Supporting Information

Organocatalytic Insertion of Isatins into Aryl Difluoronitromethyl Ketones

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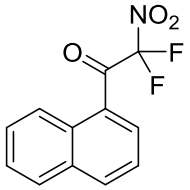
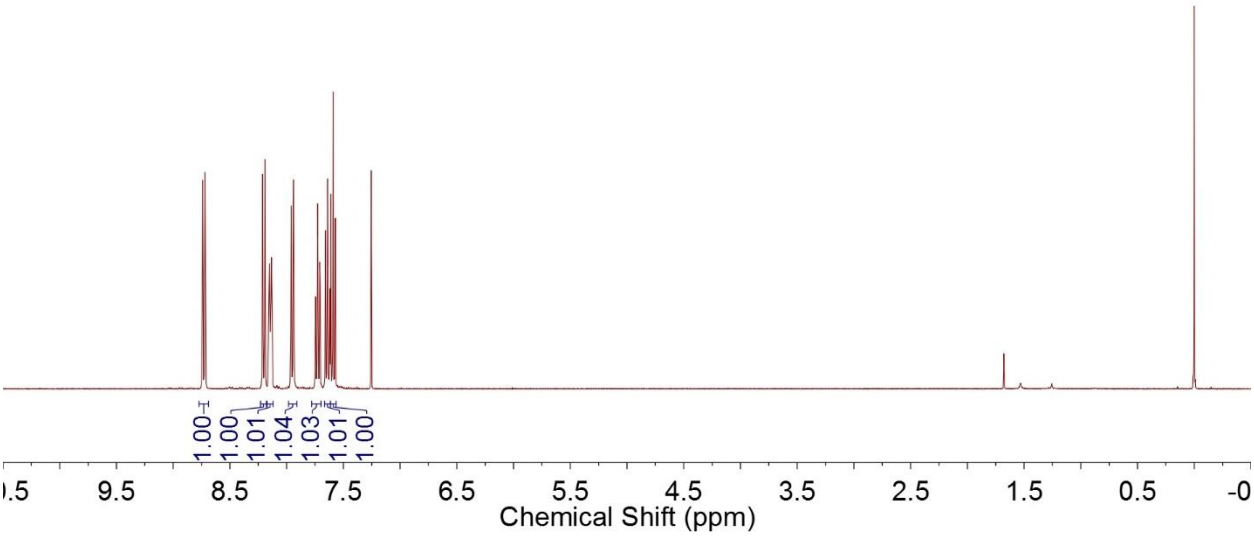
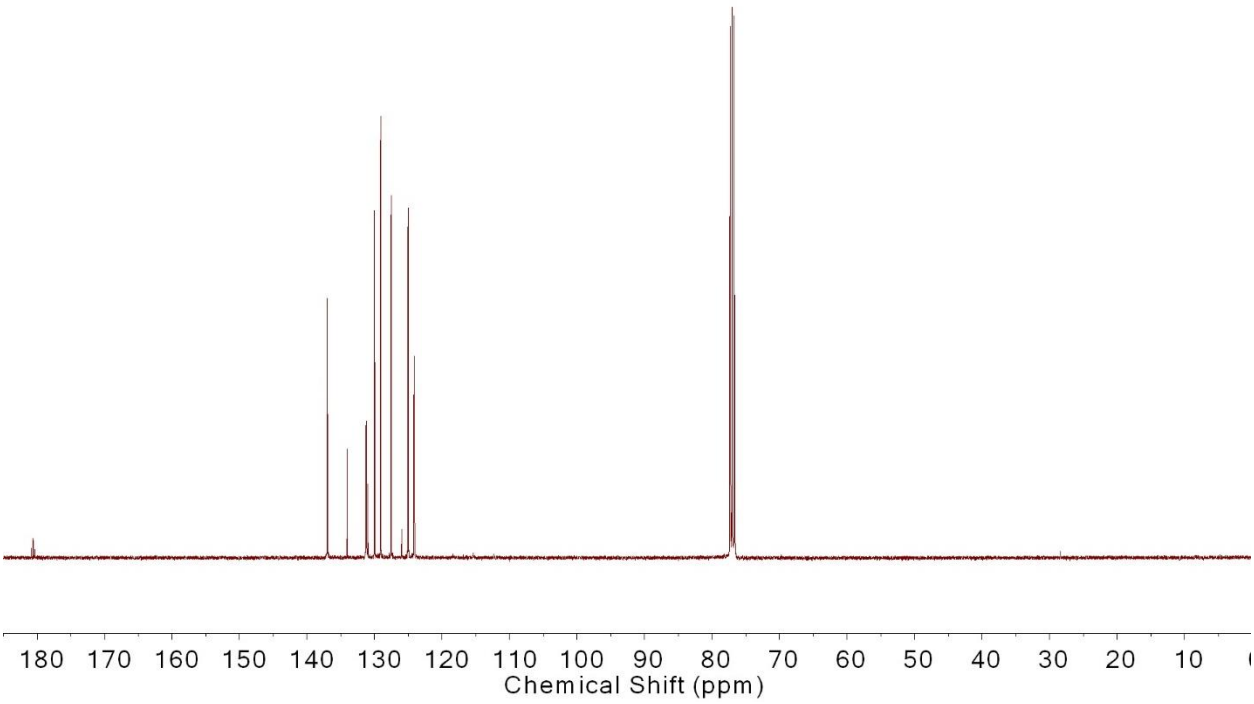
Contents:

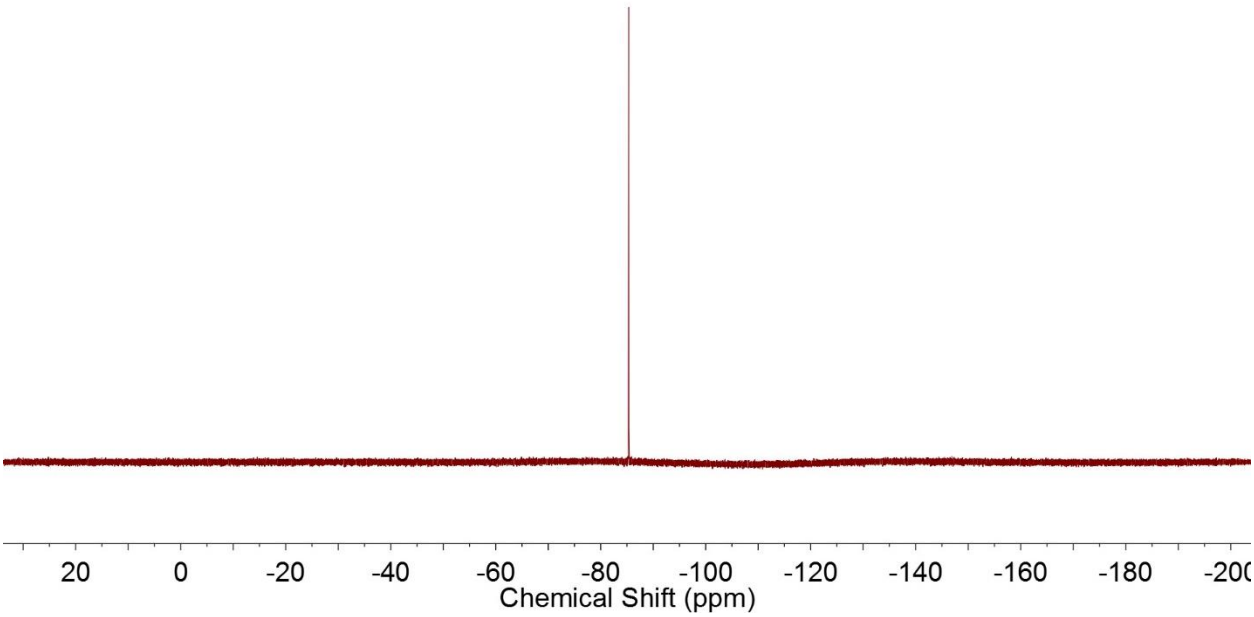
1. NMR Spectra

1-Difluoronitroacetonaphthone (**20**)

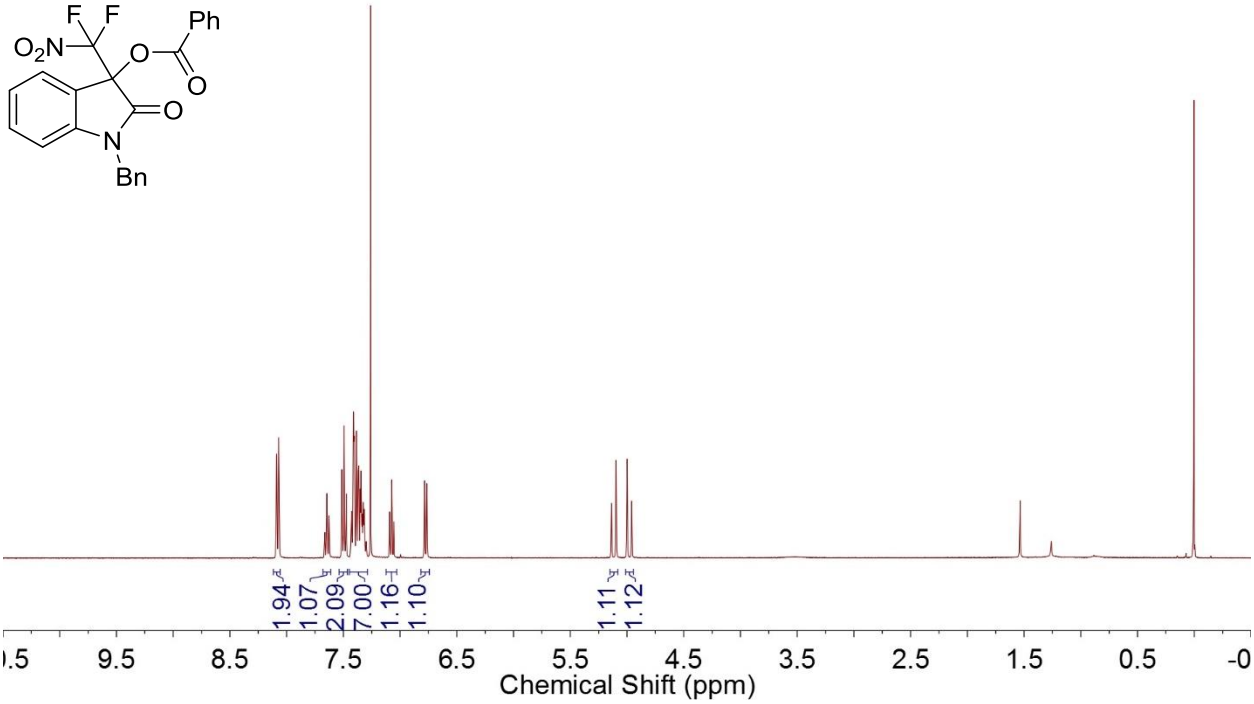


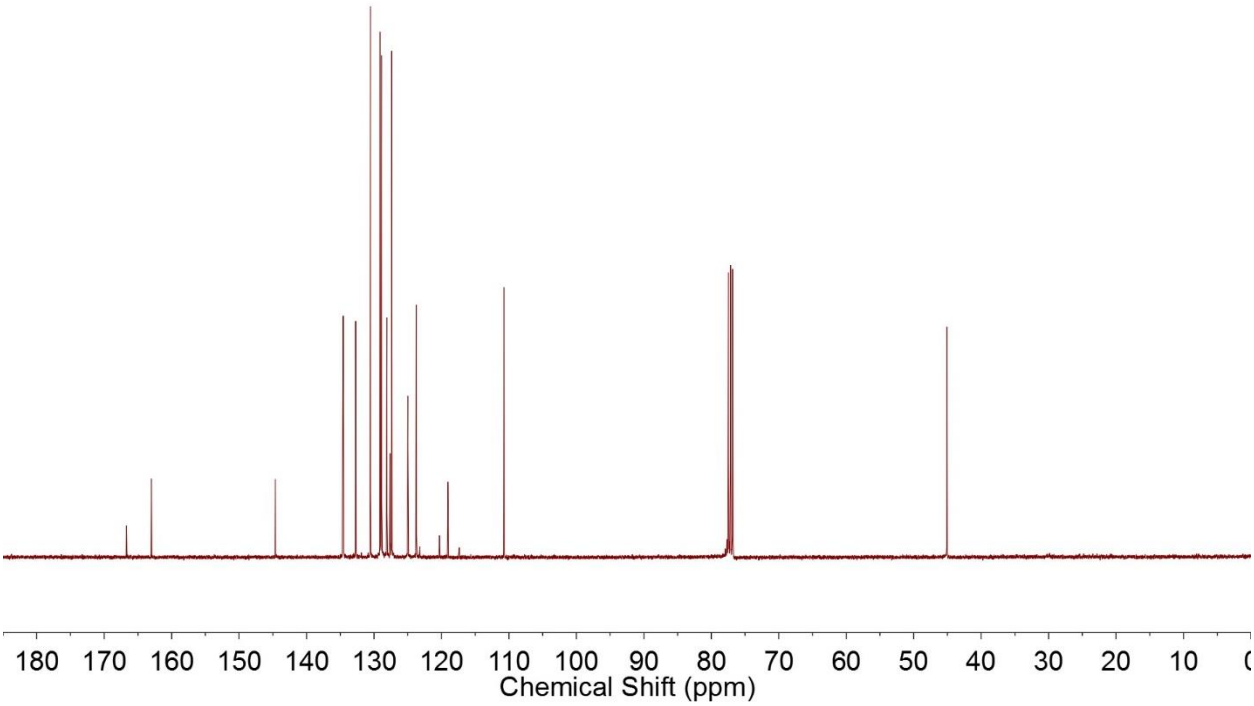






N-Benzyl 3-(difluoronitromethyl)-2-oxoindolin-3-yl benzoate (**3**)

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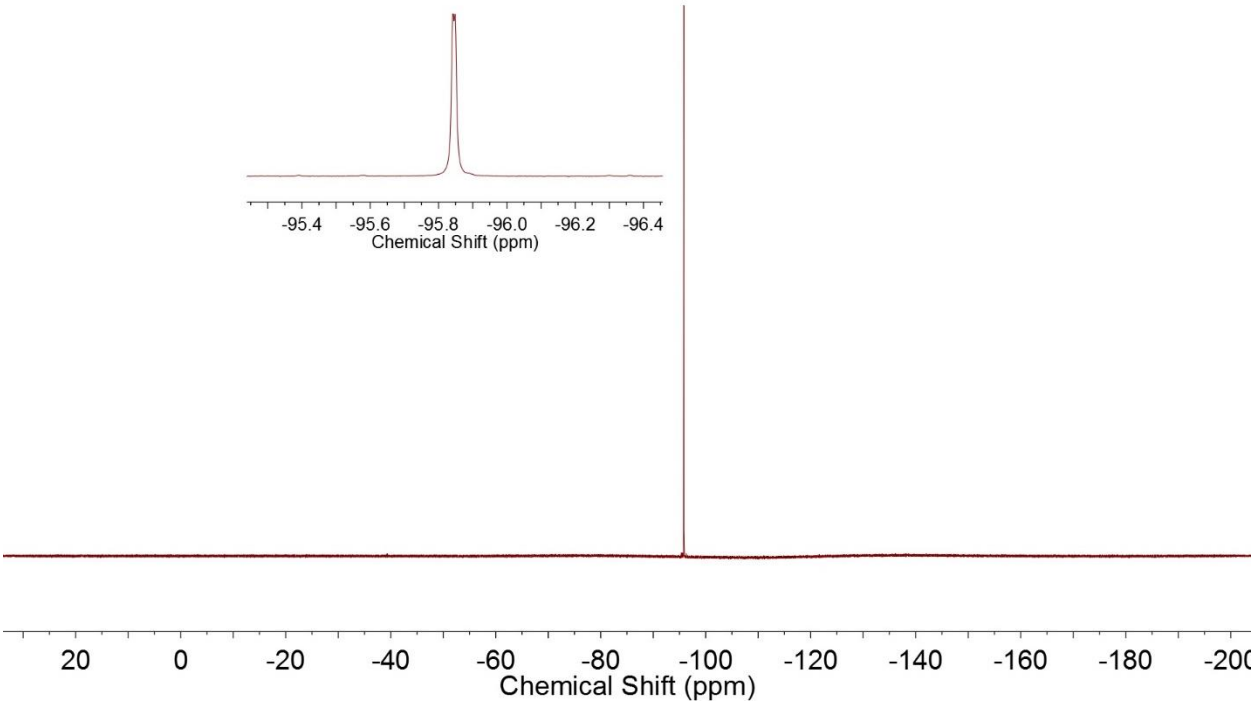
Chemical Shift (ppm)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Chemical Shift (ppm)
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Chemical Shift (ppm)

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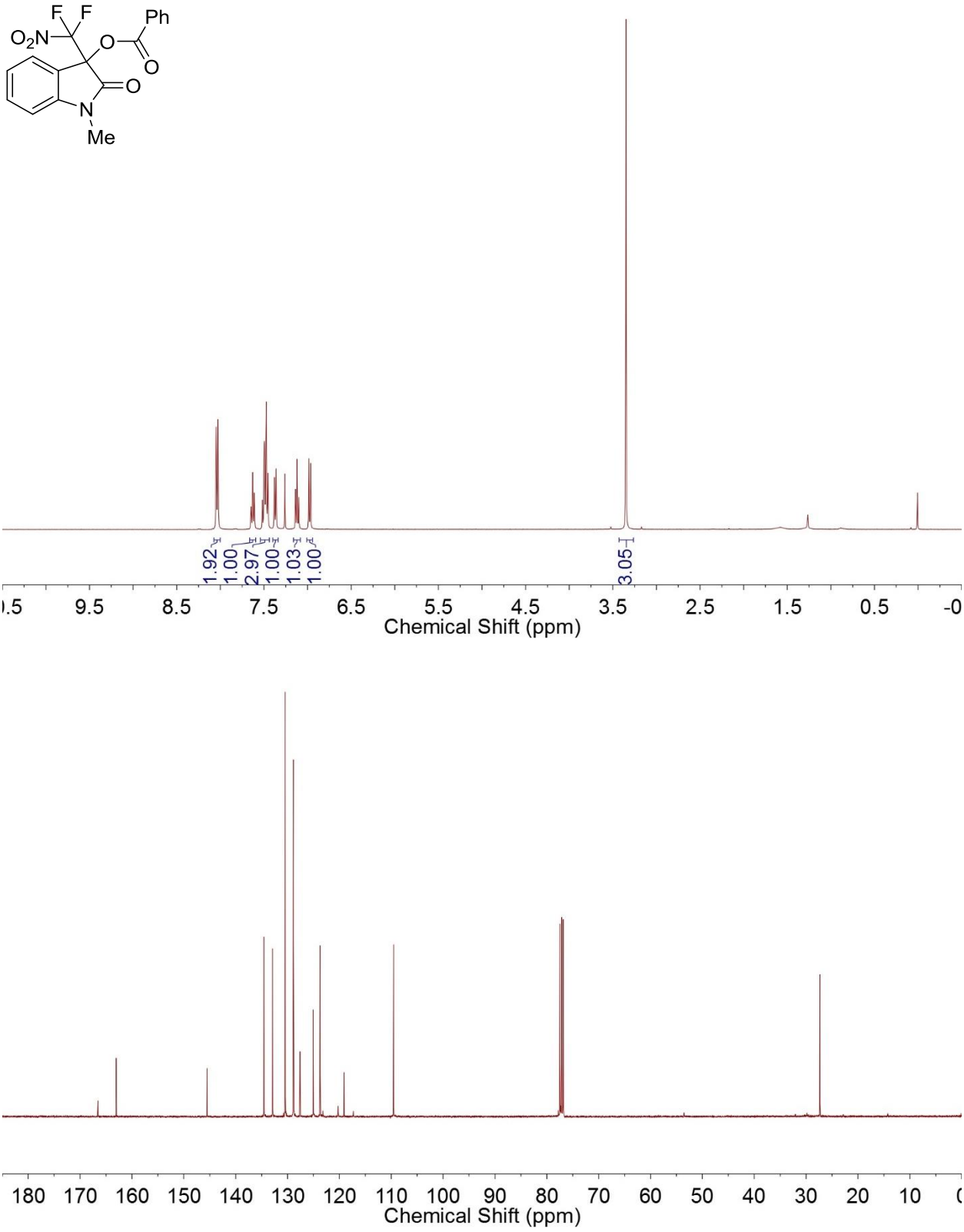

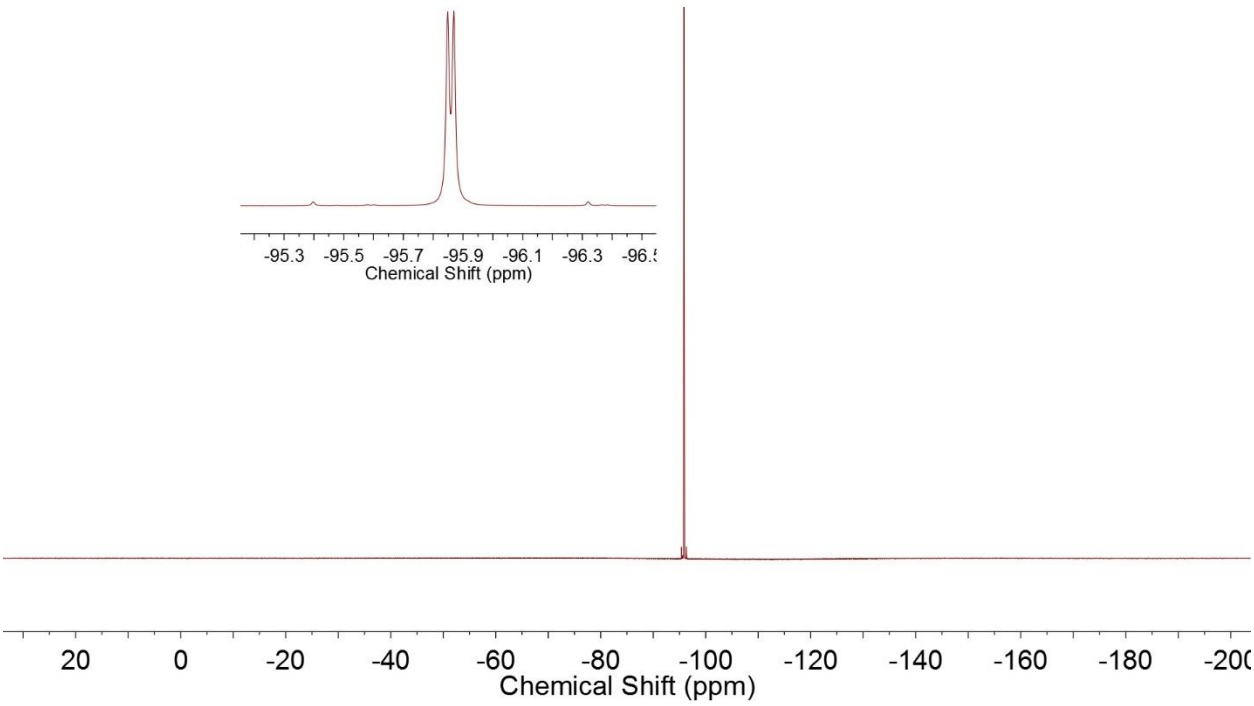

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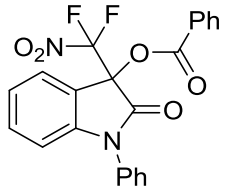

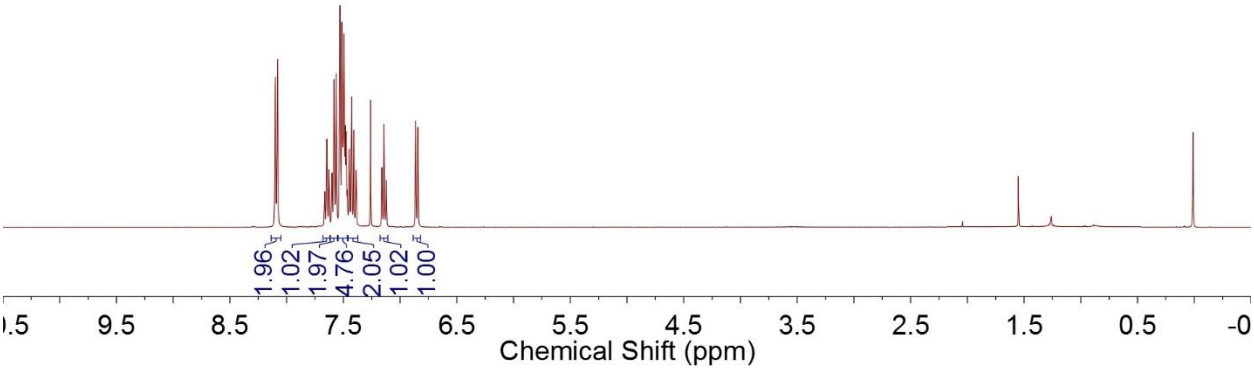

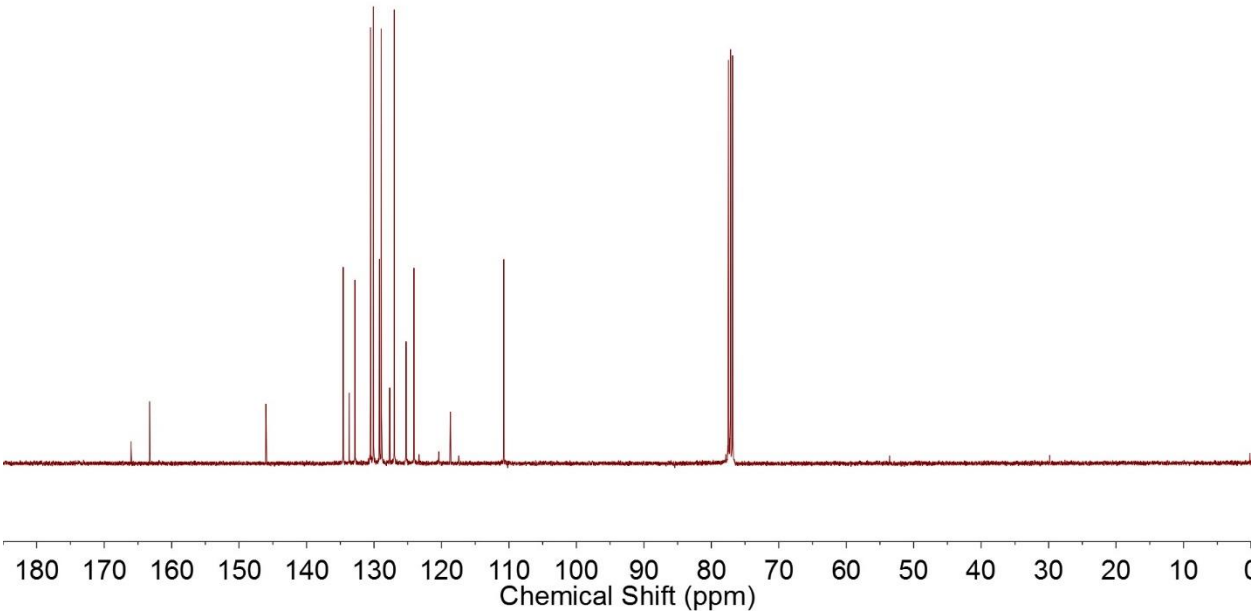
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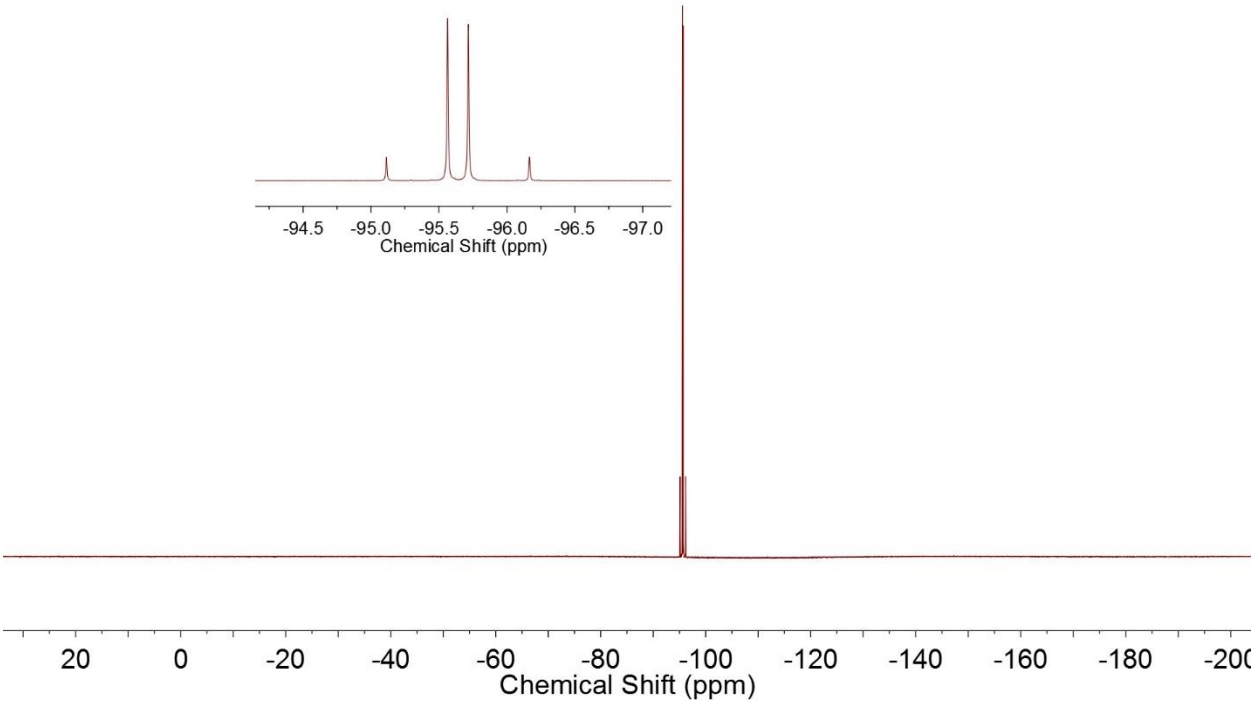
Chemical Shift (ppm)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Chemical Shift (ppm)
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Chemical Shift (ppm)

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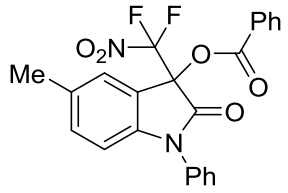

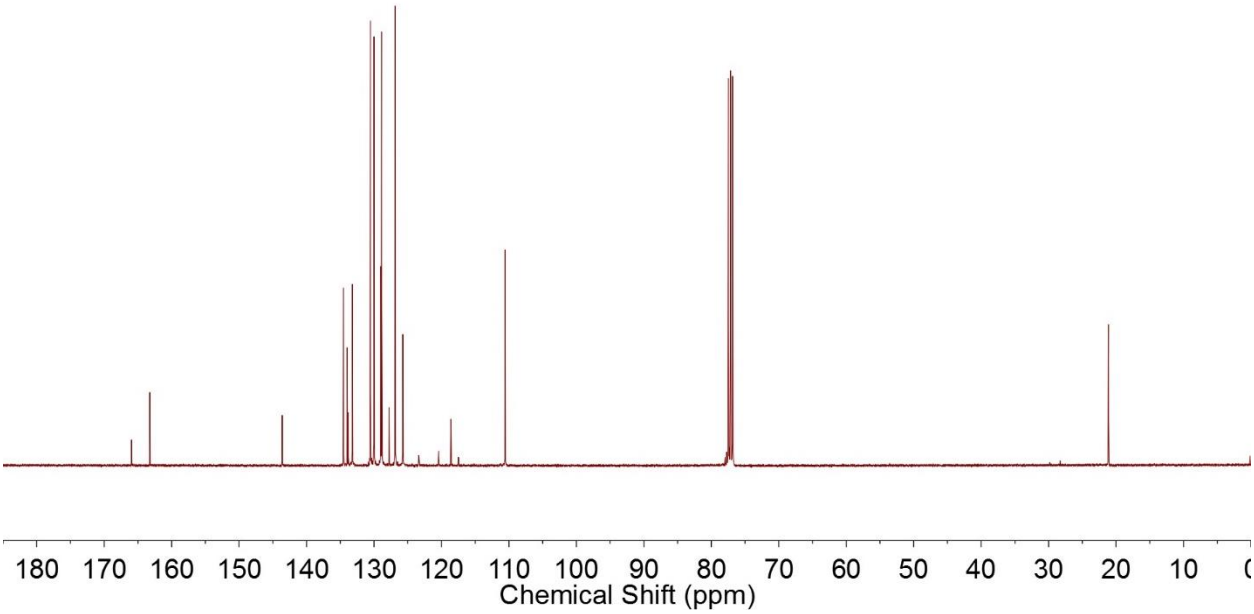

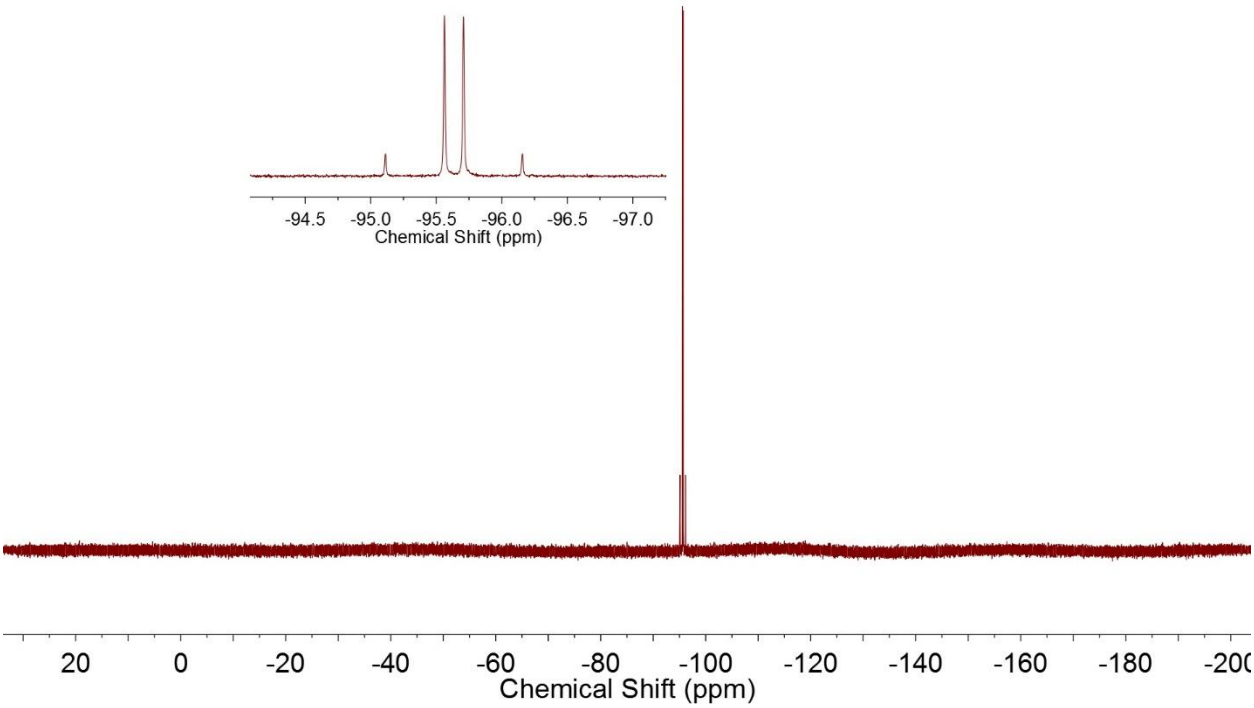

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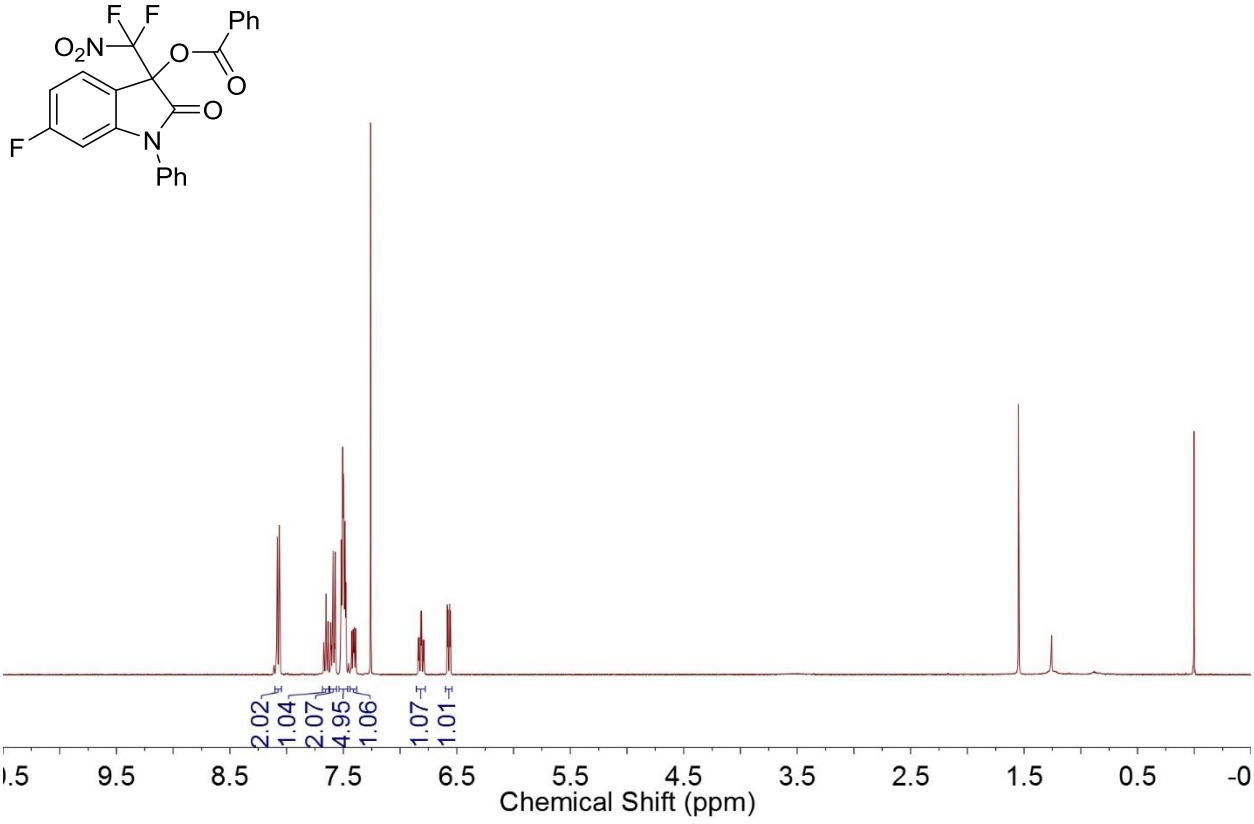

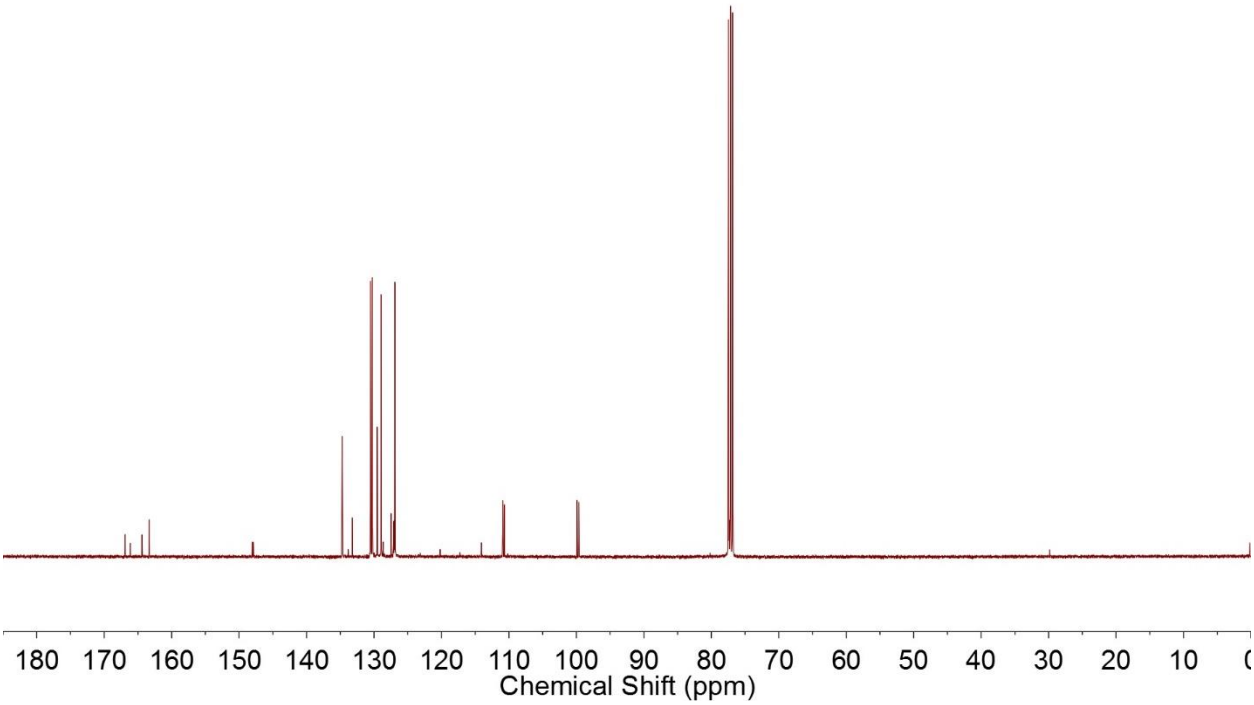
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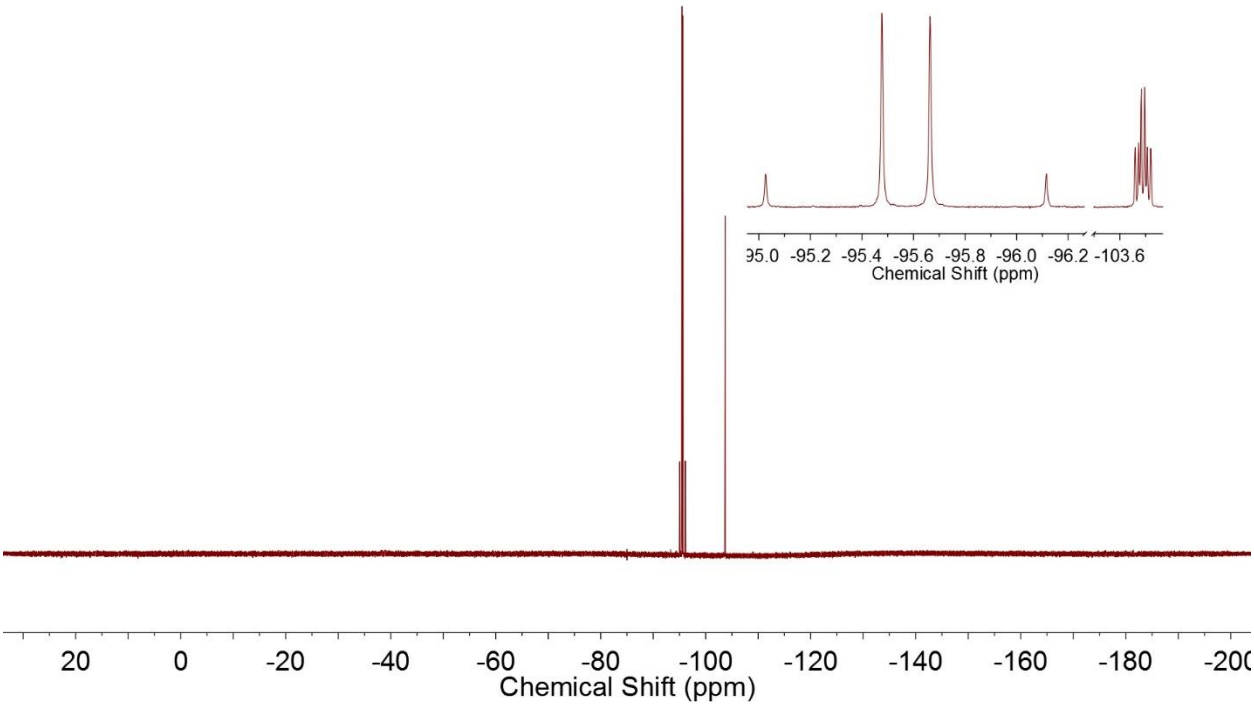
Chemical Shift (ppm)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Chemical Shift (ppm)
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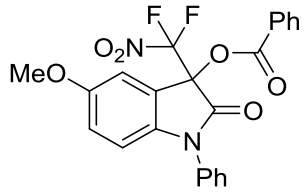
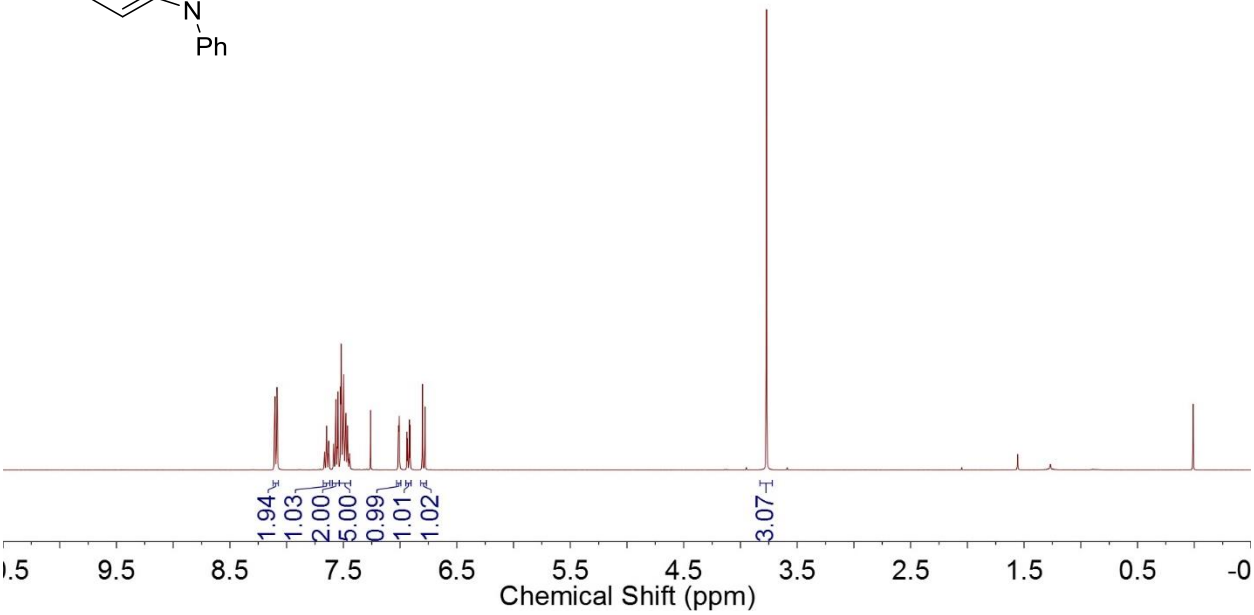
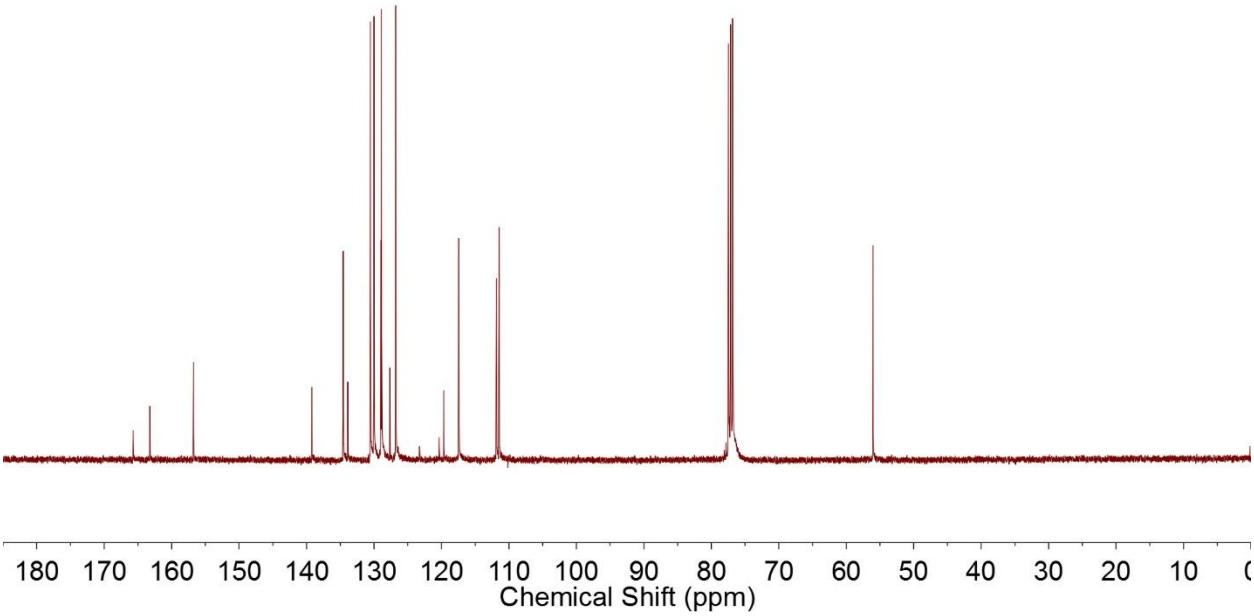
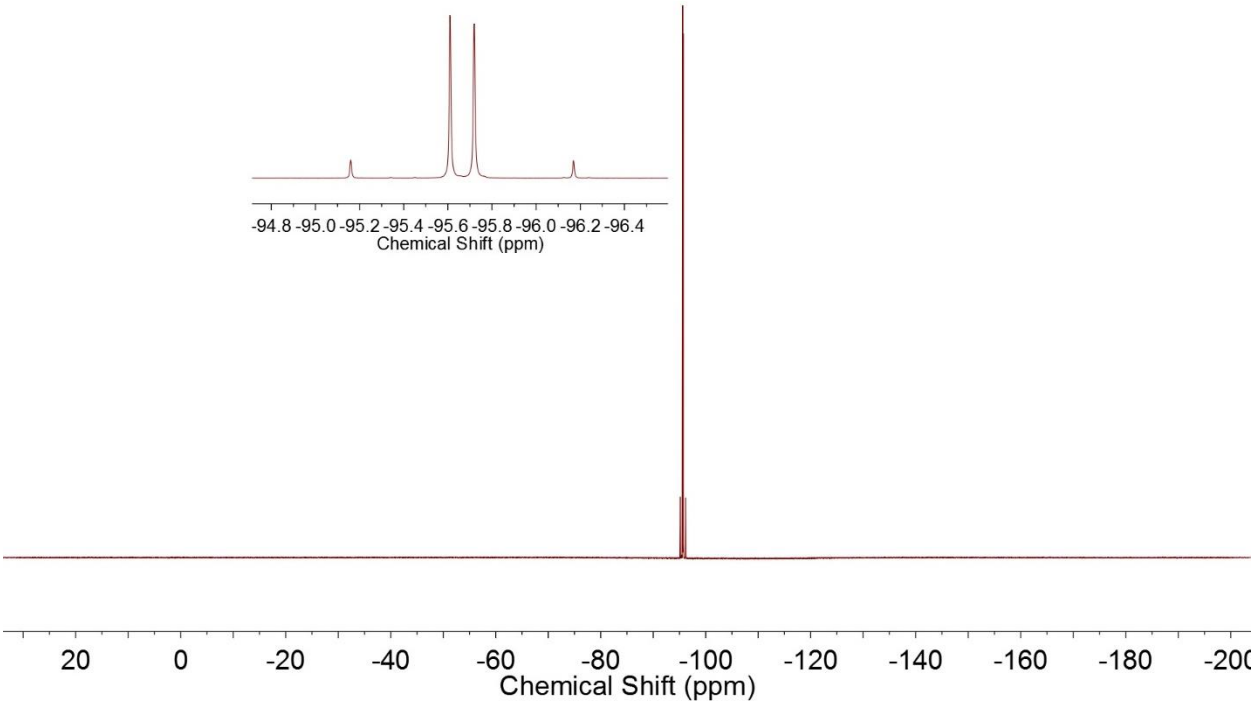
Chemical Shift (ppm)

N-Phenyl 3-(difluoronitromethyl)-5-methoxy-2-oxoindolin-3-yl benzoate (**13**)









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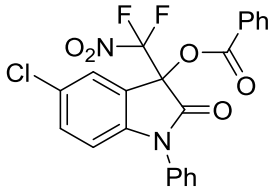

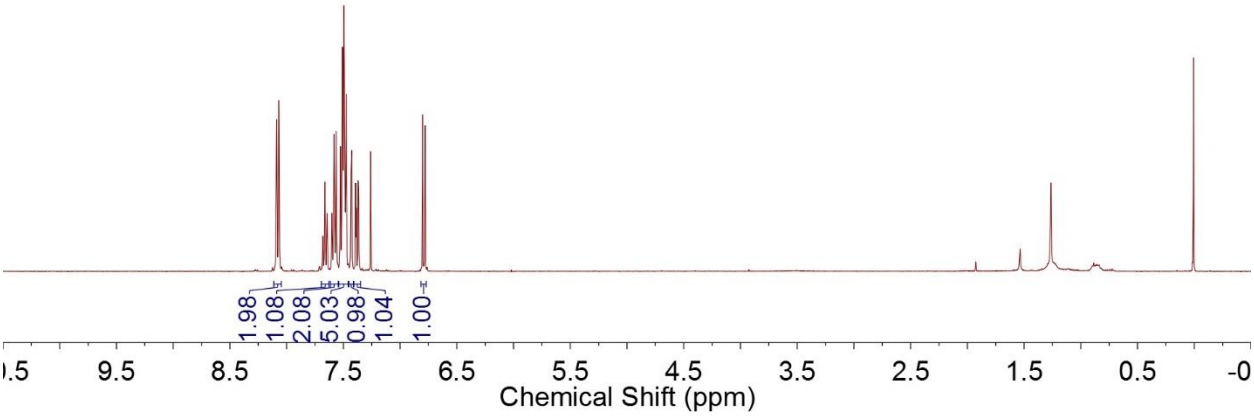

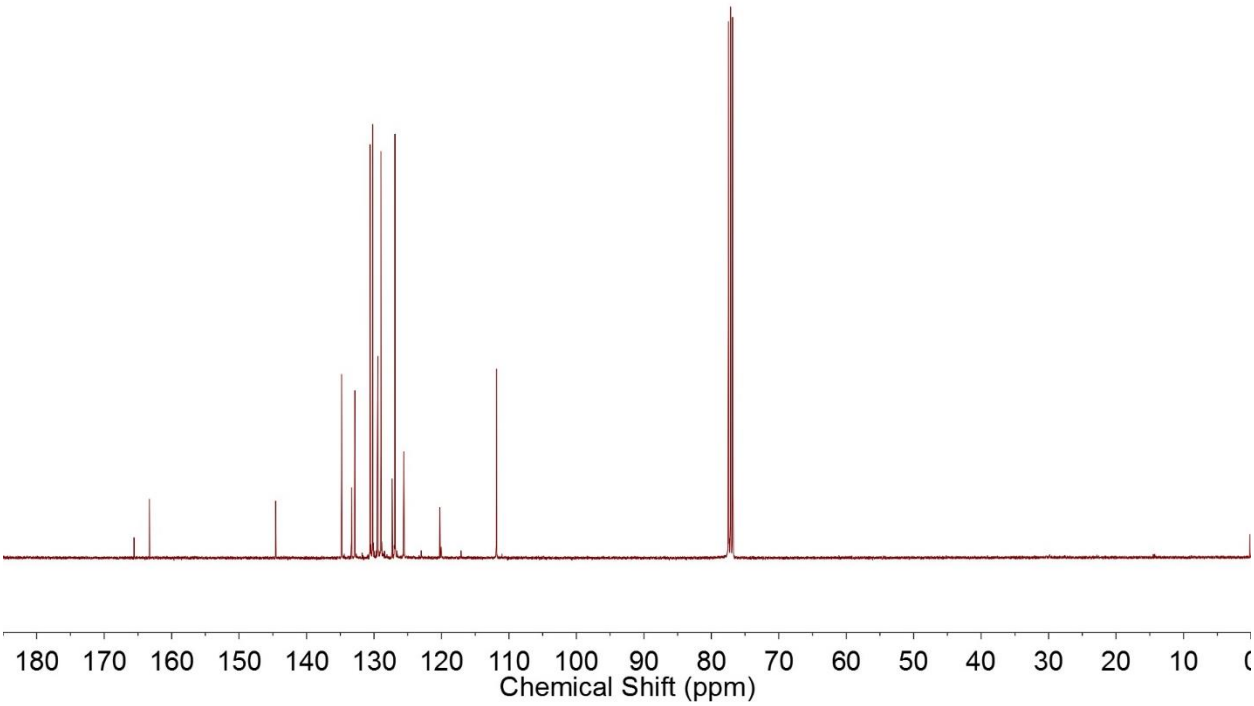
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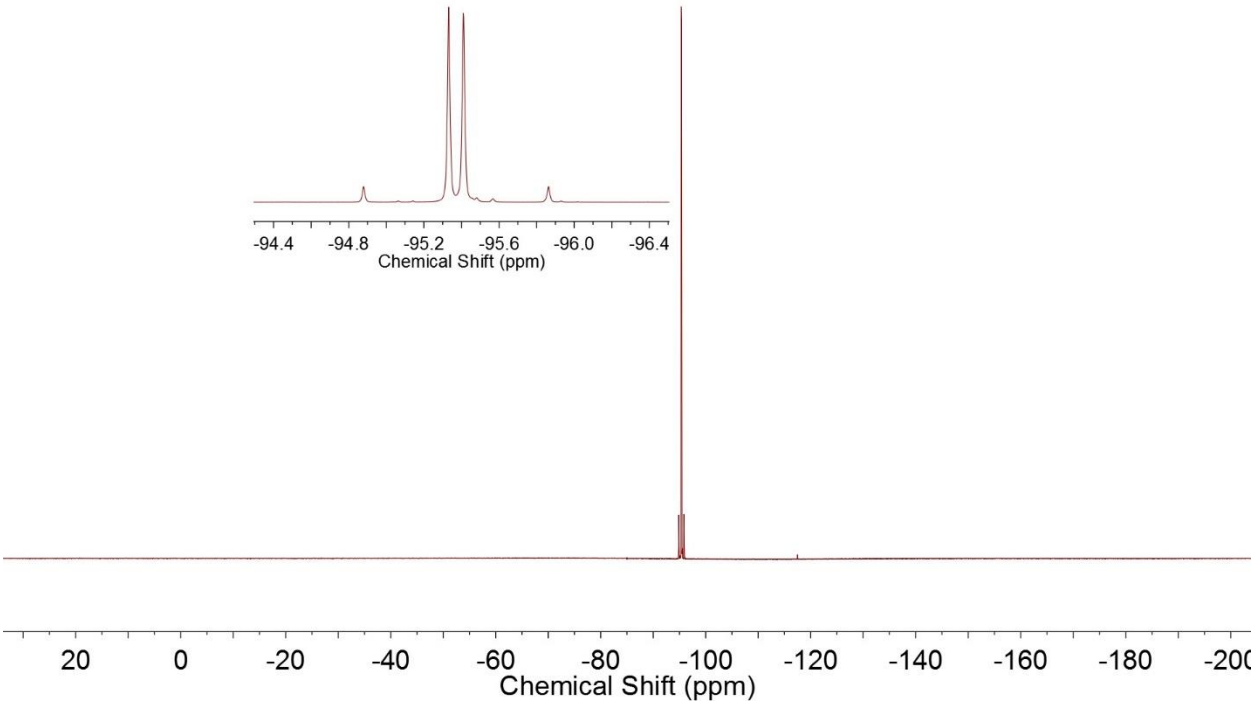
Chemical Shift (ppm)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Chemical Shift (ppm)
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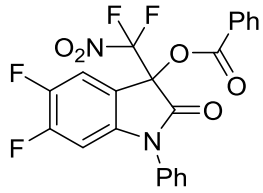
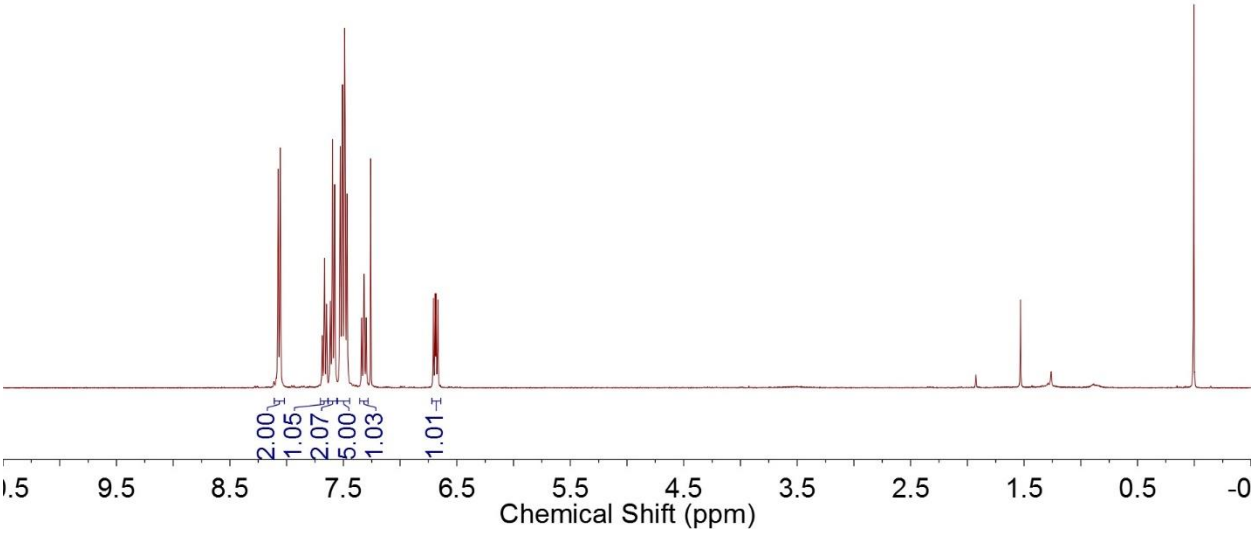
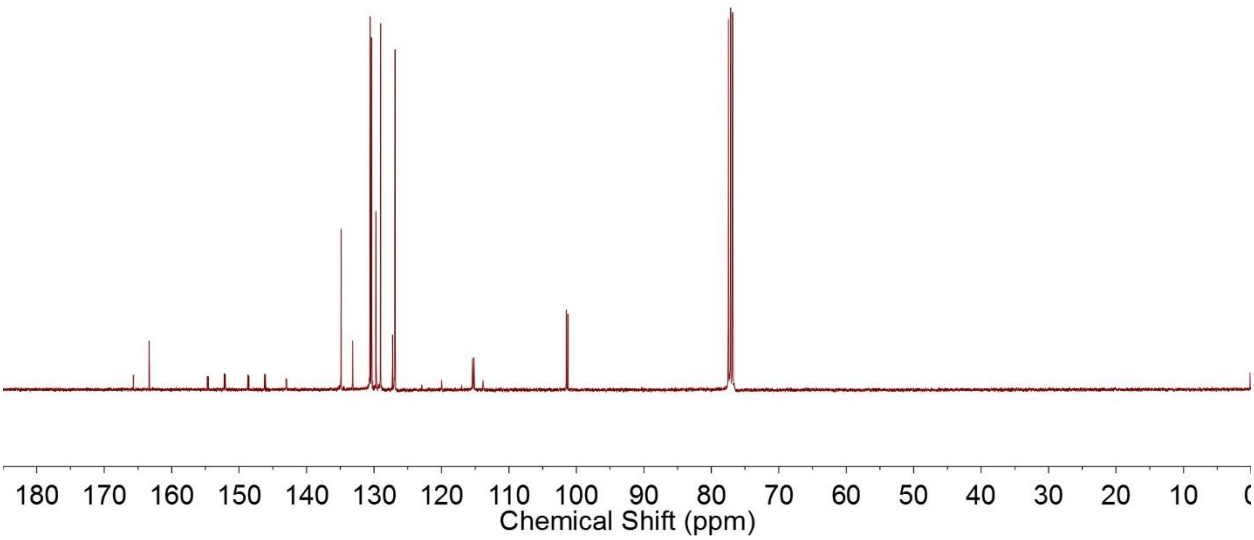
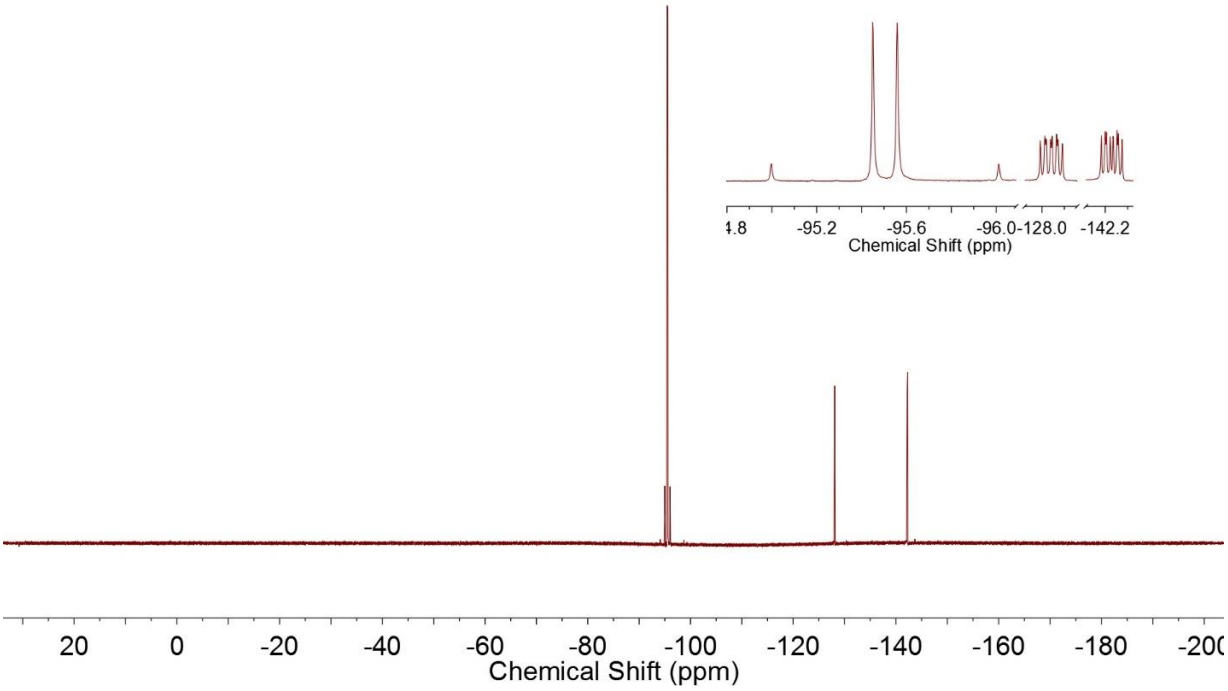
Chemical Shift (ppm)

N-Phenyl 3-(difluoronitromethyl)-5,6-difluoro-2-oxoindolin-3-yl benzoate (**17**)

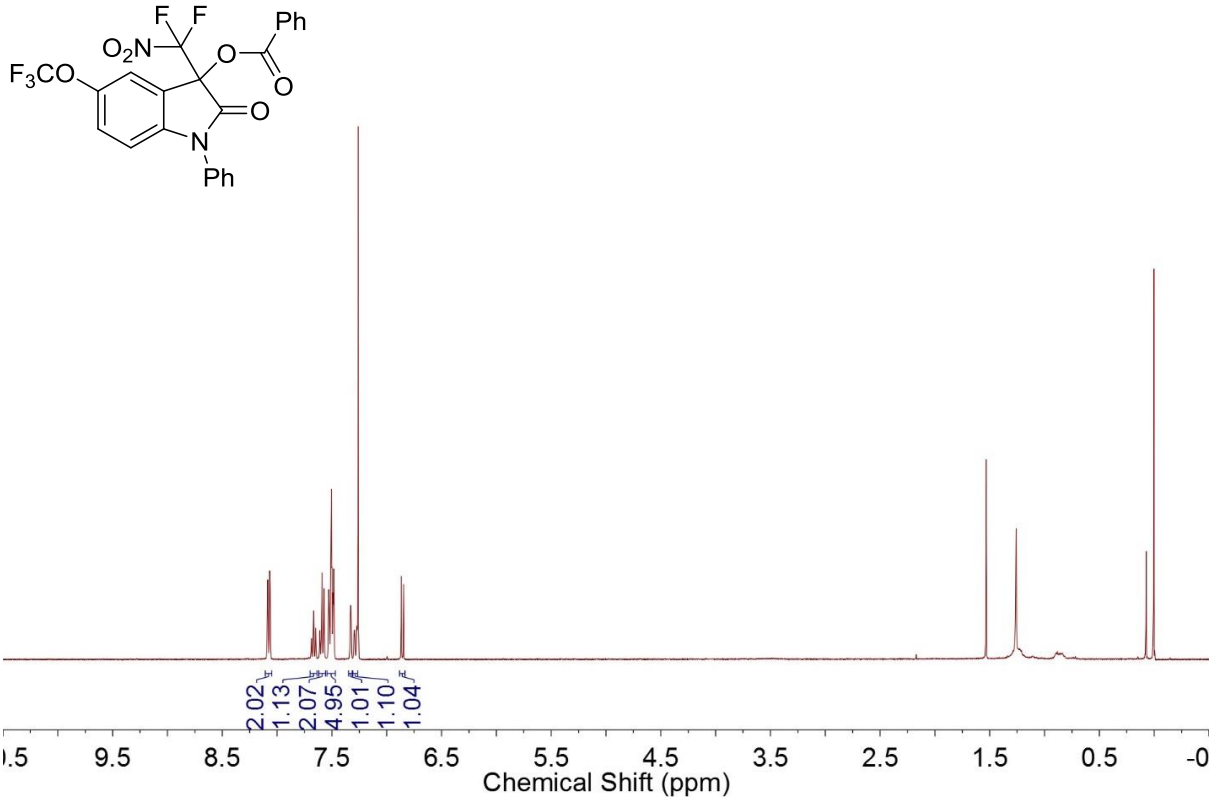


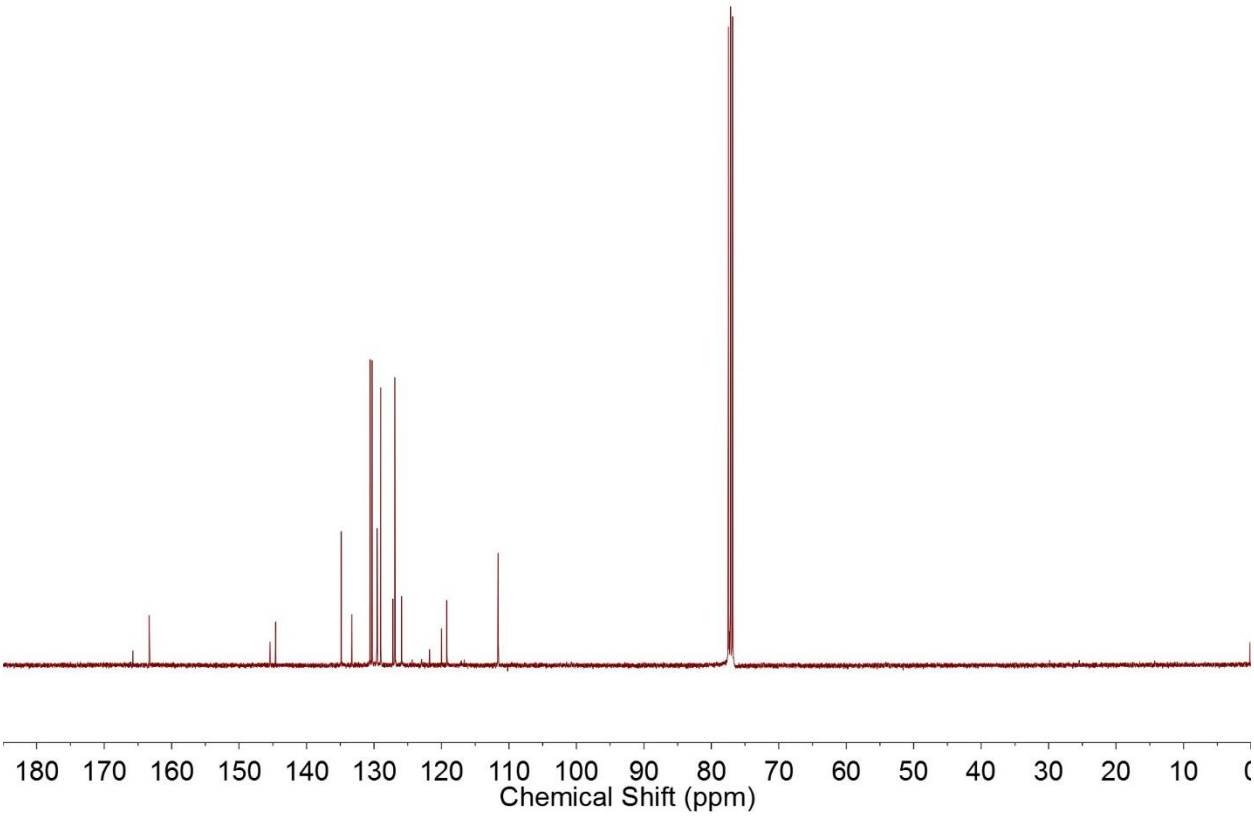






N-Phenyl 3-(difluoronitromethyl)-5-trifluoromethoxy-2-oxoindolin-3-yl benzoate (**19**)

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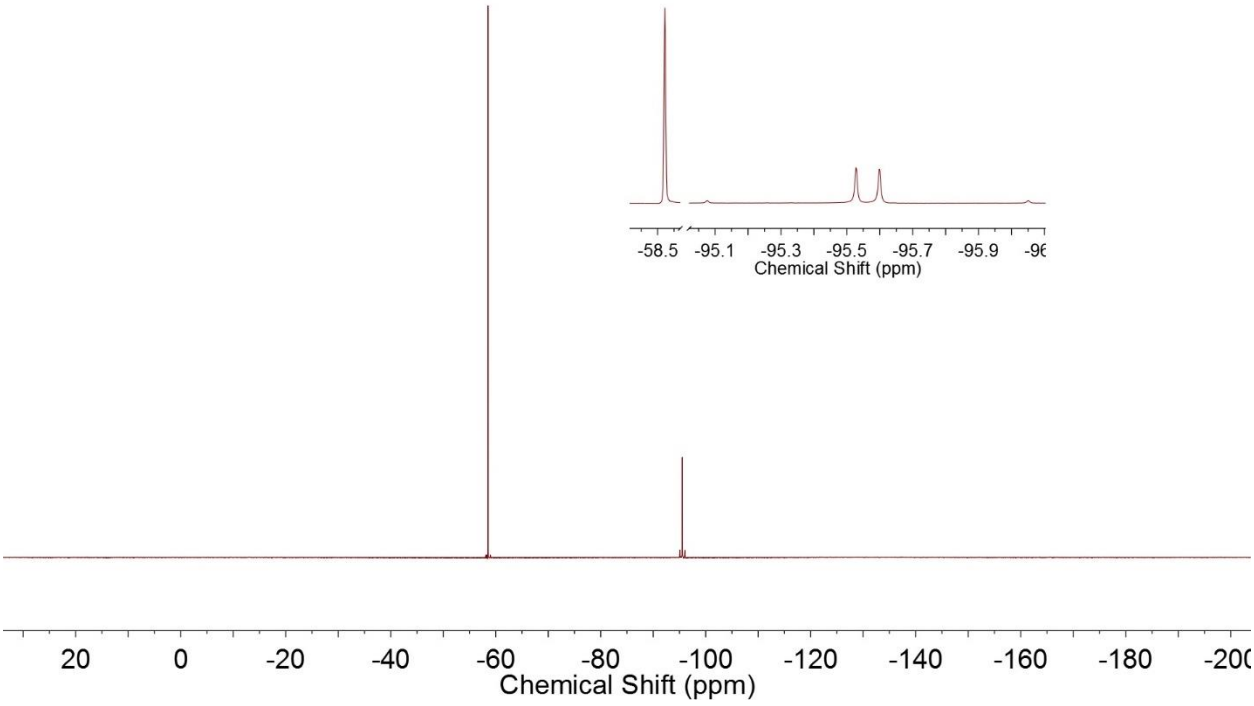
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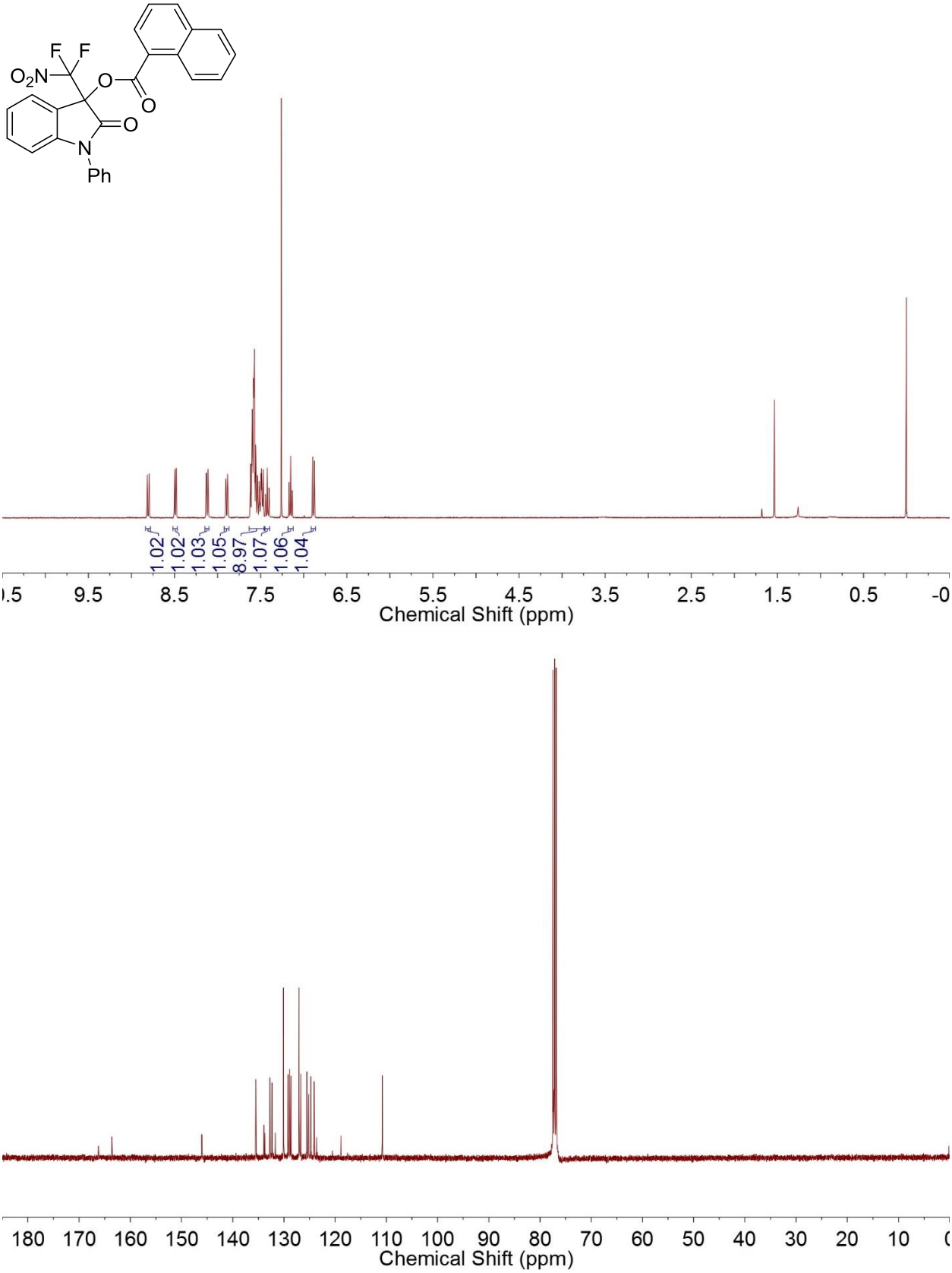
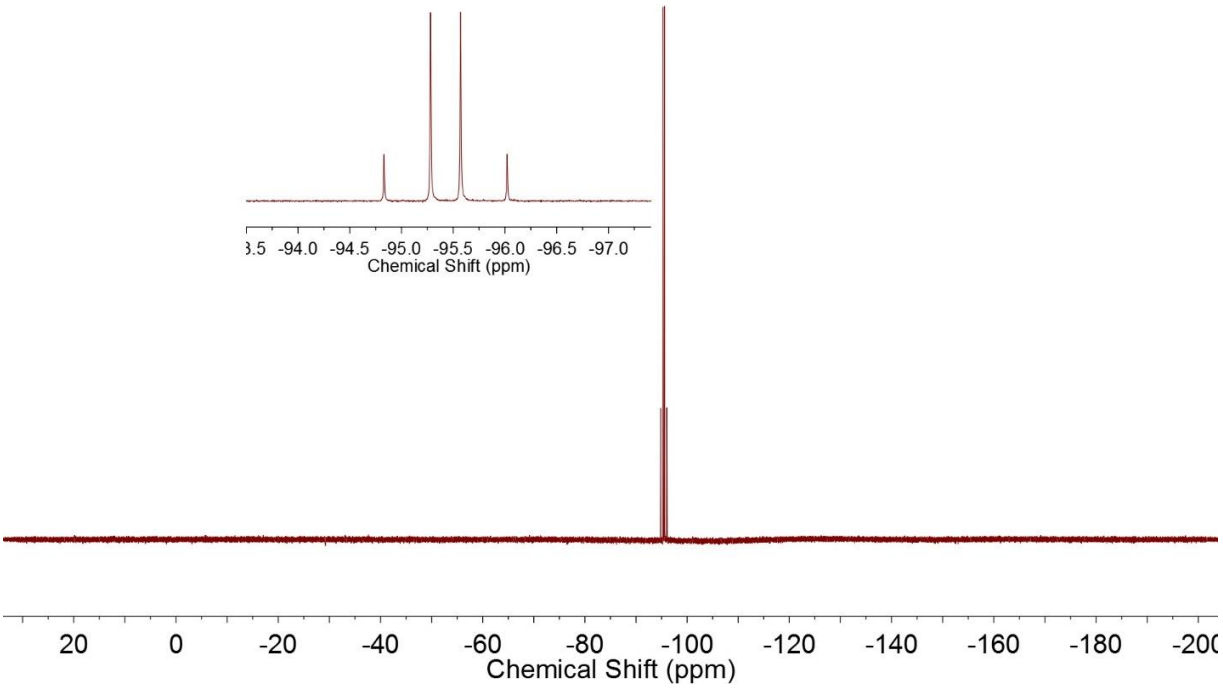
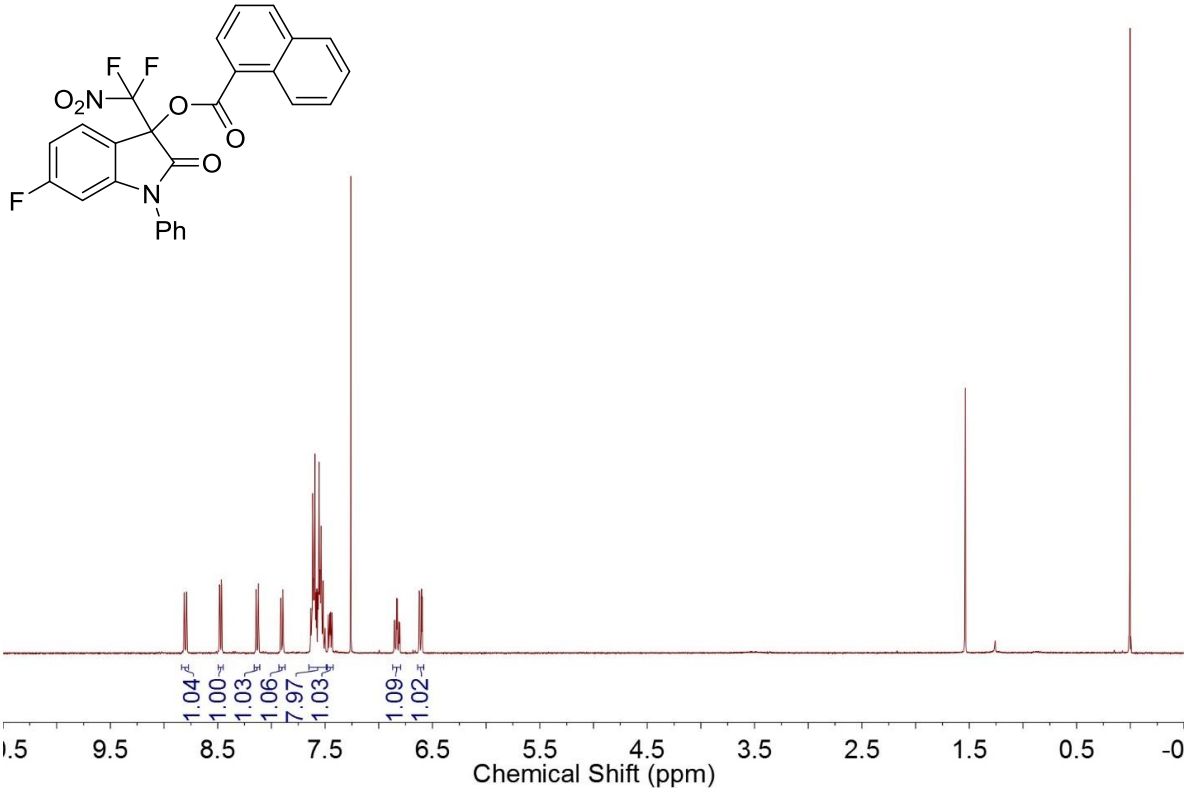
Chemical Shift (ppm)

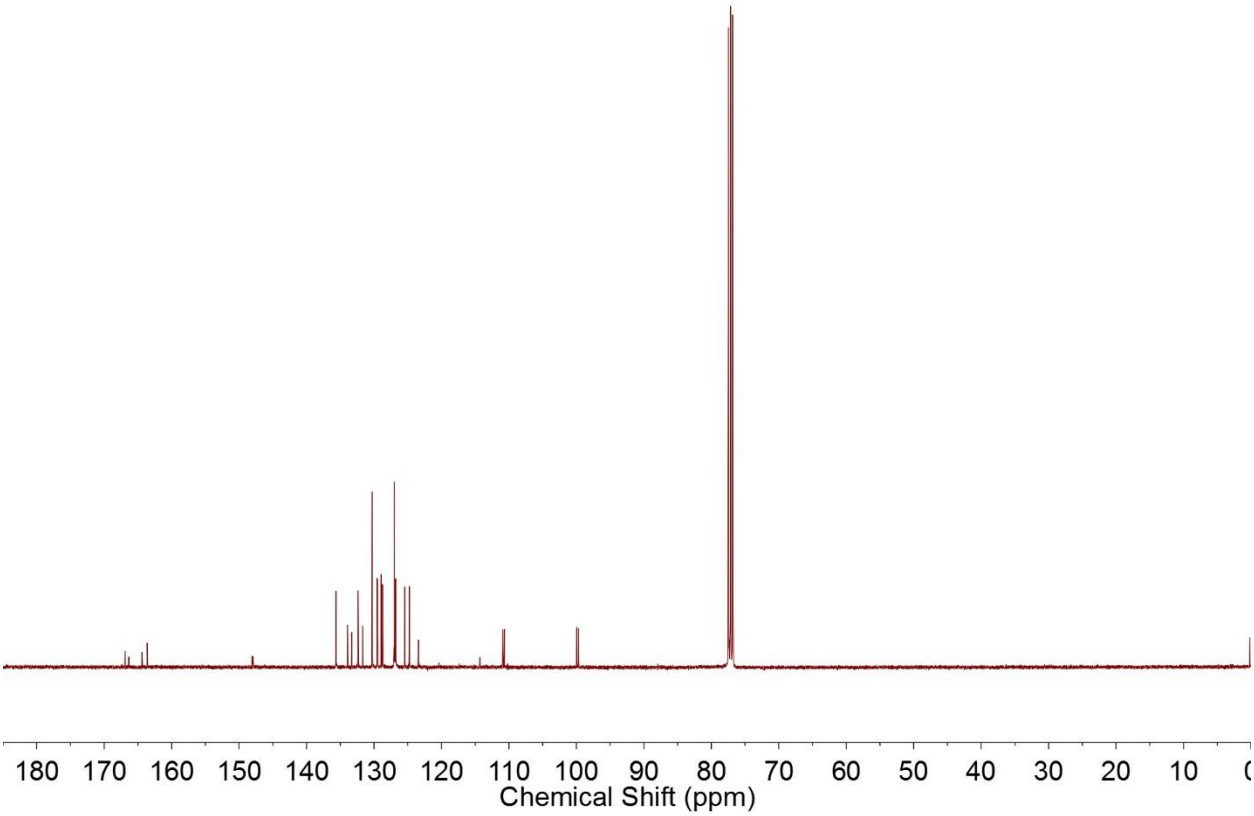
N-Phenyl 3-(difluoronitromethyl)-2-oxoindolin-3-yl 1-naphthoate (**21**)





N-Phenyl 3-(difluoronitromethyl)-6-fluoro-2-oxoindolin-3-yl 1-naphthoate (**22**)

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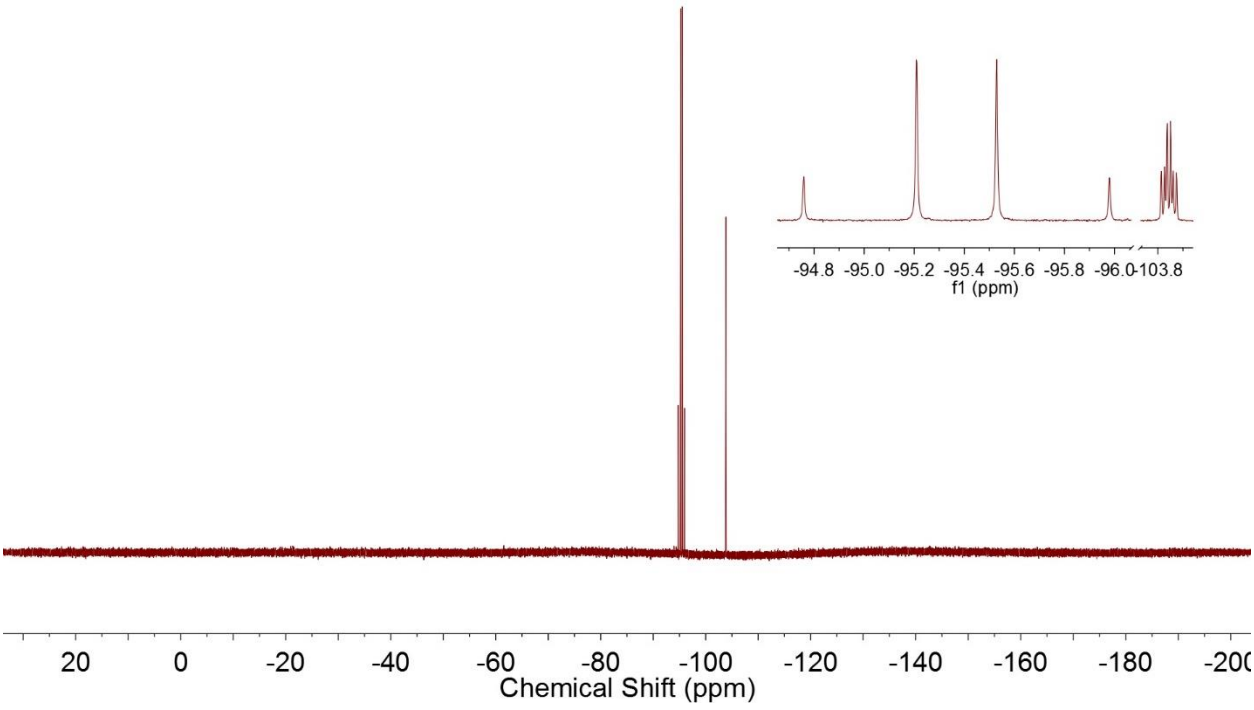
Chemical Shift (ppm)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f1 (ppm)
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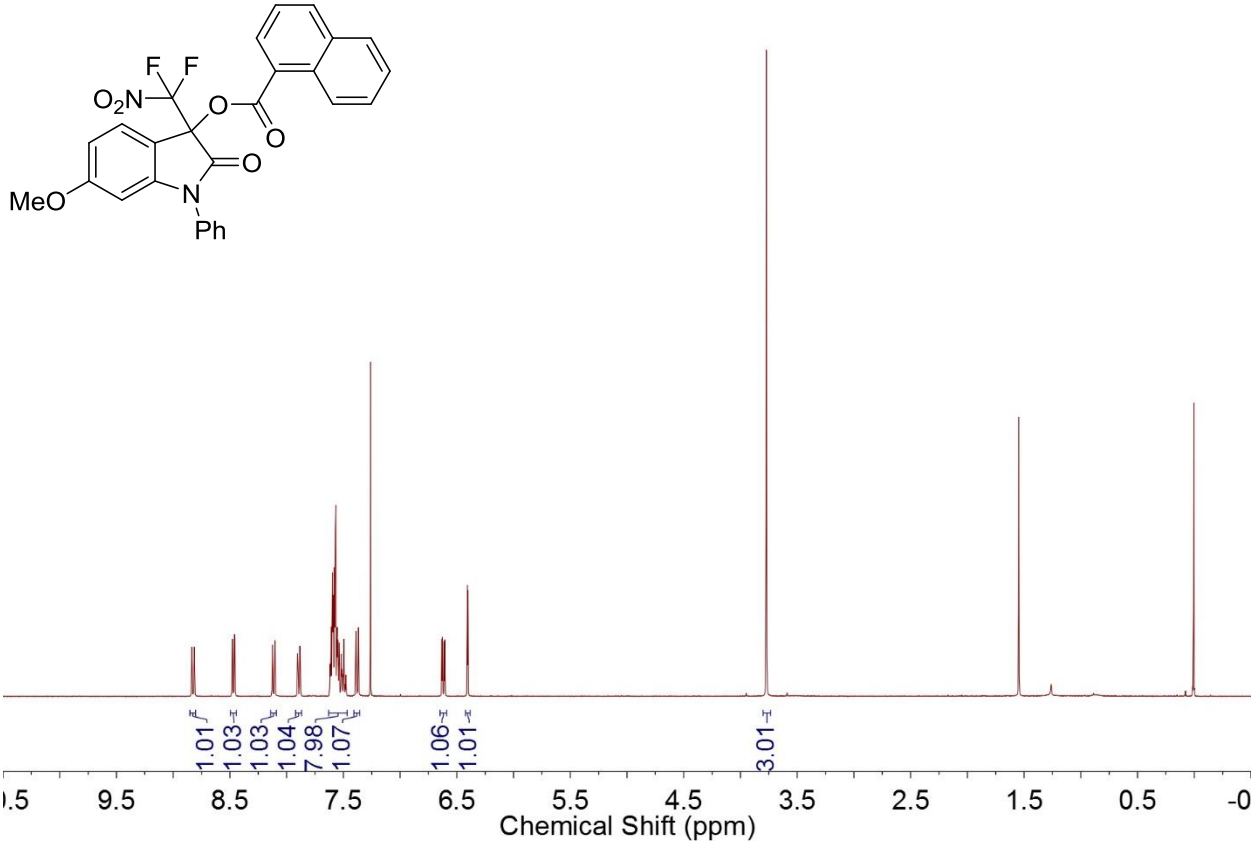
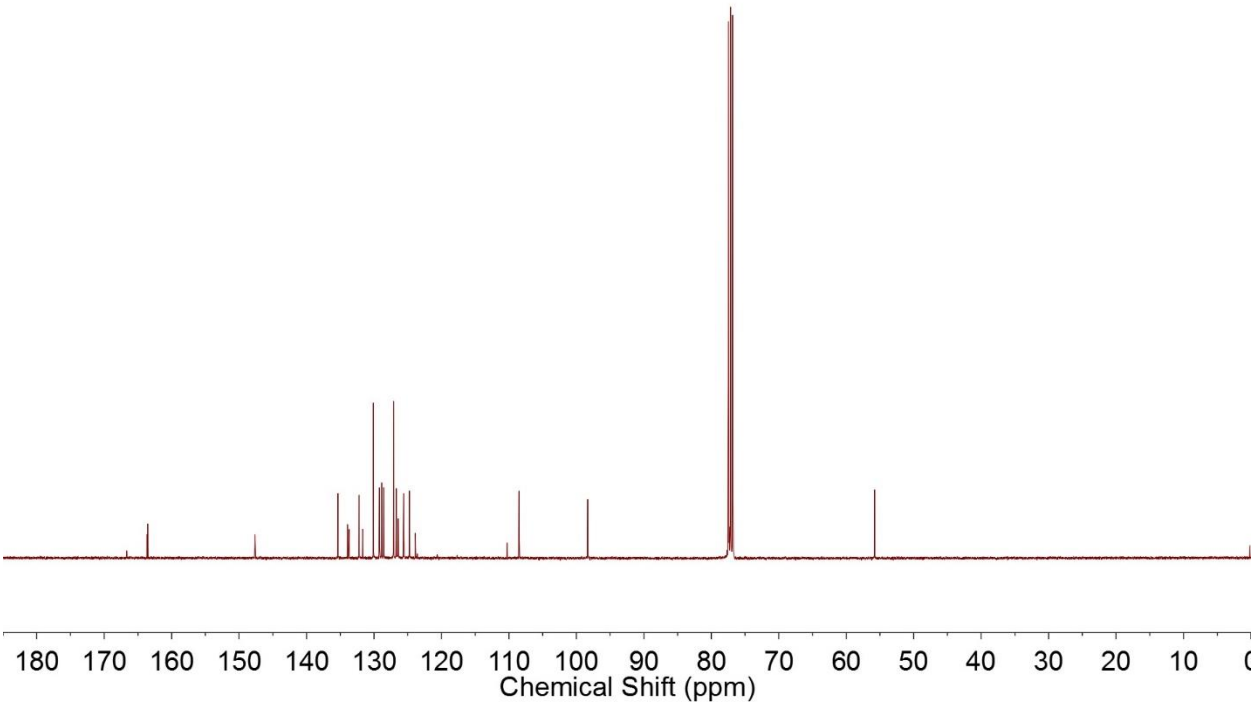
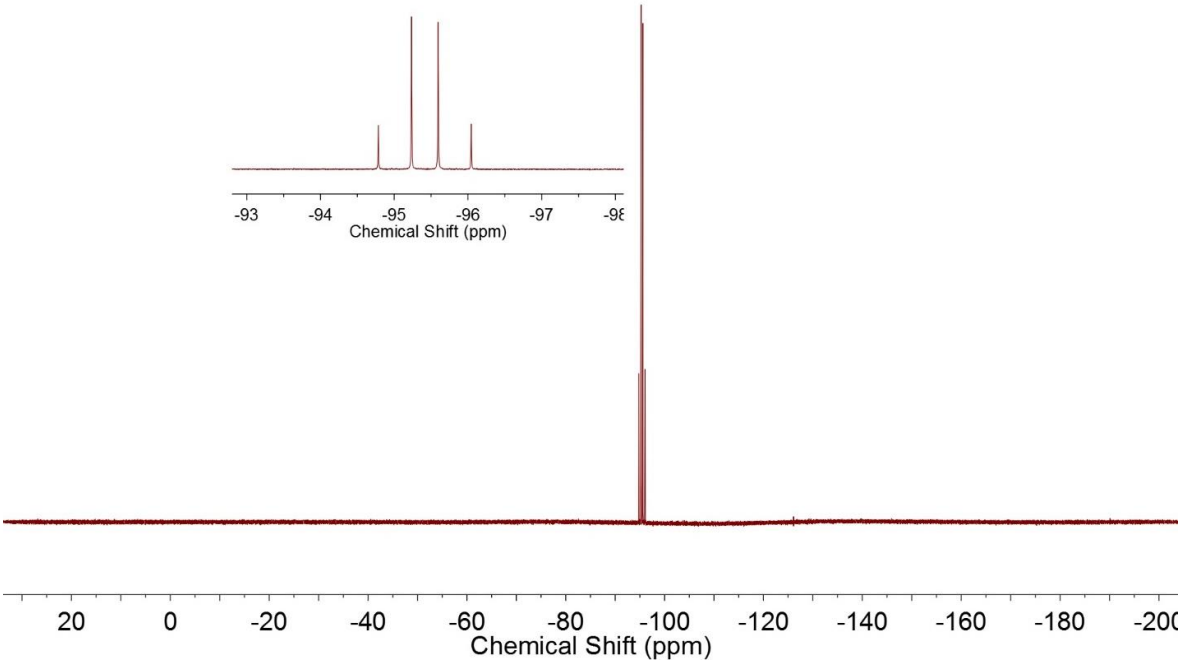
Chemical Shift (ppm)

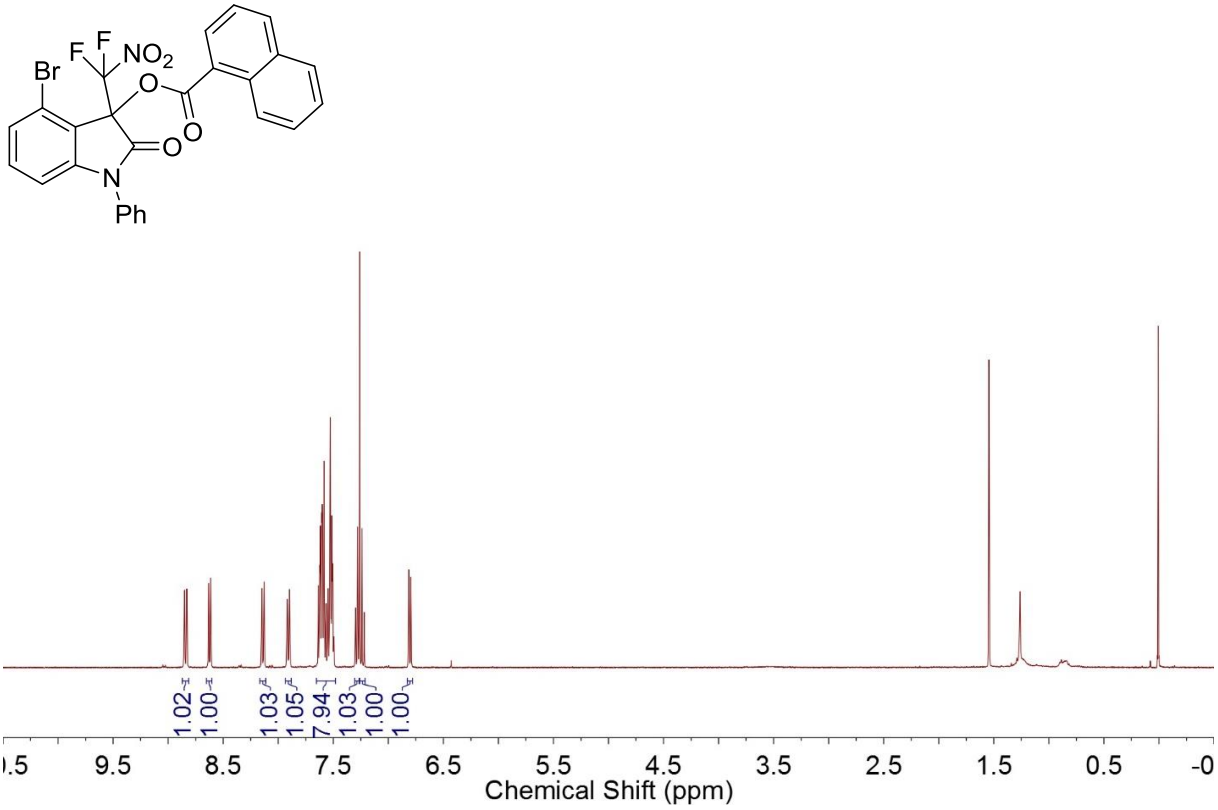
N-Phenyl 3-(difluoronitromethyl)-6-methoxy-2-oxoindolin-3-yl 1-naphthoate (**24**)

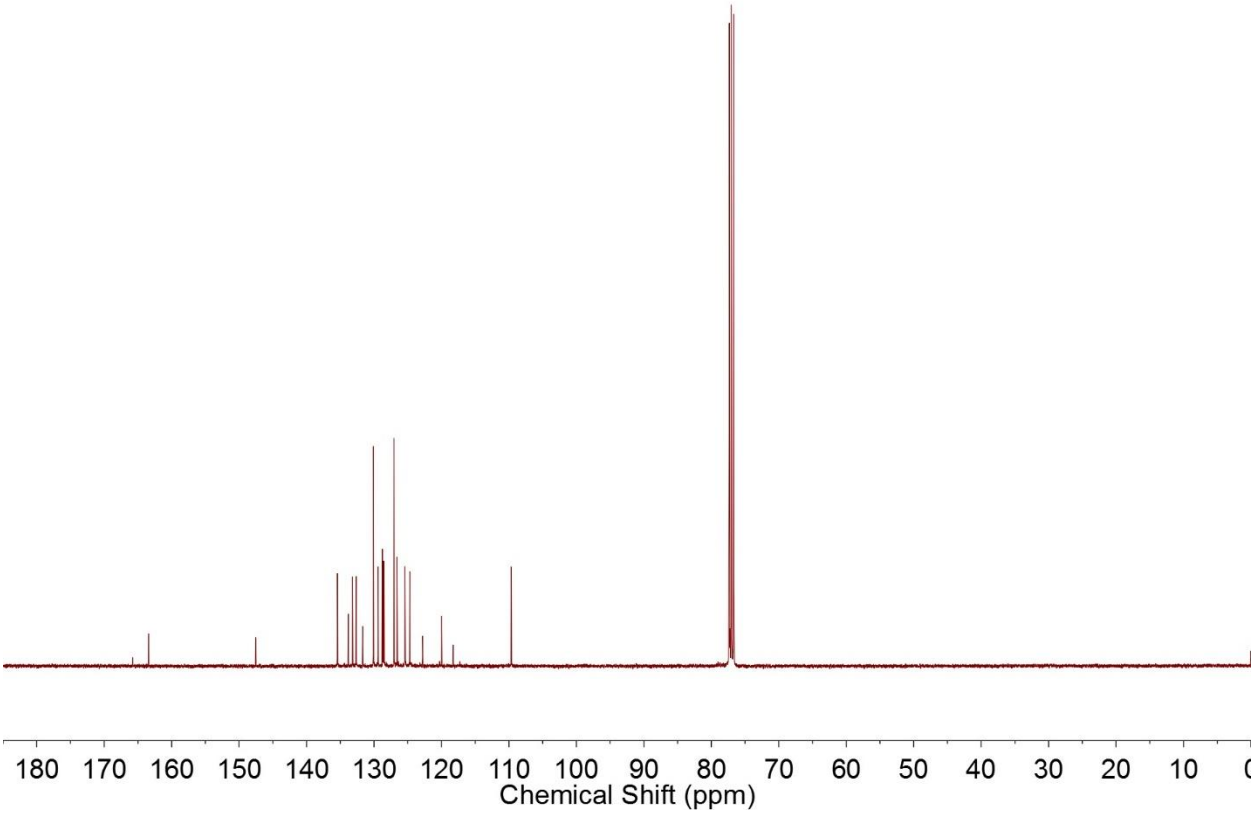






N-Phenyl 3-(difluoronitromethyl)-4-bromo-2-oxoindolin-3-yl 1-naphthoate (**26**)

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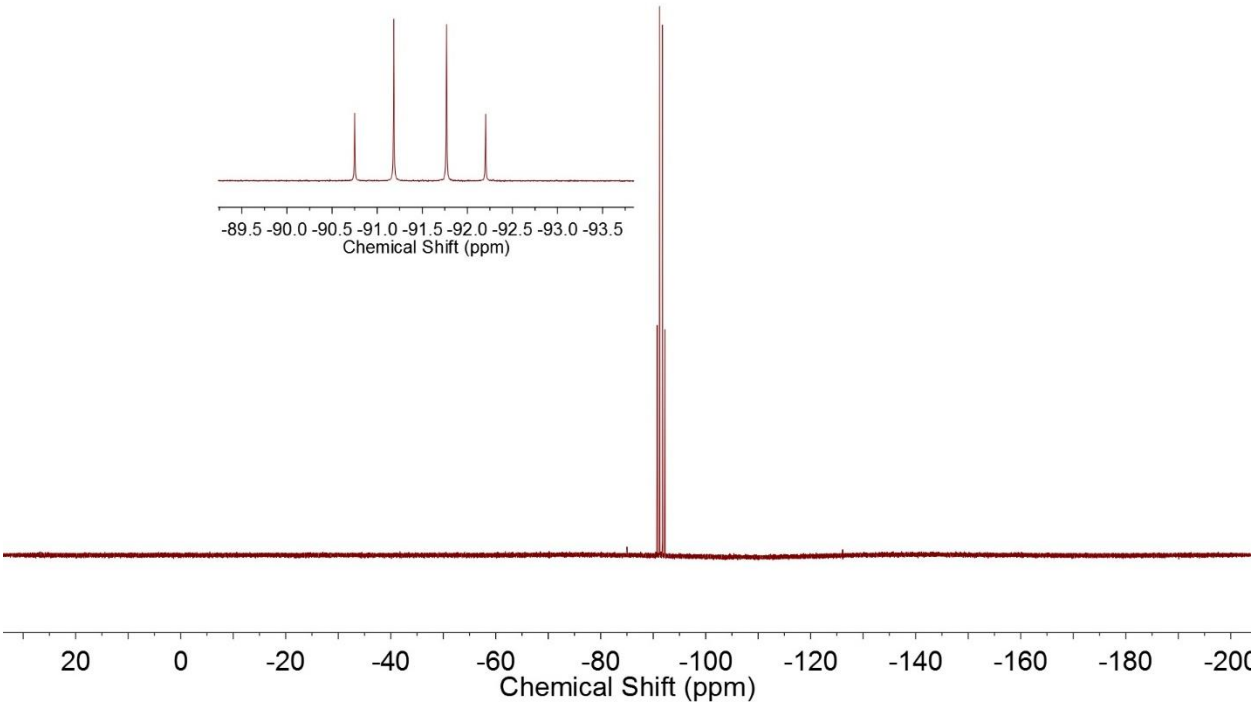
Chemical Shift (ppm)


-89.5 -90.0 -90.5 -91.0 -91.5 -92.0 -92.5 -93.0 -93.5
Chemical Shift (ppm)
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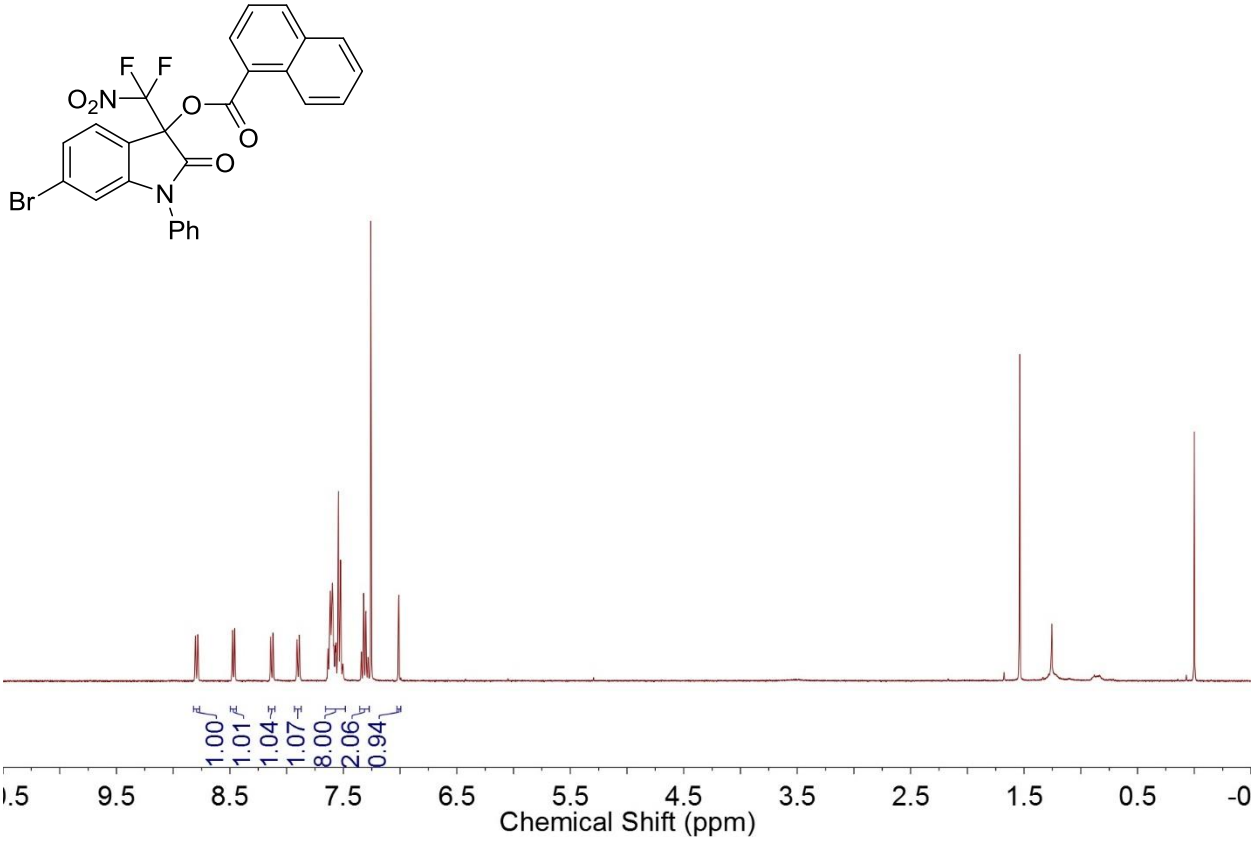
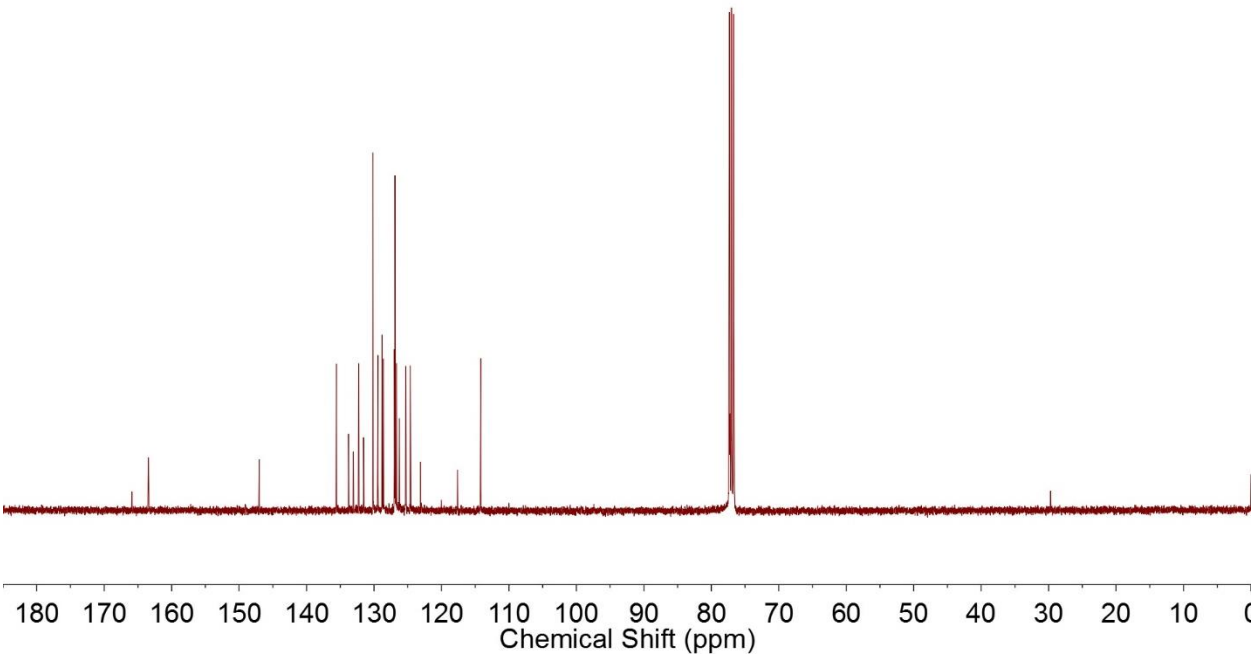
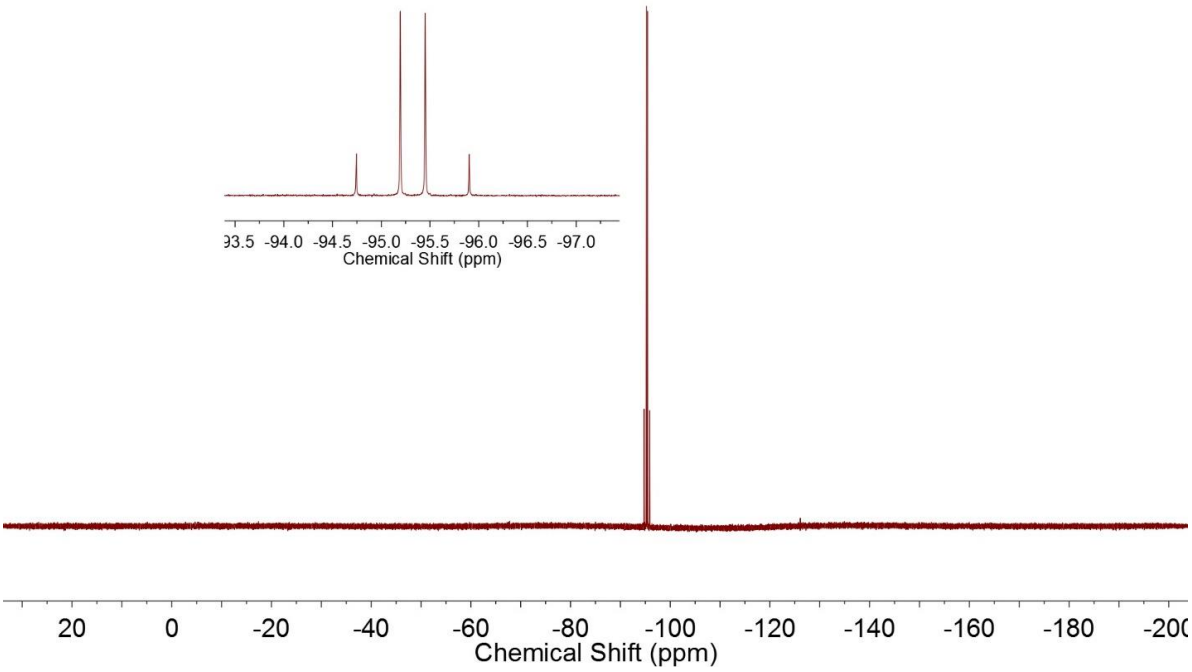
Chemical Shift (ppm)

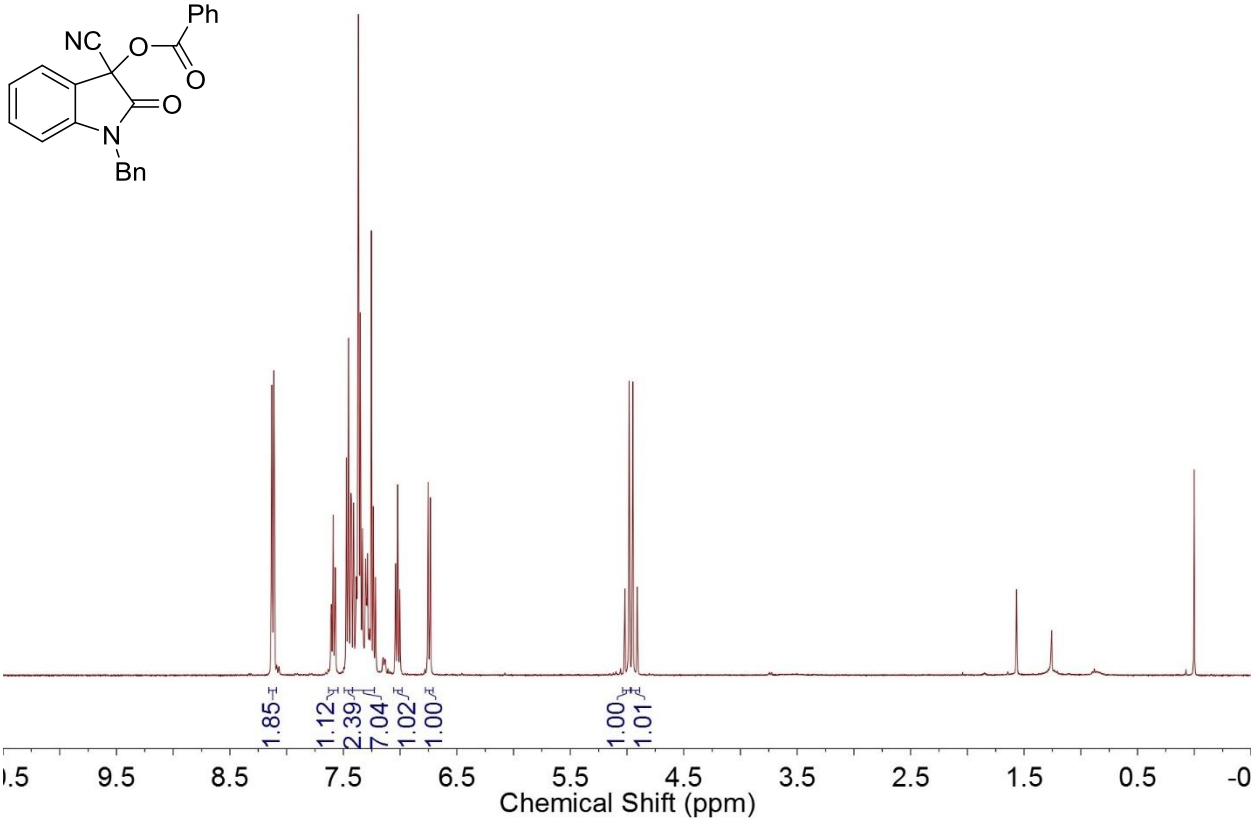
N-Phenyl 3-(difluoronitromethyl)-6-bromo-2-oxoindolin-3-yl 1-naphthoate (**28**)

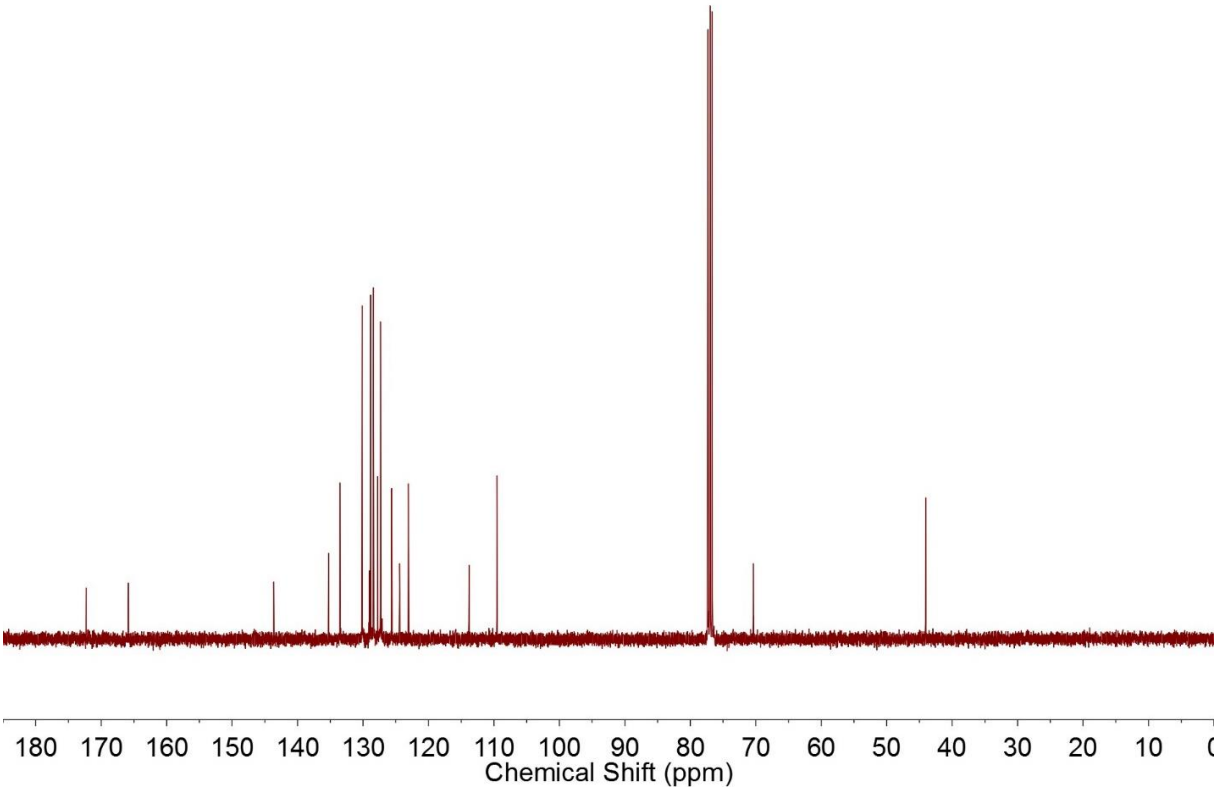




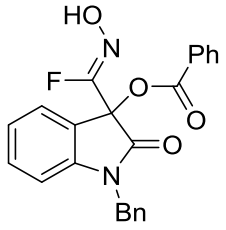


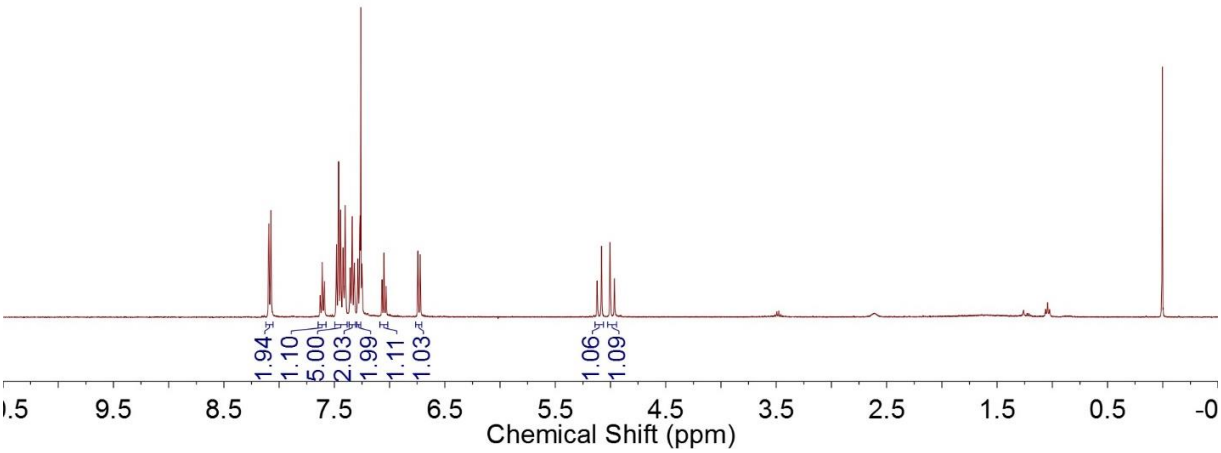
N-Benzyl 3-cyano-2-oxoindolin-3-yl benzoate (**29**)

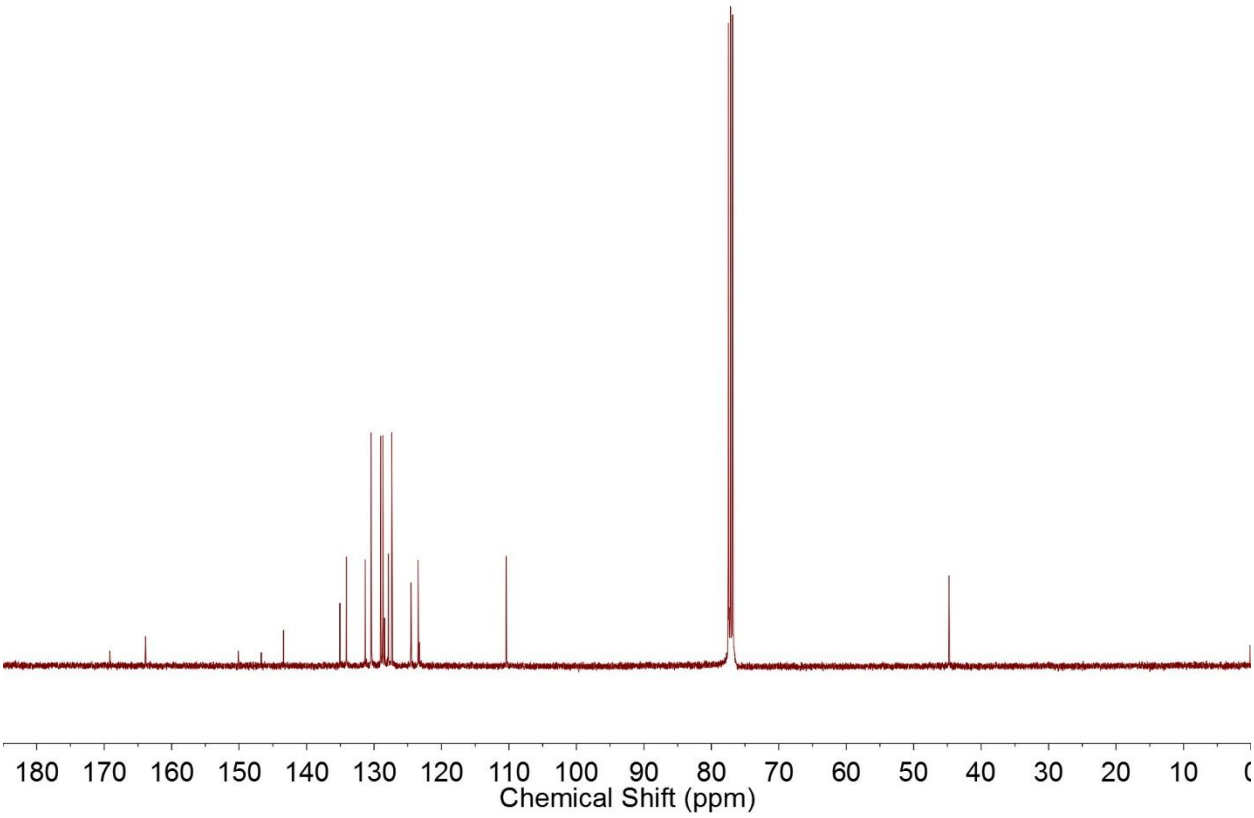


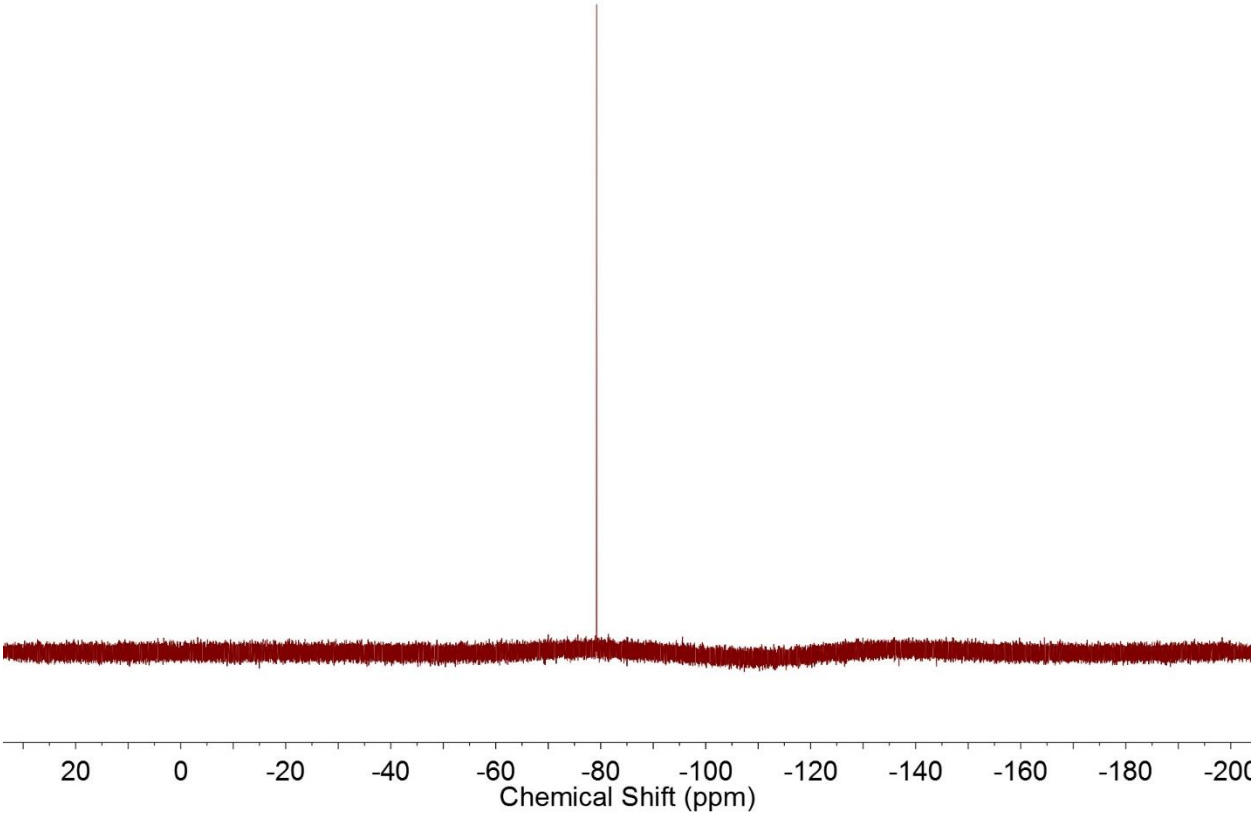


N-Benzyl (*Z*)-3-(fluoro(hydroxyimino)methyl)-2-oxoindolin-3-yl benzoate (**30**)

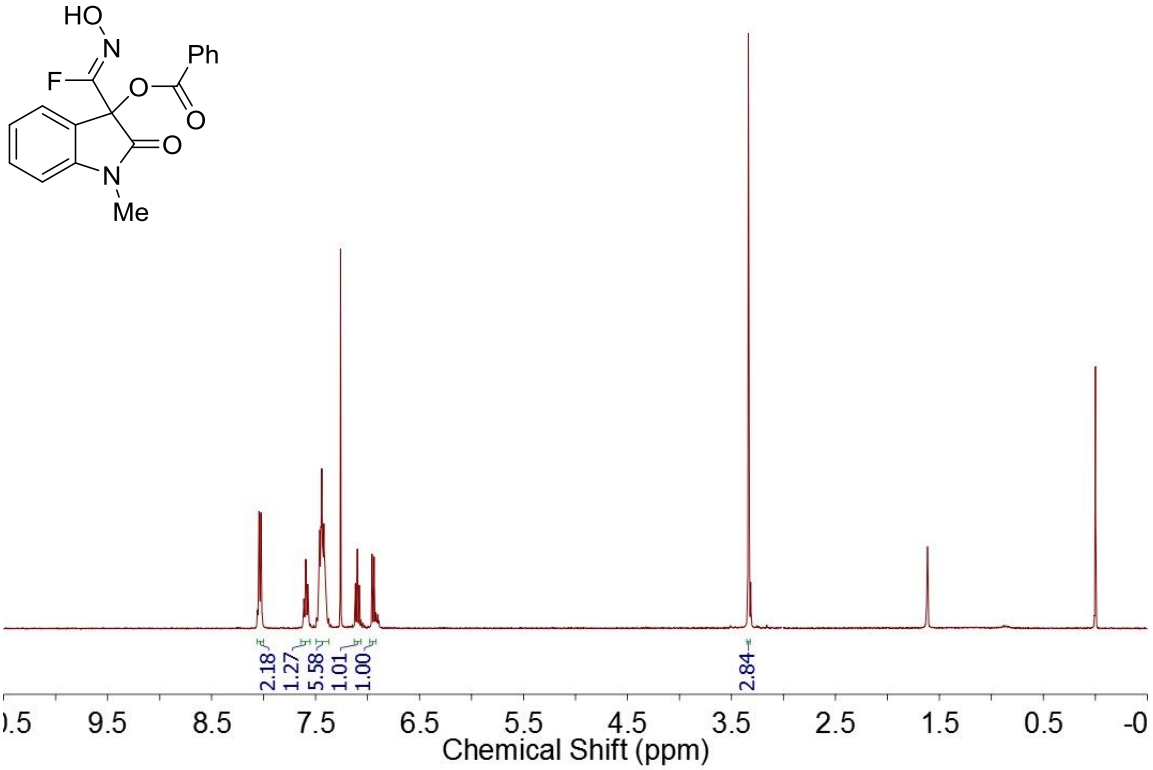


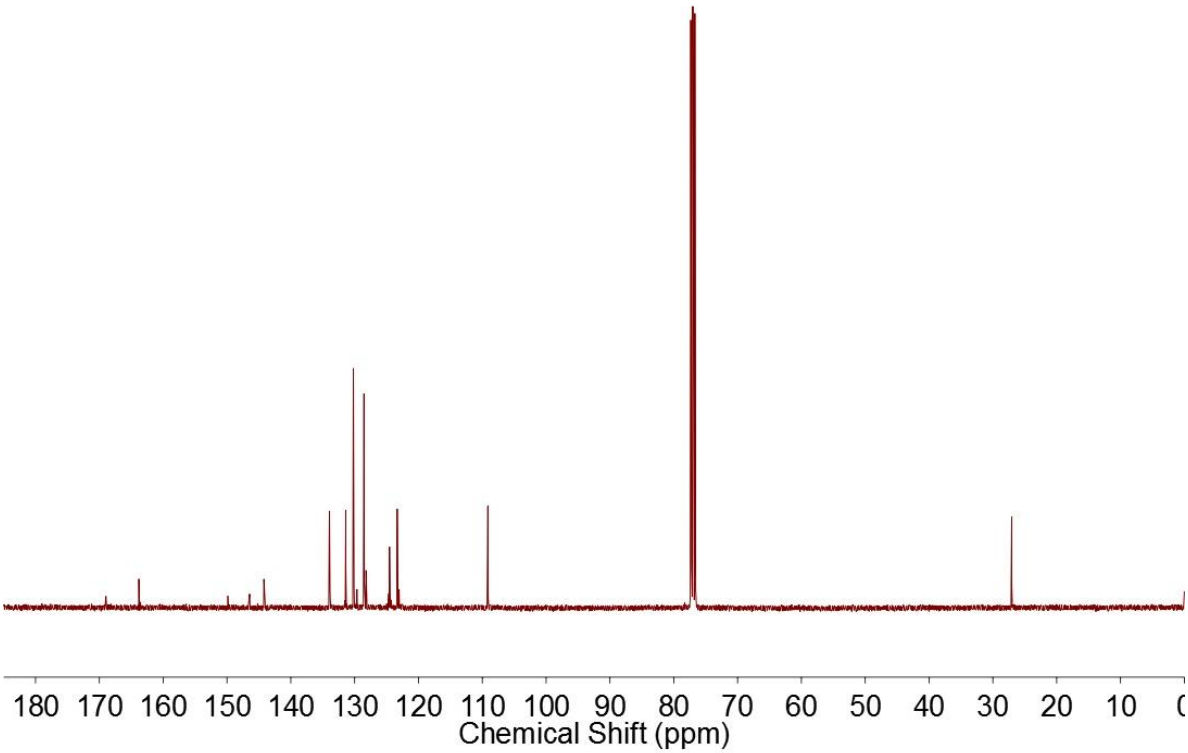


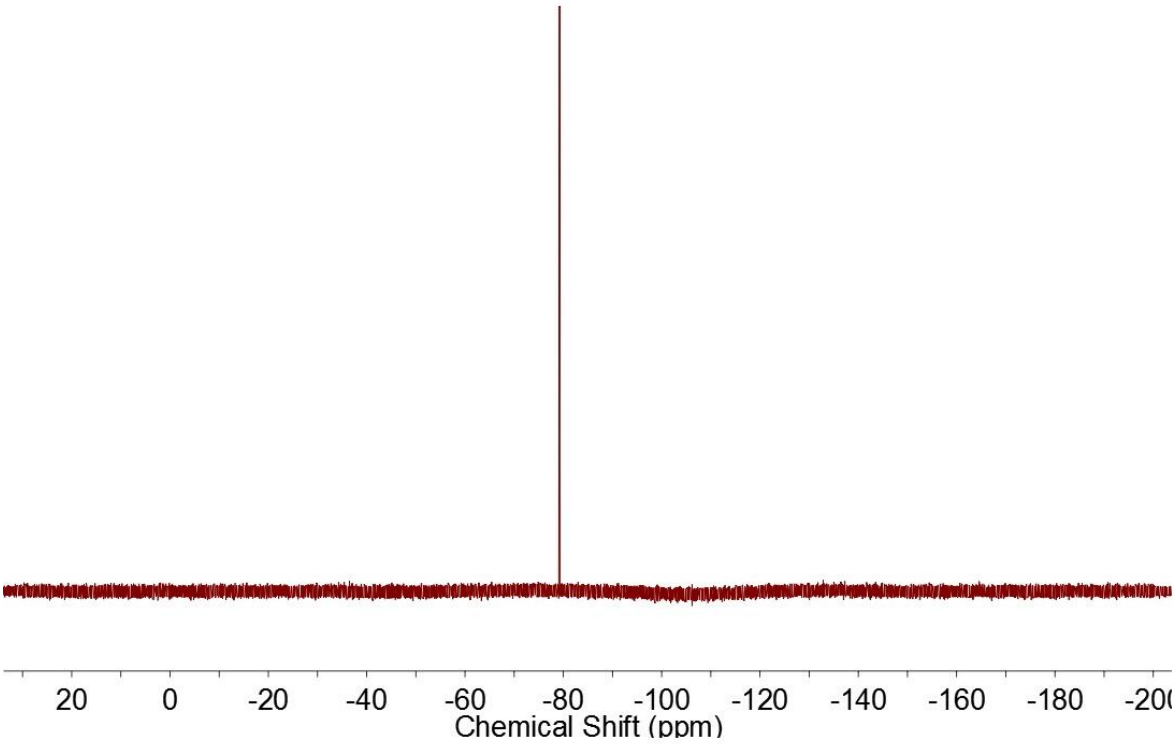

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
Chemical Shift (ppm)

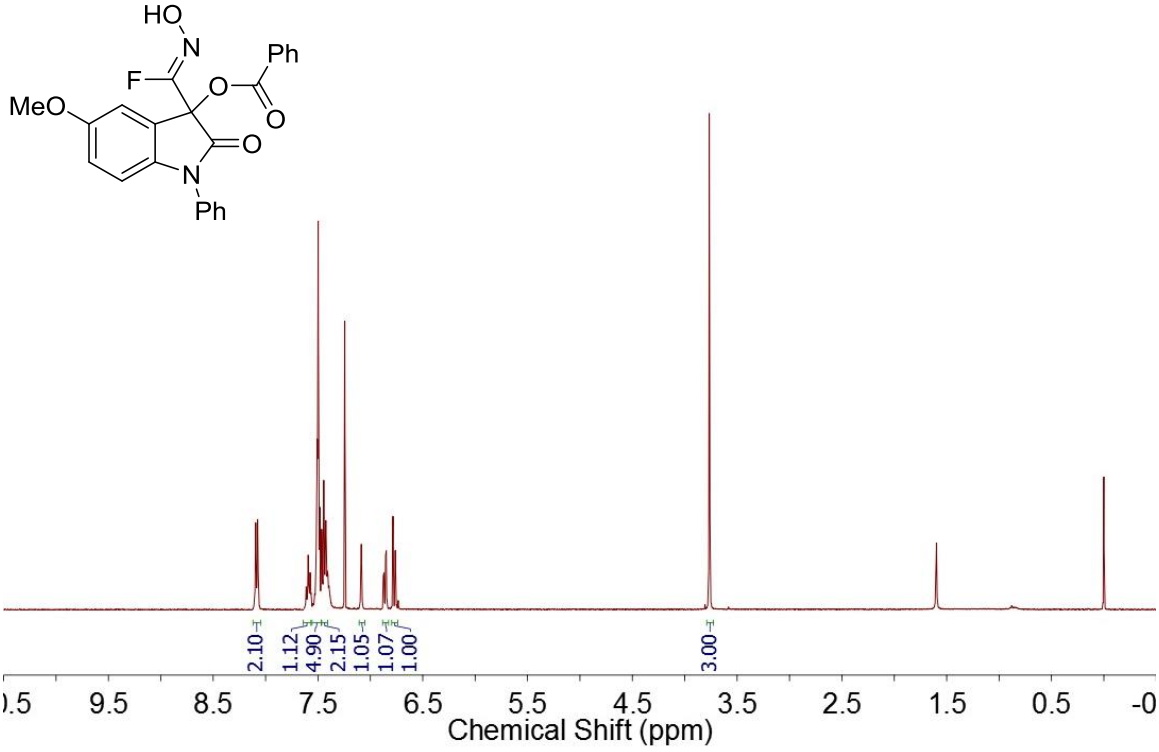
N-Methyl (*Z*)-3-(fluoro(hydroxyimino)methyl)-2-oxoindolin-3-yl benzoate (**31**)

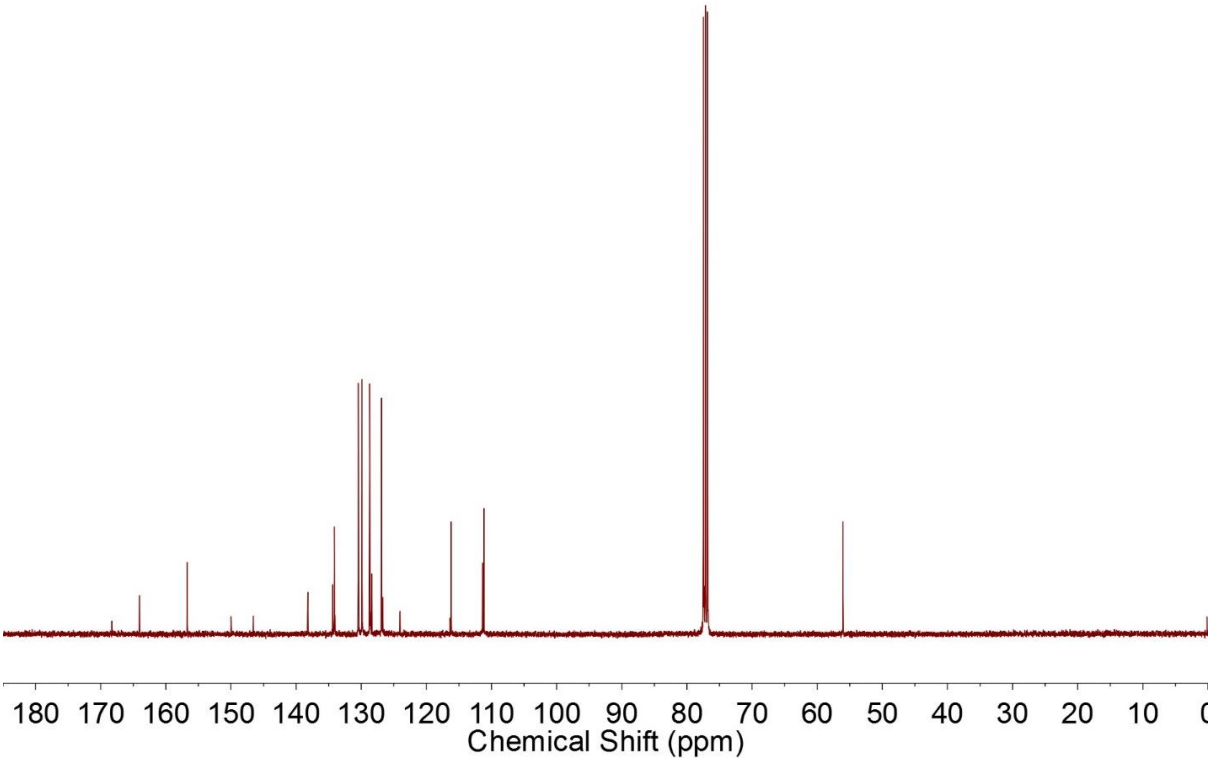


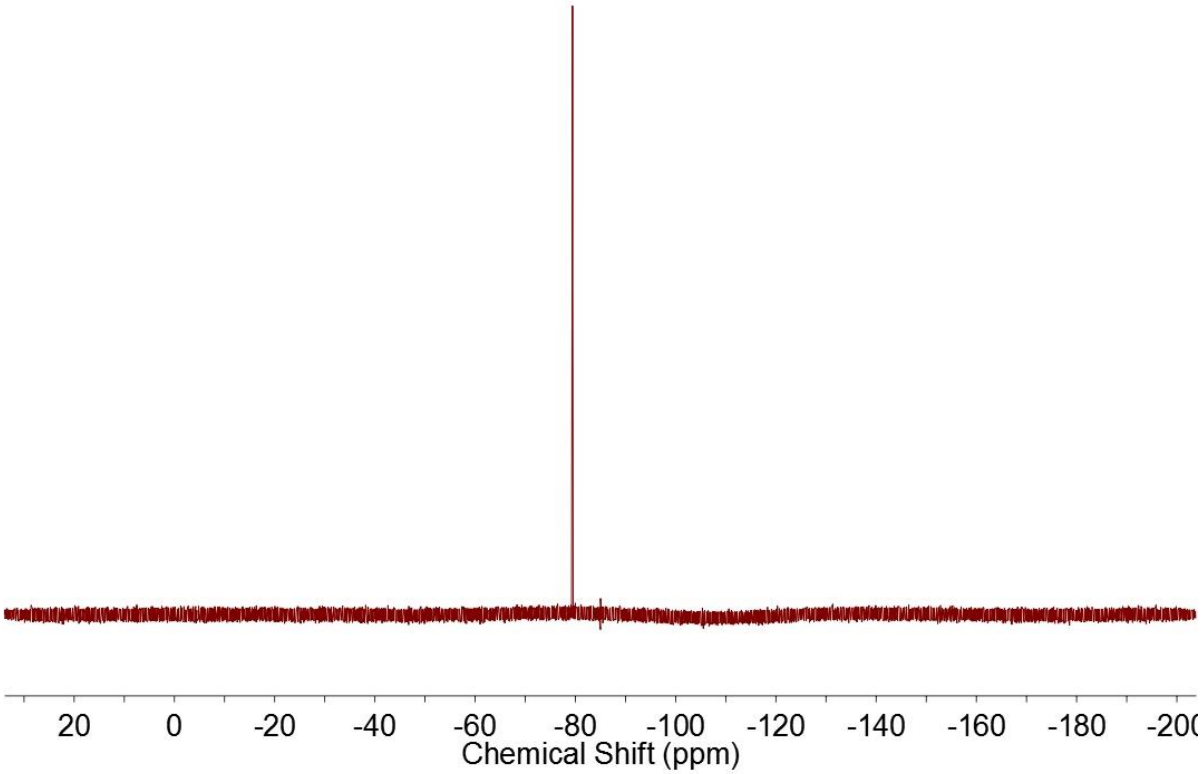




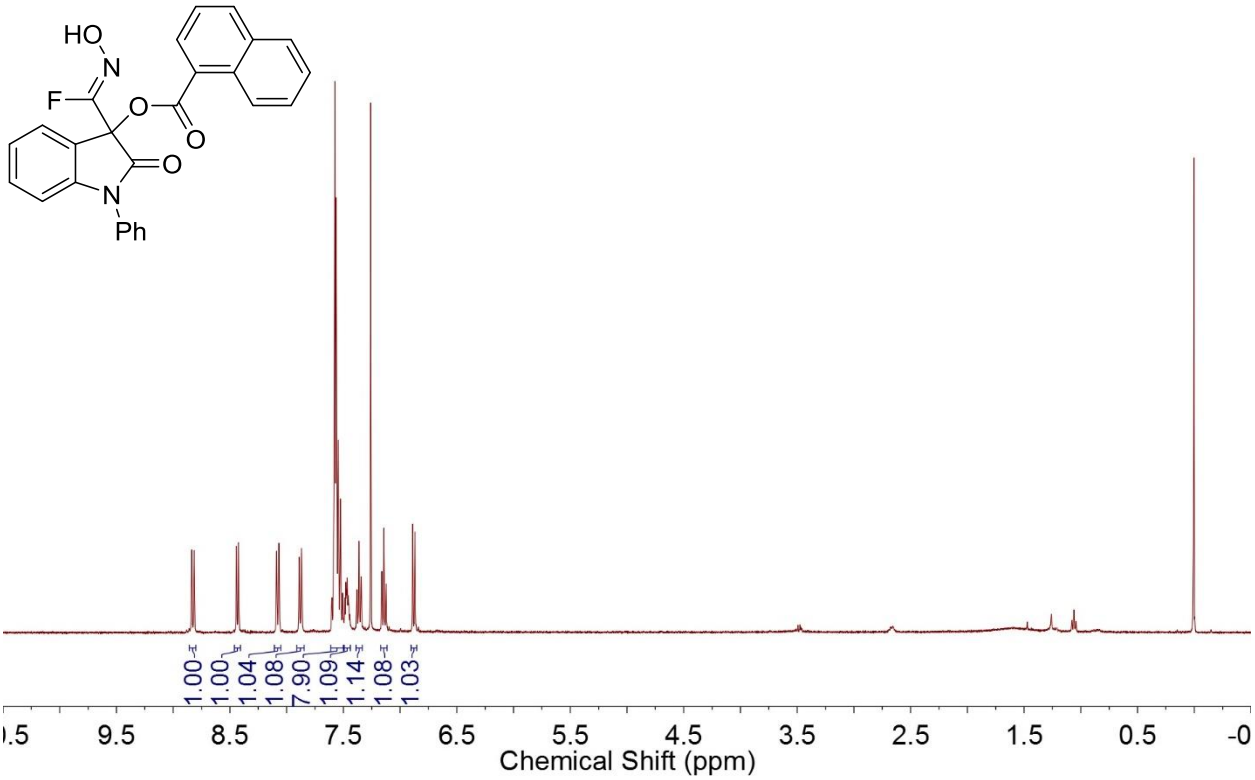
N-Phenyl (*Z*)-3-(fluoro(hydroxyimino)methyl)-5-methoxy-2-oxoindolin-3-yl benzoate (**32**)

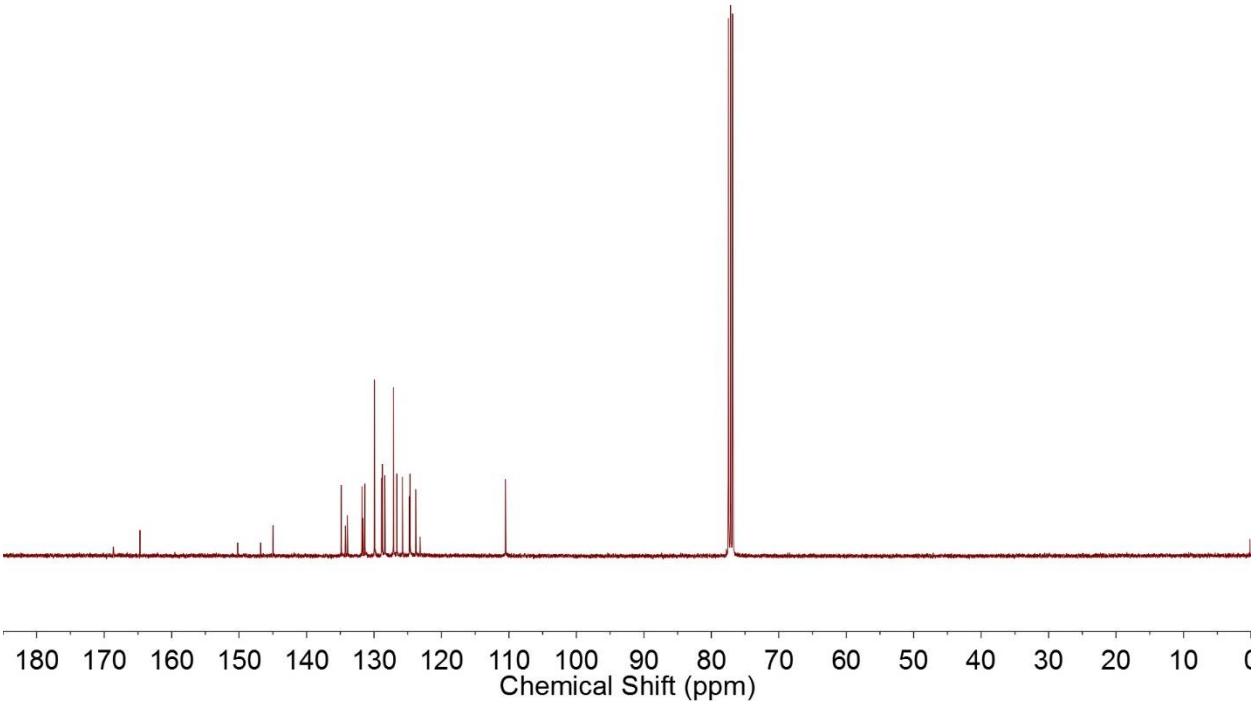


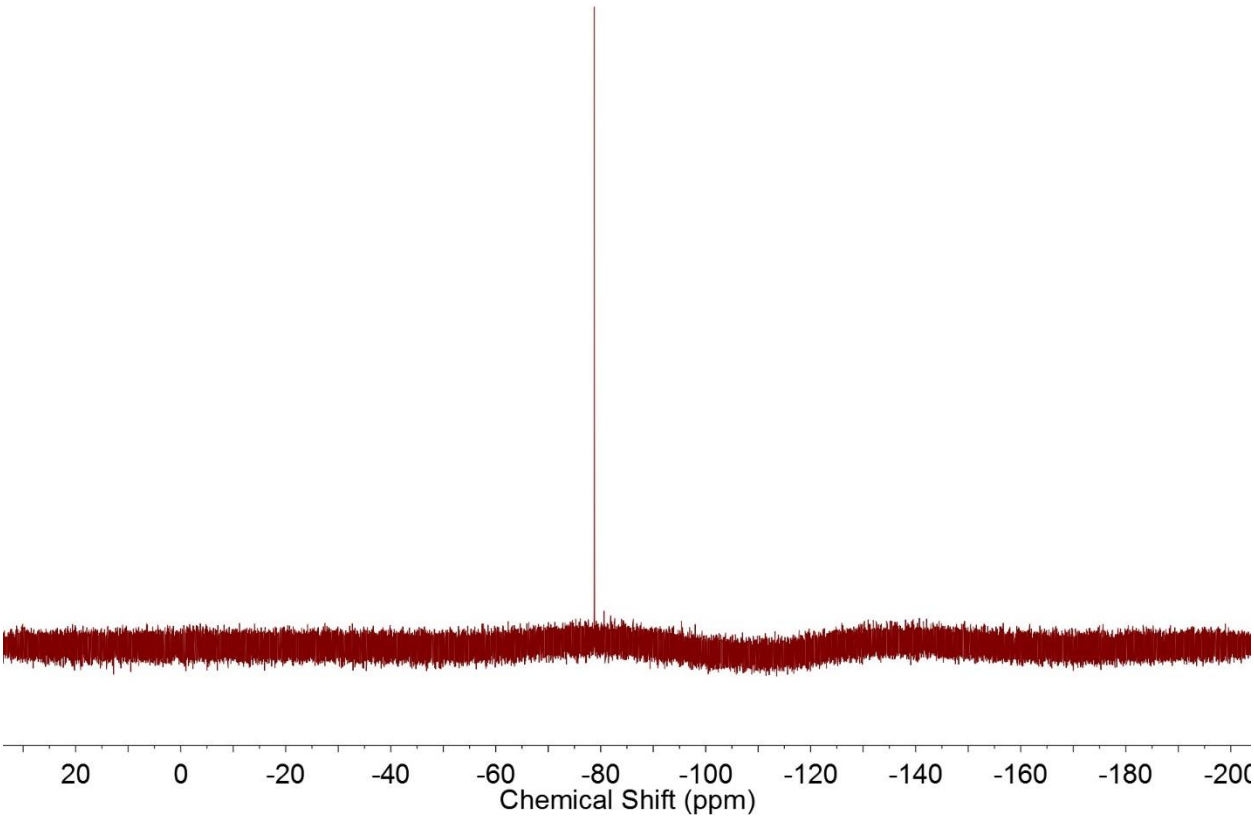

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180
Chemical Shift (ppm)

N-Phenyl (*Z*)-3-(fluoro(hydroxyimino)methyl)-2-oxoindolin-3-yl 1-naphthoate (**33**)



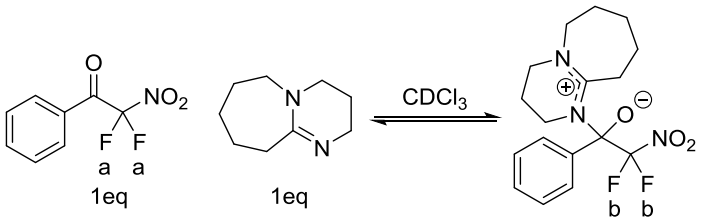


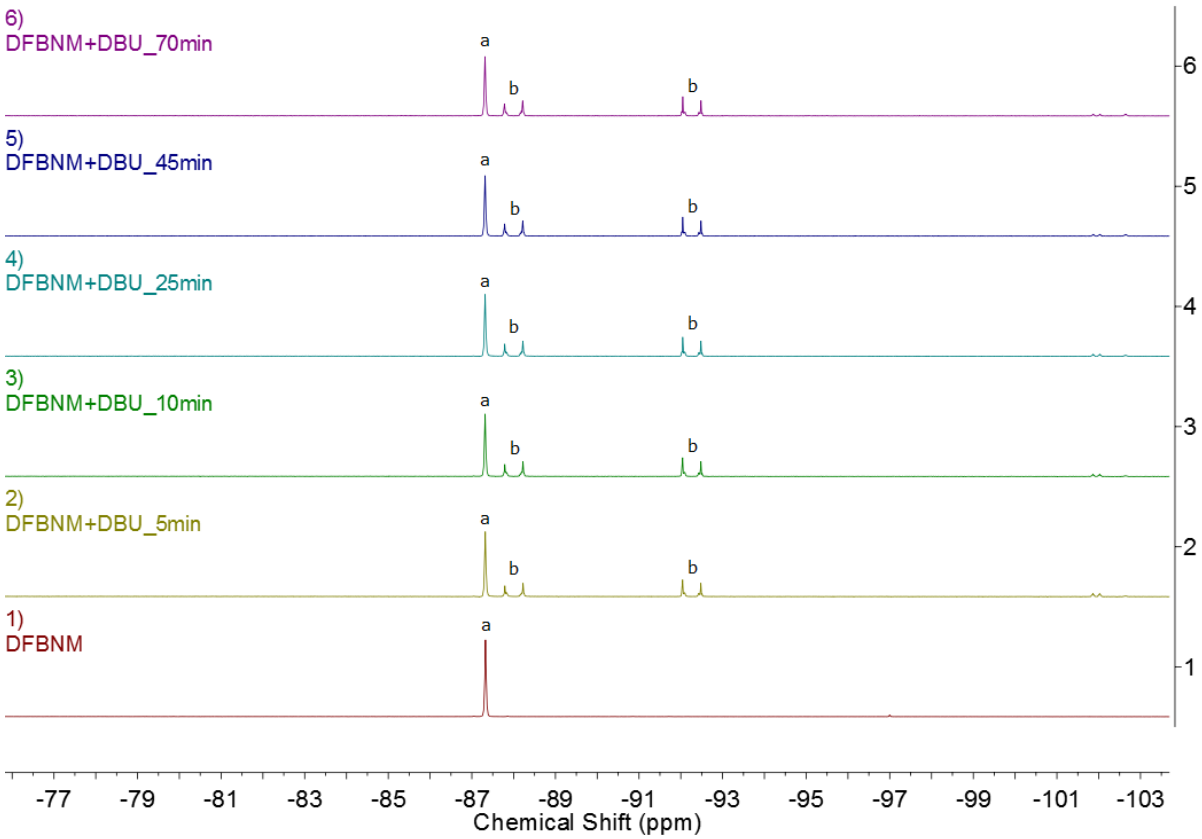

20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
Chemical Shift (ppm)

2. Mechanistic Study

^{19}F NMR analysis of the reaction between difluoronitroacetophenone and DBU

Addition of one equivalent of DBU into a solution of difluoronitroacetophenone, **1**, in $CDCl_3$ led to the formation of a difluoronitroacetophenone-DBU adduct showing diastereotopic fluorine NMR signals at -88.0 and -92.1 ppm within 5 minutes. The difluoronitroacetophenone signal did not fully disappear and the ratio of the two species did not change after 5 minutes which suggests a rapidly established equilibrium.

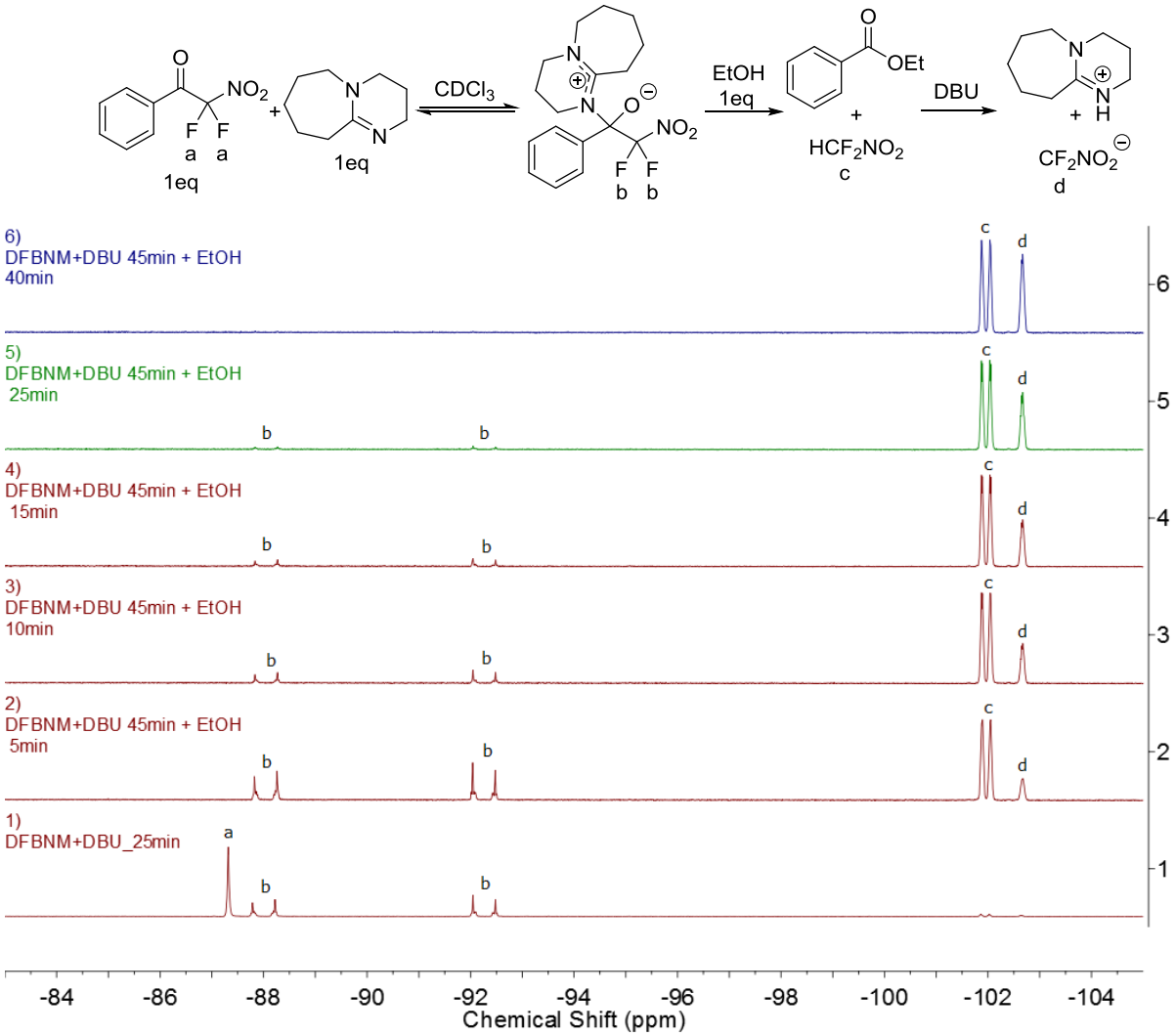




All ^{19}F NMR were obtained in $CDCl_3$. From bottom to top: Stack 1: Difluoronitroacetophenone **1** (DFBNM). Stack 2: **1** + DBU after 5 minutes (DFBNM+DBU 5min). Stack 3: **1** + DBU after 10 minutes (DFBNM+DBU 10min). Stack 4: **1** + DBU after 25 minutes (DFBNM+DBU 25min). Stack 5: **1** + DBU after 45 minutes (DFBNM+DBU 45min). Stack 6: **1** + DBU after 70 minutes (DFBNM+DBU 70min).

NMR analysis of DBU mediated cleavage of difluoronitroacetophenone using ethanol

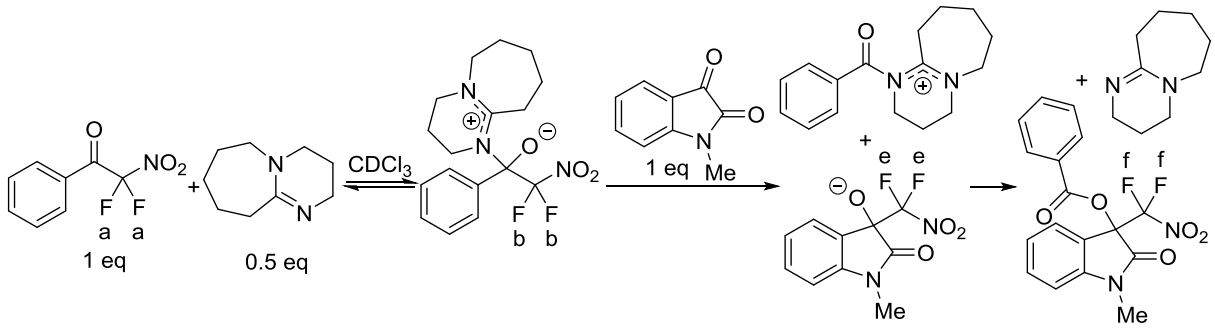
An equimolar amount of difluoronitroacetophenone, **1**, and DBU were first mixed in $CDCl_3$ to establish the **1**-DBU adduct formation. After 45 minutes, one equivalent of ethanol was added into the reaction mixture. Complete consumption of **1** and formation of difluoronitromethane (HCF_2NO_2, doublet at -101.9 ppm) and difluoronitronate ($CF_2NO_2^-$, singlet at -102.7 ppm) were observed after 5 minutes. Ethyl benzoate was detected in the corresponding H NMR. The amount of **1**-DBU adduct decreased over time due to the reaction with ethanol. The $CF_2NO_2^-/HCF_2NO_2$ ratio increased over time which can be explained to deprotonation of HCF_2NO_2 by the regenerated DBU.

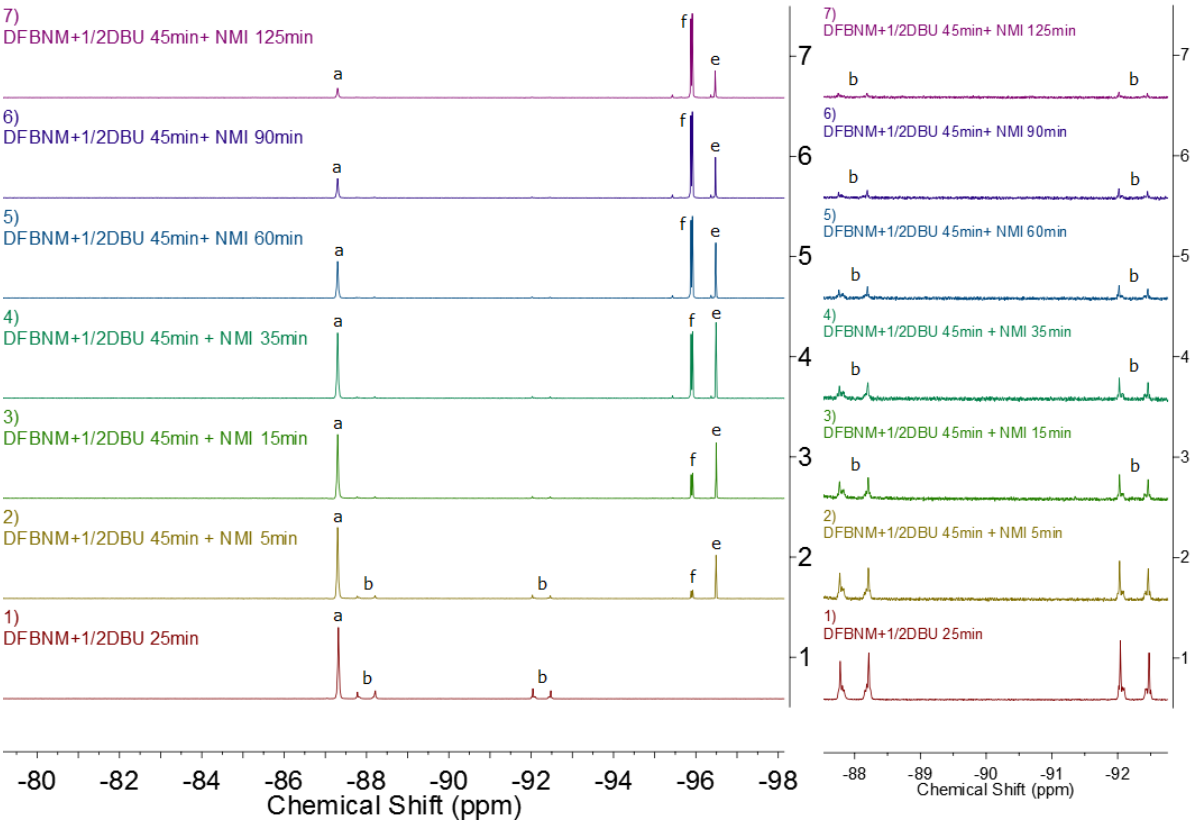


All ^{19}F NMR spectra were obtainerd in $CDCl_3$. From bottom to top: Stack 1: Difluoronitroacetophenone **1** + DBU after 25 minutes (DFBNM+DBU 25min). Stack 2: 5 minutes after methanol addition into the mixture of **1** + DBU which was previously stirred for 45 minutes (DFBNM+DBU 45min + EtOH 5min). Stack 3: 10 minutes after methanol addition (DFBNM+DBU 45min + EtOH 10min). Stack 4: 15 minutes after methanol addition (DFBNM+DBU 45min + EtOH 15min). Stack 5: 25 minutes after methanol addition (DFBNM+DBU 45min + EtOH 25min). Stack 6: 40 minutes after methanol addition (DFBNM+DBU 45min + EtOH 40min).

NMR analysis of the insertion of *N*-methyl isatin into difluoronitroacetophenone in the presence of DBU

One equivalent of difluoronitroacetophenone, **1** and a half equivalent of DBU were first mixed in $CDCl_3$ and the **1**-DBU adduct formation was observed. After 45 minutes, one equivalent of *N*-methyl isatin was added into the reaction mixture. Formation of the alkoxide (-96.5 ppm) and benzoyl ester (two doublets at -96.1 and -95.6 ppm) were observed spontaneously. As the reaction proceeded, the amount of **1** and **1**-DBU adduct decreased while the amount of the alkoxide and benzoyl ester increased. The ratio between the alkoxide and benzoyl ester decreased over time, indicating that the benzoyl transfer is relatively slow.





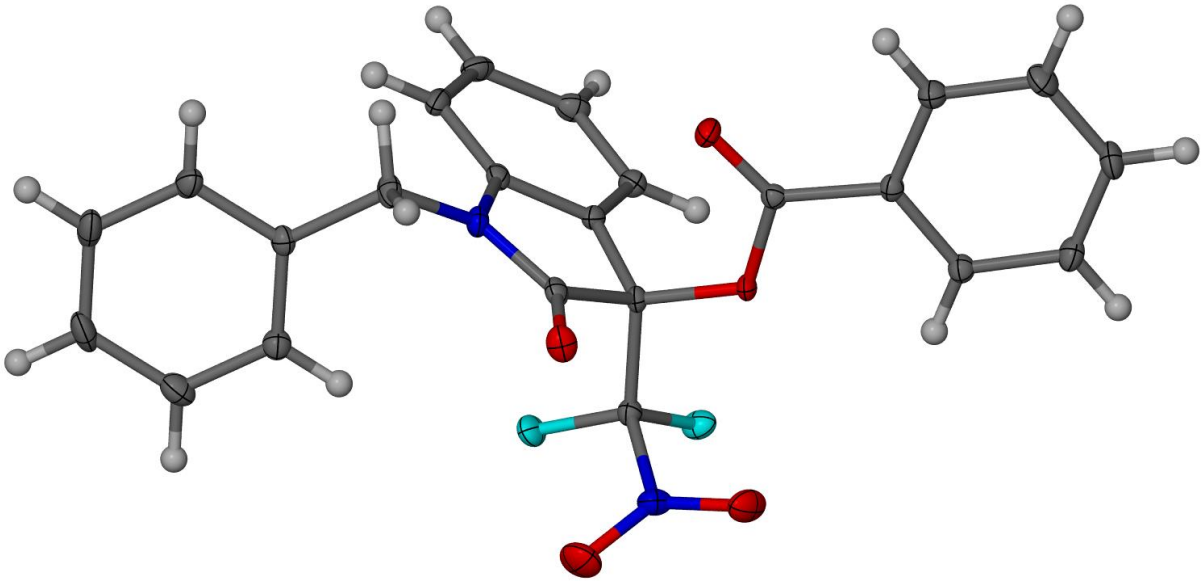
All ^{19}F NMR were obtained in $CDCl_3$. From bottom to top: Stack 1: Difluoronitroacetophenone **1** + DBU after 25 minutes (DFBNM+DBU 25min). Stack 2: 5 minutes after *N*-methyl isatin addition to the mixture of **1** + DBU previously stirred for 45 minutes (DFBNM+DBU 45min +

NMI 5min). Stack 3: 15 minutes after *N*-methyl isatin addition (DFBNM+DBU 45min + NMI 15min). Stack 4: 35 minutes after *N*-methyl isatin addition (DFBNM+DBU 45min + NMI 35min). Stack 5: 60 minutes after *N*-methyl isatin addition (DFBNM+DBU 45min + NMI 60min). Stack 6: 90 minutes after *N*-methyl isatin addition (DFBNM+DBU 45min + NMI 90min). Stack 7: 125 minutes after *N*-methyl isatin addition (DFBNM+DBU 45min + NMI 125min).

3. Crystallographic Analysis

N-Benzyl 3-(difluoronitromethyl)-2-oxoindolin-3-yl benzoate (3)

A single crystal was obtained by slow evaporation of a solution of the product in CH_2Cl_2. Single crystal X-ray analysis was performed at 296 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and corrected using the Apex 2 program. The structures were solved by direct methods and refined with full-matrix least-square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameter. Crystal data: $C_{23}H_{16}F_2N_2O_5$, M = 438.38, colorless needle, 1.0 x 0.4 x 0.4 mm^3, orthorhombic, space group *Pbca*, a = 19.5111(9), b = 10.0621(5), c = 20.2837(10) Å, V = 3982.2(3) $Å^3$, Z = 8. The X-ray structures are shown at the 50% ellipsoid contour percent probability level.



***N*-Benzyl (*Z*)-3-(fluoro(hydroxyimino)methyl)-2-oxoindolin-3-yl benzoate (30)**

A single crystal was obtained by slow evaporation of a solution of the product in $CHCl_3$. Single crystal X-ray analysis was performed at 296 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and corrected using the Apex 2 program. The structures were solved by direct methods and refined with full-matrix least-square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameter. Crystal data: $C_{23}H_{17}FN_2O_4$, *M* = 404.39, colorless needle, 1.0 x 0.4 x 0.3 mm^3, monoclinic, space group *C2/c*, *a* = 17.187(2), b = 15.4893(19), c = 15.3026(18) Å, *V* = 3831.9(8) $Å^3$, *Z* = 8. The X-ray structures are shown at the 50% ellipsoid contour percent probability level.