ONE-POT SYNTHESIS AND ANTIMICROBIAL SCREENING OF NEW [1,5] –BENZODIAZEPINE DERIVATIVES CATALYZED BY TBAB

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ABSTRACT:

A new [1,5]-benzodiazepines **(VI)** were synthesized by the reaction of *o*-phenylenediamine with 2-chloro-3-acetylquinoline in the presence of tetrabutyl ammonium bromide (TBAB) in short reaction time with excellent yield.

Keywords: tetrabutyl ammonium bromide ,[1,5]- Benzodiazepine,2-chloro-3-acetylquinoline derivatives, *o*-phenelendiamine .

INTRODUCTION

Benzodiazepines are one of the most important class that have various therapeutic applications. Many members of the benzodiazepine family have a wide range of biological activity as anticonvulsants, anti-anxiety, analgesic, sedative, anti-depressant, hypnotic **(Randall, 1974)** anti-inflammatory **(Roma, *et al.,* 1991)**, anti-viral **(Kavali and Badami, 2000)**, anti-HIV **(Di Braccio, *et al.,* 2001)**, antimicrobial, **(Kumar and Joshi, 2007)** and anti-tumor **(Kamala, *et al.,* 2008)** ctivities. Accordingly 1, 5-Benzodiazepine and its derivatives attract our attention to synthesize new members depending on wide range of pharmacological activity and industrial applications, the development of mild and efficient protocols for their preparation continues to be a challenging endeavor in the synthetic organic chemistry **(Herbert, *et al.,* 1974)**. The common procedure for the synthesis of these compounds is a one pot condensation between *o*-phenelendiamine and newly synthesized carbonyl compounds . However, from the modified literature survey a variety of catalysts such as BF_3O, $NaBH_4$, $PPA-SiO_2$, $MgO-POCl_3$, $Yb(OTf)_3$, amberlyst-15, $Ag_3PW12O40$, solid super acid sulphated zirconia, acetic acid – under MWI, AgNO3, zinc montmorilonite as catalyst at room temperature were used. These reactions also occur with various catalysts under solvent free conditions **(Chen and Lu, 2005; Kumar, *et al.,* 2006; Li, *et al.,* 2007; An, *et al.,* 2008; Mohamed and Asgar, 2012; Heravi, *et al.,* 1985).** Indeed these methodologies have several disadvantages such as harsh reaction condition, long reaction time, a large amount of catalysts, expensive reagents, unsatisfactory product yields, critical product isolation procedures, tedious workup and formation of side products. Keeping in mind in the present study we have developed one pot synthesis of [1,5]-benzodiazepines by condensation of *o*-phenelendiamine with ketones catalyzed by tetrabutylammonium bromide (Scheme 1).

R = H , CH$_3$, OCH$_3$,NO$_2$, Br

VIa ; R = H
VIb ; R = CH$_3$
VIc ; R = OCH$_3$
VId ; R = NO$_2$
VIe ; R = Br
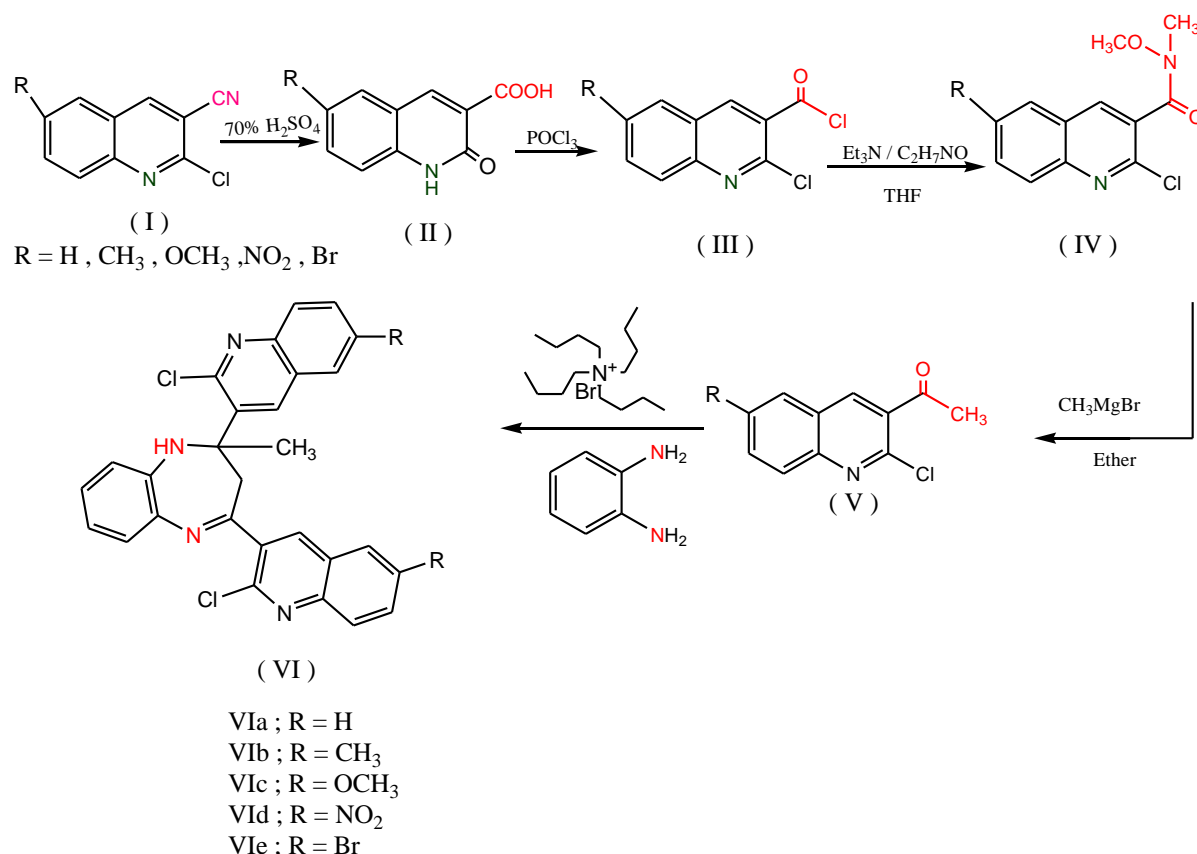
(Scheme1)

3. EXPERIMENTAL

3.1. General

Melting points were measured in capillary tube on a Graffin melting point apparatus and are uncorrected. The IR spectra were recorded on Pye Unicam SP 1000 IR spectrophotometer using KBr discs (λmax in cm^{-1}). ^{1}HNMR spectra were performed either on a Jeol ECA (500 MHz) or Gemini 300BB (300MHz) spectrometer, using TMS as internal standard and DMSO-*d6* as solvent; the chemical shifts are reported in ppm (δ) and coupling constant (J) values are given in Hertz (Hz). Signal multiplicities are represented by s (singlet), d (doublet), t (triplet), q (quadruplet), and m (multiplet). All of the new compounds were analyzed for C, H and N and agreed with the proposed structures within ±0.4% of the theoretical values by the automated CHN analyzer at the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Cairo, Egypt. Mass spectra were recorded on Hewlett Packard 5988 spectrometer at the RCMB. The purity of the compounds was checked by thin layer chromatography (TLC) on Merck silica gel 60 F254 precoated sheets.The starting Compounds(I-III) were prepared according to reported method (**Wright, 1985; Neelima, *et al.,* 1986; Cyrous, *et al.,* 2006; Monir, *et al.,* 2004; Hang and Browne, 2010**).

3.1.1 Chemistry

The synthesis of the target compounds was achieved following the routes depicted in Scheme 1. Hydrolysis of (**I**) with H$_2$SO$_4$ (70%) in ethanol gave 6-substituted 2-oxo1,2-dihydroquinoline-3-carboxylic acids (**II**) in good yields, which when heated in boiling phosphoryl chloride it gave 6-substituted 2-chloroquinoline-3-carbonyl chloride (**III**) , which

recrystallized from ethanol. Subsequently, **(III)** were reacted with *N,O*-dimethyl hydroxylamine in the presence of triethylamine (1.58g) and THF, to give 2-chloro-N-methoxy-N-methylquinoline-3-carboxamide derivatives **(IV)** that dried and crystallized from ethanol . This on further reaction with Grignard reagent (methyl magnesium bromide) in ammonium chloride and ether at room temperature gave 2-chloro-3-acetylquinoline derivatives **(V)** the structure of compounds **(V)** was confirmed on the basis of analytical and spectral data. The started compound **(I-III)** were synthesized according to reported procedures **(Wright, 1985; Neelima,** *et al.,* **Cyrous,** *et al.,* **2006; Monir,** *et al.,***2004; Hang,** *et al.,* **2010).**

General procedure for the synthesis of 6- substituted-2-Chloro-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVa-e)

To a solution of **(III)** in dry THF (10 mL), a solution of *N,O*-dimethyl hydroxylamine in THF (prepared from 2.2 mmol of *N,O*-dimethyl hydroxylamine hydrochloride, and 2.2 mmol of triethylamine in 5 mL of dry THF was added at 20 ^{o}C over 5min. The reaction mixture was stirred at r.t. for 24 h. The solvent was removed in vacuo and the residue was dissolved in EtOAc. The organic layer was washed sequentially with saturated citric acid, satd. Na_2CO_3, H_2O, and dried over $MgSO_4$. Evaporation in vacuo to dryness gave the desired products **(IVa-e)**, which were recrystallized from the appropriate solvent.

2-Chloro-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVa)

Yield 70 %, m.p. 205-206 ^{o}C. IR (KBr) cm^{-1}, 2980, 2830, 1640. Anal. Calc. For $C_{12}H_{11}ClN_2O_2$: C, 57.49; H, 4.42; N, 11.17 . Found C, 57.12; H, 4.66; N, 11.09

2-Chloro-6-methyl-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVb)

Yield 80 %, m.p. 221-222 ^{o}C. IR (KBr, cm^{-1}): 2975, 2825, 1630, ^{1}HNMR (CDCl$_3$), δ 2.30 (s, 3H, N-Me); 2.52 (s, 3H, 6-Me); 3.1 (s, 3H, O-CH$_3$), 7.30 (s, 1H, H$_5$-quinoline), 7.80-7.82 (d, 1H, H$_7$-quinoline), 7.95-7.98(d, 1H, H$_8$-quinoline), 8.20 (s, 1H, H$_4$-quinoline), . Mass: *m/z* 264.68 (45.12, M+) , 249 (35, M-CH$_3$) , 234(100,M-C$_2$H$_6$), 218(62.1M-C$_2$H$_6$O) 176 (52,M-C$_3$H$_6$NO$_2$), 161 (23.9, M-C$_4$H$_9$NO$_2$). . Anal. Calc. For $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58. Found C, 58.76; H, 4.51; N, 11.00

2-Chloro-6-methoxy-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVc).

Yield 65 %, m.p. 235-236 ^{o}C. IR (KBr, cm^{-1}): 2980, 2830, 1635. ^{1}HNMR (CDCl$_3$) δ 2.20 (s, 3H, , N-Me); 2.40 (s, 3H, 6-OMe); 3.22 (s, 3H, O-CH$_3$), 7.38 (s, 1H, H$_5$-quinoline), 7.88-7.90 (d, 1H, H$_7$-quinoline), 8.14-8.16(d, 1H, H$_8$-quinoline), 8.36 (s, 1H, H$_4$-quinoline),. Mass: *m/z* 280.71 (40.3,M+) , 265 (25,M-CH$_3$) , 250(100,M-C$_2$H$_6$),234(55.80M-C$_2$H$_6$O) 220(44.2,M-C$_2$H$_6$NO), 192 (25.9, M-C$_3$H$_6$NO$_2$),161(15.2M-C$_4$H$_9$NO$_3$). Anal. Calc. For $C_{13}H_{13}ClN_2O_3$: C, 55.62; H, 4.67; N, 9.98. Found C, 55.35; H, 4.83; N, 10.12

i2-Chloro-6-nitro-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVd).

Yield 40 %, m.p. 259-260 ^{o}C. IR (KBr, cm^{-1}): 2976, 2830, 1632. Mass: *m/z* 295.68 (33.50, M+). Anal. Calc. For $C_{12}H_{10}ClN_3O_4$: C, 48.74; H, 3.41; N, 14.21. Found. C, 49.02; H, 3.26; N, 14.45.

2-Chloro-6-bromo-*N*-methoxy-*N*-methylquinoline-3-carboxamide (IVe).

Yield 55 %, m.p. 243-244 ^{o}C. IR (KBr, cm^{-1}): 2982, 2835, 1633. ^{1}HNM R (CDCl$_3$), δ 2.35 (s, 3H, N-Me); 2.60 (s, 3H, N- O-CH$_3$), 7.25-7.27 (d, 1H, H$_8$-quinoline), 8.60 (s, 1H, H$_4$-quinoline), 7.40-7.42 (d, 1H, H$_7$-quinoline), 7.55 (d, 1H, H$_5$-quinoline),. Mass: *m/z* 329.70 (12., M+) , 331.02 (3.9., M+2) 314 (5,M-CH$_3$) , 299(7, M-C$_2$H$_6$),283(16.81, M-C$_2$H$_6$O) 269(18, M-C$_2$H$_6$NO), 190(23.9, M-C$_3$H$_6$BrNO$_2$). Anal. Calc. For C$_{12}$H$_{10}$Br ClN$_2$O$_2$: C, 43.73; H, 3.06; N, 8.50. Found C, 44.05; H, 3.32; N, 8.17

General procedure for the synthesis of 1-(2-chloro-6-substituted-quinolin-3-yl)ethanone (Va-e)

In a typical flask experiment's 0.02 mol of Grignard reagent was added at once to stirred solution of (IV) in 100 cc of dry ether that previously cooled by ice / acetone mixture ,the added Grignard reagent were cooled also previously . After stirring for 2-3h the cool bath was removed and the mixture treated with ammonium chloride solution to get the crud product of compounds **(Va-e)** at room temperature.

1-(2-chloroquinolin-3-yl)ethanone (Va)

Yield 75 %, m.p. 173-174 ^{o}C. IR (KBr, cm^{-1}): 2985,2834, 1690 .^{1}HNMR (CDCl$_3$), δ 1.90 (s, 3H, CH$_3$), 7.30-7.32 (d, 1H, H$_5$-quinoline),7.40-7.42 (t, 1H, H$_6$-quinoline), 7.65-7.68(t, 1H, H$_7$-quinoline), 7.90-7-92(t, 1H, H$_8$-quinoline), 8.36 (s, 1H, H$_4$-quinoline),. Anal. Calc. For C$_{11}$H$_8$ ClNO: C, 64.25; H, 3.92; N, 6.81. Found. C, 64.11; H, 4.18; N, 6.59

1- (2-chloro-6-methylquinolin-3-yl)ethanone (Vb)

Yield 85 %, m.p. 189-190 ^{o}C. ^{1}HNMR (CDCl$_3$), δ 1.88 (s, 3H, CH$_3$), 2.55 (s,3H, CH$_3$-quinoline),   7.32-7.34 (s, 1H, H$_5$-quinoline), 7.70-7.72(d, 1H, H$_7$-quinoline), 7.90-7-92(d, 1H, H$_8$-quinoline), 8.20 (s, 1H, H$_4$-quinoline), . Anal. Calc. For C$_{12}$H$_{10}$ ClNO: C, 65.61; H, 4.59; N, 6.38 .Found C, 65.55; H, 4.57; N, 6.70.

1- (2-chloro-6-methoxyquinolin-3-yl)ethanone (Vc)

Yield 72 %, m.p. 206-207 ^{o}C. ^{1}HNMR (CDCl$_3$), δ 1.85 (s, 3H, CH$_3$), 2.59(s,3H, OCH$_3$-quinoline), 7.37 (s, 1H, H$_5$-quinoline), 7.71-7.73(d, 1H, H$_7$-quinoline), 7.90-7-92(d, 1H, H$_8$-quinoline), 8.26 (s, 1H, H$_4$-quinoline),. Anal. Calc. For C$_{12}$H$_{10}$ ClNO$_2$: C, 61.16; H, 4.28; N, 5.94 . Found C, 61.43; H, 4.55; N, 5.90.

1- (2-chloro-6-nitroquinolin-3-yl)ethanone (Vd)

Yield 42 %, m.p. 214-215 ^{o}C. (KBr, cm^{-1}): 3090, 2870, 1695. ^{1}HNMR (CDCl$_3$), δ 1.85 (s, 3H, CH$_3$), 7.60-7.62(d, 1H, H$_8$-quinoline). 7.80-7.82 (d, 1H, H$_7$-quinoline), 7.95 (s, 1H, H$_5$-quinoline), 8.35 (s, 1H, H$_4$-quinoline),. Anal. Calc. For C$_{11}$H$_7$ ClN$_2$O$_3$: C, 52.71; H, 2.82; N, 11.18. Found C, 53.07; H, 3.14; N, 11.02.

1- (2-chloro-6-bromoquinolin-3-yl)ethanone (Ve)

Yield 49 %, m.p. 195-196 ^{o}C. Mass: *m/z* 284.54 (19, M+) . Anal. Calc. For C$_{11}$H$_7$ Br ClNO: C, 46.43; H, 2.48; N, 4.92. Found C, 46.19; H, 2.76; N, 4.98 .

General procedure for the synthesis of substituted 2,4-bis(2-chloro-quinolin-3-yl) -2,3 - dihydro-1*H*-benzo[b][1,5]- diazepine (VIa-e)

A mixture of *o*-phenylenediamine (10 mmole), and (**Va-e**) (0.01mole) and phase transfer catalyst tetrabutylammonium bromide (catalytic amount) was heated under reflux for 50 min in ethyl alcohol (10 mL) at 60 ^{o}C with stirring ,after completion of reaction (monitored by TLC) the reaction mixture was cooled and poured on crushed ice, extracted from ethyl acetate (30 mL) and washed with water and brine (20 mL each). The solvent was removed by distillation under reduced pressure. The crude product was purified by column chromatography (eluent, ethyl acetate – pet-ether).The corresponding new 1, 5 – benzodiazepines derivatives were obtained in 80-95% yield.

2,4-bis(2-chloroquinolin-3-yl) -2-methyl -2,3 -dihydro-1*H*-benzo[b][1,5]- diazepine (VIa)

Yield 85 %, m.p. 142-143 ^{o}C. (KBr, cm^{-1}): 3335, 3105, 2959, 2861. Anal. Calc. For $C_{28}H_{20}Cl_2N_4$: C, 69.57; H, 4.17; N, 11.59. Found. C, 69.20; H, 4.36; N, 11.63 .

2,4-bis(2-chloro-6-methylquinolin-3-yl) -2-methyl -2,3 -dihydro-1*H*-benzo[b][1,5]-diazepine (VIb)

Yield 95 %, m.p. 138-139 ^{o}C. (KBr, cm^{-1}): 3330, 3097, 2843. ^{1}HNMR (DMSO, D_2O), δ: 1.1(s,3H, CH_3 at C2), 1.84 (s, 2H –H_3 -diazepine), 2.39(s, 6H-2(CH_3)), 4.17 (s, 1H, NH of BDP that exchangeable with D_2O). 6.17-6.20(t, 2H, -H_4,H_5 of phenyl), 6.25-6.27(d, 2H, -H_3, H_6 of phenyl), 7.13(s, 2H, H_5 of quinoline), 7.20-7.24(d, 2H, H_7-quinolin), 7.26-7.28(d, 2H, H_8 of quinoline), 8.12(s, 2H-H_4 of quinoline), Anal. Calc. For $C_{30}H_{24}Cl_2N_4$: C, 70.45; H, 4.73; N, 11.95. Found, C, 70.80; H, 4.50; N, 11.59 .

2,4-bis(2-chloro-6-methoxyquinolin-3-yl) -2-methyl -2,3 -dihydro-1*H*-benzo[b][1,5]-diazepine (VIc)

Yield 92 %, m.p. 121-122 ^{o}C. IR (KBr, cm^{-1}): 3340, 3118, 2830. ^{1}HNMR (DMSO, D_2O), δ: 1.2(s,3H, CH_3), 1.88 (s, 2H –H_3 -diazepine), 3.39(s, 6H-2(O-CH_3)), 4.25 (s, 1H, NH of BDP that exchangeable with D_2O) 6.21-6.25(t, 2H, -H_4,H_5 of phenyl), 6.29-6.32(d, 2H, -H_3, H_6 of phenyl), 6.9(s, 2H, H_5 of quinoline), 7.32-7.34(d, 2H, H_7-quinolin)7.46-7.48(d, 2H, H_8 of quinoline), 8.02(s, 2H-H_4 of quinoline) . Mass: m/z 543.44 (15.6,M$^+$) .Anal. Calc. For $C_{30}H_{24}Cl_2N_4O_2$: C, 66.30; H, 4.45; N, 10.31. Found. C, 66.03; H, 4.48; N, 10.15 .

2,4-bis(2-chloro-6-nitroquinolin-3-yl) -2-methyl -2,3 -dihydro-1*H*-benzo[b][1,5]-diazepine (VId)

Yield 92 %, m.p. 150-152 ^{o}C. IR (KBr, cm^{-1}): 3395 , 3125, 2842. ^{1}HNMR (DMSO, D_2O), δ: 1.11(s,3H, CH_3 at C2-diazepine), 1.88 (s, 2H –H_3 -diazepine), 4.19 (s, 1H, NH , that exchangeable with D_2O) 6.21-6.23(t, 2H, H_4, H_5 of phenyl), 6.33-6.35(d, 2H , H_3, H_6 of phenyl), 7.37-7.39(d, 2H, H_8-quinolin), 8.10(s, 2H, H_4 of quinoline), 8.48-8.50(d, 2H, H_7 of quinoline), 8.63 (s, 2H, H_5 of quinoline) . Mass: m/z 573.39 (11.5, M$^+$), Anal. Calc. For $C_{28}H_{18}Cl_2N_6O_4$: C, 58.65; H, 3.16; N, 14.66. Found, C, 58.77; H, 3.47; N, 14.91 .

2,4-bis(2-chloro-6-bromoquinolin-3-yl) -2-methyl -2,3 -dihydro-1H-benzo[b][1,5]-diazepine (VIe)

Yield 92 %, m.p. 150-152 ^{o}C. IR (KBr, cm^{-1}): 3435 , 3092, 2810, . Mass: m/z 641.18 (9.14, M^{+}), 643(4.5, M^{+2}) . Anal. Calc. For C$_{28}$H$_{18}$ Br$_2$Cl$_2$N$_4$: C, 52.45; H, 2.83; N, 8.74. Found, C, 52.23; H, 2.65; N, 8.80 .

RESULT AND DISCUSSION

Tetrabutylammonium bromide is a cheap and readily available reagent it efficiently catalyze the condensation of ketones with *o*-phenelendiamine at 60 ^{o}C under mild conditions in short reaction time (50 min) with excellent yield of the product. In our work a series of [1,5]- Benzodiazepine derivatives were prepared from starting intermediate 2-oxo-1,2-dihydroquinoline-3-carboxylic acid derivatives which prepared according to the reported procedure[14-18].The structures of compound (II) were confirmed by ^{1}HNMR,^{13}C-NMR, In the ^{1}H-NMR spectra, where two sharp proton signal observed at the δ 5.4 and 11.68 ppm, one belong OH at C-2 and one belong COOH respectively, and due to resonance isomerism the NH(secondry amine) it appear at higher chemical shift at 8.9 as abroad signal more than expected due to neighboring carbonyl group, In the ^{13}C-NMR spectra of these compounds one C=O peak at about 178 ppm and one around 166 ppm corresponded to the signals of the 3-carboxylic acid and carbonyl groups in the quinoline rings. On contrary the IR spectra of compound (III) showed the disappearance of OH streatching band and this explaine the conversion of acid into acid chloride and the mass spectra of compound (III) confirm the conversion of carbonyl at C-2 into chloride moiety , so when the compound (III) react *N,O*-dimethyl hydroxylamine it produce the compound (IV) which IR spectra confirm the presence of these compound because it showed clearly decreasing of stretching absorption band of C=O from 1812 cm^{-1} and appearance of sharp medium stretching absorption bands at range of 1636 cm^{-1} which belong to (C=O) for amide, when compound (IV) react with alkyl Grignard reagent it produce compound (V), which upon cyclocondensation with *o*-phenelendiamine it afford new 1,5-benzodiazepine derivatives (VI), where the elemental analysis and spectral data confirm the existence of this cyclocondensation in which the ^{1}HNMR of new 1,5-benzodiazepines contain singlet signal due to CH$_3$ at C-2, in addition the presence of NH singlet signal at 4.17- 4.25, furthermore the presence of singlet signal due to the two hydrogen at C-3 of benzodiazepine ring and all this fact will prove this cyclocondensation reaction and formation of 1,5-benzodiazepine ring .

Antimicrobial activity:

The newly synthesized of [1,5]-benzodiazepine compounds were screened for their *in-vitro* antibacterial activity against Staphylococcus aureus , Bacillus subtilius , Pseudomonas aeruginosa , Escherichia coli   and candida albicans bacterial stains by serial plate dilution method **(Barry, 1991),** Serial dilutions of the drug in Muller Hinton broth were taken in tubes and their pH was adjusted to 5.0 using phosphate buffer. A standardized suspension of the test bacterium was inoculated for 16 to 18 hours at 37^{0}C. The minimum inhibitory concentration (MIC) was noted by observing the lowest concentration of the drug at which there was no visible growth. Numbers of antibacterial discs were placed on the agar for the sole purpose of producing zones of inhibition in the bacterial lawn. Twenty milliliters of agar media was poured into each petri dish. Excess of suspension was decanted and plates were dried by placing in an incubator at 37 ^{0}C for an hour. Using a punch, wells were made on these seeds agar plates and minimum inhibitory concentrations of the test compounds in

dimethyl sulfoxide were added into each labeled well. A control was also prepared for the plates in the same way using DMSO as a solvent. The petri dishes were prepared in triplicate and maintained at 37 0C for 3 to 4 days. Antibacterial activity was determined by measuring the diameter of inhibition zone. Activity of each compound was compared with ampicillin and Nystatin as standard. All the synthesized compounds were taken at different concentration of 500 and 600 μg/ml .The result was compared with the ampicillin (500 μg/ml)and Nystatin (500 μg/ml)as in the (Table 1).

Table 1: Antimicrobial activity of synthesized 1,5-Benzodiazepines (VIa – e)

COMP. NO.	CONCENT-RATION (MG/ML)	MICROORGANISM (INHIBITION ZONE(MM))				
		Staphylococcus aureus	Basillus subtilis	Escherichia coli	Pseudomonas aeruginosa	Candida albicans
VIa	500	16.2	18.2	16.3	15.2	15.3
	600	17.6	19.5	17.3	16.5	15.4
VIb	500	17.1	15.8	16.3	15.3	-
	600	17.9	16.3	16.9	16.2	-
Vic	500	15.4	17.3	17.3	17.4	14.1
	600	16.8	18.9	18.8	18.3	15.5
Vid	500	18.3	15.7	16.6	16.6	15.7
	600	20.1	16.7	17.8	16.9	16.8
Vie	500	19.7	16.6	16.5	16.5	16
	600	21.3	17.3	17.7	17.1	17.3
Ampicillin	500	22.0	20.3	23.0	19.1	-
Nystatine	500	-	-	-	-	18.5

From screening results of the final compounds, It showed moderate antimicrobial activity. The discussion and comparison of antibacterial activity were given with respect to ampicillin antibiotic and antifungal screening were compared with Nystatin.Microbiological testing of the newly synthesized compounds were performing in the regional center for Mycology and Biotechnology, Department of microbiology , Faculty of science , Al-Azher university , Cairo , Egypt .

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تشييد فى وعاء واحد وفحص مضادات الميكروبات لمشتقات ١,٥ ـبينزودايزبين الجديدة محفزا بتترابيوتيل امونيم بروميد

كمال محمد الجمل

قسم الكيمياء العضوية كلية الصيدلة (بنين) ـ جامعة الأزهر بالقاهرة

تم تفاعل ٢ـكلوروكينولين ـ٣ـكربونيتريل الذى أعطى ٢ـاوكسوكينولين ـ٣ـكربوكسيليك أسيد والذى تم تحويله الى مشتق الأسيد كلوريد والذى بتفاعله مع ان ــ أوـهيدروكسيل أمين أعطى المشتقات والتى بتفاعلها مع عامل جرينيارد فانه يعطى المشتقات الجديدة من ٢ـكلورو كينولين-٣- ايثانون والذى بتكاثفه مع الأورثوفينيلين داى أمين فى وجود التيترابيوتيل أمونيم بروميد فانه فى وقت قصير يعطى مشتقات جديدة تحتوى على نواة ٥,١ـبينزودايزبين وقد تم أختبار المركبات الجديدة بيولوجيا كمضـادات للبكتريا و الفطريات حيث أظهرت بعض المركبات فاعلية مضادة لهذه الميكروبات

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