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Synthesis of novel 2-propenoyl amides, esters, heterocyclic compounds and their screening as antifungal and antibacterial agents

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ABSTRACT

Compound, 2-cyano-3-(2′,4′-dichlorophenyl)-2-prpoenoyl chloride, **3**, was reacted with nitrogen, sulfur, and oxygen nucleophilic reagents to give new 2-propenoyl amide and ester derivatives. Some of these derivatives were cyclized under the reaction conditions and/or with $POCl_3$ or Ac_2O to give new derivatives of heterocyclic systems. Some of these compounds were tested as antibacterial and antifungal agents.

1. Introduction

The recent wide importance of 2-propenoylamides [1,2], 2-propenoates [3-6], besides, the interesting biological and pharmacological activities of many heterocyclic systems, like, benzoxazoles [7], pyrimidines [8], pyridopyrimidines [9], oxazoles [10], benzoxazines [11,12], oxadiazoles [13] and pyrazoles [14] encourage the authors to gather these moieties hoping to produce a valuable new compounds of expected antibacterial and antifungal activity. We report here the synthesis of 2-propenoyl amides, 2-propenoyl esters and some heterocyclic systems by developed, simple convenient and efficient procedure. Also this modified method is fast, cheap and unequivocal preparation with improved yields.

2. Experimental

2.1. Instrumentation

Melting points were taken on Griffin and Geory melting point apparatus and are uncorrected. FT-IR spectra were recorded on Pye Unicam SP 1200 spectrophotometer using the KBr wafer technique. ^{1}H NMR spectra were determined on Varian Gemini 300 MHz using TMS as internal standard. All chemical shifts (δ) are expressed in ppm. All the NH or OH protons are exchangeable on addition of D_2O. The elemental analyses were investigated by Elemental analyzer Vario EL III.

2.2. Syntheses

2.2.1. 2-cyano-3-(2′,4′-dichlorophenyl)acryloyl chloride (3)

A mixture of **2** (10 g) and thionyl chloride (15 mL) was heated on water bath for 3 hours. The excess thionyl chloride was distilled under reduced pressure; the solid separated was collected, triturated with petroleum ether 40-60 °C, dried and recrystallized from benzene to give **3** (Scheme 1). Yellow. Yield: 90%. M.p.: 88-90 °C. FT-IR (KBr, ν, cm^{-1}): 2205 (C≡N), 1738 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.39 (s, 1H, =CH), 8.04 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.77 (s, 1H, Ar-H) 7.60 (d, 1H, *J* = 8.4 Hz, Ar-H). Anal. calcd. for $C_{10}H_4Cl_3NO$: C, 46.42; H, 1.55; N, 5.38. Found: C, 45.89; H, 1.51; N, 5.34%.

2.2.2. General procedure for the formation of compounds 4-9

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol), and phenol, 4-chlorothiophenol, 4-methoxyaniline, 4-chloroaniline, 4-methylaniline (0.005 mol) in dry benzene (50 mL) was refluxed for 2 hours. The solid separated was filtered, washed with water (80 mL), dried and recrystallized from toluene to give **4**-**9**, respectively (Scheme 2).

Phenyl 2-cyano-3-(2,4-dichlorophenyl) acrylate (**4**): Yellow. Yield: 75%. M.p.: 120-122 °C. FT-IR (KBr, ν, cm^{-1}): 2232 (C≡N), 1743 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.37 (s 1H, *=CH*), 8.16 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.98 (s, 1H, *Ar-H*) 7.75 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.75-7.12 (m, 5H, *Ar-H*). Anal. calcd. for $C_{16}H_9Cl_2NO_2$: C, 60.40; H, 2.85; N, 4.40. Found: C, 60.44; H, 2.81; N, 3.92%.

S(4-Chlorophenyl)-2-cyano-3-(2,4-dichlorophenyl) prop-2-enethioate (**5**): Yellow. Yield: 82%. M.p.: 162-163 °C. ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.34 (s, 1H, *=CH*), 8.03 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.83 (s, 1H, *Ar-H*), 7.62 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.62-7.02 (m, 4H, *Ar-H*). Anal. calcd. for $C_{16}H_8Cl_3NOS$: C, 52.13; H, 2.19; N, 3.80. Found: C, 52.15; H, 2.22; N, 3.84%.

2-Cyano-3-(2,4-dichlorophenyl)-N-(4-methoxyphenyl) acrylamide (**6**): Yellow. Yield: 80%. M.p.: 218-220 °C. FT-IR (KBr, ν, cm^{-1}): 3355 (NH), 2222 (C≡N), 1686 (C=O).

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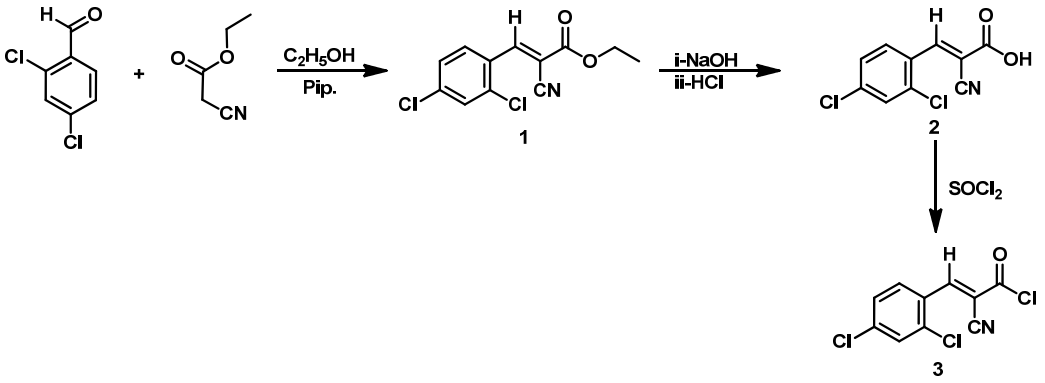


Scheme 1

^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.35 (s, 1H, *NH*), 8.36 (s, 1H, *=CH*), 8.06 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.88 (s, 1H, *Ar-H*), 7.69 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.58 (d, 2H, *J* = 8.4 Hz, *Ar-H*), 6.9 (d, 2H, *J* = 8.4, *Ar-H*), 3.74 (s, 3H, *OCH$_3$*). Anal. calcd. for $C_{17}H_{12}Cl_2N_2O_2$: C, 58.81; H, 3.48; N, 8.07. Found: C, 58.85; H, 3.56; N, 7.98%.

2-Cyano-3-(2,4-dichlorophenyl)-N-4-tolylacrylamide (**7**): Yellow. Yield: 90%. M.p.: 198-200 °C. FT-IR (KBr, ν, cm^{-1}): 3342 (NH), 2217 (C≡N), 1682 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.42 (s, 1H, *NH*), 8.36 (s, 1H, *=CH*), 8.0 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.89 (s, 1H, *Ar-H*), 7.69 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.55 (d, 2H, *J* = 8.4 Hz, *Ar-H*), 7.18 (d, 2H, *J* = 8.4 Hz, *Ar-H*), 2.39 (s, 3H, *CH$_3$*). Anal. calcd. for $C_{17}H_{12}Cl_2N_2O$: C, 61.65; H, 3.65; N, 8.46. Found: C, 61.60; H, 3.67; N, 8.12%.

N-(4-chlorophenyl)-2-cyano-3-(2,4-dichlorophenyl) acrylamide (**8**): Yellow. Yield: 80%. M.p.: 158-159 °C. FT-IR (KBr, ν, cm^{-1}): 3323 (NH), 2228 (C≡N), 1687 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.64 (s, 1H, *NH*), 8.39 (s 1H, *=CH*), 8.06 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.89 (s, 1H, *Ar-H*), 7.72 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.70-7.42 (m, 4H, *Ar-H*). Anal. calcd. for $C_{16}H_9Cl_3N_2O$: C, 54.65; H, 2.58; N, 7.97. Found: C, 54.61; H, 2.62; N, 8.10%.

2-Cyano-3-(2,4-dichlorophenyl)-N-(pyridine-3-yl) acrylamide (**9**): Yellow. Yield: 75%. M.p.: 176-178 °C. FT-IR (KBr, ν, cm^{-1}): 3338 (NH), 2225 (C≡N), 1692 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 9.64 (s, 1H, *NH*), 8.42 (s 1H, *=CH*), 8.09 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.98 (s, 1H, *Ar-H*), 7.70 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 7.70-7.42 (m, 4H, *Ar-H*). Anal. calcd. for $C_{15}H_9Cl_2N_3O$: C, 56.63; H, 2.85; N, 13.21. Found: C, 56.59; H, 2.79; N, 13.02%.

2.2.3. N'-(2-Cyano-3-(2,4-dichlorophenyl)acryloyl) benzohydrazide (10)

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol) and benzoyl hydrazine (0.68 g, 0.005 mol) in dry benzene (50 mL) was stired for an hour. The solid separated was filtered, washed with water (80 mL), dried and recrystallized from toluene to give 10 (Scheme 2). Yellow. Yield: 86%. M.p.: 180-181 °C. FT-IR (KBr, ν, cm^{-1}): 3188, 3209 (NH), 2218 (C≡N), 1675 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.81 (s, 1H, *N*H), 10.64 (s, 1H, *NH*), 8.4 (s, 1H, *=CH*), 7.89-7.49 (m, 8H *Ar-H*). Anal. calcd. for $C_{17}H_{11}Cl_2N_3O_2$: C, 56.69; H, 3.08; N, 11.67. Found: C, 56.65; H, 2.99; N, 11.61%.

2.2.4. (E)-3-(2,4-ichlorophenyl)-2-(5-phenyl-1,3,4-oxadiazol-2-yl)acrylonitrile (11)

A mixture of **10** (1 g) and phosphorus oxychloride (10 mL) was heated on water bath for 6 hours. After cooling the reaction mixture was poured on crushed ice (20 g). The solid separated was filtered, washed with water (50 mL), dried and recrystallized ftom ethanol to give **11** (Scheme 2). Green. Yield: 75%. M.p.: 176-178 °C. FT-IR (KBr, ν, cm^{-1}): 2205 (C≡N). ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 8.56 (s, 1H, *Ar-H*) 8.27 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 8.14 (d, 1H, *J* = 8.1 Hz, *Ar-H*), 7.54-7.43 (m, 6H, *Ar-H, 5ph+1aryl*). Anal. calcd. for $C_{17}H_9Cl_2N_3O$: C, 59.67; H, 2.65; N, 12.28. Found: C, 59.72; H, 2.61; N, 12.33%.

2.2.5. 6-(2,4-Dichlorophenyl)-4-hydroxy-1-methyl-2-thioxo-1,2-dihydropyrimidine- 5-carbonitrile (12)

N-methylthiourea (0.45 g, 0.005 mol) was added to a solution of **3** (1.30 g, 0.005 mol) in dry benzene (50 mL) and triethylamine (0.505 g, 0.005 mol), the reaction mixture was refluxed for one hour. The solid formed was collected, washed with water (80 mL), dried and recrystallized from ethanol to give **12** (Scheme 2). Yellow. Yield: 80%. M.p.: 186-188 °C. FT-IR (KBr, ν, cm^{-1}): 3449 (OH), 2211 (C≡N), 1633 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.9 (d, 1H, *J* = 7.9 Hz, *Ar-H*), 7.8 (d, 1H, *J* = 7.8 Hz, *Ar-H*), 7.76 (s, 1H, *Ar-H*), 3.79 (s, 3H, *NCH$_3$*), 1.6 (s, 1H, *OH*). Anal. calcd. for $C_{12}H_7Cl_2N_3OS$: C, 46.17; H, 2.26; N, 13.46. Found: C, 45.81; H, 2.81; N, 13.43%.

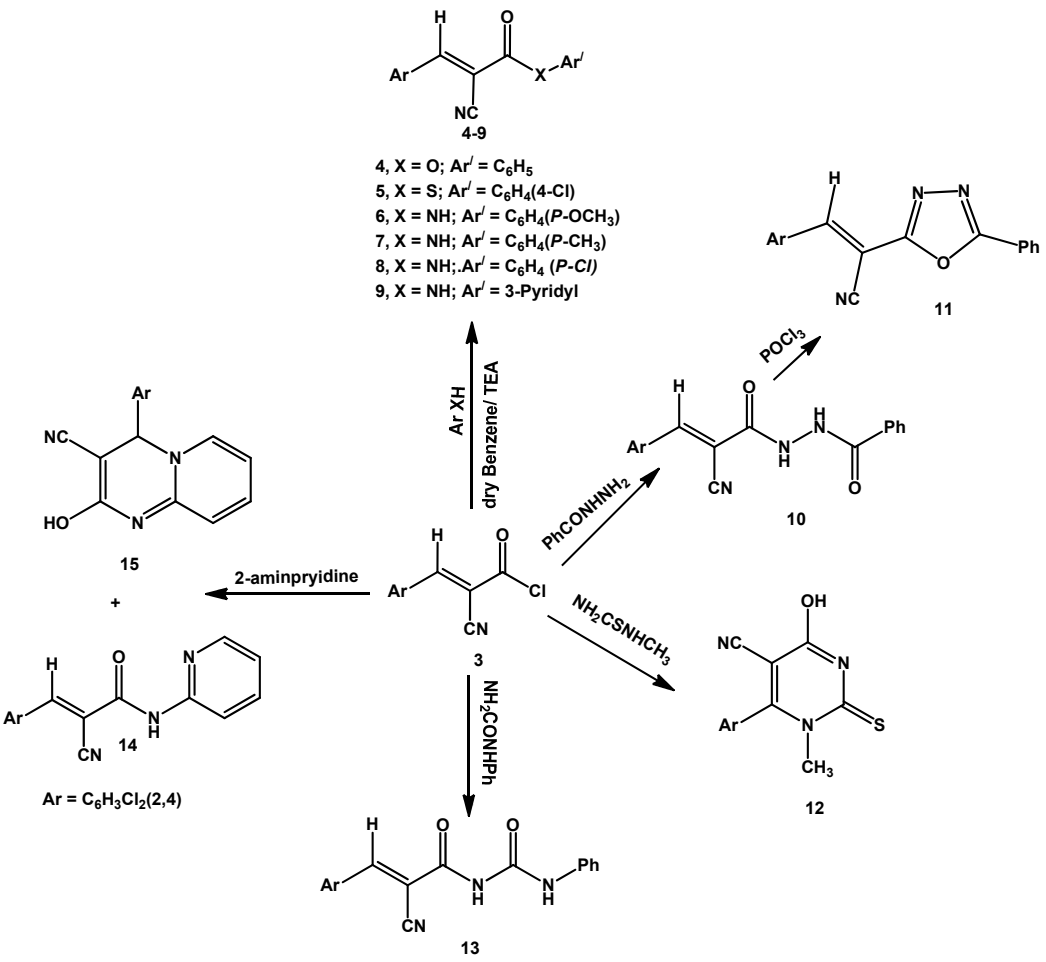
2.2.6. 1-(2-Cyano-3-(2,4-dichlorophenyl)acryloyl)-3-phenylurea (13)

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol) and phenylurea (0.681 g), 0.005 mol) in dry benzene (50 mL) was stirred for 2 hours. The separated solid was filtered, washed with water (80 mL), dried and recrystallized from benzene to give **13** (Scheme 2). Yellow. Yield: 60%. M.p.: 180-181 °C. FT-IR (KBr, ν, cm^{-1}): 3231, 3129 (NH), 2228 (C≡N), 1704, 1660 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.23 (s, 1H, *NH*,), 8.5 (s, 1H, *=CH*), 8.06-6.53 (m, 8H, *Ar*-H), 5.8 (s, 1H, *NH*). Anal. calcd. for $C_{17}H_{11}Cl_2N_3O_2$: C, 56.69; H, 3.08; N, 11.67. Found: C, 56.62; H, 3.12; N, 11.59%.

2.2.7. Synthesis of compounds 14 and 15

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol) and 2-aminopyridine (0.47 g, 0.005 mol) in dry benzene (50 mL) was stirred for 2 hours. The separated solid was filtered, washed with water, dried and recrystallized from benzene to give **14** and then from ethanol to give **15** (Scheme 2).

2-Cyano-3-(2,4-dichlorophenyl)-N-(pyridin-2-yl) acrylamide (**14**): Yellow. Yield: 90%. M.p.: 210-211 °C. FT-IR (KBr, ν, cm^{-1}): 3305 (NH), 2216 (C≡N), 1669 (C=O). ^{1}H-NMR (300 MHz, DMSO-d_6, δ, ppm): 8.3 (s, 1H, *=CH*), 8.07 (d, 1H, *J* = 8.4 Hz, *Ar-H*), 6.03 (m, 3H, *Ar-H*), 7.6 (s, 1H, *NH*) 6.7-6.6 (m, 3H, *Ar-H*). Anal. calcd. for $C_{15}H_9Cl_2N_3O$: C, 56.63; H, 2.85; N, 13.21. Found: C, 56.59; H, 2.89; N, 13.28%.



Scheme 2

4-(2,4-dichlorophenyl)-2-hydroxy-4H-pyrimido[1,2-a] pyrimidine-3-carbonitrile (**15**): Yellow. Yield: 65%. M.p.: 152-153 °C. FT-IR (KBr, ν, cm^{-1}): 3444 (NH), 2186 (C≡N), 1681 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 9.63 (s, 1H, *OH*), 8.56 (d, 1H, *J* = 6.9 Hz, *Ar-H*), 7.8-6.8 (m, 6H, *Ar-H*), 5.9 (s, H, *benzylic H*). Anal. calcd. for $C_{15}H_9Cl_2N_3O$: C, 56.63; H, 2.85; N, 13.21. Found: C, 56.56; H, 2.93; N, 13.21%.

2.2.8. Synthesis of compounds 16 and 17

Thiosemicarbazide (0.45 g, 0.005 mol) was added to a solution of **3** (1.30 g, 0.005 mol) in dioxane (20 mL) and triethylamine (0.505 g, 0.005 mol). The reaction mixture was refluxed for an hour. The solid formed was ammonium salt, the filtrate was concentrated, and the remaining semisolid was recrystallized from benzene to give **16** and then from benzene/ethanol mixture to give **17** (Scheme 3)

1-(2,4-Dichlorobenzylidene)thiosemicarbazide ***(16)*** the structure was confirmed by m.p. with an authentic sample [15].

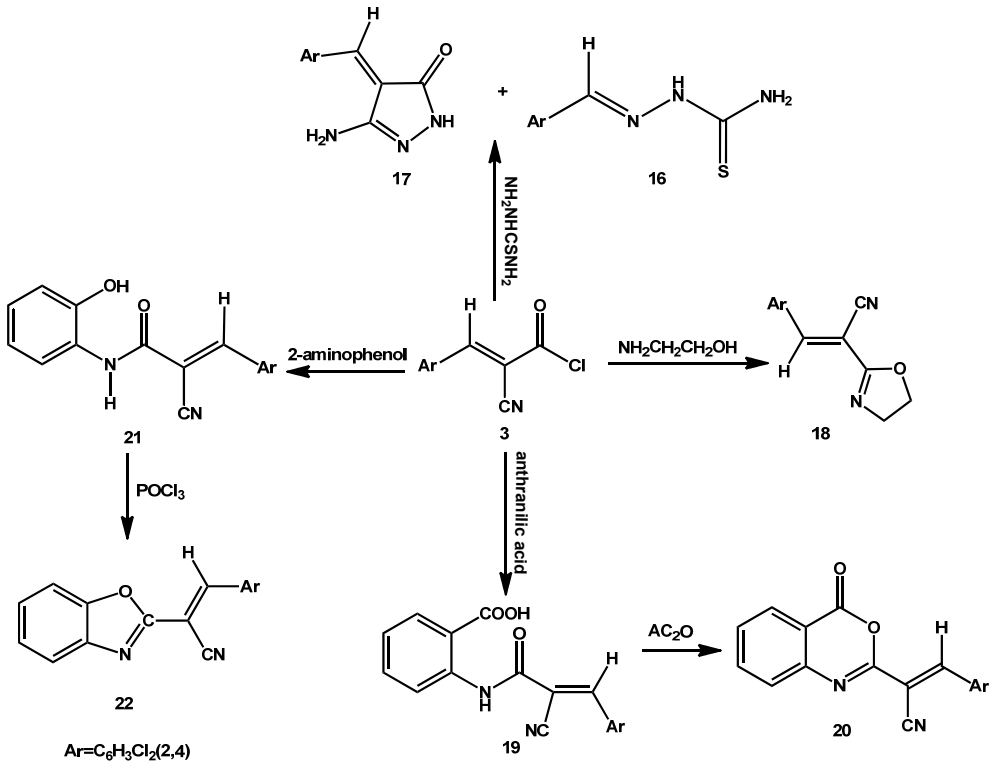
4-(2,4-dichlorobenzylidene)-3-amino-1H-pyrazol-5-(4H)-one (**17**): Reddish brown. Yield: 84%. M.p.: 150-151 °C. FT-IR (KBr, ν, cm^{-1}): 3179, 3263, 3369 (NH, NH_2), 1645 (C=O), 1619(C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.54 (s, 1H, *NH*), 8.35 (s, 1H, *=CH*), 7.4-7.2 (m, 3H, *Ar-H*), 4.4 (s, 2H, *NH_2*). Anal. calcd. for $C_{10}H_7Cl_2N_3O$: C, 46.90; H, 2.76; N, 16.41. Found: C, 46.85; H, 2.71; N, 16.38%.

2.2.9. 3-(2,4-Dichlorophenyl)-2-(4,5-dihydrooxazol-2-yl) acrylonitrile (18)

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol) and ethanolamine (0.305 g, 0.005 mol) in dry benzene (50 mL) was stirred for 2 hours. The separated solid was filtered, washed with water (50 mL), dried and recrystallized from ethanol to give **18** (Scheme 3): Yellow. Yield: 90%. M.p.: 220-222 °C. FT-IR (KBr, ν, cm^{-1}): 2209 (C≡N), 1642 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.77 (s, 1H, *=CH*), 7.69-7.40 (m, 3H, *Ar-H*), 3.61 (t, 2H, *J* = 6.90 Hz, *CH_2-O*), 1.84 (t, 2H, *J* = 6.90 Hz, N-*CH_2*). Anal. calcd. for $C_{12}H_8Cl_2N_2O$: C, 53.96; H, 3.02; N, 10.49. Found: C, 53.89; H, 2.98; N, 10.51%.

2.2.10. 2-(2-Cyano-3-(2,4-dichlorophenyl)acrylamido) benzoic acid (19)

A mixture of **3** (2.60 g, 0.01 mol), triethylamine (1.01 g, 0.01 mol) and anthranilic acid (1.37 g, 0.01 mol) in dry benzene (100 mL) was refluxed for an hour. The solid separated was filtered, washed with water (100 mL), dried and recrystallized from benzento give **19** (Scheme 3): Brown. Yield: 84%. M.p.: 172-173 °C. FT-IR (KBr, ν, cm^{-1}): 3359 (NH), 2220 (C≡N), 1689 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.75 (s, 1H, *COOH*), 8.39 (s, 1H, *=CH*), 8.07-7.94 (m, 4H, *Ar-H*), 7.89 (s, 1H, *NH*), 7.81-7.62 (m, 3H, *Ar-H*). Anal. calcd. for $C_{17}H_{10}Cl_2N_2O_3$: C, 56.53; H, 2.79; N, 7.76. Found: C, 56.68; H, 2.82; N, 7.68%.



Scheme 3

2.2.11. 3-(2,4-Dichlorophenyl)-2-(4-oxo-4H-benzo[d][1,3] oxazin-2-yl)acrylonitrile (20)

A mixture of **19** (2 g) and freshly distilled acetic anhydride (5 mL) was heated on a water bath for 6 hours. After cooling the solid separated was collected, washed with dry petroleum ether (40-60 °C), dried and recrystallized from ethanol to give **20** (Scheme 3): Green . Yield: 85%. M.p.: 172-173 °C. FT-IR (KBr, ν, cm^{-1}): 2205 (C≡N), 1758 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.52 (s, 1H, *=CH*), 8.21-7.94 (m, 3H, *Ar*-H), 7.93-7.96 (m, 4H, *Ar-H*). Anal. calcd. for $C_{17}H_8Cl_2N_2O_2$: C, 59.50; H, 2.35; N, 8.16. Found: C, 60.01; H, 2.33; N, 8.19%.

2.2.12. 2-Cyano-3-(2,4-dichlorophenyl)-N-(2-hydroxy phenyl) acrylamide (21)

A mixture of **3** (1.30 g, 0.005 mol), triethylamine (0.505 g, 0.005 mol) and 2-amino phenol (0.54 g, 0.005 mol) in dry benzene (50 mL) was refluxed for an hour. The solid separated was filtered, washed with water (80 mL), dried and recrystallized from toluene to give **21** (Scheme 3) Yellow. Yield: 92%. M.p.: 108-110 °C. FT-IR (KBr, ν, cm^{-1}): 3247, 3353 (NH), 2213 (C≡N), 1669 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.15 (s, 1H, *NH*), 9.4 (s, 1H, *OH*), 8.43 (s, 1H, *=CH*), 8.10-6.80 (m, 7H, *Ar-H*). Anal. calcd. for $C_{16}H_{10}Cl_2N_2O_2$: C, 57.68; H, 3.03; N, 8.41. Found: C, 57.56; H, 2.98; N, 8.32%.

2.2.13. 2-(Benzo[d]oxazol-2-yl)-3-(2,4-dichlorophenyl) acrylonitrile (22)

A mixture of **21** (1 g) and phosphorus oxychloride (10 mL) was heated on water bath for 6 hours. After cooling the reaction mixture was poured on crushed ice (20 g). The solid separated was filtered, washed with water (50 mL), dried and recrystallized from ethanol to give **22** (Scheme 3). Green. Yield: 82%. M.p.: 150-152 °C. FT-IR (KBr, ν, cm^{-1}): 2205 (C≡N) and 1622 (C=N) ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 8.6-7.8 (m, 3H, *Ar-H*), 7.43- 7.40 (m, 4H, *Ar-H*), 7.25 (s, 1H, *=CH*). Anal. calcd. for $C_{16}H_8Cl_2N_2O$: C, 60.98; H, 2.56; N, 8.89. Found: C, 60.86; H, 2.51; N, 8.81%.

2.3. Antimicrobial and antifungal activities

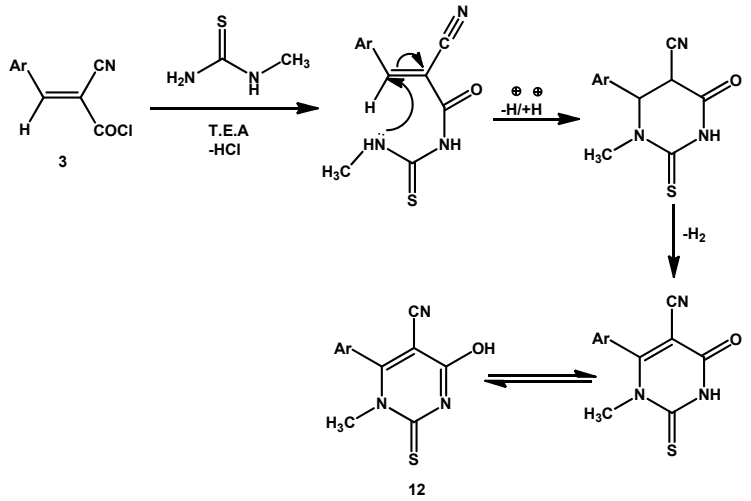
A filter paper sterilized disc saturated with measured quantity of the sample with concentration of 20 mg/mL was placed on a plate containing solid bacterial medium (nutrient agar broth) or fungal medium (Dox's medium) which was heavily seeded with the spore suspension of the tested organism. After incubation, the diameter of the clear zone of inhibition surrounding the sample was taken as a measure of the inhibitory power of the sample against the particular test organism [16-19].

The selected samples were screened against Gram-positive; *Staphylococcus aureus* and Gram-negative *Escherichia coli*. Antifungal activity was tested using *Aspergillus flavus* and *Candida albicans* (Table 1).

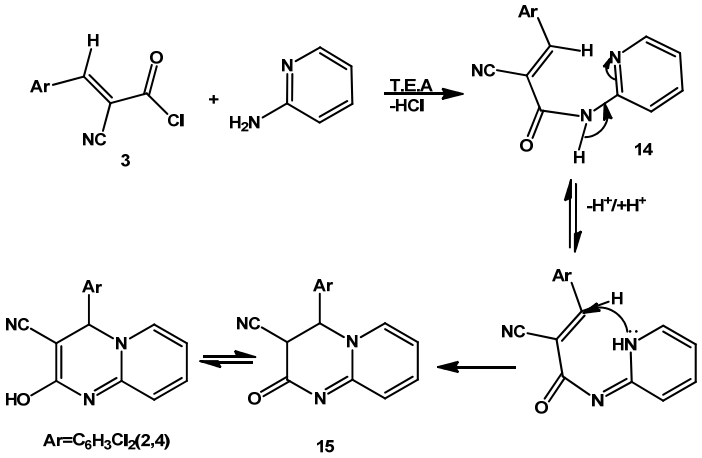
Table 1. The antimicrobial and antifungal activities of the selected compounds*.

Sample	*Escherichia coli*	*Staphylococcus aureus*	*Aspergillus flavus*	*Candida albicans*
4	13	12	0	0
5	16	20	0	0
6	10	13	0	0
7	13	13	0	0
9	10	11	0	0
10	17	15	0	13
12	19	18	0	12
17	13	15	0	0
Tetracycline	32	30	---	---
Amphotericin B	---	---	16	18
DMSO	0	0	0	0

* Solvent: Chloroform; 0: no activity (inhibition zone less than 7mm); 7-10 weak activity; 11-15 moderate activity; more than 15 strong activity.



Scheme 4



Scheme 5

3. Results and discussion

In continuation of our efforts to study the reactivity of 2-propenoyl chlorides towards some nitrogen and oxygen nucleophilic reagents [20-23], we reported herein, the synthesis of a new compound, *(E)*2-cyano-3-(2,4-dichloro phenyl)acryloyl chloride **3** via the common route condensation of 2,4-dichlorobenzaldehyde with ethyl cyanoacetate in the presence of piperidine, to give the corresponding *(E)*-ethyl 2-cyano-3-(2,4-dichlorophenyl) acrylate, **1**, [24]. Hydrolysis of **1** in alcoholic solution of sodium hydroxide (1:1 mole) gave *(E)*-2-cyano-3-(2,4-dichlorophenyl)acrylic acid, **2**, [25]. Refluxing the acid **2** with thionyl chloride yielded the new acryloyl chloride derivative **3** in good yield (Scheme 1).

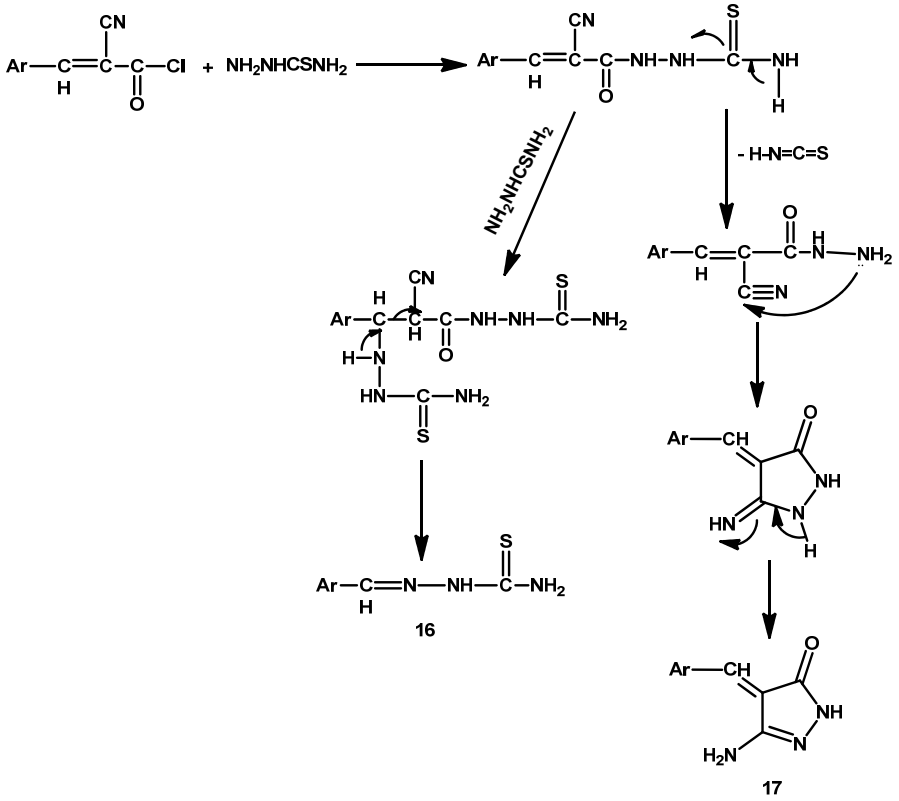
The acryloyl chloride derivative **3** was reacted with phenol, 4-chlorothiophenol and primary amines such as, 4-methoxyaniline, 4-methylaniline4chloroaniline and 3-amino pyridine in dry benzene in the presence of triethylamine to give acrylate, thioacrylate and acrylamides, **4**-**9**, respectively (Scheme 2).

On the other hand, reaction of the acryloyl chloride derivative **3** with benzoyl hydrazine as a bifunctional nucleophile under the same conditions gave the benzoyl hydrazide derivative **10** which underwent ring closure upon heating with $POCl_3$ to give the oxadiazole derivative **11** (Scheme 2). When the acryloyl chloride derivative **3** was allowed to react with methylthiourea, phenylurea and 2-aminopyridine as 1,3-binucleophilic reagents, it gave the tetrahydropyrimidine-2-thione derivative **12**, 1-acryloyl-3-phenyl urea derivative **13** and a mixture of acrylamide derivative **14** and pyridopyrimidine derivative **15**, respectively (Scheme 2).

The formation of compound **12** can be represented by the following pathway (Scheme 4).

The formation of compounds **14** and **15** can be explained by the following pathway (Scheme 5).

When the acryloyl chloride derivative **3** was allowed to react with thiosemicarbazide, it gave a mixture of the thiosemicarbazone **16** and the pyrazolone derivative **17** (Scheme 3). The acryloyl derivative **3** condensed with ethanolamine to give the dihydrooxazole derivative **18** (Scheme 3). 2-Propenoyl amide **19** was prepared by condensation of **3** with anthranilic acid in the presence of triethylamine (TEA). The structure of **19** was confirmed chemically by ring closure using acetic anhydride whereby the benzoxazinone **20** was obtained (Scheme 3).



Scheme 6

The acrylamide derivative **21**, which was prepared by the reaction of **3** with 2-aminophenol, gave the benzoxazole derivative **22** upon heating with phosphorus oxychloride (Scheme 3).

The formation of compounds **16** and **17** can be represented by the following pathway Scheme 6.

4. Conclusion

2-Propenoyl derivatives and some heterocyclic compounds with antibacterial and antifungal activities were synthesized from readily obtainable starting materials such as 2-cyano-3-(2′,4′-dichlorophenyl)acryloyl chloride, **3**.

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