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ALTERNATIVE APPROACH TO THE 2-OXOPYRANO[3,2-*c*]-QUINOLINE CORE

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Abstract – An alternative route to access the pyrano[3,2-*c*]quinoline or benzo[7,8]-6-azacoumarin core form readily available quinoline *N*-oxides is presented. The key reaction involves an unusual rearrangement of tetrahydroquinolin-2-ylacetic acids in the presence of triethylamine and acetic anhydride.

2-Oxopyrano-fused quinolines and structurally related azacoumarins have attracted much attention in the field of medicinal chemistry as they have displayed a wide range of biological properties including anti-malarial,[1] anti-microbial,[2] anti-cancer[3] and anti-inflammatory[2] activity (Figure 1). The photochemical properties of these compounds have also led to applications as fluorescent probes[4] and for use in caging chemistry.[5] Unfortunately, the lack of advancement in their synthesis has limited the study of their applications in the field of medicine.[6]

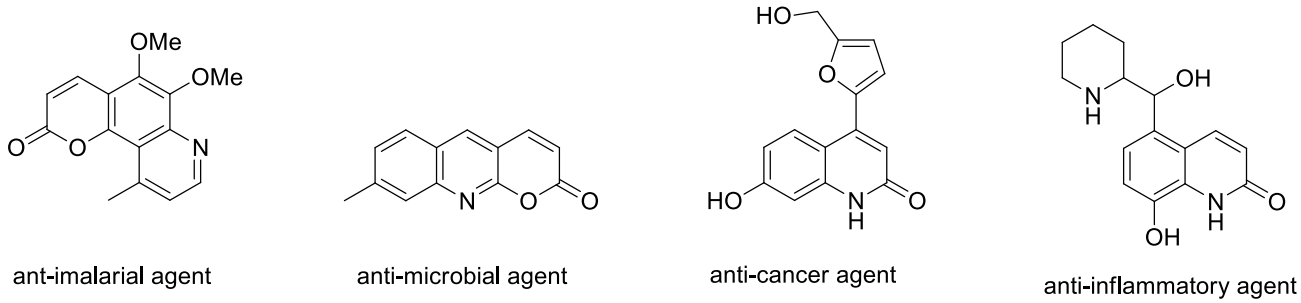
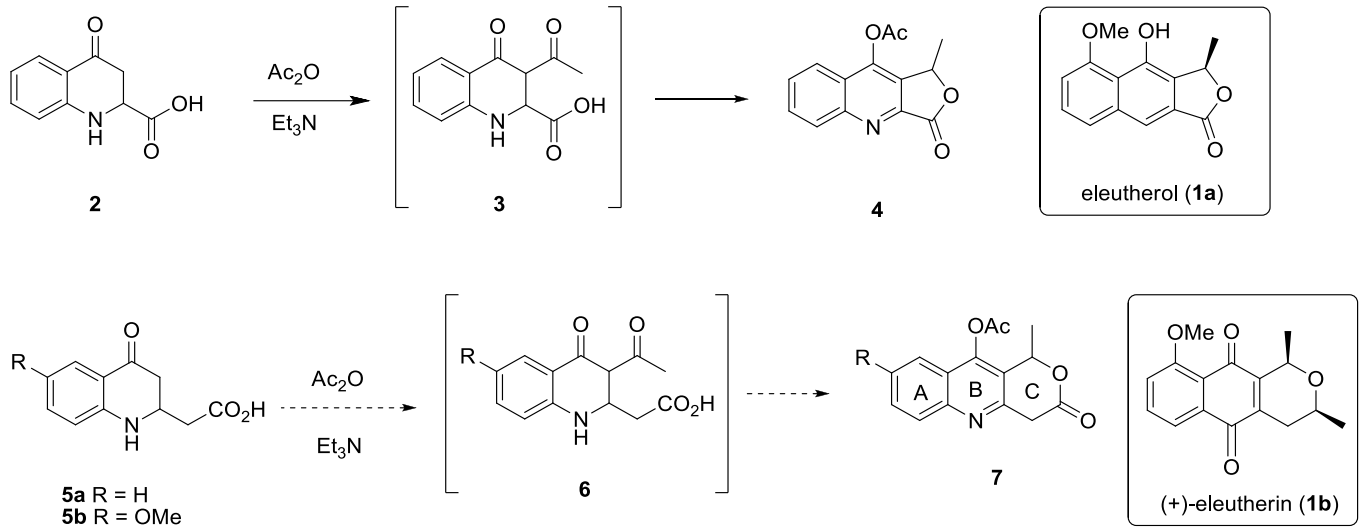


Figure 1. Bioactive 2-oxopyranoquinolines and 1-azacoumarins

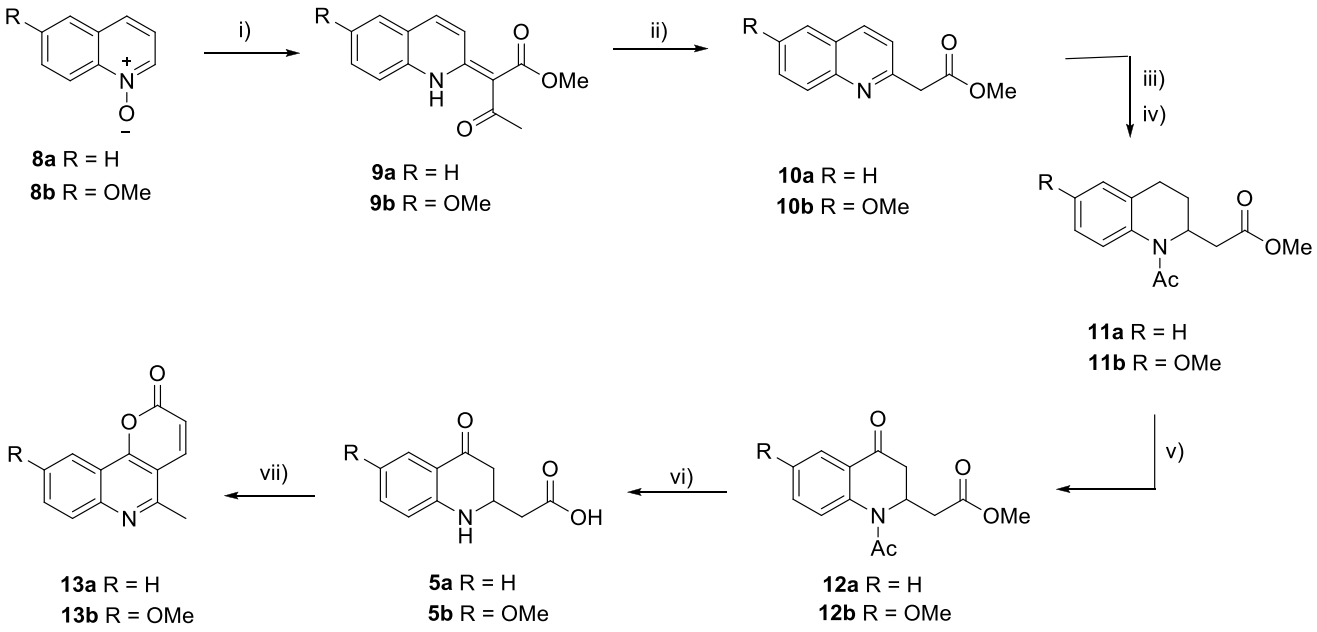
Eleutherol (**1a**) and eleutherin (**1b**) are two biologically active natural products that were isolated from *Eleutherine bulbosa*. Both compounds have demonstrated use in the treatment of heart disease. Additionally, eleutherol (**1a**) is an inhibitor of tyrosinase and melanin formation *in vitro* while eleutherin (**1b**) has been found to be a reversible inhibitor of topoisomerase II.[7-9] The incorporation of nitrogen into polyaromatic systems such as these can positively affect their biological activity by improving solubility and metabolic stability.[10] We have previously reported the synthesis of a demethoxy 9-aza-analogue (**4**) of eleutherol (**1a**) by treatment of dihydrokynurenic acid (**2**) with acetic anhydride in triethylamine.[11] Acetylation of **2** gave rise to intramolecular cyclization, followed by C=C isomerization to give the more stable 4-quinolone (**3**), and then aromatization to produce eleutherol analogue **4** (Scheme 1). It was envisaged that using this methodology, acid **5** with extended side chain at position 2, could produce the corresponding eleutherin aza-analogue **7** and allow ready access to the pyrano[3,4-*b*]quinoline core. Our efforts in this area, with the unexpected formation of the pyrano[3,2-*c*]quinoline core, are reported here.



Scheme 1. Synthesis of eleutherol and eleutherin aza analogues

Synthesis of compound **5a** was achieved as shown in Scheme 2. Gilchrist and Rahman[12] reported the synthesis of methyl 2-(quinolin-2-yl)acetate (**10a**) *via* quinolinylidene ester **9a** from quinoline *N*-oxide. Commercially obtained quinoline *N*-oxide and 6-methoxyquinoline *N*-oxide were each treated with methyl acetoacetate and acetic anhydride at 40 ˚C followed by acid mediated hydrolysis. This yielded 6-methoxyquinoline ester **10b** in 88% while the unsubstituted quinoline ester **10a** was obtained in 54%. The difference in the yield is attributed to the strong electron donating properties of the methoxy group making 6-methoxyquinoline *N*-oxide more nucleophilic in the attack on acetic anhydride (step i). On obtaining esters **10a** and **10b**, the tetrahydroquinolines **11a** and **11b** were prepared by reduction using

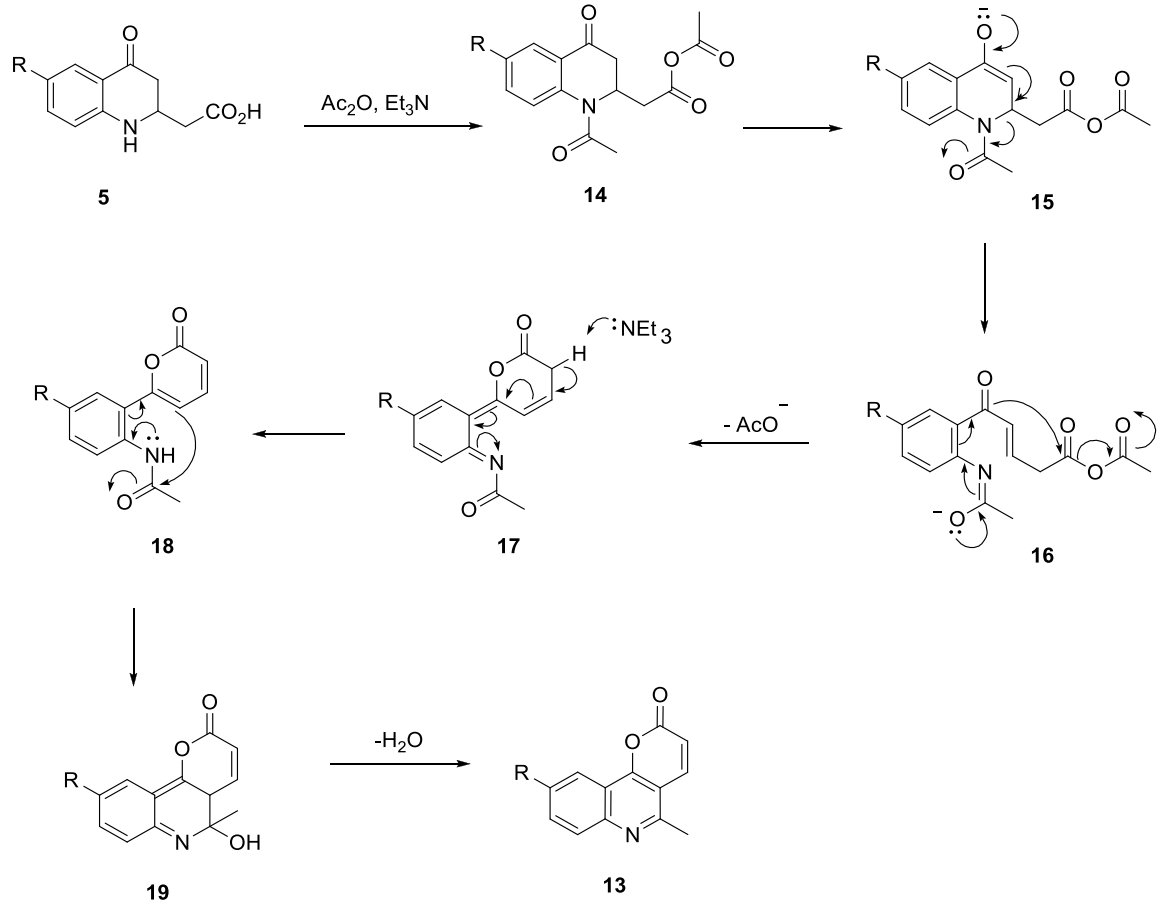
$NaCNBH_3$, followed by acetylation. Reduction of **10b** required longer reaction time (4 days compared to 3 hours) and a greater amount of $NaCNBH_3$ (4 compared to 3 molar equivalents) than for **10a**, owing perhaps to the higher electron density of its heterocyclic ring. We proceeded to carry out benzylic oxidation[13] of **11a** and **11b** prior to base hydrolysis, and obtained compounds **5a** and **5b** in very good yield. Acetylation of the amino acids **5a** and **5b** was now the only step remaining in our proposed synthesis of the eleutherin analogues (Scheme 1). We proceeded as reported by Townsend and Jackson,[12] that is, acid **5a** was dissolved in acetic anhydride, triethylamine was added, and the mixture was stirred overnight.[15] On isolation of the product, a white crystalline solid was obtained. NMR data showed a highly conjugated system, with no methylene protons. There were six protons resonating downfield of 6.5 ppm and three protons at 2.9 ppm. From elemental analysis, the molecular formula was $C_{13}H_9NO_2$, and on comparison with the literature,[14] the product was assigned as 2-oxopyrano[3,2-*c*]quinoline **13a** (47%).



Scheme 2. *Reagents and conditions*: i) methyl acetoacetate, Ac_2O, 40 ˚C; ii) HCl, rt (54% **10a**, 88% **10b** over two steps); iii) $NaCNBH_3$, AcOH, rt; iv) Ac_2O, 90 ˚C, 24 h, (87% **11a**, 54% **11b** over two steps); v) $Cr(CO)_6$, MeCN, TBHP, 70 wt% in H_2O), reflux, 24 – 48 h, 100% **12a**, 73% **12b**; vi) K_2CO_3, MeOH, reflux, 24 h, 91% **5a**, 76% **5b**; vii) Ac_2O, Et_3N, rt, 24 h, 47% **13a**, 53% **13b**.

When acid **5b** was subjected to the same protocol, pyranoquinoline **13b** was obtained in 53% yield. The mechanism shown in Scheme 3 is proposed for formation of compounds **13a** and **13b** by this route. Firstly, amino acids **5a** and **5b** are acetylated, and abstraction of the α-hydrogen allows opening of the heterocyclic ring and cyclization to form a δ-lactone **16a** and **16b**. This results in a series of reactions – recyclization, dehydration and aromatization, to produce **13a** and **13b**.

Our pathway provides pyranoquinoline **13a** *via* an unusual rearrangement and cyclization reaction of a 4-oxotetrahydroquinoline using simpler and milder reaction conditions compared to the previous synthesis by Galariniotou *et al.*[14] which required harsh conditions and long reaction times. Our route was successfully applied to provide an analogue, pyranoquinoline **13b**, in 14% yield from the respective quinoline *N*-oxide. The single crystals of pyranoquinoline **13b**, which was confirmed by X-ray, is an orthorhombic system with an asymmetric unit consisting of two molecules of pyranoquinoline **13b** (Figure 2). Non-classical hydrogen bonds (C-H---O) and (C-H---N) are evident throughout the unit cell for pyranoquinoline **13b** (Figure 3).



Scheme 3. Mechanism for the synthesis of pyranoquinolines

This is consistent with a previous report of the C-H bond behaving as a proton donor to lone pair acceptor atoms including oxygen and the less electronegative sulfur.[15] Additionally, there appears to be weak intermolecular interaction between the *ortho* carbon (C11B) and *ortho* hydrogen (H11A) of neighbouring molecules. Admittedly, this intermolecular interaction owing to the high electron density at the *ortho* carbon and the slight polarization of the C-H bond is very weak. However, the cumulative strength of these interactions as well as the non-classical hydrogen bonds particularly involving the methoxy group appears to be significant in the ordering and self-assembling of pyranoquinoline **13b** (Figure 3).

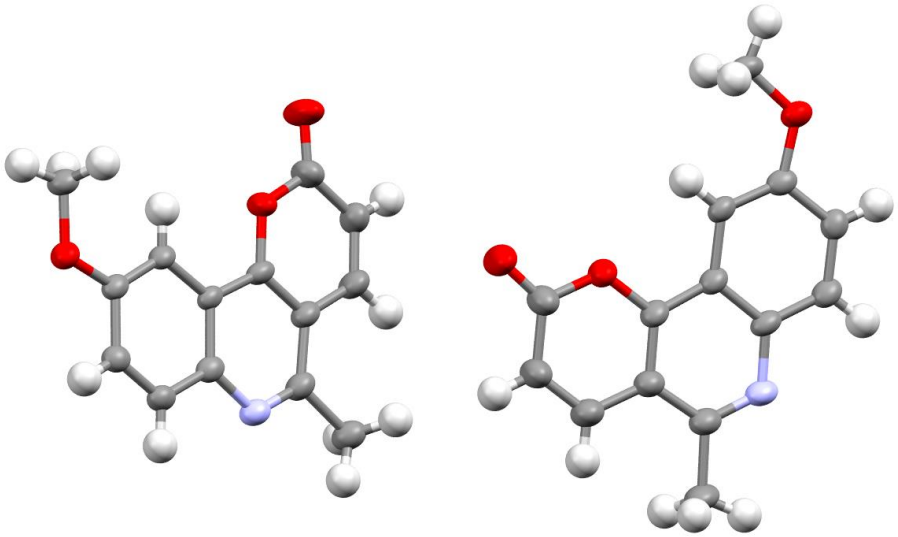


Figure 2. Asymmetric unit of pyranoquinoline **13b**

In concluding, 2-oxopyrano[3,2-*c*]quinolines can be efficiently prepared from quinoline *N*-oxides using the synthetic route presented, thereby facilitating exploration of these compounds in medicinal and material chemistry. There is scope for extending the work using these mild conditions to include assembly of other substituted pyranoquinolines from either substituted quinoline *N*-oxide or 4-oxotetrahydroquinoline type compounds.

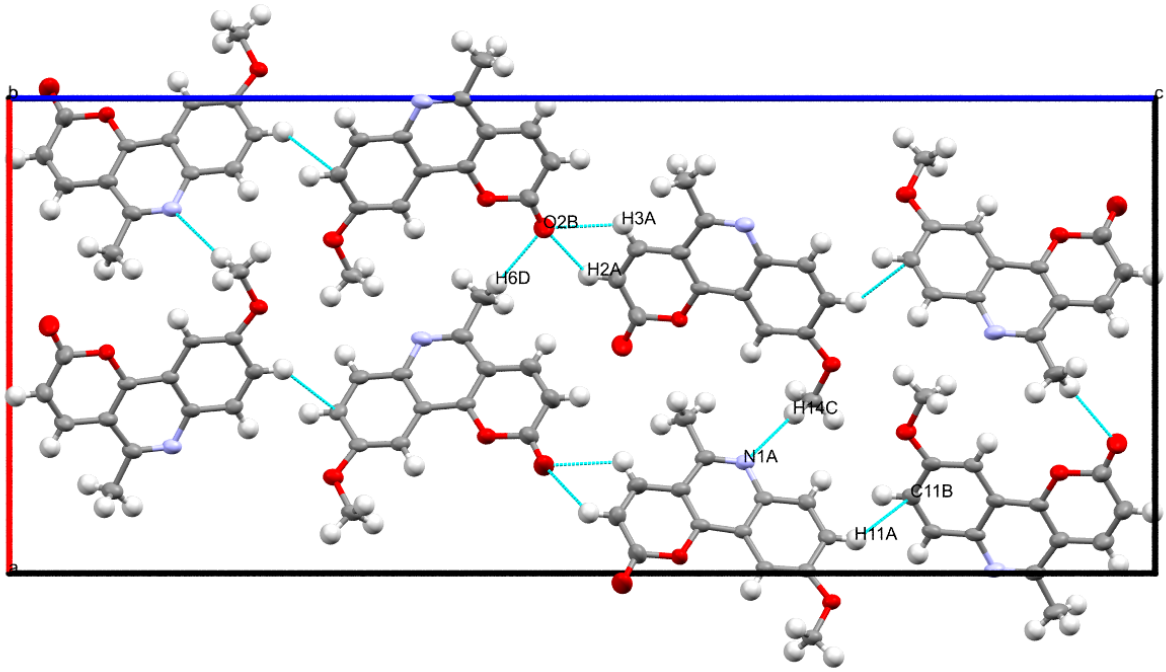


Figure 3. Unit cell of pyranoquinoline **13b** crystal structure depicting non-classical hydrogen bonds

EXPERIMENTAL

General methods

^{1}H NMR and ^{13}C NMR spectra were recorded at 200 and 500 MHz with TMS as an internal standard on a Bruker Avance spectrometer. Unless otherwise stated, the spectra were obtained in $CDCl_3$ solution and resonances are reported in δ units downfield from. FT-IR spectra were obtained on a Vector 22 or Bruker Tensor 37 with Pike Technology MIRacle single reflection ATR instruments. Column chromatography was carried out using silica gel as adsorbent. Elemental analyses were done at the University of the West Indies, Mona on a PE 2400 CHNS/O Analyzer or on a Thermo Flash EA112 CHN Analyzer at MEDAC Ltd., Surrey, United Kingdom. HR-MS analyses were carried out on a Waters LCT Premier (Es-Tof)/ Acquiring i-Class instrument at MEDAC Ltd., Surrey, United Kingdom. Melting points (uncorrected) were determined on a Gallenkamp instrument.

General Procedure for the Preparation of Dihydroquinolines. To the corresponding *N*-oxide (1.81 mmol) was added acetic anhydride (7 mL per g) and the mixture stirred at 40 ˚C for 7-10 min. Methyl acetoacetate (2 mmol equiv.) was then added in portions and the mixture stirred at 40 ˚C for 16-22 h, then poured into crushed ice (132 mL per g). The yellow precipitate was filtered off, washed with cold water (7 mL per g) and recrystallized from EtOH.

Methyl 2-(1,2-dihydroquinolin-2-ylidene)-3-oxobutanoate (9a). Reaction time: 7 min then 16 h; yield: (66% from **8a**); yellow crystals; mp 99-101 ˚C (EtOH/water) [lit 103-104 ˚C (MeOH)].[12] IR ν_{max} 1629, 1560 cm^{-1}; ^{1}H NMR δ 2.46 (3H, s, H-12), 3.86 (3H, s, H-11), 7.38 (1H, t, *J* = 7.6 Hz, H-7), 7.60 (3H, m, H-5,6, 8), 7.93 (2H, m, H-3,4). ^{13}C NMR δ 29.9, 51.0, 98.1, 118.7, 120.3, 123.2, 124.8, 127.5, 131.3, 136.4, 137.6, 154.7, 169.8, 195.3.

Methyl (2*E*)-2-(6-methoxyquinolin-2(1*H*)-ylidene)-3-oxobutanoate (9b). Reaction time: 10 min then 22 h; yield: (93% from **8b**); yellow crystals; mp 122-124 ˚C (EtOH). IR ν_{max} 2921, 1694, 1621 cm^{-1}; ^{1}H NMR δ 2.46 (3H, s, H-12), 3.85 (3H, s, H-11), 3.90 (3H, s, H-13), 7.02 (1H, d, *J* = 2.6 Hz, H-5), 7.27 (1H, m, H-7), 7.53 (1H, d, *J* = 9.0 Hz, H-8), 7.87 (1H, d, *J* = 9.6 Hz, H-3), 8.02 (1H, d, *J* = 9.6 Hz, H-4); ^{13}C NMR δ 29.6, 50.9, 55.7, 97.5, 107.1, 120.5, 120.7, 122.2, 124.4, 131.6, 137.0, 153.8, 156.9, 169.9, 194.0. HRMS (ES-ToF) *m/z*: calcd. for $C_{15}H_{16}NO_4$ $[M + H]^+$, 274.1079; found 274.1071.

Methyl 2-(quinolin-2-yl)acetate (10a). To quinoline *N*-oxide (1.00 g, 6.89 mmol) was added acetic anhydride (10 mL) and the mixture stirred at 40 ˚C for 1 h. Methyl acetoacetate (0.30 mL, 2.76 mmol) was then added in small portions and the mixture stirred at 40 ˚C for 20 h, then poured onto crushed ice (100 mL). The yellow precipitate was filtered, washed with cold water (10 mL) and the solid added slowly to hydrochloric acid (10%, 30 mL). After 50 min the solution was diluted with water (20 mL) and basified to pH 9 with sodium hydrogen carbonate solids. Brine (20 mL) was added and the organic layer extracted with EtOAc (4 × 20 mL). The combined organic layers were washed with water (10 mL), dried

over magnesium sulfate and the solvent was removed *in vacuo* to give compound **10a**[12] as an orange oil, (0.76 g, 54%). IR ν_{max} 2950, 1738, 1666 cm^{-1}; ^{1}H NMR δ 3.73 (3H, s, H-11), 4.06 (2H, s, H-9), 7.43 (1H, d, *J* = 8.5 Hz, H-3), 7.52 (1H, t, *J* = 7.4 Hz, H-6), 7.70 (1H, t, *J* = 7.6 Hz, H-7), 7.80 (1H, d, *J* = 8.2 Hz, H-5), 8.09 (1H, d, *J* = 8.5 Hz, H-8), 8.13 (1H, d, *J* = 8.5 Hz, H-4); ^{13}C NMR δ 44.6, 52.2, 121.8, 126.5, 127.1, 127.5, 129.1, 129.7, 136.7, 147.8, 154.7, 170.9.

Methyl (6-methoxyquinolin-2-yl)acetate (10b). Compound **9b** (0.50 g, 1.84 mmol) was added in small portions to hydrochloric acid (10%, 5 mL) and the mixture stirred at room temperature for 13 min. The mixture was basified using aqueous sodium hydrogen carbonate solution (11 mL). The organic layer was extracted with EtOAc (4 × 10 mL), washed with water (10 mL), dried over magnesium sulfate and the solvent removed *in vacuo*. Compound **10b**[16] was obtained as a yellow oil (0.41 g, 95%). IR ν_{max} 2952, 2920, 1723 cm^{-1}; ^{1}H NMR δ 3.72 (3H, s, H-11), 3.90 (3H, s, H-12), 4.01 (2H, s, H-9), 7.05 (1H, d, *J* = 3.0 Hz, H-5), 7.36 (2H, m, H-7, 8), 7.98 (2H, dd, *J* = 8.6, 10.7 Hz, H-3, 4); ^{13}C NMR δ 44.3, 52.1, 55.5, 105.1, 121.9, 122.2, 128.0, 130.5, 135.4, 143.9, 152.0, 157.7, 171.1.

Methyl (1-acetyl-1,2,3,4-tetrahydroquiniln-2-yl)acetate (11a). A solution of the quinoline **10a** (0.50 g, 2.50 mmol) in glacial acetic acid was cooled to below 30 ˚C and sodium $NaCNBH_3$ (3.00 mmol) added in small portions. The mixture was then allowed to stir at room temperature for 3 h, neutralized with saturated aqueous sodium hydrogen carbonate then extracted with Et_2O (3 × 15 mL). The combined extract was dried over sodium sulfate then concentrated under reduced pressure. The crude product was treated with acetic anhydride (10 mL) and the resulting solution heated at 90-100 ˚C for 4 h. After allowing the mixture to cool to room temperature it was diluted with water (50 mL) and solid sodium hydrogen carbonate was then added until no further evolution of carbon dioxide was observed. The mixture was then extracted with Et_2O, and the organic extract dried over sodium sulfate then evaporated under vacuum. The crude product was purified by flash column chromatography (hexane: EtOAc – 3:1) to give compound **11a**[17] as a yellow oil (0.54 g, 87%). IR ν_{max} 2927, 1731, 1642 cm^{-1}; ^{1}H NMR δ 2.07 (3H, s, Ac), 2.48 (6H, m, 3-H, 4, 9), 3.62 (3H, s, H-11), 5.11 (1H, m, H-2), 7.21 (4H, m, H-5, 6, 7, 8). ^{13}C NMR: δ = 22.9, 25.9, 30.5, 39.2, 49.3, 51.6, 125.9, 126.0, 126.4, 127.5, 135.4, 137.5, 169.9, 171.3.

Methyl (1-acetyl-6-methoxy-1,2,3,4-tetrahydroquinolin-2-yl)acetate (11b). A solution of quinoline **10b** (0.92 g, 3.88 mmol) in glacial acetic acid (5 mL) was added to a solution of $NaCNBH_3$ (0.98 g, 15.6 mmol) in glacial acetic acid (5 mL) and the mixture cooled to 20 ˚C under nitrogen. The mixture was stirred at 20 ˚C for 1 h and then warmed to room temperature. The mixture was heated at 50 ˚C for 1 h then stirred at room temperature for 6 d. Water (30 mL) was added after which the mixture was basified to pH 9 using sodium hydrogen carbonate solids. Brine (10 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL), washed with water (10 mL) and the solvent removed *in vacuo*. The crude product was treated with acetic anhydride (10 mL) and the resulting solution heated at 90-100 ˚C

overnight. After allowing the mixture to cool to room temperature it was diluted with water (50 mL) and sodium hydrogen carbonate solid was added. The mixture was then extracted with EtOAc (5 × 20 mL), and the combined organic layers dried over magnesium sulfate then evaporated *in vacuo*. The crude was purified by column chromatography (EtOAc: hexane; 1:3). Compound **11b** was obtained as yellow oil, (0.58 g, 54%). Anal. Calcd for $C_{15}H_{19}O_4$: C, 64.97; H, 6.91; N, 5.05%. Found: C, 64.76; H, 7.08; N, 5.05. $C_{15}H_{19}NO_4$. IR ν_{max} 2950, 1733, 1646 cm^{-1}; ^1H NMR δ 2.10 (3H, s, Ac), 2.38 (6H, m, H-3, 4, 9), 3.63 (3H, s, H-11), 3.81 (3H, s, H-12), 5.13 (1H, bs, H-2), 6.73 (1H, s, H-5), 6.77 (1H, m, H-7), 6.99 (1H, m, H-8); ^{13}C NMR δ 22.8, 26.5, 30.8, 39.3, 49.1, 51.6, 55.4, 111.7, 112.7, 127.0, 130.5,139.0, 157.6, 169.9, 171.3.

General Procedure for Oxidation of *N*-Acyltetrahydroquinolines using Chromium Hexacarbonyl. *N*-Acetyl-1,2,3,4-tetrahydroquinoline (0.540 mmol), chromium hexacarbonyl (0.6 mol. equiv.) and *tert*-butyl hydroperoxide (70 wt.% in water, 13 mL per g) were added to a round bottom flask containing MeCN (67 mL per g). The mixture was heated at reflux for 24–48 h, then cooled to room temperature, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (hexane: EtOAc; 2:1 or 3:1).

Methyl (1-acetyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)acetate (12a).[17] Reaction time: 48 h; (100% from **11a**); brown viscous oil. IR ν_{max} 1733, 1664, 1600 cm^{-1}; ^1H NMR δ 2.38 (3H, s, Ac), 2.51 (1H, dd, *J* = 15.8, 6.9, H-3_a), 2.59 (1H, m, H-3_b), 2.77 (1H, d, *J* = 18.0 Hz, H-9_a), 3.07 (1H, dd, *J* = 18.3 Hz, 6.0, H-9_b), 3.65 (3H, s, H-11), 5.56 (1H, bs, H-2), 7.30 (1H, t, *J* = 7.6 Hz, H-6), 7.43 (1H, bs, H-5), 7.59 (1H, t, *J* = 8.5 Hz, H-7), 8.02 (1H, d, *J* = 8.6 Hz, H-8). ^{13}C NMR δ 23.3, 36.7, 43.4, 50.0, 52.0, 125.7, 125.8, 127.3, 134.6, 141.0, 169.5, 170.5, 192.5.

Methyl (1-acetyl-6-methoxy-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)acetate (12b). Reaction time: 24 h; (73% from **11b**); yellow oil. IR ν_{max} 1734, 1688, 1661 cm^{-1}; Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81%. Found: C, 61.75; H, 6.22; N, 4.79. ^1H NMR δ 2.36 (3H, s, Ac), 2.55 (3H, m, H-3, 9a), 3.07 (1H, dd, *J* = 5.9 Hz, 18.3, H-9b), 3.65 (3H, s, H-11), 3.86 (3H, s, H-12), 5.55 (1H, bs, H-2), 7.16 (1H, m, H-8), 7.43 (2H, m, H-5, 7); ^{13}C NMR δ 23.0, 36.6, 43.3, 49.9, 51.9, 55.7, 109.1, 122.3, 126.6, 127.3, 134.3, 157.2, 169.4, 170.5, 192.4.

General Procedure for the Preparation of Tetrahydroquinolin-2-ylacetic Acids. Ester (0.37 mmol) was dissolved in MeOH (50 mL per g) and potassium carbonate (3-4 mol equiv.) added. The mixture was heated at reflux for 6-14 h, filtered and then concentrated *in vacuo*. The residue was diluted with water (10 mL), and the mixture extracted with EtOAc (2 × 10 mL) and washed with water (10 mL). The combined aqueous layer was acidified with hydrochloric acid (1M, 25 mL per g) and EtOAc (400 mL per g) added. The EtOAc solution was removed and reduced to two thirds of its volume then filtered to remove the remaining potassium carbonate solids. The filtrate was washed with brine (10 mL). The organic layer was collected, dried over magnesium sulfate and the solvent was removed *in vacuo*. The

crude was purified by column chromatography (hexane:EtOAc; 2:1).

(4-Oxo-1,2,3,4-tetrahydroquinolin-2-yl)acetic acid (5a).[18] Reaction time: 6 h; yield: (91% from **12a**); brown viscous oil. IR ν_{max} 3324, 1710, 1650 cm^{-1}; ^1H NMR δ 2.60 (2H, m, H-3), 2.77 (2H, m, H-9), 4.08 (1H, m, H-2), 6.71 (1H, d, *J* = 8.2 Hz, H-8), 6.77 (1H, t, *J* = 7.4 Hz, H-6), 7.32 (1H, t, *J* = 7.5 Hz, H-7), 7.83 (1H, d, *J* = 7.8, H-5). ^{13}C NMR δ 38.4, 43.5, 49.5, 116.4, 118.5, 119.0, 127.4, 135.6, 150.9, 175.4, 192.9.

(6-Methoxy-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)acetic acid (5b). Reaction time: 14 h; yield: (76% from **12b**); yellow oil; IR ν_{max} 3316, 2920, 1719, 1651 cm^{-1}; ^1H NMR (MeOD) δ 2.59 (4H, m, H-3, 9), (2H, s, br, NH, OH), 3.73 (3H, s, H-11), 3.91 (1H, m, H-2), 6.78 (1H, d, *J* = 9.0 Hz, H-8), 7.01 (1H, dd, *J* = 3.0, 9.0 Hz , H-7), 7.19 (1H, d, *J* = 3.0 Hz, H-5); ^{13}C NMR (MeOD) δ 40.7, 44.4, 46.2, 51.6, 55.8, 108.2, 119.0, 119.3, 125.4, 148.2, 152.7, 193.3. HRMS (ES-ToF) *m/z*: calcd. for $C_{12}H_{14}NO_4$ $[M + H]^+$, 236.0923; found 236.0929.

General Procedure for the Preparation of Pyranoquinolines. Amino acid **5a** or **5b** (0.25 mmol) was dissolved in acetic anhydride (81 mL per g) and triethylamine (2 mL per g) added. The mixture was heated at reflux overnight. After allowing the mixture to cool to room temperature it was diluted with water (163 mL per g) and solid sodium hydrogen carbonate was then added until the mixture was neutral. The mixture was then extracted with EtOAc, and the organic extract dried over sodium sulfate then evaporated under reduced pressure. The crude product was purified by column chromatography (EtOAc: hexane; 1:3).

5-Methyl-2*H*-pyrano[3,2-*c*]quinolin-2-one (13a). Yield: (47%); white solid**;** mp 176-178 ˚C [lit.[14] 159-161 ˚C (DCM/hexane)]. IR ν_{max} 1626, 1733, 2923, 3057 cm^{-1}; ^1H NMR δ 2.88 (3H, s, H-11), 6.55 (1H, d, *J* = 9.8 Hz, H-3), 7.62 (1H, t, *J* = 7.6 Hz, H-9), 7.80 (1H, t, *J* = 7.6 Hz, H-8), 8.03 (2H, m, H-4,10), 8.39 (1H, d, *J* = 8.2 Hz, H-7). ^{13}C NMR δ 22.5, 109.8, 116.3, 117.4, 122.0, 127.0, 128.7, 132.0, 140.7, 148.5, 156.1, 157.3, 159.4.

9-Methoxy-5-methyl-2*H*-pyrano[3,2-*c*]quinolin-2-one (13b). Yield: (53%); pale brown solid; mp 150-151 ˚C (MeOH/hexane); IR ν_{max}/cm^{-1} 2922, 1731, 1231; ^1H NMR: δ 2.06 (3H, s, H-11), 4.02 (3H, s, H-12), 6.57 (1H, d, *J* = 9.7 Hz, H-3), 7.48 (1H, m, H-8), 7.59 (1H, s, H-10), 7.90 (1H, d, *J* = 9.2 Hz, H-7), 8.30 (1H, d, *J* = 9.7 Hz, H-4); ^{13}C NMR: δ 22.2, 56.2, 100.2, 111.0, 116.9, 118.9, 124.5, 131.3, 142.4, 145.3, 150.0, 154.6, 159.1, 159.6. HR-MS (ES-ToF) *m/z*: calcd. for $C_{14}H_{12}NO_3$ $[M + H]^+$, 242.0817; found 242.0813.

Single Crystals for 9-Methoxy-5-methyl-2*H*-pyrano[3,2-*c*]quinolin-2-one (13b). Crystallographic data for the X-ray structural analysis has been deposited with the Cambridge Crystallographic Data Centre with deposition number, CCDC-2087727 for compound **13b**. Free copies of the data can be obtained via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre,

12 Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk). Selectee crystal data for **13b**: orthorhombic, a = 15.370(2) Å, b = 3.8436(6) Å, c = 37.083(7) Å, α = 90º, β = 90º, γ = 90º, V = 2190.7 (6) $Å^3$, D_{calc} = 1.463 gcm^{-3}, μ (Cu Kα) = 8.58 cm^{-1}, R = 0.0721 (3452), wR2 = 0.2198 (4333), S = 1.075.

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