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TETRAHEDRON

Synthesis of Two Pyranoquinolinones. What is the Structure of Cherimoline ?

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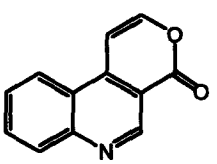
Abstract: Ethyl quinolin-4-one-3-carboxylate has been converted in 4 steps into 4*H*-pyrano[3,4-*c*]quinolin-4-one and 3-methoxyquinolin-4-one has been converted in 3 steps into 3*H*-pyrano[2,3-*c*]quinolin-3-one. Neither of these tricyclic lactones corresponds to natural cherimoline.

Plants of the family Annonaceae cultivated in Taiwan have yielded alkaloids of the oxoaporphine, aporphine, benzylisoquinoline, proaporphine, and phenanthrene types.[1] An examination of the sub-tropical fruit tree *Annona cherimola* (Annonaceae) revealed[2] the presence of several alkaloids amongst which was a new base named cherimoline, a substance with the formula $C_{12}H_7NO_2$, which was assigned the structure shown below – 4*H*-pyrano[3,4-*c*]quinolin-4-one. This ring system had not been described before in either a natural product or in a synthetic material. Nonetheless, the construction of a compound with this constitution (**Scheme 1**) seemed to present a straightforward challenge the successful conclusion of which would be confirmation for the novelty of the structure deduced[2] spectroscopically. In particular, our interest in the synthesis of quinoline-containing alkaloids[3] and our previous experience[4] with the use of 4-trifluoromethylsulfonyloxyquinolines for the introduction of functionalised two-carbon units at a quinoline 4-position by Pd(0)-catalysed coupling processes led us to suppose that 4*H*-pyrano[3,4-*c*]quinolin-4-one might be accessible using this methodology.

cherimoline
according to reference 2



In contrast to our previous studies,[4] the 4-quinolone (precursor to a 4-triflate) required in the present case needed to carry a carboxylic acid/ester function at C-3. Fortunately, such quinolones are readily available *via* the thermal ring closure of arylaminomethylenemalonates, thus, following earlier work,[5] reaction of aniline with diethyl ethoxymethylenemalonate gave **1** which in turn was converted into the 4-quinolone-3-ester **2** on heating in Dowtherm® A. The quinolone was transformed into the corresponding triflate **3** by reaction with $(CF_3SO_2)_2O$ in the presence of 2,6-lutidine. Coupling to a functionalised two-carbon unit – trimethylsilylacetylene – albeit in only modest yield was brought about using tris(dibenzylideneacetone) palladium(0)-chloroform adduct as catalyst giving **4**. Following removal of the silicon protection (→ **5**) in the standard way, formation of the lactone took place in the same pot as alkaline hydrolysis of the ester, giving 4*H*-pyrano[3,4-*c*]quinolin-4-one **6**.

The ^1H and ^{13}C NMR spectra of **6** were compared with those reported[2] for the alkaloid. Although there was considerable similarity, the spectra were clearly not identical, in particular the synthetic lactone had a ^{13}C

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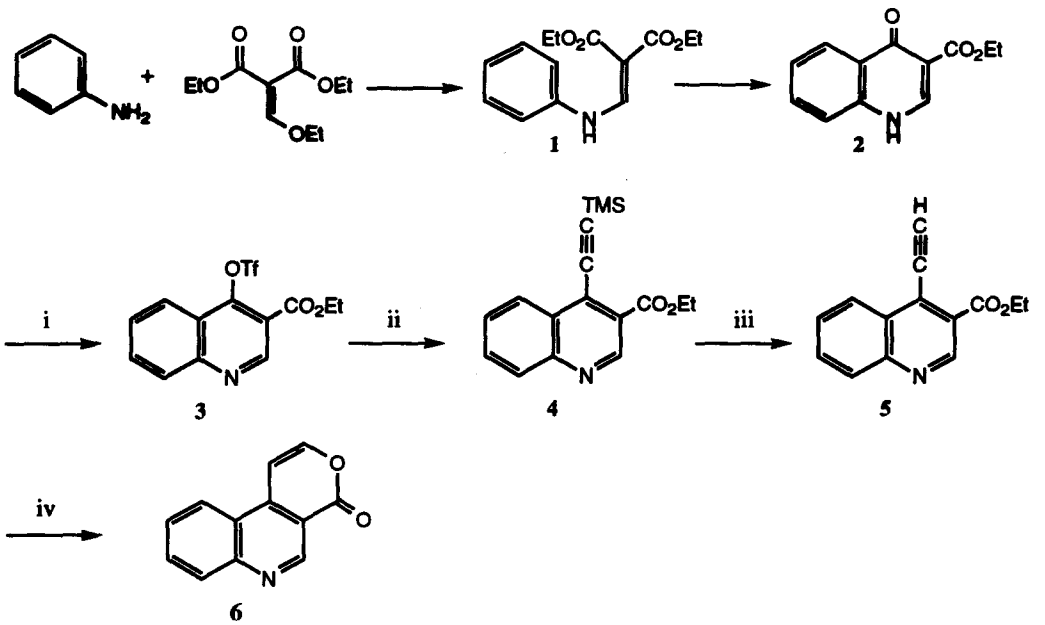


Scheme 1

Reagents: i, Tf_2O, DMAP, 2,6-lutidine, CH_2Cl_2, rt (63%); ii, $HC{\equiv}CSiMe_3$, $Pd_2(dba)_3.CHCl_3$, PPh_3, *i*-Pr_2NEt, DMF, rt (30%); iii, KF, MeOH, reflux (80%); iv, LiOH, H_2O, THF, rt (20%).

NMR signal at 150.0 for C-2 (numbering according to Fig 1), compared to 134.3 for the equivalent carbon in the alkaloid, reflecting its linkage in **6** to the electronegative oxygen – indeed the shift of C-2 in **6** is very similar to that of the quinoline α-carbon (C-5; 150.7; the hetero-ring α-carbon in cherimoline resonates at 149.5). The protons at C-2 in **6** and the equivalent position in cherimoline also reflect this difference, the former resonating some 0.5 ppm to lower field. As a final verification that we had indeed synthesised the structure proposed for cherimoline we carried out an extensive series of ^1H-^{13}C (COSY) correlations and long range ^1H-^{13}C (HMBC) correlations, these are summarised in **Figure 1**.

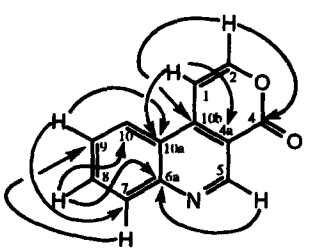
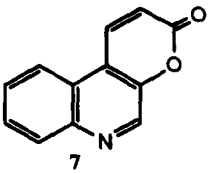


Figure 1

We were fortunate in being supplied with a small quantity of cherimoline by Professor Wu and were thus able to carry out a direct tlc comparison – cherimoline and **6** are not the same.

The availability of the small sample of the natural material allowed us to attempt to verify the high carbonyl stretching frequency reported for cherimoline – 1760 cm^{-1} – which might have been consistent with the enol-lactone structure proposed; the synthetic lactone **6** had a carbonyl absorption at 1732 cm^{-1}. Measured as a

film, cherimoline had a strong absorption at 1670 cm^{-1}; we assume that a simple typographical transposition of '6' and '7' must have occurred in the preparation of the original report.[2]



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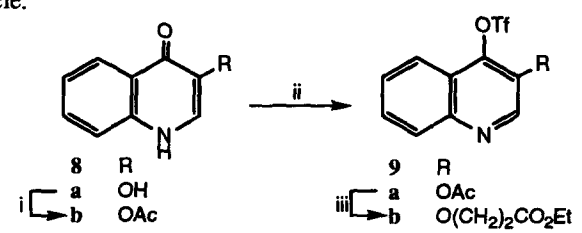
The true carbonyl frequency of the natural material clearly suggests a conjugative influence. It seemed possible that the structure of cherimoline might be **7** – 3*H*-pyrano[2,3-*c*]quinolin-3-one – which also had not been previously described as either a natural or synthetic material. Accordingly we undertook a synthesis (**Scheme 3**) of this tricycle.

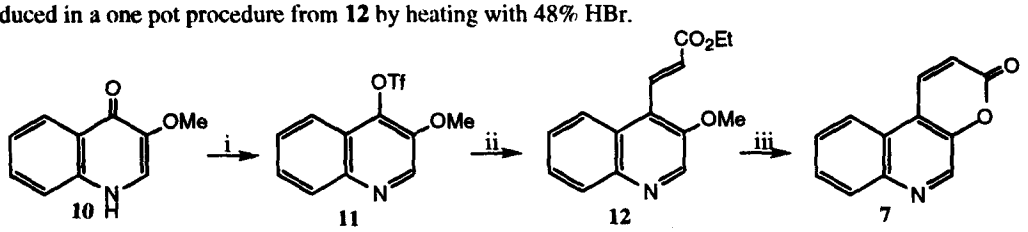


Scheme 2

Reagents: i, Ac_2O, rt (66%); ii, Tf_2O, DMAP, 2,6-lutidine 0 °C → rt (61%); iii, CH_2=$CHCO_2Et$, $Pd_2(dba)_3.CHCl_3$, Ph_3P, *i*-Pr_2NEt, DMF, rt (10%) plus **8a** (*ca.* 70%).

3-Hydroxyquinolin-4-one[6] **8a** was converted into its acetate **8b** and thence into the triflate **9a**. The conditions applied in an attempt to bring about coupling of **9a** with ethyl acrylate resulted mainly in hydrolysis to 3-hydroxyquinolin-4-one **8a**, which was accompanied by a little of the Michael adduct **9b** (**Scheme 2**).

It was clear that a more robust protection for the 3-hydroxyl would need to be put in place. 3-Methoxyquinolin-4-one[7] **10** was converted into the 4-trifluoromethylsulfonyloxy-quinoline **11** and this now did couple satisfactorily with ethyl acrylate (→ **12**) to install the three-carbon unit required for formation of **7**, which was produced in a one pot procedure from **12** by heating with 48% HBr.



10 11 12 7

Scheme 3

Reagents: i, Tf_2O, DMAP, 2,6-lutidine 0 °C → rt (57%); ii, CH_2=$CHCO_2Et$, $Pd(OAc)_2$, DMF, Bu_4NCl, $NaHCO_3$, 80 °C, 24 h (95%); iii, HBr (aq., 48%, 2 ml), AcOH (70 μl), Ac_2O (64 μl), heat, 24 h (60%).

A comparison of the spectroscopic data for the synthetic **7** with that for cherimoline again showed considerable similarities, but there were irreconcilable discrepancies. The introduction of α,β-unsaturation did not bring the carbonyl stretching frequency (observed at 1730 cm^{-1} in **7**) anywhere near that of cherimoline but did have the effect of bringing the chemical shift of the signal for the proton equivalent to the C-1-hydrogen in **6**, down to 8.05 (*cf.* corresponding cherimoline signal at 7.21). Neither of the ^{13}C NMR signals for the CH

carbons of the acrylate unit is consistent with the equivalent signals from cherimoline. A direct tlc comparison confirmed that cherimoline and **7** are not the same. The ^{1}H and ^{13}C NMR and IR data for **6** and **7** and for the natural material are compared in **Tables 1, 2, and 3.**

Table 1 ^{1}H NMR data (hydrogens numbered according to Fig. 1)

	6	**6**	cherimoline[2]	**7**	**13**[8]	**14**[8]
solvent	$CDCl_3$	CD_3OD	CD_3OD	$CDCl_3$	$CDCl_3$	$CDCl_3$
proton/field	500 MHz	500 MHz	400 MHz	300 MHz	200 MHz	200 MHz
H-1	7.25, d, *J* 5.5	7.67*	7.21*, d, *J* 7.2	8.05*, d, *J* 9.7	7.88, d, *J* 5.5	8.20, d, *J* 7.8
H-2	7.71, d, *J* 5.5	8.00	7.47, d, *J* 7.2	6.80, d, *J* 9.7	8.92, d, *J* 5.5	8.80, d, *J* 7.8
H-5	9.62, s	9.54, s	9.54, s	8.03, s	9.52, s	8.59, s
H-7	8.24, dd, *J* 8.0, 1.5	8.24	8.07, dd *J* 7.8, 1.2	7.91, dd, *J* 8.0, 1.4	1H of 3H at 7.35-7.61, m	1H of 2H at 7.89-7.98, m
H-8	7.95, ddd, *J* 8.0, 7.5, 1.0	8.10	7.79, td *J* 7.8, 7.8, 1.2	7.65, ddd, *J* 8.0, 7.5, 1.0	1H of 3H at 7.35-7.61, m	7.75, dd, *J* 8.1, 1.2
H-9	7.75, ddd, *J* 7.5, 7.5, 1.5	7.92	7.63, td *J* 7.8, 7.8, 1.2	7.76, ddd, *J* 8.8, 7.5, 1.4	8.07, dd, *J* 8.2, 1.0	8.48, dd, *J* 8.1, 1.2
H-10	8.26, dd, *J* 7.5, 1.0	8.62*	8.30*, dd *J* 7.8, 1.2	8.16*, dd, *J* 8.8, 1.0	1H of 3H at 7.35-7.61, m	1H of 2H at 7.89-7.98, m

* An nOe was found between these protons

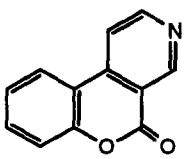
Table 2 ^{13}C NMR data (carbons numbered according to Fig. 1)

	6	cherimoline[2]	**7**
solvent	$CDCl_3$	CD_3OD	$CDCl_3$
carbon	75.4 MHz	100 MHz	75.4 MHz
1	101.7	100.4	122.4
2	150.0	134.3	120.5
4	161.0	162.8	159.3
4a	113.1	117.5	146.9
5	150.7	149.5	144.7
6a	149.5	147.6	145.9
7	130.6	129.6	129.5
8	132.7	131.5	129.5
9	128.0	127.4	128.6
10	123.8	123.6	122.4
10a	121.2	122.2	128.8
10b	142.3	142.8	139.1

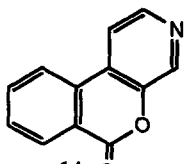
Table 3 IR carbonyl frequencies (cm^{-1})

6	cherimoline	7	13[8]	14[8]
film	not specified[2]	film	nujol	nujol
1732	1760[2] 1670*	1730	1738	1747

* The carbonyl absorption frequency of the cherimoline sample provided by Professor Wu and measured by us as a film.



13



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There are currently 94 substances listed in the Beilstein data base with the molecular formula $C_{12}H_7NO_2$. Of these only 2 can be considered as possible structures for cherimoline, namely the lactones **13** and **14**[8] but a comparison (**Tables 1** and **3**) of the published IR and ^1H NMR data for these two substances with those for cherimoline show conclusively that neither of these two structures represents the natural material.

A consideration of the types of alkaloid previously reported from plants of the Annonaceae, which all have isoquinoline or isoquinoline-derived structures, may give some guidance as to the true structure of cherimoline, but the number of possibilities which this still leaves open is too large to contemplate further synthetic work until more evidence becomes available on the natural material.

ACKNOWLEDGEMENTS

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EXPERIMENTAL

General

Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on SiO_2 (silica Gel 60 F_{254}, Merck 0.063-0.200 mm) and spots were located with UV light. Column chromatography was carried out on SiO_2 (silica Gel 60 SDS 0.060-0.2 mm). Flash chromatography was carried out on SiO_2 (silica Gel 60 A CC (Merck). Organic extracts were dried over anhydrous Na_2SO_4, and solutions were evaporated under reduced pressure with a rotatory evaporator. IR spectra were performed on a Nicolet 205 FT-IR and peaks are given in cm^{-1}. NMR spectra were measured with Varian Gemini-200 (200 MHz), Varian Gemini-300 (300 MHz) and Varian VXR-500 (500 MHz) spectrometers; data are given in δ referenced to TMS with ^1H-NMR coupling constants (J) in Hz. Mass spectra were measured in the electron impact (EI) and chemical ionisation (CI) modes with a Hewlett-Packard model 5989A; ions are recorded as *m/z* with percentage abundances relative to the molecular ion given in parentheses. High resolution mass spectra were performed on a Autospec/VG by Departamento de Química Orgánica Biológica (C.S.I.C.) Barcelona.

Ethyl 4-trifluoromethylsulfonyloxyquinoline-3-carboxylate 3

To a solution of **2**[5] (250 mg, 1.2 mmol) in dry CH_2Cl_2 (15 ml) were successively added under N_2, 4-dimethylaminopyridine (DMAP) (30 mg, 0.24 mmol), 2,6-lutidine (0.2 ml, 1.68 mmol) and $(CF_3SO_2)_2O$ (Tf_2O) (0.25 ml, 1.44 mmol). The mixture was stirred at 0 °C for 2 h then 1 h at rt. The organic solution was washed with H_2O, dried and evaporated *in vacuo* and the residue was purified by column chromatography. Elution with hexane/CH_2Cl_2 (70:30) afforded **3** as an oil (265 mg, 63%). IR (film) 1710 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33 (t, J =7.1 Hz, 3H); 4.34 (q, J =7.1 Hz, 2H); 7.51 (ddd, J = 8.0, 8.0, 0.8 Hz, 1H); 7.69 (ddd, J = 8.0, 8.0, 1.8 Hz, 1 H); 8.16 (dd, J =8.0, 0.8 Hz, 1H); 8.39 (dd, J = 8.0, 1.8 Hz, 1H); 8.82 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 14.2 (q); 62.0 (t); 118.4 (d); 121.9 (q); 127.5 (s); 127.8 (d); 128.3 (d); 133.9 (d); 137.6 (s); 143.1 (d); 155.0 (s); 162.8 (s); 173.7 (s). MS (EI) 349 (M^+, 3); 172 (100); 144 (21); 132 (31).

Ethyl 4-trimethylsilylethynylquinoline-3-carboxylate 4

To a solution of **3** (260 mg, 0.74 mmol) in dry DMF (5 ml) were successively added under N_2, $Pd_2(dba)_3.CHCl_3$ (77 mg, 0.074 mmol), Ph_3P (64 mg, 0.5 mmol), *i*-Pr_2NEt (0.4 ml, 2.2 mmol), and trimethylsilylacetylene (0.3 ml, 2.2 mmol). The mixture was stirred at rt for 16 h after which time Et_2O (20 ml) was added and the organic solution was washed with H_2O, dried and evaporated *in vacuo*. The residue was purified by column chromatography, elution with hexane/CH_2Cl_2 (70:30) giving **4** as an oil (67 mg, 30%). IR (film) 2130, 1730 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.38 (s, 9H); 1.48 (t, J = 7.1 Hz, 3H); 4.50 (q, J = 7.1 Hz, 2H); 7.68 (ddd, J = 8.5, 8.5, 1.2 Hz, 1H); 7.82 (ddd, J = 8.5, 8.5, 1.4 Hz, 1H); 8.13 (dd, J = 8.5, 1.2 Hz, 1H); 8.45 (dd, J = 8.5, 1.4 Hz, 1H); 9.36 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ -0.3 (q); 14.3 (q); 61.6 (t); 98.4 (s); 113.0 (s); 124.5 (s); 127.2 (d); 127.4 (s); 128.0 (d); 129.7 (d); 130.2 (s); 131.4 (d); 148.8 (s); 150.2 (d); 165.3 (s). MS (EI) 297 (M^+, 13); 282 (23); 268 (29); 254 (45); 238 (100); 223 (29). Found M^+ 297.1169; $C_{17}H_{19}NO_2Si$ requires M 297.1185.

Ethyl 4-ethynylquinoline-3-carboxylate 5

To a solution of **4** (100 mg, 0.34 mmol) in MeOH (5 ml) was added KF (60 mg, 1 mmol) and the mixture was stirred at reflux for 1 h. After this time the solvent was evaporated and the residue was dissolved in CH_2Cl_2 and washed with H_2O. The organic solution was dried and evaporated to give **5** as a gum (60 mg, 80%). IR (film) 2250, 1735 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ 1.47 (t, J = 7.0 Hz, 3H); 4.13 (s, 1H); 4.51 (q, J = 7.0 Hz, 2H); 7.68 (ddd, J = 7.6, 7.6, 1.4 Hz, 1H); 7.84 (ddd, J = 7.6, 7.6, 1.8 Hz, 1 H); 8.15 (dd, J = 7.6, 1.4 Hz, 1H); 8.49 (dd, J = 7.6, 1.8 Hz, 1H); 9.39 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 14.2 (q); 61.8 (t); 93.5 (d); 116.0 (s); 124.5 (s); 127.1 (d); 128.2 (d); 129.8 (d); 131.7 (d); 142.5 (s); 133.0 (s); 148.5 (s); 150.0 (d); 168.5(s). MS (EI) 225 (M^+, 79); 197 (49); 180 (100); 152 (87). Found M^+ 225.0789; $C_{14}H_{11}NO_2$ requires M 225.0789.

***4H*-pyrano[3,4-*c*]quinolin-4-one 6**

A solution of LiOH (53 mg, 1.3 mmol) in H_2O (0.5 ml) was added to a solution of **5** (60 mg, 0.26 mmol) in THF (3 ml) and the mixture was stirred for 48 h at rt. The organic solvent was evaporated, H_2O (3 ml) was added to the residue, the aq. solution was neutralized with 1N HCl and extracted with CH_2Cl_2. The organic solution was dried and evaporated to give a residue which was purified by column chromatography. Elution with CH_2Cl_2 gave **6** (10 mg, 20%), mp 144-146 °C (Et_2O). IR ($CHCl_3$) 1732 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.25 (d, J = 5.5 Hz, 1 H); 7.71 (d, J = 5.5 Hz, 1 H); 7.75 (ddd, J = 7.5, 7.5, 1.5 Hz, 1H); 7.95 (ddd J

= 8.0, 7.5, 1.0 Hz, 1 H); 8.24 (dd, J = 8.0, 1.5 Hz, 1 H); 8.26 (dd, J = 7.5, 1.0 Hz, 1H); 9.62 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 101.7 (d); 113.1 (s); 121.2 (s); 123.8 (d); 128.0 (d); 130.6 (d); 132.7 (d); 142.3 (s); 149.5 (s); 150.0 (d); 150.7 (d); 161.0 (s). MS (EI) 197 (M^+, 99); 169 (100); 141(37); 140 (37). Found M^+ 197.0481; $C_{12}H_7NO_2$ requires M 197.0477.

3-Acetoxyquinolin-4-one 8b

3-Hydroxyquinolin-4-one[6] **8a** (95 mg, 0.6 mmol) was dissolved in Ac_2O (3 ml) and after 1 h at rt, saturated aq. $NaHCO_3$ was added until the solution was basic then product extracted into CH_2Cl_2. The organic layer was dried and evaporated to give **8b** (80 mg, 66%), mp 202-205 °C (CH_2Cl_2). IR (KBr) 1765 cm^{-1}. ^{1}H NMR (d_6-DMSO, 300 MHz) δ 2.24 (s, 3H); 7.34 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H); 7.58 (dd, J = 7.8, 1.2 Hz, 1H); 7.67 (ddd, J = 7.8, 7.5, 1.5 Hz, 1H); 8.00-8.14 (m, 2H). ^{13}C NMR (d_6-DMSO, 75.4 MHz) δ 20.5 (q); 118.6 (d); 123.3 (d); 125.2 (d); 125.9 (s); 131.9 (d); 132.5 (d); 133.8(s); 139.3 (s); 168.7 (s); 170.0 (s). MS (EI) 203 (M^+, 5); 161 (100); 133 (46); 104 (42).

3-Acetoxy-4-trifluoromethylsulfonyloxyquinoline 9a

To a solution of **8b** (170 mg, 0.8 mmol) in dry CH_2Cl_2 (5 ml) cooled at 0 °C under N_2 were successively added DMAP (20 mg, 0.2 mmol), 2,6-lutidine (140 ml, 1.2 mmol) and Tf_2O (170 µl). The mixture was stirred for 2 h at 0 °C and for 1 h at rt. The organic solution was washed with H_2O, dried and evaporated to give a residue which was purified by column chromatography, elution with hexane/CH_2Cl_2 (70:30) affording **9a** (170 mg, 61%) as an oil. IR (film) 1800 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.45 (s, 3H); 7.70 (ddd, J= 8.2, 7.7, 1.2 Hz, 1H); 7.80 (ddd, J= 8.8, 7.7, 1.4 Hz, 1H); 8.00 (dd, J= 8.8, 1.2 Hz, 1H); 8.19 (dd, J= 8.2, 1.4 Hz, 1H); 8.92 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 20.5 (q); 120.5 (d); 124.4 (q); 128.8 (d); 129.8 (d); 130.3 (d); 133.8 (s); 135.2 (s); 141.7 (s); 147.1 (d); 147.6 (s); 167.6 (s). MS (EI) 335 (M^+, 7); 292 (36); 160 (100); 132 (53).

3-(2-Ethoxycarbonylethoxy)-4-trifluoromethylsulfonyloxyquinoline 9b

To a solution of **9a** (170 mg, 0.5 mmol) in dry DMF (3 ml) were successively added under N_2, $Pd_2(dba)_3.CHCl_3$ (52 mg, 0.05 mmol), Ph_3P (43 mg, 0.2 mmol), i-Pr_2NEt (260 ml, 1.5 mmol) and ethyl acrylate (160 ml, 0.8 mmol). The reaction mixture was stirred at rt for 24 h, Et_2O was added and the organic solution was washed with H_2O dried and evaporated. The residue was purified by column chromatography, elution with hexane/CH_2Cl_2 (70: 30) affording **9b** as an oil (20 mg, 10 %). IR (film) 1737 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, J= 7.2 Hz, 3H); 2.92 (t, J= 6.2 Hz, 2H); 4.17 (q, J= 7.2 Hz, 2H); 4.53 (t, J= 6.2 Hz, 2H); 7.40-7.52 (m, 2H); 7.76 (ddd, J= 8.0, 8.0, 1.6 Hz, 1H); 8.04 (s, 1H); 8.55 (dd, J= 8.0, 0.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 14.0 (q); 33.2 (t); 48.8 (t); 61.7 (t); 115.0 (d); 118.8 (q); 123.7 (s); 124.8 (d); 128.0 (d); 128.4 (s); 133.1 (d); 133.3 (s); 137.8 (d); 138.4 (s); 170.2 (s). MS (EI) 393 (M^+, 9%); 260 (56); 232 (63); 146 (100). Found M^+ 393.0492; $C_{15}H_{14}F_3NSO_6$ requires M 393.0494.

3-Methoxy-4-trifluoromethylsulfonyloxyquinoline 11

To a solution of **10**[7] (200 mg, 1.1 mmol) in CH_2Cl_2 (5 ml) cooled at 0 °C were successively added DMAP (30 mg, 0.2 mmol), 2,6-lutidine (185 ml, 1.6 mmol) and Tf_2O (250 ml, 1.5 mmol) and the mixture stirred 1 h at 0 °C and 1 h at rt. After this time, the organic solution was washed with H_2O, dried and evaporated. The residue was purified by column chromatography, elution with hexane/CH_2Cl_2 (80:20) giving **11** (200 mg, 57%) as an oil. IR (film) 1403, 1220 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.00 (s, 3H); 7.50-7.65 (m, 3H); 7.75 (dd, J =

7.7, 1.9 Hz, 1H); 7.95 (dd, J = 8.1, 1.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 56.3 (q); 117.0 (d); 118.6 (q); 126.3 (d); 128.1 (2d); 128.6 (d); 129.5 (s); 139.8 (s); 144.4 (s); 145.2 (s). MS (EI) 307 (M^+, 100); 174 (34); 159 (68); 146 (83). Found M^+ 307.0114; $C_{11}H_8F_3NSO_4$ requires M 307.0126.

Ethyl 3-(3-methoxyquinolin-4-yl)propenoate 12

A mixture of **11** (150 mg, 0.5 mmol), ethyl acrylate (110 ml, 1 mmol), $Pd(OAc)_2$ (10 mg, 0.01 mmol), Bu_4NCl (140 mg, 1 mmol), $NaHCO_3$ (105 mg, 1.2 mmol) in dry DMF (3 ml) was stirred under N_2 for 24 h at 80 °C. To the cooled solution, Et_2O was added, solid was removed by filtration and the organic layer washed with H_2O, dried and evaporated to give **12** (122 mg, 95%), mp 112-115 °C (AcOEt). IR ($CHCl_3$) 1713 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.35 (t, J = 6.8 Hz, 3H); 4.30 (q, J = 6.8 Hz, 4H); 7.24 (d, J = 15.6 Hz, 1H); 7.38 (s, 1H); 7.45-7.60 (m, 2H); 7.67 (dd, J = 7.8, 1.4 Hz, 1H); 8.00 (dd, J = 8.0, 1.0 Hz, 1H); 8.21 (d, J = 15.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.2 (q); 55.4 (q); 60.5 (t); 112.5 (d); 124.3 (d); 126.2 (d); 127.1 (d); 127.5 (d); 134.3 (s); 138.0 (d); 142.8 (s); 145.7 (s); 152.0 (s); 166.9 (s). MS (EI) 257 (M^+, 91); 228 (20); 226 (20); 212 (100); 184 (97); 170 (65). Found M^+ 257.1051; $C_{15}H_{15}NO_3$ requires M 257.1052.

3*H*-Pyrano[2,3-*c*]quinolin-3-one 7

A solution of **12** (50 mg, 0.2 mmol), AcOH (70 µl), Ac_2O (64 µl), and 48% HBr (2 ml) was refluxed during 24 h. The cooled solution was made basic with sat. aq. $NaHCO_3$ and organic material extracted into CH_2Cl_2. The organic layer was dried and evaporated to give **7** (25 mg, 60%), mp 192-194 °C (AcOEt). IR ($CHCl_3$) 1730 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.80 (d, J = 9.7 Hz, 1H); 7.65 (ddd, J = 8.0, 7.5, 1.0 Hz, 1H); 7.76 (ddd, J = 8.8, 7.5, 1.4 Hz, 1H); 7.91 (dd, J = 8.0, 1.4 Hz, 1H); 8.03 (s, 1H); 8.05 (d, J = 9.7 Hz, 1H); 8.16 (dd, J = 8.8, 1.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 120.5 (d); 122.4 (d); 127.4 (d); 128.6 (d); 128.8 (s); 129.5 (2d); 139.1 (s); 144.7 (d); 145.9 (s); 146.9 (s); 159.3 (s). MS (EI) 197 (M^+, 100); 169 (87); 141 (70). Found M^+ 197.0478. $C_{12}H_7NO_2$ requires M 197.0477.

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