Research Article

New Class of Antibiotics from Some Modified Pyrano Quinoline

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Abstract

Treatment of 8-hydroxy quinoline 1a and 8-hydroxy-2-methyl quinoline 1b with various chalcones (E)-3-phenyl-1-(pyridin-4-yl)prop-2-en-1-ones 2a-c and (E)-3-phenyl-1-(pyridin-3-yl)prop-2-en-1-ones 3a-c in presence of iodine and acetic acid under reflux condition various 4-phenyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline 4a-f and 4-phenyl-2-(pyridin-3-yl)-4H-pyrano[3,2-h]quinoline 5a-f have been obtained. All the synthesised compounds were characterized with spectral study and screened for antimicrobial studies.

Keywords: Quinoline, Pyranoquinoline, Michael addition and Antimicrobial studies

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Introduction

The plant family Balfourodedron riedelianum (Rutaceae) is considered to be a prolific source of pyranoquinoline alkaloids [1]. Balfourodedron riedelianum (Rutaceae) is a small Brazilian tree which has been used as medicine for the treatment of gastrointestinal ailments [2]. The biological activity of these alkaloids depends not only on the bicyclichetero-aromatic pharmacophore but also on the nature of the peripheral substituent and their spatial relationship. They also exhibit antimalarial [3], antitumor [4], antioxidant [5], antileishmanial [6] and antiplatelet activities [7]. In addition they function as pharmacologically active synthetic compounds [8] such as DNA binding capabilities [9] and DNA-intercalating carrier [10]. A series of compounds derived from 8-hydroxyquinoline as potential HIV-1 integrate inhibitors were synthesized recently [11a-f]. In addition pyranoquinoline derivatives have gained strong attention recently due to their activities as perspective HIV integrase inhibitors [12] and also, for their extensive biological activities [13].

Prompted by these observation and in continuation of our interest in synthesizing newer modified pyrano[3,2-h]quinoline derivatives, The pyrano[3,2-h]quinoline nucleus incorporated in quinoline moiety fused with substituent group and therefore in the present work various 4-phenyl-2-(pyridine-4-yl)- 4H-pyrano [3,2-h] quinoline 4a-f and 4-phenyl-2- (pyridine- 3-yl)-4H-pyrano[3,2-h] quinoline 5a-f have been synthesized, characterized and evaluate an antimicrobial activity against various microbial strains.

Materials and Methods

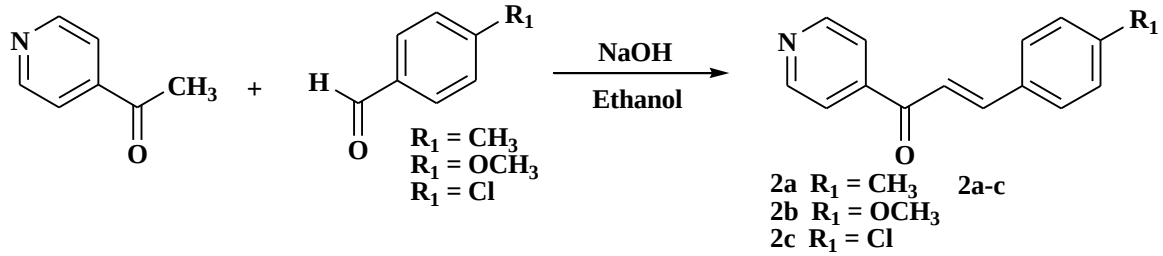
All chemicals were purchased from Sigma-Aldrich, German. Melting points were determined by the open capillary method and were uncorrected. FTIR spectra of the synthesized compounds were recorded on a Shimadzu-8400S, using KBr pellets in 10^{-4} resolution and 30 scans. ^{1}H NMR spectra were recorded on a Varian spectrometer, USA at 400 MHz at room temperature. Samples were prepared in CD_3COCD_3, CD_3OD, $CDCl_3$ and DMSO-d_6 containing TMS as an internal standard. Splitting patterns were designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Chemical shift values were given in parts per million (ppm). ^{13}C NMR were recorded on Varian 400 spectrometer, operating at 400 MHz. The Liquid Chromatography Mass Spectra (LC-MS) were recorded on a Varian Inc, USA, 410 Prostar Binary LC with 500 MS IT PDA detectors.

Experimental

Preparation of (E)-3-phenyl-1-(pyridin-4-yl)prop-2-en-1-one (2a-c) (Scheme 1) and (E)-3-phenyl-1-(pyridin-3-yl) prop-2-en-1-one (3a-c) (Scheme 2)

In a 100 mL three necked flask equipped with a thermometer and magnetic needle, an aqueous 10% sodium hydroxide solution (25 ml) and ethanol (20 ml) were added with stirring and the mixture was cooled to 0-10°C in an ice bath. An appropriate aromatic aldehyde (0.02 mol) was introduced in one portion. Then 3-acetyl pyridine or 4-acetylpyridine (0.02 mol) was added in small portions over a period of 10 minutes. The mixture was stirred for three hours at 10°C under stirring. The resulting solid was isolated by filtration and was washed with cold ethanol. The solid was then dried and recrystallized from ethanol to give yellow crystals.

Characterization of synthesized compounds



Scheme 1

(E)-1-(pyridin-4-yl)-3-p-tolylprop-2-en-1-one (Scheme-1)2a

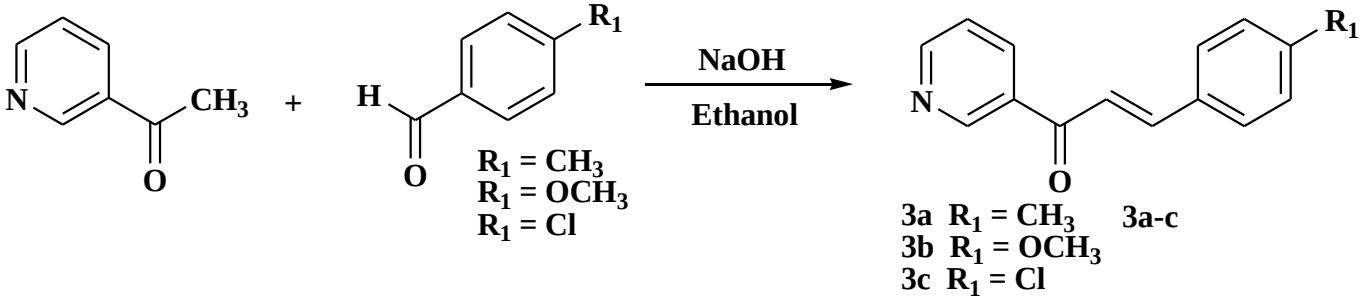
R_1 = CH_3, Yield: 85%, mp 132°C, *IR (cm^{-1})* ν_{max} 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 802 (C-H bending vibration of p-disubstituted benzene ring), 3032 (aromatic C-H stretching), *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.41 (3H, singlet, CH_3), 7.24-7.84 (8H, multiplet, aromatic protons except protons at C_2 and C_6 of pyridine ring + two olefinic protons at C_2 and C_3), 8.85 (2H, apparently doublet, protons at C_2 and C_6 of pyridine ring).

(E)-3-(4-methoxyphenyl)-1-(pyridin-4-yl)prop-2-en-1-one (Scheme-1)2b.

R_1 = OCH_3, Yield: 80%, mp 115°C, *IR (cm^{-1})* ν_{max} 1660 (C=O stretching), 1590 and 1510 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3053 (aromatic C-H stretching), *^{1}H NMR (δ, ppm) ($CDCl_3$)* 3.89 (3H, singlet, OCH_3), 6.96-7.84 (8H, multiplet, aromatic protons except protons at C_2 and C_6 of pyridine ring + two olefinic protons at C_2 and C_3), 8.84 (2H, apparently doublet, protons at C_2 and C_6 of pyridine ring).

(E)-3-(4-chlorophenyl)-1-(pyridin-4-yl)prop-2-en-1-one (Scheme-1)2c.

R_1 = Cl, Yield: 75%, mp 139°C, *IR (cm^{-1})* ν_{max} 1660 (C=O stretching), 1600 and 1490 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3034 (aromatic C-H stretching), *^{1}H NMR (δ, ppm) ($CDCl_3$)* 7.43-7.82 (8H, multiplet, aromatic protons except protons at C_2 and C_6 of pyridine ring + two olefinic protons at C_2 and C_3), 8.86 (2H, apparently doublet, protons at C_2 and C_6 of pyridine ring).



Scheme 2

(E)-1-(pyridin-3-yl)-3-p-tolylprop-2-en-1-one (Scheme-2) 3a

R_1 = CH_3, Yield: 84%, mp 102°C, *IR (cm^{-1})* ν_{max} 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 802 (C-H bending vibration of p-disubstituted benzene ring), 3032 (aromatic C-H stretching), *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.42 (3H, singlet, CH_3), 7.25-8.82 (9H, multiplet, aromatic protons except proton at C_2 of pyridine ring + two olefinic protons at C_2 and C_3), 9.25 (1H, poorly resolved doublet, proton at C_2 of pyridine ring).

(E)-3-(4-methoxyphenyl)-1-(pyridin-3-yl)prop-2-en-1-one (Scheme-2) 3b

R_1 = OCH_3, Yield: 82%, mp 96°C, ν_{max} 1659 (C=O stretching), 1589 and 1512 (aromatic C=C and C=N stretching), 810 (C-H bending vibration of p-disubstituted benzene ring), 3040 (aromatic C-H stretching), *^{1}H NMR (δ, ppm)*

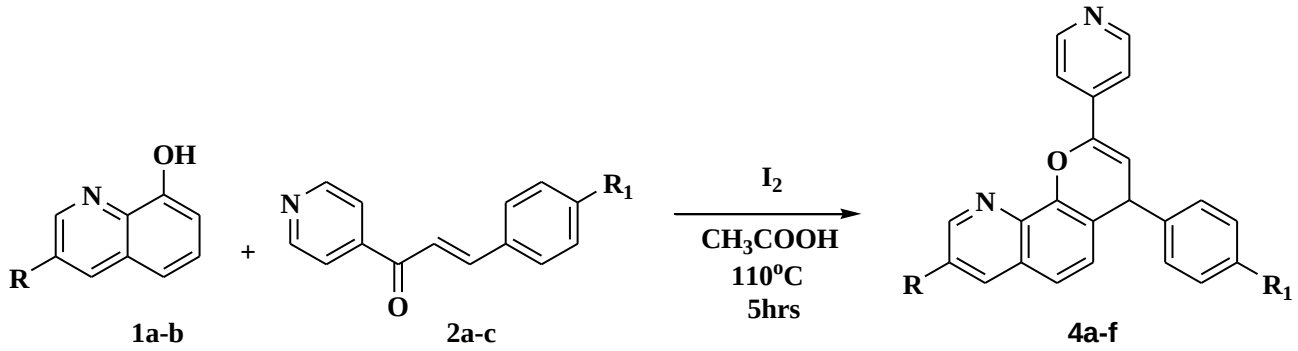
($CDCl_3$) 3.89 (3H, singlet, OCH_3), 6.96-8.82 (9H, multiplet, aromatic protons except protons at C_2 of pyridine ring + two olefinic protons at C_2 and C_3), 9.24 (1H, poorly resolved doublet, proton at C_2 of pyridine ring).

(E)-3-(4-chlorophenyl)-1-(pyridin-3-yl)prop-2-en-1-one (Scheme-2) 3c

R_3 = Cl, Yield: 77%, mp 134°C, ν_{max} 1659 (C=O stretching), 1589 and 1489 (aromatic C=C and C=N stretching), 802 (C-H bending vibration of p-disubstituted benzene ring), 3086 (aromatic C-H stretching), *^1H NMR (δ, ppm) ($CDCl_3$)* 7.42-8.84 (9H, multiplet, aromatic protons except protons at C_2 of pyridine ring + two olefinic protons at C_2 and C_3), 9.24 (1H, poorly resolved doublet, proton at C_2 of pyridine ring).

Preparation of 4-phenyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (4a-f) (Scheme 3), 4-phenyl-2-(pyridin-3-yl)-4H-pyrano[3,2-h]quinoline (5a-f) (Scheme 4)

A mixture of a selected chalcone (0.5 mmol), 8-hydroxy quinoline (0.5 mmol), and iodine (0.5 mmol) was dissolved in 15 mL acetic acid. Then, the mixture was stirred under reflux at 100℃ for four hours. The reaction mixture was cooled to room temperature and diluted with water, followed by $Na_2S_2O_3H_2O$ solution to quench excess iodine. The reaction mixture was filtered invacuo, and the residue was purified by column chromatography on silica gel (60-120 mesh) using $CHCl_3$: Pet-Ether (80:20) as an eluent to give the pure product.



Scheme 3

Characterization of synthesized compounds

2-(pyridin-4-yl)-4-p-tolyl-4H-pyrano[3,2-h]quinoline (Scheme-3) 4a

R=H, R_1 = CH_3, Yield: 90%, mp 197°C, *IR (cm^{-1})*, ν_{max} 1730 (C=O stretching of δ-lactone of coumarin), 1612 and 1518 (aromatic C=C and C=N stretchings), 3010 (aromatic C-H stretching), 751 and 972 (C-H bending vibrations of mono substituted benzene ring), 2930 (aliphatic C-H stretching), 1050 (C-O-C stretching of benzopyran ring). *^1H NMR (δ, ppm) ($CDCl_3$)* 2.20 (3H, singlets, 1 × CH_3), 4.62 (1H, poorly resolved doublet), 6.11(1H, poorly resolved doublet), 7.21-8.10 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 25.32(CH_3), 44.20(CH), 110.21(CH), 1115.29(CH), 111.74(CH), 1117.9(CH), 125.3(C), 126.51(C), 128.24(CH), 129.42(CH), 128.65(CH), 141.57(CH), 132.19(C), 138.45(C), 137.65(C), 144.38(C), 149.78(CH), 150.19(CH), 151.50(C), 151.78(C).

4-(4-methoxyphenyl)-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme-3) 4b

R=H, R_1 = OCH_3, Yield: 78%, mp 188°C, *IR (cm^{-1})*, ν_{max} 1715 (C=O stretching of δ-lactone of coumarin), 1615 and 1507 (aromatic C=C and C=N stretchings), 3012 (aromatic C-H stretching), 760 and 972 (C-H bending vibrations of mono substituted benzene ring), 2937 (aliphatic C-H stretching), 1113 (C-O-C stretching of benzopyran ring). *^1H NMR (δ, ppm) ($CDCl_3$)* 3.64 (3H, singlets, 1 × OCH_3), 4.70 (1H, poorly resolved doublet), 6.21(1H, poorly resolved doublet), 7.12-8.54 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 47.28(CH), 57.66(OCH_3), 101.21(CH), 120.29(CH), 120.74(CH), 120.9(CH), 121.3(C), 127.41(C), 128.24(CH), 128.44(CH), 129.64(CH), 135.57(CH), 136.11(C), 137.45(C), 137.68(C), 144.33(C), 149.72(CH), 150.11(CH), 151.45(C), 151.66(C).

4-(4-chlorophenyl)-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme-3) 4c

R=H, R_1 = OCH_3, Yield: 79%, mp 194°C, *IR (cm^{-1})*, ν_{max} 1745 (C=O stretching of δ-lactone of coumarin), 1653 and

1512 (aromatic C=C and C=N stretchings), 3010 (aromatic C-H stretching), 760 and 934 (C-H bending vibrations of mono substituted benzene ring), 2955 (aliphatic C-H stretching), 1117 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 4.12 (1H, poorly resolved doublet), 6.37(1H, poorly resolved doublet), 7.87-8.16 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 45.31(CH), 56.66(OCH_3), 101.11(CH), 120.19(CH), 120.74(CH), 121.1(CH), 121.53(C), 127.50(C), 128.74(CH), 128.44(CH), 129.12(CH), 135.57(CH), 136.11(C), 137.45(C), 137.56(C), 144.41(C), 149.82(CH), 150.11(CH), 151.85(C), 151.16(C).

8-methyl-2-(pyridin-4-yl)-4-p-tolyl-4H-pyrano[3,2-h]quinoline (Scheme-3) 4d

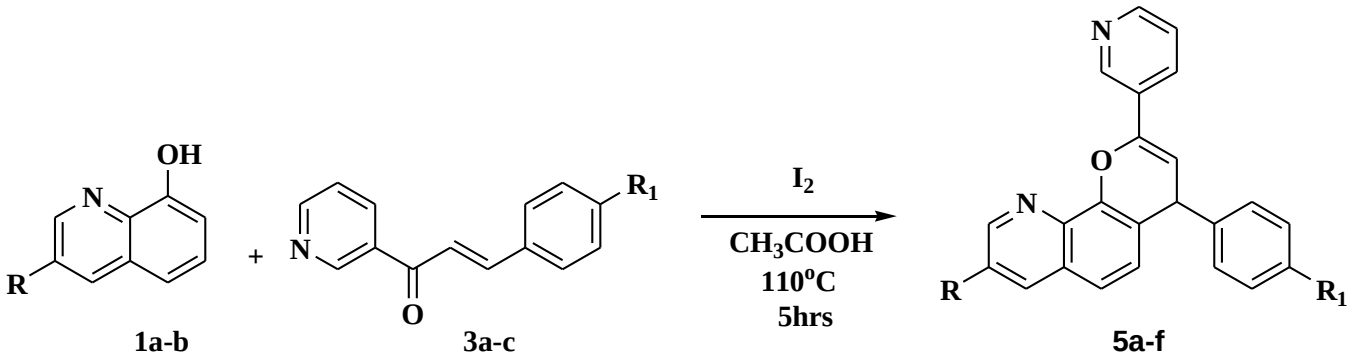
R=CH_3, R_1 = CH_3, Yield: 88%, mp 183°C, *IR (cm^{-1}),* ν_{max} 1764 (C=O stretching of δ-lactone of coumarin), 1614 and 1518 (aromatic C=C and C=N stretchings), 3020 (aromatic C-H stretching), 768 and 967 (C-H bending vibrations of mono substituted benzene ring), 2922 (aliphatic C-H stretching), 1063 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.14 (6H, singlets, 2 × CH_3), 4.11 (1H, poorly resolved doublet), 6.47(1H, poorly resolved doublet), 7.32-8.21 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 21.55(CH_3), 21.18(CH_3), 44.38(CH), 100.11(CH), 120.12(CH), 121.60(C), 127.51(C), 128.14(CH), 128.40(CH), 129.17(C), 130.52(C), 135.87(CH), 135.91(C), 137.45(C), 137.70(C), 145.12(C), 149.72(CH), 150.11(CH), 150.95(C), 151.60(C).

4-(4-methoxyphenyl)-8-methyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme-3) 4e

R=CH_3, R_1 = OCH_3, Yield: 79%, mp 184°C, *IR (cm^{-1}),* ν_{max} 1725 (C=O stretching of δ-lactone of coumarin), 1611 and 1527 (aromatic C=C and C=N stretchings), 3075 (aromatic C-H stretching), 768 and 967 (C-H bending vibrations of mono substituted benzene ring), 2897 (aliphatic C-H stretching), 1089 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.34 (3H, singlets, 1 × CH_3), 3.92 (3H, singlets, 1 × OCH_3), 4.72 (1H, poorly resolved doublet), 6.17(1H, poorly resolved doublet), 7.44-8.72 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 20.23(CH_3), 21.28(CH_3), 45.31(CH), 100.21(CH), 120.29(CH), 120.3(C), 128.12(C), 128.24(CH), 128.42(CH), 129.64(CH), 130.33(C), 135.70(CH), 136.21(C), 137.11(C), 137.60(C), 145.32(C), 149.72(CH), 150.11(CH), 151.45(C), 151.66(C).

4-(4-chlorophenyl)-8-methyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme-3) 4f

R=CH_3, R_1 = Cl, Yield: 75%, mp 193°C, *IR (cm^{-1}),* ν_{max} 1708 (C=O stretching of δ-lactone of coumarin), 1632 and 1514 (aromatic C=C and C=N stretchings), 3020 (aromatic C-H stretching), 740 and 932 (C-H bending vibrations of mono substituted benzene ring), 2937 (aliphatic C-H stretching), 1091 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.54 (3H, singlets, 1 × CH_3), 4.64 (1H, poorly resolved doublet), 6.21(1H, poorly resolved doublet), 7.17-8.45 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 21.12(CH_3), 21.82(CH_3), 44.31(CH), 100.22(CH), 120.29(CH), 121.7(C), 127.51(C), 128.24(CH), 128.63(CH), 129.64(CH), 130.33(C), 135.57(CH), 135.91(C), 137.45(C), 137.60(C), 145.10(C), 149.72(CH), 150.11(CH), 150.45(C), 151.30(C).



Scheme 4

2-(pyridin-3-yl)-4-p-tolyl-4H-pyrano[3,2-h]quinoline (Scheme 4) 5a

R=H, R_1 = CH_3, Yield: 79%, mp 195°C, *IR (cm^{-1}),* ν_{max} 1733 (C=O stretching of δ-lactone of coumarin), 1595 and 1512 (aromatic C=C and C=N stretchings), 3023 (aromatic C-H stretching), 759 and 957 (C-H bending vibrations of

mono substituted benzene ring), 2912 (aliphatic C-H stretching), 1081 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.14 (3H, singlets, 1 × CH_3), 4.23 (1H, poorly resolved doublet), 6.47(1H, poorly resolved doublet), 7.34-8.16 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 21.18(CH_3), 44.20(CH), 100.84(CH), 120.23(CH), 120.24(CH), 121.09(CH), 121.30(C), 127.51(C), 128.17(CH), 128.42(CH), 129.64(CH), 135.84(CH), 135.91(C), 137.32(C), 137.60(C), 144.12(C), 149.72(CH), 150.23(CH), 151.50(C), 151.66(C).

4-(4-methoxyphenyl)-2-(pyridin-3-yl)-4H-pyrano[3,2-h]quinoline (Scheme 4) 5b

R=H, R_1 = OCH_3, Yield: 91%, mp 186C, *IR (cm^{-1})*, ν_{max} 1737 (C=O stretching of δ-lactone of coumarin), 1609 and 1519 (aromatic C=C and C=N stretchings), 3034 (aromatic C-H stretching), 752 and 957 (C-H bending vibrations of mono substituted benzene ring), 2927 (aliphatic C-H stretching), 1102 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 3.54 (3H, singlets, 1 × OCH_3), 4.66 (1H, poorly resolved doublet), 6.72(1H, poorly resolved doublet), 7.32-8.18 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 45.31(CH), 58.20(OCH_3), 100.41(CH), 120.40(CH), 120.10(CH), 120.9(CH), 121.3(C), 128.51(C), 128.94(CH), 129.02(CH), 129.64(CH), 135.57(CH), 135.91(C), 137.45(C), 137.60(C), 144.20(C), 149.72(CH), 150.11(CH), 151.10(C), 151.56(C).

4-(4-chlorophenyl)-2-(pyridin-3-yl)-4H-pyrano[3,2-h]quinoline (Scheme 4) 5c

R=H, R_1 = OCH_3, Yield: 84%, mp 190°C, *IR (cm^{-1})*, ν_{max} 1723 (C=O stretching of δ-lactone of coumarin), 1594 and 1512 (aromatic C=C and C=N stretchings), 3019 (aromatic C-H stretching), 758 and 961 (C-H bending vibrations of mono substituted benzene ring), 2937 (aliphatic C-H stretching), 1182 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 4.14 (1H, poorly resolved doublet), 6.20(1H, poorly resolved doublet), 7.47-8.88 (13H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 45.31(CH), 58.66(OCH_3), 101.21(CH), 120.29(CH), 120.74(CH), 120.91(CH), 121.3(C), 127.51(C), 127.91(CH), 128.12(CH), 129.10(CH), 135.57(CH), 135.91(C), 137.45(C), 137.60(C), 144.32(C), 149.80(CH), 150.11(CH), 151.45(C), 152.16(C).

8-methyl-2-(pyridin-3-yl)-4-p-tolyl-4H-pyrano[3,2-h]quinoline (Scheme 4) 5d

R=CH_3, R_1 = CH_3, Yield: 87%, mp 182°C, *IR (cm^{-1})*, ν_{max} 1747 (C=O stretching of δ-lactone of coumarin), 1611 and 1497 (aromatic C=C and C=N stretchings), 3015 (aromatic C-H stretching), 751 and 930 (C-H bending vibrations of mono substituted benzene ring), 2947 (aliphatic C-H stretching), 1091 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.11 (6H, singlets, 2 × CH_3), 4.67 (1H, poorly resolved doublet), 6.88(1H, poorly resolved doublet), 7.45-8.28 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 23.34(CH_3), 23.88(CH_3), 44.31(CH), 101.21(CH), 120.14(CH), 121.3(C), 128.11(C), 128.24(CH), 128.42(CH), 129.64(C), 130.33(C), 135.57(CH), 135.91(C), 137.45(C), 137.60(C), 145.32(C), 149.42(CH), 150.11(CH), 151.15(C), 151.67(C).

4-(4-methoxyphenyl)-8-methyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme 4) 5e

R=CH_3, R_1 = OCH_3, Yield: 80%, mp 180°C, *IR (cm^{-1})*, ν_{max} 1708 (C=O stretching of δ-lactone of coumarin), 1609 and 1542 (aromatic C=C and C=N stretchings), 3010 (aromatic C-H stretching), 775 and 912 (C-H bending vibrations of mono substituted benzene ring), 2940 (aliphatic C-H stretching), 1101 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.35 (3H, singlets, 1 × CH_3), 3.99 (3H, singlets, 1 × OCH_3), 4.12 (1H, poorly resolved doublet), 6.25(1H, poorly resolved doublet), 7.55-8.48 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 21.55(CH_3), 21.75(CH_3), 44.31(CH), 100.21(CH), 120.29(CH), 121.3(C), 127.51(C), 128.24(CH), 128.42(CH), 130.14(CH), 130.37(C), 135.57(CH), 135.91(C), 137.15(C), 137.60(C), 144.42(C), 149.12(CH), 150.21(CH), 151.20(C), 151.63(C).

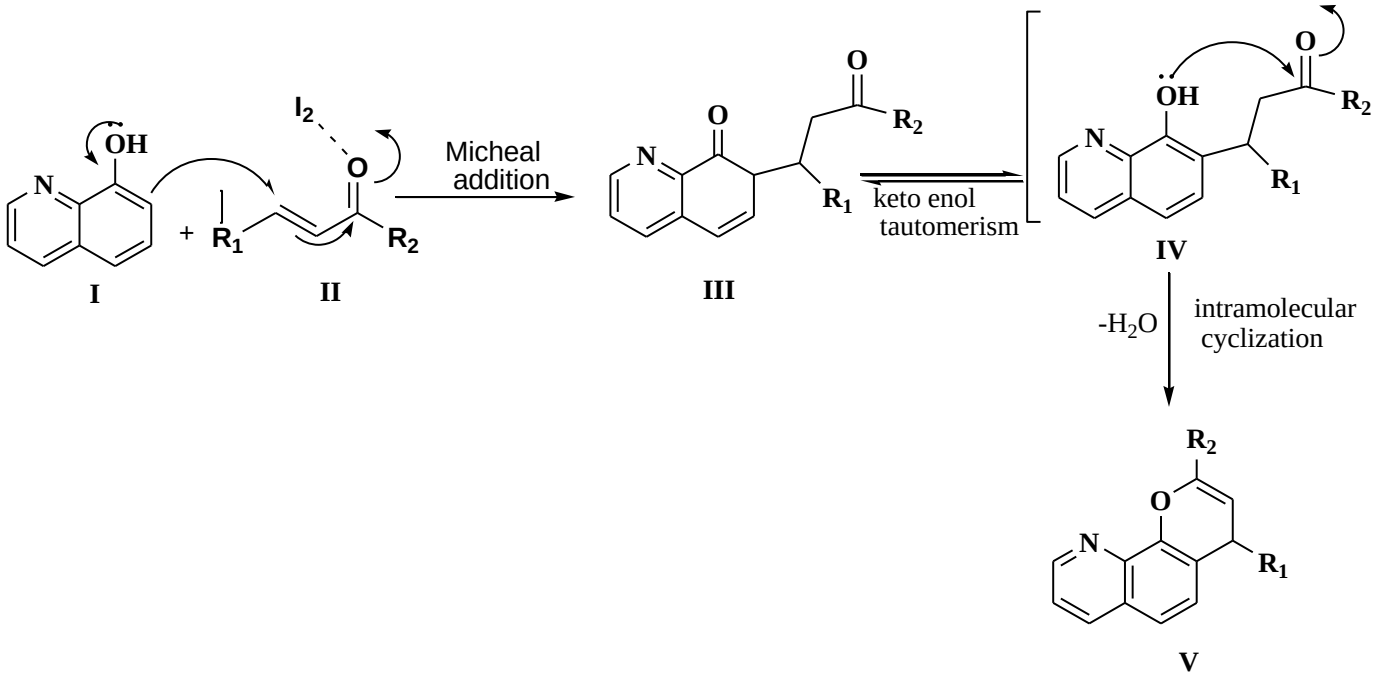
4-(4-chlorophenyl)-8-methyl-2-(pyridin-4-yl)-4H-pyrano[3,2-h]quinoline (Scheme 4) 5f

R=CH_3, R_1 = Cl, Yield: 83%, mp 195°C, *IR (cm^{-1})*, ν_{max} 1761 (C=O stretching of δ-lactone of coumarin), 1594 and 1497 (aromatic C=C and C=N stretchings), 3042 (aromatic C-H stretching), 710 and 937 (C-H bending vibrations of mono substituted benzene ring), 2940 (aliphatic C-H stretching), 1110 (C-O-C stretching of benzopyran ring). *^{1}H NMR (δ, ppm) ($CDCl_3$)* 2.44 (3H, singlets, 1 × CH_3), 4.50 (1H, poorly resolved doublet), 6.54(1H, poorly resolved doublet), 7.47-8.74 (12H, multiplet, aromatic protons except protons), ^{13}C NMR *(δ, ppm) ($CDCl_3$)* 21.10(CH_3),

21.75(CH_3), 44.12(CH), 100.10(CH), 120.34(CH), 121.7(C), 127.94(C), 128.24(CH), 128.74(CH), 129.22(CH), 130.10(C), 135.57(CH), 135.91(C), 137.40(C), 137.60(C), 144.10(C), 149.72(CH), 151.11(CH), 151.45(C), 151.41(C).

Results and Discussion

A possible mechanism is proposed in Scheme 5, where molecular iodine ligated with chalcone (II) activates Michael addition [14] with 8-hydroxyquinoline (I) and forms a 1,5-diketone (III) intermediate. The unstable intermediate is equilibrated in keto-enol (IV) forms. Further, the intermediate undergoes intramolecular cyclization by the loss of a water molecule to form the desired product (V).



Scheme 5

The newly synthesized target compounds (4a-f) and (5a-f) were evaluated for their *in vitro* antibacterial activity against two Gram positive bacteria *Staphylococcus aureus* (MTCC 96) and *Bacillus subtilis* (MTCC 441) and two Gram negative bacteria *Escherichia coli* (MTCC 443) and *Salmonella typhi* (MTCC 98). They were also evaluated for their *in vitro* antifungal activity against *Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 282) as fungal strains. Broth dilution method was used for the determination of the antibacterial and antifungal activity as recommended by NCCLS [15]. Ampicillin, Chloramphenicol and Norfloxacin were used as standard antibacterial drugs, whereas Griseofulvin and Nystatin were used as standard antifungal drugs. All MTCC cultures were collected from Institute of Microbial Technology, Chandigarh and tested against above mentioned known drugs. Mueller-Hinton broth was used as the nutrient medium for the test bacteria and Sabouraud Dextrose broth was used for the test fungi. Inoculum size for the test strains was adjusted to 10^8 CFU (Colony Forming Unit per milliliter) per milliliter by comparing the turbidity. Each synthesized compound was diluted with DMSO so as to have the stock solution of 2000 $\mu g/$mL concentration as a stock solution. The results were recorded in the form of primary and secondary screening. The synthesized compounds (4a-f) and (5a-f) were screened for their antibacterial and antifungal activity at the concentration of 1000, 500 and 250 $\mu g/$mL for the primary screening. The synthesized compound showing activity against microbes in the primary screening were further screened in a second set of dilution at concentrations of 200, 100, 62.5, 50 and 25 $\mu g/$mL. The suspention of 10 μL from each well was further incubated and growth was noted at 37°C after 24 hour for bacteria and 48 hour for fungi. The lowest concentration which showed no visible growth (turbidity) after spot subculture was considered as the minimum inhibitory concentration (MIC) for each compound.

The investigation of the data summarized in (**Table 1**) reveals that many compounds were found to be active against Gram-positive bacteria while some of the compounds were found to be active against Gram-negative bacterial and fungal species as compared to that of the standard antimicrobial drugs.

Table 1 Biological Activity of (4a-f) and (5a-f) against standard drugs

Compound	Minimum Inhibitory Concentration (MIC, $\mu g mL^{-1}$)					
	Gram +ve bacteria		Gram –ve bacteria		Fungi	
	B.s.	***S.a.***	***E.c.***	***S.t.***	***A.n.***	***C.a.***
4a	200	250	100	250	>1000	1000
4b	100	100	200	100	>1000	250
4c	200	250	250	100	1000	500
4d	100	200	250	100	>1000	1000
4e	100	125	200	62.5	1000	1000
4f	100	200	250	125	>1000	500
5a	250	500	100	125	>1000	>1000
5b	250	200	100	250	>1000	500
5c	500	250	200	200	>1000	>1000
5d	250	200	125	250	>1000	>1000
5e	200	125	200	100	>1000	500
5f	100	62.5	250	200	1000	>1000
Ampicillin	250	250	100	100	-	-
Chloramphenicol	50	50	50	50	-	-
Ciprofloxacin	50	50	25	25	-	-
Norfloxacin	100	10	10	10	-	-
Gentamycin	0.5	0.25	0.05	1	-	-
Griseofulvin	-	-	-	-	100	500
Nystatin	-	-	-	-	100	100

B.s.: Bacillus subtilis, S.a.: Staphylococcus aureus, E.c.: Escherichia coli, S.t.: Salmonella typhi, A.n.: Aspergillus niger, C.a.: Candida albicans

Conclusion

In conclusion, we have developed a molecular iodine–promoted efficient and regioselective synthetic method for highly functionalized pyranocoumarin derivatives in good to excellent yield from various 8-hydroxy quinolines and chalcones derivatives in AcOH solvent at 100°C. Our protocol has synthesized functionalized pyranoquinoline and has advantages such as cheap catalyst, nontoxic and commercially available substrates, economic viability, and environmental compatibility.

Three series of newer pyrano[3,2-h]quinolines derivatives were synthesized in reasonably good yields. They were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectrometry. All the newly synthesized compounds were screened for antimicrobial activity by Broth dilution method. Upon evaluating the antimicrobial activity data, it has been observed that compounds 4b, 4d, 4e, 4f and 5f (MIC = 100µg/mL) exhibited excellent activity against gram positive bacteria *Bacillus subtilis* compared to Ampicillin (MIC = 250µg/mL) and equal activity to Norfloxacin (MIC = 100µg/mL). Compounds 4a, 4c and 5e (MIC = 200µg/mL) showed better activity compared to Ampicillin (MIC = 250µg/mL) whereas 5a, 5b and 5d (MIC = 250µg/mL) were found to be equipotent to Ampicillin (MIC = 250µg/mL).

Compounds 5f (MIC = 62.5 µg/mL), 4b (MIC = 100 µg/mL), 4e and 5e (MIC = 125 µg/mL) showed excellent activity against gram positive bacteria *Staphylococcus aureus* compared to Ampicillin(MIC = 100 µg/mL). Compounds 4d, 4f, 5b and 5d (MIC = 200 µg/mL) showed better activity compared to Ampicillin (MIC = 250µg/mL) whereas 4a, 4c and 5c (MIC = 250µg/mL) were found to be equipotent to Ampicillin (MIC = 250µg/mL) against *Escherichia coli*.

Compounds 4a, 5a and 5b (MIC = 100 µg/mL) were found to be equipotent to Ampicillin (MIC = 100µg/mL) against *Escherichia coli*.

Compound 4e (MIC = 62.5 µg/mL) exerted excellent activity against gram negative bacteria *Salmonella typhi* compared to Ampicillin (MIC = 100 µg/mL). Compounds 4b, 4c, 4d, 5e (MIC =100µg/mL) were found to be equipotent to Ampicillin (MIC = 100µg/mL) against *Salmonella typhi.*

Compound 4b (MIC = 250µg/mL) was found to be more active than Griseofulvin (MIC = 500µg/mL) against fungal pathogen *Candida albicans* while compounds 4c, 4f, 5b and 5e (MIC = 500µg/mL) were found to be equipotent to Griseofulvin against *Candida albicans.* None of the tested compounds showed better activity towards the *Aspergillus niger*.

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