

Supporting Information

Organocatalytic Asymmetric Hetero-Diels–Alder Reaction of in-situ Generated Dienes: Access to α,β -Unsaturated δ -Lactones Featuring CF₃-Substituted Quaternary Stereocenter

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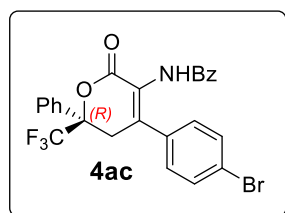
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1. X-ray crystal structure and crystallographic data of 4ac (CCDC 1951698):



Sample preparation: 50.0 mg of compound **4ac** was taken in a vial and dissolved in 5 mL of ethyl acetate then 0.2 mL n-hexane was added to it (dropwise). The solvents were allowed to evaporate slowly at room temperature, which yielded block-shaped transparent crystals of compound **4ac** in two weeks.

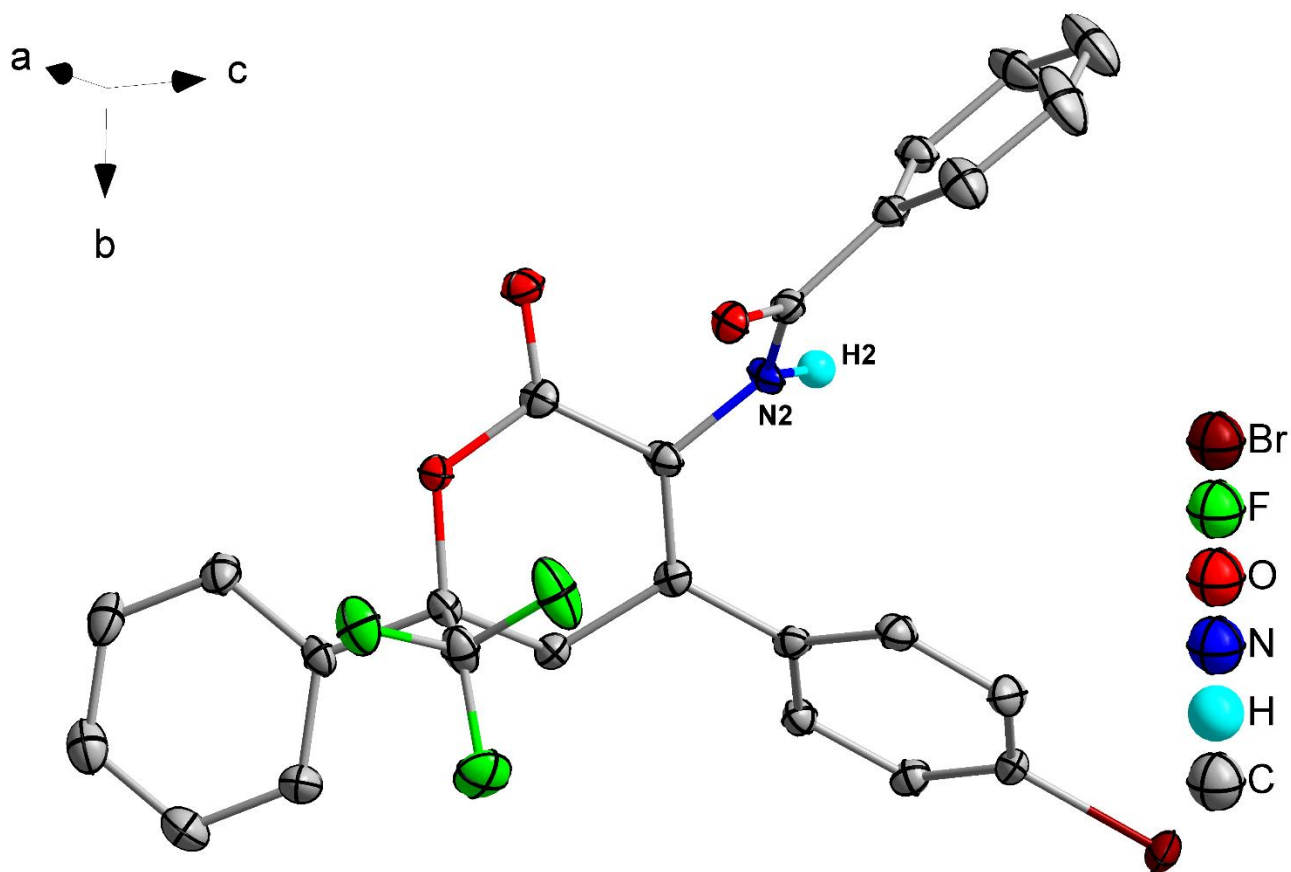


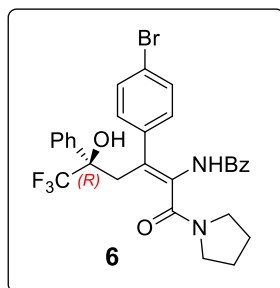
Figure S1: Molecular structure of **4ac** with ellipsoids set at 50% probability. All hydrogen atoms except N-H are omitted for clarity.

Crystal structure determination for compound 4ac: The crystal structure was solved by SHELXT^{1a} structure solution program and refined by full matrix least-squares method based on F^2 by SHELXL^{1b} program in the Olex 2^{1c} software. All the crystallographic figures were generated using the Diamond 3.2k software.^{1d}

Table S1: Crystal data for 4ac

Identification code	4ac
Empirical formula	C ₂₅ H ₁₇ BrF ₃ NO ₃
Formula weight	516.30
Temperature/K	273.15
Crystal system	monoclinic
Space group	P2 ₁
a/Å	9.8347(5)
b/Å	22.0058(12)
c/Å	10.1652(6)
$\alpha/^\circ$	90
$\beta/^\circ$	94.998(2)
$\gamma/^\circ$	90
Volume/Å ³	2191.6(2)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.565
μ/mm^{-1}	1.929
F(000)	1040.0
Crystal size/mm ³	0.052 × 0.023 × 0.015
Radiation	MoK α (λ = 0.71073)
2 θ range for data collection/ $^\circ$	5.468 to 56.556
Index ranges	-13 ≤ h ≤ 13, -29 ≤ k ≤ 29, -13 ≤ l ≤ 13
Reflections collected	33659
Independent reflections	10757 [R_{int} = 0.0466, R_{sigma} = 0.0610]
Data/restraints/parameters	10757/1/595
Goodness-of-fit on F^2	1.013
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0293, wR_2 = 0.0685
Final R indexes [all data]	R_1 = 0.0329, wR_2 = 0.0701
Largest diff. peak/hole / e Å ⁻³	0.86/-0.58
Flack parameter	0.034(3)

2. X-ray crystal structure and crystallographic data of **6** (CCDC 1951699):



Sample preparation: 30.0 mg of compound **6** was taken in a vial and dissolved in 5 mL of ethyl acetate then 0.2 mL n-hexane was added to it in a dropwise manner. The solvents were allowed to evaporate slowly at room temperature, which yielded block-shaped transparent crystals of compound **6** in one week.

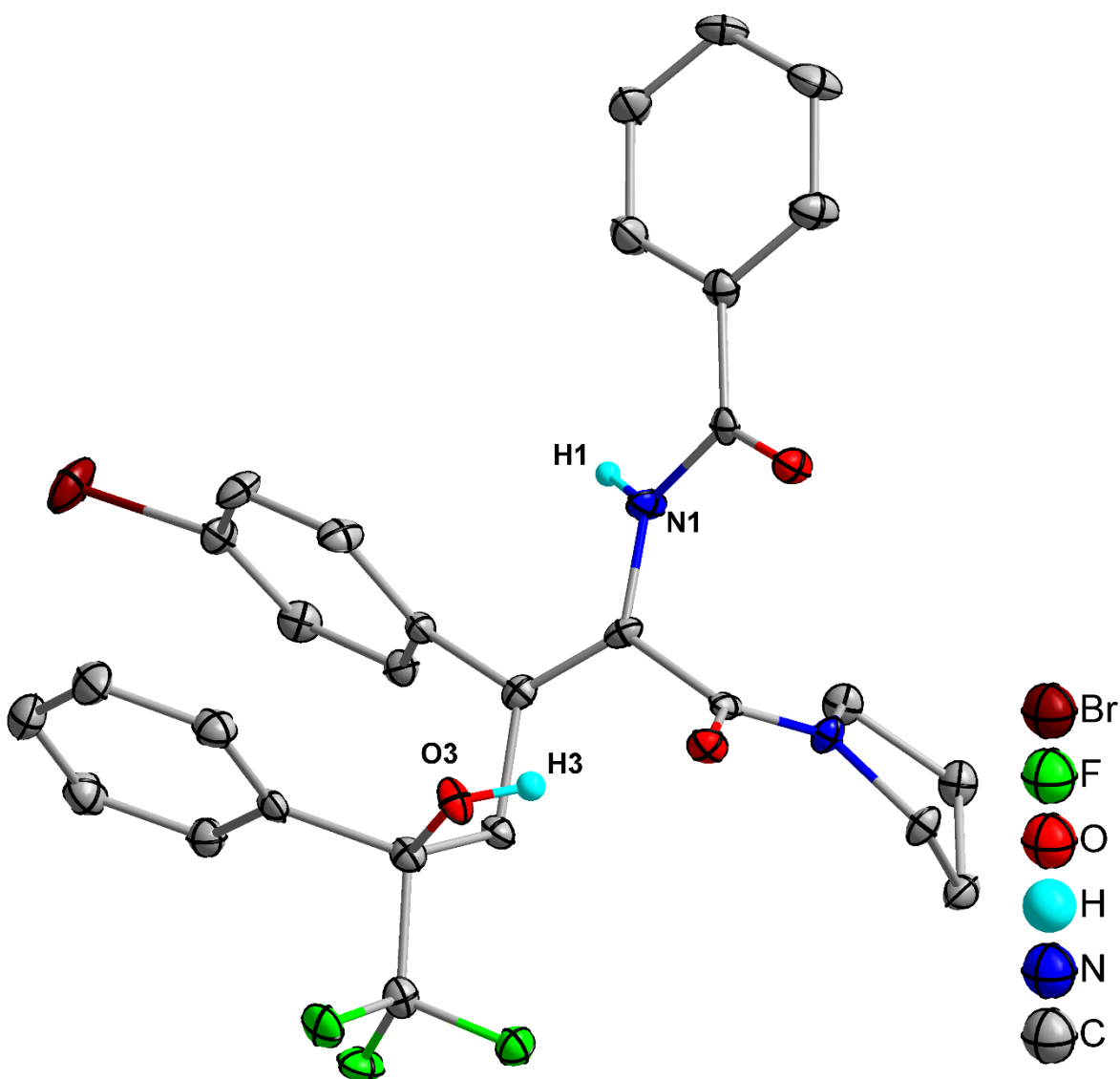


Figure S2: Molecular structure of **6** with ellipsoids set at 50% probability. All hydrogen atoms except N-H and O-H are omitted for clarity.

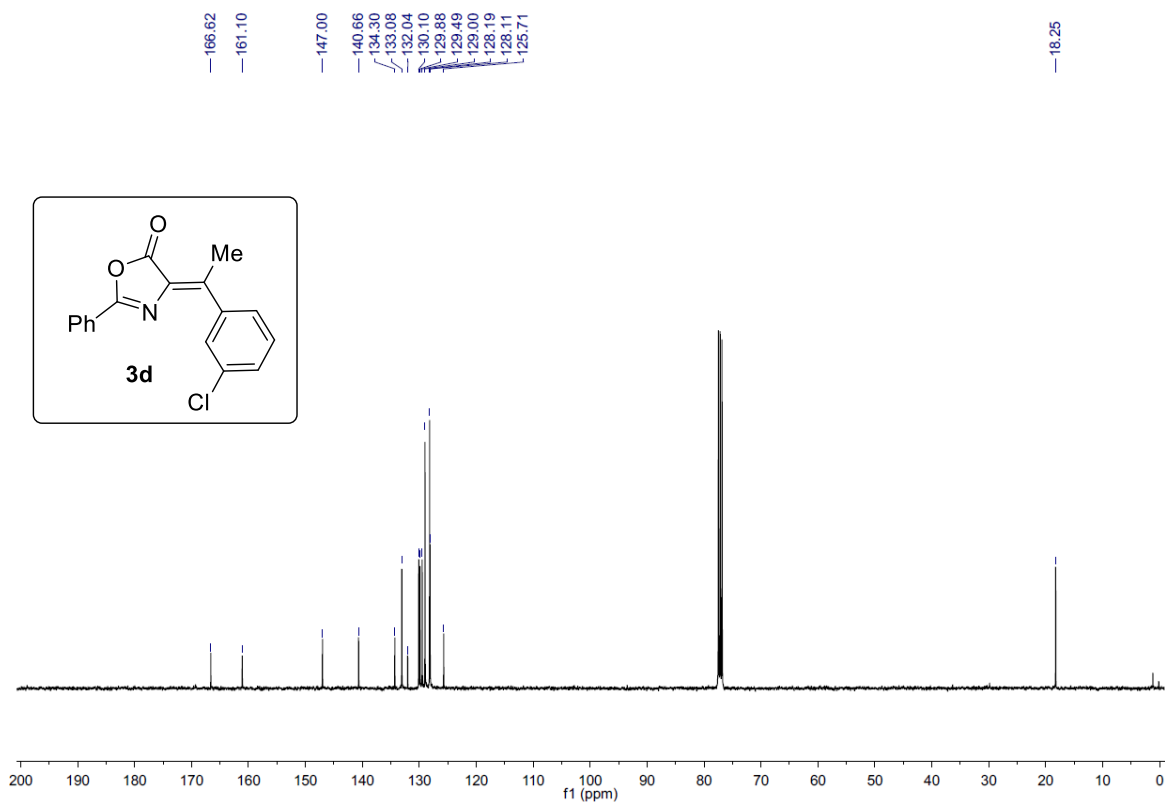
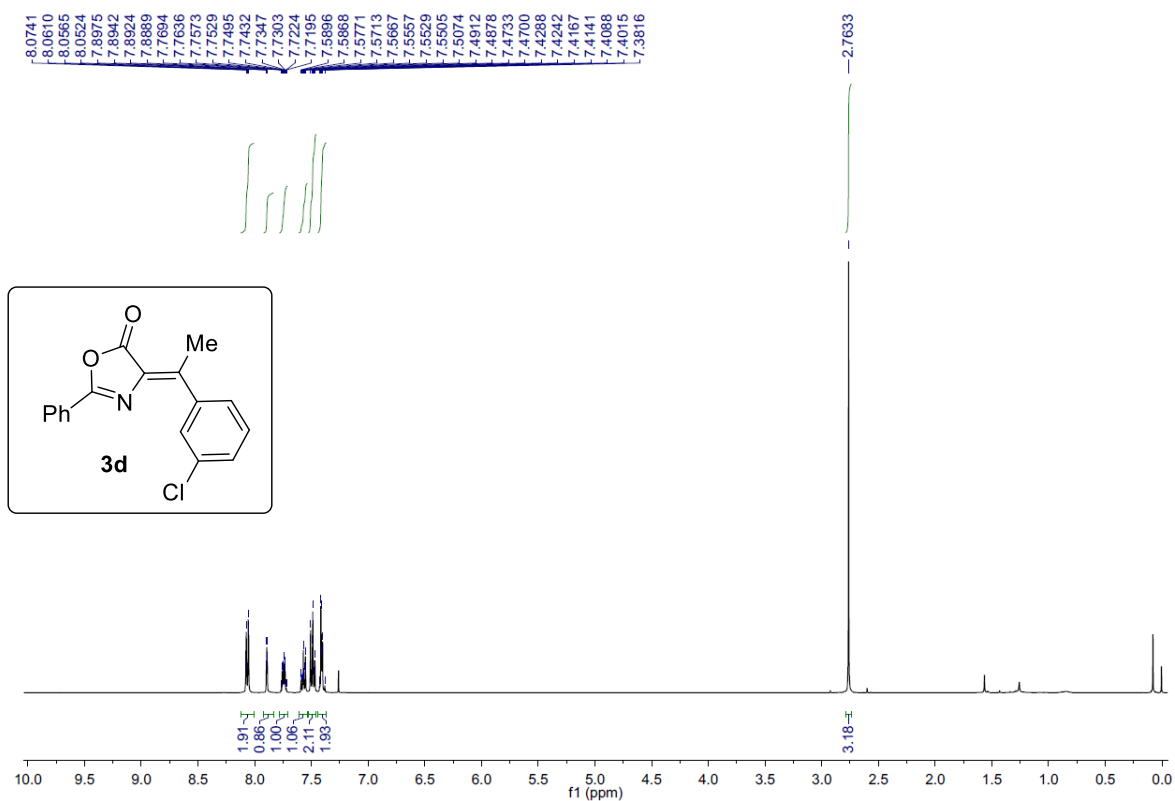
Crystal structure determination for compound 6: The crystal structure was solved by SHELXT^{1a} structure solution program and refined by full matrix least-squares method based on F^2 by SHELXL^{1b} program in the Olex 2^{1c} software. All the crystallographic figures were generated using the Diamond 3.2k^{1d} software.

Table S2: Crystal data for compound 6

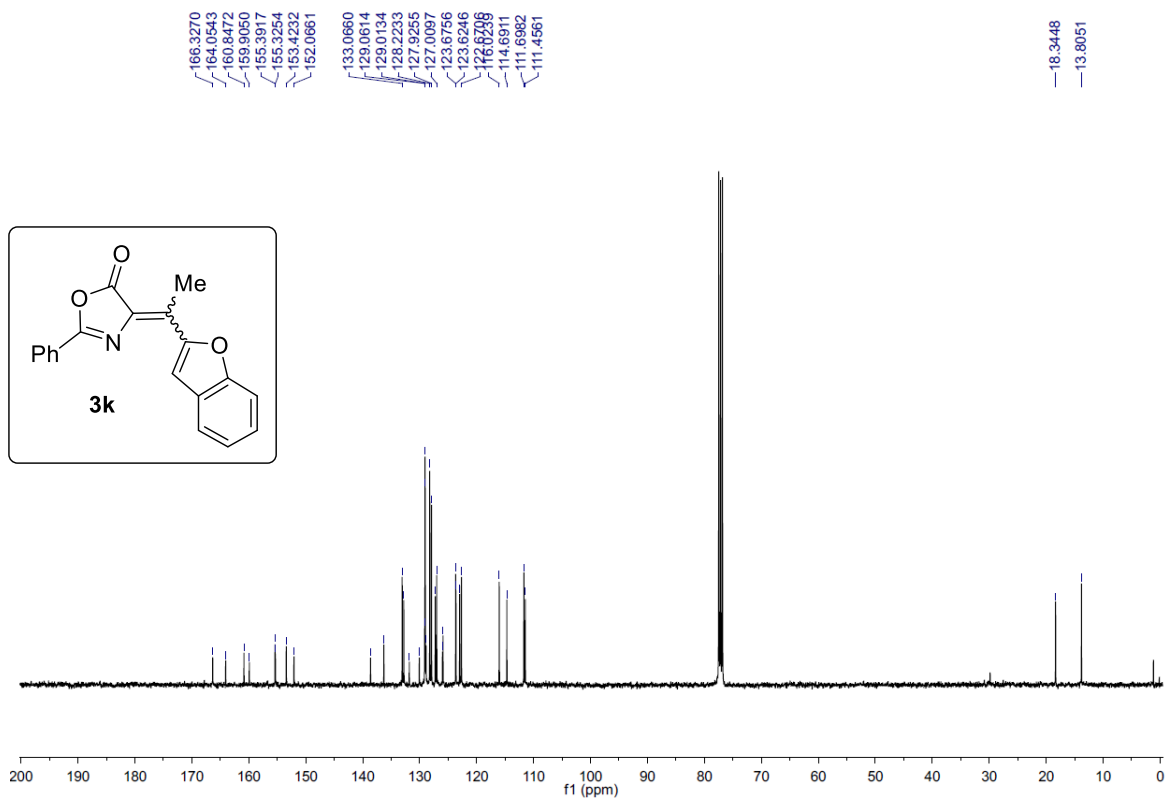
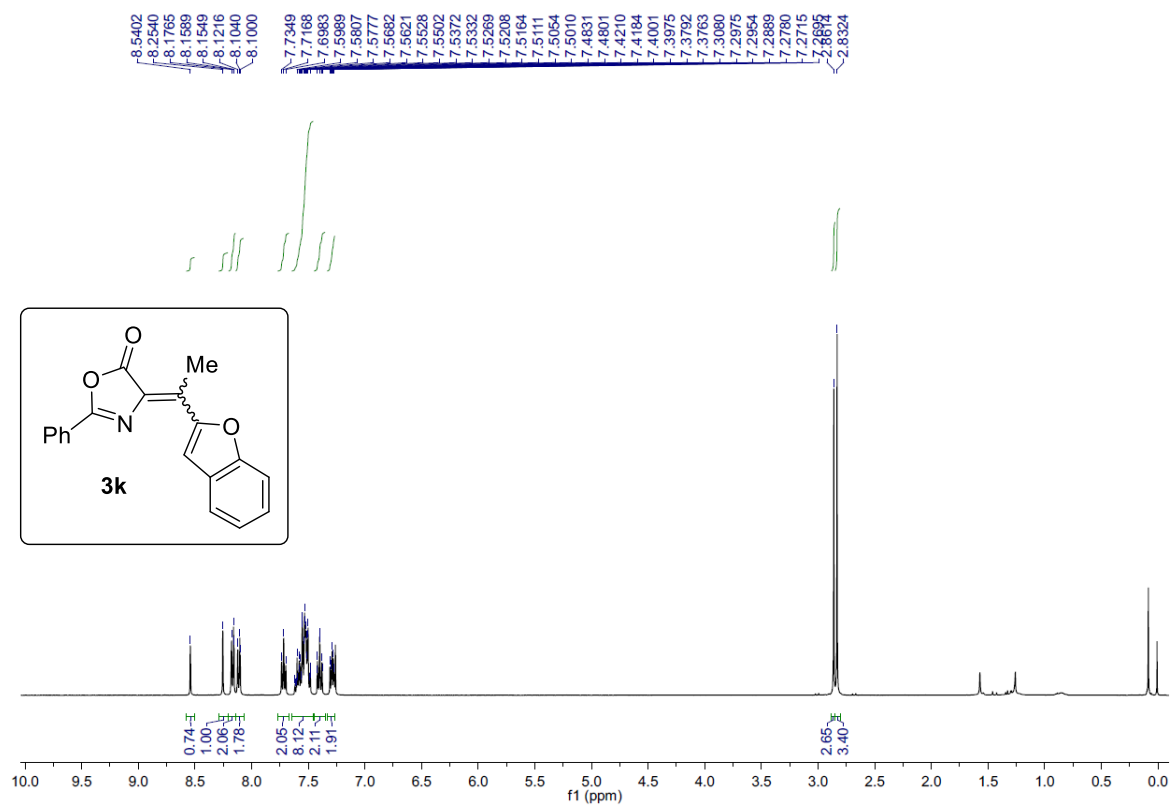
Identification code	6
Empirical formula	C ₂₉ H ₂₆ BrF ₃ N ₂ O ₃
Formula weight	587.42
Temperature/K	273.15
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	10.6343(5)
b/Å	11.7382(5)
c/Å	20.6645(10)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	2579.5(2)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.513
μ/mm^{-1}	1.650
F(000)	1200.0
Crystal size/mm ³	0.029 × 0.026 × 0.023
Radiation	MoK α (λ = 0.71073)
2 θ range for data collection/ $^\circ$	5.532 to 51.988
Index ranges	-13 ≤ h ≤ 13, -14 ≤ k ≤ 14, -25 ≤ l ≤ 25
Reflections collected	34484
Independent reflections	5062 [R _{int} = 0.0841, R _{sigma} = 0.0541]
Data/restraints/parameters	5062/0/344
Goodness-of-fit on F ²	1.064
Final R indexes [I ≥ 2 σ (I)]	R ₁ = 0.0292, wR ₂ = 0.0636
Final R indexes [all data]	R ₁ = 0.0375, wR ₂ = 0.0688
Largest diff. peak/hole / e Å ⁻³	0.26/-0.30
Flack parameter	0.022(5)

- 3. References:** 1 (a) Sheldrick, G. M. SHELXT - Integrated Space-Group and Crystal-Structure Determination. *Acta Cryst.* **2015**, A71, 3. (b) Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Cryst.* **2015**, C71, 3. (c) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr.* **2009**, 42, 339. (d) Brandenburg, K.; DIAMOND. Version 3.2k, Crystal Impact GbR, Bonn, Germany, **2014**.

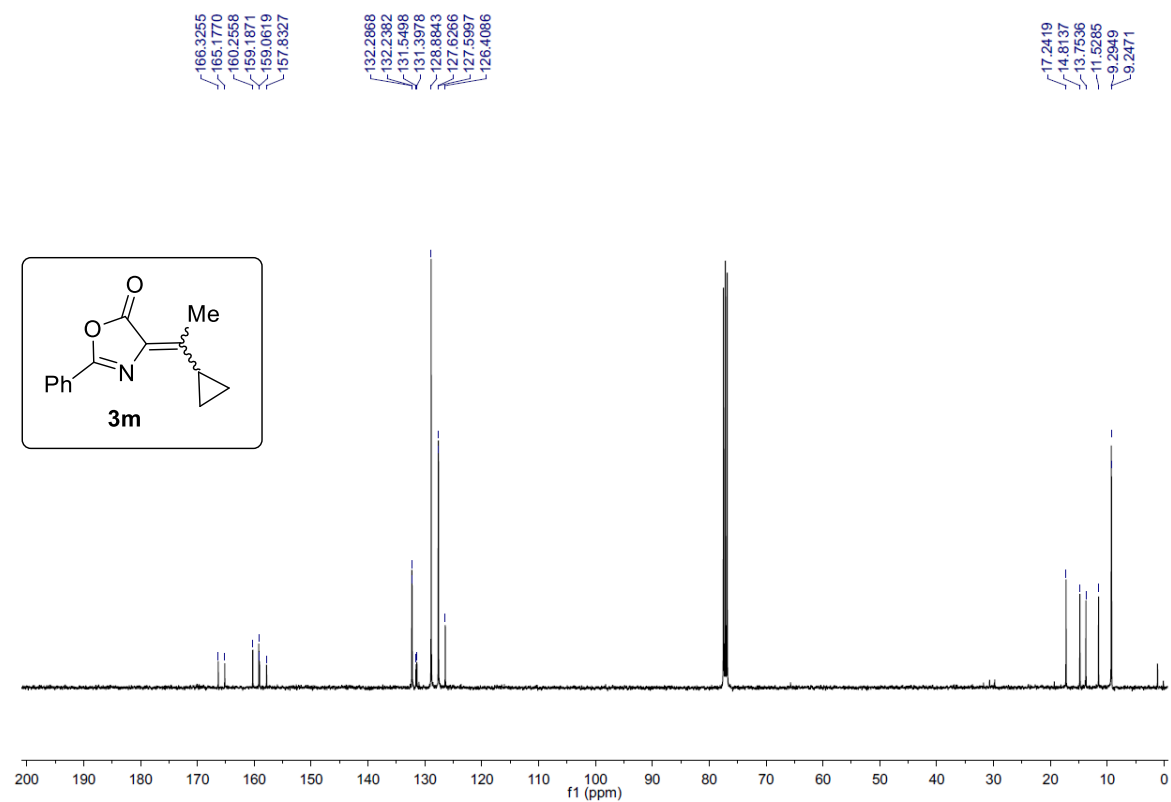
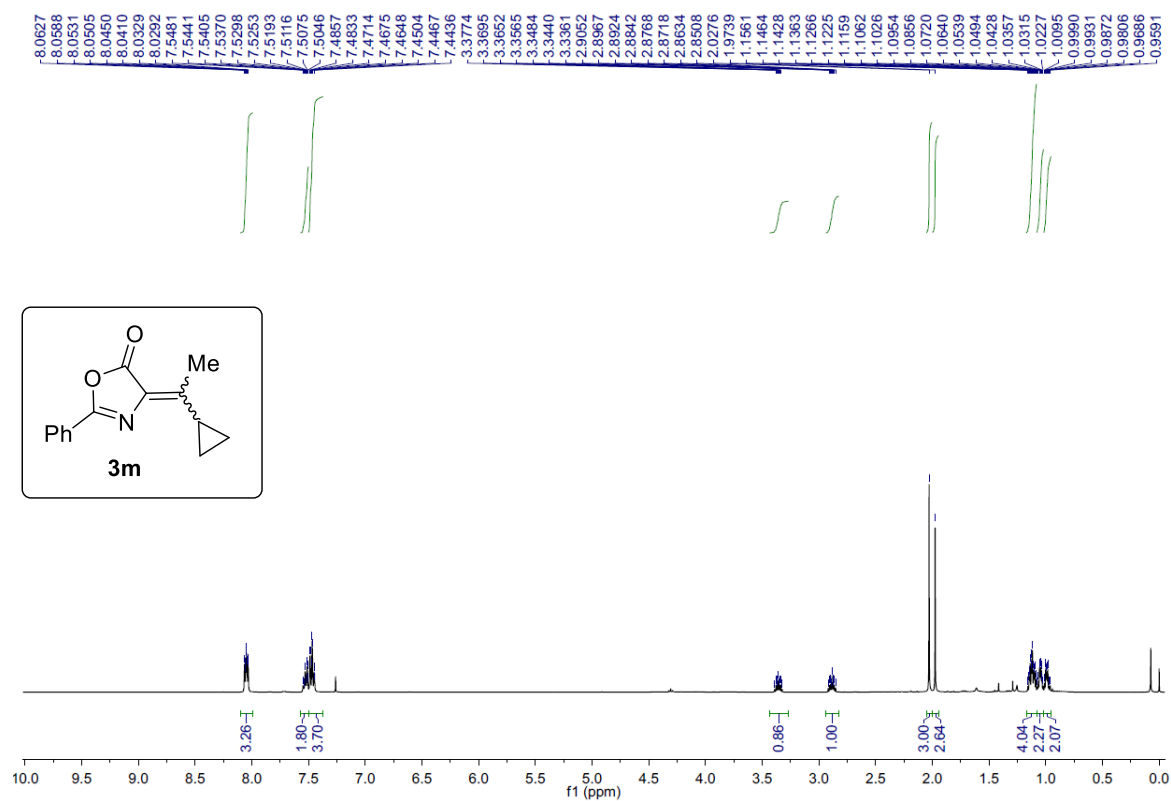
4. NMR spectra:



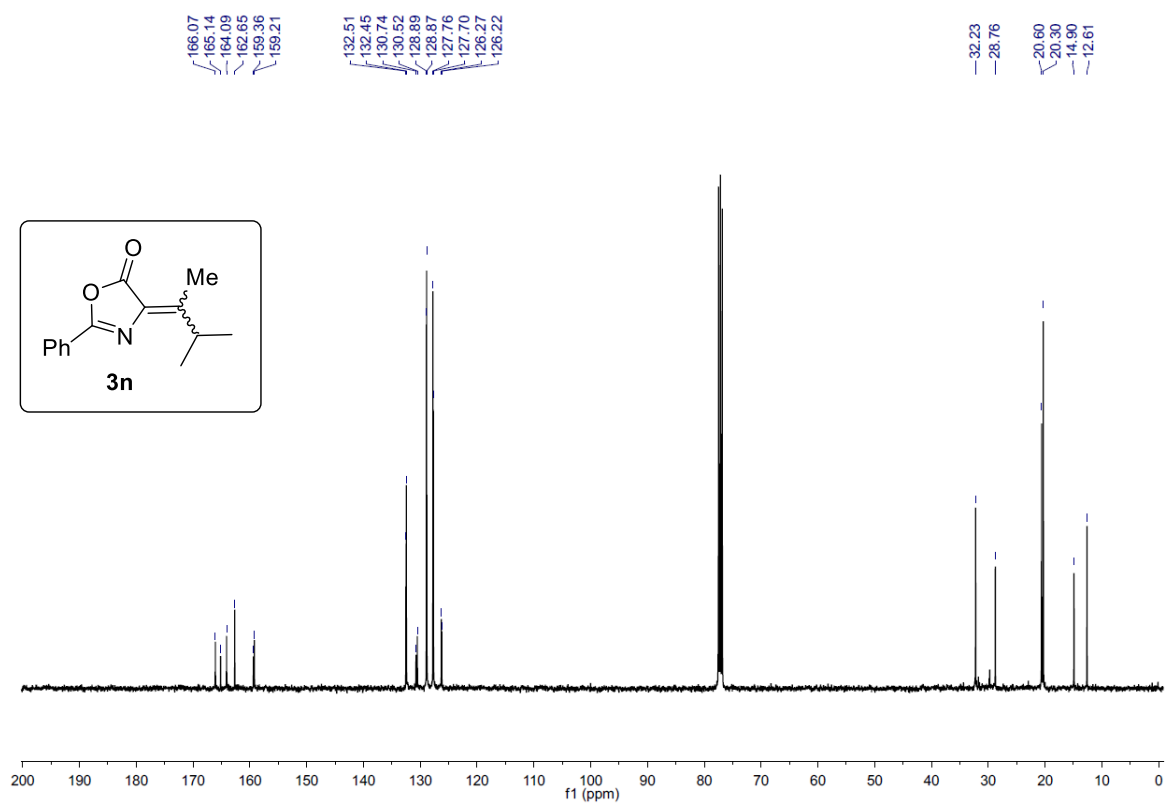
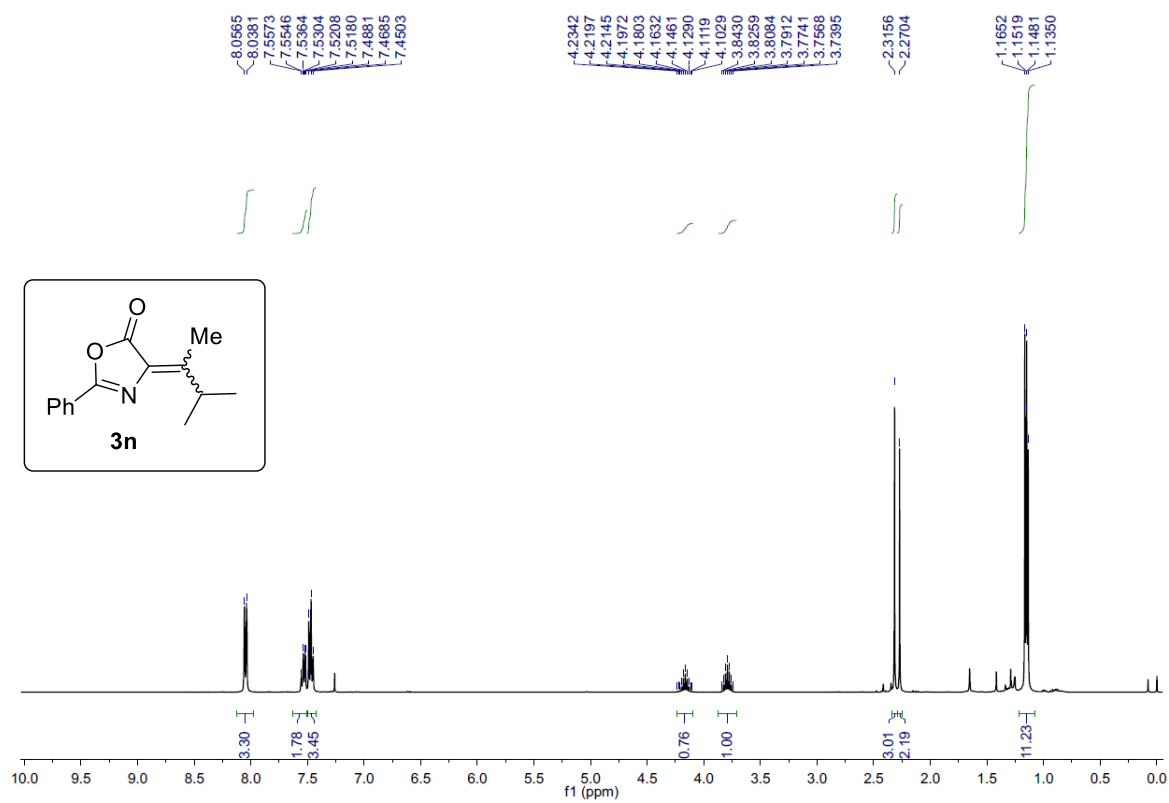
400 MHz ¹H NMR and 100 MHz ¹³C NMR spectra of compound **3d** in CDCl₃



400 MHz ¹H NMR and 100 MHz ¹³C NMR spectra of compound **3k**, *E/Z* (1:1.3), in CDCl₃



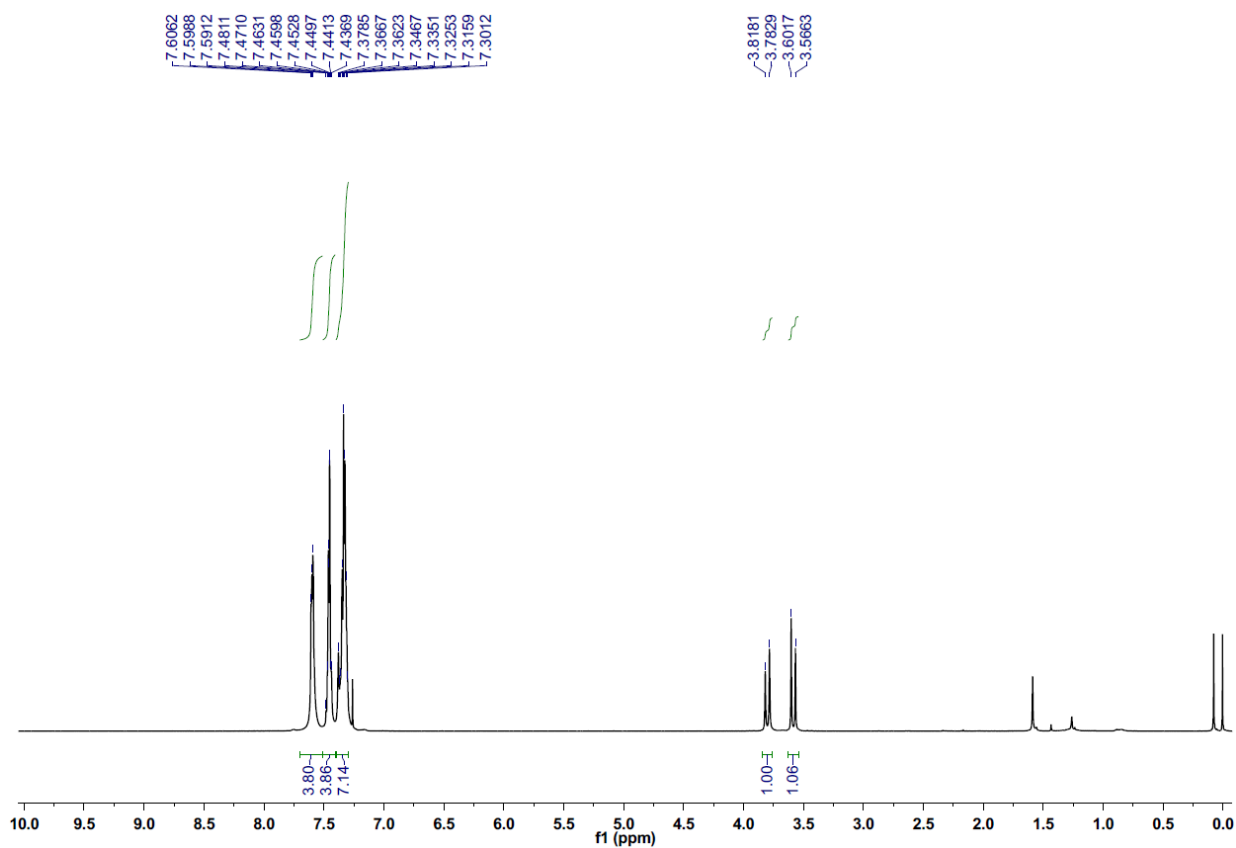
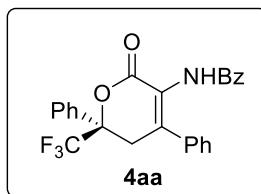
400 MHz ¹H NMR and 100 MHz ¹³C NMR spectra of compound **3m**, *E/Z* (1:1.1), in CDCl₃



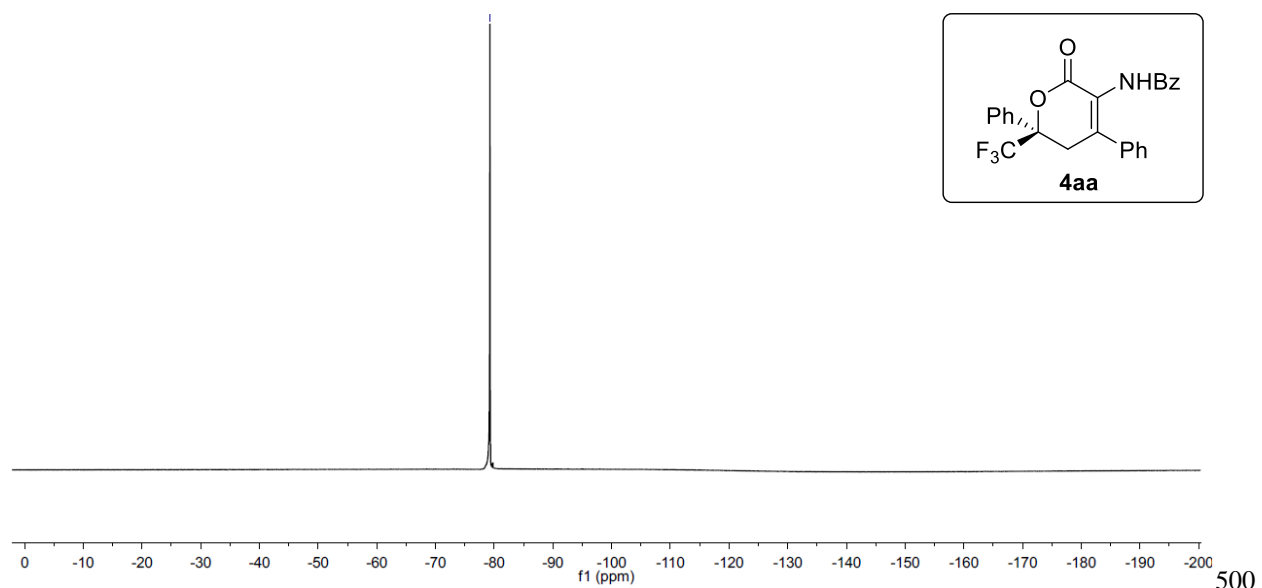
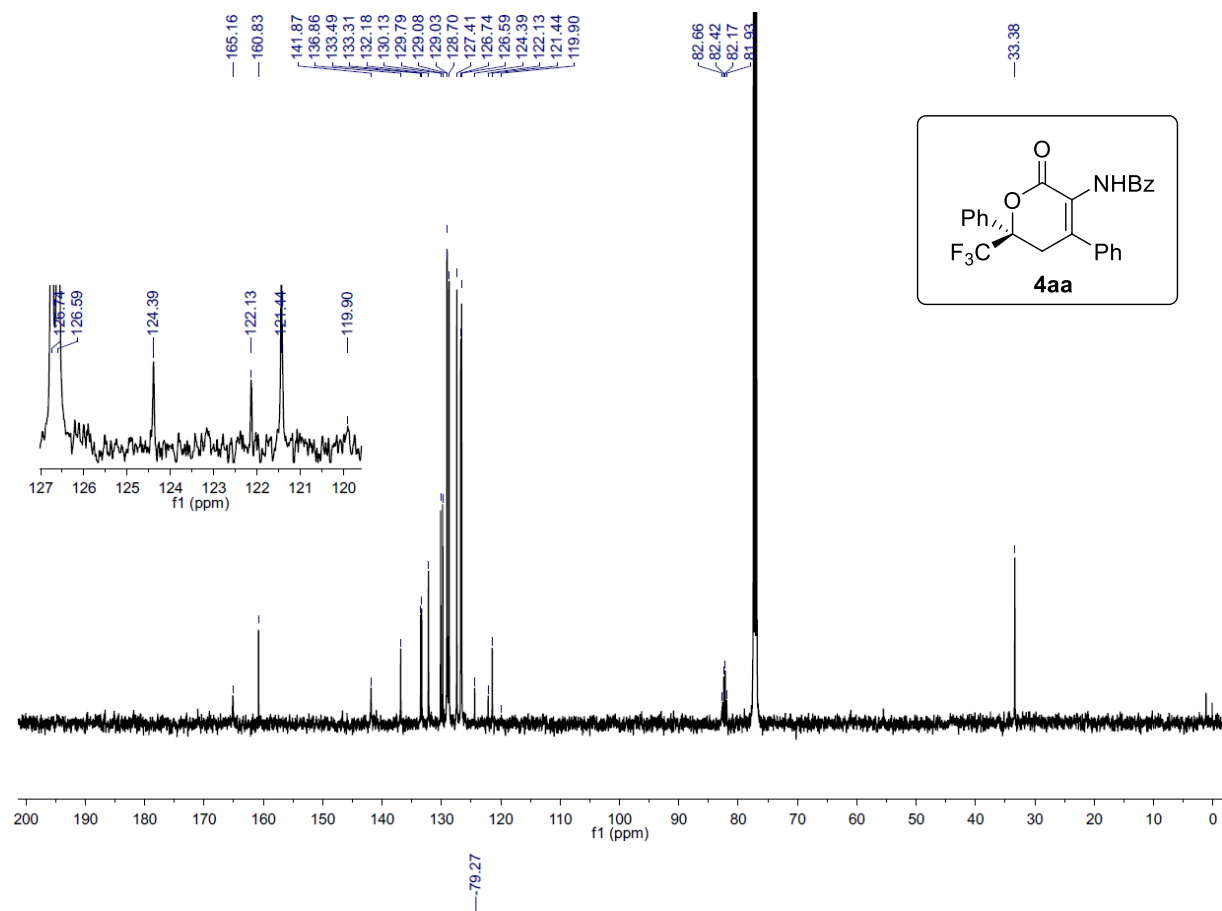
400 MHz ¹H NMR and 100 MHz ¹³C NMR spectra of compound **3n**, *E/Z* (1:1.3), in CDCl₃

NMR spectra of HDA adducts (4), transformation products (5) and (6)

(i) (*R*)-*N*-(2-oxo-4,6-diphenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4aa)

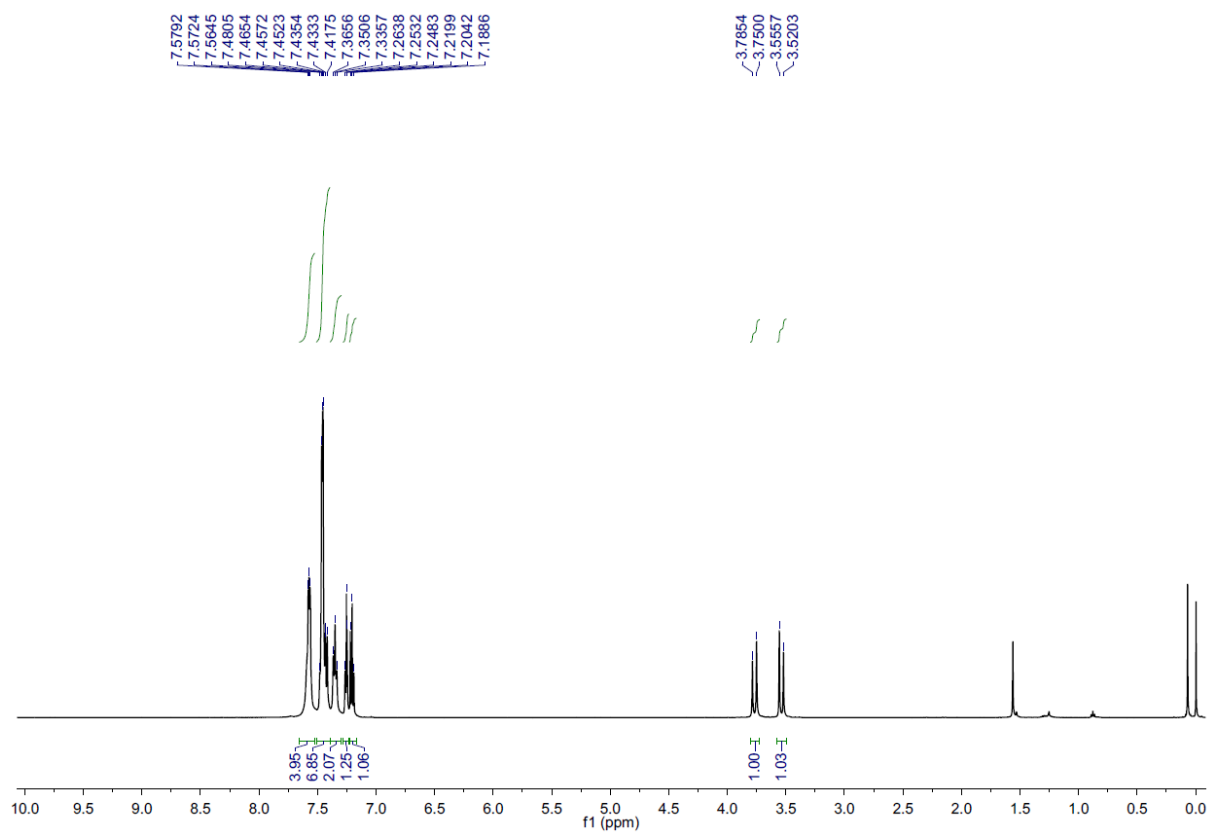
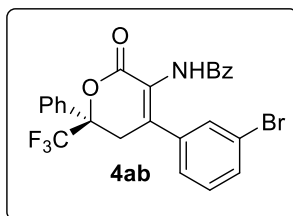


500 MHz ^1H NMR spectrum of compound **4aa** in CDCl_3

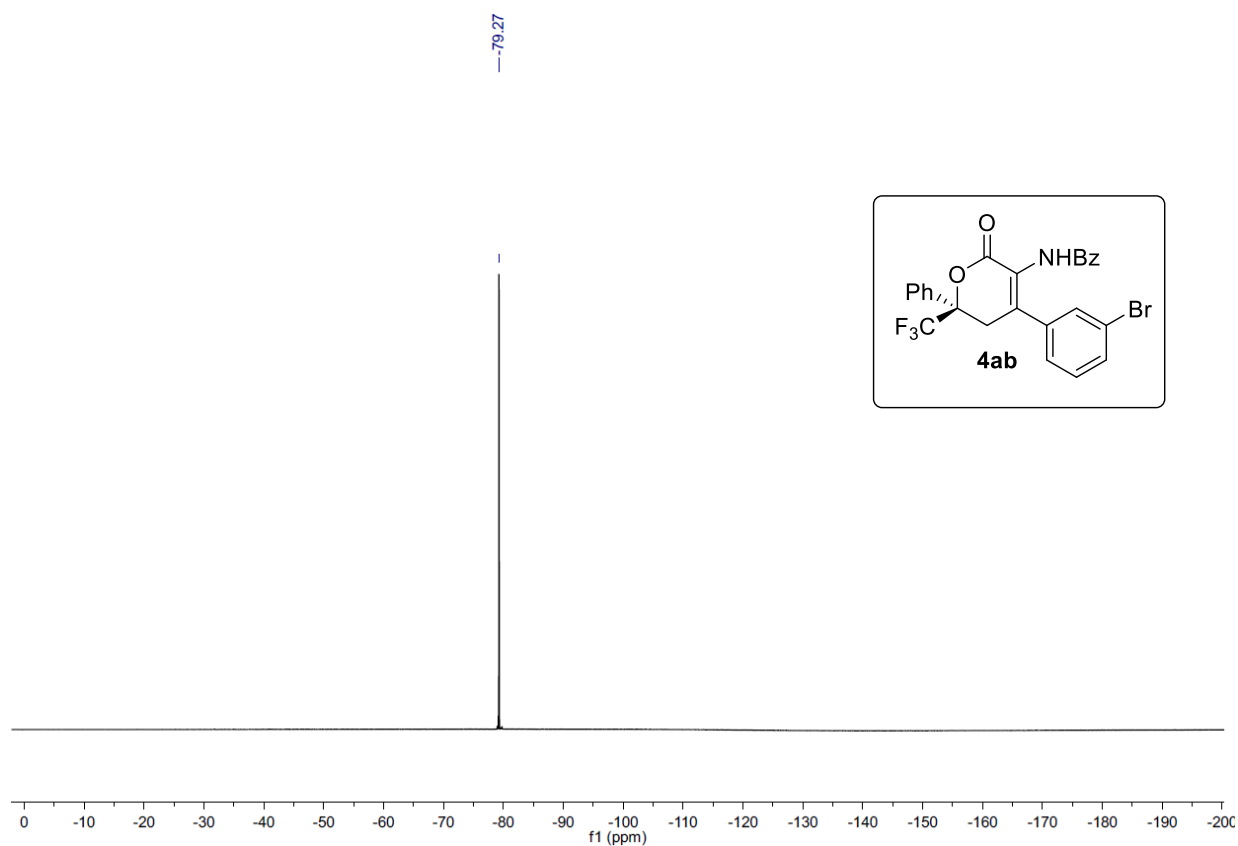
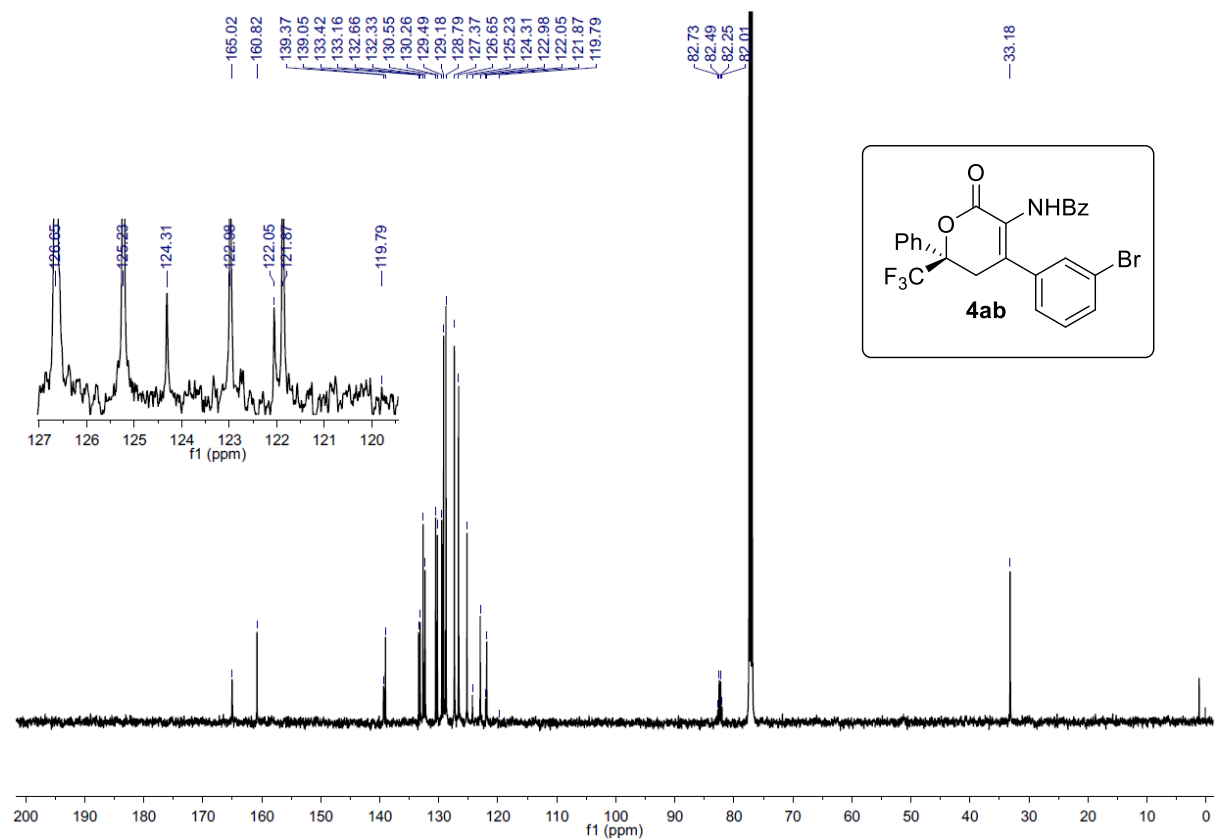


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4aa** in CDCl_3

- (ii) **(*R*)-*N*-(4-(3-bromophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4ab**)**

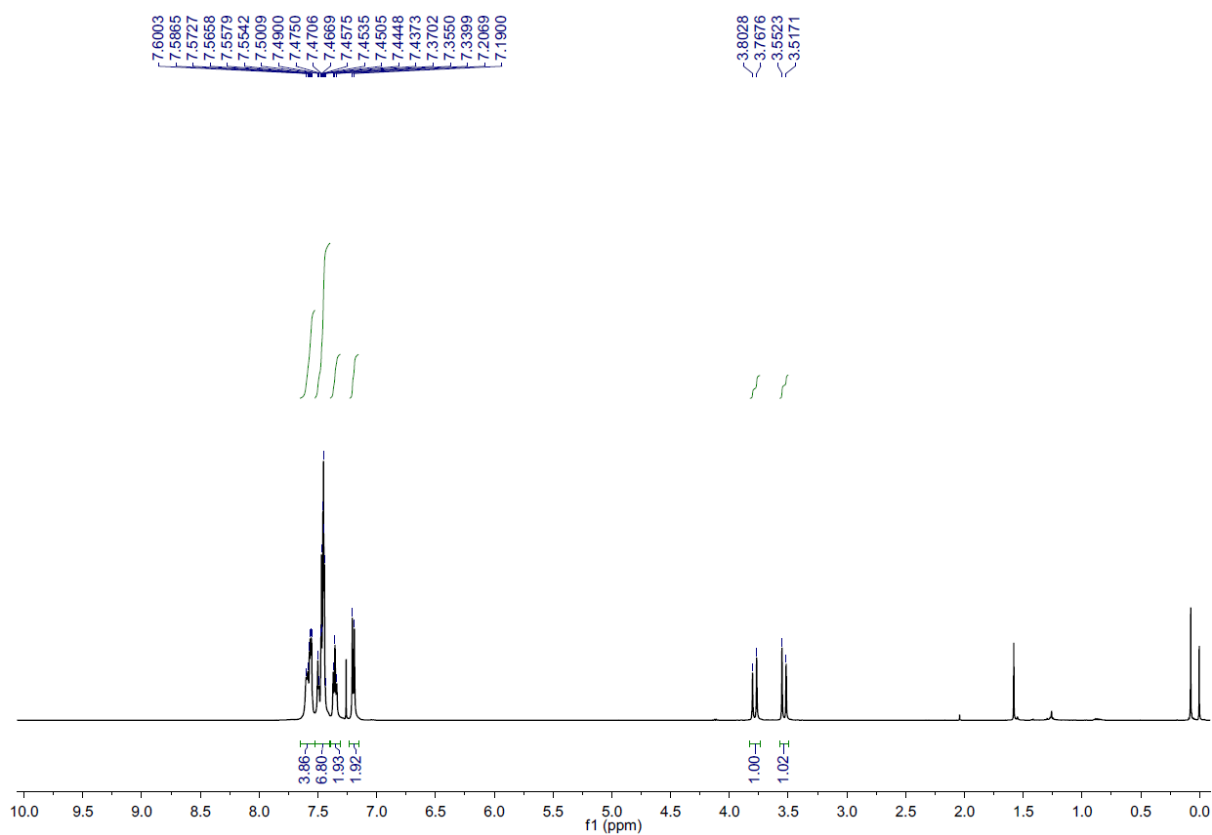
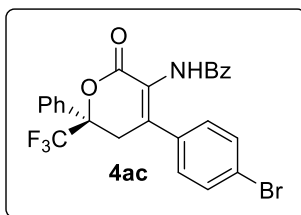


500 MHz ^1H NMR spectrum of compound **4ab** in CDCl_3

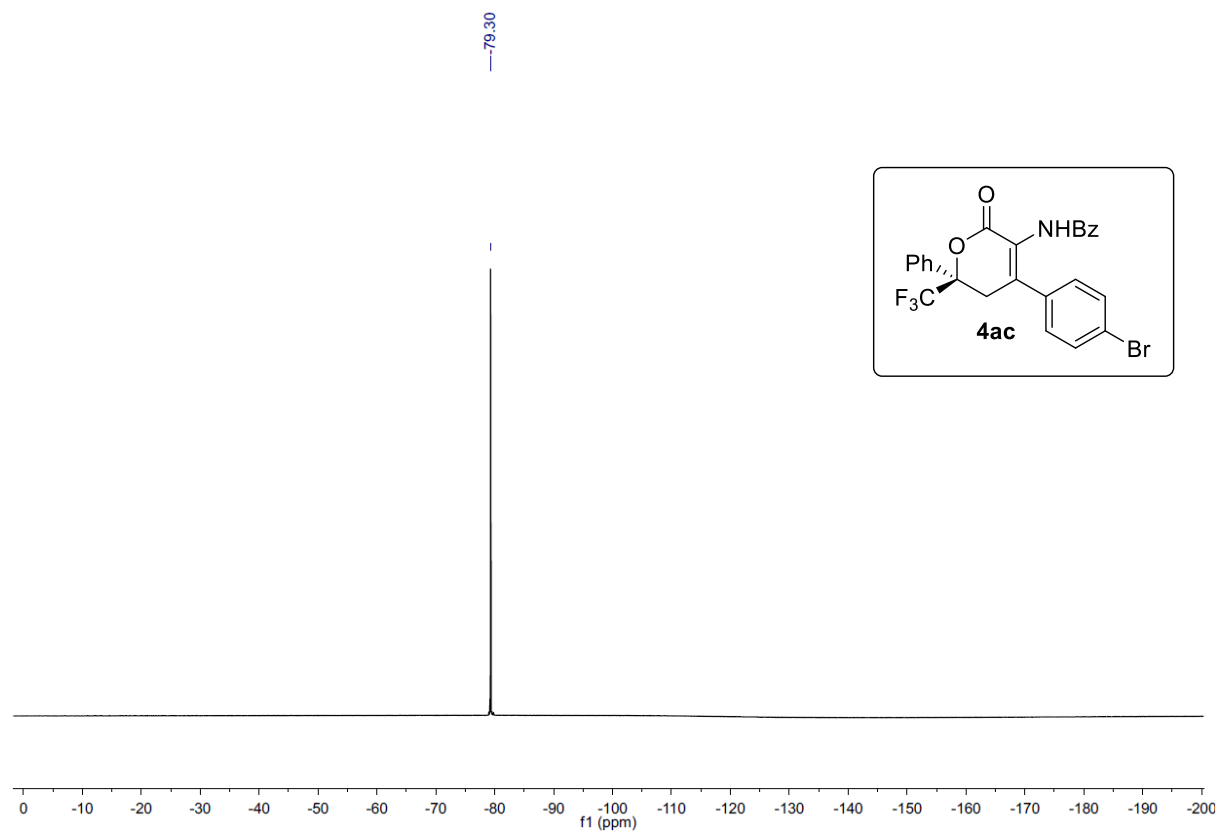
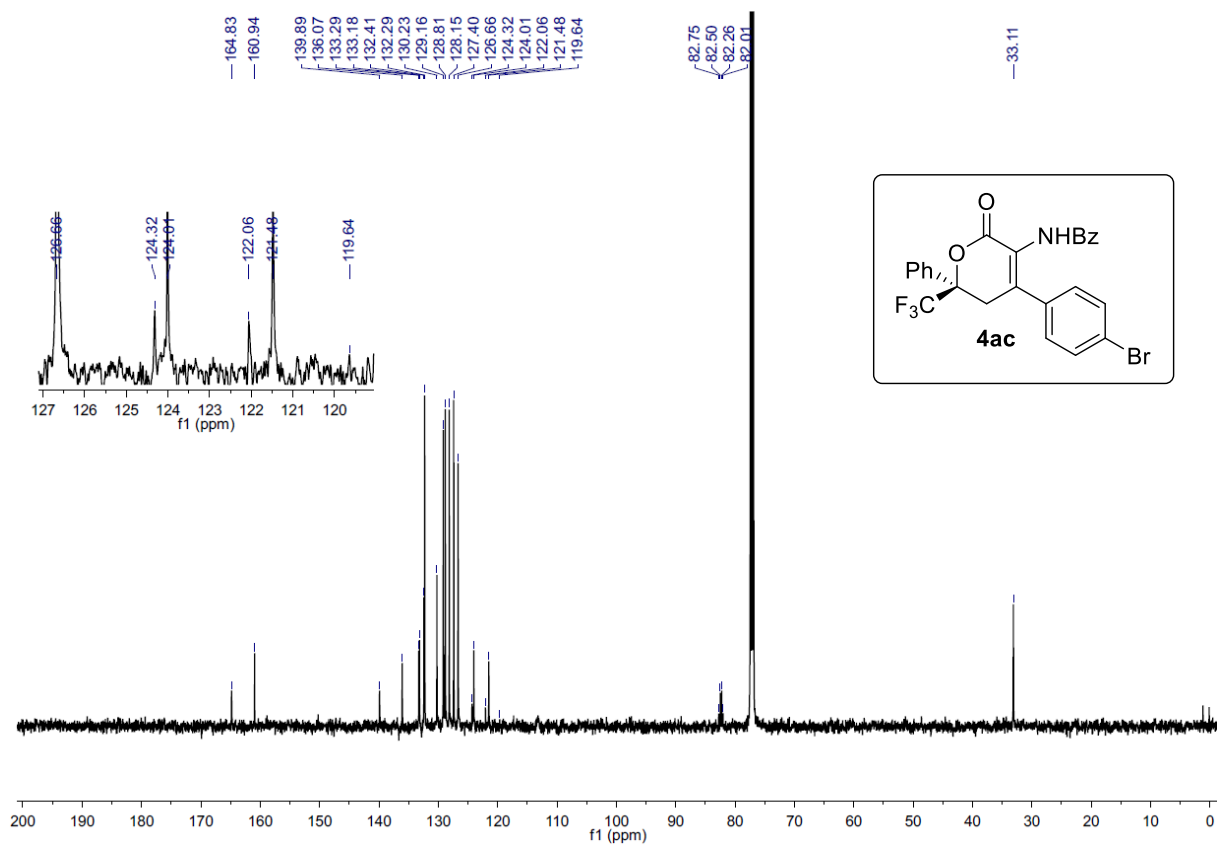


125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4ab** in CDCl₃

- (iii) **(*R*)-*N*-(4-(4-bromophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ac)**

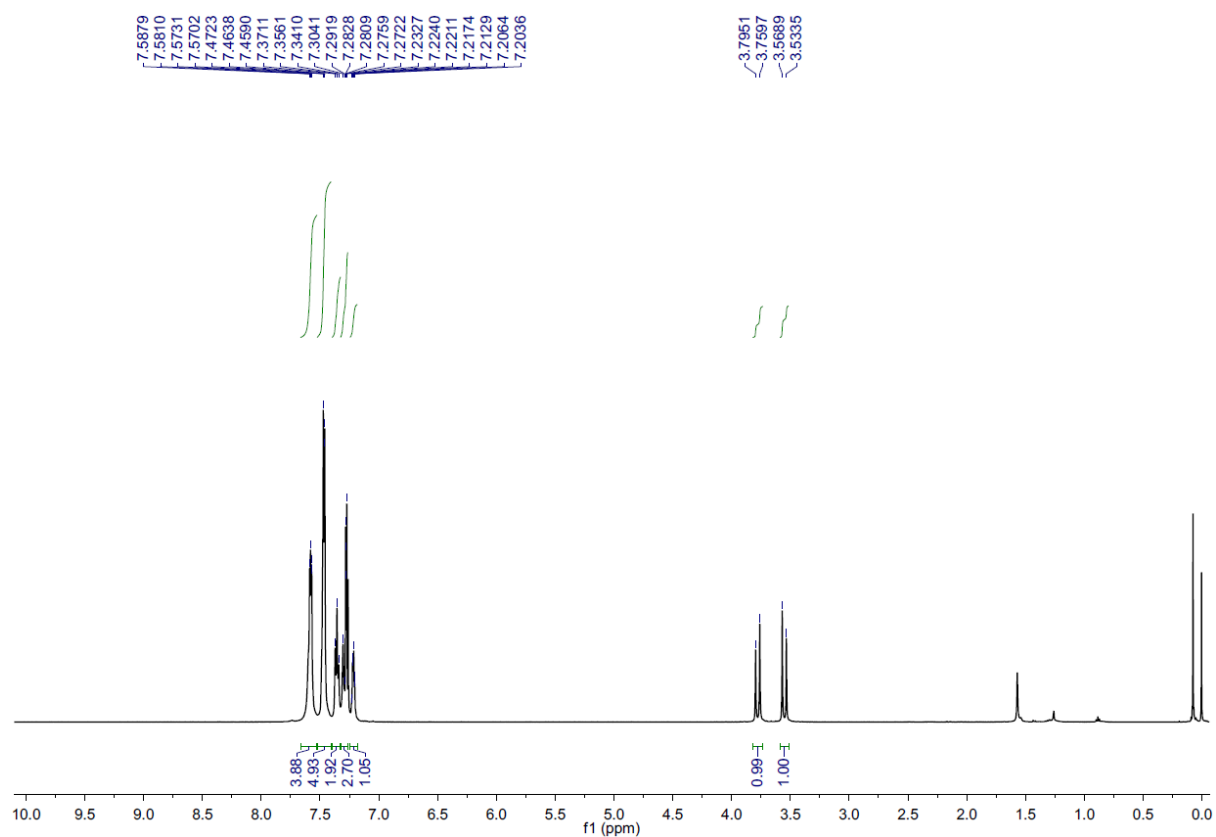
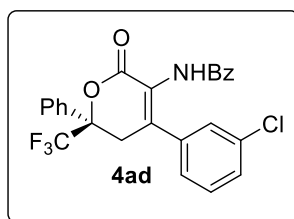


500 MHz ^1H NMR spectrum of compound **4ac** in CDCl_3

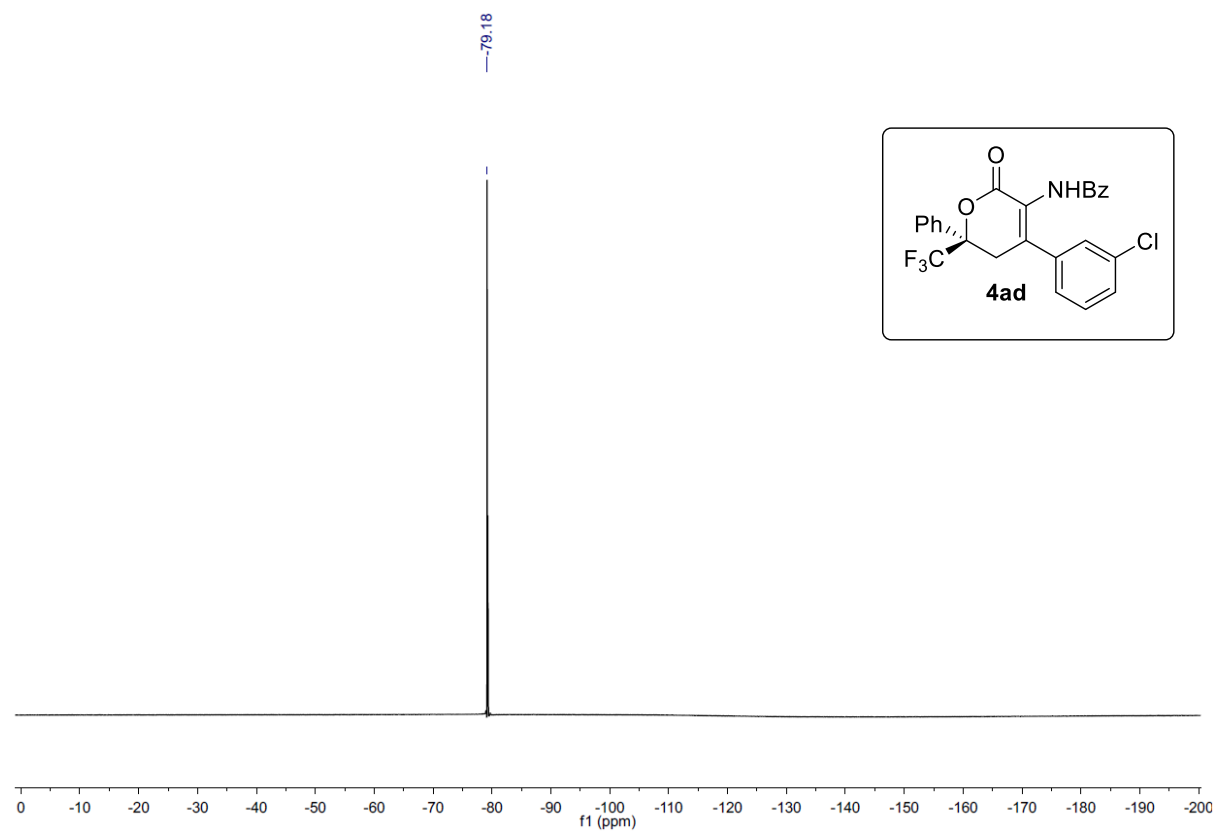
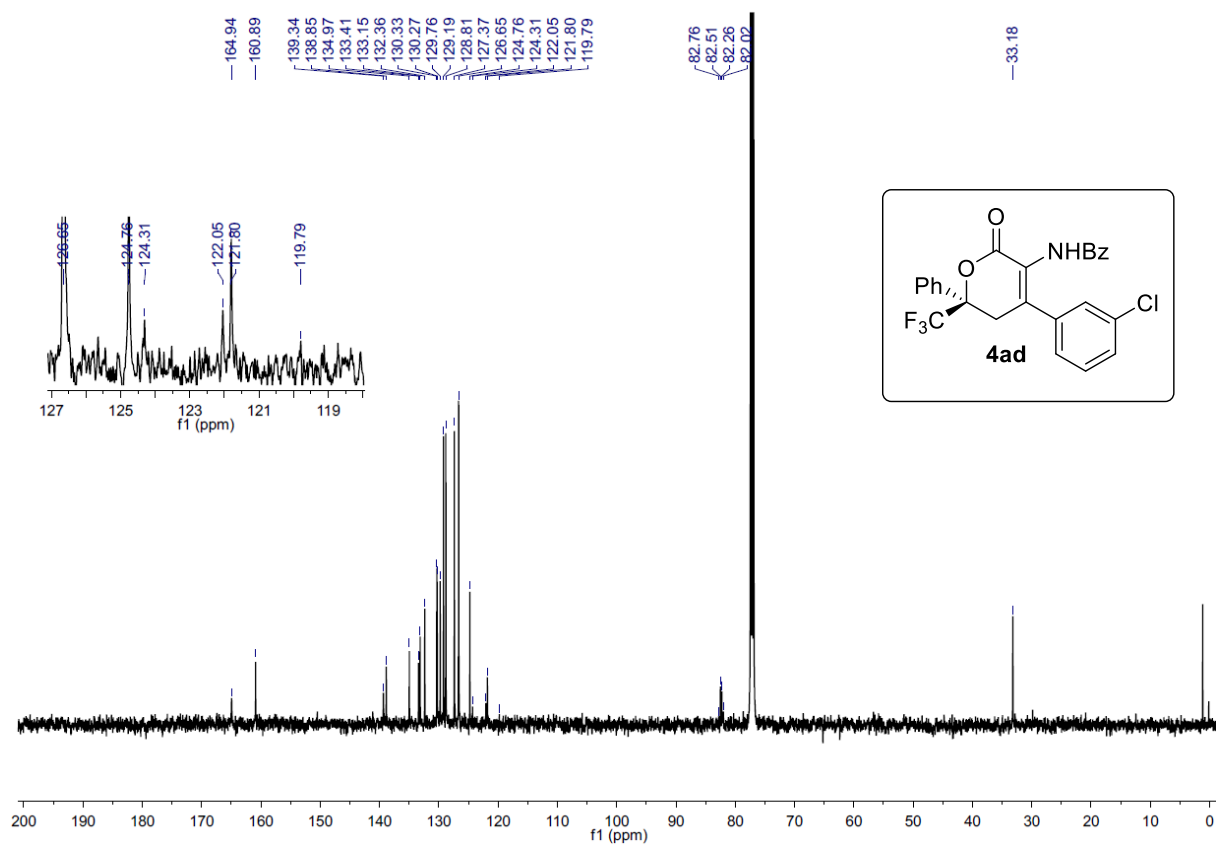


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ac** in CDCl_3

- (iv) **(*R*)-*N*-(4-(3-chlorophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ad)**

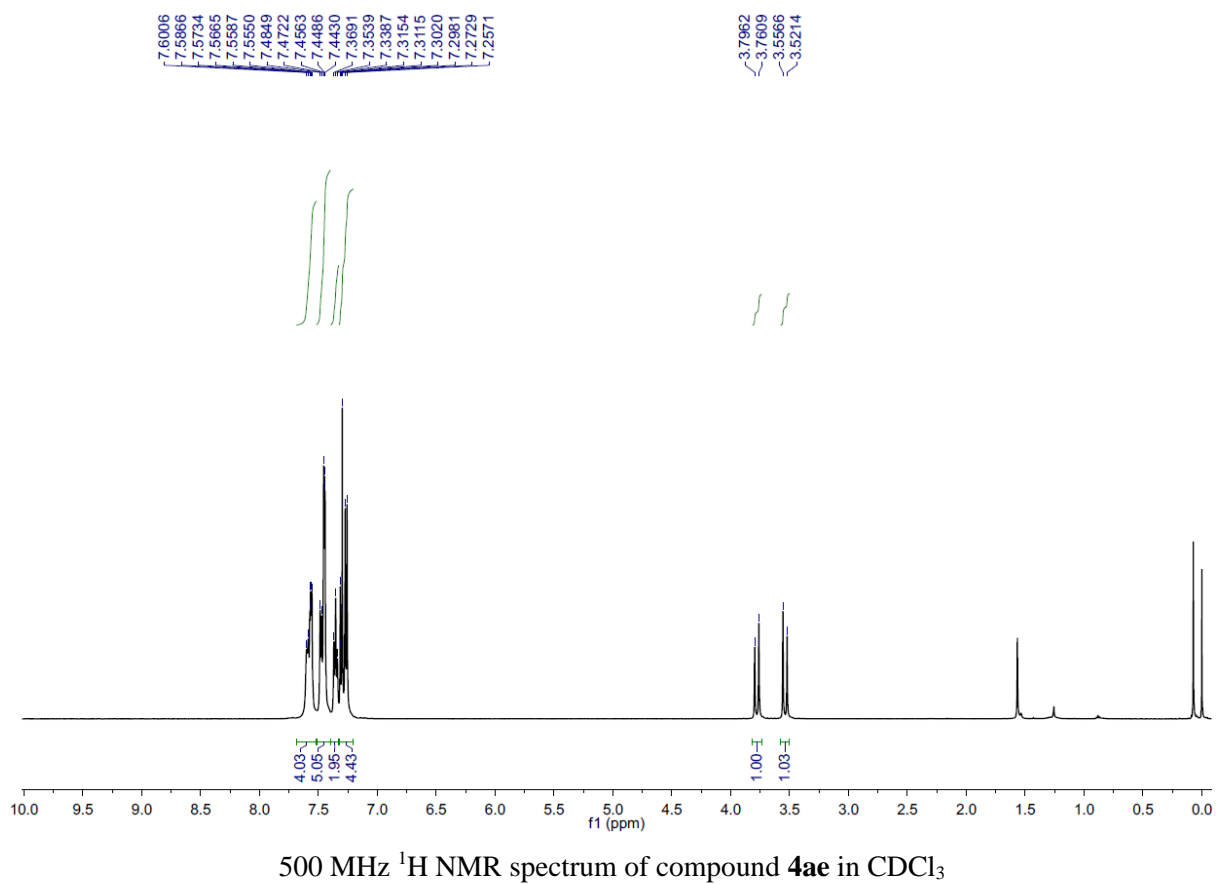
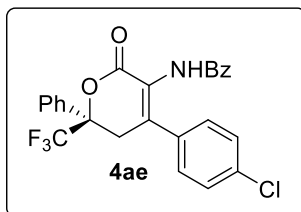


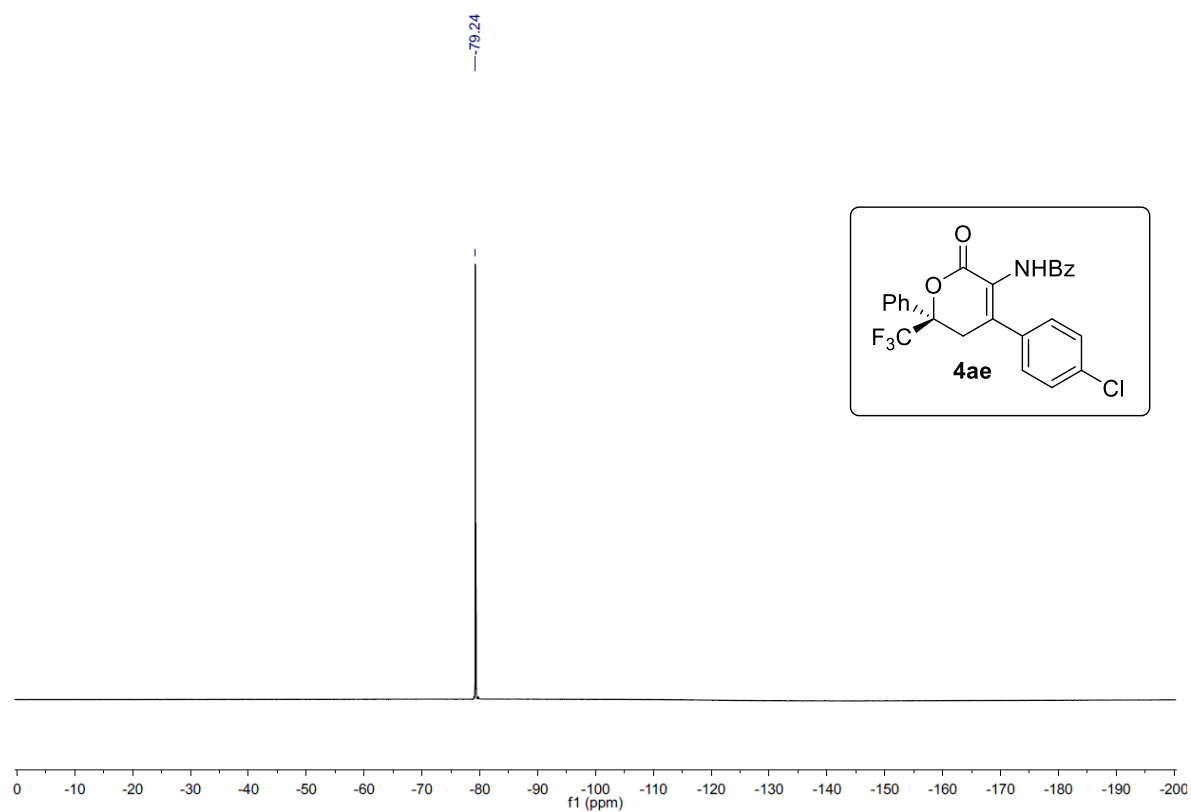
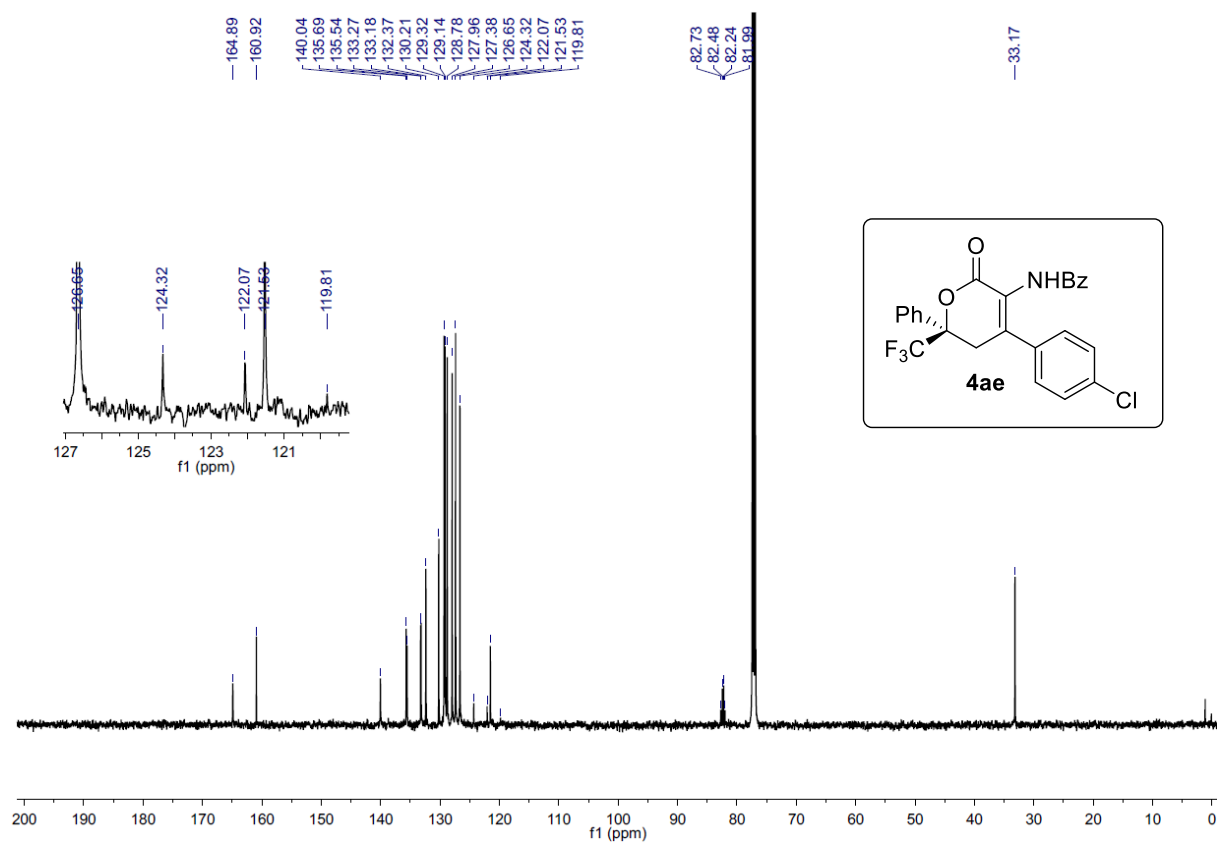
500 MHz ^1H NMR spectrum of compound **4ad** in CDCl_3



125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4ad** in CDCl₃

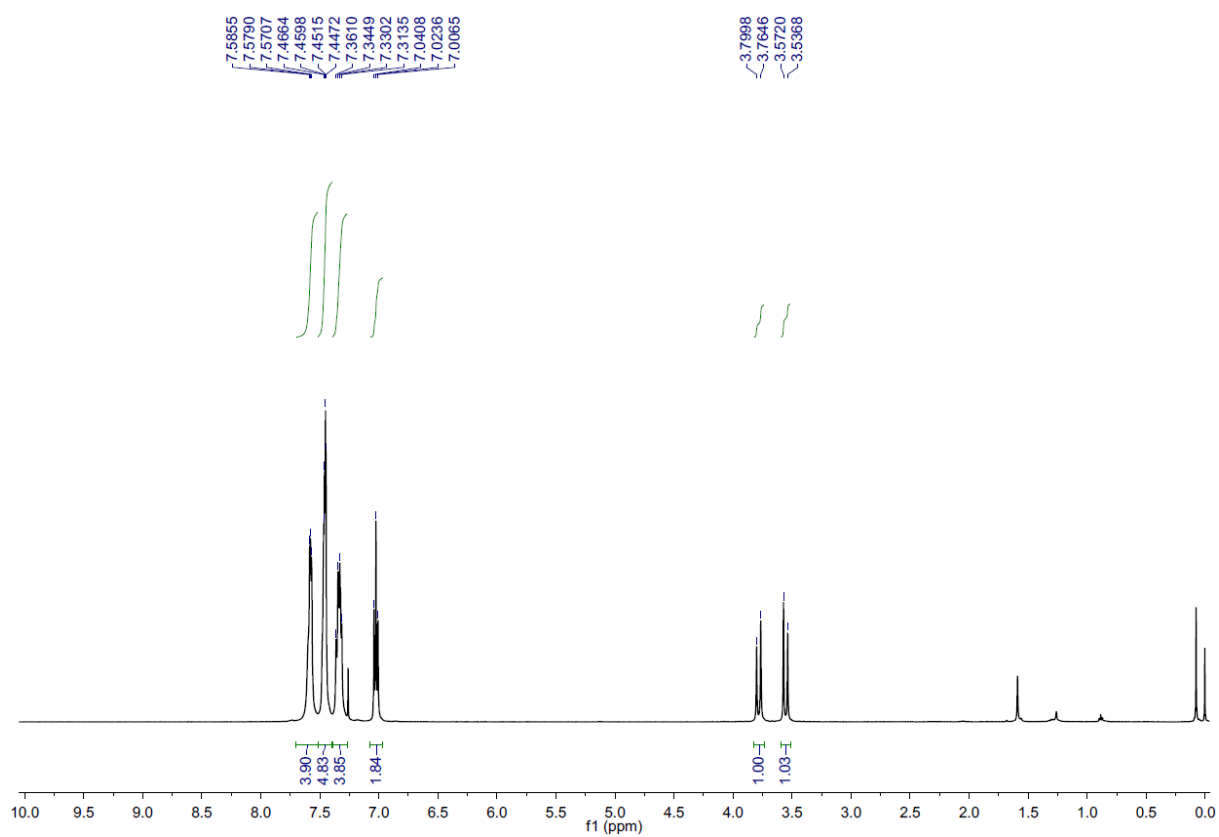
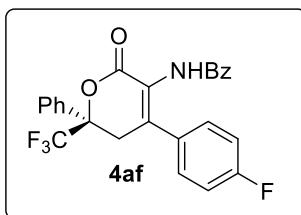
- (v) (*R*)-*N*-(4-(4-chlorophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4ae**)



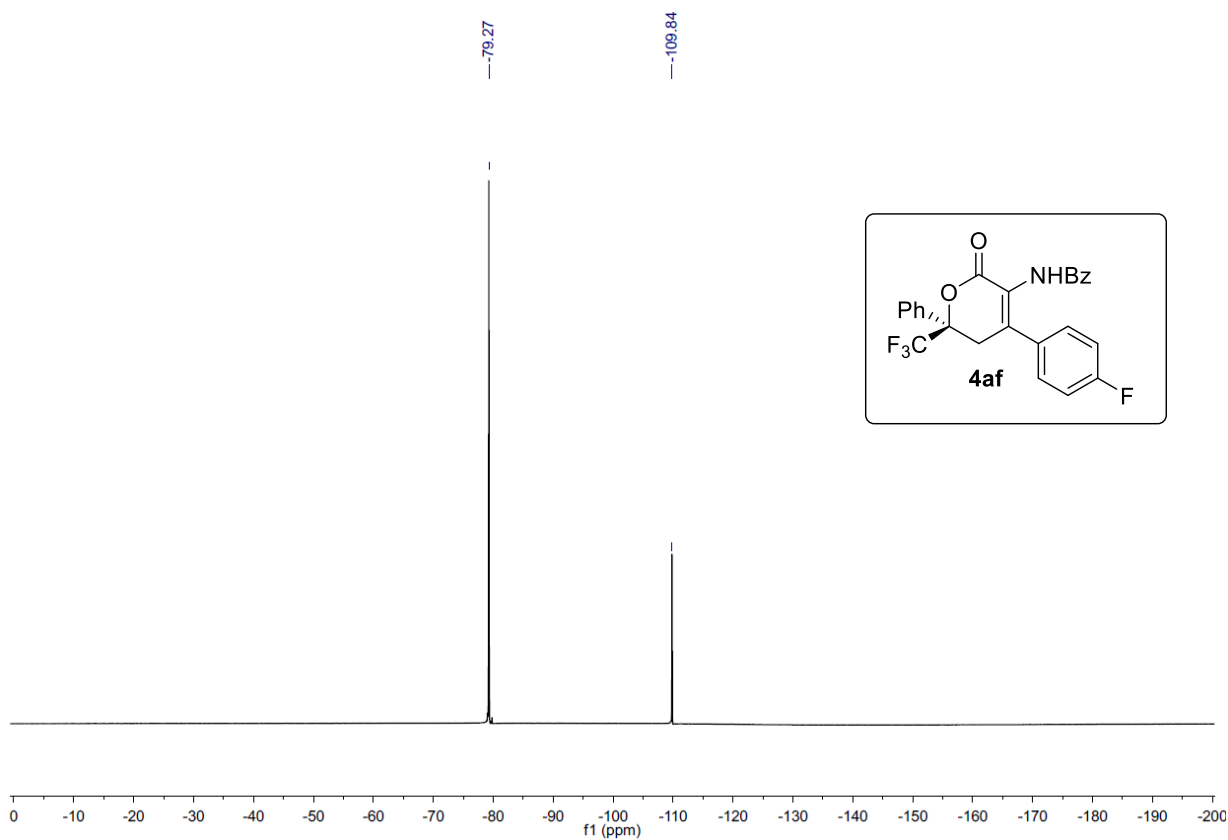
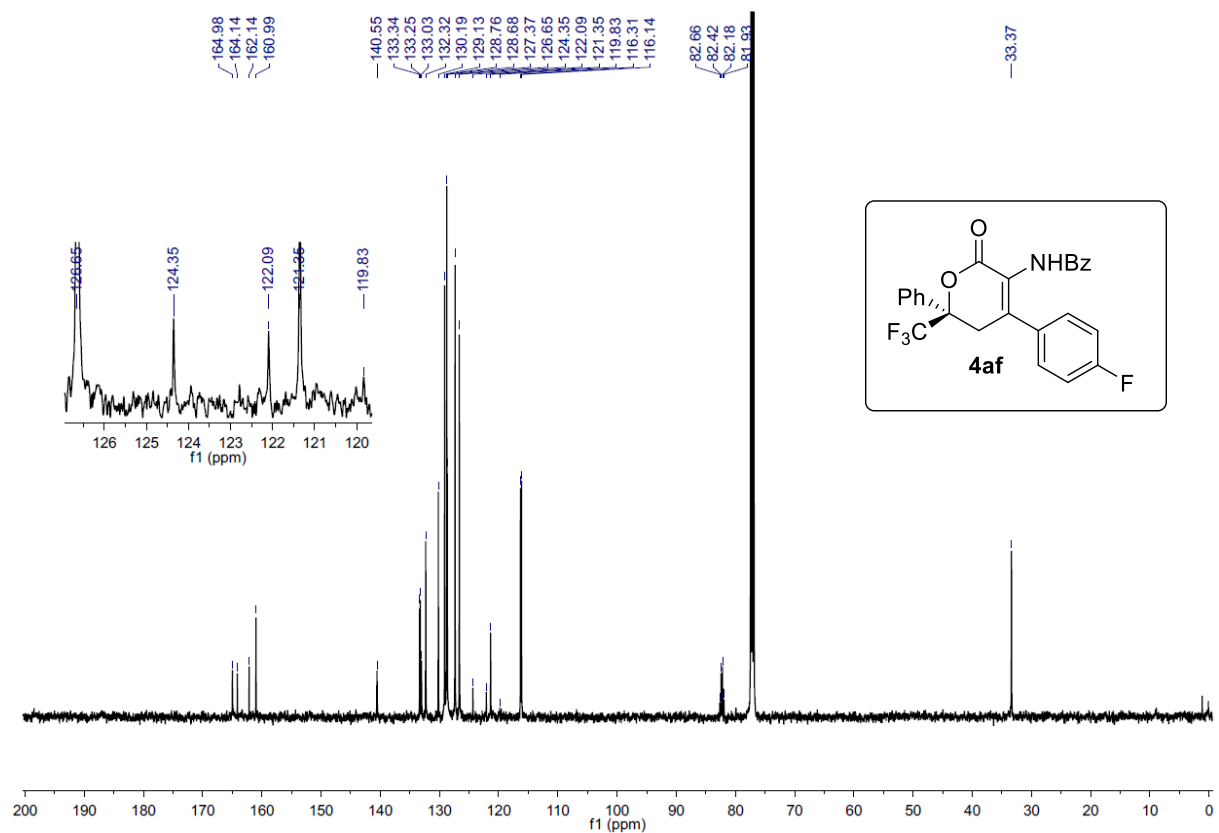


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ae** in CDCl_3

(vi) **(*R*)-*N*-(4-(4-fluorophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4af**)**

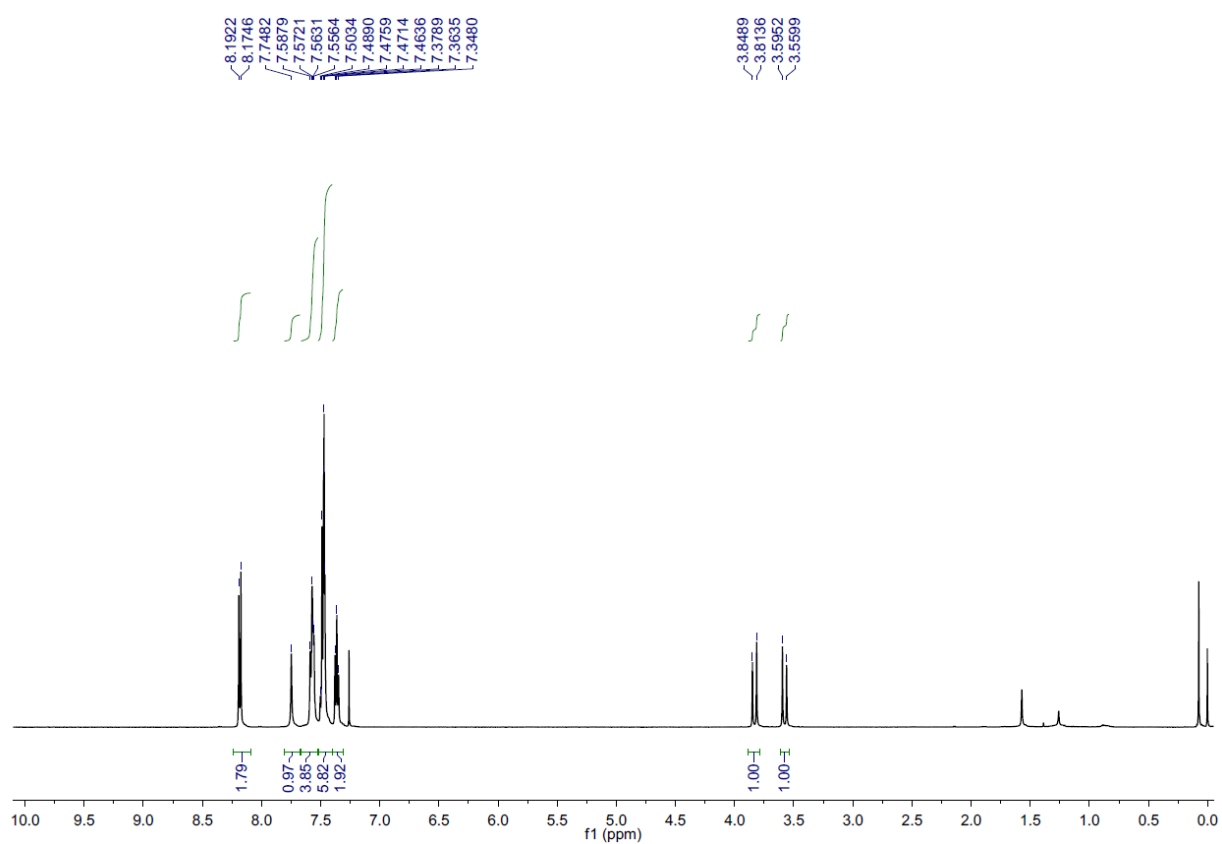
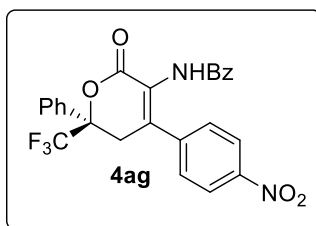


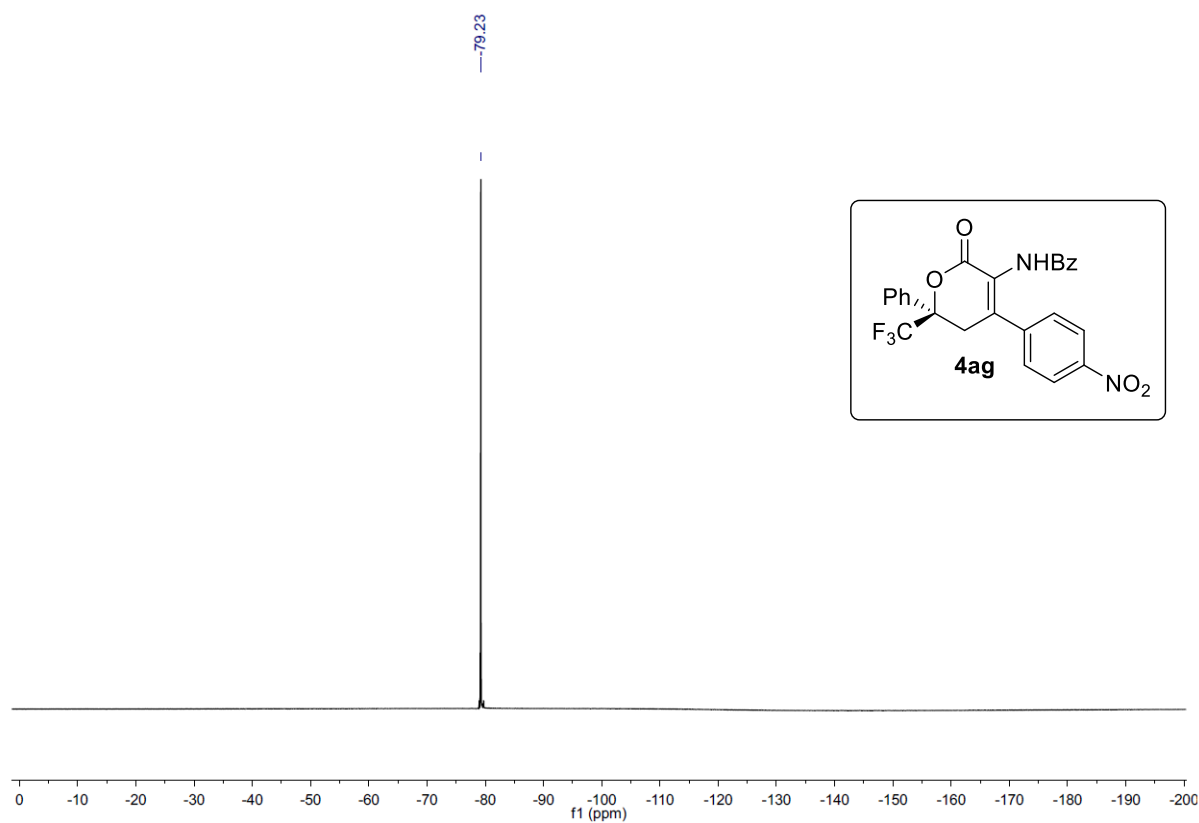
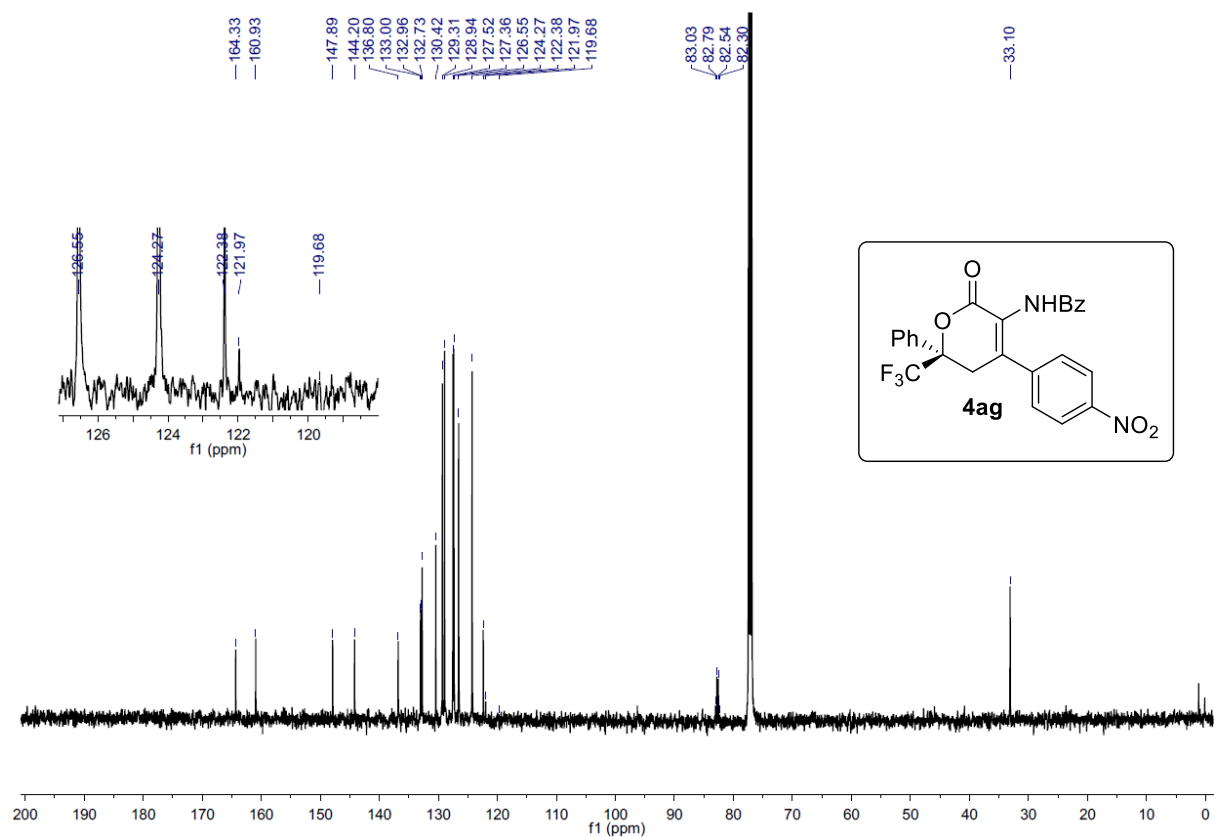
500 MHz ^1H NMR spectrum of compound **4af** in CDCl_3



125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4af** in CDCl_3

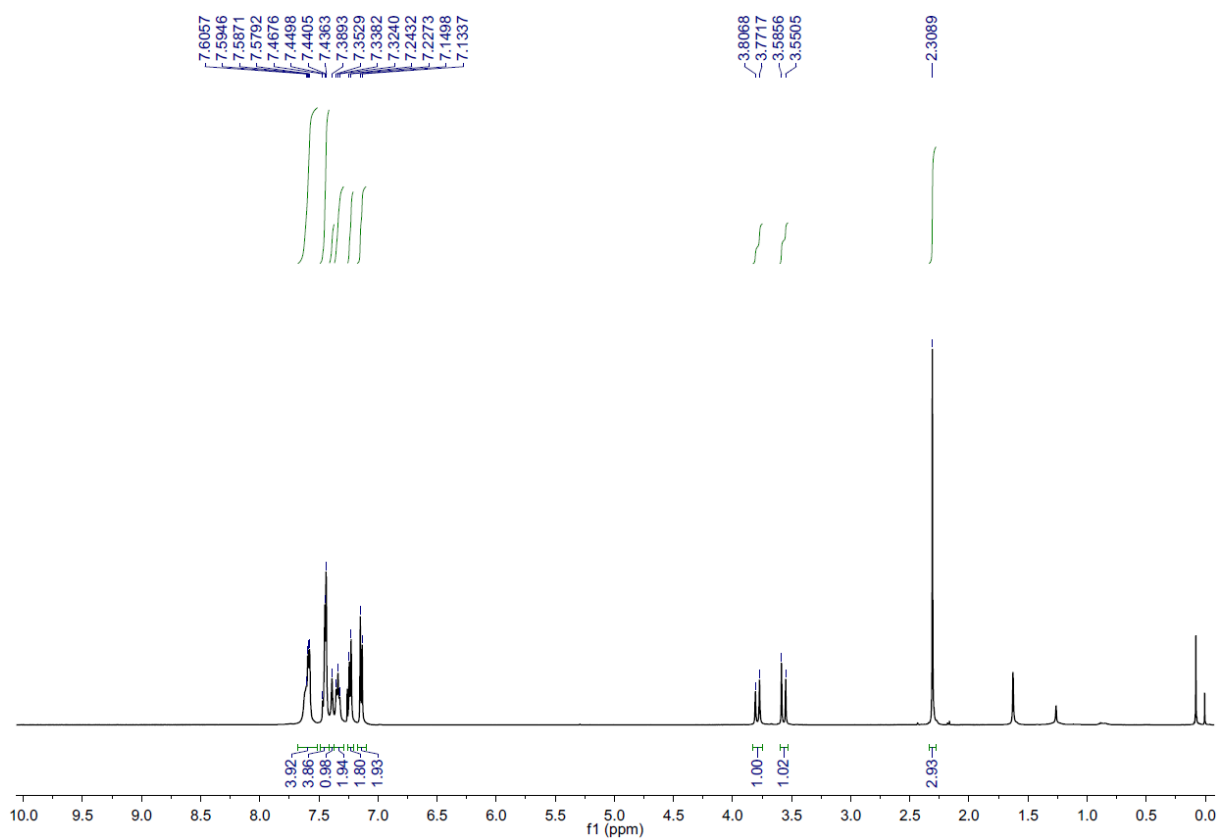
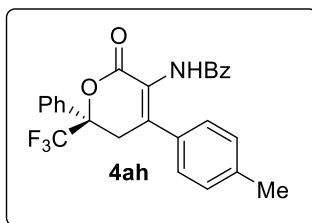
(vii) **(*R*)-*N*-(4-(4-nitrophenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ag)**



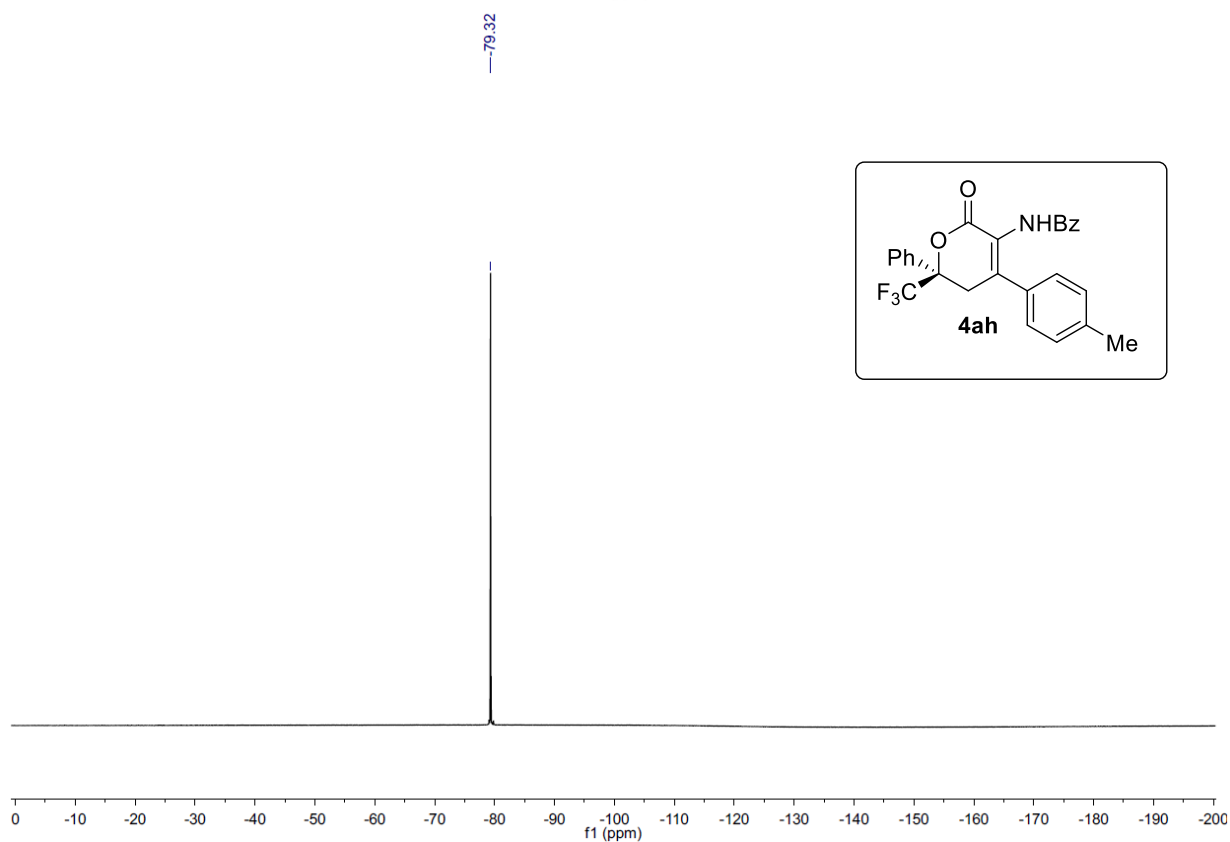
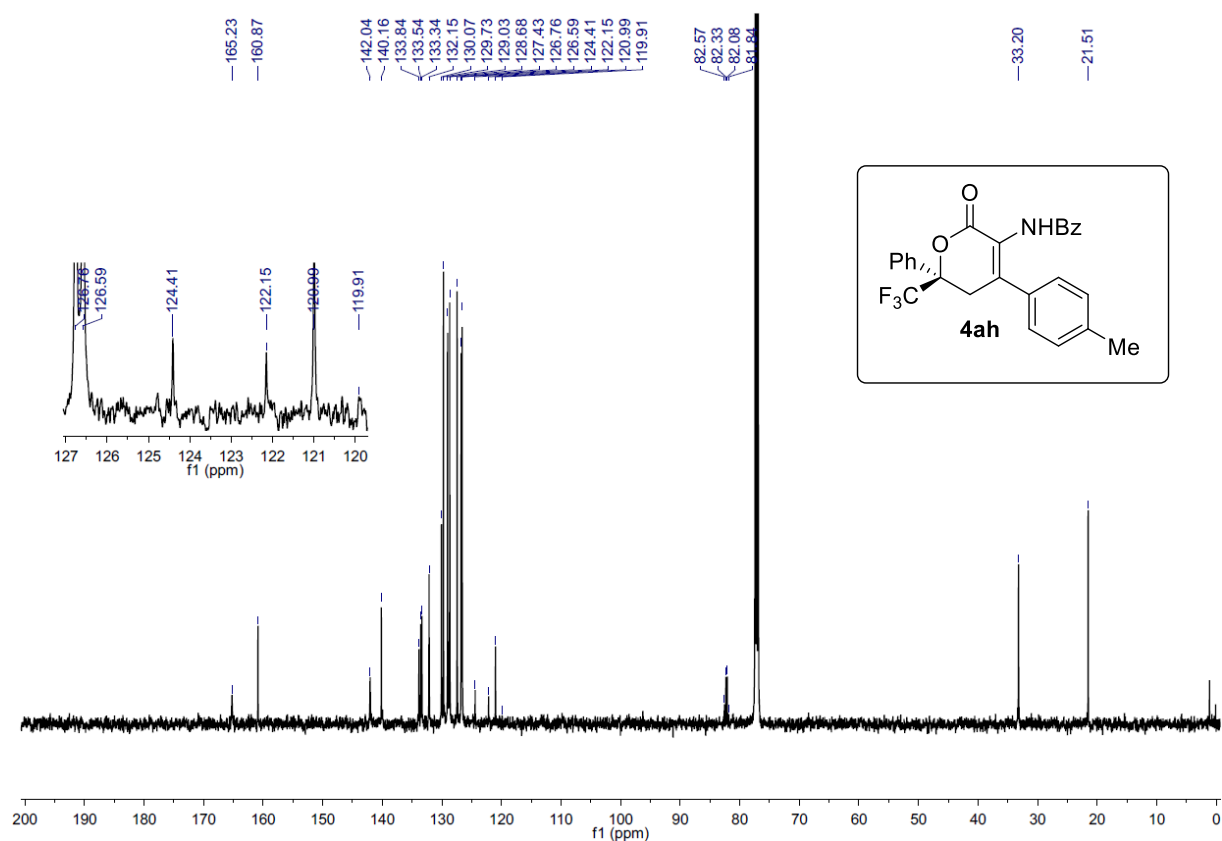


125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4ag** in CDCl₃

(viii) (*R*)-*N*-(2-oxo-6-phenyl-4-(*p*-tolyl)-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4ah**)

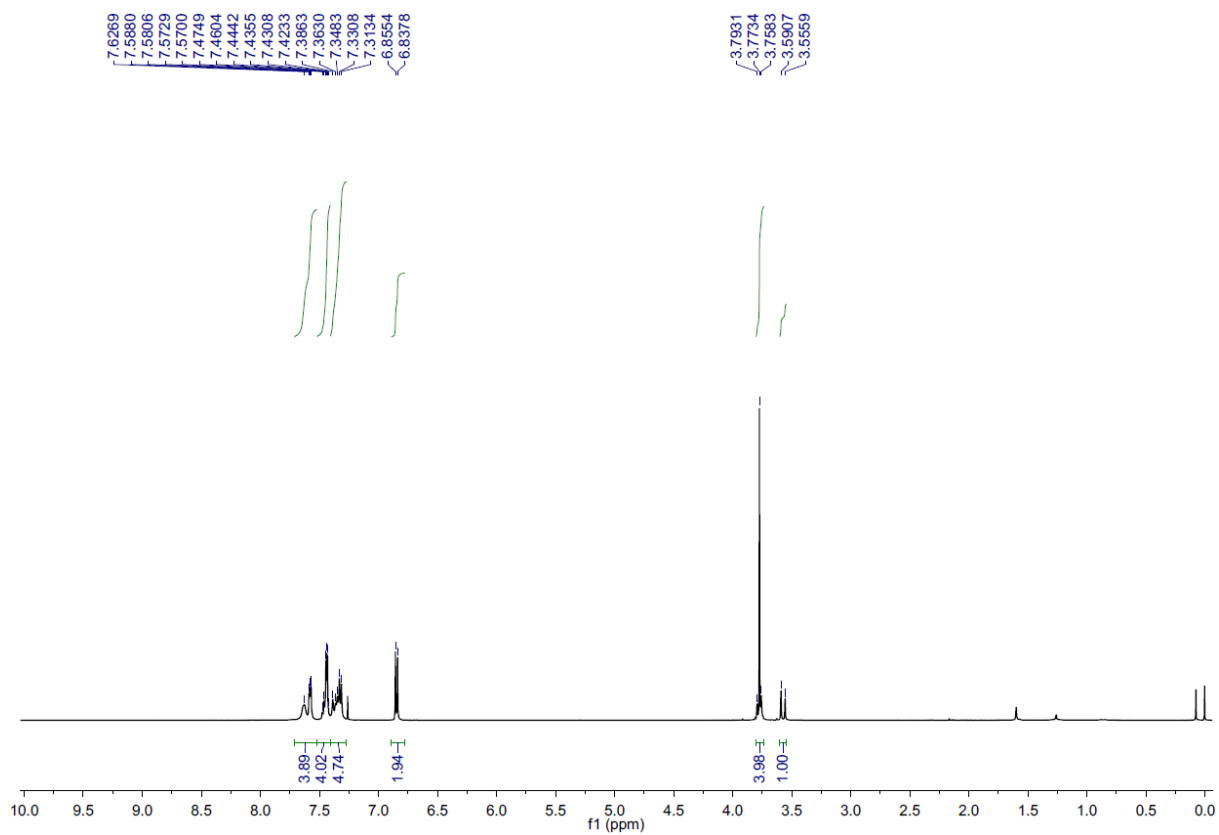
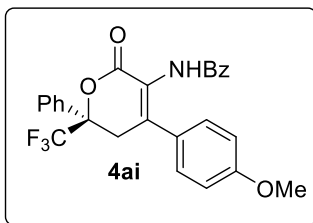


500 MHz ^1H NMR spectrum of compound **4ah** in CDCl_3

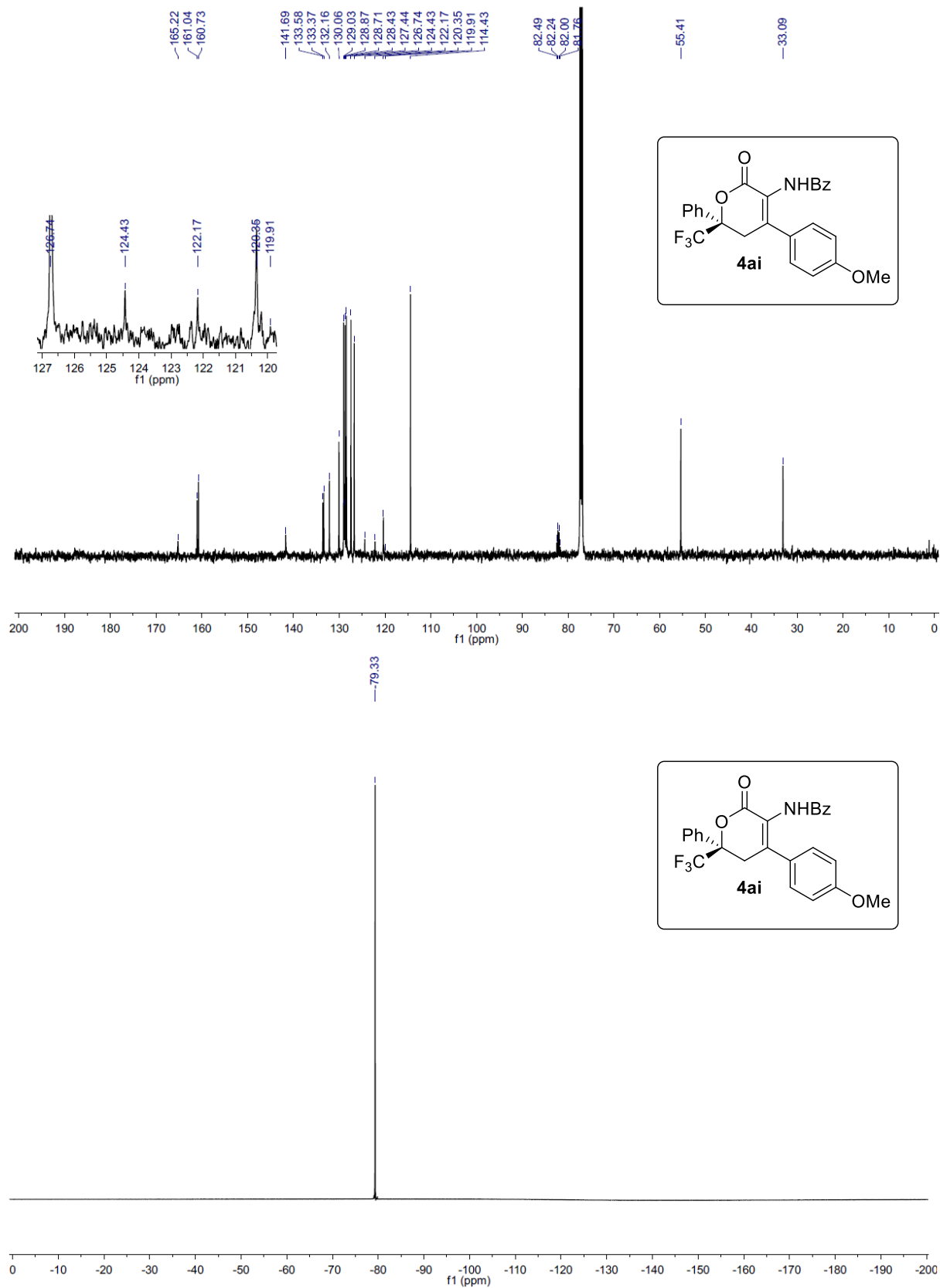


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ah** in CDCl_3

(ix) **(*R*)-*N*-(4-(4-methoxyphenyl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4ai**)**

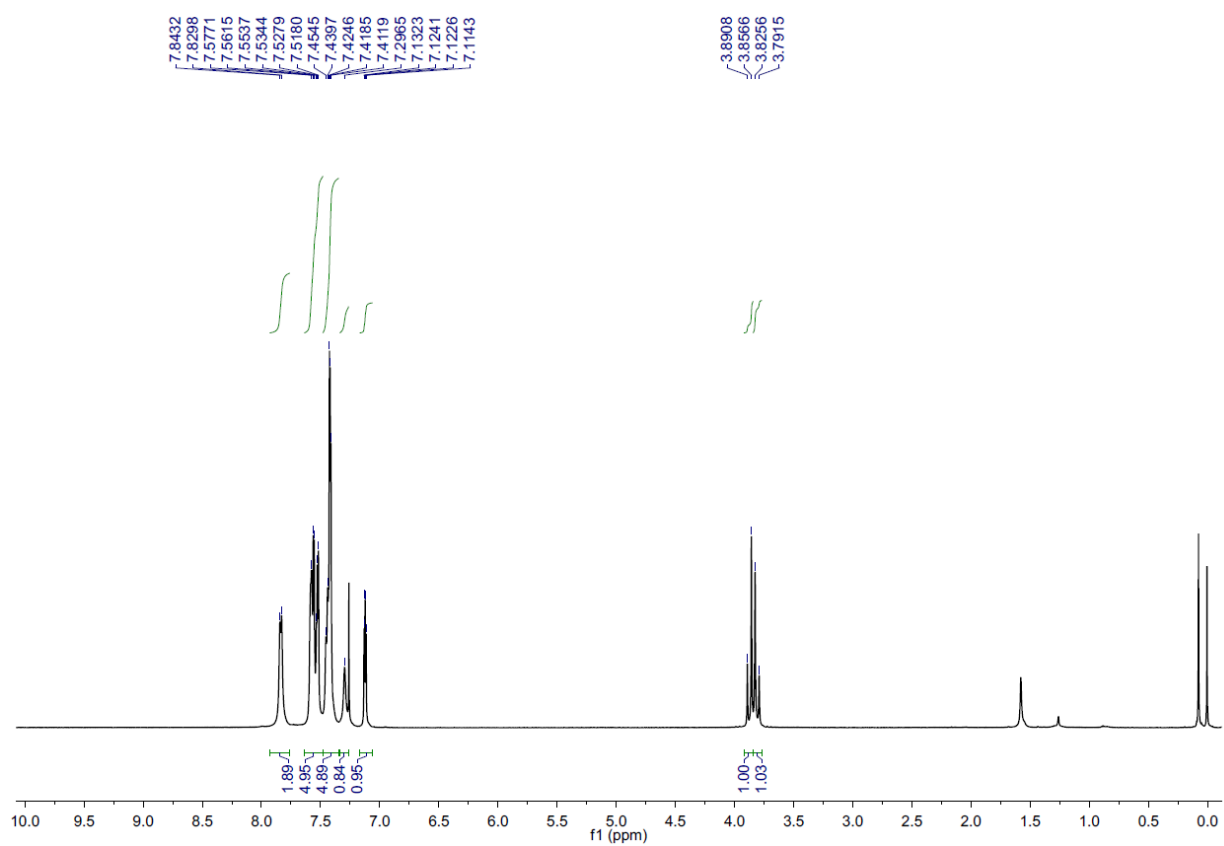
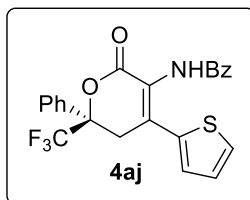


500 MHz ^1H NMR spectrum of compound **4ai** in CDCl_3

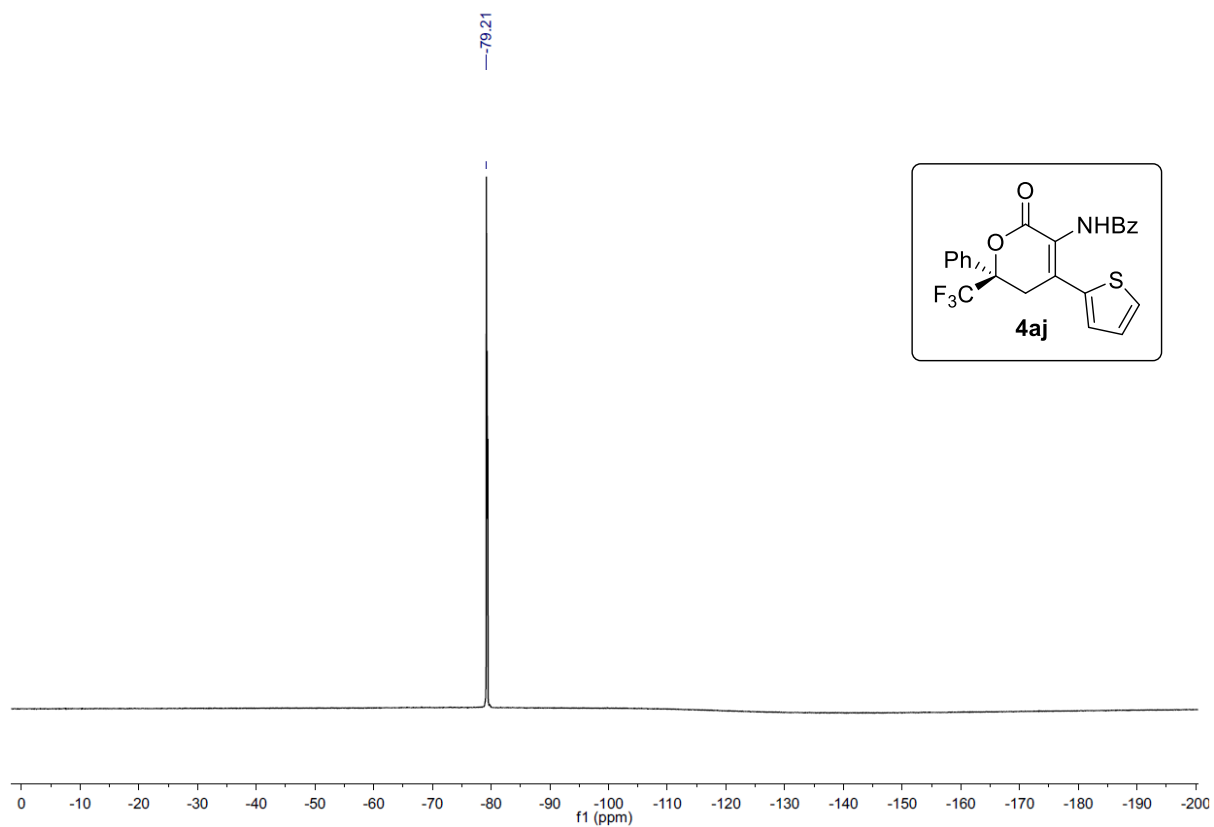
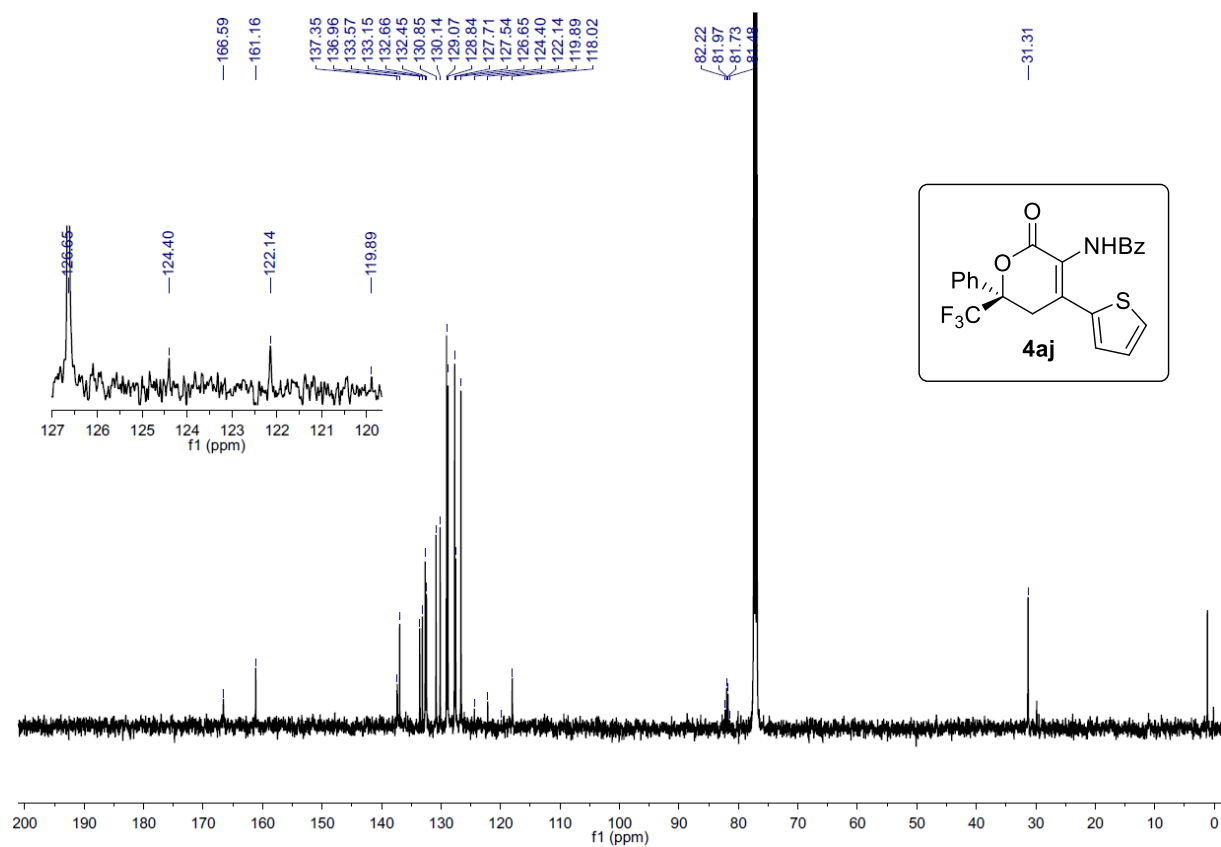


125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4ai** in CDCl₃

- (x) **(*R*)-*N*-(2-oxo-6-phenyl-4-(thiophen-2-yl)-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4aj)**

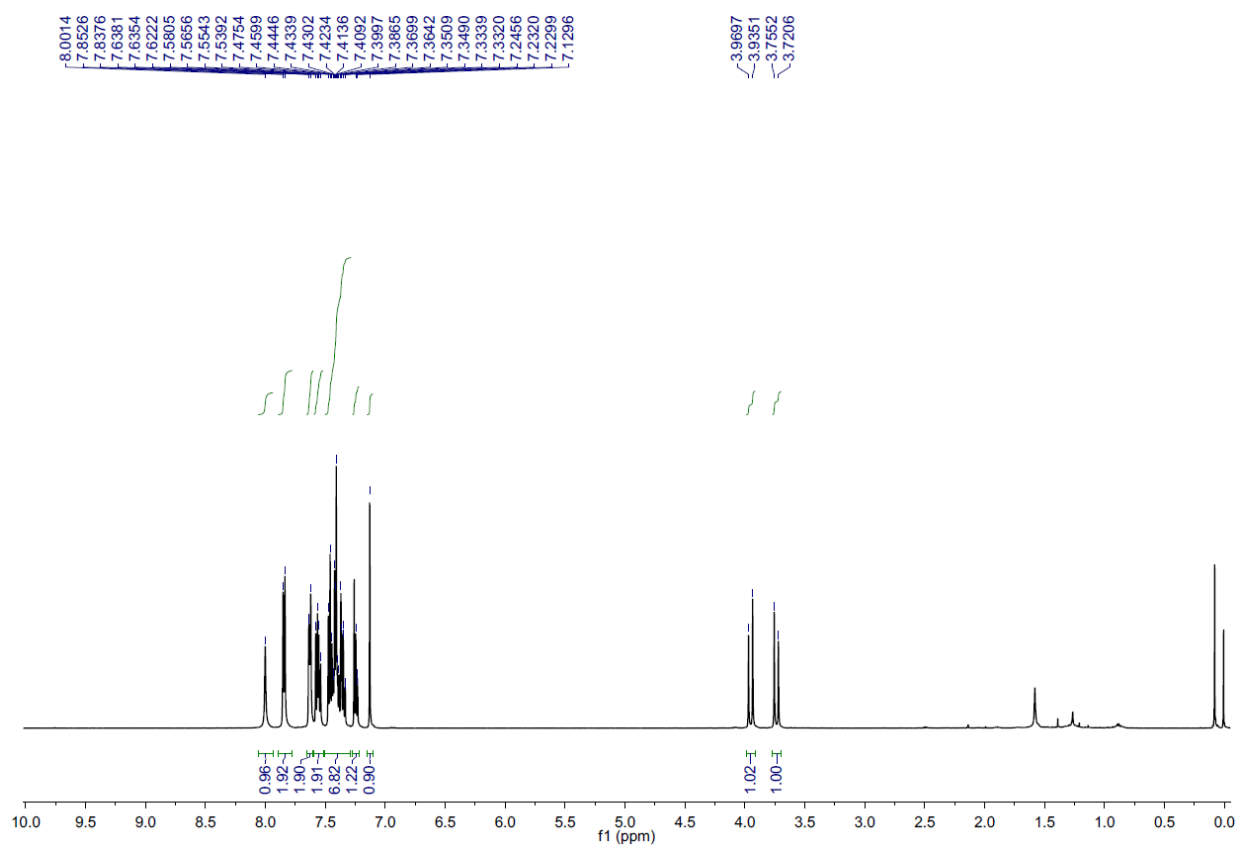
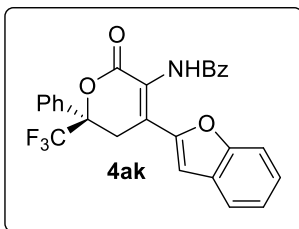


500 MHz ^1H NMR spectrum of compound **4aj** in CDCl_3

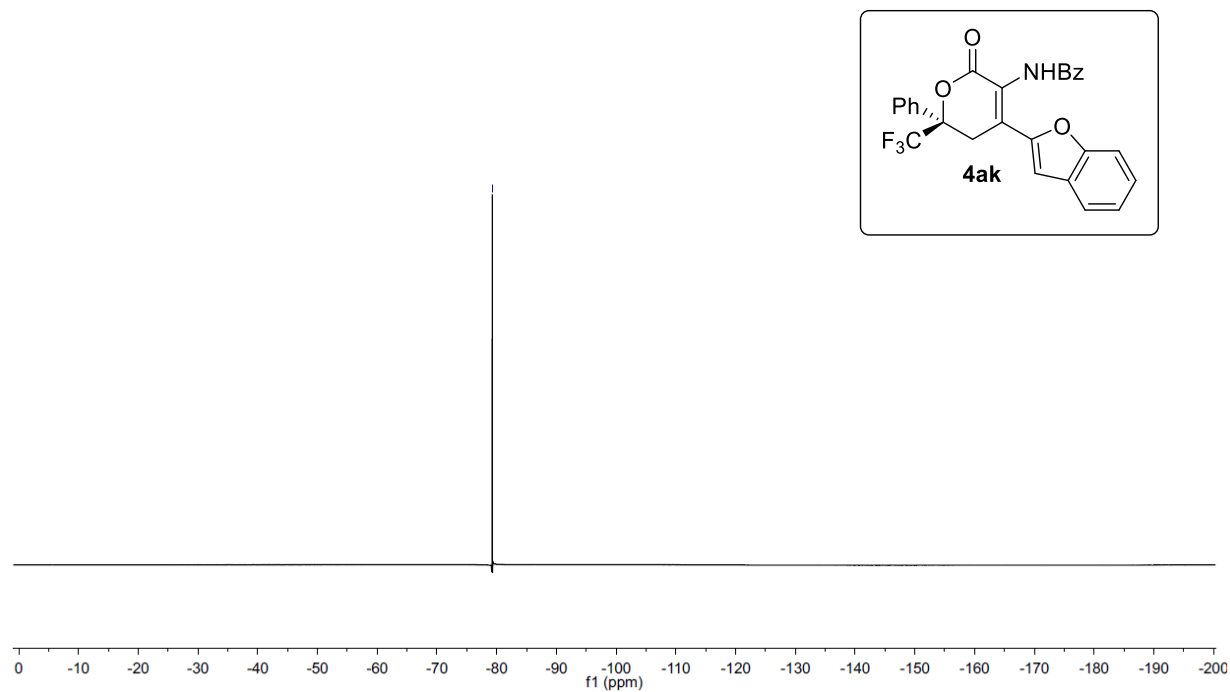
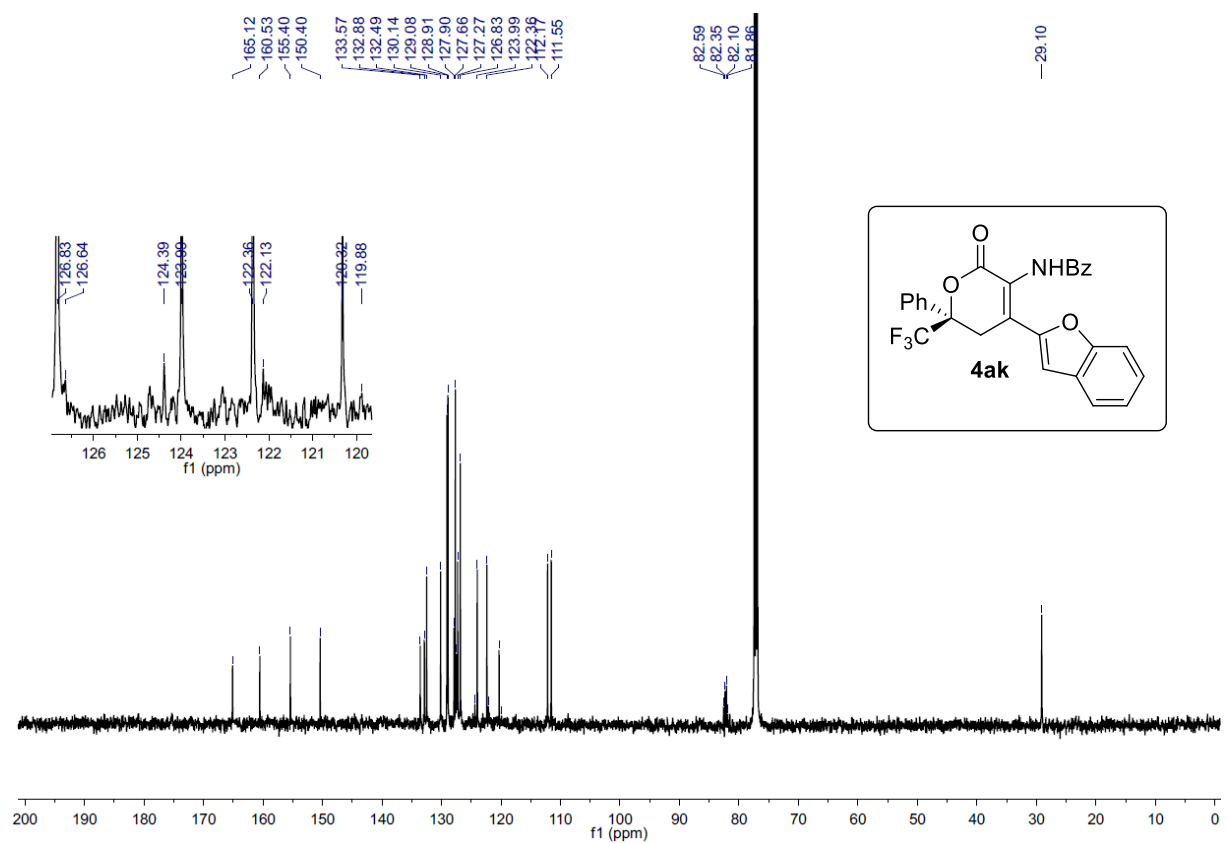


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4aj** in CDCl_3

- (xi) **(*R*)-*N*-(4-(benzofuran-2-yl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ak)**

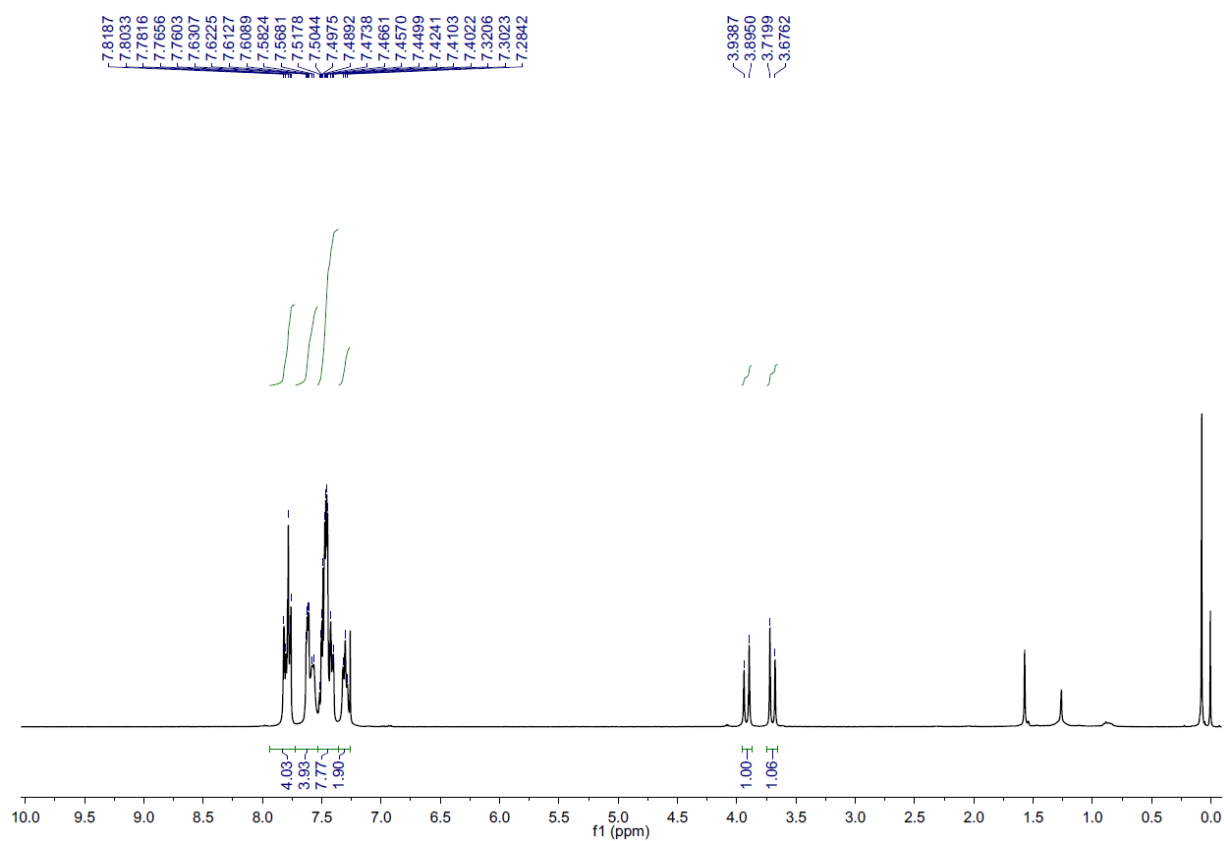
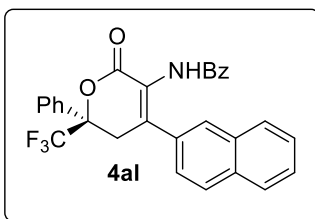


500 MHz ^1H NMR spectrum of compound **4ak** in CDCl_3

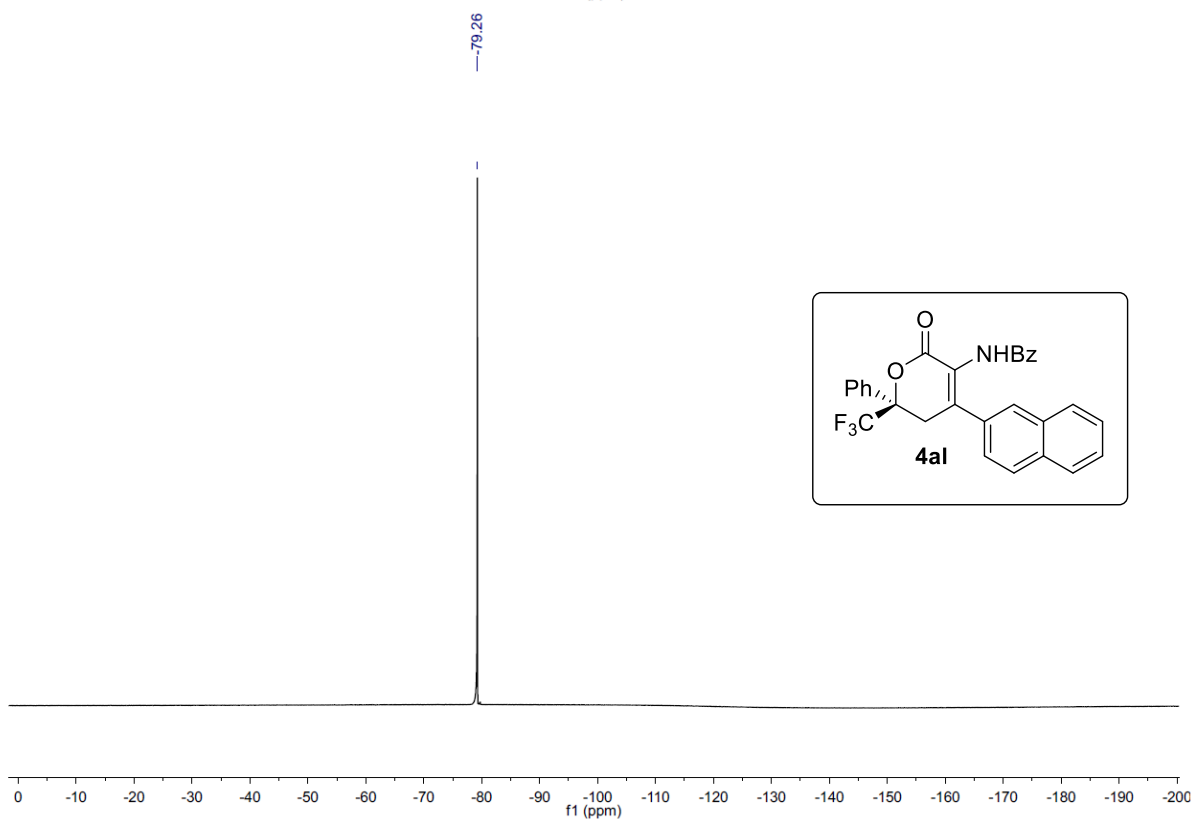
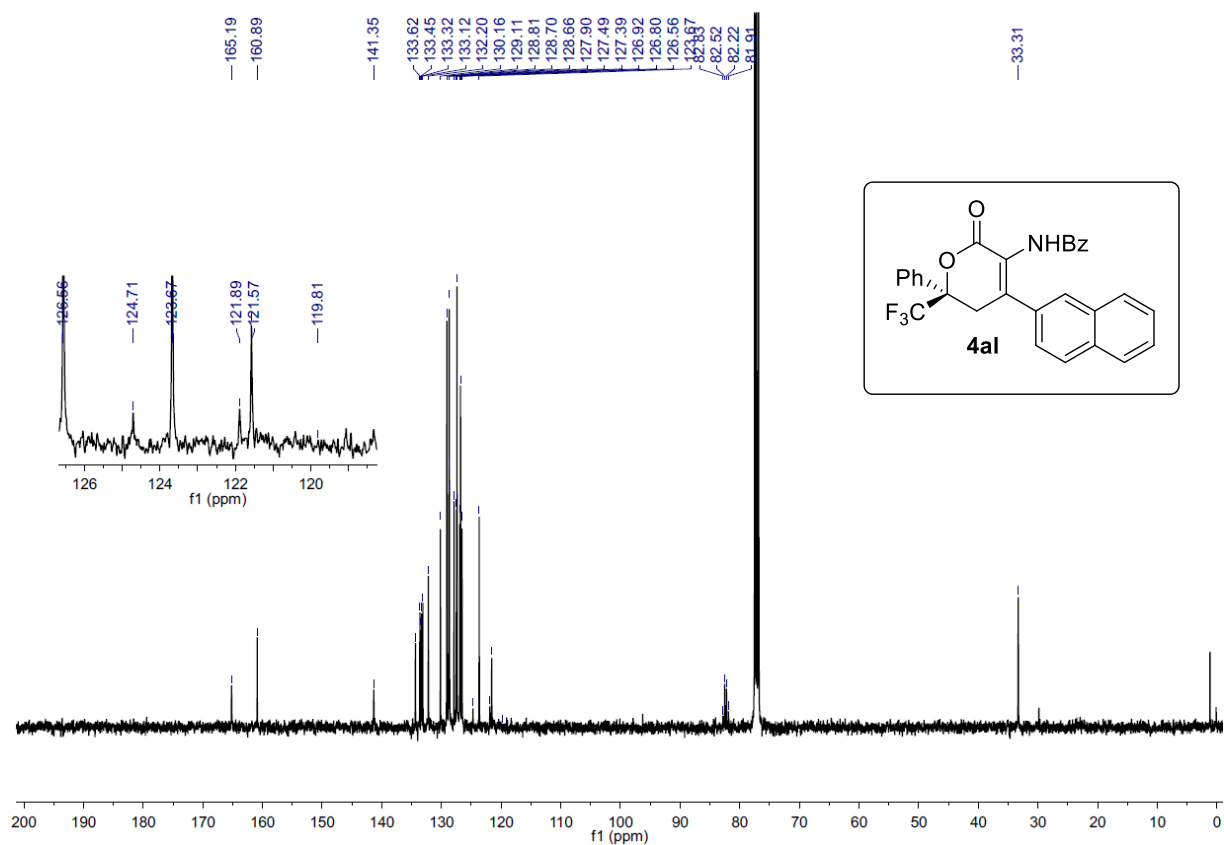


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ak** in CDCl_3

- (xii) **(*R*)-*N*-(4-(naphthalen-2-yl)-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4al)**

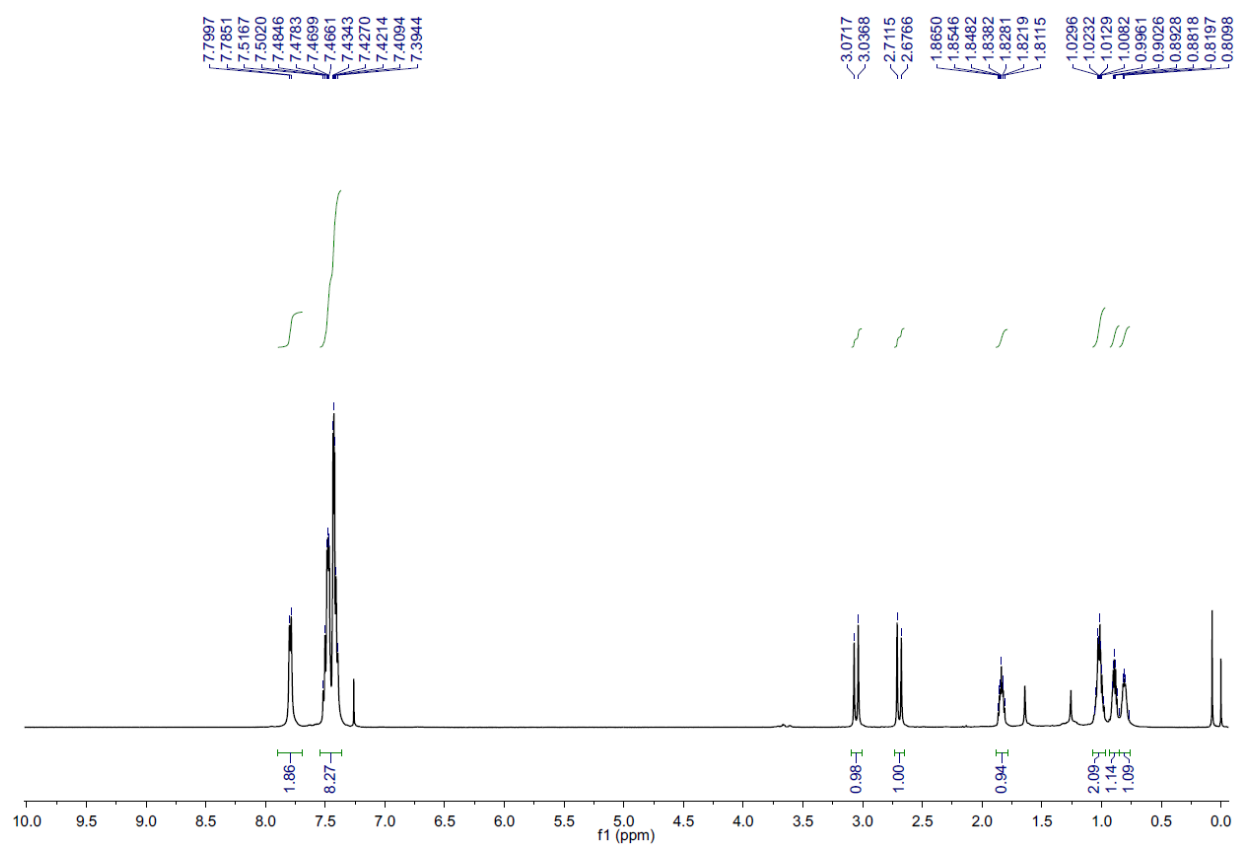
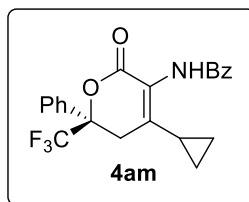


400 MHz ^1H NMR spectrum of compound **4al** in CDCl_3

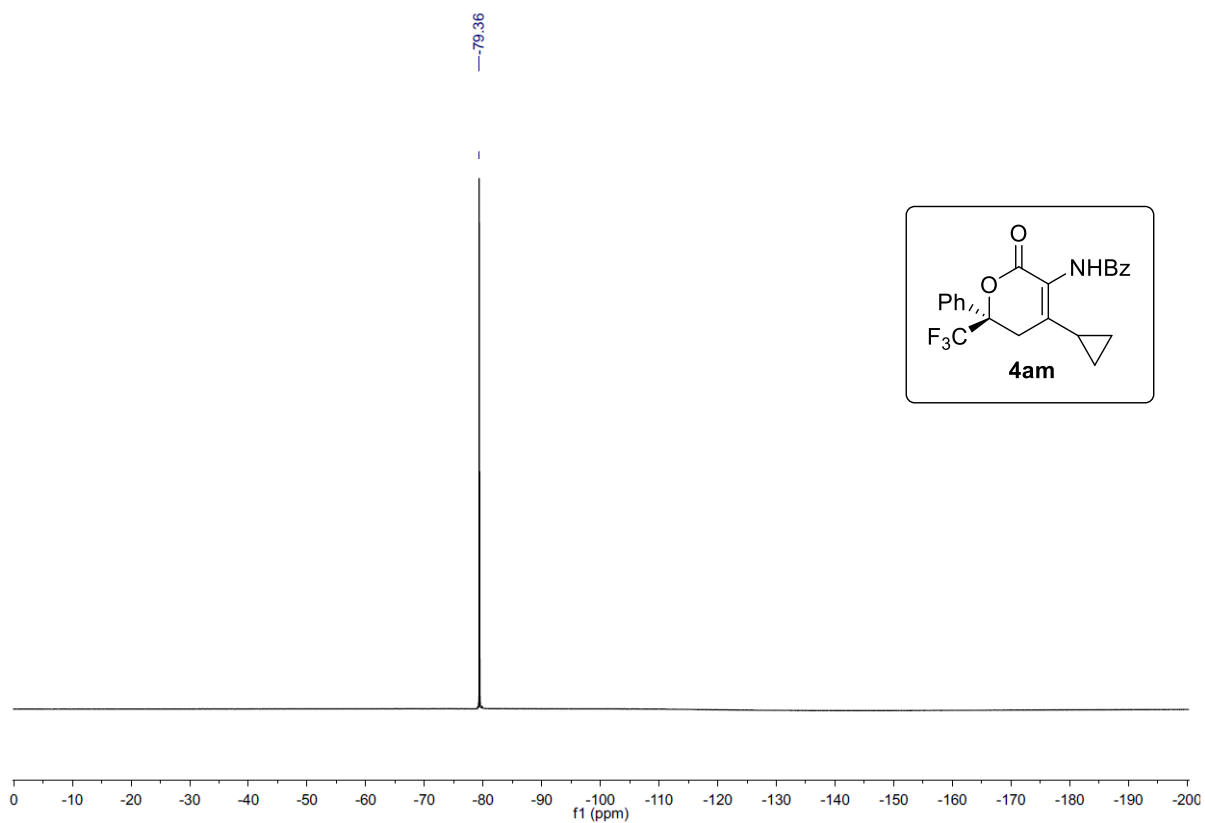
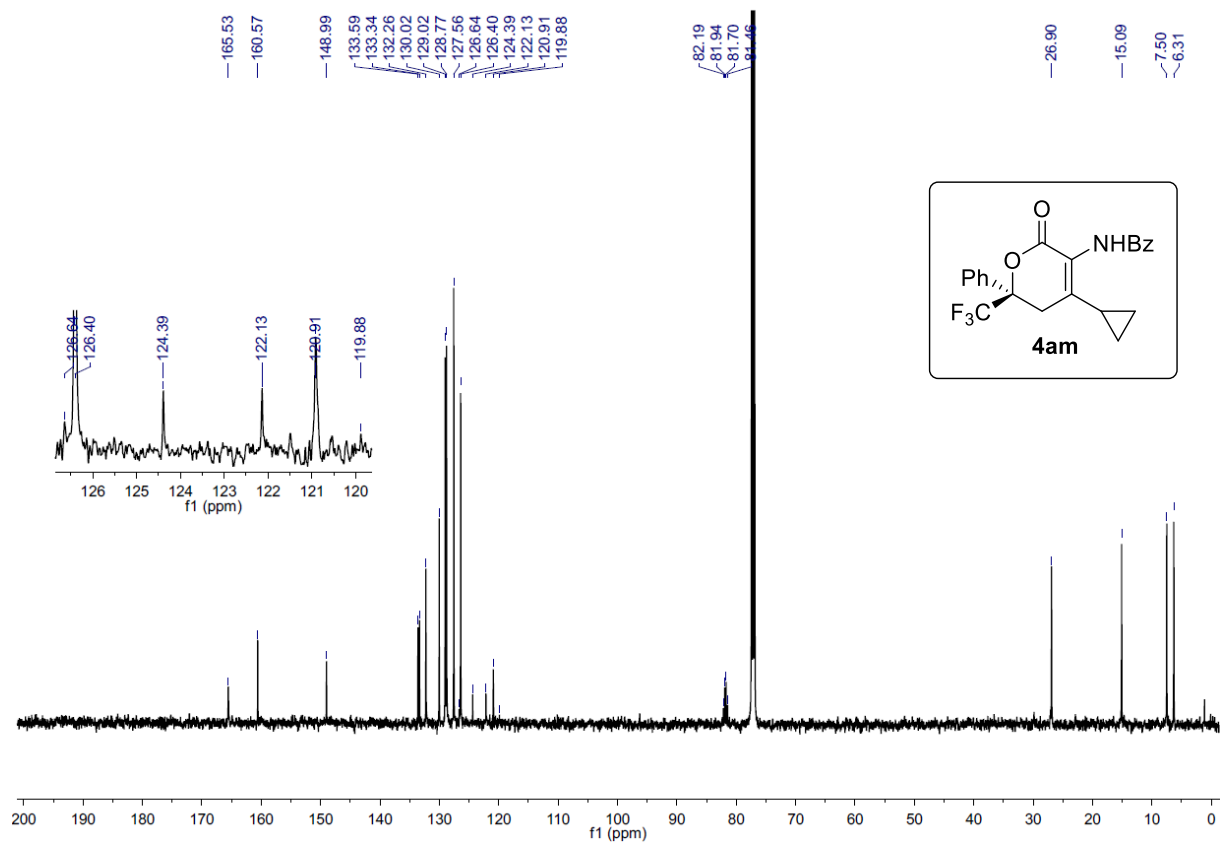


100 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4al** in CDCl_3

(xiii) (*R*)-*N*-(4-cyclopropyl-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4am**)

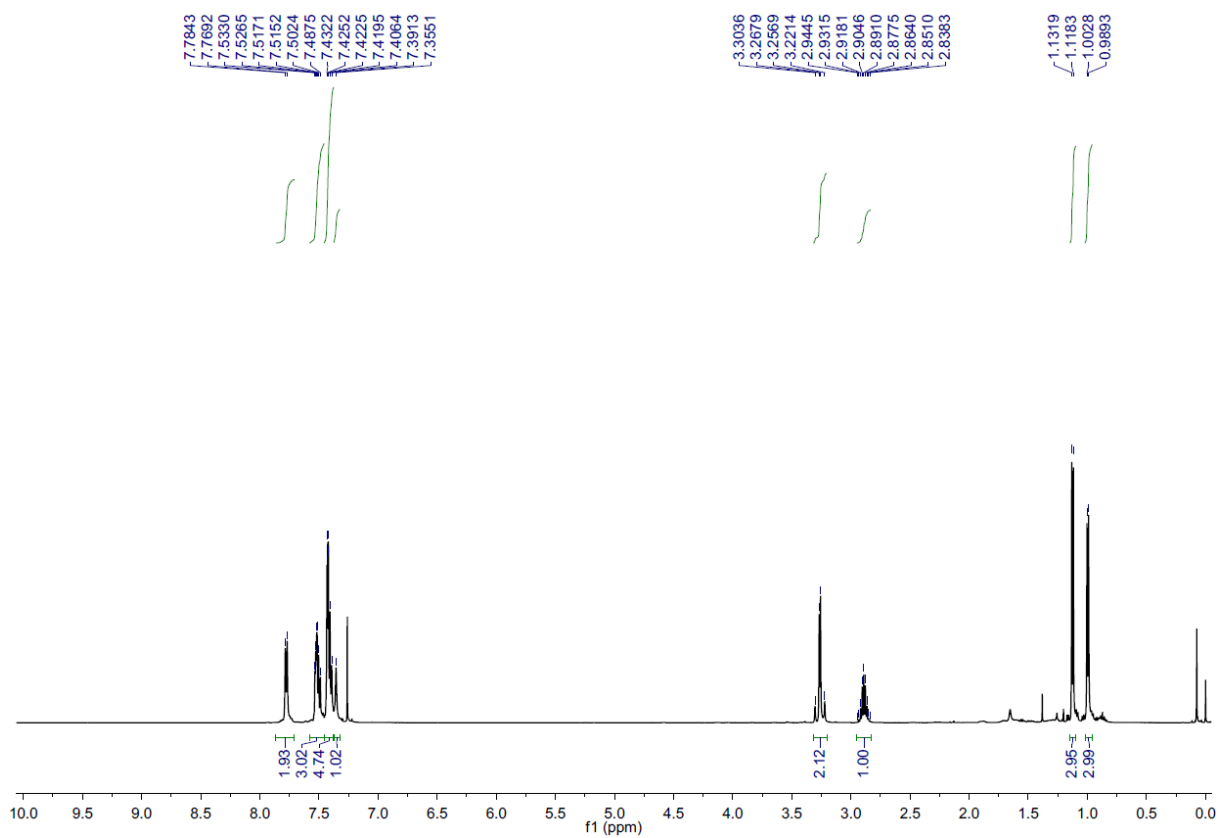
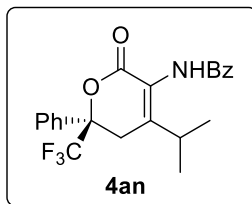


500 MHz ^1H NMR spectrum of compound **4am** in CDCl_3

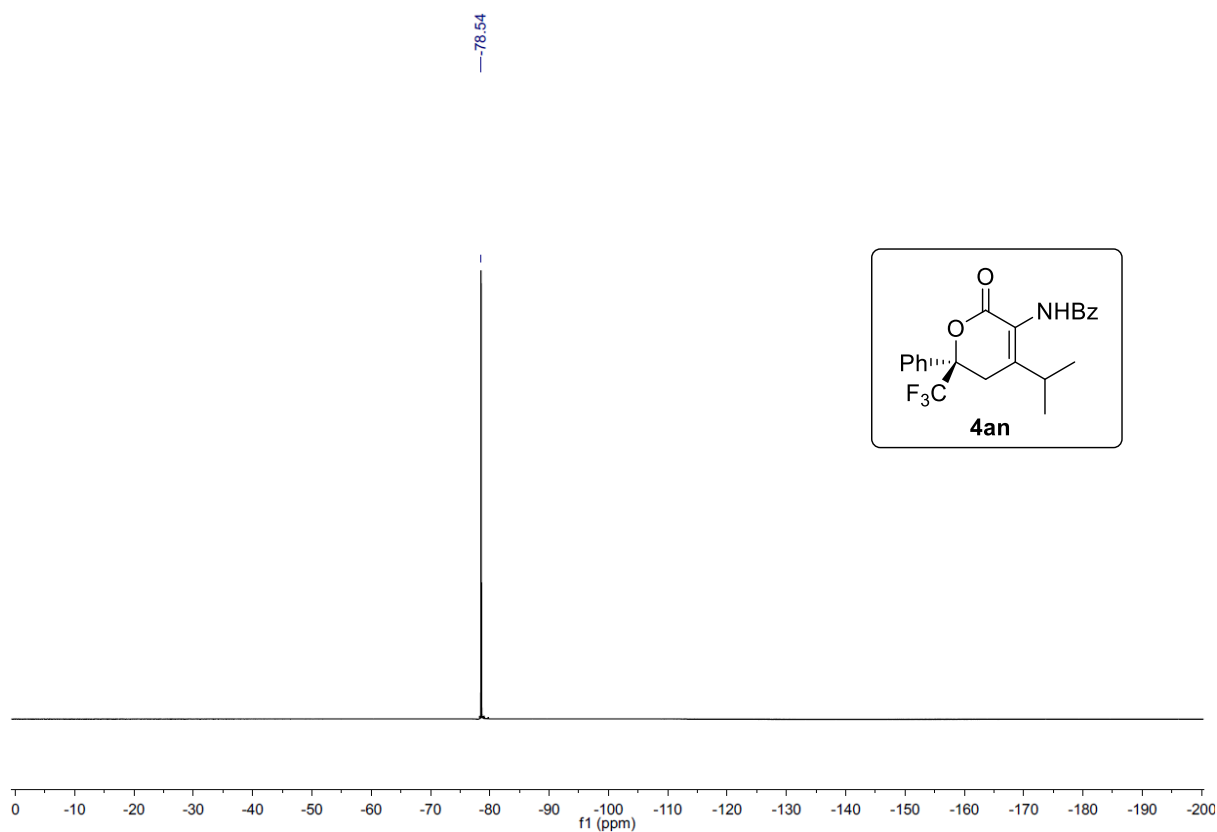
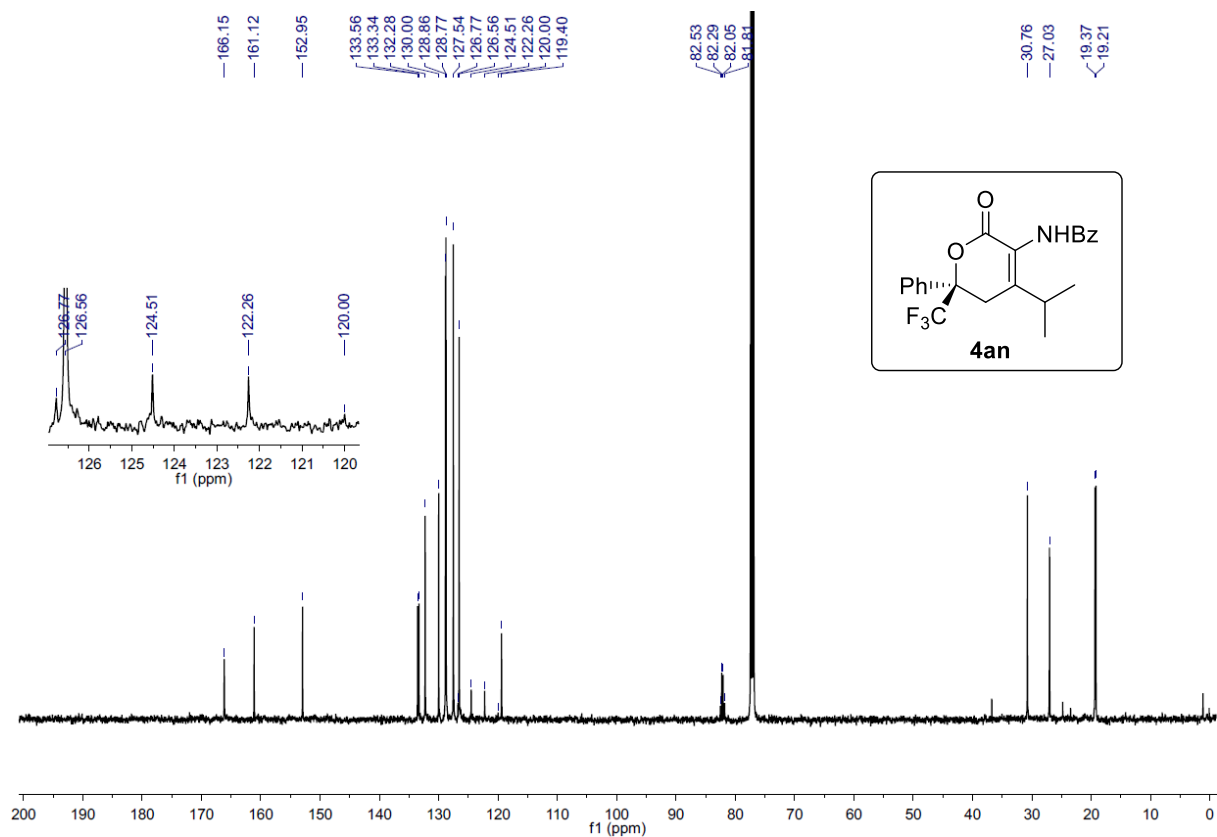


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4am** in CDCl_3

- (xiv) (*R*)-*N*-(4-isopropyl-2-oxo-6-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4an**)

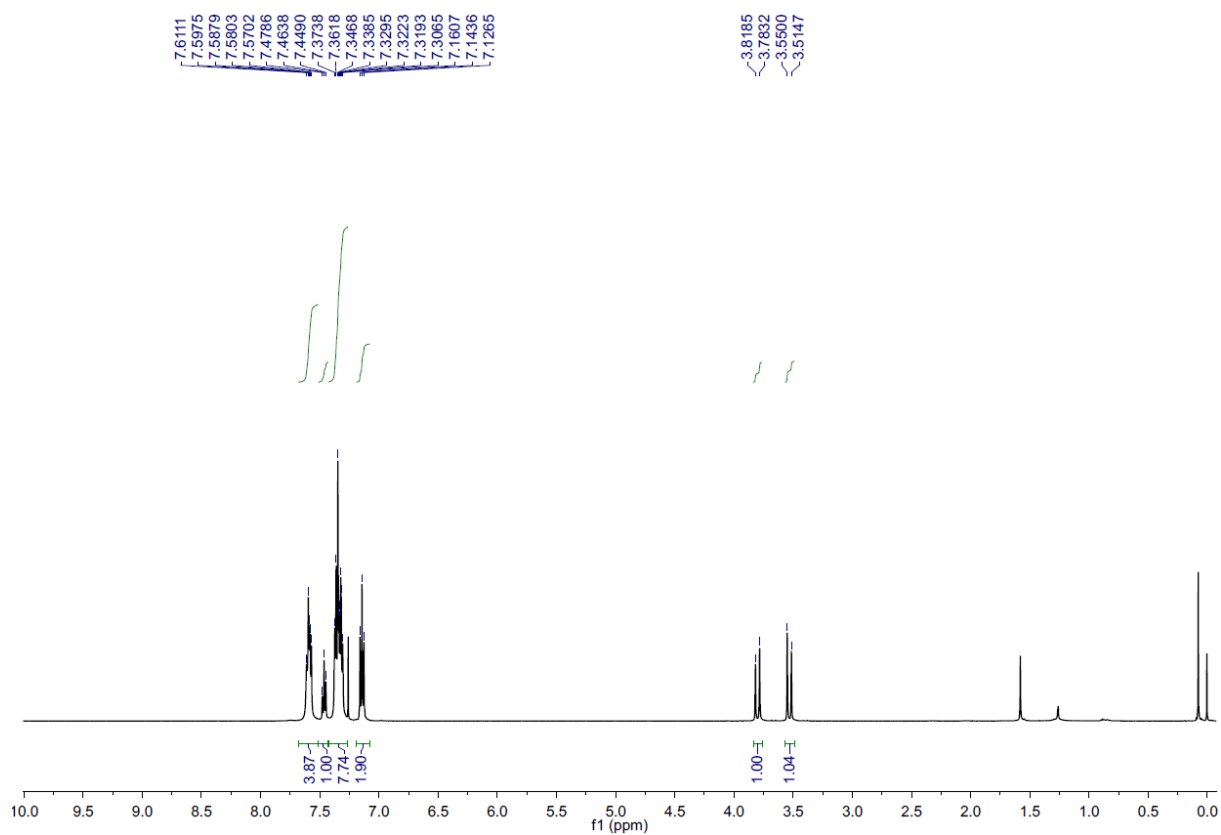
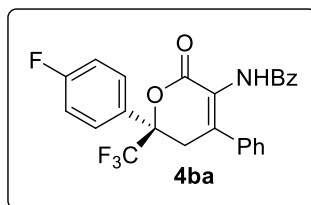


500 MHz ^1H NMR spectrum of compound **4an** in CDCl_3

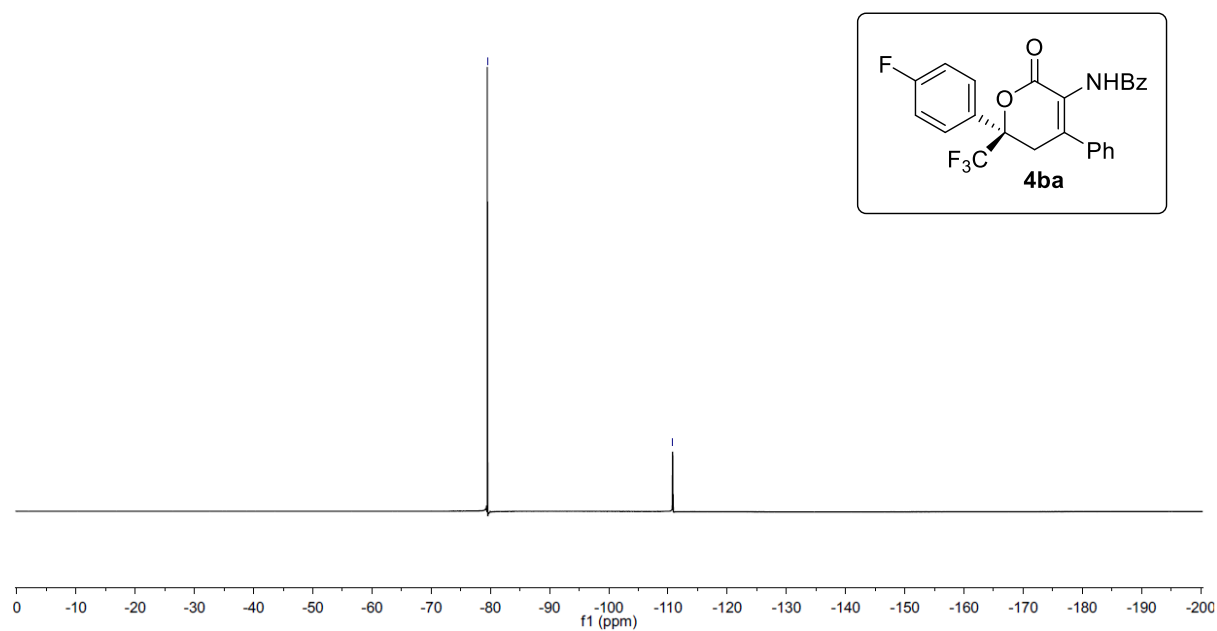
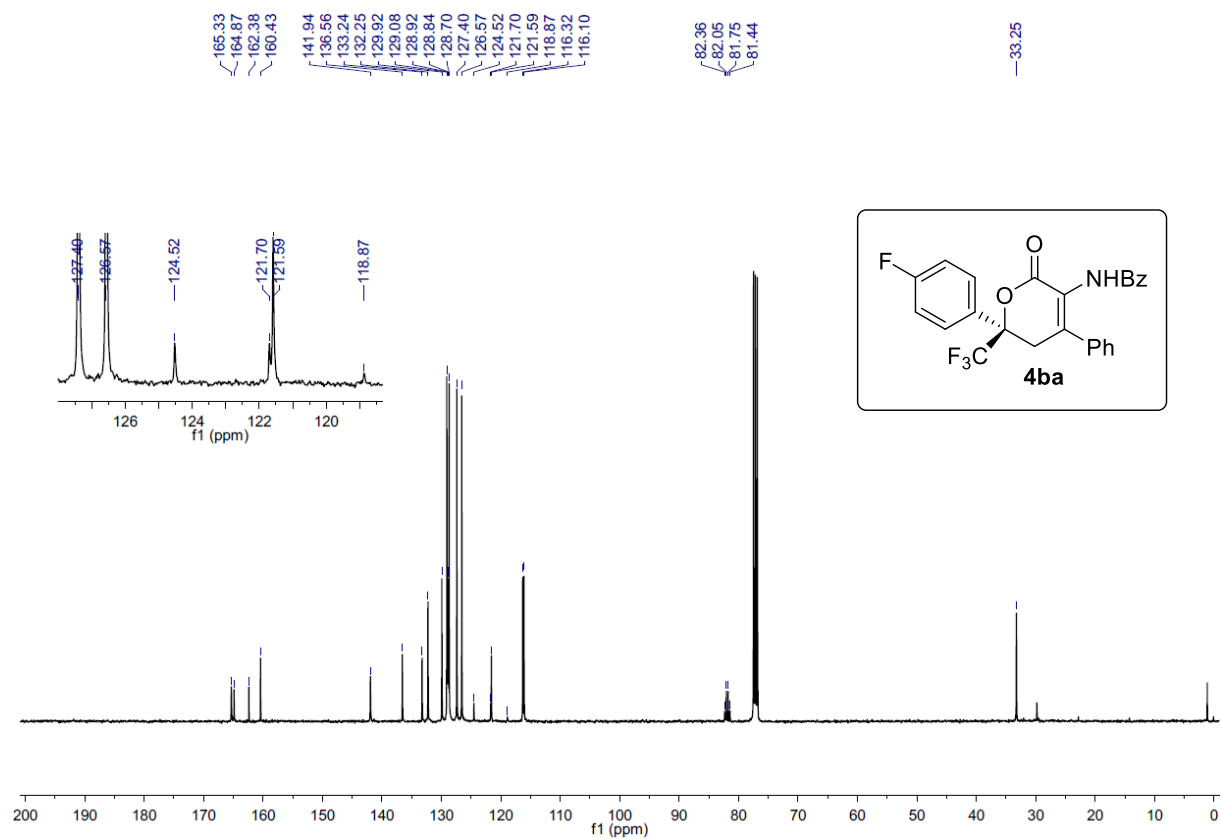


125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4an** in CDCl₃

(xv) **(*R*)-*N*-(6-(4-fluorophenyl)-2-oxo-4-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ba)**

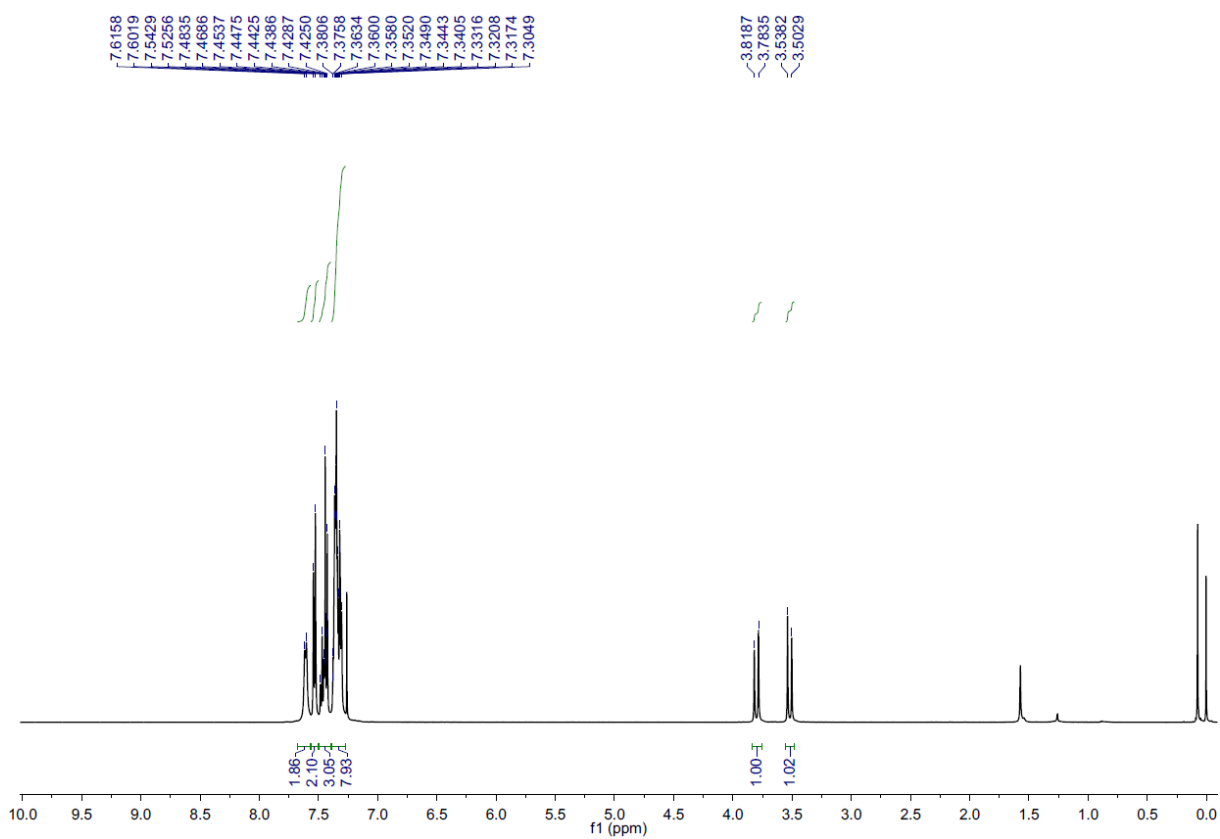
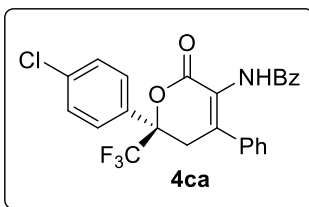


500 MHz ^1H NMR spectrum of compound **4ba** in CDCl_3

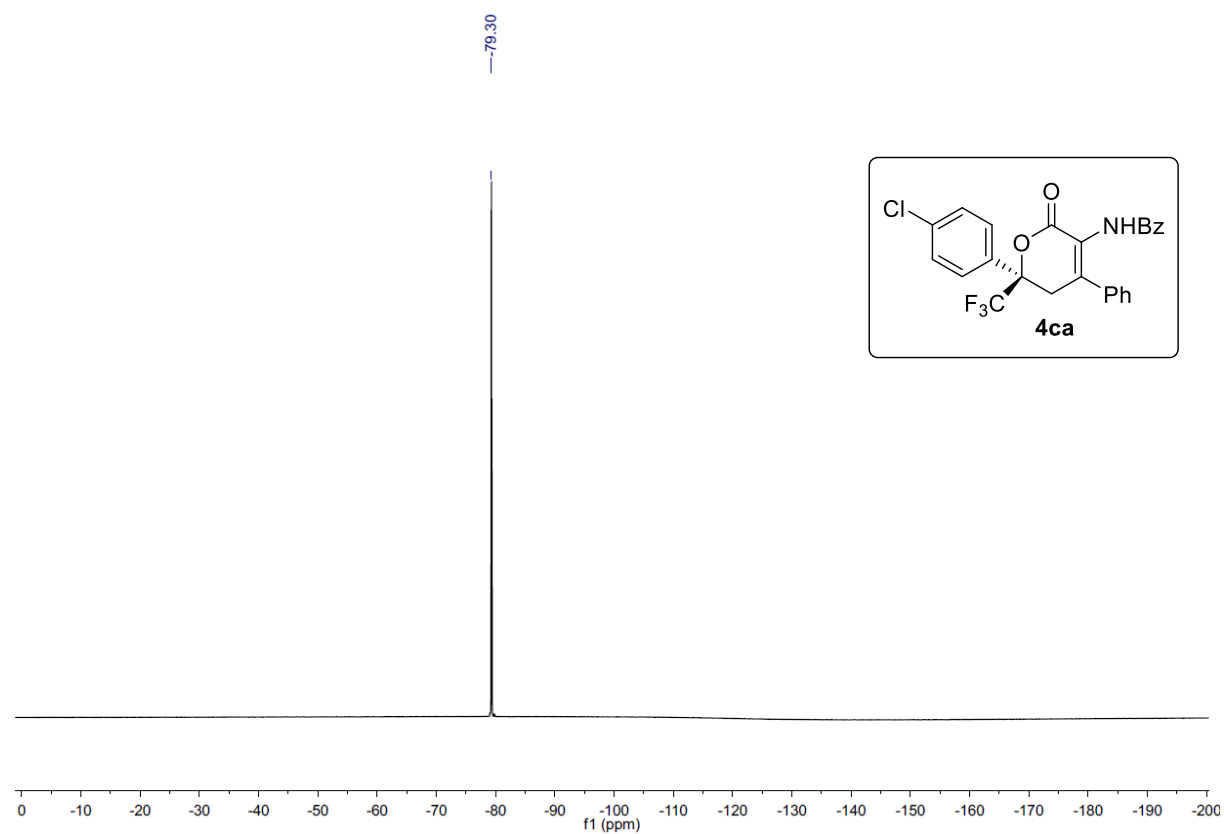
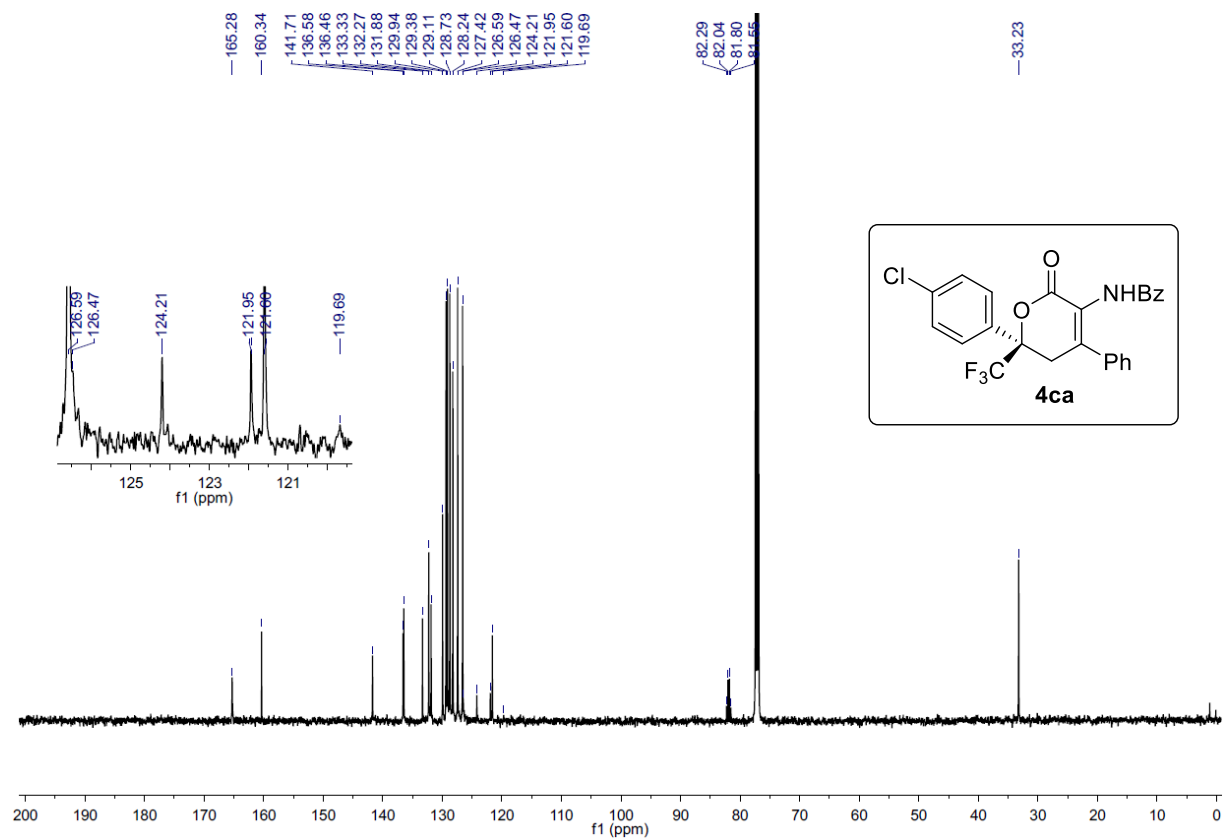


100 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ba** in CDCl_3

(xvi) **(*R*)-*N*-(6-(4-chlorophenyl)-2-oxo-4-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ca)**

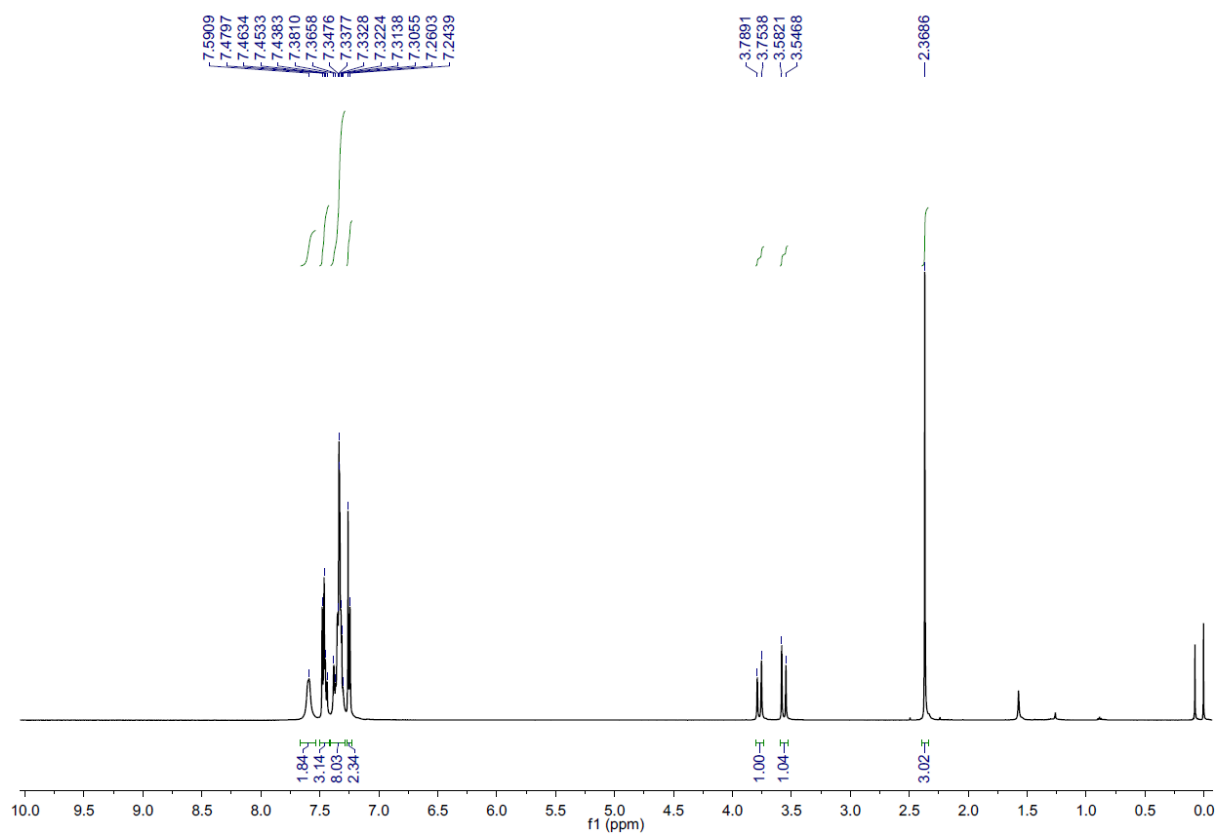
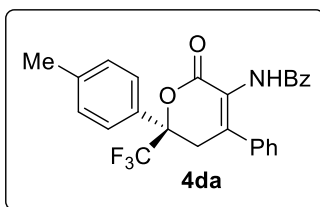


500 MHz ^1H NMR spectrum of compound **4ca** in CDCl_3

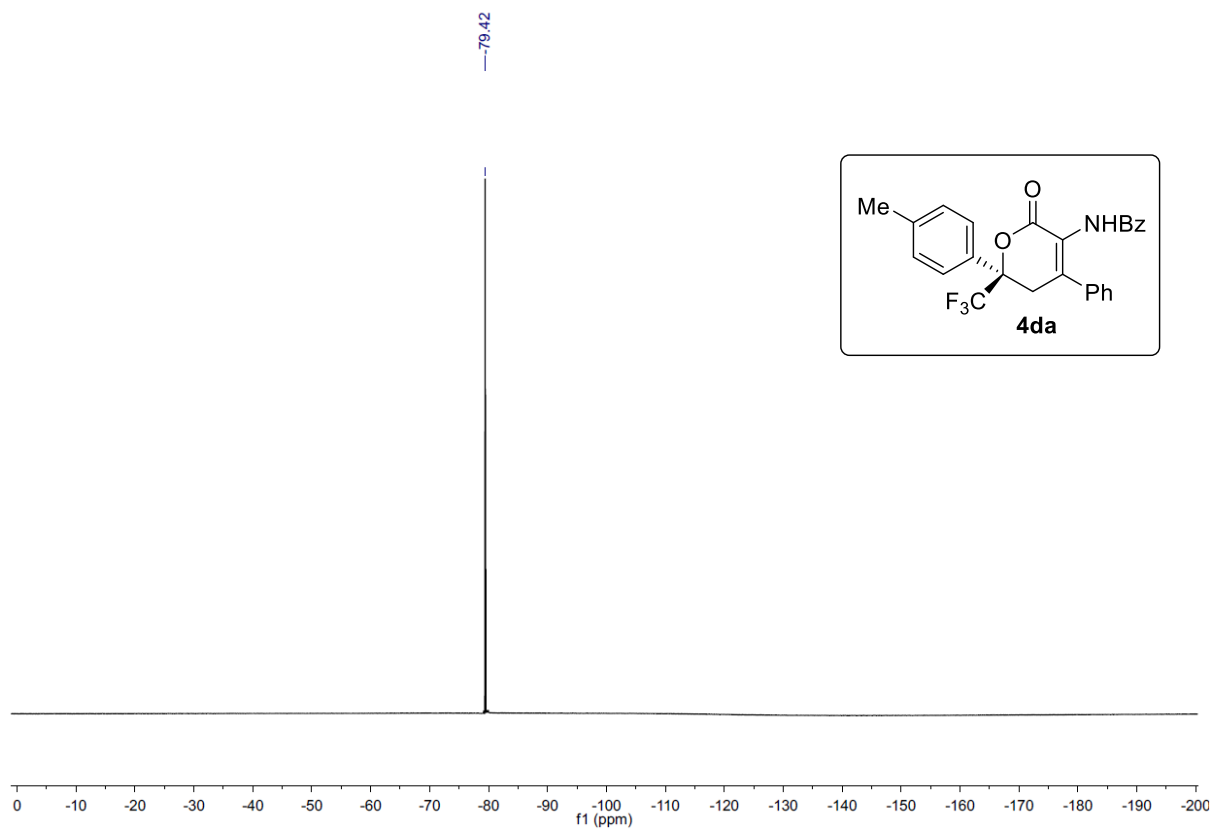
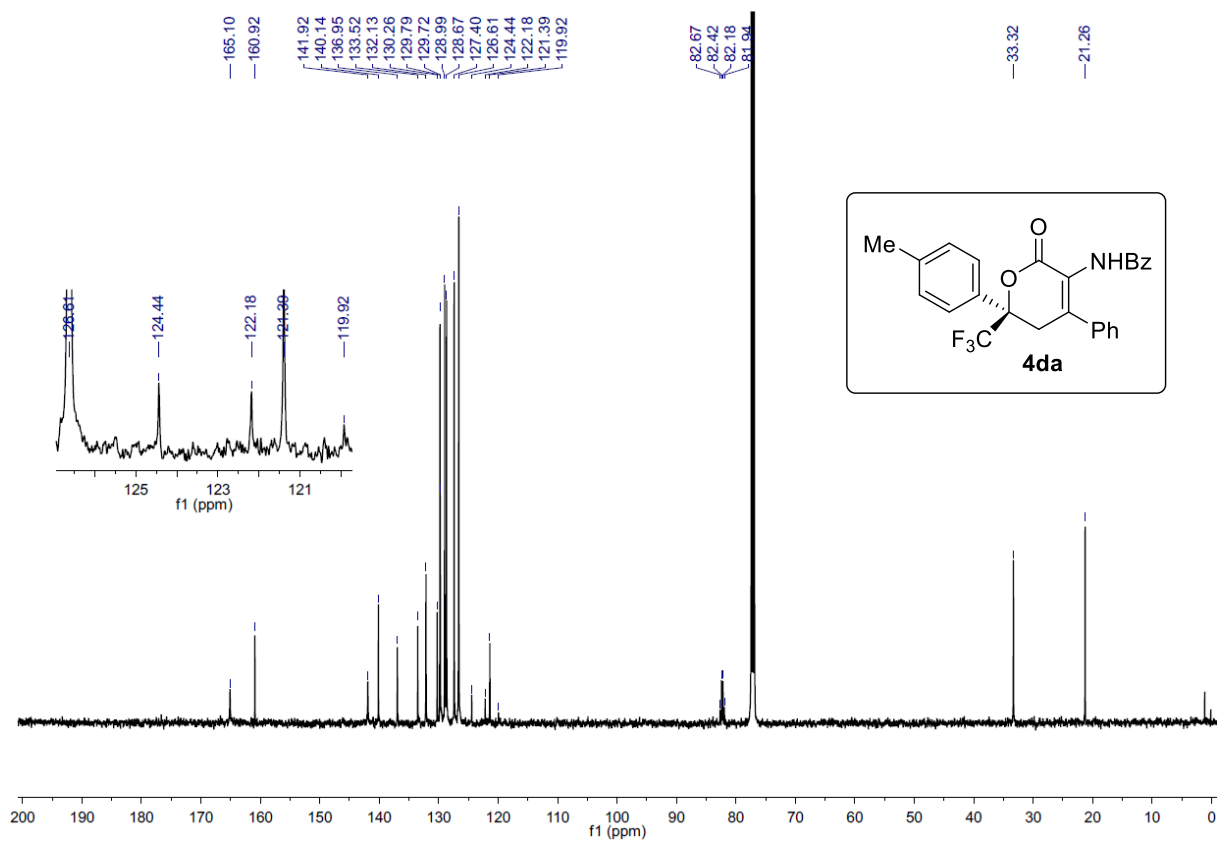


125 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **4ca** in CDCl₃

(xvii) (*R*)-*N*-(2-oxo-4-phenyl-6-(*p*-tolyl)-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4da**)

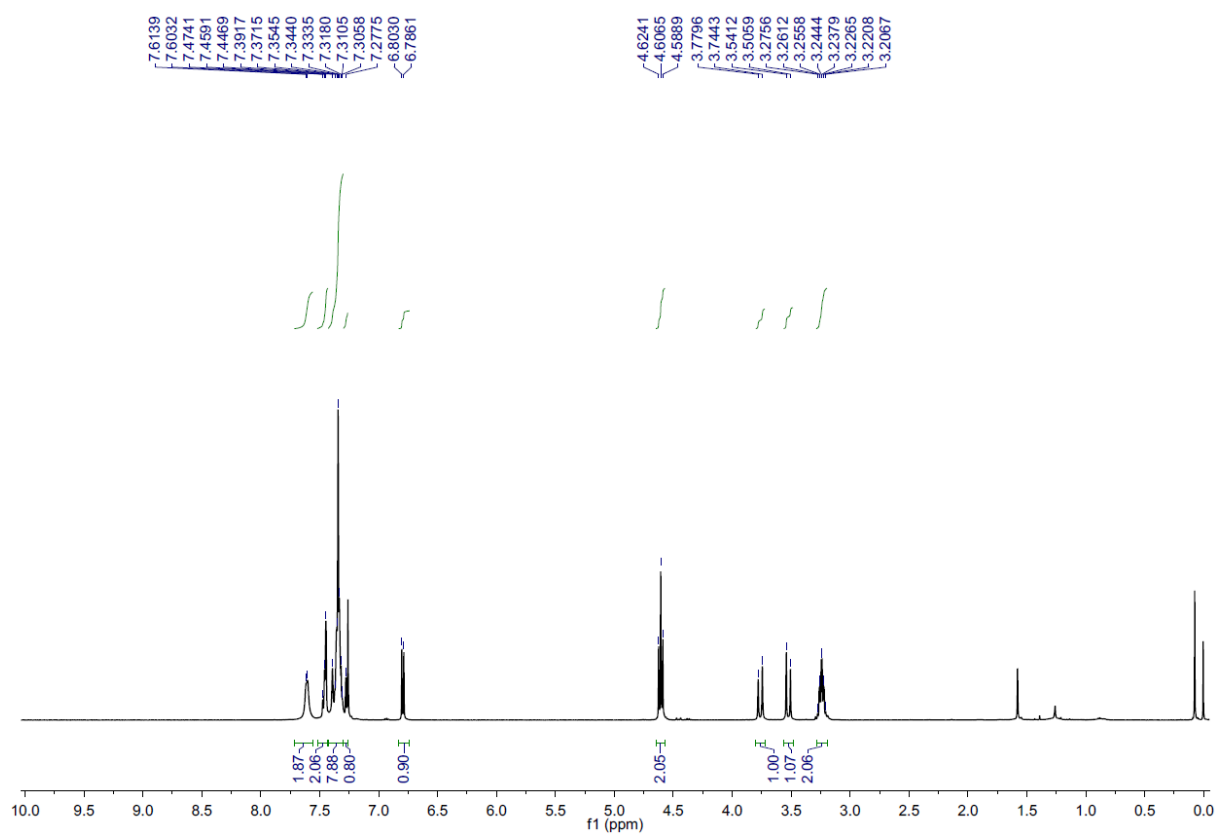
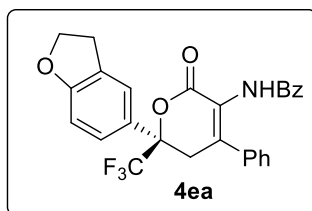


500 MHz ^1H NMR spectrum of compound **4da** in CDCl_3

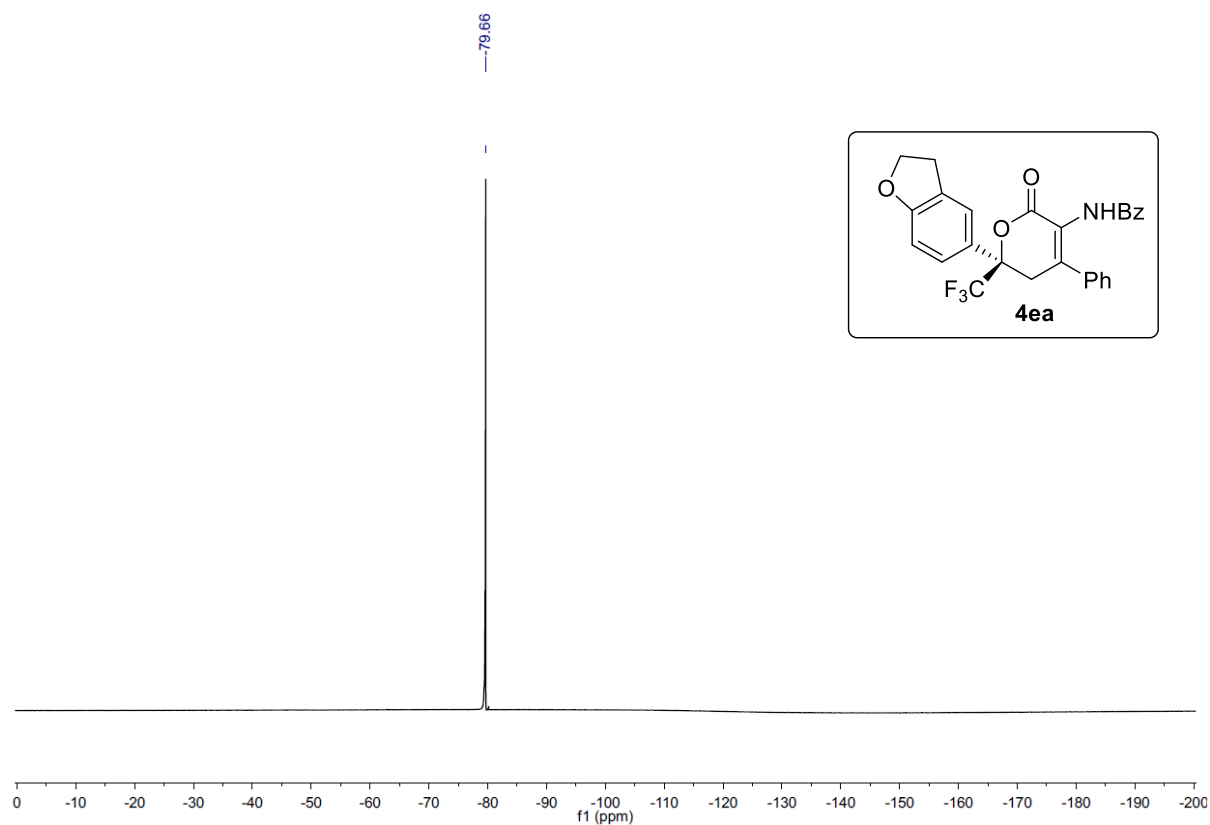
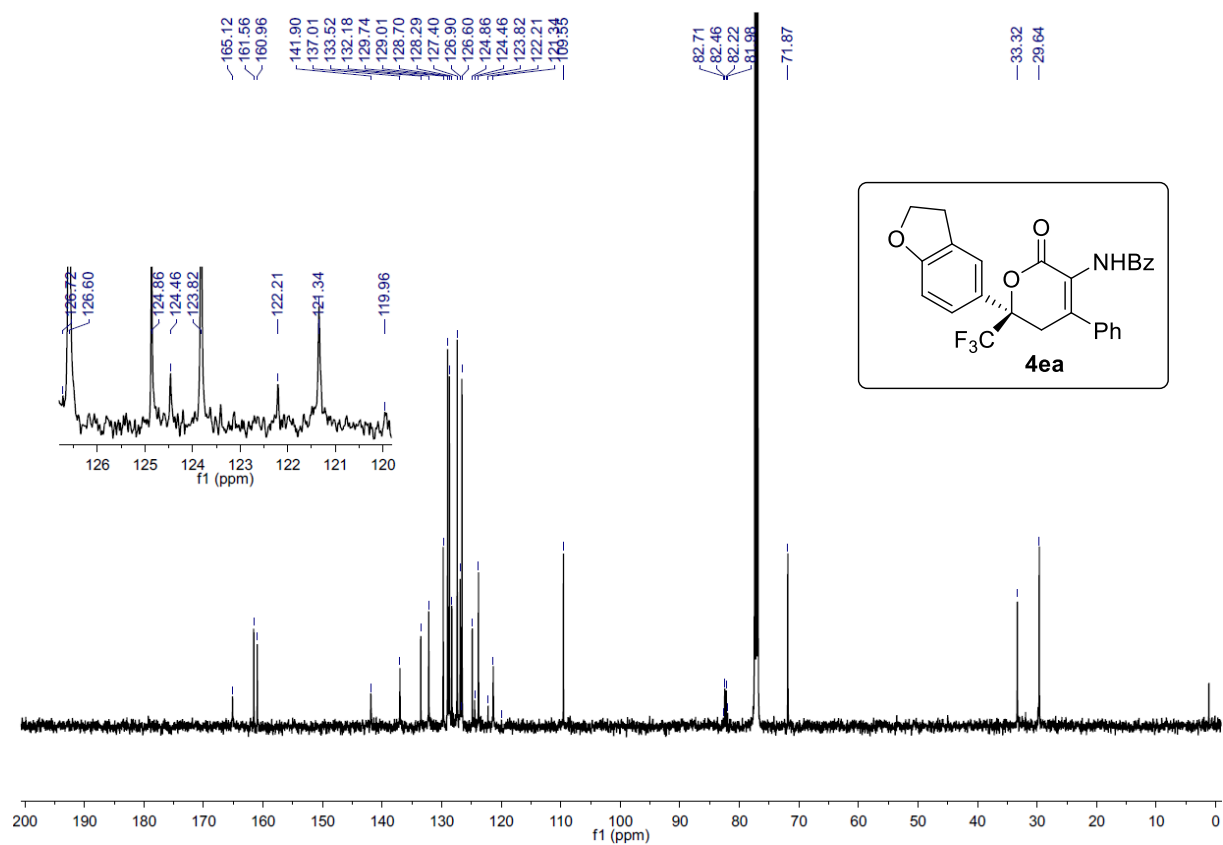


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4da** in CDCl_3

(xviii) (*R*)-*N*-(6-(2,3-dihydrobenzofuran-5-yl)-2-oxo-4-phenyl-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (**4ea**)

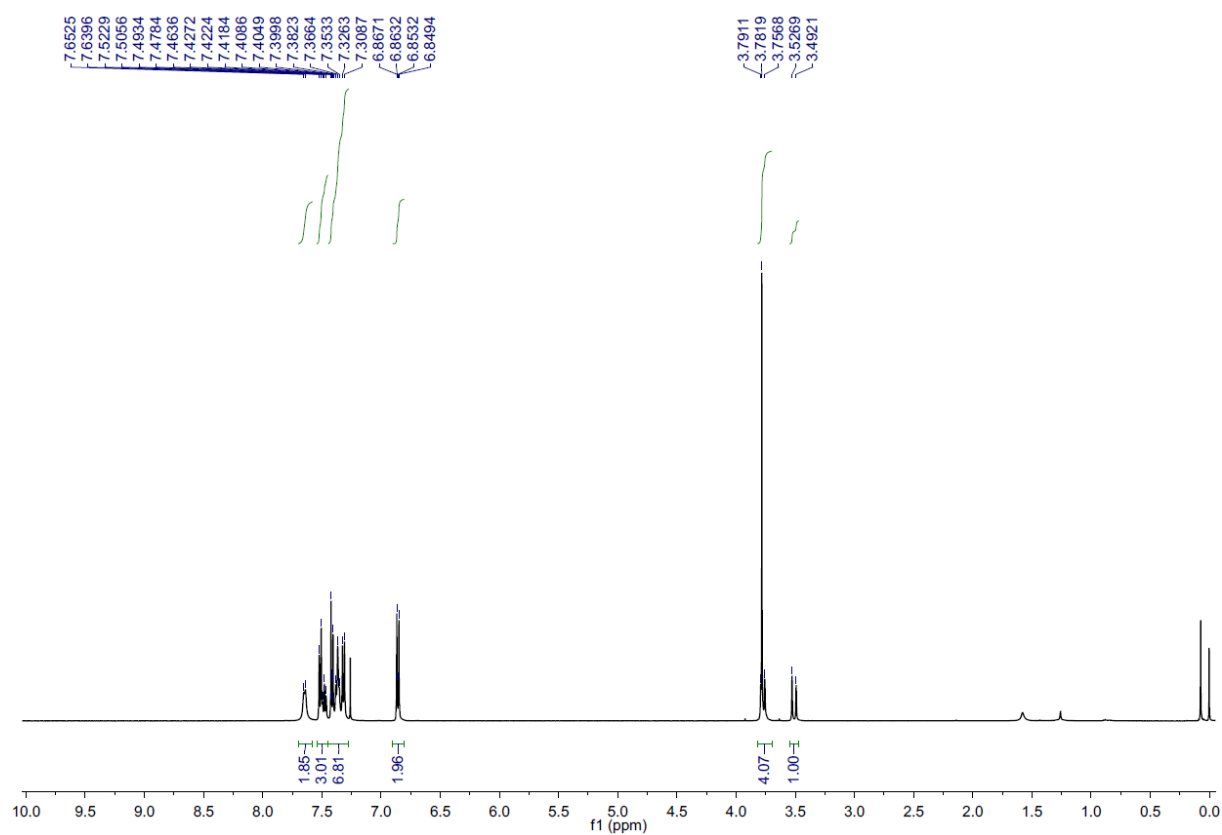
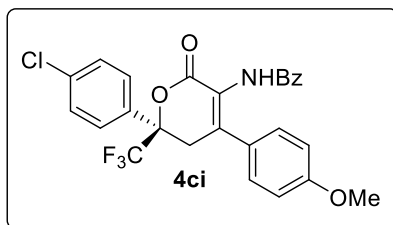


500 MHz ^1H NMR spectrum of compound **4ea** in CDCl_3

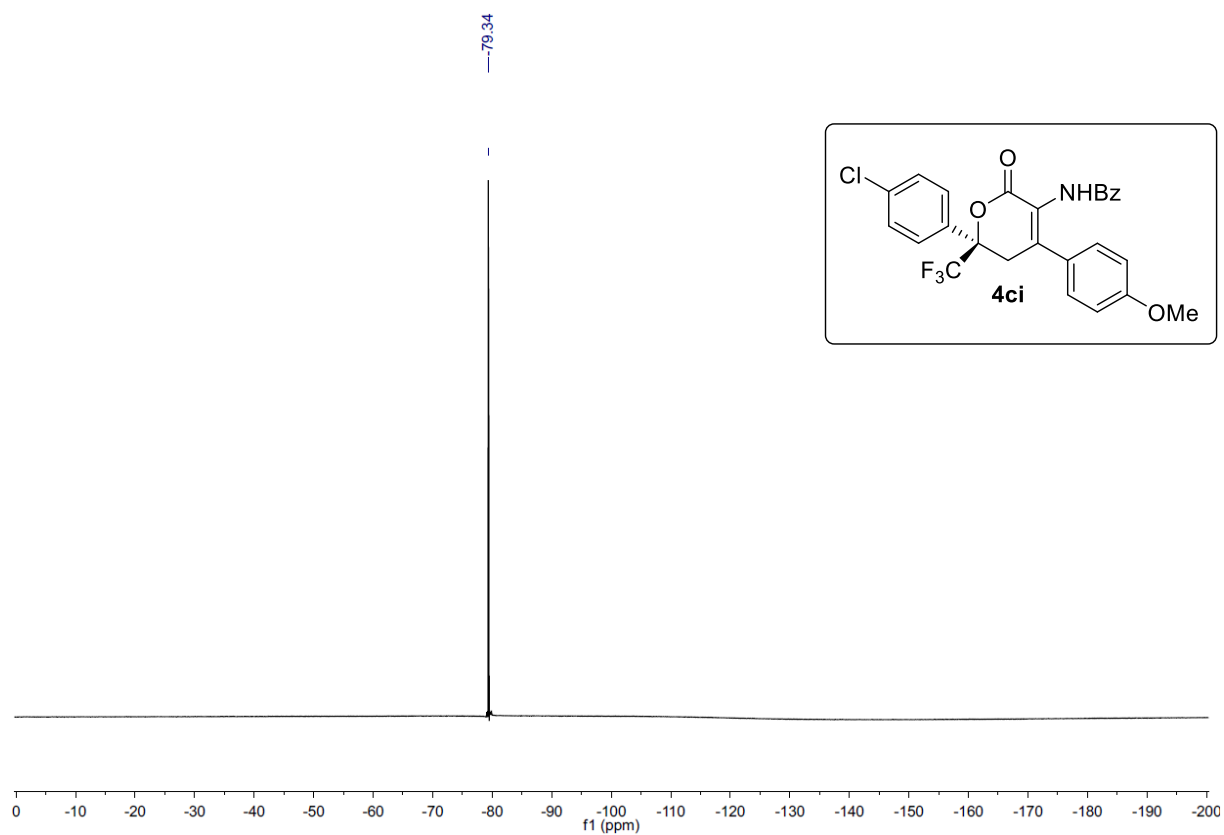
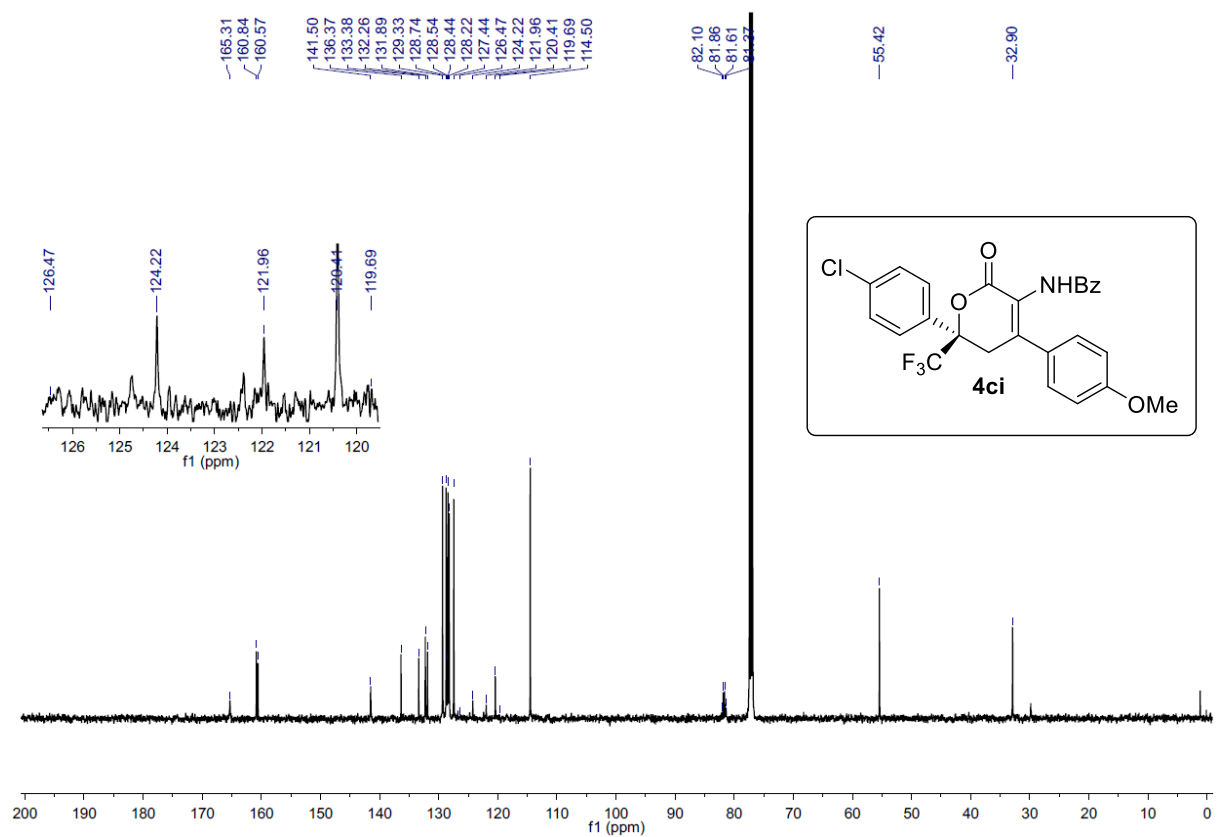


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ea** in CDCl_3

(xix) **(*R*)-*N*-(6-(4-chlorophenyl)-4-(4-methoxyphenyl)-2-oxo-6-(trifluoromethyl)-5,6-dihydro-2*H*-pyran-3-yl)benzamide (4ci)**

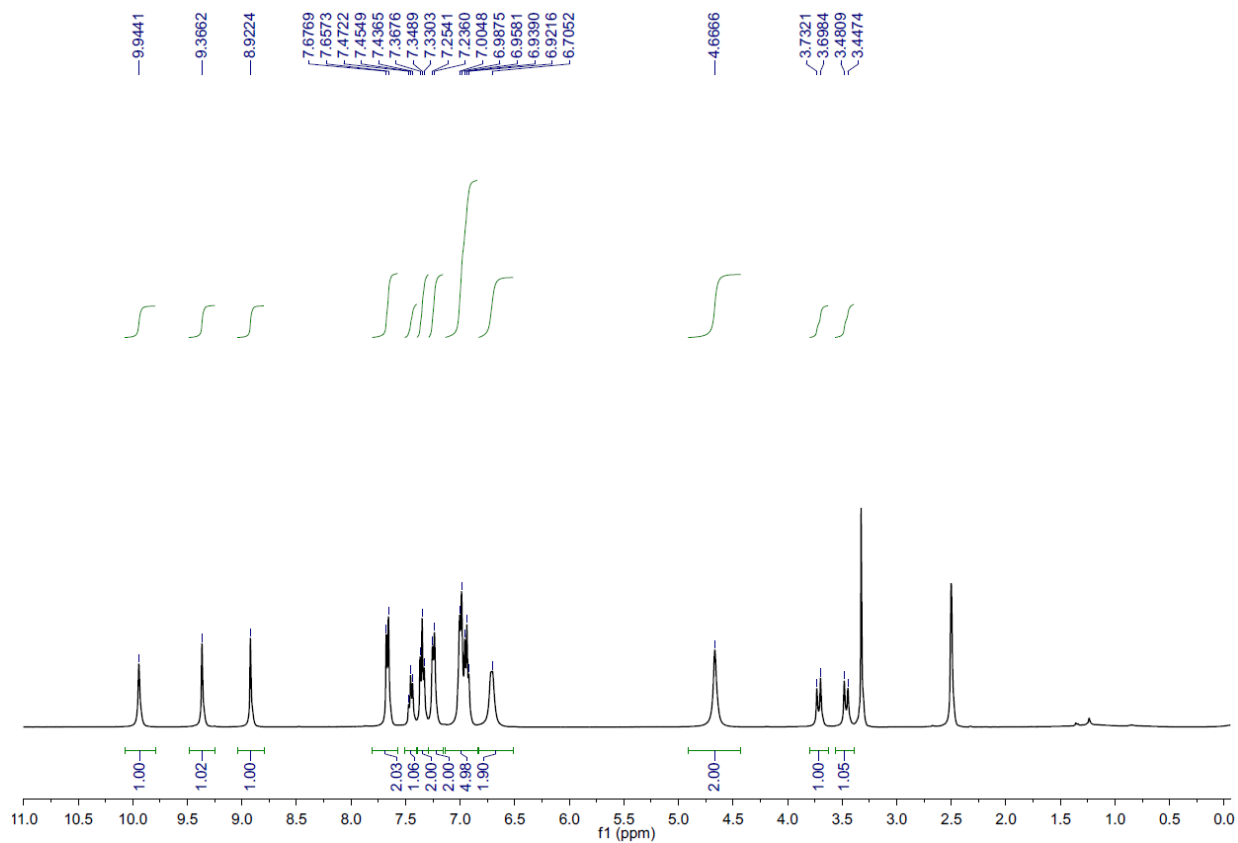
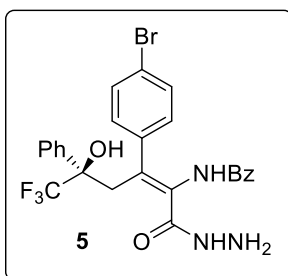


500 MHz ^1H NMR spectrum of compound **4ci** in CDCl_3

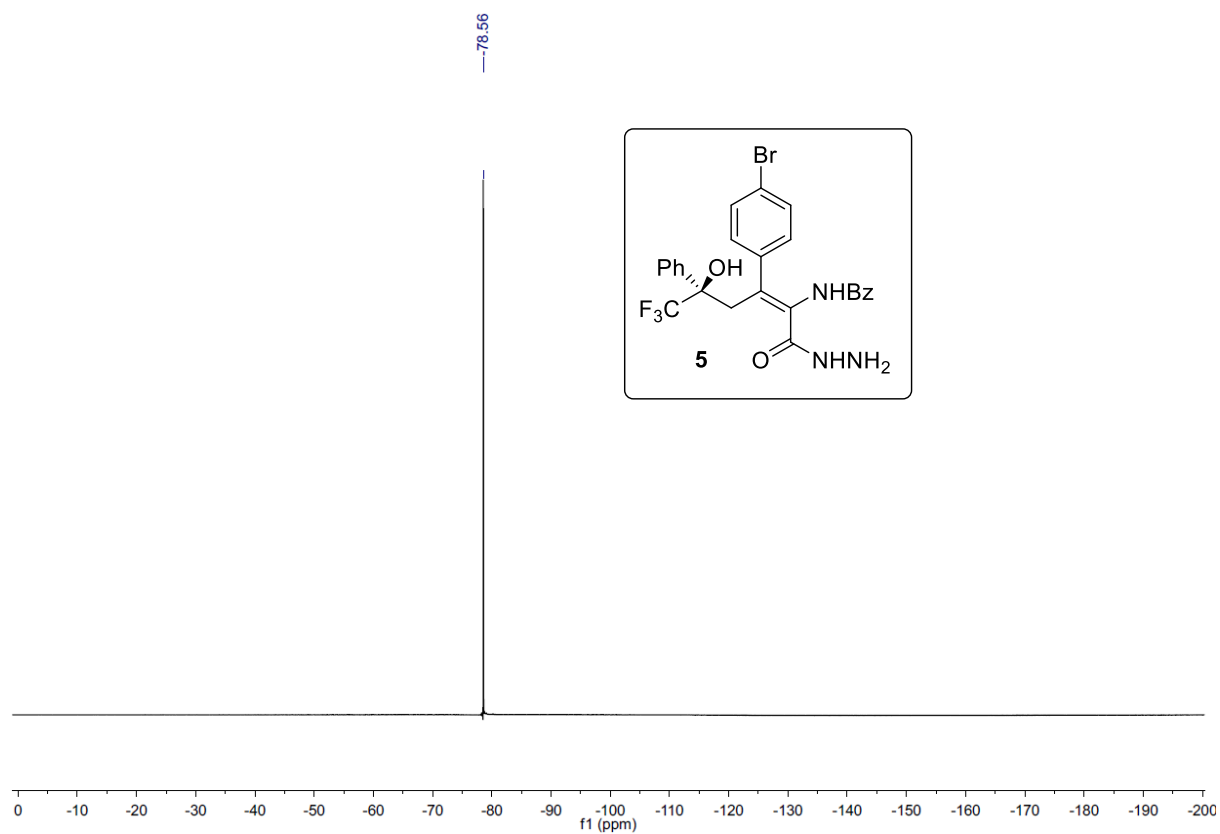
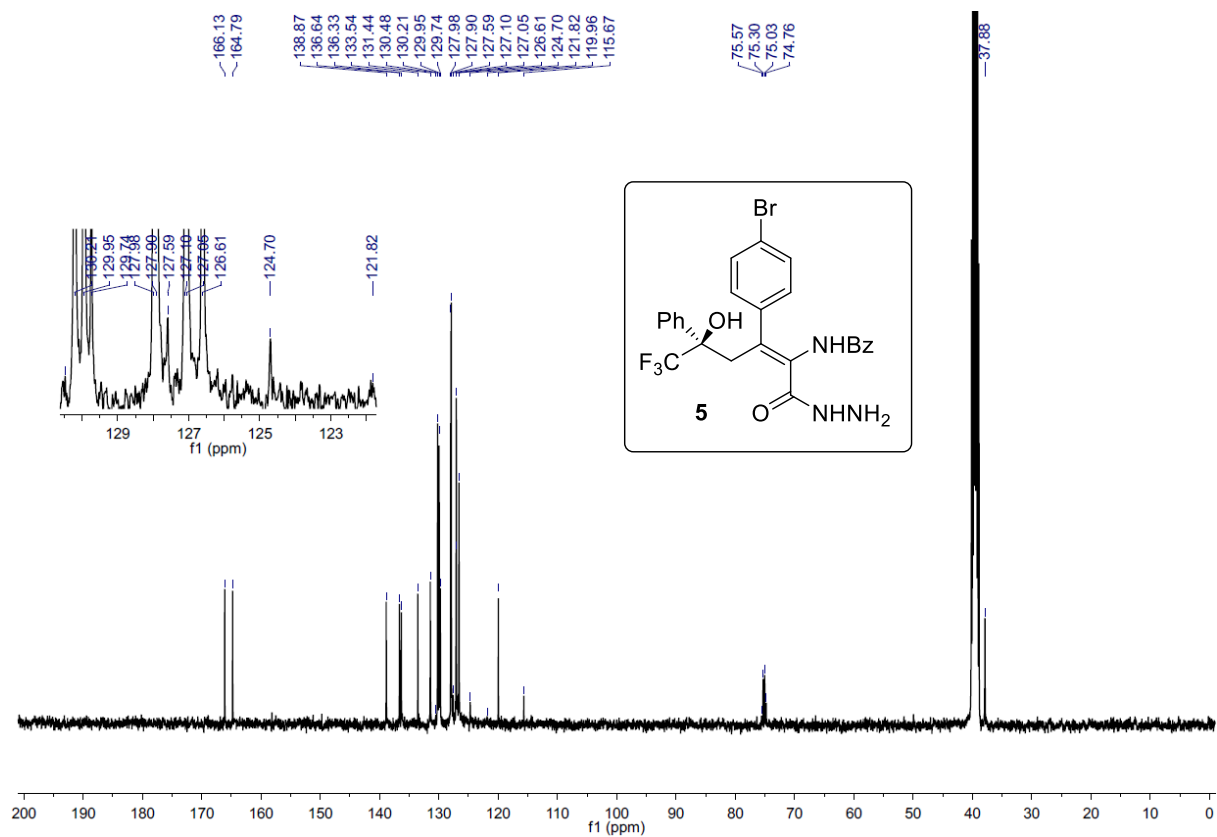


125 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **4ci** in CDCl_3

(xx) **(*R,Z*)-*N*-(3-(4-bromophenyl)-6,6,6-trifluoro-1-hydrazinyl-5-hydroxy-1-oxo-5-phenylhex-2-en-2-yl)benzamide (5)**

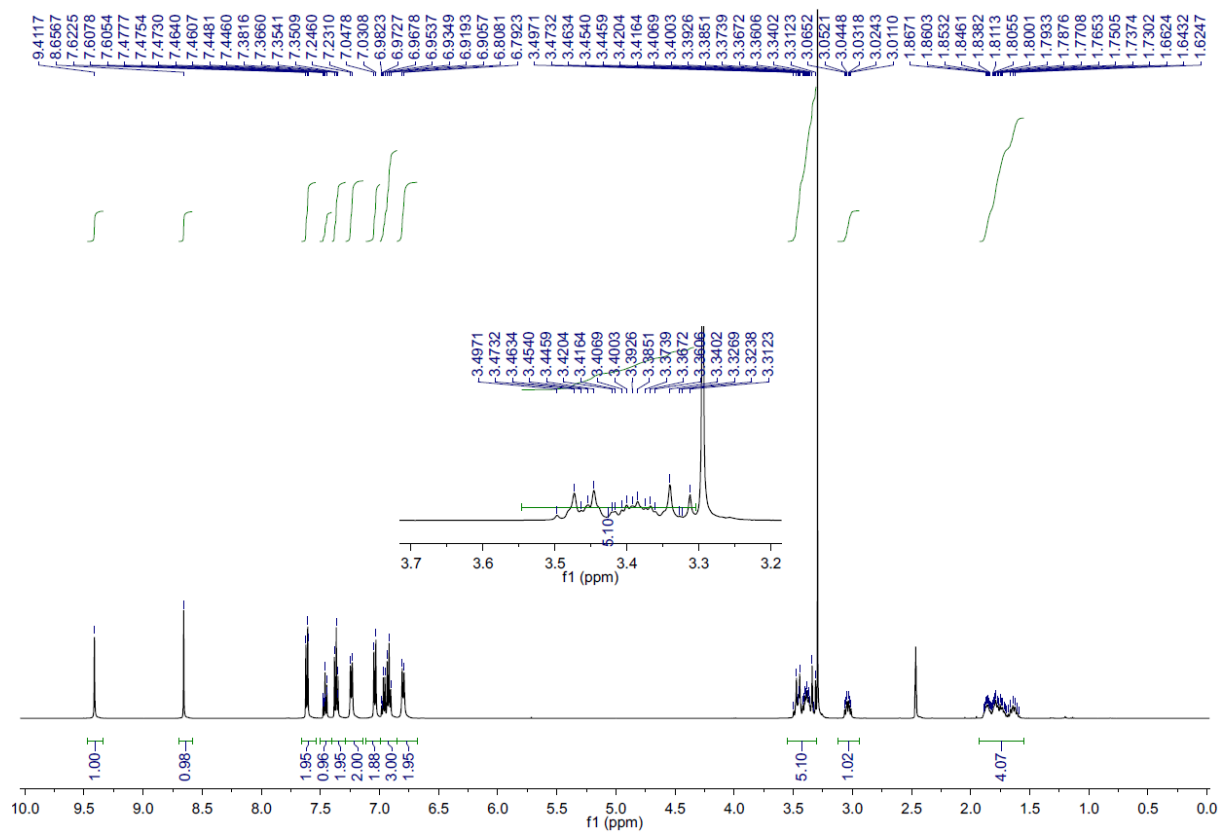
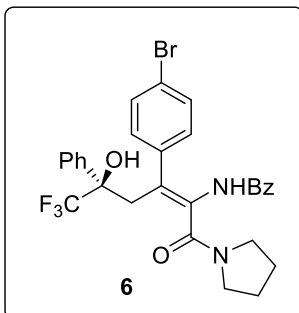


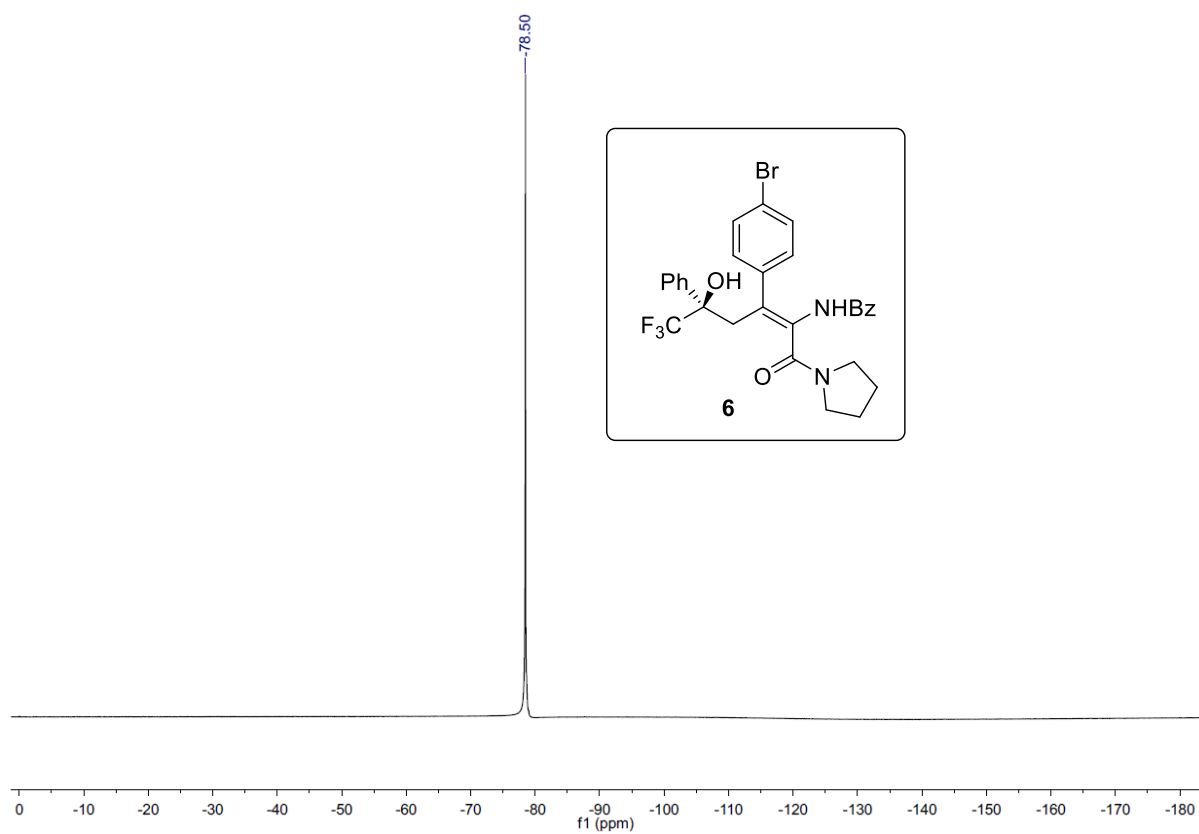
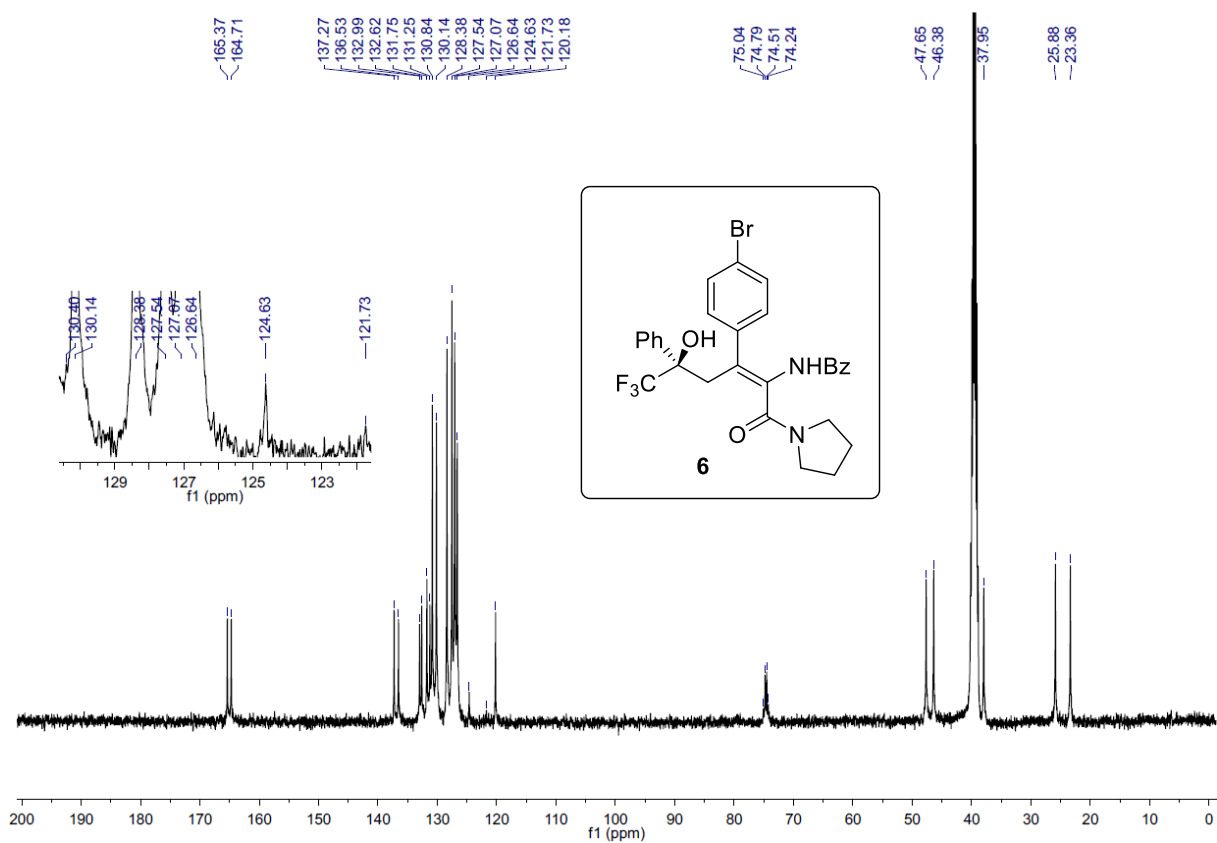
400 MHz ^1H NMR spectrum of compound **5** in $\text{DMSO}-d_6$



100 MHz ^{13}C NMR and 373 MHz ^{19}F NMR spectra of compound **5** in $\text{DMSO-}d_6$

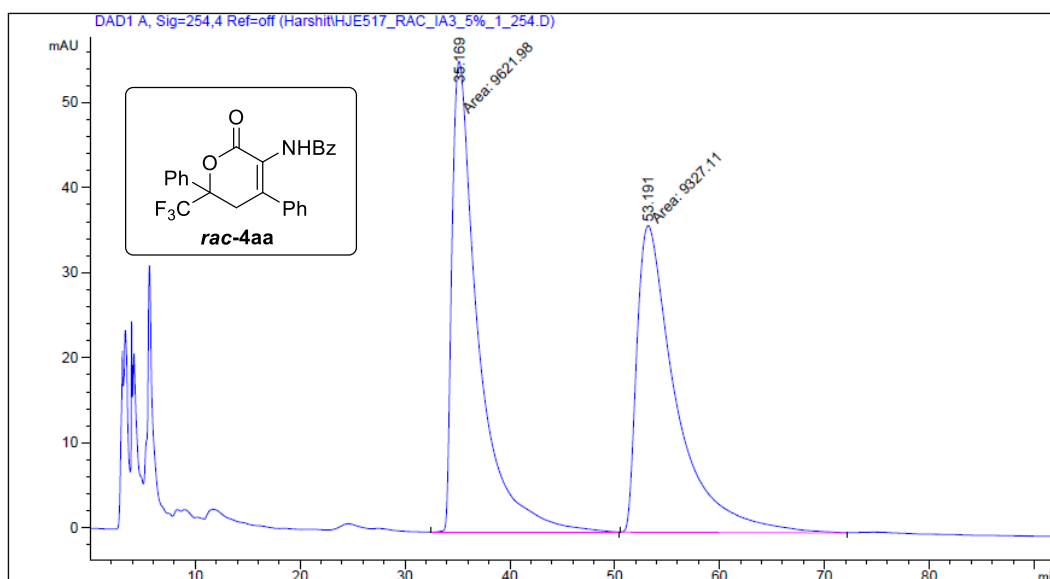
(xxi) **(*R,Z*)-*N*-(3-(4-bromophenyl)-6,6,6-trifluoro-5-hydroxy-1-oxo-5-phenyl-1-(pyrrolidin-1-yl)hex-2-en-2-yl)benzamide (6)**



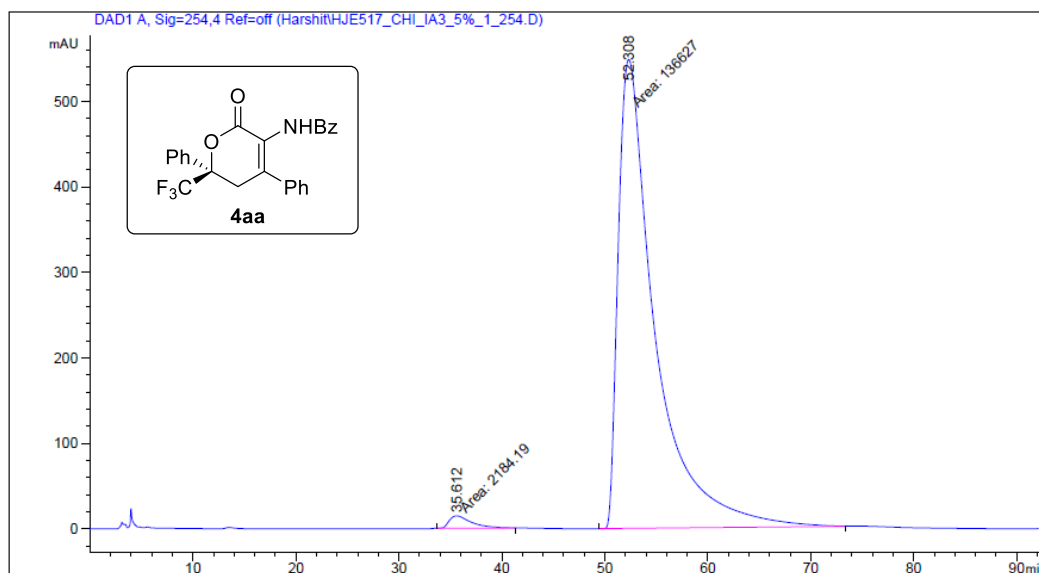


100 MHz ¹³C NMR and 373 MHz ¹⁹F NMR spectra of compound **6** in DMSO-*d*₆

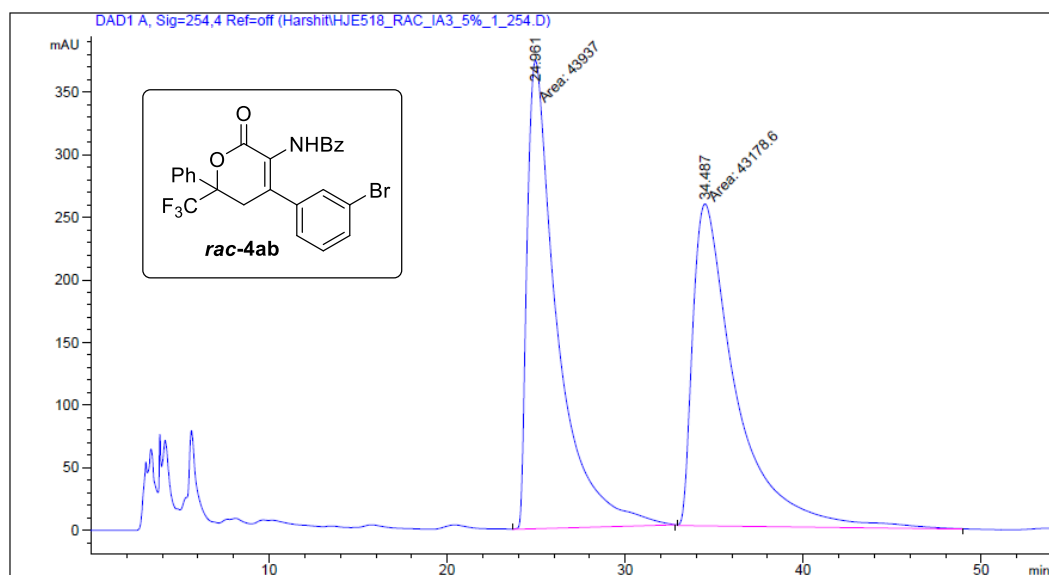
5. HPLC graphs:



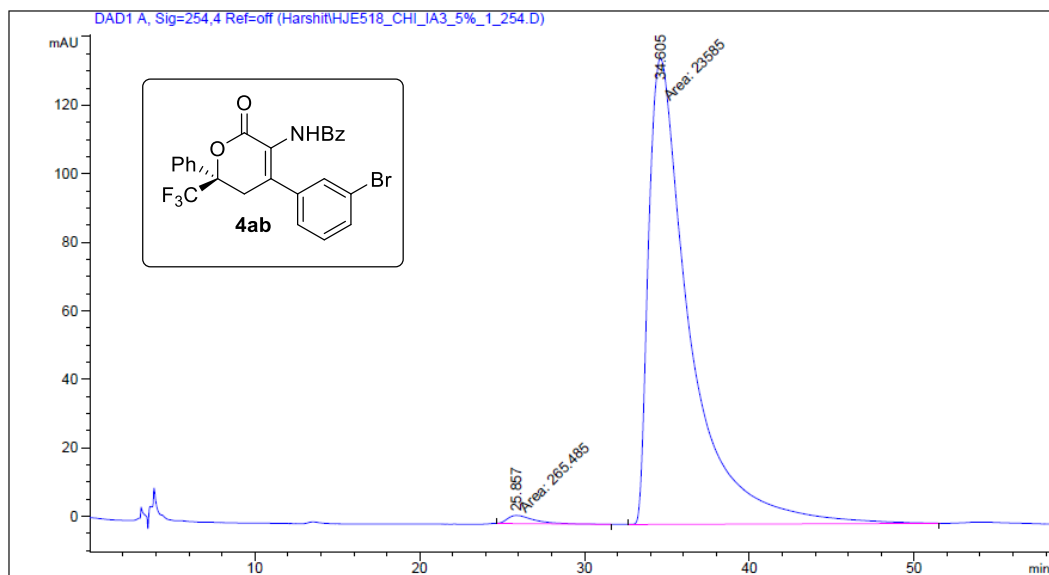
HPLC graph of racemic **4aa**



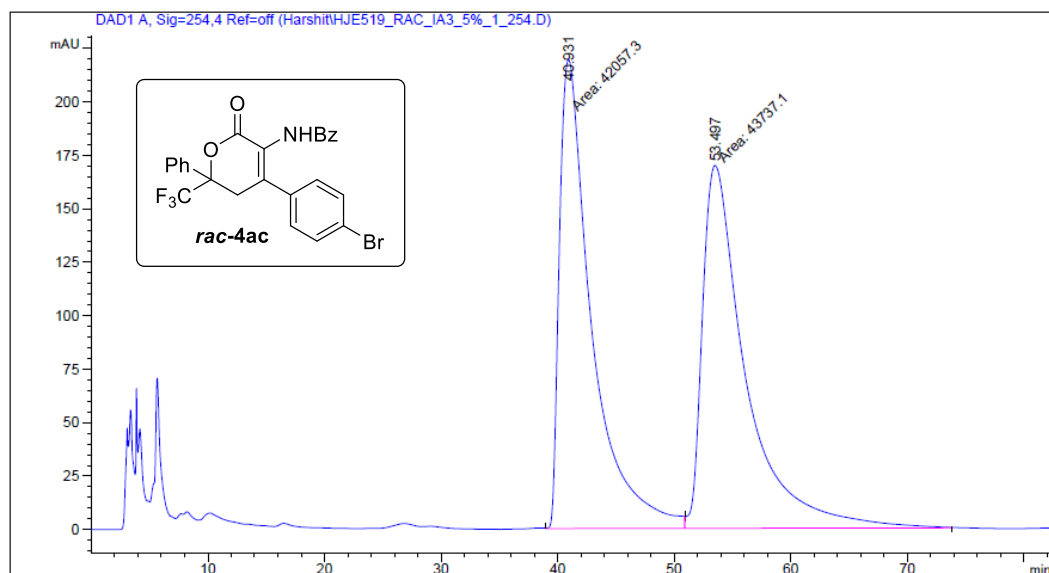
HPLC graph of enantioenriched **4aa**



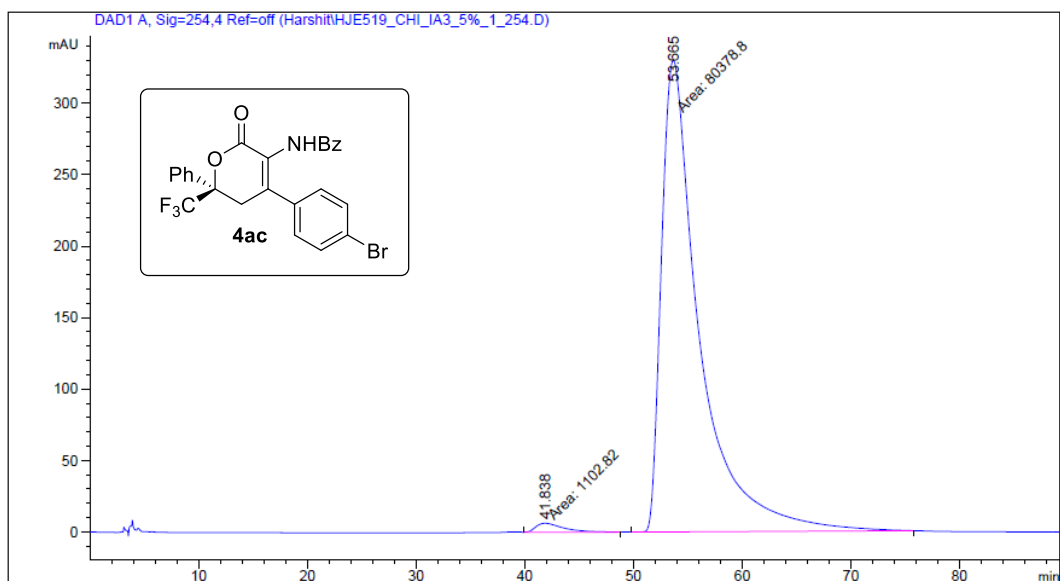
HPLC graph of racemic **4ab**



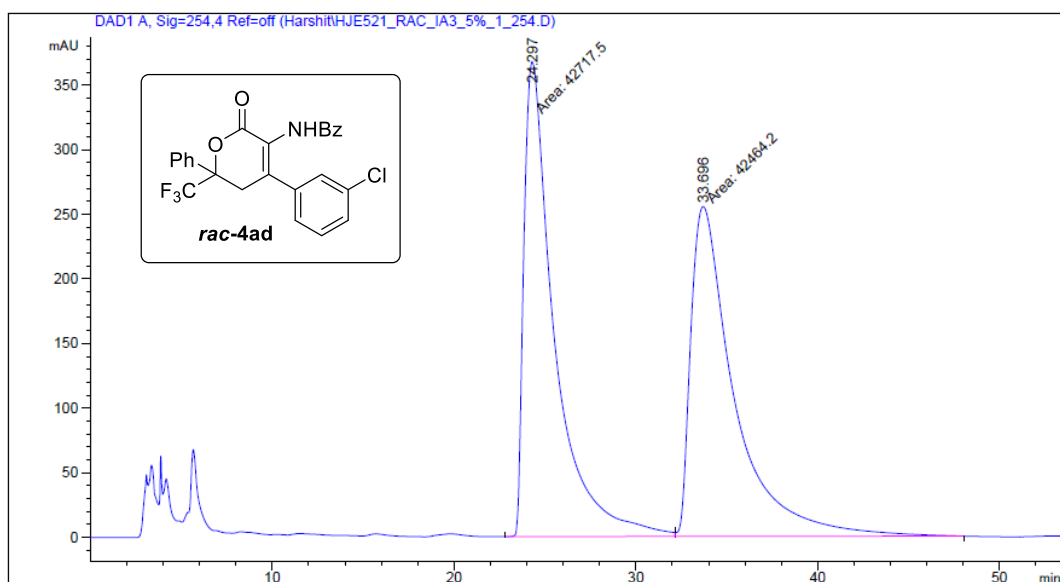
HPLC graph of enantioenriched **4ab**



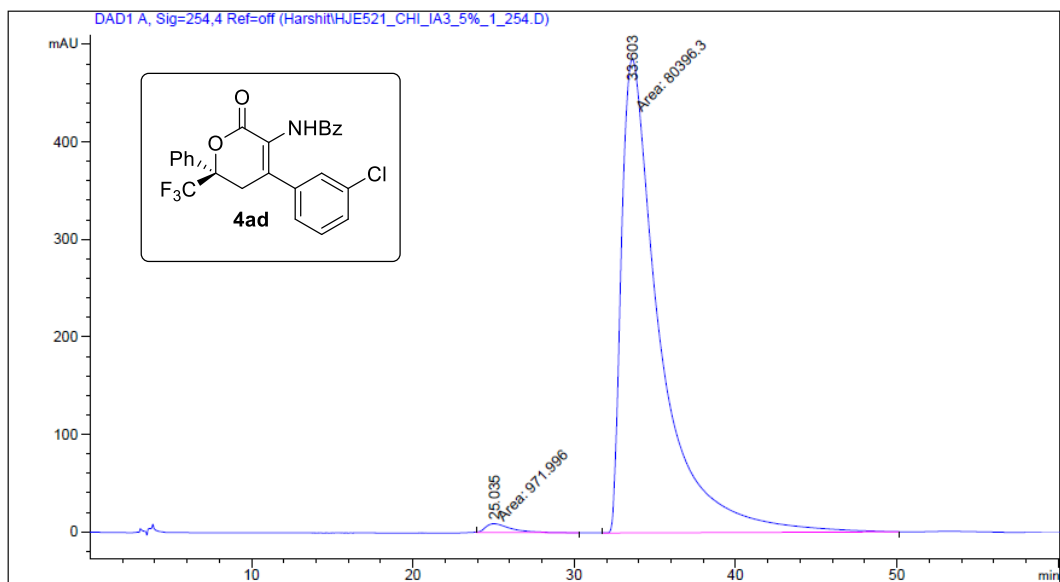
HPLC graph of racemic **4ac**



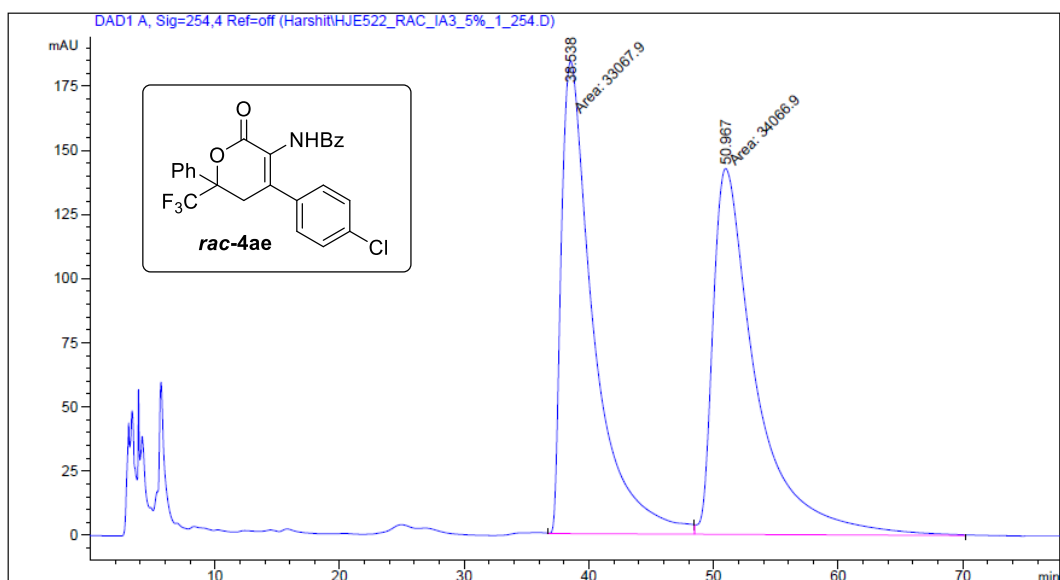
HPLC graph of enantioenriched **4ac**



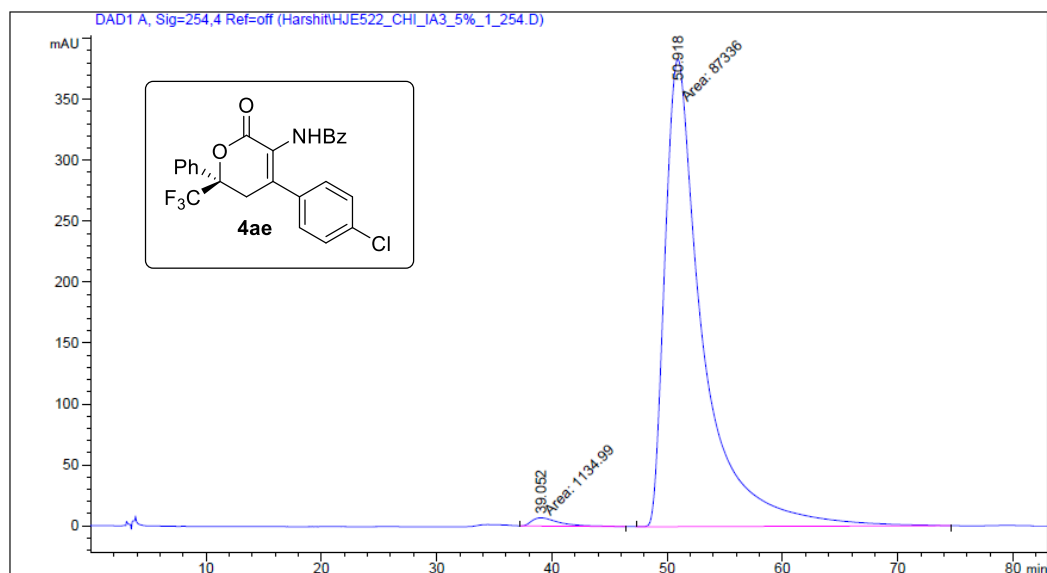
HPLC graph of racemic **4ad**



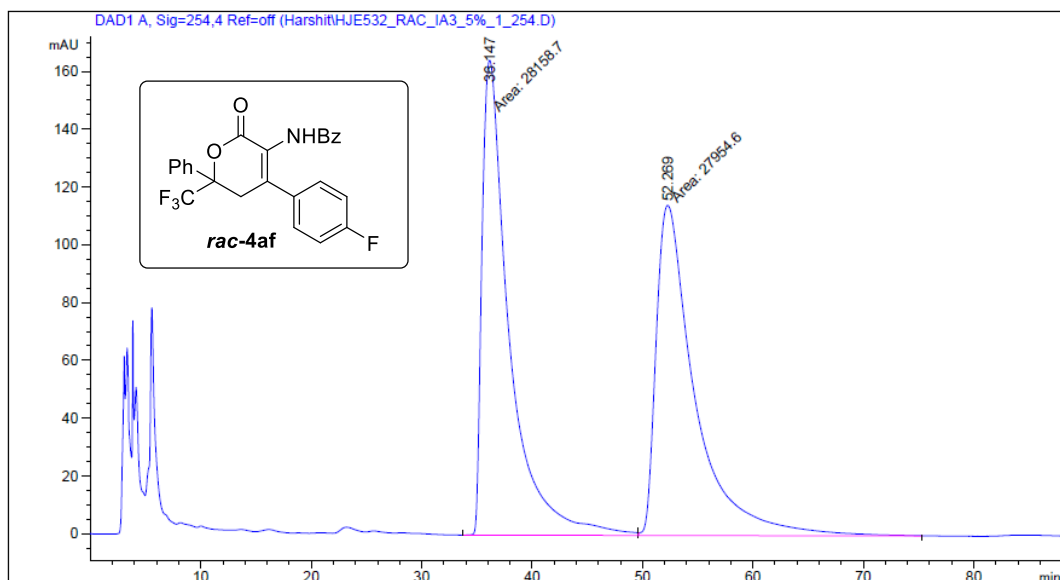
HPLC graph of enantioenriched **4ad**



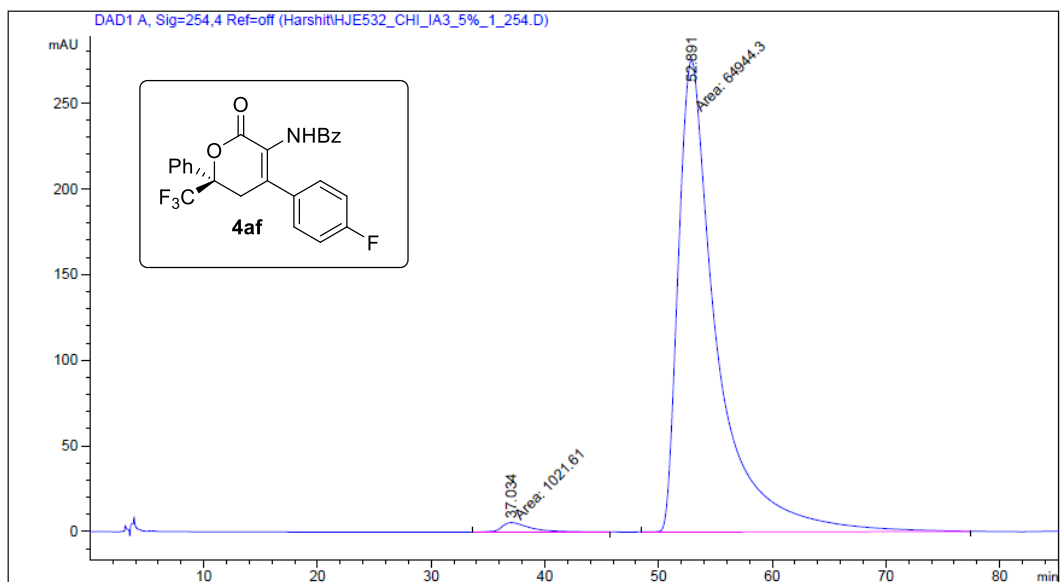
HPLC graph of racemic **4ae**



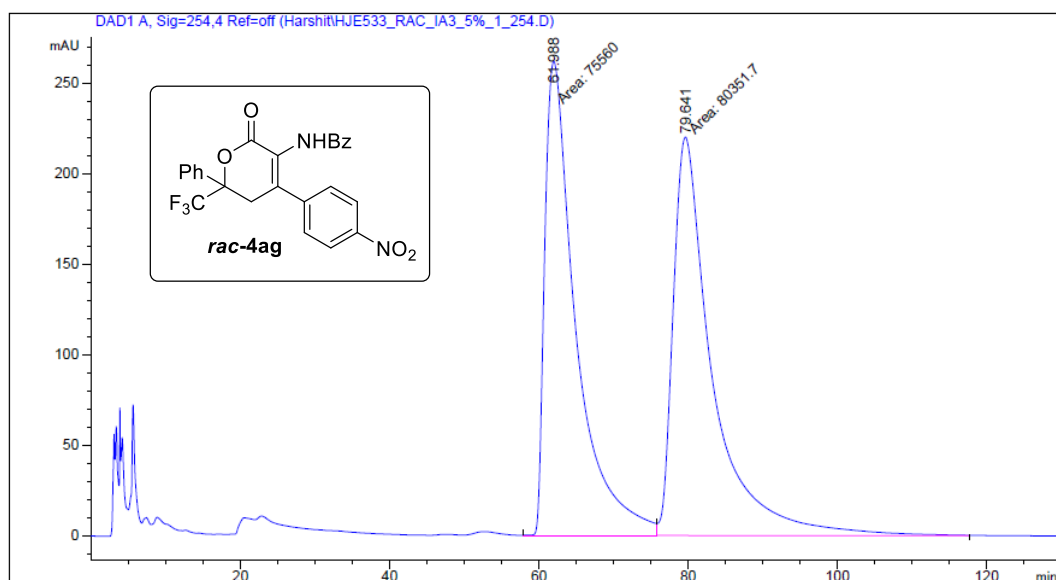
HPLC graph of enantioenriched **4ae**



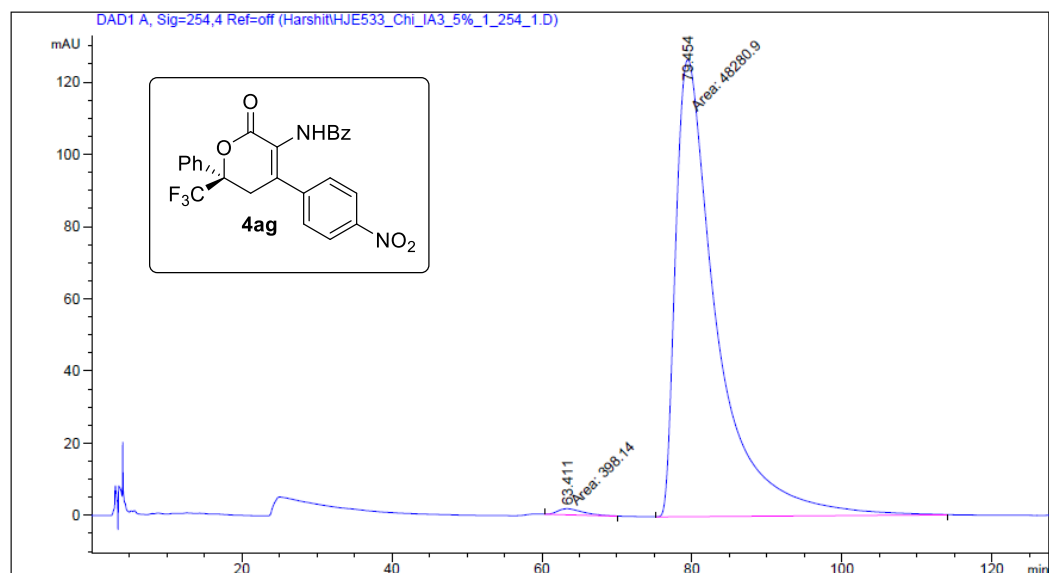
HPLC graph of racemic **4af**



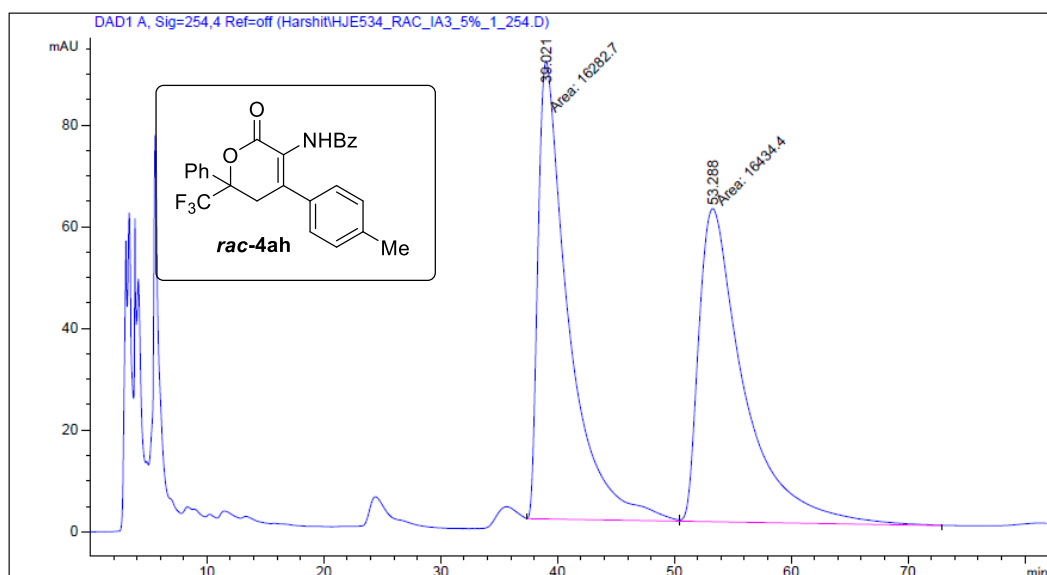
HPLC graph of enantioenriched **4af**



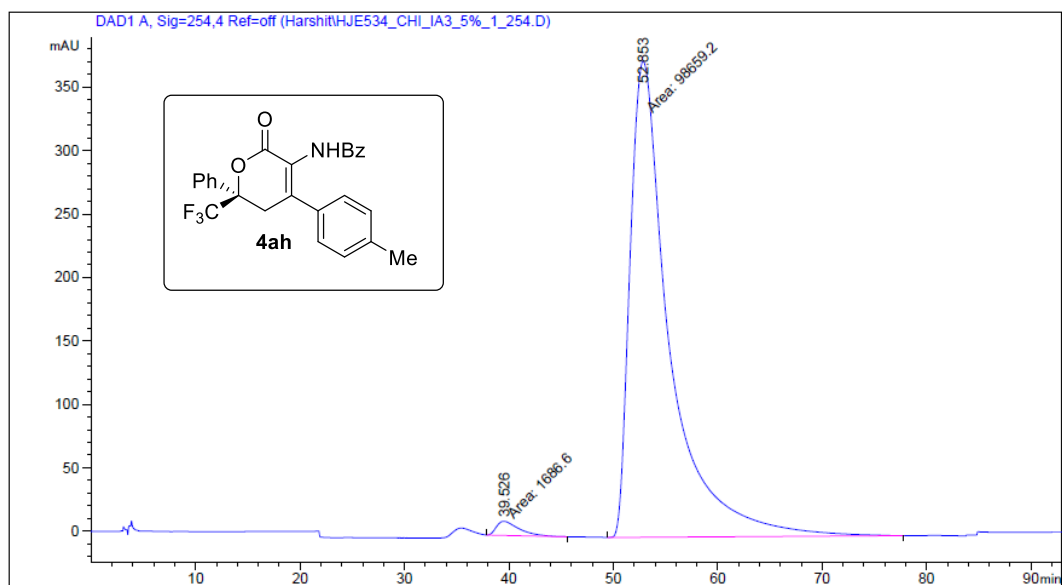
HPLC graph of racemic **4ag**



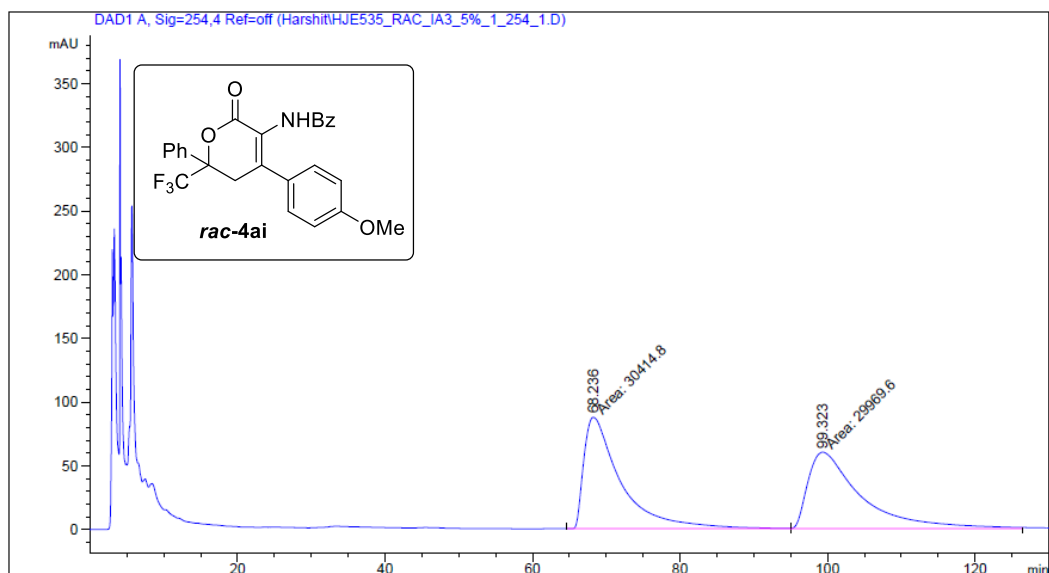
HPLC graph of enantioenriched **4ag**



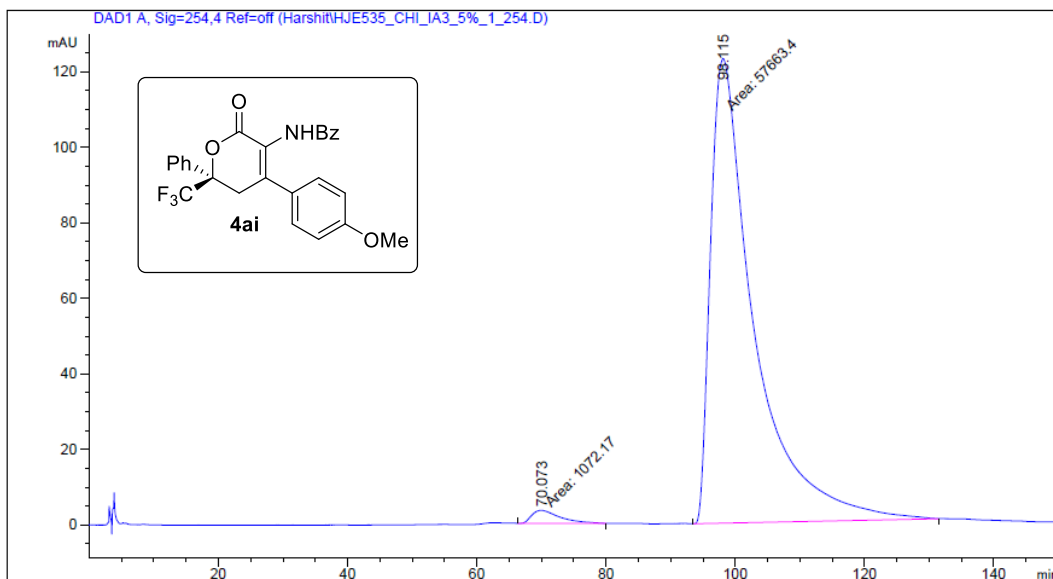
HPLC graph of racemic **4ah**



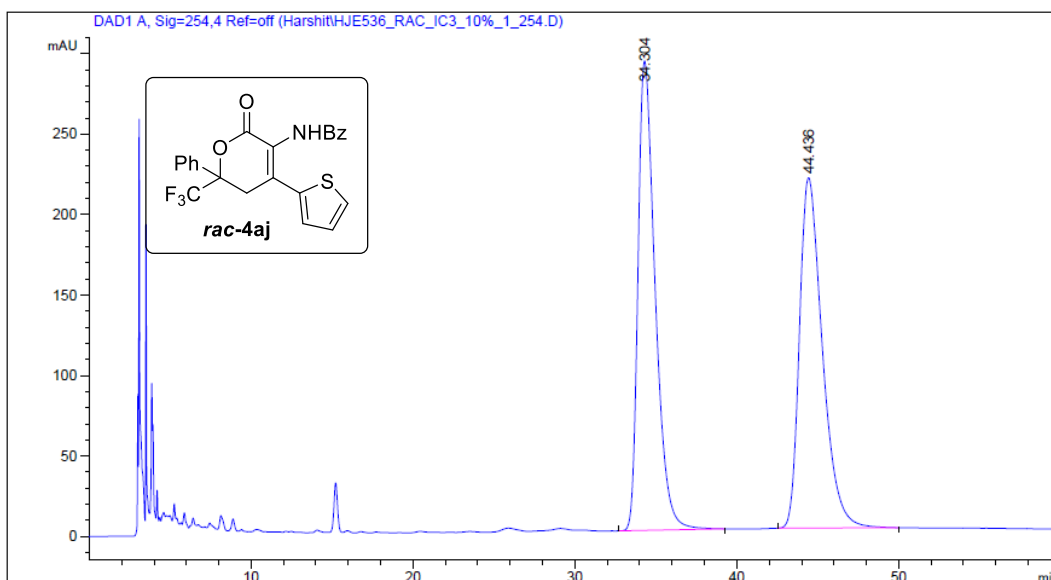
HPLC graph of enantioenriched **4ah**



HPLC graph of racemic **4ai**

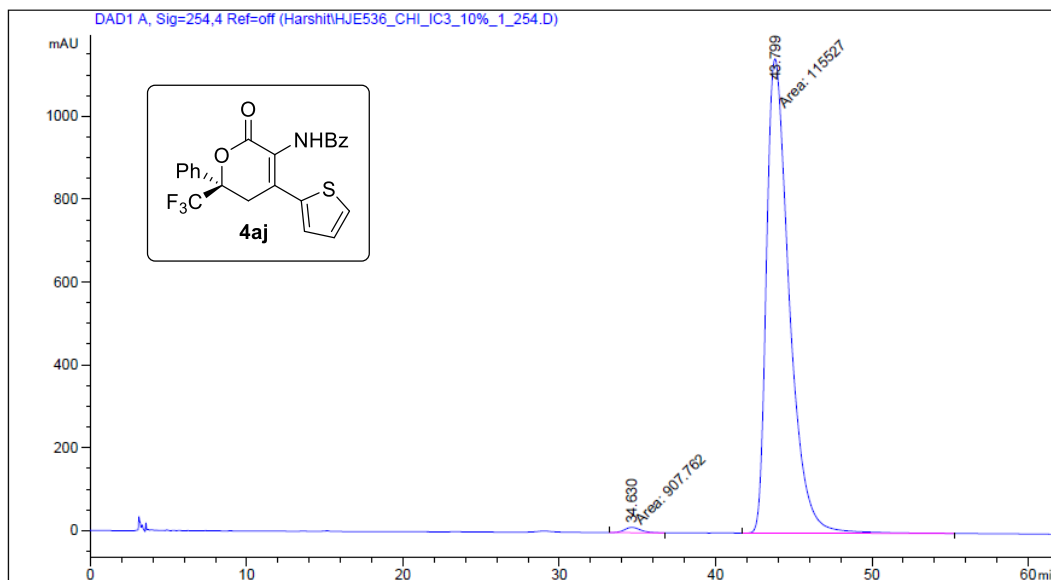


HPLC graph of enantioenriched **4ai**



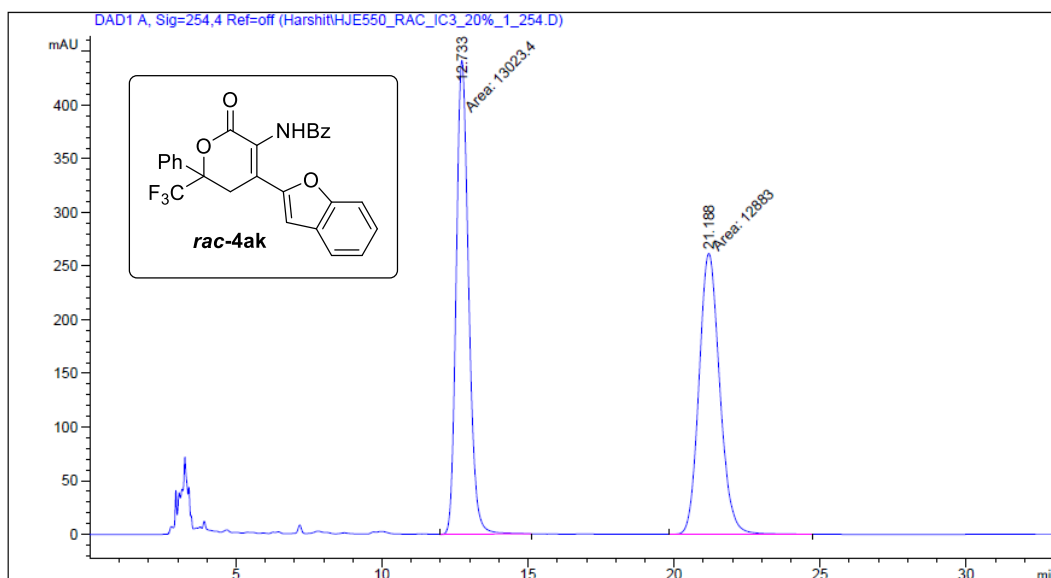
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.304	BB	1.1157	2.14452e4	291.70615	50.0935
2	44.436	BB	1.4874	2.13652e4	217.62785	49.9065

HPLC graph of racemic **4aj**

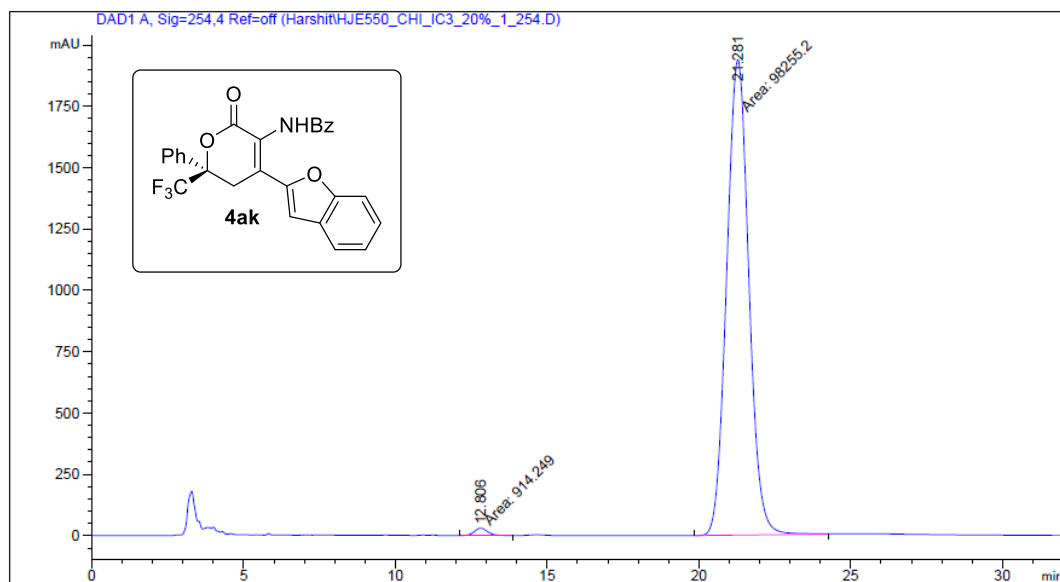


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.630	MM	1.1869	907.76239	12.74672	0.7796
2	43.799	MM	1.6813	1.15527e5	1145.20691	99.2204

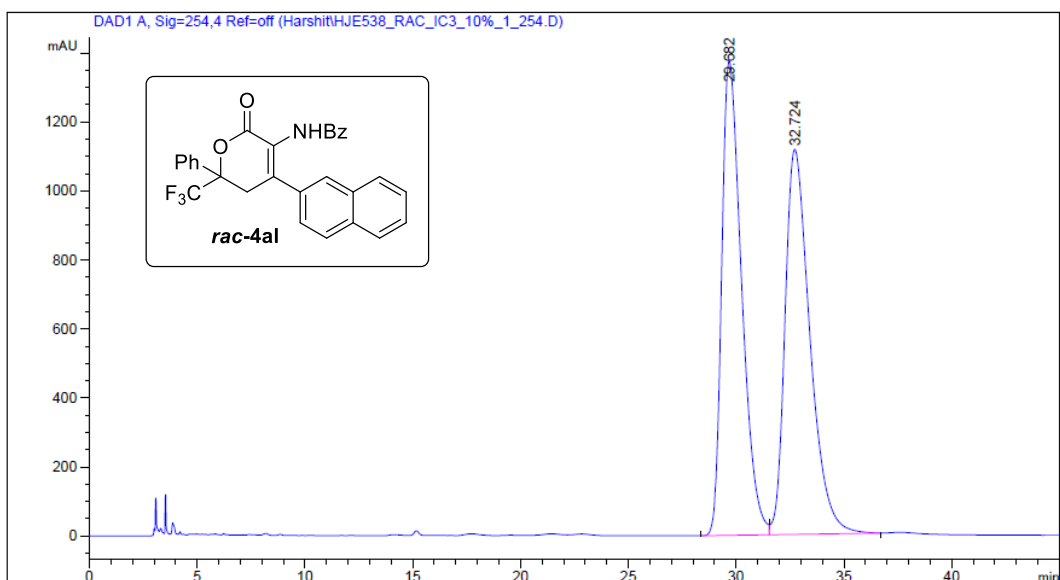
HPLC graph of enantioenriched **4aj**



HPLC graph of racemic **4ak**

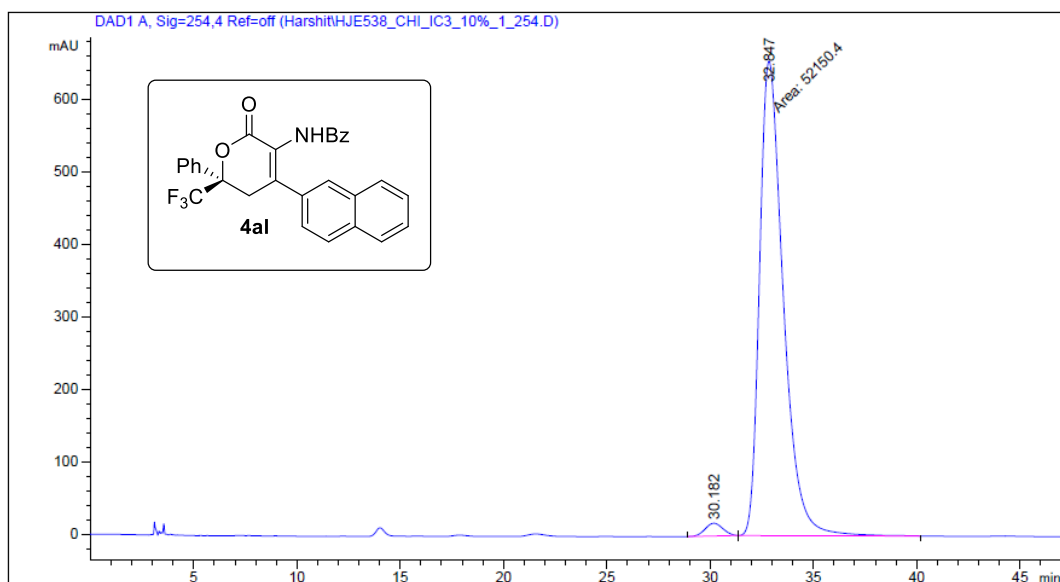


HPLC graph of enantioenriched **4ak**



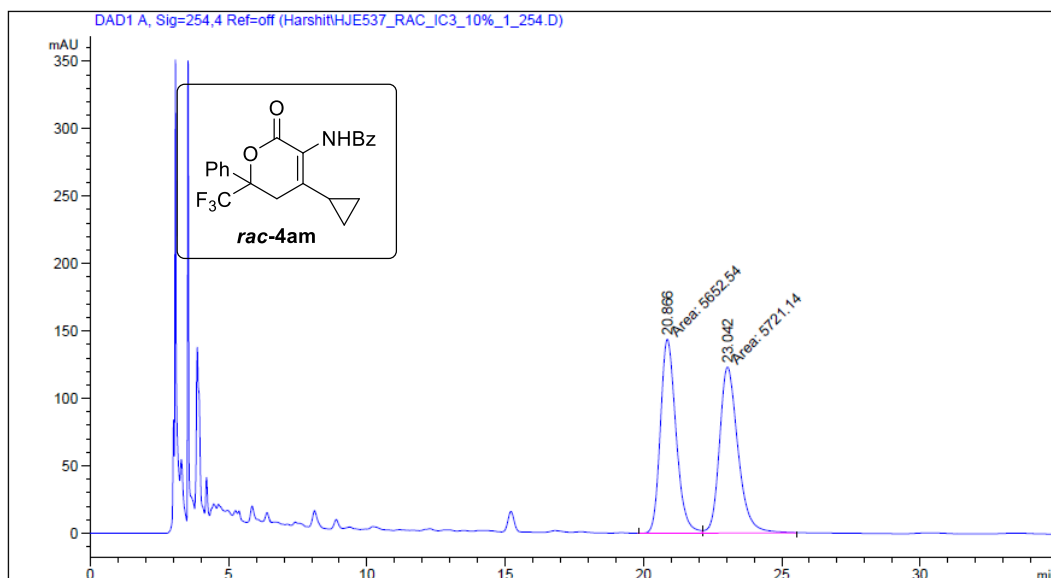
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.682	BV	0.9826	8.82047e4	1374.67322	49.6344
2	32.724	VB	1.2119	8.95040e4	1115.67712	50.3656

HPLC graph of racemic **4al**

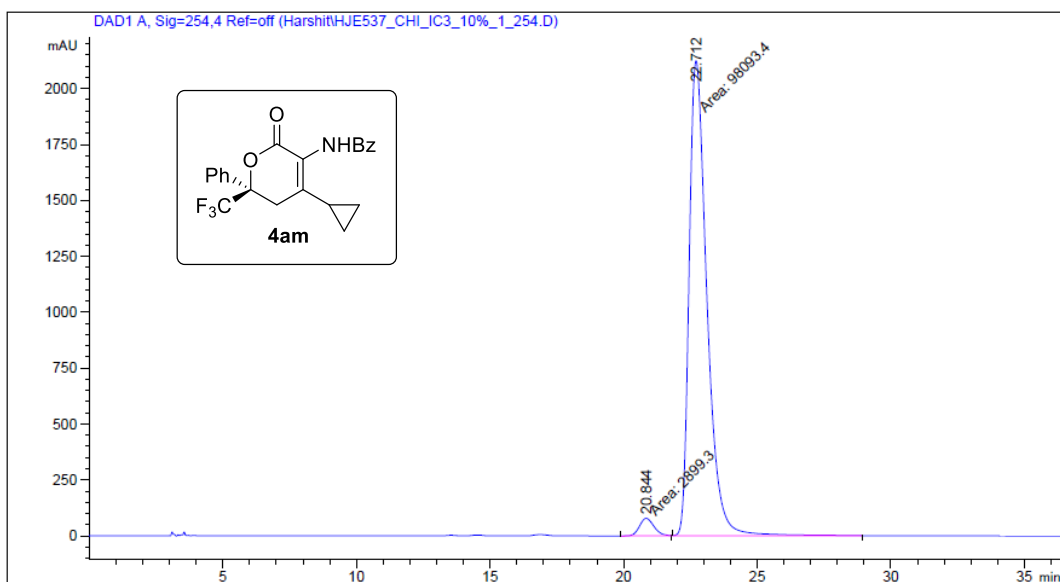


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.182	BB	0.8760	1053.44263	17.65934	1.9800
2	32.847	MM	1.3284	5.21504e4	654.30878	98.0200

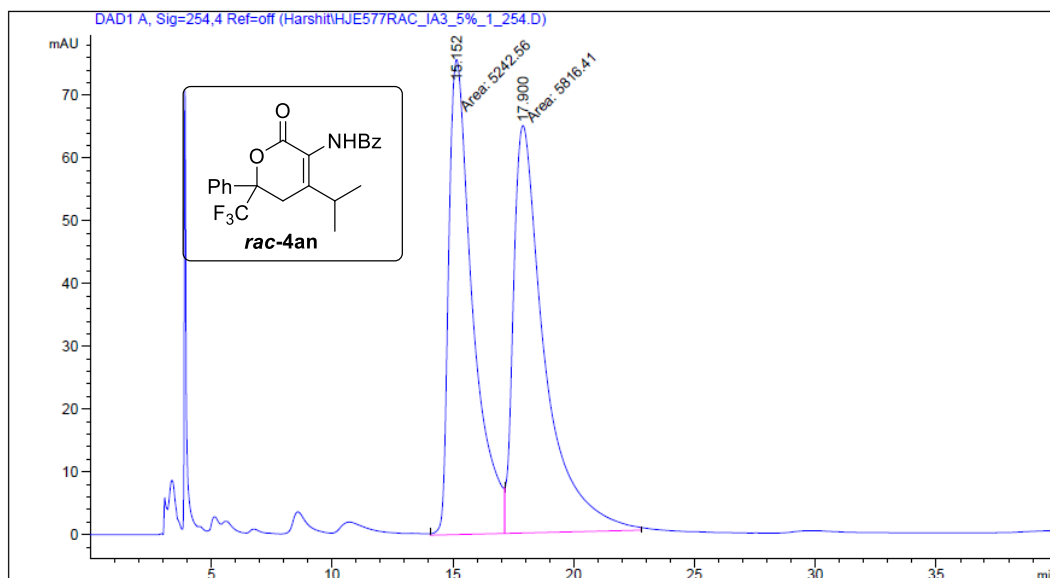
HPLC graph of enantioenriched **4al**



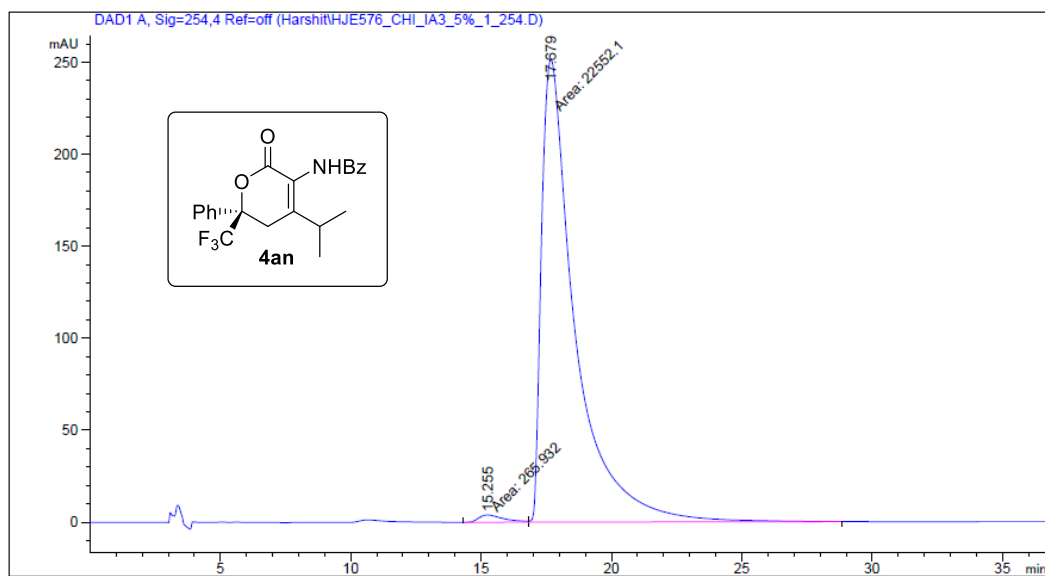
HPLC graph of racemic **4am**



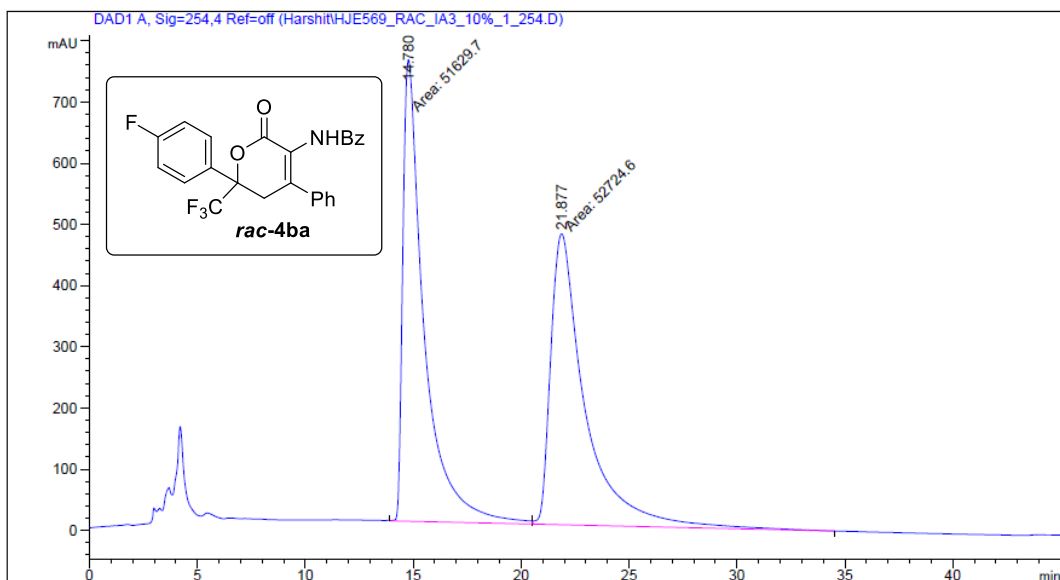
HPLC graph of enantioenriched **4am**



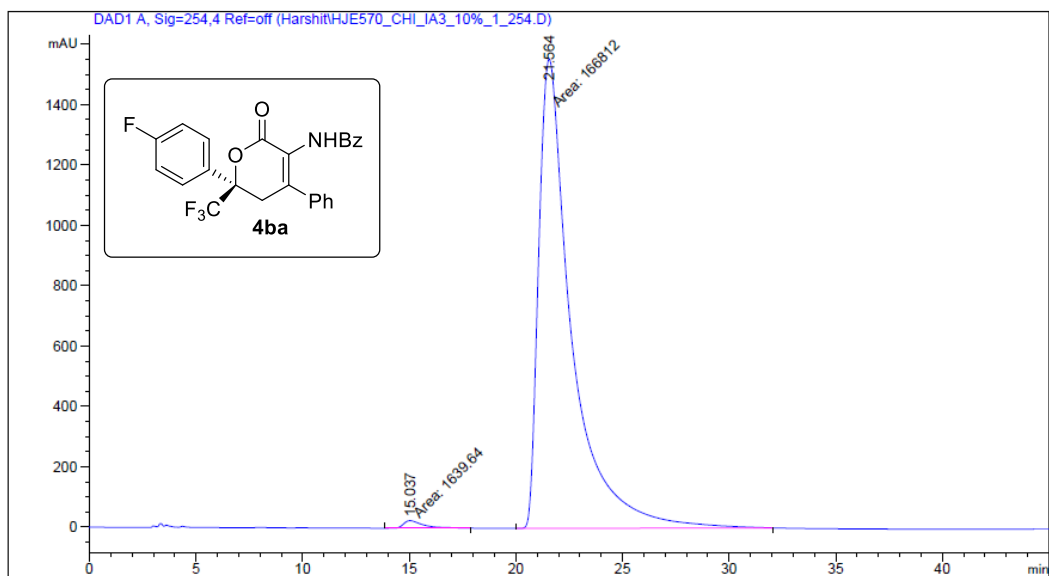
HPLC graph of racemic **4an**



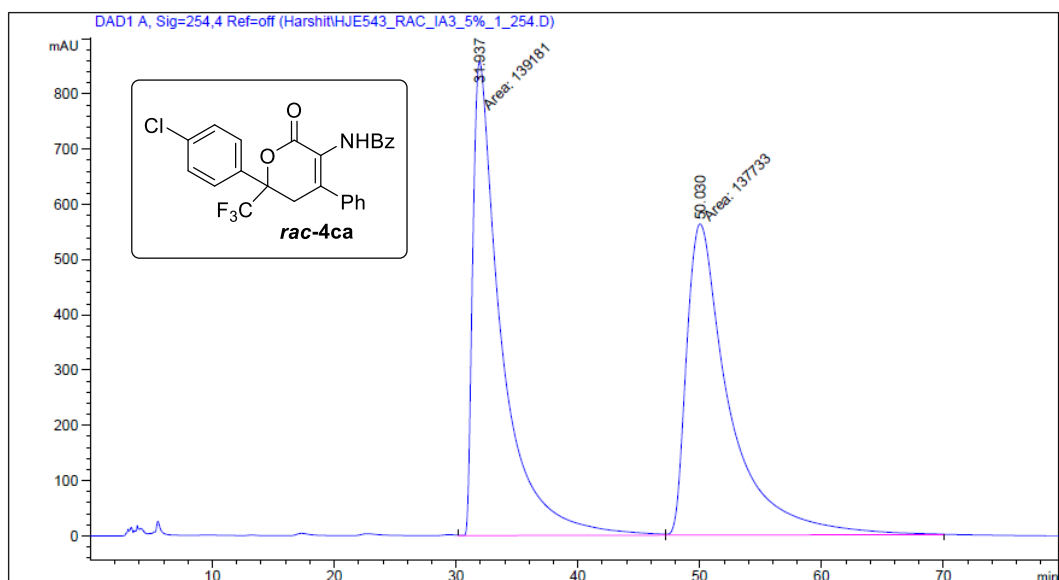
HPLC graph of enantioenriched **4an**



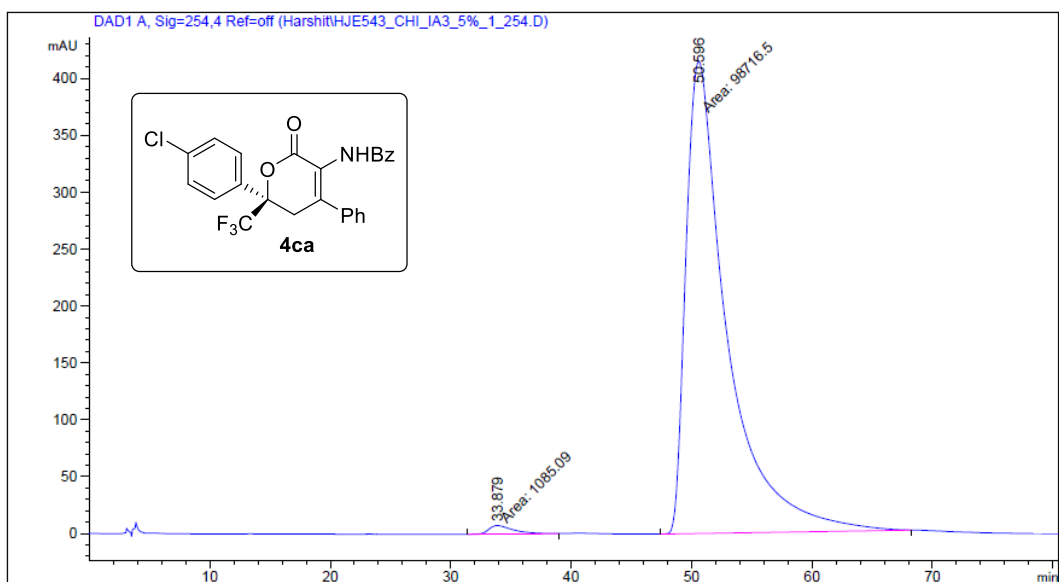
HPLC graph of racemic **4ba**



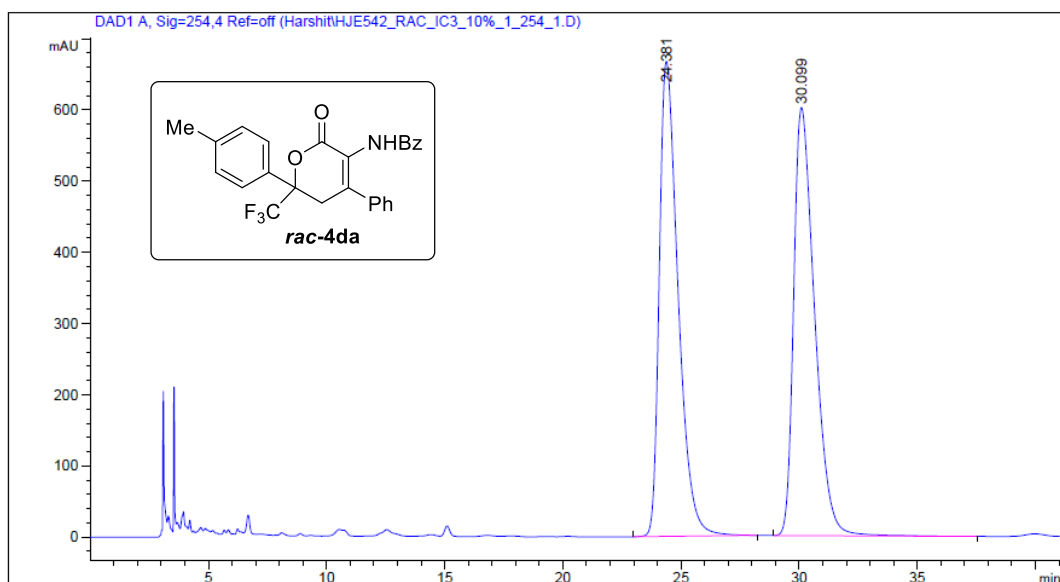
HPLC graph of enantioenriched **4ba**



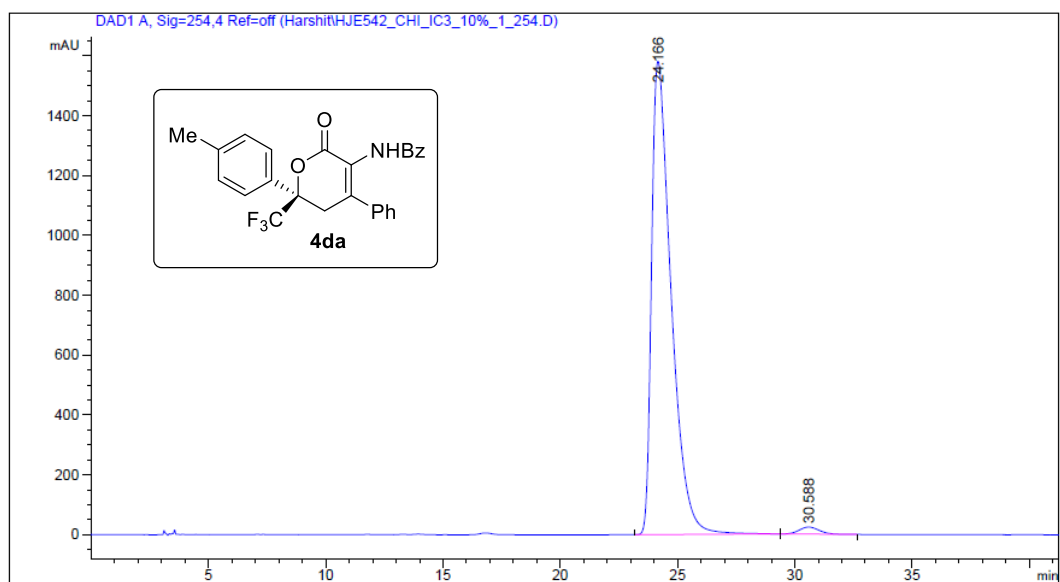
HPLC graph of racemic **4ca**



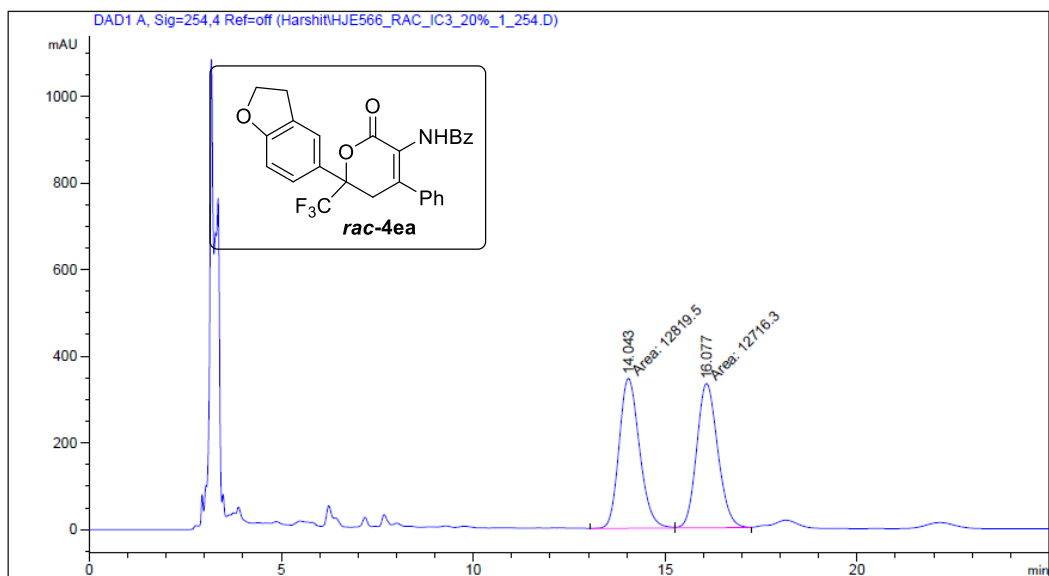
HPLC graph of enantioenriched **4ca**



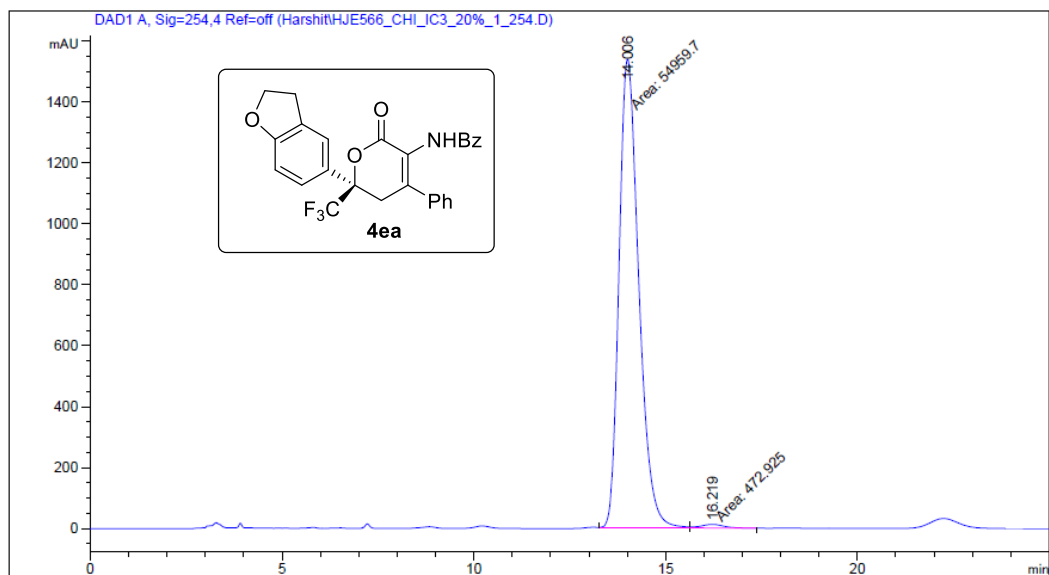
HPLC graph of racemic **4da**



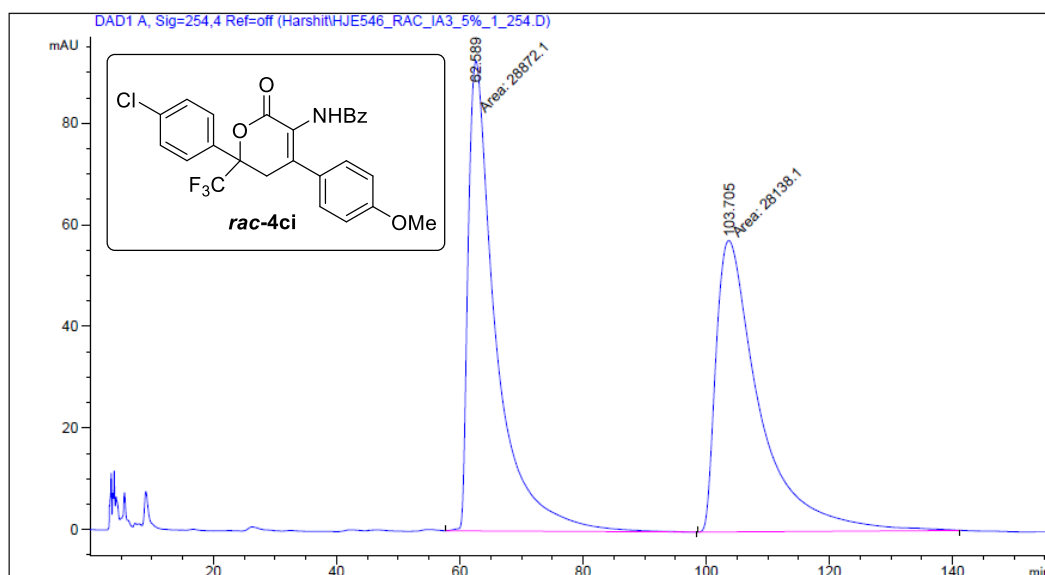
HPLC graph of enantioenriched **4da**



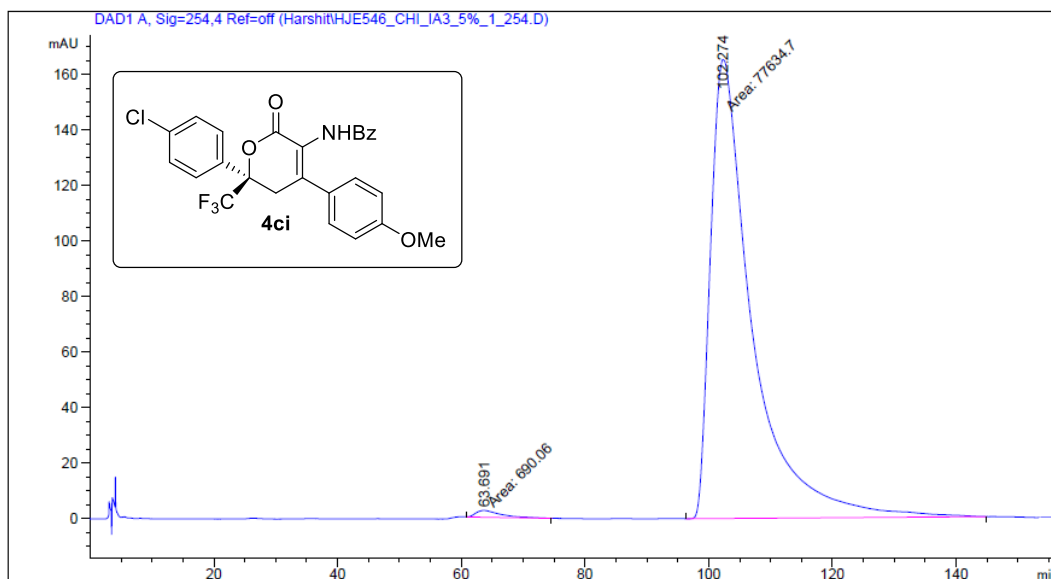
HPLC graph of racemic **4ea**



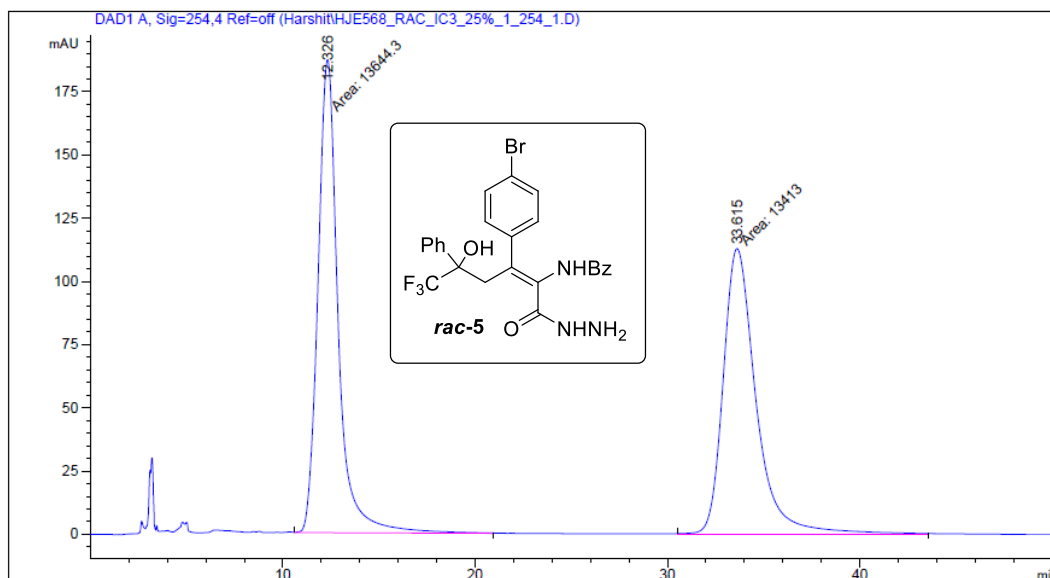
HPLC graph of enantioenriched **4ea**



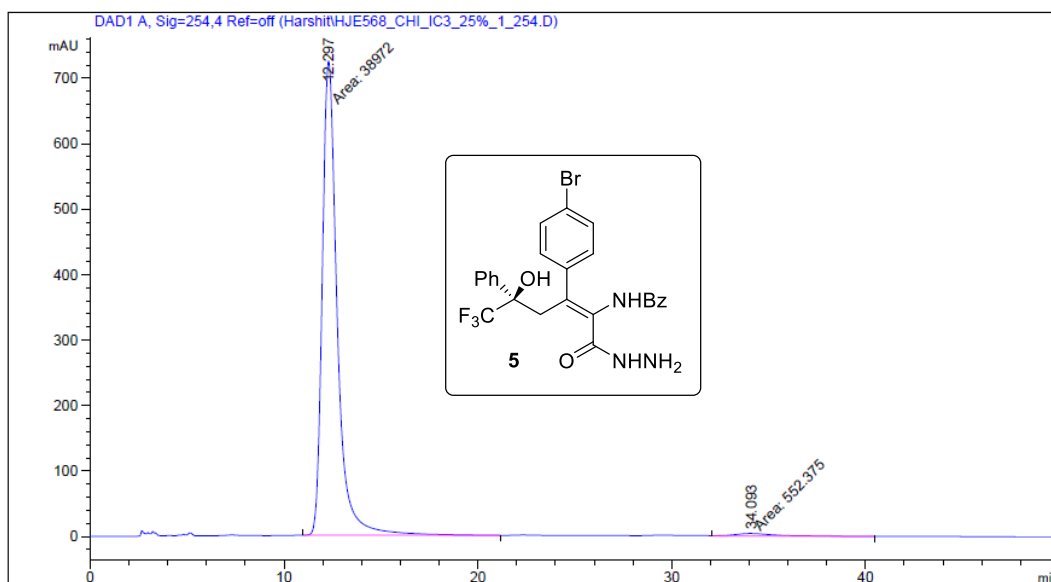
HPLC graph of racemic **4ci**



HPLC graph of enantioenriched **4ci**



HPLC graph of racemic **5**



HPLC graph of enantioenriched **5**