$H-NMR spectrum of compound [b_5]

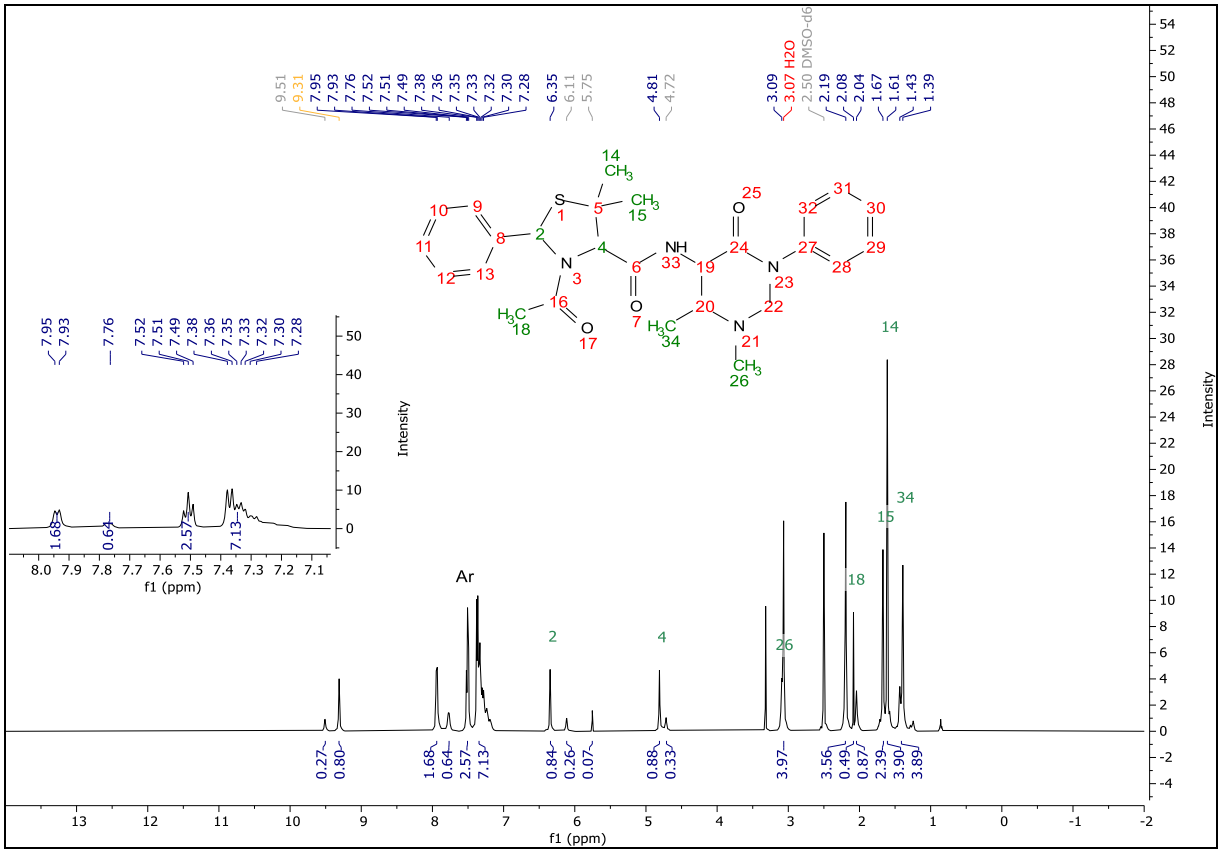


Figure 3–19 : $_1$H-NMR spectrum of compound [b_6]

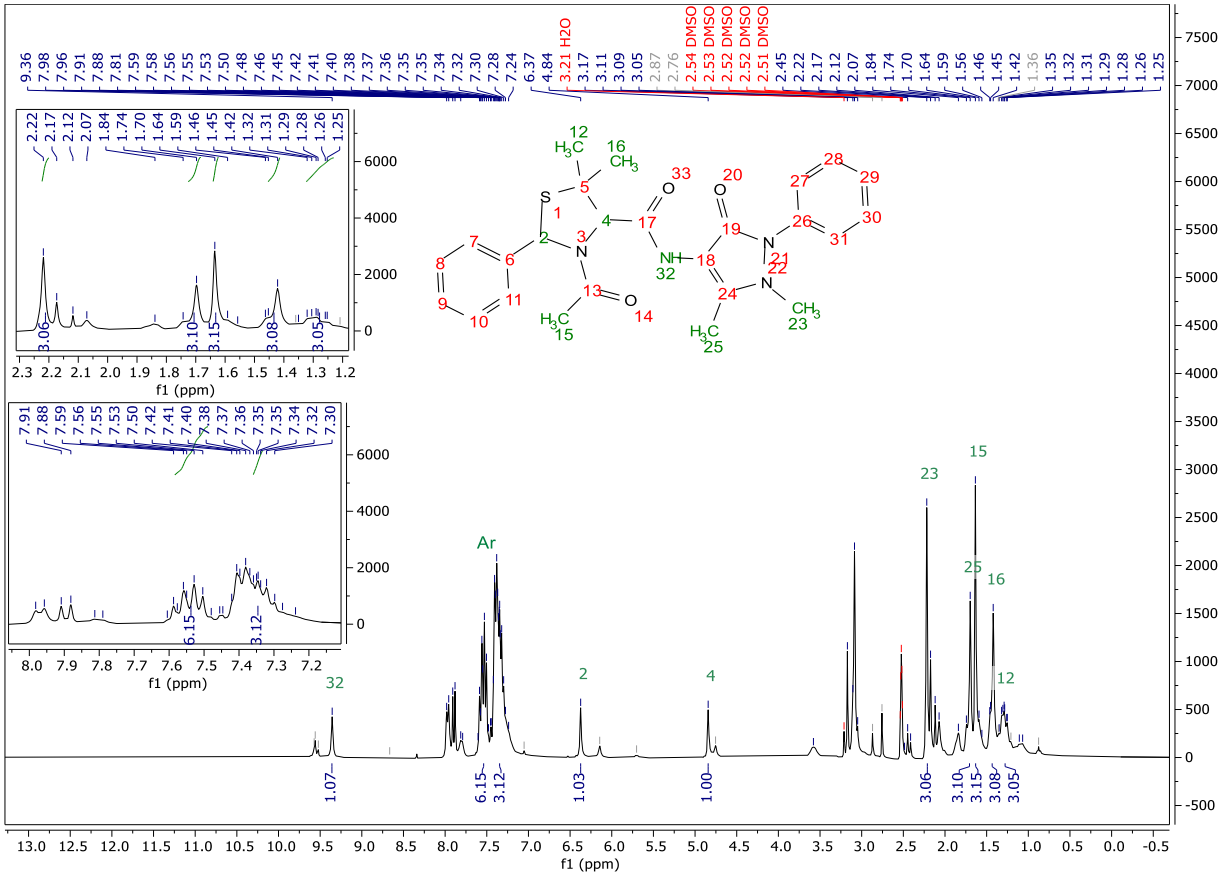


Figure 3–20 **:** $_1$H-NMR spectrum of compound [b_7]

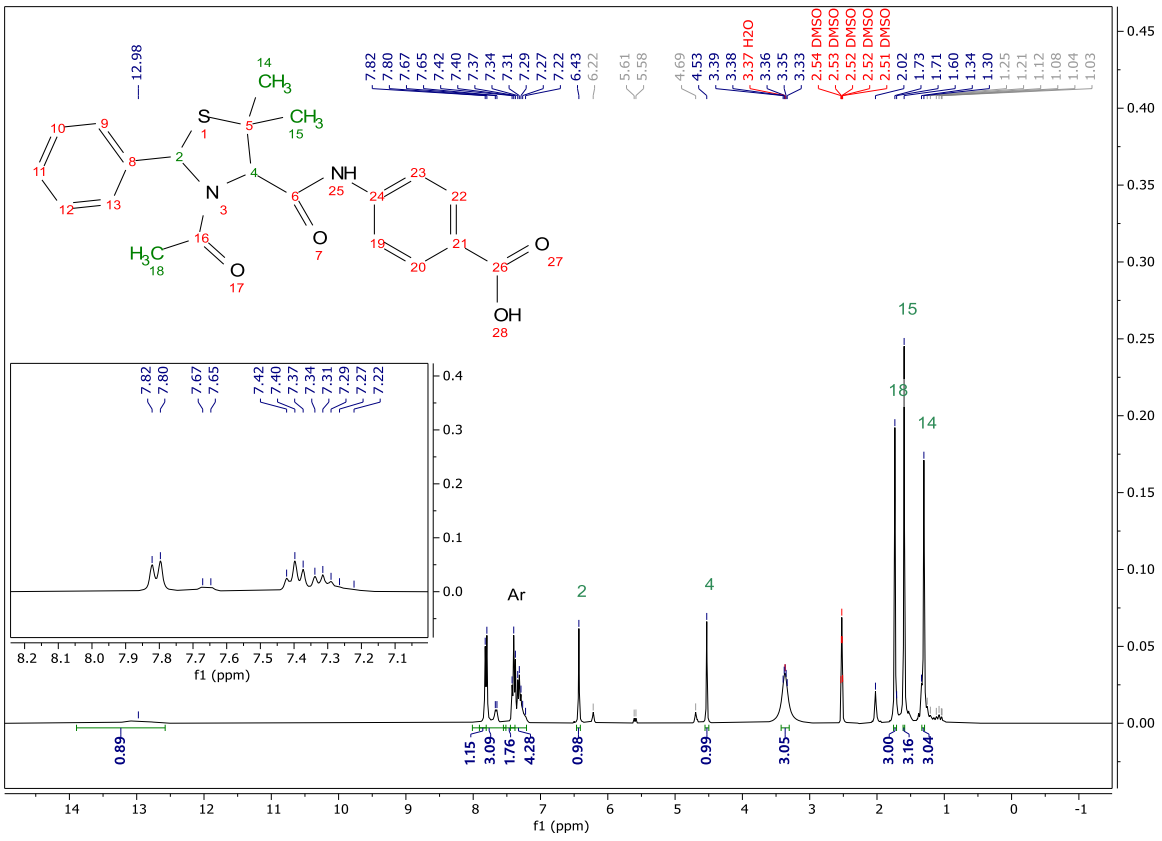


Figure 3–21 **:** $_1$H-NMR spectrum of compound [b_8]

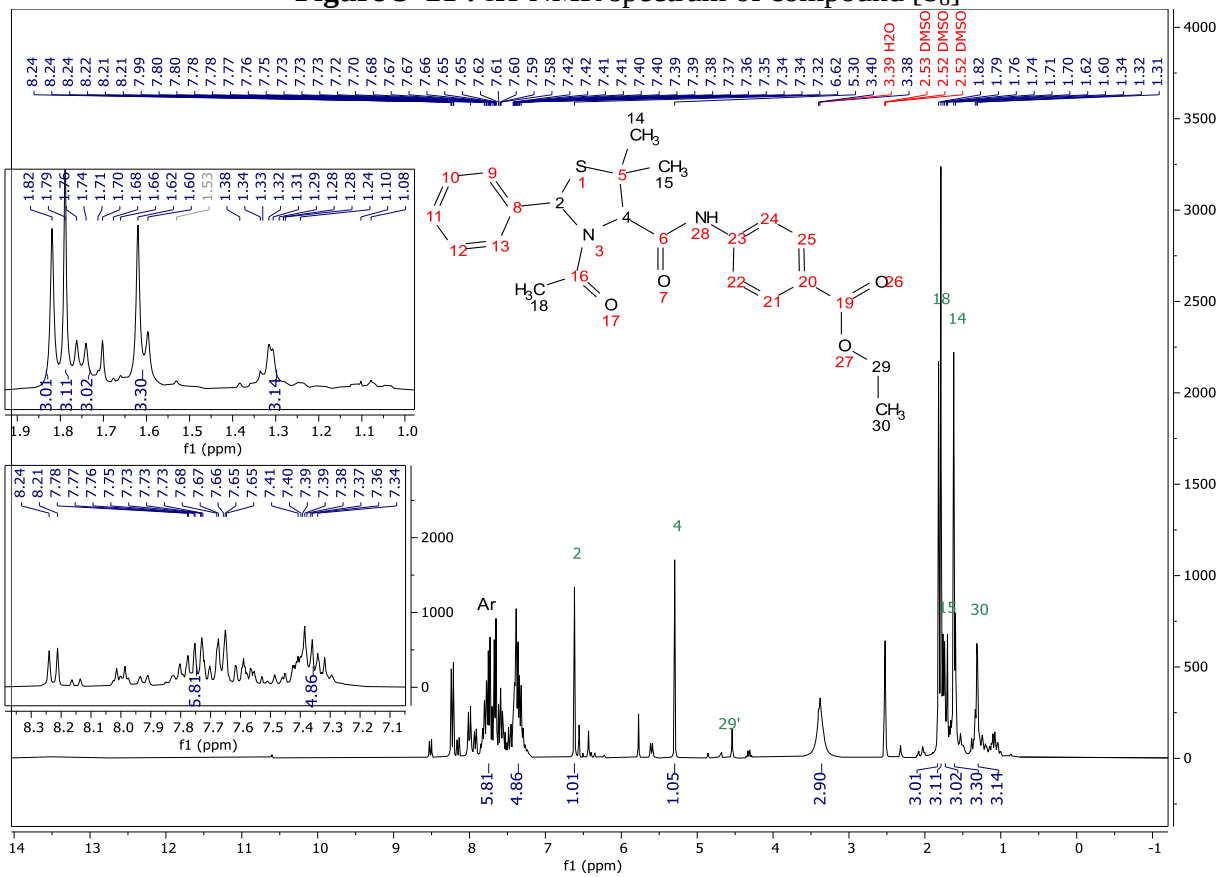


Figure 3–22 **:** $_1$H-NMR spectrum of compound [b_9]

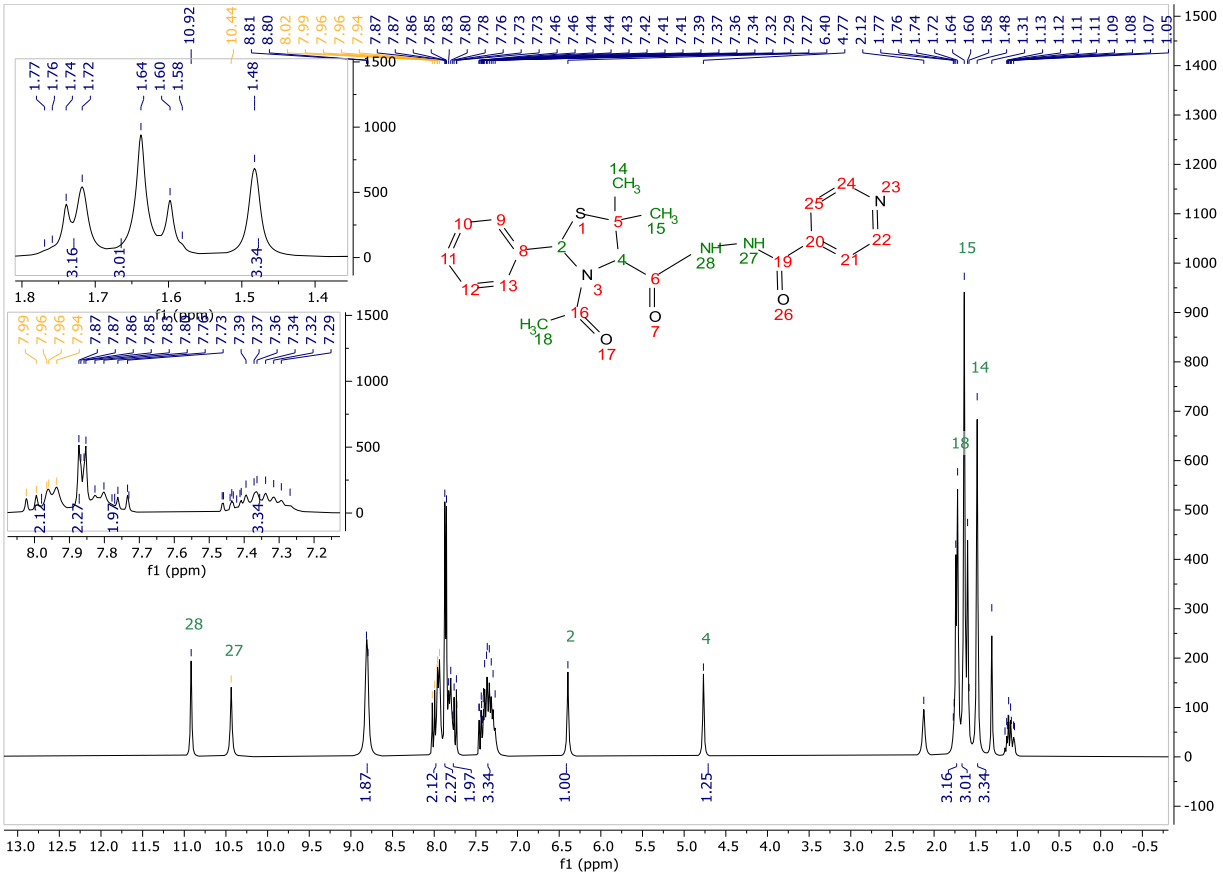


Figure 3–23 : $_1$H-NMR spectrum of compound [b_{10}]

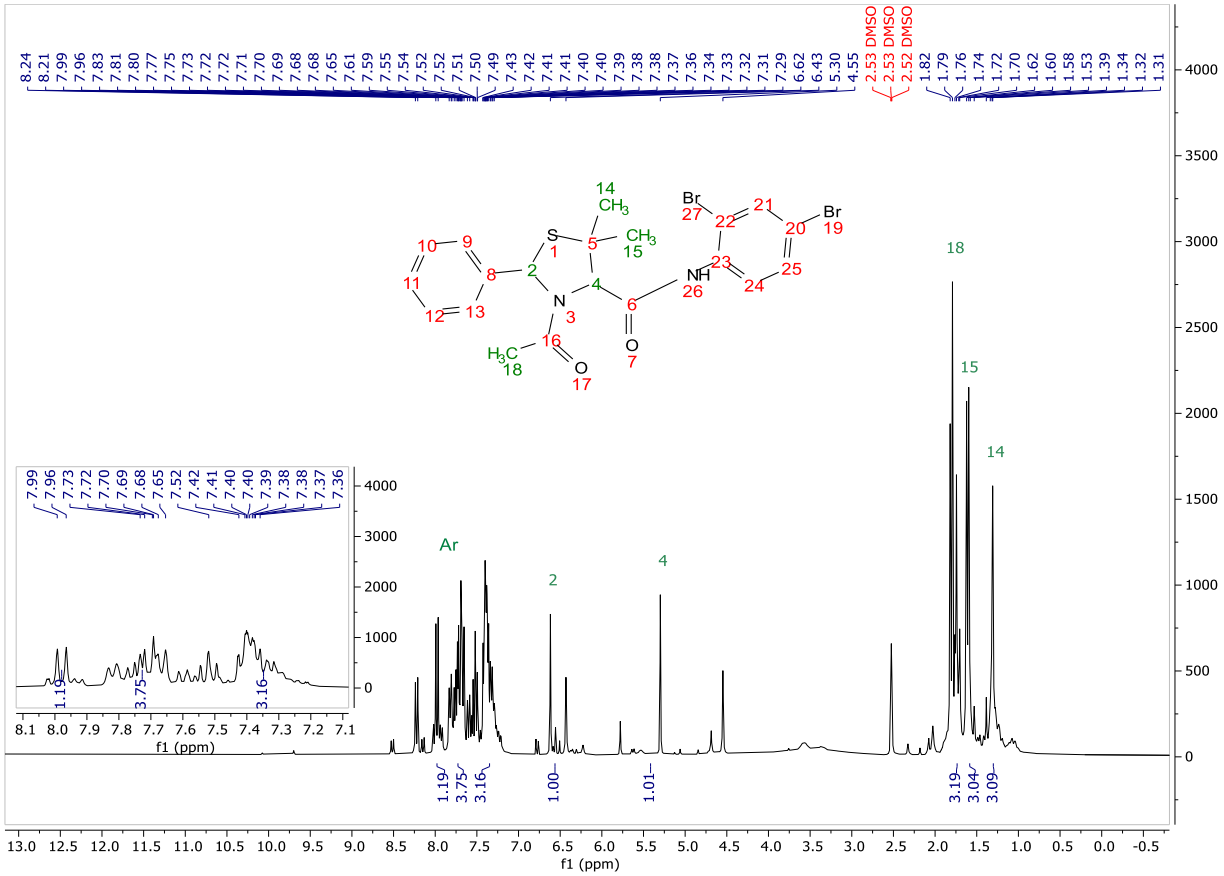


Figure 3–24 : $_1$H-NMR spectrum of compound [b_{11}]

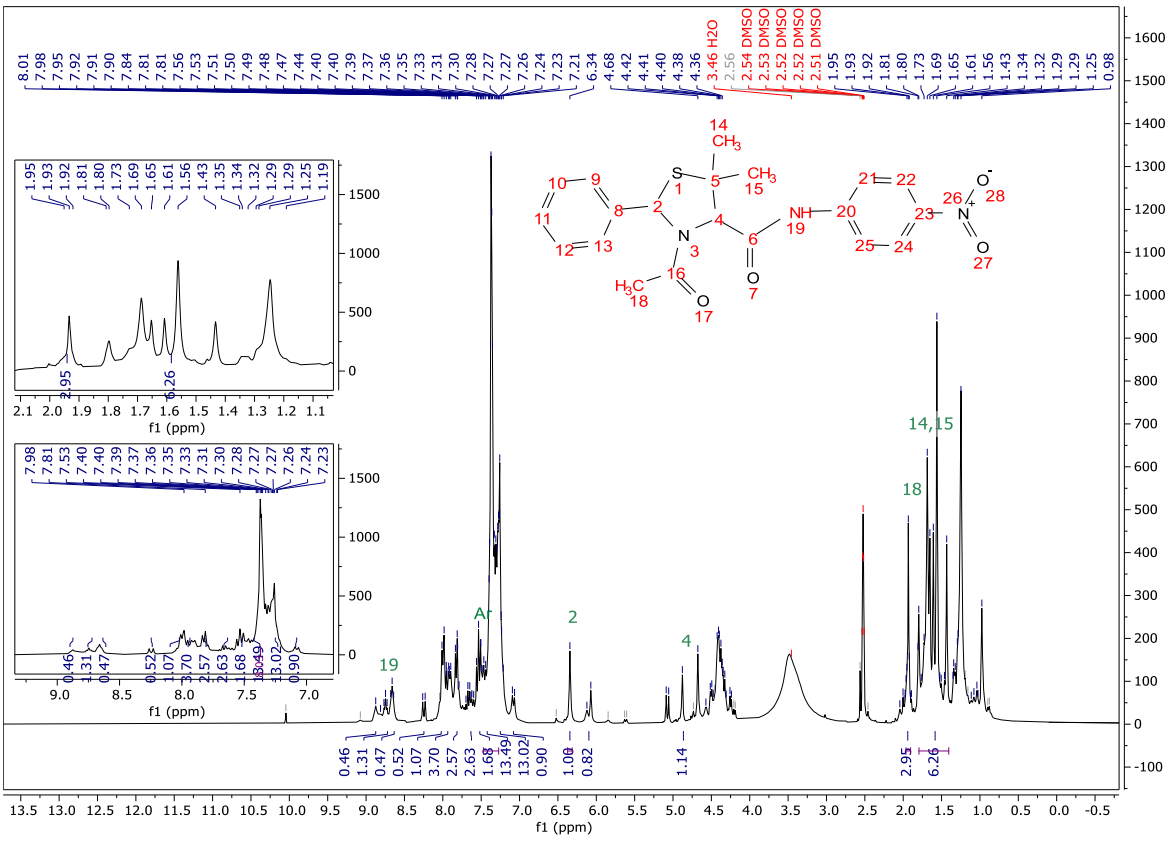


Figure 3–25 : $_1$H-NMR spectrum of compound [b_{12}]

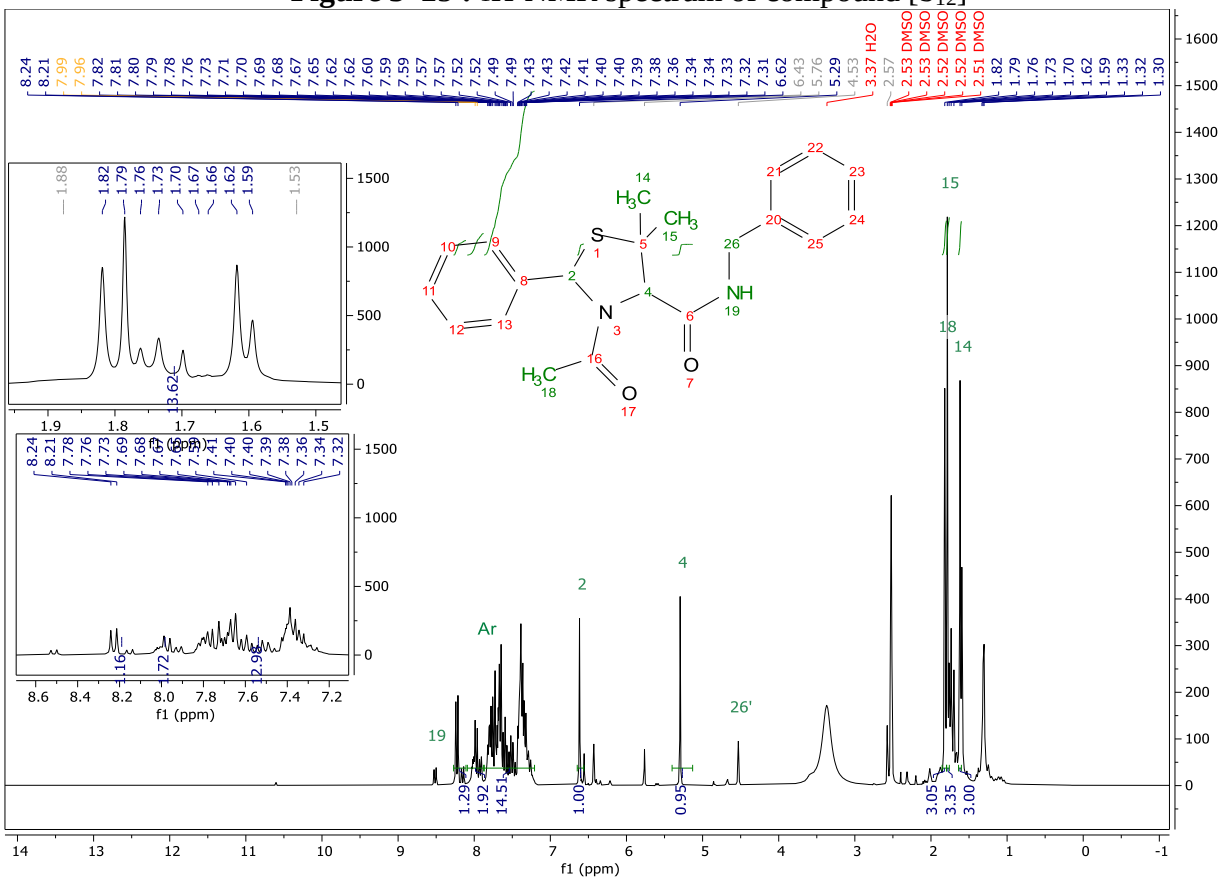
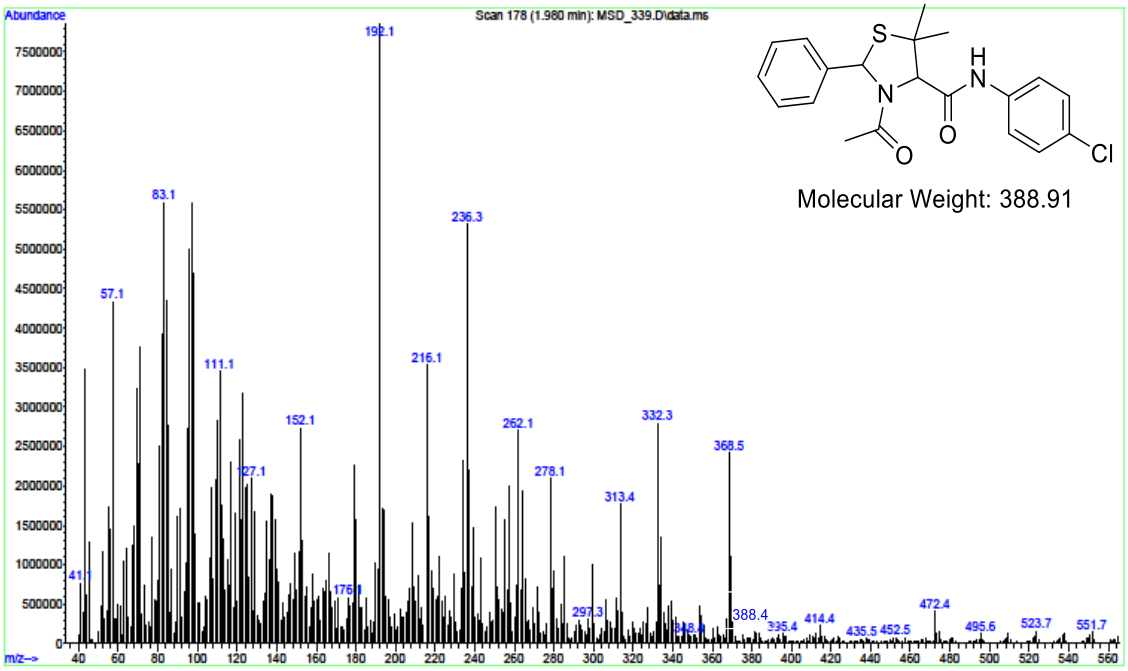


Figure 3–26 : $_1$H-NMR spectrum of compound [b_{13}]



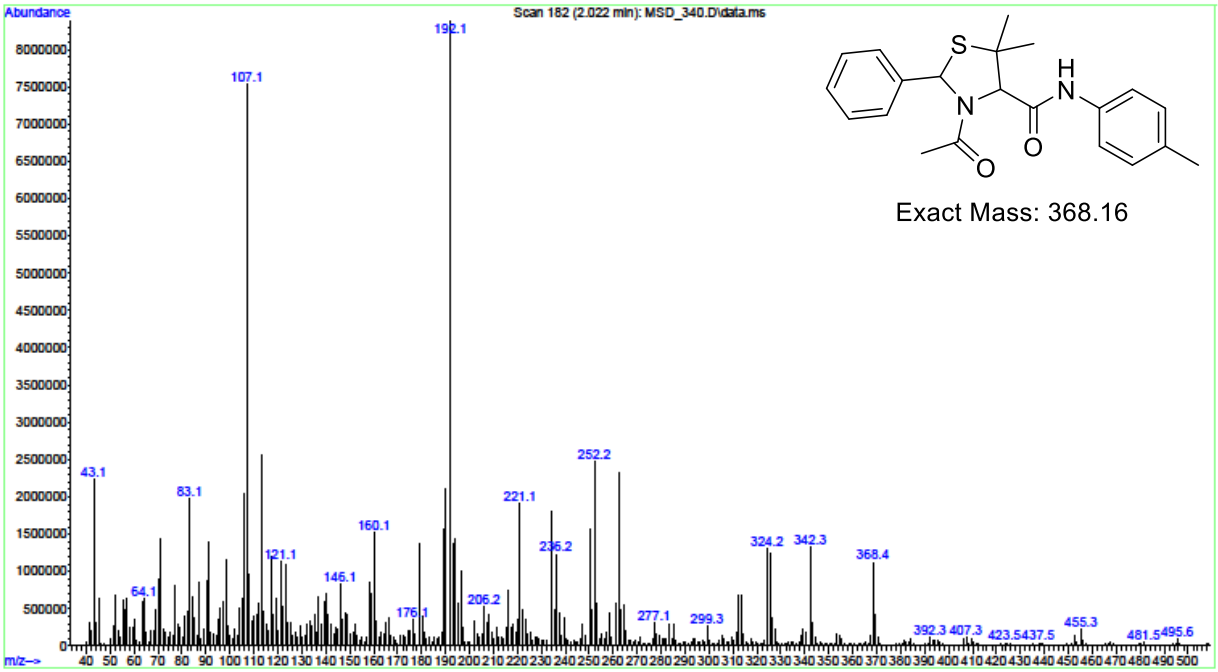


Figure 3–28 **:** mass spectrum of compound [b_2]

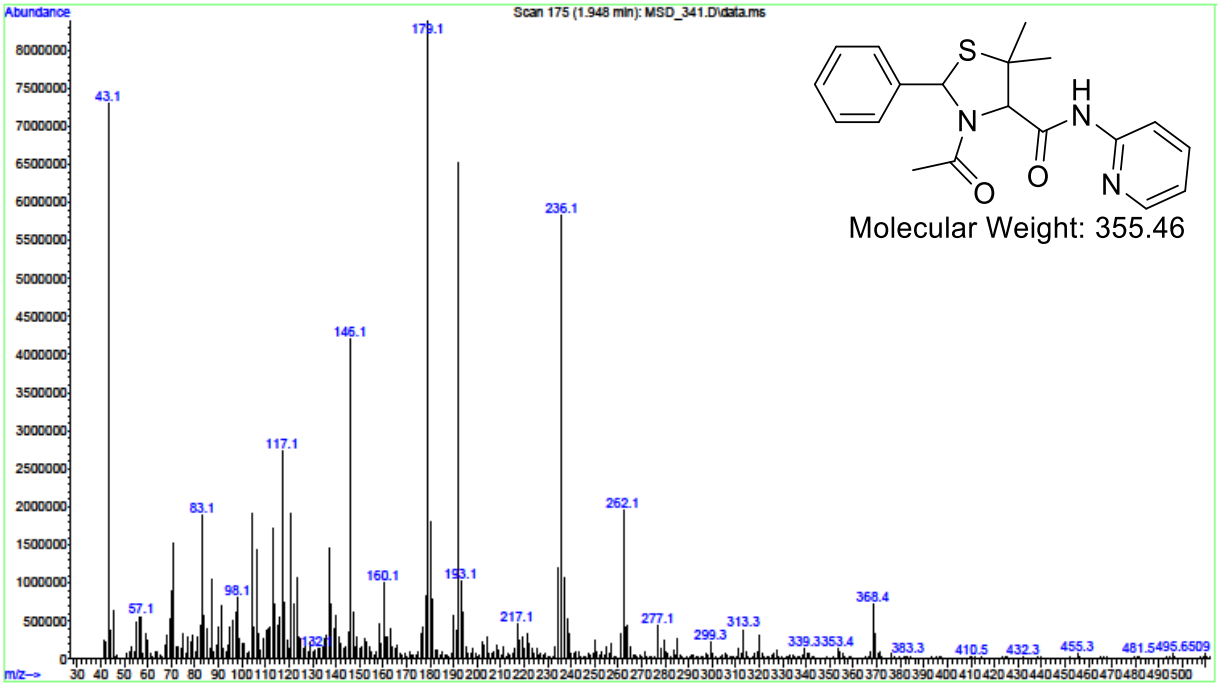


Figure 3–29 **:** mass spectrum of compound [b_3]

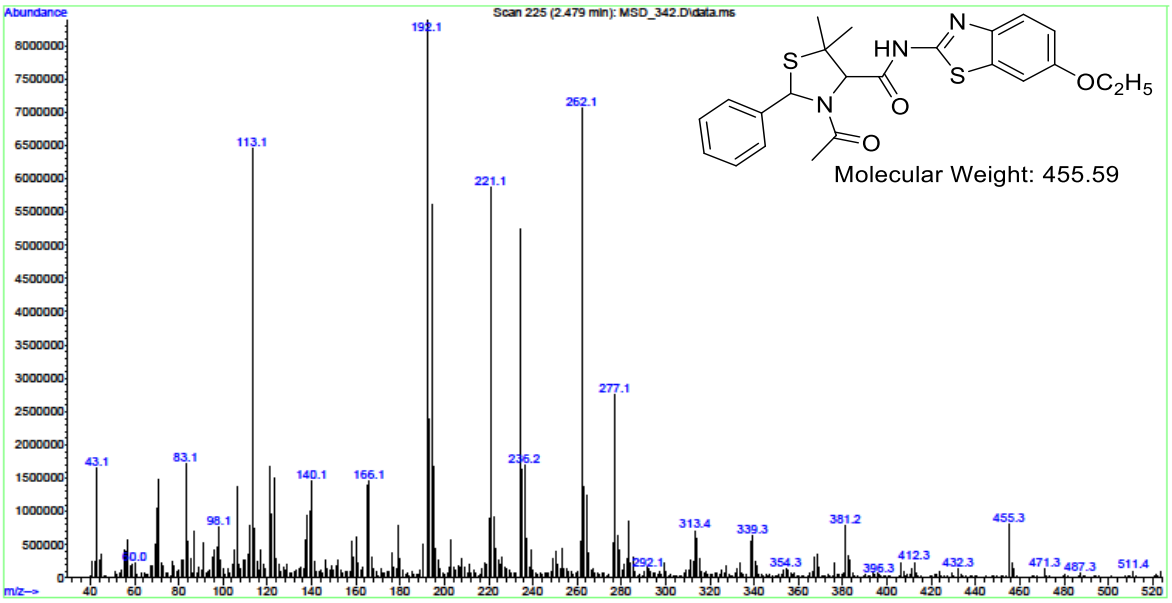


Figure 3–30**:** mass spectrum of compound [b_4]

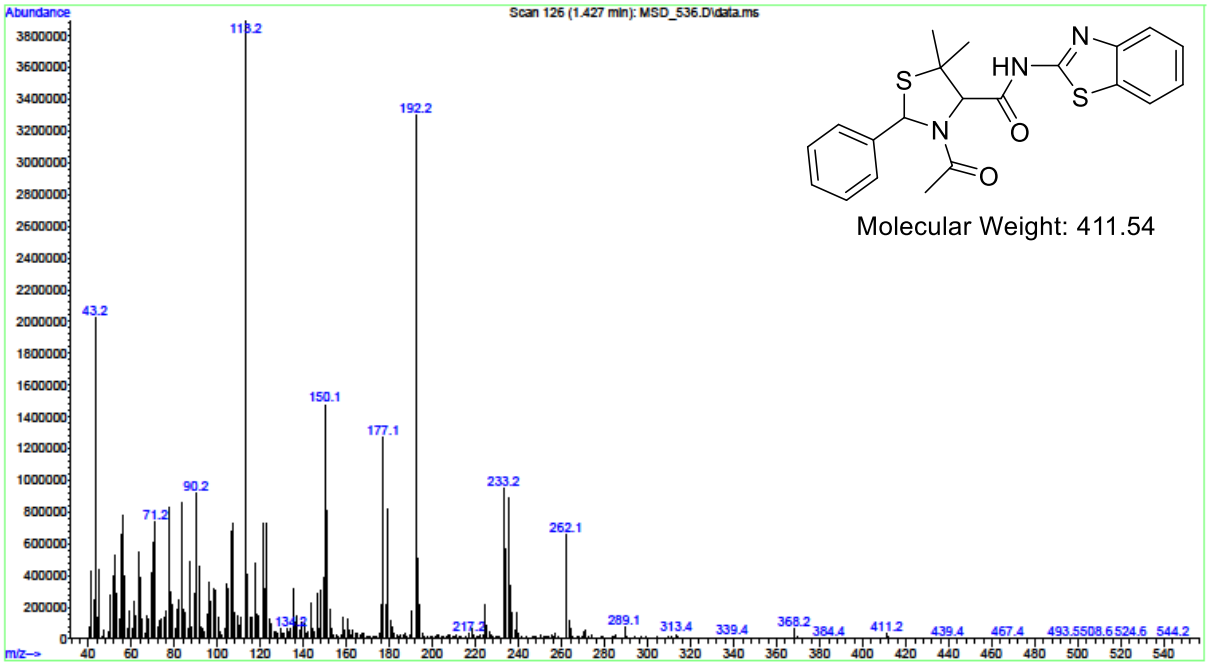


Figure 3–31**:** mass spectrum of compound [b_5]

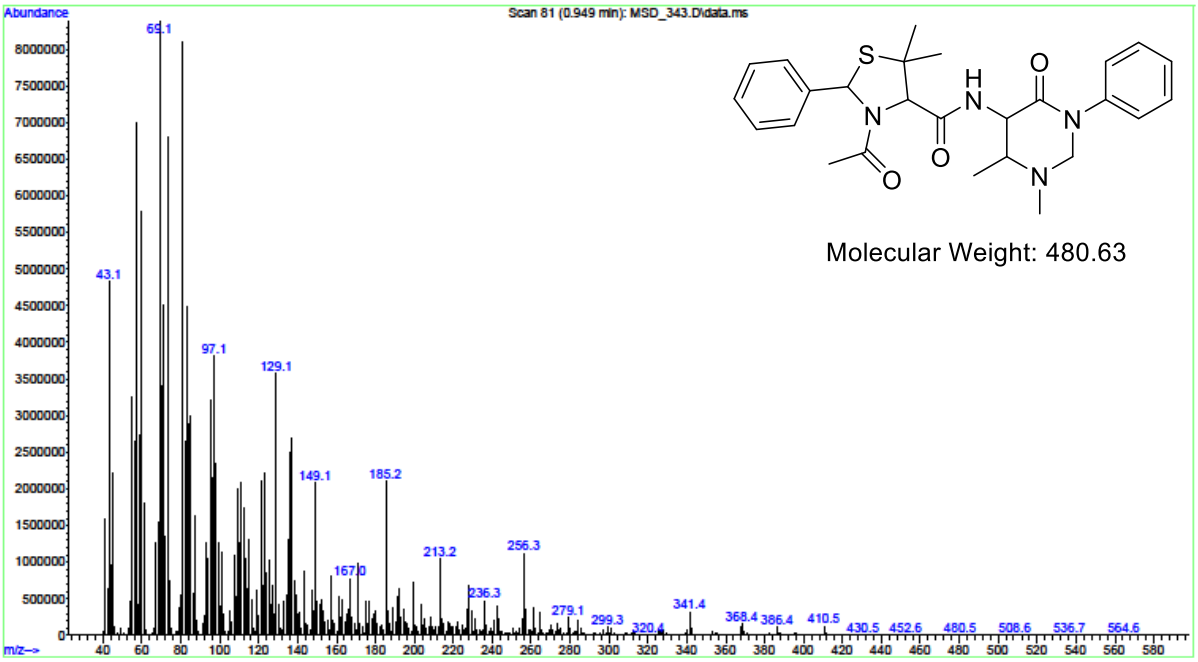


Figure 3–32**:** mass spectrum of compound [b_6]

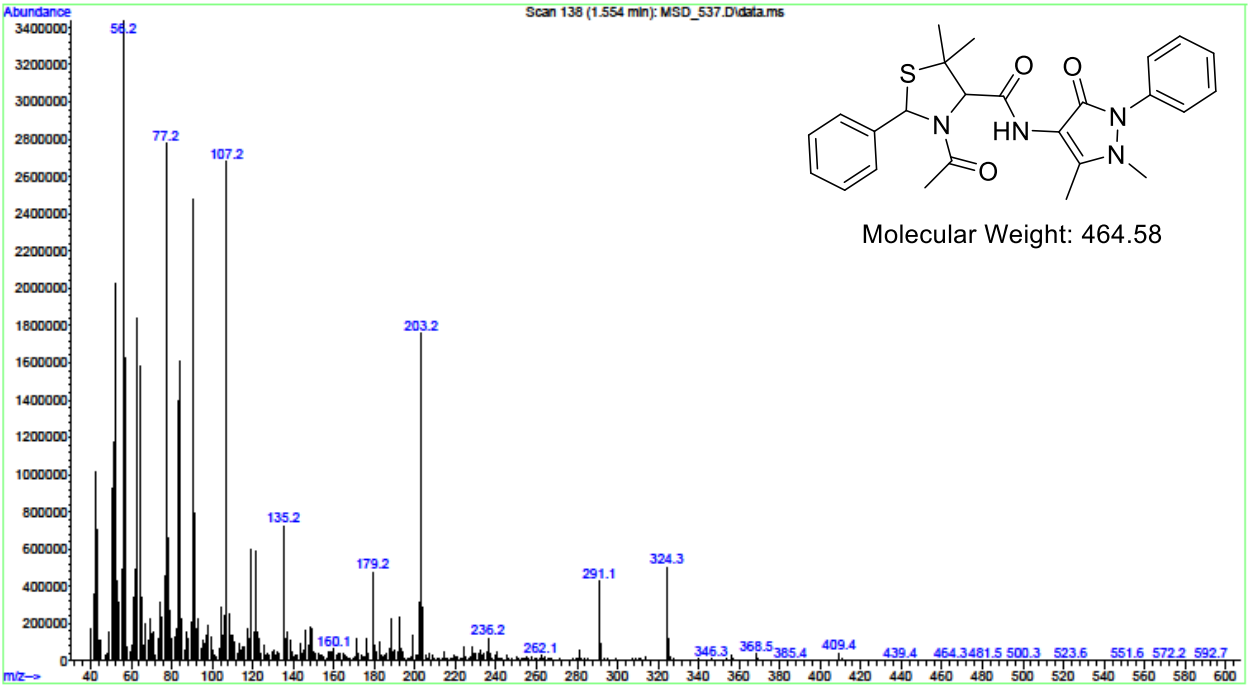


Figure 3–33**:** mass spectrum of compound [b_7]

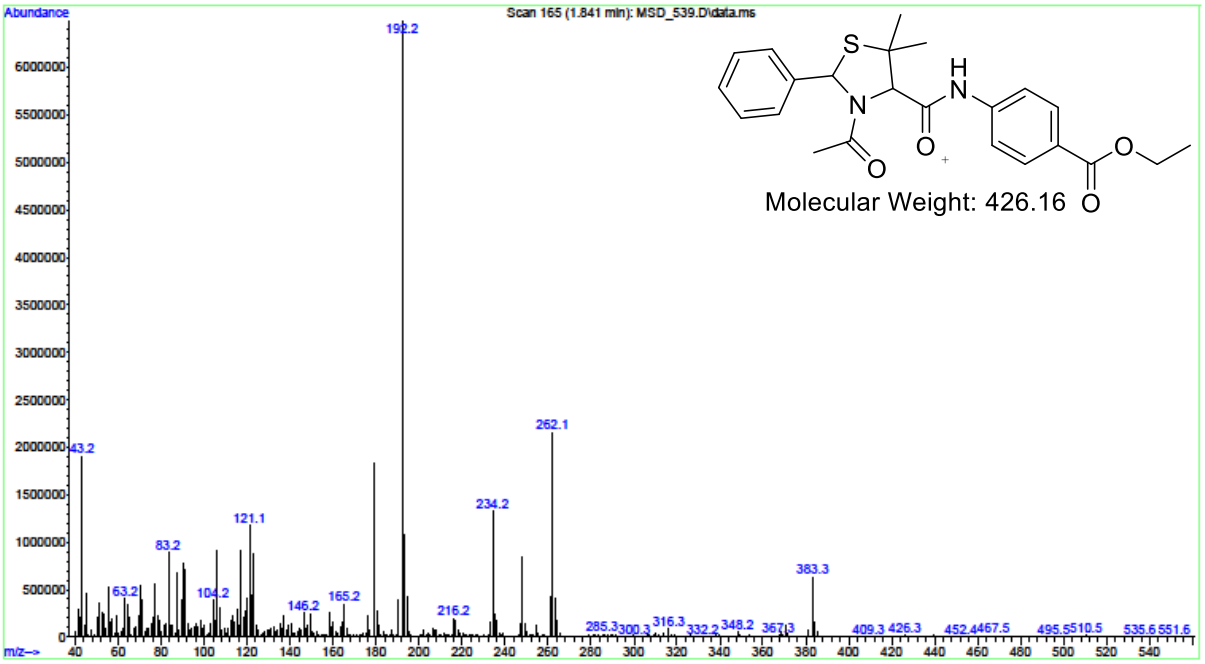


Figure 3–34**:** mass spectrum of compound [b_8]

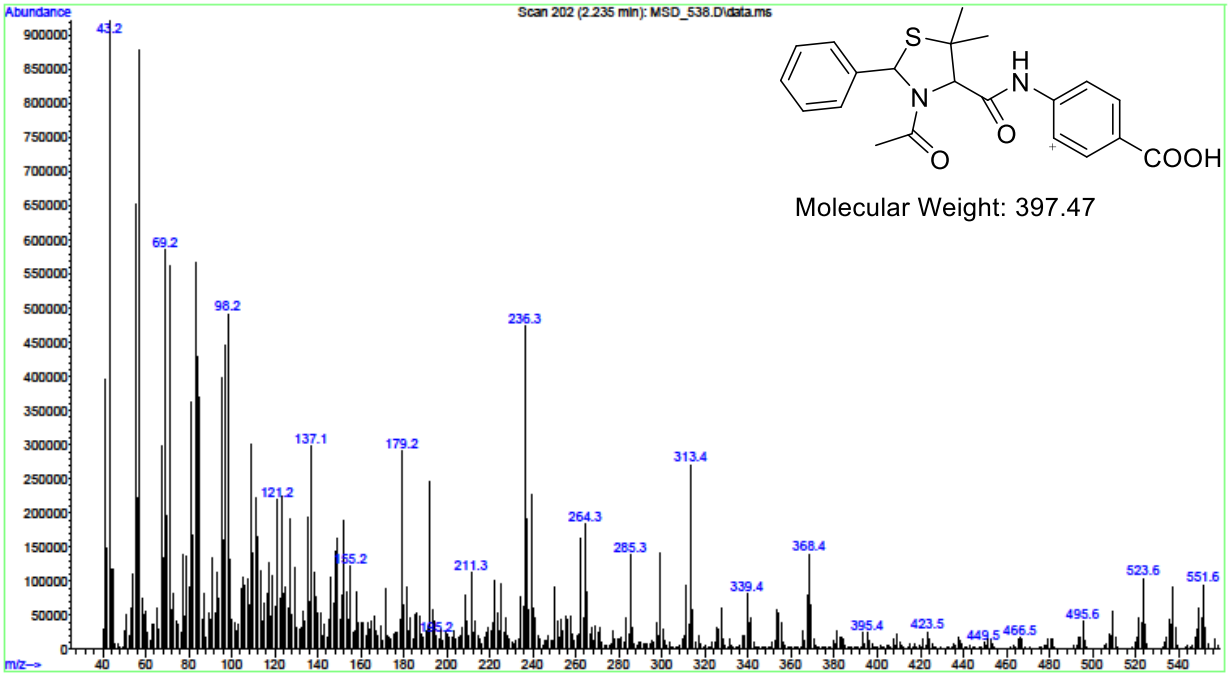


Figure 3–35**:** mass spectrum of compound [b_9]

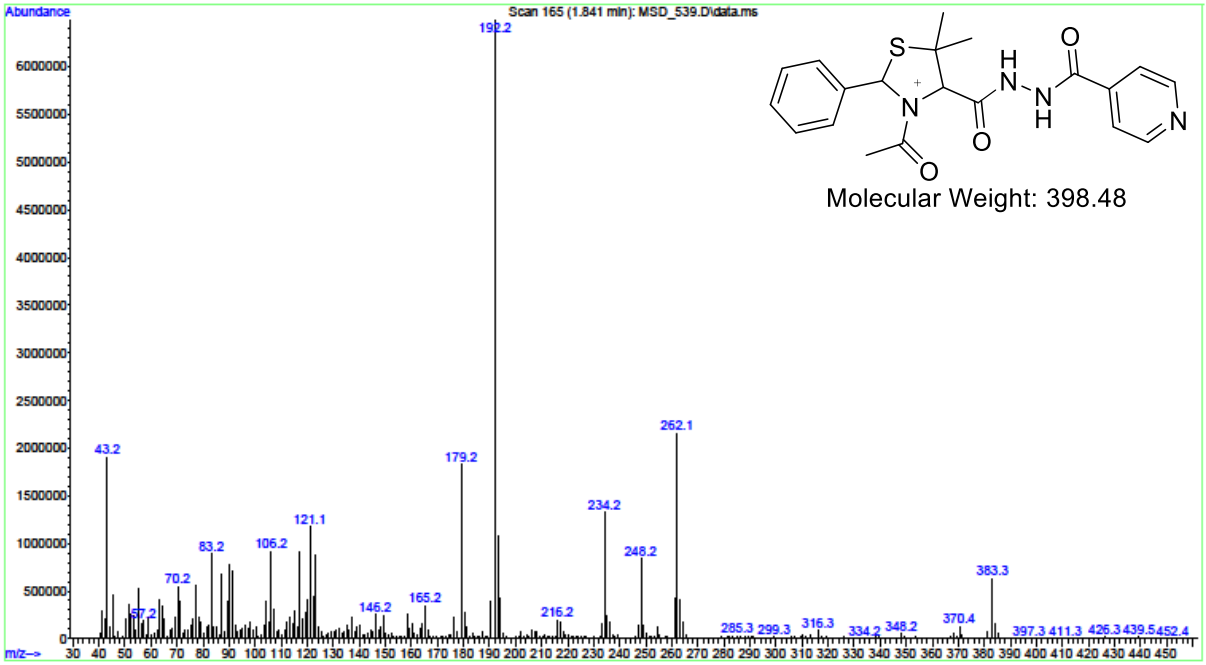


Figure 3–36**:** mass spectrum of compound [b_{10}]

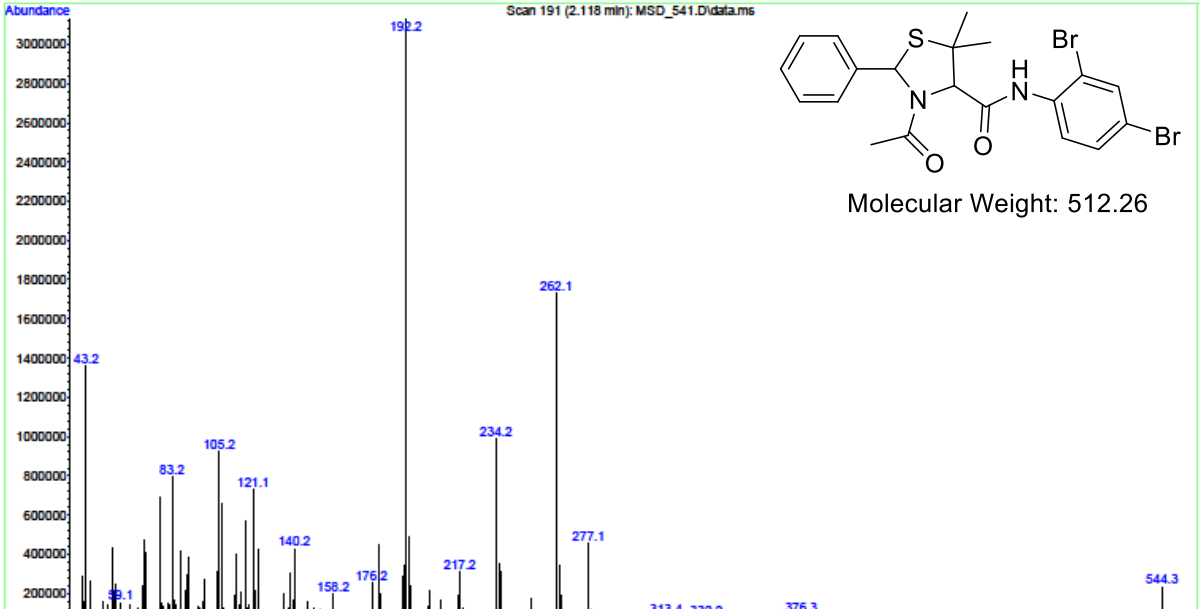


Figure 3–37**:** mass spectrum of compound [b_{11}]

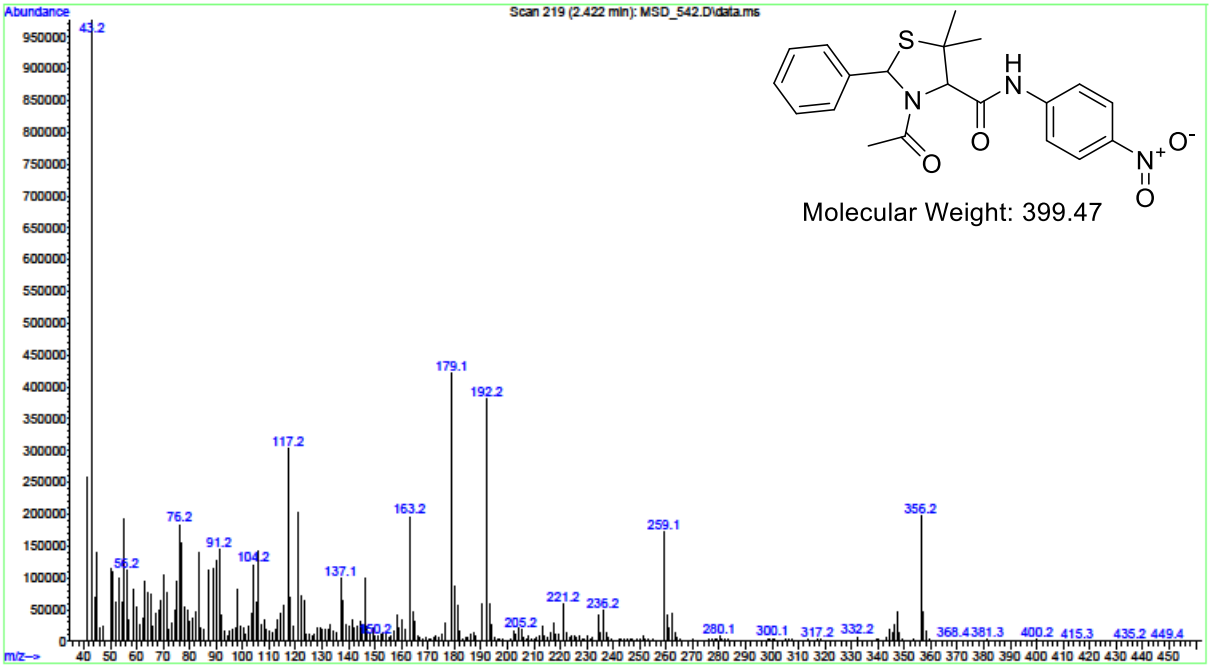


Figure 3–38**:** mass spectrum of compound [b_{12}]

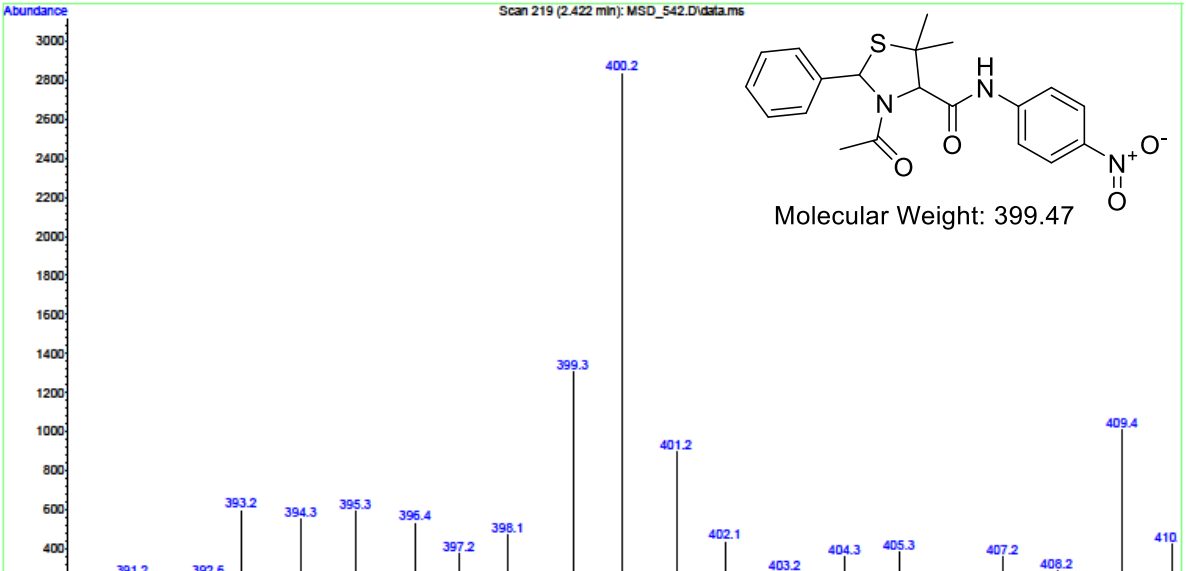


Figure 3–39**:** mass spectrum ,expanded spectrum for compound [b_{12}]

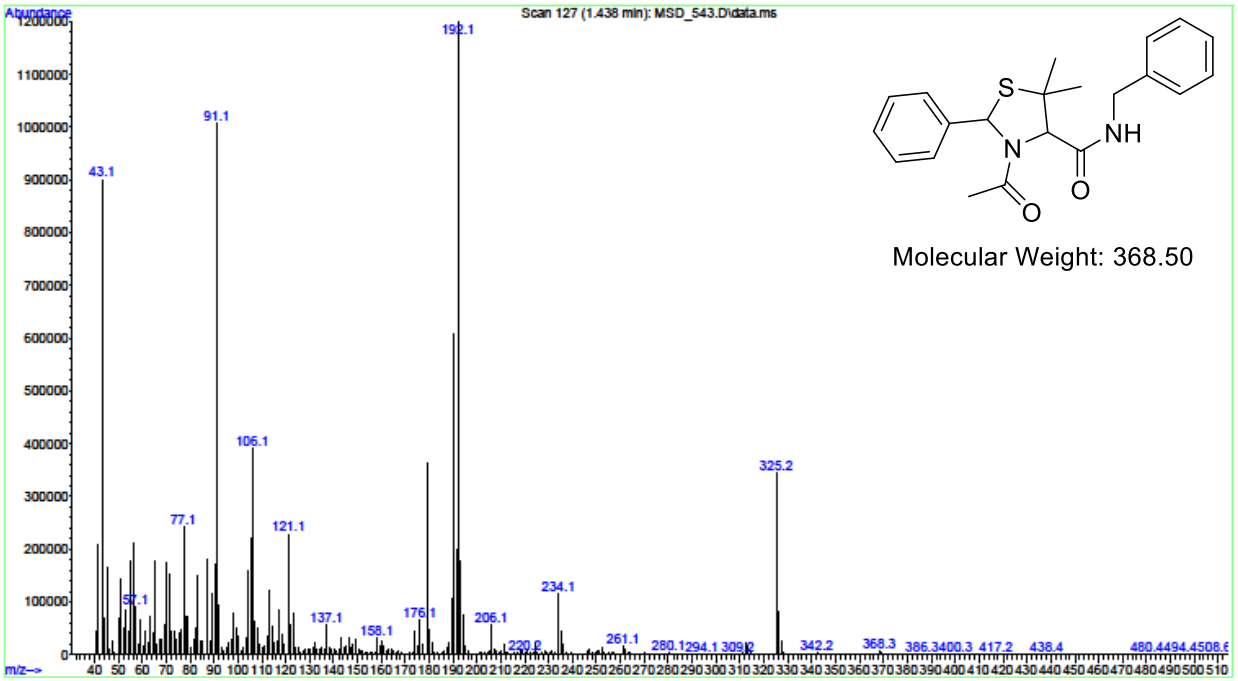


Figure 3–40**:** mass spectrum of compound [b_{13}]

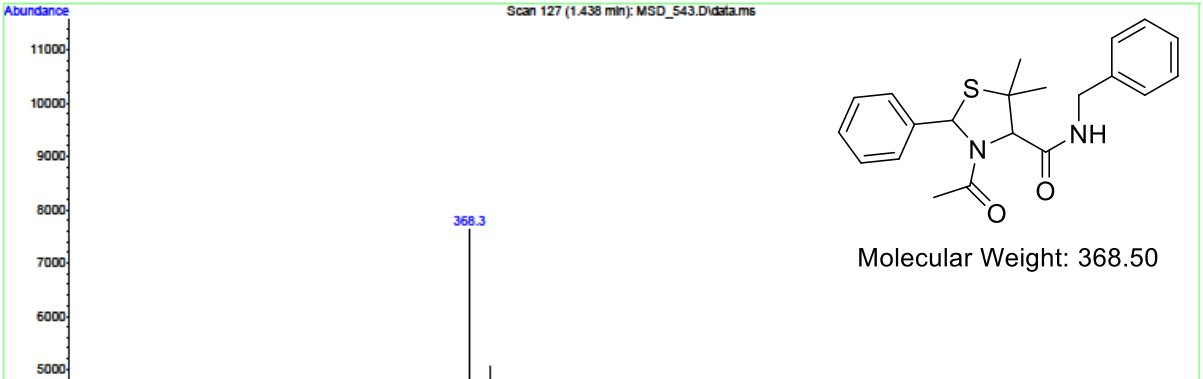


Figure 3–41**:** mass spectrum, expanded spectrum for compound [b_{13}]

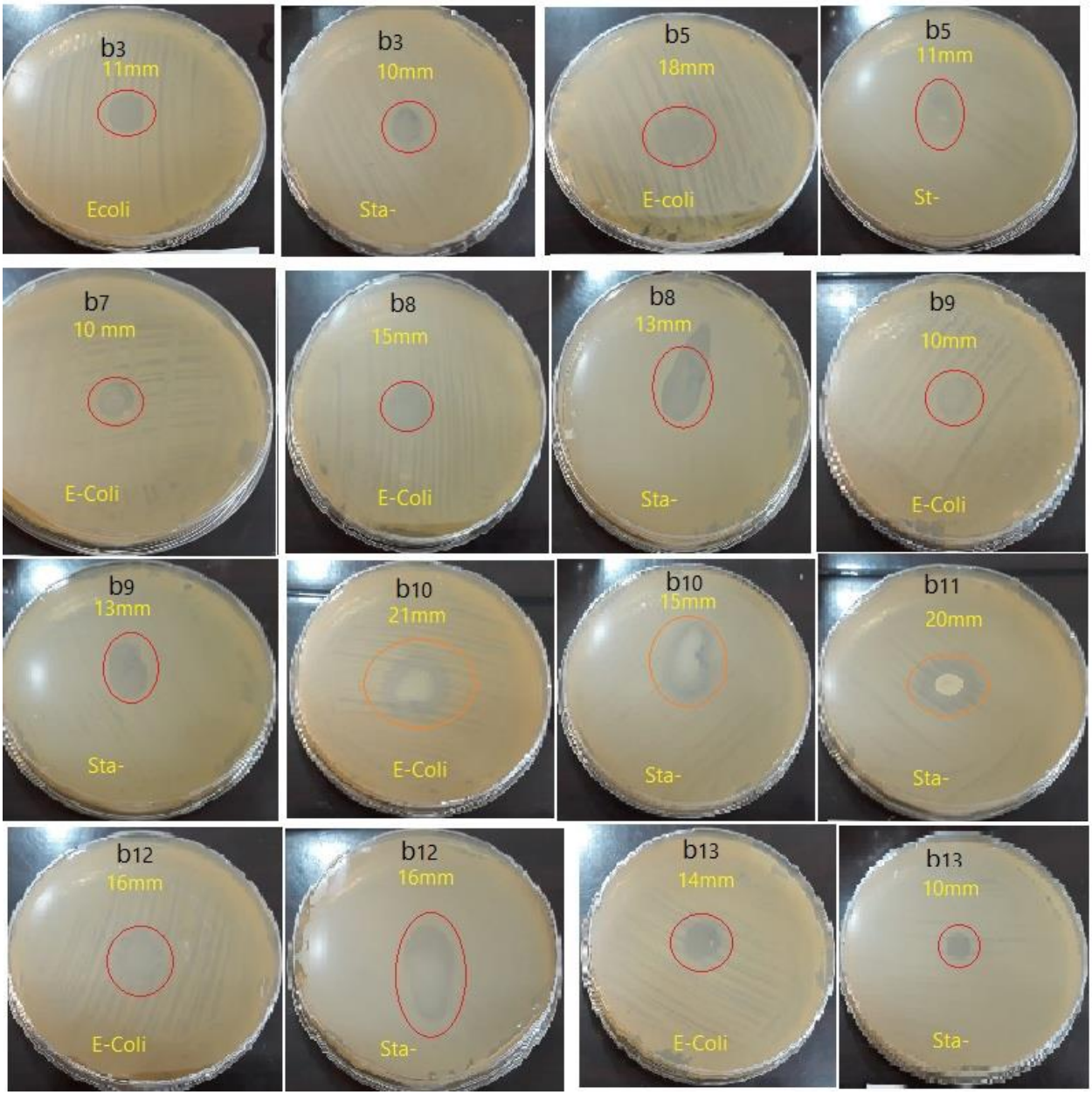


Figure 3–42: Inhibition zone of the compounds on (+Ve) bacteria (*staphylococcus*), (-Ve) bacteria (*E.coli*)