Supporting Information

Catalyst and Solvent-Free alkylation of Quinoline *N*-oxide with olefins: Direct Access to Quinoline Substituted α-Hydroxy Carboxylic Derivatives

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Table of Contents

1. General consideration

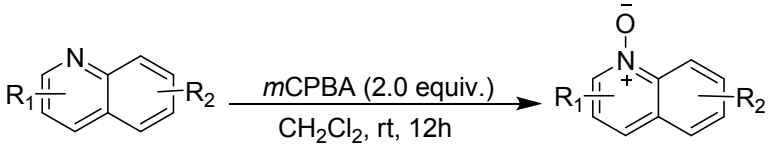
Reagent Information: Unless otherwise stated, all reactions were carried out under air atmosphere in screw cap reaction vials. All solvents were bought from Aldrich in sure-seal bottle and used as such. All chemicals were bought from Sigma Aldrich, Alfa-aesar and TCI. For column chromatography, silica gel (230-400 mesh) from Merck was used. A gradient elution using *n*-hexane and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel $60F_{254}$).

Analytical information: The melting points were recorded on a Bronsted Electro thermal 9100. All isolated compounds are characterized by ^{1}H NMR, ^{13}C NMR and LC-MS. In addition, all the compounds are further characterized by HRMS. Mass spectra were recorded on Water Q-ToF-Micro Micromass. Copies of ^{1}H, ^{13}C NMR can be found in the NMR supporting information.

Nuclear magnetic resonance spectra were recorded either on a Bruker-Avance 600 or 300 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm) and were measured relative to the signals for residual chloroform (7.26) in the deuterated solvents. All ^{13}C NMR spectra were reported in ppm relative to deuterated chloroform (77.23) and all were obtained with ^{1}H decoupling. Optimization studies were done by NMR and NMR yield were calculated by using TCE as internal standard.

2. Preparation of Quinoline *N*-Oxides

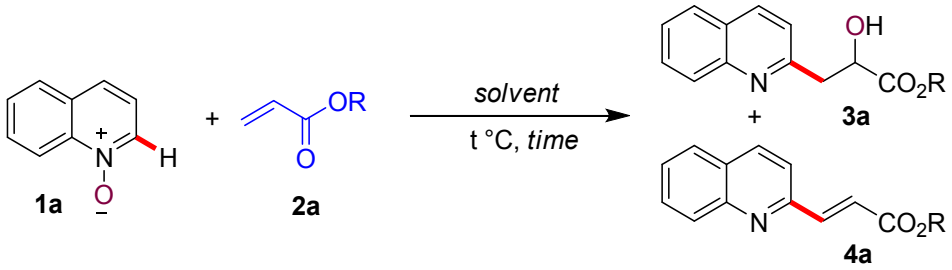
General procedure for the preparation of Quinoline *N*-Oxide[1]



All quinoline *N*-oxide were prepared according to literature procedure with slight modification. All solid reactants, *m*-CPBA (4.0 mmol) and quinoline (2.0 mmol) were added in schlenk tube and put under vaccum for 2h, then CH_2Cl_2 (4 ml) was added at 0°C. The reaction was allowed to stir at room temperature for 12h. On completion, the reaction mixture was extracted with ethyl

acetate and organic extract was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (230-400 mesh size) with *n*-hexane: EtOAc to afford desired *N*-Oxide.

3. Quinoline *N*-oxide Reaction with Acrylates



3.1 Optimization detail

To an oven-dried screw cap reaction vial charged with a spin vane magnetic stir-bar, quinoline *N*-oxide (0.1 mmol), acrylate (X equiv.), and solvent (0.5 ml) were added. The reaction vial was closed with screw cap and kept for vigorous stirring on a preheated oil bath at variable temperature for variable time. After completion, reaction mixture was allowed to cool down to room temperature and extracted with ethyl acetate. Ethyl acetate layer was dried over anhydrous Na_2SO_4. Ethyl acetate was removed completely under reduced pressure. The crude yield was measured by 1H NMR using 1,1,2,2-tetrachloroethane as internal standard.

Table S1: Optimization Study.

Entry	2a (equiv.)	T (°C)	Time	Solvent	Conv.	NMR Yield (%)[b]	3a/4a
1	5	110	24h	*N*- methyl pyrrolidone	<5	n.d.	-
2	5	110	24h	*N*- methyl pyrrolidine	100	46	94:6
3	5	110	24h	*N*-methyl morpholine	22	16	73:27
4	5	110	24h	DMSO	21	9	43:57
5	5	110	24h	Toluene	<5	n.d.	-
6	5	110	24h	DCE	<5	n.d.	-
7	5	110	24h	DMF	<5	n.d.	-
8	5	110	24h	TFT	<5	n.d.	-
9	5	110	24h	1-4 dioxane	<5	n.d.	-

10	5	110	24h	HFIP	<5	n.d.	-
11	20	r.t.	24h	-	<5	n.d.	-
12	20	60	24h	-	15	15	100:0
13	20	90	24h	-	35	33	100:0
14	20	110	24h	-	65	58	94:6
15	20	130	24h	-	73	28	49:51
16	15	110	24h	-	91	64	82:18
17	10	110	24h	-	86	63	81:19
18	5	110	24h	-	100	43	55:45
19	4	100	24h	-	100	53	66:34
20	20	100	48h	-	100	67	71:29
21	4	100	20h	-	100	66	78:22
22	**4**	**100**	**15h**	**-**	**84**	**78**	**95:5**
23	4	100	12h	-	75	63	94:6
24	4	100	5h	-	25	25	100:0
25	4	100	10h	-	59	56	100:0
26	4	100	11h	-	64	57	>99:1
27	4	100	14h	-	76	70	96:4
28	4	100	16h	-	86	75	90:10
29	4	100	18h	-	90	75	90:10
30	4	100	20h	-	100	66	77:23
31	4	100	24h	-	100	53	66:34

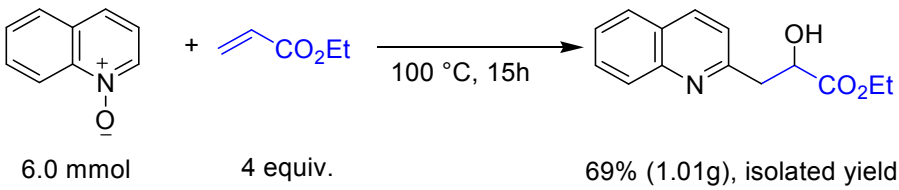
3.2 General Procedure for C-2 alkylation of Quinoline *N*-Oxides with Acrylates

Unless otherwise stated, to an oven-dried screw cap reaction vial charged with a spin vane magnetic stir-bar, quinoline *N*-oxide (0.3 mmol) and acrylate (4 equiv.) were added. The reaction vial was closed with screw cap and kept for vigorous stirring on a preheated oil bath at 90-110°C for 5-36 h depending on the particular substrate. After completion, reaction mixture was allowed to cool down to room temperature and extracted with ethyl acetate. Ethyl acetate layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Residue was purified by flash chromatography using silica gel (230-400 mesh size) and *n*-hexane: EtOAc as eluent.

3.3 Procedure for gram scale reaction

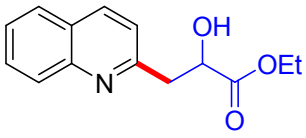
To a screw capped vial with a spin vane triangular shaped stir bar, quinoline *N*-oxide (6.0 mmol, 1.086 g) and ethyl acrylate (4.0 equiv., 2.56 ml) were added. The reaction was stirred at 100°C

for 15h. After completion, reaction mixture was allowed to cool down to room temperature and extracted with ethyl acetate. Ethyl acetate layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Residue was purified by flash chromatography using silica gel (230-400 mesh size) and *n*-hexane: EtOAc as eluent to give the final product in 69% (1.01 g) yield.



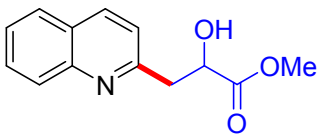
3.4 Characterization data

ethyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2 , entry 3a)[2] Colourless



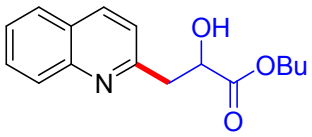
crystals (78%); mp 109 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.67 – 7.70 (m, 1H), 7.49 – 7.52 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 4.75 – 4.77 (m, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.49 (dd, J = 15.6, 4.2 Hz, 1H), 3.40 (dd, J = 15.6, 7.2 Hz, 1H), 1.22 – 1.23 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8, 158.9, 147.3, 136.9, 129.9, 128.9, 127.7, 127.0, 126.4, 122.1, 70.6, 61.4, 41.1, 14.3; HRMS (ESI) m/z calcd for $C_{14}H_{16}NO_3$ $[M+H]^+$ 246.1150, found 246.1109.

methyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry 3b) Orange solid



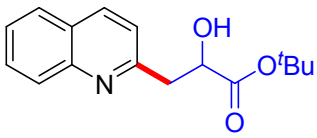
(48%); mp 90 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 9.0 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.50 – 7.53 (m, 1H), 7.30 (d, J = 8.4 Hz, 1H). 4.78 – 4.80 (m, 1H), 3.76 (s, 3H), 3.50 (dd, J = 15.6, 3.6 Hz, 1H), 3.42 (dd, J = 15.6, 7.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 158.8, 147.1, 137.1, 130.0, 128.7, 127.7, 127.1, 126.5, 122.1, 70.5, 52.5, 40.8; HRMS (ESI) m/z calcd for $C_{13}H_{14}NO_3$ $[M+H]^+$ 232.0968, found 232.0988.

butyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry 3c) Yellow resin



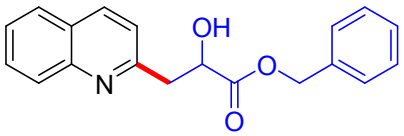
(73%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.65-7.68 (m, 1H), 7.47-7.50 (m, 1H), 7.28 (d, J = 8.4 Hz, 1H), 4.75 - 4.76 (m, 1H), 4.12 - 4.14 (m, 2H), 3.37 - 3.49 (m, 2H), 1.52 - 1.56 (m, 2H), 1.23-1.28 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.9, 158.9, 147.2, 136.8, 129.8, 128.8, 127.6, 127.0, 126.3, 122.1, 70.5, 65.2, 41.1, 30.6, 19.1, 13.6; HRMS (ESI) m/z calculated for $C_{16}H_{20}NO_3$ $[M+H]^+$ 274.1438, found 274.1415.

tert-butyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry 3d) Orange resin



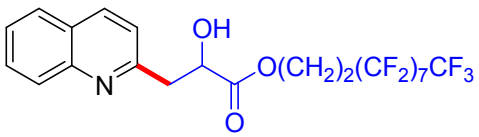
(75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.63 - 7.69 (m, 1H), 7.45 - 7.50 (m, 1H), 7.30 (d, J = 8.4 Hz, 1H), 4.62 (dd, J = 6.6, 4.2 Hz, 1H), 3.30 - 3.48 (m, 2H), 1.39 (s, 9H);^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 158.9, 147.5, 136.5, 129.7, 128.9, 127.6, 127.0, 126.2, 122.2, 82.0, 70.7, 41.9, 28.1; HRMS (ESI) m/z calcd for $C_{16}H_{20}NO_3$ $[M+H]^+$ 274.1438, found 274.1419.

benzyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry 3e) White solid



(77%); mp 102 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.72 – 7.74 (m, 1H), 7.55 – 7.57 (m, 1H), 7.26 – 7.30 (m, 6H), 5.21 (s, 2H), 4.85 (dd, J = 6.0, 4.2 Hz, 1H), 3.55 (dd, J = 15.6, 4.2 Hz, 1H), 3.48 (dd, J = 15.6, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6, 158.8, 137.1, 137.1, 135.6, 130.0, 128.8, 128.8, 128.6, 128.4, 127.7, 127.1, 126.5, 122.1, 70.6, 67.1, 40.7; HRMS (ESI) m/z calcd for $C_{19}H_{18}NO_3$ $[M+H]^+$ 308.1281, found 308.1265.

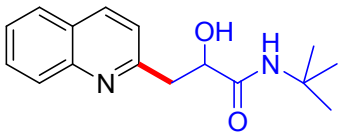
3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry 3f) Yellow solid



(59%); mp 82 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.68 - 7.71 (m, 1H), 7.51 – 7.53 (m, 1H), 7.29 (d, J = 8.4 Hz, 1H), 4.78 – 4.80 (m, 1H), 4.40 – 4.48 (m, 2H), 3.50 – 3.53 (m, 1H), 3.43 – 3.48 (m, 1H), 2.35 – 2.46 (m, 2H); ^{13}C NMR

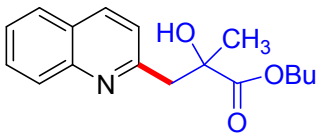
(150 MHz, $CDCl_3$) δ 173.4, 158.6, 147.1, 137.2, 130.1, 128.7, 127.1, 126.6, 122.0, 119.9 – 120.4 (m), 119.0 – 119.5 (m), 117.3 – 118.5 (m), 115.6 – 116.6 (m), 114.2 – 114.7 (m), 112.0 – 113.0 (m), 110.2 – 111.3 (m), 108.2 – 109.3 (m), 70.4, 57.1, 40.5, 30.5 - 30.8 (m); HRMS (ESI) m/z calcd for $C_{22}H_{15}F_{17}NO_3$ $[M+H]^+$ 664.0275, found 664.0265.

N-tert-butyl-2-hydroxy-3-(quinolin-2-yl)propanamide (Table 2, entry 3g) Yellow



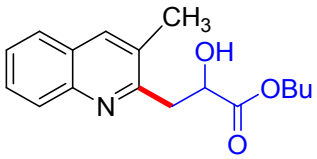
resin (36%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.51 – 7.54 (m, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.99 (s, 1H), 4.51 (dd, J = 7.8, 3.6 Hz, 1H), 3.50 (dd, J = 15.6, 3.6 Hz, 1H), 3.28 (dd, J = 15.6, 7.8 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.3, 160.2, 146.6, 137.4, 130.1, 128.2, 127.9, 127.1, 126.5, 122.5, 71.7, 50.8, 40.0, 28.8; HRMS (ESI) m/z calcd for $C_{16}H_{21}N_2O_2$ $[M+H]^+$ 273.1598, found 273.1579.

butyl 2-hydroxy-2-(quinolin-2-yl)methyl)propanoate (Table 2, entry 3h) Pale



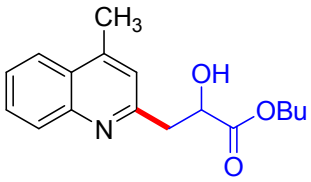
yellow liquid (56%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.66 – 7.69 (m, 1H), 7.48 – 7.51 (m, 1H), 7.26 (d, J = 8.4 Hz, 1H), 3.99 – 4.03 (m, 2H), 3.55 (d, J = 15.0 Hz, 1H), 3.26 (d, J = 15.0 Hz, 1H), 1.58 (s, 3H), 1.40 – 1.45 (m, 2H), 1.11 – 1.17 (m, 2H), 0.71 – 0.73 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.2, 159.2, 146.9, 136.9, 129.9, 128.8, 127.6, 127.0, 126.4, 122.3, 75.3, 65.1, 46.4, 30.7, 26.6, 19.0, 13.6.

butyl 2-hydroxy-3-(3-methylquinolin-2-yl)propanoate (Table 2, entry 3i) Green



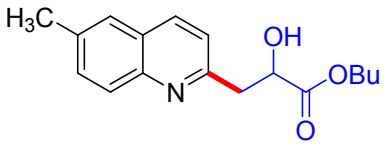
resin (66%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 1H), 7.88 (s, 1H), 7.70 (d, J = 8.4 Hz, 1H), 7.60 – 7.62 (m, 1H), 7.45 - 7.48 (m, 1H), 4.83 (dd, J = 6.0, 4.2 Hz, 1H), 4.13 - 4.16 (m, 2H), 3.37 - 3.45 (m, 2H), 2.44 (s, 3H), 1.54 – 1.59 (m, 2H), 1.24 - 1.27 (m, 2H), 0.80 - 0.82 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 158.8, 145.6, 136.3, 130.1, 128.9, 128.4, 127.4, 126.9, 126.4, 70.2, 65.1, 37.5, 30.7, 19.1, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{17}H_{22}NO_3$ $[M+H]^+$ 288.1594, found 288.1584.

butyl 2-hydroxy-3-(4-methylquinolin-2-yl)propanoate (Table 2, entry 3j) Orange



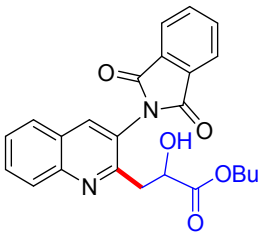
resin (55%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, J = 13.8, 8.4 Hz, 2H), 7.62-7.67 (m, 1H), 7.49-7.52 (m, 1H), 7.11 (s, 1H), 4.74 (dd, J = 6.6, 3.9 Hz, 1H), 4.13 (t, J = 6.6 Hz, 2H), 3.32-3.44 (m, 2H), 2.65 (s, 3H), 1.49-1.56 (m, 2H), 1.24 – 1.30 (m, 2H), 0.79-0.84 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 158.6, 147.1, 145.1, 129.4, 127.1, 126.1, 123.7, 122.7, 70.6, 65.2, 41.0, 30.7, 19.1, 18.6, 13.6; HRMS (ESI) m/z calcd for $C_{17}H_{22}NO_3$ $[M+H]^+$ 288.1594, found 288.1581.

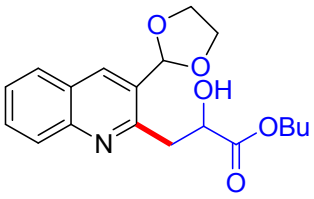
butyl 2-hydroxy-3-(6-methylquinolin-2-yl)propanoate (Table 2, entry 3k) orange



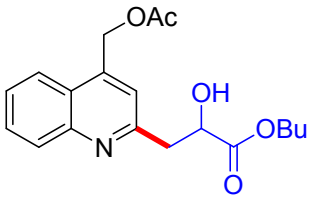
solid (68%); mp 44 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 9.0 Hz, 1H), 7.49 – 7.52 (m, 2H), 7.23 (d, J = 8.4 Hz, 1H), 4.73 – 4.75 (m, 1H), 4.12 (t, J = 6.6 Hz, 2H), 3.44 – 3.47 (m, 1H), 3.34 – 3.38 (m, 1H), 2.50 (s, 3H), 1.52 – 1.57 (m, 2H), 1.23 – 1.29 (m, 2H), 0.81 – 0.83 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 157.9, 145.8, 136.2, 132.0, 128.5, 127.0, 126.5, 122.0, 70.6, 65.2, 40.9, 30.6, 29.8, 21.6, 19.1, 13.6; HRMS (ESI) m/z calculated for $C_{17}H_{22}NO_3$ $[M+H]^+$ 288.1594, found 288.1574.

butyl 2-hydroxy-3-(3-(1,3-dioxoisoindolin-2-yl)quinolin-2-yl)propanoate (Table 2, entry 3m) Yellow solid (46%); mp 127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.99 - 8.00 (m, 2H), 7.83 – 7.86 (m, 3H), 7.77 – 7.80 (m, 1H), 7.57 – 7.60 (m, 1H), 4.75 (dd, J = 6.6, 3.6 Hz, 1H), 4.09 (t, J = 6.6 Hz, 2H), 3.36 – 3.40 (m, 1H), 3.29 - 3.33 (m, 1H), 1.48 – 1.52 (m, 2H), 1.18 - 1.22 (m, 2H), 0.76 – 0.78 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6, 167.2, 167.1, 156.9, 146.9, 137.0, 134.9, 132.0, 131.9, 131.0, 128.8, 127.9, 127.3, 127.0, 125.0, 124.2, 70.0, 65.3, 36.8, 30.6, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{24}H_{23}N_2O_5$ $[M+H]^+$ 419.1601, found 419.1589.

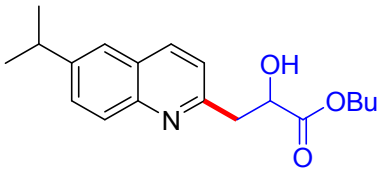


butyl 3-(3-(1,3-dioxolan-2-yl)quinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3n) 

Yellow semi-solid (53%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.67 - 7.70 (m, 1H), 7.49 - 7.52 (m, 1H), 6.08 (s, 1H), 4.81 (dd, J = 6.0, 4.2 Hz, 1H), 4.07 - 4.14 (m, 6H), 3.57 - 3.59 (m, 2H), 1.52 - 1.57 (m, 2H), 1.23-1.27 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 157.7, 146.8, 134.6, 130.3, 129.7, 128.5, 128.0, 126.7, 126.5, 101.4, 70.3, 65.5, 65.4, 65.1, 37.6, 30.7, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{19}H_{24}NO_5$ $[M+H]^+$ 346.1649, found 346.1635.

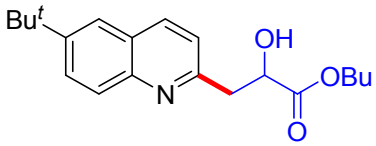
butyl 3-(4-(acetoxymethyl)quinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3p) 

Orange resin (61%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.67 – 7.73 (m, 1H), 7.52 – 7.57 (m, 1H), 7.34 (s, 1H), 5.55 (s, 2H), 4.76 (dd, J = 6.6, 4.2 Hz, 1H), 4.14 (t, J = 6.6 Hz, 2H), 3.36 – 3.53 (m, 2H), 2.17 (s, 3H), 1.52 – 1.61 (m, 2H), 1.24 – 1.33 (m, 2H), 0.80 – 0.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 170.5, 158.8, 147.4, 141.8, 129.8, 129.8, 126.8, 124.9, 122.9, 120.8, 70.5, 65.3, 62.6, 41.3, 30.7, 20.9, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{19}H_{24}NO_5$ $[M+H]^+$ 346.1649, found 346.1631.

butyl 2-hydroxy-3-(6-isopropylquinolin-2-yl)propanoate (Table 2, entry 3q) 

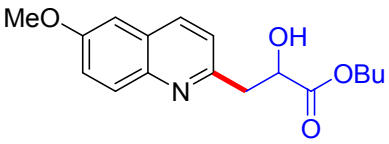
Orange resin (76%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.58 – 7.60 (m, 1H), 7.56 (d, J = 1.8 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 4.74 (dd, J = 6.6, 3.6 Hz, 1H), 4.12 - 4.14 (m, 2H), 3.45 – 3.48 (m, 1H), 3.36 – 3.39 (m, 1H), 3.05 – 3.08 (m, 1H), 1.52 – 1.56 (m, 2H), 1.33 (d, J = 7.2 Hz, 6H), 1.23 – 1.28 (m, 2H), 0.81 – 0.83 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 158.0, 147.0, 146.1, 136.6, 129.7, 128.7, 127.1, 123.7, 122.0, 70.7, 65.2, 40.9, 34.1, 30.7, 24.0, 24.0, 19.1, 13.7; HRMS (ESI) m/z calculated for $C_{19}H_{26}NO_3$ $[M+H]^+$ 316.1907, found 316.1894.

butyl 3-(6-tert-butylquinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3r) Brown resin (55%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.76 - 7.78 (m, 1H), 7.68 (d, J =



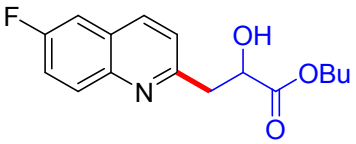
2.4 Hz, 1H),7.25(d, J = 8.4 Hz, 1H), 4.74 (dd, J = 6.6, 4.2 Hz, 1H), 4.12 (t, J = 6.6 Hz, 2H), 3.45 - 3.48 (m, 1H), 3.35 – 3.39 (m, 1H), 1.52 – 1.57 (m, 2H), 1.40 (s, 9H), 1.22 - 1.28 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 158.1, 149.2, 145.7, 136.9, 128.8, 128.3, 126.7, 122.6, 122.0, 70.7, 65.2, 40.9, 34.9, 31.3, 30.7, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{20}H_{28}NO_3$ $[M+H]^+$ 330.2064, found 330.2055.

butyl 2-hydroxy-3-(6-methoxyquinolin-2-yl)propanoate (Table 2, entry 3s) Brown



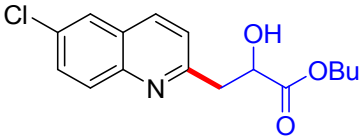
resin (53%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 9.6 Hz, 1H), 7.31 – 7.33 (m, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 4.72 – 4.74 (m, 1H), 4.12 (t, J = 6.6 Hz, 2H), 3.89 (s, 3H), 3.42 – 3.45 (m, 1H), 3.32 – 3.36 (m, 1H), 1.52 – 1.57 (m, 2H), 1.24 – 1.29 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 157.7, 156.2, 143.3, 135.6, 130.2, 128.0, 122.4, 122.3, 105.2, 70.7, 65.2, 55.6, 40.8, 30.6, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{17}H_{22}NO_4$ $[M+H]^+$ 304.1543, found 304.1533.

butyl 3-(6-fluoroquinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3t) Orange



solid (69%); mp 70 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, J = 9.0 Hz, 1H), 7.98 (dd, J = 9.0, 5.4 Hz, 1H), 7.43 – 7.46 (m, 1H), 7.38 (dd, J = 8.4, 3.0 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 4.73 – 4.75 (m, 1H), 4.13 – 4.15 (m, 2H), 3.46 – 3.49 (m, 1H), 3.36 – 3.40 (m, 1H), 1.53 – 1.58 (m, 2H), 1.24 – 1.29 (m, 2H), 0.82 – 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 160.3 (d, J = 246.3 Hz), 158.1 (d, J = 2.7 Hz), 144.4, 136.1 (d, J = 5.1 Hz), 131.3 (d, J = 9.0 Hz), 127.6 (d, J = 9.9 Hz), 122.9, 119.9 (d, J = 25.5 Hz), 110.7 (d, J = 21.6 Hz), 70.4, 65.4, 41.2, 30.7, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{16}H_{19}FNO_3$ $[M+H]^+$ 292.1343, found 292.1328.

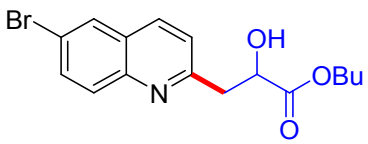
butyl 3-(6-chloroquinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3u) Brownish



resin (73%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.75 (d, J = 2.4 Hz, 1H), 7.59 - 7.61 (m, 1H), 7.31 (d, J = 8.4 Hz, 1H), 4.73 - 4.75 (m, 1H), 4.14 (td, J = 6.6, 1.2 Hz, 2H), 3.46 - 3.49 (m, 1H), 3.36 - 3.40 (m, 1H), 1.53 - 1.58 (m, 2H), 1.24 - 1.30 (m, 2H), 0.82 - 0.84 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 159.1, 145.7, 135.8, 132.1,

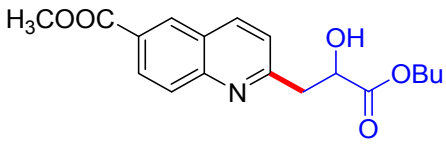
130.7, 130.5, 127.6, 126.3, 123.1, 70.4, 65.4, 41.3, 30.7, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{16}H_{19}ClNO_3$ $[M+H]^+$ 308.1048, found 308.1031.

butyl 3-(6-bromoquinolin-2-yl)-2-hydroxypropanoate (Table 2, entry 3v) Brown



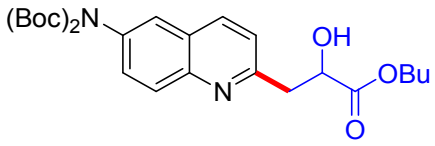
resin (73%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 1.8 Hz, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.73 (dd, J = 9.0, 2.1 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 4.72 – 4.76 (m, 1H), 4.14 (t, J = 6.6 Hz, 2H), 3.44 – 3.50 (m, 1H), 3.37 (dd, J = 15.6, 6.6 Hz, 1H), 1.51 – 1.60 (m, 2H), 1.23 – 1.33 (m, 2H), 0.81 – 0.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 159.3, 146.0, 135.7, 133.2, 130.7, 129.7, 128.2, 123.1, 120.1, 70.4, 65.4, 41.5, 30.7, 19.1, 13.7; HRMS (ESI) m/z calculated for $C_{16}H_{19}BrNO_3$ $[M+H]^+$ 352.0543, found 352.0538.

methyl 2-(2-(butoxycarbonyl)-2-hydroxyethyl)quinoline-6-carboxylate (Table 2,



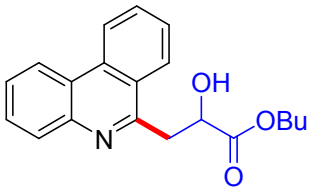
entry 3w) Greenish yellow resin (43%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.26 (d, J = 9.0 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 4.76 – 4.77 (m, 1H), 4.15 (t, J = 6.6 Hz, 2H), 3.98 (s, 3H), 3.50 - 3.53 (m, 1H), 3.42 (dd, J = 15.6, 6.6 Hz, 1H), 1.54 – 1.58 (m, 2H), 1.24 – 1.30 (m, 2H), 0.81 - 0.84 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 166.7, 161.3, 149.2, 138.0, 130.8, 129.4, 129.2, 128.0, 126.2, 123.0, 70.3, 65.5, 52.5, 41.6, 30.7, 19.1, 13.7; HRMS (ESI) m/z calculated for $C_{18}H_{22}NO_5$ $[M+H]^+$ 332.1492, found 332.1481.

di-tert-butyl 2-(2-(2-(butoxycarbonyl)-2-hydroxyethyl)quinolin-6-yl)malonate



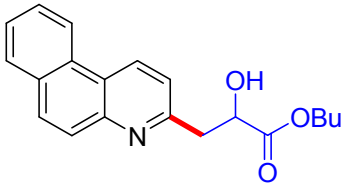
(Table 2, entry 3x) Yellow resin (57%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 9.0 Hz, 1H), 7.56 (d, J = 2.4 Hz, 1H), 7.46 (dd, J = 9.0, 2.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 4.75 - 4.77 (m, 1H), 4.14 – 4.16 (m, 2H), 3.49 (dd, J = 15.6, 4.2 Hz, 1H), 3.38 – 3.42 (m, 1H), 1.56 – 1.60 (m, 2H), 1.40 (s, 16H), 1.26 – 1.31 (m, 2H), 0.83 - 0.86 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 159.3, 151.8, 146.2, 137.3, 136.9, 130.4, 129.4, 126.9, 126.0, 122.5, 83.2, 70.4, 65.4, 41.2, 30.7, 28.0, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{26}H_{37}N_2O_7$ $[M+H]^+$ 489.2595, found 489.2584.

butyl 2-hydroxy-3-(phenanthridin-6-yl)propanoate (Table 2, entry 3z) Orange solid



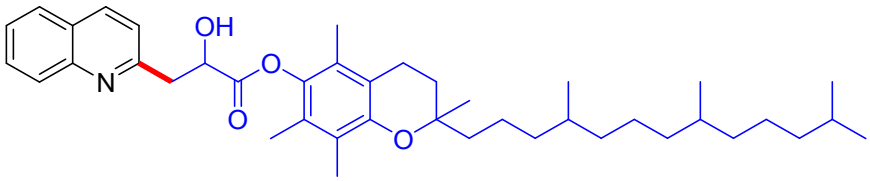
(71%) mp 90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, J = 8.1 Hz, 1H), 8.47 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H), 8.02 (d, J = 8.1 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 7.58 – 7.69 (m, 3H), 4.92 – 4.95 (m, 1H), 4.15 (t, J = 6.6 Hz, 2H), 3.83 – 3.85 (m, 2H), 1.49 – 1.57 (m, 2H), 1.17 – 1.30 (m, 2H), 0.75 – 0.80 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 158.5, 142.6, 132.9, 130.9, 129.4, 128.8, 127.6, 126.9, 125.7, 125.5, 123.7, 122.5, 122.0, 69.9, 65.1, 37.2, 30.7, 19.1, 13.6; HRMS (ESI) m/z calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found 324.1579.

butyl 3-(benzo[f]quinolin-3-yl)-2-hydroxypropanoate (Table 2, entry 3za) Yellow



solid (46%); mp 107 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.88 (d, J = 8.4 Hz, 1H), 8.58 (d, J = 8.4 Hz, 1H), 7.9 (d, J = 9.0 Hz, 1H), 7.89 – 7.98 (m, 2H), 7.68 – 7.70 (m, 1H), 7.64 (t, J = 7.2 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 4.78 - 4.80 (m, 1H), 4.15 (t, J = 6.6 Hz, 2H), 3.52 - 3.55 (m, 1H), 3.42 – 3.46 (m, 1H), 1.54 – 1.60 (m, 2H), 1.26 – 1.31 (m, 2H), 0.81 – 0.84 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 158.2, 147.3, 131.7, 131.6, 131.3, 129.6, 128.9, 127.7, 127.3, 124.1, 122.6, 122.1, 70.7, 65.4, 40.9, 30.7, 19.1, 13.7; HRMS (ESI) m/z calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found 324.1585.

3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-chromen-6-yl 2-hydroxy-3-(quinolin-2-yl)propanoate (Table 2, entry zb)



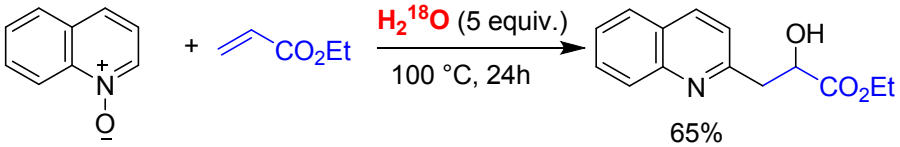
Greenish yellow resin (49%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.71 – 7.74 (m, 1H), 7.53 – 7.56 (m, 1H), 7.39 (d, J = 8.4 Hz, 1H), 5.09 (dd, J = 6.6, 3.6 Hz, 1H), 3.73 – 3.76 (m, 1H), 3.63 – 3.67 (m, 1H), 2.53 (t, J = 6.6 Hz, 2H), 2.04 (s, 3H), 1.86 (s, 3H), 1.83 (s, 3H), 1.76 -1.79 (m, 2H), 1.71 – 1.74(m, 1H), 1.49 -1.54 (m, 4H), 1.34 – 1.40 (m, 4H), 1.23 – 1.28 (m, 10H), 1.21 (s, 3H), 1.12 – 1.15 (m, 2H), 0.87 (s, 3H), 0.86 (s, 3H), 0.85 (d, J = 3.0 Hz, 3H), 0.84 (d, J = 3.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4, 159.1, 149.6, 140.5, 140.1, 130.2, 128.7, 128.7, 127.7, 127.1, 126.7, 126.7,

125.0, 123.2, 122.2, 117.5, 75.2, 70.7, 40.5, 39.5, 37.6, 37.6, 37.5, 37.5, 37.4, 32.9, 32.9, 32.8, 28.1, 25.0, 24.9, 24.6, 22.9, 22.8, 21.2, 21.2, 20.7, 19.8, 12.9, 12.1, 11.9; HRMS (ESI) m/z calcd for $C_{41}H_{60}NO_4$ $[M+H]^+$ 630.4517, found 630.4501.

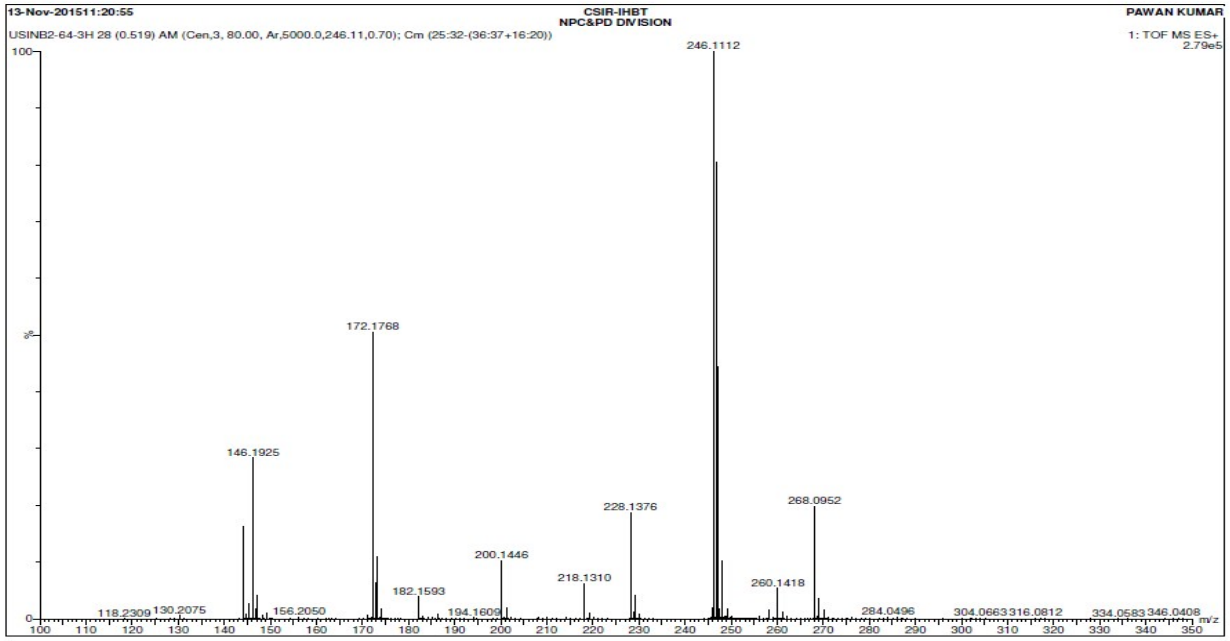
4. Mechanistic study

^{18}O isotopic labeling experiment (Scheme 3b)

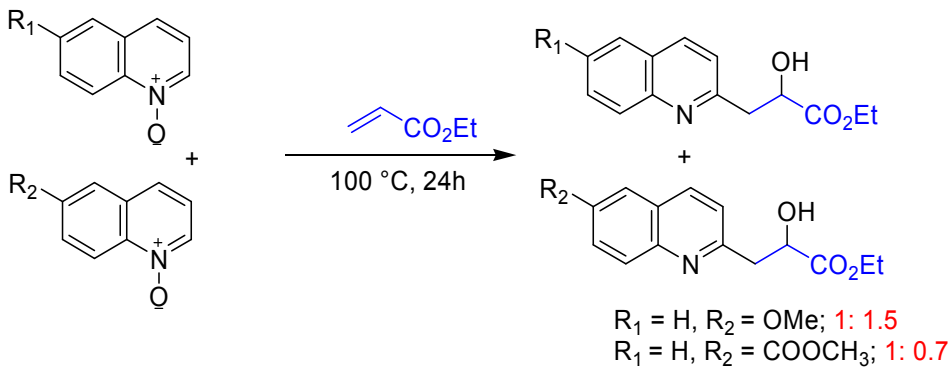
To a screw capped vial with a spin vane triangular shaped stir bar, quinoline *N*-oxide (0.1 mmol), ethylacrylate (0.4 mmol) and ^{18}O labeled water (5 equiv.) were added. The reaction was stirred at 100°C for 15h, filtered and washed with EtOAc. 65% product was observed in NMR and no ^{18}O incorporation in the final product was observed based on HRMS.



no ^{18}O incorporation as HRMS observed for 3a = 246.1112

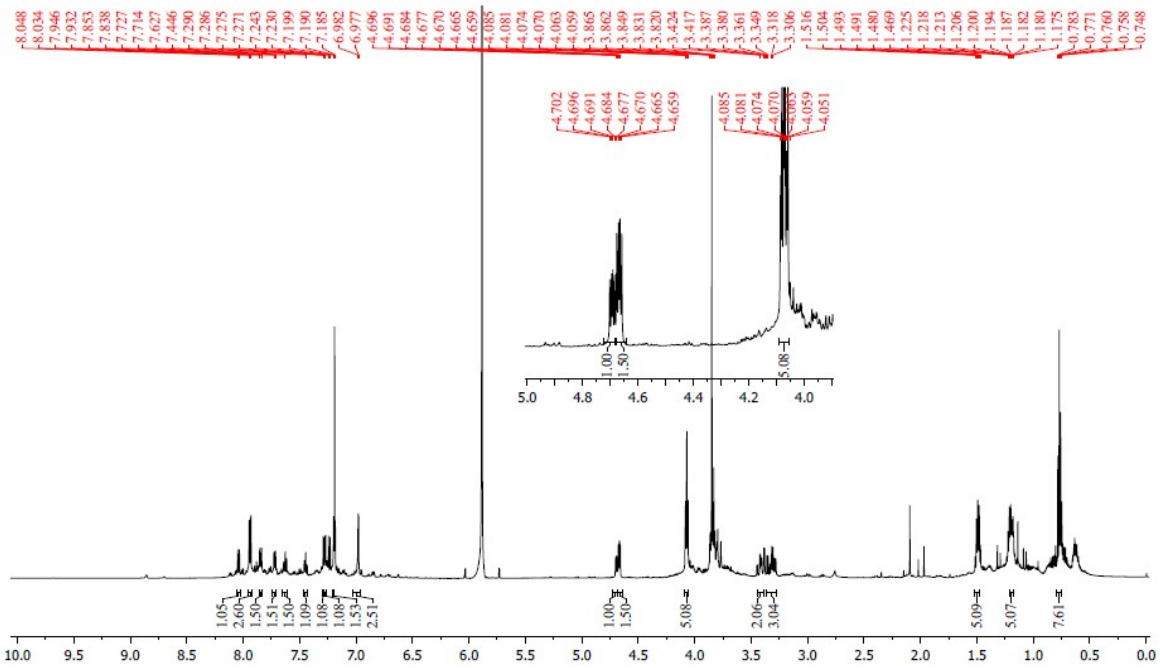


Competition Experiments Between Electronically Differentiatedquinoline N-oxide (Scheme 4)

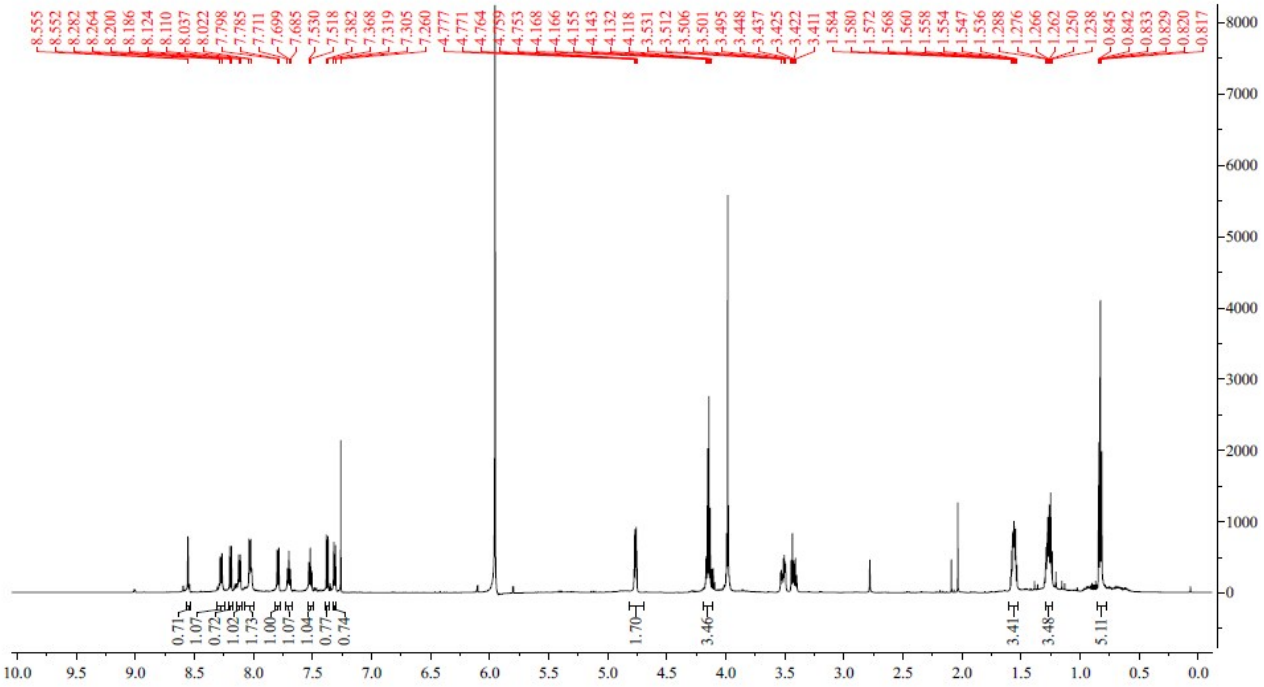


To a screw capped vial with a spin vane triangular shaped stir bar, quinoline *N*-oxide (**A)** (0.05 mmol), 6-OMe (**B)** / 6-$COOCH_3$(**C**) quinoline *N*-Oxide (0.05 mmol), butylacrylate (0.4 mmol) were added. The reaction was stirred at 100°C for 15h, filtered and washed with EtOAc.

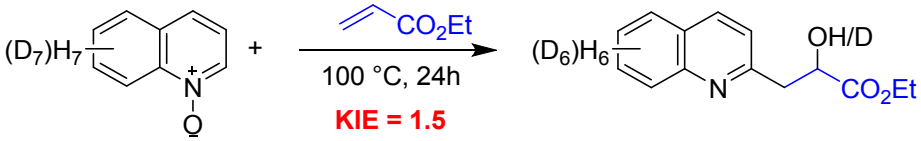
1H NMR (A+B)



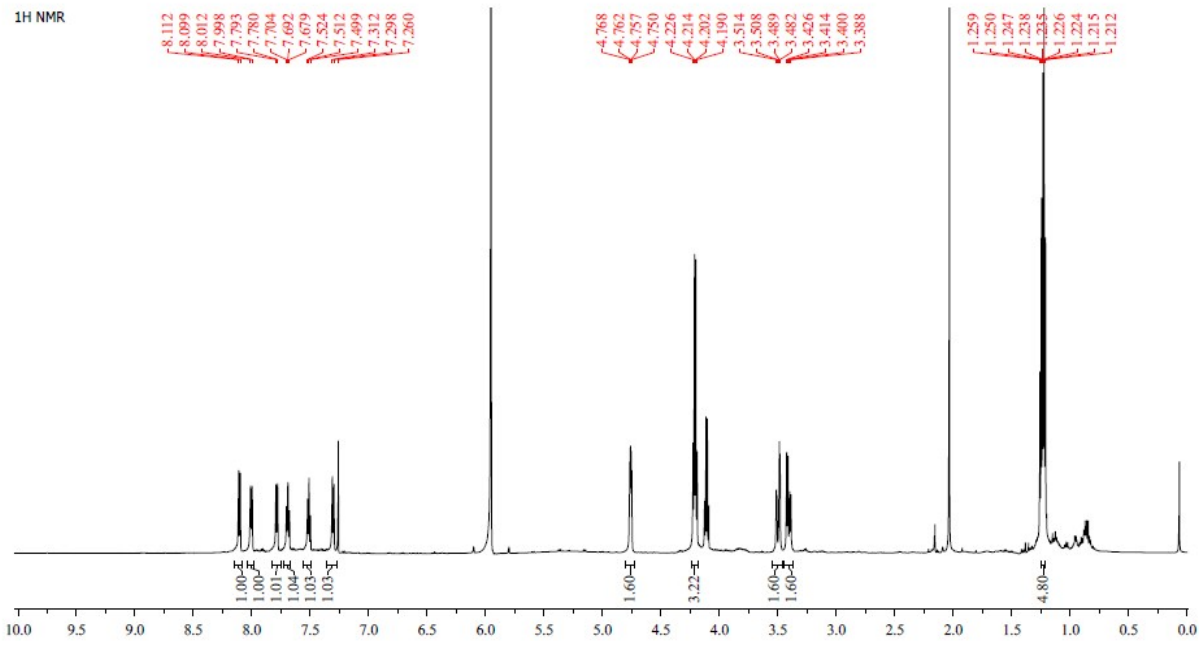
1H NMR (A+C)



KIE study *(Scheme 5)*



To a screw capped vial with a spin vane triangular shaped stir bar, quinoline *N*-oxide (0.05 mmol), quinoline-D_7 *N*-oxide (0.05 mmol), ethyl acrylate (0.4 mmol) were added. The reaction was stirred at 100°C for 15h, filtered and washed with EtOAc. Solvent was removed under reduced pressure and residue was purified by flash chromatography on silica gel (hexane: EtOAc) to give the mixture of desired product P+[D6]-P. the ratio of P/[D6]-P was obtained by ^{1}H-NMR to give KIE value of **1.5**.



5. General Procedure for Conversion of 3a to 4a[3]

To an oven-dried screw cap reaction vial charged with a spin vane magnetic stir-bar, ethyl 2-hydroxy-3-(quinolin-2-yl)propanoate (**3a**) (0.1 mmol) was added. The reaction vial was closed with screw cap and kept for vigorous stirring on a preheated oil bath at 100°C for 24h. After completion, reaction mixture was allowed to cool down to room temperature and extracted with ethyl acetate. Ethyl acetate layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Residue was purified by flash chromatography using silica gel (230-400 mesh size) and *n*-hexane: EtOAc as eluent to give (*E*)-ethyl 3-(quinolin-2-yl)acrylate (**4a**) in 46% yield.[3]

References

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