Supporting Information

Regio-controlled nitration of 4-quinolones at ambient condition

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Experimental

Theoretical calculation

Table S1:

Fukui function (f_k^-) and local softness (s_k^-) calculation at B3LYP/6-31G(d,p).

Entry	Sites	Fukui function(f_k^-)	Local softness (s_k^-)	Theoretically preferred carbon
C-5	0.0215	0.1311	C-7
	C-6	0.0173	0.1055	
	C-7	0.0293	0.1786
C-5	0.0330	0.1938	C-5
	C-6	0.0284	0.1668	
	C-7	0.0163	0.0957
C-5	0.0298	0.1816	C-5
	C-7	0.0187	0.1140	
	C-8	0.0272	0.1655
C-5	0.0383	0.2226	C-5
	C-7	0.0134	0.0777	
	C-8	0.0377	0.2191
C-5	0.032	0.183	C-5
	C-7	0.013	0.074	
	C-8	0.025	0.143	

Characterization of compounds:

Ethyl 1, 4-dihydro-5-nitro-4-oxoquinoline-3-carboxylate (1a)

Greenish yellow solid, melting point: $>253^{\circ}\text{C}$; ^1H NMR (DMSO- d_6 , 300 MHz) δ 1.26 (t, $J=7.2$ Hz, 3H), 4.23 (q, $J=7.2$ Hz, 2H), 7.56 (t, $J=8.1$ Hz, 1H), 8.53-8.55 (m, 2H), 8.61 (d, $J=8.1$ Hz, 1H), 12.2 (s, 1H) ^{13}C NMR (DMSO- d_6 , 75 MHz) δ 14.59, 60.43, 111.75, 124.06, 129.48, 130.57, 133.47, 134.25, 137.08, 146.60, 164.24, 172.36; MS (ESI $^{+}$) m/z 263.10 $[\text{M}+\text{H}]^{+}$; Anal. Calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_5$: C, 54.97; H, 3.84; N, 10.68; Found: C, 54.76; H, 3.79; N, 10.51.

Ethyl 1, 4-dihydro-8-methyl-5-nitro-4-oxoquinoline-3-carboxylate (2b)

Yellowish white solid, melting point: 225°C - 228°C ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 1.22 (t, $J=7.2$ Hz, 3H), 2.54 (s, 3H), 4.21 (q, $J=7.2$ Hz, 2H), 7.53 (d, $J=7.8$ Hz, 1H), 7.70 (d, $J=8.4$ Hz, 1H), 8.43 (s, 1H), 11.60 (s, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz) δ 14.70, 17.74, 60.47, 111.35, 118.26, 118.99, 131.45, 133.28, 139.06, 145.59, 147.52, 164.64, 171.18; MS (ESI $^{+}$) m/z 298.95 $[\text{M}+\text{Na}]^{+}$; Anal. Calcd for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_5$: C, 56.52; H, 4.38; N, 10.14; Found: C, 56.38; H, 4.32; N, 9.96.

Ethyl 8-fluoro-1,4-dihydro-5-nitro-4-oxoquinoline-3-carboxylate (3c)

Yellowish white solid, melting point: 234°C - 236°C ; ^1H NMR (DMSO- d_6 , 300 MHz): δ 1.03 (t, $J=7.2$ Hz, 3H), 3.98 (q, $J=7.2$ Hz, 2H), 7.46-7.50 (m, 1H), 7.56-7.62 (m, 1H), 8.19 (s, 1H), 12.80 (s, 1H). ^{13}C NMR (DMSO- d_6 , 75 MHz) δ 14.67, 60.62, 112.28, 117.67, 117.92, 119.51, 119.61, 120.10, 129.97, 130.16, 144.93, 144.98, 145.59, 151.11, 154.49, 164.29, 170.23; HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^{+}$ found 281.0486. $\text{C}_{12}\text{H}_{10}\text{FN}_2\text{O}_5$ requires 281.0574.

Ethyl 1,4-dihydro-8-methoxy-5,7-dinitro-4-oxoquinoline-3-carboxylate (4d)

Bright yellow solid, melting point: 175⁰C-178⁰C; ¹H NMR (DMSO-d₆, 300 MHz) δ 1.27 (t, *J*=7.2 Hz, 3H), 4.12 (s, 3H), 4.23 (q, *J*=7.2 Hz, 2H), 8.37 (s, 1H), 8.49 (s, 1H); ¹³C NMR (DMSO-d₆, 75 MHz) δ 14.66, 60.75, 64.38, 113.25, 114.83, 121.48, 136.79, 142.12, 143.54, 146.13, 146.30, 164.18, 170.26; HRMS (ESI-TOF) *m/z*: [M+H]⁺, found 338.0522. C₁₃H₁₁N₃O₈ requires 338.0624.

Ethyl 1-((ethoxycarbonyl) methyl)-1,4-dihydro-8-methoxy-5-nitro-4-oxoquinoline-3-carboxylate (5e)

Yellow solid, melting point: 148⁰C-150⁰C ¹H NMR (300 MHz, DMSO-d₆): δ 1.26-1.36 (m, 6H), 3.91 (s, 3H), 4.22-4.35 (m, 4H), 5.07 (s, 2H), 7.03 (d, *J*=8.7 Hz, 1H), 7.24 (d, *J*=8.4 Hz, 1H), 8.19 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 14.17, 14.28, 56.64, 60.21, 61.13, 61.93, 111.96, 112.67, 120.37, 130.85, 143.31, 151.00, 152.32, 164.14, 167.30, 170.31. HRMS (EI⁺): [M]⁺, found 378.1041. C₁₇H₁₈N₂O₈ requires 378.1063.

Ethyl 1, 4-dihydro-8-methoxy-7-nitro-4-oxoquinoline-3-carboxylate (6f)

Yellow solid, melting point: 190⁰C-193⁰C ¹H NMR (300MHz, DMSO-d₆): δ =1.27 (t, *J*=7.2 Hz, 3H), 3.98 (s, 3H), 4.22 (q, *J*=7.2 Hz, 2H), 7.87 (dd, *J*=9 and 0.9 Hz, 1H), 8.00 (dd, *J*=9 and 0.9Hz, 1H), 8.44 (s, 1H), 12.40 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆): δ 14.61, 60.33, 63.97, 111.75, 119.76, 121.86, 131.01, 134.74, 143.92, 144.09, 146.09, 164.57, 172.77; (ESI⁺) *m/z* 293.00 [M+H]⁺; Anal. Calcd for C₁₃H₁₂N₂O₆: C, 53.43; H, 4.14; N, 9.59. Found: C, 52.96; H, 4.21; N, 9.74.

Ethyl 1, 4-dihydro-6-methyl-8-nitro-4-oxoquinoline-3-carboxylate (7g)^{8d}

Yellowish white solid, melting point: 239⁰C-241⁰C ¹H NMR (300 MHz, DMSO-d₆): δ 1.25 (t, *J*=7.2 Hz, 3H), 2.24 (s, 3H), 4.19 (q, *J*=7.2 Hz, 2H), 7.73 (d, *J*=2.7 Hz, 2H), 8.58 (d, *J*=6.3 Hz, 1H), 12.7 (bs, 1H). ¹³C NMR (75 MHz, DMSO-d₆): δ 14.23, 15.45, 59.86, 110.76,

117.59, 120.69, 125.62, 135.10, 138.15, 145.04, 147.29, 164.27, 170.31; (ESI⁺) m/z 277.00 [M+H]⁺; Anal. Calcd for C₁₃H₁₂N₂O₅: C, 56.52; H, 4.38; N, 10.14. Found: C, 56.32; H, 4.29; N, 9.65.

Ethyl 1-((ethoxycarbonyl) methyl)-1, 4-dihydro-6-methyl-5-nitro-4-oxoquinoline-3-carboxylate (8h)

Light yellow solid, melting point: 203⁰C-206⁰C ¹H NMR (300MHz, DMSO-d₆): δ 1.09-1.19 (m, 6H), 2.16 (s, 3H), 4.04-4.15 (m, 4H), 5.30 (s, 2H), 7.64 (d, *J*=9 Hz, 1H), 7.72 (d, *J*=9 Hz, 1H), 8.68 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 14.05, 14.38, 16.11, 55.01, 61.13, 62.78, 112.32, 117.02, 119.56, 127.15, 135.13, 138.26, 148.87, 149.76, 164.33, 166.29, 170.79. HRMS (EI⁺): [M]⁺, found 362.1123. C₁₇H₁₈N₂O₇ requires 362.1114.

Preparation of compound 5 and 8

Compound 4 or 7 (1 mmol, 0.247g/ 0.231g) and 1.5 mmol (0.207g) of K₂CO₃ were stirred in a 100 ml round bottomed flask in requisite amount of DMF (solvent) at room temperature. The stirring was continued until H₂ gas was ceased to evolve. Then, ethyl bromoacetate (0.324g/ ~0.3 ml) was introduced into the reaction vessel and continued the stirring for next 1h at 60⁰C. After completion of reaction as detected by the TLC, the reaction mixture was diluted with water and the product was extracted with DCM (3 x10 ml). The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography using the mixture of ethyl acetate and petroleum ether as eluent.

Ethyl 1-((ethoxycarbonyl) methyl)-1, 4-dihydro-8-methoxy-4-oxoquinoline-3-carboxylate (5)

White solid, melting point: 159⁰C-162⁰C ¹H NMR (300 MHz, CDCl₃): δ 1.25 (t, *J*=6.9 Hz, 3H), 1.38 (t, *J*=6.9 Hz, 3H), 3.83 (s, 3H), 4.24 (q, *J*=6.9 Hz, 2H), 4.36 (q, *J*=6.9 Hz, 2H), 5.05 (s, 2H), 7.07-7.10 (m, 1H), 7.27-7.34 (m, 1H), 8.11 (dd, *J*=8.1 and 1.2 Hz, 1H), 8.25 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 14.24, 14.42, 56.16, 60.10, 60.89, 61.77, 110.82, 114.40, 119.87, 125.52, 130.09, 131.02, 149.44, 152.15, 165.46, 167.65, 173.76.

Ethyl 1-((ethoxycarbonyl) methyl)-1, 4-dihydro-6-methyl-4-oxoquinoline-3-carboxylate (8)

White solid, Melting Point: 205⁰C-208⁰C, ¹H NMR (300 MHz, CDCl₃): δ 1.26 (t, *J*=6.9 Hz, 3H), 1.41(t, *J*=6.9 Hz, 3H), 4.26 (q, *J*=6.9 Hz, 2H), 4.39 (q, *J*=6.9 Hz, 2H), 4.89 (s, 2H), 7.12(d, *J*=8.4 Hz, 1H), 7.48 (dd, *J*=8.7 and 2.1 Hz 1H), 8.31 (s, 1H), 8.46 (s, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 14.06, 14.40, 20.99, 54.68, 61.05, 62.65, 110.95, 115.01, 127.47, 128.25, 134.37, 135.76, 137.27, 149.65, 165.51, 166.63, 174.46.

Preparation of compound 6

Compound **4** (1 mmol, 0.247g), TBAHS (0.01 mmol, 3.23mg) and powdered NaOH (2.5 mmol, 100 mg) were dissolved in 8 ml of DCM. Then 1.5 mmol (0.423 g) of (CF₃SO₂)₂O in 1 ml DCM was introduced in a single portion and continue the reaction for 30 minutes at room temperature. Immediately after completion of reaction, the reaction medium was neutralized by adding solid NaHCO₃. The crude reaction mixture was filtered out and purified by the column chromatography.

Ethyl 1,4-dihydro-8-methoxy-1-trifluoromethanesulfonate-4-oxoquinoline-3-carboxylate (6)

Colourless liquid, ¹H NMR (300 MHz, CDCl₃): δ 1.50 (t, *J*=7.2 Hz, 3H), 4.17 (s, 3H), 4.60 (q, *J*=7.2 Hz, 2H), 7.46 (d, *J*=7.5 Hz, 1H), 7.75-7.80 (m, 1H), 8.01 (dd, *J*=8.4 and 0.6 Hz, 1H),

9.41 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 13.99, 57.00, 64.41, 105.30, 115.14, 115.22, 118.39, 121.16, 130.28, 131.21, 145.18, 150.23, 167.93, 172.56.

^1H NMR and ^{13}C spectra of 1a:

^1H NMR and ^{13}C spectra of 2b:

^1H NMR and ^{13}C spectra of 3c:

^1H NMR and ^{13}C spectra of 4d:

^1H NMR and ^{13}C spectra of **5**:

^1H NMR and ^{13}C spectra of 5e:

^1H NMR and ^{13}C spectra of **6**:

^1H NMR and ^{13}C spectra of 6f:

^1H NMR and ^{13}C spectra of 7g:

^1H and ^{13}C spectra of 8:

^1H and ^{13}C NMR of 8h: