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3-(1-Naphthoyl)Acrylic Acid as Substrate for the Synthesis of Novel Heterocyclic Compounds with Expected Antimicrobial Activity

MA. EL-Hashash[1], A. Essawy[2], SA. Rizk[1], I. E. El-Shamy[2], Ahmed Sobhy Fawzy[1]*

1. Chemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt.
2. Chemistry Department, Faculty of Science, Fayoum University, Fayoum, Egypt

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For Correspondence:

Ahmed Sobhy Fawzy

Chemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt

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ABSTRACT:

This research describe the reaction of 3-(1-naphthoyl)acrylic acid1with different Nitrogen nucleophiles under Aza-Michael reaction conditions to afford the corresponding Aza-Michael adduct 2(a-h)which allowed to react with hydrazine hydrate, hydroxyl amine hydrochloride and acetic anhydride to form novelpyridazinone3(a-c),oxazinone4(a-c) and furanone5(a-c) derivatives respectively. Some of the new products showed antimicrobial activities.

KEY WORDS: β–aroylacrylic acids, Aza-Michael, Pyridazinone, Oxazinone, Furanone, 3-(1-naphthoyl)acrylic acid, Antimicrobial.

INTRODUCTION:

β–aroylacrylic acid derivatives have antimicrobial activities against a wide variety of gram positive and gram negative organisms[1, 2], moreover they exhibit abroad spectrum of physiological activities and in recovery of Alzheimerdisease[3].And they have antiproliferative activity against human cervix carcinoma[4, 5] .β–aroylacrylic acids also are convenient polyelectrophilic reagents in the synthesis of heterocyclic compounds, for which the addition reaction of Nitrogen, Sulfur, Phosphorus, or Carbon nucleophiles occurs exclusively at theα-carbonyl electrophilic position of the molecule[6-12]. These reports of interesting chemical reactivity and biological activities prompt us to continue our research on β–aroylacrylic acid derivatives[1] to build new heterocyclic compounds starting with 3-(1-naphthoyl)acrylic acid, and studying their antimicrobial activity.

MATERIALS AND METHODS:

Melting points were determined on electrothermal apparatus using open capillary method and are uncorrected. Elemental analyses were carried out by the Micro Analytical Center at Cairo University. The IR spectra were recorded on FT/IR- 300E Jasco spectrophotometer as potassium bromide discs. The mass spectra were run by a Shimadzu-GC-MS-QP 1000 EX apparatus at 70 eV. (1H&13C)NMR spectra were recorded on Varian Mercury 300MHz spectrometer using TMS as internal standard.

General method for the synthesis of Aza-Michael adduct (2):

A mixture of 4-(naphthalen-1-yl)-4-oxobut-2-enoic acid (1) (2.26 g; 0.01 mol) and Nitrogen nucleophile (0.01 mol) namely benzyl amine, morpholine, 4-Aminoacetophenone, 2-(diphenylphosphino) ethylamine,Dimethylaminopropylamine, p-Anisidine, 1-(3-

aminopropyl)imidazole and 2-(Aminomethyl)pyridine in ethanol (50 ml) was refluxed for 2 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from appropriate solvent, afforded compounds (**2a-h)**.

2-(benzylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2a): (81% yield, mp 230 °C). IR (KBr): 1625, 1688, 3057 and 3442 (cm^{-1}).^{1}HNMR (DMSO)δ ppm: 2.31 (s, 1H, NH), 3.72 (s, 2H, methylene protons), 3.97 (d, *J* = 7 Hz, 2H, methylene protons), 4.12 (dd, J = 6 Hz, 1H, methine proton), 7.14, 7.28, 7.39 (m, 5H of benzyl moiety), 7.42 – 8.90 (m, 7H, ArH), 9.75 (s, 1H, OH exchangeable with D_2O).EIMS m/e: 333 [M^+]. Anal. Calcd. (%) for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found (%): C, 75.52; H, 5.73; N, 4.32%.

2-morpholino-4-(naphthalen-1-yl)-4-oxobutanoic acid (2b): (84% yield, mp 218 °C). IR (KBr):1628, 1683, 3058 and 3427 (cm^{-1}). ^{1}HNMR (DMSO)δ ppm: 2.63 (m, 4H of morpholine ring), 2.76 (d, *J*= 6 Hz, 2H methylene proton), 3.68 (m, 4H, of morpholine ring), 4.45 (dd, *J*= 6 Hz, 1H methane proton), 7.45-9.02 (m, 7H, ArH), 9.12 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 313 [M^+]. Anal. Calcd. (%) for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found (%):C, 68.83; H, 6.22; N, 4.53.

2-(4-acetylphenylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2c): (62% yield, mp227°C). IR (KBr): 1584, 1671, 1727, 3338 and 3398 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.45 (s, 3H of methyl group), 3.21 (d, *J* = 6 Hz, 2H methylene protons), 3.95 (s, 1H, NH), 4.13 (dd, *J* = 4 Hz, methine proton), 6.78, 7.65 (dd, *J* = 9 Hz, 4H of acetylphenol moiety), 7.42 – 9.32 (m, 7H, ArH), 9.41 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 361 [M^+]. Anal. Calcd. (%) for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found (%): C, 72.96; H, 5.21; N, 3.91.

2-(2-(diphenylphosphino)ethylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2d): (58% yield, mp 271 °C). IR (KBr): 1628, 1677, 1724, 3053 and 3366 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.12, 2.71 (dd, *J* = 4 Hz, 4H of 2 methylene groups), 3.22 (s, 1H, NH), 3.85 (d, J = 7 Hz, 2H, methylene protons), 4.15 (dd, J = 7 Hz, 1H, methine proton), 7.29 – 7.65 (m, 10H of 2 phenyl moiety), 7.55 – 9.34 (m, 7H, ArH), 9.73 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 455 [M^+]. Anal. Calcd. (%) for $C_{28}H_{26}NO_3P$: C, 73.83; H, 5.75; N, 3.08. Found (%): C, 73.71; H, 5.82; N, 3.17.

2-(3-(dimethylamino)propylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2e): (53% yield, mp186°C). IR (KBr): 1595, 1682, 3065, 3227 and 3436(cm^{-1}).^{1}HNMR (DMSO) δ ppm: 1.93 (m, 2H, methylene protons), 2.31 (s, 6H of 2 methyl groups), 2.12 (s, 1H, NH), 2.46, 2.59 (dd, *J* = 3 Hz, 4H of 2 methylene groups), 4.12 (dd, *J* = 6 Hz, 1H, methine proton), 4.23 (d, *J* = 6 Hz, 2H, methylene protons), 7.32 – 9.17 (m, 7H, ArH), 9.24 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 328 [M^+]. Anal. Calcd. (%) for$C_{19}H_{24}N_2O_3$: C, 69.49; H, 7.37; N, 8.53. Found (%): C, 69.54; H, 7.43; N, 8.65.

2-(4-methoxyphenylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2f): (47% yield, mp198°C). IR (KBr): 1624, 3051, 3230 and 3448(cm^{-1}).^{1}HNMR (DMSO) δ ppm: 3.22 (d, *J* = 4 Hz, 2H, methylene protons), 3.91 (s, 3H, methyl group), 4.12 (dd, *J* = 4 Hz, 1H, methine proton), 4.35 (s, 1H, NH), 6.63 (dd, *J* = 3 Hz, 4H, phenyl moiety), 7.41 – 9.52 (m, 7H, ArH), 9.32 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 349 [M^+]. Anal. Calcd. (%) for$C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01. Found (%): C, 71.92; H, 5.59; N, 4.12.

2-(3-(1H-imidazol-1-yl)propylamino)-4-(naphthalen-1-yl)-4-oxobutanoic acid (2g): (48% yield, mp220°C). IR (KBr): 1594, 1672, 3115 and 3434 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.13 (m, 2H, methylene protons), 2.24 (s, 1H, NH), 2.61 (dd, *J* = 4 Hz, 2H, methylene protons), 3.08 (d, J = 6 Hz, 2H, methylene protons), 4.14 (dd, *J* = 3 Hz, 1H, methine proton), 6.71, 7.19, 7.87 (dd, *J* = 3 Hz, 3H, imidazole moiety), 7.35 – 9.33 (m, 7H, ArH), 9.72 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 351 [M^+]. Anal. Calcd. (%) for$C_{20}H_{21}N_3O_3$: C, 68.36; H, 6.02; N, 11.96. Found (%): C, 68.02; H, 6.21; N, 12.09.

4-(naphthalen-1-yl)-4-oxo-2-(pyridin-2-ylmethylamino)butanoic acid (2h): (48% yield, mp 220 °C). IR (KBr): 1625, 1688, 3098 and 3198 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.27 (s, 1H, NH), 3.81 (d, *J* = 7 Hz, 2H, methylene protons), 4.09 (dd, *J* = 7 Hz, 1H, methine proton), 4.26 (s, 2H, methylene protons), 7.21 - 8.41 (m, 4H of pyridine moiety), 7.42 – 9.15 (m, 7H, ArH), 9.63 (s, 1H, OH exchangeable with D_2O). EIMS m/e: 334 [M^+]. Anal. Calcd. (%) for$C_{20}H_{18}N_2O_3$:C, 71.84; H, 5.43; N, 8.38. Found (%): C, 71.51; H, 5.52; N, 8.47.

44-(benzylamino)-6-(naphthalen-1-yl)-4,5-dihydropyridazin -3(2H)-one (3a): A mixture of Aza-Michael adduct **(2a)** (3.33 g; .01 mol) and hydrazine hydrate (3 ml) in ethanol (50 ml) was refluxed for 3 hours.

The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from acetic acid afforded compound **(3a)** (41% yield, mp 197 °C). IR (KBr): 1607, 1669, 3246, 3290, 3439 and 3641 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm:2.06 (dd, *J*= 6 Hz, 2H,CH_2 in pyridazinone moiety), 2.40 (s, 1H, NH group), 3.60 (dd, J = 6 Hz, 1H, CH in pyridazinone moiety), 3.92 (m, 2H, methylene protons), 7.21- 8.93 (m, 7H, ArH), 8.75 (s, 1H, NH of pyridazinone moiety exchangeable with D2O).EIMS m/e: 329 [M^+]. Anal. Calcd. (%) for $C_{21}H_{19}N_3O$: 76.57; H, 5.81; N, 12.76. Found (%):76.46; H, 5.77; N, 12.87.

4-morpholino-6-(naphthalen-1-yl)-4,5-dihydropyridazin-3(2H)-one (3b): A mixture of Aza-Michael adduct **(2b)** (3.13 g; .01 mol) and hydrazine hydrate (3 ml) in ethanol (50 ml) was refluxed for 3 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from acetic acid afforded compound **(3b)** (43% yield, mp186°C). IR (KBr): 1631, 1736, 3213 and 3441 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 1.85 (dd, *J* = 4 Hz, 2H, CH*2* of pyridazinone moiety), 2.71, 3.61 (m, 8H of morpholine moiety), 3.72 (dd, *J* = 4 Hz, 1H CH of pyridazinone moiety), 6.91 (s, 1H, NH of pyridazinone moiety), 7.51 – 8.77 (m, 7H, ArH). EIMS m/e: 309 [M^+]. Anal. Calcd. (%) for$C_{18}H_{19}N_3O_2$: C, 69.88; H, 6.19; N, 13.58. Found (%):C, 69.77; H, 6.14; N, 13.63.

4-(4-acetylphenylamino)-6-(naphthalen-1-yl)-4,5-dihydropyridazin-3(2H)-one (3c): A mixture of Aza-Michael adduct **(2c)** (3.61 g; .01 mol) and hydrazine hydrate (3 ml) in ethanol (50 ml) was refluxed for 3 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from acetic acid afforded compound **(3c)** (39% yield, mp192°C). IR (KBr): 1570, 1604, 3309, 3392 and 3495 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.11 (dd, *J* = 6 Hz, 2H, CH_2 in pyridazinone moiety), 2.43 (s, 3H, methyl group), 3.60 (dd, *J* = 6 Hz, 1H, CH in pyridazinone moiety), 3.92 (s, 1H, NH group), 6.82 (dd, *J* = 9 Hz, 2H of benzene ring), 7.12 (s, 1H, NH of pyridazinone moiety exchangeable with D2O), 7.62 (dd, *J* = 6 Hz, 2H of benzene ring), 7.51 - 8.97 (m, 7H,ArH).EIMS m/e: 357 [M^+]. Anal. Calcd. (%) for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found (%): C, 73.81; H, 5.30; N, 11.82.

5-(benzylamino)-3-(naphthalen-1-yl)-4H-1,2-oxazin-6(5H)-one (4a): A mixture of Aza-Michael adduct **(2a)** (3.33 g; 0.01 mol) and hydroxylamine hydrochloride (0.69 g, 0.01) and few drops of sodium hydroxide 50% solution in isopropyl alcohol (50 ml) was refluxed for 2 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from isopropyl alcohol afforded compound **(4a)** (37% yield, mp182°C). IR (KBr): 1635, 1663, 3053, 3220 and 3412 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.83 (s, 1H, NH group), 3.41 (dd, *J* = 6 Hz, 2H of CH_2in pyridazinone moiety),3.63 (dd, *J* = 6 Hz, 1H, CH in pyridazinone moiety),3.92 (s, 2H, methylene protons), 7.17 (d, *J* = 6 Hz, 2H of benzene ring), 7.24 (m, 1H of benzene ring), 7.33 (d, *J* = 6 Hz, 2H of benzene ring), 7.52 – 9.07 (m, 7H, ArH). EIMS m/e: 330 [M^+]. Anal. Calcd. (%) for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found (%): C, 76.22; H, 5.52; N, 8.54.

5-morpholino-3-(naphthalen-1-yl)-4H-1,2-oxazin-6(5H)-one (4b): A mixture of Aza-Michael adduct (2b) (3.13 g; 0.01 mol) and hydroxylamine hydrochloride (0.69 g, 0.01) and few drops of sodium hydroxide 50% solution in isopropyl alcohol (50 ml) was refluxed for 2 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from isopropyl alcohol afforded compound (4b) (40% yield, mp 197 °C). IR (KBr): 1689, 1713, 1794, 2904 and 3201 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.41 (m, 4H of morpholine moiety), 3.21 (dd, *J* = 4 Hz, 2H, CH_2 of pyridazinone moiety), 3.45 (dd, *J* = 4 Hz, 1H, CH of pyridazinone moiety), 3.62 (m, 4H of morpholine moiety), 7.47 – 9.10 (m, 7H, ArH). EIMS m/e: 310 [M^+]. Anal. Calcd. (%) for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found (%): C, 69.53; H, 5.79; N, 9.15.

5-(4-acetylphenylamino)-3-(naphthalen-1-yl)-4H-1,2-oxazin-6(5H)-one (4c): A mixture of Aza-Michael adduct **(2c)** (3.61 g; .01 mol) and hydroxylamine hydrochloride (0.69 g, 0.01) and few drops of sodium hydroxide 50% solution in isopropyl alcohol (50 ml) was refluxed for 2 hours. The reaction mixture was allowed to cool and the separated product was filtered off, dried and crystallized from isopropyl alcohol afforded compound **(4c)** (33% yield, mp 185 °C). IR (KBr): 1596, 161, 3325, 3436 and 3493 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.59 (s, 3H, methyl group), 3.34 (dd, *J* = 4 Hz, 2H, CH_2 of pyridazinone moiety), 3.61 (dd, *J* = 4 Hz, 1H, CH of pyridazinone moiety), 4.64 (s, 1H, NH), 6.61, 7.81 (dd, *J* = 6 Hz, 4H, phenyl moiety), 7.45 – 8.92 (m, 7H, ArH). EIMS m/e: 358 [M^+]. Anal. Calcd. (%) for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06; N, 7.82. Found (%): C, 73.61; H, 5.17; N, 7.91.

3-(benzylamino)-5-(naphthalen-1-yl)furan-2(3H)-one (5a): A mixture of Aza-Michael adduct **(2a)** (3.33 g; 0.01 mol) and acetic anhydride (9.42mL, 0.1mol) was refluxed

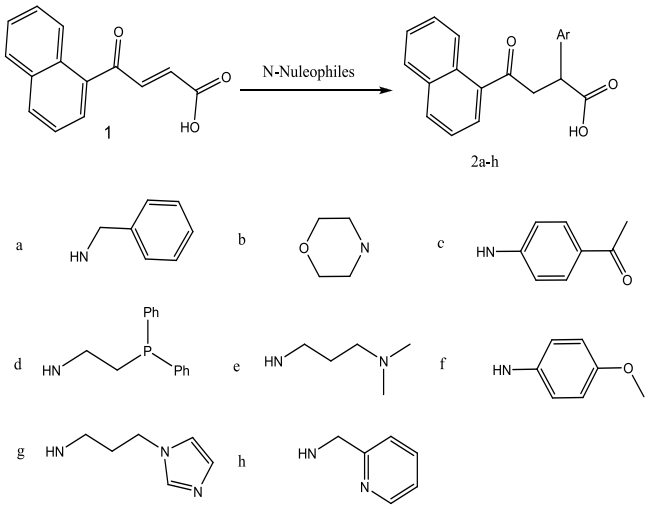
on boiling water bath for 1 h. The reaction mixture was allowed to cool then poured into ice-water and the separated product was filtered off, dried and crystallized from toluene afforded compound **(5a)** (38% yield, mp 219 °C). IR (KBr): 1648, 1778, 3057 and 3428 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.44 (s, 1H, NH), 3.91 (s, 2H, methylene protons), 4.23 (d, J = 3 Hz, 1H, CH of furanone moiety), 5.42 (d, J = 3 Hz, 1H, CH of furanone moiety), 7.18, 7.39 (d, J = 6 Hz, 4H, benzyl moiety), 7.29 (m, 1H, benzyl moiety), 7.51 – 9.02 (m, 7H, ArH). EIMS m/e: 315 [M^+]. Anal. Calcd. (%) for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found (%): C, 79.81; H, 5.56; N, 4.59.

3-morpholino-5-(naphthalen-1-yl)furan-2(3H)-one (5b): A mixture of Aza-Michael adduct (**2b**) (3.13 g; .001 mol) and acetic anhydride (9.42mL, 0.1mol) was refluxed on boiling water bath for 1 h. The reaction mixture was allowed to cool then poured into ice-water and the separated product was filtered off, dried and crystallized from toluene afforded compound **(5b)** (41% yield, mp 233 °C). IR (KBR): 1630, 1765, 3051 and 3439 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.71 (m, 4H of morpholine), 3.62 (m, 4H of morpholine), 4.26 (d, *J* = 2.2 Hz, 1H, CH of furanone moiety), 6.13 (d, *J* = 2.2 Hz, 1H, CH of furanone moiety), 7.35 – 8.54 (m, 7H, ArH). EIMS m/e: 295 [M^+]. Anal. Calcd. (%) for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found (%): C, 73.13; H, 5.77; N, 4.85.

3-(4-acetylphenylamino)-5-(naphthalen-1-yl)furan-2(3H)-one (5c): A mixture of Aza-Michael adduct **(2c)** (3.61 g; .01 mol) and acetic anhydride (9.42mL, 0.1mol) was refluxed on boiling water bath for 1 h. The reaction mixture was allowed to cool then poured into ice-water and the separated product was filtered off, dried and crystallized from toluene afforded compound **(5c)** (37% yield, mp 191 °C). IR (KBr): 1638, 1702, 1797, 3203, 3302 and 3452 (cm^{-1}). ^{1}HNMR (DMSO) δ ppm: 2.67 (s, 3H, methyl group), 4.18 (s, 1H, NH), 4.23, 5.67 (d, *J* = 3 Hz, 2H of 2 CH of furanone moiety), 6.64, 7.82 (dd, *J* = 6 Hz, 4H, phenyl moiety), 7.18 – 8.73 (m, 7H, ArH). EIMS m/e: 343 [M^+]. Anal. Calcd. (%) for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found (%): C, 76.82; H, 4.87; N, 3.95.

RESULTS AND DISCUSSIONS

3-(1-naphthoyl)acrylic acid **(1)** was prepared following a reported procedure[13]. Reaction of **1** with N-Nucleophiles namely benzyl amine, p-aminoacetophenone, N,N-dimethylamino-propylamine, 1-(3-aminopropyl)imidazole, morpholine, 2-(diphenylphosphino)ethylamine, p-anisidine and 2-picolylamine gave Aza-Michael adduct derivatives **(2a-h)** respectively (**Scheme 1**). The structures of compounds **(2a-h)** were confirmed by elemental analysis and spectral data. IR spectrum of compound **2a** revealed strong absorption bands at1625, 1688, 3057 and 3442 cm^{-1} attributable to $\upsilon_{C=O}$, υ_{OH} and υ_{NH} bonded and nonbonded, respectively, while the ^{1}H-NMR spectrum of compound **(2b)** shows signals at δ ppm2.63 (m, 4H of morpholine ring), 2.76 (d, *J*= 6 Hz, 2H methylene proton), 3.68 (m, 4H, of morpholine ring), 4.45 (dd, *J*= 6 Hz, 1H methine proton), 7.45-9.02 (m, 7H, ArH), 9.12 (s, 1H, OH exchangeable with D2O), and EIMS of compound **(2c)** exhibits m/e 361 (M^+).



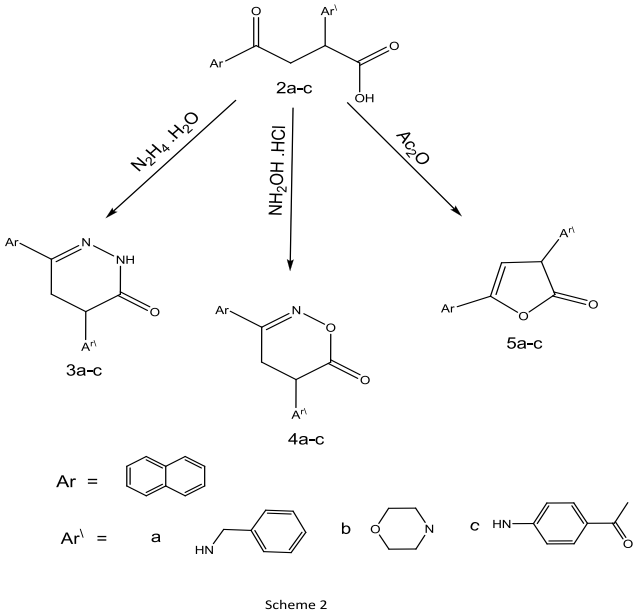
Scheme 1

Furthermore the structure of **(2a-c)** was established chemically by:

(i) Cyclocondensation of **(2a-c)** with hydrazine hydrate afforded pyridazinone derivatives **(3a-c), (Scheme 2).**The structures of compounds **(3a-c)** were confirmed by elemental analysis and spectral data^{1}H-NMR spectrum of compound **(3a)** shows signals at δ ppm 2.06 (dd, *J*= 6 Hz, 2H,CH_2 in pyridazinone moiety), 2.40 (m, 1H, NH group), 3.60 (dd, J = 6 Hz, 1H, CH in pyridazinone moiety), 3.92 (s, 2H, methylene protons), 7.21- 8.93 (m, 7H, ArH), 8.75 (s, 1H, NH of pyridazinone moiety exchangeable with D2O), and EIMS of compound **(3b)** exhibits m/e 309 (M^+), while ^{1}H-NMR spectrum of compound **(3c)** shows signals at δ ppm 2.11 (dd, *J* = 6 Hz, 2H, CH_2 in pyridazinone moiety), 2.43 (s, 3H, methyl group), 3.60 (dd, *J* = 6 Hz, 1H, CH in pyridazinone moiety), 3.92 (s, 1H, NH group), 6.82 (dd, *J* = 9 Hz, 2H of benzene ring), 7.12 (s, 1H, NH of pyridazinone moiety exchangeable with D_2O), 7.62 (dd, *J* = 6 Hz, 2H of benzene ring), 7.51 - 8.97 (m, 7H,ArH).

(ii) Interaction of **2(a-c)** with hydroxyl amine hydrochloride gave oxazinone derivatives **(4a-c),** (Scheme 2).The structures of compounds **(4a-c)** were confirmed by elemental analysis and spectral data. ^{1}H-NMR spectrum of compound **(4a)** shows signals at δ ppm 2.83 (s, 1H, NH group), 3.41 (dd, *J* = 6 Hz, 2H of CH_2in pyridazinone moiety),3.63 (dd, *J* = 6 Hz, 1H, CH in pyridazinone moiety),3.92 (s, 2H, methylene protons), 7.17 (d, *J* = 6 Hz, 2H of benzene ring), 7.24 (m, 1H of benzene ring), 7.33 (d, *J* = 6 Hz, 2H of benzene ring), 7.52 – 9.07 (m, 7H, ArH) and EIMS of compound **(4b)** exhibits m/e 310 (M^+), while IR spectrum of compound **(4c)** revealed strong absorption bands at 1596, 1618, 3493 and 3602 cm^{-1} attributable to $\upsilon_{C=O}$ and υ_{NH} bonded and nonbonded.

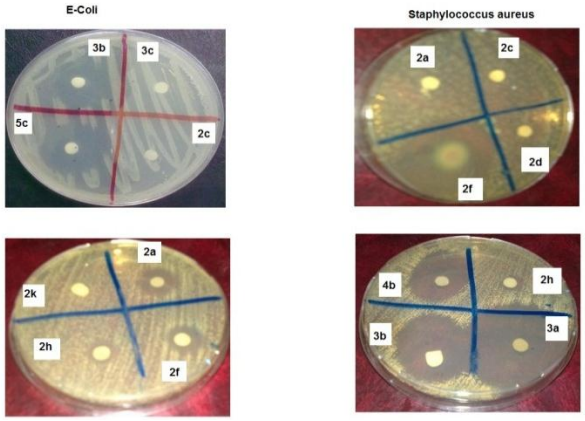
(iii) Reaction of **(2a-c)** with acetic anhydride yielded furanone derivatives **(5a-c),** (Scheme 2).The structures of compounds **(5a-c)** were confirmed by elemental analysis and spectral data. EIMS of compound **(5a)** exhibits m/e 315 (M^+), while ^{1}H-NMR spectrum of compound **(5b)** shows signals at δ ppm 2.71 (m, 4H of morpholine), 3.62 (m, 4H of morpholine), 4.26 (d, *J* = 2.2 Hz, 1H,methine proton furanone moiety), 6.13 (d, *J* = 2.2Hz, 1H, CH of Furanone moiety), 7.35 – 8.54 (m, 7H, ArH), and IR spectrum of compound **5c** revealed strong absorption bands at1702, 1797, 1823, 3302 and 3452 cm^{-1}attributable to $\upsilon_{C=O}$ and υ_{NH} bonded and nonbonded.



Scheme 2

Biological Activity

β-aroylacrylic acid and its derivatives represent one of the most active classes of compounds possess a wide spectrum of biological activity[1]. 3-(1-naphthoyl)acrylic acid relates to a group of compounds having a wide spectrum of chemotherapeutics activity, and they have also been to have fungistatic activity[14]. Some of the newly synthesized compounds have been tested for their antibacterial activity against gram –ve bacteria (Escherichia coli) and gram +ve bacteria (Staphylococcus aureus), and for their antifungal activity against (Candida albicans and Aspergillus flavus). Antimicrobial activity of the tested samples was determined using a modified Kirby-Bauer disc diffusion method [15]. Briefly, 100 μl of the test bacteria was grown in 10 mL of fresh media (Mueller-Hinton agar) until they reached a count of approximately 108 cells/mL for bacteria or 105 cells/ml for fungi [16]. 100 µl of microbial suspension was spread onto agar plates corresponding to the broth in which they were maintained. The tested organisms were the gram +ve bacteria (Staphylococcus aureus) and the gram –ve bacteria (Escherichia coli), and fungus (**Candida albicans** and Aspergillus flavus*)* by using sterile Whatman-No1 filter paper disks (8.0mm diameter). Each compound was dissolved in DMSO. Filter paper disks were loaded with certain amount of the tested material (30μg/disk) and then left with care under hot air to complete dryness. The disks were deposited on the surface of agar plates and the disks were incubated at 5°C for 1h, to permit good diffusion. All the plates were then incubated for 24 h at 37°C. The diameter of inhibition zones was measured in mm. **(Table 1)** represents the antimicrobial activity of some new synthesized compounds.



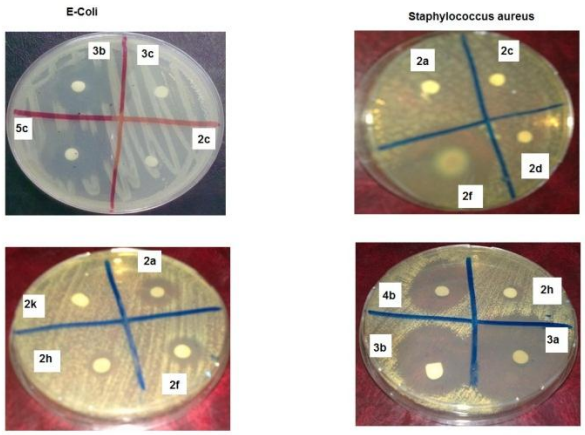


Table 1

Sample	Inhibition zone diameter (mm / mg Sample)			
	Escherichia coli	***Staphylococcus aureus***	***Candida albicans***	*Aspergillus flavus*
2a	**++**	**+**	**++**	**++**
2c	**+**	**+**	**+++**	**++**
2d	**-**	**+**	**++**	**++**
2f	**++**	**++**	**++**	**+++**
2h	**++**	**++**	**++**	**+++**
3a	**++**	**+++**	**+++**	**++**
3b	**+++**	**++**	**++**	**+++**
4b	**++**	**++**	**+++**	**+++**
4c	**++**	**++**	**+++**	**++**
5c	**+++**	**++**	**+++**	**++**

- = no activity, + = weak activity (diameter 5 :10mm), ++ = moderate activity (diameter 10 :15mm), +++ = strong activity(diameter >15mm)

CONCLUSION

Novel β-aroylacrylic acid derivatives, pyridazinone, oxazinone, furanone and other heterocyclic compounds were successfully synthesized through simple methods. The structures for the new synthesized compounds were confirmed by elemental analysis, FTIR, NMR, and mass spectra. These compounds were evaluated for in vitro antimicrobial activities against some strains of bacteria and fungi. And some of them showed significant activities for both gram positive and gram negative bacteria as well as for fungi, where it was it was found that Aza-Michael adduct compounds (2a,c,d,f,h) showed moderate to no activity against bacteria while strong to moderate activity against fungi which may be due to naphthalene oxobutanoic acid moiety, and compounds (3a, 3b) showed strong to moderate activity against both bacteria and fungi which may be due the pyridazinone moiety, while compounds (4b, 4c) showed strong to moderate activity against both bacteria and fungi which may be due the oxazinone moiety, and compound (5c) showed strong to moderate activity against both bacteria and fungi which may be due the furanone moiety.

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