Synthesis of Some New Benzoxazole Acetonitrile Derivatives and Evaluation of Their Herbicidal Efficiency.

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Abstract: Twenty three new 2-cyanomethyl benzoxazole derivatives were synthesized by different methods. Their structures were elucidated by many ways as elemental analysis, spectroscopic analysis and chemical methods. The herbicidal activity of the newly synthesized compounds was evaluated against wheat as pattern for monocotyledonous plants, three plant parameters were studied, seed gerimination, root and shoot growth under laboratory conditions. Compounds that showed an observable inhibition on one or more of the growth parameters under study were considered as promising compounds and needs more studies from the toxicological, soil, environmental and formulation points of view to stand on the most potent derivative that can be formulated in a suitable formulation form to be used in the field of pest control. Compounds (**16a**),(**16b**),(**16f**),(**13b**),(**10a**),(**7a**) and (**3b**) inhibited all growth parameters under study by different degrees. While compounds (**13b**) and (**13a**) were more effective on root and gerimination respectively. Most synthesized compounds inhibited markedly shoot growth.

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Introduction

Our present work is a continuation of our ongoing programme in utilizing readily obtainable materials in the synthesis of different biologically active heterocylces [1].2-cyanomethyl benzoxazole and its related compounds play an important role in pharmaceutical and agricultural fields due to their broad spectrum of biological activities. Such a ring system has been reported to be used as herbicides [2-14], bactericides [15], fungicides [16-25], antiviral [26-30] and antimicrobial agents [22]. Also , 2-cyanomethyl benzoxazole connected to pyridine carbonitriles have been found to be of great interest due to their broad spectrum of biological activities [31]. So that depending on the biological activities and due to the high chemical activity of 2-cyanomethyl benzoxazole ring system , it was found that synthesis and study of the herbicidal activity of some new 2-cyanomethyl benzoxazole derivatives is a subject of great interest hoping that these new compounds could be applied as a new herbicidal agents in the field of pest control.

Results and discussion

1-Chemistry part

The key starting material 2-cyanomethyle benzoxazole (**1**) is characterized by the presence of an active methylene as well as nitrile group which makes it chemically very active so it can be used as a precursor to synthesize many biologically and chemically active ring systems. Condensation of acetonitrile (**1**) with different heterocyclic or aromatic aldehydes in ethanol and triethylamine as an organic base under reflux afforded -2- arylidene benzoxazole-2- acetonitrile (**za-e**),[31](c.f.Schem1). both elemental and spectral data of the obtained compounds are consistent with the assigned structure (c.f.Experimental). benzoxazole (**1**) as a result of the presence of the active methylene, it was allowed to react with o-hydroxy napthaldhyde (**4**) in ethanol and ammonium acetate to give coumarine (**5**)[32,33], the structure that was supported by the disappearance of the characteristic absorption band of CN with the appearance of carbonyl group band in IR spectra as well as the appearance of the signal corresponding to the ethylenic proton of coumarine ring as singlet at

9.92 ppm in 1H-NMR spectrum of compound (**5**) due to oxidation of nitrile group followed by elimination of water and cyclization on coumarine ring .

Moreover , mass spectrum of compound (**5**) showed the expected molecular ion peak at m/z=313 with relative abundance of 27.7 corresponding to the correct molecular formula . in the same way ,2-cyanomethyle benzoxaole (**1**) on treatment with different ketones (**6**) in ethanol in the presence of piperidine as a basic catalyst under reflux afforded α-(benzoxazole -2-yl)-B- alkyl (aryl) crotonitrile (**7a-c**).

Structural elucidation of derivatives (**7a-c**) was carried out by different ways as elemental analyses as well as spectroscopic data, whereas, IR spectra of compound (**7a**) revealed the appearance of the characteristic absorption band for CH aliphatic at 2225 cm^{-1} region. Also, ^{1}H-NMR (DMSO-d6) of the same derivative showed two singlets at 2.40 and 2.55 ppm corresponding to two methyl groups of compound (**7a**)

Moreover , mass spectrum of this compound showed the expected molecular ion peak at m/z= 198 with relative abundance of 50.0 corresponding to the correct molecular formula.

On the other hand, compound (**1**) was reacted with α,B – unsaturated nitriles (**8a-c**) in ethanol in the presence of piperidine as a basic catalyst under reflux to afford the corresponding dicarbonitrile derivatives (**10a-d**). structural elucidation of derivatives (**10a-d**) was carried out by different ways as elemental analyses, spectroscopic data as well as chemical ways. Whereas, IR spectra of all obtained compounds revealed two absorption bands at 1940 and 2198 cm $^{-1}$ region due to the presence of two (CN) functional groups . Also, structure (**10**) was confirmed by the presence of the characteristic signal at 5.23 ppm in ^{1}H-NMR spectrum of compound (**10b**) due to the formation of NH_2 functional group. More over the mass spectrum of compound (**10b**) showed the expected molecular ion peak at m/z=346 with relative abundance of 2.6 corresponding to the correct molecular formula .

Refluxing arylidene (**3**) with malononitrile (**a**) in ethanol in the presence of sodium ethoxide gave dicarbonitrile (**10d**) which was confirmed by m.p,mixed m.p and IR spectrum that revealed the presence of two absorption bands at 1940, 2195 cm $^{-1}$ region corresponding to two (CN) functional groups and mass spectrum of the same derivative that displayed molecular ion peak at m/z =401 with relative abundance of 2.9corresponding to the molecular formula $C_{22}H_{18}N_4O_4$.

Benzoxoazole (**1**) on treatment with the arylidene ethyl α-cyanocinnamate (**11**) in ethanol in the presence of sodium ethoxide as a basic catalyst afforded pyridine carboxylic esters (**13a-d**).

Structures (**13a-d**) was confirmed by different ways as elemental analyses and spectroscopic analyses. whereas , IR spectra of all obtained compounds revealed new absorption bands at 3375, 3237 and 1662 cm $^{-1}$ region due to the presence of NH_2 and C=O group . Also, ^{1}H-NMR (DMSO-d6) of compound (**13b**) showed signals at 1.28-1.33 (t,3H,CH_3),4.26-4.36 (q,2H,CH_2), 7.34-7.39 (m,3H,thiophene – H) , 8.07-8.23(m-5H,Ar-H)and 8.62(s,2H,NH_2). Moreover ,treatment of arylidene (3)with ethyl cyano acetate (**12**) in ethanol and sodium ethoxide as a basic catalyst under reflux gave pyridine carboxy ester(**13 a**), which was considerd as chemical tool for structural elucidation of compounds (**13b-d**) . Structure of (**13 a**) was confirmed by compatible elemental analysis and spectral data (c.f. Experimental).

In addition, 2-cyanomethyl benzoxazole (**2**)was reacted with α,β-unsaturated nitriles(**14**) in ethanol and sodium ethoxide under reflux to afford 3-cyanopyridine -2(1H)-(thi)ones(**16a-f**) was carried out by different ways as elemental analysis, Spectroscopic data as well as chemical ways. Where as IR spectra of all obtained compounds revealed new observation band at 1244 and 1657 cm^{-1} region due to the presence of c=s and c=o functional groups in pyridine thions and pyridine ones respectively .Also, ^{1}H-NMR (DMSO-d6) of compound (**16e**) showed signals at 2.72 (a,3H,cH_3) 6.62-6.86 (br.s,2H,NH_2), 7.7.49-7.96 (m,8H,Ar-H) and 8.0 (s,1H,pyridine –NH). Moreover, mass spectrum of compound (**16e**) showed the expected molecular ion peak at m/z=371 with relative abundance of 8.9 corresponding to the correct molecular formula.

As another method to elucidate structure of compound (**16**), arylidene (**3**) was treated with cyano(thio)acetamidein ethanol in the presence of catalyst amount of sodium ethoxide to afford compounds (**16d,f**).both elemental and spectral data of compounds (**16d,f**) provided satisfying evidence for the proposed structures (c.f. Experimental).

EXPERMENTAL

All melting points are uncorrected and were determined on an electric melting point (Gallenkamp) 9200 A apparatus. IR spectra were recorded (KBr) on pye Unicam SP-1000 Spectrophotometer. 1H–NMR spectra were obtained from Varian Gemini 200 MHz spectrometer and chemical shifts are expressed in δ (ppm) using TMS as internal reference. Mass spectra were recorded on a GCMS–QP 1000 mass spectrometer opening at 70 eV. Microanalytical data were obtained from the microanalytical data center at Cairo University.

2-Arylidene benzoxazole–2–acetonitrile (3a–e).

Method A

Solution of (1,3–benzoxazole–2–yl) acetonitrile (1) (1.58g, 0.01 mole) in absolute ethanol (30 ml) was stirred with triethylamine or piperidine (seven drops) for 1h and the appropriate aldhyde (2) (0.01 mole) was added gradually to the reaction mixture and stirring was maintained for about 4 hrs. The formed crystalline precipitate was filtered off, washed with ethanol, dried and crystallized from the proper solvent to afford arylidenes (3a–e).

Method B

A mixture of (1,3–benzoxazole–2–yl) acetonitrile (1) (1.58g, 0.01 mole), aromatic or heterocyclic aldhyde (2) (0.01 mole) and piperidine (five drops) in ethanol (30 ml) was heated under reflux for 2 hrs. The reaction mixture was left aside at room temperature to cool, poured into an acidified crushed ice and filtered off. The obtained solid product was crystallized from suitable solvent to give arylidenes (3a–e).

(3a) yield (2.45g, 90%); (pet.ether); mp 163–65ºC. IR (cm1): 3083 (CH–arom), 2925 (CH–aliph.), 2221 (CN), 1606 (C=N), 1583 (C=C), 1030 (C-O-C); 1H–NMR (DMSO–d6): 7.33-7.48 (m, 3H, thiophene-H), 7.81-8.18 (m,4H, benzoxazole–H), 8.73 (s, 1H, =CH). MS m/z (%): 254 (M+ +2, 19.2), 253 (M+ +1, 13.1), 252 (M+ , not detected), 251 (M+ -1, 41.5), 196 (16.9), 179 (10.8), 158 (5.4), 63 (100). Ana. calcd. for C14H8N2OS (252.27) C66.65, H3.19, N11.10, S12.71. Found: C66.29, H3.09, N11.19, S12.85%.

(3b) yield (2.73g, 80%); (n–Hexane); mp 159-61ºC. IR (cm^{-1}): 3064 (CH–arom.), 2923 (CH-aliph.) 2227 (CN), 1601 (C=N), 1542 (C=C), 1031 (C-O-C); ^{1}H–NMR (DMSO–d6): 7.49–7.90 (m, 4H, benzoxazole–H), 8.14–8.18 (m, 4H, Ar–H), 8.57 (S, 1H, =CH). MS m/z (%): 328 (M^+ + 3, 0.1), 327 (M^+ + 2, 1.0), 326 (M^+ + 1, 4.2), 325 (M^+, 4.7), 324 (M^+ -1, 4.4), 245 (100), 123 (11.3), 63 (100). Ana. calcd. for $C_{16}H_9BrN_2O$ (325.16) C 59.10, H 2.79, Br 24.57, N 8.62. Found: C 59.07, H 2.70, Br 24.53, N 8.57%.

(3c) yield (2.53g, 85%); (pet. ether); mp 163–65ºC. IR (cm^{-1}): 3055 (CH–arom.), 2926 (CH–aliph), 2229 (CN), 1608 (C=N), 1583 (C=C), 1042 (C-O-C); MS m/z (%): 282 (M^+ + 2, 2.0), 281 (M^+ + 1, 3.7), 280 (M^+ , 8.1), 279 (M^+ -1, 7.3), 245 (66.1), 216 (12.16), 63 (100). Ana. Calcd for. $C_{16}H_9ClN_2O$ (280.71) C 68.46, H 3.23, Cl 12.63, N 9.98. Found: C 68.39, H 3.17, C l12.48, N 9.75%.

(3d) yield (2.60g, 85%); (EtOH); mp 160-62ºC. IR (cm^{-1}): 3067 (CH-arom.), 2919 (CH-aliph.), 2230 (CN), 1606 (C=N), 1549 (C=C), 1060 (C-O-C); MS m/z (%): 288 (M^+, not detected), 287 (M^+ -1, 60.0), 245 (80.0), 128 (66.7), 56 (100). Ana. calcd. for C_{19} H_{16} N_2O (288.34) C 79.14, H 5.59, N 9.72. Found: C 79.06, H 5.54, N 9.57%.

(3e) yield (2.76g, 90%); (Toluene); mp 246–48ºC. IR (cm^1): 3022 (CH–arom.), 2915 (CH–aliph), 2211 (CN), 1603 (C=N), 1570 (C=C), 1063 (C–O–C); ^{1}H–NMR (DMSO–d6): 3.13(s, 6H, 2CH3), 6.88–8.08 (m, 8H, Ar-H), 8.28 (s, 1H,=CH). MS m/z (%): 290 (M^+ + 1, 13.9), 289 (M^+, 89.7), 288 (M^+ -1, 100), 144 (11.8), 127 (7.5), 63 (86.9). Ana. Calcd. for. $C_{18}H_{15}N_3O$ (289.33) C 74.42, H 5.23, N 14.52. Found: C 74.55, H 5.18, N 14.44%.

2-(-2`H-Chromn-2`-oxo-3`-yl-(5`,6`-e)-napthyl)benzoxazole (5).

To a solution of (1,3-benzoxazole-2-yl) acetonitrile **(1)** (1.58g, 0.01 mole), ammonium acetate (7.79, 0.01 mole) in ethanol (40 ml), 2-hydroxyl napthaldhyde **(4)** (1.72g, 0.01 mole) was added and the reaction mixture was heated under reflux for 4 hrs. The reaction mixture was left to cool at room temperature, poured into crushed ice, filtered off and the finally obtained solid product was crystallized from toluene to afford coumarine derivative **(5)**.

(5) yield (2.31g, 70%); (Toluene); mp 242-44ºC. IR (cm^1): 3055 (CH-arom.), 2922 (CH-**aliph**), 1746 (C=O), 1622 (C=N), 1563 (C=C), 1030 (C-O-C); ^{1}H–NMR (DMSO–d6): 7.52–7.90 (m, 6H, Ar-H), 8.10–8.73 (m, 4H, benzoxazole–H), 9.92 (s, 1H, =CH). MS m/z (%): 314 (M^+ + 1, 8.0), 313 (M^+ , 27.7), 312 (M^+ -1, 8.8), 285 (19), 228 (13.9), 164 (18.2), 138 (10.2), 63 (100). Ana. Calcd. for. $C_{20}H_{11}NO_3$ (313.31) C 76.67, H 3.54, N 4.47. Found: C 76.65, H 3.47, N 4.45%.

α-(Benzoxazole-2`-yl)-β-alkyl (aryl) crotonitrile (7).

(1,3-Benzoxazole-2-yl) acetonitrile (1.58g, 0.01 mole) was stirred in ethanol (40 ml) containing catalytic amount of piperidine (0.5 ml, 0.02 mole) for l h, ketone **(6)** (0.01 mole) was added. The reaction mixture was heated under reflux, left to cool at room temperature, poured into an acidified crushed ice, filtered off and the finally obtained solid product was crystallized from ethanol to give crotonitrile derivatives **(7a-c)**.

(7a) yield (1.94g, 90%); (EtOH); mp 128–30ºC. IR (cm^{-1}): 3060 (CH–arom.), 2922 (CH–aliph), 2225 (CN), 1603 (C=N), 1550 (C=C), 1038 (C–O–C); ^{1}H–NMR (DMSO–d6): 2.40 (S, 3H, CH_3) 2.55 (s, 3H, CH3), 7.40–7.48 (s, 2H, benzoxazole–H), 7.78–7.83 (s, 2H, benzoxazole–H). MS m/z (%): 199 (M^+ + 1, 16.7), 198 (M^+, 50.5), 159 (25.0), 158 (58.3), 63 (100). Ana. Calcd. for. $C_{12}H_{10}N_2O$ (198.22) C 72.71, H 5.08, N 14.13. Found: C 72.70, H 5.01, N 14.9%.

(7b) yield (1.619, 70%); (EtOH); mp 66–68ºC. IR (cm^{-1}): 3057 (CH–arom.), 2975 (CH-aliph), 2225 (CN), 1612 (C=N), 1552 (C=C), 1045 (C–O–C); MS m/z (%): 213 (M^+ + 1, 10.06), 212 (M^+ , 79.8), 211 (M^+ -1, 34.6) 198 (5.8), 158 (29.8), 133 (39.4), 93 (22.1), 63 (100). Ana. Calcd. for. $C_{13}H_{12}N_2O$ (212.25) C 73.56, H 5.70, N 13.20. Found: C 73.49, H 5.65, N 13.14%.

(7c) yield (2.519, 80%); (EtOH); mp 88–90ºC. IR (cm^{-1}): 3105 (CH-arom.), 2935 (CH-aliph), 2210 (CN), 1604 (C=N), 1523 (C=C), 1106 (C-O-C). Ana. Calcd. for. $C_{17}H_{11}N_3O_3$ (305.29) C 66.88, H 3.63, N 13.76. Found: C 66.64, H 6.53, N 13.72%.

1-Amino-3-aryl-3H-pyrido[2,1–b]benzoxazole-2,4-dicarbo–nitriles (10a-d).

Method A

A mixture of arylidene malonoitrile **(8a–c)** (0.01 mole), (1,3-benzoxazole-2-yl) acetonitrile **(1)** (1.58g, 0.01 mole) in ethanol (30 ml) containing catalytic amount of piperidine (0.5 ml, 0.02 mole) were heated under reflux for 5 hrs. The reaction mixture was left to cool at room temperature, poured into an acidified crushed ice, filtered off, left to dry and the obtained solid product was crystallized from a suitable solvent to afford the substituted amino pyridine dicarbonitrile derivatives **(10a–c)**.

Method B

2-arylidene benzoxazole–2–acetonitrile **(3)** (0.01 mole), sodium ethoxide [prepared from sodium metal (0.46 g, 0.02 mole) in ethanol (30 ml)] and malonoitrile **(9)** (0.66 g, 0.01 mole) was heated under reflux for 7 hrs. The reaction mixture was left aside at room temperature to cool, poured into an acidified crushed ice and the precipitated solid product was filtered off, dried and crystallized from ethanol to give dicarbonitrile derivative **(10d)**.

(10a) yield (2.54 g, 80%); (EtOH); mp 180–82ºC. IR (cm^{-1}): 3327, 3219 (NH_2), 3085 (CH–arom.), 2210, 2340 (CN), 1611 (C=C), 1033 (C–O–C); MS m/z (%): 319 (M^+ + 1, 20.7), 318 (M^+ , 31.0), 291 (34.5), 226 (17.2), 194 (20.71), 127 (17.2), 63 (100). Ana. Calcd. for. $C_{17}H_{10}N_4OS$ (318.35): C 64.14, H 3.17, N 17.60, S 10.07. Found: C 64.11, H 3.12, N 17.48, S 10.10%.

(10b) yield (2.78 g, 80%); (Acetonitrile); mp 245-47ºC. IR (cm^{-1}): 3460, 3437 (NH_2), 3061 (CH-arom.), 2198, 1940 (CN), 1642 (C=C), 1039 (C–O–C); ^{1}H-NMR (DMSO–d_6): 5.23 (s, 2H, NH_2), 6.69 (s, 1H, pyridine-H), 7.32–7.53 (m, 4H, Ar-H), 7.66–7.78 (m, 4H, benzoxazole-H). MS m/z (%): 347 (M^+ + 1, 1.1), 346 (M^+ , 2.6), 345 (M^+ -1, 1.1), 309 (2.4), 279 (12.8), 245 (100), 216 (15.6), 158 (9.6), 126 (10.4), 63 (89.8). Ana. Calcd. for. $C_{19}H_{11}ClN_4O$ (346.77): C 65.81, H 3.20, Cl 10.22, N 16.16. Found: C 65.76, H 3.11, Cl 10.19, N 16.11%.

(10c) yield (3.19 g, 90%); (EtOH); mp 248–50ºC. IR (cm^{1}): 3433, 3313 (NH_2), 3060 (CH–arom.), 2922 (CH–aliph), 2195, 1941 (CN), 1598 (C=C), 1039 (C-O-C); MS m/z (%): 358 (M^+ + 3, 29.4), 355 (M^+ , not detected), 305 (100), 262 (17.6), 181 (29.4), 174 (23.5), 77 (94.1). Ana. Calcd. for. $C_{21}H_{17}N_5O$ (355.39): C 70.97, H 4.82, N 19.71. Found: C 70.78, H 4.73, N 19.64%.

(10d) yield (3.61g, 90%); (EtOH); mp 140–42ºC.IR (cm^{-1}): 3313, 3227 (NH_2), 3081 (CH–arom.), 2920 (CH–aliph), 2195, 1940 (CN), 1627 (C=C), 1040 (C–O–C); MS m/z (%): 402 (M^+, not detected), 401(M^+ -1, 2.9), 327 (9.8), 291 (2.9), 245 (46.8), 158 (24.9), 63 (100). Ana. Calcd for. $C_{22}H_{18}N_4O_4$ (402.4): C 65.66, H 4.51, N 13.92. Found: C 65.54, H 4.41, N 13.64%.

1-Amino-3-aryl-3H-pyrido[2,1-b)benzoxazole-4-carbonitrile-2-ethyl carboxylate (13a-d).

Method A

To a solution of (1,3-benzoxazole-2-yl) acetonitrile **(1)** (1.58 g, 0.01 mole), sodium ethoxide [prepared from sodium metal (0.46 g, 0.02 mole) in absolute ethanol (40 ml)], arylidene ethyl α-cyanocinnamate **(11)** (0.01 mole) was added, and the reaction mixture was heated under reflux for 10 hrs. The reaction mixture was left to cool at room temperature, poured into an acidified crushed ice, filtered off, dried and crystallized from ethanol to afford pyridine ethyl carboxylate derivatives **(13b–d)**.

Method B

2-Arylidene benzoxazole-2-acetonitrile **(3)** (0.01 mole), catalytic amount of sodium ethoxide [prepared from sodium metal (0.46 g, 0.02 mole) in ethanol (40 ml)] and ethyl cyanoacetate **(12)** (1.13 g, 0.01 mole) was heated under reflux for 10 hrs. The reaction mixture was left to cool, then poured into ice cold water mixture and neutralized with dilute hydrochloric acid. The solid product which

precipitate was collected by filtration, washed with ethanol, dried and crystallized from ethanol to afford compound **(13a)**.

(13a) yield (2.72 g, 70%); (EtOH); mp 175–77ºC. IR (cm^{-1}): 3431, 3330 (NH_2), 3042 (CH-arom.), 2978 (CH-aliph), 2220 (CN), 1704 (C=O), 1600 (C=C) and 1023 (C–O–C); MS m/z (%): 389 (M^+ , not detected), 386 (M^+ -3, 0.17), 305 (36.38), 275 (100), 232 (15.72), 181 (13.54), 149 (13.64). Ana. Calcd. for. $C_{22}H_{19}N_3O_4$ (389.40): C 67.86, H 4.92, N 10.79. Found: C 67.84, H 4.74, N 10.65%.

(13b) yield (2.37 g, 65%); (EtOH); mp 200–02ºC. IR (cm^{-1}): 3375, 3237 (NH2), 3103 (CH–arom.), 2923 (CH–aliph), 2221 (CN), 1662 (C=O), 1584 (C=C), 1034 (C–O–C); ^{1}H–NMR (DMSO–d_6): 1.28–135 (t, 3H, CH_3), 4.26–4.36 (q, 2H. CH2), 7.34–7.39 (m, 3H, thiophene-H), 8.07–8.23 (m, 5H, Ar-H), 8.62 (s, 2H, NH_2). MS m/z (%): 366 (M^+ + 1, 9.8), 365 (M+, 4.9), 289 (100), 288 (85.2), 144 (31.1), 63 (73.8). Ana. Calcd for. $C_{19}H_{15}N_3O_3S$ (365.41): C 62.45, H 4.14, N 11.56, S 8.78. Found: C 62.34, H 4.11, N 11.44, S 8.75%.

(13c) yield (3 g, 75%); (EtOH); mp 195–97ºC. IR (cm^{-1}): 3648, 3616 (NH_2), 3022 (CH–arom.), 2912 (CH–aliph), 2211 (CN), 1793 (C=O), 1605 (C=C), 1033 (C-O-C). Ana. Calcd. for. $C_{23}H_{22}N_4O_3$ (402.45): C 68.64, H 5.51, N 13.92. Found: C 68.34, H 5.24, N 13.69%.

(13d) yield (2.74 g, 70%); (EtOH); mp 180–82ºC. IR (cm^{-1}): 3389 (NH_2), 3059 (CH-arom.), 2930 (CH-aliph), 2218 (CN), 1742 (C=O), 1613 (C=C), 1046 (C-O-C). Ana. Calcd. for. $C_{21}H_{16}N_3O_3$ (393.82): C 64.05, H 4.09, Cl 9.00, N 10.67. Found: C 63.69, H 3.97, Cl 8.93, N 10.55%.

6–Amino-5-(benzoxazole-2-yl)-4-aryl-3-cyanopyridine-2 (1H)-thio) nes) (16a-f).

Method A

A mixture of α,β-unsaturated nitrile **(14)** (0.01 mole), (1,3-benzoxazole-2-yl) acetonitrile **(1)** (1.58 g, 0.01 mole), sodium ethoxide [prepared from sodium metal (0.46 g, 0.02 mole) in ethanol (40 ml)] was heated under reflux for 12 hrs. The reaction mixture was left to cool at room temperature, poured into an acidified crushed ice, filtered off and the finally obtained solid product was crystallized from a suitable solvent to afford the substituted 3-cyano-pyridine-2(1H)-(thi) ones **(16a-c,e)**.

Method B

Equimolar amount of 2-arylidene benzoxazole-2-acetonitrile (**3**), cyano (thio) a cetamide (**15**) in ethanol (40 ml) containing sodium metal (0.46 g, 0.02 mole) was heated under reflux for 12 hrs. The reaction mixture was treated as before to produce the corresponding 3-cyanopyridine-2(1H)-(thi)one derivatives (**16d,f**).

(16a) yield (3.16 g, 90%); (ACOH); 219–20ºC. IR (cm-1): 3329, 3206 (NH2, NH), 2216 (CN), 1614 (C=N), 1555 (C=C), 1244 (C=S), 1048 (C–O–C); 1H–NMR (DMSO–d6): 6.86–7.20 (br.s, 2H, NH2), 7.5 (s, 3H, thiophene-H), 7.73 (s, 4H, benzoxazole–H), 8.98 (s, 1H, pyridine–NH). MS m/z (%): 350 (M+, 12.5), 298 (12.5), 287 (18.1), 236 (100), 146 (50), 125 (51.4). Ana. Calcd. for C17H10N4OS3 (350.42): C 58.27, H 2.88, N 15.99, S 18.30. Found: C 58.18, H 2.75, N 15.86, S 18.09%.

(16b) yield (3.19 g, 85%); (EtOH); mp 195-97ºC. IR (cm^{-1}): 3358, 3250 (NH_2, NH), 2967 (CH-aliph.), 2211 (CN), 1608 (C=N), 1564 (C=C), 1247 (C=S), 1027 (C-O-C). Ana. Calcd. for $C_{20}H_{14}N_4O_2$ (372.42): C 64.16, H 3.77, N 14.96, S 8.56. Found: C 64.03, H 3.66, N 14.89, S 8.49%.

(16c) yield (2.96, 78%); (EtOH); mp 115-17ºC. IR (cm^{-1}): 3345, 3250 (NH_2, NH), 2212 (CN), 1613 (C=N), 1552 (C=C), 1242 (C=S), 1173 (C-O-C). Ana. Calcd. for $C_{19}H_{11}ClN_4OS$ (378.83): C 60.24, H 2.93, Cl 9.36, N 14.79, S 8.46. Found: C60.18, H 2.85, Cl 9.23, N 14.64, S 8.42%.

(16d) yield (3.11 g, 80%); (ACOH); mp 183-85ºC. IR (cm^{-1}): 3353, 3206 (NH_2, NH), 2918 (CH-aliph..), 2210 (CN), 1606 (C=N), 1560 (C=C), 1242 (C=S), 1193 (C-O-C); ^{1}H–NMR (DMSO–d6): 2.94-3.02 (s, 6H, $(CH_3)_2N$), 4.5 (br.s, 2H, NH_2), 6.87-7.73 (m, 8H, Ar-H), 9.98 (s, 1H, pyridine-NH). Ana. Calcd. for $C_{21}H_{17}N_5OS$ (387.46): C 65.10, H 4.42, N 18.08, S 8.28. Found: C 64.98, H 4.38, N 17.88, S 8.19%.

(16e) yield (2.23 g, 60%); (DMF); mp > 300°C. IR (cm^{-1}): 3370, 3157 (NH_2, NH), 2924 (CH–aliph.), 2210 (CN), 1657 (C=O), 1607 (C=N), 1523 (C=C), 1168 (C-O-C); ^{1}H–NMR (DMSO–d6): 2.72 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 6.62–6.86 (br.s, 2H. NH_2), 7.49-7.96 (m, 8H, Ar-H), 8.0 (s, 1H, pyridine–NH). MS m/z (%): 372 (M^+ + 1, 2.5), 371 (H^+, 8.9), 369 (M^+ -2, 2.5), 368 (M^+ -3, 10.1), 338 (29.1), 327 (25.3), 299 (12.7), 275 (26.6), 247 (19.0), 191 (12.7), 158 (24.1), 134 (26.6), 98 (60.8), 60 (100). Ana. Calcd. for $C_{21}H_{17}N_5OS$ (371.39): C

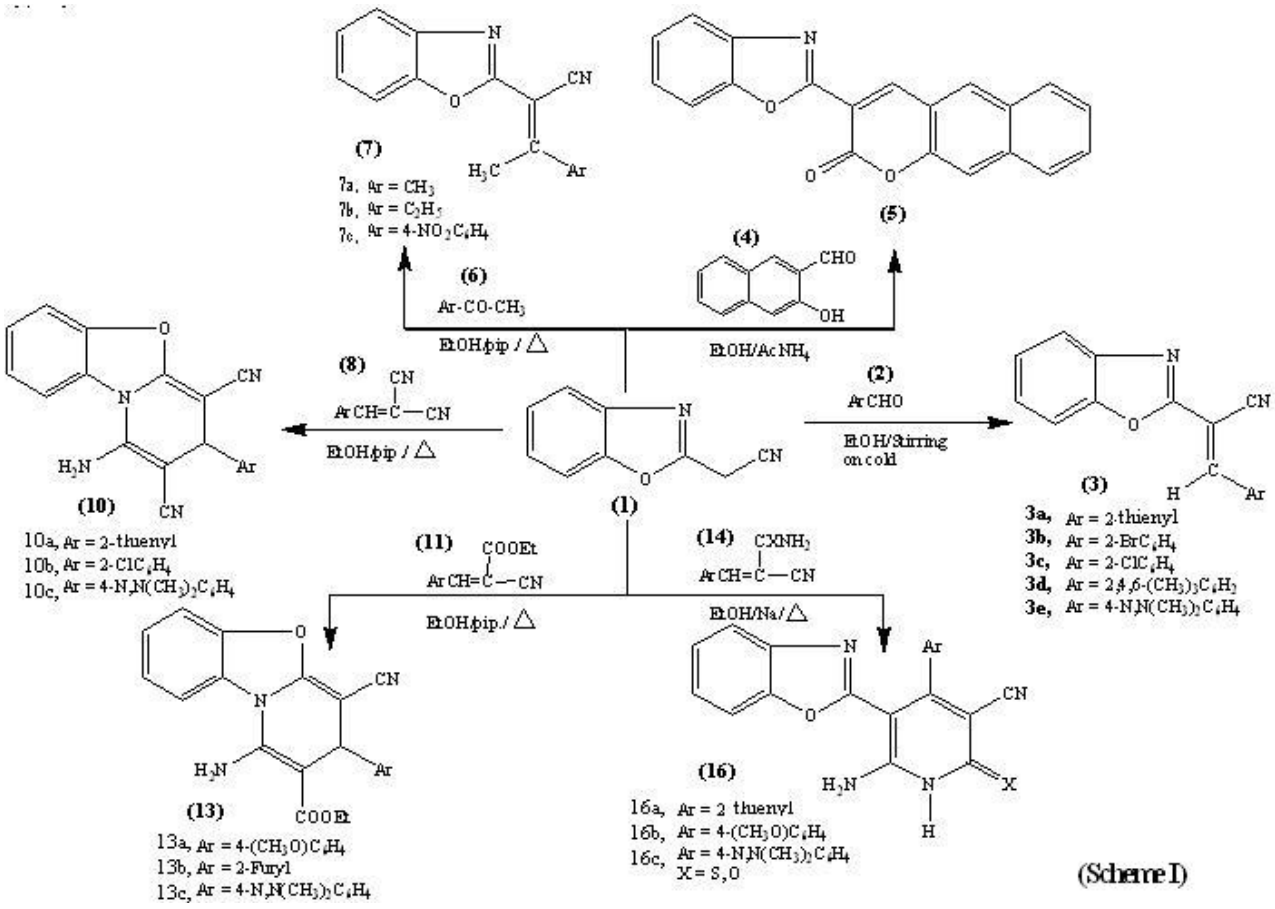
67.91, H 4.61, N 18.86. Found: C 67.88, H 4.56, N 18.79%.

(16f) yield (3.28 g, 90%); (EtOH/H_2O); mp 168–70ºC.
IR (cm^{-1}): 3743, 3357 (NH_2, NH), 2217 (CN), 1619 (C=O), 1572 (C=N), 1048 (C-O-C); ^{1}H–NMR (DMSO–d_6): 4.78 (s, 2H, NH_2), 6.95–7.68 (m, 8H, Ar–H), 11.90 (s, 1H, pyridine–NH). Ana. Calcd. for $C_{19}H_{11}ClN_4O_2$ (362.77): C 62.91, H 3.03, Cl 9.77, N 15.44. Found: C 62.75, H 3.11, Cl 9.65, N 15.37%.

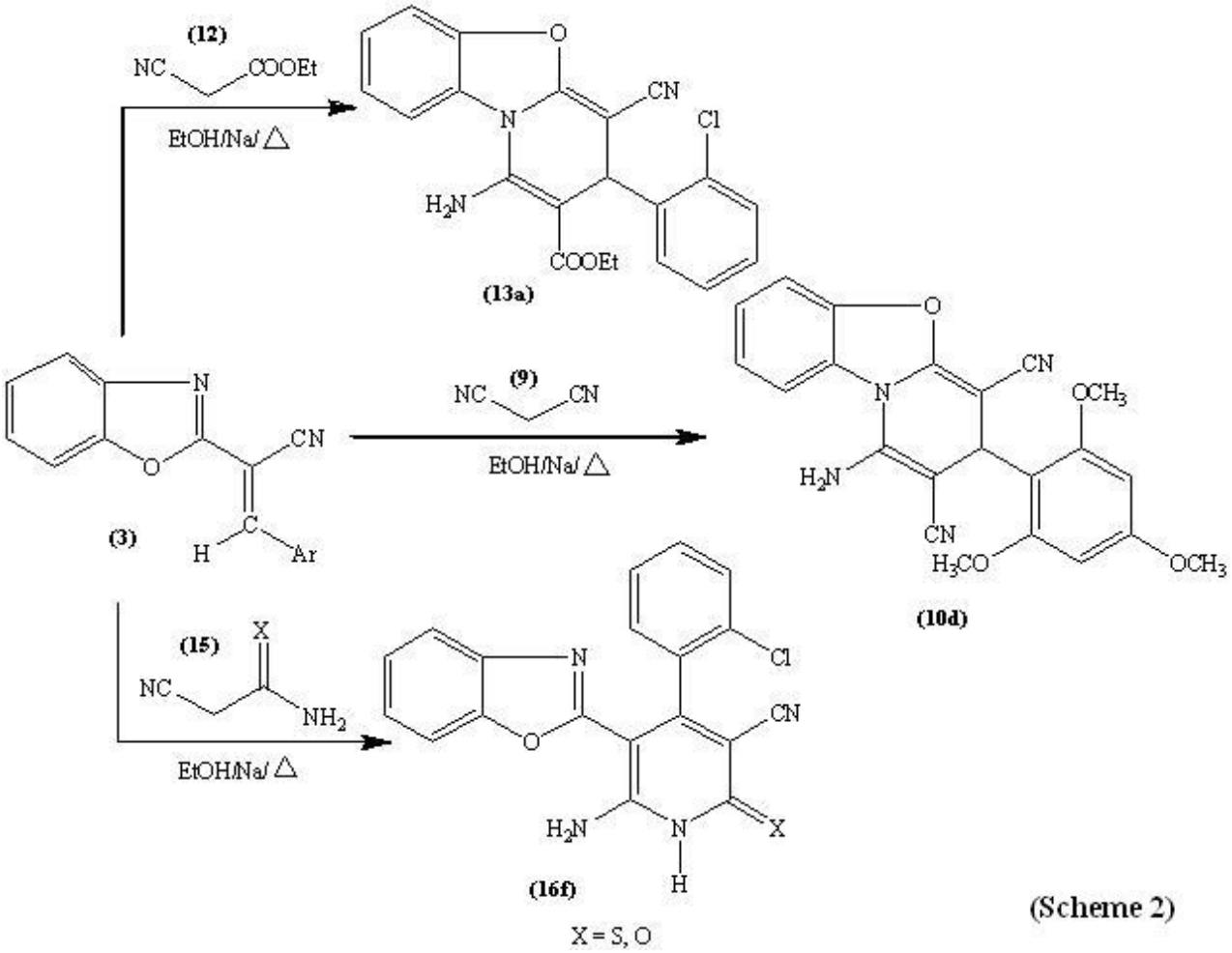
2- Biological study

The herbicidal evaluation of the newly synthesized compounds on wheat as pattern for monocotyledonous plants.

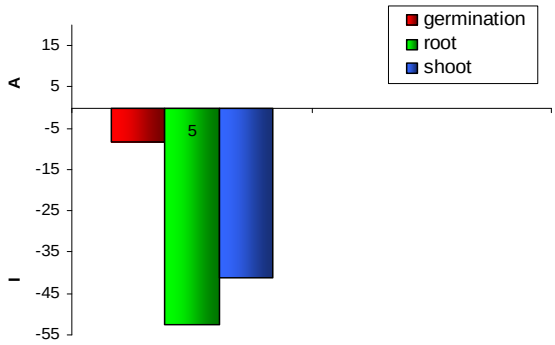
The herbicidal efficiency of the newly synthesized compounds and their derivatives was evaluated laboratory conditions against wheat as pattern for monocotyledonous plants with concentration of 2000 ppm. the percentages of inhibition of wheat growth parameters such as gerimination, root and shoot growth were taken as indicators to determine the herbicidal effect of these compounds .



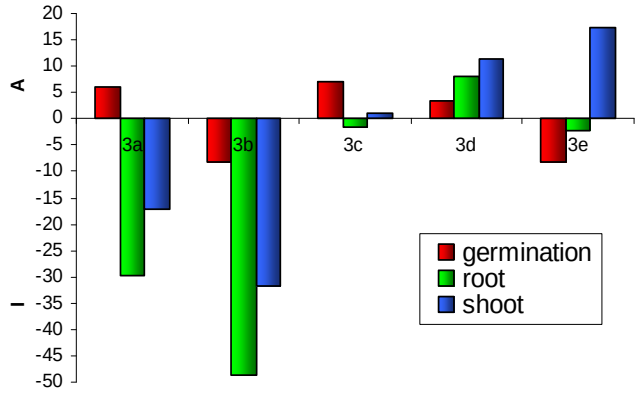
(Scheme I)



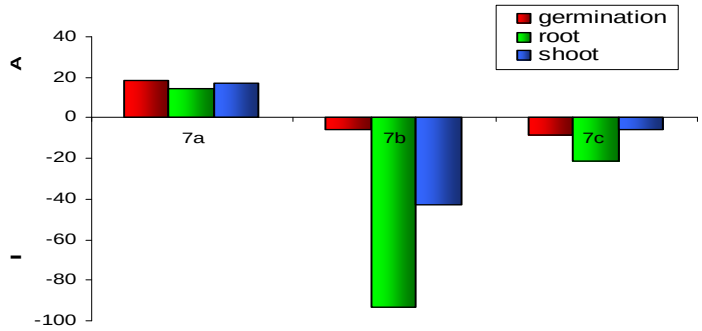
(Scheme 2)



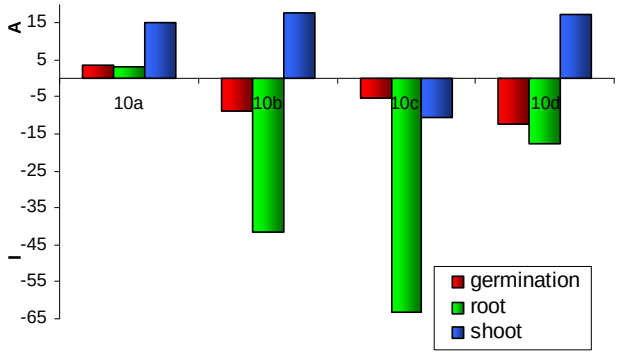
The effect of arylidenes (3a-e) on germination, root and shoot growth of wheat.



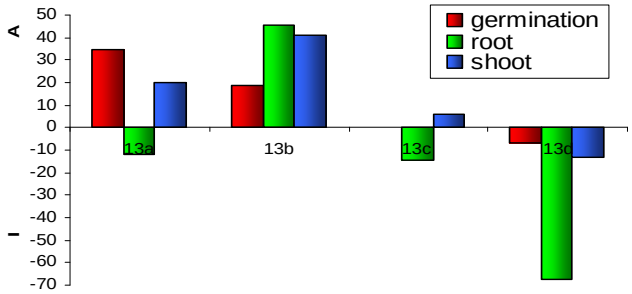
The effect of Coumarine (5) on germination, root and shoot growth of wheat.



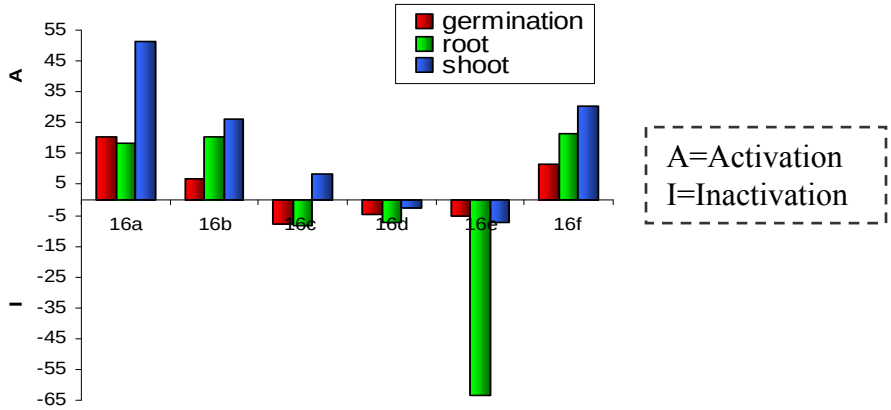
The effect of benzoxazoles (7a-c) on germination, root and shoot growth of wheat.



The effect of pyridobenzoxazoles (10a-d) on germination, root and shoot growth of wheat.



The effect of benzoxazoles (13a-d) on germination, root and shoot growth of wheat.



The effect of pyridine(thi)ones (16a-f) on germination, root and shoot growth of wheat.

According to figures (1-6) all compounds showed biological changes in growth parameters of wheat these changes were between activation to inhibition. Depending on the biological activity against growth parameters of wheat, the tested compounds could be classified as follow:

a) Compounds activated all growth parameters.
Compounds (**3b**),(**5**),(7b),(**7c**),(**10c**),(**13d**) and (**16e**) activated all growth parameters under study.

b) Compounds activated one or more of the growth parameters and inhibited the other parameter.
Compounds (**3e**),(**10d**) and(**16e**) activated gerimination and root growth, while compounds (**3c**),(1**3a**) and (**13c**) activated root growth and compound (**3a**) that activated both root and shoot growth.

c) Compounds inhibited all growth parameters.
Compounds (**16a**),(**16**b), (**16f**), (**13b**),(**10a**),(**7a**) and (**3b**) inhibited all growth parameters under study. Generally compounds that showed high inhibition percentage against all growth parameters were considered as promising compounds followed by that showed high inhibition effect against two growth parameters. So that, compounds (**16a**) ,(**16b**) ,(**16f**), (**13b**) and (**13a**) were considered as promising herbicide active ingredients . on the other hand all promising compounds except (**13b**) and (**13a**) were more effective against shoot growth than the other

growth parameters, whereas compounds (**13b**) and (**13a**) were more effective against root and gerimination respectively than the other growth parameters.

According to the obtained data , differences were found in activity between derivatives of the same compound. This differences may be explained on the basis of substitution, for example the presence of thienyl group, 2-chlorophenyl and methoxy phenyl substituents in (**16a**),(**16b**),(**16f**) respectively inhibited all growth parameters , while the presence of dimethyl amino phenyl in derivatives (**16a**) and (**16e**) resulted in an activation of all growth parameters.

From another point of view there is a relationship between some substituents and the herbicidal activity of the synthesized compounds as in case of compounds (**10a**),(**13b**) and (**16f**) due to the presence of thienyl group and as in compounds (**10a**) and (**10f**) due to the presence of 2-chorophenyl.

Conclusion

1. All synthesized compounds showed biological activity against growth parameters of wheat, the effect that was between activation to inhibition.
2. Compounds (**16a**),(**16b**),(**16f**) and (**13b**) were considered as promising herbicide active ingredients. These compounds caused high inhibition effect on all or on two from the growth parameters under study
3. Substituents play an important role in effectiveness of different derivatives of the same compound
4. There is a relationship between some Substituents and the herbicidal efficiency of the synthesized compounds including them such as thienyl and 2-chorophenyl groups .

Eperimental

Evaluation of Herbicidal Efficiency of the Newly synthesized compounds. Bioassay. Under laboratory conditions.

- Seed germination, root and shoot growth inhibition were carried out according to the procedure described by Powel and Spencer [34], some modifications were made for this work as described below.
- Serial concentrations from each compound was prepared by dissolving it in dimethyl sulfoxide and dilution with water. The calculated amount from each concentration was pipetted on thirty seeds of wheat as a test plant and agitated to coat the seed surface. Each ten seeds were transferred to petridish (90 mm diameter), lined with a dry filter paper and left at 25°C without led to grant solvent evaporation. After that, 6 ml distilled water was pipetted on the filter paper, Petridish was sealed with (PVC) electrical insulting tape. After complete germination of control (Petridishes containing untreated seeds), the number of germinated and non germinated seeds and radical length were recorded. Three replicates were done for each treatment.

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