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Supplementary Information

Mono and di *ortho*-C–H acetoxylation of 2-aryloxyquinoline-3-carbaldehydes

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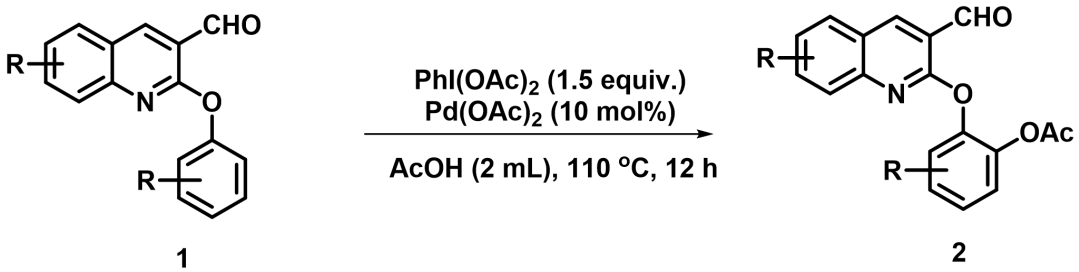
CONTENTS

1. General Information:

Commercial reagents were used without further purification. For compounds ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra were recorded in deuterochloroform-d_3 ($CDCl_3$) or dimethyl sulfoxide-d6 (DMSO) on a Bruker 400 MHz spectrometer using tetramethylsilane (TMS, $\delta = 0$) as an internal standard. Spin multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m). Mass spectra were recorded on Agilent 6530-B Accurate Mass Q-TOF LC/MS.

2. General Experimental Procedures:

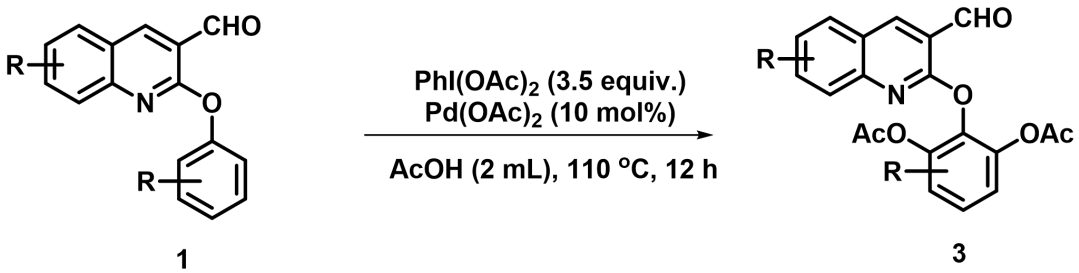
a) General experimental procedure for the syntheses of mono acetoxylated 2-aryloxyquinoline-3-carbaldehydes



1 2

To a mixture of 2-aryloxyquinoline-3-carbaldehyde 1 (1.0 mmol), iodobenzene diacetate (1.5 equiv.), 10 mol% $Pd(OAc)_2$ were added in acetic acid (2 mL) and the resulting mixture was heated at 110 °C for 12 h. After monitoring by TLC, the reaction mixture was cooled to room temperature and was diluted with water (10 mL), and extracted with ethyl acetate (3x10 mL). The combined organic layer was dried over Na_2SO_4. The solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel 100-200 mesh, 15:85 Ethyl acetate: Hexane) to provide the pure products **2a-k**.

b) General experimental procedure for the syntheses of di acetoxylated 2-aryloxyquinoline-3-carbaldehydes

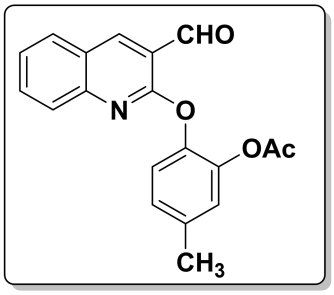


1 3

To a mixture of 2-aryloxyquinoline-3-carbaldehyde 1 (1.0 mmol), iodobenzene diacetate (3.5 equiv.), 10 mol% $Pd(OAc)_2$ were added in acetic acid (2 mL) and the resulting mixture was heated at 110 °C for 12 h. After monitoring by TLC, the reaction mixture was cooled to room temperature and was diluted with water (10 mL), and extracted with ethyl acetate (3x10 mL). The combined organic layer was dried over Na_2SO_4. The solvent was evaporated and the crude product thus obtained was purified by column chromatography (silica gel 100-200 mesh, 15:85 Ethyl acetate: Hexane) to provide the pure products **3a**–**f**.

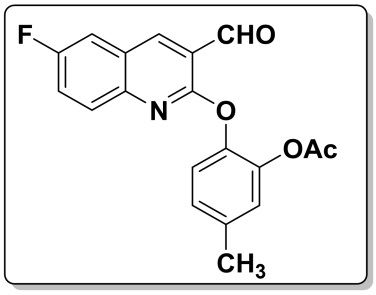
3. Spectroscopic data of the compounds:

2-((3-Formylquinolin-2-yl)oxy)-5-methylphenylacetate (2a)



White solid; Yield: 85%; M.P: 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 8.74 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.73 (dd, J = 14.3, 7.3 Hz, 2H), 7.58 – 7.43 (m, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 7.09 (s, 1H), 2.43 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.90, 168.59, 159.78, 148.67, 142.27, 141.85, 140.67, 136.27, 133.00, 129.74, 128.02, 127.41, 126.01, 125.28, 124.34, 123.45, 119.78, 21.18, 20.69; HRMS (ESI): Calc. for $[(C_{19}H_{15}NO_4)]$ $(M+H)^+$ 322.1079, found 322.1067.

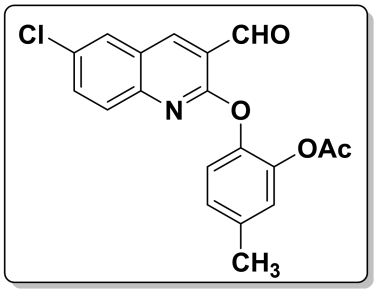
2-((6-Fluoro-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2b)



White solid; Yield: 72%; M.P: 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 8.67 (s, 1H), 7.74 (dd, J = 9.2, 5.1 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.30 (d, J = 8.2 Hz, 1H), 7.15 – 7.13 (m, 1H), 7.09 (d, J = 1.5 Hz, 1H), 2.42 (s, 3H), 1.95 (s, 3H). δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.67, 168.55, 145.55, 142.26, 141.76, 139.82 (d, $J_{C\text{-}F}$ = 5.3 Hz), 136.41, 130.28 (d, $J_{C\text{-}F}$ = 8.7 Hz), 127.44, 124.37, 123.42, 122.99, 122.73, 120.32, 112.69 (d, $J_{C\text{-}F}$ =

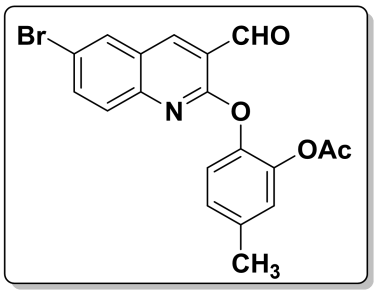
8.7 Hz), 21.18, 20.70; HRMS (ESI): Calc. for [($C_{19}H_{14}FNO_4$)] $(M+H)^+$ 340.0985, found 340.0974.

2-((6-Chloro-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2c)



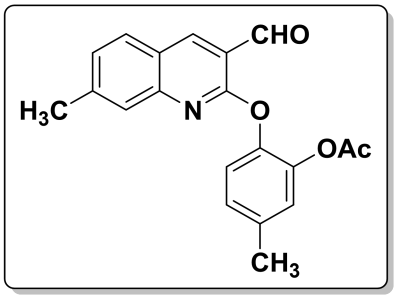
White solid; Yield: 75%; M.P: 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.63 (s, 1H), 7.86 (d, *J* = 2.1 Hz, 1H), 7.66 (dd, *J* = 19.7, 5.6 Hz, 1H), 7.63 (dd, J = 9.0 Hz, 2.2 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.14 (dd, J = 8.2, 1.9 Hz, 1H), 7.09 (s, 1H), 2.42 (s, 3H), 1.95 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 188.51, 168.51, 159.92, 146.99, 142.22, 141.65, 139.59, 136.50, 133.64, 131.61, 129.52, 128.12, 127.44, 125.85, 124.38, 123.40, 120.38, 21.18, 20.70; HRMS (ESI): Calc. for [($C_{19}H_{14}ClNO_4$)] $(M+H)^+$ 356.0690, found 356.0683.

2-((6-Bromo-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2d)



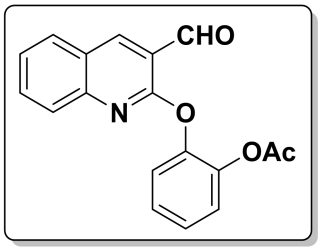
White solid; Yield: 60%; M.P: 165-167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.63 (s, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.75 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.15 (dd, *J* = 4.8, 3.4 Hz, 1H), 7.09 (s, 1H), 2.42 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.48, 168.51, 159.96, 147.23, 142.20, 141.61, 139.51, 136.52, 136.17, 131.45, 129.64, 127.44, 126.39, 124.38, 123.38, 120.32, 119.44, 21.18, 20.70; HRMS (ESI): Calc. for [($C_{19}H_{14}BrNO_4$)] $(M+H)^+$ 400.0184, found 400.0176.

2-((3-Formyl-7-methylquinolin-2-yl)oxy)-5-methylphenylacetate (2e)



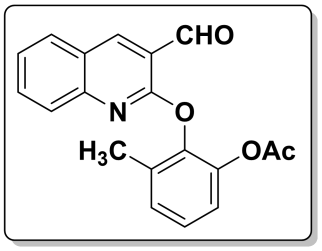
White solid; Yield: 65%; M.P: 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.69 (s, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.54 (s, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 1.7 Hz, 1H), 2.48 (s, 3H), 2.42 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.94, 148.95, 144.26, 142.31, 141.96, 140.27, 136.20, 129.40, 128.24, 127.41, 127.30, 124.29, 123.49, 123.30, 120.05, 118.99, 22.23, 21.19, 20.70; HRMS (ESI): Calc. for [($C_{20}H_{17}NO_4$)] $(M+H)^+$ 336.1236, found 336.1226.

2-((3-Formylquinolin-2-yl)oxy)phenylacetate (2f)



White solid; Yield: 65%; M.P: 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.63 (s, 1H), 8.75 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.75 – 7.71 (m, 2H), 7.50 – 7.44 (m, 2H), 7.38 – 7.30 (m, 3H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.78, 168.44, 159.62, 148.60, 144.29, 142.72, 140.76, 133.07, 129.74, 128.01, 126.80, 126.16, 126.10, 125.31, 123.92, 123.87, 119.74, 20.67; HRMS (ESI): Calc. for [($C_{18}H_{13}NO_4$)] $(M+H)^+$ 308.0923, found 308.0936.

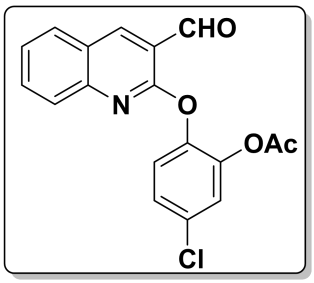
2-((3-Formylquinolin-2-yl)oxy)-3-methylphenylacetate (2g)



White solid; Yield: 52%; M.P: 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.69 (s, 1H), 8.76 (s, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.71 – 7.69 (m, 2H), 7.47 (ddd, *J* = 8.1, 5.3, 2.8 Hz, 2H), 7.23 (d, *J* = 2.4 Hz, 1H), 7.13 – 7.10 (m, 1H), 2.27 (s, 3H), 1.91 (s, 3H).^{13}C NMR (100

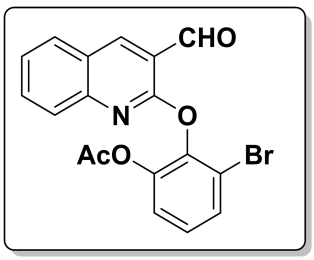
MHz, $CDCl_3$) δ 188.88, 168.61, 148.84, 143.13, 142.97, 140.69, 133.29, 133.04, 129.78, 128.50, 128.07, 125.99, 125.86, 125.24, 121.21, 119.44, 20.69, 16.78; HRMS (ESI): Calc. for $[(C_{19}H_{15}NO_4)]$ $(M+H)^+$ 322.1079, found 322.1071.

5-Chloro-2-((3-formylquinolin-2-yl)oxy)phenylacetate (2h)



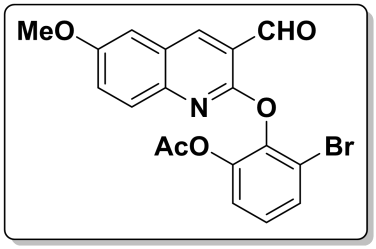
White solid; Yield: 51%; M.P: 130-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.60 (s, 1H), 8.76 (s, 1H), 7.92 (d, *J*=7.8, 1H), 7.74 (dd, *J*= 4.7, 1.1 Hz, 2H), 7.52 – 7.48 (m, 1H), 7.41 – 7.39 (m, 1H), 7.33 (dd, *J*=7.6, 2.1 Hz, 2H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.53, 148.50, 148.46, 145.95, 143.13, 143.04, 141.05, 133.26, 129.80, 127.97, 126.89, 126.30, 125.39, 124.76, 124.42, 20.60; HRMS (ESI): Calc. for $[(C_{18}H_{12}ClNO_4)]$ $(M+H)^+$ 342.0533, found 342.0523.

3-Bromo-2-((3-formylquinolin-2-yl)oxy)phenylacetate (2i)



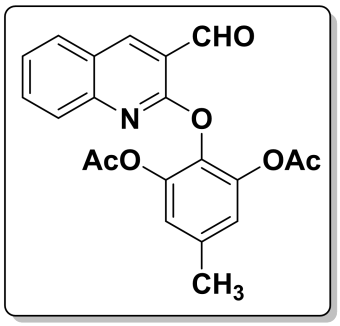
White solid; Yield: 56%; M.P: 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.78 (s, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 3.4 Hz, 2H), 7.57 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.28 (d, *J* = 1.8 Hz, 1H), 7.24 (s, 1H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.74, 168.22, 148.56, 144.71, 140.77, 133.11, 130.62, 129.82, 128.09, 126.95, 126.24, 125.51, 123.21, 119.44, 118.17, 20.74; HRMS (ESI): Calc. for $[(C_{18}H_{12}BrNO_4)]$ $(M+H)^+$ 386.0028, found 386.0044.

3-Bromo-2-((3-formyl-6-methoxyquinolin-2-yl)oxy)phenylacetate (2j)



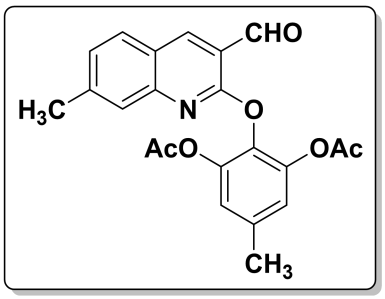
Yellow solid; Yield: 65%; M.P: 140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.67 (s, 1H), 7.61 (d, *J* = 9.2 Hz, 1H), 7.56 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.36 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.28 (d, *J* = 1.7 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.17 (d, *J* = 2.8 Hz, 1H), 3.91 (s, 3H), 1.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.80, 168.09, 157.51, 157.39, 144.61, 144.26, 142.64, 139.03, 130.46, 129.22, 126.67, 126.19, 125.52, 123.07, 119.22, 118.08, 106.91, 55.67, 20.61. HRMS (ESI): Calc. for [($C_{19}H_{14}BrNO_5$)] $(M+H)^+$ 416.0134, found 416.0130.

2-((3-Formylquinolin-2-yl)oxy)-5-methyl-1,3-phenylenediacetate (3a)



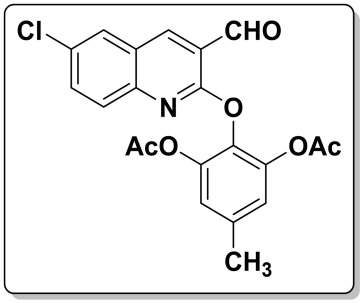
Light brown solid; Yield: 78%; M.P: 126-128 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.61 (s, 1H), 8.74 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.48 (dd, J = 10.7, 4.0 Hz, 1H), 7.01 (s, 2H), 2.42 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.56, 168.21, 158.71, 148.52, 143.65, 140.71, 135.97, 134.07, 133.19, 129.69, 127.98, 126.17, 125.31, 121.67, 119.34, 21.38, 20.69; HRMS (ESI): Calc. for [($C_{21}H_{17}NO_6$)] $(M+H)^+$ 380.1134; found value, 380.1122.

2-((3-Formyl-7-methylquinolin-2-yl)thio)-5-methyl-1,3-phenylenediacetate (3b)



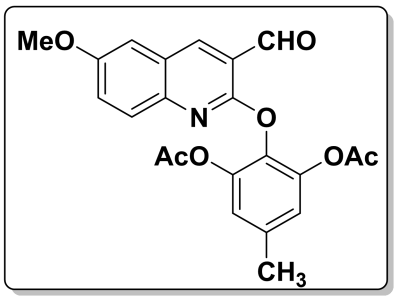
White solid; Yield: 52%; M.P: 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.58 (s, 1H), 8.69 (s, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.54 (s, 1H), 7.30 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.01 (d, *J* = 0.6 Hz, 2H), 2.48 (s, 3H), 2.43 (s, 3H), 1.97 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) 188.66, 168.30, 159.08, 148.86, 144.54, 143.72, 140.31, 135.96, 134.22, 129.37, 128.45, 127.28, 123.38, 121.67, 118.55, 22.24, 21.44, 20.74; HRMS (ESI): Calc. for [($C_{22}H_{19}NO_6$)] $(M+H)^+$ 394.1291, found 394.1293.

2-((6-Chloro-3-formylquinolin-2-yl)thio)-5-methyl-1,3-phenylenediacetate (3c)



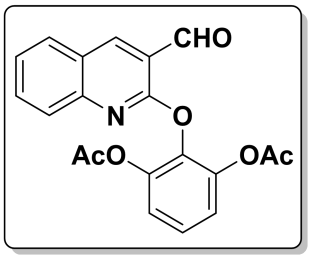
White solid; Yield: 68%; M.P: 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.64 (s, 1H), 7.87 (d, *J* = 1.9 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.01 (s, 2H), 2.43 (s, 3H), 1.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.23, 168.20, 158.88, 146.87, 143.59, 139.68, 136.24, 133.88, 131.86, 129.54, 128.11, 125.93, 121.72, 119.99, 21.42, 20.73; HRMS (ESI): Calc. for [($C_{21}H_{16}ClNO_6$)] $(M+H)^+$ 414.0744, found 414.0739.

2-((3-Formyl-6-methoxyquinolin-2-yl)oxy)-5-methyl-1,3-phenylenediacetate (3d)



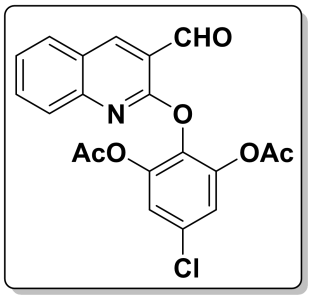
Yellow crystals; Yield: 72%; M.P: 151-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.57 (s, 1H), 8.63 (s, 1H), 7.65 (d, *J* = 9.1 Hz, 1H), 7.36 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.15 (s, 1H), 7.00 (s, 2H), 3.90 (s, 3H), 2.42 (s, 3H), 1.95 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.82, 168.31, 157.56, 157.47, 144.35, 143.67, 139.15, 135.84, 134.21, 129.28, 126.14, 125.75, 121.69, 119.24, 106.97, 55.74, 21.37, 20.71; HRMS (ESI): Calc. for [($C_{22}H_{19}NO_7$)] (M+H) 410.1240, found 410.1242.

2-((3-Formylquinolin-2-yl)oxy)-1,3-phenylenediacetate (3e)



Light brown solid; Yield: 69%; M.P: 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 8.76 (s, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 4.9 Hz, 2H), 7.51 – 7.47 (m, 1H), 7.37 – 7.32 (m, 2H), 7.21 (d, *J* = 8.0 Hz, 1H), 1.97 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.53, 168.15, 148.50, 144.25, 140.85, 133.32, 129.73, 128.04, 126.35, 126.30, 125.55, 125.38, 121.15, 119.31, 20.74; HRMS (ESI): Calc. for [($C_{20}H_{15}NO_6$)] $(M+H)^+$ 366.0978, found 366.0996.

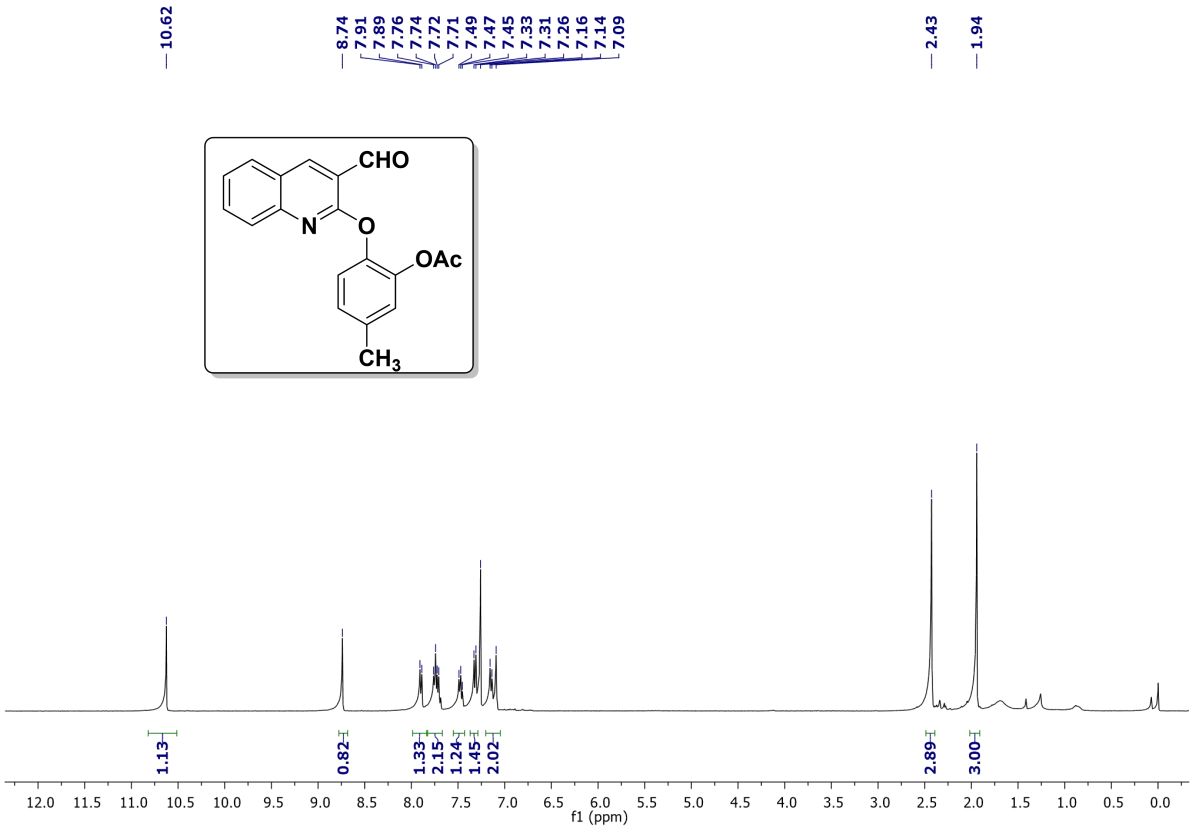
5-Chloro-2-((3-formylquinolin-2-yl)oxy)-1,3-phenylene diacetate (3f)

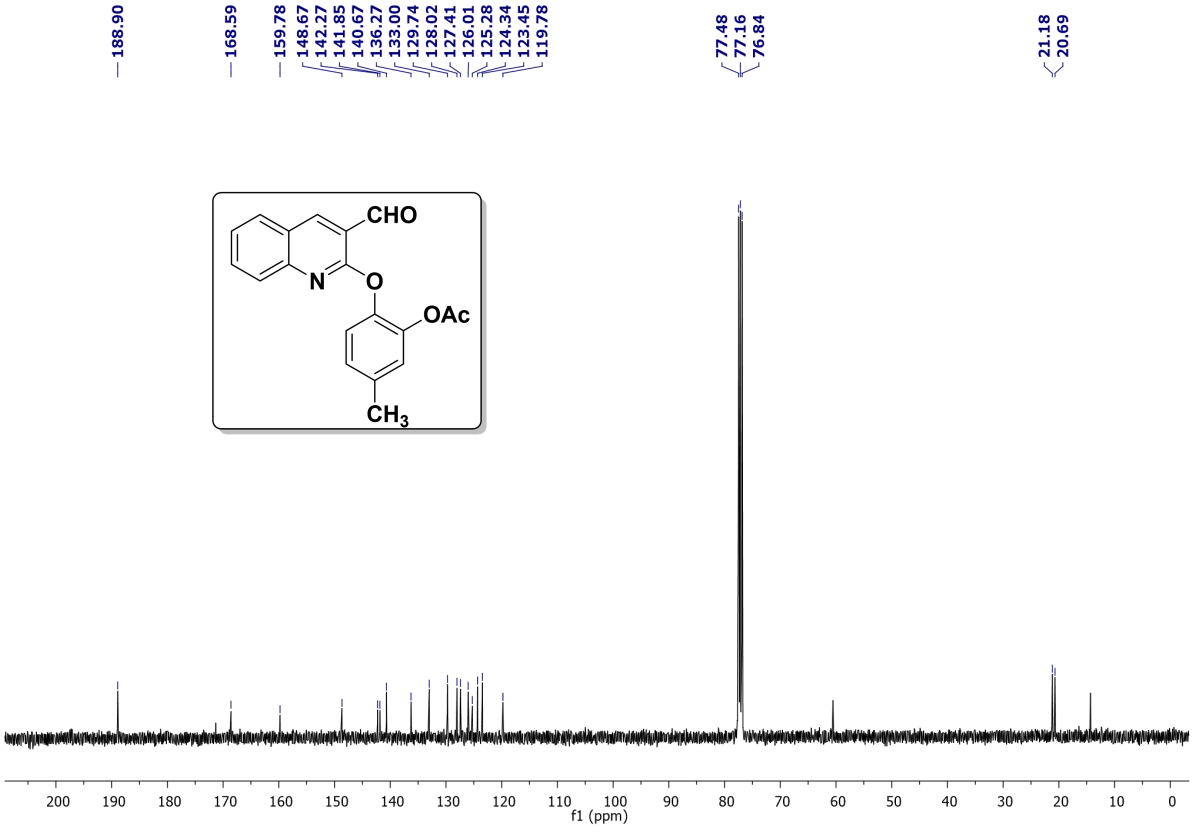


Light brown solid; Yield: 65%; M.P: 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.76 (s, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 3.5 Hz, 2H), 7.51 (dd, *J* = 8.3, 3.8 Hz, 1H), 7.24 (s, 2H), 1.97 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.24, 167.66, 158.35, 148.40, 144.44, 141.06, 135.62, 133.43, 130.53, 129.76, 127.99, 126.45, 125.47, 121.71, 119.29, 20.62. HRMS (ESI): Calc. for [($C_{20}H_{14}ClNO_6$)] $(M+H)^+$ 400.0588, found 400.0600.

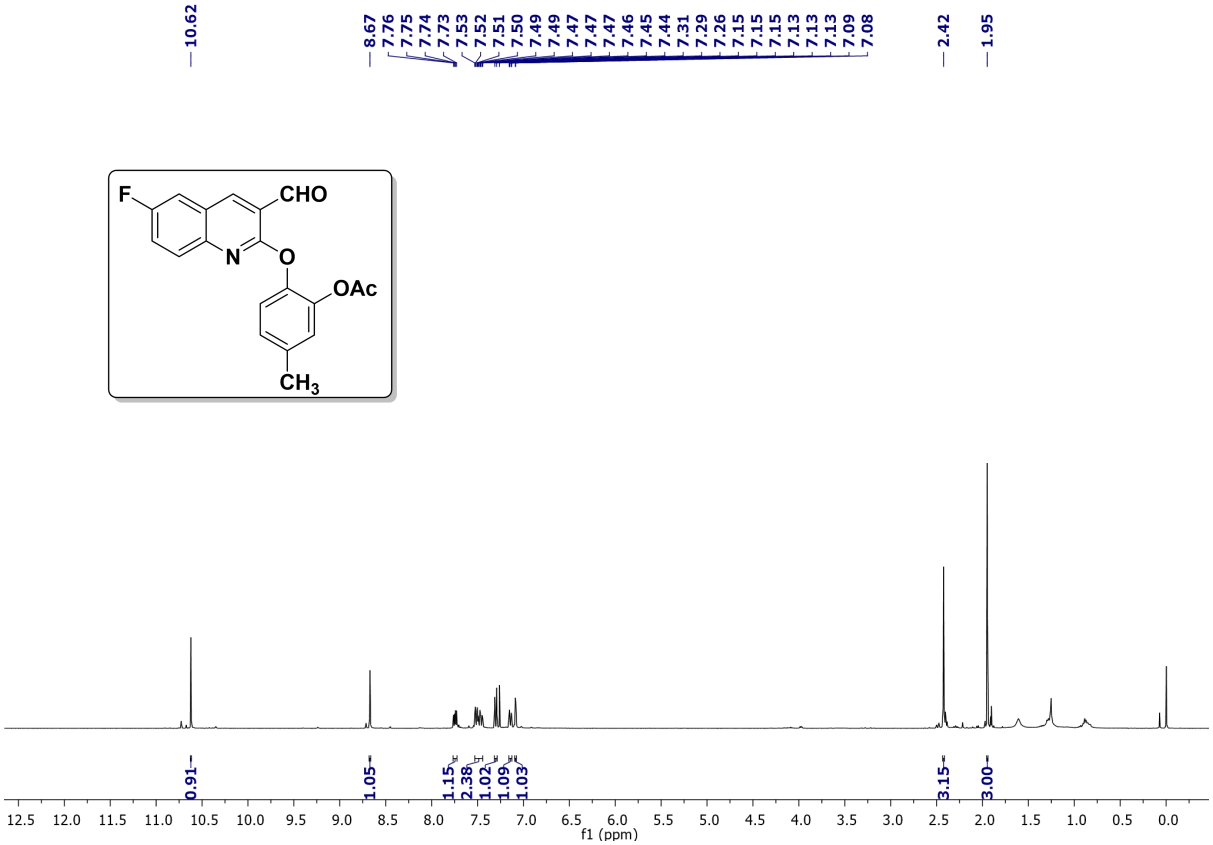
4. Copies of ^{1}H and ^{13}C NMR spectra of the products

2-((3-Formylquinolin-2-yl)oxy)-5-methylphenylacetate (2a)





2-((6-Fluoro-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2b)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8.67
7.76
7.75
7.74
7.73
7.53
7.52
7.51
7.50
7.49
7.49
7.47
7.47
7.47
7.46
7.45
7.44
7.31
7.29
7.26
7.15
7.15
7.13
7.13
7.09
7.08
2.42
1.95
F
CHO
N
O
OAc
CH3
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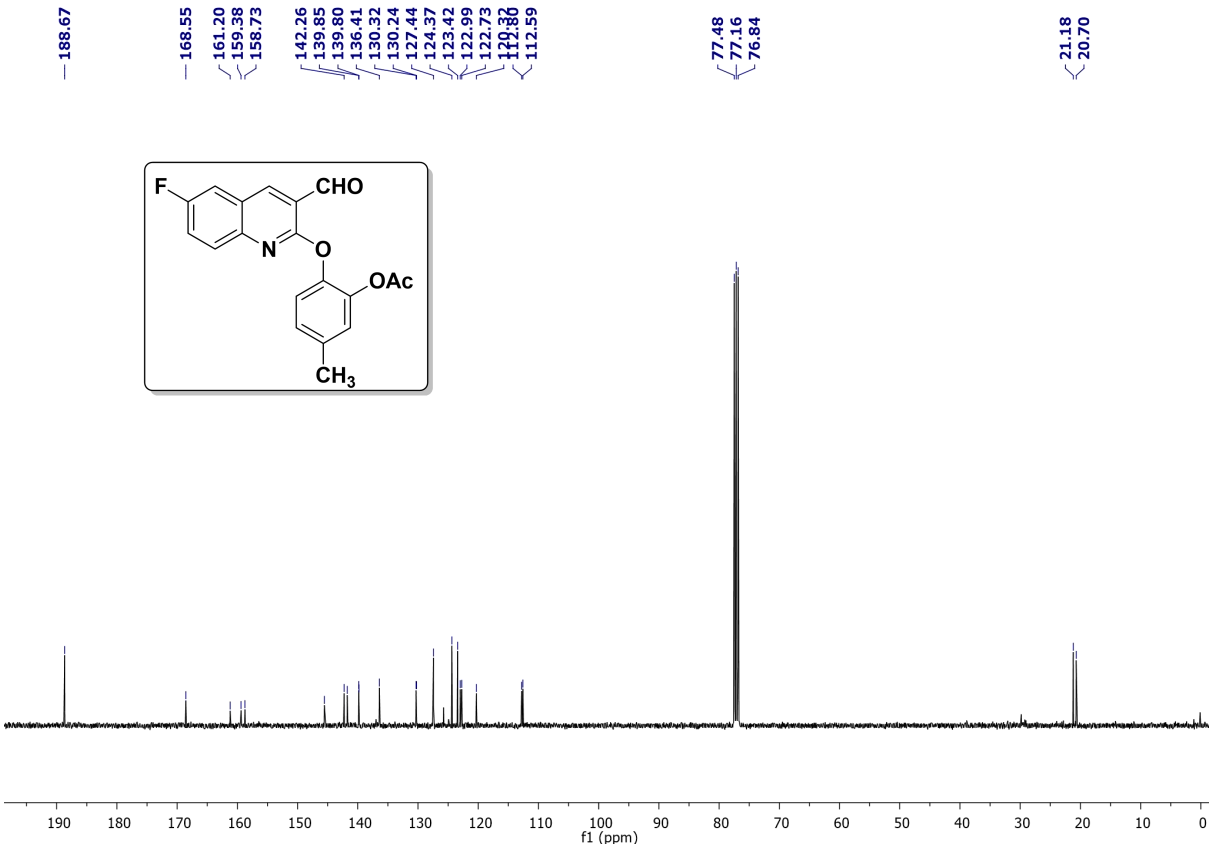
1.05
1.15
2.38
1.02
1.09
1.03
3.15
3.00
f1 (ppm)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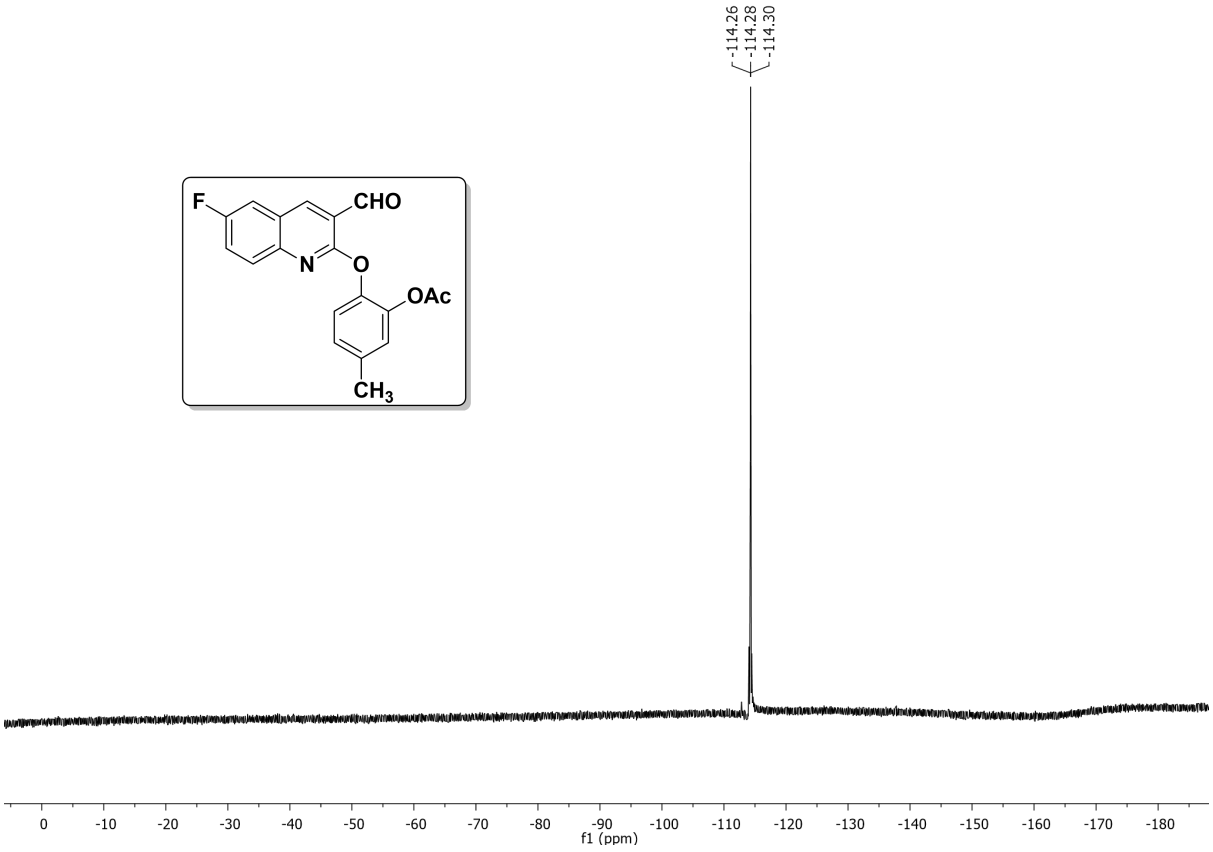
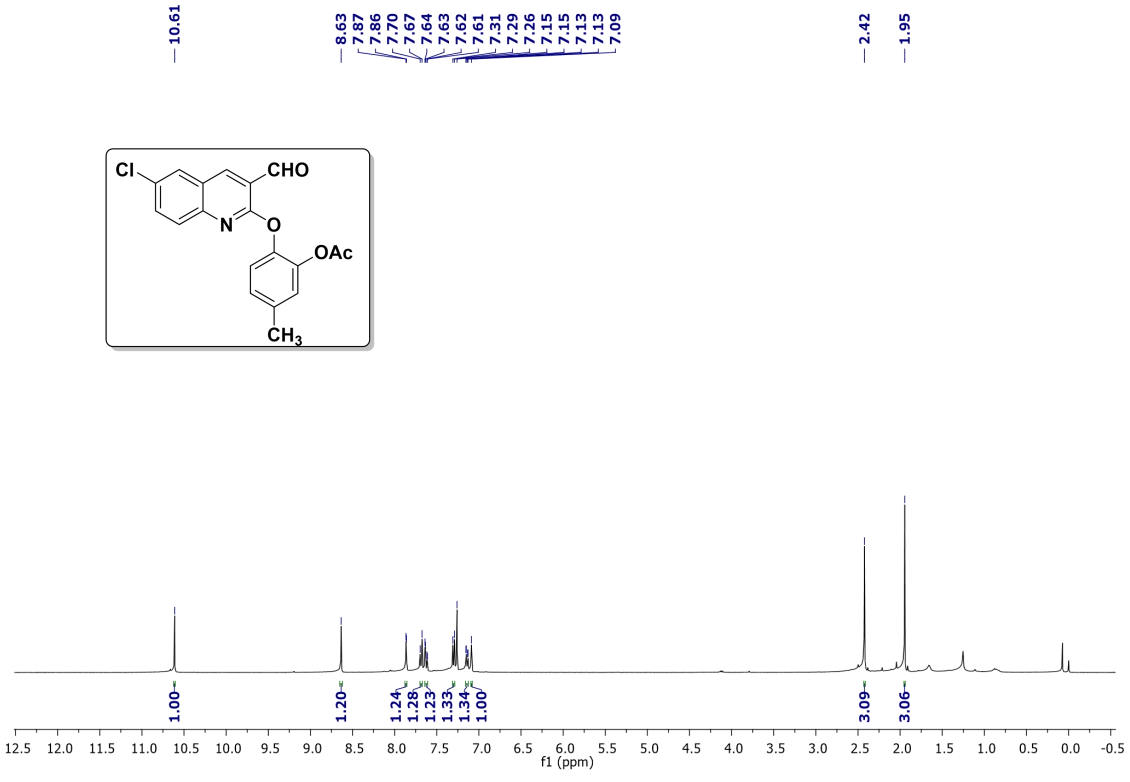
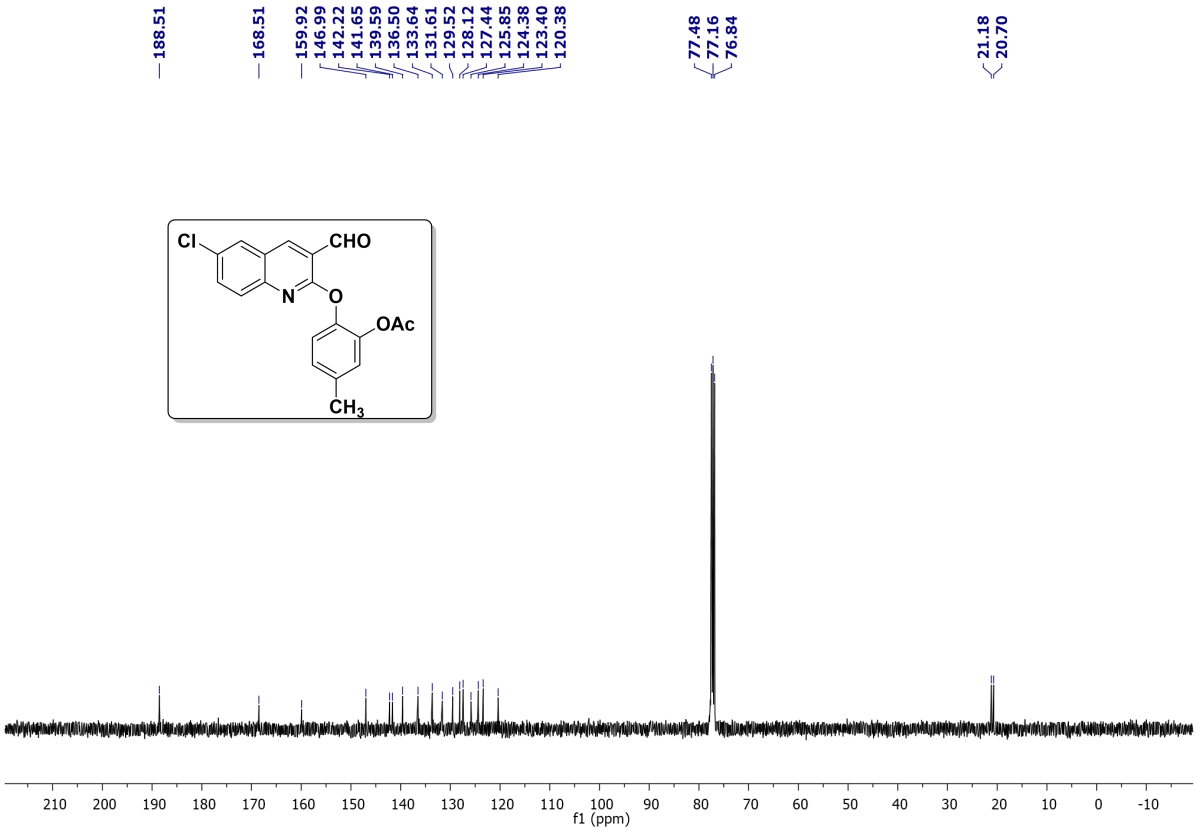
168.55
161.20
159.38
158.73
142.26
139.85
139.80
136.41
130.32
130.24
127.44
124.37
123.42
122.99
122.73
112.59
77.48
77.16
76.84
21.18
20.70
F
CHO
N
O
OAc
CH3
f1 (ppm)

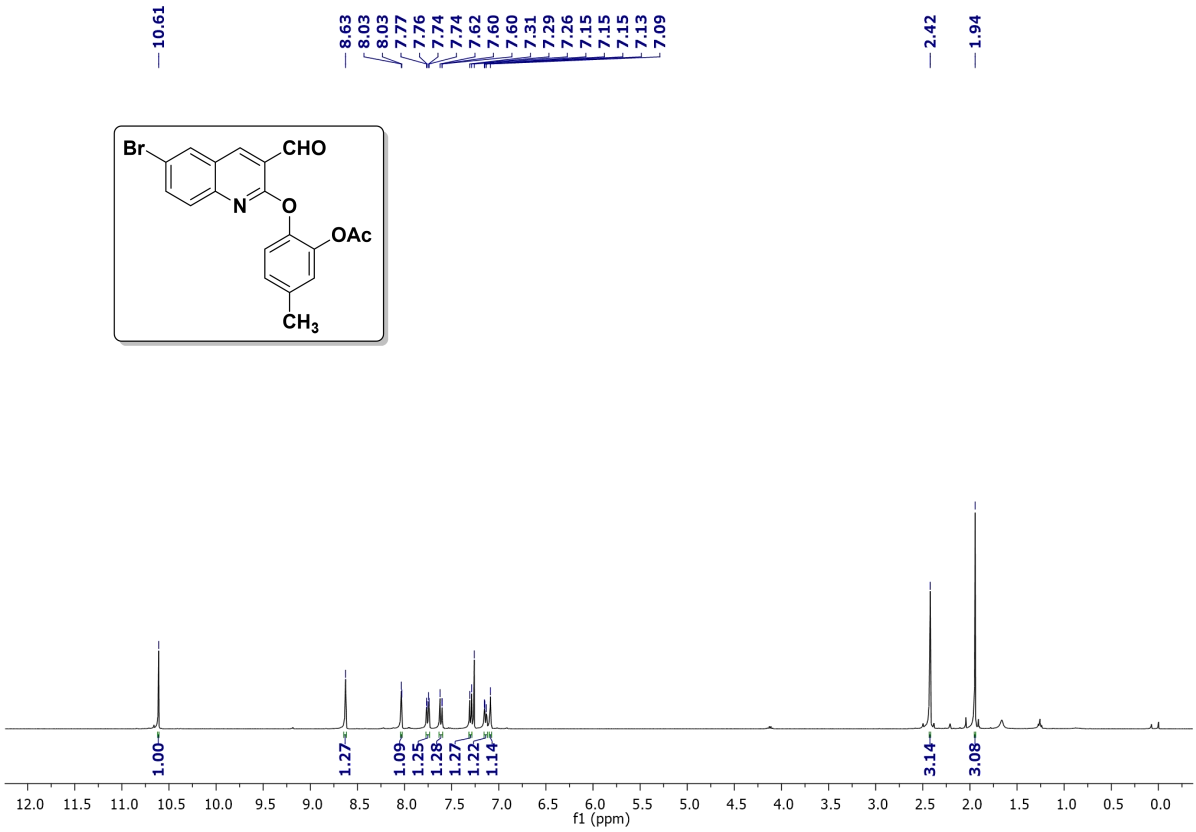


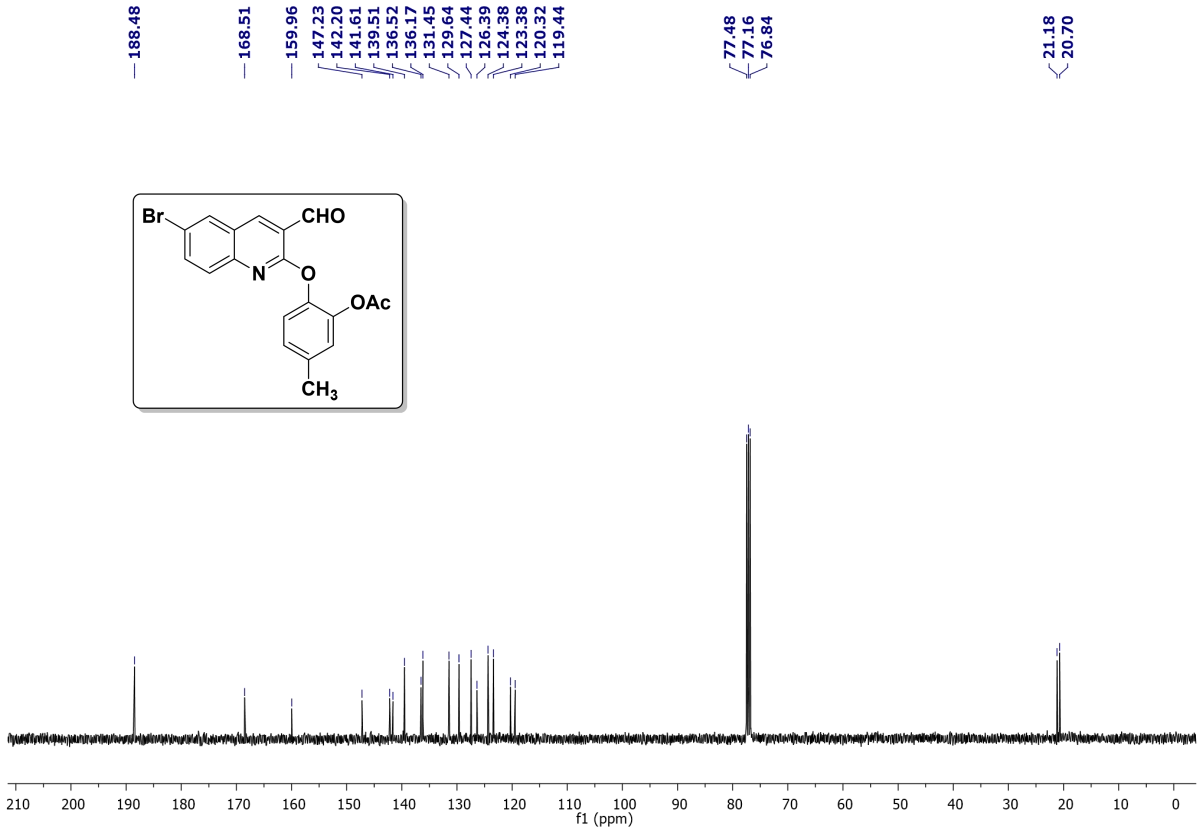
2-((6-Chloro-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2c)



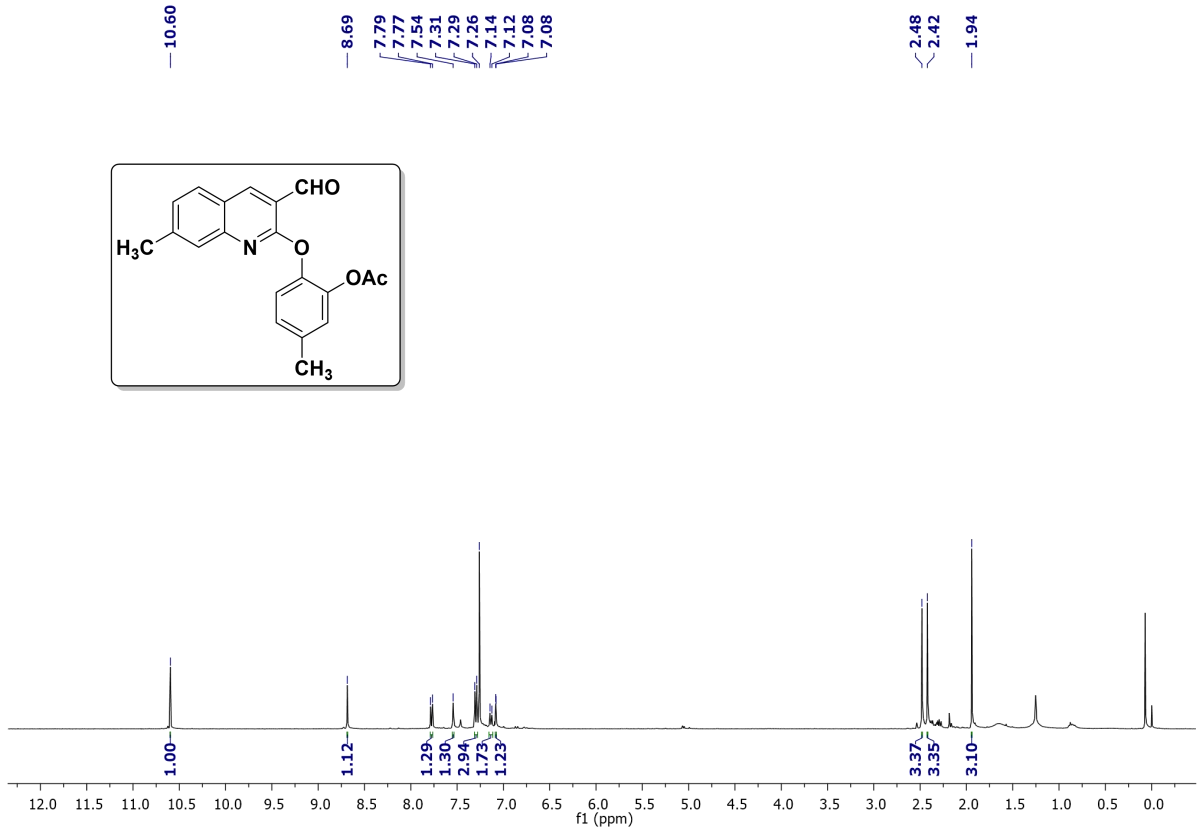


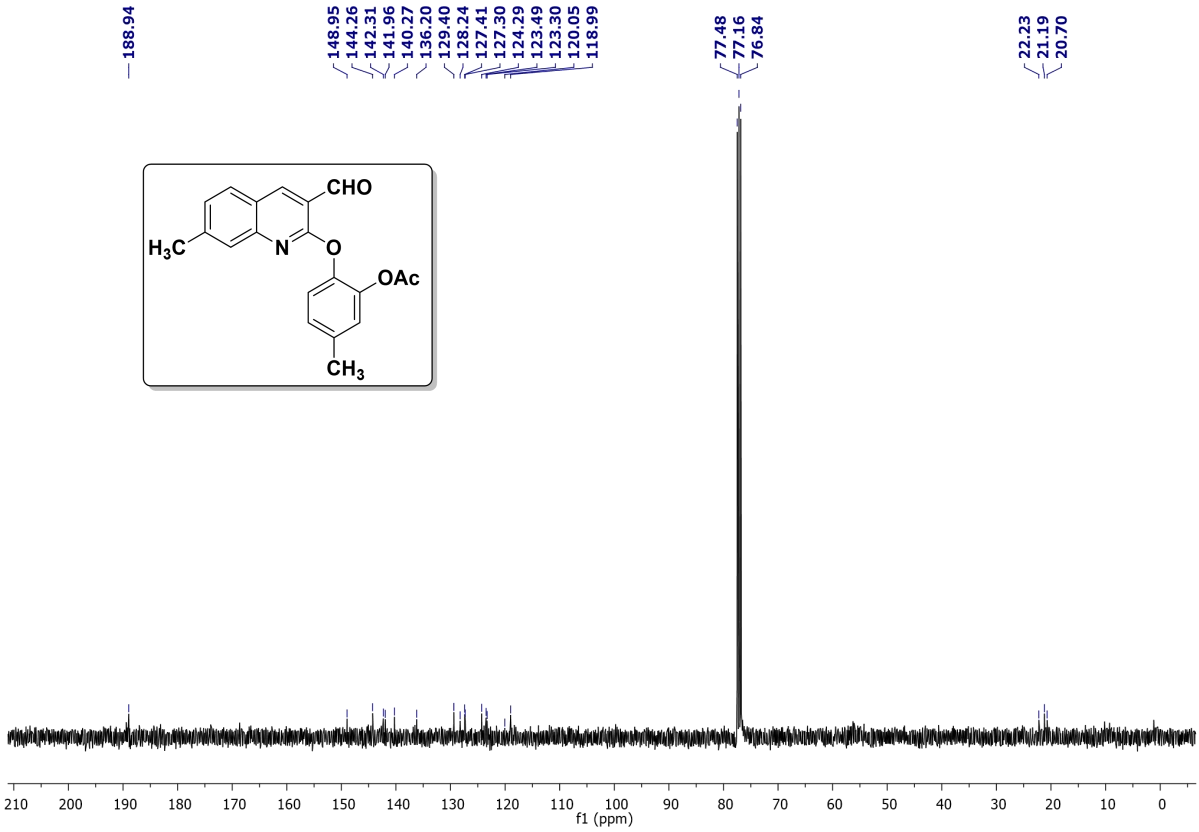
2-((6-Bromo-3-formylquinolin-2-yl)oxy)-5-methylphenylacetate (2d)



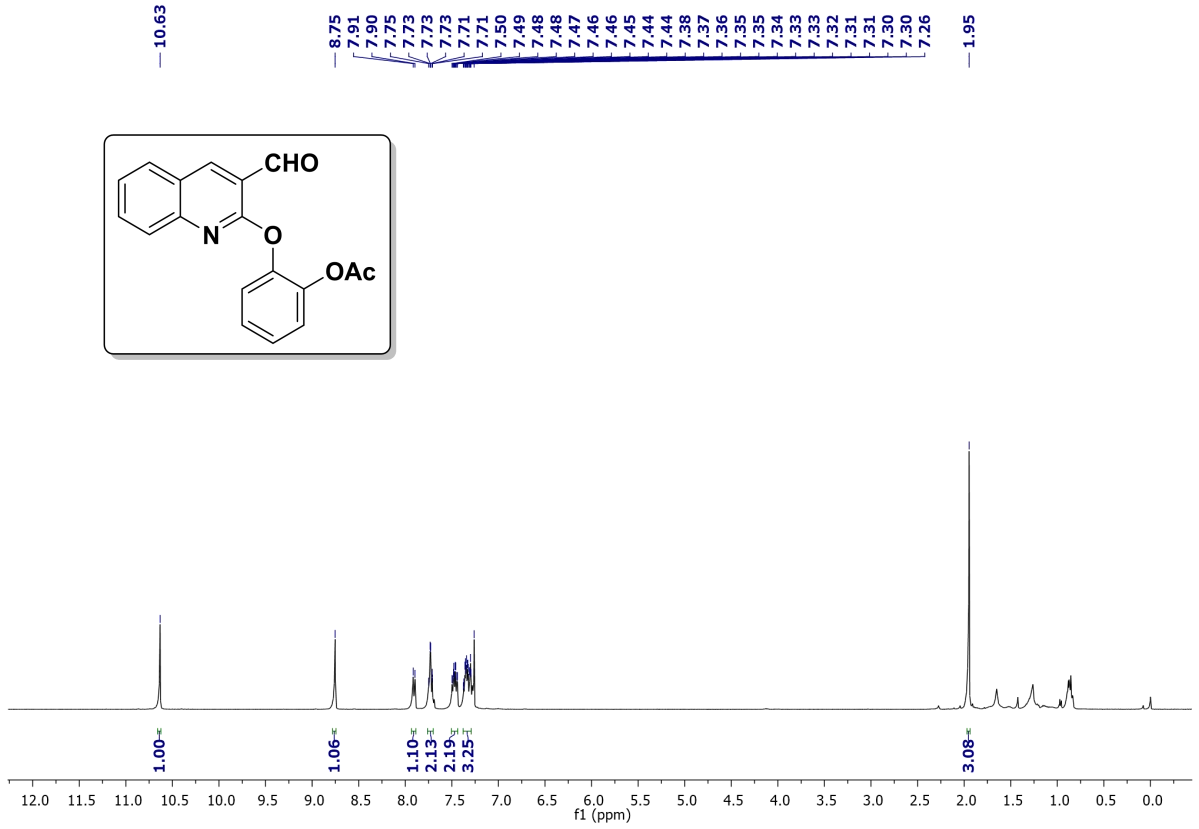


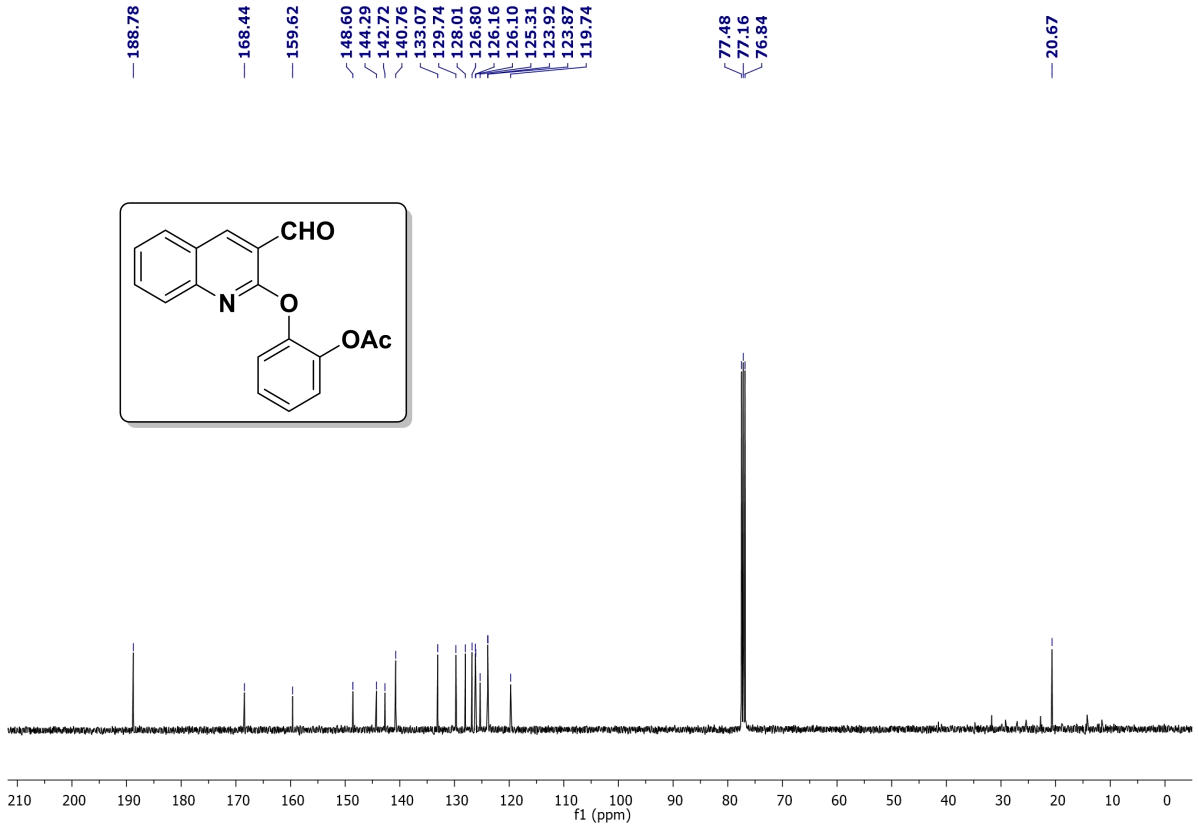
2-((3-Formyl-7-methylquinolin-2-yl)oxy)-5-methylphenylacetate (2e)



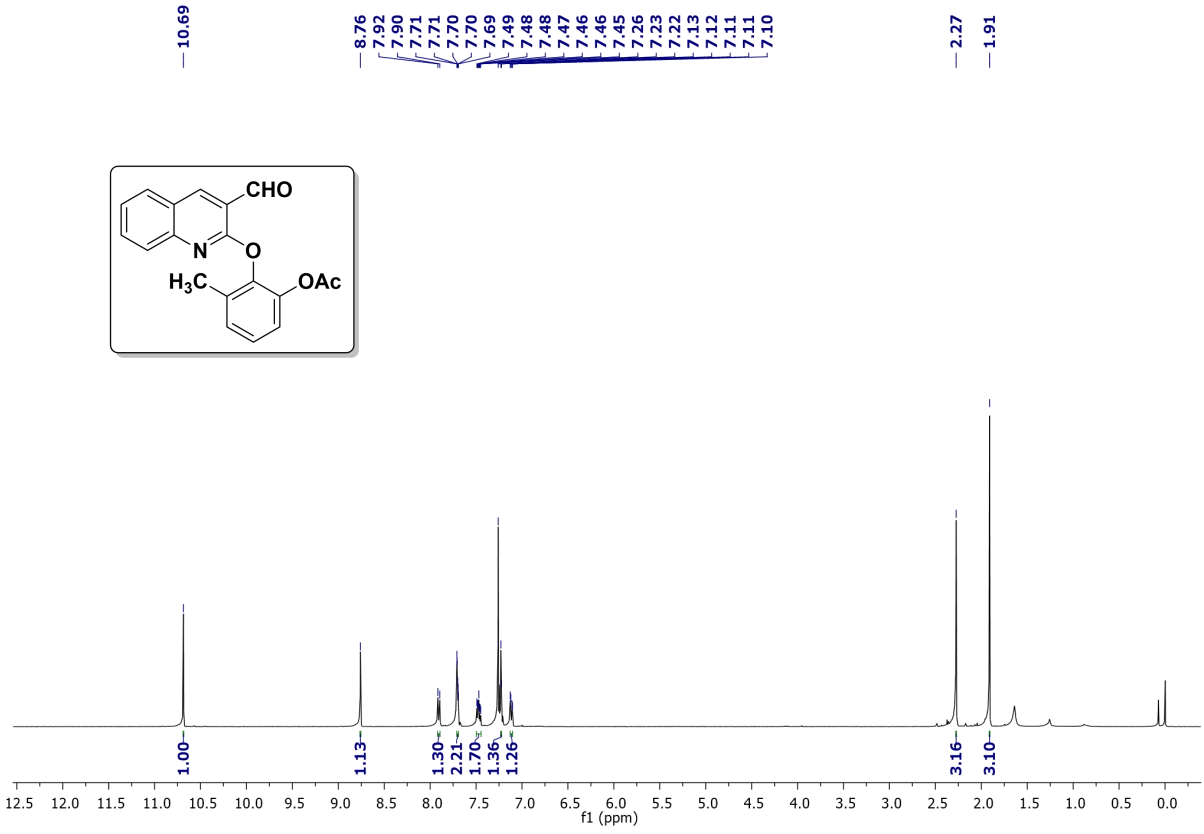


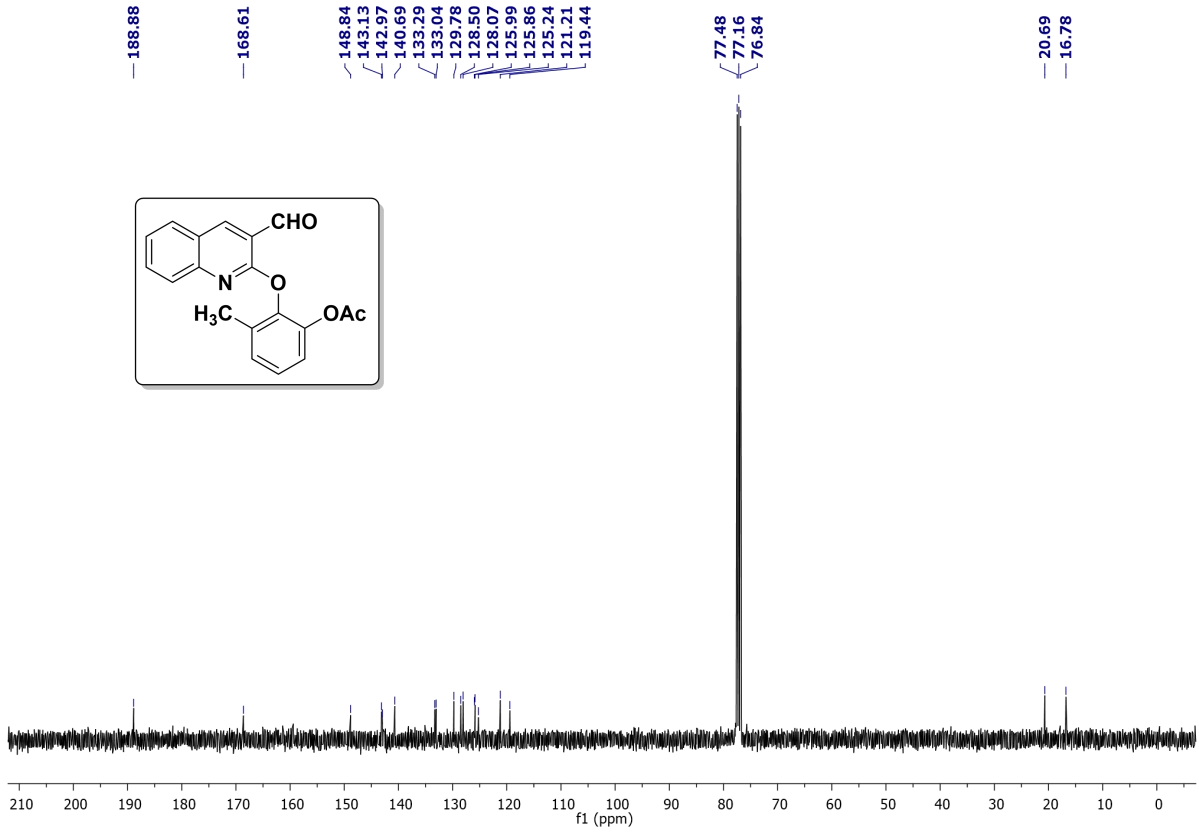
2-((3-Formylquinolin-2-yl)oxy)phenylacetate (2f)



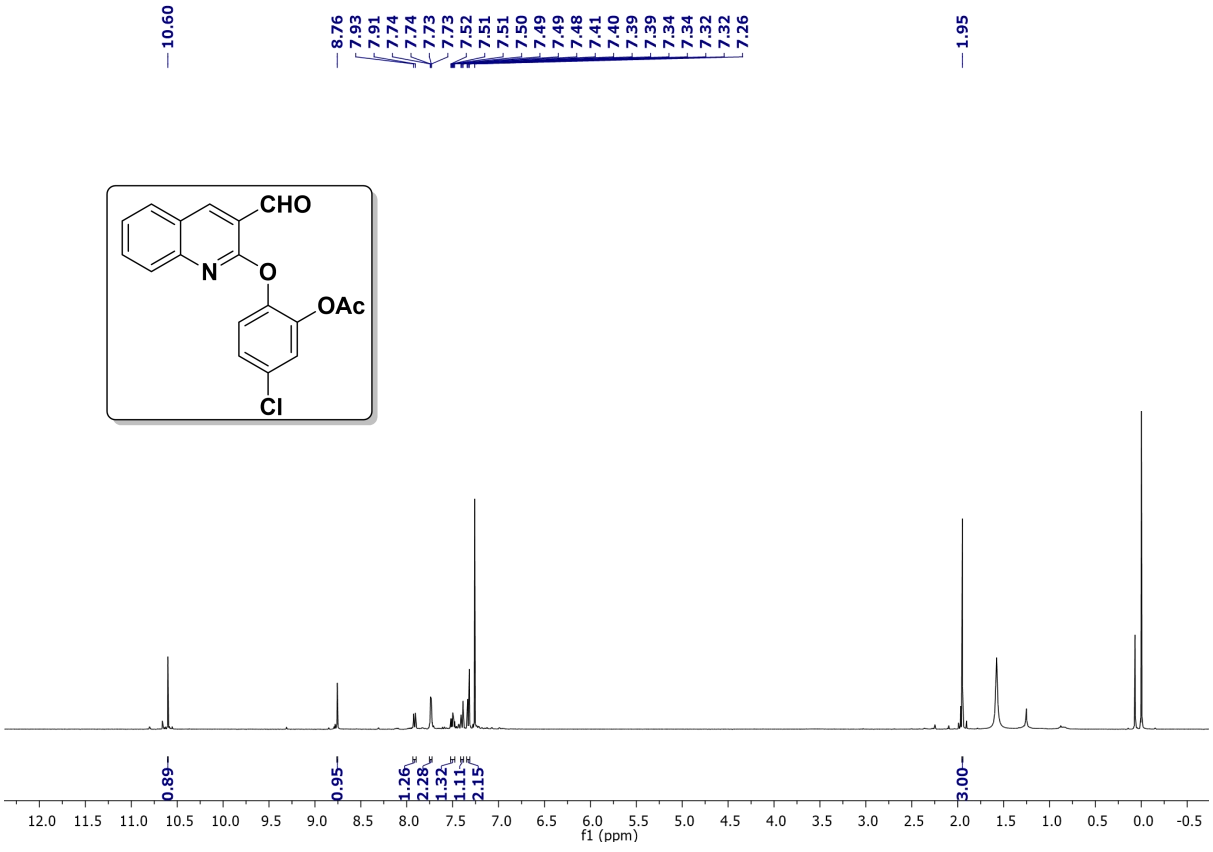


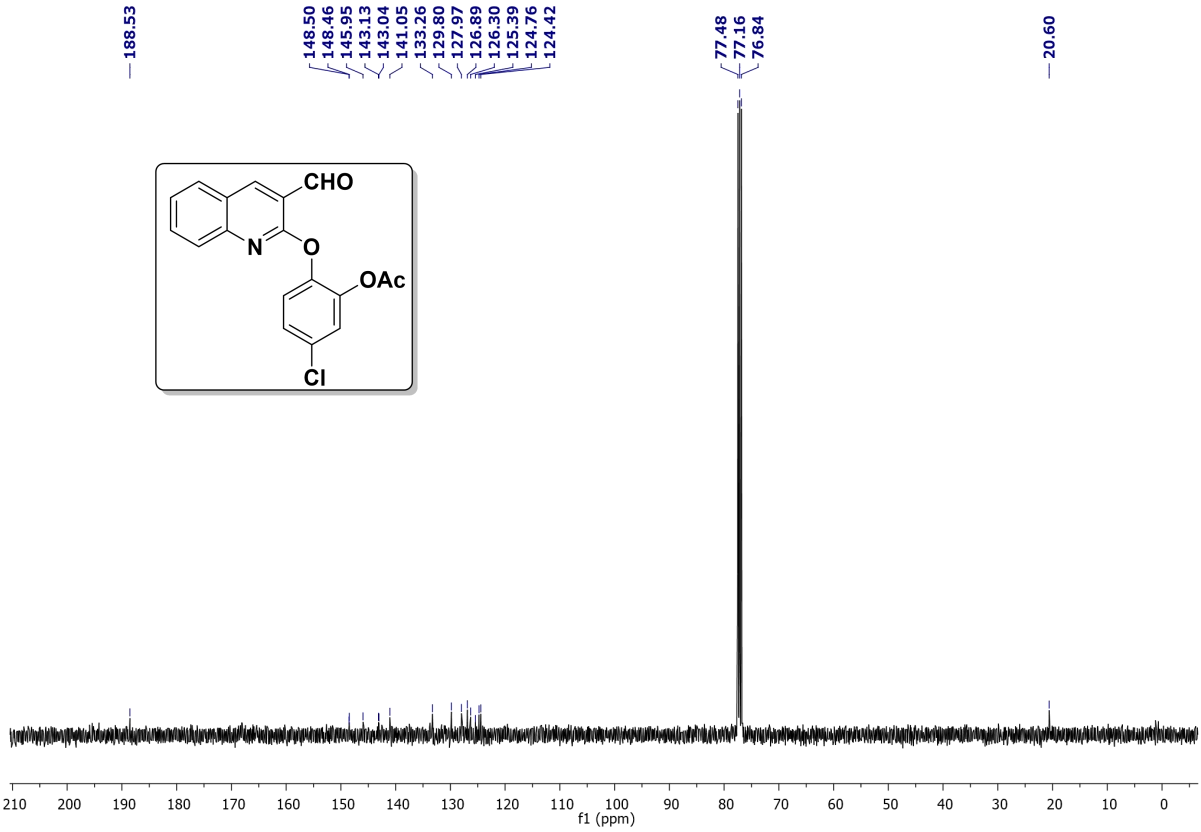
2-((3-Formylquinolin-2-yl)oxy)-3-methylphenylacetate (2g)



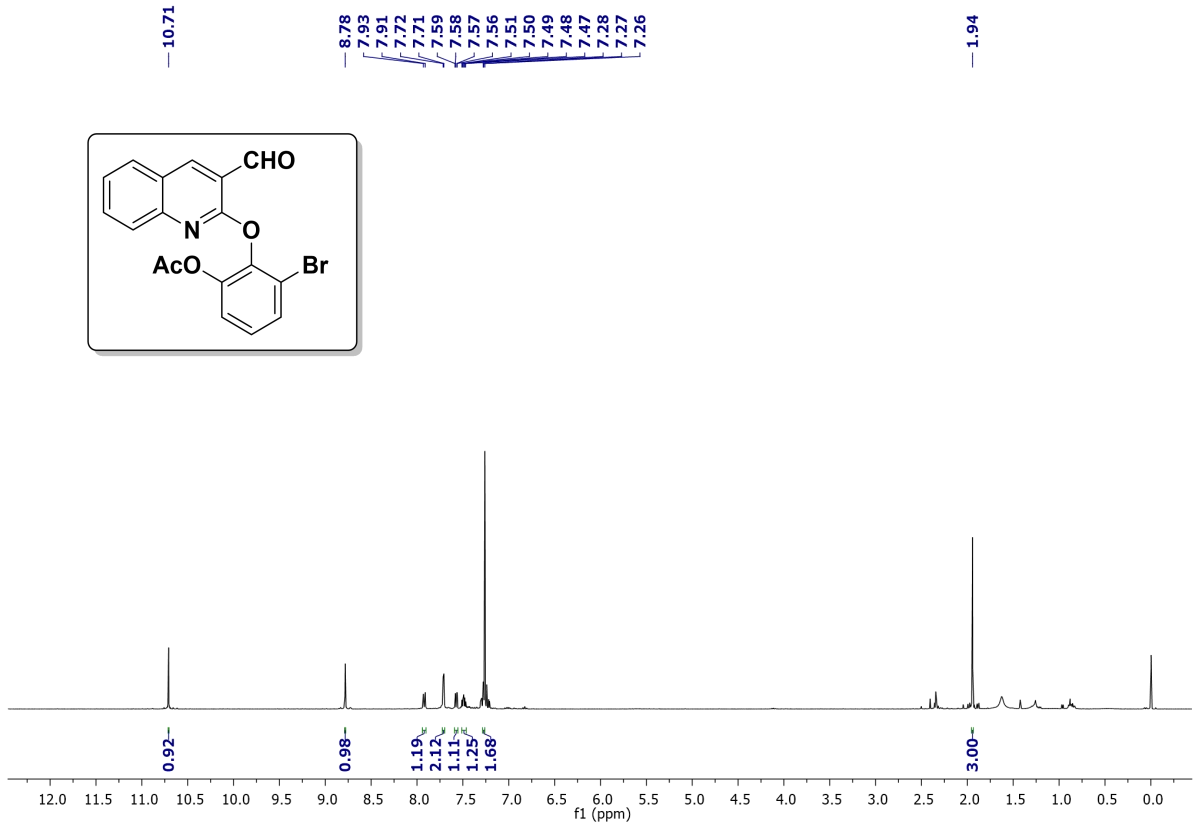


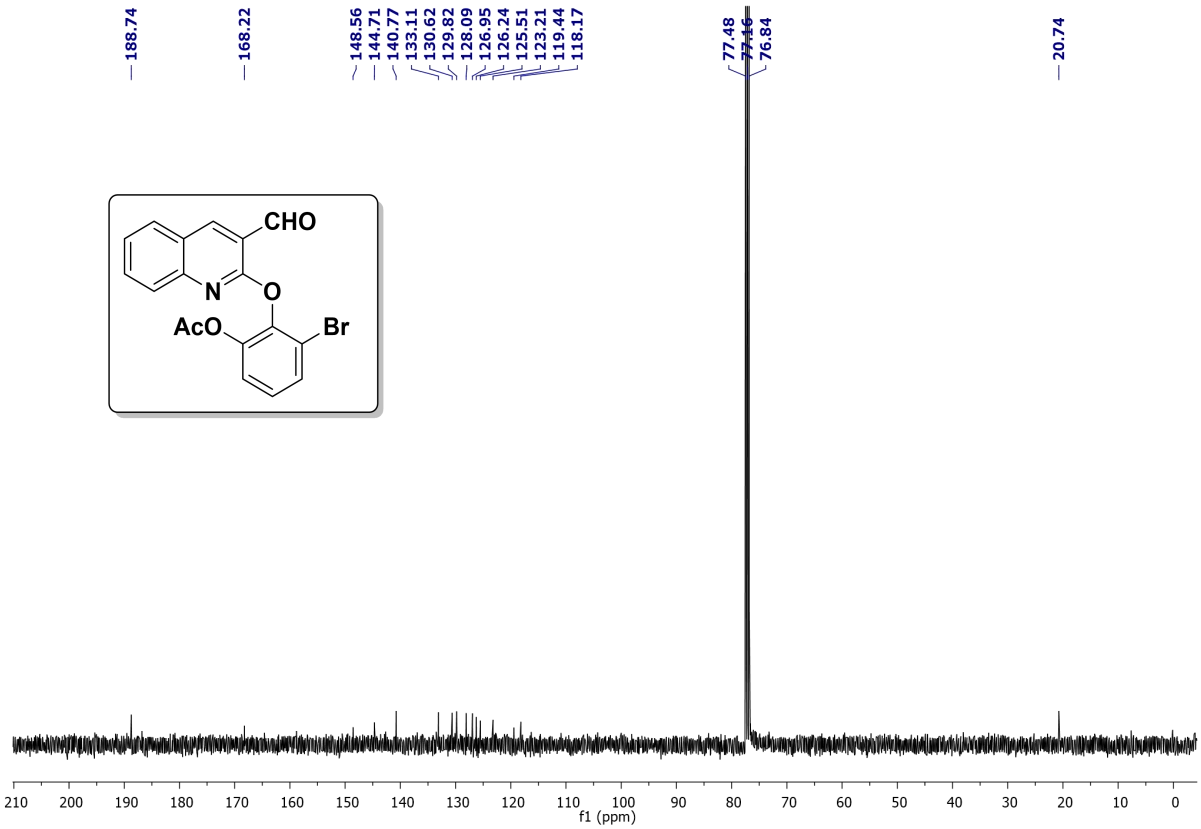
5-Chloro-2-((3-formylquinolin-2-yl)oxy)phenylacetate (2h)



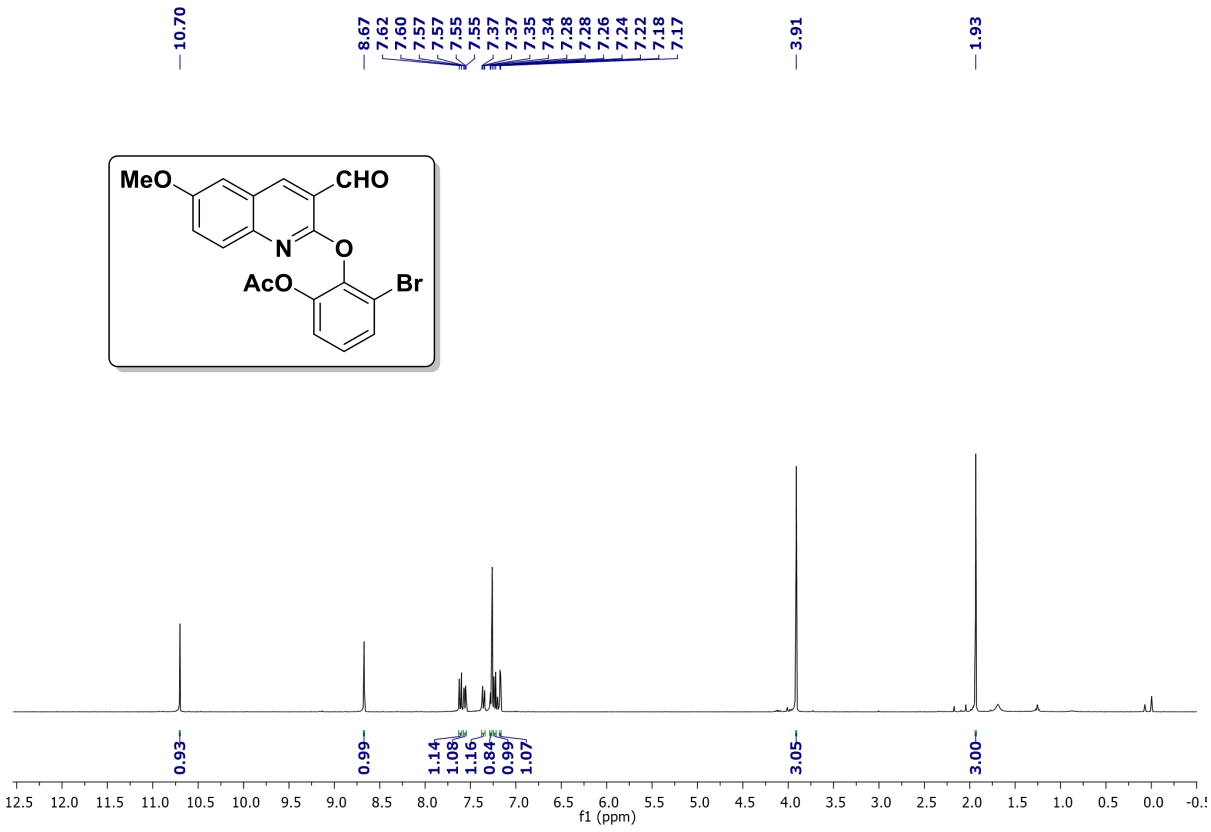


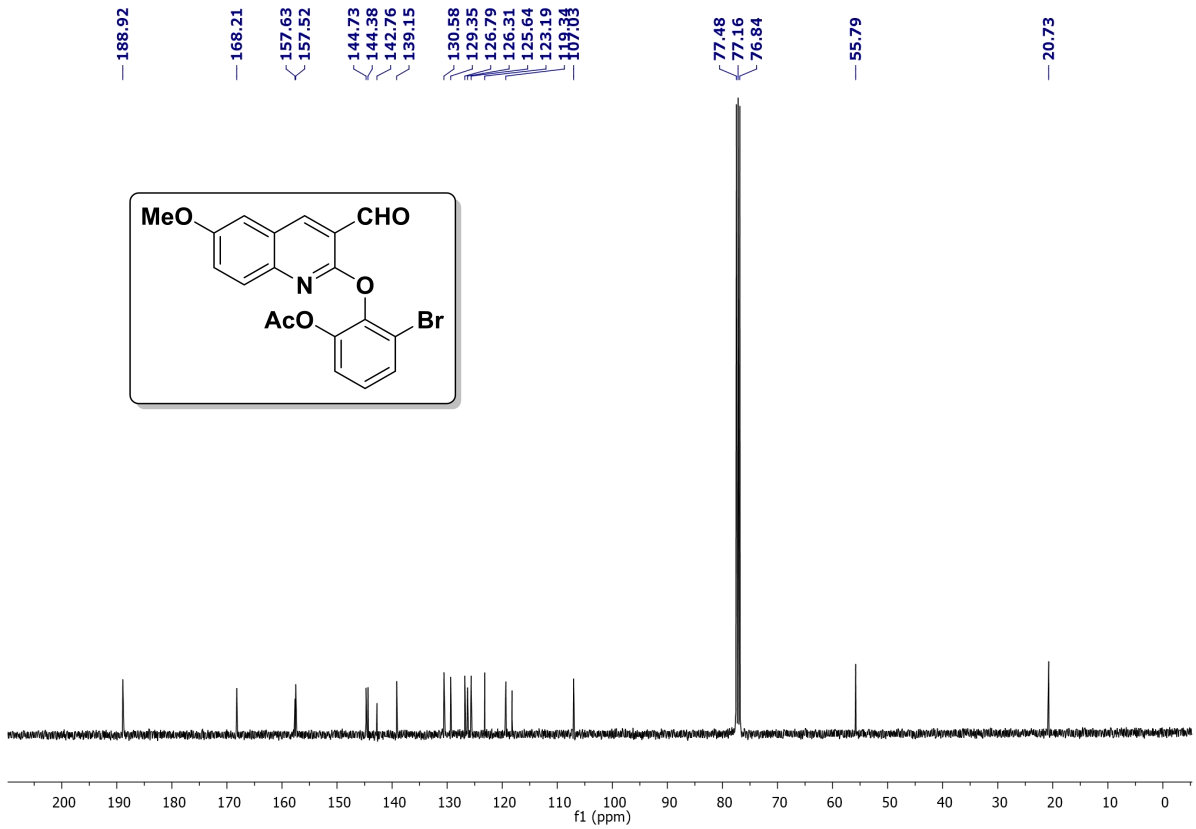
3-Bromo-2-((3-formylquinolin-2-yl)oxy)phenylacetate (2i)



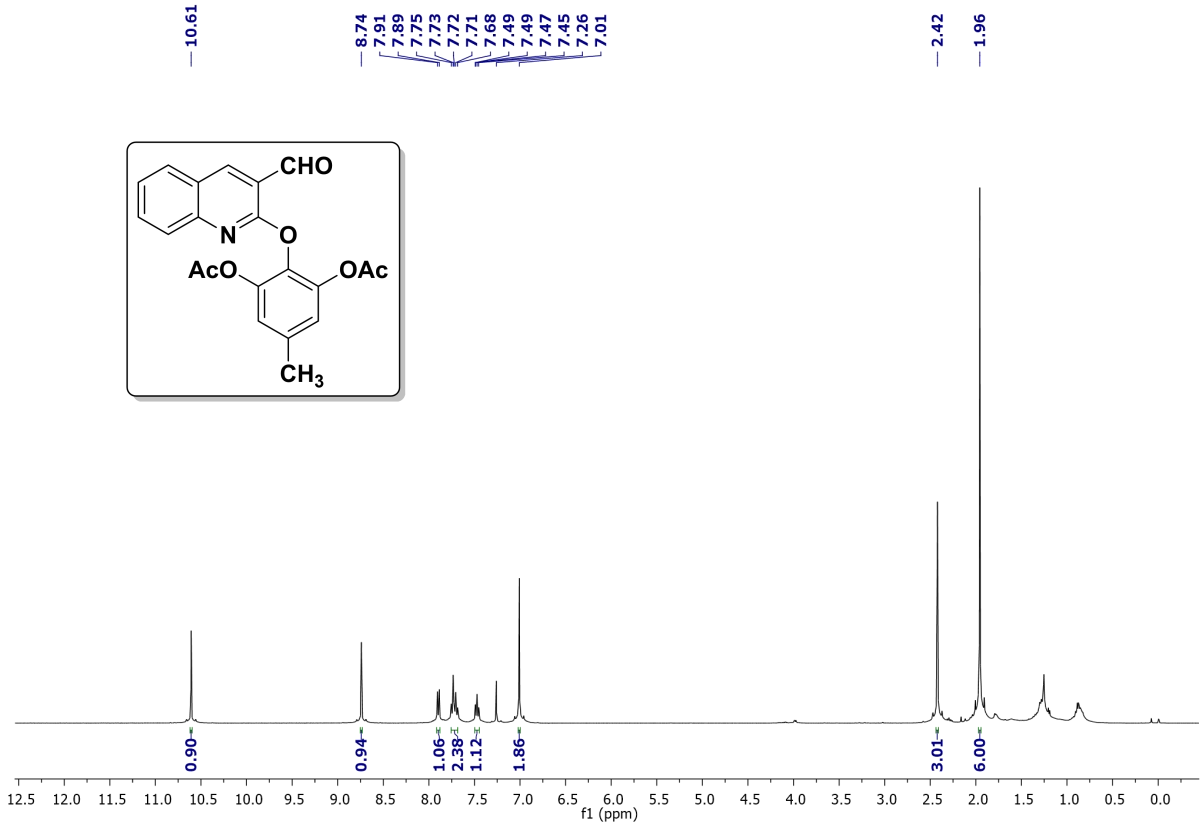


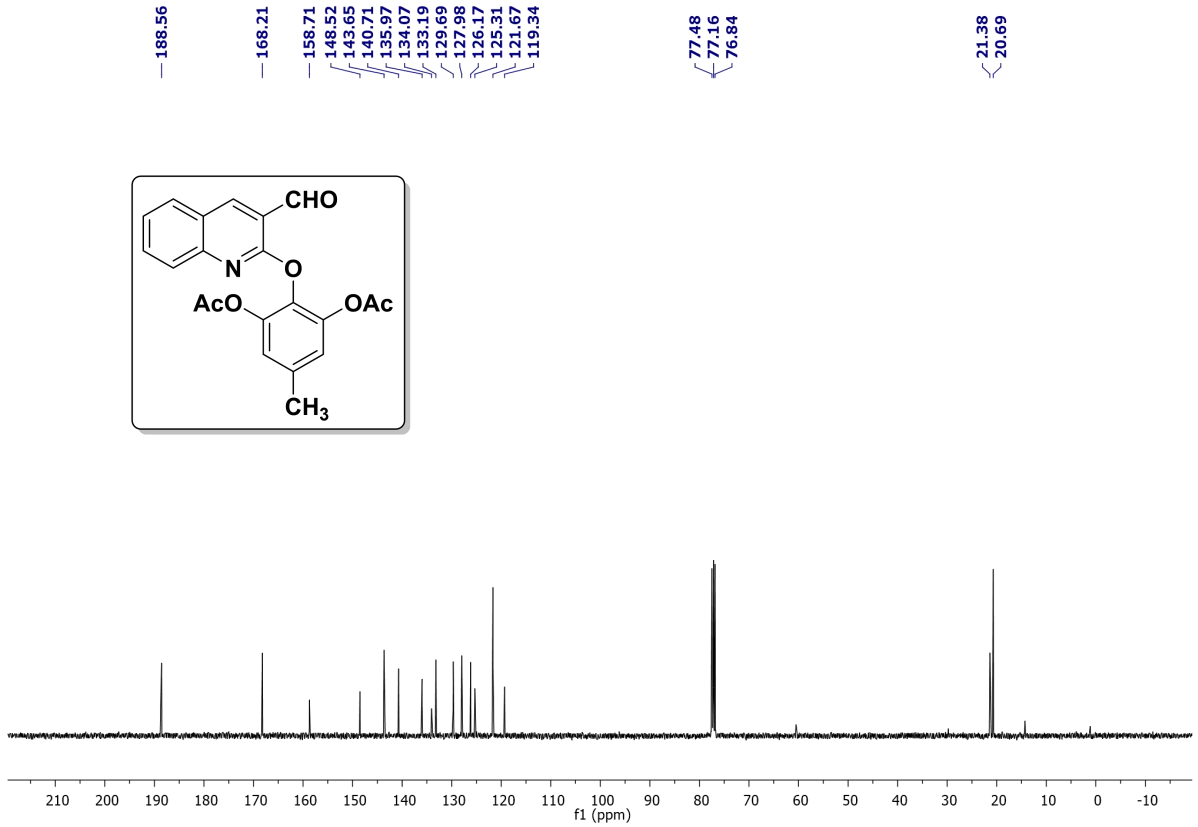
3-Bromo-2-((3-formyl-6-methoxyquinolin-2-yl)oxy)phenylacetate (2j)



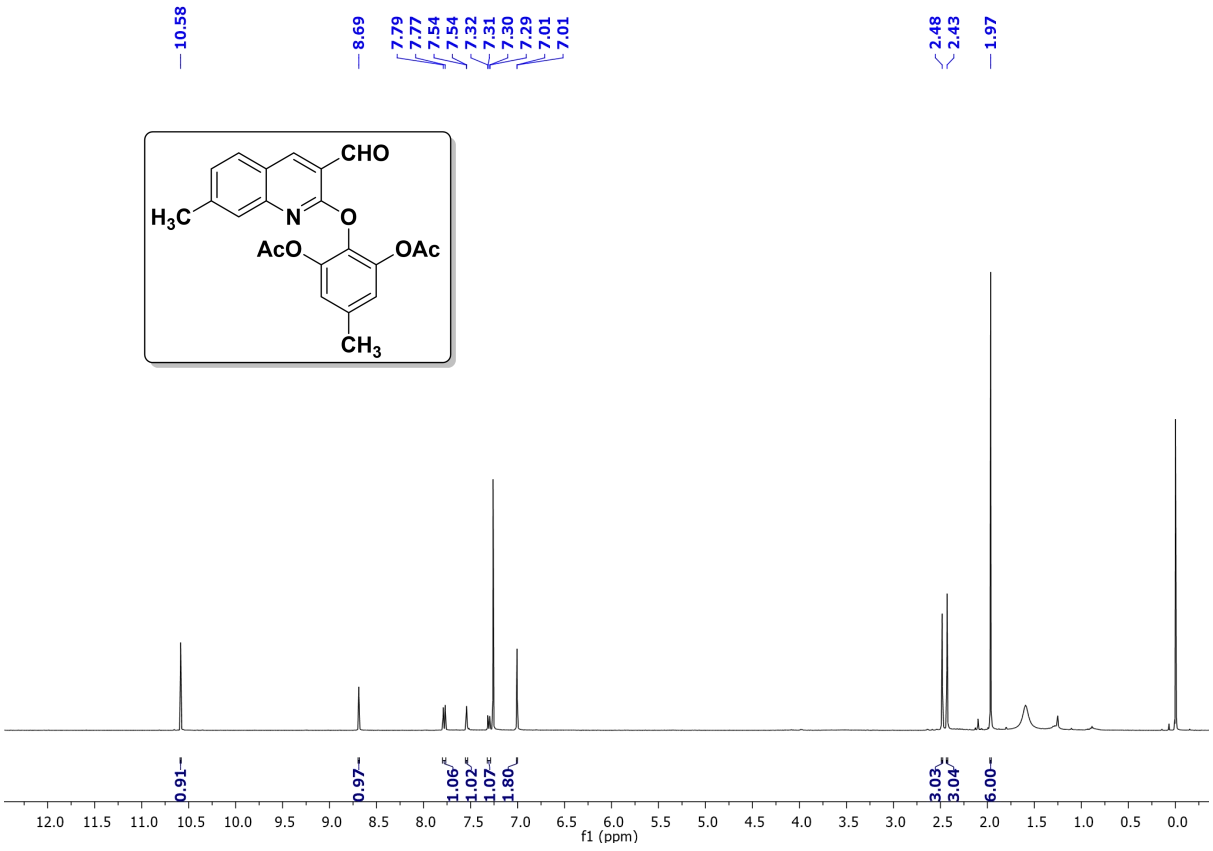


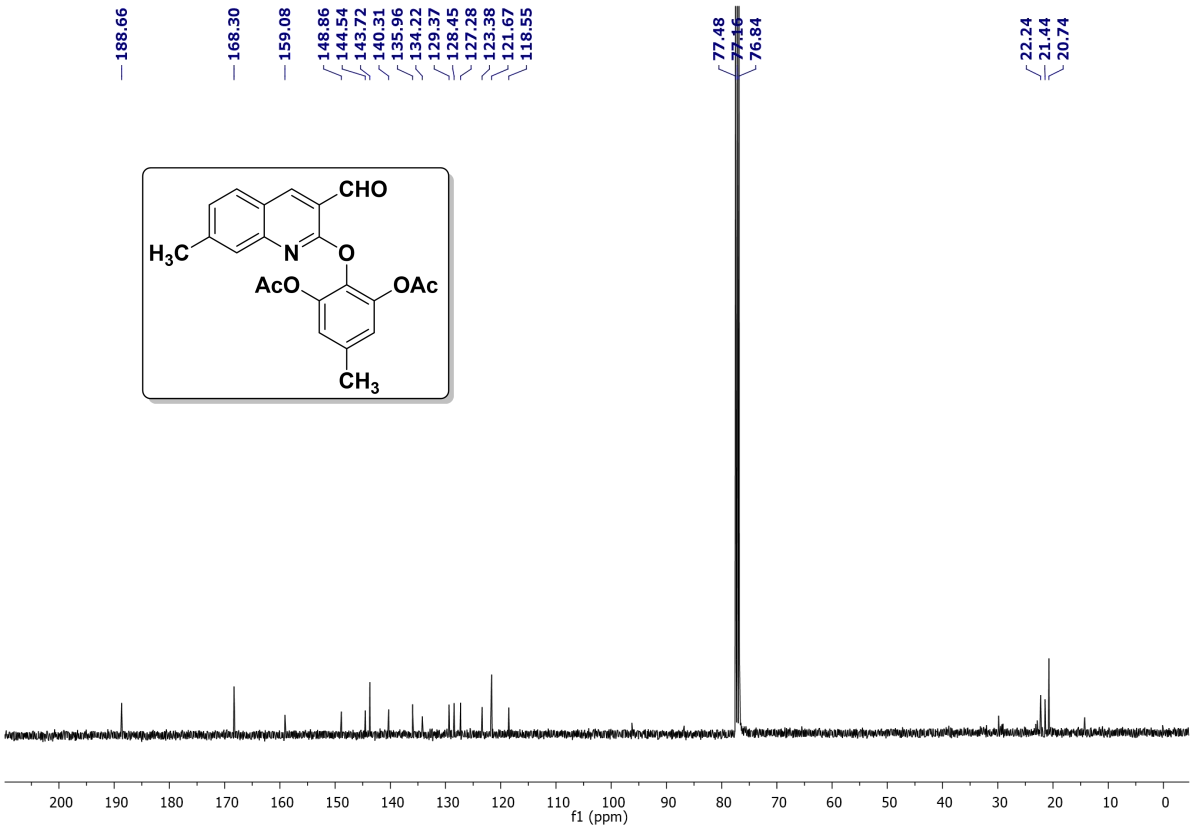
2-((3-Formylquinolin-2-yl)oxy)-5-methyl-1,3-phenylenediacetate (3a)



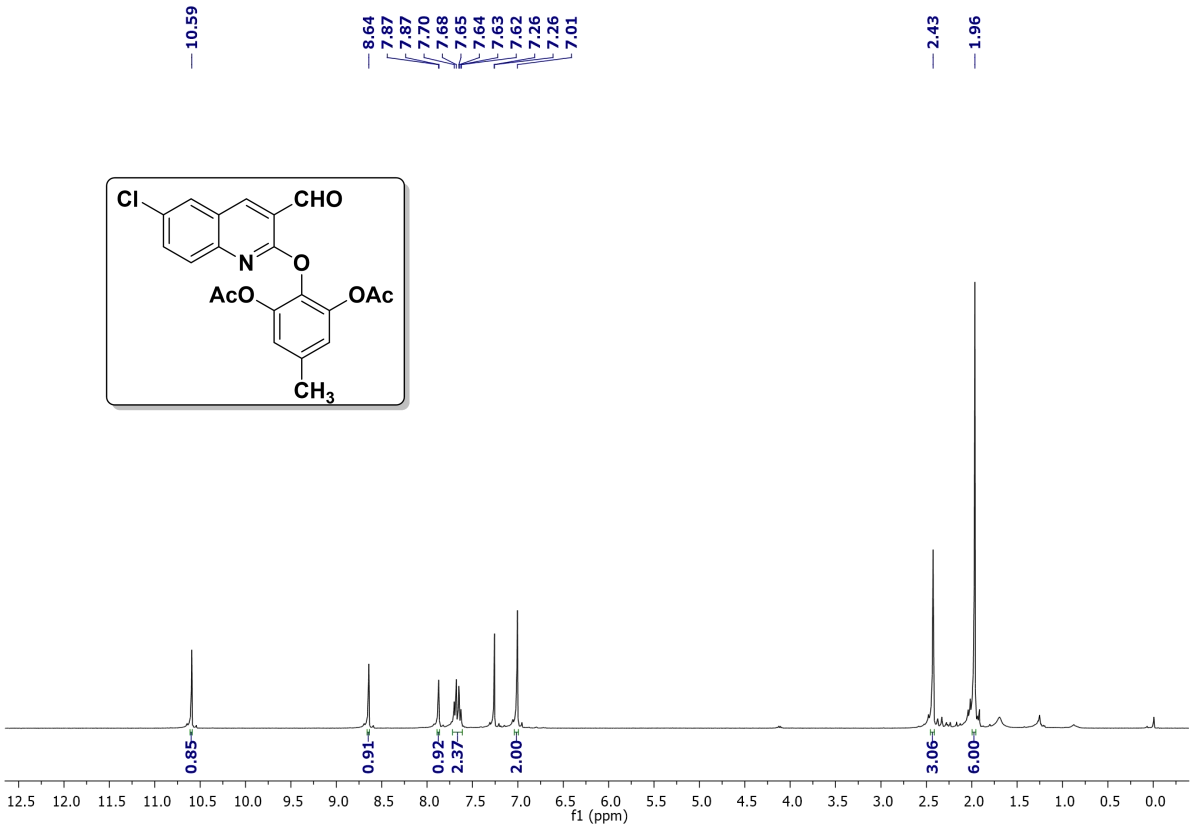


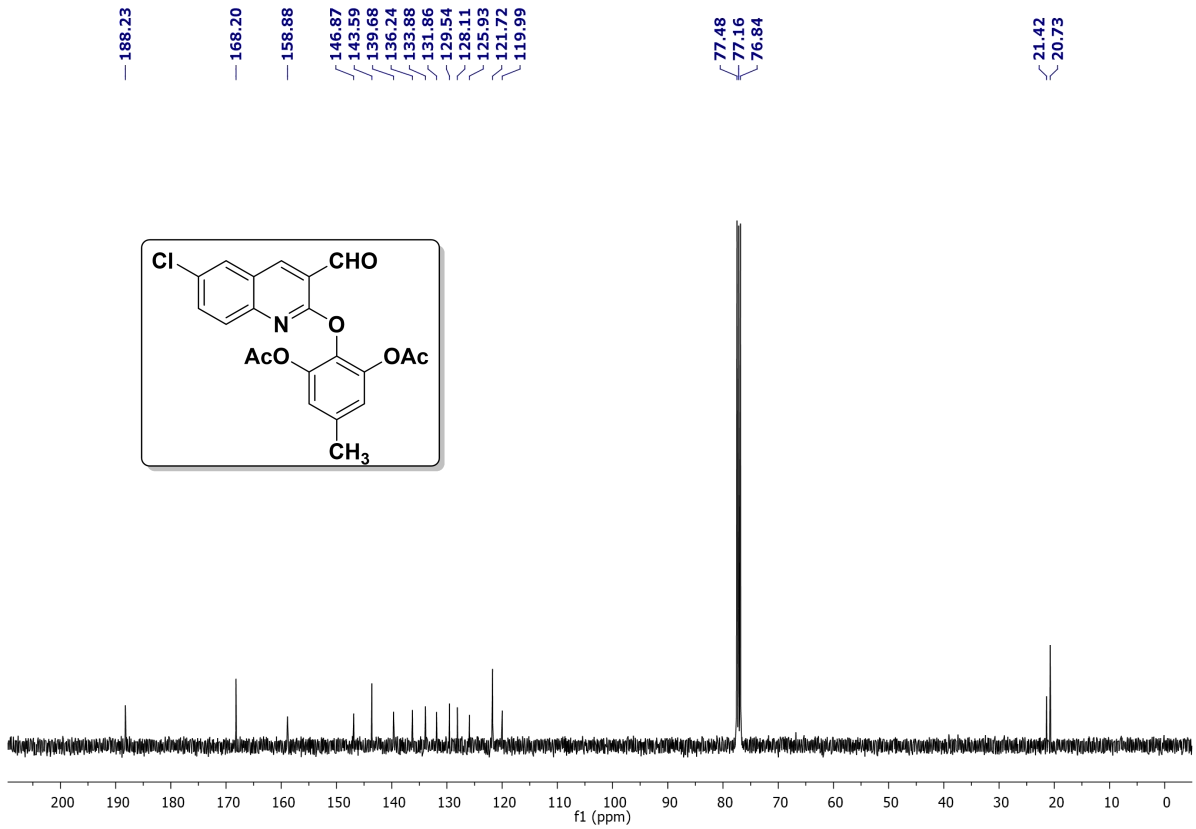
2-((3-Formyl-7-methylquinolin-2-yl)thio)-5-methyl-1,3-phenylenediacetate (3b)



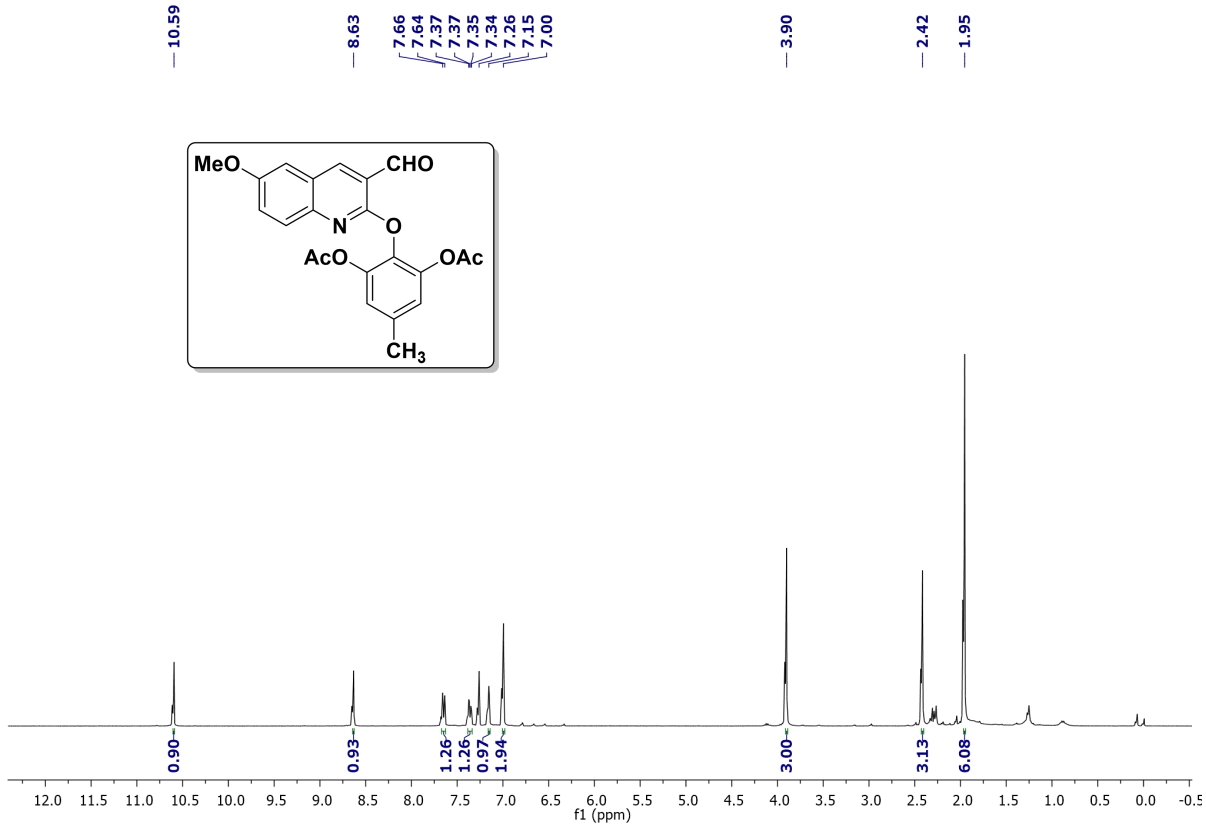


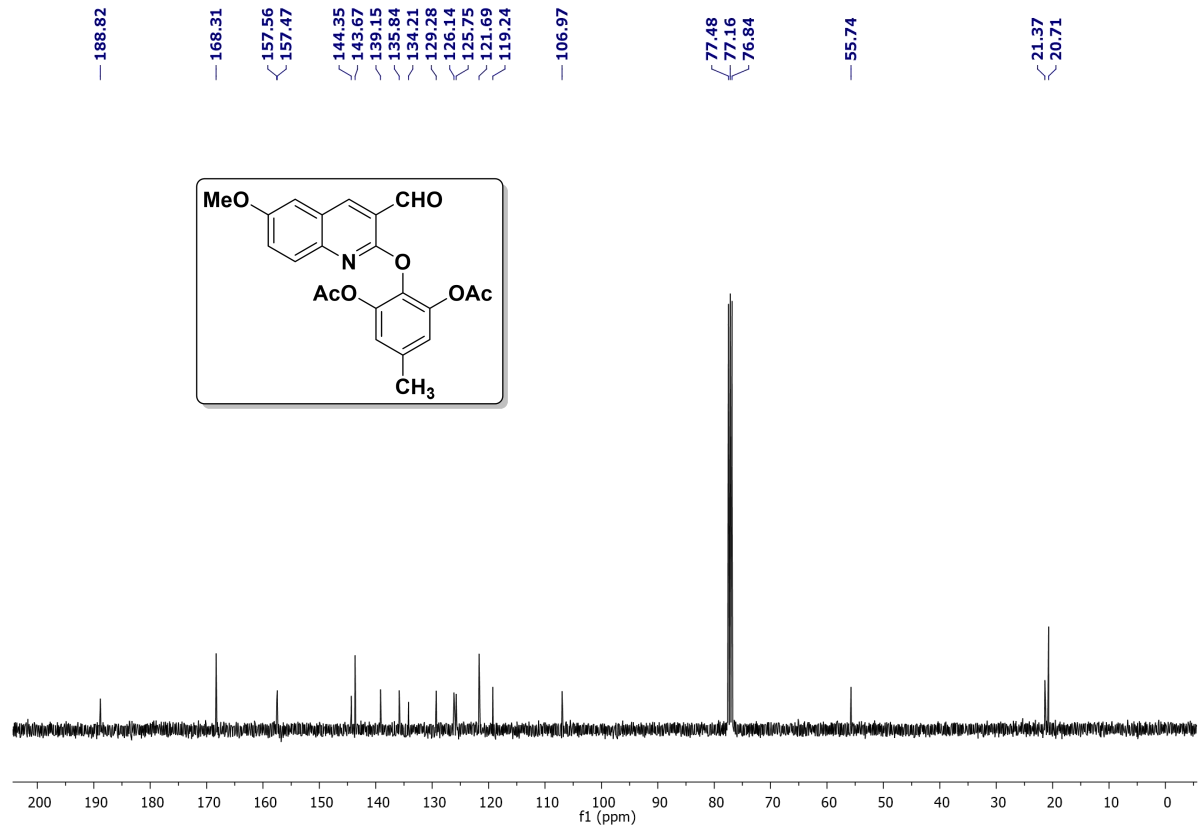
2-((6-Chloro-3-formylquinolin-2-yl)thio)-5-methyl-1,3-phenylenediacetate (3c)



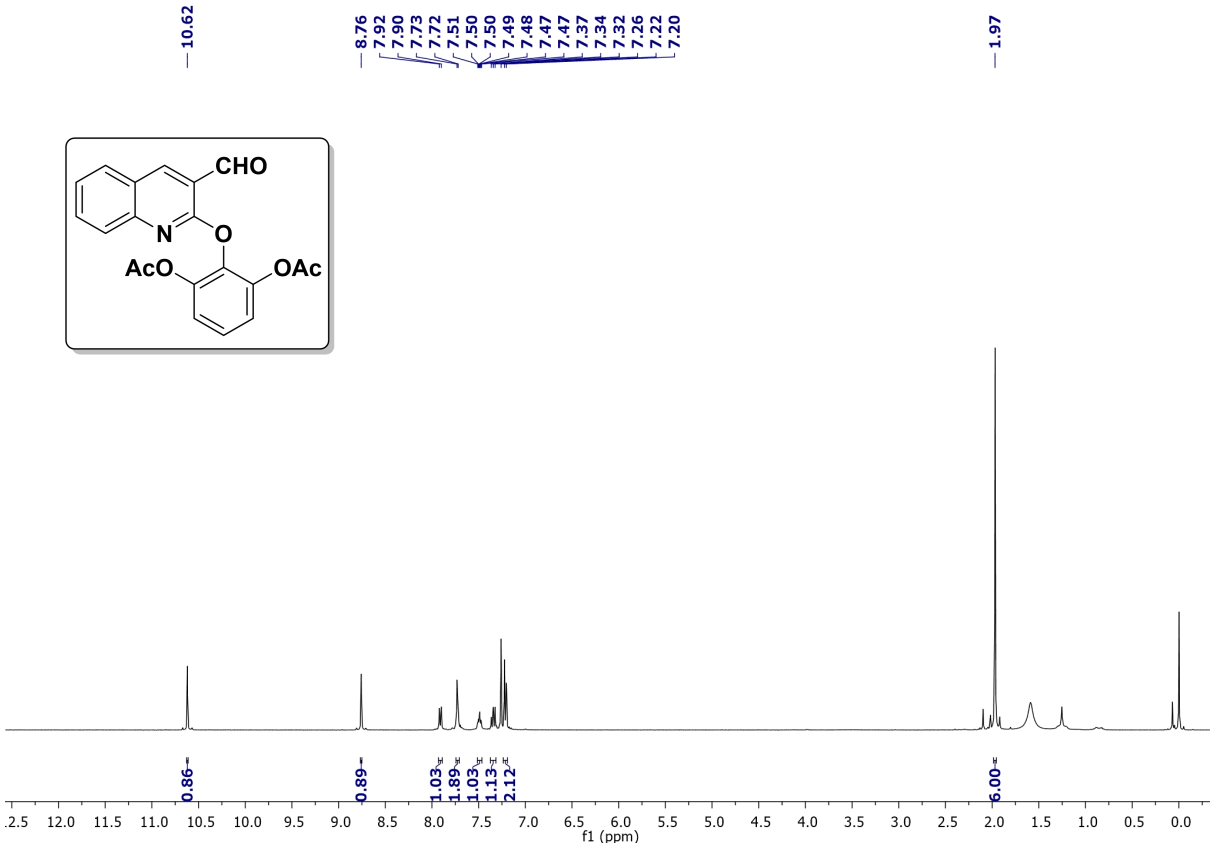


2-((3-Formyl-6-methoxyquinolin-2-yl)oxy)-5-methyl-1,3-phenylenediacetate (3d)





2-((3-Formylquinolin-2-yl)oxy)-1,3-phenylenediacetate (3e)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8.76
7.92
7.90
7.73
7.72
7.51
7.50
7.50
7.49
7.48
7.47
7.47
7.37
7.34
7.32
7.26
7.22
7.20
1.97
CHO
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O
AcO
OAc
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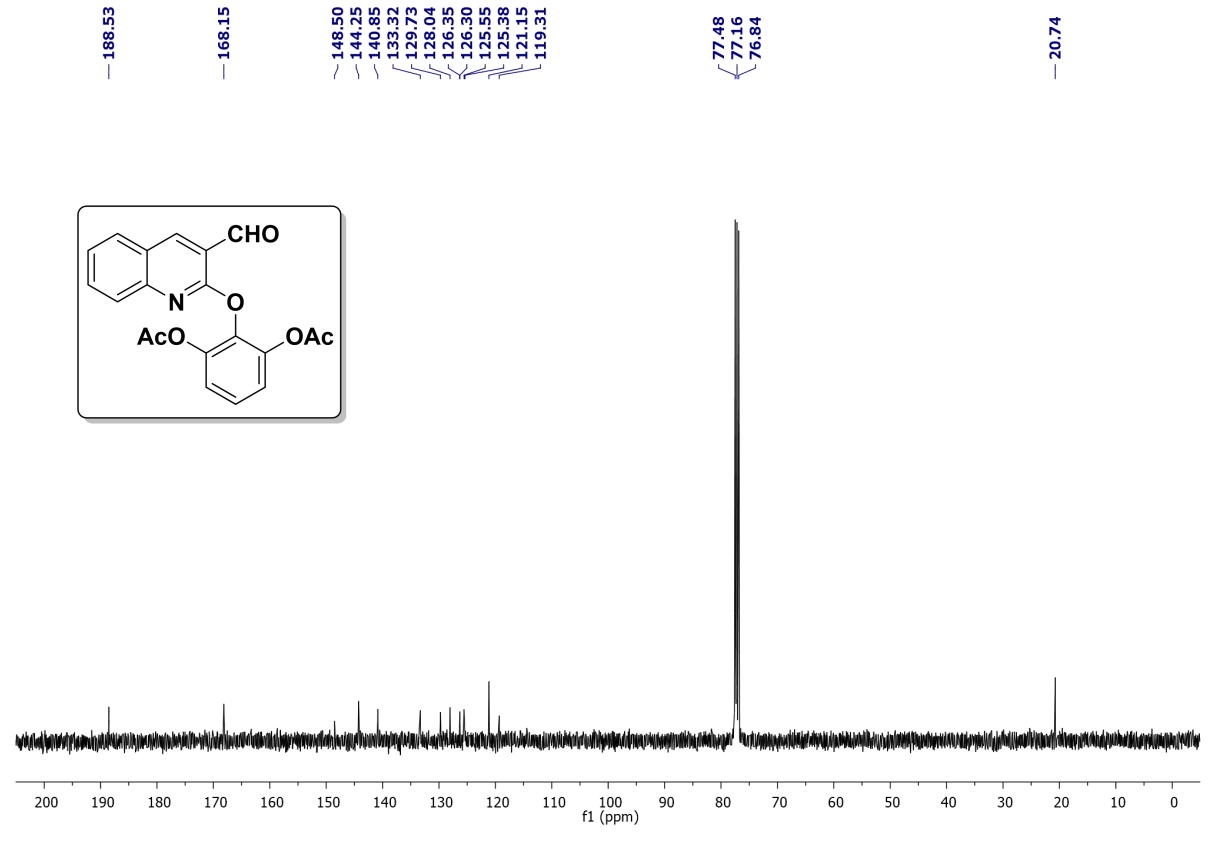
0.89
1.03
1.89
1.03
1.13
2.12
6.00
f1 (ppm)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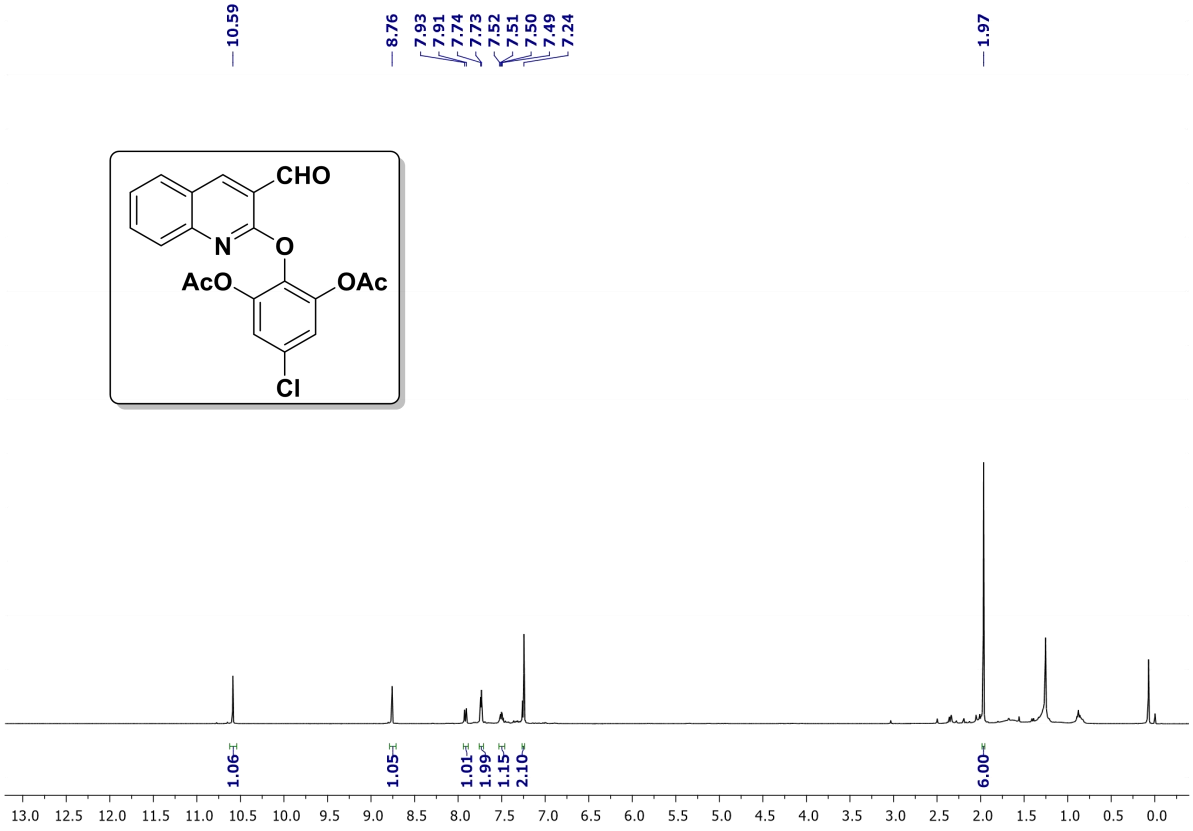
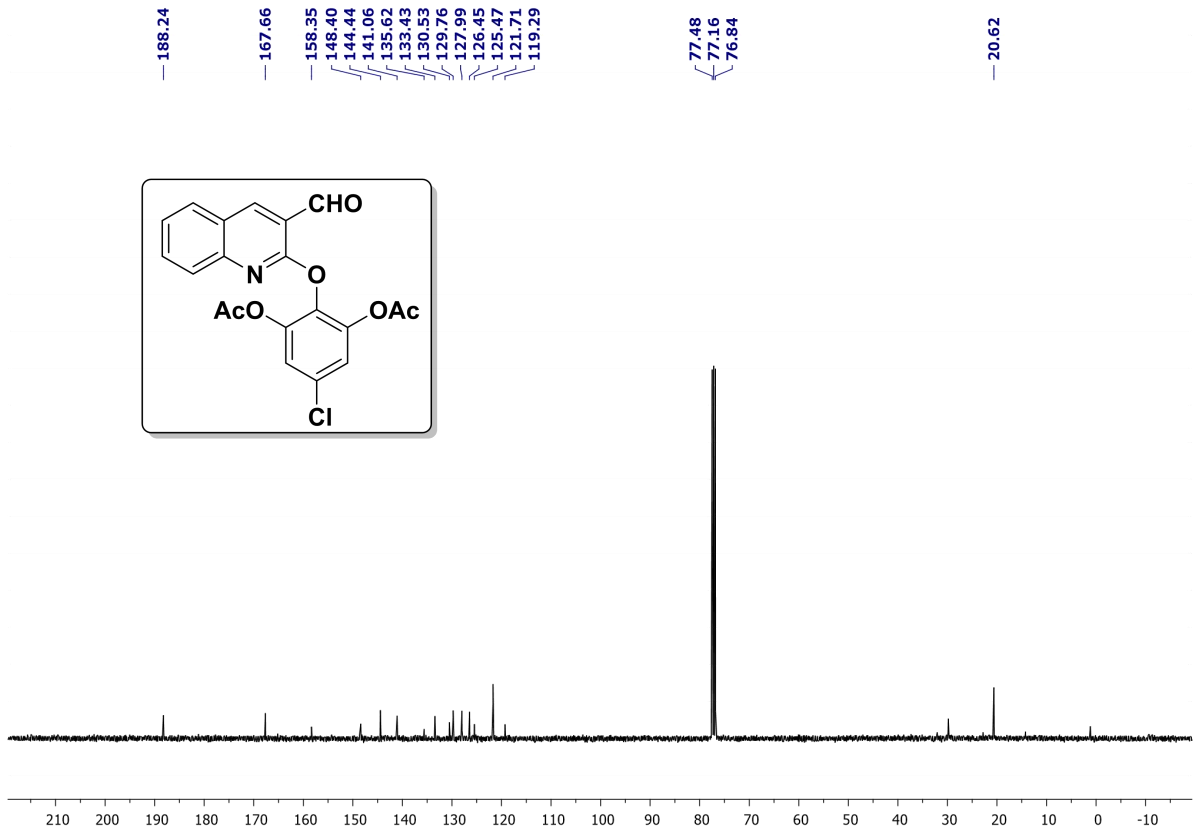
168.15
148.50
144.25
140.85
133.32
129.73
128.04
126.35
126.30
125.55
125.38
121.15
119.31
77.48
77.16
76.84
20.74
CHO
N
O
AcO
OAc
f1 (ppm)

5-Chloro-2-((3-formylquinolin-2-yl)oxy)-1,3-phenylene diacetate (3f)

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144.44
141.06
135.62
133.43
130.53
129.76
127.99
126.45
125.47
121.71
119.29
77.48
77.16
76.84
20.62
CHO
N
O
AcO
OAc
Cl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10