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FACILE SYNTHESIS OF *IN-VIVO* INSECTICIDAL AND ANTIMICROBIAL EVALUATION OF BIS HETEROCYCLIC MOIETY FROM PET WASTE

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ABSTRACT

Recycling of Plastic Solid Waste (PSW) using green tool such as solar energy which used for degradation of plastic solid bottles (PET) to afford terepthalic acid which estrified using butanol/H_2SO_4 to afford dibutyl terephthalate as a starting material which has been chemically modified to yield new bis (1,2,4-triazole-3-thiol) 5, 1,3,4-oxadiazole 6, 8, 15, 1,3-thiazolidine 9, 1 *H*-pyrazole 10, 11 and 13 derivatives. Interestingly all the synthesized compounds exhibited good *in-vivo* insecticidal activity against the *Cluex pipiens* and *musca domestica* and also they were assayed to have high antimicrobial activity.

Keywords: Poly Ethylene Terephthalate (PET), Heterocyclic, Insecticidal and Antimicrobial

1. INTRODUCTION

1,2,4-Triazoles are associated with diverse pharmacological screening for analgesic, antiasthmatic, diuretic, antihypertensive, anticholinergic, antibacterial, antifungal and anti-inflammatory activities (Abu-Zaied *et al*., 2011; Kumar *et al*., 2013; Yakout *et al*., 1999). It was also reported that a large number of compounds containing triazole ring possess a moderate antiviral drug (EI-Fattah, 1998). Moreover, it was found that the pyrazole-4-carboxylic acid hydrazides and its hydrazones have antimicrobial activity (Ragavan *et al*., 2010). 1,3,4-Oxadiazoles and pyrazole-4-carboxylic acid hydrazides are known to have a broad spectrum of biological applications (Soural *et al*., 2006; Al-Salem *et al*., 2009; Chenot, 2007; Kawamura *et al*., 2002). Furthermore, 1,2,4-triazoles, 1,3,4-oxadiazoles and pyrazoles were found to be an effective insecticides toward houseflies, faceflies and hornflies (Wojciechowski and Wyrębak, 2003; Zhuang *et al*., 2006; Jun *et al*., 2011). Because of our interest in the synthesis of new heterocycles of biological interest, (Fahim *et al*., 2013; Abd El Salam *et al*., 2013) we have decided to synthesize the title compounds from plastic waste for evaluation of their antimicrobial and insecticidal activities.

2. MATERIALS AND METHODS

2.1. Chemical Protocols

All melting points were measured on a Gallenkamp melting point apparatus and uncorrected. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP-3-300 and Shimadzu FT IR 8101 PC infrared spectrophotometers. The NMR spectra were recorded on a Varian Mercury VX-500 NMR spectrometer. ^{1}HNMR spectra were run at 500 MHz and ^{13}CNMR spectra were run at 75.46 MHz in Dimethyl Sulphoxide (DMSO-d_6). Chemical shifts were related that of the solvents. Mass spectra were recorded on a Shimadzu GCMS-QP-1000EX mass spectrometer at 70 e.v.

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2.2. Prepartion of Terephthalic Dihydrazide (3) *Via* Hydrolysis of Polyethylene Terepthalate (PET)

Plastic bottles (22 g) were cut into a small strips and mixed with 50% NaOH solution placed in sun light for 5 weeks to obtain the sodium salt of terephthalte and then dissolved in water then acidify by (5 mol L^{-1}) H_2SO_4 to afford white precipitate of terephthalic acid (1), yield 90%; m.p. above 300°C. Then, terephthalic acid (10 g, 1.66 moL) was refluxed in absolute butanol (30 mL) and H_2SO_4 (5 mL) for 6h to get dibutyl terephthalate (2). A mixture of 2 (10 mL) and hydrazine hydrate (6.0 mL, 99%) in 50 mL of absolute ethanol was refluxed for 5 h. The reaction mixture was left to cool and the separated solid was filtered off and recrystallized from EtOH/DMF to give terephthalic dihydrazide (3) (Palekar *et al*., 2009).

2.3. Synthesis of 1,4 Di-Benzoyl-*N*-Phenyl Hydrazine Carbothioamide (4)

A mixture of terephthalic dihydrazide 3 (5 mmoL) was refluxed with phenyl isothiocyanate (10 mmoL) in dry benzene (25 mL) for 5 h. After the solution has been cooled, the solid was filtered-off and recrystallized from EtOH to afford 4, yield 90%, mp: 209°C; IR (KBr) ν_{max}/cm^{-1}: 3619, 3450 (NH), 1650 (C = O); ^{1}H NMR (DMSO-d_6): δ 4.3 (d, 2H, NH D_2O exchangable), 6.81-8.21(m, 14H, Ars H), 10.75(d, 2H, NH D_2O exchangable), 12.52(s, 2H, NH D_2O exchangable); MS (*m/z*): 464.1 (M^+, 100.0%), 465.11 (27.7%); Anal calcd: $C_{22}H_{20}N_6O_2S_2$ (464.56); C, 56.88; H, 4.34; N, 18.09; S, 13.80%; Found: C, 56.90; H, 4.39; N, 18.12; S, 13.88%.

2.4. Synthesis of 5,5'-(1,4-Phenylene) Bis (4-Phenyl-4*H*-1,2,4-Triazole-3-Thiol) (5)

Compound 4 (1 mmoL) was refluxed with 20% KOH solution (5 mL) for 4 h. The reaction mixture was filtered off on hot and kept overnight, then the solid formed was collected, washed with water and finally recrystallized from ethanol to afford product 5, yield 75% mp: 298°C; IR (KBr) ν_{max}/cm^{-1}: 2908 (CH), 2793, 2742 (SH); ^{1}H NMR (DMSO-d_6): δ 4.4 (s, 2H, 2 SH), 7.05-7.4 (m, 14 H, Ars H); ^{13}C NMR (DMSO-*d6*): 125(4 CH), 128 (4 CH), 134.3 (2 CH), 143.3(2 CH), 156 (2 CH), 169 (2 CH); MS (*m/z*): 428, (M^+, 100.0%), 147 (22.6%); Anal calcd: $C_{22}H_{16}N_6S_2$ (428.09); C, 61.66; H, 3.76; N, 19.61; S, 14.97%; Found: C, 61.70; H, 3.80; N, 19.69; S, 15.02%.

2.5. Synthesis of 5,5'-(1,4-Phenylene) Bis ((*N*-Phenyl-1,3,4-Oxadiazol-2-Amine) (6)

To a mixture of bisthiosemicarbazide 4 with with potassium iodide and iodine in DMF (20 mL), was added and the reaction mixture was heated under reflux for 8 h, then left to cool and pour into crushed ice. The solid that separated was collected by filtration, washed with ethanol and finally recrystallized from EtOH/DMF to obtain 6; yield 75% mp: 233°C; IR (KBr) ν_{max}/cm^{-1}: 3411 (NH), 2926 (CH); ^{1}H NMR (DMSO-d_6): δ 6.82-7.97 (m, 14H, ArsH), 10.52 (s, 2H, 2 NH D_2O exchangable); ^{13}C NMR (DMSO-*d6*): 117 (4 CH), 125 (2 CH), 129(2 CH), 138 (4 CH), 164 (4 CH), 169 (2 CH); MS (*m/z*): 369 (M^+, 10.6%), 267 (6.2%) 102 (100.0%); Anal calcd: $C_{22}H_{16}N_6O_2$ (369.13); C, 66.66; H, 4.07; N, 21.20%; Found: C, 66.69; H, 4.12; N, 21.25%.

2.6. Synthesis of Bis-Pottasiumdithio Carbazinate (7)

Terephthalic hydrazide (3) (1 mmoL) in ethanol (10 mL) was added with stirring to Potassium hydroxide (3 mmol) ethanolic solution in an ice bath. Then, carbon disulfide (2 nmmoL) in ethanol was supplied to the potassium salt solution dropwise continuously and the mixture was stirred for 12 h at room temperature. The precipitate potassium dithio carbazinate was collected by filtration, washed with cooled ethanol (50 mL) and dried on vacuum. The potassium salt that obtained was used in the next step without further purification (Palekar *et al*., 2009).

2.6.1. Syntheis of Diethyl 2,2'-(5,5'-(1,4-Phenylene) Bis (1,3,4-Oxadiazole-5,2-Diyl)) Bis (Sulfanediyl) Diacetate (8)

Ethyl 2-bromoacetate (10 mmoL) was added to a soultion of potassium salt (7) (1.8 g, 5 mmoL) in ethanol. The reaction mixture was heated under reflux for 2 h and the precipitated solid was collected by filtration, washed with ethanol, dried and recrystallized from ethanol to obtain 8; yield 70%, mp: 285°C; IR (KBr) ν_{max}/cm^{-1}: 1725 (C = O); ^{1}H NMR (DMSO-d_6): δ 1.18 (t, 6H, $2CH_3$), 4.11 (s, 2H, CH_2), 4.28 (q, 4H, $2CH_2$), 8.12 (m, 4H, Ars H); ^{13}C NMR (DMSO-*d6*): 14.1 (2-CH_3), 32.2 (2-CH_2), 60.6 (2 CH), 127 (2 CH), 129 (4 CH), 133 (2 CH), 164 (2 CH), 167 (2 C = O); MS (*m/z*): 451 (M^+, 6.8%), 166 (60.2%), 149 (100.0%), Anal calcd: $C_{18}H_{18}N_4O_6S_2$ (450.49); C,79.51.; H, 5.01; N, 15.46%; Found: C, 79.58; H, 4.97; N, 15.50%.

2.6.2. Synthesis of N_1,N_4-Bis (4-Phenyl-2-Thioxothiazol-3(2*H*)-yl) Terephthalamide (9)

Reaction of soultion of potassium salt (7) (1.8 g, 5 mmoL) in ethanol with phencyl bromide (10 mmoL) was carried out. After boiling the reaction mixture for 4 h. the formed precipitate was collected by filtration, washed with ethanol and dried. recrystallization from ethanol to afford compound 9, yield 72%, mp:175°C; IR (KBr) ν_{max}/cm^{-1}: 3057 (NH), 1686 (C = O); ^{1}H NMR (DMSO-d_6): δ 7.04 (s, 2H,CH), 7.5-8.5 (m, 14H, Ars H), 9.4 (s, 2H, NH, D_2O exchangable); ^{13}CNMR (DMSO-*d6*): 66.9 (2 CH_2), 127-128 (10 CH), 129 (4 CH), 148 (2 CH),150 (2 CH), 169 (2 CH), 172 (2 C = O), 193 (2 C = S); MS (*m/z*): 546 (M^+, 100%) M^+; Anal calcd $C_{26}H_{18}N_4O_2S_4$ (546.71); C,57.12; H,3.,32; N,10.25; S,23.46; Found: C,57.16; H,3.39; N,10.29; S,23.48.

2.7. Synthesis of 1,4-Phenylene Bis ((3,5-Dimethyl-1 H-Pyrazol-1-yl) Methanone (10)

A mixture of terephthalic dihydrazide 3 (2 mmoL), pentane-2, 4-dione (4 mmoL) and few drops of DMF in glacial acid (10 mL) was stirred at room temperature over night. After dilution with water the solid precipitate was filtered, dried and crystallized from (Ethanol/DMF) to afford compound 10, yield 75%, mp: 215°C; IR (KBr) ν_{max}/cm^{-1}: 1646 (C = O), 1431 (CH_3); ^{1}H NMR (DMSO-d_6): δ 1.83 (s, 6H, 2CH_3), 2.1 (s, 6H, 2CH_3), 6.2 (s, 2H, 2CH pyrazole), 7.87 (s, 4H, Ars H); ^{13}CNMR (DMSO-*d6*): 13.2 (4 CH_3), 110 (2 CH), 129 (4 CH), 134 (2 CH), 143 (2 CH), 152 (2 CH), 167(2 C = O); MS (*m/z*): 322 (M^+, 100.0%), 228 (6.2%), 226 (14.4%); Anal calcd $C_{18}H_{18}N_4O_2$ (322.14); C, 67.07; H, 5.63; N, 17.38; Found: C, 67.10; H, 5.66; N, 17.40.

2.8. Synthesis of 1, 4-Phenylene Bis (5-Amino-3-Hydroxy-1 *H*-Pyrazol-1-yl) Methanone (11)

A mixture of the hydrazide 3 (2 mmoL) in 10% KOH solution (10 mL) and ethyl cyanoacetate was refluxed in ethanol (20 mL) for 10 h, the reaction mixture was then cooled, diluted with water and neutralized with HCl. The resulting solid was filtered off, washed with water, dried and recrystallized from ethanol/DMF to obtain compound 11; yield 72% mp: 254°C; IR (KBr) ν_{max}/cm^{-1}: 3423 (OH), 3010 (NH_2), 1677 (C = O); ^{1}H NMR (DMSO-d_6): δ 4.69 (s, 4H, 2 NH_2, D_2O exchangable); 7.9 (s, 4H, Ars H), 8.85 (s, 2H, 2 CH pyrazole), 11.64 (s, 2H, 2 OH, D_2O exchangable); ^{13}C NMR (DMSO-*d6*): 91 (2 CH), 129 (4 CH), 136 (2 CH), 150 (2 CH), 152 (2 CHOH), 165 (2 C = O), MS (*m/z*): 328 (M^+, 100.0%), 146 (14.7%); Anal calcd $C_{14}H_{12}N_6O_4$ (328.28); C,51.22; H,3.68; N,25.60; Found: C,51.25; H,3.60; N; 25.58.

2.9. Synthesis of N'^1, N'^4-Bis (3-Oxobutanoyl) Tere Phthalo Hydrazide (12)

A mixture of the hydrazide 3 (2 mmoL) and ethylacetoacetate (10 mL) was refluxed for 5 h. The mixture was diluted with petroleum ether (60-80 br) and the resulting solid was filtered, washed with water, dried and recrystallized from ethanol to get compound 12, yield 70%; mp: 245°C; IR (KBr) ν_{max}/cm^{-1}: 3450, 3242 (NH), 1736 (C = O,ester), 1658 (C = O, amide); ^{1}H NMR (DMSO-d_6): δ 1.29 (s, 6H, 2CH_3), 4.21 (s, 4H, CH_2), 8.21(m, 4H, Ars H), 10.38 (br s, 4H, 4NH, D_2O exchangable); MS (*m/z*): 390 (M^+, 85.3%), 362.34 (100.0%); Anal calcd $C_{16}H_{18}N_4O_6$ (390.39); C,53.04; H, 5.01; N,15.46; Found: C,53.10; H,5.08; N,15.50.

2.10. Synthesis of 2,2'-Terephthaloyl-Bis-(5-Methyl-1*H*-Pyrazol-3(2*H*)-one) (13)

Compound 12 (2 mmoL) was dissolved in 20% KOH (20 mL) solution and refluxed for 5 h and the reaction mixture was then cooled, acidified with conc. HCl. The resulting solid was filtered, washed with water, dried and recrystallized from ethanol to produce 13, yield 73%; mp: 295°C; IR (KBr) ν_{max}/cm^{-1}: 3067 (OH), 1686 (C = O); ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 6H, 2 CH_3), 6.1 (s, 2H, 2 CH), 8.04 (s, 4H, Ars H), 13.24 (s, 2H, 2 NH); ^{13}C NMR (DMSO-*d6*): 17.8 (2 CH_3), 44.6 (2 CH_2), 119 (2 CH), 128 (4 CH), 149 (4 CH), 170 (2 C = O); MS (*m/z*): 326 (M^+, 84%) 166 (6.2%), 149 (100%); Anal calcd $C_{16}H_{14}N_4O_4$ (326.31); C, 58.89; H,4.32; N,17.17; Found: C, 58.92; H, 4.35; N, 17.20.

2.11. Synthesis of N'^1, N'^4-Dibenzoyl Terephthalo Hydrazide (14)

A mixture of the hydrazide 3 (2 mmoL) and benzoyl chloride (2 mmoL) in pyridine (20 mL) was refluxed for 24 h, then the reaction mixture was then cooled, diluted with water and acidified with dil HCl. The resulting solid was filtered, washed with water, dried and recrystallized from ethanol/DMF to afford 14; yield 65% mp: 185°C; IR (KBr) ν_{max}/cm^{-1}: 3325 (NH), 1687 (C = O), 1611 (C = O). ^{1}H NMR(DMSO-d_6): δ 7.63-8.21 (m, 14H, Ars H), 10.74 (s, 4H, 2NH D_2 Oexchangable); MS (*m/z*): 402 (M^+, 100.0%); Anal

calcd $C_{22}H_{18}N_4O_4$ (402.40); C, 65.66; H, 4.51; N, 13.92; C, 65.61; H, 4.47; N, 13.85.

2.12. Synthesis of 1,4-Bis (5-Phenyl-1,3,4-Oxadiazol-2-yl) Benzene (15)

Compound 14 (2 mmoL) was dissolved in dry xylene (20 mL) and refluxed with phosphourous pentaoxide (0.5 g) for 12 h. Then, the reaction mixture was cooled, diluted with water and neutralized with ammonia. The solid separated was filtered off, washed with water, dried and recrystallized from ethanol/DMF to afford 15, yield 74%; mp: 226°C; ^{1}H NMR (DMSO-d_6): δ 7.5-8.21 (m, 14H, Ars H); ^{13}C NMR (DMSO-*d6*): 127-130 (14 CH), 134 (2 CH), 133 (2 CH), 146 (2 CH), 164 (2 C-O); MS (*m/z*): 366(M^+, 5.3%), 266(34.8%), 105 (100.0%); Anal calcd $C_{22}H_{14}N_4O_2$ (366.37); C,72.12; H, 3.85; N,15.29; Found: C,72.18; H,3.83; N,15.40.

3.RESULTS

3.1. Biological Activity

3.1.1. Insecticidal Activity

Tested insects: *Culex pipiens* (Culicidae: Diptera) and *Musca domestica* (Mucidae: Diptera). Larvae of *Culex pipiens* and *Musca domestica* were provided from Medical Entomology Institute and transferred to the laboratory of Entomology Department-Faculty of Science-Ain Shams University where self-perpetuating colonies were established and maintained during the present study as described by (Kamel *et al*., 2005) for *Culex pipiens*. Preliminary, toxicological bioassay tests were carried out on tested compounds as a modification for the described method. Mortality data was analyzed by using log-probit analysis to estimate probity regression line and calculate LC_{50}, LC_{95}, slope function by applying the computer program (Chornous *et al*., 2005). If the control mortality was between 5 and 20%, the percentage mortalities were corrected by Abbott's formula (Wright, 1971; Abbott, 1925; Chornous *et al*., 2005). Ten tested compounds were bioassay against the 3rd instars of the *Cluex pipiens* larvae and *musca domestica* larvae in the laboratory (**Table 1** and **2**). Which were statistically calculated for LC_{50} and LC_{95} at p = 0.05. The tested compounds showed different toxicity against them (**Fig. 1-4**). All the tested compounds showed a certain effect on *Culex pipiens* and *Musca domestica* as illustrated in (**Table 1** and **2**) which clear that 1,3,4-oxadiazol derivative 16 gave higher more potent activity than open chain compound N^1,N^4-dibenzoyl terephthalo hydrazide (14) Despite of other derivatives were closely resulted in potency which were found to possess crossing regression lines of nearly equal slope values. This may suggest that these compounds have different mode of action against the tested insect larvae and homogenous effect on the population (Busvine, 1971).

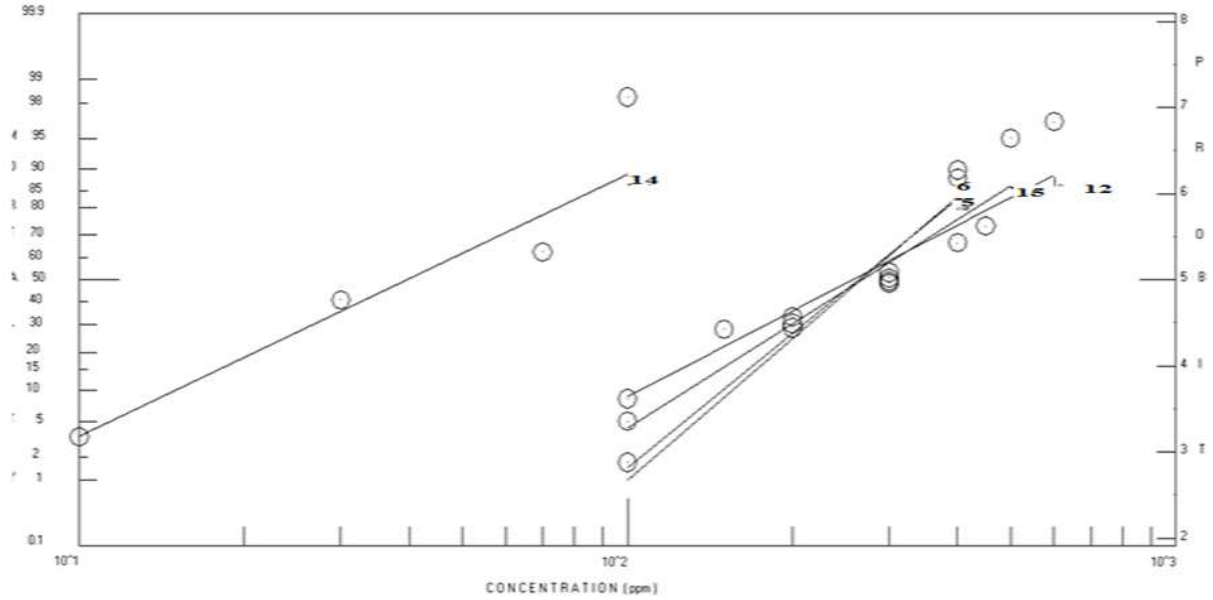

Fig. 1. Susceptibility of Culex pipiens larvae to group one Group one of compounds (14, 6, 5, 15 and 12)

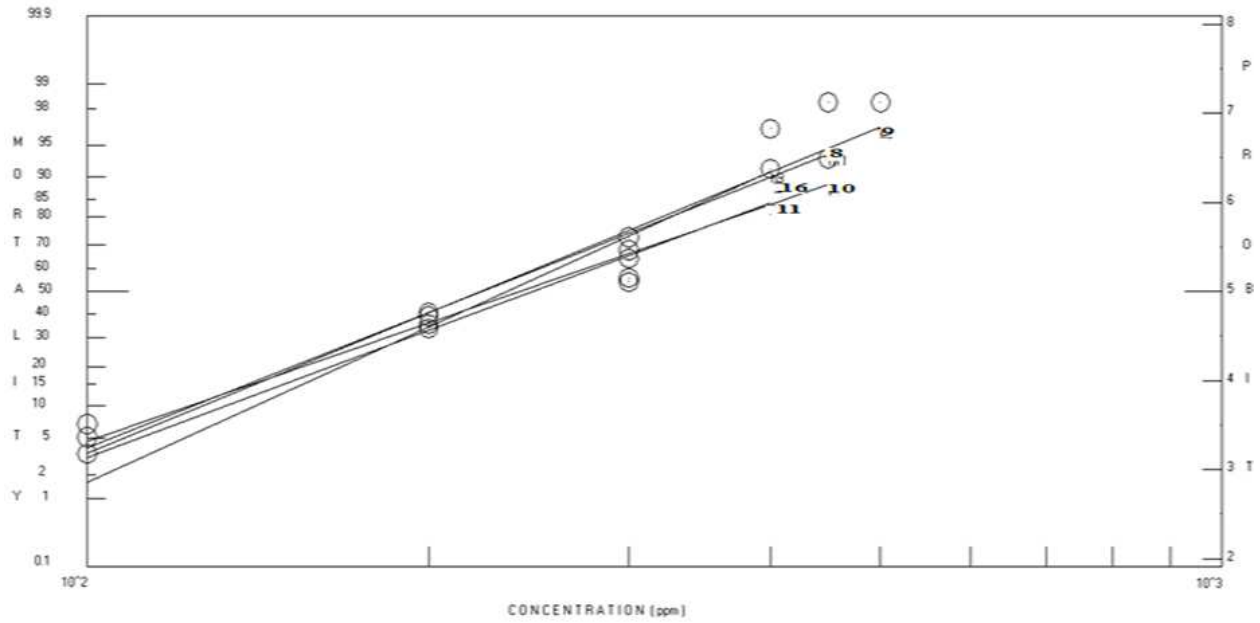

Fig. 2. Susceptibility of Culex pipiens larvae to group two Group two of compounds (9, 8, 16, 11 and 10)

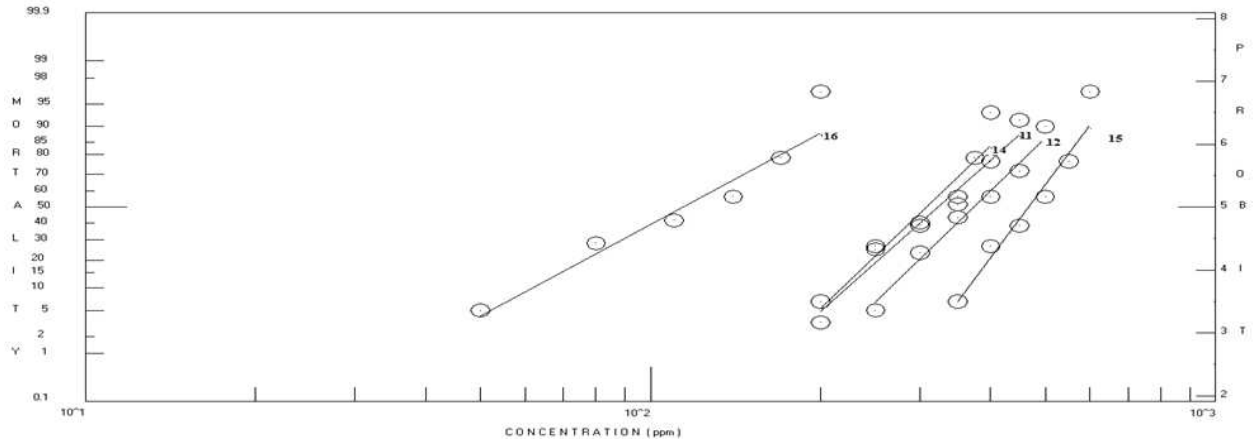

Fig. 3. Susceptibility of Musca domestica larvae to group one Group one of compounds (16, 14, 11, 12 and 15)

Also compound 1*H*-pyrazol derivative 10 exhibited high activity in action of *Culex pipiens* rather than *Musca domestica*. In general mosquitoes were more susceptible than housefly to tested compounds. The susceptibility of *Culexpipiens* and *Musca domestica* larvae to a pyrethroid insecticide (Deltamethrine) and an insect growth regulator (Flufenoxuron) to compare them with the tested compounds. The results presented in **Table 3** and illustrated in **Fig. 5** which shows that *Culexpipiens* and *Muscadomestica* larvae are generally most susceptible to Deltamethrine insecticide then Flufenoxuron at the basis of LC_{50} values.

Although decreasing potency of the newly synthesized compounds in comparing with traditional insecticides, the new compound 15 is still promising because of it was produced from waste material and needs more investigations to detect its mode of action:

- Lines 1 and 2 represent Deltamethrine for *Muscadomestica* and *Culexpipiens* respectively
- Lines 3 and 4 represent Flufenoxuron for Musca domestica and Culex *pipiens* respectively

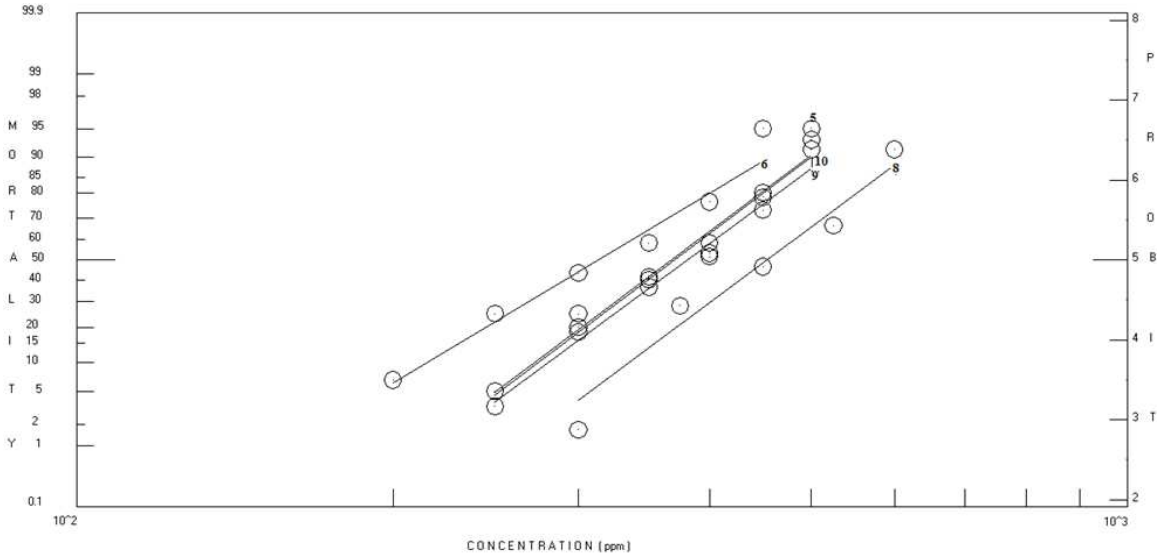

Fig. 4. Susceptibility of Musca domestica larvae to group two Group two of compounds (6, 9, 10, 8 and 5)

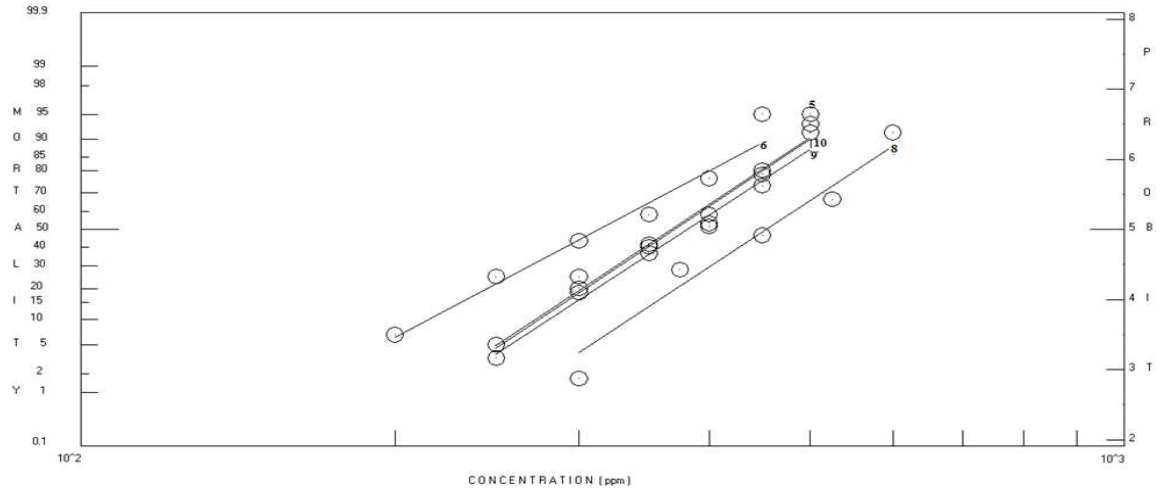

Fig. 5. Susceptibility of Cluexpipiens and Muscadomestica larvae exposed to Deltamethrine (Pyrethroid) and Flufenoxuron (LGR)

3.1.2. Antimicrobial Activity

Ten of the newly synthesized target compounds were evaluated for *S. pneumonia*, *S. aureus (B*), *S. typhimurium* and *E.coli* (30) for Gram+ve and -ve Bacteria, respectively and antifungal activites for *C. albicans* (*A*) and *A. flavu*. The results were recorded for each of the tested compounds as the average diameter of the Inhibition Zone (IZ) of bacterial or fungal growth around the disks in mm. The results, depicted in **Table 4** revealed that the most of the tested compounds displayed variable inhibitory effects on the growth of *G+* and *G-* bacterial strain and antifungal strains. In general, most of the tested compound 1,2,4 triazole derivative 5 exhibited high degree of inhibition against all types of strains. Agar well diffusion method showing Antimicrobial activities of the tested compounds compared with reference (µm) and also compound 1,3,4-oxadiazol-2-amine derivative 6 has high activity against all strains except *S.pneumonia* (s), These bulky substituent deteriorate the antibacterial and antifungal activity of these compounds (8, 9, 14, 12, 15 and 10) show a moderate activity against bacteria and fungi strains (**Table 5** and **6**) and shows the inhibition zone in (**Fig 6-8**).

Table 1. Larval mortality and LC_{50} and LC_{95} values for the Culex pipiens larvae exposed to some novel compound

Name of sub.	LC_{50} (Co. limits)	LC_{95} (Co. limits)	Slope
8	217.3(197.3-238.9)	468.4(392.9-558.6)	4.9
9	216.9(196.9-238.8)	483.1(403.6-578.4)	4.7
6	227.4(208.3-248.3)	468.6(397.5-552.6)	5.2
16	38(32.6- 44.6)00000	140.8(105.5-188.7)	2.9
10	235.7(212.6-261.20)	580.6(467.3-721.8)	4.2
11	241.5(219.1-266.10)	571.2(460.6-708.6)	4.3
14	258.4(235.8 -283.10)	564(461-690.3)	4.7
5	260.1(237.9-284.50)	573.3(465.8-705.9)	4.8
12	268.02(243.56-294.92)	686.45(560.08-841.74)	4.0
15	258.05(229.71- 289.88)	814.22(640.79-1035.55)	3.3

Table 2. Larval mortality and LC_{50} and LC_{95} values for the *Musca demostica* larvae exposed to some novel compound

Name of sub	LC_{95} (Co. limits)	LC_{50} (Co. limits)	Slope
8	453.64 (435.6-472.03)	668.87 (613.99728.67)	09.7
9	381.59 (368.11-395.55)	563.02 (519.49610.22)	09.7
6	313.31 (29.83-327.390)	506.78 (460.67-557.53)	07.8
16	114.06 (106.08-122.63)	249.41 (213.3-290.870)	04.8
10	367.99 (355.08-381.360	540.17 (500.8-582.440)	09.8
11	322.94 (309.25-337.200	519.18 (471.16-572.12)	07.9
14	308.06 (296.02-320.580	478.61 (437.69-523.28)	08.5
5	371.21 (358.24-384.650	544.32 (504.55-587.23)	09.8
12	373.32 (359.0 - 388.22)	577.26 (526.95-632.40)	08.6
15	467.74 (454.39-481.490	641.69 (602.59-683.32)	11.9

Table 3. Larval mortality and LC_{50} and LC_{95} values for the *Cluex pipiens* and *Musca domestica* larvae exposed to Deltamethrine (Pyrethroid) and Flufenoxuron (LGR)

	Culex pipiens			Musca domestica		
Insecticide	LC_{50}	LC_{95}	Slope	LC_{50}	LC_{95}	Slope
Deltamethrine	0.00034 (0.0003-0.0004)	0.0012 (0.001-0.0015)	3.5	0.03 (0.025-0.035)	0.18 (0.12-0.27)	2.12
Flufenoxuron	0.0036 (0.0031-0.0042)	0.017 (0.013-0.022)	2.4	0.63 (0.58-0.67)	1.36 (1.15-1.64)	4.80

Table 4. Well diffusion method showing Antimicrobial activities of tested compounds compared with reference drugs, results given in (μm)

Strain sample	*S*.pneumonia	Gram+ve bacteria *S*.aureus (B)	Gram-ve bacteria *S*.typhimurium	Fungi *E*.coli (30)	*C*.albicans sample (A)	*A*.flavu (s)
5	13	14	15	11	23 13	
10	-ve	10 s	-ve	12	-ve	13
12	-ve	-ve	-ve	-ve	-ve	10 s
14	-ve	20	-ve	11	-ve	16
11	-ve	-ve	-ve	-ve	-ve	-ve
15	12	12 s	16	16	-ve	18
16	-ve	22	-ve	20	-ve	18
8	-ve	12	21	11	-ve	12
6	-ve	18	22	11	12	13
9	15	19	-ve	12	-ve	13
Cefoperazone 75 μg mL^{-1}						
Ciprofloxacin 200 μg mL^{-1}	13	50	21	45	-	-
Fluconazole 100 μg mL^{-1}	-	-	-		20	-ve

Table 5. MIC of tested compounds against tested strains compared with reference drugs

Strains samples	*S. pneumonia* Gram+ve bacteria (s)	*S. aureus*(B)	*S. typhimurium* Gram+ve bacteria (3)	*E. coli*-30	*C. albicans* Fungi(A)	*A. flavu*-58s
5	25	25	25	50	3.125	50
10	ND*	50	ND	50	ND	50
12	ND	-ve	ND	-ve	ND	-ve
14	25	25	12.5	50	-ve	25
11	ND	-ve	ND	-ve	ND	-ve
15	-ve	-ve	3.125	25	-ve	25
16	-ve	25	3.125	25	25	25
8	25	50	-ve	50	-ve	50
6	ND	25	ND	50	ND	50
9	ND	25	ND	50	ND	50
Cefoperazone 75µg mL^{-1}	25	0.78	3.125	1.56	-	-
Ciprofloxacin 200µg mL^{-1}						
Fluconazole 100µg mL^{-1}	-	-	-	-	6.25	-
Control negative |(DMSO)	-	-	-	-	-	-

ND*: Not detected

Table 6. MIC of tested compounds against tested strains compared with reference drugs

Strains samples	*S. pneumonia* Gram+ve bacteria (s)	*S. typhimurium* Gram+ve bacteria	*C. albicans* Fungi (A)
5	25	25	3.125
15	25	12.5	-ve
8	-ve	3.125	-ve
6	-ve	3.125	25
9	25	-ve	-ve
Cefoperazone	25	3.125	-
Fluconazole	-	-	6.25

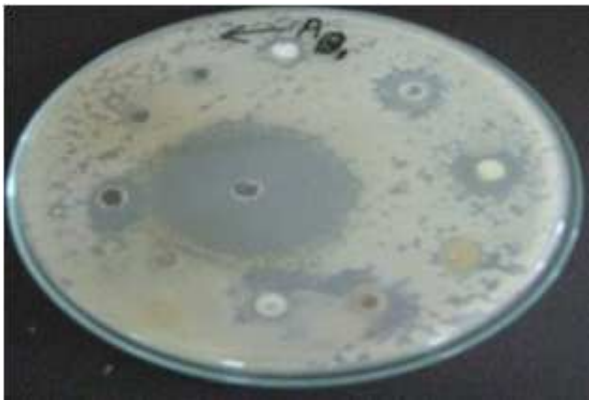

Fig. 6. Zone of inhibition of tested samples in sequence with the arrow (anti clock wise); samples 1-10. then CIP 200 µg mL^{-1} Samples were tested against *S. aureus*

Fig. 7. Zone of inhibition of tested samples sequence with arrow (anti clock wise); samples 1-10 CIP 200 µg mL^{-1} Samples were tested against *E.coli*

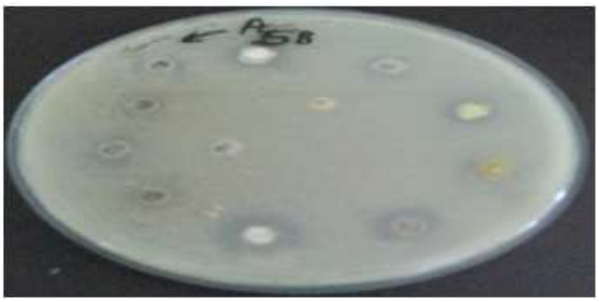

Fig. 8. Zone of inhibition of tested samplesin sequence with the arrow (anti clock wise); samples 1-10. CIP 200 µg mL^{-1} Samples were tested against A.flavus

Table 4. Agar well diffusion method showing Antimicrobial activities of tested compounds compared with reference (mm) and also compound 1,3,4-oxadiazol-2-amine derivative 6 has high activity against all strains except *S. pneumonia* (s), These bulky substituent deteriorate the antibacterial and antifungal activity of these compound (8, 9, 14, 12, 16 and 10) show a moderate activity against bacteria and fungi strains **Table 4**.

Also the MIC activity were assayed in **Table 5 and 6** and it was showed that the 1,2,4 triazole derivatives 5 exhibited resemble activity such the reference drug against *S. typhimurium* (*G*+) against *E. coli* by measuring theaverage diameter of the Inhibition Zone (IZ):

4. DISCUSSION

Degradation of Poly Ethylene Terephthalate (PET) utilizing Sun energy as a source of heat to afford terephthalic acid (1) which was esterified to dibutyl terephthalate (2) which was treated with hydrazine hydrate to afford terephthalic dihydrazide (3). Treatment of (3) with phenylisothiocynate in refluxing benzene gave the bisthiosemicarbazide 4 (Shaker *et al*., 2005; Pradip, 2008; Ram and Vlietinck, 1988). Furthermore, the intramolecular cyclization of 4 takes place upon heating with KOH to produce the 1,2,4 triazole derivative 5. Its mass spectrum revealed a peak corresponding to the molecular ion at *m/z* 428(M^+) and its IR spectrum was free of NH and C = O absorption bands. Interestingly, when bis-thiosemicarbazide 4 was boiled with potassium iodide and iodine in DMF, it gave 1,3,4-oxadiazol-2-amine derivative 6 (**Fig. 9**) which was confirmed on the basis of its elemental analysis and spectral data; (*cf. experimental*).

The required bis-dithiocarbazinate **7** was synthesized by reacting dihydrazide 3 with carbon disulfide and potassium hydroxide in ethanol. This salt underwent ring closure with an ethyl 2-bromoacetate to give bis-1,3,4-oxadiazole derivative 8. The structure was confirmed by IR, ^{1}H NMR and mass spectra. For example, the ^{1}H NMR of 8 showed a triplet signal at δ 1.18 ppm due to methyl group and singlet signal at 4.16 due to active methylene, whereas its mass spectrum revealed molecular ion peak at *m/z* 450 (M^+). While the reaction of the salt 7 with 1-phenyl-2-bromoethanone yilded 1,3-thiazolidine derivative 9 which was confirmed by spectral data (**Fig. 10**). For example IR spectrum of 9 showed a strong absorption band due to NH of Pyrazole at 3057cm^{-1}, its ^{1}H NMR spectrum showed a singlet at δ 4.25 (NH, D_2O exchangable) and its mass spectrum showed a peak corresponding to its molecular ion at *m/z* 362 (M^+).

Reaction of dihydrazide 3 with the active methylene of pentane-2,4-dione in glacial acetic acid afforded 1,4 phenylene-bis ((3,5-dimethyl-1*H*-pyrazol-1-yl) methanone (10). The structure of the obtained product was established *via* its spectral data. For example, IR spectrum of 10 revealed the presence of strong absorption band at 1646 cm^{-1} for C = O function group; ^{1}H NMR spectrum showed a characteristic singlet signal at δ 6.29 of 4H pyrazole protons, Its mass spectrum showed its molecular ion peak at *m/z* 322. In addition, when the hydrazide 3 was allowed to react with ethylcyanoacetate in basic condition, it gave the corresponding 1,4 phenylene bis (5-amino-3-hydroxy-1*H*-pyrazol-1-yl) methanone (11) and its mass spectrum revealed the molecular ion peak at *m/z* 328 as shown in (**Fig. 11**). The reactivity of the terephthalicdihydrazide (3) towards ethyl acetoacetate was also investigated to afforded *N'*^{1},*N'4*-bis (3-oxobutanoyl) terephthalohydrazide (12). IR spectrum of the latter product showed two carbonyl absorption bands at 1736 and 1658 cm^{-1}. Its mass spectrum revealed a peak corresponding to the molecular ion at *m/z* 390 (M^+). Cyclization of *N'*^{1},*N'4*-bis (3-oxobutanoyl) terephthalo hydrazide (12) in aqueous potassium hydroxide gave the corresponding 2,2'-terephthaloyl bis(5-methyl-1*H*-pyrazol-3 (2*H*)-one) (14). The IR spectrum showed an absorption band due OH at 3067 and at 1686 cm^{-1} for carbonyl group. Its mass spectrum revealed the molecular ion peak at *m/z* 326 (**Fig. 12**) (*cf. experiental*). Benzoylation of bishydrazide 3 took place in boilig pyridine to yield *N*^{1}, *N*^{4}-dibenzoyl terephthalohydrazide (15) which afforded 1,4-bis (5-phenyl-1,3,4-oxadiazol-2-yl) benzene (16) *via* cyclocondensation in the presence of P_2O_5 in refluxing xylene.

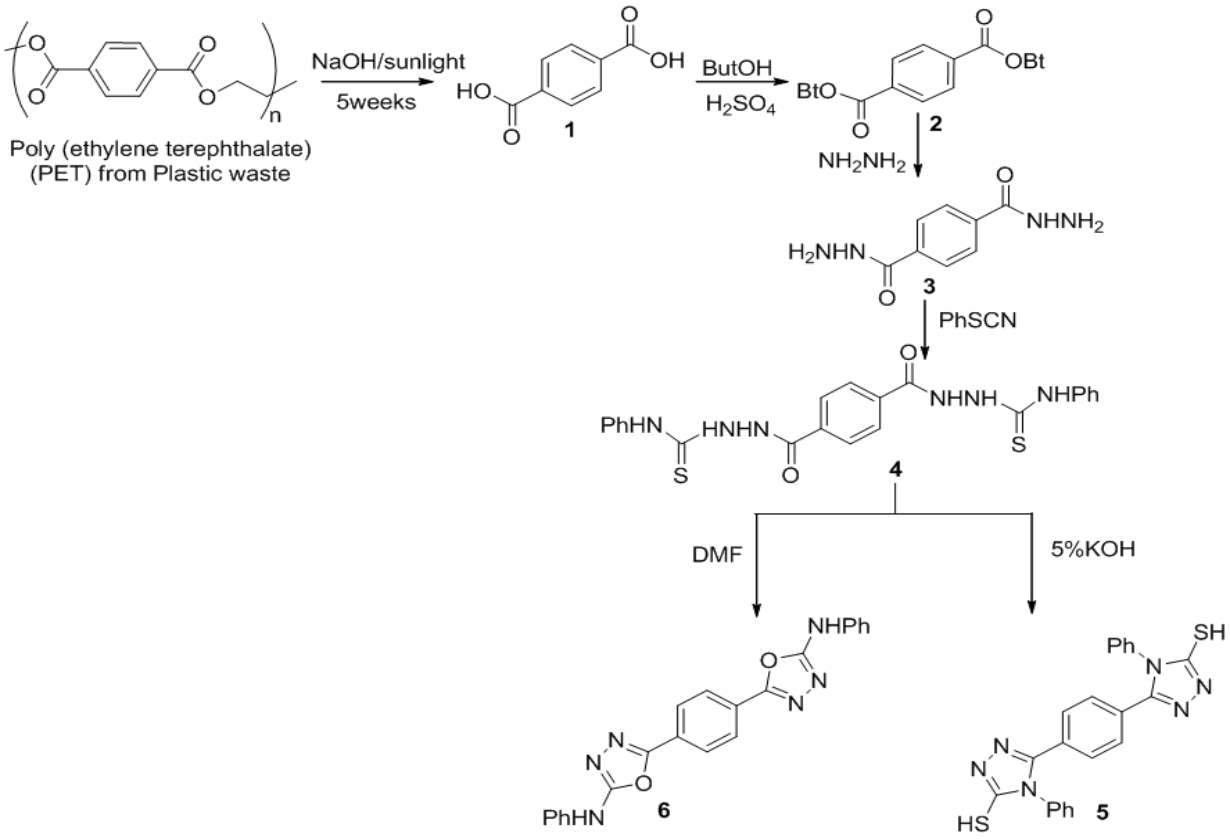

Fig. 9. Scheme (1)

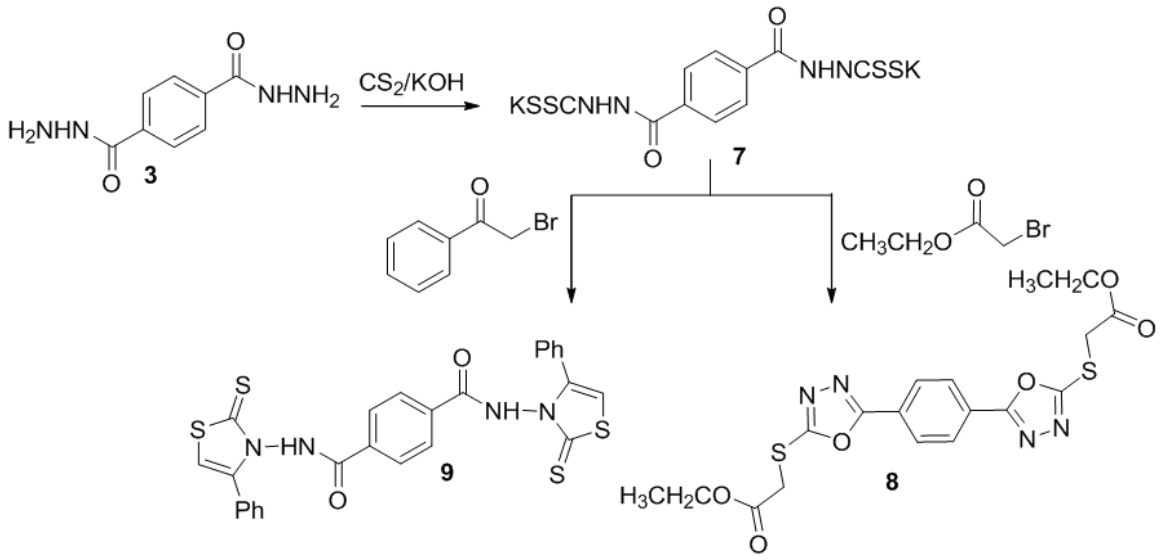

Fig. 10. Scheme (2)

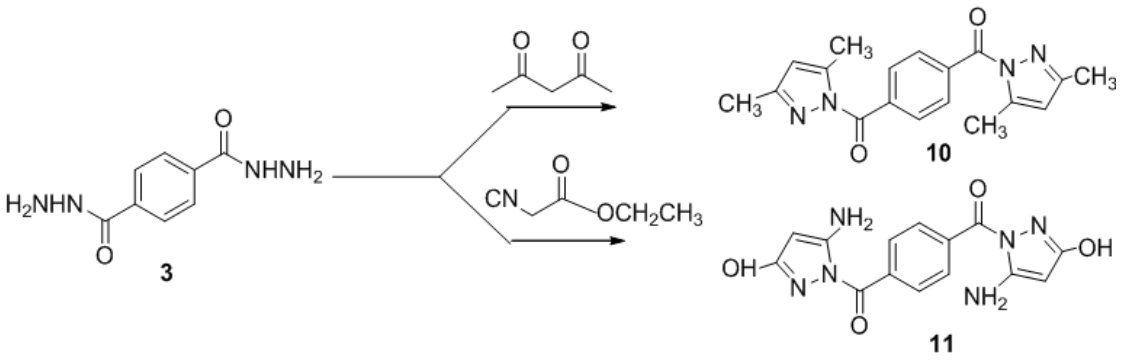

Fig. 11. Scheme (3)

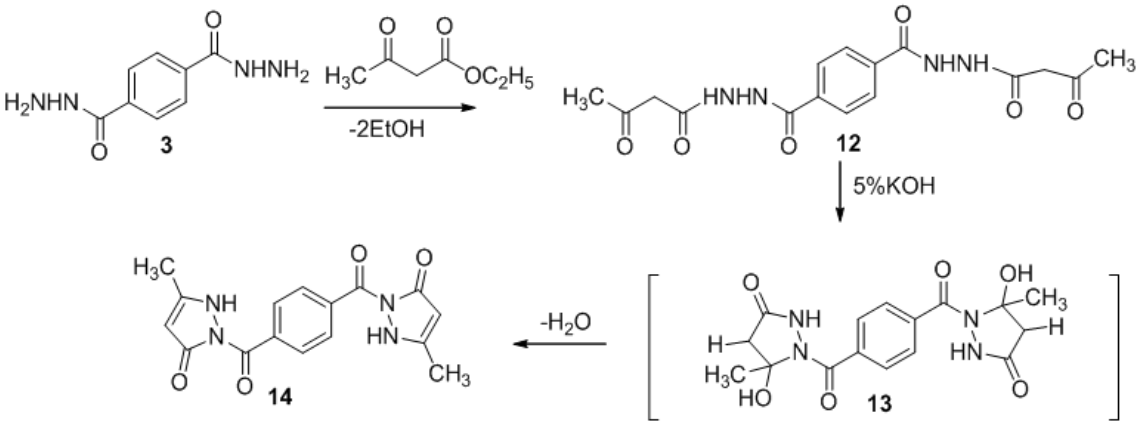

Fig. 12. Scheme (4)

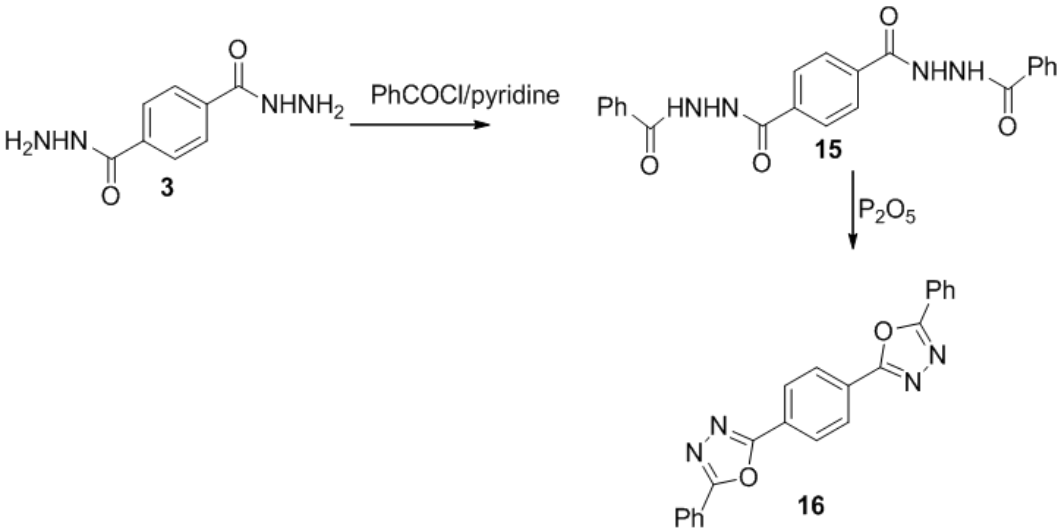

Fig. 13. Scheme (5)

The structure of 16 was confirmed by the spectral data, For example its IR spectrum showed the absence of the absorbtion bands of NH and C = O groups, while ^{1}H NMR spectrum of 15 reaveled multiplet at δ 8.21 due to the aromatic protons (**Fig. 13**).

5. CONCLUSION

PET waste was utilized as chemical feed stock for preparing new cheap compounds. Thus, the preparation of the novel compounds 5, 6, 8, 9, 10, 11, 13 and 15 were carried out starting from terepthalic dihydrazide which is being obtained from PET waste. Insecticidal and antimicrobial activities of the synthesized heterocycles were studied and we concluded that 1,3,4-oxadiazol derivative 16 displayed an insecticidal activity against *Cluexpipiens* larvae and *muscadomestica* larvae; where the most promising 1,2,4-triazole derivative 5 show high activity in all strain media comparable with to commercial compounds.

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