

Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base
Mustafa Y. Jamal , Saadon A. Aowda

Synthesis and spectroscopic studies of some Azetidin-2-one derivatives from Benzidine and S-Benzylthioglycolic acid via Schiff base

Mustafa Y. Jamal , Saadon A. Aowda
Chemistry department -College of Science - Babylon University

Received 8 December 2013 ; Accepted 11 February 2014

Abstract

A series of four membered ring of azetidin-2-one (11-20) have been synthesized via Schiff bases(1-10) by reaction of different aromatic aldehyde with unsubstituted benzidine in absolute ethanol and two or three drops of glacial acetic acid then reflux for (2-3) hours. Schiff bases then reacted with S-Benzylthioglycolic in the presence of triethylamine with phosphorus oxychloride using dry methylene dichloride under inert nitrogen atmosphere at 0 °C. to give us the corresponding azetidin-2-one. The structural of these compounds were monitored and confirmed by using TLC , spectroscopic tools as IR , ¹H NMR, and Elemental analysis.

Keywords : Imines, Schiff bases, Benzidine , β -lactam , Four member ring , Staudinger reaction , Ketene

تحضير و دراسة طيفيه لبعض مشتقات الازتدين-2-اون من البنزدين وحامض بنزيلثايوكلايكوليك من خلال مشتقات قواعد شف

المخلص

تم تحضير سلسلة من مركبات الازتدين الرباعية الحلقة غير المتجانسة (٢٠-١١) من تفاعل قواعد شف المحضرة مع تفاعل اورثوتوليدين مع مركبات البنزليدهايد الاروماتيه المختلفه بوجود الايثانول المطلق وبضع قطرات من استيك اسيد الثلجي والتصعيد (٣-٢) ساعه. ثم تم مفاعله قواعد الشف المحضرة (١٠-١) مع حامض بنزيلثايوكلايكوليك وبوجود ثلاثي اثيل امين و فسفورس اوكسي كلورايد ومثيلين كلورايد في جو خامل من النتروجين وبدرجه الصفر المئوي لينتج مشتق الازتدين-٢-اون.

وقد تم متابعه وتشخيص النواتج المحضرة بواسطه تقنيات كروموتوغرافيا الطبقة الرقيقه، الاشعه تحت الحمراء، كاربون وبروتون الرنين النووي المغناطيسي، بالاضافه الى تحليل العناصر.

INTRODUCTION

All β -lactam antibiotics chemically possess a four-membered cyclic amide, known as azetidin-2-one or β -lactam, which can be isolated or fused to form a bicyclic or tricyclic ring system as showed in (figure 1). A fused heterocyclic ring can be either saturated or unsaturated with a double bond positioned either between C-2 and C-3 of the five membered heterocycle or C-3 and C-4 of the six-membered heterocycle.

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base
Mustafa Y. Jamal , Saadon A. Aowda**

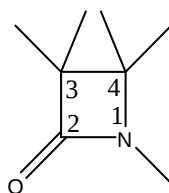


Figure (1) : azetidin-2-one structure

The ring can be formed in several different ways, Staudinger reaction being the one most often used. Recent discoveries have shown also other biological properties that have further increased the significance of β -lactams as synthetic intermediates for the preparation of heterocycles of biological interest. Although they can serve as inhibitors of serine proteases [1], cholesterol acyltransferase, human cytomegalovirus and proteasome inhibitors [2] their antibacterial activity remains the principal mode of action [3,4]. Because of good characteristics (wide spectrum, relatively low host toxicity, appropriate pharmacokinetics, synergistic effect...) β -lactam antibiotics (Figure 2) are the most used antibacterial agents in clinical practice [5,6,7,8], where they are represented with around forty compounds [9], the β -lactam compound used as anticancer agents [10,11], a series of bicyclic N-substituted and unsubstituted β -lactams were synthesized and evaluated as targeted potential antimalarials [12].

However, a widely used method is via the [2+2] cyclocondensation of ketenes to imines, a process known as the Staudinger reaction, which has important application in pharmaceutical and synthetic chemistry [13,14,15], this reaction has been used to construct macrocyclic bisazetidinone polyethers by the reaction of the appropriate ketene precursors with macrocyclic diimines [16].

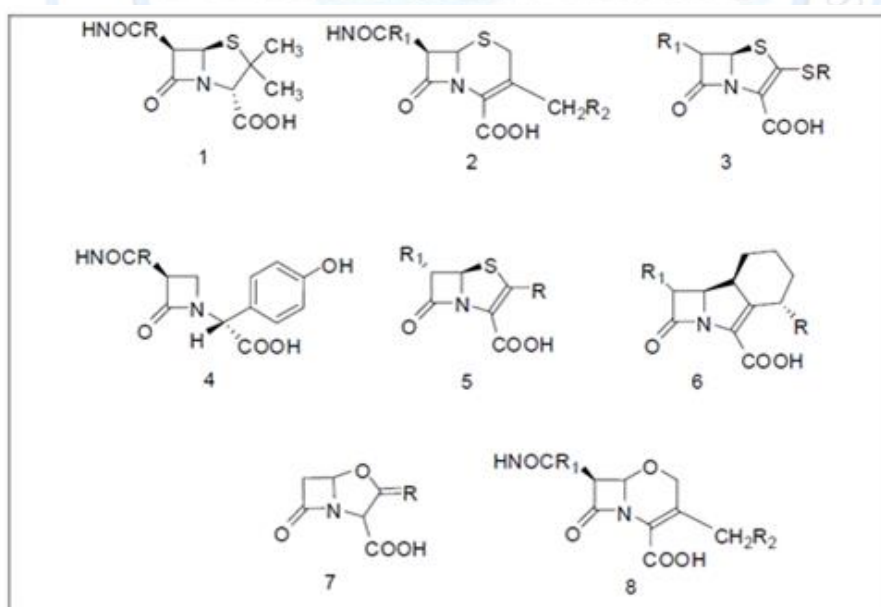


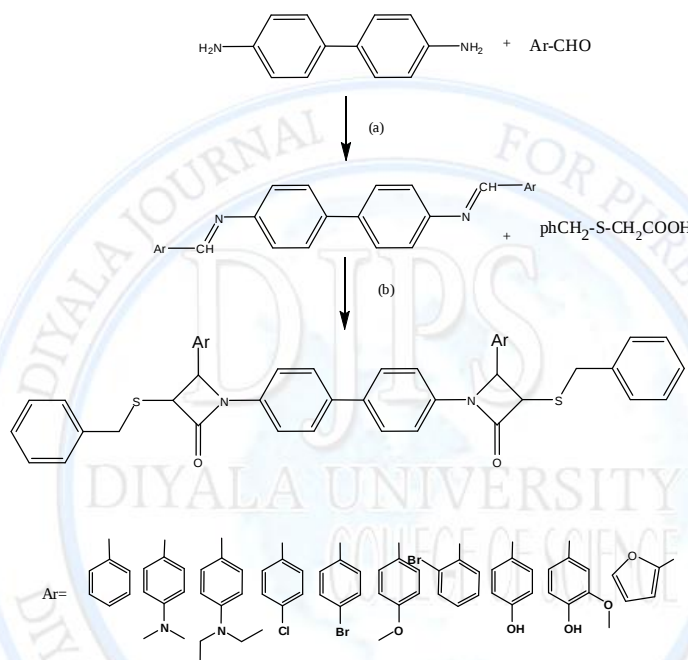
Figure 2: Classification of β -lactam antibiotics based on structure: penams (1), cephems (2), penems (3), monobactams (4), carbapenems (5), trinems (6), clavams (7), oxacephems (8)

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

EXPERIMENTAL

All melting points are uncorrected and are expressed in degree(°C), using melting point SMP3 . IR spectra were recorded as KBr disks using shimadzu FT-IR 8400. ¹H NMR spectra were recorded using Varian VnmrJ 400 spectrometer (400 MHz) and tetramethylsilane (TMS) as internal standard using DMSO-d₆ as solvent the peaks showed at δ=(2.5-2.4)ppm, ¹³C NMR spectra were recorded using Varian VnmrJ 400 spectrometer (100 MHz) and tetramethylsilane (TMS) as internal standard using DMSO-d₆ as solvent Elemental analysis using Leco CHNS-933 Leco corporation st.Joseph .



Scheme (1): (a) reflux in ethanol(2-3) h ;(b) slow addition POCl₃ with stirring (30-55) mint in N₂ at 0°C using dichloromethane as solvent.

Synthesis of imines derivatives (1-10):

(E)-N⁴,N^{4'}-dibenzylidenebiphenyl-4,4'-diamine. (1)

Benzidine (2 mmol, 0.368gm) was dissolved in absolute ethanol and added to benzaldehyde 4mmol, 0.2gm) in presence of few drops of glacial acetic acid under refluxing for 2 hours. A yellow precipitate was observed then by section filtration a product yield= (89%) with m.p.=(240-241) C°. FT-IR-spectra in figure (3) showed absorption bands appeared at the range of 3057 and 2883 cm⁻¹ which belong to both (C-H) aromatic and aliphatic respectively. While (C=N) appeared at 1622 cm⁻¹ , (C-N) appeared at stretching frequency at 1183 cm⁻¹ , beside that the (C=C) aromatic appeared at range of 1573 – 1492 cm⁻¹. Elemental analysis confirmed the molecular formula C₂₆H₂₀N₂ (calculated /**found**): (C, 86.64 /**86.92**; H, 5.59/**5.63**; N, 7.77/ **7.87**).

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

(E)- N⁴,N^{4'}-Bis[4- (dimethyl amino) benzylidene] biphenyl-4,4'-diamine. (2)

Benzidine (2mmol, 0.368gm) was dissolved in absolute ethanol and added to *p*-dimethyl amino benzaldehyde (4mmol, 0.60 gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours. The resulting yellow-orange precipitated product was observed, filtrated yield=87%. The following criteria of the precipitated product were recorded: m.p.= (318-319) C° of the desired product. FT- IR spectra, showed a stretching frequency at 1609cm⁻¹ referring to (C=N), 1483-1583 cm⁻¹ to (C=C) aromatic, 1363 cm⁻¹ to (CH₃), 1167 cm⁻¹ to (C-N) and 3100 cm⁻¹ to (C-H), benzylic bonds. On the other hand the ¹H-NMR in DMSO-d₆ showed , at δ= 3.3ppm due to (s, 12H, CH₃) , at δ = 9.1ppm referred to (s, 2H, CH=N), at δ =7.7ppm , (dd,8H, Ar) referred to biphenyl , at δ= 7.2ppm, (d,4H, Ar) at δ= 7.3ppm and (m,4H, Ar) due to substituted phenyl. Elemental analysis of the molecular formula C₃₀H₃₀N₄ (calculated / **found**): (C, 80.68 / **80.91** ; H, 6.77 / **6.68** ; N, 12.55 / **12.66**) .

(E)-N⁴,N^{4'}Bis [4-(diethyl amino) benzylidene] biphenyl-4,4'-diamine.(3)

Benzidine (2 mmol, 0.368gm) was dissolved in absolute ethanol and added to *p*-diethyl amino benzaldehyde (4 mmol, 0.70gm) in presence of few drops of glacial acetic acid under refluxing for 2 hours. A yellow light precipitated yield= 88 % was observed. The m.p. = (288-289)C°.FT- IR spectra was confirmed the suggested product, the stretching frequency of imines (C=N)group observed at 1607cm⁻¹, (C=C, aromatic) at 1521-1582 cm⁻¹, (CH₂) at 1400,(CH₃) 1354cm⁻¹ and (C-H ,aliphatic) appear at range 2972 cm⁻¹. On the other hand the ¹H-NMR in DMSO-d₆ showed , at δ= 3.2 -3.3ppm and (q,8H, CH₂) at δ= 1.2ppm in addition to (t, 12H, CH₃),at δ = 8.8ppm referred to (s, 2H, CH=N), at δ =7.5ppm (dd,8H, Ar) due to biphenyl ,at δ= 7.3ppm, (m,4H, Ar) and δ=7.6ppm (m,4H, Ar) referred to substituted phenyl .Elemental Analysis of compound with molecular formula C₃₄H₃₈N₄ (calculated /**found**) C, 81.24 / **81.67** ; H, 7.62 / **8.04** ; N, 11.15 / **11.35** .

(E)-N⁴,N^{4'}Bis (4-chlorobenzylidene) biphenyl-4,4'-diamine.(4)

Benzidine (2 mmol,0.368gm) was dissolved in absolute ethanol and added to *p*-chlorobenzaldehyde (4mmol, 0.56 gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours. Yellow precipitate observed , after workup of the reaction mixture , The yield = 91% , m.p. = (269-270)°C ,FT-IR showed the sharp absorption band at stretching frequency (C=N) 1622 cm⁻¹ for imines group , 1489-1586 cm⁻¹ (aromatic ,C=C) , 1091cm⁻¹ (Ar-N) ,and (C-Cl) observed at stretching frequency 839 cm⁻¹ and. On the other hand elemental analysis confirmed the suggested the molecular formula C₂₆H₁₈N₂Cl₂ (calculated / **found**) C, 72.73 / **72.85**; H, 4.23 / **4.33**; N, 6.52 / **6.64**.

(E)-N⁴,N^{4'} Bis (4-bromobenzylidene) biphenyl-4,4'-diamine. (5)

Benzidine (2mmol, 0.368gm) was dissolved in absolute ethanol and added to *p*-bromobenzaldehyde (4mmol, 0.73 gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours.

A yellow light precipitated product directly observed with a percentage yield = 92 % , m.p. = 300-301 C° .FT- IR showed data such as 1622 cm⁻¹ (C=N), 1402-1583 cm⁻¹ (aromatic C=C), 1070 cm⁻¹ (C-N) except stretching absorption at 540 cm⁻¹ which belong to (Ar-Br). On the

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal, Saadon A. Aowda

other hand the data in figure (4), $^1\text{H-NMR}$ in DMSO-d_6 as a solvent showed, at $\delta = 8.9\text{ppm}$ referred to (s, 2H, CH=N), at $\delta = 7.7\text{ppm}$ (dd, 8H, Ar) due to biphenyl, at $\delta = 7.3\text{ppm}$ (m, 4H, Ar) and $\delta = 7.4\text{ppm}$ (m, 4H, Ar) referred to substituted phenyl. Elemental analysis of the molecular formula $\text{C}_{26}\text{H}_{18}\text{N}_2\text{Br}_2$ (calculated / **found**) C, 60.26 / **60.45**; H, 3.50 / **3.63**; N, 5.41 / **5.73**.

(E)-N⁴,N^{4'}-bis(4-methoxybenzylidene)biphenyl-4,4'-diamine.(6)

Benzidine (2mmol, 0.368gm) was dissolved in absolute ethanol and added to *p*-methoxy benzaldehyde (4mmol, 0.54gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours. Yellow-orange precipitate, after work up of compound the percentage yield was 93%, m.p. = (255-256) $^\circ\text{C}$. The FT- IR spectra showed two adsorption bands appear in the range of 3050 cm^{-1} and 2959 cm^{-1} which belong to (C-H) aromatic and aliphatic respectively, while (C=N) appear at 1606 cm^{-1} , (C-O-C) appear in the range 1250 cm^{-1} , (C-N) appear at stretching frequency 1169 cm^{-1} , beside that the (aromatic C=C) appear at range between $1510\text{--}1574\text{ cm}^{-1}$. On the other hands the $^1\text{H-NMR}$ in DMSO-d_6 showed, at $\delta = 3.9\text{ppm}$ in addition to (s, 6H, CH_3), at $\delta = 8.5\text{ppm}$ referred to (s, 2H, CH=N), at $\delta = 7.3\text{ppm}$ and 7.6ppm , (m, 8H, Ar) due to biphenyl, at $\delta = 7.0\text{ppm}$, (m, 4H, Ar) at $\delta = 7.9\text{ppm}$, (m, 4H, Ar) referred to substituted phenyl. The elemental analysis of the molecular formula $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_2$ (calculated / **found**): (C, 79.98 / **80.51**; H, 5.75 / **5.90**; N, 6.66 / **6.88**)

(E)-N₄,N_{4'}-bis(2-bromobenzylidene)biphenyl-4,4'-diamine. (7)

Benzidine (2mmol, 0.368gm) was dissolved in absolute ethanol and added to *o*-bromo benzaldehyde (4mmol, 0.74gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours. Slightly yellow precipitate with m.p. = (185-186) $^\circ\text{C}$, yield = 93 %, FT- IR data showed, weak absorption band at $3053\text{--}2912\text{ cm}^{-1}$ (C-H, aromatic, C-H, aliphatic), 1616 cm^{-1} (C=N), $1487\text{--}1557\text{ cm}^{-1}$ (aromatic C=C), sharp peak at 752 cm^{-1} (C-Br). Elemental analysis of the molecular formula $\text{C}_{26}\text{H}_{18}\text{N}_2\text{Br}_2$ (calculated / **found**): (C, 60.26 / **61.12**; H, 3.50 / **4.21**; N, 5.41 / **5.83**).

(E)-N⁴,N^{4'}- Bis (4-hydroxybenzylidene) biphenyl-4,4'-diamine. (8)

Benzidine (2mmol, 0.368gm) was dissolved in absolute ethanol and added to *p*-hydroxyl benzaldehyde (4mmol, 0.50 gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours, brown color of precipitate were obtained, after filtration and drying the yield = 91 % and the m.p. = (277-278) $^\circ\text{C}$, FT- IR data showed two absorption band at 3289 cm^{-1} (OH, phenol), $3034\text{--}3010\text{ cm}^{-1}$ (C-H, aromatic), at 1607 cm^{-1} due to (C=N), $1512\text{--}1587\text{ cm}^{-1}$ due to (C=C, aromatic), and 1255 cm^{-1} (C-O). On the other hands the $^1\text{H-NMR}$ in DMSO-d_6 showed, at $\delta = 9.75\text{ppm}$ (s, 2H, OH), at $\delta = 8.5\text{ppm}$ referred to (s, 2H, CH=N), at $\delta = 7.5$ and 7.7 ppm (m, 8H, Ar) for biphenyl group, at $\delta = 7.3\text{ppm}$ (m, 4H, Ar) and at $\delta = 8.0\text{ppm}$ (m, 4H, Ar) referred to substituted phenyl. Elemental analysis of the molecular formula $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_2$ (calculated / **found**): C, 79.57 / **79.78**; H, 5.14 / **5.8944**; N, 7.14 / **7.31**)

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

(E)-N⁴,N^{4'}-Bis (3-methoxy-4-hydroxybenzylidene)biphenyl-4,4'-diamine. (9)

Benzidine (2 mmol, 0.368 gm) was dissolved in absolute ethanol and added to vanillin (3-methoxy -4- hydroxyl benzaldehyde) (4 mmol, 0.60 gm) in presence of few drops of glacial acetic acid under refluxing for 3 hours. after workup bright yellow precipitation observed with m.p.=(226 -227) °C and yield = 91% . FT-IR spectra showed the following bands (broad band appear at 3422 cm⁻¹ (OH), 1624 cm⁻¹ (C=N) , 1512-1586 cm⁻¹ (aromatic C=C) , 1284 cm⁻¹ (C-O-C) ,and 1150 cm⁻¹ (C-O). On the other hands the ¹H-NMR in DMSO-d₆ showed , (s, 2H, OH) singlet at δ= 9.8 ppm , at δ = 8.4 ppm referred to (s, 2H, CH=N), at δ= 7.0 ppm (m, 4H, Ar) and 7.4 ppm (m, 2H ,Ar) due to substituted phenyl. at δ=7.3 ppm (m, 4H, Ar) and δ=7.7 ppm (m, 4H, Ar) referred to biphenyl. Elemental analysis of the molecular formula C₂₈H₂₄N₂O₄ (calculated /**found**): C, 74.32 /**74 .51**, H, 5.35 / **5.47**; N, 6.19 /**6.37**).

(E)- N₄,N_{4'}-bis(furan-2-ylmethylene)biphenyl-4,4'-diamine .(10)

Benzidine (2 mmol, 0.368 gm) was dissolved in absolute ethanol and added to furan (4 mmol, 1.36 gm) in presence of few drops of glacial acetic acid under refluxing for more than 3 hours. after workup bright yellow precipitation observed with m.p.=(232-233)°C and yield = 90% . FT- IR spectra showed the following bands at 3110 cm⁻¹ (C-H aromatic) , 1624 cm⁻¹ (C=N) , 1470-1590 cm⁻¹ (C=C aromatic) . On the other hands the ¹H-NMR in DMSO-d₆ showed , at δ = 8.3 ppm referred to (s, 2H, CH=N), at δ= 7.7 ppm and (d, 4H ,Ar) of biphenyl group, at δ=6.6 ppm (m, 2H, Ar), δ=7.0 ppm (m, 2H, Ar) and at δ=7.78 ppm due to furfural group. at δ= 6.6 ppm (m, 4H, Ar) and at δ=7.85 ppm (m, 4H, Ar) referred to biphenyl . Elemental analysis of the molecular formula C₂₂H₁₆N₂O₂ (calculated /**found**): C, 77.63 /**78 .11**, H, 4.74 / **5.13**; N, 8.23 /**8.57**).

General method to synthesis of azetidin-2-one (11-20):

To solution of S-Benzylthioglycolic acid (0.55 g, 3 mmol), imine, (1 mmol) and triethylamine (1 g, 6 mmol, 1.5 ml) in 80 mL dry methylenechloride was added drop wise (30-55 m) under nitrogen atmosphere at 0°C, a solution of phosphorus oxychloride (POCl₃) (0.82 g, 0.48 mL, 3 mmol) in 20 mL of dry methylene chloride with constant stirring[17]. The reactant was stirred overnight at room temperature. The completion of reaction was monitored by TLC. After the completion, the contents were washed successively with 1N HCl (30 ml), water (3x30 ml ,5% NaHCO₃ (30 ml) and brine (30 mL). The organic layer was separated and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by column chromatography using silica gel mesh (60-120)

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-phenylazetidin-2-one). (11)

Using imine (1), (0.36 g, 1 mmol) and followed the general method of synthesis above then , the product was purified by column chromatography using silica gel eluting with (7:3 hexanes /ethyl acetate). After solvent evaporation bright yellow precipitation observed with m.p.=(105-106) °C , yield = 64% . FT-IR-spectra showed absorption bands appeared at the range of 3055 cm⁻¹ and 2922 cm⁻¹ which belong to both (C-H) aromatic and aliphatic

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

respectively. While (C=O) appeared at 1757 cm^{-1} , beside that the (C=C aromatic) appeared at range of $1502\text{--}1585\text{ cm}^{-1}$. On the other hand the data in figure(21) of $^1\text{H-NMR}$ in DMSO-d_6 showed, at $\delta=(7.2\text{--}7.6)\text{ ppm}$ (m, 24H, Ar) of aromatic ring, at $\delta=5.7\text{ ppm}$ (d, 2H, C4-H), at $\delta=4.9\text{ ppm}$ and (d, 2H, C3-H), at $\delta=3.9\text{ ppm}$ and (s, 4H, SCH_2). Elemental analysis of the molecular formula $\text{C}_{44}\text{H}_{36}\text{N}_2\text{O}_2\text{S}_2$ (calculated /found): C, 76.71/77.06; H, 5.27/5.63; N, 4.07/4.41; S, 9.31/9.70.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-(dimethylamino)phenyl)azetidin-2-one).(12)

Using imine (2), (0.447g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (8:2 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.= $(84\text{--}85)^\circ\text{C}$, yield = 54%. FT-IR-spectra showed absorption bands appeared at the range of 3028 and 2920 cm^{-1} which belong to both (C-H) aromatic and C-H aliphatic respectively. While (C=O) appeared at 1747 cm^{-1} , beside that the (C=C aromatic) appeared at range of $1598\text{--}1524\text{ cm}^{-1}$, bands appeared at the range of $1452\text{--}1375\text{ cm}^{-1}$ which belong to both groups (CH_2) (CH_3) respectively. On the other hand the $^1\text{H-NMR}$ in DMSO-d_6 showed, at $\delta=(7.0\text{--}7.6)\text{ ppm}$ (m, 26H, Ar) broad band due to aromatic protons, at $\delta=5.3\text{ ppm}$ (d, 2H, C4-H), at $\delta=4.6\text{ ppm}$ and (d, 2H, C3-H), at $\delta=2.9\text{ ppm}$ (d, 12H, CH_3), at $\delta=3.8\text{ ppm}$ (d, 4H, SCH_2). $^{13}\text{CNMR}$ in CDCl_3 showed, at $\delta=51\text{ ppm}$ and at $\delta=58\text{ ppm}$ due to C_3 & C_4 of azetidin-2-ones ring respectively, at $\delta=40\text{ ppm}$ due to the N- CH_3 and at $\delta=36\text{ ppm}$ due to (S-CH_2), the (C=O) of azetidin-2-ones ring appeared at $\delta=172\text{ ppm}$, the aromatic carbons appeared at range $112\text{--}136\text{ ppm}$. Elemental analysis of the molecular formula $\text{C}_{48}\text{H}_{46}\text{N}_4\text{O}_2\text{S}_2$ (calculated /found): C, 74.39/75.06; H, 5.98/6.33; N, 7.23/7.46; S, 8.27/8.49.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-(diethylamino)phenyl)azetidin-2-one).(13)

Using imine (3), (0.502 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (8:2 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.= $(88\text{--}89)^\circ\text{C}$, yield = 53%. FT-IR-spectra showed absorption bands appeared at the range of 3030 and 2922 cm^{-1} which belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1751 cm^{-1} , beside that the (C=C aromatic) appeared at range of $1525\text{--}1499\text{ cm}^{-1}$ bands appeared at the range of $1454\text{--}1379\text{ cm}^{-1}$ which belong to both groups (CH_2) (CH_3) respectively. Elemental analysis of the molecular formula $\text{C}_{52}\text{H}_{54}\text{N}_4\text{O}_2\text{S}_2$ (calculated /found): C, 75.14/75.56; H, 6.55/6.49; N, 6.74/6.98; S, 7.72/8.22.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-chlorophenyl)azetidin-2-one).(14)

Using imine (4), (0.428 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (7:3 hexanes /ethyl acetate). After solvent evaporation bright yellow precipitation observed with m.p.= $(68\text{--}69)^\circ\text{C}$, yield = 65%. FT-IR spectra showed absorption bands appeared at the range of 3059 and 2922 cm^{-1} which belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1751 cm^{-1} ,

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal, Saadon A. Aowda

beside that the (C=C aromatic) appeared at range of 1600– 1492 cm^{-1} and at 1454 cm^{-1} due to (CH₂). formula C₄₄H₃₄Cl₂N₂O₂S₂ (calculated /found): C, 69.74/70.22; H, 4.52/4.72; N, 3.70/3.90; S, 8.46/8.74.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-bromophenyl)azetidin-2-one).(15)

Using imine (5), (0.518 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (7:3 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.=(111-112) °C, yield = 61%. FT-IR-spectra showed absorption bands appeared at the range of 3052 and 2927 cm^{-1} which belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1748 cm^{-1} , beside that the (C=C aromatic) appeared at range of 1587– 1526 cm^{-1} and at 1456 cm^{-1} due to (CH₂). ¹³CNMR in CDCl₃ showed, at δ =51ppm and at δ =62ppm due to C₃ & C₄ of azetidin-2-ones ring respectively, at δ =36ppm due to (S-CH₂), the (C=O) of azetidin-2-ones ring appeared at δ =169ppm, the aromatic carbons appeared at range 121-133ppm. Elemental analysis of the molecular formula C₄₄H₃₄Br₂N₂O₂S₂ (calculated /found) C, 62.42/62.66; H, 4.05/4.13; N, 3.31/3.57; S, 7.57/7.78.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-methoxyphenyl)azetidin-2-one).(16)

Using imine (6), (0.42 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (8:2 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.=(96-97)°C, yield = 52%. FT-IR-spectra showed absorption bands appeared at the range of 3051 and 2880 cm^{-1} which belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1755 cm^{-1} , beside that the (C=C aromatic) appeared at range of 1518– 1582 cm^{-1} at 1122 cm^{-1} peak due to (C-O) and at 1439 cm^{-1} a peak due to (CH₂). On the other hand the ¹H-NMR in DMSO-d₆, at δ = 7.2-7.6ppm (m, 26H, Ar) of aromatic protons, at δ = 3.9ppm (s, 6H, OCH₃), at δ = 3.4ppm (s, 4H, SCH₂), at δ = 4.3ppm and (d, 2H, C3-H) at δ = 5.2ppm and (d, 2H, C4-H). ¹³CNMR in CDCl₃ showed, at δ =51ppm and at δ =62ppm due to C₃ & C₄ of azetidin-2-ones ring respectively, at δ =36ppm due to (S-CH₂), the (C=O) of azetidin-2-ones ring appeared at δ =169ppm, the aromatic carbons appeared at range 121-133ppm. Elemental analysis of the molecular formula C₄₆H₄₀N₂O₄S₂ (calculated /found): C, 73.31/73.69, H, 5.03/ 5.31; N, 3.89/4.09, S, 8.90/9.08).

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(2-bromophenyl)azetidin-2-one).(17)

Using imine (7), (0.518 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (7:3 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.=(80-81)°C, yield = 51%. FT-IR-spectra in showed absorption bands appeared at the range of 3053 and 2972 cm^{-1} which belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1748 cm^{-1} , beside that the (C=C aromatic) appeared at range of 1584– 1522 cm^{-1} and at 1436 cm^{-1} a peak due to (CH₂). On the other hand the ¹H-NMR in DMSO-d₆ showed, at δ =7.1=7.7ppm (m, 26H, Ar) due to aromatic protons, at δ = 5.2ppm

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal, Saadon A. Aowda

(d,2H, C4-H)ppm, at $\delta = 4.5$ (d,2H, C3-H)ppm and at $\delta = 3.3$ ppm, (s,4H,SCH₂). Elemental analysis of the molecular formula C₄₄H₃₄Br₂N₂O₂S₂ (calculated /**found**): C, 62.42/62.68; H, 4.05/4.17; N, 3.31/3.44; S, 7.57/7.88.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-hydroxyphenyl)azetidin-2-one). (18)

Using imine (8), (0.392 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (8:2 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.=(71-72)^oC, yield = 48%. FT-IR-spectra showed absorption abroad band appeared at 3296cm⁻¹ belong to(O-H), at the range of 3028, 2920cm⁻¹ showed bands belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1749 cm⁻¹ and at 1452 cm⁻¹ a peak due to (CH₂), beside that the (C=C aromatic) appeared at range of 1597– 1495 cm⁻¹. On the other hand the data in figure (5) of ¹H-NMR in DMSO-d₆ showed, at $\delta = 7.1$ -7.6ppm (m,26H,Ar) due to aromatic protons, at $\delta = 5.4$ ppm and (d,2H, C4-H) at $\delta = 4.6$ ppm and (d,2H, C3-H), at $\delta = 9.5$ ppm (s,2H, OH) of phenolic protons, and at $\delta = 3.3$ ppm, (s,4H,SCH₂). ¹³CNMR using DMSO-d₆ in figure(6), showed at $\delta = 49$ ppm and at $\delta = 64$ ppm due to C₃ & C₄ of azetidin-2-ones ring respectively, at $\delta = 36$ ppm due to (S-CH₂), the (C=O) of azetidin-2-ones ring appeared at $\delta = 169$ ppm, the aromatic carbons appeared at range 120-155ppm. Elemental analysis of the molecular formula C₄₄H₃₆N₂O₄S₂ (calculated /**found**): C, 73.31/73.52; H, 5.03/5.24; N, 3.89/3.99; S, 8.90/9.32.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(4-hydroxy-3-methoxyphenyl)azetidin-2-one). (19)

Using imine (9), (0.452 g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (8:2 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with m.p.=(100-101)^oC, yield = 47%. FT-IR-spectra showed absorption abroad band appeared at 3230 cm⁻¹ belong to(O-H), at the range of 3057 and 2924 cm⁻¹ showed bands belong to both (C-H) aromatic and (C-H) aliphatic respectively. While (C=O) appeared at 1746 cm⁻¹, beside that the (C=C aromatic) appeared at range of 1593– 1516 cm⁻¹ and at 1437 cm⁻¹ a peak due to (CH₂). On the other hand the ¹H-NMR in DMSO-d₆ showed, at $\delta = 7.1$ -7.7ppm (m,24H,Ar) due to aromatic protons, at $\delta = 5.3$ ppm (d,2H, C4-H) at $\delta = 4.6$ ppm (d,2H, C3-H), at $\delta = 9.98$ ppm (s,2H, O-H) of phenol, at $\delta = 3.5$ ppm, (s,4H,SCH₂) and at $\delta = 3.9$ ppm, (s,6H,OCH₃). ¹³CNMR in CDCl₃ showed, at $\delta = 50$ ppm and at $\delta = 64$ ppm due to C₃ & C₄ of azetidin-2-ones ring respectively, at $\delta = 36$ ppm due to (S-CH₂), at $\delta = 56$ ppm due to (O-CH₃), the (C=O) of azetidin-2-ones ring appeared at $\delta = 167$ ppm, the aromatic carbons appeared at range 110-135ppm. Elemental analysis of the molecular formula C₄₆H₄₀N₂O₆S₂ (calculated /**found**): C, 70.75/70.89; H, 5.16/5.31; N, 3.59/3.64; S, 8.21/8.55.

1,1'-(biphenyl-4,4'-diyl)bis(3-(benzylthio)-4-(furan-2-yl)azetidin-2-one). (20)

Using imine (10), (0.34g, 1 mmol) and followed the general method of synthesis above then, the product was purified by column chromatography using silica gel eluting with (7:3 hexanes /ethyl acetate). After solvent evaporation bright brown precipitation observed with

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

m.p.=(62-63)^oC , yield = 58% .FT-IR-spectra showed at the range of 3028 and 2924 cm⁻¹ bands belong to both (C-H) aromatic and aliphatic respectively. While (C=O) appeared at 1753cm⁻¹ , beside that the (C=C aromatic) appeared at range of 1608– 1499 cm⁻¹ and at 1454 cm⁻¹ a peak due to (CH₂) . On the other hand the of ¹H-NMR in DMSO-d₆ showed , at δ =7.1-7.5ppm, (m ,24H, Ar) due to aromatic protons, at δ= 5.4ppm, (d,2H, C4-H), at δ= 4.6ppm and (d,2H, C3-H) , at δ= 3.8ppm, (d,4H,SCH₂). ¹³CNMR in CDCl₃ showed, at δ =50ppm and at δ =61ppm due to C₃ & C₄ of azetidin-2-ones ring respectively ,at δ =36ppm due to (S-CH₂) , the (C=O) of azetidin-2-ones ring appeared at δ =171ppm, the aromatic carbons appeared at range 110-143ppm . Elemental analysis of the molecular formula C₄₀H₃₂N₂O₄S₂ (calculated /**found**): C, 71.83/**71.98**; H, 4.82/**5.01**; N, 4.19/**4.27**; S, 9.59/**9. 76**.

Result and Discussion

The mixture of 1 mmol of benzidine and 2 mmol of suitable aromatic aldehyde were heated in presence of approximately 25 ml of absolute ethanol with (2-3) drops of glacial acetic acid in water bath at 70- 80 C for approximately(2-3)hours[18].The process of reaction was followed by TLC ,then filtration or evaporation of the solvent then recrystallized from ethanol .A series of different azetidin-2-one (11-20) were synthesized by the Staudinger ketene-imine [2+2] cycloaddition using phosphors compound[19][20], In this paper work we used POCl₃ as condensation reagent [21][22][23] as shown below Scheme(1) .The FT-IR spectra of the different azetidin-2-one were characterized by the presence of the carbonyl group (C=O) of amide carbonyl at (1755-1674)cm⁻¹ of β-lactam ring and ¹H-NMR of β-lactam (11-20) showed at regions (8.0-7.0) ppm corresponding to to aromatic protons ,at the δ=(4.3-4.9)ppm region referred to (C3-H) and at δ=(5.2-5.7) ppm referred to (C4-H) of β-lactam ring beside peaks at region δ=(3.3-3.9)ppm due to (SCH₂). The disappearance of FT-IR in region (1624-1607) cm⁻¹ due to (C=N) ,and in ¹H-NMR the (CH=N) of imine disappearance in δ=(9.1-8.4)ppm , which confirm the formation of β-lactam ring . The ¹³C-NMR of β-lactams compounds (11-20) ,the δ=(49-54)ppm region appeared carbons due to (C3-H), at δ= (59-65) ppm referred to carbons (C4-H) of β-lactam ring and at region δ=(35-30)ppm due to (SCH₂).

References

- 1- Powers J.C., AsgianJ.L., Ekici O.D. and James K.E, Chem. Rew., (2002), 102, 4639-4750
- 2- Imbach P., Lang M., García-Echeverría C., Guagnano V., Noorani M., Roesel J., Bitsch F., Rihs G.,Furet P.,Bioorganic & Medicinal Chemistry Letters, (2007), 17(2), 358-362
- 3- Alcaide B. and Almendros P.,(2004), 11, 1921-1949
- 4- Desmukh A.R.A.S., bhawal B.M., Krishnaswamy D., Govande V.V., Shinkre B.A., Jayanthi A., Current Medicinal Chemistry,(2004), 11, 1889-1920
- 5- Modugno di E., Erbeti I., Ferrai L., Galasi G., Hammond S. M., Xerri L., Antimicrobial Agents and Chemotherapy, (1994), 38, 10(10), 2362 – 2368
- 6- Hall B. G., Barlow M.,Drug Resistance Updates,(2002), 7(2), 111-123
- 7- Bulytchev A., Belletini J, R., O'Brien M., Crocker P. J., Samama J.P., Miller M. J., Mobashery, Tetrahedron, (2000), 56, 5719 – 5728
- 8- Sader H.S., Gales A.C, Drugs (2001), 61(5), 553-564
- 9-Bassetti M., Righi E., Viscoli C.,Drugs, (2008), 17(3), 285-296

**Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base**

Mustafa Y. Jamal , Saadon A. Aowda

- 10-Bimal K. Banik, Frederick F. Becker and Indrani Banik.,Bioorganic & Medicinal Chemistry., (2004), 12, 2523–2528
- 11-Bimal K. Banik,a, Indrani Banikb and Frederick F. Beckerb.,Bioorganic & Medicinal Chemistry., (2005), 13,3611–3622
- 12-Manisha Nivsarkar, D. Thavaselvam, S. Prasanna, Mamta Sharma and M. P. Kaushik, Bioorganic & Medicinal Chemistry Letters .,(2005), 15,1371–1373
- 13- Staudinger, H. Ann.(1907), 356, 51–123
- 14-Tidwell, T. T. Eur. J. Org. Chem. (2006), 563–568
- 15-Jiao, L.; Zhang, Q. F.; Liang, Y.; Zhang, S. W.; Xu, J. X. J. Org. Chem. (2006), 71, 815–818.
- 16-Arumugam, N.; Raghunathan, R. Tetrahedron Lett. (2006), 47, 8855–8857
- 17- AL-Tamemay ,S. M, Iraqi National Journal of Chemistry,(2011), 44,571-581
- 18- Brian S., Antony J., Peter W., Austin R., "Vogel's " 5th ed. Johan and Wiley ,Inc. New York , (1989).
- 19- Krishnaswamy D., Govanda, V.V., Gumaste,V.K., Bhawal, B.M. and Deshmukh, A.R.S., (2002) ,58 ,22215-22225.
- 20- Alcaide B., Almendros P., Vicentea A. R.and M. Pilar Ruiz, Tetrahedron(2005), 61, 2767–2778.
- 21- Bhalla A., Madan S., Venugopalany P. and Shamsher S. B.,Tetrahedron (2006),62,5054–5063.
- 22- Bhalla A., Madan S., Venugopalany P. and Shamsher S. B.,Tetrahedron, Tetrahedron., (2006),62,8291–8302
- 23-S. S. Bari a, Aman Bhalla a, Reshma, Geeta Hundal, Tetrahedron Letters., (2013),54, 483–486.

Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base
Mustafa Y. Jamal , Saadon A. Aowda

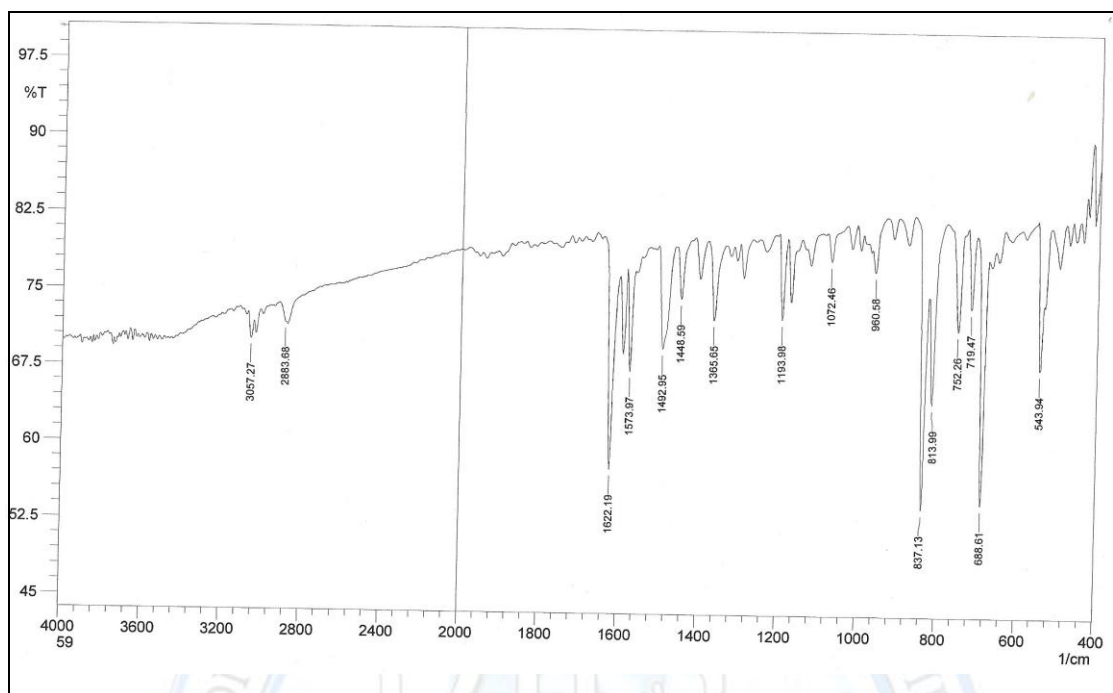


Figure (3): FT-IR spectra of (E)-N⁴,N^{4'}-dibenzylidenebiphenyl-4,4'-diamine.(1)

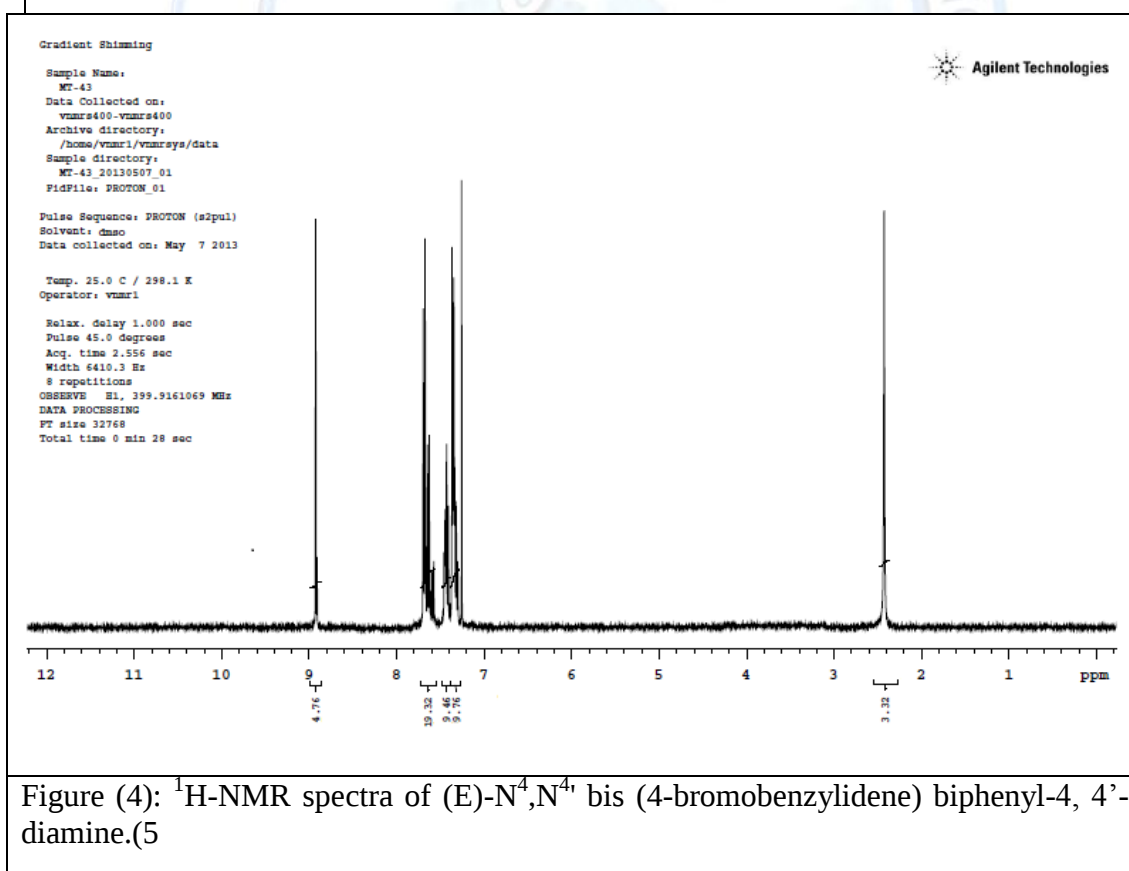


Figure (4): ¹H-NMR spectra of (E)-N⁴,N^{4'} bis (4-bromobenzylidene) biphenyl-4, 4'-diamine.(5)

Synthesis and spectroscopic studies of some Azetidin-2-one derivatives
from Benzidine and S-Benzylthioglycolic acid via Schiff base
Mustafa Y. Jamal , Saadon A. Aowda

