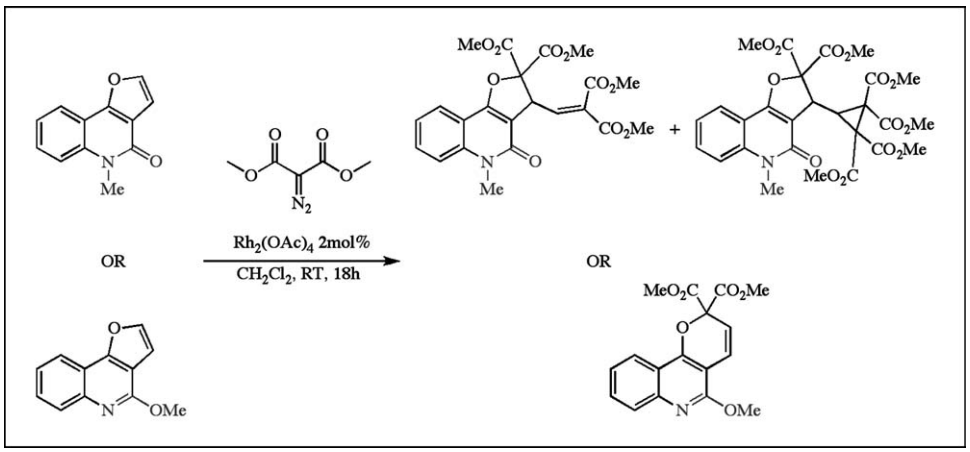
Karl-Fredrik Lindahl,* Anthony Carroll, Ronald J. Quinn, and Justin A. Ripper

Eskitis Institute, Griffith University, Brisbane, Queensland 4111, Australia
*E-mail: f.lindahl@imb.uq.edu.au or kflindahl@hotmail.com
Received November 17, 2009
DOI 10.1002/jhet.463
Published online 17 June 2010 in Wiley InterScience (www.interscience.wiley.com).



Novel double CH-insertion and rearrangement products (**5**, **6**, and **7**) were isolated from treatment of **1** or **2** with dimethyl diazomalonate (**3**) under dirhodiumtetrakis mediated carbenoid chemistry conditions. A new possible reaction pathway is suggested and discussed. Also other diazo compounds were tested.

J. Heterocyclic Chem., **47**, 998 (2010).

INTRODUCTION

Furoquinolinones belong to a class of molecules exhibiting a wide variety of biological activities, including antifungal, antibacterial, antiviral (HIV), antimicrobial, antimalarial, insecticidal, antineoplastic, antidiuretic, antiarrhythmic, and sedative properties [1,2]. Examples of natural alkaloids containing the furoquinolinone core structure include oligophyline [3], araliopsine [4], and almeine [5] (Fig. 1).

These naturally occurring alkaloids, and others belonging to the furoquinolinone class of molecules, are obvious derivatives of a common core structural unit **1**, having a double bond in the **C** ring. Structure **1** is therefore a good choice for functionalization to important synthons for natural product synthesis and medicinal chemistry applications. To our knowledge, this potentially reactive core structure has not yet been exploited in synthesis.

It was envisaged that an electrophilic metal carbenoid, which is readily generated by metal catalyzed decomposition of a diazo reagent [6], could be used to probe reactivity of the **C** ring double bond of the furoquinolinone core structure. Previous studies on related structures have used metal carbenoid chemistry, such as simple furans [7], benzofurans [8], and tris-2-furylmethane derivatives [9].

RESULTS AND DISCUSSION

We wish to report unexpected results from metal carbenoid-mediated chemistry using two analogues, **1** and **2**, as substrates and dimethyl diazomalonate (**3**) as the carbene precursor (Fig. 2). We have previously reported a novel synthesis of the common furoquinolinone core structure (**1**), describing the use of a palladium mediated intramolecular Heck coupling as a key step [10] and an alternative route to literature precedents [11]. The second core structure **2** was synthesized through modification of that protocol by using SEM in place of a methyl substituent as protecting group to facilitate formation of intermediate **9**. Treatment of **9** with dry HCl yielded the unprotected core structure **4**, which could easily be converted to the corresponding imine form **2** by further treatment with $POCl_3$ and sodium methoxide in two separate steps (Scheme 1). The carbene precursor **3** was synthesised by known methods [12].

All reactions were carried out in dichloromethane, with 2 mol % dirhodiumtetraacetate as catalyst and

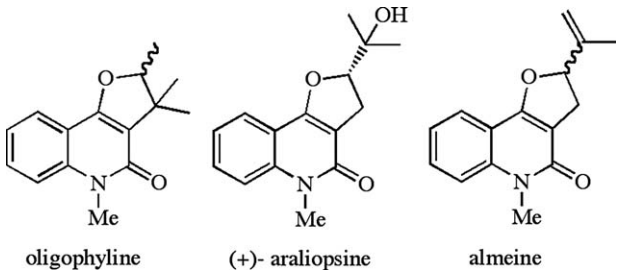


Figure 1. Natural alkaloids with furoquinolinone core structure.

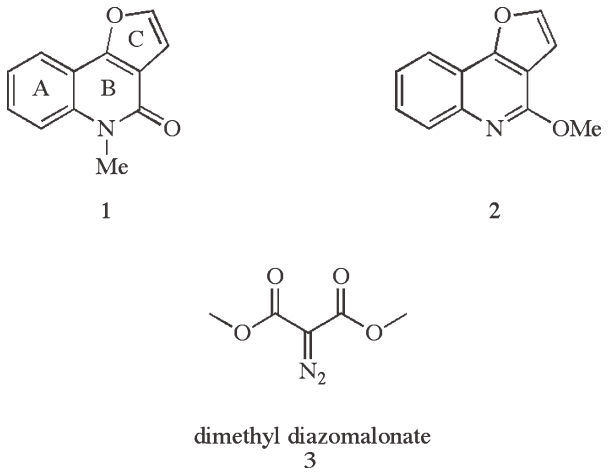


Figure 2. Starting materials (**1** and **2**) and carbene precursor (**3**).

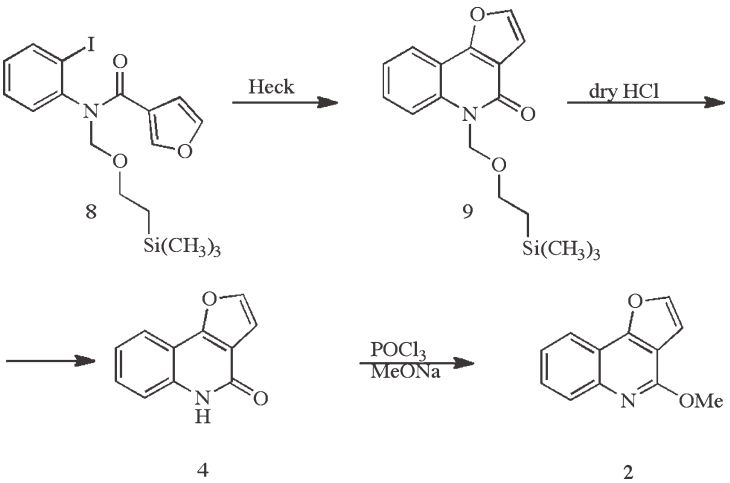
substrate **1** serving as a template for optimizing the reaction conditions. Treating **1** with **3** using previous reported literature procedures [8] with the aim of installing a cyclopropane functionality, did not consume starting material (**1**) in all cases (<5%). Optimized reaction conditions were found using 3.2 eq of **3** (Experimental), leading to 100% consumption of **1** and formation of furo products. Strikingly, the major product was the double CH-insertion product **5**, and the minor product was a cyclopropanated double CH-insertion product **6** (Scheme 2).

However, treatment of the analogue substrate **2** with **3**, under the same optimized conditions used as above, gave only the unsaturated product **7** (Scheme 3). Two aliquots of the carbene species must have reacted with one substrate giving two CH-insertions on the one scaffold, followed by ring opening of the furan ring, rearrangement and ring closure to give **5**. Due to the excess of the metal carbenoid present in the reaction mixture, product **5** can also react further to the minor product **6**. Opening of the furan ring has been noticed before for related structures under similar reaction conditions [7(d),13] This is similar here, indicated by the presence of the quarternary carbon at the C-2 position in both products **5** and **7**. Interestingly, when reacting **2** with **3**, only the pyrano structure **7** was produced.

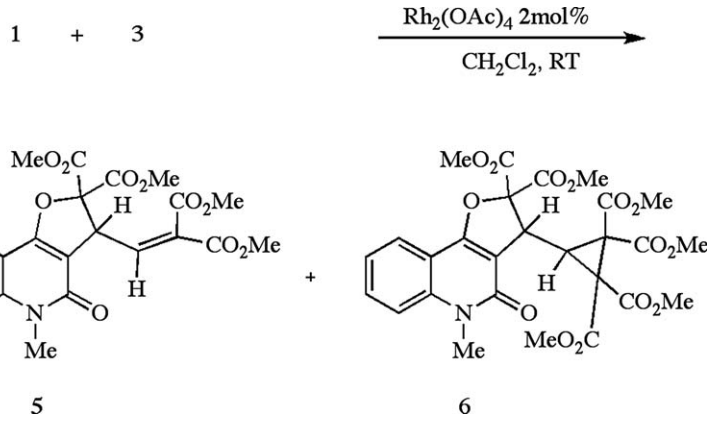
These quite different outcomes are most likely due to two different initial reaction intermediates/transition states **A** and **A'** forming from **1** and **2**, respectively, as substrates (Scheme 4). Possibly substrate **1** reacts with **3** in the C-3 position first, while substrate **2** reacts with **3** in the C-2 position. This suggests that intermediate **A** is formed and is sufficiently stable to undergo a second addition to form transition state **B**, followed by ring opening/ring closing to form **5** (Scheme 5).

In contrast, transition state **A'** cannot undergo such addition and is further stabilized by ring opening/rearrangement to give product **7** (Scheme 6). The ring closing pathway to form **7** proceeds most likely in a similar fashion as suggested for product **5**. These two early reaction intermediates/transition states (**A** and **A'**) can explain the two different outcomes observed and, ultimately, this reflects the inherent electronic differences

Scheme 1



Scheme 2



5 6

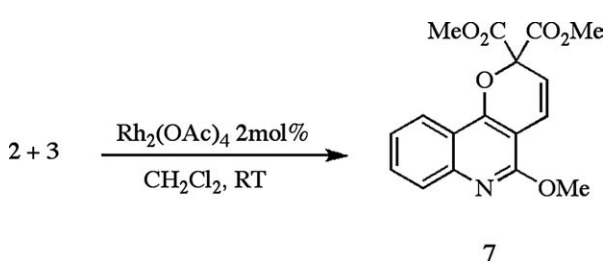
of **1** and **2**. Interestingly, it was noted product **7** does not react further in the presence of excess of **3**.

When changing dimethyl diazomalonate (**3**) for ethyl 2-diazopropionate (**8**) and optimizing the reaction protocol (Experimental), reaction of either **2** or **3** with **8** [14] gave the expected cyclopropanated outcomes **9** and **10** in isolated yields of 43 and 69%, respectively (Scheme 7). No ring opened product was observed in either case. Treatment of either **2** or **3** with the less stabilized carbene precursor 2-diazopropane under a range of conditions, including with/without catalyst and/or lowered/elevated temperatures, starting material was recovered quantitatively in all attempts.

In summary, three novel rearrangement products (**5**, **6**, and **7**) can be derived from two relatively similar substrates **1** and **2**, both belonging to the furoquionolinone class of molecules. The outcomes can be explained by different initial reaction intermediates/transition states, such as **A**, **B**, and **A'**, due to inherently different electronic properties of **1** and **2**. Thus, changing the relatively remote functionality from an amide to an imine (**1** to **2**) determines the reaction under the carbene chemistry conditions. Other reaction intermediates such as a dimerized diazomalonate in the presence of rhodium could possibly act as a carbene precursor. However, this may only be formed in higher concentrations of dimethyl diazomalonate, low consumption of **1** being observed until a certain excess of **3** is present. Alternatively, a direct rhodium mediated opening of the furan ring between the oxygen and C1 occurs [7(b),15]. Further, the expected cyclopropanated products **9** and **10** were obtained from treatment of **1** and **2** with ethyl 2-diazopropionate, however, no reaction was observed when using 2-diazopropane as the carbene precursor.

Most interestingly products **5**, **6**, and **7** are, to our knowledge, unprecedented rearrangement products. Thus, for product **5** (and **6**), this suggests a new reaction pathway is taking place and might serve as a useful application in related areas.

Scheme 3

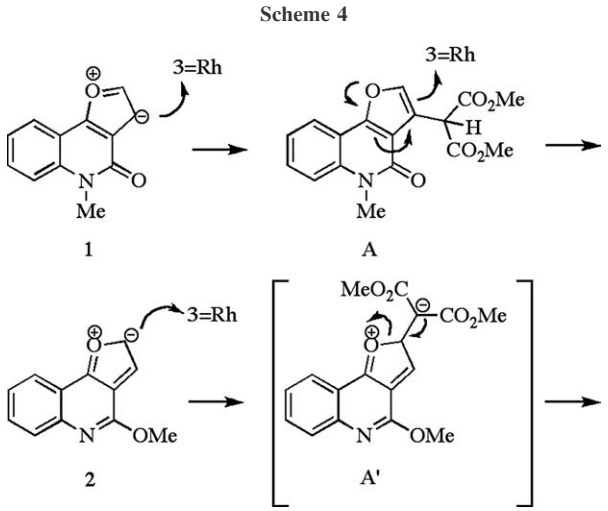


7

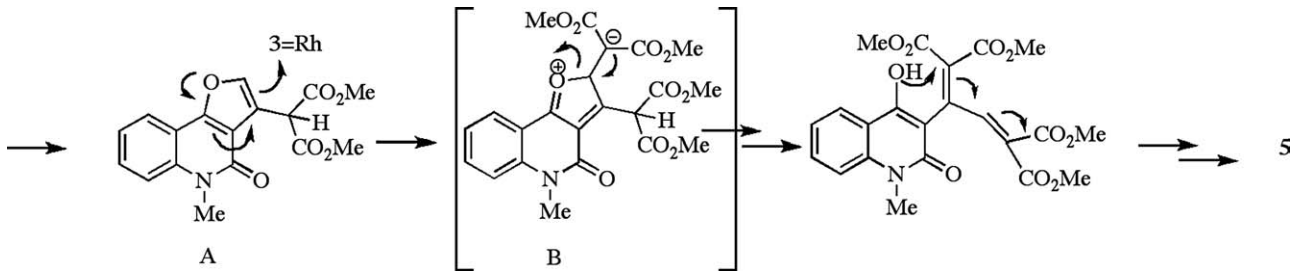
EXPERIMENTAL

***N*-(2-Iodophenyl)-*N*-((2-(trimethylsilyl)ethoxy)methyl)-furan-3-carboxamide (8).** (2-(Chloromethoxy)ethyl)trimethylsilane (1.49 mL, 8.42 mmol) was added dropwise to a solution of *N*-(2-iodophenyl)furan-3-carboxamide (635 mg, 2.03 mmol) and sodium hydride (202 mg, 8.42 mmol) in THF (20 mL) at 0°C under a nitrogen atmosphere. The reaction mixture was allowed to stir for 11 h (mean while slowly warming up to RT) and was then quenched by adding water (20 mL). The

Scheme 4



Scheme 5



reaction mixture was extracted with EtOAc (3 × 50 mL), washing the combined organic layers with 1M NaOH (30 mL), 1*M* HCl (30 mL) and brine (20 mL), dried with $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (EtOAc:hexane/1:9) afforded 855 mg of **8** (95 %) as an oil. IR (KBr, ν_{max}): 2946, 2921, 2357, 2324, 1655, 1581, and 1471 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 206.0 nm (14577), 226.2 nm (10829). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.03 (s, 9H, $SiMe_3$), 0.99 (m, *J* 10 Hz, 2H, H-2‴), 3.77 (app d, *J* 5 Hz, 2H, H-1‴), 4.57 (d, *J* 10.5 Hz, 1H, H-1″), 5.81 (d, *J* 9 Hz, 1H, H-1b″), 6.28 (s, 1H, H-4), 6.73 (s, 1H, H-5), 7.16 (app t, *J* 7.5 Hz, 1H, H-4′), 7.20 (s, 1H, H-2), 7.37 (d, *J* 8.0 Hz, 1H, H-6′), 7.45 (app t, *J* 8.0 Hz, 1H, H-5′), 7.96 (d, *J* 8.0 Hz, 1H, H-3′). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 0.0 ($SiMe_3$), 18.5 (C-2‴), 66.9 (C-1‴), 77.3 (C-1″), 101.4 (C-2′), 111.4 (C-4), 121.9 (C-3), 129.7 (C-5′), 130.9 (C-4′), 132.0 (C-6′), 140.4 (C-3′), 142.5 (C-5), 143.8 (C-1′), 145.9 (C-2), 163.7 (C=O). MS (ESI): *m*/*z* 445 $[M+H]^+$, 467 $[M+Na]^+$, 910 $[2M+Na]^+$. Anal. Calcd. for $C_{17}H_{22}INO_3Si$: C, 46.05; H, 5.00; N, 3.16. Found: C, 46.09; H, 5.01; N, 3.02.

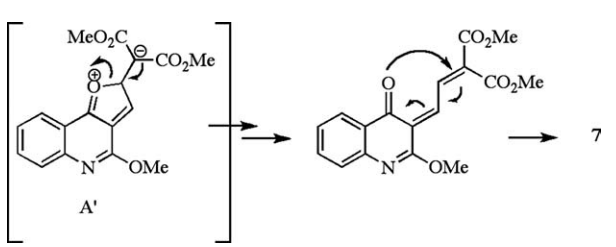
5-((2-(Trimethylsilyl)ethoxy)methyl)furo[3,2-c]quinolin-4(5*H*)-one (9). A mixture of **8** (90 mg, 0.20 mmol), KOAc (26 mg, 0.26 mmol), *n*-Bu_4NCl (11 mg, 0.04 mmol), and PdO (2.5 mg, 0.02 mmol) was stirred in DMA (0.4 mL) at 150°C under a nitrogen atmosphere for 18 h. The crude mixture was then concentrated under reduced pressure followed by flash chromatography (EtOAc:hexane/15:85) to afford 55 mg of **9** (87%) as a slightly yellowish solid. Mp 61–62°C. IR (KBr, ν_{max}): 3158, 3133, 2949, 2900, 1662, 1584, and 1499 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 227 nm (38358), 276 nm (7485), 286 nm (8934), 316 nm (9261), 331 nm (9435). ^1H NMR ($CDCl_3$, 500 MHz): δ -0.022 (s, 9H, H-SiMe3), 0.96 (t, *J* 8.5, 7.5 Hz, 2H, H-2″), 3.74 (t, *J* 8.5, 8 Hz, 2H, H-1″), 5.86 (s, 2H, H-1′), 7.08 (s, 1H, H-3), 7.35 (app t, *J* 7.5 Hz, 1H, H-8), 7.56 (app t, *J* 8.0 Hz, 1H, H-7), 7.65 (s, 1H, H-2), 7.72 (d, *J* 8.0 Hz, 1H, H-6), 8.02 (d, *J* 8.1 Hz, 1H, H-9). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 0.0 (SiMe3), 18.4 (C-2″), 66.6 (C-1″), 71.7 (C-1′), 108.8 (C-3), 113.7 (C-3a), 115.1 (C-9a), 116.8 (C-6), 121.3 (C-9), 123.1 (C-8), 129.8 (C-2), 137.9 (C-5a), 144.3 (C-7), 156.1 (C-9b), 160.2 (C=O). MS (ESI): *m*/*z* 316 [M+H]+, 338 [M+Na]+. Anal. Calcd. for $C_{17}H_{21}NO_3Si$: C, 64.73; H, 6.71; N, 4.44. Found: C, 64.76; H, 6.70; N, 4.45.

Furo[3,2-c]quinolin-4(5*H*)-one (4). To a premixed solution of acetyl chloride (43 mL), ethanol (73 mL) and water (5 mL), was added **9** (1.82 g, 5.77 mmol) at RT with stirring. After all substrate was dissolved, the reaction flask was fitted with a reflux condenser and heated to 80°C for 11 h, and the reaction mixture was then concentrated under reduced pressure. Purification was straightforward by flash chromatography when using (EtOAc:hexane/1:1) as eluent mixture which afforded 0.90 g of furo[3,2-*c*]quinolin-4(5*H*)-one (84%) as an off white solid. ^1H NMR (DMSO-d_6, 400 MHz): δ 7.04 (d, *J* 2.0 Hz, 1H, H-3), 7.25 (app t, *J* 7.4 Hz, 1H, H-8), 7.47 (app d, *J* 7.4 Hz, 1H, H-7), 7.53 (app t, *J* 7.4 Hz, 1H, H-9) 7.88 (d, *J* 7.4 Hz, 1H, H-6), 8.06 (d, *J* 2.0 Hz, 1H, H-2), 11.73 (br s, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 108.4, 111.9, 116.2, 116.7, 120.8, 122.9, 130.1, 137.7, 146.1, 156.1, 159.5. MS (ESI): *m*/*z* 185 $[M+H]^+$.

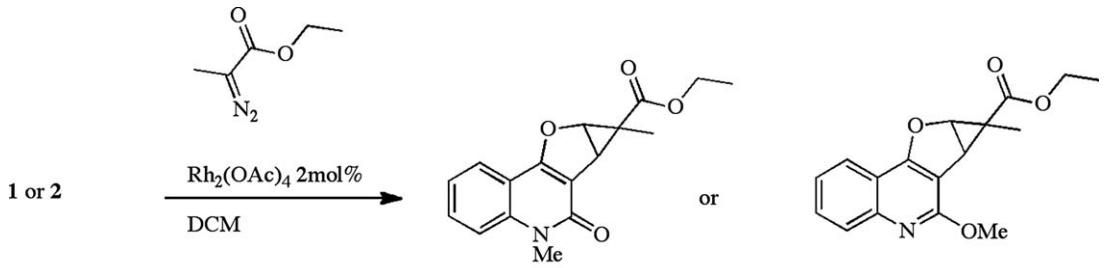
(4-Chlorofuro[3,2-c]quinoline). A mixture of furo[3,2-*c*]quinolin-4(5*H*)-one (0.87 g, 4.7 mmol), phosphorusoxychloride (10.0 mL) and water (0.5 mL) was refluxed at 135 °C for 4 h. The cold reaction mixture was quenched by adding water (10 mL) and with 25% ammonia. The aqueous layer was extracted with DCM (3 × 150 mL) and EtOAc (3 × 150 mL). The organic layers were combined, dried with $MgSO_4$ and concentrated under reduced pressure to afford 0.90 g of the desired 4-chlorofuro[3,2-*c*]quinoline (94%). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.03 (d, *J* 2.2 Hz, 1H, H-3), 7.64 (m, 1H, H-8), 7.73 (m, 1H, H-7), 7.82 (d, *J* 2.2 Hz, 1H, H-2), 8.14 (dd, *J* 8.0, 2.0 Hz, 1H, H-9), 8.25 (dd, *J* 7.4, 2.0 Hz, 1H, H-6). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 106.3, 116.6, 119.8, 120.1, 127.2, 128.8, 129.2, 144.3, 145.0, 145.2, 156.4. MS (ESI): *m*/*z* 204 $[M+H]^+$.

4-Methoxyfuro[3,2-c]quinoline (2). A mixture of the 4-chlorofuro[3,2-*c*]quinoline (125 mg, 0.49 mmol) and a methanolic solution of sodium methoxide (approximately 1.2 M, generated from 230 mg sodium in 10 mL of methanol) at RT under nitrogen atmosphere, was stirred until all starting material was consumed (monitored by TLC). The reaction mixture was extracted with EtOAc (3 × 100 mL). The organic layers were combined, dried with $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (EtOAc:hexane/0 to 2.5:100 to 97.5) afforded 100 mg of **2** (80%). ^1H NMR ($CDCl_3$, 400 MHz): δ 4.20 (s, 3H, OMe), 6.95 (m, 1H, H-3), 7.46 (app t, *J* 7.2 Hz, 1H, H-8), 7.61 (app t, *J* 7.2 Hz, 1H, H-7), 7.72 (m, 1H, H-2), 7.95 (app d, *J* 7.2 Hz, 1H, H-6), 8.15 (app d, *J* 7.2 Hz, 1H, H-9). ^{13}C NMR ($CDCl_3$, 100

Scheme 6



Scheme 7



9 **10**

MHz): δ 53.7 (OMe), 105.4 (C-3), 111.4 (C-3a), 116.0 (C-9a), 120.1 (C-9), 124.4 (C-8), 127.7 (C-6), 128.6 (C-7), 144.3 (C-1), 144.5 (C-5a), 157.64 (C-9b), 157.68 (C-4). MS (ESI): *m*/*z* 200 $[M+H]^+$.

Rearrangement/CH-insertion products (5) and (6). To a solution of 1.30 (100 mg, 0.50 mmol) and dirhodium tetraacetate (5 mg, 0.01 mmol, 2 mol %) in DCM (2.5 mL) under a nitrogen atmosphere was added a solution of dimethyl diazomalonate (293 mg, 1.85 mmol, 3.7 eq) in DCM (0.5 mL) over 3 h period followed by 17 h stirring at ambient temperature (monitored by tlc). The crude was then filtered through a short silica plug using EtOAc as eluent (2 × 20 mL), dried with MgSO4 and concentrated *in vacuo*. Flash chromatography (EtOAc:hexane/1:1) afforded 180 mg of a clear oil as a mixture of the two products, **5** and **6**, in the ratio of 75:25. Reverse phase chromatography (HPLC, MeOH:H_2O/7:3) afforded an analytically pure sample of each product.

(**5**): Mp 179°C. IR (KBr, ν_{max}): 3464, 3003, 2954, 1744, 1670, 1633, 1593, and 1437 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 226 (12355), 283 (1738), 292 (1922) nm. ^1H NMR ($CDCl_3$, 600 MHz): δ 3.63 (s, 3H, NMe), 3.73 and 3.91 (2 × s, 2 × OMe, C-2′), 3.80 and 3.85 (2 × s, 2 × OMe, C-2), 5.61 (d, *J* 10.8 Hz, 1H, H-3), 6.73 (d, *J* 10.8 Hz, 1H, H-1′), 7.26 (dd, *J* 7.2, 3.0 Hz, 1H, H-8), 7.36 (d, *J* 8.4 Hz, 1H, H-6), 7.62 (app. t, *J* 7.8 Hz, 1H, H-7), 7.88 (d, *J* 7.8 Hz, 1H, H-9). ^{13}C NMR (CDCl3, 125 MHz) δ 29.4 (C-5), 46.7 (C-3), 52.8 and 53.1 (C-2′, 2 × OMe), 53.7 and 54.2 (C-2, 2 × OMe), 93.5 (C-2), 108.0 (C-2′), 111.7 (C-9a), 115.0 (C-6), 122.5 (C-8), 124.0 (C-9), 131.4 (C-3a), 132.5 (C-7), 141.4 (C-5a), 142.3 (C-1′), 159.9 (C-4), 161.9 (C-9b), 164.1, and 164.7 (C-2′, 2 × COOR), 165.1 and 166.1 (C-2, 2 × COOR) MS (ESI): *m*/*z* 460 $[M+H]^+$, 482 $[M+Na]^+$. HRMS Calcd. for $C_{22}H_{22}NO_{10}$ $[M+H]^+$: 460.1238. Found: 460.1252.

(**6**): Mp 199°C. IR (KBr, ν_{max}): 3460, 3007, 2954, 1752, 1666, 1638, and 1433 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 229 (14802), 279 (2944), 290 (2931), 326 (2379) nm. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.61 (d, *J* 11.0 Hz, 1H, H-3′), 3.66 (s, 3H, NMe), 3.73, 3.82, 3.87, and 3.95 (4 × s, 4 × OMe), 3.78 (s, 2 × OMe), 5.15 (d, *J* 11.0 Hz, 1H, H-3), 7.28 (m, 1H, H-8), 7.37 (d, *J* 8.5 Hz, 1H, H-6), 7.63 (app t, *J* 7.5 Hz, 1H, H-7), 7.88 (d, *J* 8.0 Hz, 1H, H-9). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 29.6 (C-5), 36.7 (C-3′), 43.7 (C-2′), 43.9 (C-3), 45.3 (C-1′), 53.0, 53.2, 53.5, 53.6, 53.7 and 53.9 (6 × OMe), 92.7 (C-2), 108.9 (C-3a), 111.9 (C-9a), 114.7 (C-6), 122.1 (C-8), 123.8 (C-9), 132.1 (C-7), 141.4 (C-5a), 160.1 (C-4), 161.1 (C-9b), 164.4 and 166.0 (C-1′, 2 x COOR), 166.2 and 166.3 (C-2′, 2 × COOR), 167.5 and 167.9 (C-2, 2 × COOR). (ESI): *m*/*z* 590 $[M+H]^+$, 612 $[M+Na]^+$. HRMS Calcd. for $C_{27}H_{28}NO_{14}$ $[M+H]^+$: 590.1504. Found: 590.1495.

Dimethyl 5-methoxy-2*H*-pyrano[3,2-*c*]quinoline-2,2-dicarboxylate (7). To a solution of **2** (100 mg, 0.5 mmol) and dirhodium tetraacetate (4.95 mg, 0.01 mmol, 2 mol %) in DCM (2.5 mL) under nitrogen atmosphere, was added a solution of dimethyl diazomalonate (293 mg, 1.85 mmol, 3.7 eq) in DCM (0.5 mL) over 3 h period followed by 17 h stirring at ambient temperature (monitored by tlc). The crude reaction mixture was then filtered through a short silica plug using EtOAc as eluent (2 × 20 mL), dried with MgSO4 and concentrated *in vacuo*. Flash chromatography (EtOAc:hexane/1:9) afforded 63 mg of **7** as a white solid (38%). Mp 85–86°C. IR (KBr, ν_{max}): 3101, 3015, 2954, 1761, 1740, 1642, 1605, 1569, 1507, 1475 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 229 (4083), 254 (2936), 263 (2520), 317 (982) nm. ^1H NMR ($CDCl_3$, 500 MHz): δ 3.86 (s, 2 × 3H, 2 × COOMe), 4.09 (s, 3H, OMe), 6.05 (d, *J* 10.0 Hz, 1H, H-3), 6.97 (d, *J* 10.0 Hz, 1H, H-4), 7.39 (dd, *J* 7.0, 1.0 Hz, 1H, H-9), 7.62 (dd, *J* 7.0, 1.0 Hz, 1H, H-8), 7.77 (d, *J* 8.0 Hz, 1H, H-7), 8.19 (d, *J* 8.0 Hz, 1H, H-10). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 53.86 (C-2, 2 × COOMe), 53.89 (C-5, OMe), 101.4 (C-4a), 82.3 (C-2), 116.9 (C-3), 117.7 (C-10a), 120.9 (C-4), 122.4 (C-10), 124.2 (C-9), 127.2 (C-7), 130.7 (C-8), 147.2 (C-6a), 155.4 (C-10b), 158.7 (C-5), 167.0 (C-2, 2 × COOR). MS (ESI): *m*/*z* 330 $[M+H]^+$, 352 $[M+Na]^+$, 298 $[M-CH_3O]^+$. HRMS Calcd. for $C_{17}H_{16}NO_6$ $[M+H]^+$: 330.0972. Found 330.0960.

Ethyl 5,7-dimethyl-6-oxo-5,6b,7,7a-tetrahydro-6*H*-cyclopropa[4,5]furo[3,2-*c*]quinoline-7-carboxylate (9). To a solution of **2** (482 mg, 2.41 mmol) and dirhodium tetraacetate (24 mg, 0.05 mmol, 2 mol %) in DCM (15 mL) under a nitrogen atmosphere was added a solution of ethyl 2-diazopropanoate (**8**) (988 mg, 7.71 mmol, 3.2 eq) in DCM (5 mL) over 1 h period followed by 1 h stirring at ambient temperature. The crude reaction mixture was then filtered through a short silica plug using EtOAc as eluent (3 × 20 mL), dried with $MgSO_4$ and concentrated *in vacuo*. Reverse phase flash chromatography (MeOH:H_2O/7:3) afforded 314 mg of **9** as a white solid (43%). Mp 141–142°C. IR (KBr, ν_{max}): 3081, 2974, 2929, 1716, 1659, 1593, and 1569 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 224 (25226), 298 (3488), 324 (3880) nm. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.93 (s, 3H, H-1′), 1.29 (t, *J* 7.2 Hz, 3H, H-2″), 3.50 (d, *J* 5.6 Hz, 1H, H-6b), 3.73 (s, 3H, NMe), 4.19 (q, *J* 7.2 Hz, 2H, H-1″), 5.18 (d, *J* 5.6 Hz, 1H, H-7a), 7.26 (dd, *J* 7.6, 1.2 Hz, 1H, H-2), 7.41 (d, *J* 8.4 Hz, 1H, H-4), 7.61 (dd, *J* 7.6, 1.6 Hz, 1H, H-3), 7.77 (dd, *J* 7.6, 1.2 Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 6.6 (C-1′), 14.5 (C-2″), 20.2 (C-7), 29.6

(NMe), 34.4 (C-6b), 61.5 (C-1″), 72.8 (C-7a), 110.3 (C-6a), 111.8 (C-8b), 115.0 (C-4), 122.2 (C-2), 122.8 (C-1), 131.5 (C-3), 140.6 (C-4a), 161.1 (C-6), 164.0 (C-8a), 173.3 (COOR). MS (ESI): *m*/*z* 300 $[M+H]^+$, 322 $[M+Na]^+$. HRMS Calcd. for $C_{17}H_{17}NO_4Na$ $[M+Na]^+$: 322.1049. Found: 322.1041.

Ethyl 6-methoxy-7-methyl-7,7a-dihydro-6b*H*-cyclopropa[4,5]-furo[3,2-*c*]quinoline-7-carboxylate (10). To a solution of **3** (100 mg, 0.50 mmol) and dirhodium tetraacetate (5 mg, 0.01 mmol, 2 mol %) in DCM (3.1 mL) under a nitrogen atmosphere was added a solution of ethyl 2-diazopropanoate (**8**) (209 mg, 1.60 mmol, 3.2 eq) in DCM (1 mL) over 1 h period followed by 1 h stirring at ambient temperature. The crude reaction mixture was then filtered through a short silica plug using EtOAc as eluent (2 × 20 mL), dried with $MgSO_4$ and concentrated *in vacuo*. Flash chromatography (EtOAc:hexane/5:95) afforded 103 mg of **10** as a white solid (69%). Mp 105°C. IR (KBr, ν_{max}): 2979, 2949, 2938, 2899, 1707, 1637, 1604, and 1576 cm^{-1}. UV (MeOH) $\lambda_{max}(\varepsilon)$: 234 (52189), 320 nm (22709) nm. ^1H NMR ($CDCl_3$, 500 MHz): δ 0.86 (s, 3H, H-1′), 1.33 (t, *J* 6.0 Hz, 3H, H-2″), 3.48 (d, *J* 5.6 Hz, 1H, H-6b), 4.14 (s, 3H, OMe), 4.23 (q, *J* 6.0 Hz, 2H, H-1″), 5.25 (d, *J* 5.6 Hz, 1H, H-7a), 7.36 (dd, *J* 6.8, 1.2 Hz, 1H, H-2), 7.61 (dd, *J* 7.2, 1.6 Hz, 1H, H-3), 7.86 (m, 2H, H-4 and H-1). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 6.6 (C-1′), 14.5 (C-2″), 20.1 (C-7), 33.1 (C-6b), 53.7 (OMe), 61.6 (C-1″), 72.9 (C-7a), 106.5 (C-6a), 114.6 (C-8b), 121.1 (C-4), 124.0 (C-2), 127.5 (C-1), 130.1 (C-3), 147.4 (C-4a), 160.4 (C-6), 166.2 (C-8a), 173.7 (COOR). MS (ESI): *m*/*z* 300 $[M+H]^+$, 322 $[M+Na]^+$. HRMS Calcd. for $C_{17}H_{18}NO_4$ $[M+H]^+$: 300.1230. Found: 300.1221.

Acknowledgments. This work was supported through a Griffith Postgraduate Research Scholarship.

REFERENCES AND NOTES

[1] Grundon, M. F. The Alkaloids: Quinoline Alkaloids Related to Anthranilic Acid; Academic Press: London, 1988, 32, 341.

[2] Michael, J. P. Nat Prod Rep 1998, 61, 595.

[3] Xu, W. H.; Xue, Z. Acta Chim Sin 1984, 42, 899.

[4] Vaquette, J.; Hifnawy, M. S.; Pousset, J. L.; Fournet, A.; Bouquet, A.; Cave, A. Phytochemistry 1976, 15, 743.

[5] Moulis, C.; Wirasutisna, K. R.; Gleye, J.; Loiseau, P.; Stanislas, E.; Moretti, C. Phytochemistry 1983, 22, 2095.

[6] (a) Dorwald, F. Z. Metal Carbenes in Organic Syntheses; Wiley-VCH, 1999; (b) Taber, D. F.; Joshi, P. V. In Modern Rhodium-Catalyzed Organic Reactions; Evans, P. A., Ed.; Wiley-VCH, 2005; p 357; (c) Davies, H. M. L.; Walji, A. M. In Modern Rhodium-Catalyzed Organic Reactions; Evans, P. A., Ed.; Wiley-VCH, 2005; p 301; (d) Doyle, M. P. In Modern Rhodium-Catalyzed Organic Reactions; Evans, P. A., Ed.; Wiley-VCH, 2005; p 341; (e) Davies, H. M. L.; Jin, Q. Proc Natl Acad Sci USA 2004, 101, 5472; (f) Davies, H. M. L.; Jin, Q. J Am Chem Soc 2004, 126, 10862.

[7] (a) Wenkert, E.; Khatuya, H.; Klein, P. S. Tetrahedron Lett 1999, 40, 5171; (b) Matlin, S. A.; Chan, L.; Catherwood, B. J Chem Soc Perkin Trans 1 1990, 89. (c) Davies, H. M. L.; Hedley, S. J Chem Soc Rev 2007, 36, 1109; (d) Wenkert, E.; Guo, M.; Lavilla, R.; Porter, B.; Ramachandran, K.; Sheu, J.-H. J Org Chem 1990, 55, 6203.

[8] Wenkert, E.; Alonso, M. E.; Gottlieb, H. E.; Sanchez, E. L.; Pellicciari, R.; Cogolli, P. J Org Chem 1977, 42, 3945.

[9] Nair, V.; Thomas, S.; Mathew, S. C.; Vidya, N.; Rath, N.P. Tetrahedron 2005, 61, 9533.

[10] Lindahl, K.-F; Carroll, A.; Quinn, R. J.; Ripper, J. A. Tetrahedron Lett 2006, 47, 7493.

[11] (a) Boyd, D. R.; Sharma, N. D.; Barr, S. A.; Carroll, J. G.; Mackerracher, D.; Malone, J. F. J Chem Soc Perkin Trans 1 2000, 3397; (b) Bar, G.; Parsons, A. F.; Thomas, C. B. Tetrahedron 2001, 57, 4719; (c) Lee, Y. R.; Kim, B. S,; Kweon, H. I. Tetrahedron 2000, 56, 3867; (d) Pirrung, M. C.; Blume, F. J Org Chem 1999, 64, 3642.

[12] Doyle, M. P.; Davies, S. B.; Hu, W. Org Lett 2000, 2, 1145.

[13] (a) Davies, H. M. L.; Antoulinakis, E. G. Org React 2001, 57; (b) Manning, J. R.; DaviesH. M. L. Tetrahedron, 2008, 64, 6901; (c) Wood, J. L.; Moniz, G. A. Org Lett 1999, 1, 371; (d) Baird, M. S. Chem Rev 2003, 103, 1271.

[14] (a) Bachmann, S.; Fielenbach, D.; Jorgensen, K. A. Org Biomol Chem 2004, 2, 3044; (b) Benati, L; Nanni, D.; Spagnolo, P. J Org Chem 1999, 64, 5132; (c) Taber, D. F.; Herr, R. J.; Pack, S. K.; Geremia, J. M. J Org Chem 1996, 61, 2908.

[15] (a) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Chem Rev 2010, 110, 704; (b) West, F. F. Modern Rhodium-Catalyzed Organic Reactions; Wiley-VCH, 2005, p 417.