Supporting Information

Redox and non-redox mechanism of in vitro cyclooxygenase inhibition by natural quinones

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Analytical chemistry related to synthesis of juglone derivatives

NMR spectra were recorded on Bruker Avance 400 (Bruker Corporation). $^1$H NMR spectra were recorded at 400 MHz and $^{13}$C spectra at 100 MHz. Spectra were taken at room temperature in deuterated solvents as indicated, using the solvent peak as internal standard. High resolution mass spectra (HR-MS) were measured on LTQ ORBITRAP XL from Thermo Fisher Scientific. For column chromatography, silica gel 60 (0.063-0.200 mm) purchased from Merck was used. From the same company we obtained TLC silica gel 60 F$_{254}$ aluminum sheets for thin-layer chromatography (TLC). Visualization was accomplished by UV-light (254 nm) and staining with vanillin solution, followed by heating.

Synthesis of O-methyljuglone

O-Methyljuglone was prepared from juglone according to published procedures [10, 11]. The obtained NMR spectroscopic data corresponded with the reported ones [10, 11]. For the
reaction, freshly prepared Ag$_2$O was needed, which was synthesized from AgNO$_3$ according to a published procedure [12].

**Synthesis of 5-acetyljuglone**

5-Acetyljuglone was prepared from juglone by a modified published procedure [13]. Juglone (0.85 g, 0.49 mmol) was dissolved in DCM. Pyridine (5×n, 0.2 mL, 2.45 mmol), acetic anhydride (5×n, 0.23 mL, 2.45 mmol), and DMAP (0.2×n, 12.5 mg, 0.1 mmol) were added. The reaction mixture was stirred at room temperature overnight, monitored by TLC, Rf = 0.6 in hexane/EtOAc, 3/1, v/v. The reaction mixture was diluted with DCM, washed with a saturated solution of CuSO$_4$ (several times to remove pyridine), NaHCO$_3$ and brine, dried over Na$_2$SO$_4$ and evaporated. The crude product was purified on a silica gel column (hexane/EtOAc, 7/3, v/v) to afford 41 mg (39%) of pure orange product (40% of the starting material was recovered). $^1$H-NMR (400MHz, CDCl$_3$): δ (ppm): 2.45 (s, 3H, Ac), 6.85 (d, J = 10.3 Hz, 1H, H-2), 6.95 (d, J = 10.3 Hz, 1H, H-3), 7.40 (d, J$_1$ = 1.3 Hz, J$_2$ = 8.1 Hz, 1H, H-8), 7.77 (t, J = 7.9 Hz, 1H, H-7), 8.05 (dd, J$_1$ = 1.3 Hz, J$_2$ = 7.8 Hz, 1H, H-6). $^{13}$C-NMR (100 MHz, CDCl$_3$): δ (ppm): 21.0 (Me), 125.0 (C-6), 129.7 (C-8), 134.8 (C-7), 137.3 (C-3), 139.9 (C-2), 183.6 (2×CO, C-1, C-4). HR-MS: m/z (M+Na$^+$, C$_{12}$H$_8$O$_4$Na): calcd. 239.0315, found 239.0315.

**Synthesis of 5-tosyljuglone**

5-Tosyljuglone was prepared from juglone according to published procedures [14, 15]. Juglone (0.1 g, 0.57 mmol) was dissolved in dry THF under argon, and K$_2$CO$_3$ (1.6×n, 127 mg, 0.92 mmol) was added. Tosylchloride (1.1×n, 121 mg, 0.63 mmol) dissolved in dry THF was added dropwise to the mixture from a syringe. The mixture was stirred at room temperature over the weekend. The reaction was very slow and not all the starting material
was consumed within the three days. The reaction mixture was diluted with DCM, washed with solution of NaHCO$_3$, water and brine, dried over Na$_2$SO$_4$, and evaporated. The crude product was purified on a silica gel column (hexane/EtOAc, 8/2 – 7/3, v/v) to afford 17 mg (15%) of pure orange product (40% of the starting material was recovered).

**Synthesis of 2-methylaminojuglone**

2-Methylaminojuglone was prepared from juglone by a modified published procedure [16]. Juglone (0.1 g, 0.57 mmol) was dissolved in dry THF under argon, and methylamine (1.5×n, 0.45 mL, 2 M solution in THF) was added dropwise from a syringe. The solution was stirred overnight at room temperature. The reaction was quenched with 0.5 M HCl; THF fraction was washed with water, dried over Na$_2$SO$_4$ and evaporated. The obtained product was purified on a silica gel column (hexane/EtOAc, 7/3, v/v) to afford 50 mg (43%) of pure red-colored product. TLC: Rf = 0.36 (hexane/EtOAc, 3/1, v/v). $^1$H-NMR (400 MHz, CDCl$_3$): δ (ppm): 2.96 (d, J = 5.4 Hz, 3H, Me), 5.62 (s, 1H, H-3), 6.12 (br.s, 1H, NH), 7.25 (dd, J$_1$ = 1.1 Hz, J$_2$ = 8.4 Hz, 1H, H-6), 7.47 (t, J = 8.0 Hz, 1H, H-7), 7.59 (dd, J$_1$ = 1.1 Hz, J$_2$ = 7.5 Hz, 1H, H-8). $^{13}$C-NMR (100 MHz, CDCl$_3$): δ (ppm): 29.2 (Me), 99.6 (C-3), 115.0 (C-10), 119.0 (C-8), 126.0 (C-6), 130.5 (C-9), 133.9 (C-7), 149.7 (C-2), 161.1 (CO, C-1), 181.1 (CO, C-4). HR-MS: m/z (M+H$^+$, C$_{11}$H$_{10}$O$_3$N): calcd. 204.0655, found 204.0655.