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Cannizzaro reaction of 2-chloro-3-formylquinolines and its synthetic utility for 2-acetylfuro[2,3-*b*]quinolines: The alkaloid analogues

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Abstract. Cannizzaro reaction of 2-chloro-3-formylquinolines was investigated under two different conditions. Under both conditions, redox and methoxylation proceeded simultaneously and gave 2-methoxy-3-formylquinolines, 2-methoxyquinolin-3-yl-methanols and 2-methoxyquinoline-3-carboxylic acids. The synthesized 2-methoxy-3-formylquinolines were then condensed with acetone in the presence of sulphuric acid to give 4-(2-methoxy-quinolin-3-yl)-but-3-en-2-ones which in turn were bromocyclized and dehydrobrominated to get 2-acetylfuro[2,3-*b*]quinolines.

Keywords. Cannizzaro reaction; bromocyclisation; 2-methoxy-3-formylquinolines; furoquinolines; 2-chloro-3-formylquinolines.

1. Introduction

Natural products bearing furo[2,3-*b*]quinoline skeleton and their synthetic analogues play a vital role in drug development and drug discovery. In recent years, many synthetic methods have been developed for furo[2,3-*b*]quinolines.[1–4] The 2-acetylfuro[2,3-*b*]quinoline alkaloids (figure 1) have been isolated from the root bark of *Melicope semecarpifolia* and the extract of this plant was used for antiplatelet aggregation activity.[5] Molecules containing furo[2,3-*b*]quinoline scaffold show a wide range of biological activities which include vasoconstructive, antidiuretic, antiarrhythmic, spamolytic, sedative, hypothermal effects,[6] antitumour, antipyretic, antiplatelet and cytotoxic activities.[7,8] This wide range of biological activities has encouraged us to develop a new route for the synthesis of acetyl substituted furo[2,3-*b*]quinolines.

2. Experimental

2.1 *General*

Melting points were determined using a Raga melting point apparatus and were uncorrected. IR spectra were recorded on Shimadzu FT IR PC (S) 8201spectrometer using KBr pellets and the absorption frequencies are expressed in reciprocal centimetres (cm^{-1}). NMR spectra were taken on BRUKER 400 MHz and 500 MHz spectrometer using TMS as an internal reference. The chemical shifts were expressed in parts per million (ppm). The mass spectra were determined on an Autospec EI^+ mass spectrometer and HRMS (ESI) mass spectrometer. Elemental analyses were performed on Vario EL IIICHNS Analyzer and Perkin Elmer Analyzer.

2.2 *General Procedure for 2-methoxyquinoline-3-carbaldehydes* **2**(**a–f**)*, 2-methoxyquinolin-3-yl)-methanols* **3**(**a–f**) *and 2-methoxyquinoline-3-carboxylic acids* **4**(**a–f**)

A solution of compound **1**(**a–f**) (**1d**, 1.025 g, 0.005 mol) in KOH (6 g) in methanol (30 mL) was stirred for 24 h at room temperature or refluxed for 12 h until starting material was disappeared. The mixture was then poured into crushed ice and neutralized with 4N HCl. The precipitate was filtered off, dried and column chromatographed over silcagel using a mixture of petroleum ether and ethylacetate as eluent. The solvent (PE: EA) combination ratio for **2**(**a–f**), **3**(**a–f**) and **4**(**a–f**) were 100:0, 90:10, 80:20, respectively.

2.2a *2-Methoxy-quinoline-3-carbaldehydes* **2**(**a–f**): The spectroscopic data and melting points are consistent with reported in literature.[10–12]

2.2b *(2-Methoxy-8-methylquinolin-3-yl)-methanol* (**3d**). *mp 101°C; IR (KBr)*: 3212 cm^{-1}; ^1H NMR

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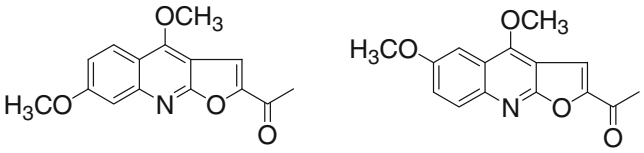


Figure 1. Acetyl derivative of furoquinoline alkaloids.

(500 MHz; DMSO-d_6): $\delta = 2.65$ (s, 3H, CH_3), 4.03 (s, 3H, OCH_3), 4.60 (d, 2H, $J = 5Hz$, CH_2OH), 5.36 (t, 1H, $J = 5Hz$, OH), 7.30 (t, 1H, $J = 7.4$ Hz C_6H), 7.49 (d, 1H, $J = 7.4$ Hz, C_7H), 7.72 (d, 1H, $J = 7.4$ Hz, C_5H), 8.15(s, 1H, C_4H); ^{13}C NMR (125 MHz, DMSO-d_6): 17.8, 53.3, 58.3,124.1, 125.3, 125.7, 126.6, 129.4, 134.3, 134.9, 143.9, 158.9. MS (ESI, m/z): 204.13 $[M+H]^+$. Anal, Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.73; H, 6.26; N, 6.70.

2.2c *(2-Methoxyquinolin-3-yl)-methanol* (**3a**). *mp 109°C; IR (KBr)*: 3215 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 4.03$ (s, 3H, OCH_3), 4.62 (d, 2H, $J = 5Hz$, CH_2OH), 5.38 (t, 1H, $J = 5Hz$, OH), 7.63 (t, 1H, $J = 8.5Hz$, C_6H), 7.85 (t, 1H, $J = 8.5Hz$, C_7H), 7.96 (d, 1H, $J = 8.5Hz$, C_8H), 8.07 (d, 1H, $J = 8.5Hz$, C_5H), 8.20 (s, 1H, C_4H); Anal, Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.62; H, 6.03; N, 7.23.

2.2d *(2-Methoxy-6-methylquinolin-3-yl)-methanol* (**3b**). *mp 127°C; IR (KBr)*: 3222 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 2.43$ (s, 3H, CH_3), 4.01 (s, 3H, 2-OCH_3), 4.52 (d, 2H, $J = 5Hz$, CH_2OH), 5.29 (t, 1H, $J = 5$ Hz, OH), 7.21 (d, 1H, $J = 9$ Hz, C_8H), 7.33 (s, 1H, C_5H), 7.64 (d, 1H, $J = 9$ Hz, C_7H), 8.06 (s, 1H, C_4H); Anal, Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.75; H, 6.25; N, 6.72.

2.2e *(2-Methoxy-7-methylquinolin-3-yl)-methanol* (**3c**). *mp 112°C; IR (KBr)*: 3234 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 2.41$ (s, 3H, CH_3), 3.97 (s, 3H, 2-OCH_3), 4.54 (d, 2H, $J = 5$ Hz, CH_2OH), 5.32 (t, 1H, $J = 5Hz$, OH), 7.15 (s, 1H, C_8H), 7.31 (d, 1H, $J = 8.4$ Hz, C_5H), 7.35 (d, 1H, $J = 8.4$ Hz, C_6H), 8.17 (s, 1H, C_4H); Anal, Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.78; H, 6.60; N, 7.05.

2.2f *2, 6-Dimethoxyquinolin-3-yl-methanol* (**3e**). *mp 105°C; IR (KBr)*: 3227 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 3.85$ (s, 3H, 6-OCH_3), 3.97 (s, 3H, 2-OCH_3), 4.57 (d, 2H, $J = 5Hz$, CH_2OH), 5.33 (t, 1H, $J = 5Hz$, OH), 7.24 (d, 1H, $J = 9$ Hz, C_8H), 7.35 (s, 1H, C_5H), 7.67 (d, 1H, $J = 9$ Hz, C_7H), 8.11(s, 1H, C_4H); Anal, Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.58; H, 5.78; N, 6.23.

2.2g *2, 7-Dimethoxyquinolin-3-yl-methanol* (**3f**). *mp 98°C; IR (KBr)*: 3230 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 3.84$ (s, 3H, 7-OCH_3), 3.94 (s, 3H, 2-OCH_3), 4.60 (d, 2H, $J = 5Hz$, CH_2OH), 5.29 (t, 1H, $J = 5Hz$, OH), 7.12 (s, 1H, C_8H), 7.28 (d, 1H, $J = 8.2Hz$, C_5H), 7.38 (d, 1H, $J = 8.2Hz$, C_6H), 8.19 (s, 1H, C_4H); Anal, Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.90; H, 5.82; N, 6.22.

2.2h *8-Methyl-2-methoxyquinoline-3-carboxylic acid* (**4d**). *mp 186°C; IR (KBr)*: 1699, 3116 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 2.65$ (s, 3H, CH_3), 4.06 (s, 3H, OCH_3), 7.37 (t, 1H, $J = 8$ Hz, C_6H), 7.64 (d, 1H, $J = 8$ Hz, C_7H), 7.84 (d, 1H, $J = 8$ Hz, C_5H), 8.15 (s, 1H, C_4H); ^{13}C NMR (125 MHz, DMSO-d_6) 17.6, 53.7, 117.1, 124, 124.8, 127, 132.1, 134.6, 142.5, 145.9, 158.5, 166.4. Anal, Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.19; H, 5.28; N, 6.24.

2.2i *2-Methoxyquinoline-3-carboxylic acid* (**4a**). *mp 174°C; IR (KBr)*: 1695, 3120 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 4.03$ (s, 3H, OCH_3), 7.68 (t, 1H, $J = 8.6$ Hz, C_6H), 7.89 (t, 1H, $J = 8.6$ Hz, C_7H), 8.12 (d, 1H, $J = 8.6$ Hz C_8H), 8.17 (d, 1H, $J = 8.6$ Hz, C_5H), 8.23 (s, 1H, C_4H); Anal, Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.16; H, 4.32; N, 6.74.

2.2j *2-Methoxy-6-methylquinoline-3-carboxylic acid* (**4b**). *mp 182°C; IR (KBr)*: 1702, 3128 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 2.44$ (s, 3H, CH_3), 4.01 (s, 3H, 2-OCH_3), 7.22 (d, 1H, $J = 8.3$ Hz, C_8H), 7.34 (s, 1H, C_5H), 7.64 (d, 1H, $J = 8.3Hz$, C_7H), 8.04 (s, 1H, C_4H); Anal, Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.19; H, 5.32; N, 6.59.

2.2k *2-Methoxy-7-methylquinoline-3-carboxylic acid* (**4c**). *mp 203°C; IR (KBr)*: 1722, 3133 cm^{-1}; ^{1}H NMR (500 MHz; DMSO-d_6): $\delta = 2.41$ (s, 3H, CH_3), 3.98 (s, 3H, 2-OCH_3), 7.19 (s, 1H, C_8H), 7.35 (d, 1H, $J = 8.2Hz$, C_5H), 7.39 (d, 1H, $J = 8.2$ Hz, C_6H), 8.20 (s, 1H, C_4H), Anal, Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.52; H, 5.27; N, 6.28.

2.2l *2,6-Dimethoxyquinoline-3-carboxylic acid* (**4e**). *mp 168°C; IR (KBr)*: 1731, 3142 cm^{-1}; ^{1}H NMR

(500 MHz; DMSO-d_6): $\delta = 3.87$ (*s*, 3H, 6-OCH_3), 3.99 (*s*, 3H, 2-OCH_3), 7.40 (*d*, 1H, *J = 9 Hz*, C_8H), 7.46 (*s*, 1H, C_5H), 7.72 (*d*, 1H, *J = 9 Hz*, C_7H), 8.60 (*s*, 1H, C_4H), 13.1(*s*, 1H, COOH); Anal, Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.64; H, 4.58; N, 6.18.

2.2m *2,7-Dimethoxyquinoline-3-carboxylic acid* (**4f**). *mp 156°C; IR (KBr)*: 1737, 3126 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): $\delta = 3.85$ (*s*, 3H, 7-OCH_3), 3.96 (*s*, 3H, 2-OCH_3), 7.14 (*s*, 1H, C_8H), 7.31 (*d*, 1H, *J = 8.4Hz*, C_5H), 7.40 (*d*, 1H, *J = 8.4 Hz*, C_6H), 8.23 (*s*, 1H, C_4H); Anal, Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.75; N, 6.01. Found: C, 61.97; H, 4.91; N, 5.83.

2.3 *General procedure for 4-(2-methoxyquinolin-3-yl)-but-3-en-2-one* **5(a–f)**

A mixture of compound **2(a–f)** (**2d**, 1.006 g, 0.005 mol) and acetone (40 mL) and few drops of sulphuric acid was refluxed in water bath for 6 h. After completion of the reaction which was checked by TLC the mixture was poured into crushed ice. The precipitate was filtered off, dried, and column chromatographed over silica gel using petroleum ether and ethyl acetate (90:10) as eluent to give compound **5(a–f)**.

2.3a *4-(8-Methyl-quinolin-3-yl)-but-3-en-2-one* (**5d**): Yield 86%; mp 83°C; IR (KBr): 1674 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): $\delta = 2.42$ (*s*, 3H, $COCH_3$), 2.69 (*s*, 3H, CH_3), 4.15 (*s*, 3H, OCH_3), 6.95 (*d*, 1H, *J = 16.4 Hz*, $C_\alpha H$), 7.27 (*t*, 1H, *J = 8.4 Hz,* C_6H), 7.50 (*d*, 1H, *J = 8.4 Hz,* C_5H), 7.57 (*d*, 1H, *J = 8.4Hz*, C_7H), 7.78 (*d*, 1H, *J = 16.4 Hz*, $C_\beta H$), 8.17 (*s*, 1H, C_4H); ^{13}C NMR (125 MHz, DMSO) 17.8,28.2, 53.3, 119.1, 124.8, 125, 126.6, 130.1, 131.5, 134.6, 136.9, 139.3, 145.3, 158.9, 199.2; MS (ESI, *m/z*): 242.20 $[M+H]^+$. Anal, Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.48; H, 6.42; N, 5.63.

2.3b *4-(2-Methoxyquinolin-3-yl)-but-3-en-2-one* (**5a**): Yield 76%; mp 74°C; IR (KBr): 1675 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$): $\delta = 2.38$ (*s*, 3H, $COCH_3$), 4.09 (*s*, 3H, OCH_3), 7.05 (*d*, 1H, *J = 16 Hz*, $C_\alpha H$), 7.46 (*t*, 1H, *J = 8.4 Hz,* C_6H), 7.70 (*t*, 1H, *J = 8.4 Hz,* C_7H), 7.73 (*d*, 1H, *J = 16 Hz*, $C_\beta H$), 7.77 (*d*, 1H, *J = 8.4 Hz,* C_8H), 7.91 (*d*, 1H, *J = 8.4 Hz*, C_5H), 8.71 (*s*, 1H, C_4H); Anal, Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.83; H, 5.92; N, 5.96.

2.3c *4-(2-Methoxy-6-methylquinolin-3-yl)-but-3-en-2-one* (**5b**): Yield 80%; mp 87°C; IR (KBr): 1656 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): $\delta = 2.42$ (*s*, 3H, CH_3), 2.48 (*s*, 3H, 6-CH_3) 4.13 (*s*, 3H, 2-OCH_3), 7.92 (*d*, 1H, *J = 16.5 Hz*, $C_\alpha H$), 7.46 (*d*, 1H, *J = 9 Hz*, C_8H), 7.49 (*s*, 1H, C_5H), 7.71 (*d*, 1H, *J = 9 Hz*, C_7H), 7.76 (*d*, 1H, *J = 16.5 Hz*, $C_\beta H$), 8.10 (*s*, 1H, C_4H); Anal, Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.50; H, 6.45; N, 5.99.

2.3d *4-(2-Methoxy-7-methylquinolin-3-yl)-but-3-en-2-one* (**5c**): Yield 82%; mp 79°C; IR (KBr): 1676 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): $\delta = 2.35$ (*s*, 3H, CH_3), 2.44 (*s*, 3H, 7-CH_3), 4.05 (*s*, 3H, 2-OCH_3), 6.99 (*d*, 1H, *J = 16.2 Hz*, $C_\alpha H$), 7.51 (*d*, 1H, *J = 8.5Hz*, C_6H), 7.63 (*s*, 1H, C_8H), 7.65 (*d*, 1H,*J = 8.5Hz*, C_5H), 7.69 (*s*, 1H, *J = 16.2 Hz*, $C_\beta H$), 8.53 (*s*, 1H, C_4H); Anal, Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.82; H, 6.11; N, 5.98.

2.3e *4-(2, 6-Dimethoxyquinolin-3-yl)-but-3-en-2-one* (**5e**): Yield 64%; mp 68°C; IR (KBr): 1682 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): $\delta = 2.36$ (*s*, 3H, CH_3), 3.81 (*s*, 3H, 6- OCH_3), 4.02 (*s*, 3H, 2-OCH_3), 6.12 (*d*, 1H, *J = 16 Hz*, $C_\alpha H$), 7.34 (*d*, 1H, *J = 9 Hz*, C_8H), 7.45 (*s*, 1H, C_5H), 7.72 (*d*, 1H, *J = 16 Hz*, $C_\beta H$), 7.81 (*d*, 1H, *J = 9 Hz*, C_7H), 8.86 (*s*, 1H, C_4H); Anal, Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.88; H, 5.72; N, 5.58.

2.3f *4-(2,7-Dimethoxyquinolin-3-yl)-but-3-en-2-one* (**5f**): Yield: 58%; mp 60°C; IR (KBr): 1686 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): $\delta = 2.41$ (*s*, 3H, CH_3), 3.92 (*s*, 3H, 7-OCH_3), 3.98 (*s*, 3H, 2-OCH_3), 7.12 (*d*, 1H, *J = 16.5 Hz*, $C_\alpha H$), 7.46 (*d*, 1H, *J = 8 Hz*, C_6H), 7.58 (*s*, 1H, C_8H), 7.63 (*d*, 1H, *J = 8 Hz*, C_5H), 7.72 (*d*, 1H, *J = 16.5 Hz*, $C_\beta H$), 8.68 (*s*, 1H, C_4H); Anal, Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.20; H, 5.73; N, 5.28.

2.4 *General procedure for 1-Furo[2,3-b]quinolin-2-yl-ethanone* **6(a–f)**

A mixture of compound **5(a–f)** (**5d**, 0.6025 g, 0.0025 mol) and excess of bromine in chloroform (15 mL) and glacial acetic acid (15 mL) was heated at 96°C for 12 h. After completion of the reaction which was checked by TLC, the excess of bromine was removed by adding 25% solution of sodium sulphite through the dropping funnel. The colourless chloroform layer was separated out, washed with water

and dried over magnesium sulphate. After a few minutes, the magnesium sulphate was removed by filtration. The solution was evaporated to dryness to give **6(a–f)** which was purified by column chromatography using petroleum ether and ethyl acetate (85:15) as eluent.

2.4a *1-Furo[2,3-b]quinolin-2-yl-ethanone* (**6a**). *IR (KBr)*: 1677 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.64 (*s*, 3H, $COCH_3$), 7.62 (*t*, 1H, *J* = *8.5Hz,* C_6H), 7.84 (*t*, 1H, *J* = *8.5Hz,* C_7H), 8.05 (*d*, 1H, *J* = *8.5Hz,* C_8H), 8.20 (*d*, 1H, *J* = *8.5Hz*, C_5H), 8.08 (*s*, 1H, C_4H), 8.97(*s*, 1H, C_3H); ^{13}C NMR (125 MHz, DMSO-d_6): 26.9, 113.3, 120.2, 125.7, 126.8, 128.4, 129.4, 131, 134.4, 146.7, 152.8, 161.1, 188.8; HRMS (ESI) Calcd for $C_{13}H_9NO_2$, (M + H) 212.0712, Found 212.0711.

2.4b *1-(6-Methylfuro[2, 3-b]quinolin-2-yl)-ethanone* (**6b**). *IR (KBr)*: 1686 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.46 (*s*, 3H, $COCH_3$), 2.49 (*s*, 3H, 6-CH_3), 7.52 (*s*, 1H, C_5H), 7.58 (*d*, 1H, *J* = *8.3Hz,* C_8H), 7.84 (*d*, 1H, *J* = *8.3Hz,* C_7H), 8.03 (*s*, 1H, C_4H), 8.92 (*s*, 1H, C_3H); Anal, Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.79; H, 4.78; N, 6.01.

2.4c *1-(7-Methylfuro[2, 3-b]quinolin-2-yl)-ethanone* (**6c**). *IR (KBr)*: 1695 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.46 (*s*, 3H, $COCH_3$), 2.49 (*s*, 3H, 7-CH_3), 7.49 (*d*, 1H, *J* = *9Hz,* C_5H), 7.54 (*s*, 1H, C_8H), 7.76 (*d*, 1H, *J* = *8.8Hz,* C_6H), 8.06 (*s*, 1H, C_4H), 8.92 (*s*, 1H, C_3H); Anal, Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.78; H, 4.72; N, 6.36.

2.4d *1-(8-Methylfuro[2,3-b]quinolin-2-yl)-ethanone* (**6d**). *IR (KBr)*: 1681 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.52 (*s*, 3H, $COCH_3$), 2.66 (*s*, 3H, 8-CH_3), 7.46 (*d*, 1H, *J* = *8Hz*, C_5H), 7.52 (*t*, 1H, *J* = *8 Hz*, C_6H), 7.92 (*d*, 1H, *J* = *8Hz,* C_7H), 8.15 (*s*, 1H, C_4H), 8.90 (*s*, 1H, C_3H); Anal, Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.44; H, 4.73; N, 6.40.

2.4e *1-(6-Methoxyfuro[2, 3-b]quinolin-2-yl)-ethanone* (**6e**). *IR (KBr)*: 1701 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.44 (*s*, 3H, $COCH_3$), 3.98 (*s*, 3H, 6- OCH_3), 7.62 (*s*, 1H, C_5H), 7.68 (*d*, 1H, *J* = *8.4 Hz,* C_8H), 7.89 (*d*, 1H, *J* = *8.4 Hz,* C_7H), 8.10 (*s*, 1H, C_4H), 8.86 (*s*, 1H, C_3H); Anal, Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.53; H, 4.75; N, 5.66.

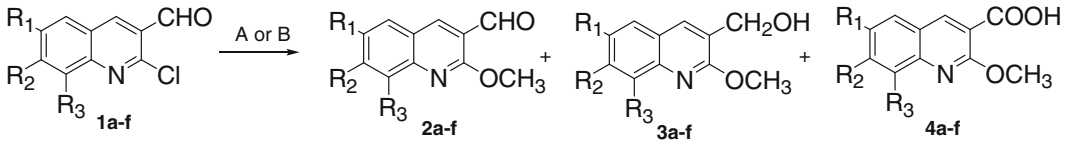
2.4f *1-(7-Methoxyfuro[2, 3-b]quinolin-2-yl)-ethanone* (**6f**). *IR (KBr)*: 1692 cm^{-1}; ^1H NMR (500 MHz; DMSO-d_6): δ = 2.42 (*s*, 3H, $COCH_3$),), 3.89 (*s*, 3H, 7-OCH_3), 7.42 (*d*, 1H, *J* = *8.6 Hz,* C_5H), 7.51 (*s*, 1H, *J* = *8.6 Hz,* C_8H), 7.82 (*d*, 1H, *J* = *8.6 Hz,* C_6H), 8.08 (*s*, 1H, C_4H), 8.89 (*s*, 1H, C_3H); Anal, Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.87; H, 4.43; N, 5.99.

3. Results and discussion

Recently we have reported[9] the synthesis of 2-benzoylfuro[2,3-*b*]quinolines from quinoline-based chalcones by bromocyclization method. We report here an extension of this methodology for the synthesis of 2-acetylfuro[2,3-*b*]quinolines started from 2-methoxy-3-formylquinolines[10–12] which in turn were synthesized from 2-chloro-3-formylquinolines in single step under the Cannizzaro reaction conditions.

Cannizzaro reaction is the redox disproportionative conversion of aldehydes into their corresponding alcohols and acids. It has been examined in heterocyclic compounds only on few cases and reported to give expected products.[13–17] But we have observed that in case of 2-chloro-3-formylquinolines, in addition to redox reaction, methoxylation also proceeded and gave 2-methoxy-3-formylquinolines **2(a–f)**, 2-methoxyquinolin-3-yl-methanols **3(a–f)** and 2-methoxyquinoline-3-carboxylic acids **4(a–f)** (scheme 1). We have investigated Cannizarro reaction of compound **1a** with KOH in methanol under two different conditions and found that, in the condition of stirring at room temperature (A), compound **2a** was major product and under the condition of reflux (B), compound **4a** was major product. The results of different derivatives are presented in table 1. For separation of these mixtures **2(a–f)**, **3(a–f)** and **4(a–f)** in column chromatography, we used PE: EA combinations in the ratio of 100:0, 90:10, and 80:20 as a solvent for elution.

Next, the conversion of **2(a–f)** to **6(a–f)** was attempted as shown in scheme 2. Reaction of **2(a–f)** with acetone in the presence of sulphuric acid afforded 4-(2-methoxy-quinolin-3-yl)-but-3-en-2-ones **5(a–f)** with good yields. The synthesized compounds **5(a–f)** were identified by spectral analysis. As an example, compound **5d** showed, two signals of vinylic protons of α, β unsaturated carbonyl were found at δ= 6.95 ppm for H_α and 7.78 ppm for H_β with a coupling constant (J) of 16.4 Hz. The same reaction was also tried with 2-hydroxy-3-formylquinoline but it was found that the desired product was not produced.



Conditions:

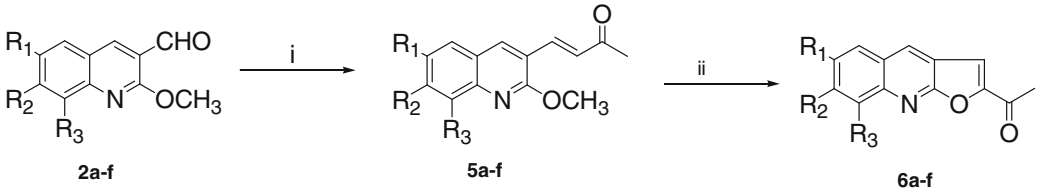
A) KOH / CH_3OH, Stirring, r.t, 24 h.
B) KOH / CH_3OH, Reflux, 12 h.

a) $R_1 = R_2 = R_3 = H$.
b) $R_1 = CH_3$, $R_2 = R_3 = H$.
c) $R_1 = R_3 = H$, $R_2 = CH_3$.
d) $R_1 = R_2 = H$, $R_3 = CH_3$.
e) $R_1 = OCH_3$, $R_2 = R_3 = H$.
f) $R_1 = H$, $R_2 = OCH_3$, $R_3 = H$.

Scheme 1. Cannizzaro reaction of 2-chloro-3-formylquinolines.

Table 1. Cannizzaro reaction of 2-chloro-3-formylquinolines.

					Products					
					Condition A			Condition B		
		Starting materials			(% of Yield)					
Entry		R_1	R_2	R_3	**2(a–f)**	**3(a–f)**	**4(a–f)**	**2(a–f)**	**3(a–f)**	**4(a–f)**
1	**1a**	H	H	H	73	6	21	22	28	50
2	**1b**	CH_3	H	H	75	7	18	20	24	56
3	**1c**	H	CH_3	H	70	7	23	16	25	59
4	**1d**	H	H	CH_3	80	6	14	20	29	51
5	**1e**	OCH_3	H	H	78	5	17	18	26	56
6	**1f**	H	OCH_3	H	72	8	20	19	32	49



i) CH_3COCH_3 / H_2SO_4, 6 h, reflux.

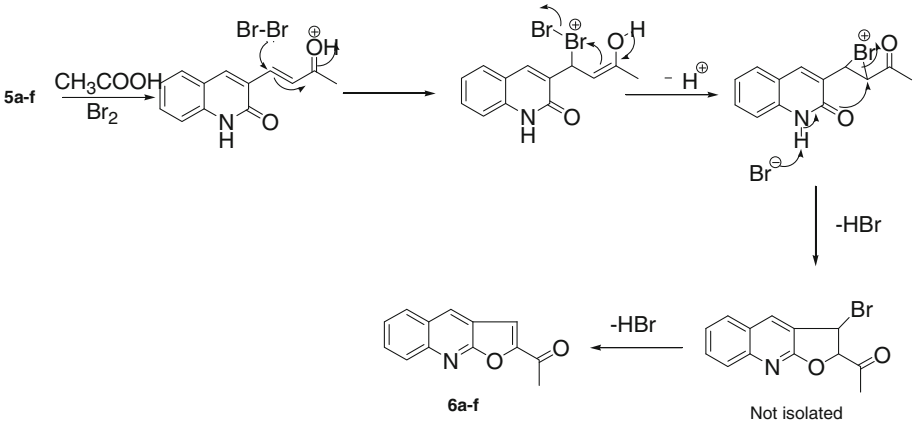
ii) Br_2, $CH_3COOH/CHCl_3$, 12 h, reflux.

a) $R_1 = R_2 = R_3 = H$.
b) $R_1 = CH_3$, $R_2 = R_3 = H$.
c) $R_1 = R_3 = H$, $R_2 = CH_3$.
d) $R_1 = R_2 = H$, $R_3 = CH_3$.
e) $R_1 = OCH_3$, $R_2 = R_3 = H$.
f) $R_1 = H$, $R_2 = OCH_3$, $R_3 = H$.

Scheme 2. Synthesis of 2-acetylfuro[2,3-*b*] quinolines.

Table 2. Synthesis of 2-acetylfuro[2,3-*b*]quinolines.

Entry	Product	R_1	R_2	R_3	Condition	Yield (%)	Mp(°C)
1	**6a**	H	H	H	96°C/ 12 h	80	156
2	**6b**	CH_3	H	H	96°C/ 12 h	82	174
3	**6c**	H	CH_3	H	96°C/ 12 h	78	182
4	**6d**	H	H	CH_3	96°C/ 12 h	87	161
5	**6e**	OCH_3	H	H	96°C/ 12 h	74	142
6	**6f**	H	OCH_3	H	96°C/ 12 h	70	134



Scheme 3. Proposed mechanism for bromocyclisation.

Furthermore, the cyclisation of synthesized compounds **5(a–f)** was carried out in the presence of bromine using acetic acid and chloroform. Reaction of **5a** at 96°C for 12 h gave the desired product **6a** in 80 % yield. The results of other reactions are presented in table 2.

The formation of **6a** from **5a** may be explained as shown in scheme 3. The methoxy group of compound **5a** was cleavaged into 2-hydroxy group. Protonation of carbonyl group followed by bromocyclisation and dehydrobromination gave cycloadduct **6a**.

4. Conclusion

In summary, we have reported an efficient synthesis of 2-acetyl furo[2,3-*b*]quinolines through the condensation reaction of 2-methoxy-3-formylquinolines with acetone in the presence of sulphuric acid followed by bromocyclisation and dehydrobromination. The starting materials were prepared from 2-chloro-3-formylquinolines under the condition of Cannizzaro reaction. The experimental procedures are also very simple.

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