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SYNTHESIS AND CHARACTERIZATION OF 3,3'-(ETHANE- 1,2-DIYLBIS(SULFANEDIYL))BIS(1,4-BIS(4- BROMOPHENYL) AZETIDIN-2-ONE)

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ABSTRACT

This study is concerned with the synthesis and characterization of the 3,3'-(ethane-1,2-diylbis(sulfanediyl)) bis(1,4-bis(4-bromophenyl) azetidin-2-one) 2a. This compound was prepared by reacting 2,2'-(ethane- 1,2-diylbis(sulfanediyl)) diacetic acid with the appropriate 4-bromo-N-(4-bromobenzlidene) aniline 1a. The structure of these azetidin-2-one was established on the basis of the spectral data: IR, 1H NMR, 13C NMR and Mass.

KEYWORDS: Imine; Azetidin-2-ones; β-lactam; IR; 1H NMR; 13C NMR; Mass spectroscopy.

1. INTRODUCTION

Azetidin-2-ones, constitute a well-known class of heterocyclic compounds. This class of cyclic amides has attended extensive investigation in last two decades from synthetic, mechanistic and medicinal chemistry viewpoints.[1-9] β-Lactam antibiotics, are a wide class of antibiotics, characterized by the presence of an azetidin-2-one, nucleus containing the carbonyl β-lactam, fundamental for the activity.

The first antibiotic-resistance strategy reported in the literature is the production of the β-lactamase penicillinase. Different subclasses of β-lactams can be defined count on the chemical substitutions of the central β-lactamic core. Chemical modification of molecular structure has also driven the development of new β-lactamase-insensitive semisynthetic β-lactams, such as penems and carbapenems.[10,11] These antibiotics possess broad-spectrum activity and enhanced stability to β-lactamases. Considering the large pharmacological potential and use of the β-lactam systems, bushy research has produced numerous methods for synthesizing this skeleton, and the topic has been profusely authenticated and reviewed several times. Moreover, as documented in the subsequent Sect. 4, the chemical reactivity of the b-lactam ring depends robustly on the substitution at the N-1, the C-3, and the C-4 locations.[12]

2. The Experimental

Imine **1a** was prepared by the reaction 4-bromoaniline (0.01 mole, 1.85 g) with 4-chloro Benzaldehyde (0.01 mole, 1.40 g), 20 mL of methanol and one drop of glacial acetic acid was heated in water bath at (70-80˚C) for 30 min[13,14], as shown in Table (2-1). To a suspension of 2,2'-(ethane-1,2-diylbis(sulfanediyl)) diacetic acid (0.38g, 1.8mmole), 4-bromo-N-(4-bromobenzylidene) aniline **1a** (1 g, 2.9mmole) and triethylamine (3mmole, 0.9 g, 1.3 ml) in 25ml of dry dichloromethane was added drop-wise, under nitrogen atmosphere, a solution of $POCl_3$ (1.5mmole, 0.7g, 0.4ml) in 20ml dry dichloromethane with constant stirring at 0˚C.[15,16]

The reactants were stirred overnight at room temperature. Thereafter, the contents were washed successively with 1N HCL (25mL) ,5% $NaHCO_3$ (25mL) and brine salt (25mL). The organic layer was separated and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the crude product was column chromatographed over silica gel using 3:7 ethyl acetate\ hexane as eluent and solvent evaporation furnished pure β-lactam (2a), as shown in Table (2-1).

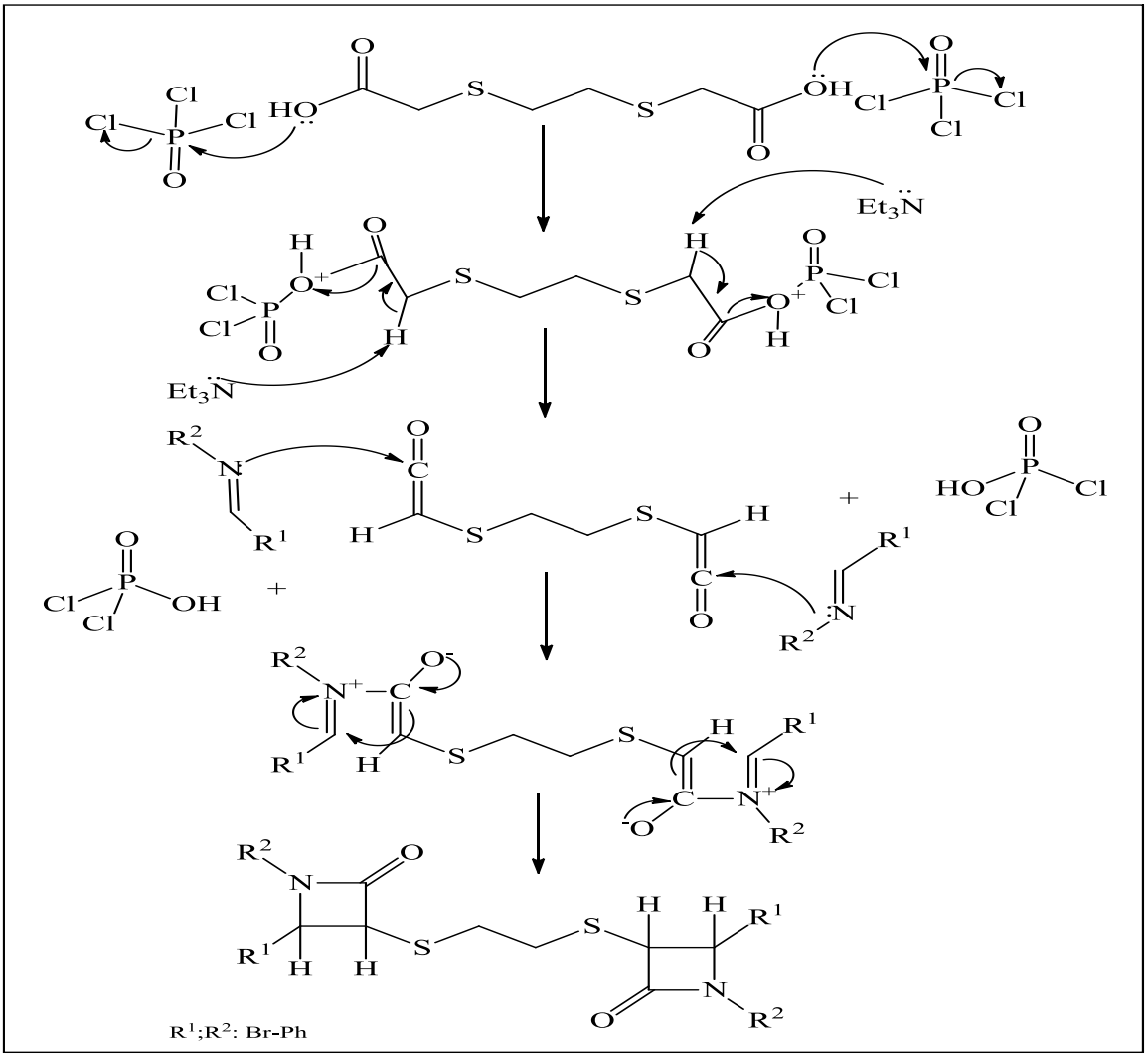
Table (2-1): Physical data for azetidine-2-one(2a) and imine (1a).

Comp.	Yield (%)	M.P. ˚C	Color
1a	83	144-146	White Yellowish
2a	78	203-205	White

3. RESULTS AND DISCUSSION

3.1. General

Taking the lead from previous studies[17,18] we considered to employ ketene-imine cyclization in the presence of triethylamine. The phosphorrusoxychloride reacted with triethylamine to generate the corresponding ketene in situ which further reacted with imine **1a**,to furnish the corresponding of 3,3'-(ethane-1,2-diylbis(sulfanediyl)) bis (1,4-bis 4-bromophenyl)azetidin-2-one) **2a**, as shown in (Scheme1).



(scheme 1)

3.2. IR spectra of 1a and 2a

The IR spectra of the imine **1a**, as KBr disc is shown in Figure (3-1). The IR spectra showed an absorption band at 1618.28 cm^{-1}, corresponding to the azomethine of imine compound. The rest of the packages can be summarized in the table (3-1).

The IR spectra of the 3,3'-(ethane- 1,2-diylbis(sulfanediyl)) bis(1,4-bis(4-bromo-phenyl) azetidin-2-one) **2a**, as KBr disc and, is listed in Table (3-1). The IR spectra of these compound **2a** showed an absorption band at (1681 cm^{-1}) for carbonyl amide group as shown in figure (3-2). The IR absorption frequency of carbonyl group depended upon the nature of substituents on phenyl ring by an electron-with drawing group such as bromo group will increased the absorption frequency.[19] w: weak. m: medium. s: strong.

Table (3-1): FT-IR spectra of imine(1a) and azetidine-2-one(2a).

absorption band	1a	2a
Aromatic C-H Str. cm^{-1}	3059 *m* 3024 *w*	3025 *w* 3082 *w* 3130 *m*
Aliphatic C-H Str. cm^{-1}	2879 *s*	2962 *m* 2937 *w* 2671 *m*
C=N Str. cm^{-1}	1618*s*	
Aromatic C=C Str. cm^{-1}	1583 *m* 1562 *m* 1481 *s*	1587 *s* 1508 *w* 1425 *m*
Aromatic C-H Ben. cm^{-1}	707 *w* 831 *s* 877 *w*	815 *m*
C=O Str. cm^{-1}		1681 *s*

3.3. NMR spectra

3.3.1. The ^{1}H-NMR spectra of 2a

The ^{1}H-NMR spectra of 2a showed three regions, an aliphatic region including tree groups of signals at the region δ 2.81 ppm corresponding SC-H and δ 4.50-5.15

ppm corresponding to methylene, C_3-H, and C_4-H protons. In the ^{1}H-NMR spectra the range of δ 7.18-8.26 ppm,corresponding to aromatic protons. which are included in Table (3-2) with their spectra, as shown in Figure (3-3).

3.3.2. ^{13}C NMR spectra of 2a

The resonance as between δ 166 ppm were assigned to the carbonyl.[20,21] group. The ^{13}C NMR spectra of the **2a** showed the carbonyl signal at δ164.4 ppm. The chemical shift values of aliphatic carbon atoms within the range δ 30.8-67.3 ppm and values of aromatic carbon atoms within the range δ 121.1-142.5 ppm. which are included in Table (3-2) with their spectra, as shown in Figure (3-4).

Table (3-2): ^{1}H-NMR and ^{13}C NMR spectra data of azetidine-2-one 2a.

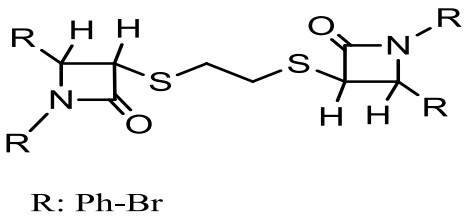
Chemical shift ppm	^{1}H-NMR /CD3OD δ ppm 2a	^{13}C NMR /$CDCl_3$ δ ppm 2a
Aliphatic protons δ ppm	2.814 4.504-4.537 5.124-5.165	30.8, 49.4 67.6 164.4
Aromatic protons δ ppm	7.182-7.189 7.920-7.927 8.117-8.262	121.1,122.3, 127.1,131.4, 136.7, 138.5 142.5

3.4: Mass spectra

The mass spectral data of the compound is shown in the Figure (3-5). The mass spectra of compound **2a**, showed the molecular ion peak corresponding to the particular compound M^+852 m/z, and the fragmentation of **2a** lead to ketene, isocyanate and imine.[22,23] The fragmentation of **2a** leading to the ketene 315 m/z and 173m/z. corresponding isocyanate 196 m/z and 118 m/z also the fragmentation of this compound **2a** showed the imine peaks 339 m/z, as shown in table (3-3) the fragmentation mechanism of compound **2a** is shown below in (scheme2).

Table (3-3): Mass spectral data of azetidin-2-one 2a.

Mass spectra	m/z
2a	(M^+)852 m/z, (R-CH=N-R) 339m/z, (R-N-C=O)196m/z, (Ph-N=C=O)118m/z, (R-N=CH-Ph) 258m/z, ($C_6H_5^+$)77m/z, (R)155 m/z, (R-CH=CH-S-$(CH_2)_2$-S-CH=C=O)315m/z, ($^+CH_2$-S-CH=C=O)87m/z, ($C_5H_5^+$)65m/z



R: Ph-Br

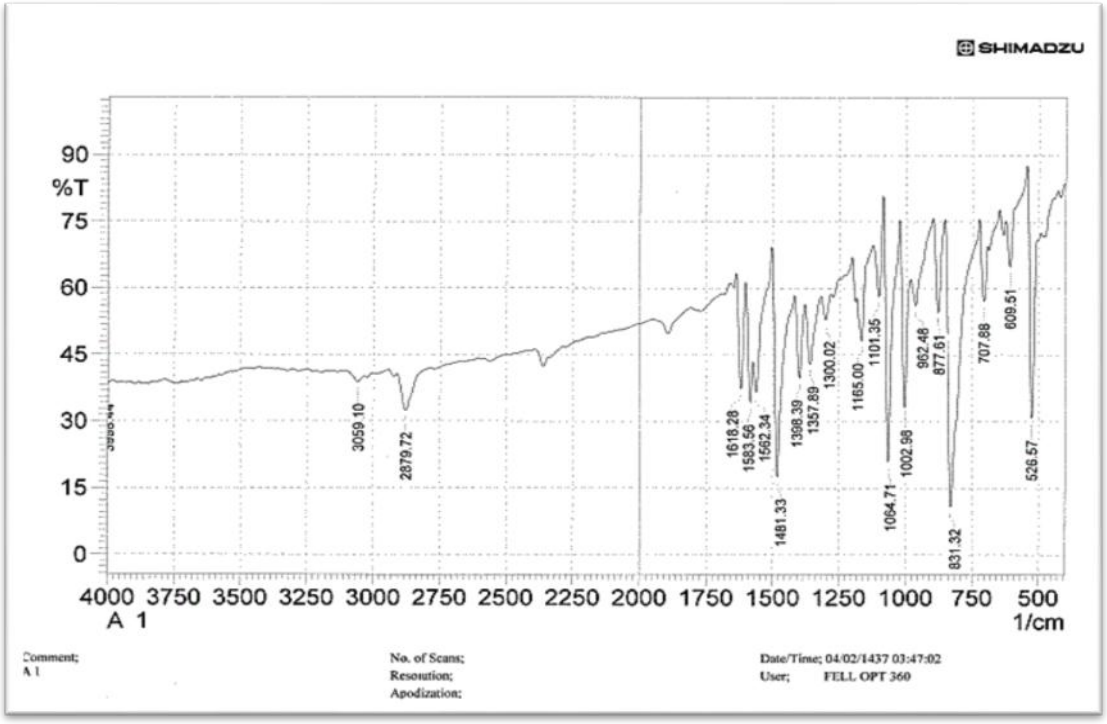


Figure (3-1): FT-IR spectrum of N-(4-bromophenyl)-4-bromobenzyldine 1a.

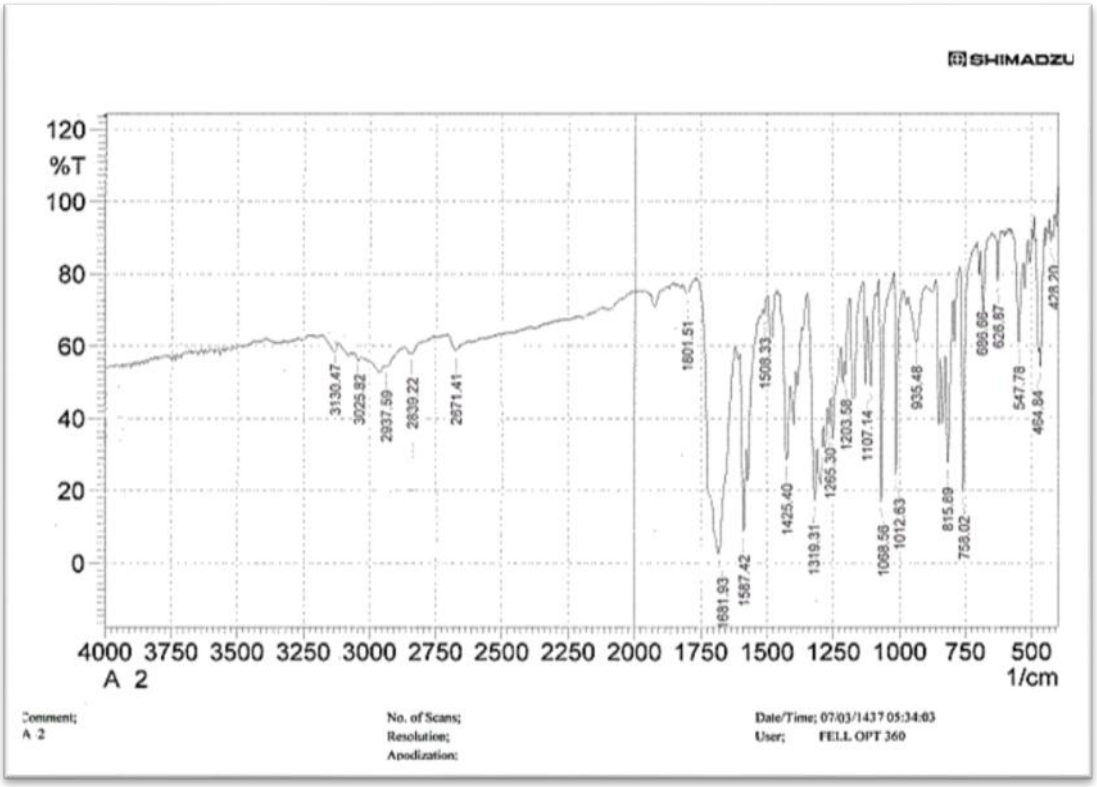


Figure (3-2): FT-IR spectrum of 3,3'-(ethane-1,2-diylbis(sulfanediyl))bis(1,4-bis(4-bromophenyl) azetidin-2-one) 2a.

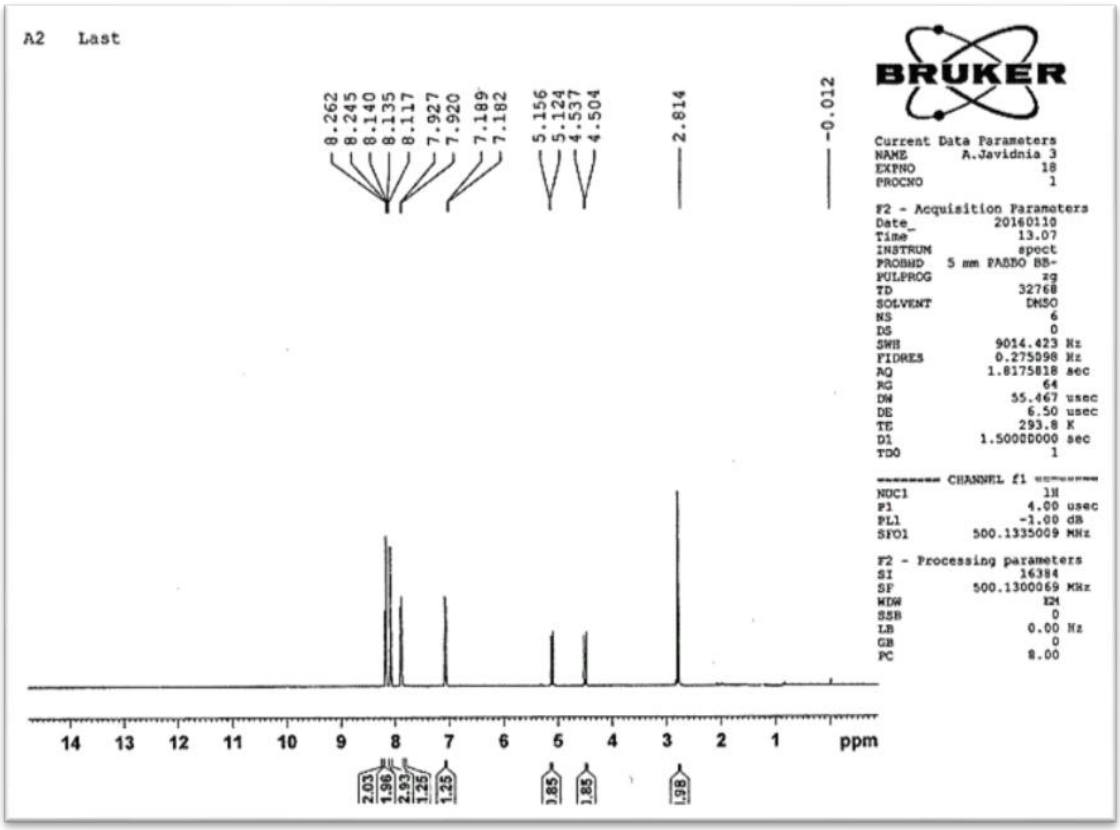


Figure (3-3): ^{1}H-NMR spectrum of 3,3'-(ethane-1,2-diylbis(sulfanediyl))bis(1,4-bis(4-bromophenyl) azetidin-2-one)2a.

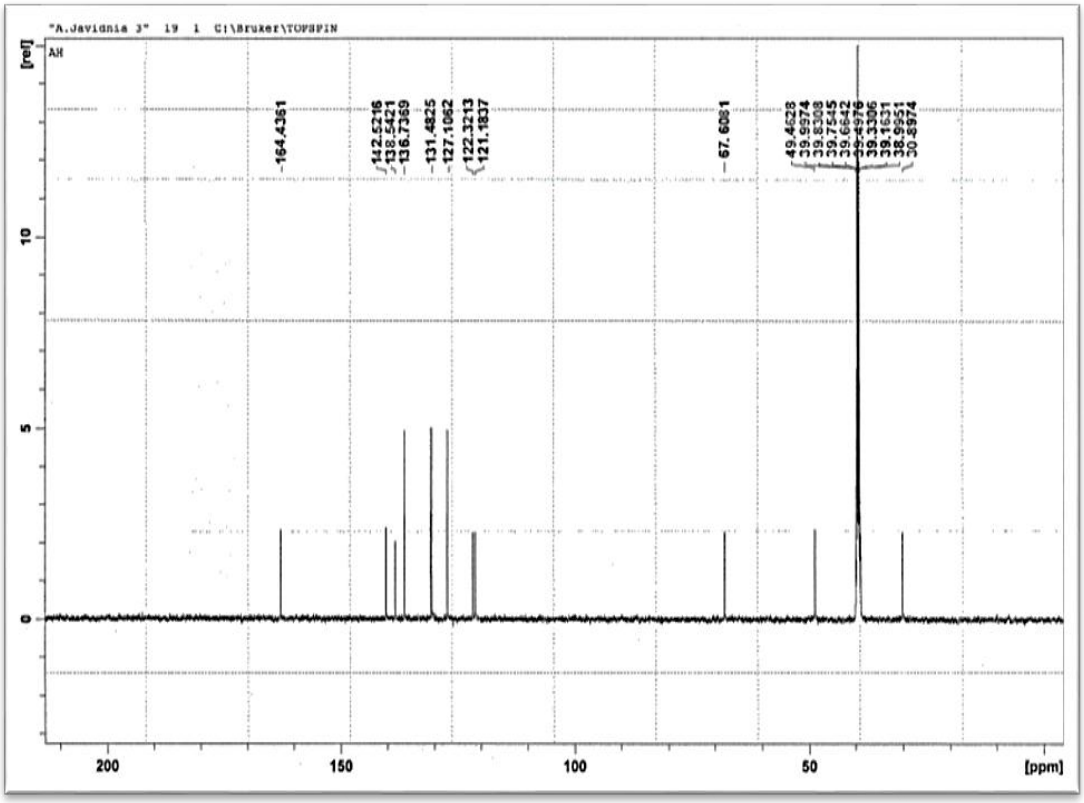


Figure (3-4): ^{13}C NMR spectrum of 3,3'-(ethane-1,2-diylbis(sulfanediyl))bis(1,4-bis(4-bromophenyl) azetidin-2-one) 2a.

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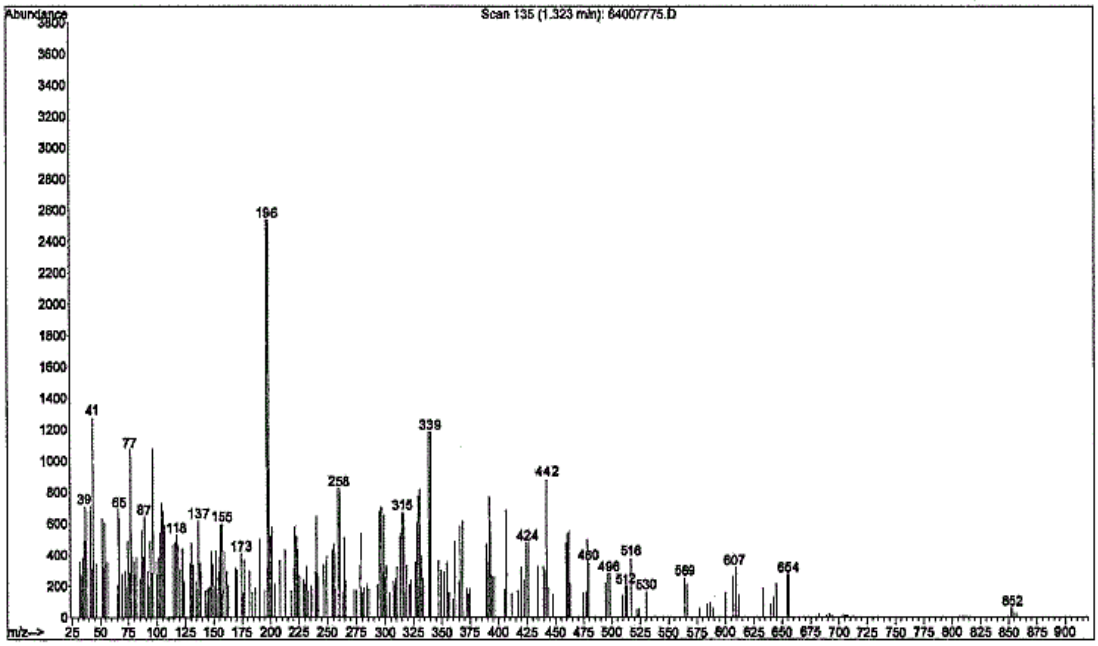

Figure (3-5): Mass spectrum of 3,3'-(ethane-1,2-diylbis (sulfanediyl))bis(1,4-bis(4-bromophenyl)azetidin-2-one) 2a.

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