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Simple method for the synthesis and antibacterial activity of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c] quinolin-5-one derivatives

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A simple method for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivative and biological evaluation of the antibacterial activity against *Pseudomonas syringae, Xanthomonas citi* and *Pectobacterium carotovorum* are reported. The structure of the isolated compounds was determined by means of $^{1}H/^{13}C$ NMR and FT-IR spectroscopy. Silica supported boron trifluoride ($BF_3.SiO_2$) is an efficient, readily available and reusable catalyst for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivatives by condensation of 4-hydroxyquinolin-2(1*H*)-one, aldehyde, and malononitrile. This reaction under normal heating is very simple affording good to excellent yields products. Some of the compound showed significant inhibition of bacteria growth.

Keywords:

INTRODUCTION.

Homogeneous acidic catalysts such as H_2SO_4, HCl and BF_3 are commonly used for organic synthesis. However, the above-mentioned catalysts have several disadvantages such as corrosiveness, toxicity or volatility, and they generate large amounts of waste. Silica supported boron trifluoride, $BF_3.SiO_2$, which is easy to prepare and shows unusually high acidity which can be controlled by activation temperature, exhibits considerable catalytic activity [1], and enables better accessibility of the reactants to the active sites. $BF_3.SiO_2$ is a solid super acid and has surface species such as Al–OBF_2 and Si–OBF_2, and the ion pairs Al–OBF_3−H^+ or Si–OBF_3-H^+ [2]. $BF_3.SiO_2$ is used in several organic transformations, such as synthesis by Claisen-Schmidt condensation [3] of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes [4], 1,2,4,5-tetrasubstituted imidazoles [5], polymerization of styrene [6], polyfunctionalized piperidin-4-ones [7], α-amino phosphonates [8], quinoxalines [9], and 3,4-dihydropyrimidin-2(1*H*)-ones [10].

Pyrans constitute one of the major classes of naturally occurring compounds [11-15]. Pyran derivatives have biological activities, and photochromic properties [16-20]. Moreover, 4*H*-pyrans are useful intermediates for the synthesis of various compounds, such as pyranopyridine derivatives [21], polyazanaphthalenes [22], pyrano[2]pyrimidines [23], and pyridin-2-ones [24]. Recently, a method has been reported for the synthesis of pyran derivatives *via* three-component condensation of 4-hydroxyquinolin-2(1*H*)-one with aldehydes and malononitrile to synthesize 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivatives. A variety of catalysts such as KF–Al_2O_3 [25], ammonium acetate [26], have been employed to effect this transformation.

Pectobacterium carotovorum is a bacterium of the family *Enterobacteriaceae*; it formerly was a member of the genus *Erwinia*. The species is a plant pathogen with a diverse host range, including potato, african violet, and other agriculturally and scientifically important plant species. It causes soft rot and blackleg of potato and vegetables, as well as slime flux on many different tree species [27, 28]. *Xanthomonas* can infect a wide variety of species including pepper, rice, citrus, cotton, tomato, broccoli, cabbage, and soybeans. Some types of *Xanthomonas* cause localized leaf spot or leaf streak while others spread systemically and cause black rot or leaf blight disease [29, 30]. *Pseudomonas syringae* is responsible for causing diseases on over 180 plant species including fruit trees, vegetable crops and flowers. Pathovars of main economic importance in Europe are the pvs *syringae*, *morsprunorum, avii* and *persicae*, causing bacterial canker on sweet and sour cherry, plum, peach, apricot and wild cherry [31, 32].

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EXPERIMENTAL

Preparation of $BF_3.SiO_2$

3.7 g of BF_3 (7.0 ml of $BF_3.Et_2O$) was added dropwise to a mixture of 6.3 g of silica gel and 10 ml of chloroform. The mixture was stirred for 1 h at room temperature. The resulting suspension was filtered. The obtained solid was washed with chloroform and dried in a domestic microwave oven for 20 min at power 100.

General procedure for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivatives:

A mixture of 4-hydroxyquinolin-2(1*H*)-one (0.32 g, 2 mmol) with various aldehydes (2.1 mmol), malononitrile (0.14 g, 2.1 mmol), and $BF_3.SiO_2$ (0.06 g, 0.5 mmol, 25 mol %) was heated at 60 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with ethanol and filtered to recover the catalyst. The filtrate was evaporated and the crude product was recrystallized from iso-propanol to afford the pure 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c] quinolin-5-one derivatives in 85-95 % yields. All products were known and were identified by comparison of their physical and spectral data with those of authentic samples.

2-amino-3-cyano-4-(4-ethyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pink powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3392, 3293, 3137, 3024, 2953, 2867, 2854, 2188, 1688, 1603, 1499, 1467, 1442, 1391, 1249, 1174, 1103, 900, 754 cm^{-1}. ^{1}H NMR (DMSO-d6, 400 MHz): d 0.60– 0.75 (m, 3H), 1.45–1.85 (m, 2H), 3.47 (br s, 1H), 7.10–7.55 (m, 5H), 7.77 (d, *J* = 7.0 Hz, 1H), 11.86 (s, 1H); ^{13}C NMR (DMSO-d6, 100 MHz): d 9.2, 27.0, 32.1, 54.8, 109.6, 112.5, 115.6, 121.5, 122.3, 123.1, 131.2, 138.0, 152.4, 160.8, 161.4.

2-amino-3-cyano-4-(n-propyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pink powder, m.p. >300 °C; 3391, 3293, 3137, 3024, 2952, 2867, 2853, 2188, 1688, 1603, 1499, 1466, 1442, 1391, 1249, 1174, 1103, 900, 754 cm^{-1}. ^{1}H NMR (DMSO-d6, 400 MHz): d 0.75– 0.86 (m, 3H), 1.07–1.30 (m, 2H), 1.45–1.71 (m, 2H), 3.47 (br s, 1H), 7.05–7.55 (m, 5H), 7.79 (d, *J* = 7.0 Hz, 1H), 11.84 (br s, 1H); ^{13}C NMR (DMSO-d6, 100 MHz): d 14.3, 18.2, 31.0, 37.2, 55.5, 110.3, 112.5, 115.7, 120.8, 121.9, 122.3, 131.3, 138.0, 152.2, 160.7, 161.3.

2-amino-3-cyano-4-(4-nitrophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Yellowish brown powder, m.p. >300 °C; 3549, 3426, 3329, 3001, 2951, 2857, 2191, 1670, 1643, 1588, 1516, 1438, 1378, 1352, 1250, 1173, 1107, 1015, 902, 825, 758, 707 cm^{-1}. ^{1}H NMR (400 MHz, DMSOd6): d 4.69 (s, 1H), 7.20–7.65 (m, 7H), 7.91 (d, 1H, *J* = 7.0 Hz), 8.15 (d, 2H, *J* = 5.6 Hz), 11.79 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 37.2, 57.4, 108.7, 112.3, 115.9, 119.9, 122.3, 122.5, 124.1, 129.3, 131.9, 138.4, 146.8, 152.0, 152.4, 159.4, 160.9.

2-amino-3-cyano-4-(3-nitrophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Yellowish brown powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3549, 3426, 3329, 3001, 2950, 2858, 2192, 1670, 1644, 1588, 1516, 1439, 1378, 1352, 1250, 1173, 1107, 1015, 902, 825, 758, 707 cm^{-1}. ^{1}H NMR (DMSO-d6) d: 4.73 (s, 1H), 7.30–7.35 (m, 2H), 7.41 (s, 2H), 7.58–7.63 (m, 2H), 7.74 (d, 1H, *J* = 7.6 Hz), 7.93 (d, *J* = 8.4 Hz, 1H), 7.95 (s, 1H), 8.10 (d, 1H, *J* = 8.4 Hz), 11.81 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 37.2, 57.1, 108.9, 112.3, 115.9, 119.9, 122.3, 122.4, 124.1, 128.8, 129.1, 131.8, 137.9, 145.6, 151.2, 152.3, 159.4, 160.8.

2-amino-3-cyano-4-(3,4-dichlorophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3452, 3334, 3201, 3063, 3017, 2950, 2849, 2208, 1696, 1593, 1470, 1439, 1373, 1332, 1250, 1168, 1117, 1019, 881, 835, 738 cm^{-1}. ^{1}H NMR (DMSO-d6) d: 4.57 (s, 1H), 7.21 (d, 1H, *J* = 8.4 Hz), 7.29–7.35 (m, 4H), 7.48 (s, 1H), 7.55 (d, 1H, *J* = 7.6 Hz), 7.57–7.61 (m, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 11.79 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 37.3, 57.1, 108.7, 112.2, 115.9, 120.0, 122.3, 122.4, 122.6, 124.1, 128.8, 129.3, 131.9, 138.4, 146.7, 141.9, 152.6, 159.4, 160.8.

2-amino-3-cyano-4-(4-methoxyphenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3324, 3288, 3170, 2996, 2950, 2863, 2193, 1665, 1593, 1501, 1440, 1388, 1322, 1260, 1173, 1112, 1035, 815, 764 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 3.72 (s, 3H), 4.47 (s, 1H), 6.86 (d, 2H, *J* = 7.4 Hz), 7.15 (d, 2H, *J* = 7.4 Hz), 7.24 (s, 2H), 7.29 (t, 1H, *J* = 7.4 Hz), 7.35 (d, 1H, *J* = 7.7 Hz), 7.58 (t, 1H, *J* = 7.3 Hz), 7.92 (d, 1H, *J* = 7.4 Hz), 11.74 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.4, 55.5, 58.5, 110.4, 112.5, 114.2, 115.8, 120.4, 122.2, 122.4, 128.9, 131.6, 136.9, 138.2, 151.4, 158.5, 159.4, 161.0.

2-amino-3-cyano-4-(4-chlorophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3355, 3304, 3155, 2955, 2853, 2203, 1675, 1598, 1486, 1393, 1255, 1173, 1096, 1025, 846, 764 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 4.56 (s, 1H), 7.25–7.42 (m, 8H), 7.60 (t, 1H, *J* = 7.0 Hz), 7.95 (d, 1H,

J = 7.2 Hz), 11.76 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.7, 57.8, 109.5, 112.4, 115.9, 120.2, 122.3, 122.4, 128.8, 129.8, 131.7, 131.8, 138.3, 143.8, 151.7, 159.4, 160.9.

2-amino-3-cyano-4-(4-bromophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pale yellow powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3324, 3310, 3150, 2950, 2853, 2197, 1680, 1593, 1486, 1383, 1327, 1291, 1260, 1163, 1107, 1004, 851, 758 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 4.55 (s, 1H), 7.21 (d, 2H, *J* = 7.2 Hz), 7.25–7.43 (m, 4H), 7.50 (d, 2H, *J* = 7.2 Hz), 7.59 (t, 1H, *J* = 7.4 Hz), 7.94 (d, 1H, *J* = 7.3 Hz), 11.73 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.8, 57.7, 109.4, 112.4, 115.9, 120.2, 120.2, 122.3, 122.5, 130.2, 131.7, 131.8, 138.3, 144.3, 151.7, 159.4, 160.9.

2-amino-3-cyano-4-(2-chlorophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pale yellow powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3324, 3288, 3170, 2996, 2950, 2863, 2193, 1665, 1593, 1501, 1440, 1388, 1322, 1260, 1173, 1112, 1035, 815, 764 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 5.03 (s, 1H), 7.15–7.41 (m, 8H), 7.57 (t, 1H, *J* = 6.8 Hz), 7.92 (d, 1H, *J* = 7.4 Hz), 11.70 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 34.5, 57.0, 108.9, 112.3, 115.9, 119.9, 122.3, 122.4, 128.0, 128.8, 129.9, 130.7, 131.8, 132.8, 138.4, 142.0, 152.3, 159.4, 160.8.

2-amino-3-cyano-4-(2,4-dichlorophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pale yellow powder, mp >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3344, 3307, 3170, 2950, 2958, 2197, 1670, 1634, 1583, 1480, 1383, 1317, 1260, 1183, 1112, 1045, 850, 748 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 5.01 (s, 1H), 7.20 (d, 1H, *J* = 7.9 Hz), 7.25–7.38 (m, 5H), 7.52 (s, 1H), 7.58 (t, 1H, *J* = 7.4 Hz), 7.90 (d, 1H, *J* = 7.7 Hz), 11.67 (br s, 1H); ^{13}C NMR (100 MHz, DMSOd6): d 34.2, 56.4, 108.4, 112.3, 115.9, 119.7, 122.3, 122.5, 128.2, 129.2, 131.8, 132.1, 132.3, 133.7, 138.4, 141.1, 152.3, 159.4, 160.7.

2-amino-3-cyano-4-(3,4-dimethoxyphenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, mp >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3355, 3314, 3160, 3068, 3001, 2964, 2884, 2197, 1680, 1593, 1496, 1440, 1378, 1245, 1168, 1112, 1035, 912, 856, 774 cm^{-1}. ^{1}H NMR (DMSO-d6) d: 4.43 (s, 1H), 5.96 (s, 2H), 6.67 (d, 2H, *J* = 8.4 Hz), 6.74 (s, 1H), 6.81 (d, 1H, *J* = 8.0 Hz), 7.22 (s, 2H), 7.27–7.34 (m, 2H), 7.55– 7.59 (m, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 11.75 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.4, 55.5, 57.5, 58.5, 110.4, 112.5, 114.2, 115.8, 120.4, 122.2, 122.4, 128.9, 128.8, 130.7, 131.6, 136.9, 138.2, 151.4, 158.5, 159.4, 161.0.

2-amino-3-cyano-4-(4-cyanophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Yellowish brown powder, m.p. >300 °C; 3355, 3304, 3155, 2955, 2853, 2225, 2203, 1675, 1598, 1486, 1393, 1255, 1173, 1025, 846, 763 cm^{-1}. ^{1}H NMR (DMSO-d6, 400 MHz): d 4.63 (s, 1H), 7.27 (t, 1H, *J* = 7.3 Hz), 7.34 (d, 1H, *J* = 8.0 Hz), 7.38 (s, 2H), 7.43 (d, 2H, *J* = 7.5 Hz), 7.57 (t, 1H, *J* = 7.0 Hz), 7.75 (d, 2H, *J* = 7.5 Hz), 7.91 (d, 1H, *J* = 7.6 Hz), 11.78 (br s, 1H); ^{13}C NMR (DMSO-d6, 100 MHz): d 37.4, 57.2, 108.8, 110.0, 112.4, 115.9, 119.3, 120.0, 122.3, 122.5, 129.1, 131.9, 132.9, 138.4, 150.4, 152.0, 159.4, 160.9.

2-amino-3-cyano-4-(phenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, m.p. >300 °C; IR (KBr) (υ_{max}/cm^{-1}): 3392, 3293, 3137, 3024, 2854, 2188, 1688, 1603, 1499, 1442, 1391, 1249, 1174, 1103, 900, 754 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 4.52 (s, 1H), 7.21–7.32 (m, 8H), 7.35 (d, 1H, *J* = 8.2 Hz), 7.58 (t, 1H, *J* = 7.7 Hz), 7.93 (d,1H, *J* = 7.7 Hz), 11.77 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 37.2, 58.2, 110.0, 112.5, 115.8, 120.3, 122.2, 122.4, 127.2, 127.8, 128.8, 131.7, 138.2, 144.8, 151.7, 159.4, 160.9.

2-amino-3-cyano-4-(4-flurophenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: Pale yellow powder, m.p. >300 °C; 3354, 3304, 3155, 2954, 2853, 2203, 1675, 1598, 1486, 1393, 1255,1248, 1173, 1025, 846, 764 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 4.52 (s, 1H), 7.05–7.35 (m, 8H), 7.56 (t, 1H, *J* = 7.2 Hz), 7.89 (d, 1H, *J* = 7.4 Hz), 11.75 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.5, 58.1, 109.8, 112.4, 115.4, 120.2, 122.3, 122.4, 129.8, 129.8, 131.7, 138.3, 141.0, 151.6, 159.4, 160.3, 160.9.

2-amino-3-cyano-4-(4-hydroxyphenyl)-1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one: White powder, m.p. >300 °C; 3403, 3324, 3310, 3150, 3058, 2950, 2920, 2853, 2197, 1680, 1620, 1593, 1486, 1383, 1327, 1291, 1260, 1163, 1107, 1004, 851, 758 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d6): d 4.40 (s, 1H), 6.67 (d, 2H, *J* = 8.3 Hz), 7.01 (d, 2H, *J* = 8.3 Hz), 7.18 (s, 2H), 7.27 (t, 1H, *J* = 7.6 Hz), 7.33 (d, 1H, *J* = 8.2 Hz), 7.55 (t, 1H, *J* = 7.6 Hz), 7.90 (d, 1H, *J* = 8.0 Hz), 11.74 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): d 36.3, 58.7, 110.6, 112.6, 115.5, 115.8 120.5, 122.2, 122.4, 128.9, 131.5, 135.2, 138.2, 151.3, 156.7, 159.4, 161.0.

In vitro antibacterial screening: Preparation of plates and microbiological assays:

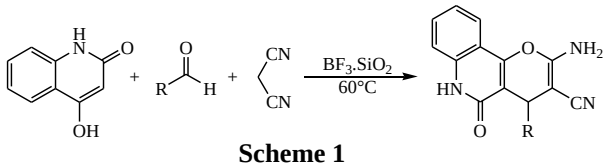
Inoculation of test bacteria (*X. campestris pvs*, *P. syringae* and *P. carotovorum*) was carried out by inoculating a loopful of organism in a 10 ml nutrient broth and incubated at 37ºC for 24 h till a moderate turbidity was developed. 0.10 ml of each suspension was thoroughly mixed with 25 ml of nutrient agar medium in a pre-sterilized petri plate and was set aside. After cooling, the seeded agar plate was used for testing compounds by the disc diffusion method. Sterilized paper discs were dipped in each compound solution. These discs were placed equidistant in the plates. The central disc without any compound was taken as control. The petri plates were then incubated at 37ºC for 24 h, after which the zones of inhibition were measured. After solidification of the medium, 0.10 ml of spore suspension was spread by a sterilized spreader in a specific zone. The compounds were dissolved in DMSO solvent at 200 ppm concentration. The paper discs were dipped in each compound solution for 5 min. Then the paper discs were placed equidistant in the plates. The central disc dipped in DMSO solvent without compound was used as control. The petri plates were kept for incubation at 28ºC for 3 days, after the completion of recommended period, the zones of inhibition were measured (Table 3).

RESULTS AND DISCUSSION

In continuation of our investigations on the application of solid acids in organic synthesis, we investigated the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano [3,2-c]quinolin-5-one derivatives in the presence of $BF_3.SiO_2$ under normal heating. Herein, we report that $BF_3.SiO_2$ is an efficient and reusable catalyst for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivatives. The reaction of 4-hydroxyquinolin-2(1*H*)-one (0.32 g, 2 mmol) with 4-nitrobenzaldehyde (0.32 g, 2.1 mmol) and malononitrile (0.14 g, 2.1 mmol) was investigated for optimization of the reaction conditions (Table 1). Reaction at different temperatures and various molar ratios of substrates in the presence of $BF_3.SiO_2$ revealed that the best conditions were solvent-free at 60 °C and a ratio of 4-hydroxyquinolin-2(1*H*)-one (mmol): 4-nitrobenzaldehyde (mmol): malononitrile (mmol): 37% $BF_3.SiO_2$ of 2 : 2.1 : 2.1 : 0.5 (Table 1).

The applicability of the present method to a large-scale process was examined with 4-hydroxyquinolin-2(1*H*)-one (3.22 g, 20 mmol), 4-nitrobenzaldehyde (3.17 g, 21 mmol), and malononitrile (1.39 g, 21 mmol) under thermal conditions which gave 2-amino-3-cyano-4-(4-nitrophenyl)-1,4,5,6-tetrahydropyrano[3,2-c] quinolin-5-one in (6.70 g, 93%) yield.

4-hydroxyquinolin-2(1*H*)-one, malononitrile and various aldehydes were used as substrates for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydro pyrano[3,2-c] quinolin-5-one derivatives under normal heating, (Scheme 1 and Table 2).



Scheme 1

Table 1. Optimization of conditions for the synthesis of 2-amino-3-cyano-4-(4-nitrophenyl) -1,4,5,6-tetrahydropyrano [3,2-c] quinolin-5-one

Entry	Catalyst (mol %)	Solvent	Conditions	Time (min)	Yield[a] %
1	$BF_3.SiO_2$ (25)	Chloroform	r.t.	30	scarce
2	$BF_3.SiO_2$ (25)	Chloroform	Reflux	30	62
3	$BF_3.SiO_2$ (25)	Ethanol	r.t.	30	scarce
4	$BF_3.SiO_2$ (25)	Ethanol	Reflux	30	75
5	$BF_3.SiO_2$ (25)	Water	r.t.	30	scarce
6	$BF_3.SiO_2$ (25)	Water	Reflux	30	58
7	$BF_3.SiO_2$ (25)	Solvent-free	r.t.	30	scarce
8	$BF_3.SiO_2$ (25)	Solvent-free	50°C	30	77
9	$BF_3.SiO_2$ (25)	Solvent-free	50°C	12	60
10	$BF_3.SiO_2$ (25)	Solvent-free	60°C	8	72
11	$BF_3.SiO_2$ (30)	Solvent-free	60°C	12	95
12	$BF_3.SiO_2$ (20)	Solvent-free	60°C	12	90
13	$BF_3.SiO_2$ (25)	Solvent-free	60°C	12	95
14	$BF_3.SiO_2$ (25) 2nd run	Solvent-free	60°C	12	93
15	$BF_3.SiO_2$ (25) 2nd run	Solvent-free	60°C	12	93

. [a] Isolated yield

Table 2. Synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one derivatives *via* Scheme 1

Entry	R[b]	Time (min)	Yield[c] %	Ref
1	CH_3CH_2	25	87	20
2	$CH_3CH_2CH_2$	25	89	20
3	4- O_2N-C_6H_4	12	95	20
4	3- O_2N-C_6H_4	12	95	19
5	3,4-Cl-C_6H_4	12	94	20
6	4-MeO-C_6H_4	15	93	20
7	4-Cl-C_6H_4	15	92	20
8	4-Br-C_6H_4	15	92	20
9	2-Cl-C_6H_4	15	92	19
10	2,4-Cl-C_6H_4	15	92	19
11	3,4-CH_3O-C_6H_4	15	90	20
12	4-CN-C_6H_4	15	90	20
13	C_6H_5	15	90	20
14	4-F-C_6H_4	18	85	20
15	4-HO-C_6H_4	18	85	20

[a]4-hydroxyquinolin-2(1*H*)-one (2 mmol) and malononitrile (2.1 mmol) were stirred with various aldehydes (2.1 mmol) in the presence of 0.5 mmol of freshly prepared 37% $BF_3.SiO_2$ under neat conditions at 60 °C [b]all products are known and were characterized by IR and ^{1}H-NMR and by comparison of their physical properties with those reported in the literature.

[c]Isolated yield

The *in vitro* antibacterial activity of the synthesized novel class of 2-amino-4*H*-pyran derivatives was tested against some important bacteria by the disc diffusion method [33, 34] using Mueller-Hinton agar No. 2 as the nutrient medium. *In vitro* antibacterial assay was performed against *X. campestris pvs, P. syringae* and *P. carotovorum*. The results obtained as zone of inhibition (mm) are presented in Table 3.

The current method for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one is simple, efficient, and less time-consuming. The materials were purchased from Sigma–Aldrich and Merck and were used without additional purification. The compounds gave satisfactory analytical and spectroscopic data. A Bruker (DRX-400 Avance) NMR apparatus was used to record the ^{1}H NMR and ^{13}C NMR spectra. All NMR spectra were recorded in DMSO-d6 at ambient temperature. Melting points were measured on an Electrothermal apparatus. All products are known and were characterized by ^{1}H NMR, ^{13}C NMR and comparison of their physical properties with those reported in the literature.

In conclusion, we have demonstrated a simple method for the synthesis of 2-amino-3-cyano-1,4,5,6-tetrahydropyrano[3,2-c]quinolin-5-one using $BF_3.SiO_2$ as an eco-friendly, inexpensive and efficient reagent. Short reaction times, high yield, simplicity of operation and easy work-up are some of the advantages of this method.

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Table 3. Analytical and antibacterial activity of compounds

Entry	R	Molecular Formula	Molecular weight	Zone of inhibition (mm)		
				X.campest-rispvs	*P. syringae*	*P. carotovorum*
1	CH_3CH_2	$C_{15}H_{13}N_3O_2$	267.28	22± 0.9	19± 1.0	17± 1.1
2	$CH_3CH_2CH_2$	$C_{16}H_{15}N_3O$	281.31	19± 1.0	20± 1.1	18± 1.2
3	4-O_2N-C_6H_4	$C_{19}H_{12}N_4O$	360.32	18± 0.4	14± 0.6	16± 0.9
4	3-O_2N-C_6H_4	$C_{19}H_{12}N_4O_4$	360.32	17± 0.8	18± 1.0	20± 1.0
5	3,4-Cl_2-C_6H_3	$C_{19}H_{11}Cl_2N_3O_3O_2$	384.22	33± 1.1	28± 1.1	35± 0.7
6	4-MeO-C_6H_4	$C_{20}H_{16}N_3O_3O_2$	345.35	19± 1.1	19± 0.9	14± 1.3
7	4-Cl-C_6H_4	$C_{19}H_{12}ClN_3O_{24}$	349.77	28± 0.4	29± 1.2	30± 1.2
8	4-Br-C_6H_4	$C_{19}H_{12}BrN_3O_{24}$	394.22	23± 1.8	25± 0.4	22± 1.1
9	2-Cl-C_6H_4	$C_{19}H_{12}ClN_3O_2$	349.77	31± 0.9	29± 1.0	32± 0.8
10	2,4-Cl_2-C_6H_4	$C_{19}H_{11}Cl_2N_3O_3$	384.22	34± 1.1	32± 1.2	36± 1.2
11	3,4-MeO-C_6H_3	$C_{21}H_{17}N_3O_4$	375.38	18± 1.4	12± 1.1	12± 0.9
12	4-CN-C_6H_4	$C_{20}H_{12}N_4O_2O_2$	340.33	21± 1.1	25±1.2	23± 1.4
13	C_6H_5	$C_{19}H_{13}N_3O_2$	315.33	22± 1.2	24± 0.9	22± 1.8
14	$C_{19}H_{12}FN_3O_2$	$C_{24}H_{20}O_2$	332.32	23± 1.2	24± 1.1	21± 1.5
15	4-HO-C_6H_4	$C_{19}H_{13}N_3O_3$	331.32	27± 1.1	29± 1.3	26± 1.2

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ПРОСТ МЕТОД ЗА СИНТЕЗА И АНТИБАКТЕРИАЛНА АКТИВНОСТ НА 2-АМИНО-3-ЦИАНО-1,4,5,6-ТЕТРАХИДРОПИРАНО[3,2-C] ХИНОЛИН-5-ОН ПРОИЗВОДНИ

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(Резюме)

Съобщава се за прост метод за синтеза на 2-амино-3-циано-1,4,5,6-тетрахидропирано[3,2-c] хинолин-5-он производни и оценката на тяхната антибактериална активност спрямо *Pseudomonas syringae, Xanthomonas citi* и *Pectobacterium carotovorum*. Структурата на изолираните съединения е определена с помощта на ^{1}H/^{13}C ЯМР и FT-IR спектроскопия. Борният трифлуорид, фиксиран със силициев диоксид ($BF_3.SiO_2$) е ефикасен, лесно достъпен и многократно използваем катализатор за синтезата на is an efficient, readily available and reusable catalyst for the synthesis of 22-амино-3-циано-1,4,5,6-тетрахидропирано[3,2-c] хинолин-5-он'ови произвдони чрез кондензацията на 4-хидроксихинолин-2(1*H*)-он, алдехид и малононитрил. Тази реакция е много проста при леко нагряване и дава добри до отлични добиви. Някои от тези продукти показват значително инхибиране на микробния растеж.