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Synthesis of 6-chloro-2-(propargyloxy)quinoline-4-carboxylic acid and propargyl 6-chloro-2-(propargyloxy)quinoline-4-carboxylate

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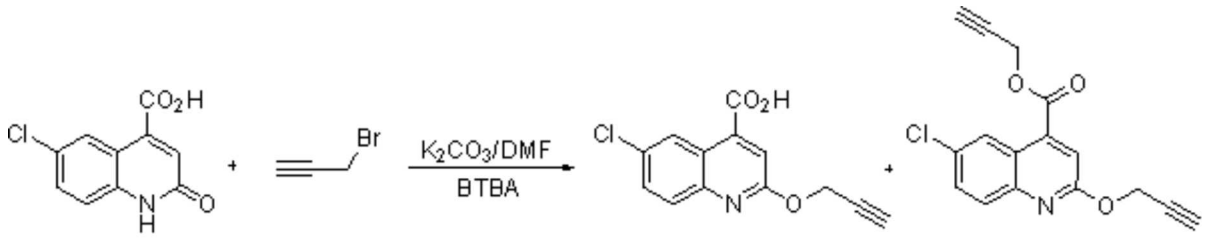
The quinoline ring systems are important structural units in naturally occurring alkaloids and synthetic analogues with interesting biological activities. Therefore, the development of new and efficient synthetic route for the preparation of their analogues is of importance in both synthetic organic chemistry and medicinal chemistry.[1-4]
We reported here the synthesis of a new quinoline derivative.



1 2 3 4

To a solution of quinoline 1 (1 g, 4.4 mmol) and K_2CO_3 (1.21 g, 8.8 mmol) in 60 mL of DMF, was added propargyl bromide (0.75 mL, 8.8 mmol) and tetra n-butylammonium bromide (TBAB) (catalytic amount). The mixture was stirred at room temperature for 24 h and the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O and the combined organic layers were washed with brine and dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel (n-hexane/AcOEt 8:2) to give 0.44 g (43 %) of 3 and 0.46 g (35 %) of 4.

6-chloro-2-(propargyloxy)quinoline-4-carboxylic acid, 3
Melting point: 170 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ= 2.62 (t, 1H, ≡CH, ^{3}J= 2.4 Hz); 5.09 (d, 2H, OCH_2, ^{3}J= 2.4 Hz); 7.61 (s, 1H, =CH); 7.64-8.53 (m, 3H, H_{Ar}).

^{13}C-NMR (300 MHz, $CDCl_3$): δ= 54.7 (OCH_2); 76.1 (≡CH); 118.1 (=CH); 127.1, 129.6, 133.7 (CH_{Ar}); 120.1, 137.3, 143.8 (Cq); 164.0 (C=N); 164.2 (CO_2H).

MS (EI, m/z): 237.

Elemental analysis: Calculated for $C_{13}H_8ClNO_3$: C, 59.67 %; H, 3.08 %; N, 5.35 %; Found: C, 59.70 %; H, 3.04 %; N, 5.41 %;

Propargyl-6-chloro-2-(propargyloxy)quinoline-4-carboxylate, 4
Melting point: 156 °C

^{1}H-NMR (300 MHz, $CDCl_3$): δ= 2.67 (t, 1H, ≡CH, ^{3}J= 2.4 Hz); 2.70 (t, 1H, ≡CH, ^{3}J= 2.4 Hz); 5.05 (d, 2H, OCH_2, ^{3}J= 2.4 Hz); 5.12 (d, 2H, OCH_2, ^{3}J= 2.4 Hz); 7.08 (s, 1H, =CH); 7.58-8.20 (m, 3H, H_{Ar}).

^{13}C-NMR (300 MHz, $CDCl_3$): δ= 52.4 (OCH_2); 54.4 (OCH_2); 78.1 (≡CH); 78.7 (≡CH); 78.9, 75.5 (≡C); 118.2 (=CH); 125.5, 126.4, 131.9 (CH_{Ar}); 118.5, 138.1, 138.2 (Cq); 159.7 (C=N); 164.3 (CO_2H).

MS (EI, m/z): 299.

Elemental analysis: Calculated for $C_{16}H_{10}ClNO_3$: C, 64.12 %; H, 3.36 %; N, 4.67 %; Found: C, 64.17 %; H, 3.29 %; N, 4.72 %;

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