

Supporting Information for

Copper salts/TBAB -catalyzed chemo- and regioselectivity β -C(sp³) –H
acyloxylation of aliphatic amides

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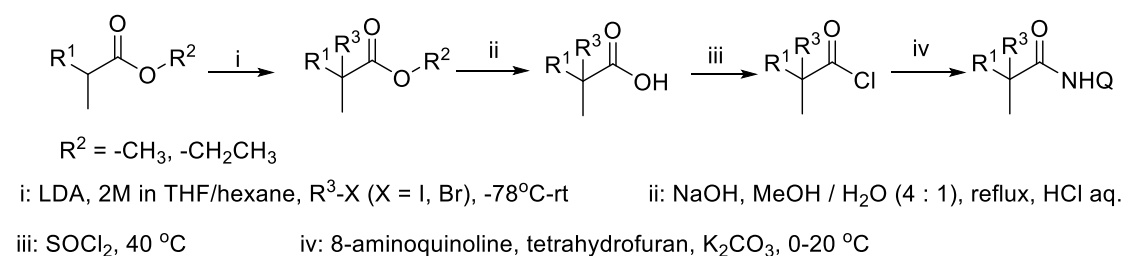
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General Information

All starting materials and reagents were commercially available and used directly without further purification. All aliphatic amides were prepared according to the literature procedures. All known products gave satisfactory analytical data by NMR spectra, corresponding to the reported literature values. In addition, unknown compounds were confirmed by HRMS. Melting points were determined using X-4 micro melting point apparatus and are uncorrected. NMR spectra were recorded at room temperature on a Bruker Avance-300, Bruker Avance-400 and Bruker Avance-500 at 300 MHz, 400 MHz and 500 MHz with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. High-resolution mass spectra (HRMS) were recorded on Agilent 6200 LC/MS TOF using ESI in positive mode.

Preparation of the Starting Materials



Scheme S1 Preparation of the starting materials

To this LDA solution (5 mL, 10 mmol), carboxylate ester (10 mmol) was added dropwise at $-78^\circ C$ and the mixture was stirred at this temperature for 1 h. Alkyl halide (15 mmol) was then added dropwise to the solution at $-78^\circ C$. After the addition, the mixture was warmed to room temperature and stirred overnight. Then the mixture was quenched with water at $0^\circ C$, and the aqueous phase was extracted with ethyl acetate (3×10 mL). The organic layer was dried over Na_2SO_4 and then evaporated in vacuo to give the crude ester.

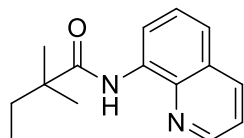
To the ester was added a solution of NaOH and methanol / H_2O (4:1, 15 mL). The mixture was stirred and reflux at $110^\circ C$ for 8 h. Then the pH of the mixture was adjusted to 3-4 with HCl. The mixture was then saturated with NaCl and extracted with ethyl acetate (3×10 mL). The combined organic layers was dried over Na_2SO_4 , and then evaporated in vacuo to give the crude carboxylic acid, which was used directly for the next step without further purification.

Thionyl chloride (10 mL) was added slowly to a stirred solution of the carboxylic

acid. The mixture was stirred for 6 h at 40 °C and evaporated in vacuo to give the crude acid chloride, which was used directly for the next step without further purification. The acid chloride was added dropwise to a solution of 8-aminoquinoline (1.44 g, 10 mmol) and K₂CO₃ (1.66 g, 12 mmol) in tetrahydrofuran (10 mL). The mixture was stirred overnight at room temperature. The reaction mixture quenched with saturated sodium chloride and diluted with ethyl acetate. The aqueous phase was extracted with ethyl acetate (3×10 mL). The organic layer was dried over Na₂SO₄. After concentration, the resulting residue was purified by flash chromatography on silica gel with petroleum ether: ethyl acetate (10:1) as eluent to afford corresponding 8-aminoquinolinyl amides.

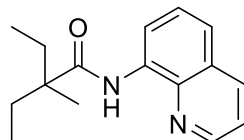
Characterization Data of Some Starting Materials

2,2-Dimethyl-N-(quinolin-8-yl)butanamide 1a



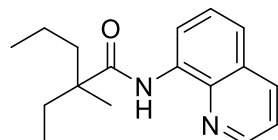
White solid (2.23 g, 92%). Mp = 39.0-40.1 °C. ¹H NMR (500 MHz, CDCl₃): δ 10.24 (s, 1H), 8.85-8.82 (m, 1H), 8.81 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.56-7.51 (m, 1H), 7.51-7.47 (m, 1H), 7.47-7.42 (m, 1H), 1.77 (q, *J* = 7.5 Hz, 2H), 1.40 (s, 6H), 0.96 (t, *J* = 7.5 Hz, 3H).

2-Ethyl-2-methyl-N-(quinolin-8-yl)butanamide 1b



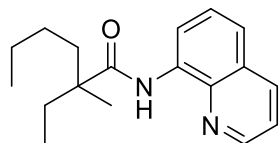
Yellow liquid (1.56 g, 61%). ¹H NMR (500 MHz, CDCl₃): δ 10.22 (s, 1H), 8.85-8.79 (m, 2H), 8.17-8.11 (m, 1H), 7.56-7.50 (m, 1H), 7.50-7.40 (m, 2H), 1.96-1.83 (m, 2H), 1.70-1.58 (m, 2H), 1.35 (s, 3H), 0.94 (t, *J* = 7.5 Hz, 6H).

2-Ethyl-2-methyl-N-(quinolin-8-yl)pentanamide 1c



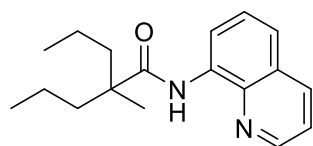
Yellow liquid (1.75 g, 65%). ¹H NMR (500 MHz, CDCl₃): δ 10.23 (s, 1H), 8.86-8.76 (m, 2H), 8.18-8.08 (m, 1H), 7.55-7.50 (m, 1H), 7.49-7.45 (m, 1H), 7.45-7.41 (m, 1H), 1.95-1.85 (m, 1H), 1.81 (td, *J* = 13.0, 4.5 Hz, 1H), 1.69-1.60 (m, 1H), 1.56 (td, *J* = 12.5, 5.0 Hz, 1H), 1.49-1.38 (m, 1H), 1.37 (s, 3H), 1.35-1.24 (m, 1H), 0.97-0.89 (m, 6H).

2-Ethyl-2-methyl-N-(quinolin-8-yl)hexanamide 1d



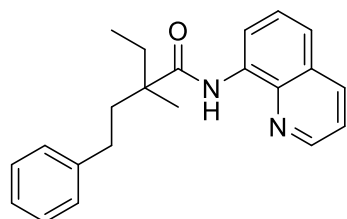
Yellow liquid (1.85 g, 65%). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.23 (s, 1H), 8.87-8.77 (m, 2H), 8.20-8.09 (m, 1H), 7.55-7.50 (m, 1H), 7.50-7.46 (m, 1H), 7.46-7.41 (m, 1H), 1.94-1.87 (m, 1H), 1.87-1.79 (m, 1H), 1.68-1.61 (m, 1H), 1.61-1.53 (m, 1H), 1.37 (s, 3H), 1.35-1.22 (m, 4H), 0.94 (t, $J = 7.5$ Hz, 3H), 0.88 (t, $J = 7.0$ Hz, 3H).

2-Methyl-2-propyl-N-(quinolin-8-yl)pentanamide 1f



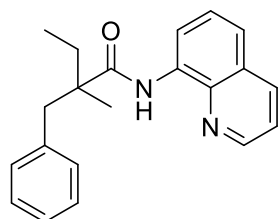
White solid (1.70 g, 60%). Mp = 69.2-71.4 °C. $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.23 (s, 1H), 8.85-8.75 (m, 2H), 8.16 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.56-7.51 (m, 1H), 7.50-7.47 (m, 1H), 7.47-7.42 (m, 1H), 1.81 (td, $J = 13.0, 4.5$ Hz, 2H), 1.56 (td, $J = 13.0, 4.5$ Hz, 2H), 1.46-1.38 (m, 2H), 1.38 (s, 3H), 1.36-1.26 (m, 2H), 0.92 (t, $J = 7.5$ Hz, 6H),

2-Ethyl-2-methyl-4-phenyl-N-(quinolin-8-yl)butanamide 1i



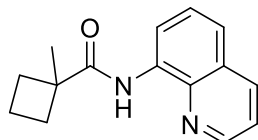
Yellow liquid (1.89g, 57%). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.28 (s, 1H), 8.87-8.80 (m, 2H), 8.21-8.13 (m, 1H), 7.58-7.53 (m, 1H), 7.52-7.48 (m, 1H), 7.48-7.43 (m, 1H), 7.26-7.18 (m, 4H), 7.17-7.12 (m, 1H), 2.75-2.58 (m, 2H), 2.18 (td, $J = 13.0, 4.5$ Hz, 1H), 2.00-1.91 (m, 1H), 1.88 (td, $J = 13.0, 5.0$ Hz, 1H), 1.76-1.65 (m, 1H), 1.47 (s, 3H), 0.98 (t, $J = 7.5$ Hz, 3H).

3-Benzyl-2-methyl-N-(quinolin-8-yl)butanamide 1j



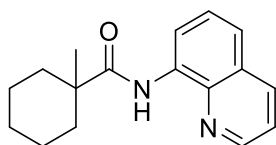
White solid (1.84 g, 58%). Mp = 71.8-74.4 °C. $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.13 (s, 1H), 8.84 (dd, $J = 7.5, 1.5$ Hz, 1H), 8.74 (dd, $J = 4.0, 1.5$ Hz, 1H), 8.15 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.58-7.53 (m, 1H), 7.52-7.48 (m, 1H), 7.45-7.40 (m, 1H), 7.21-7.14 (m, 4H), 7.14-7.09 (m, 1H), 3.30-3.20 (m, 1H), 2.88-2.77 (m, 1H), 2.09-2.00 (m, 1H), 1.64-1.56 (m, 1H), 1.34 (s, 3H), 0.99 (t, $J = 7.5$ Hz, 3H).

1-Methyl-N-(quinolin-8-yl)cyclobutane-1-carboxamide **1k**



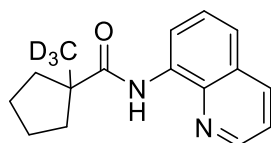
Yellow liquid (1.27 g, 53%). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 9.99 (s, 1H), 8.85-8.77 (m, 2H), 8.16 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.57-7.52 (m, 1H), 7.51-7.47 (m, 1H), 7.47-7.43 (m, 1H), 2.74-2.62 (m, 2H), 2.12-1.98 (m, 3H), 1.96-1.87 (m, 1H), 1.64 (s, 3H).

1-Methyl-N-(quinolin-8-yl)cyclohexane-1-carboxamide **1o**



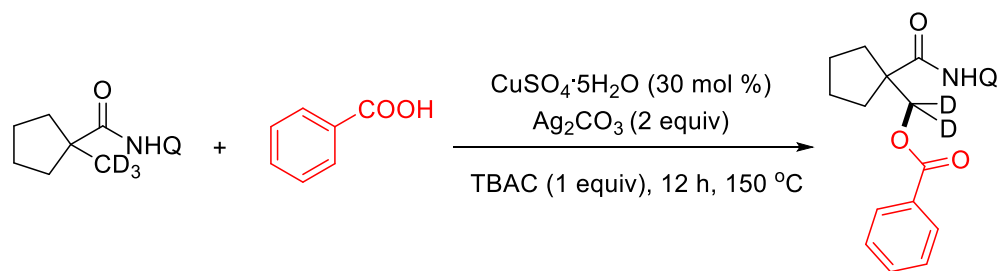
Yellow liquid (1.34 g, 50%). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.29 (s, 1H), 8.93-8.68 (m, 2H), 8.25-8.10 (m, 1H), 7.56-7.51 (m, 1H), 7.50-7.47 (m, 1H), 7.46-7.42 (m, 1H), 2.26-2.13 (m, 2H), 1.70-1.63 (m, 2H), 1.62-1.56 (m, 2H), 1.57-1.49 (m, 3H), 1.47-1.38 (m, 1H), 1.36 (s, 3H).

1-(Methyl- d_3)-N-(quinolin-8-yl)cyclopentane-1-carboxamide [D_3]-**1l**



Yellow liquid (1.44 g, 56%). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 10.20 (s, 1H), 8.84-8.74 (m, 2H), 8.19-8.10 (m, 1H), 7.55-7.50 (m, 1H), 7.49-7.45 (m, 1H), 7.45-7.41 (m, 1H), 2.34-2.24 (m, 2H), 1.88-1.75 (m, 4H), 1.74-1.64 (m, 2H).

Deuteration Experiments

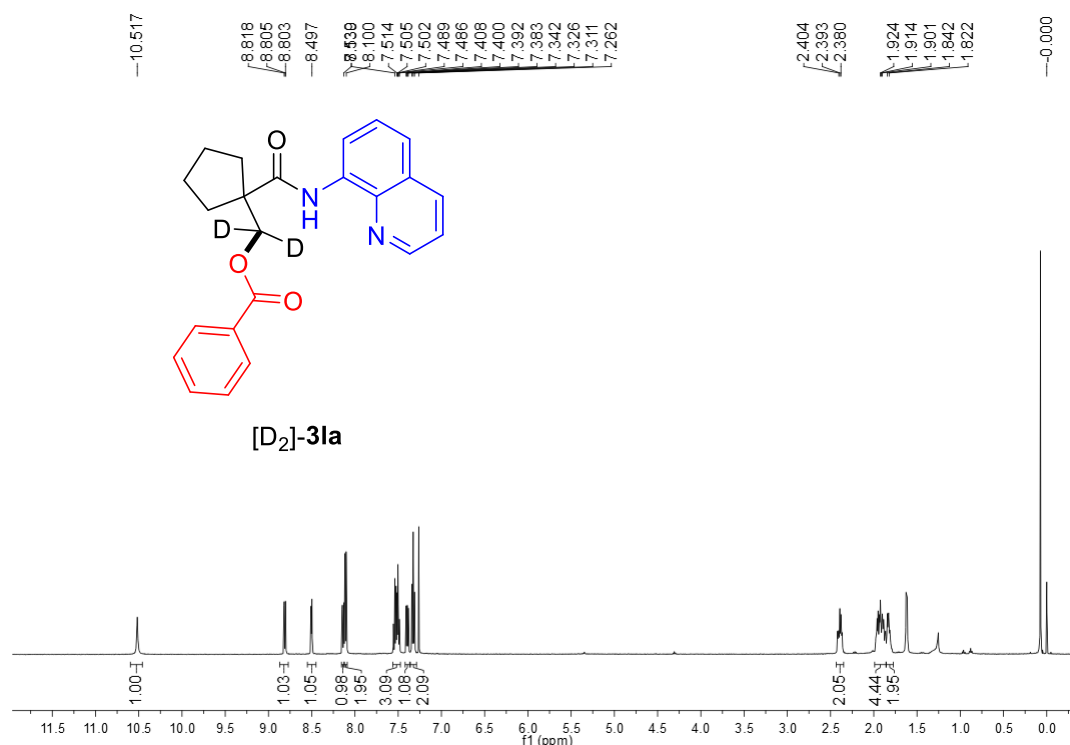


[D₃]-1I
0.1 mmol, >99% D **2a**, 0.2 mmol

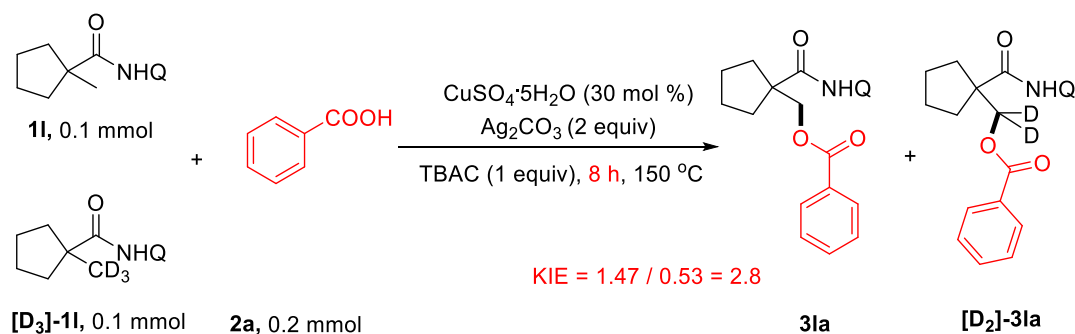
[D₂]-3Ia, 52%, >99% D

To a 10 mL reaction tube was added amide **[D₃]-1I** (0.1 mmol), acid **2a** (0.2 mmol), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (7.5 mg, 30 mol %), Ag_2CO_3 (55.1 mg, 2 equiv), TBAC (27.8 mg, 1 equiv) and toluene / DMF (1 mL / 1 mL) in air. The mixture was stirred at 150 °C for 12 h. The reaction mixture was then cooled to room temperature, diluted with ethyl acetate and quenched with saturated sodium chloride. The aqueous phase was extracted with ethyl acetate (3×10 mL). The organic layer was dried over Na_2SO_4 . After concentration, the resulting residue was purified by flash chromatography to afford the product. The product was analyzed by ^1H NMR.

Figure S1. ^1H NMR Spectra of **[D₂]-3Ia**

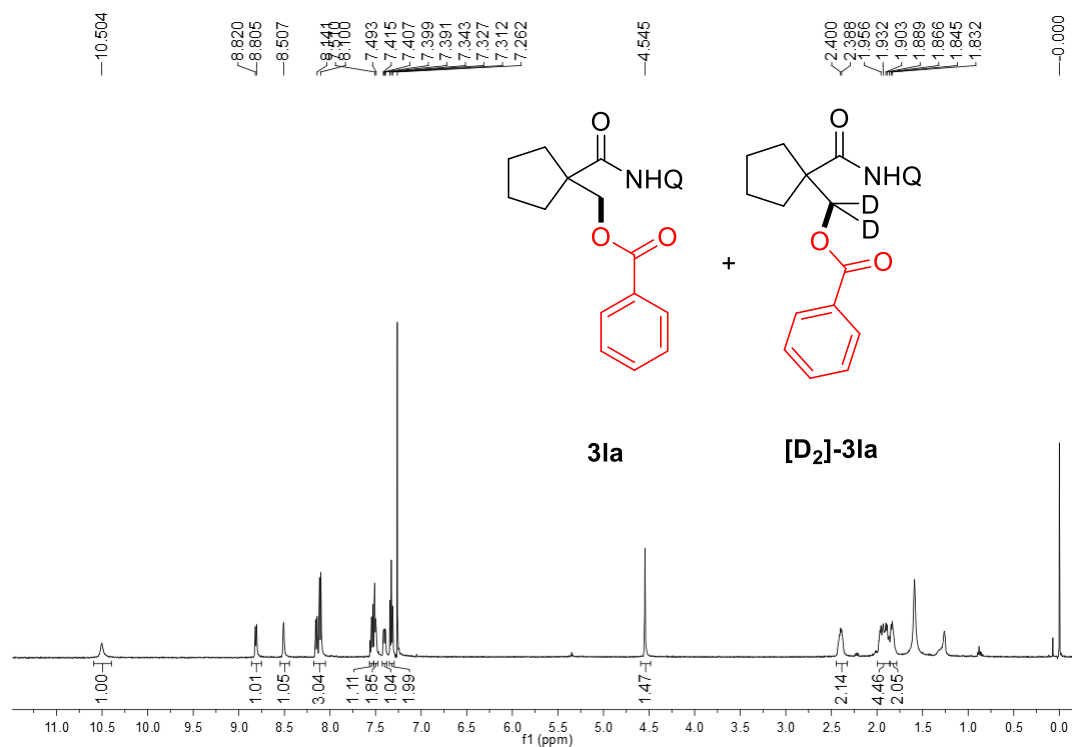


KIE Studies



To a 10 mL reaction tube was added amide $[\text{D}_3]\text{-1I}$ (0.1 mmol), 1I (0.1 mmol), acid 2a (0.2 mmol), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (7.5 mg, 30 mol %), Ag_2CO_3 (55.1 mg, 2 equiv), TBAC (27.8 mg, 1 equiv) and toluene / DMF (1 mL / 1 mL) in air. The mixture was stirred at 150 °C for 8 h. The reaction mixture was then cooled to room temperature, diluted with ethyl acetate and quenched with saturated sodium chloride. The aqueous phase was extracted with ethyl acetate (3×10 mL). The organic layer was dried over Na_2SO_4 . After concentration, the resulting residue was purified by flash chromatography to afford the product. The product was analyzed by ^1H NMR.

Figure S2. ^1H NMR Spectra of $[\text{D}_2]\text{-3Ia}$



Copies of ^1H and ^{13}C NMR Spectra

Figure S3. ^1H NMR Spectra of 1a

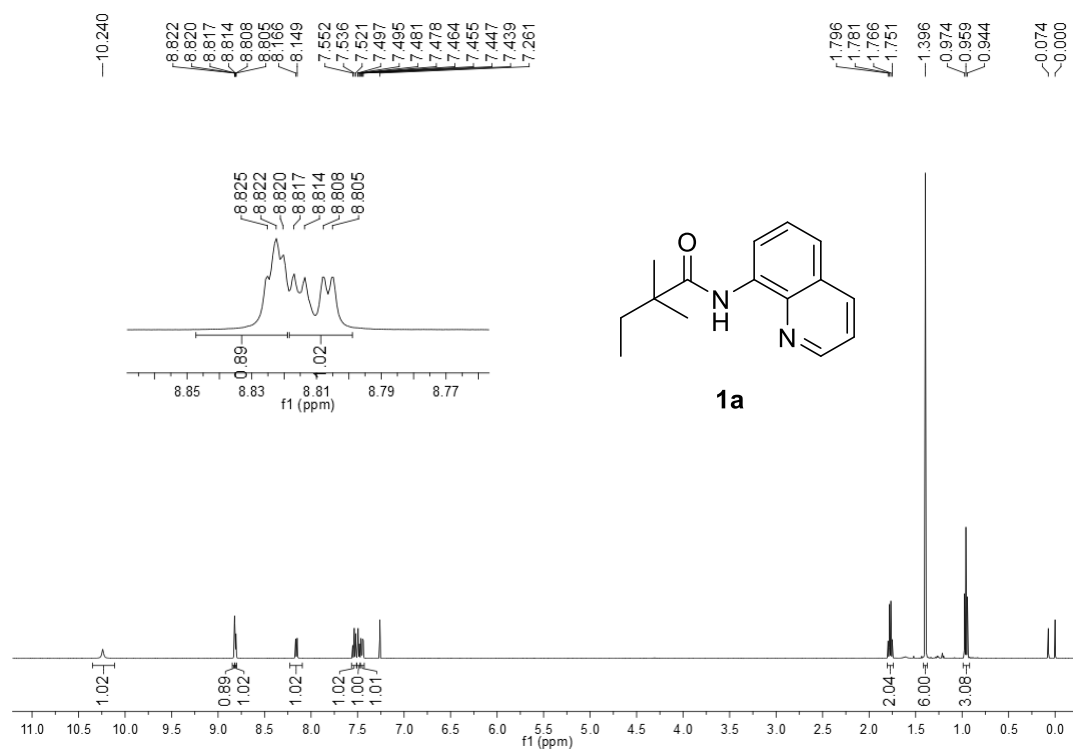


Figure S4. ^1H NMR Spectra of 1b

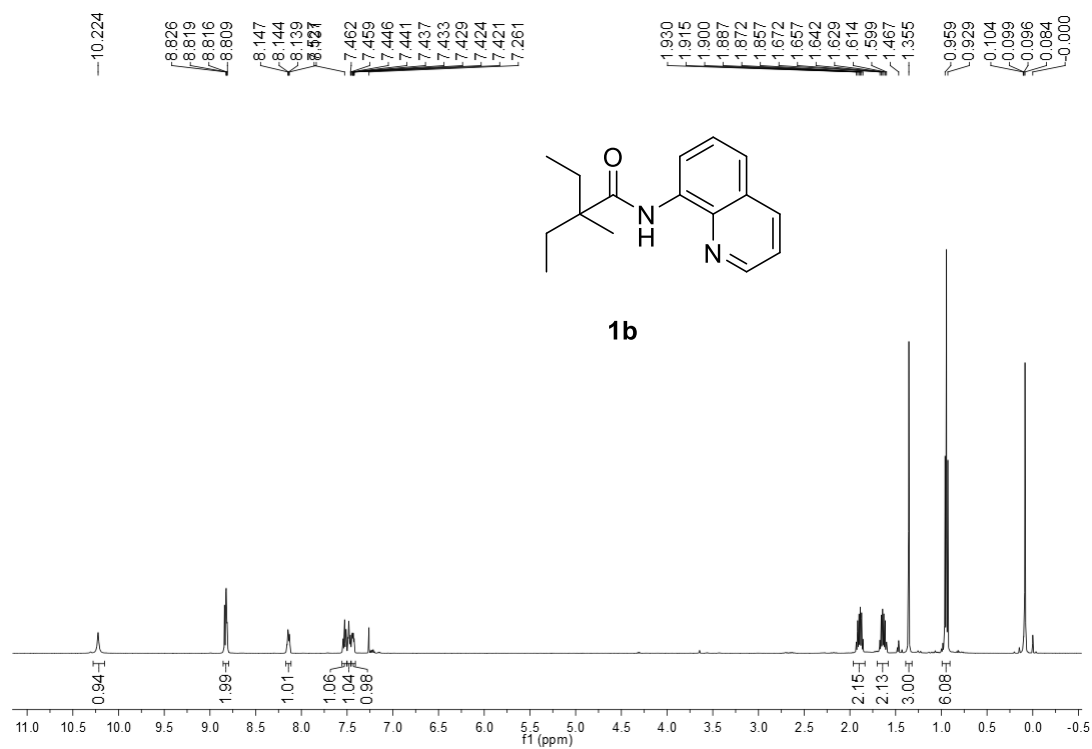


Figure S5. ¹H NMR Spectra of 1c

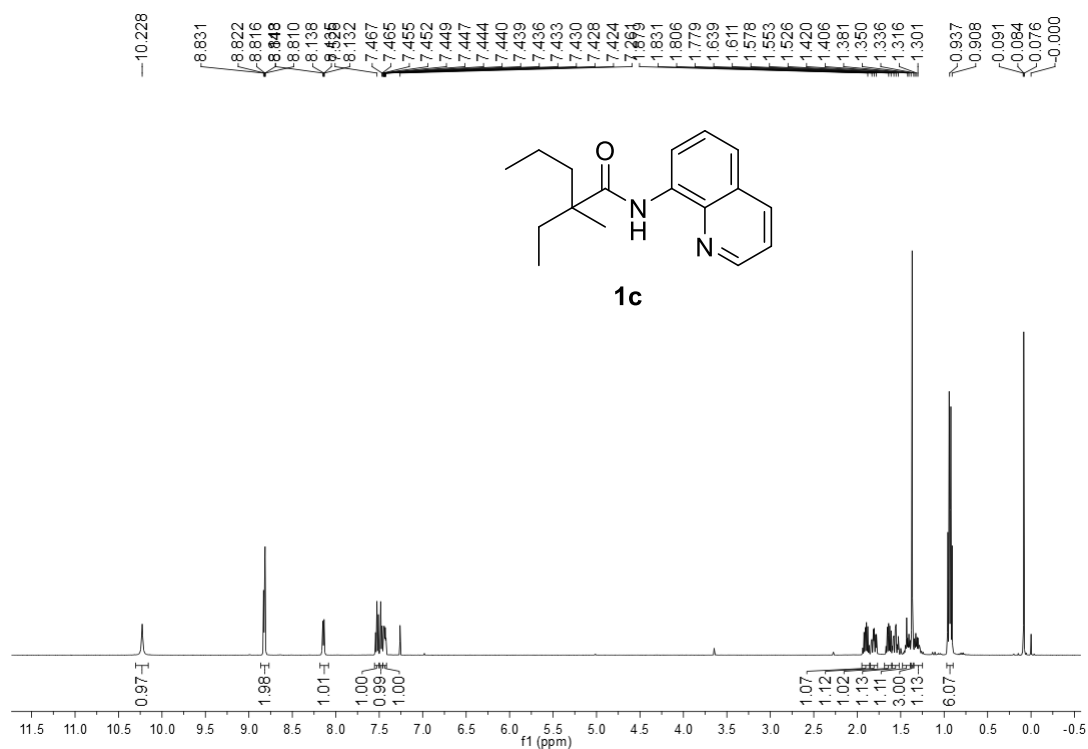


Figure S6. ¹H NMR Spectra of 1d

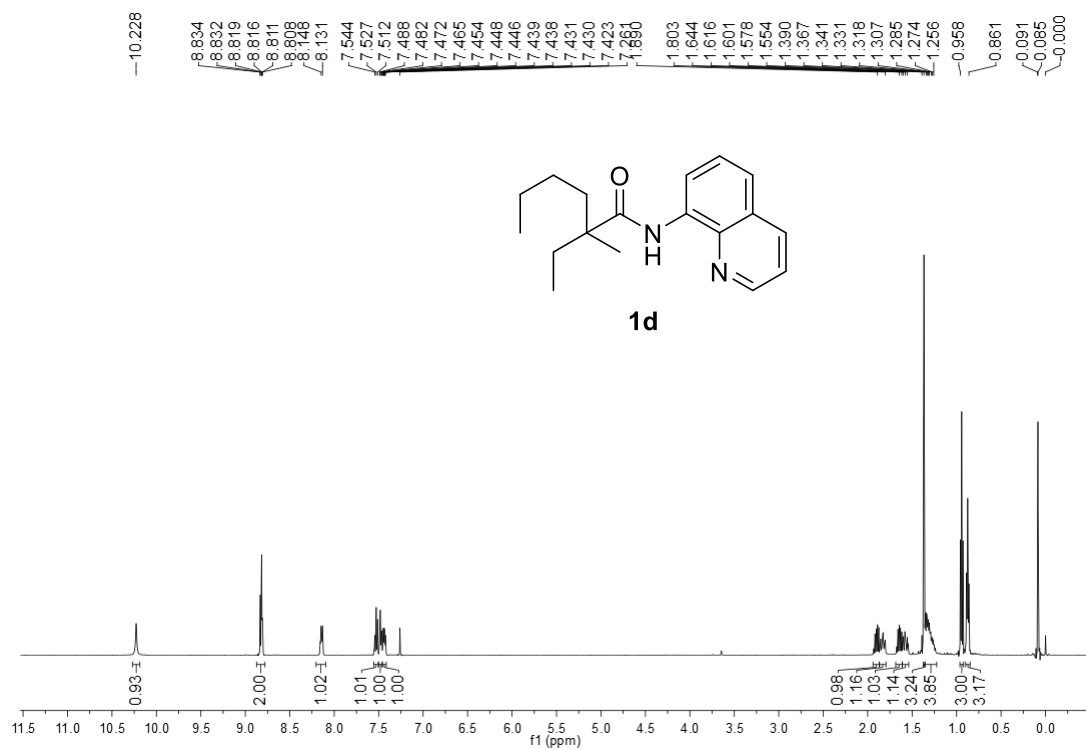


Figure S7. ¹H NMR Spectra of 1f

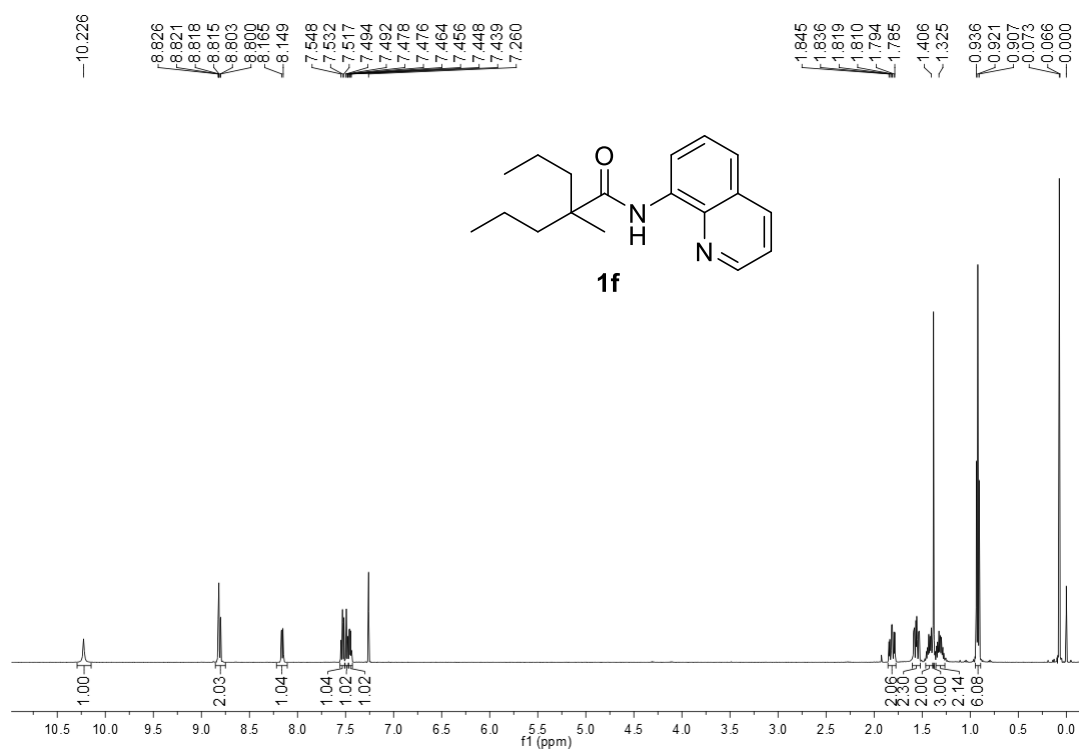


Figure S8. ¹H NMR Spectra of 1i

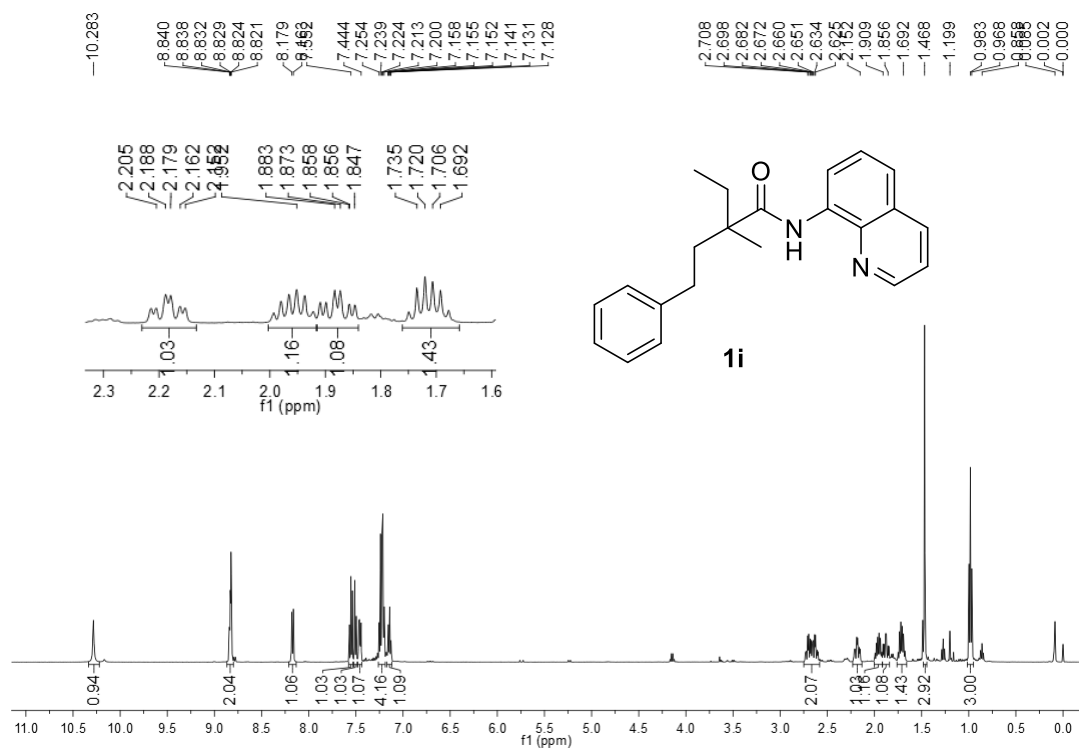


Figure S9. ¹H NMR Spectra of 1j

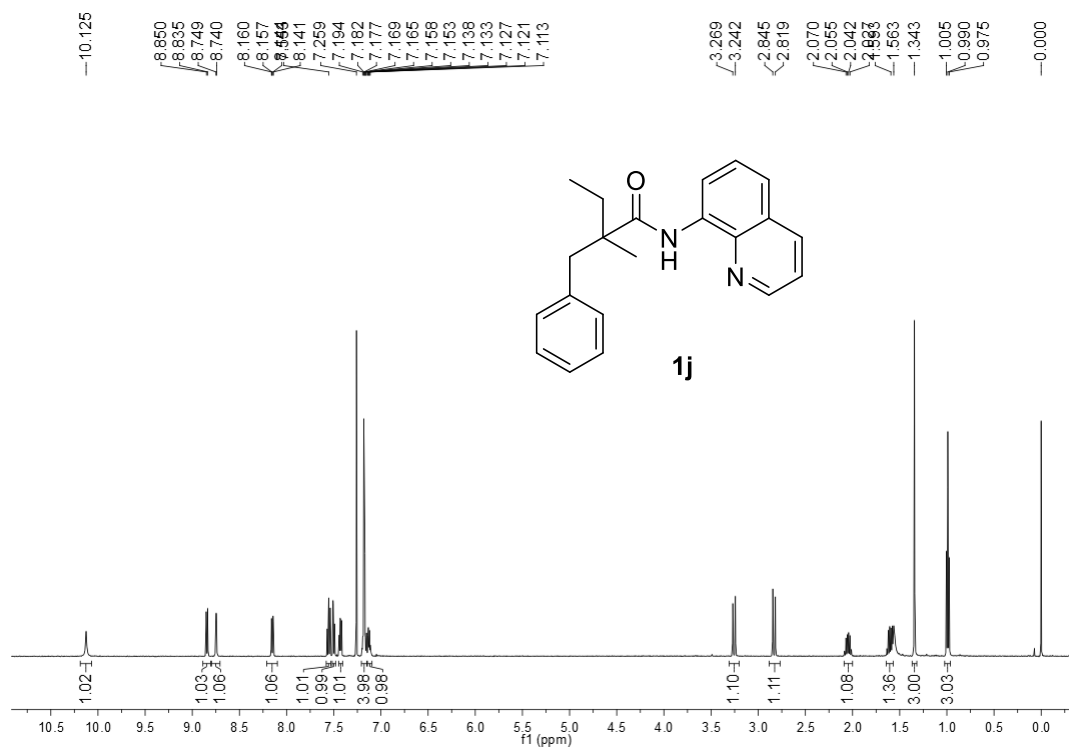


Figure S10. ¹H NMR Spectra of 1k

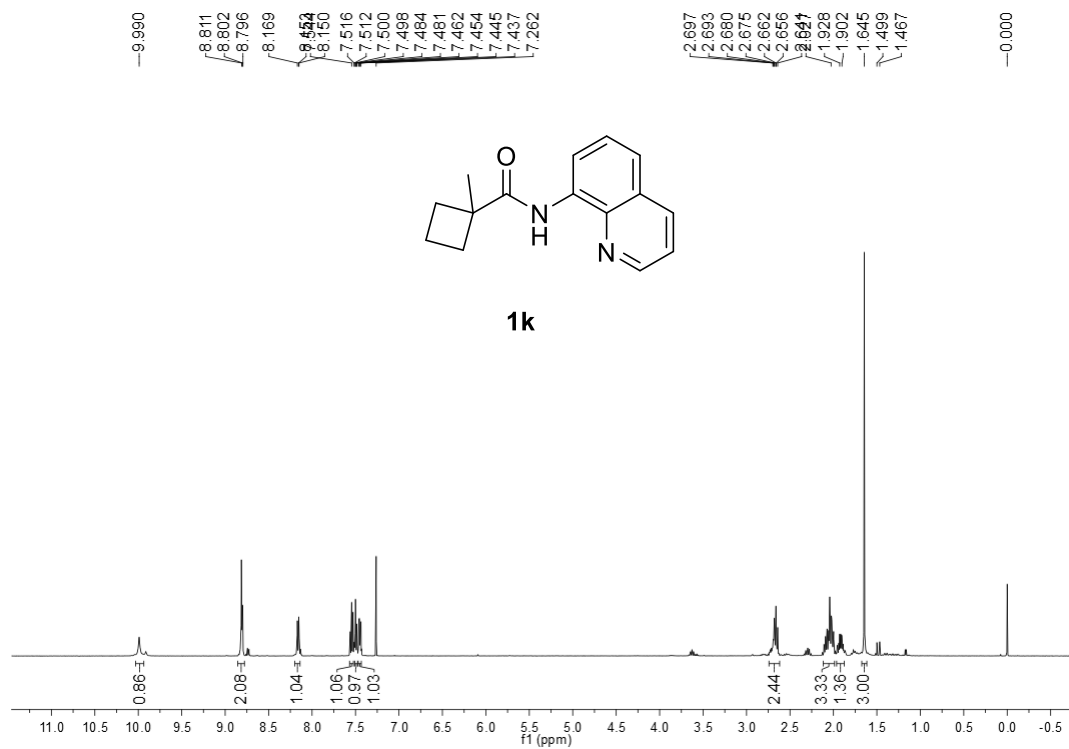


Figure S11. ¹H NMR Spectra of **1o**

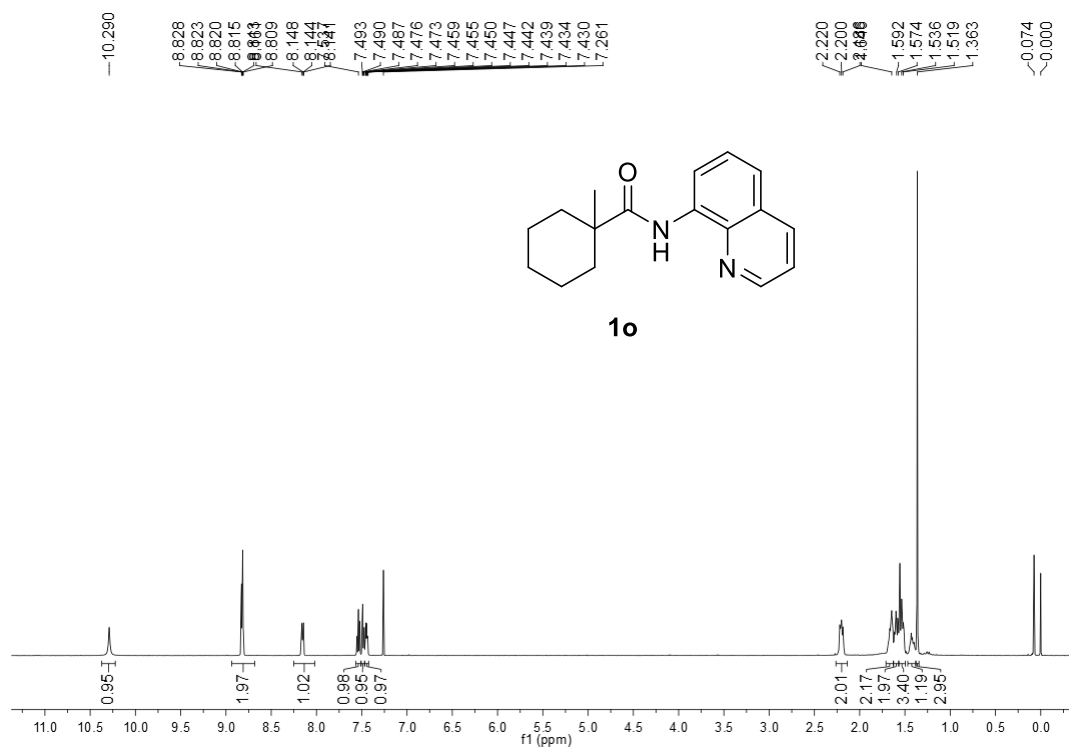


Figure S12. ¹H NMR Spectra of [D₃]-**1l**

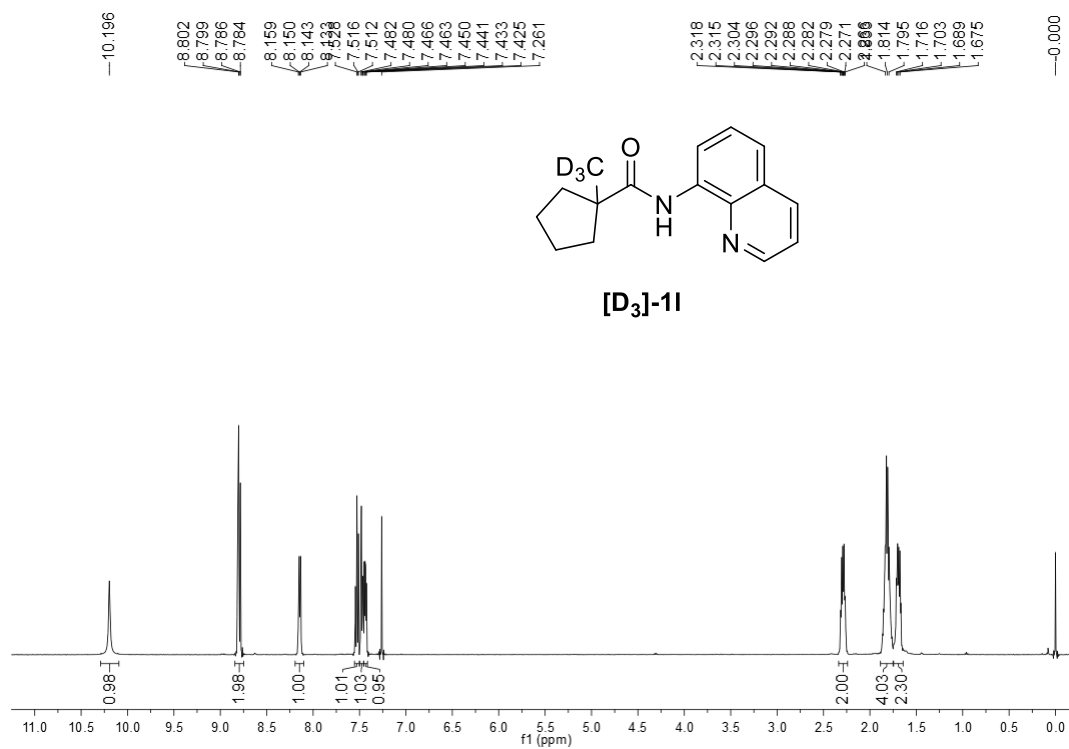


Figure S13. ¹H NMR Spectra of compound 3aa

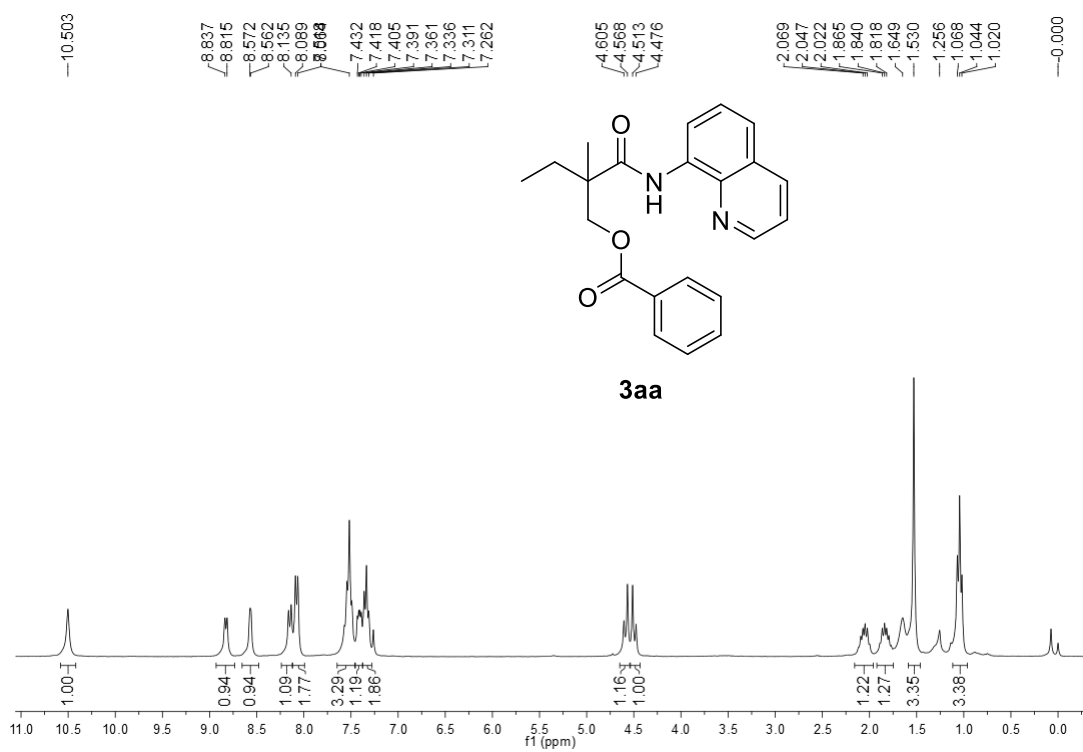


Figure S14. ¹³C NMR Spectra of compound 3aa

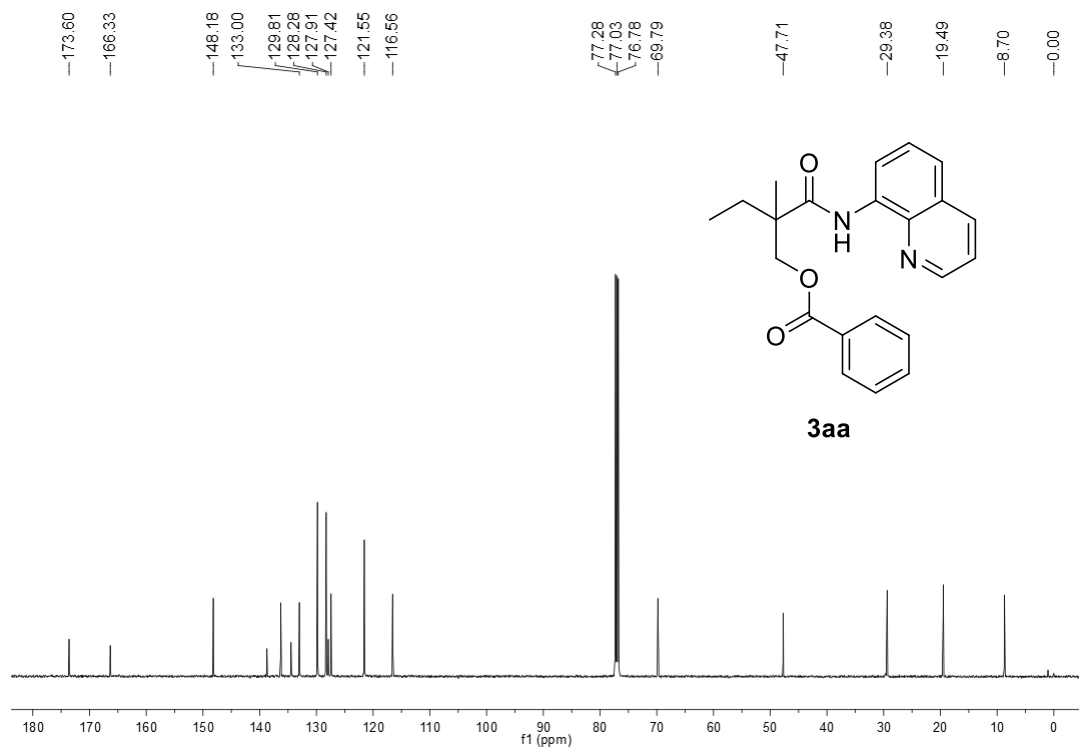


Figure S15. ¹H NMR Spectra of compound 3aa'

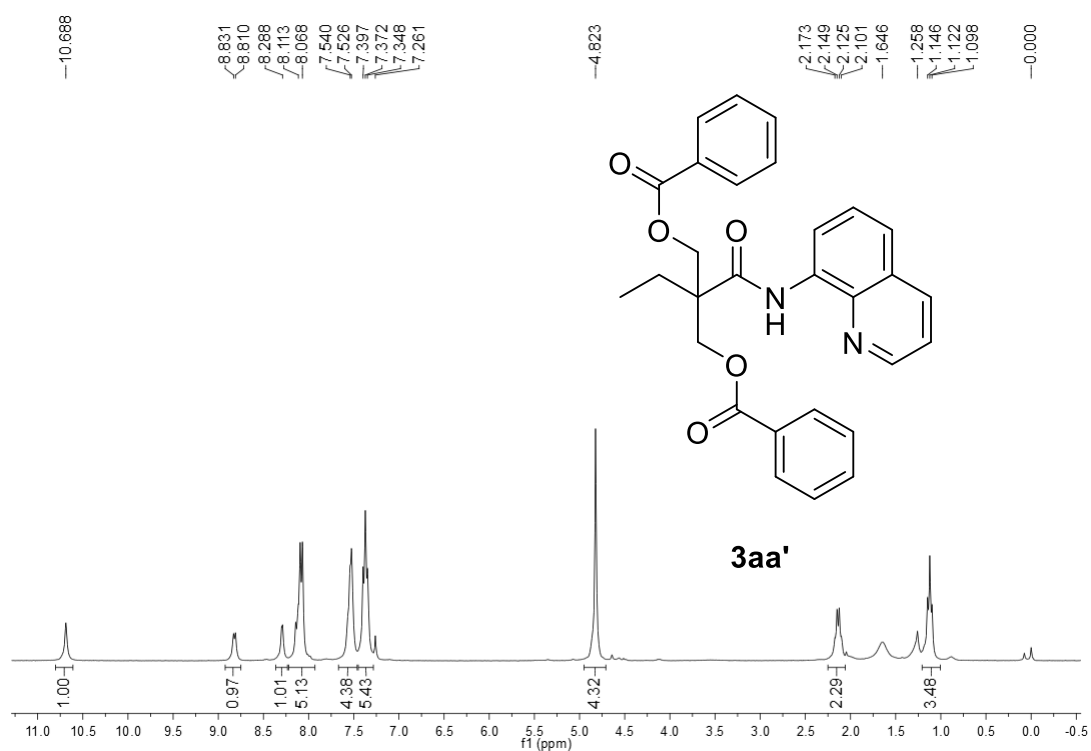


Figure S16. ¹³C NMR Spectra of compound 3aa'

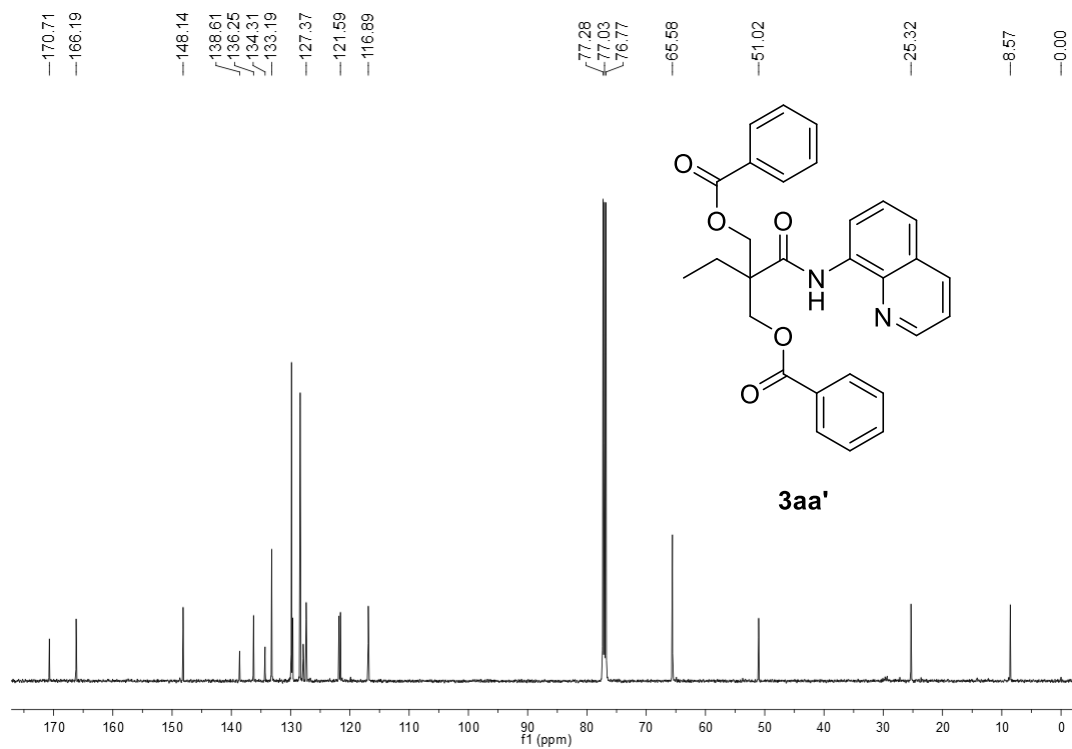


Figure S17. ¹H NMR Spectra of compound 4a

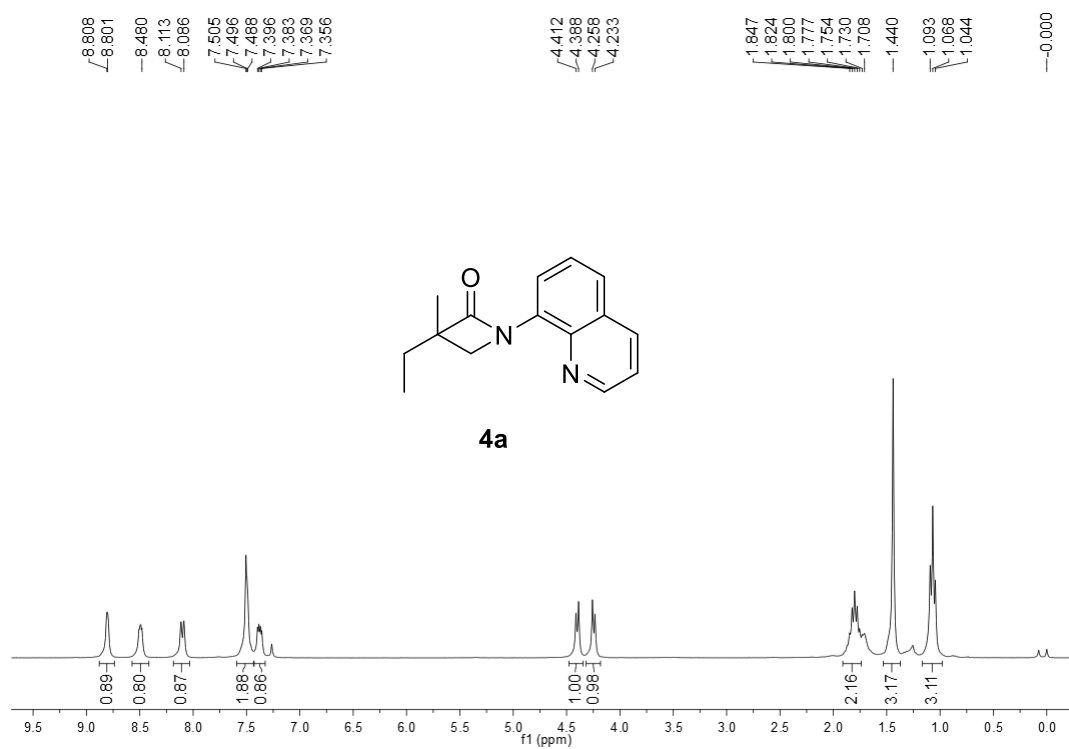


Figure S18. ¹³C NMR Spectra of compound 4a

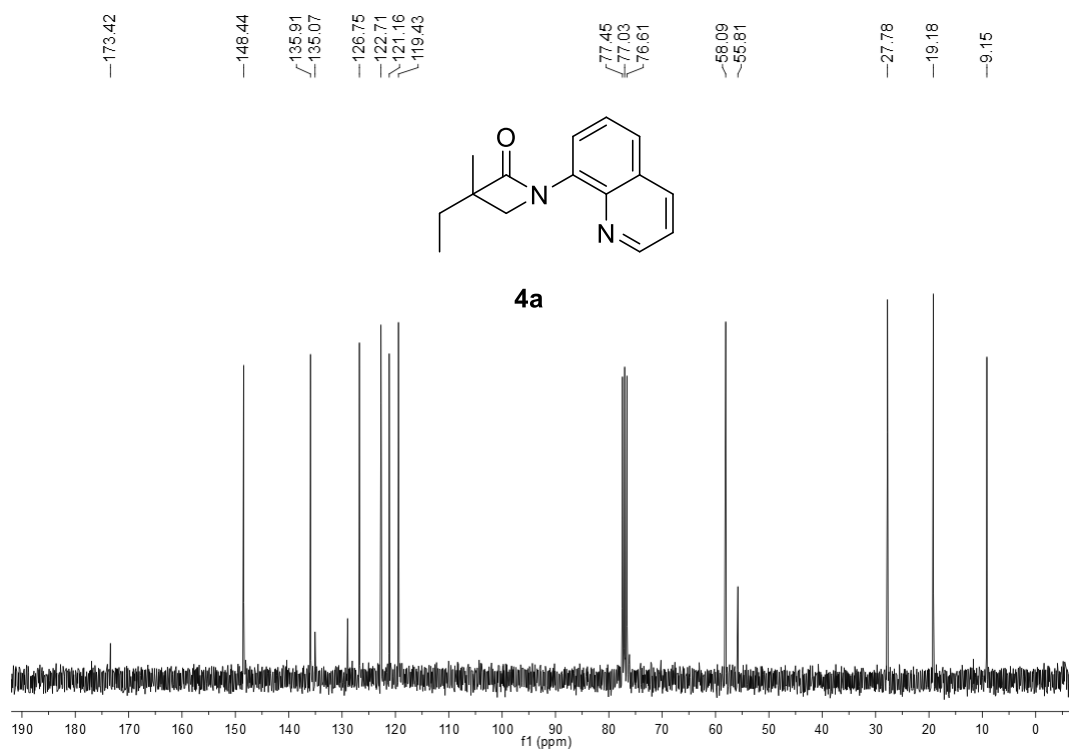


Figure S19. ¹H NMR Spectra of compound 3ab

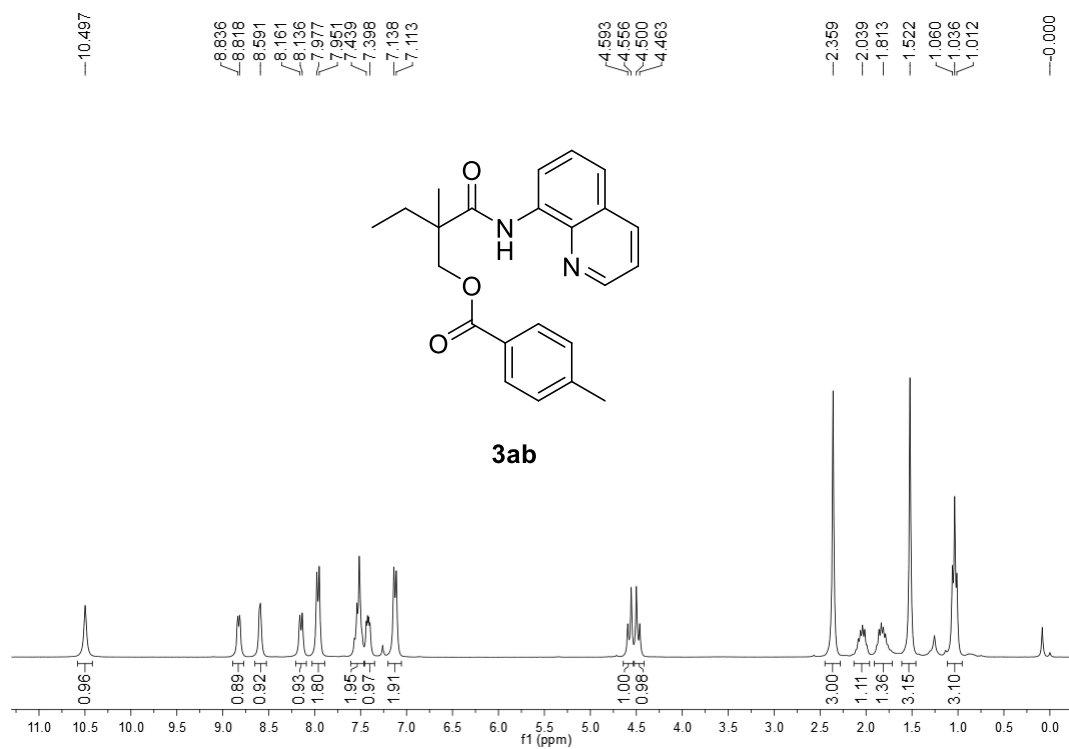


Figure S20. ¹³C NMR Spectra of compound 3ab

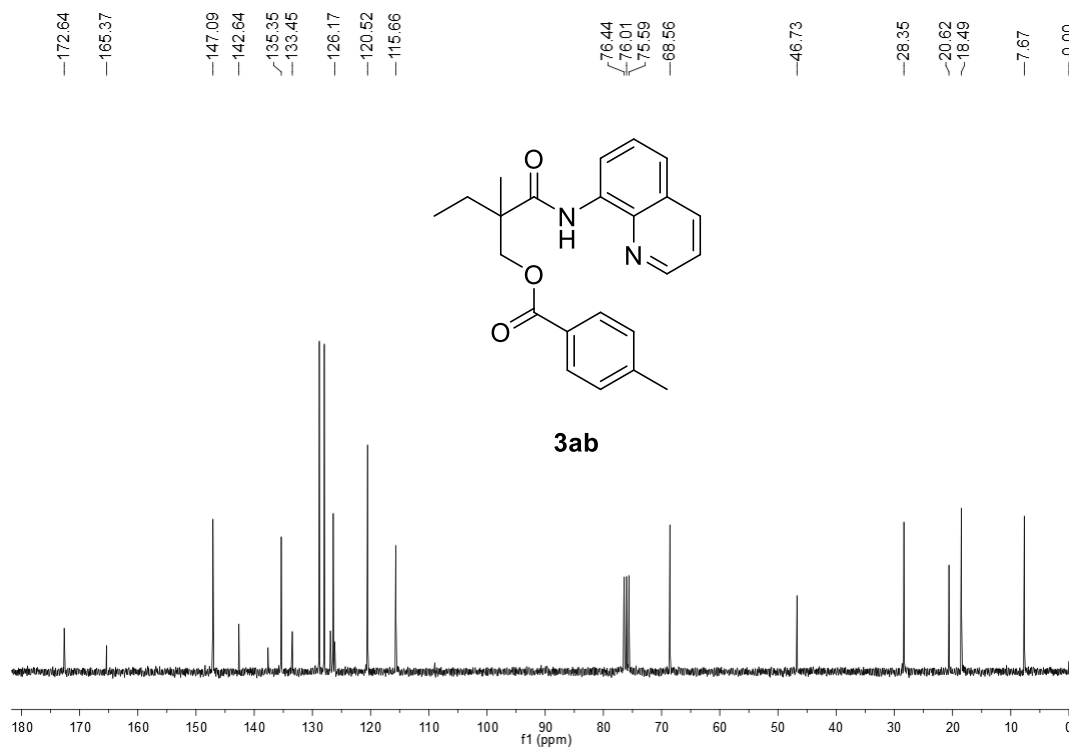


Figure S21. ¹H NMR Spectra of compound 3ab'

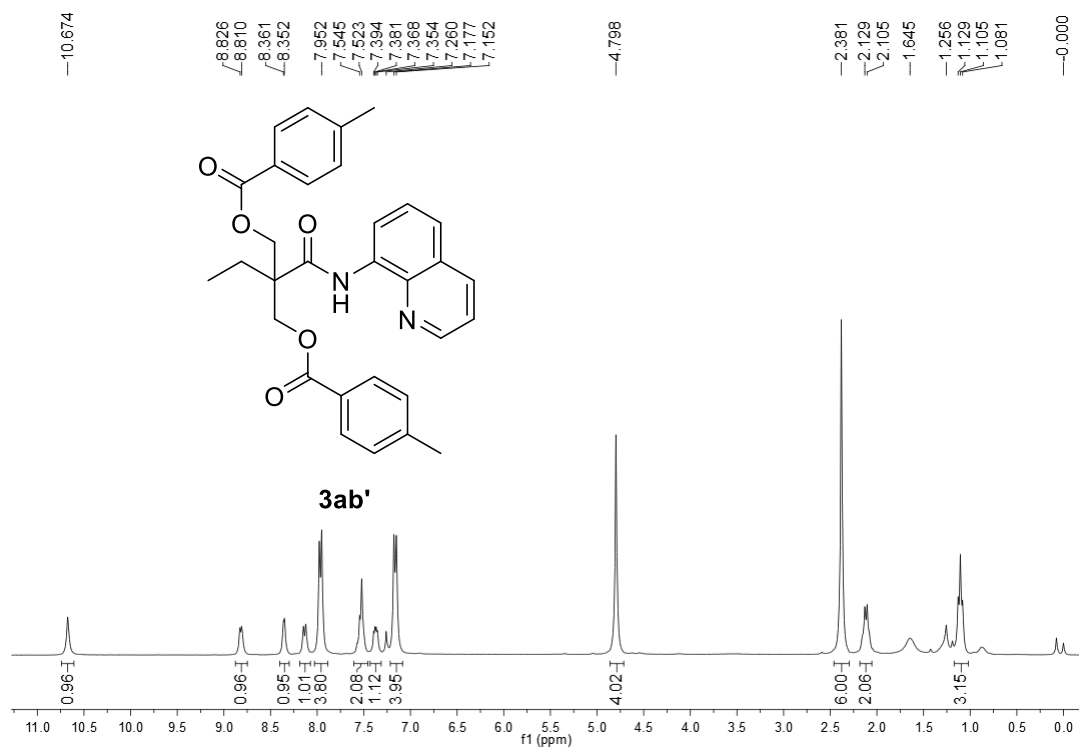


Figure S22. ¹³C NMR Spectra of compound 3ab'

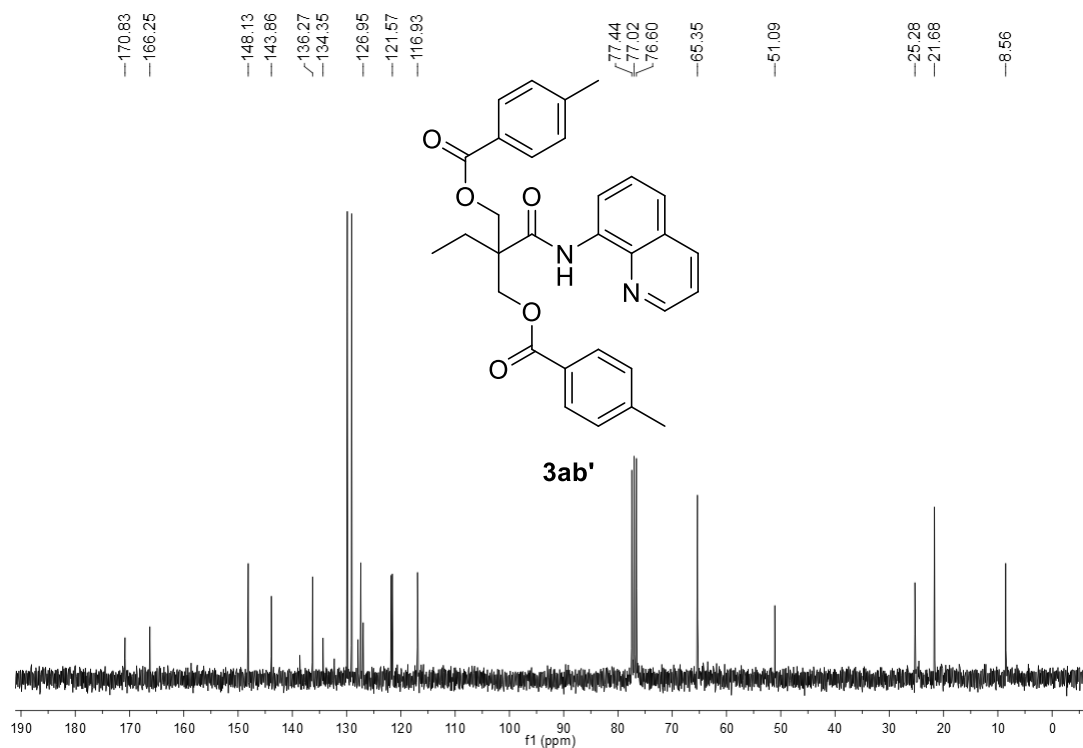


Figure S23. ¹H NMR Spectra of compound 3ac

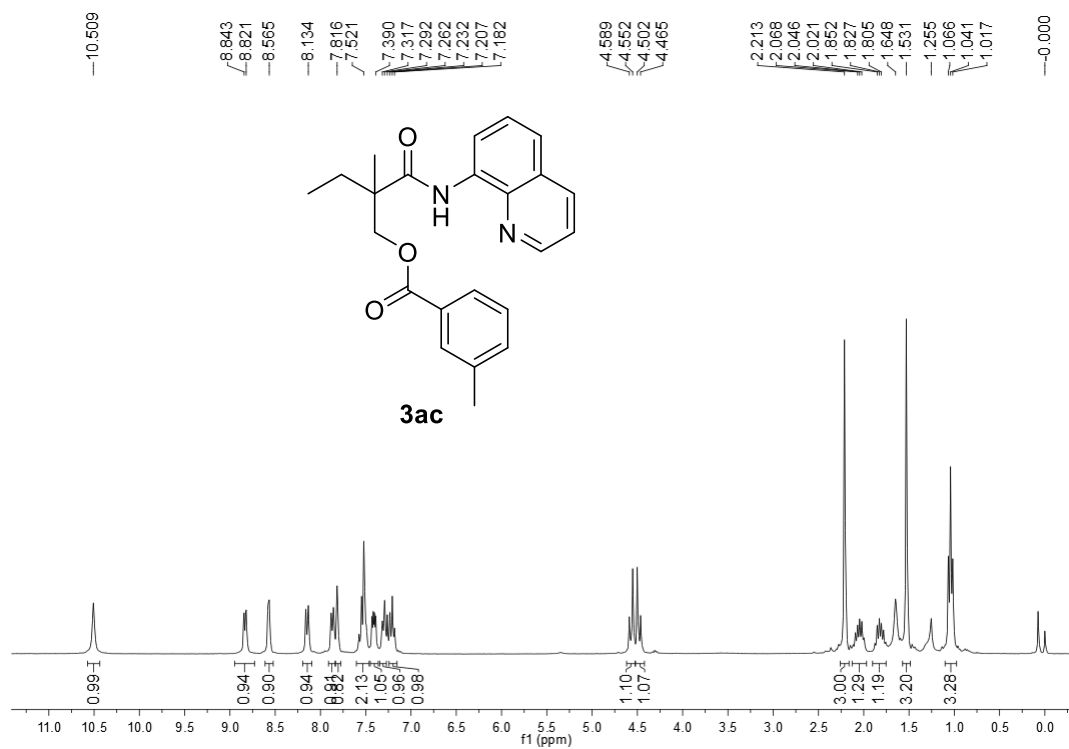


Figure S24. ¹³C NMR Spectra of compound 3ac

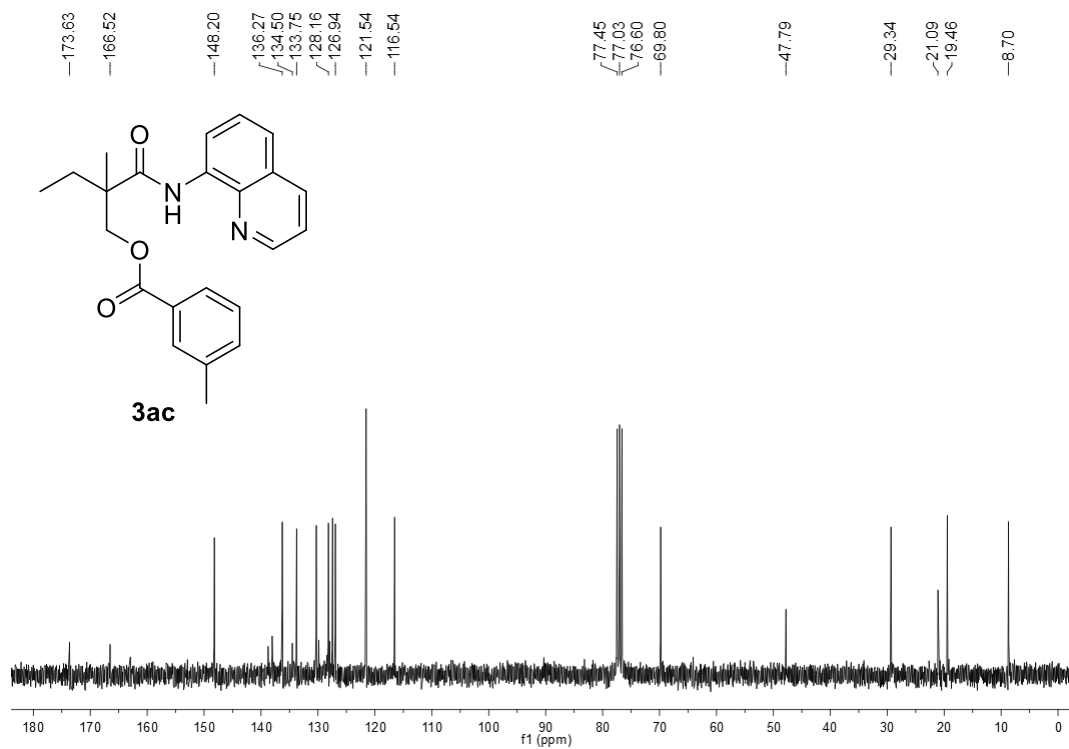


Figure S25. ¹H NMR Spectra of compound 3ac'

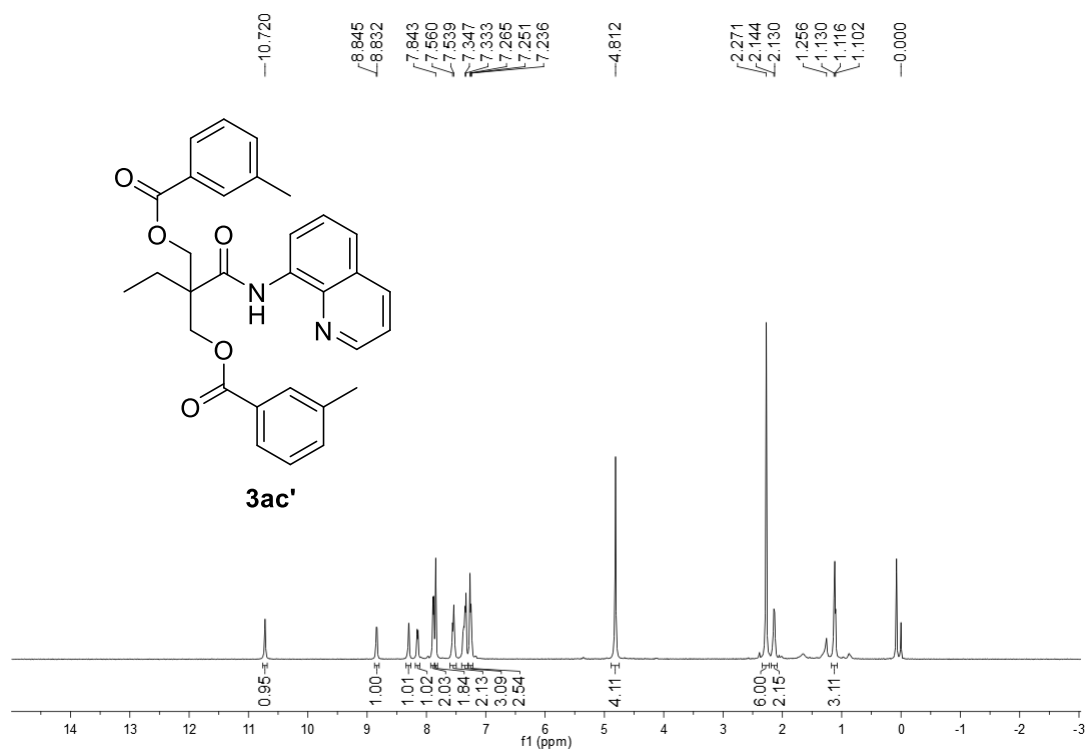


Figure S26. ¹³C NMR Spectra of compound 3ac'

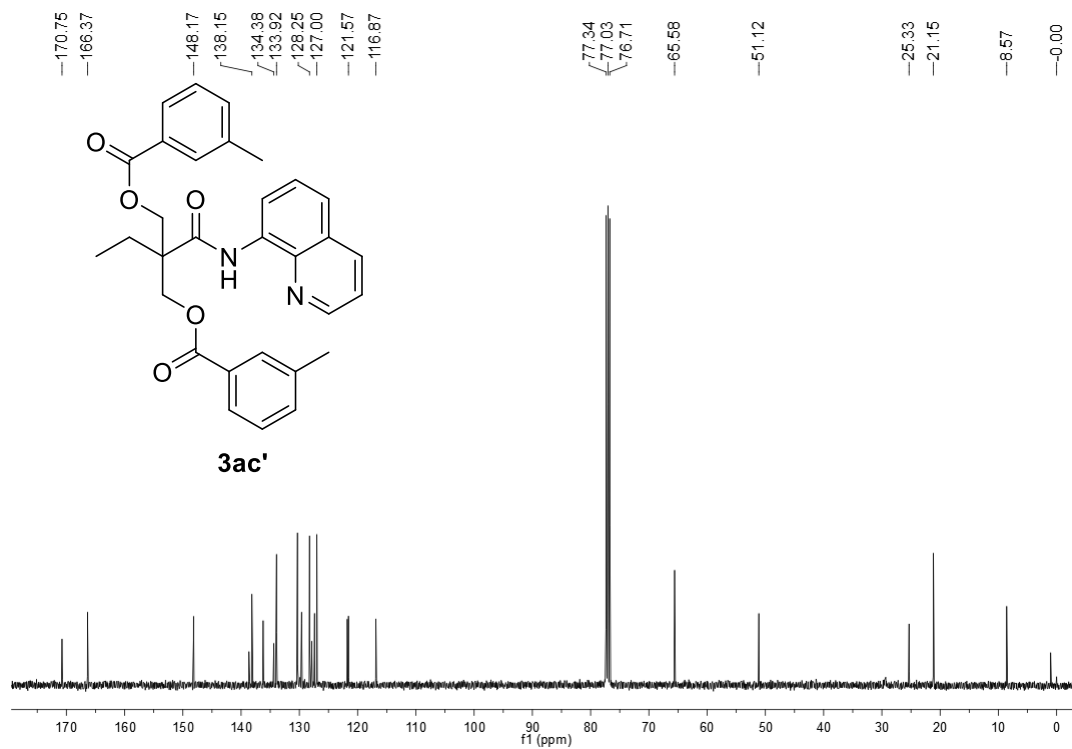


Figure S27. ¹H NMR Spectra of compound 3ad

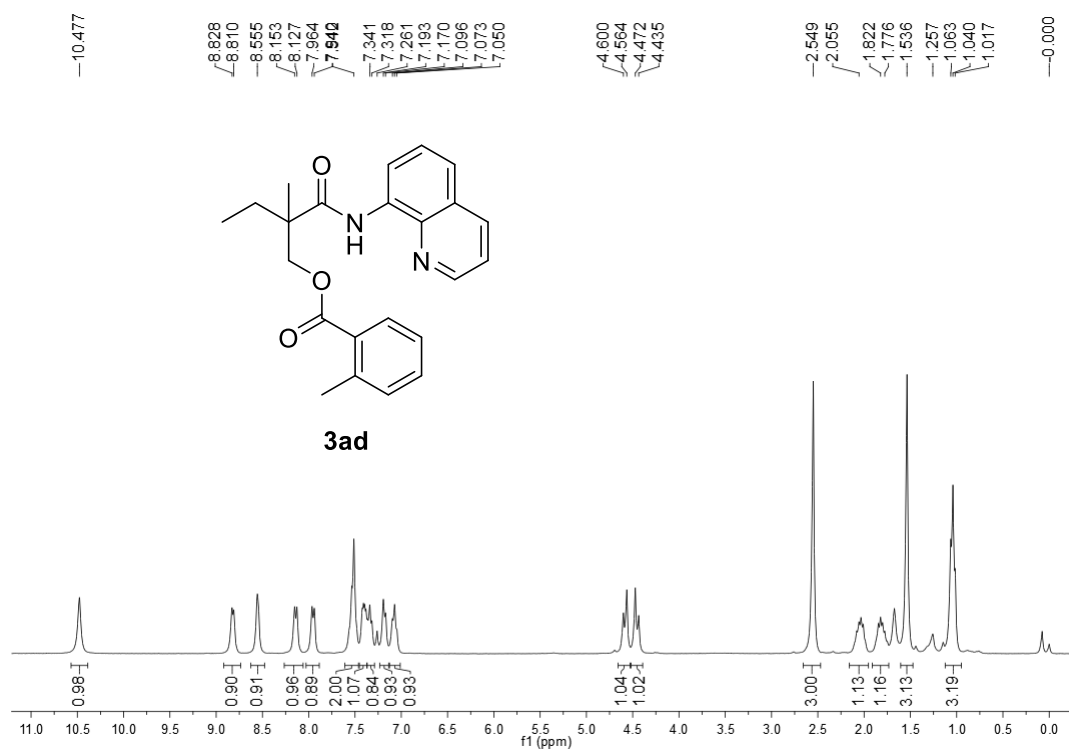


Figure S28. ¹³C NMR Spectra of compound 3ad

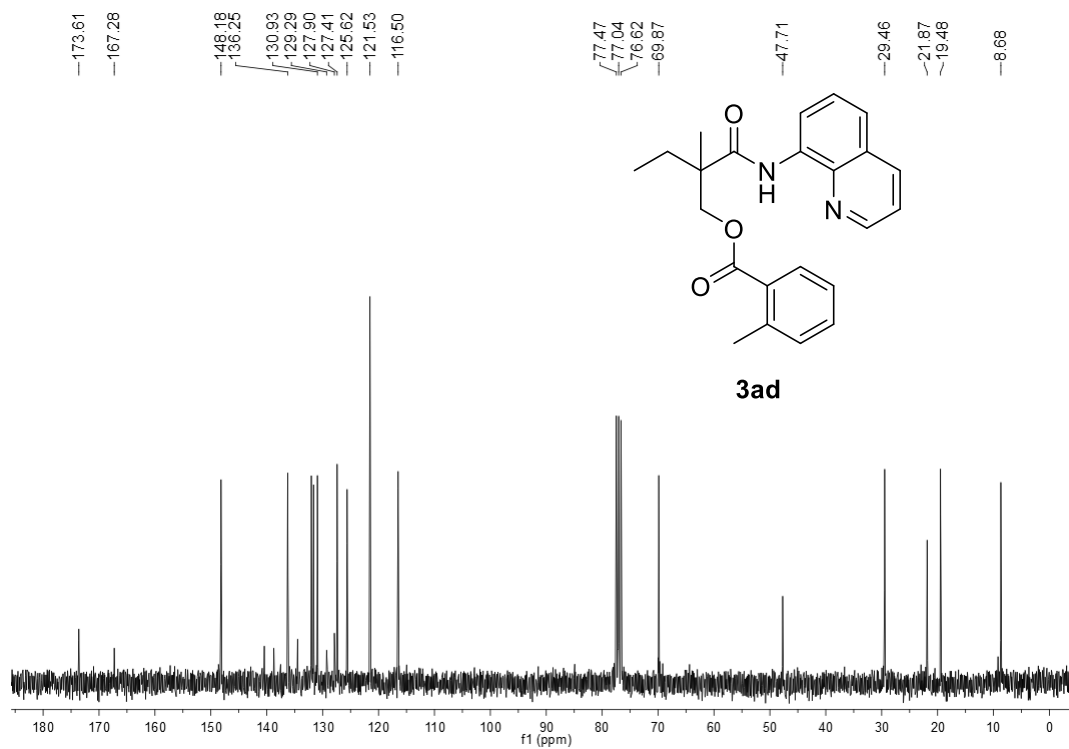


Figure S29. ¹H NMR Spectra of compound 3ad'

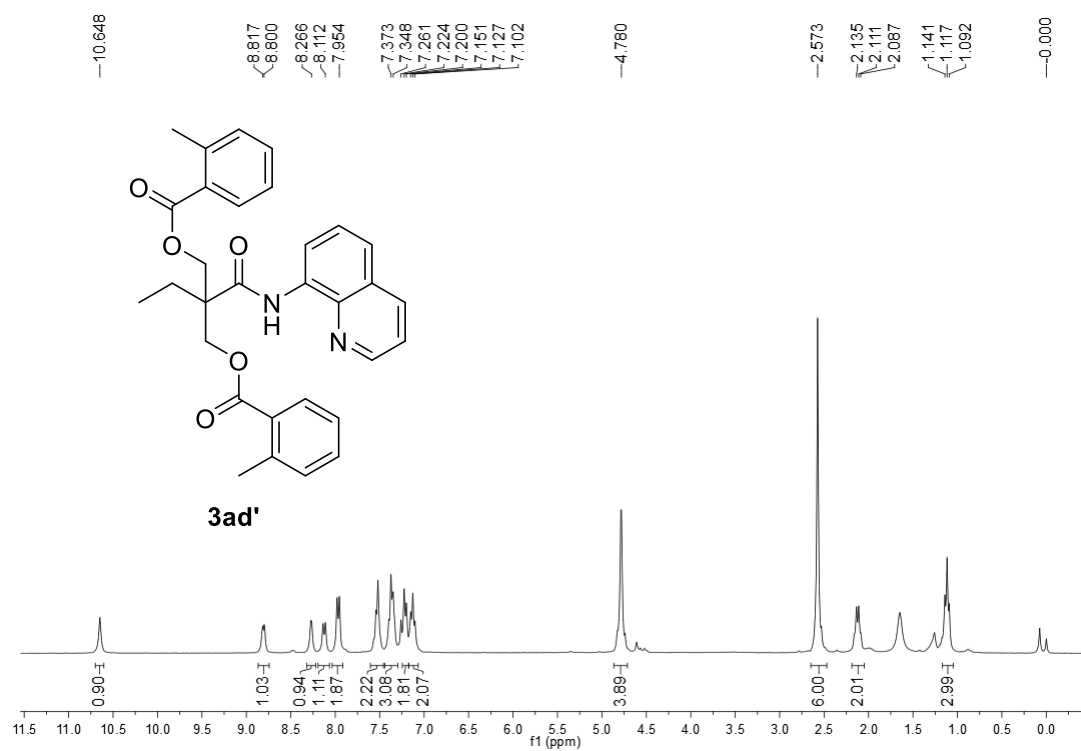


Figure S30. ¹³C NMR Spectra of compound 3ad'

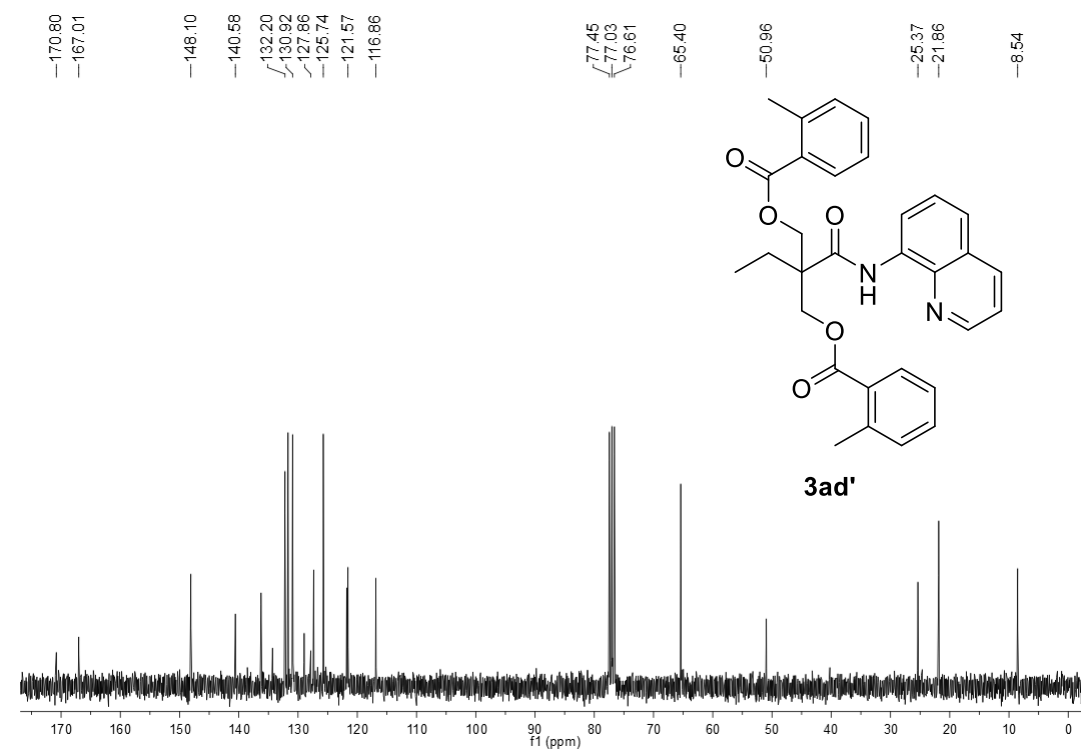


Figure S31. ¹H NMR Spectra of compound 3ae

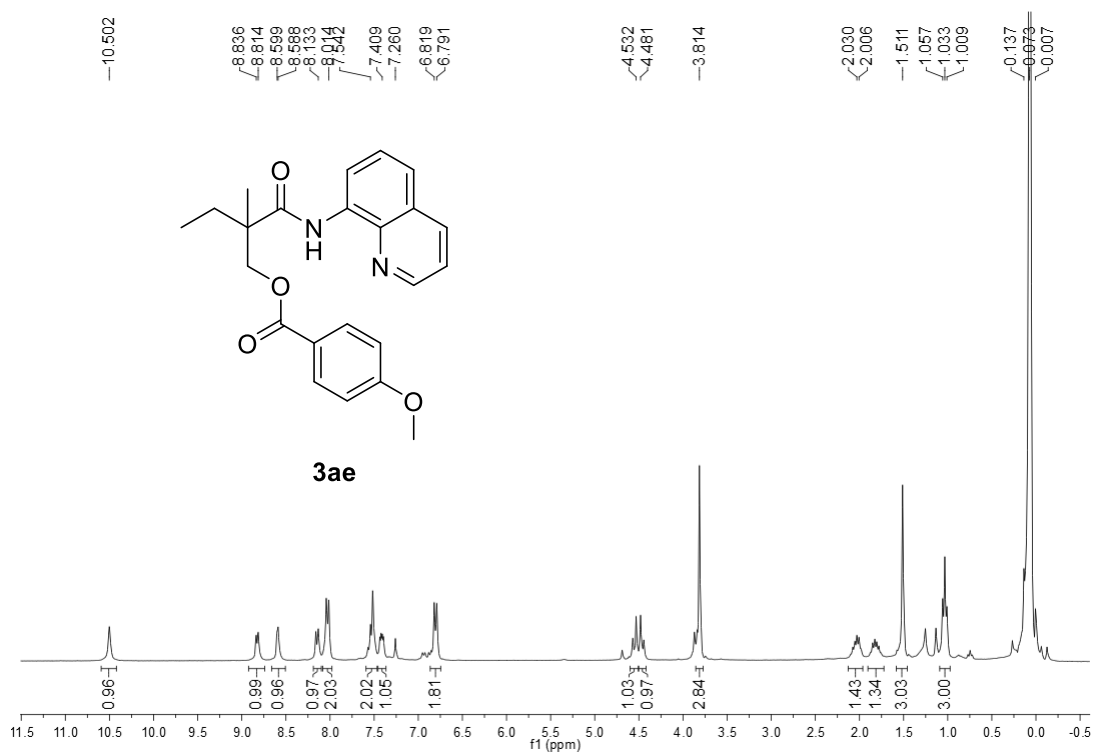


Figure S32. ¹³C NMR Spectra of compound 3ae

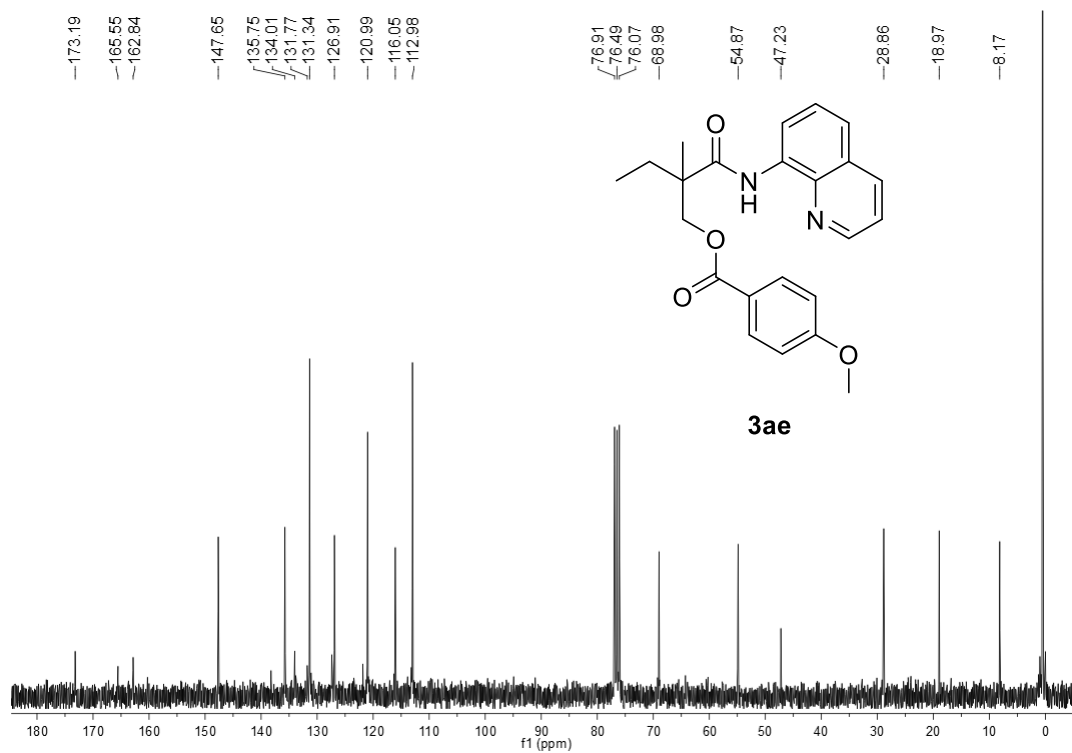


Figure S33. ^1H NMR Spectra of compound 3ae'

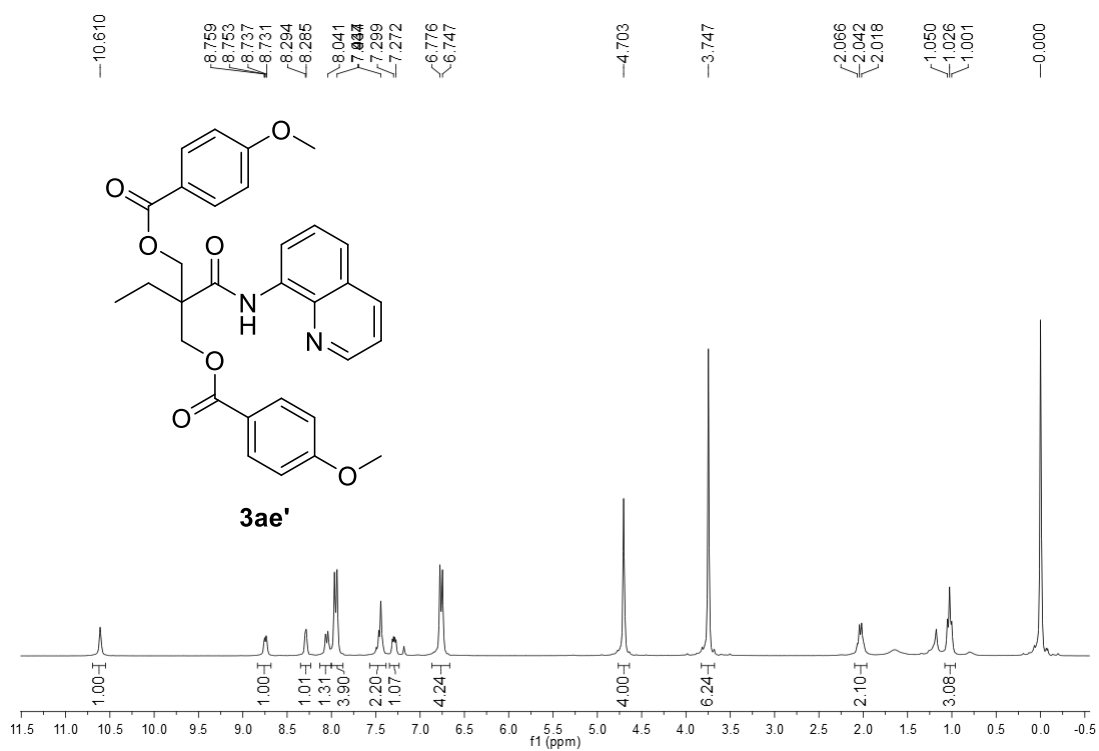


Figure S34. ^{13}C NMR Spectra of compound 3ae'

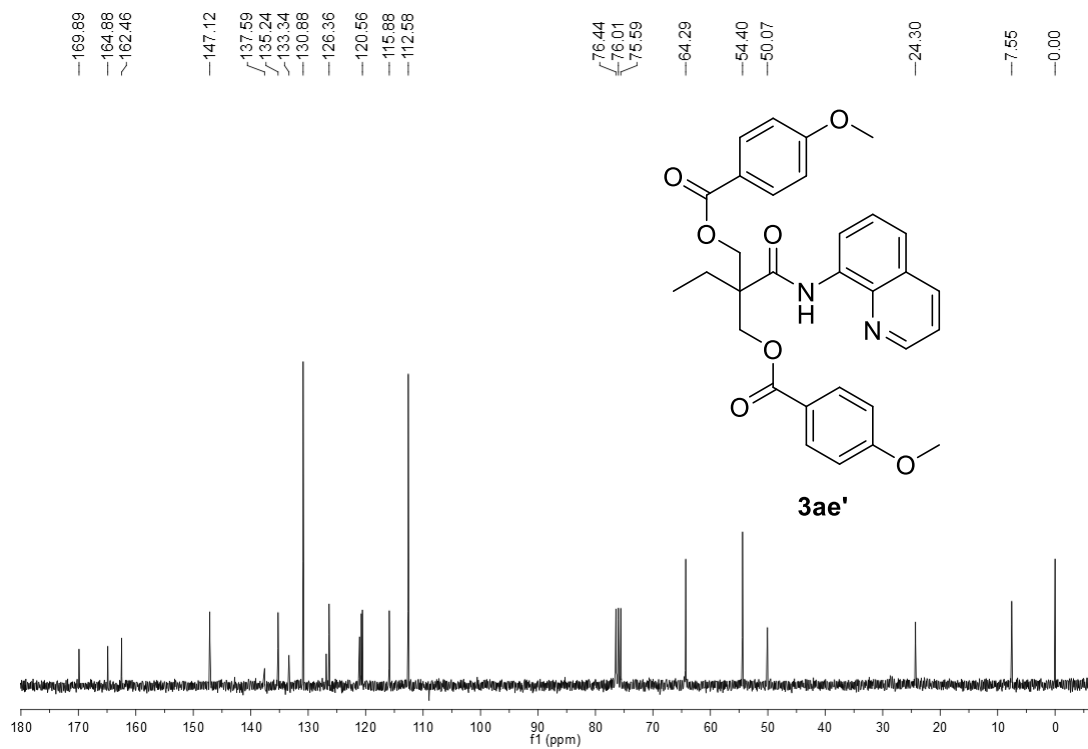


Figure S35. ¹H NMR Spectra of compound 3af

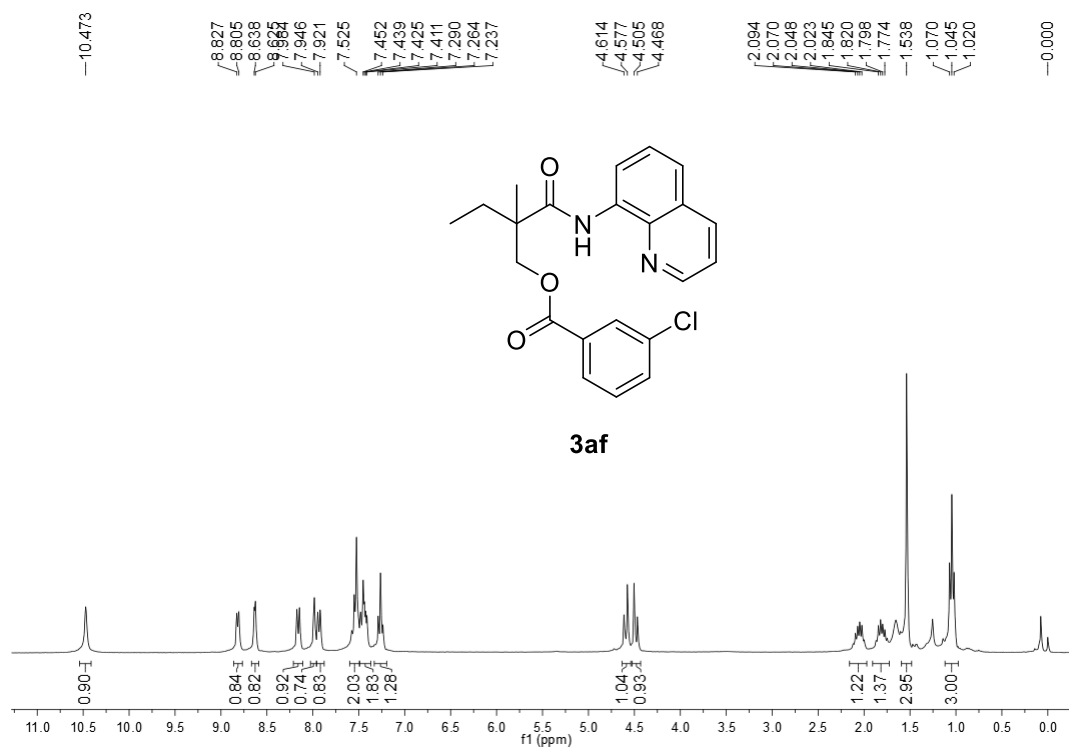


Figure S36. ¹³C NMR Spectra of compound 3af

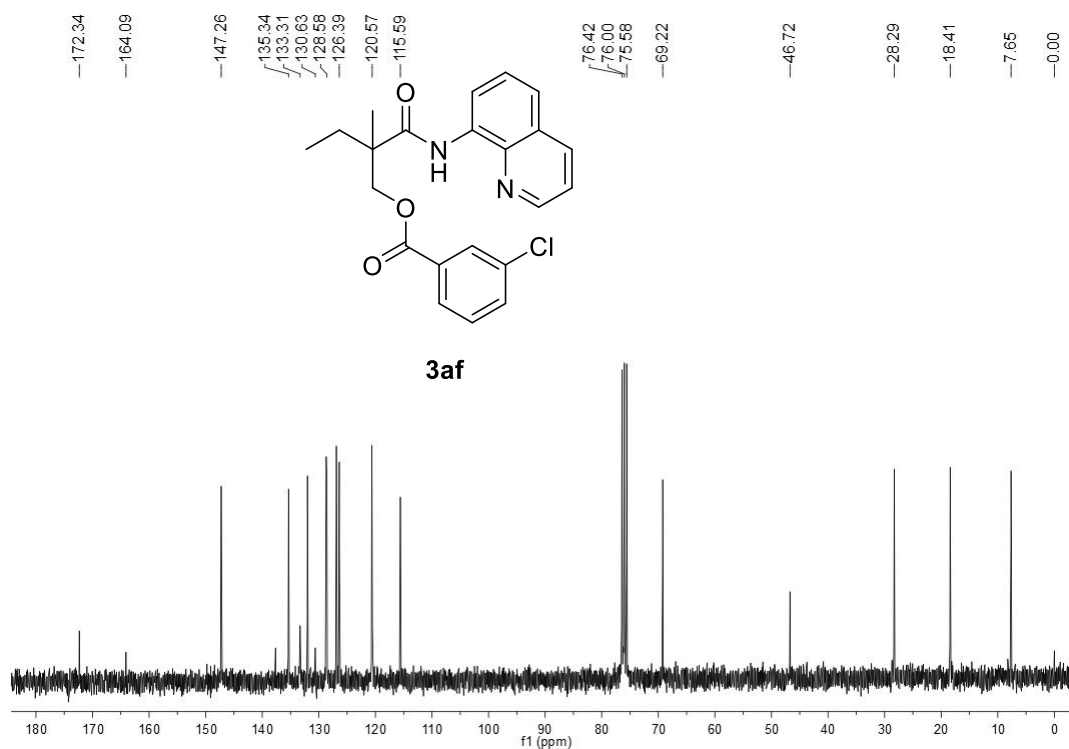


Figure S37. ¹H NMR Spectra of compound 3af'

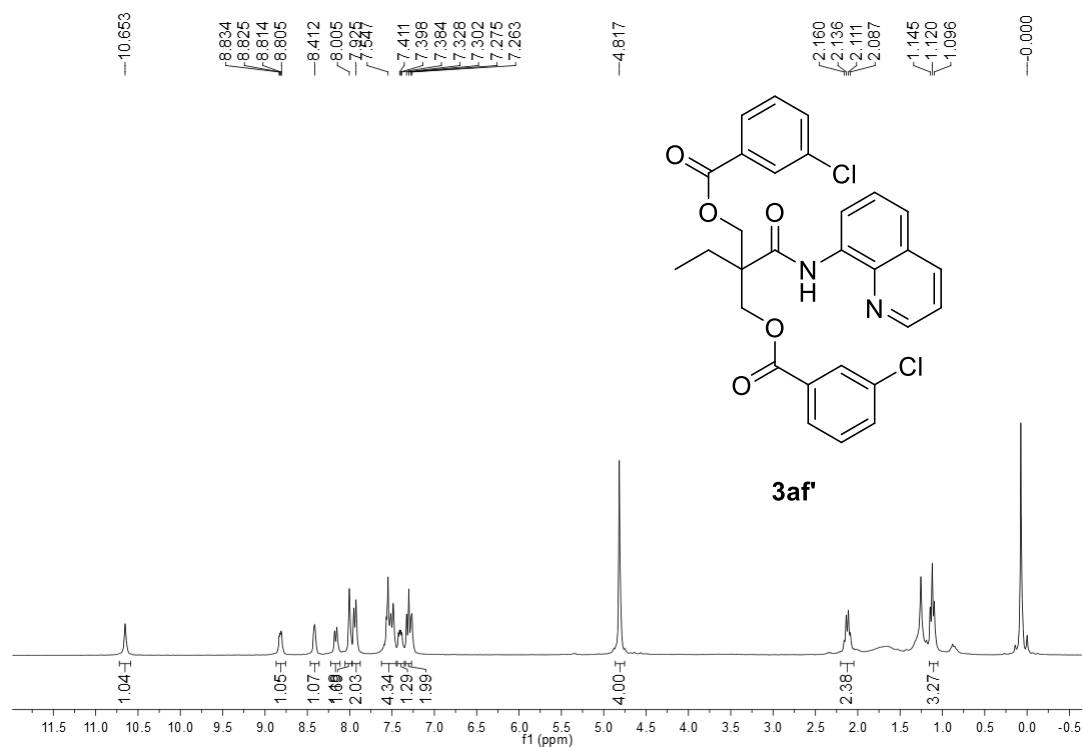


Figure S38. ¹³C NMR Spectra of compound 3af'

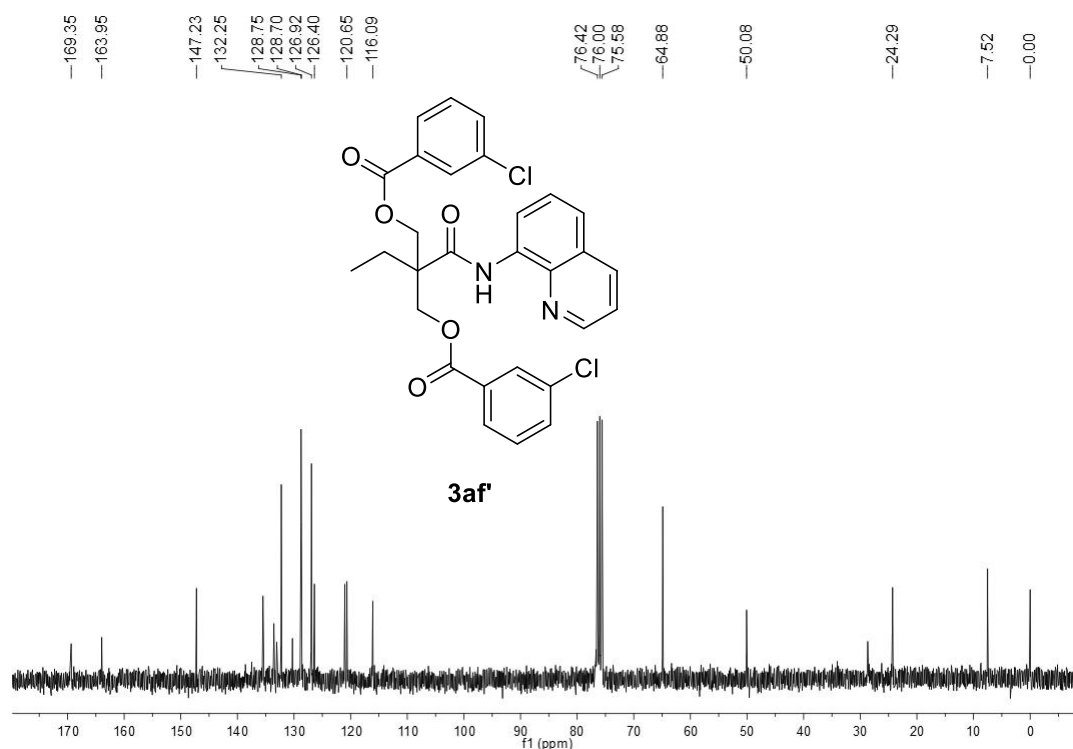


Figure S39. ¹H NMR Spectra of compound 3ag

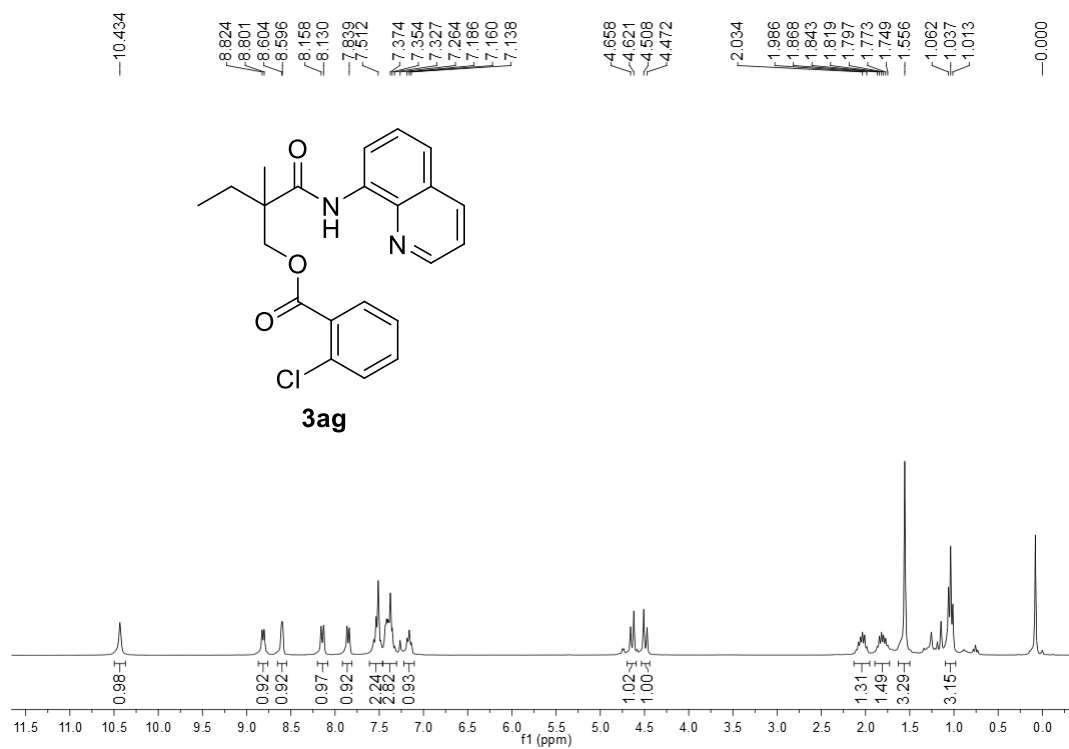


Figure S40. ¹³C NMR Spectra of compound 3ag

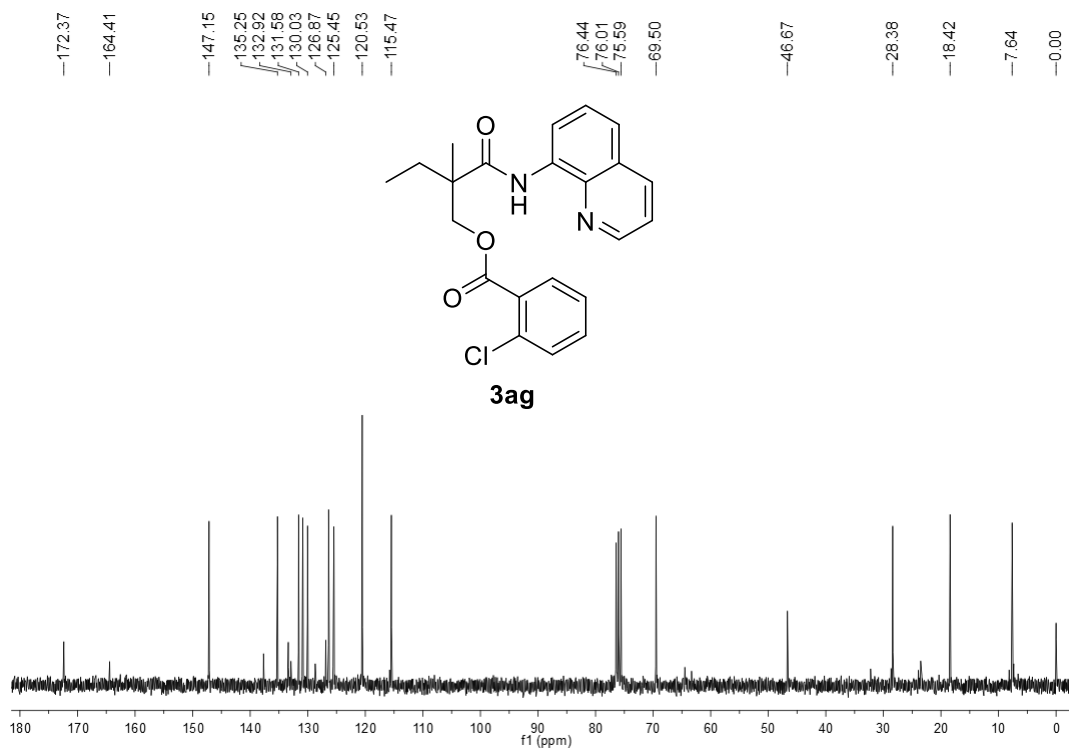


Figure S41. ¹H NMR Spectra of compound 3ag'

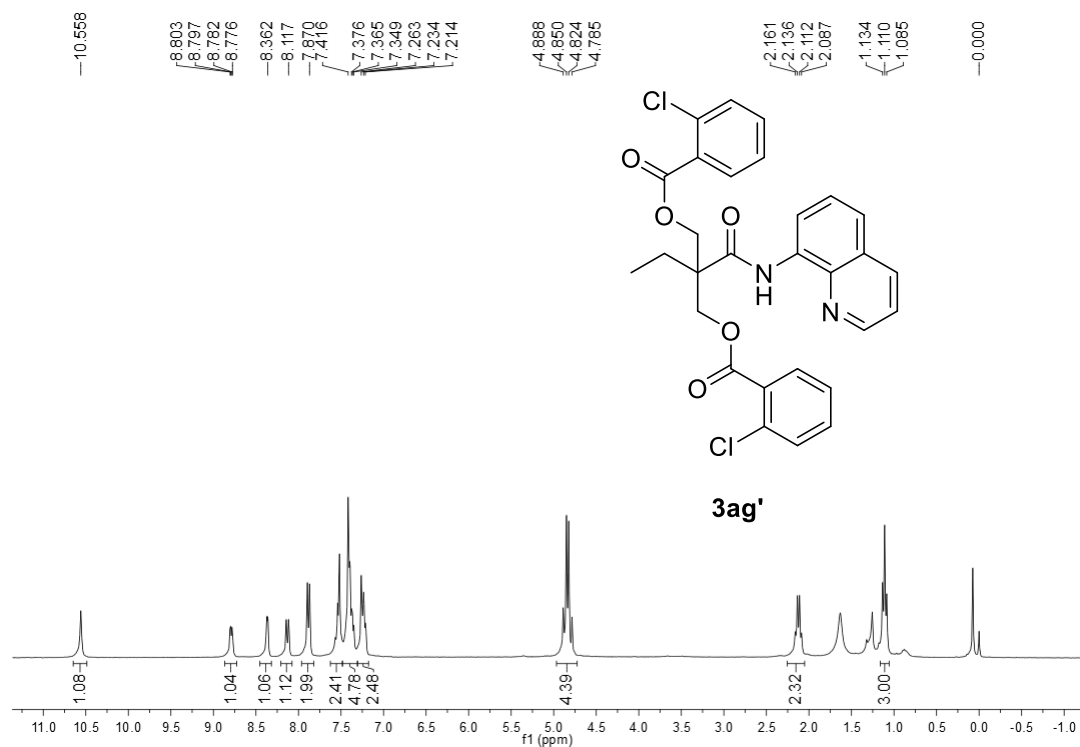


Figure S42. ¹³C NMR Spectra of compound 3ag'

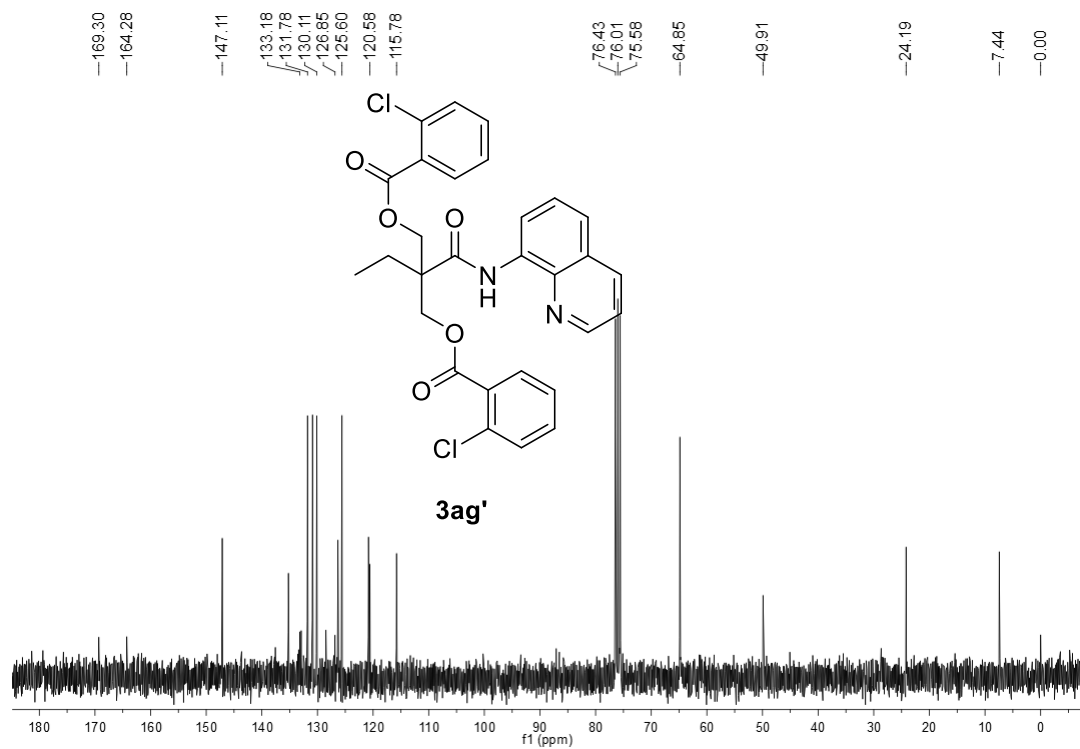


Figure S43. ¹H NMR Spectra of compound 3ah

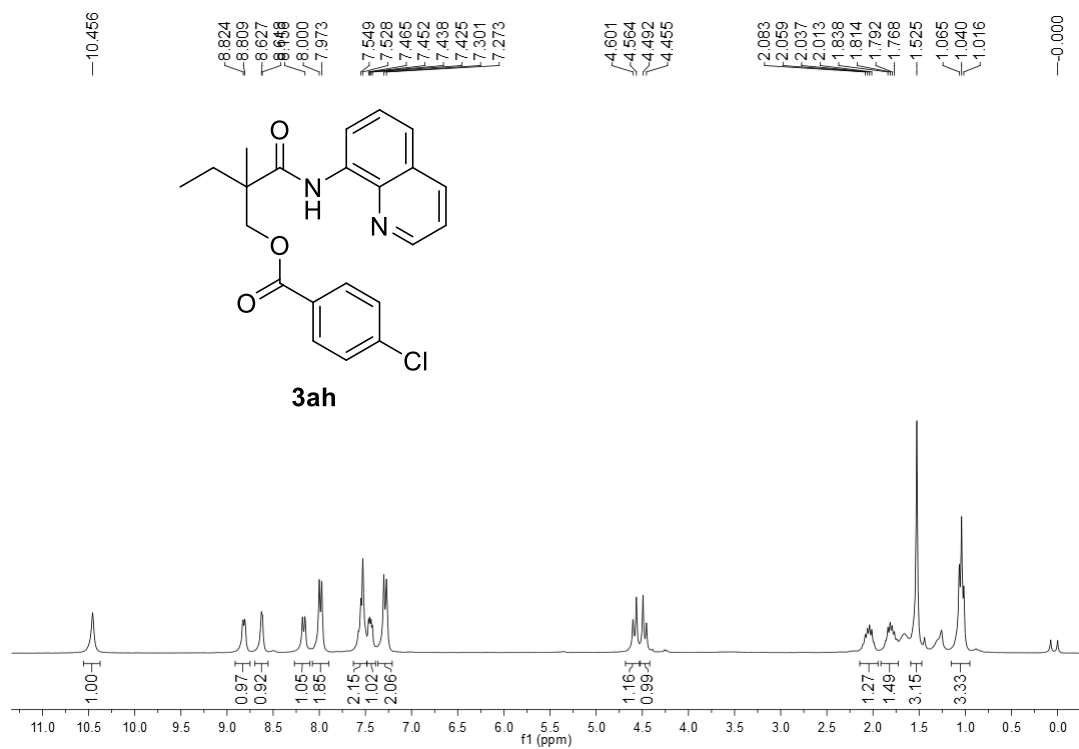


Figure S44. ¹³C NMR Spectra of compound 3ah

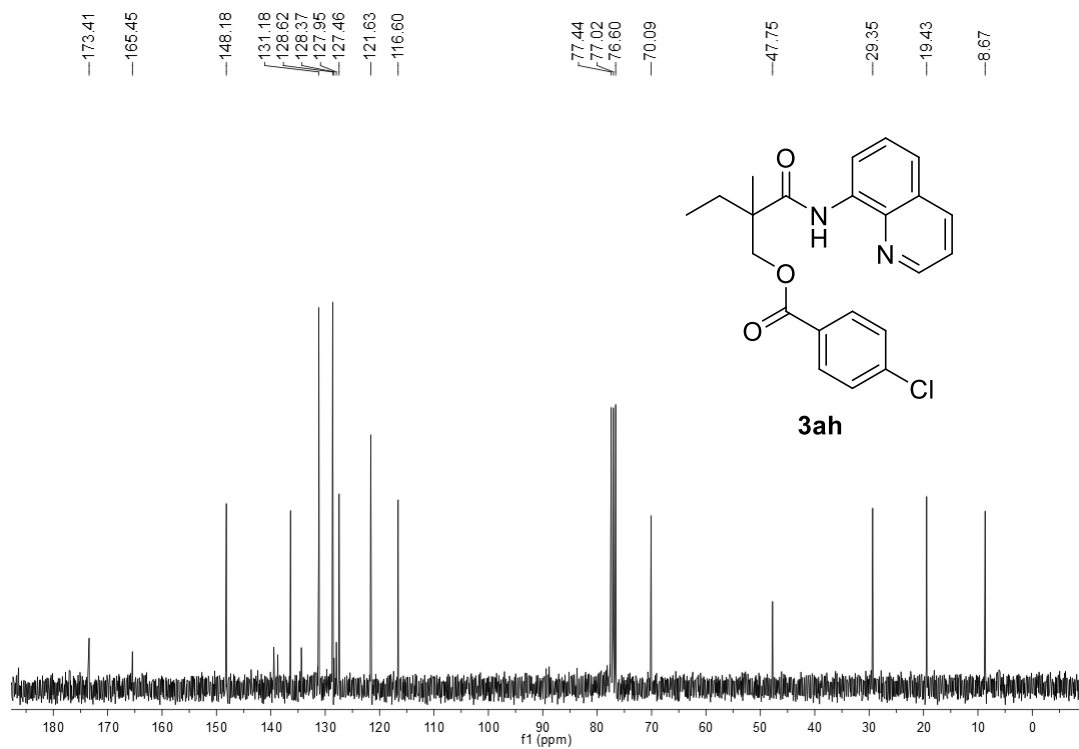


Figure S45. ^1H NMR Spectra of compound 3ah'

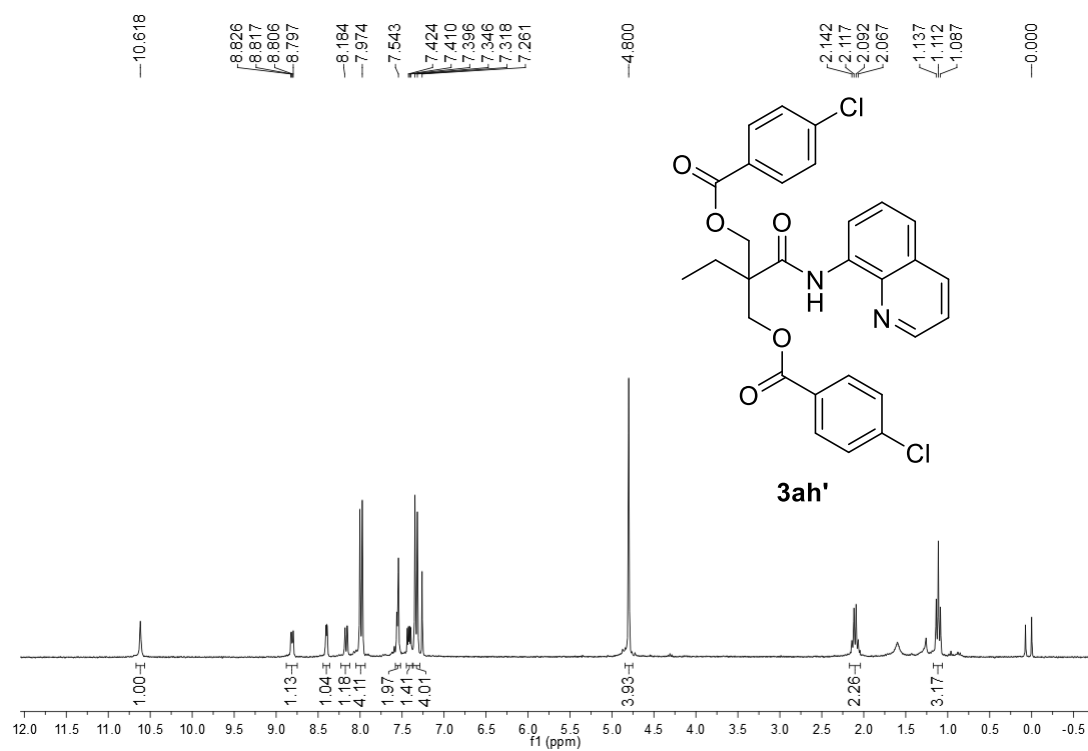


Figure S46. ^{13}C NMR Spectra of compound 3ah'

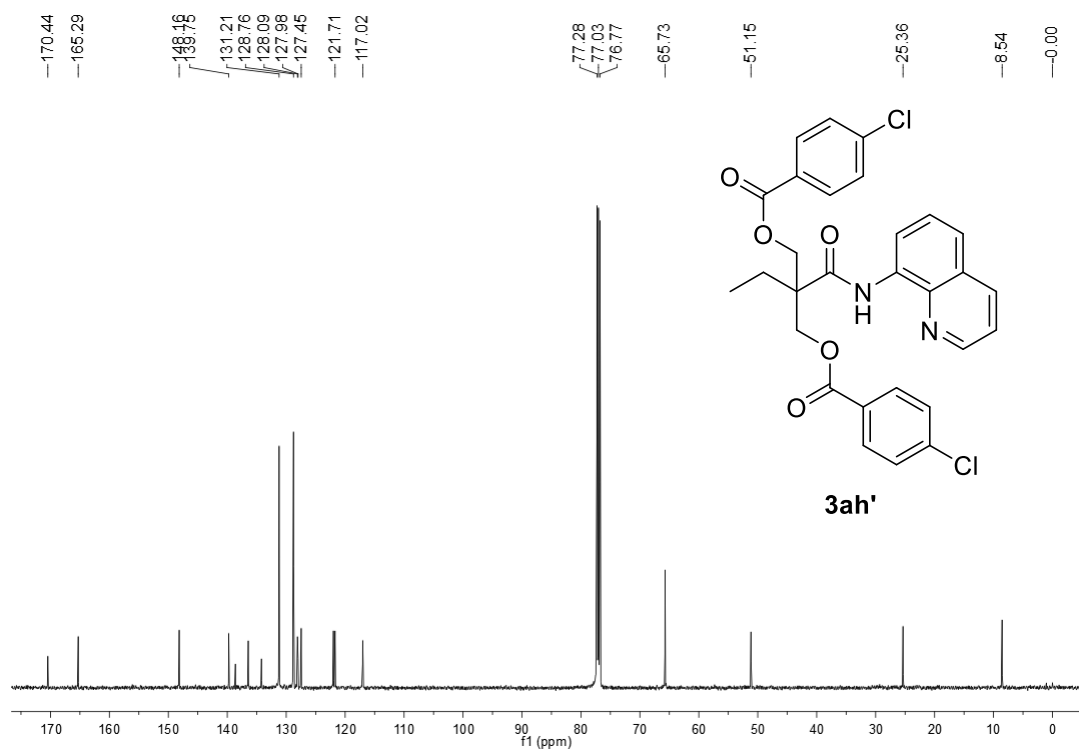


Figure S47. ¹H NMR Spectra of compound 3ai

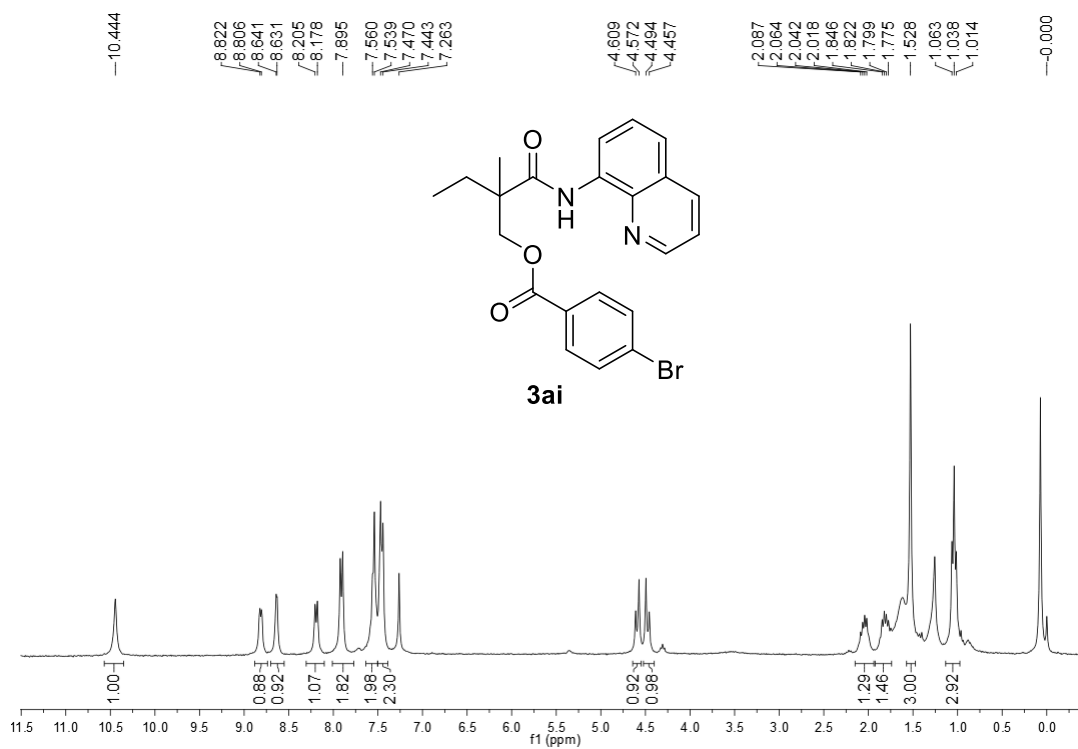


Figure S48. ¹³C NMR Spectra of compound 3ai

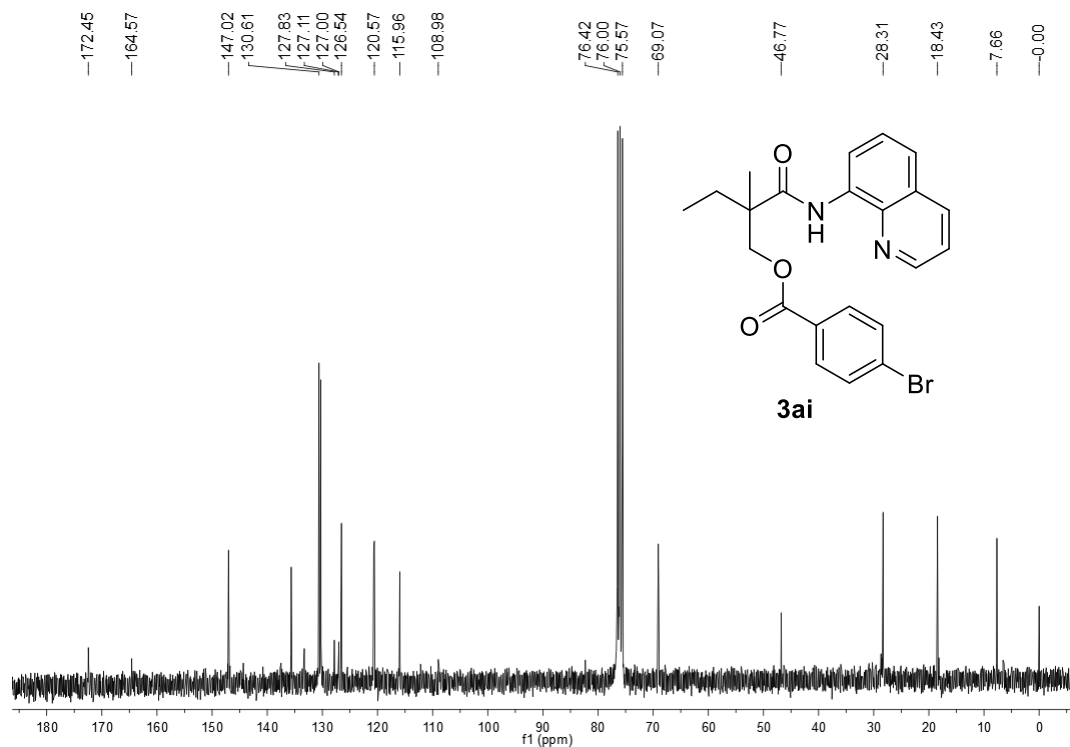


Figure S49. ¹H NMR Spectra of compound 3ai'

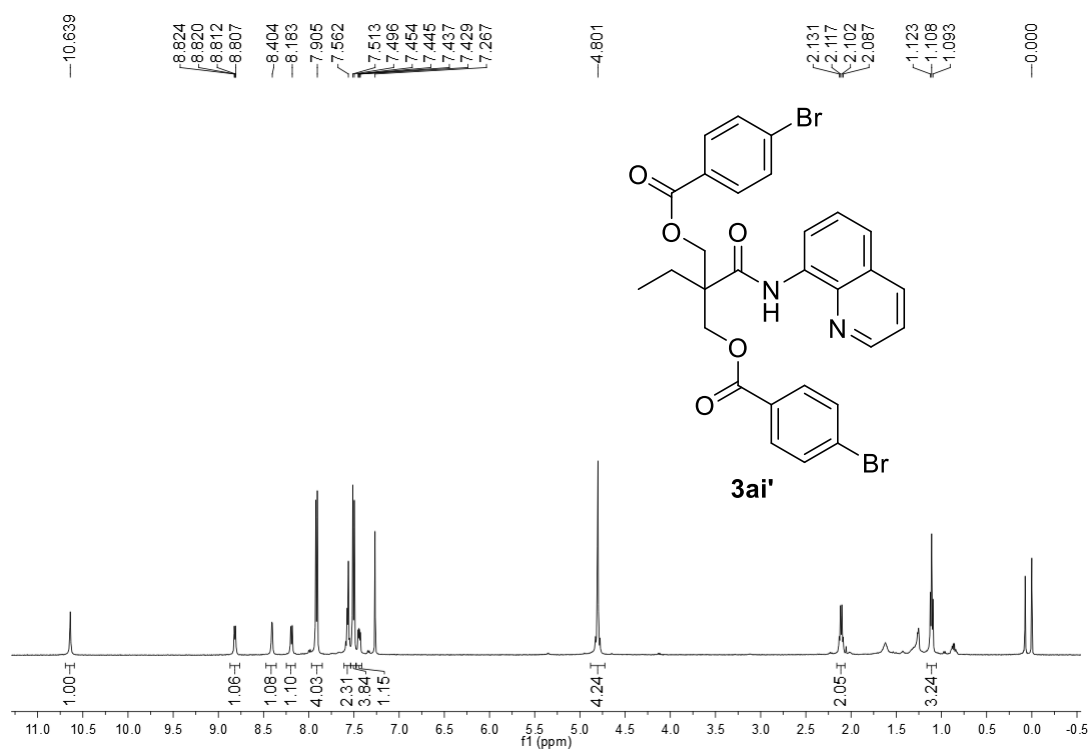


Figure S50. ¹³C NMR Spectra of compound 3ai'

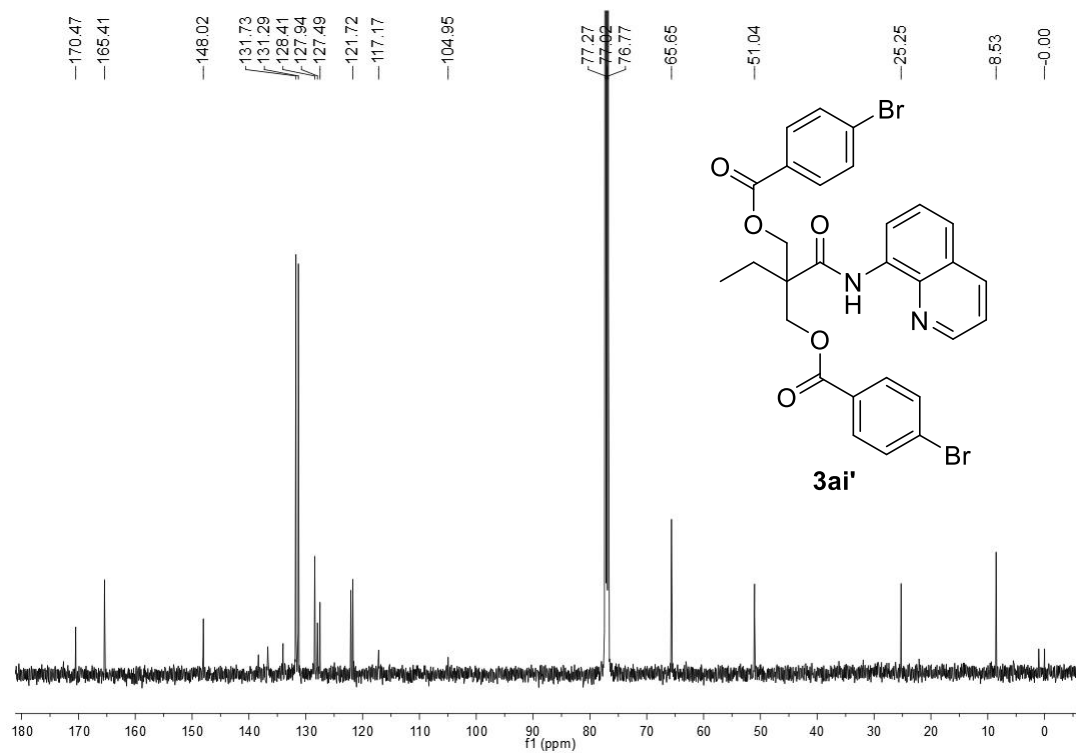


Figure S51. ¹H NMR Spectra of compound 3aj

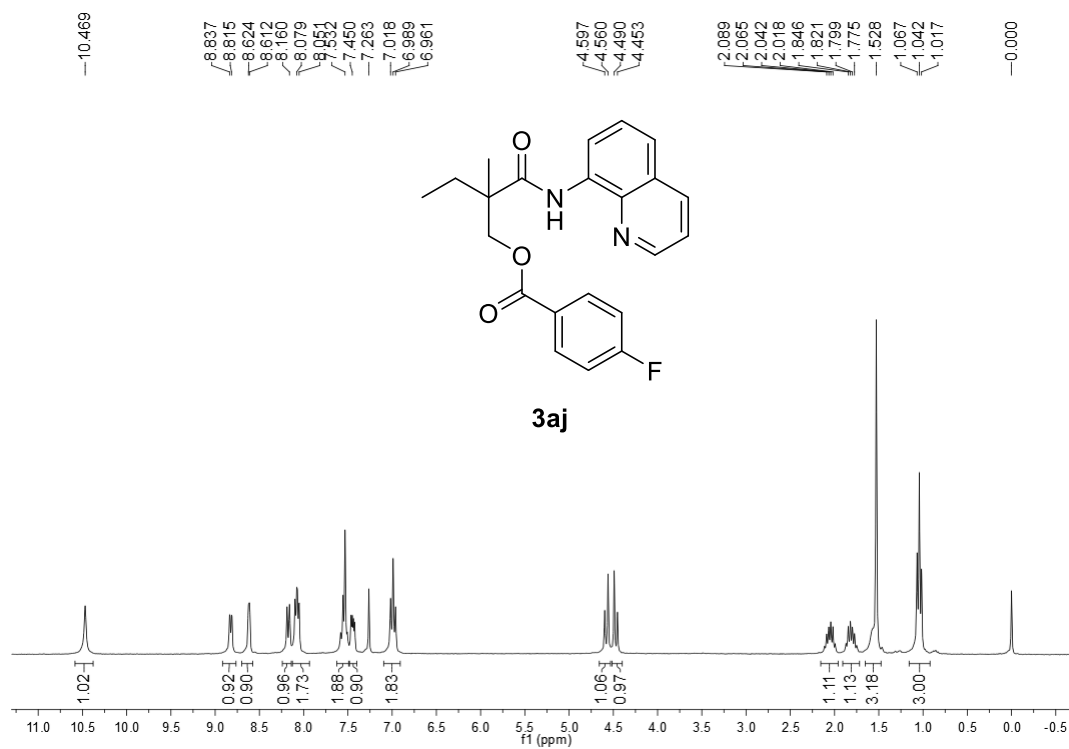


Figure S52. ¹³C NMR Spectra of compound 3aj

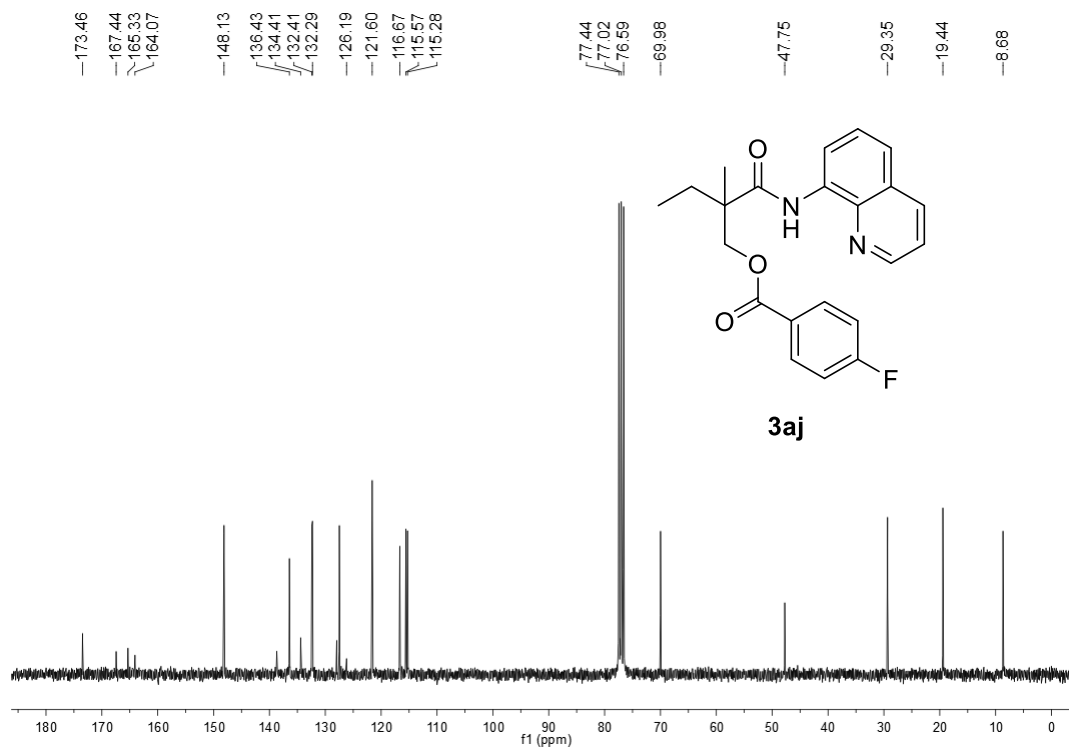


Figure S53. ¹H NMR Spectra of compound 3aj'

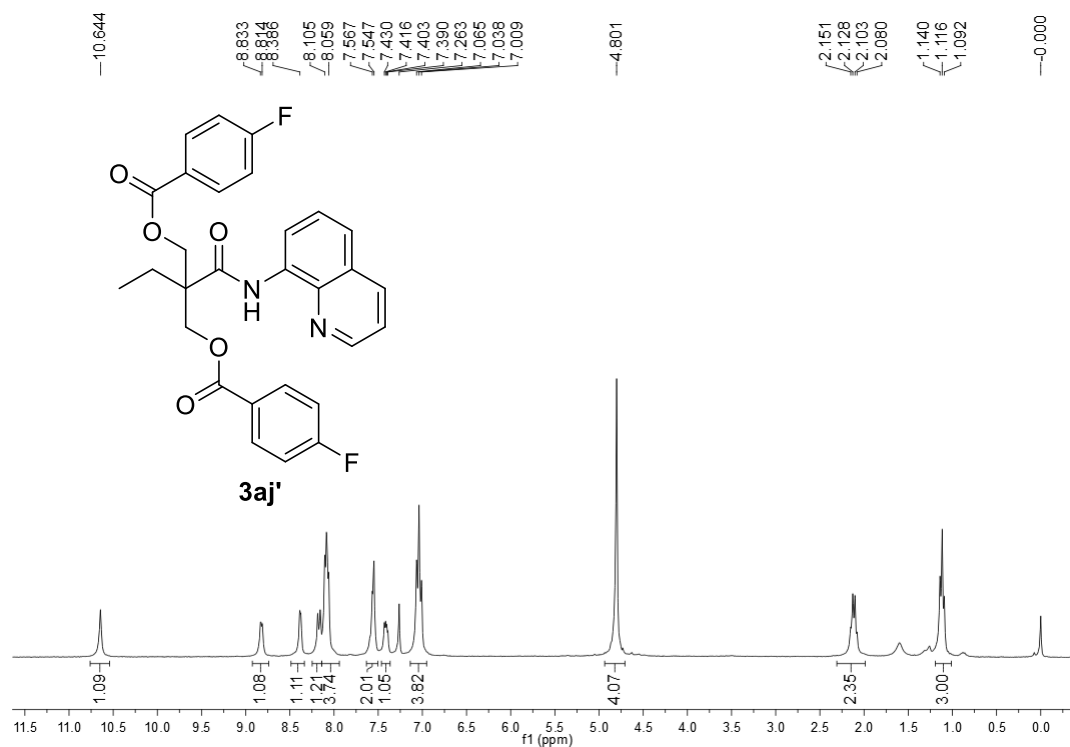


Figure S54. ¹³C NMR Spectra of compound 3aj'

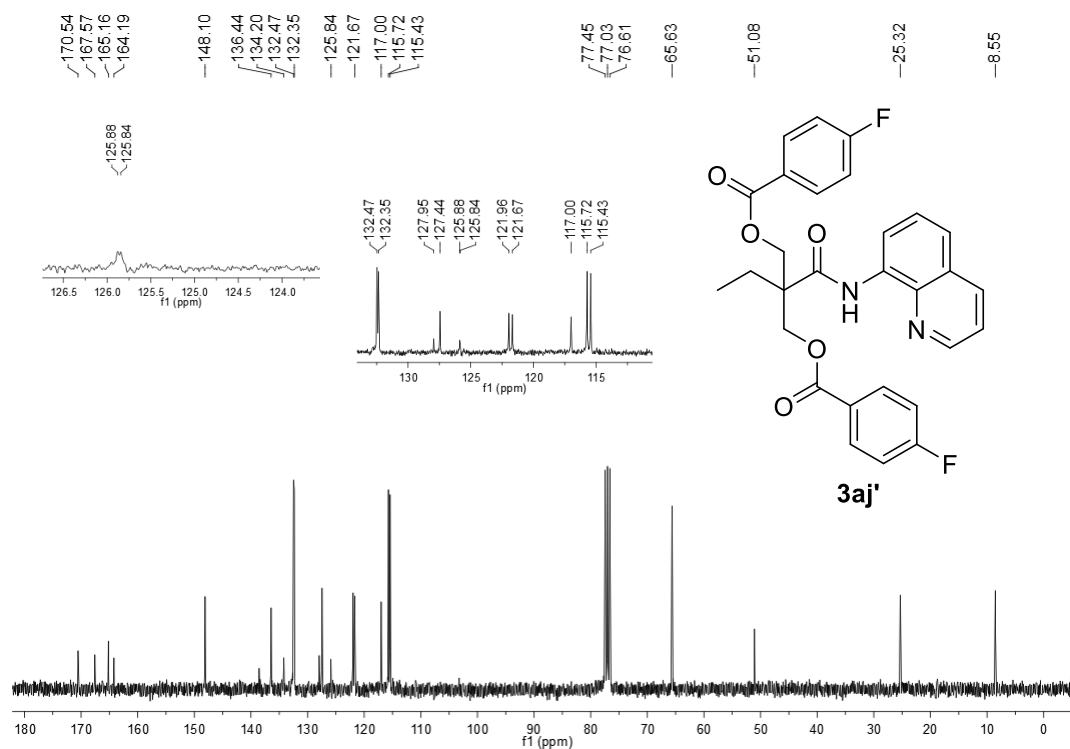


Figure S55. ¹H NMR Spectra of compound 3ak

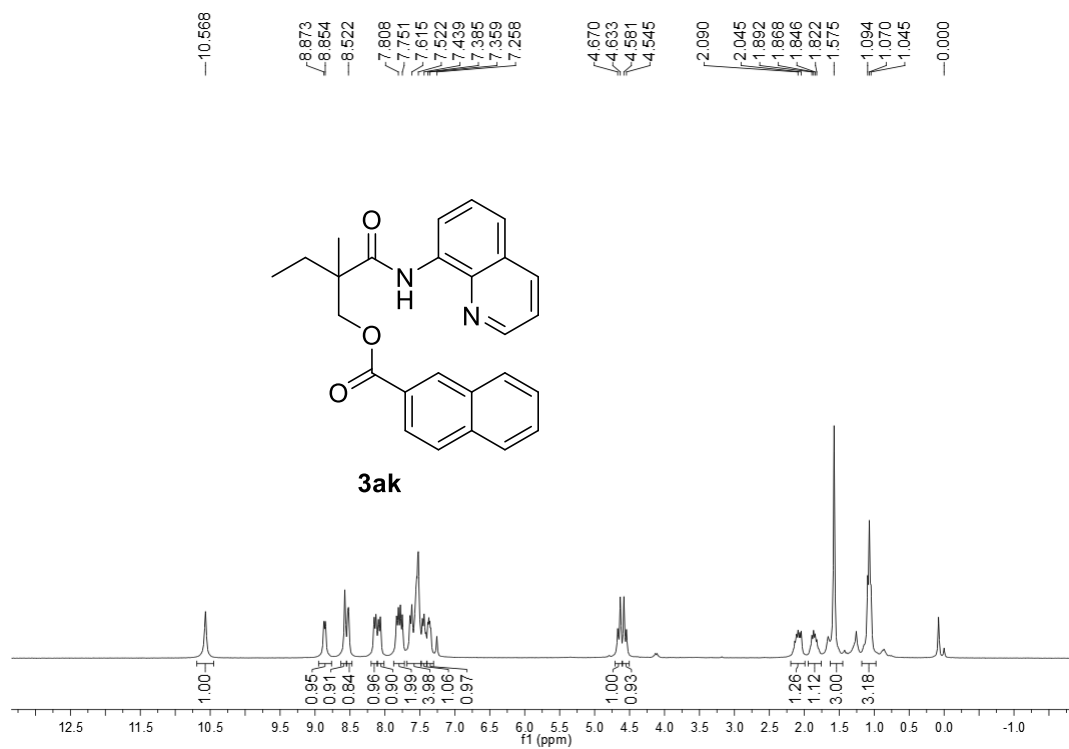


Figure S56. ¹³C NMR Spectra of compound 3ak

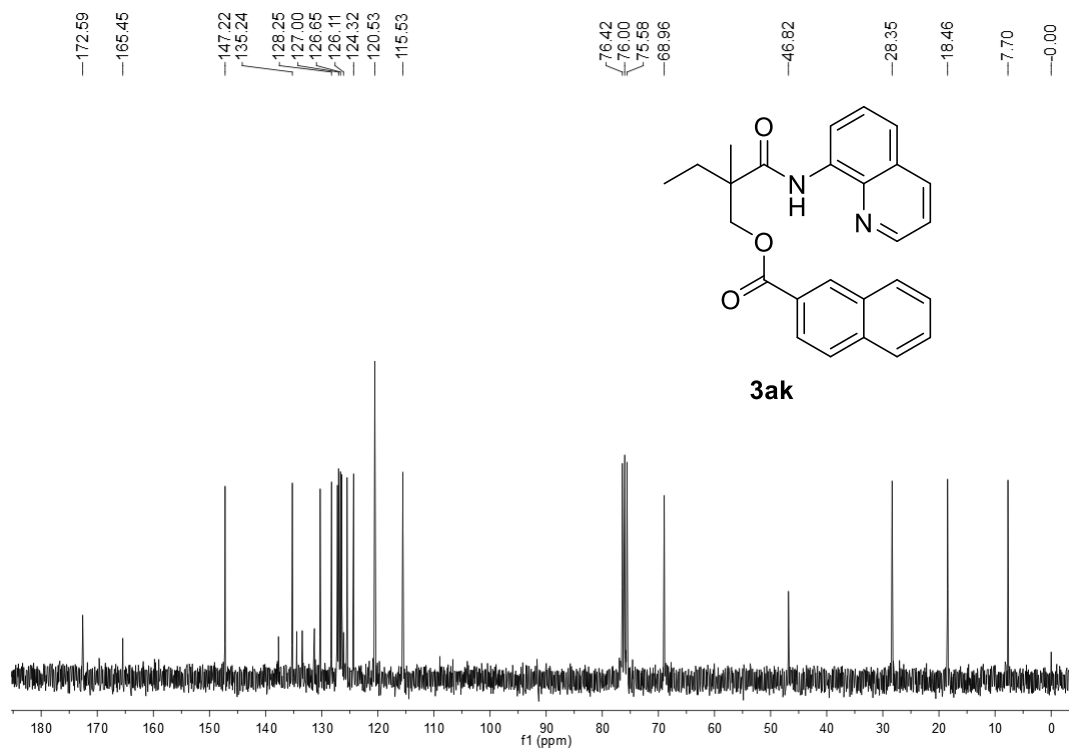


Figure S57. ¹H NMR Spectra of compound 3ak'

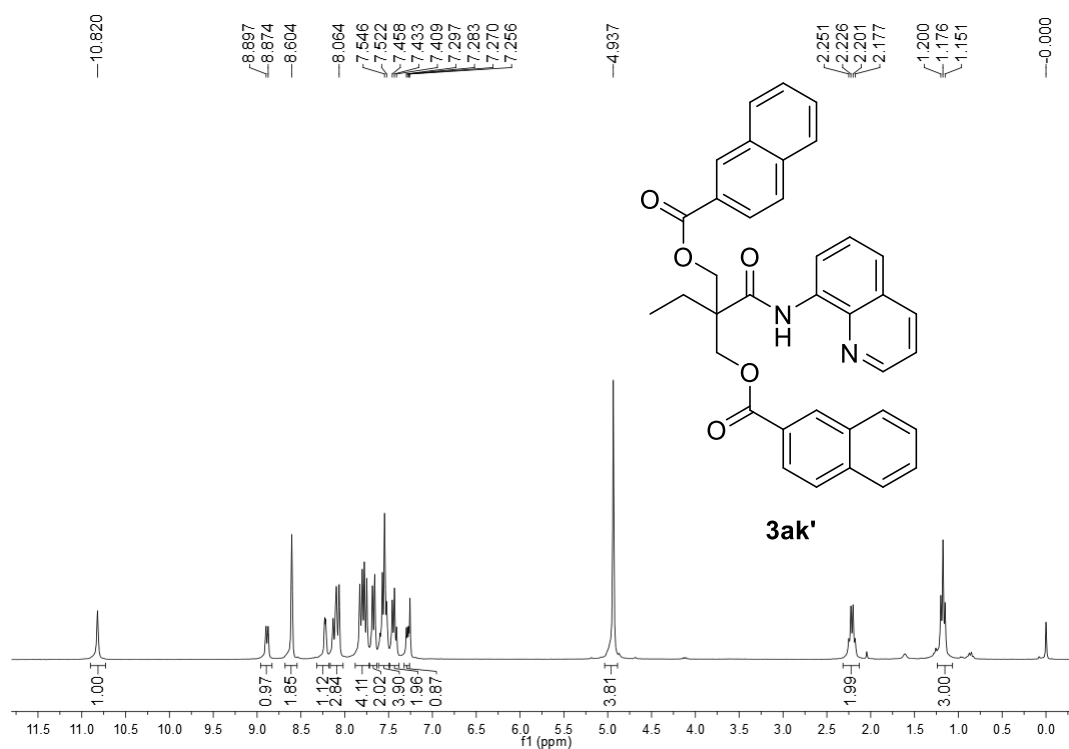


Figure S58. ¹³C NMR Spectra of compound 3ak'

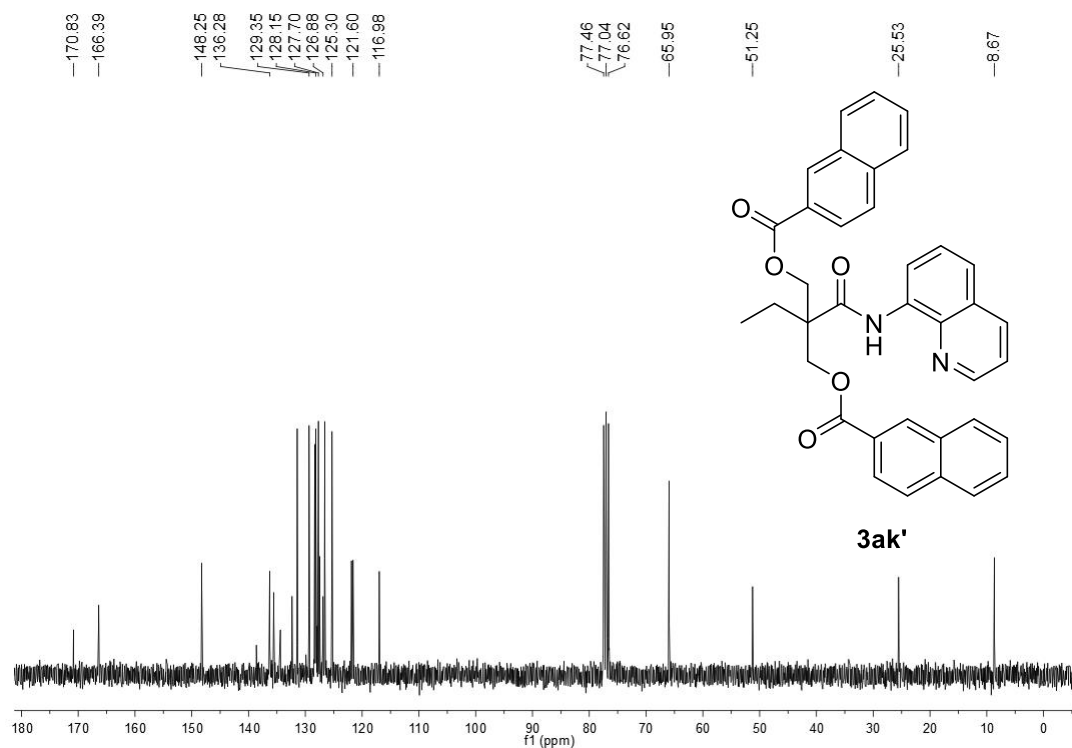


Figure S59. ¹H NMR Spectra of compound 3al

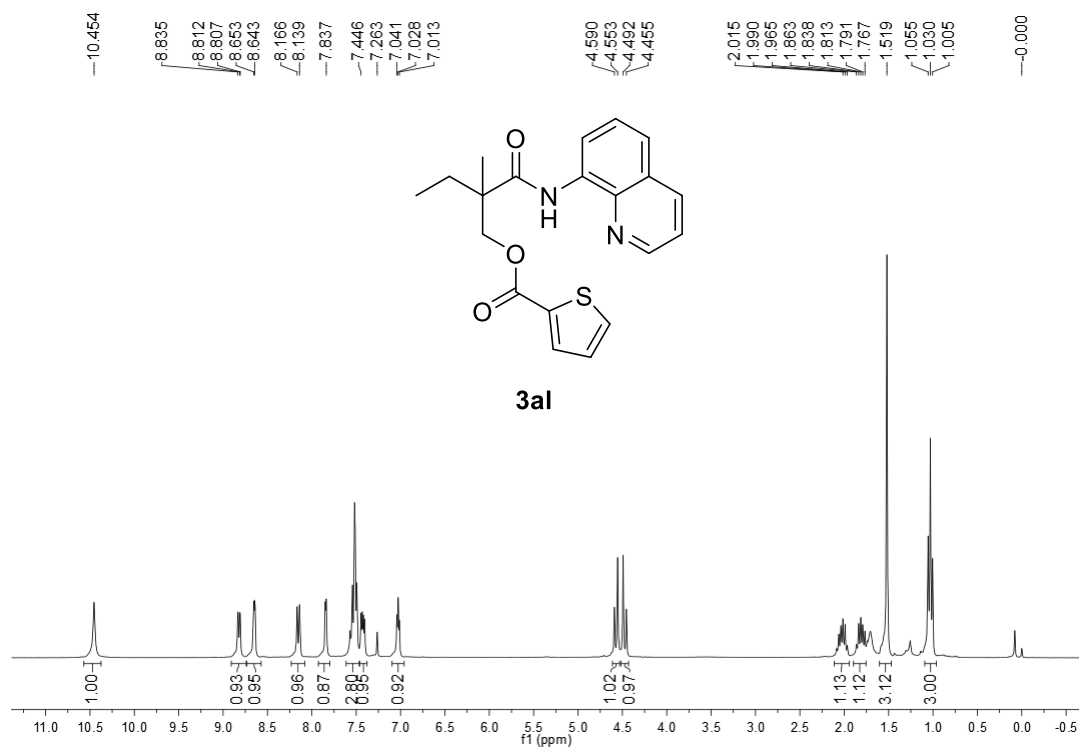


Figure S60. ¹³C NMR Spectra of compound 3al

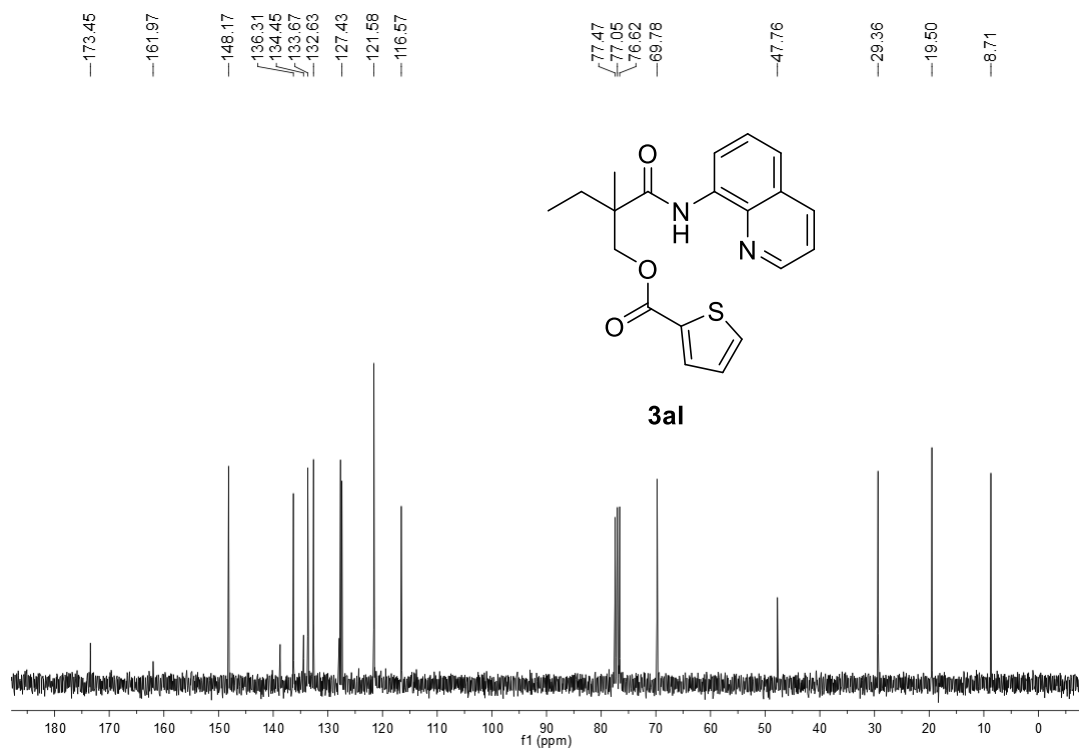


Figure S61. ¹H NMR Spectra of compound 3a'

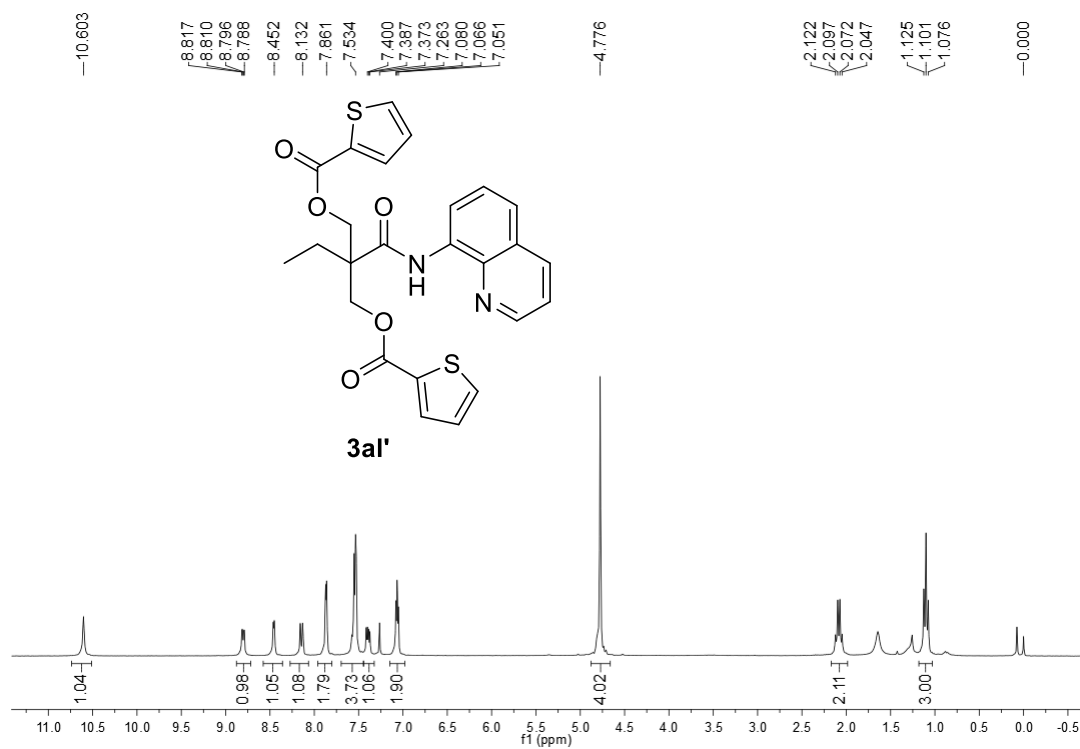


Figure S62. ¹³C NMR Spectra of compound 3a'

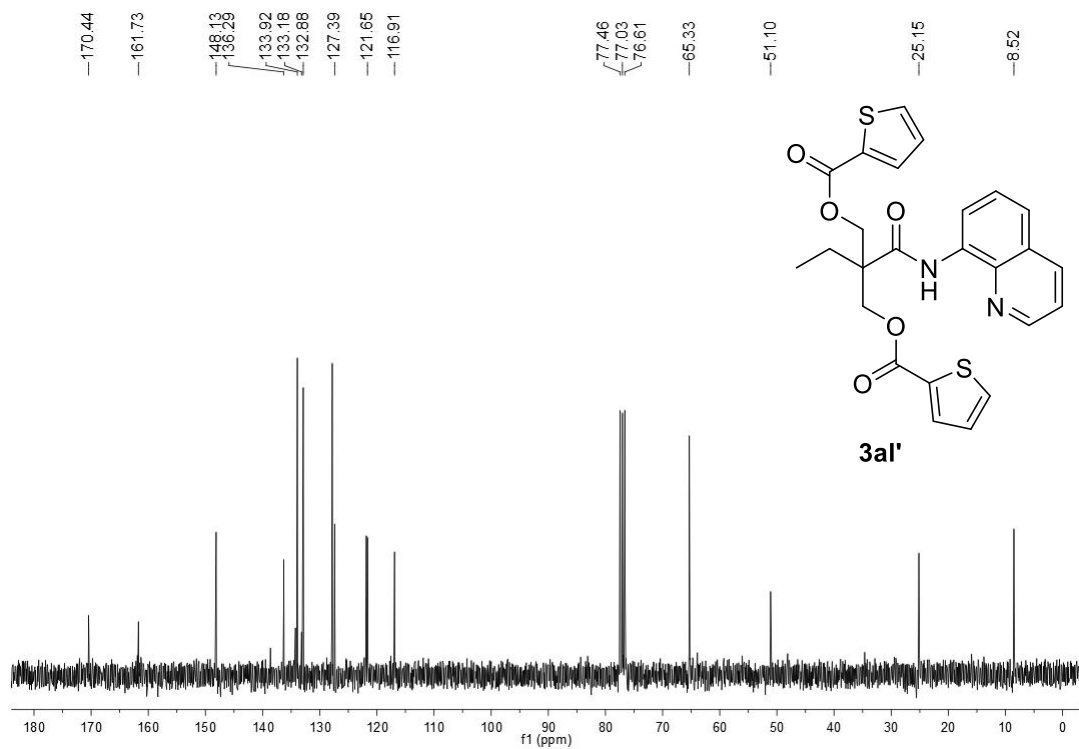


Figure S63. ¹H NMR Spectra of compound 3am

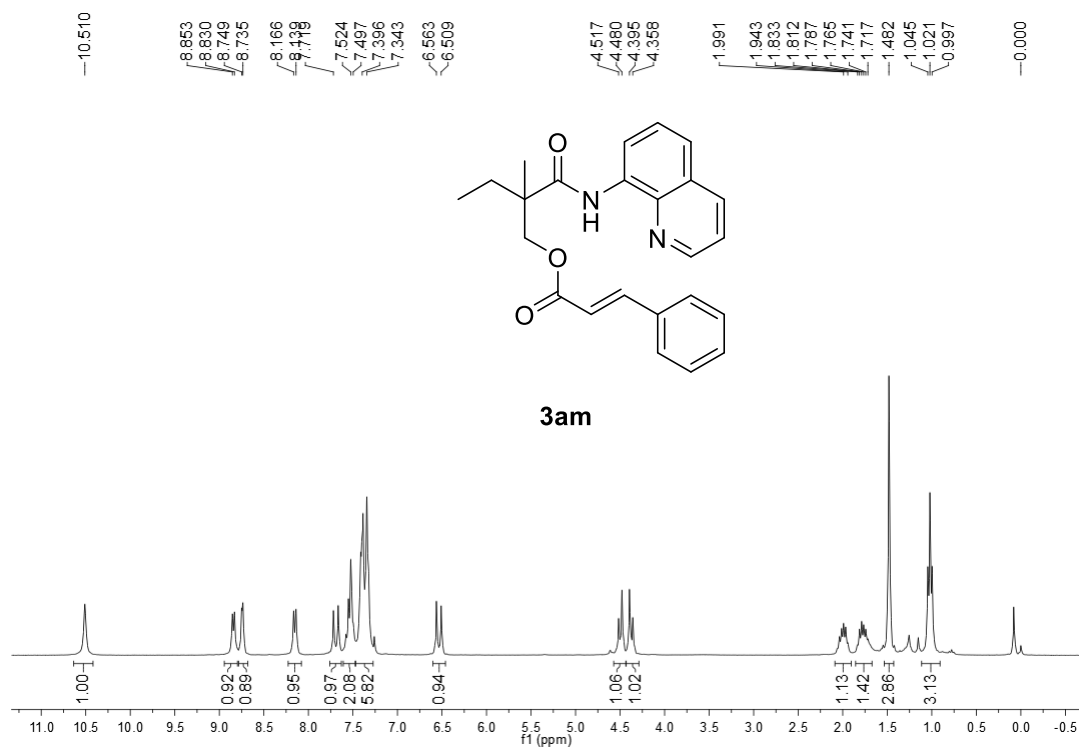


Figure S64. ¹³C NMR Spectra of compound 3am

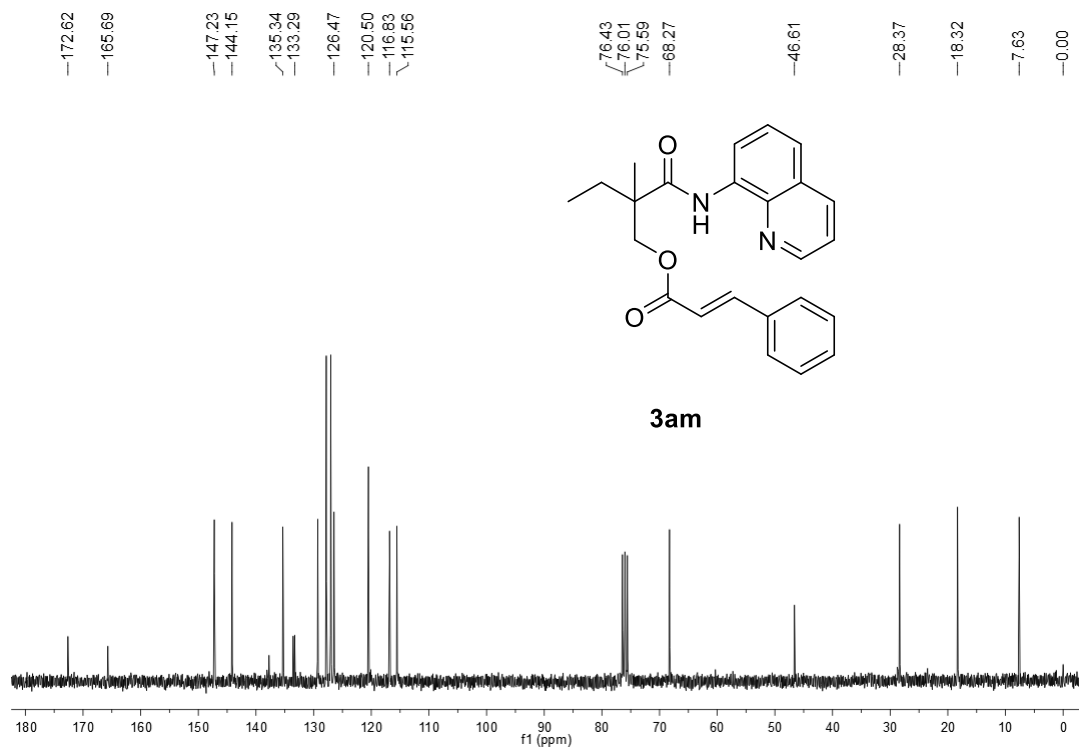


Figure S65. ¹H NMR Spectra of compound 3am'

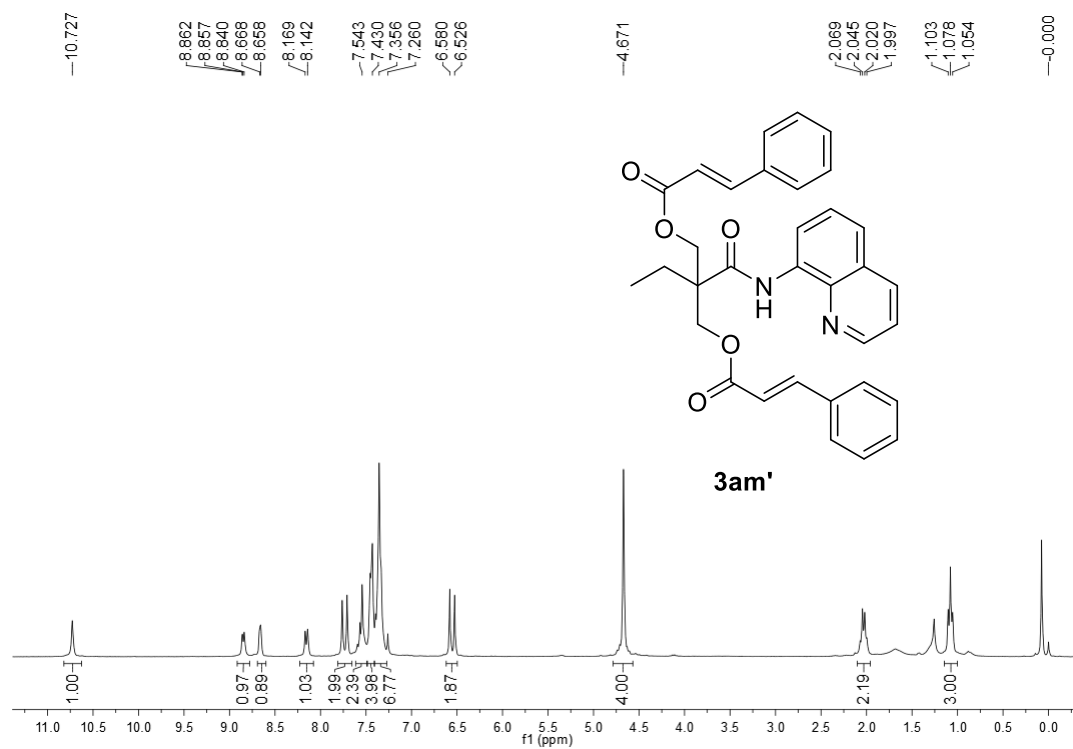


Figure S66. ¹³C NMR Spectra of compound 3am'

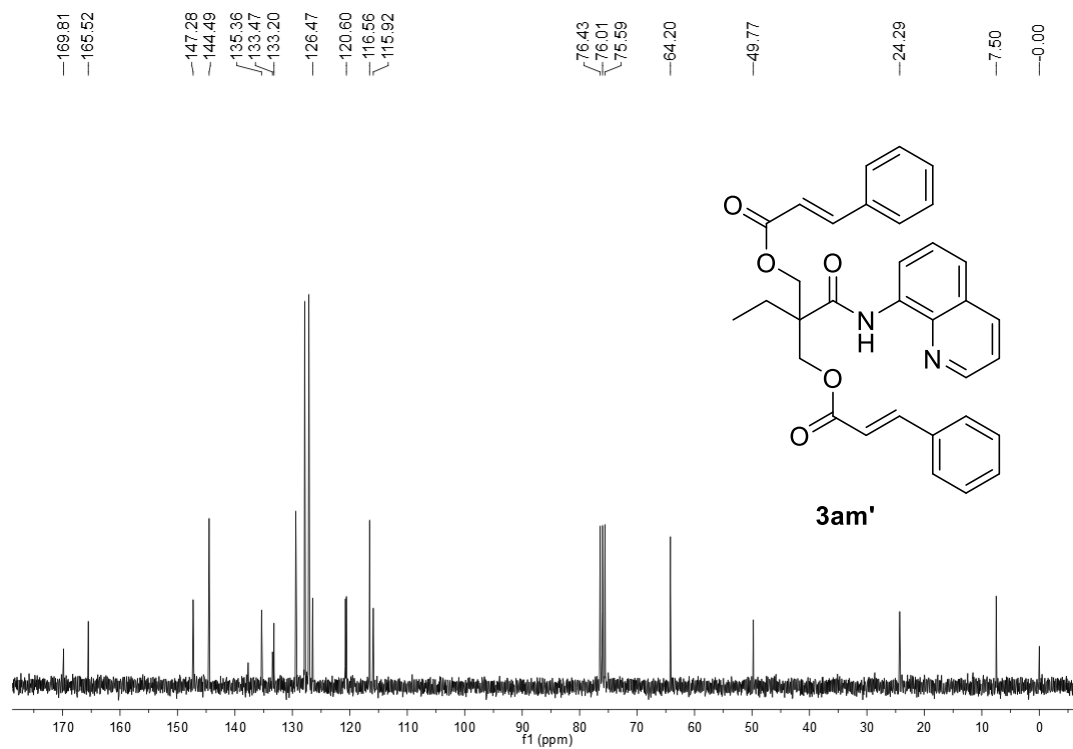


Figure S67. ¹H NMR Spectra of compound 3an

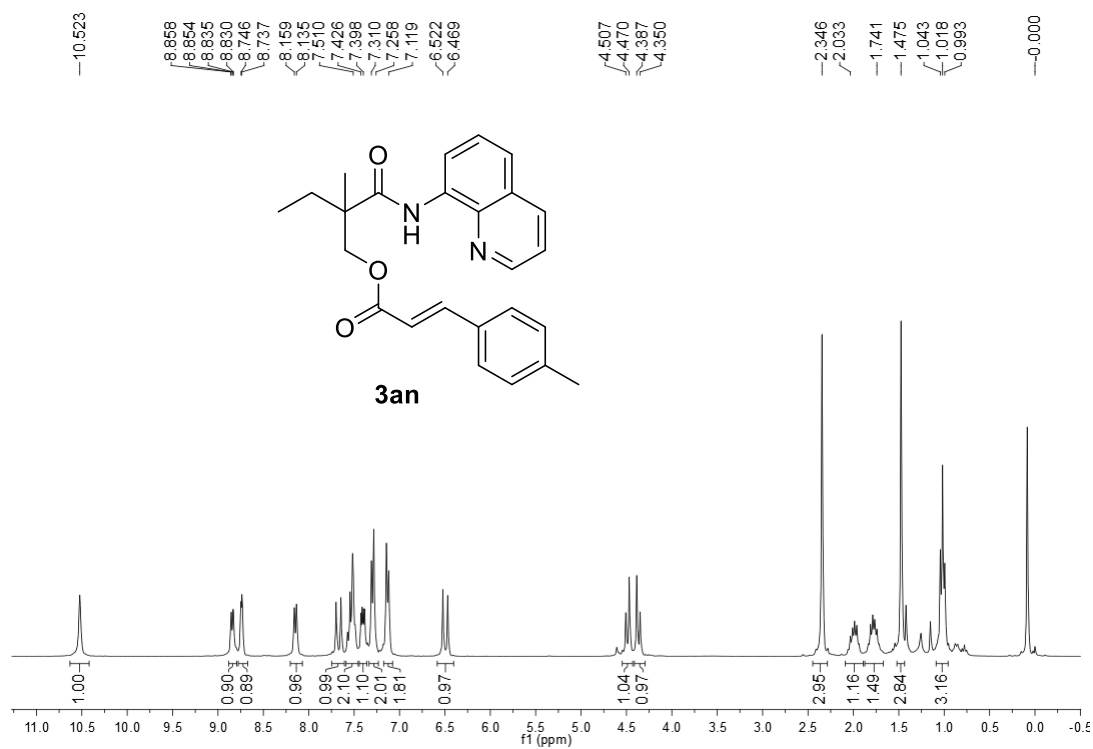


Figure S68. ¹³C NMR Spectra of compound 3an

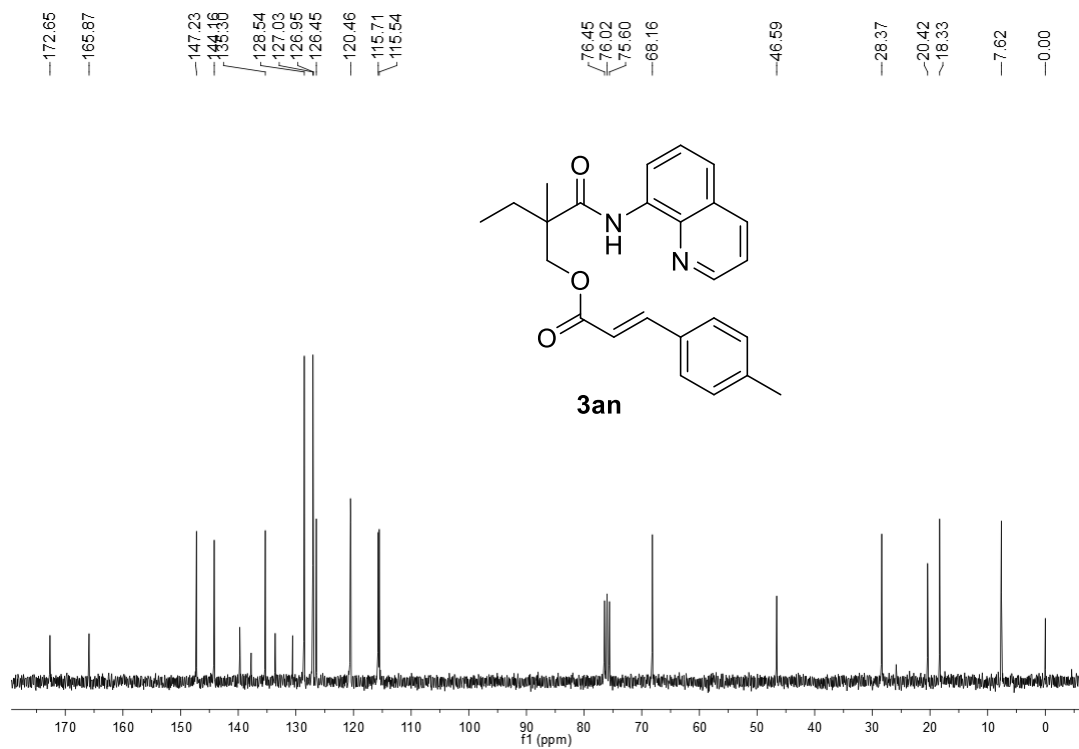


Figure S69. ¹H NMR Spectra of compound 3an'

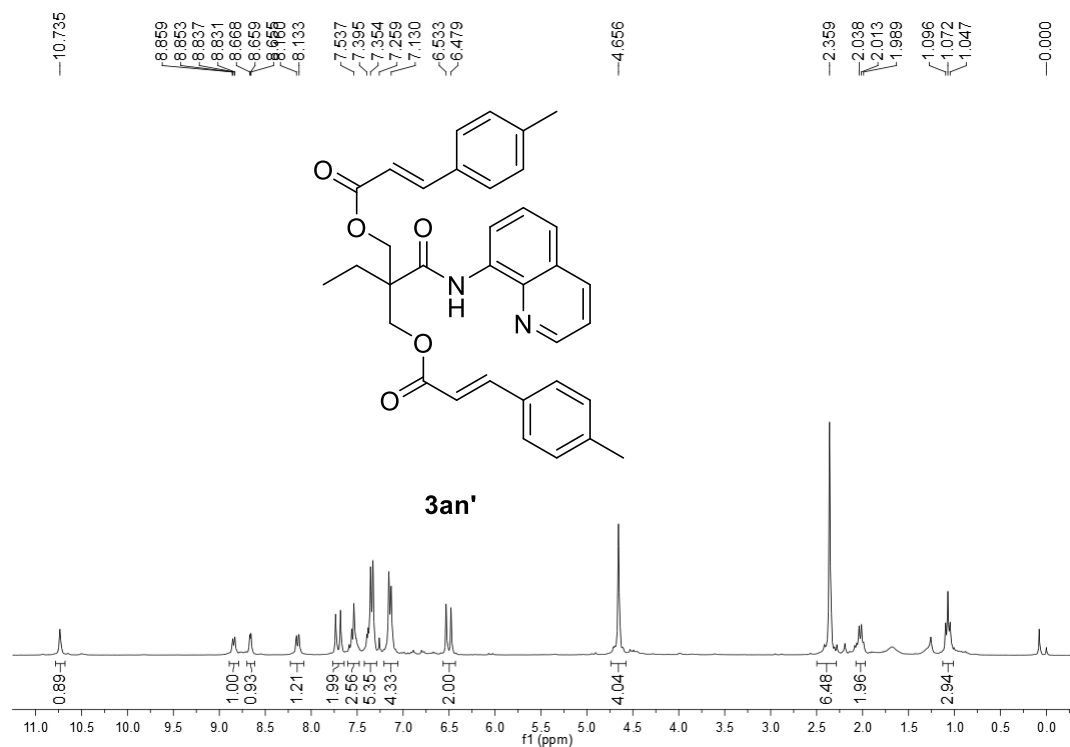


Figure S70. ¹³C NMR Spectra of compound 3an'

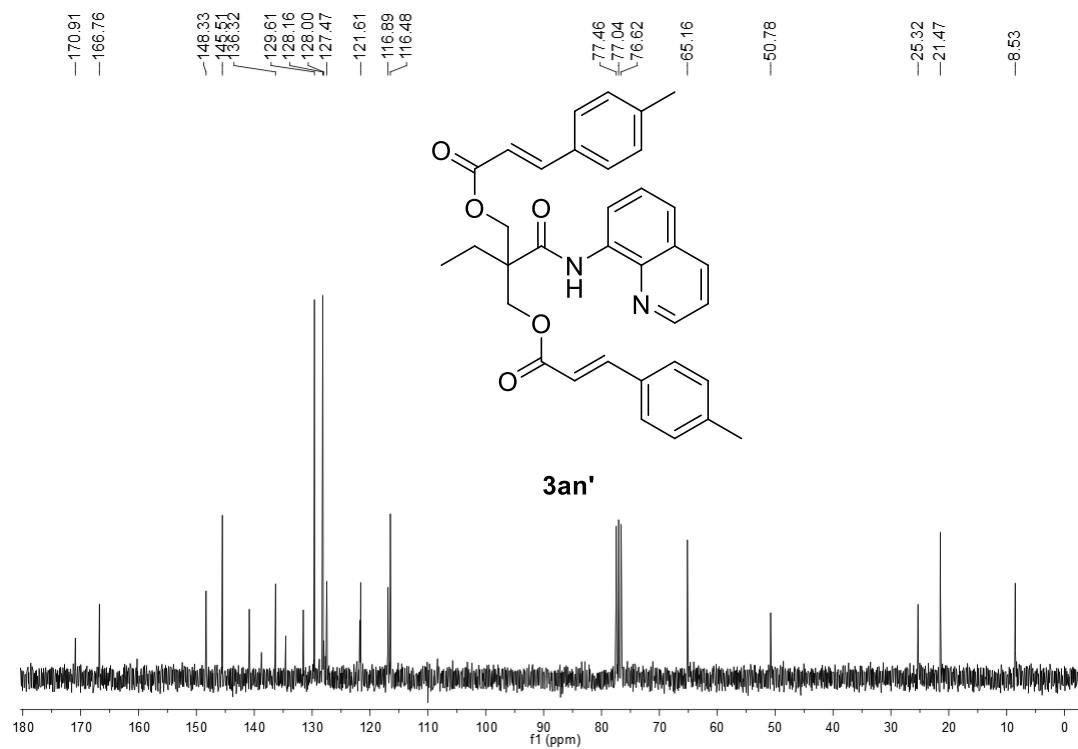


Figure S71. ¹H NMR Spectra of compound 3ao

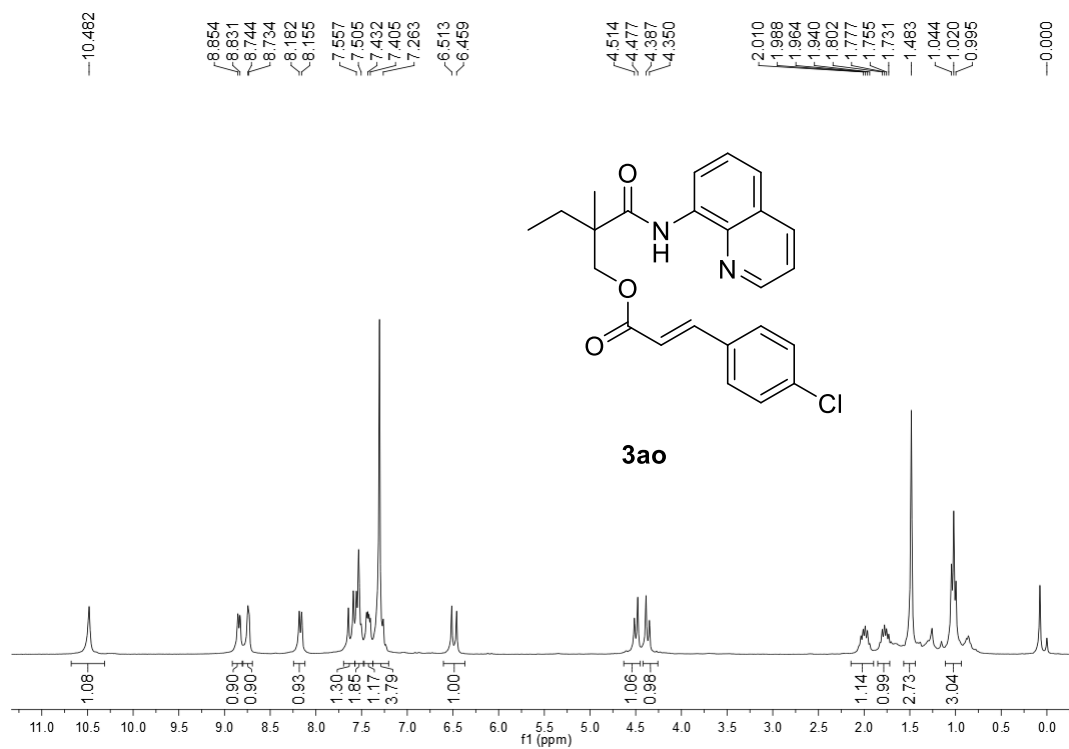


Figure S72. ¹³C NMR Spectra of compound 3ao

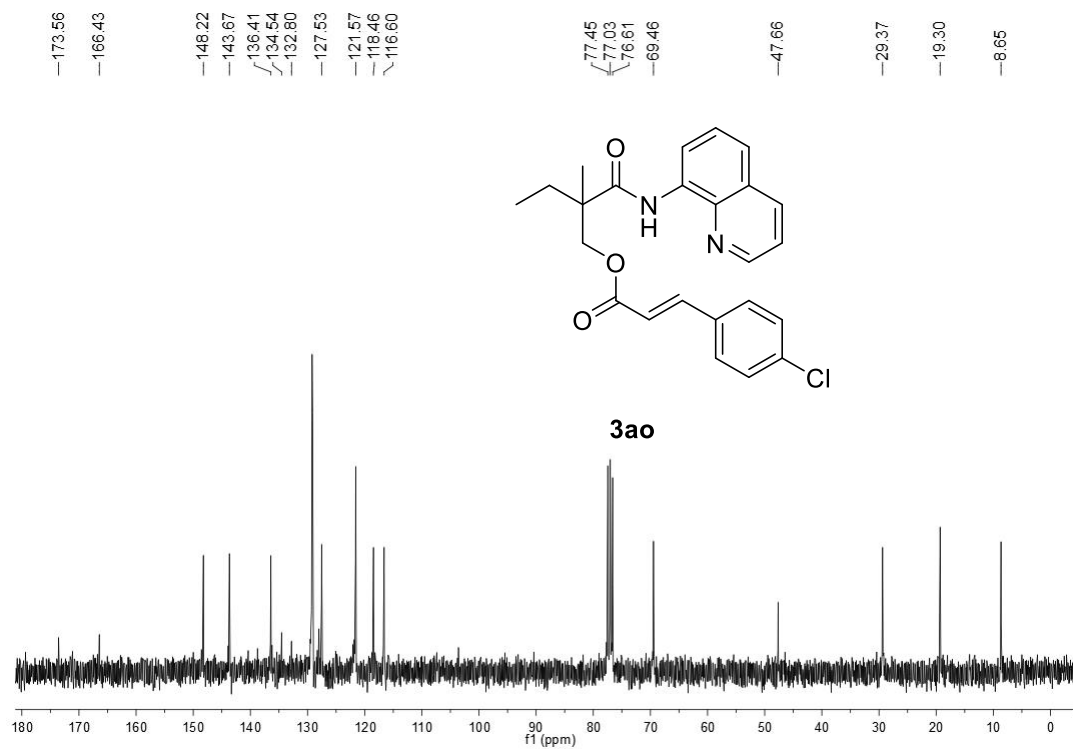


Figure S73. ^1H NMR Spectra of compound **3ao'**

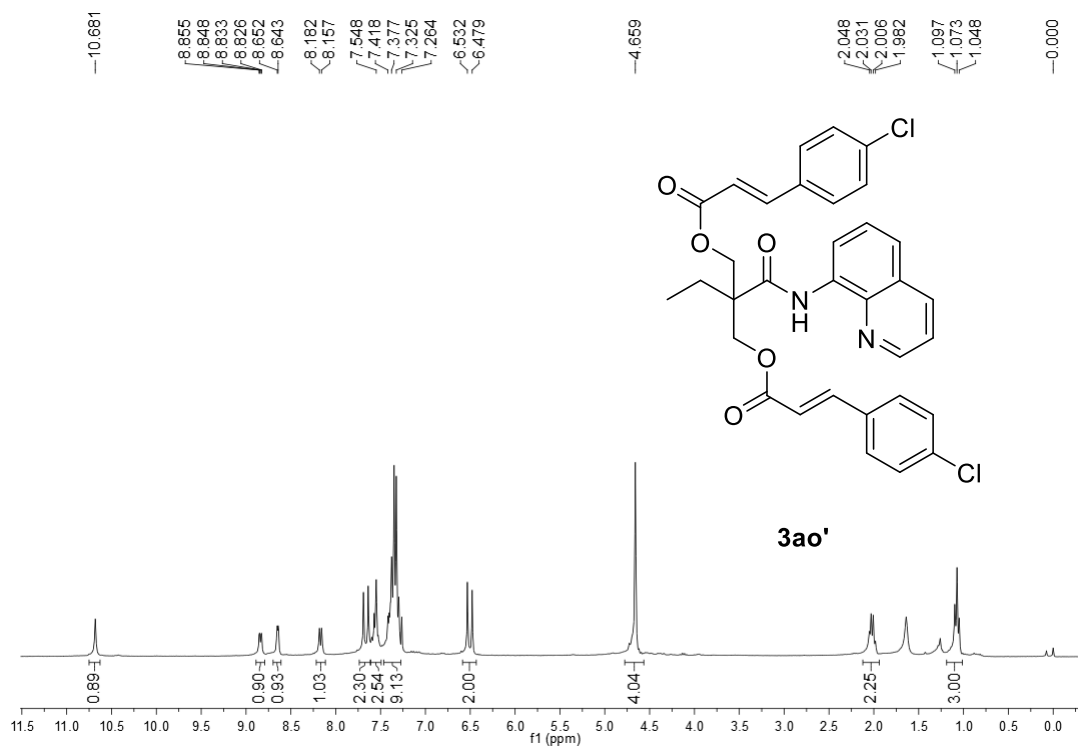


Figure S74. ^{13}C NMR Spectra of compound **3ao'**

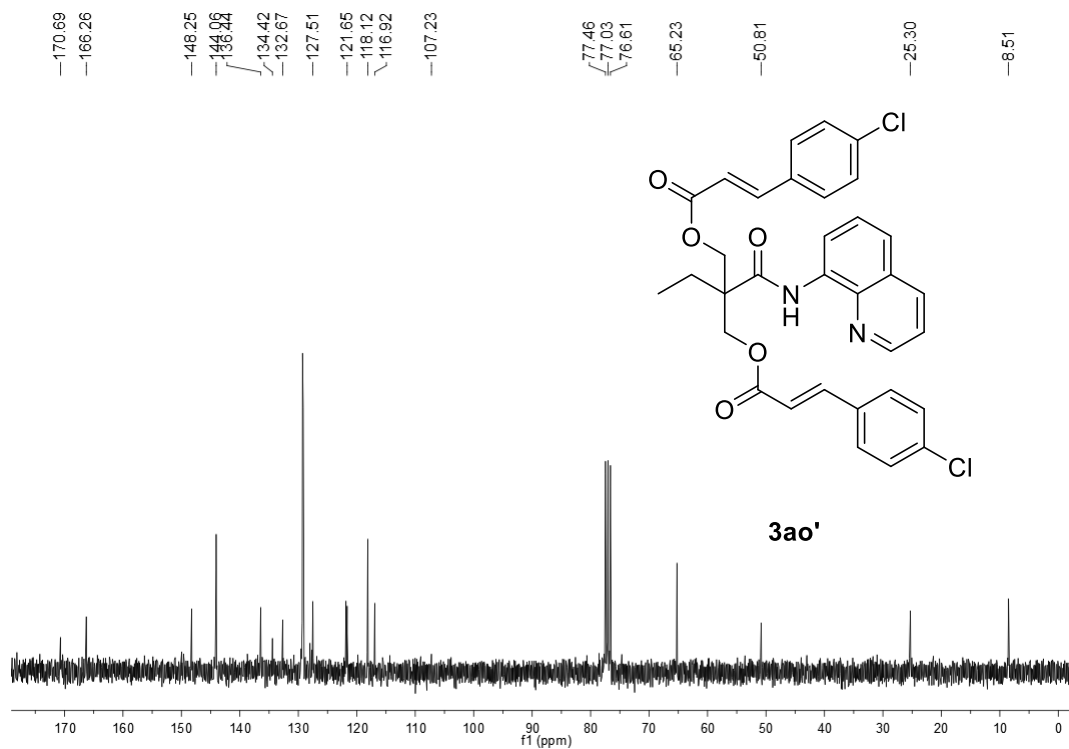


Figure S75. ¹H NMR Spectra of compound 3ap

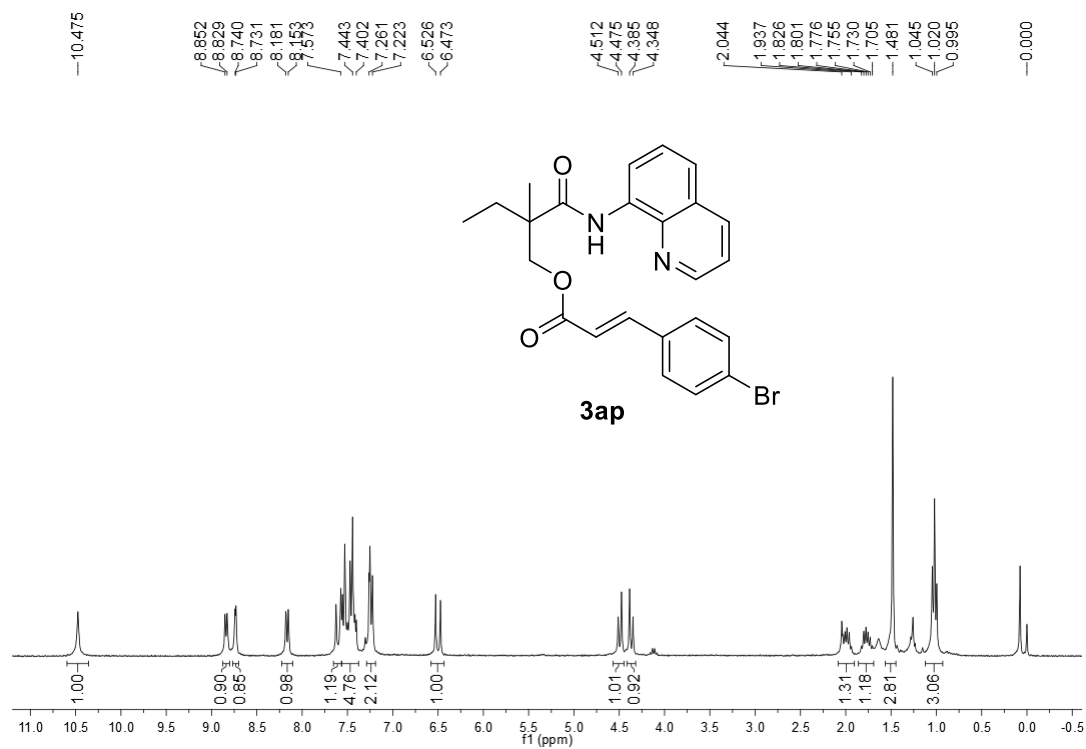


Figure S76. ¹³C NMR Spectra of compound 3ap

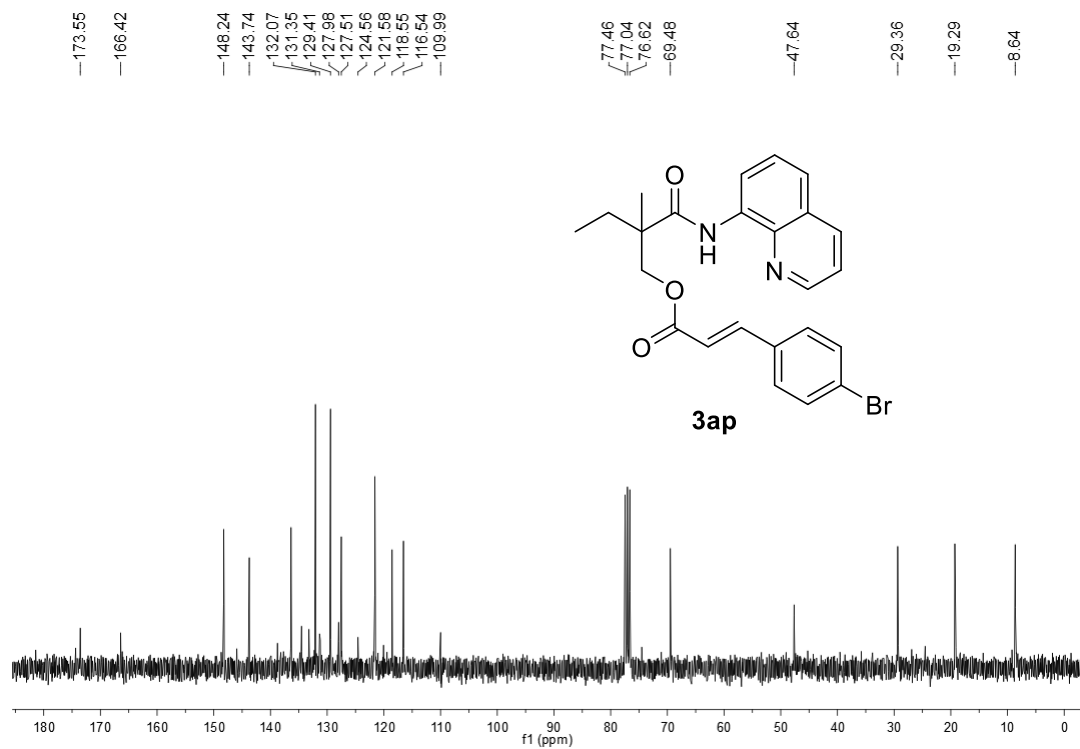


Figure S77. ¹H NMR Spectra of compound 3ap'

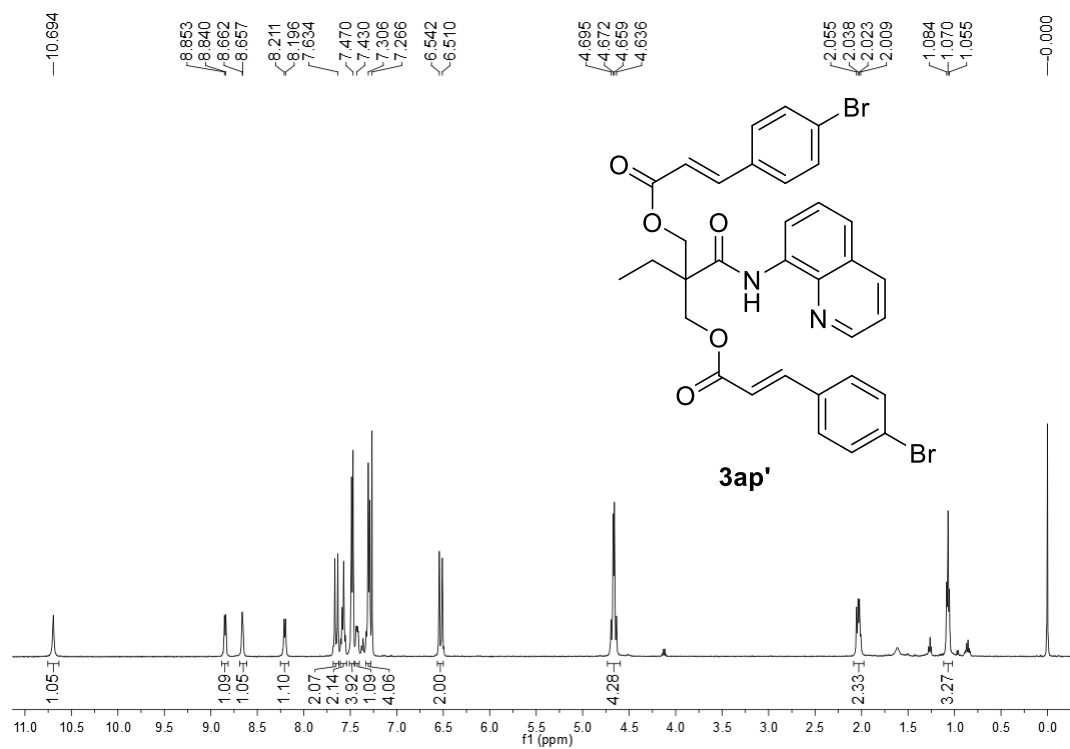


Figure S78. ¹³C NMR Spectra of compound 3ap'

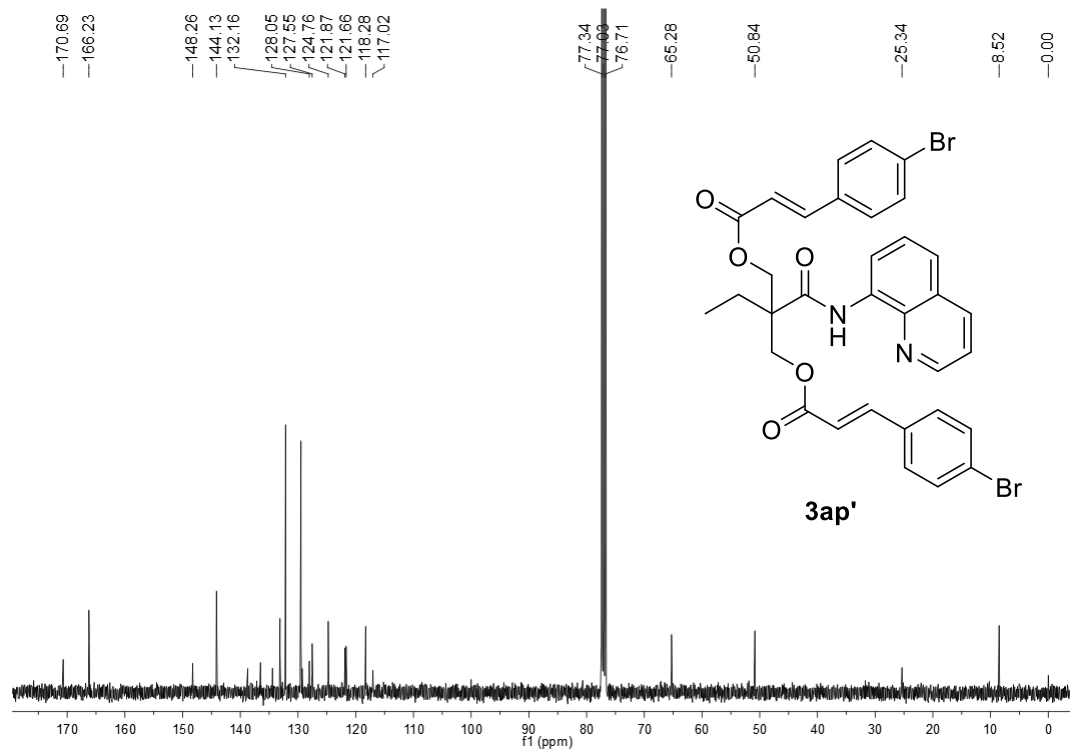


Figure S79. ¹H NMR Spectra of compound 3aq

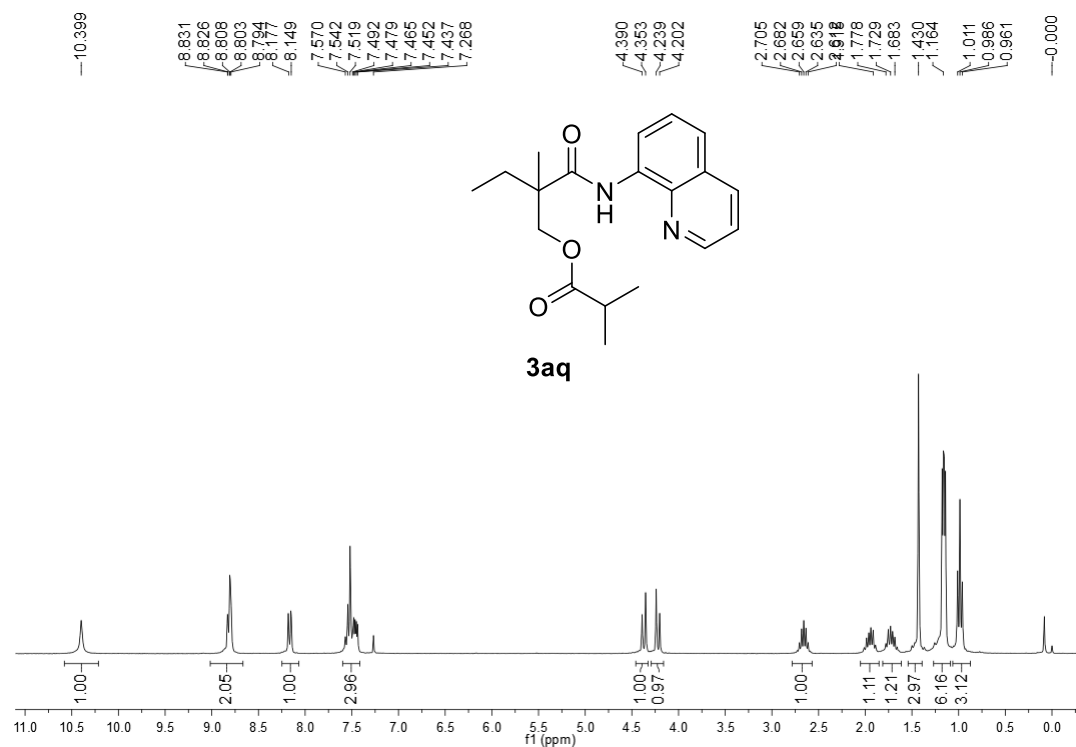


Figure S80. ¹³C NMR Spectra of compound 3aq

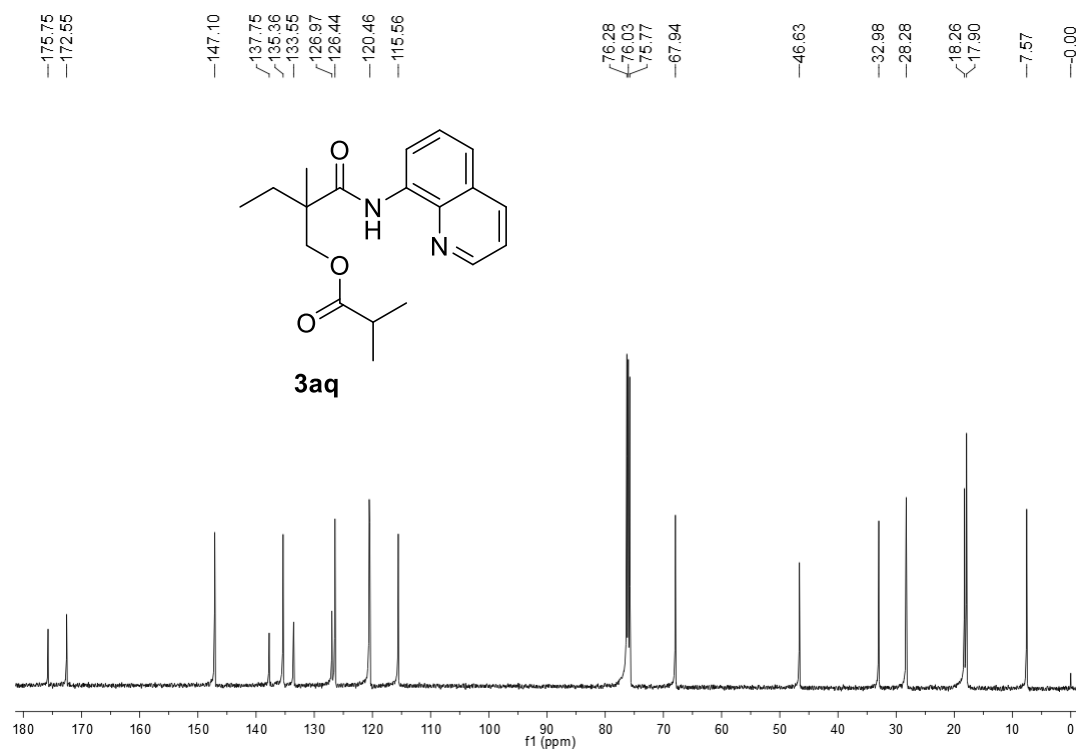


Figure S81. ¹H NMR Spectra of compound 3aq'

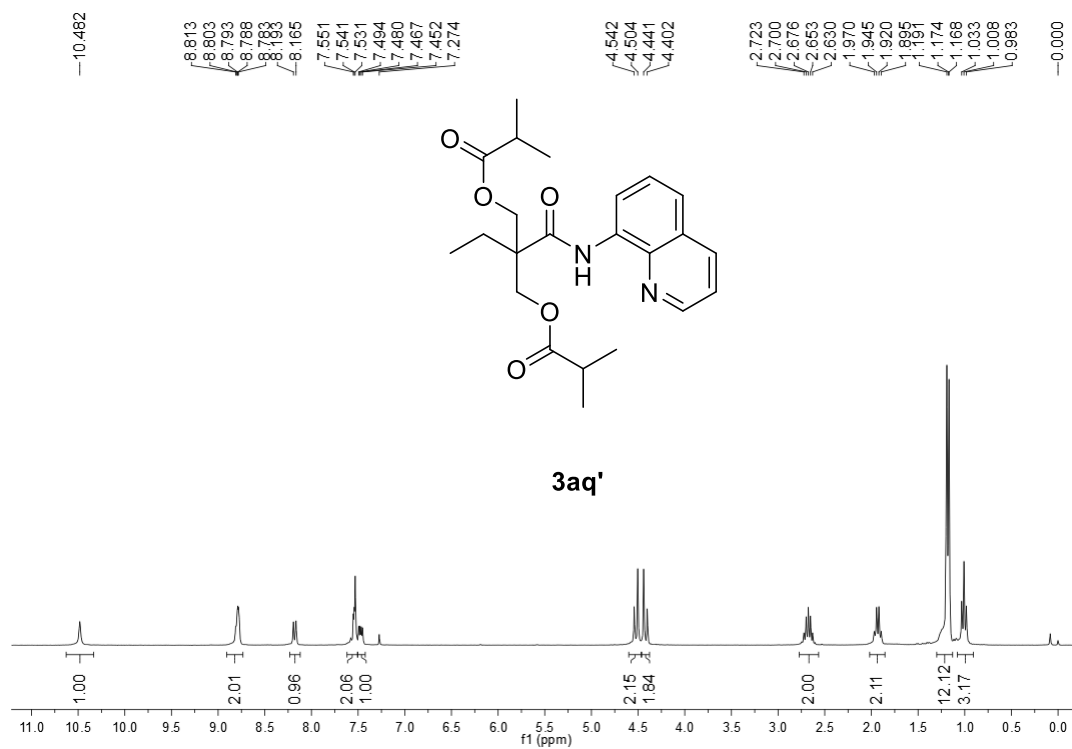


Figure S82. ¹³C NMR Spectra of compound 3aq'

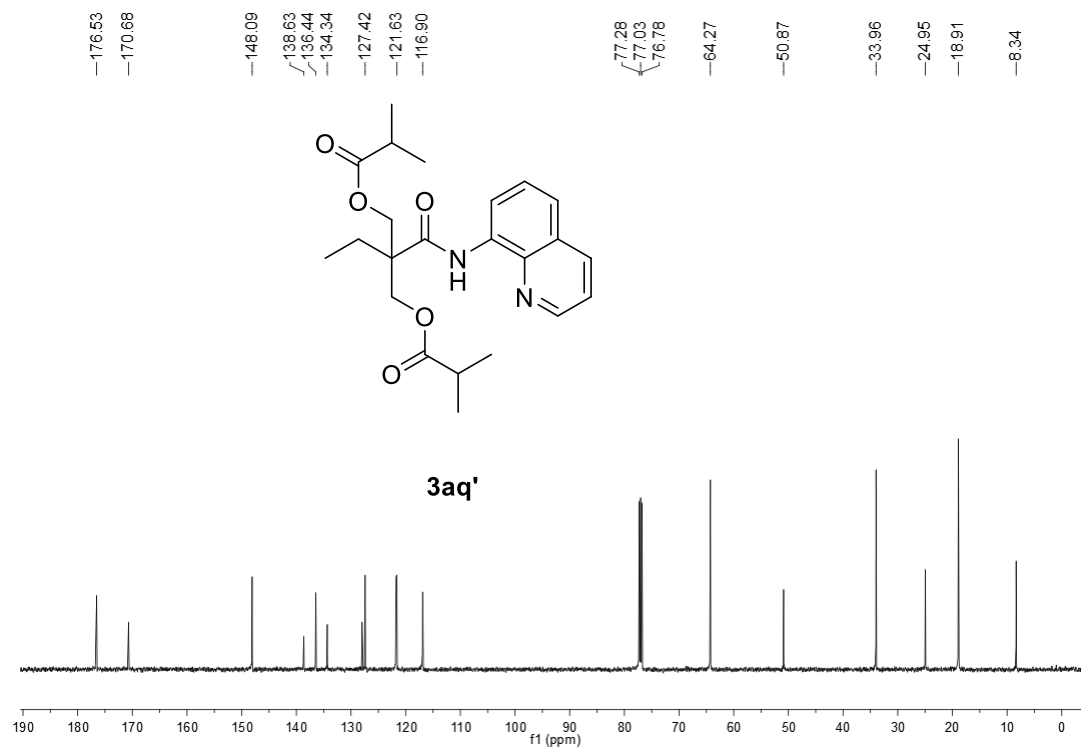


Figure S83. ¹H NMR Spectra of compound 3ar

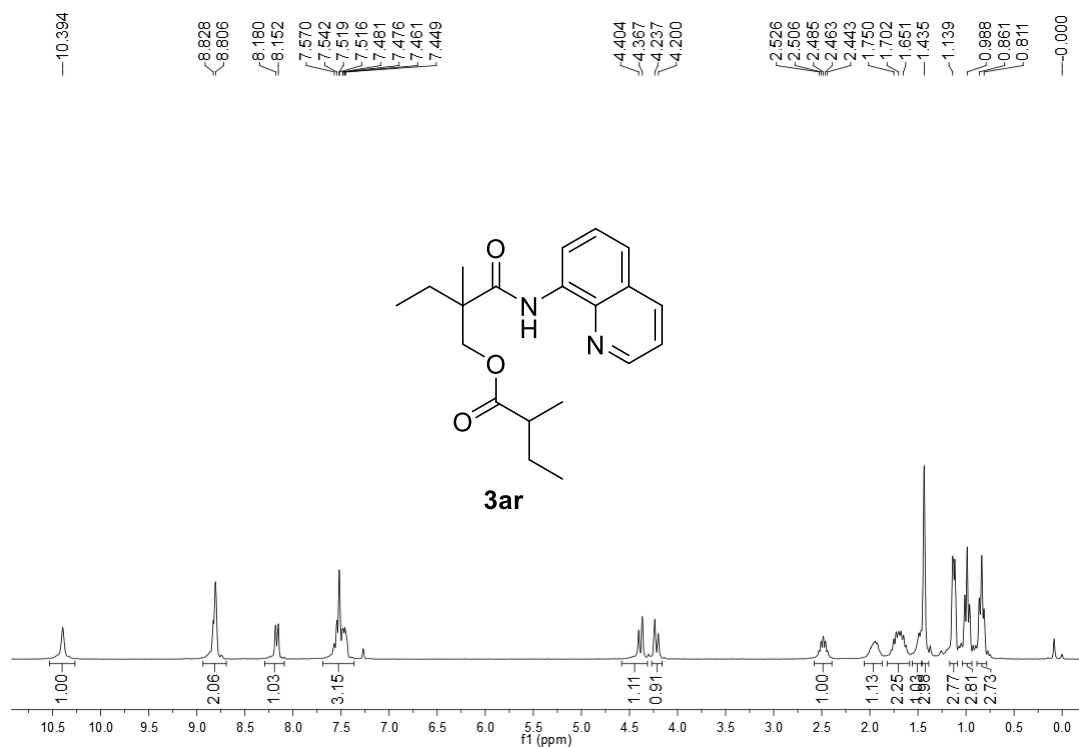


Figure S84. ¹³C NMR Spectra of compound 3ar

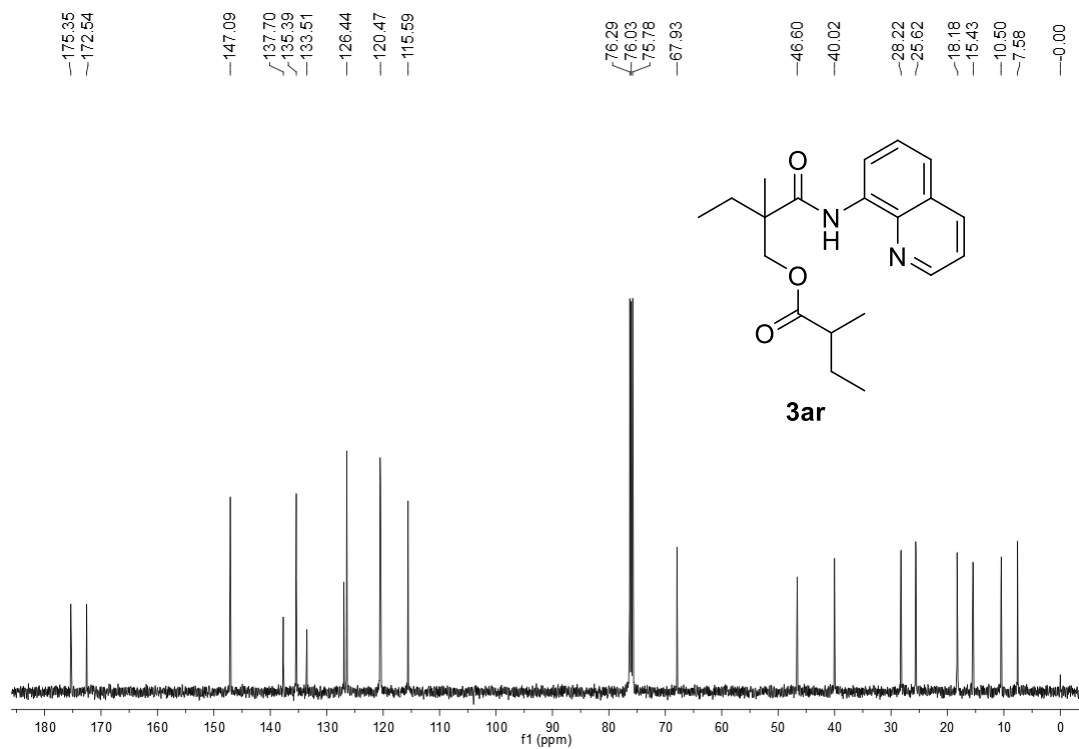


Figure S85. ¹H NMR Spectra of compound 3ar'

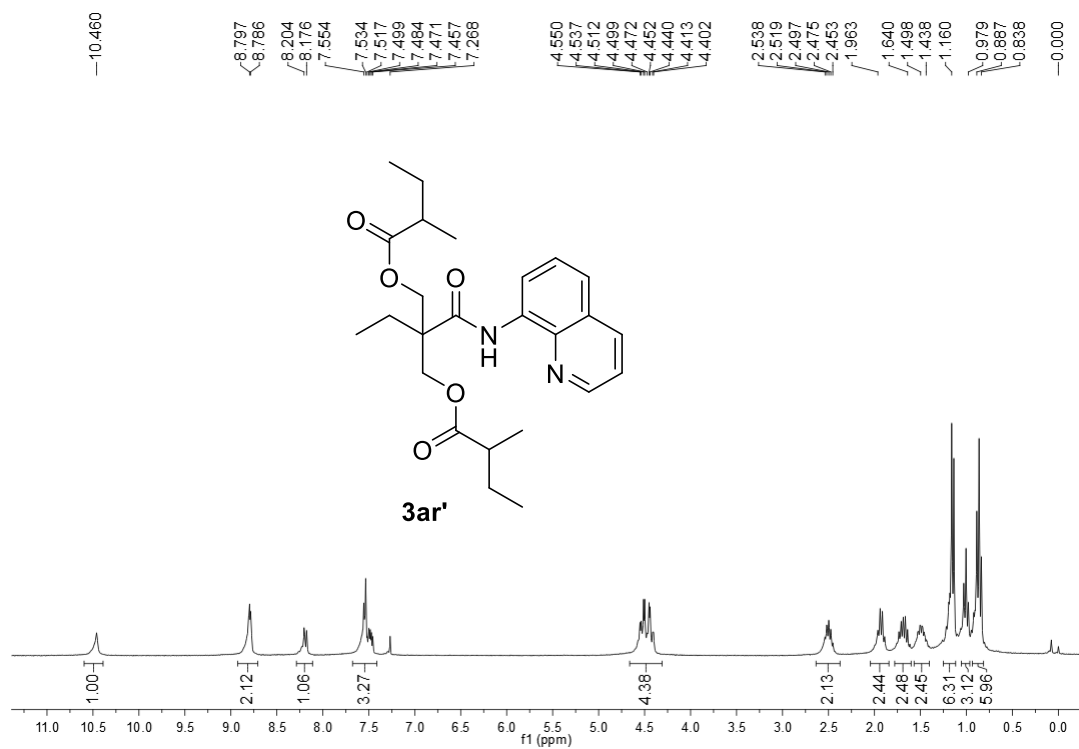


Figure S86. ¹³C NMR Spectra of compound 3ar'

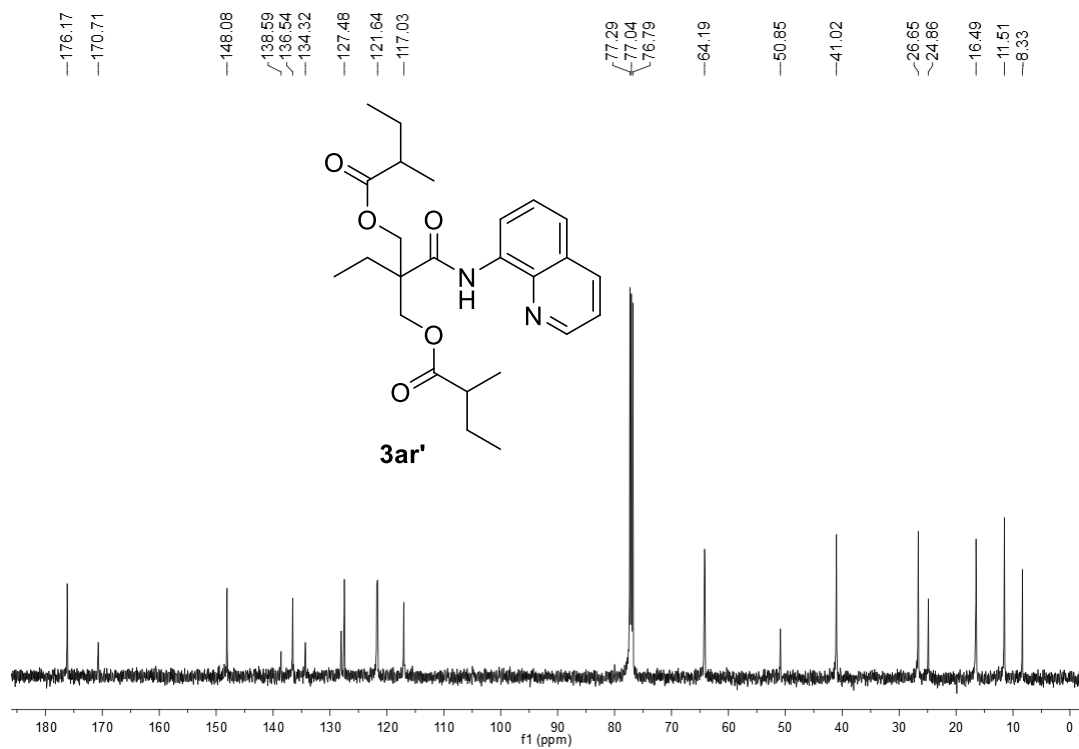


Figure S87. ¹H NMR Spectra of compound 3ba

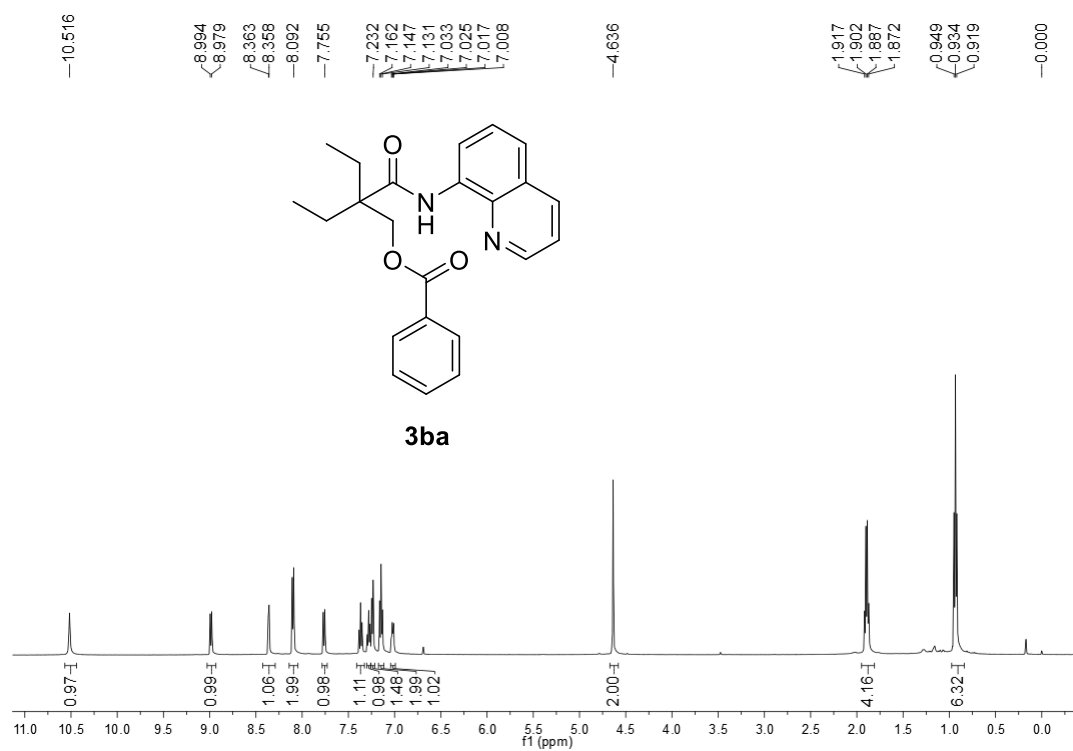


Figure S88. ¹³C NMR Spectra of compound 3ba

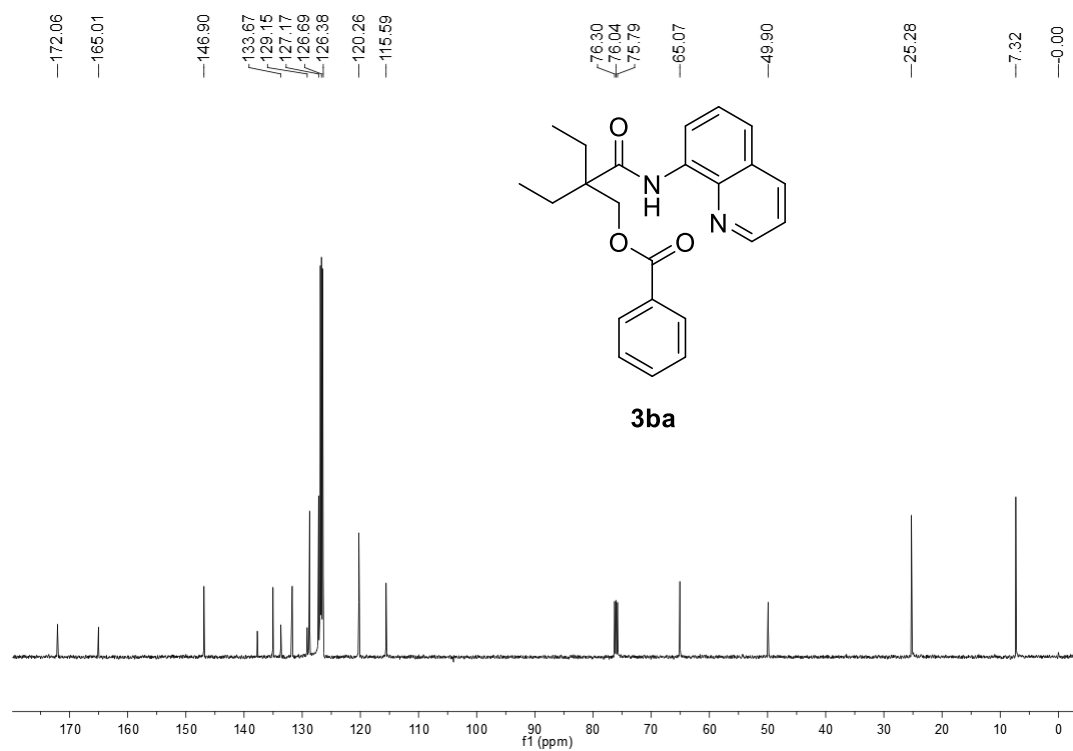


Figure S89. ¹H NMR Spectra of compound 3bb

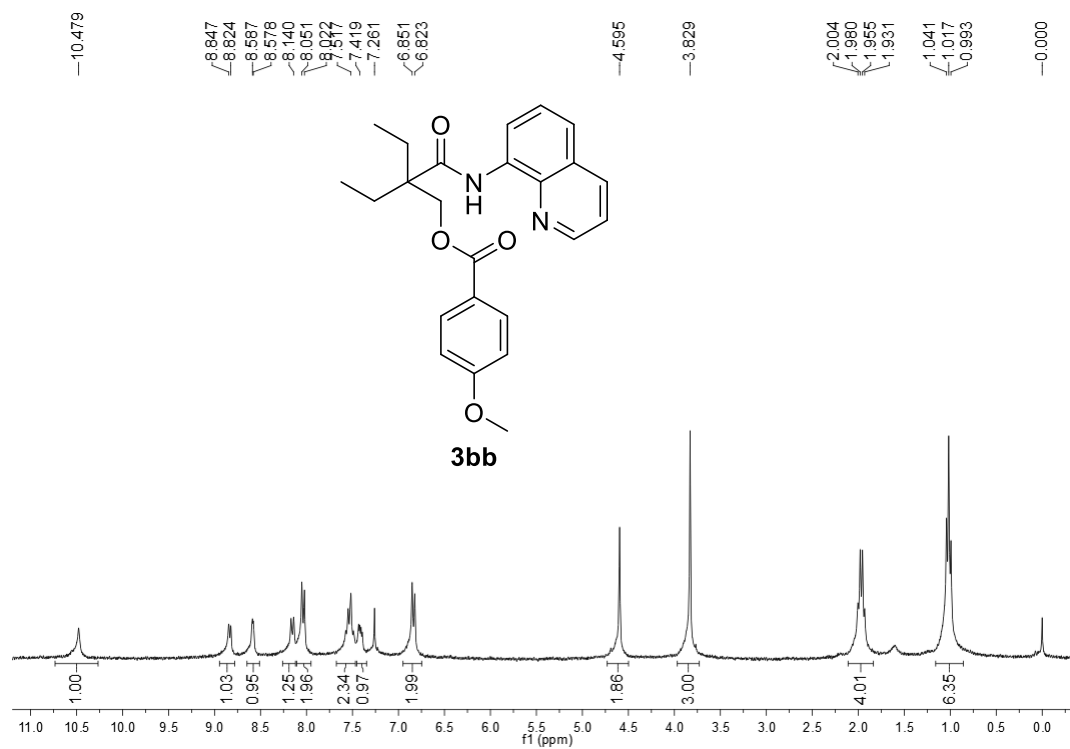


Figure S90. ¹³C NMR Spectra of compound 3bb

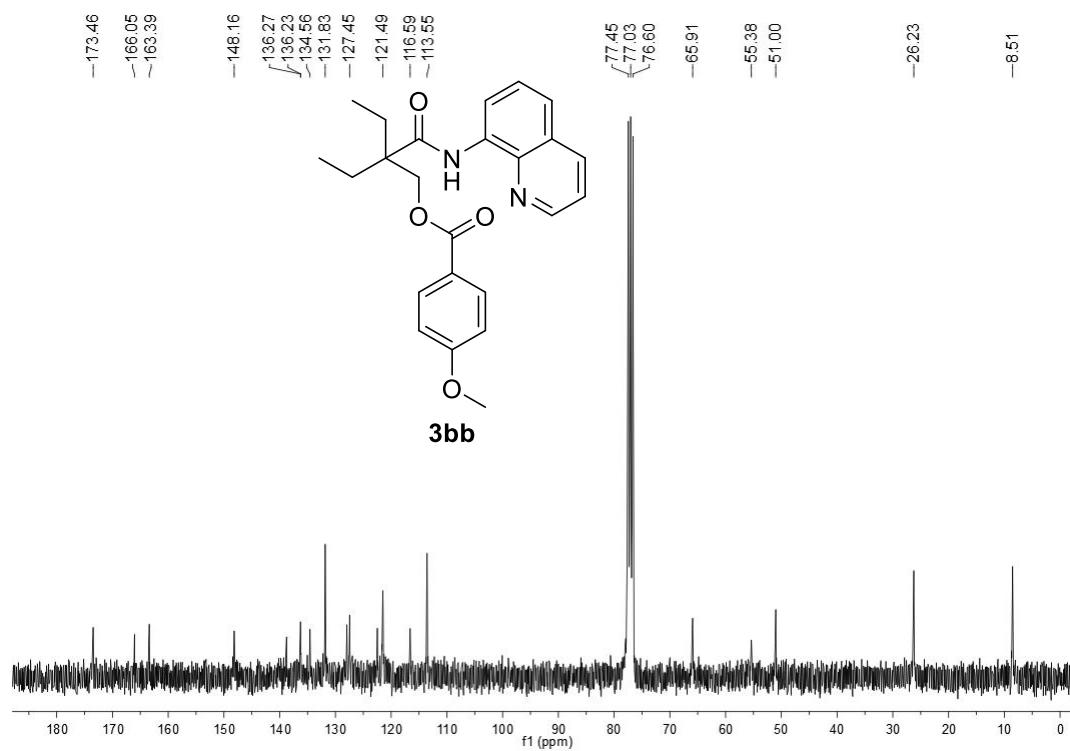


Figure S91. ¹H NMR Spectra of compound 3bc

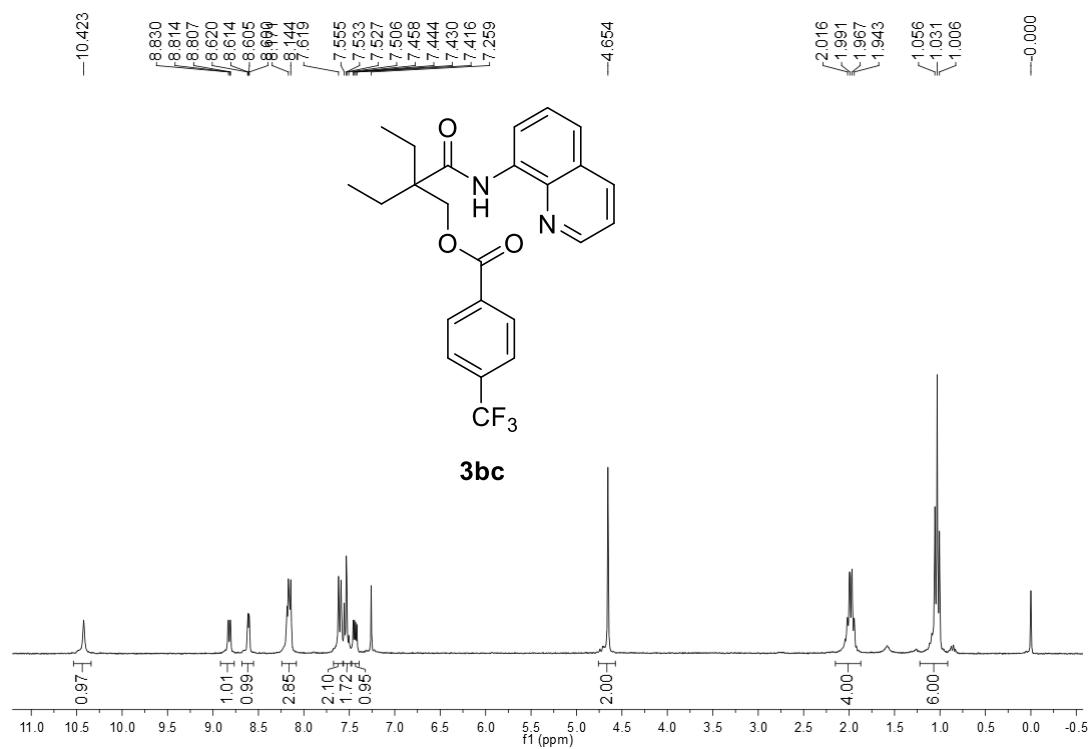


Figure S92. ¹³C NMR Spectra of compound 3bc

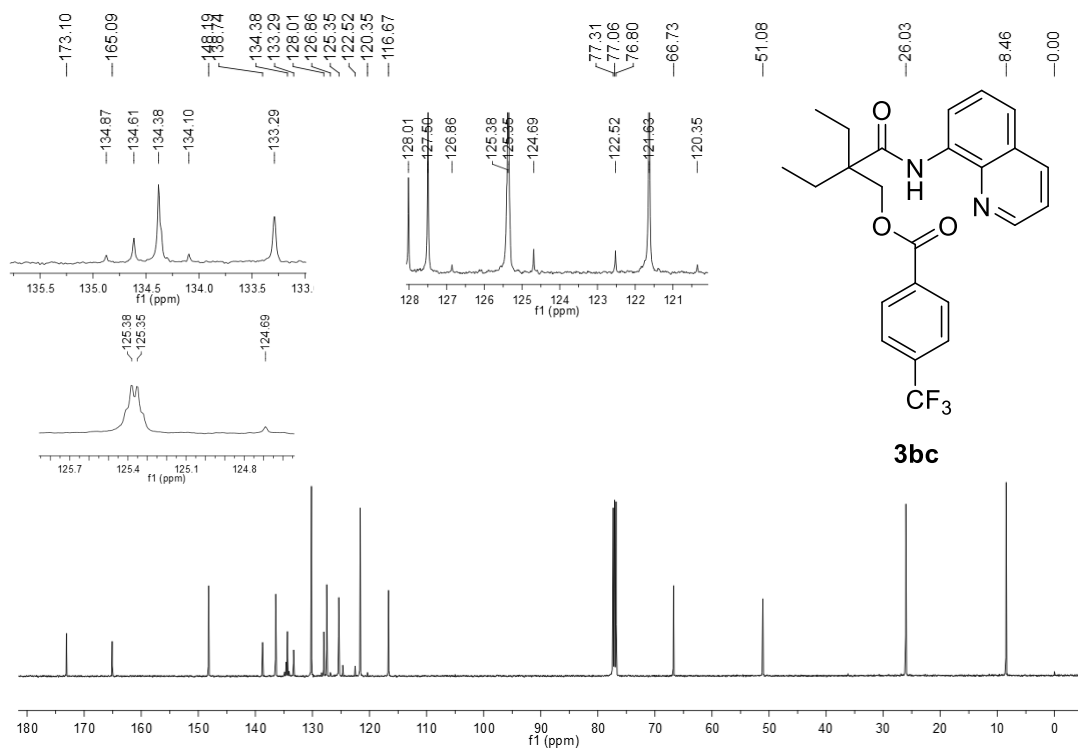


Figure S93. ¹H NMR Spectra of compound 3ca

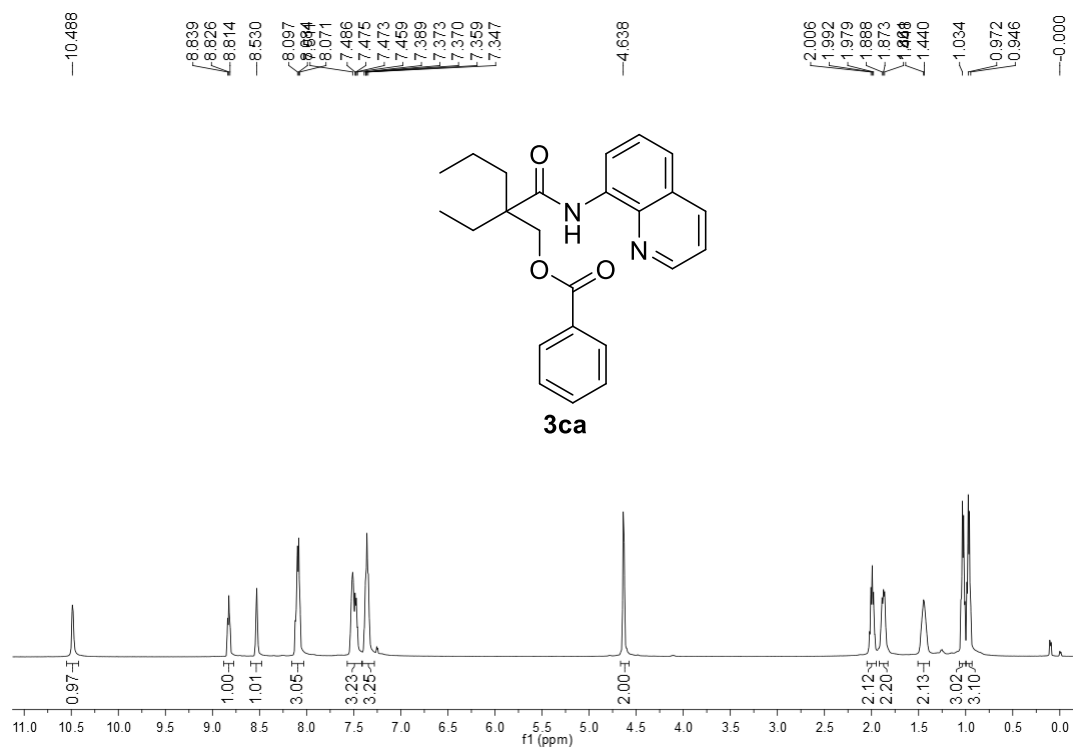


Figure S94. ¹³C NMR Spectra of compound 3ca

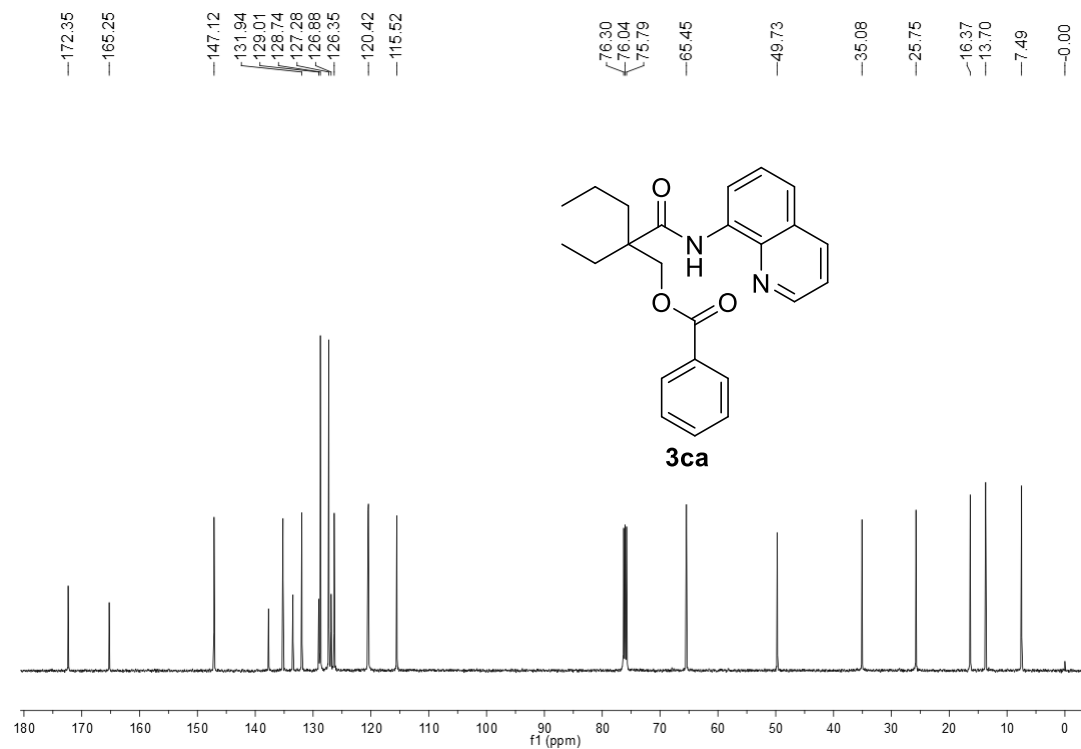


Figure S95. ¹H NMR Spectra of compound 3da

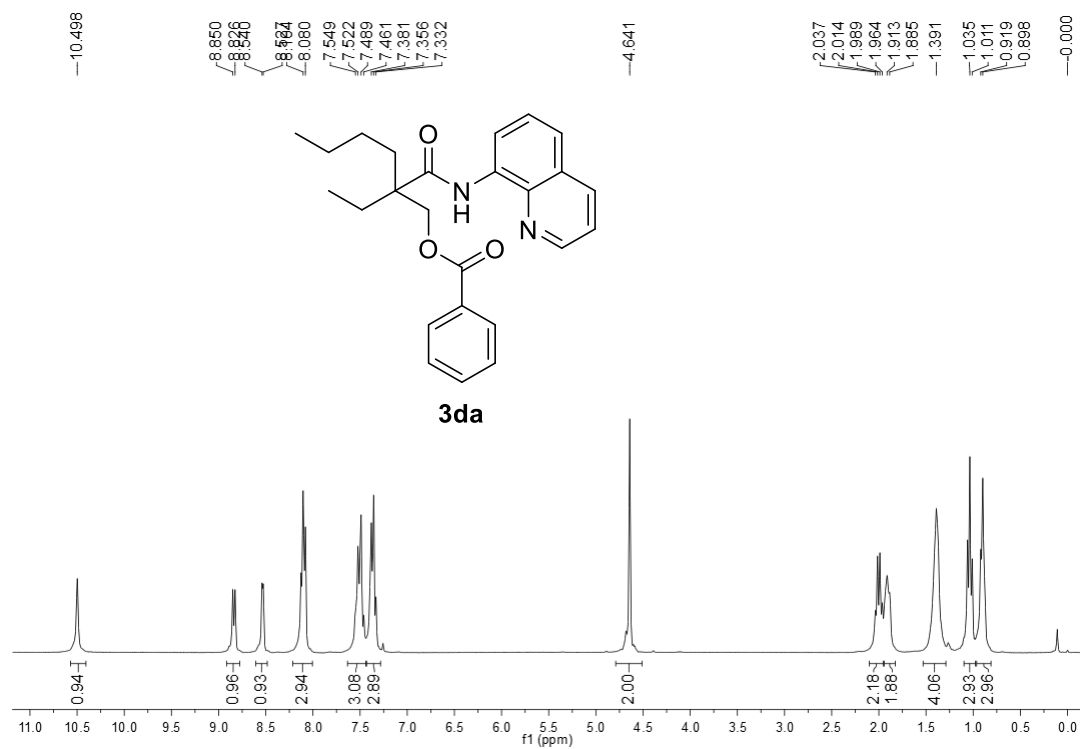


Figure S96. ¹³C NMR Spectra of compound 3da

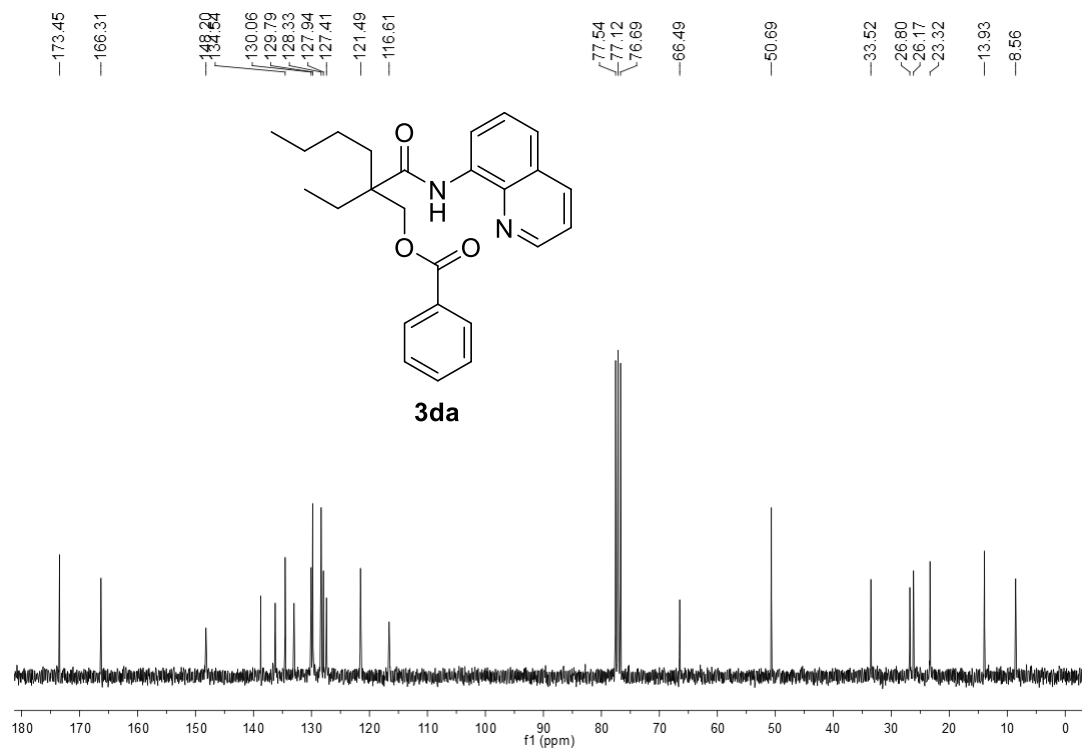


Figure S97. ¹H NMR Spectra of compound 3ea

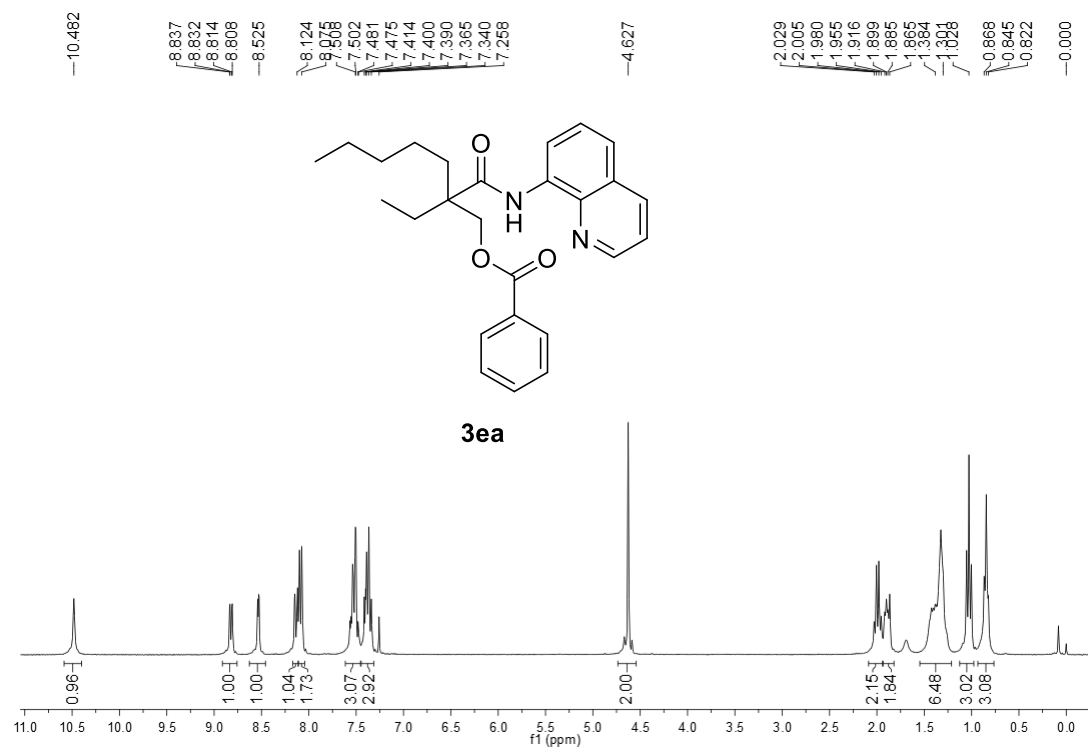


Figure S98. ¹³C NMR Spectra of compound 3ea

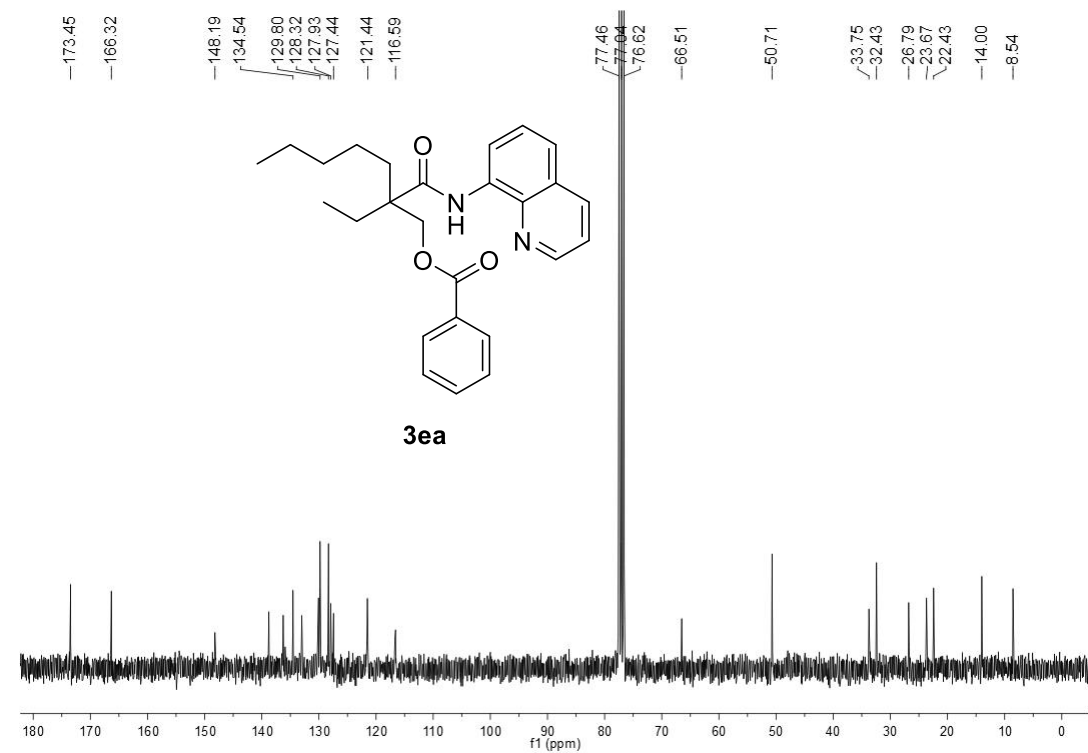


Figure S99. ¹H NMR Spectra of compound 3fa

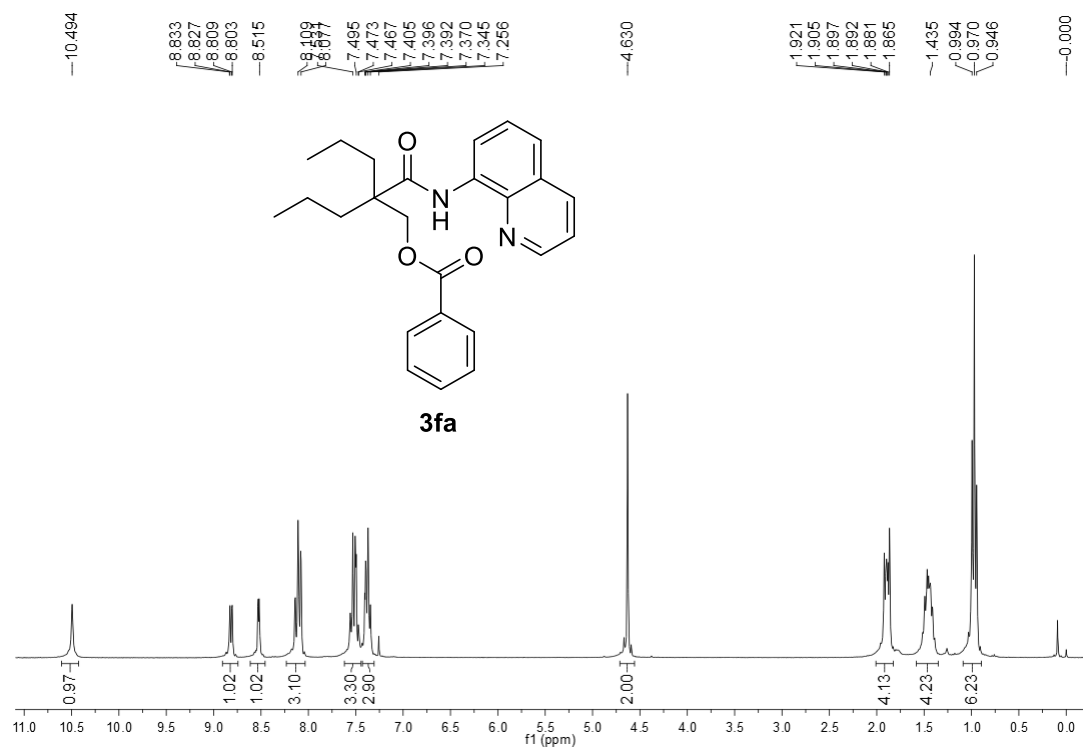


Figure S100. ¹³C NMR Spectra of compound 3fa

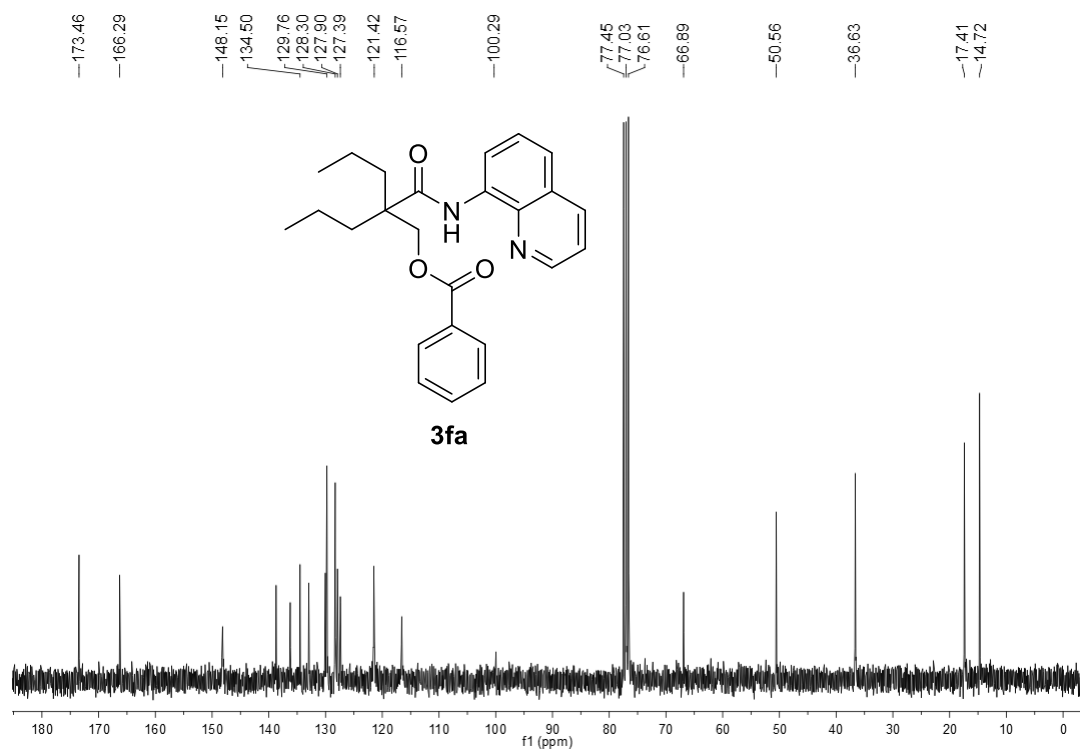


Figure S101. ¹H NMR Spectra of compound 3ga

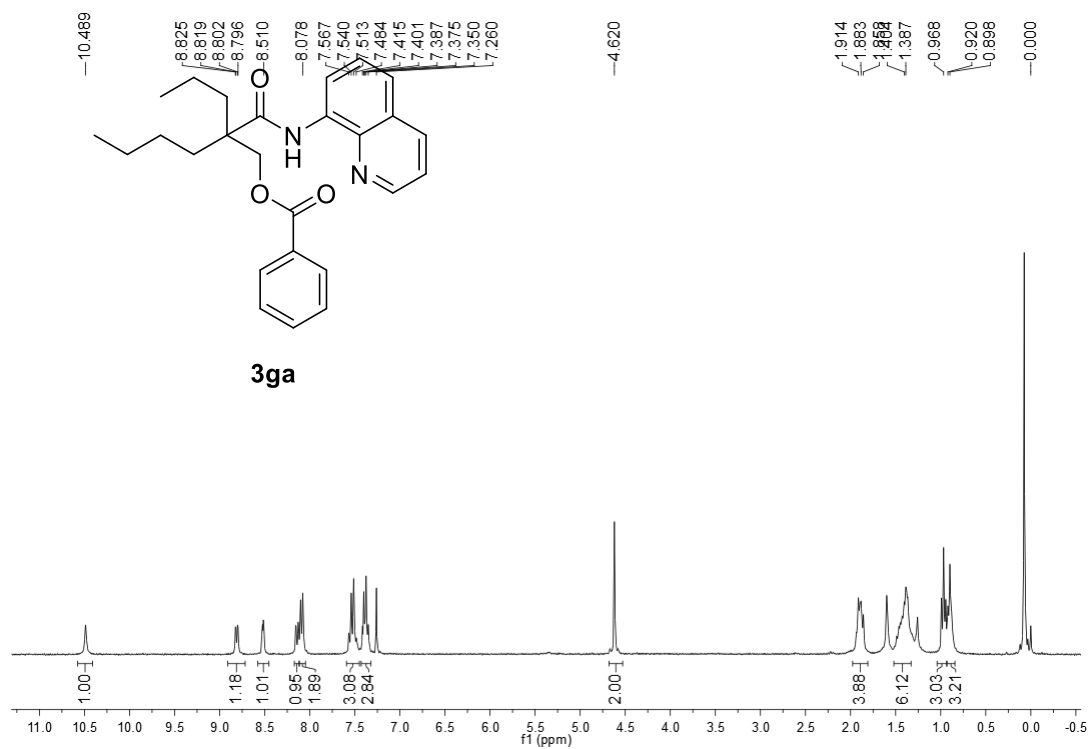


Figure S102. ¹³C NMR Spectra of compound 3ga

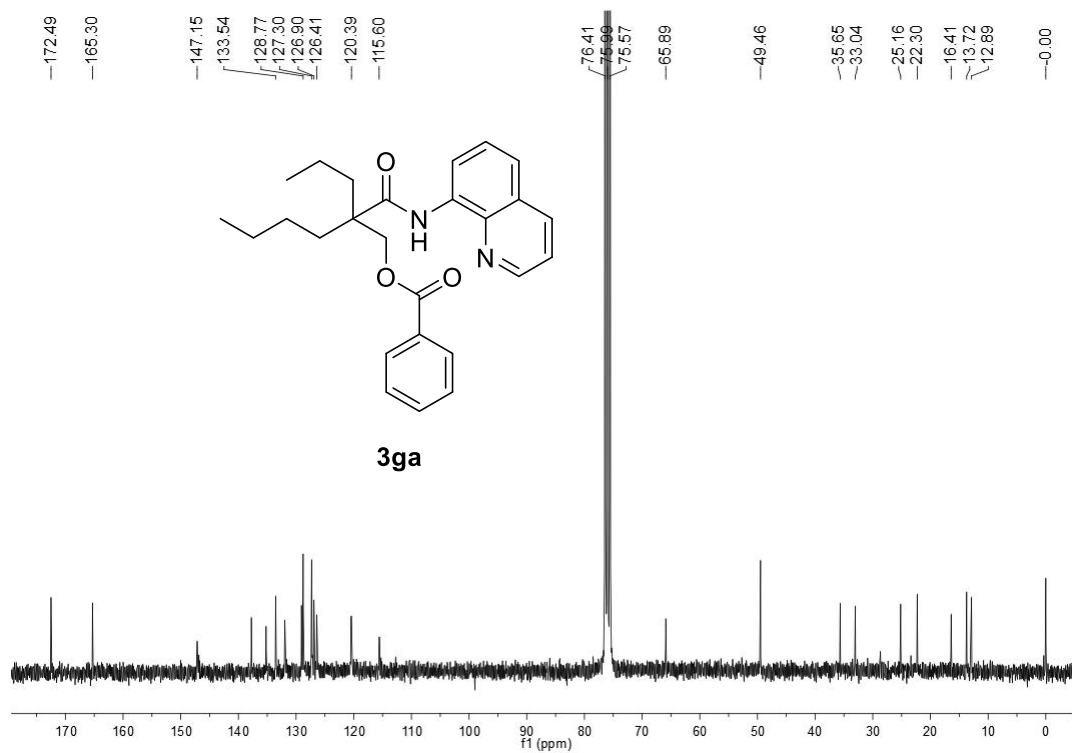


Figure S103. ¹H NMR Spectra of compound 3ha

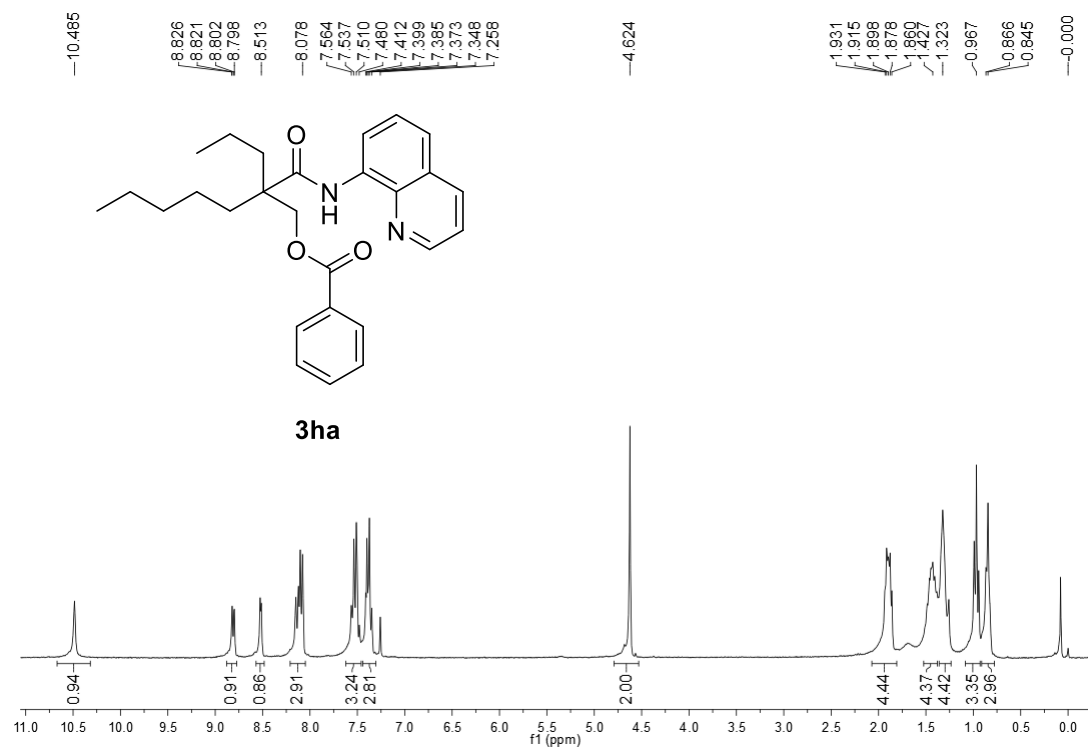


Figure S104. ¹³C NMR Spectra of compound 3ha

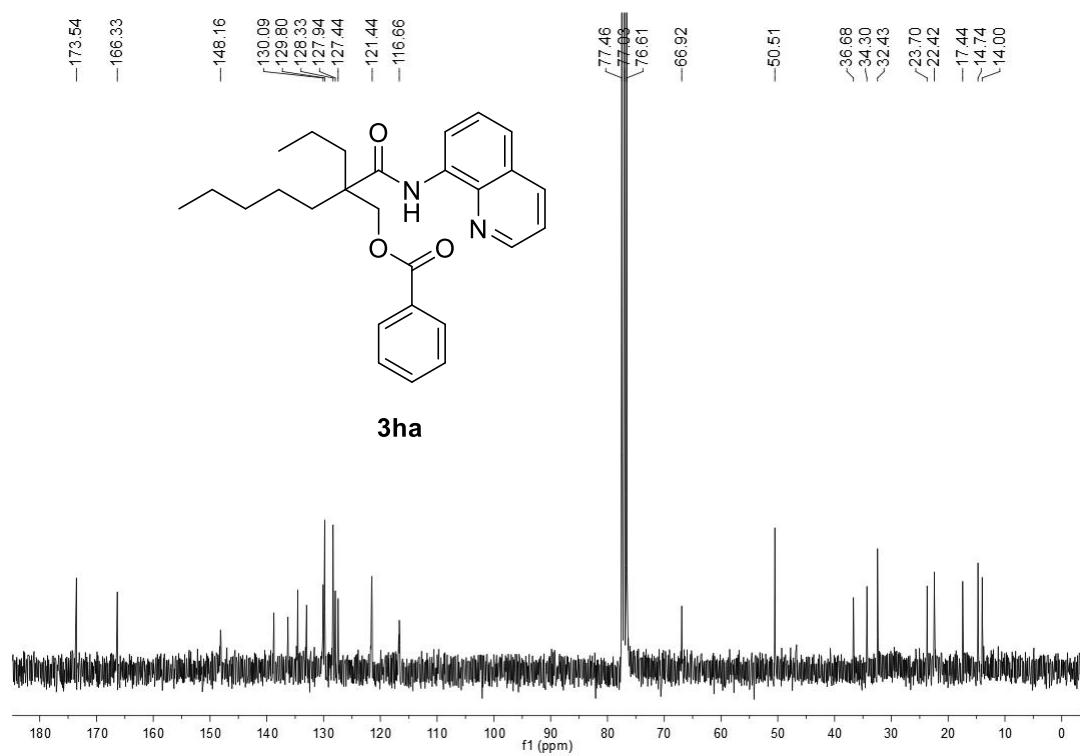


Figure S105. ¹H NMR Spectra of compound 3ia

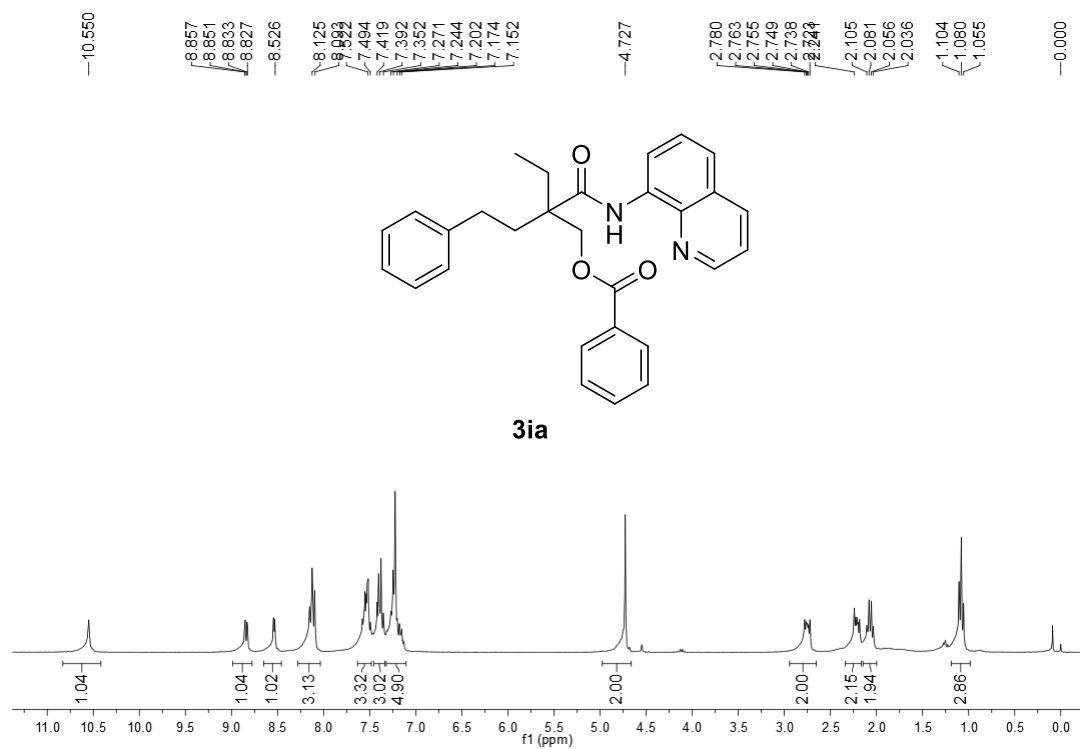


Figure S106. ¹³C NMR Spectra of compound 3ia

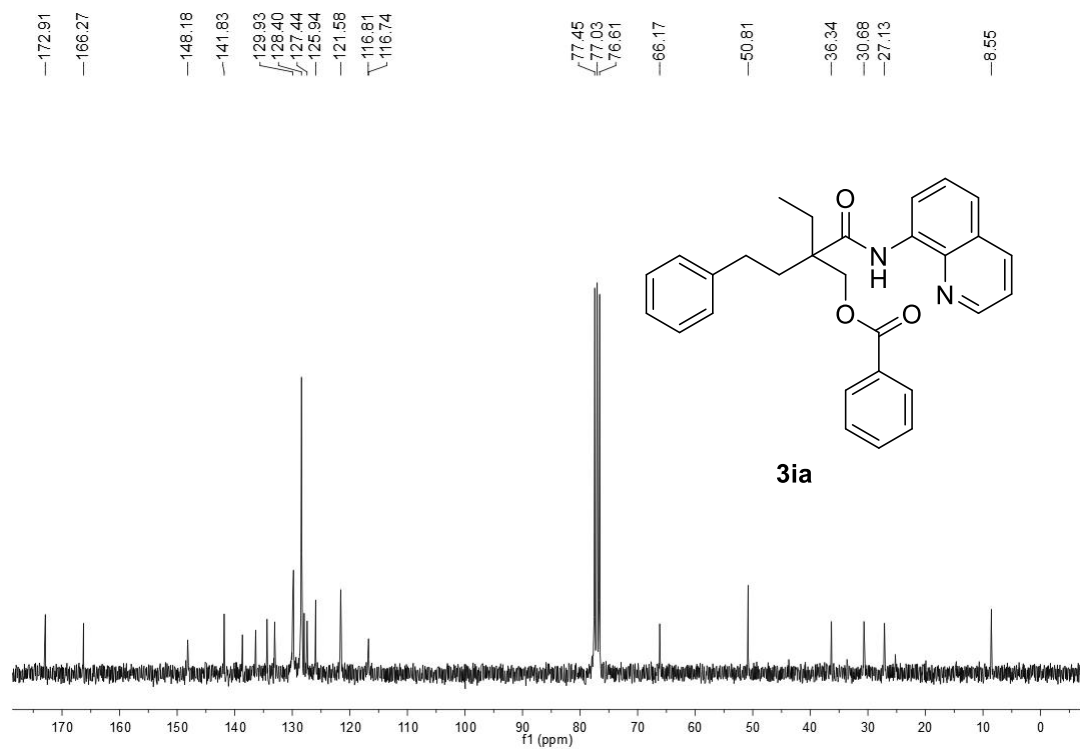


Figure S107. ¹H NMR Spectra of compound 3ja

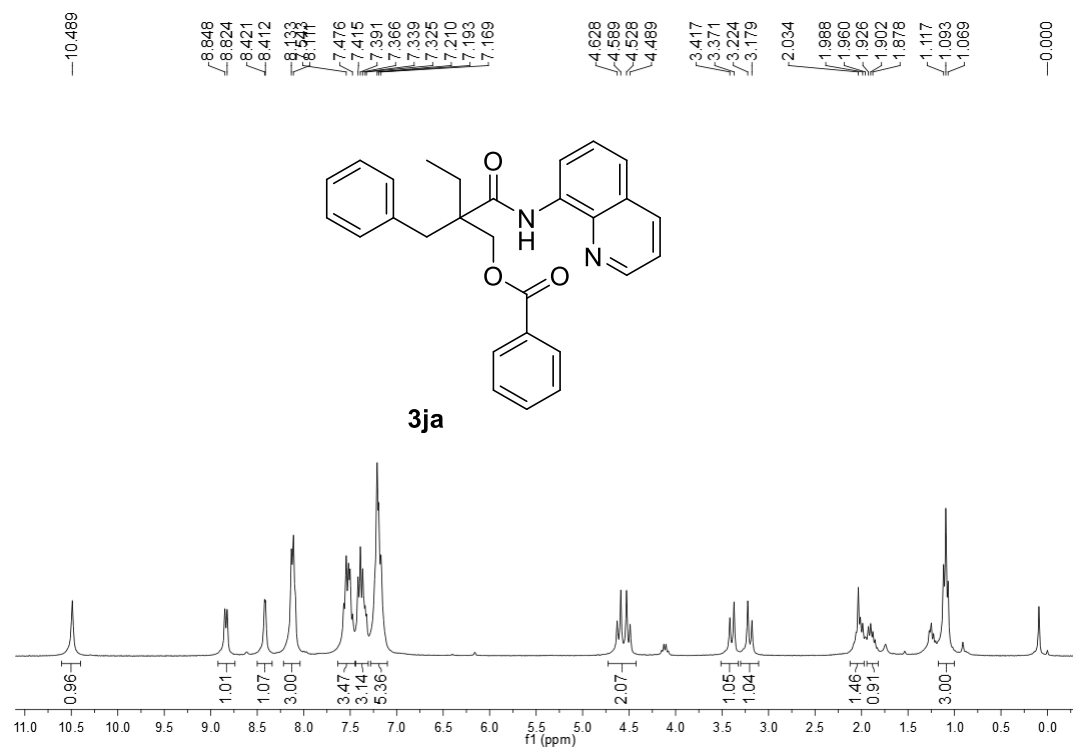


Figure S108. ¹³C NMR Spectra of compound 3ja

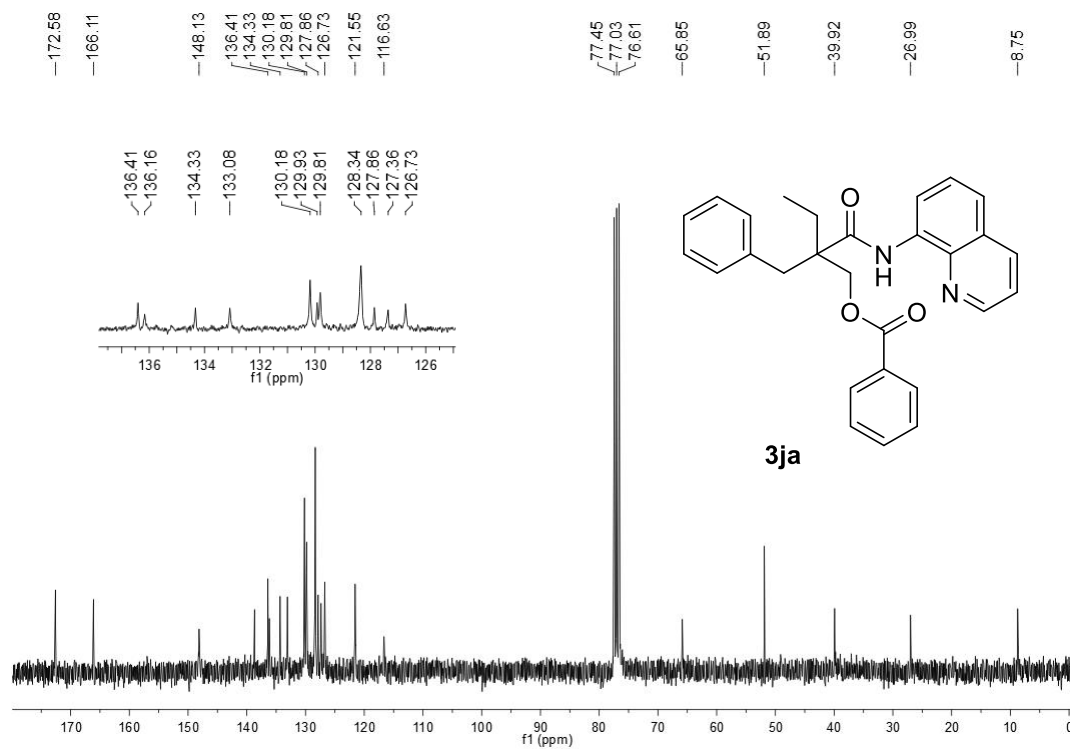


Figure S109. ¹H NMR Spectra of compound 3ka

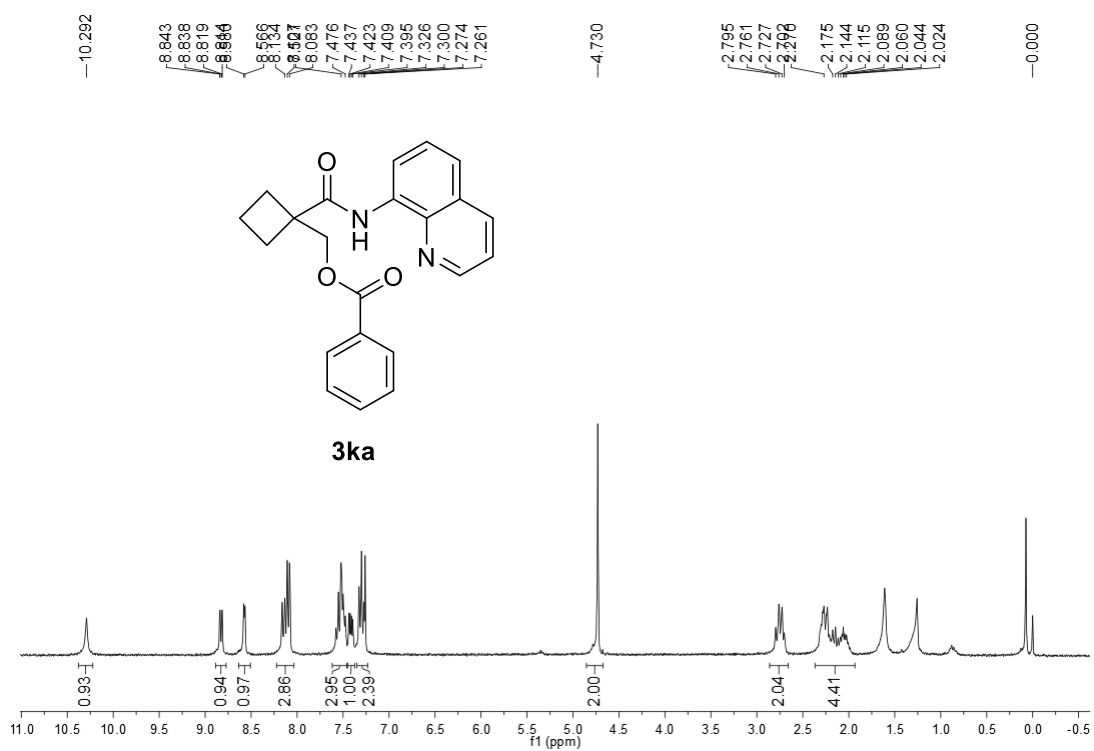


Figure S110. ¹³C NMR Spectra of compound 3ka

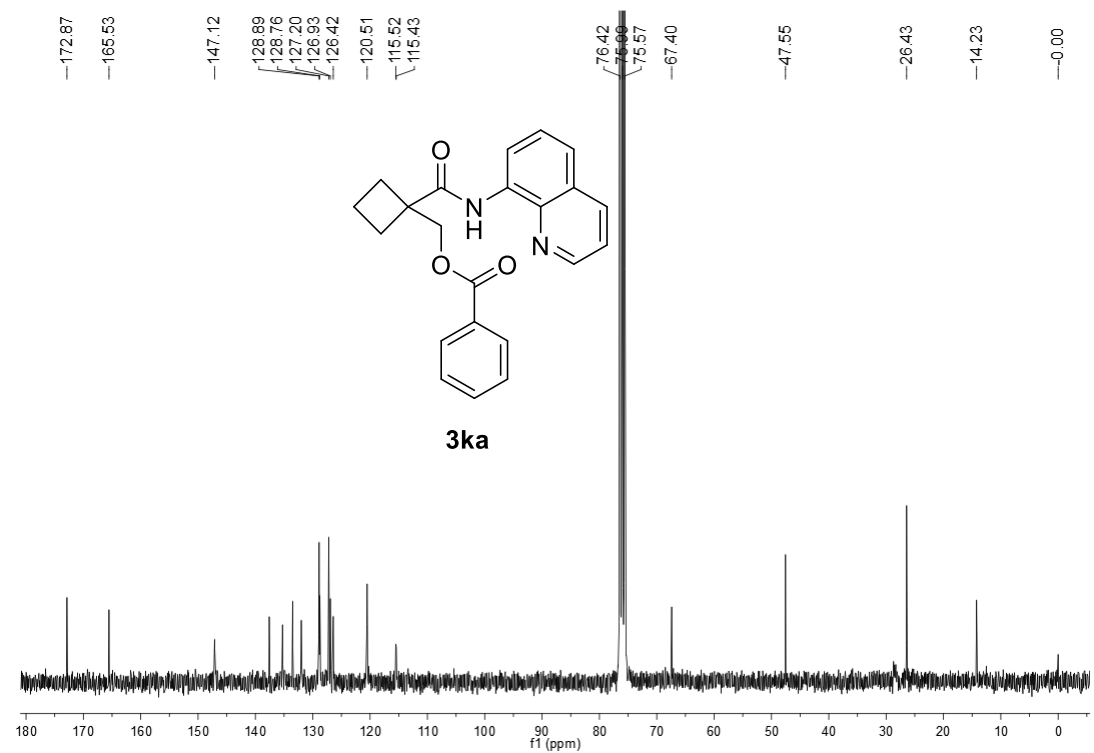


Figure S111. ¹H NMR Spectra of compound 3la

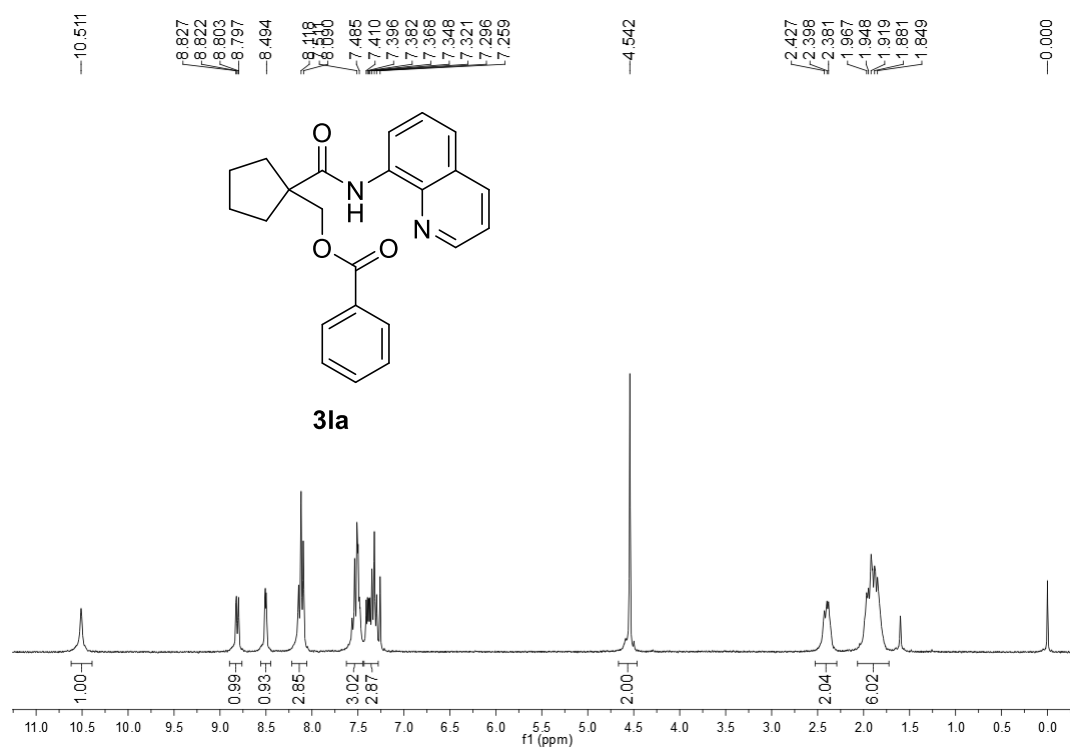


Figure S112. ¹³C NMR Spectra of compound 3la

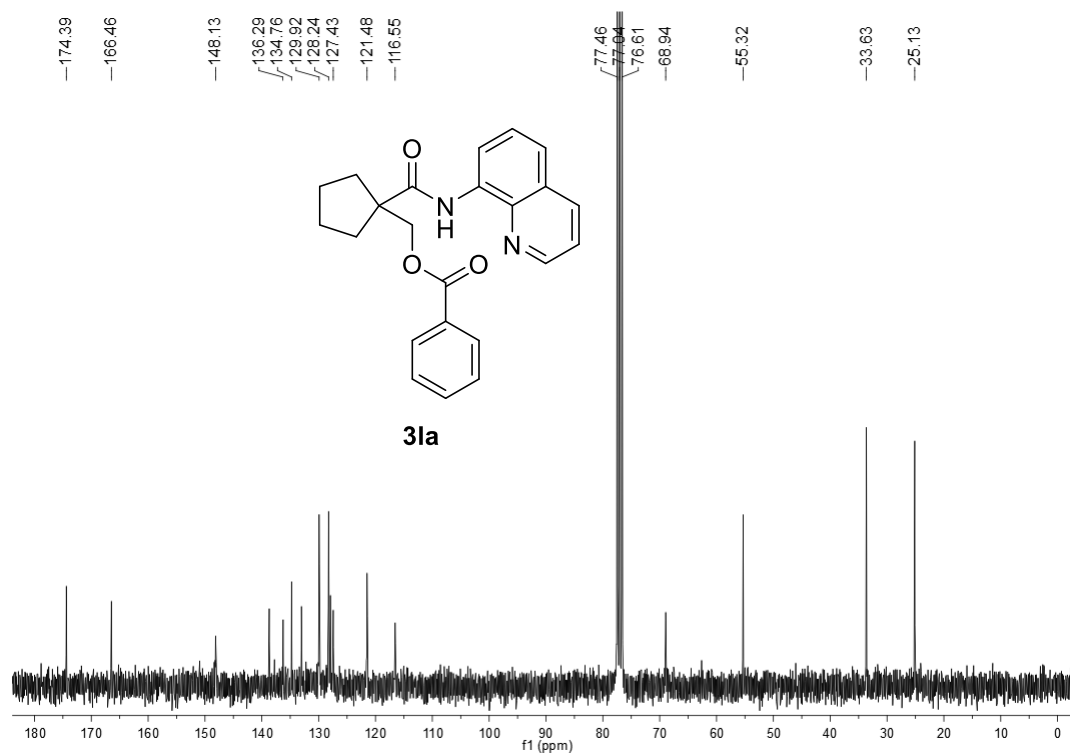


Figure S113. ¹H NMR Spectra of compound 4o

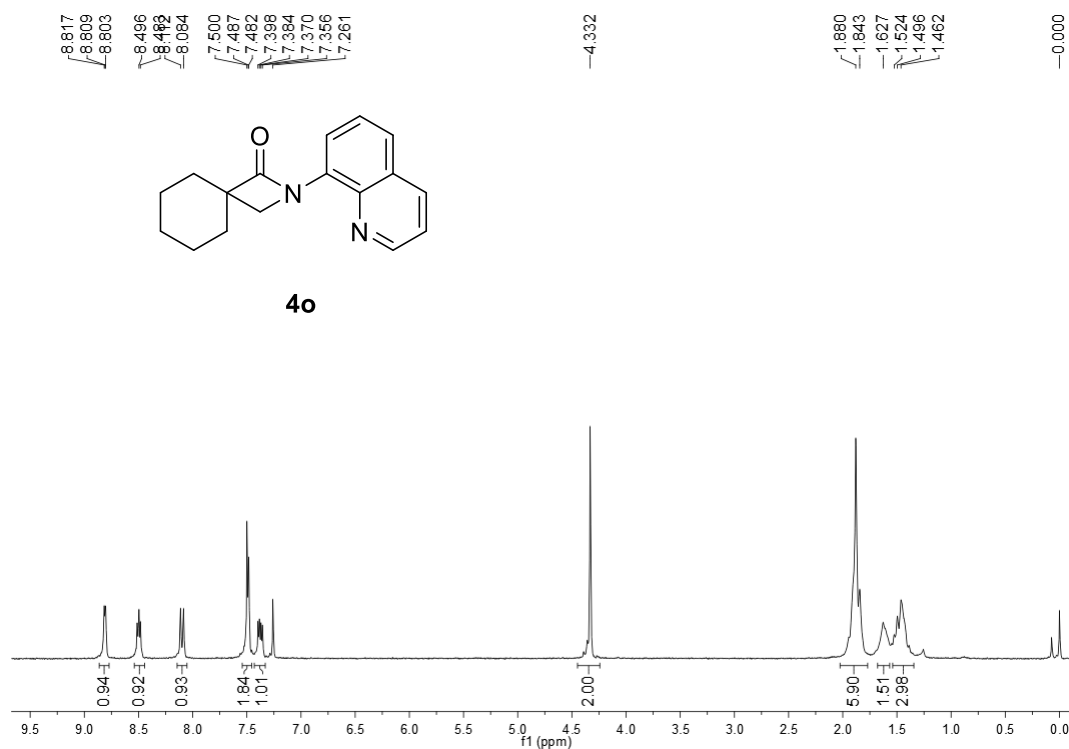


Figure S114. ¹³C NMR Spectra of compound 4o

