

Supplementary Materials

Diastereoselective ZnCl₂-Mediated Joullié-Ugi Three-Component Reaction for the Preparation of Phosphorylated *N*-Acylaziridines from 2*H*-Azirines

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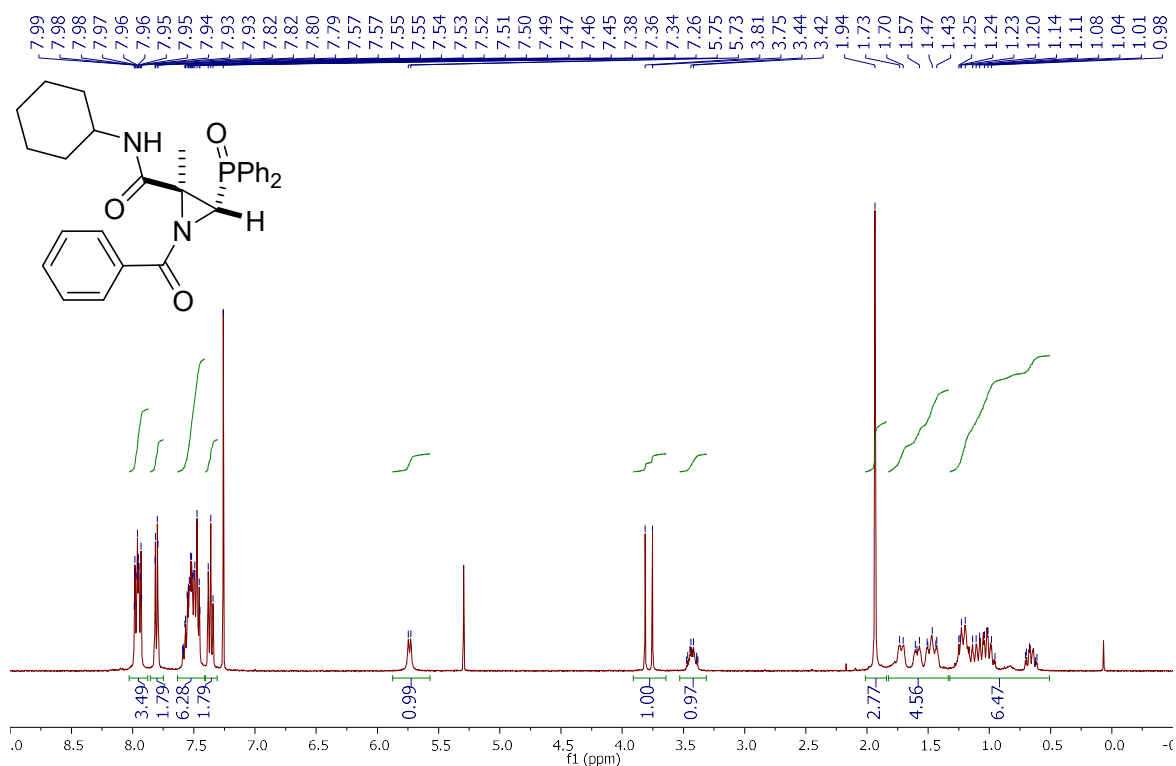
* Correspondence: jesus.delossantos@ehu.eus; Tel.: +34-945-013-104

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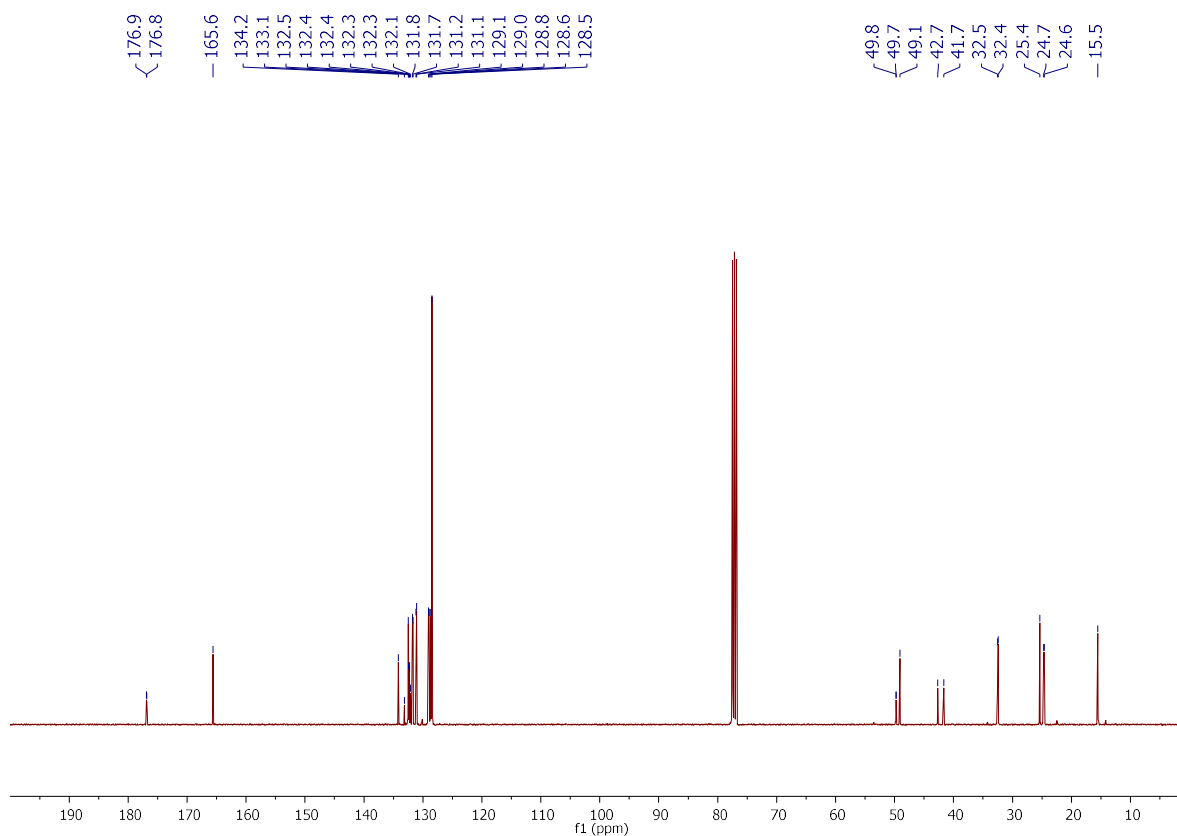
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1. ^1H NMR, ^{13}C NMR, ^{31}P NMR, ^{19}F NMR and 2D HMBC NMR $\{^1\text{H}-^{13}\text{C}\}$ spectra of compounds

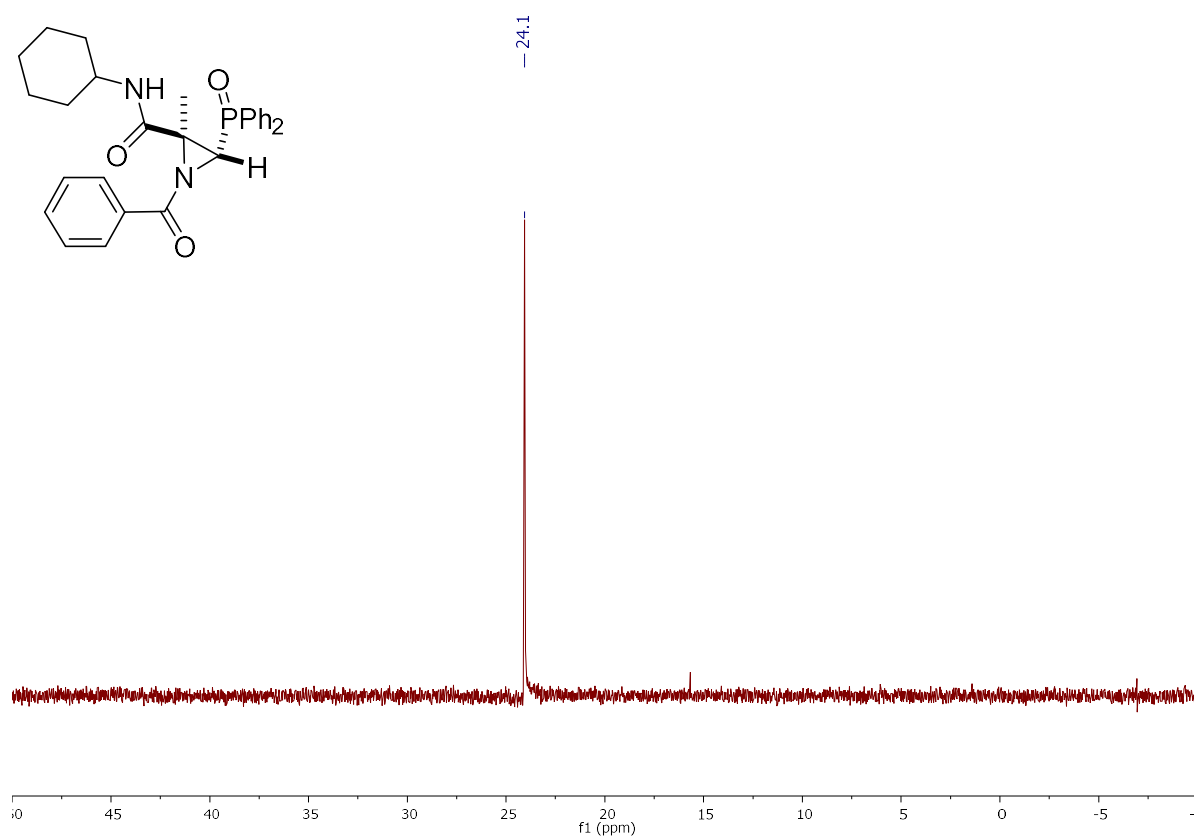
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4a**



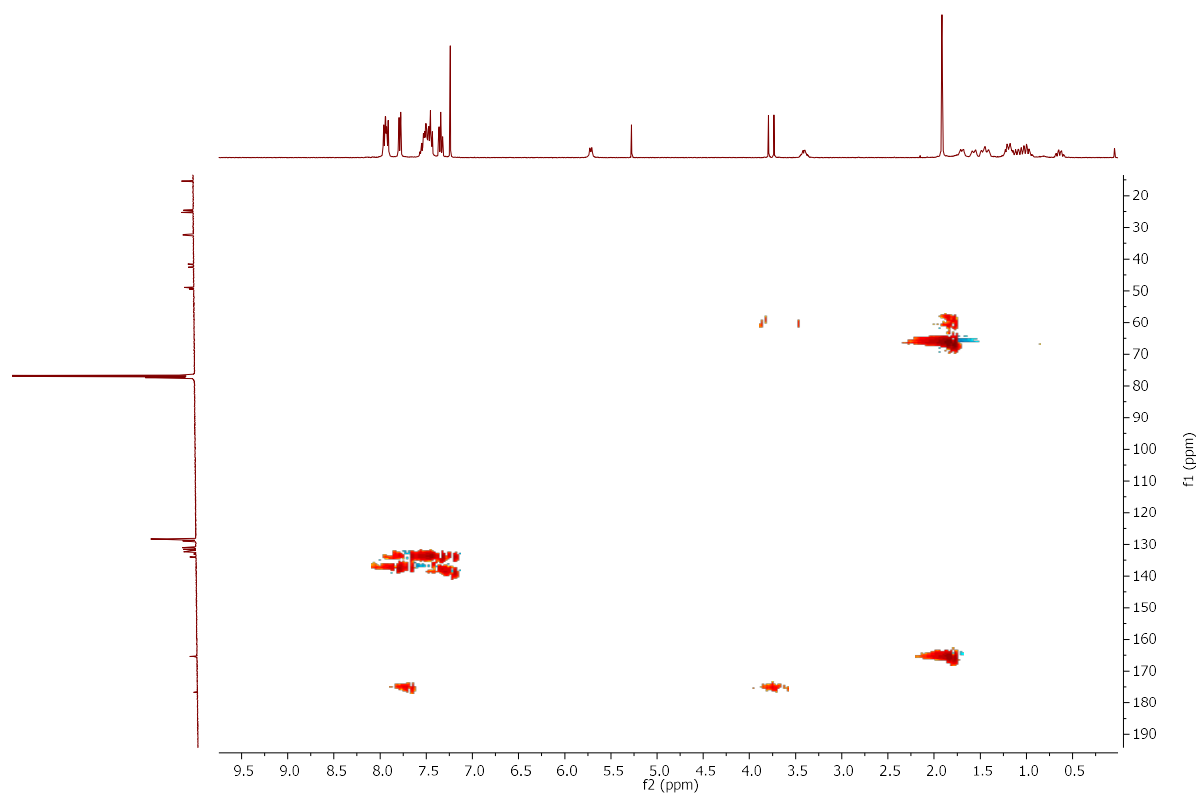
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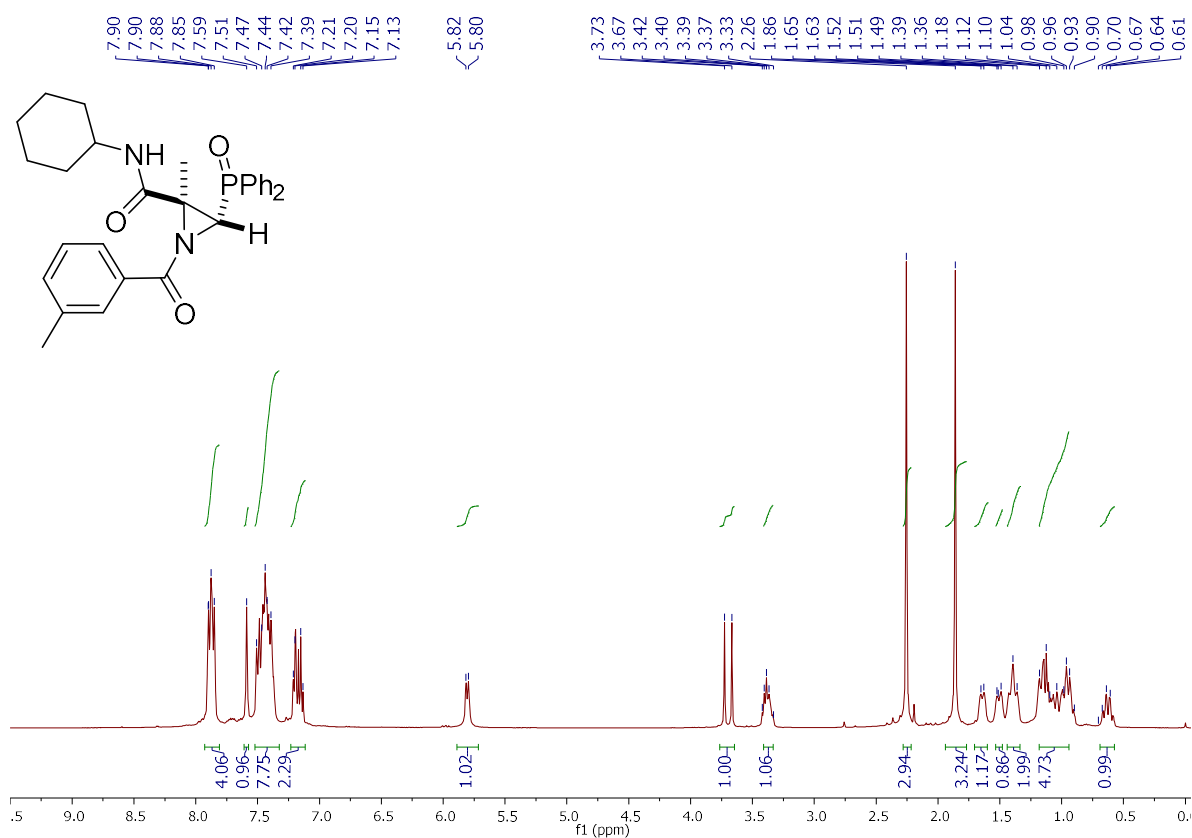
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4a**



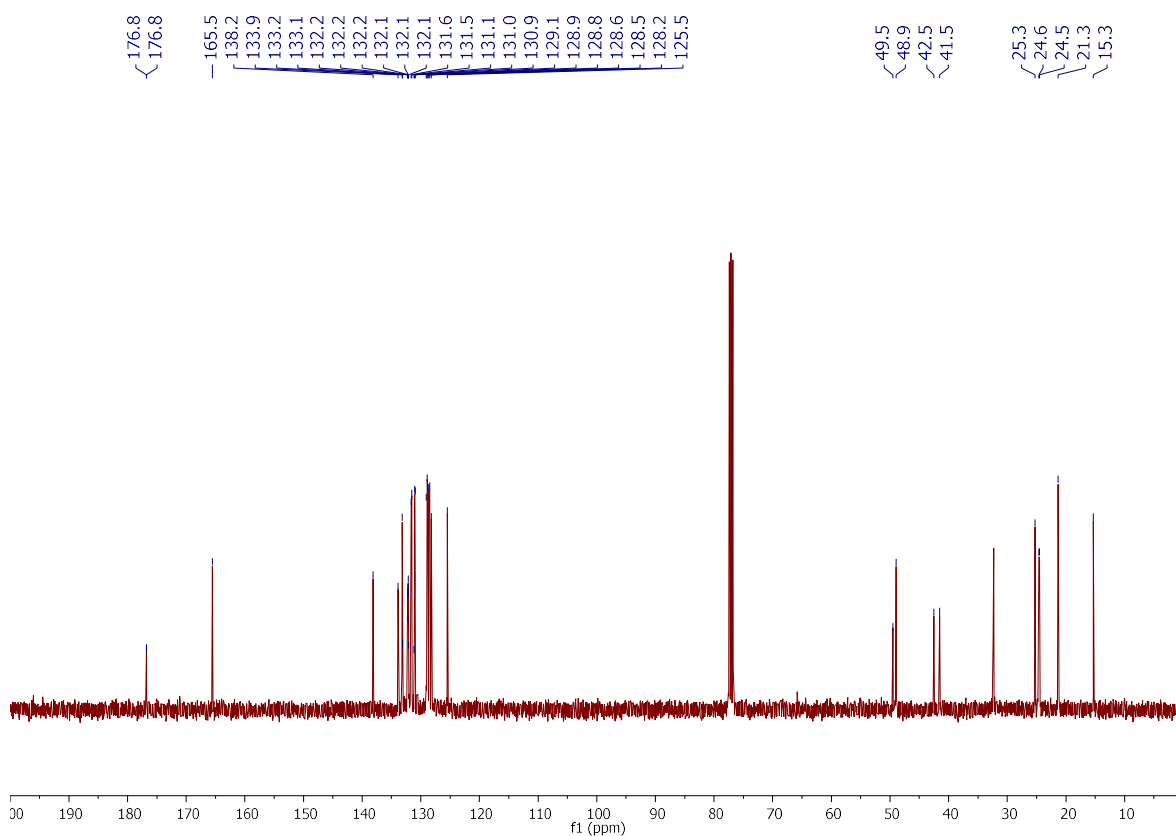
^1H - ^{13}C HMBC (CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4a**



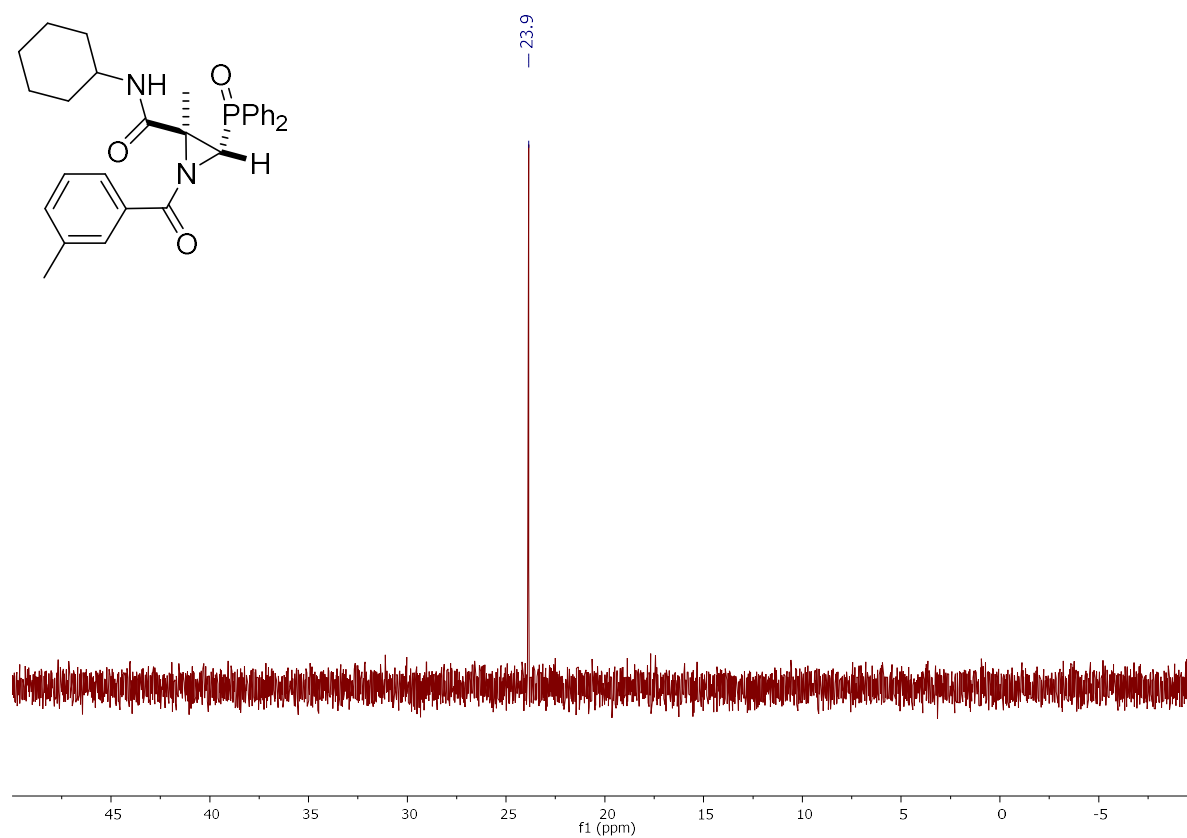
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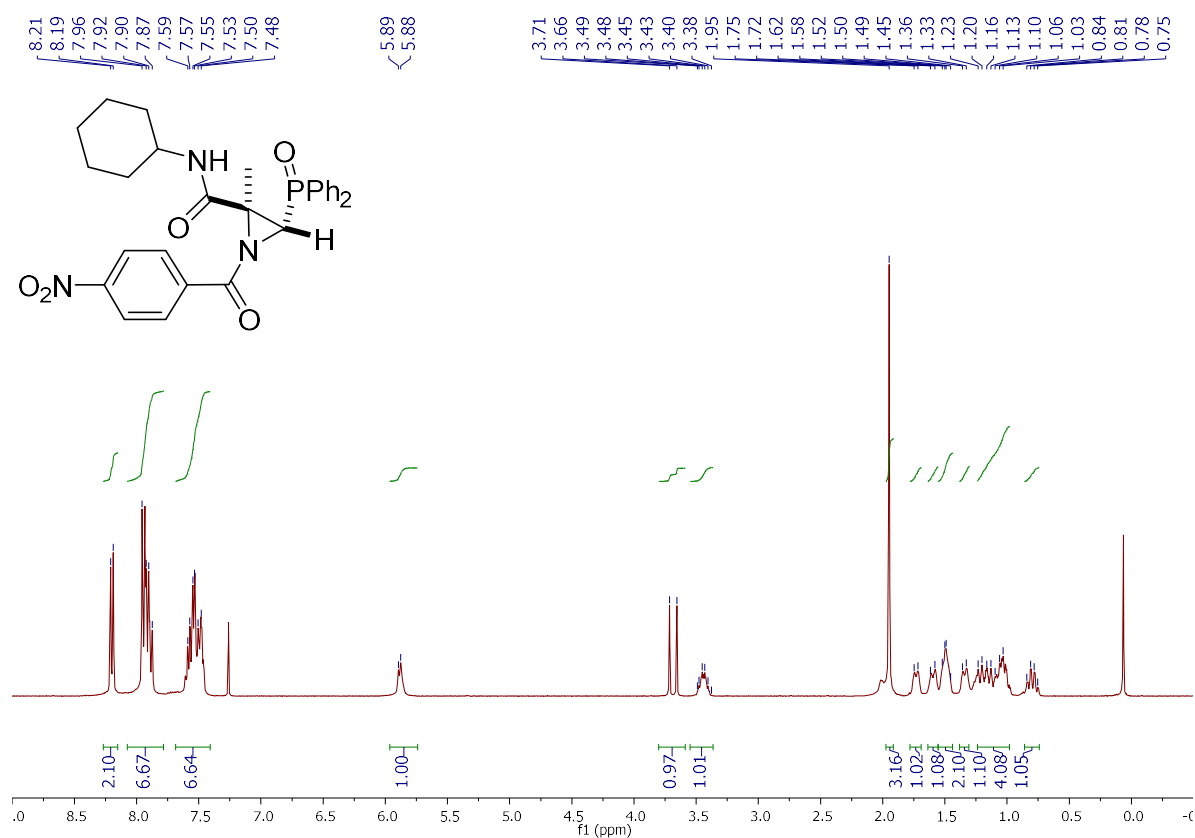
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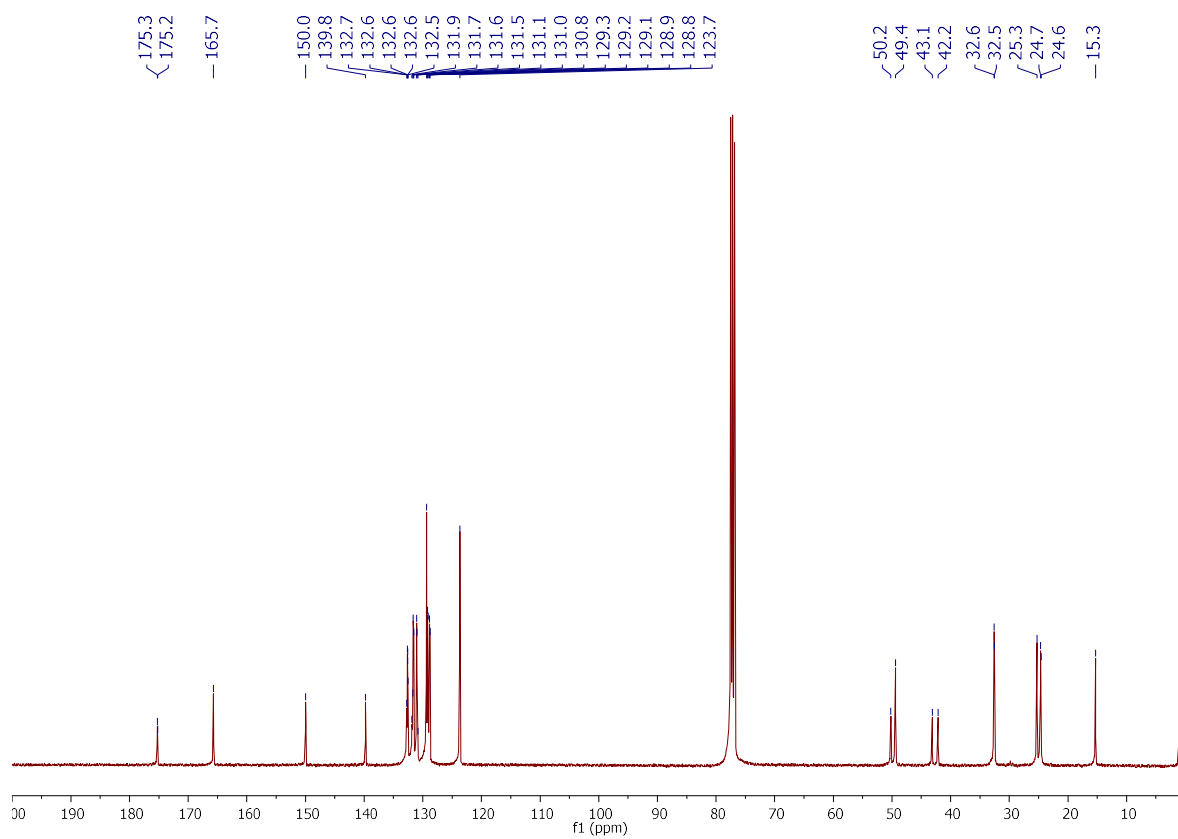
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4b**



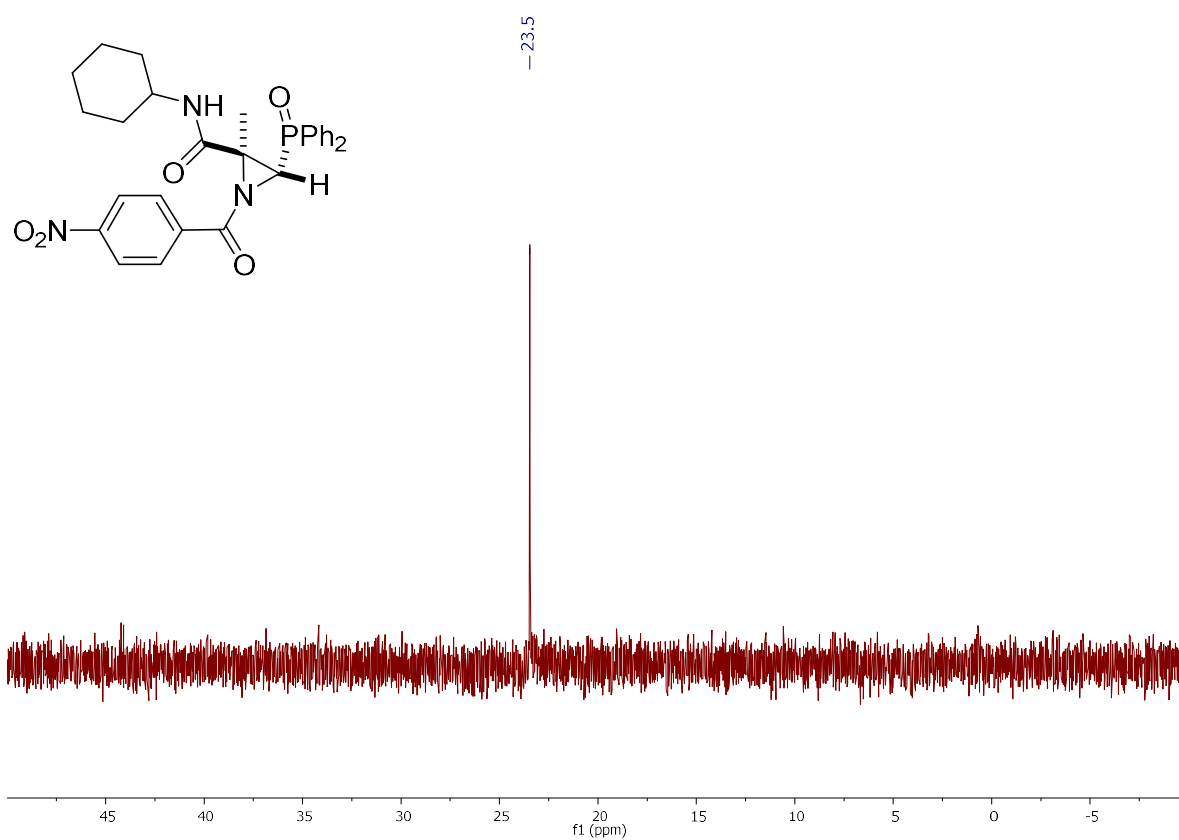
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4c**



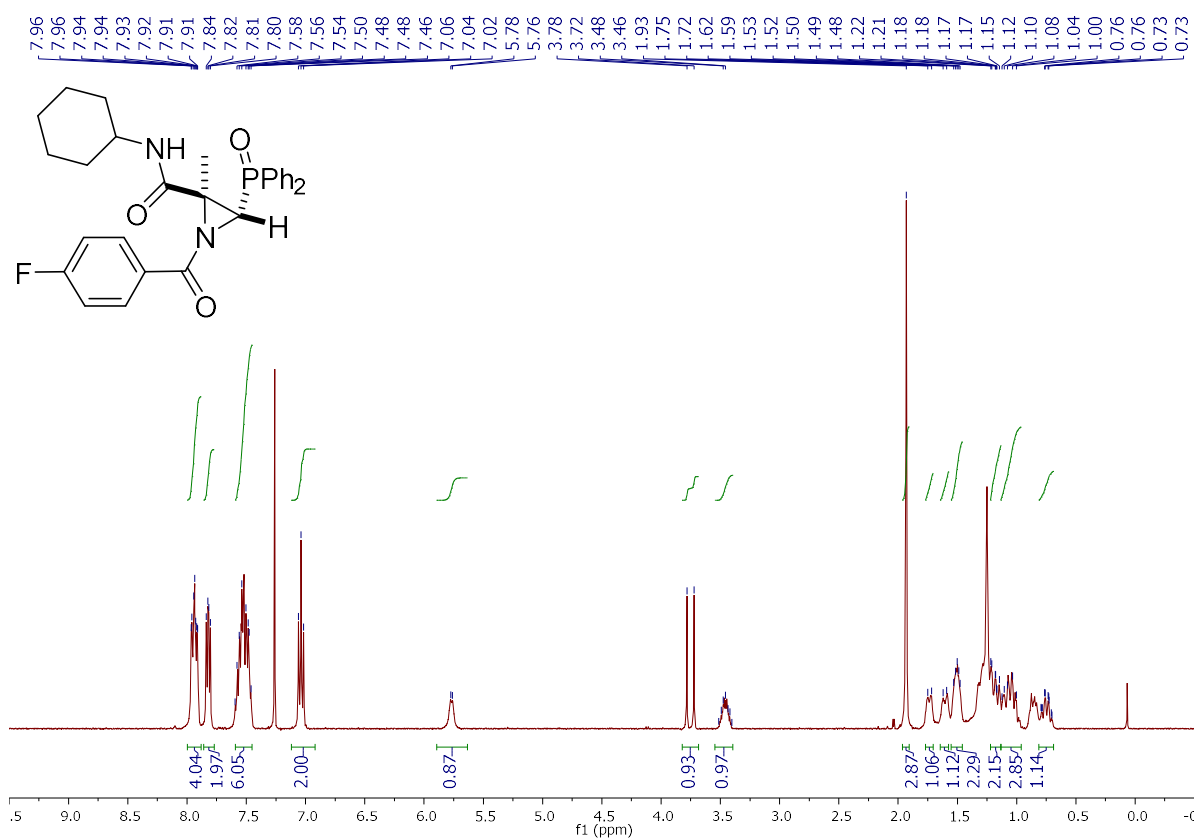
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4c**



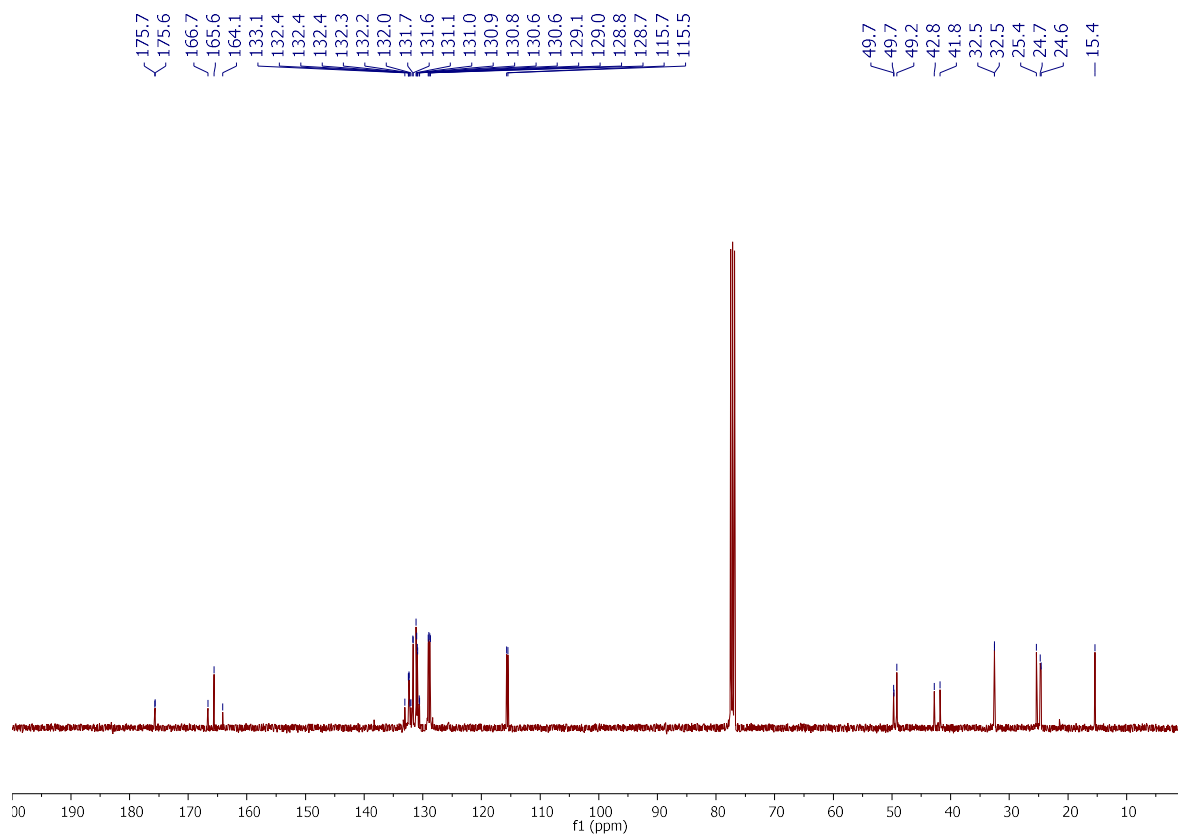
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4c**



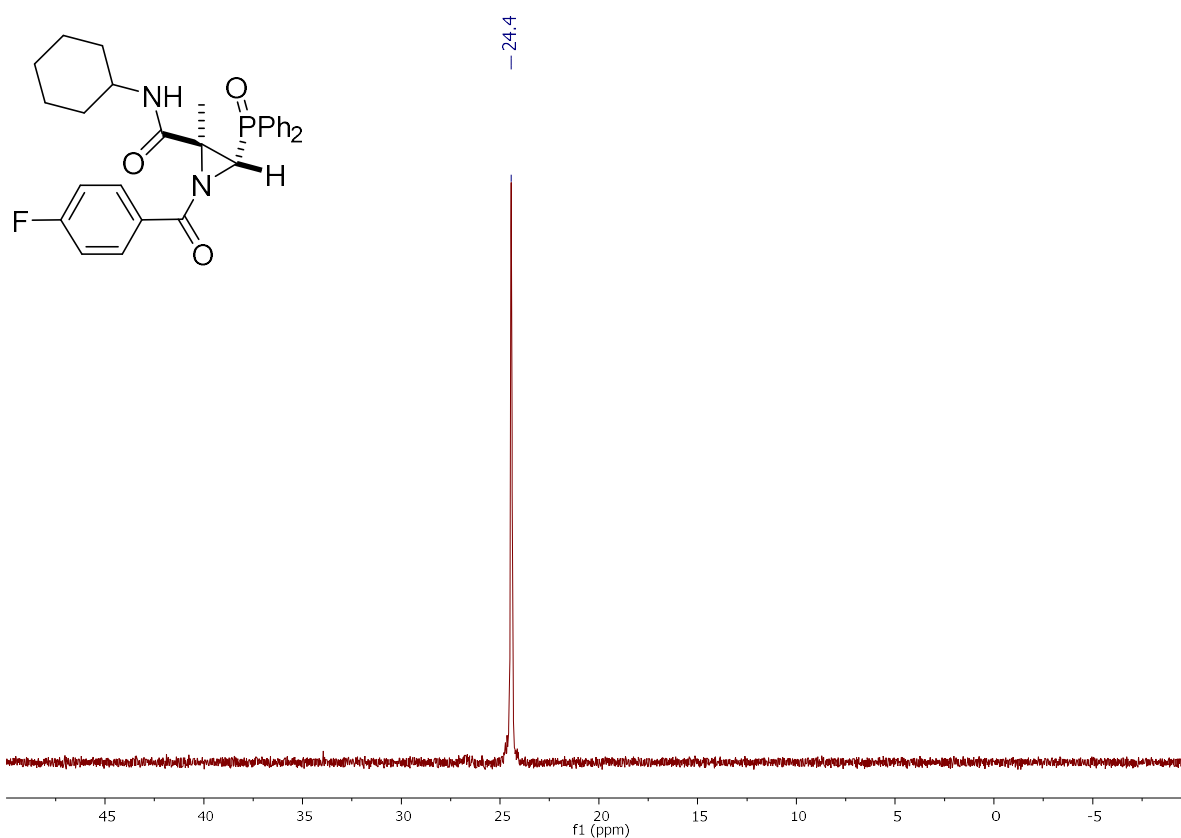
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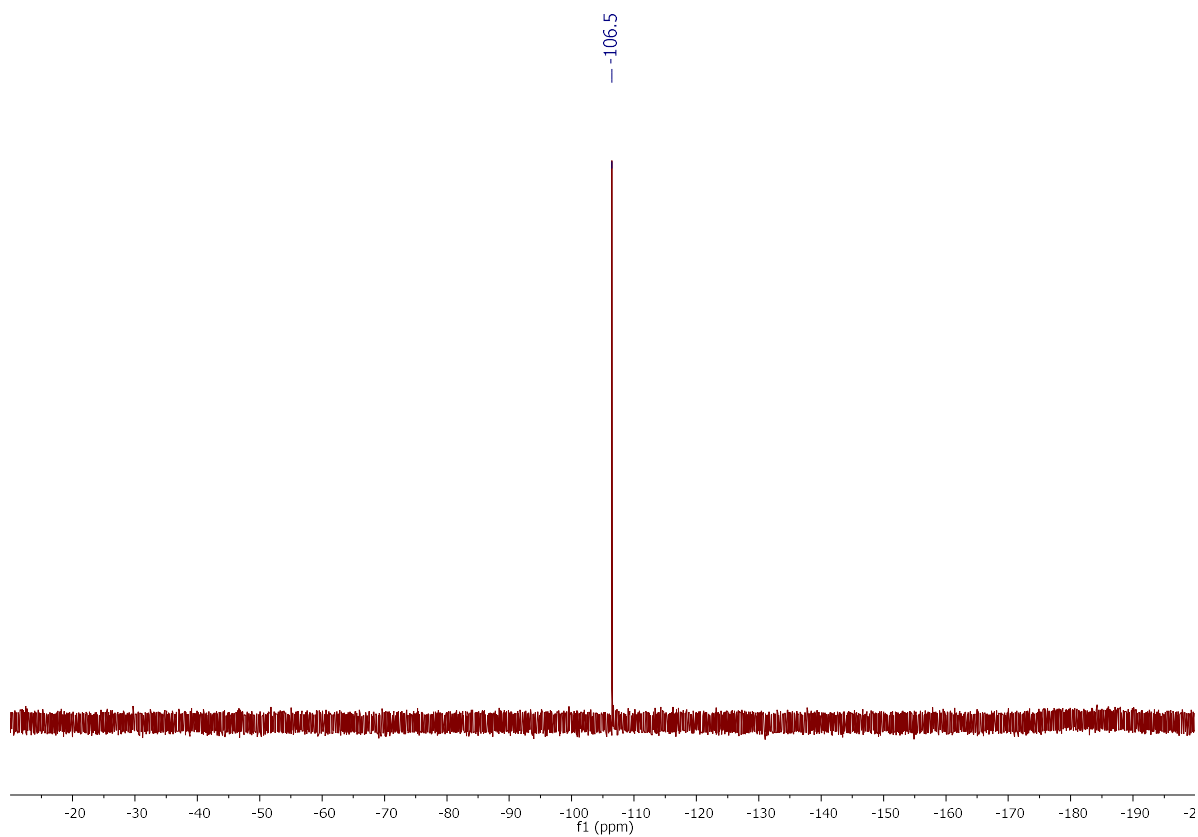
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4d**



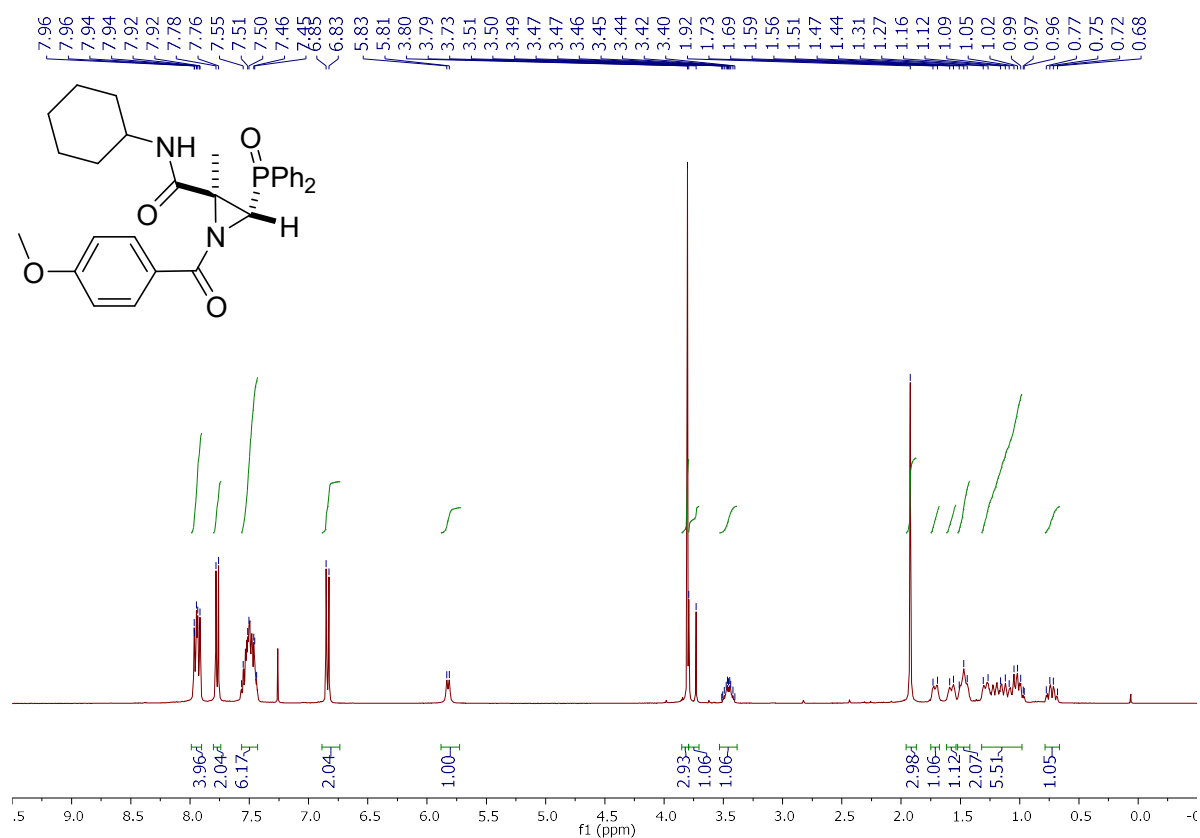
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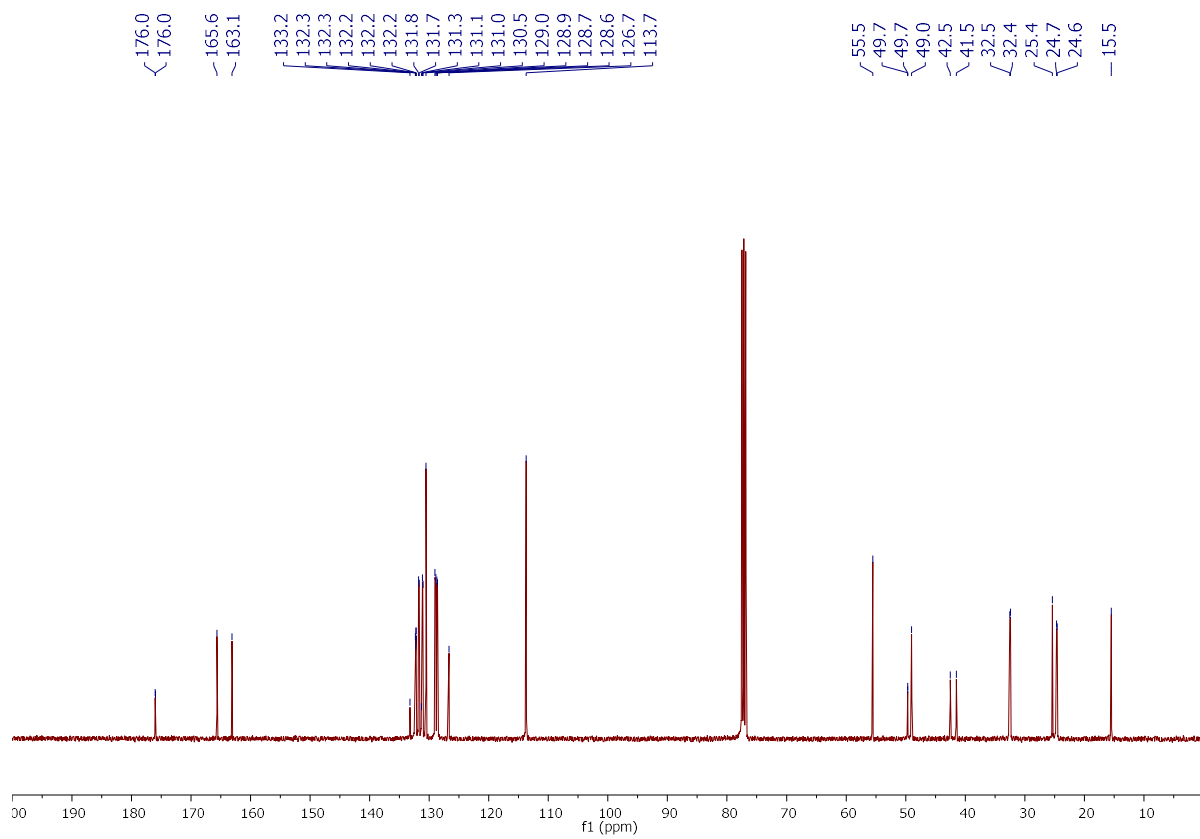
^{19}F (376 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4d**



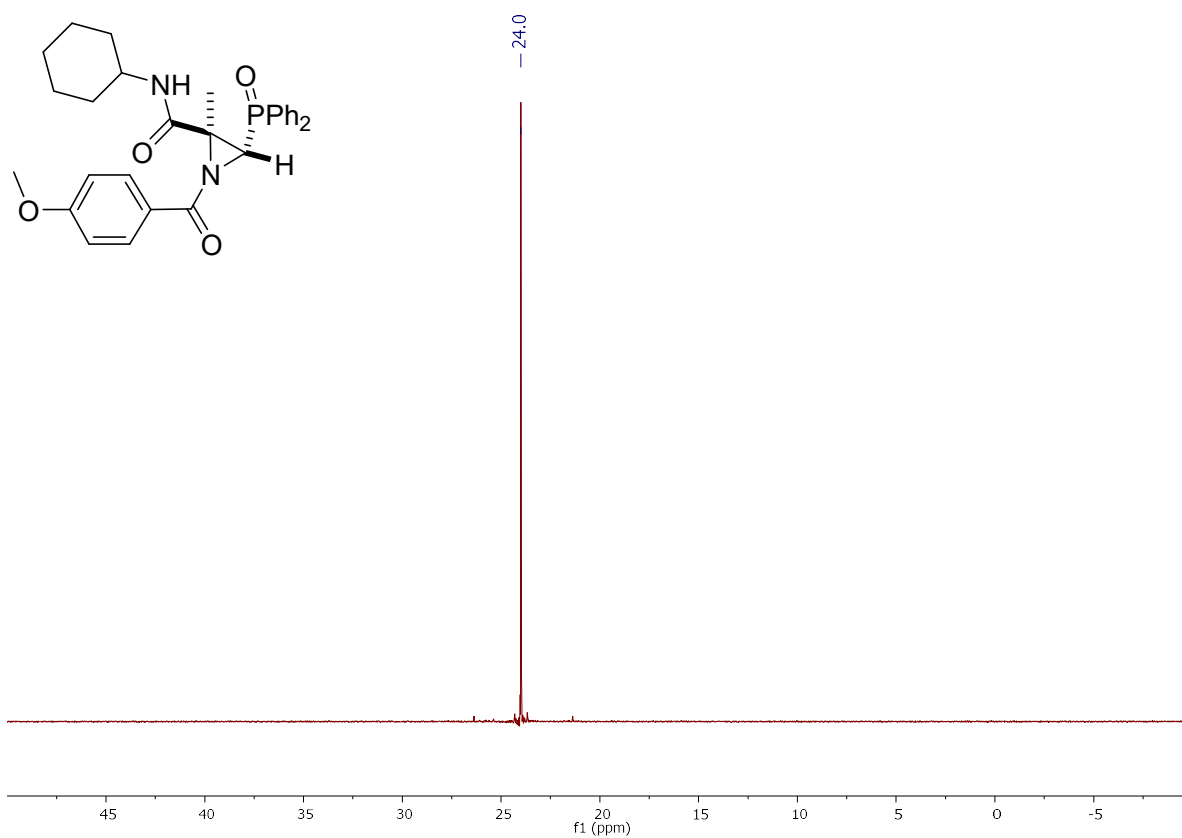
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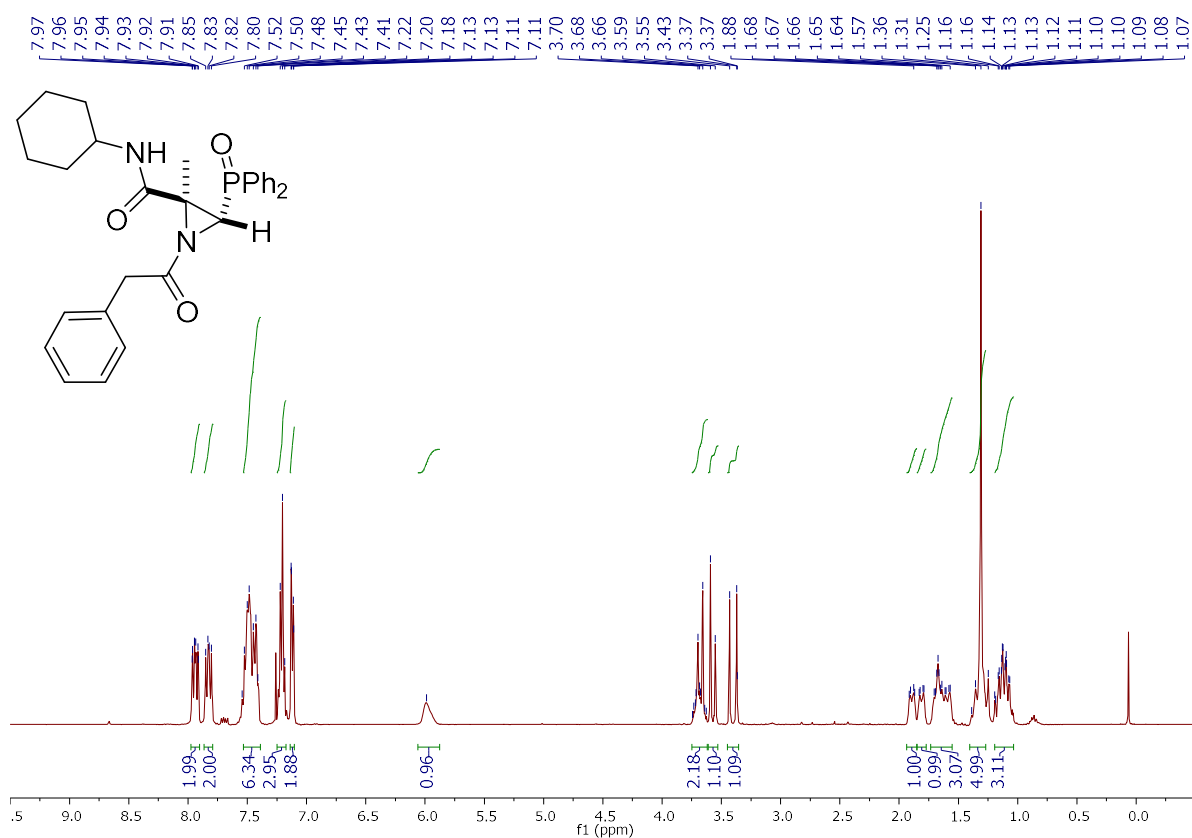
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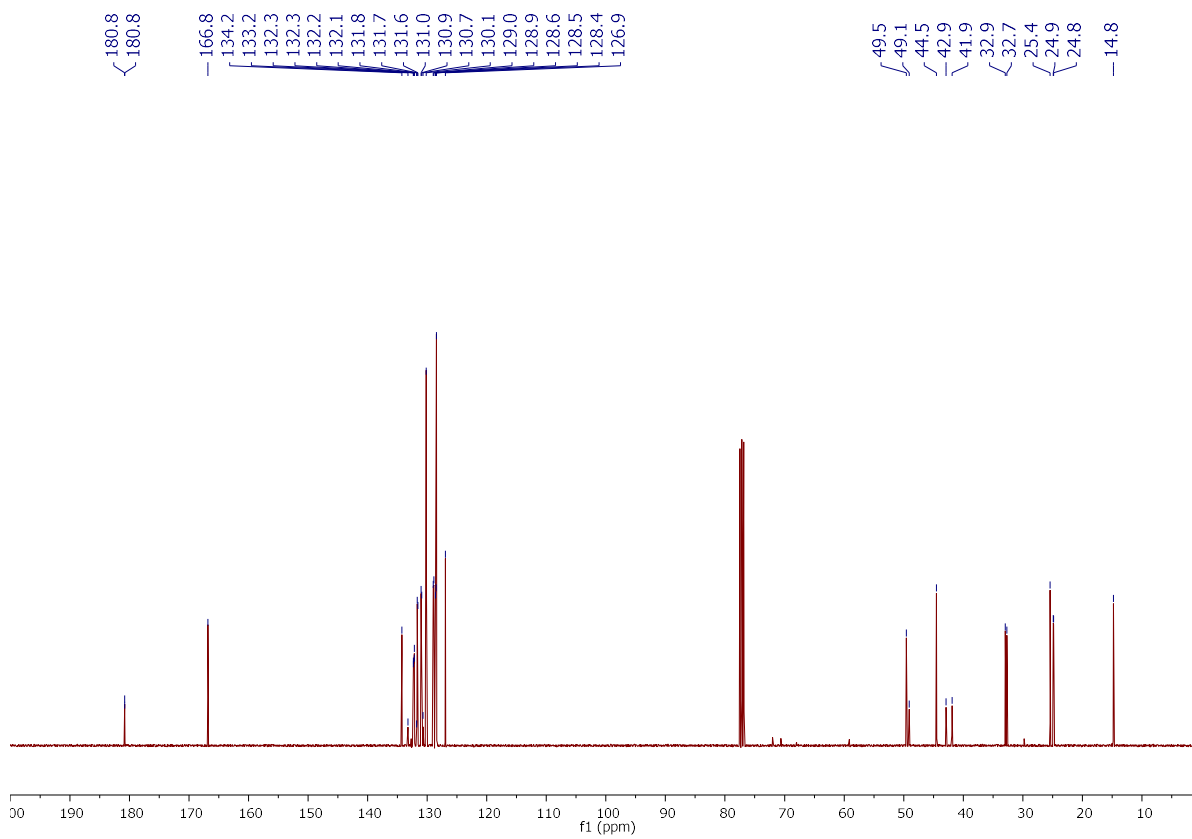
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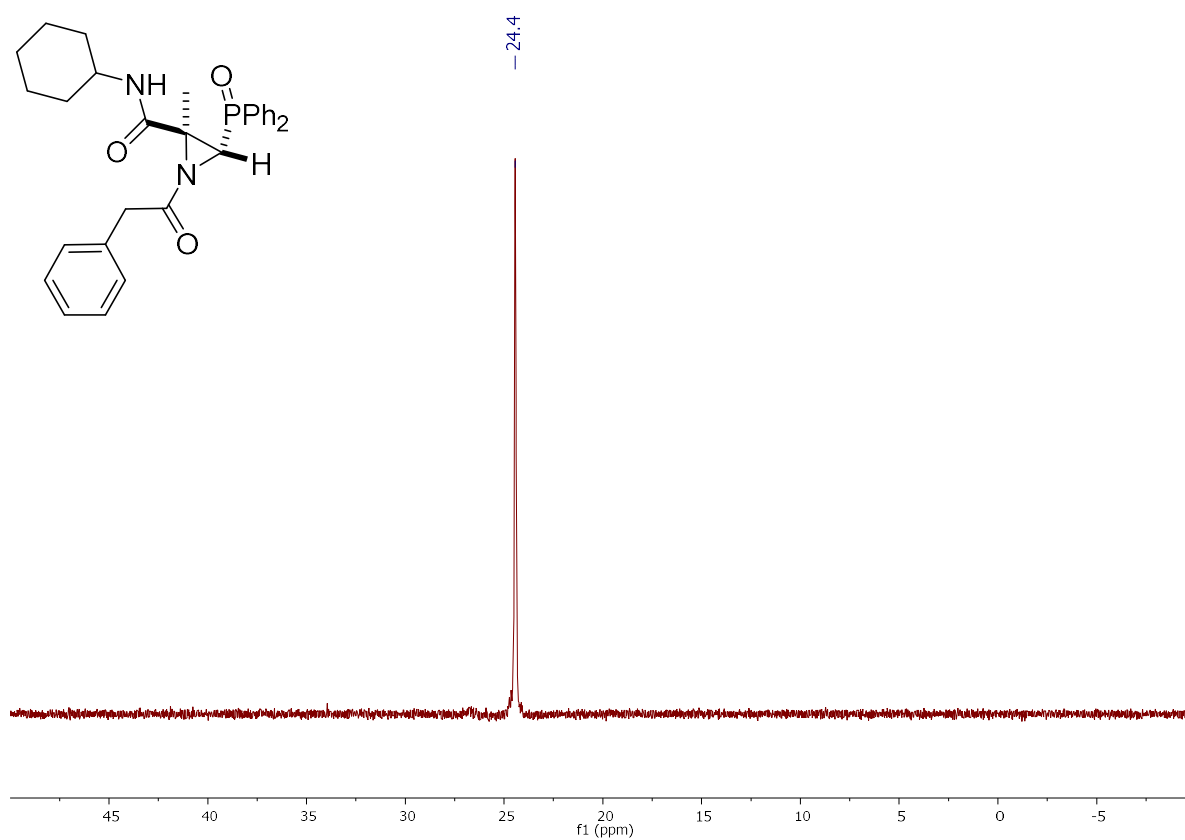
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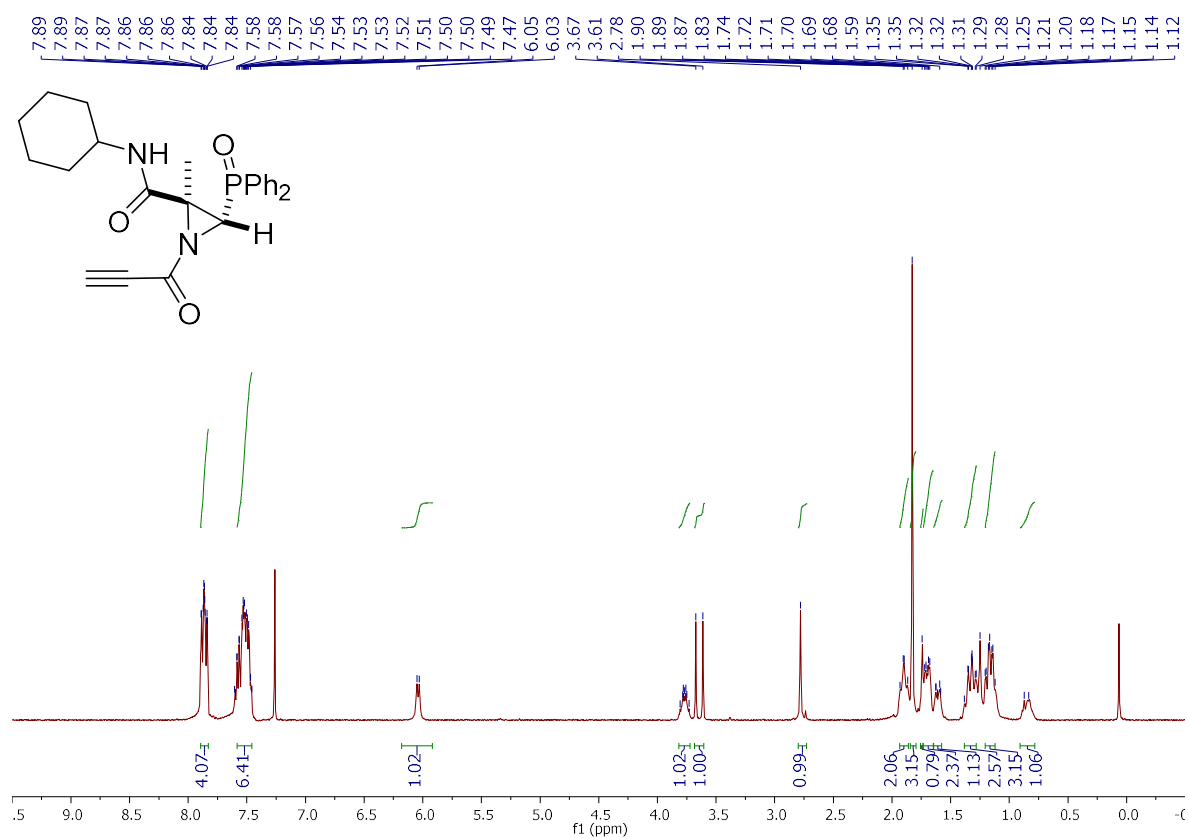
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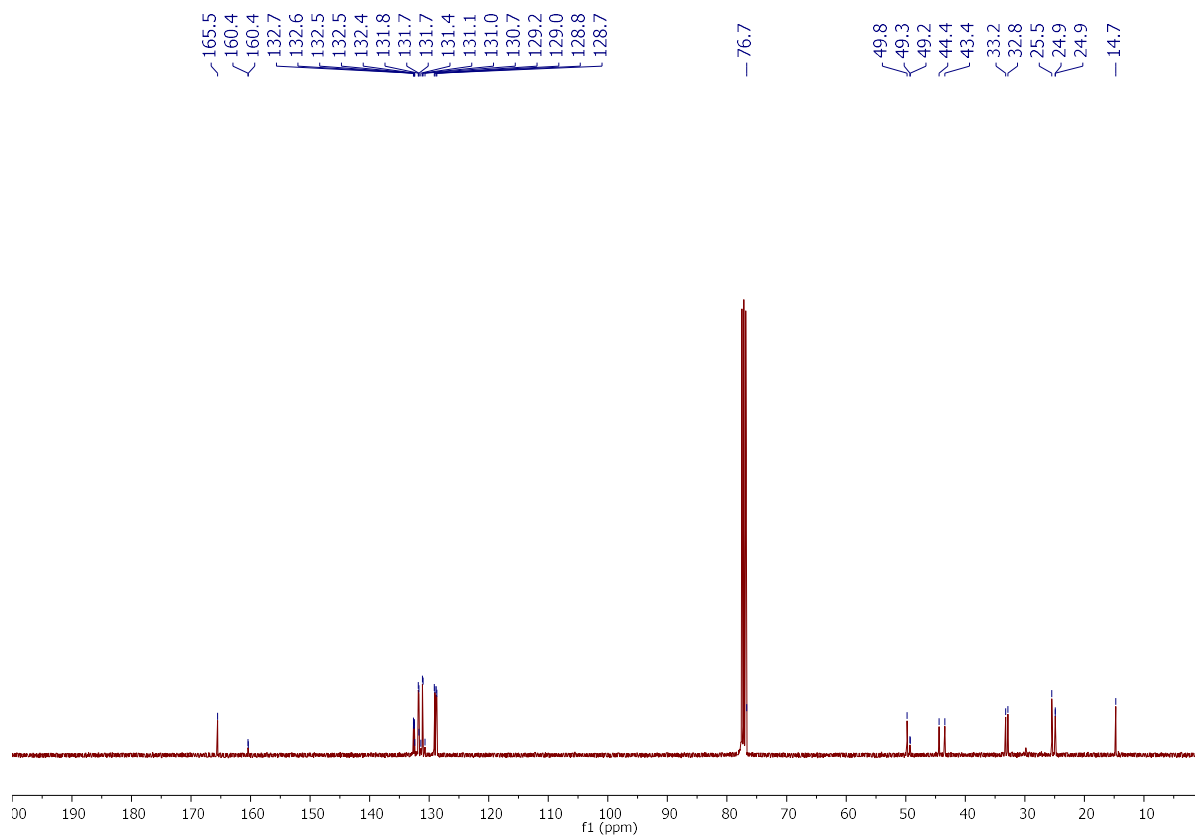
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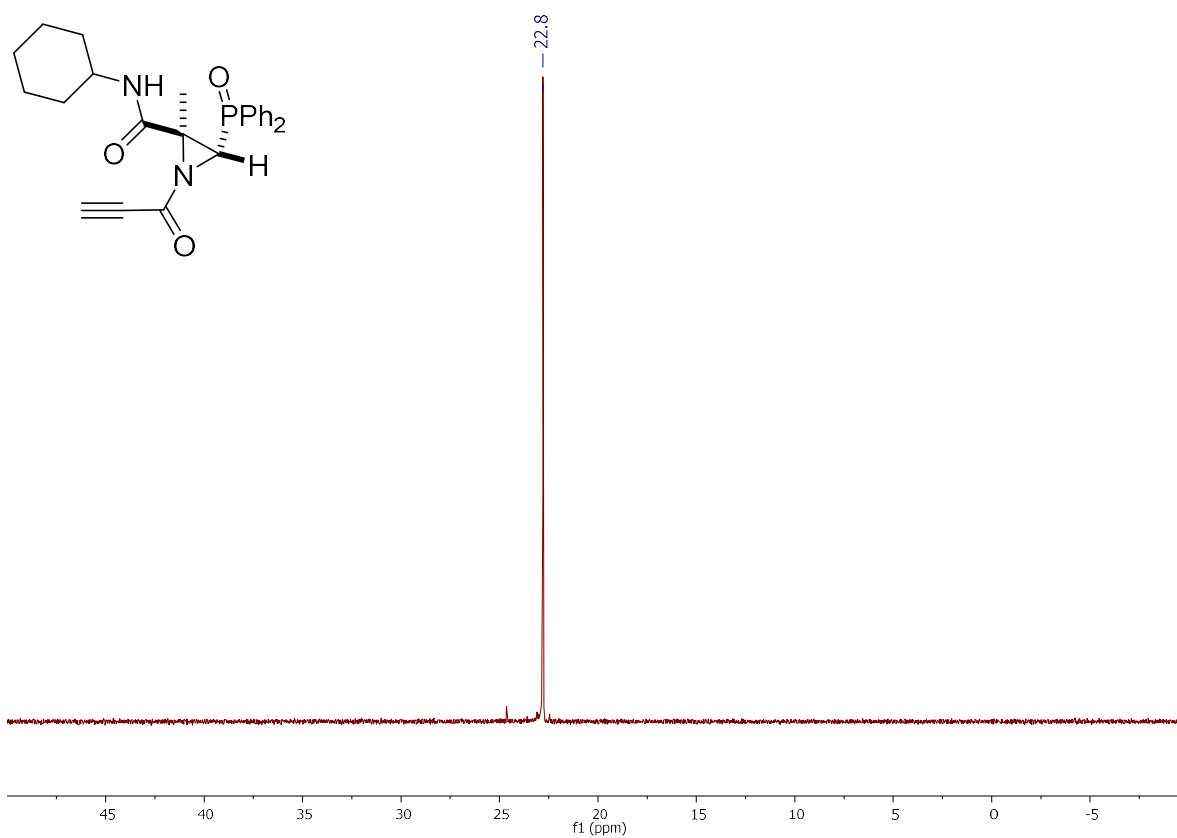
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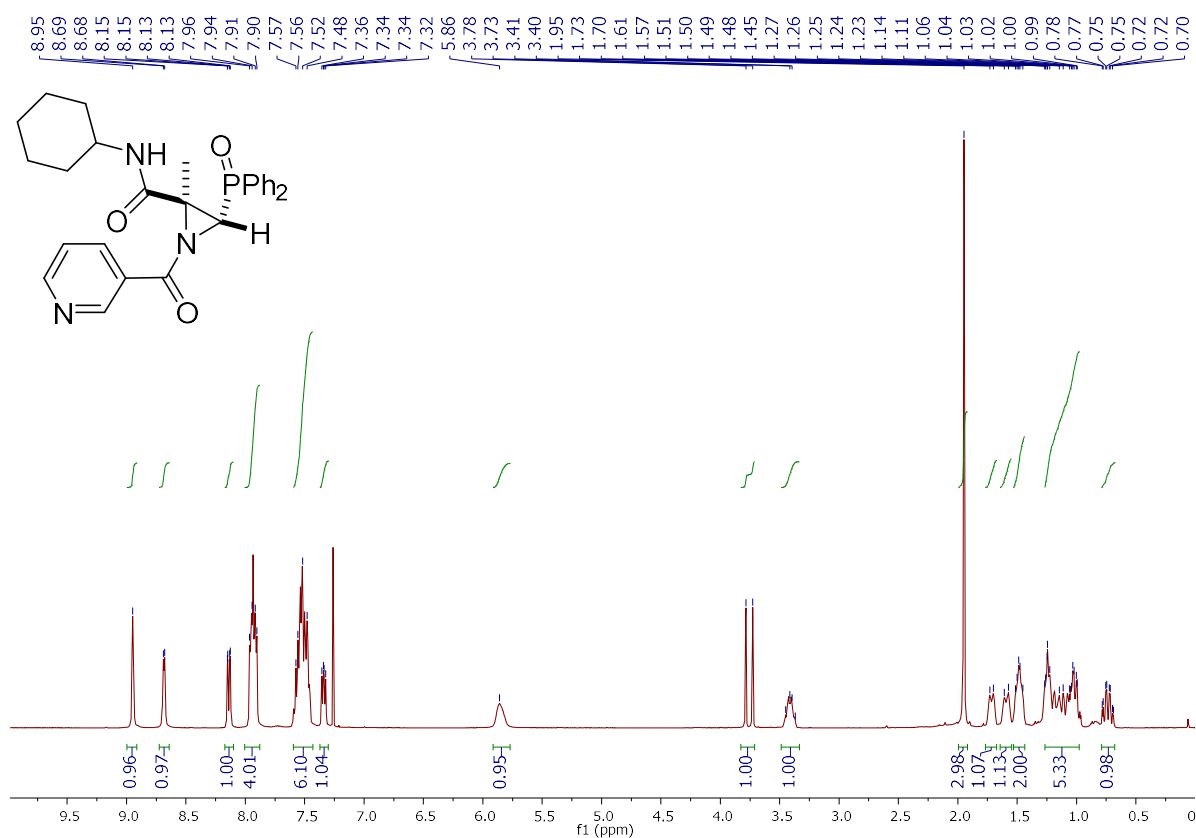
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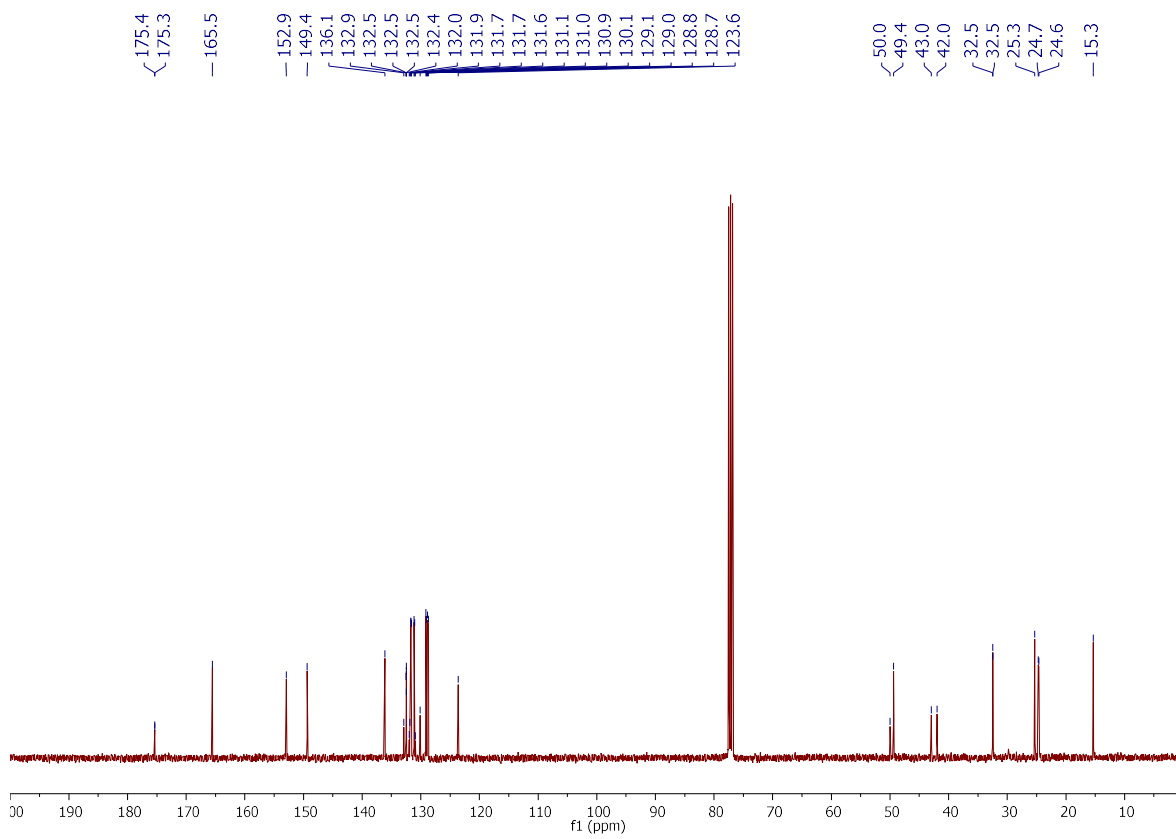
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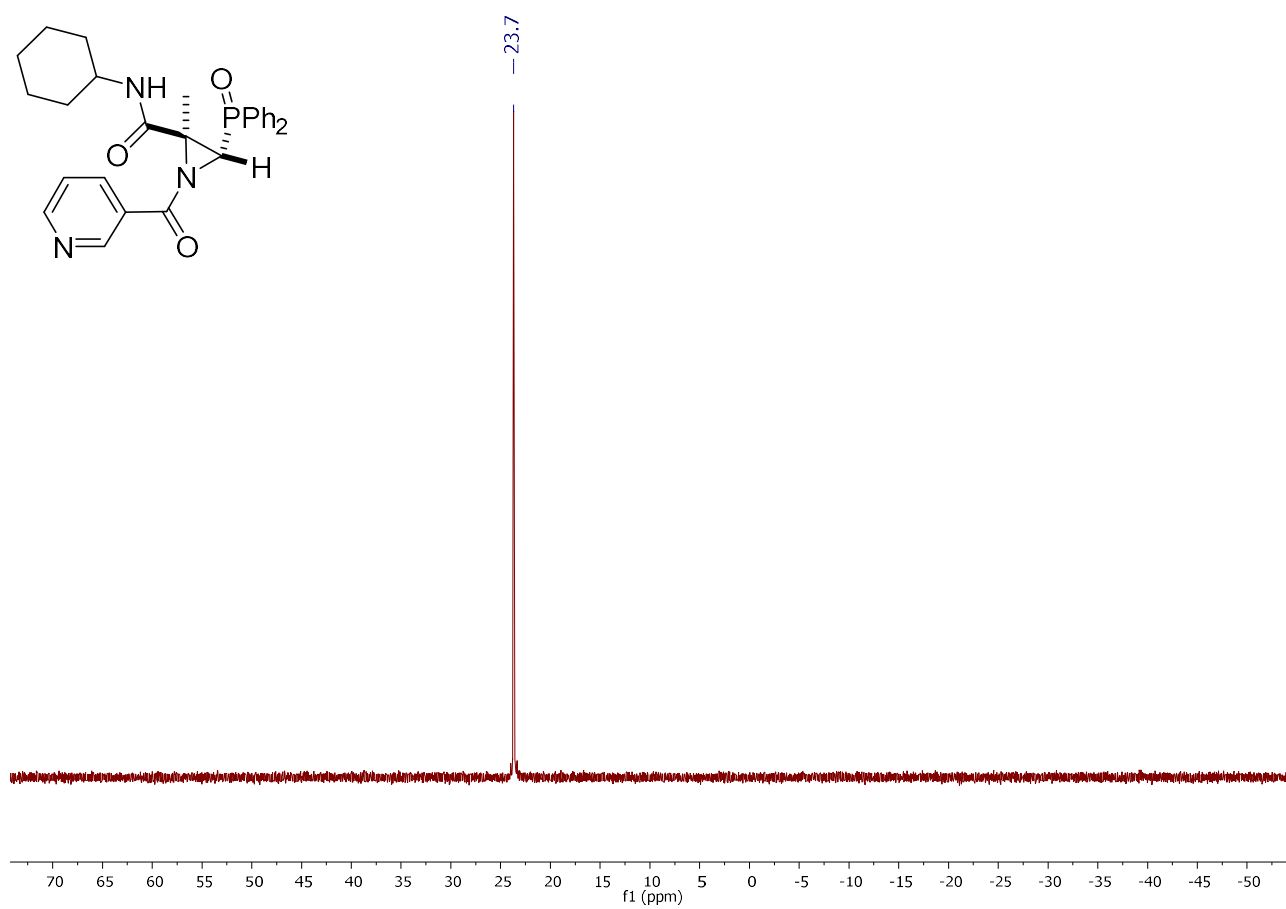
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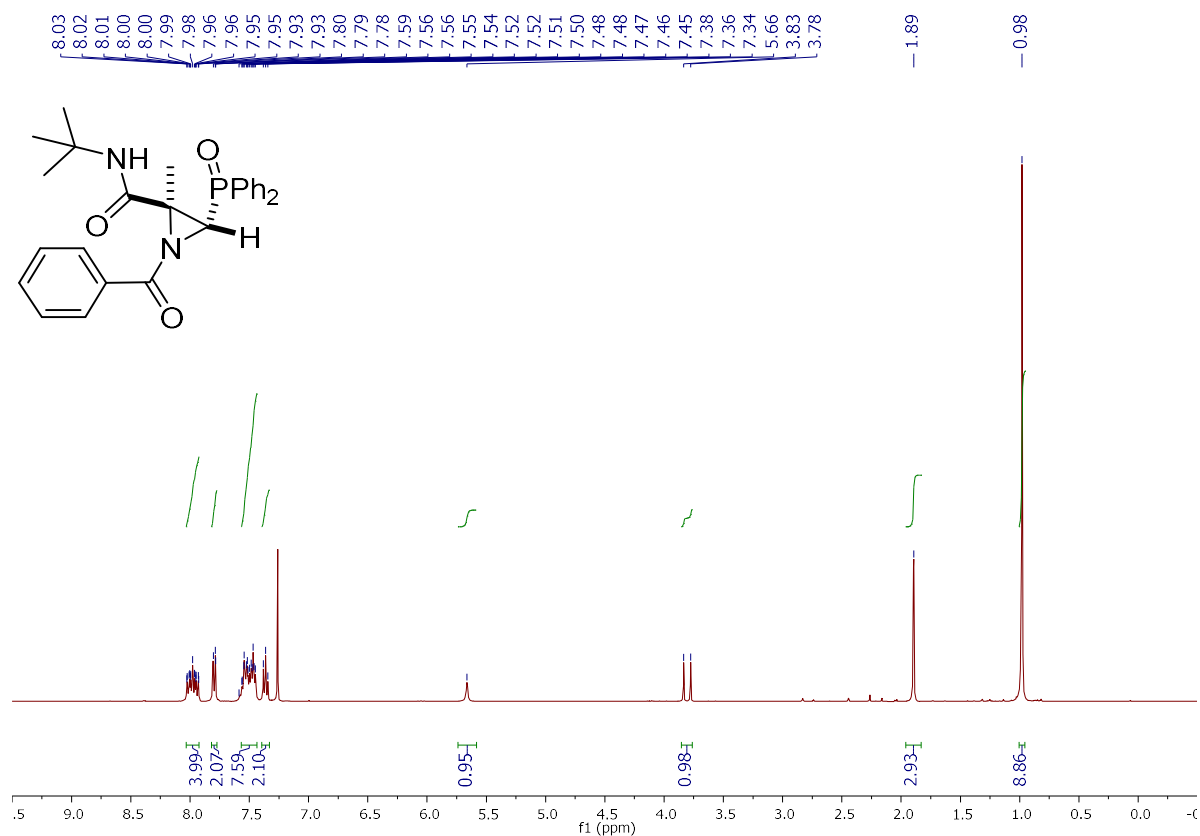
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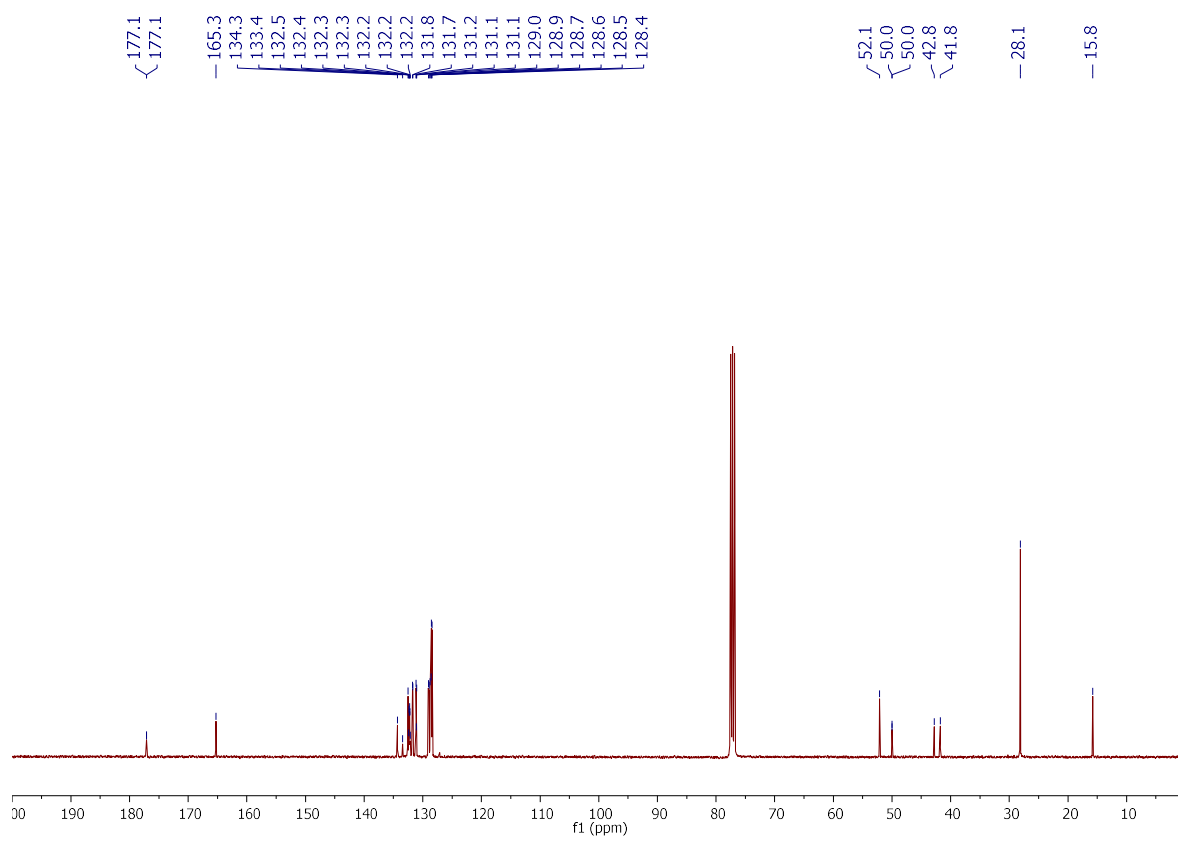
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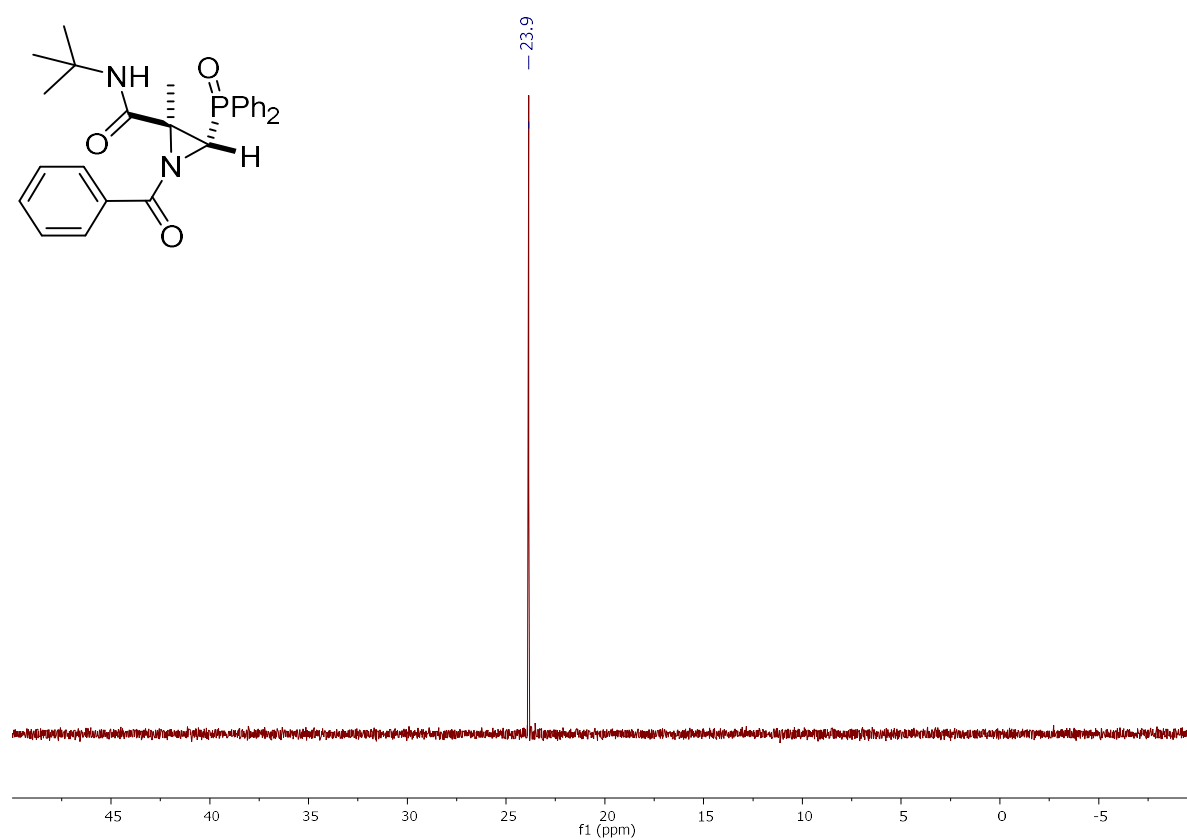


^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4i**

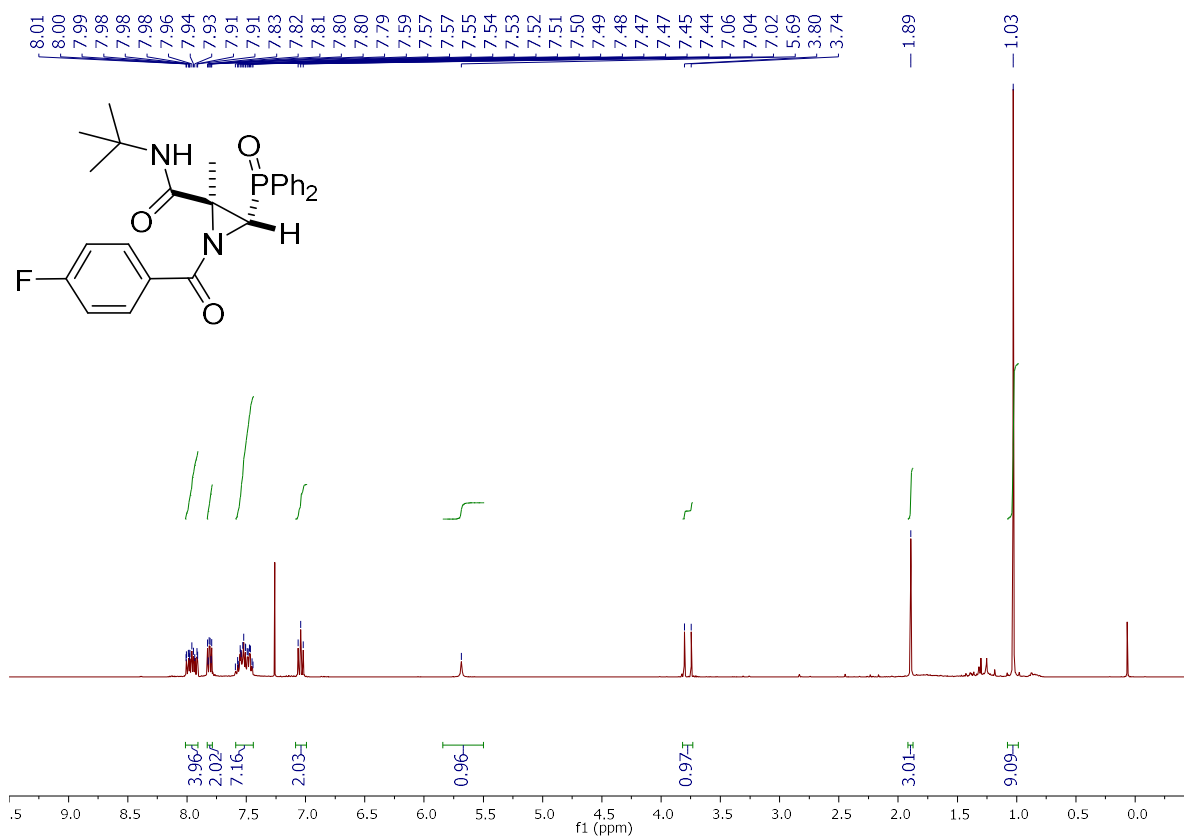


^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4i**

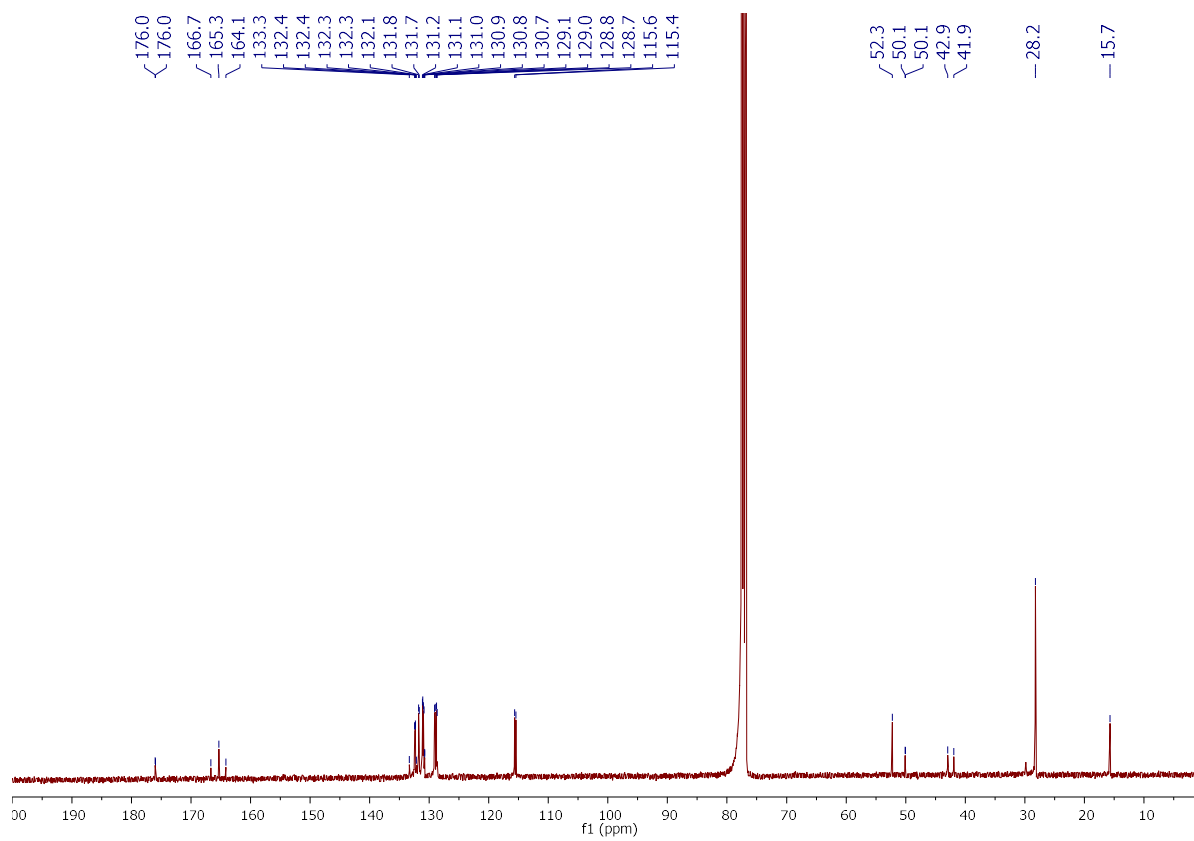


³¹P (160 MHz, CDCl₃) of *N*-Acylaziridine Phosphine Oxide **4i**

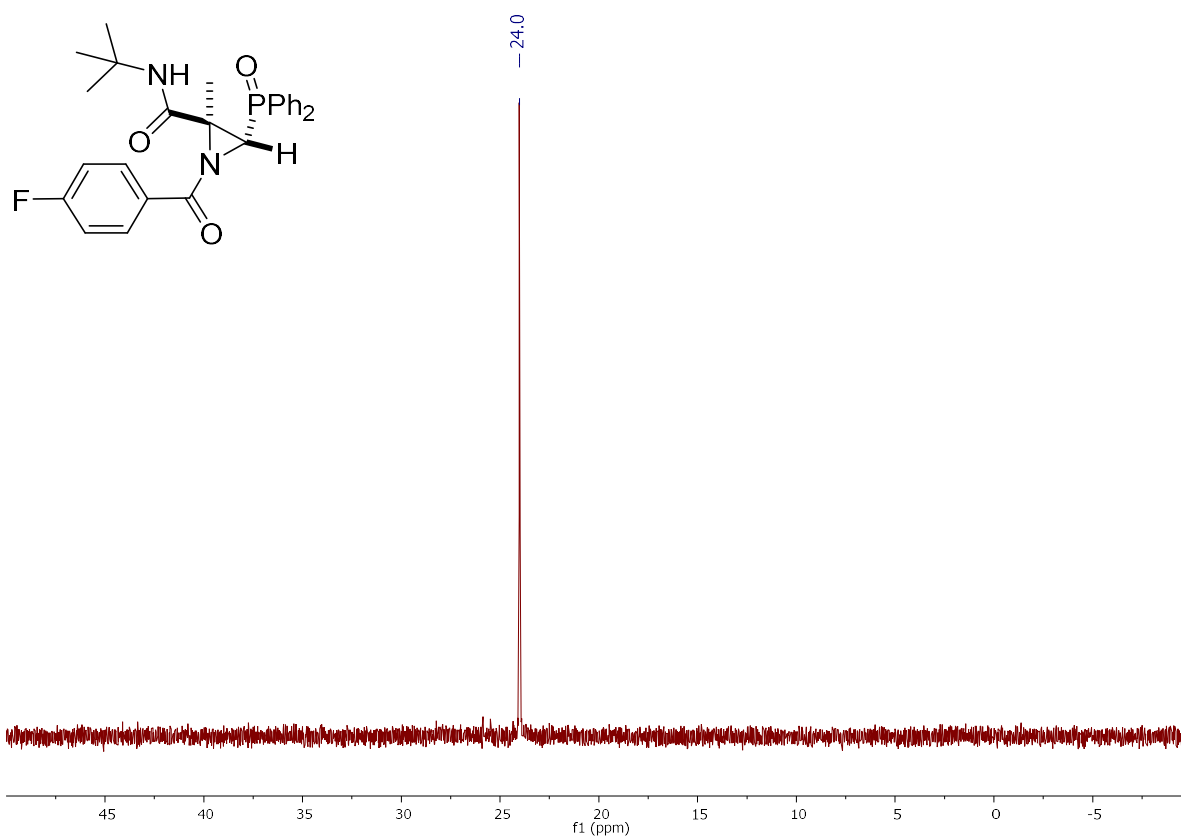
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4j**



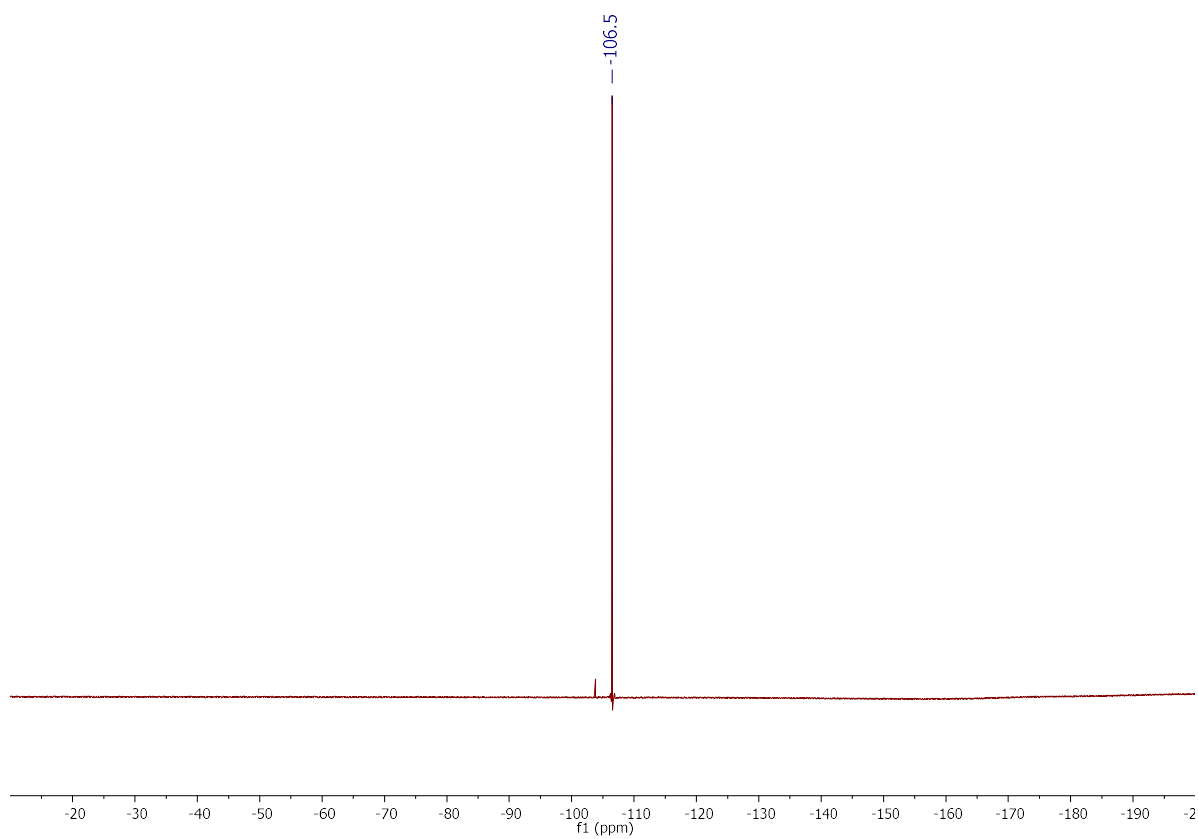
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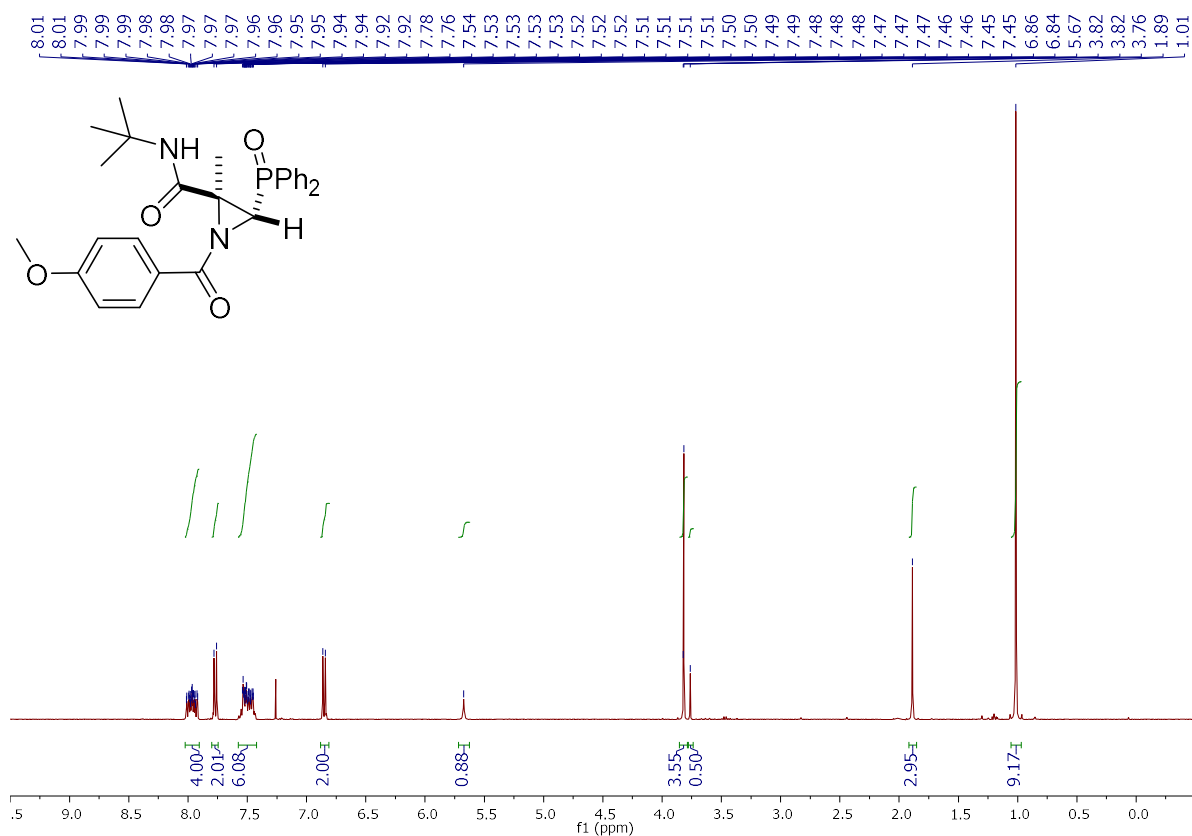
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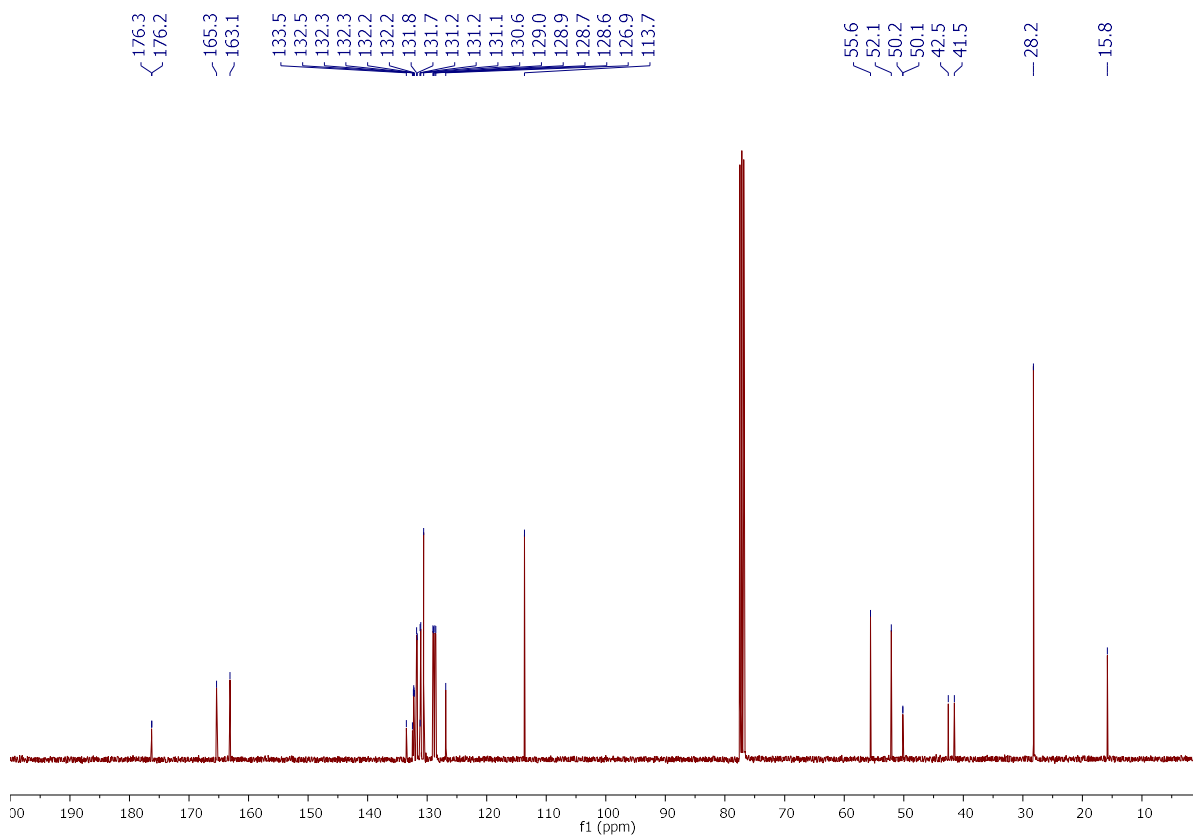
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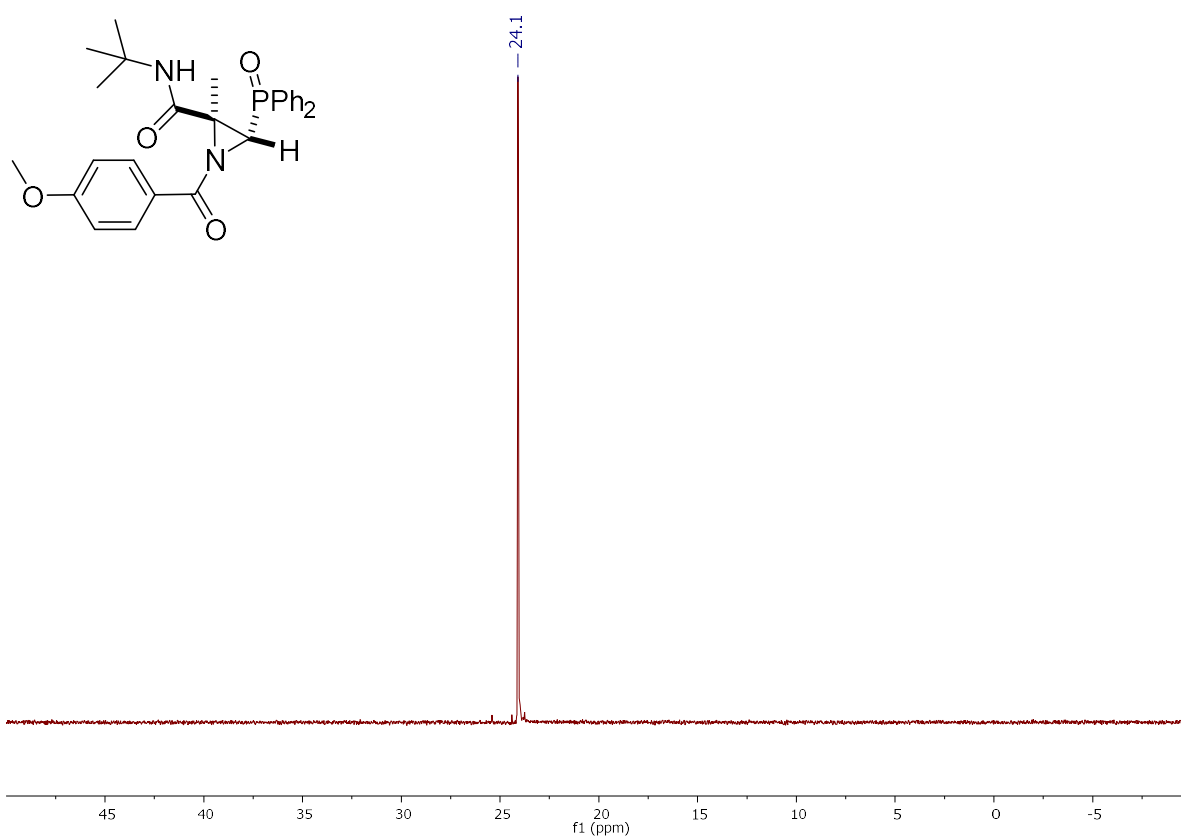
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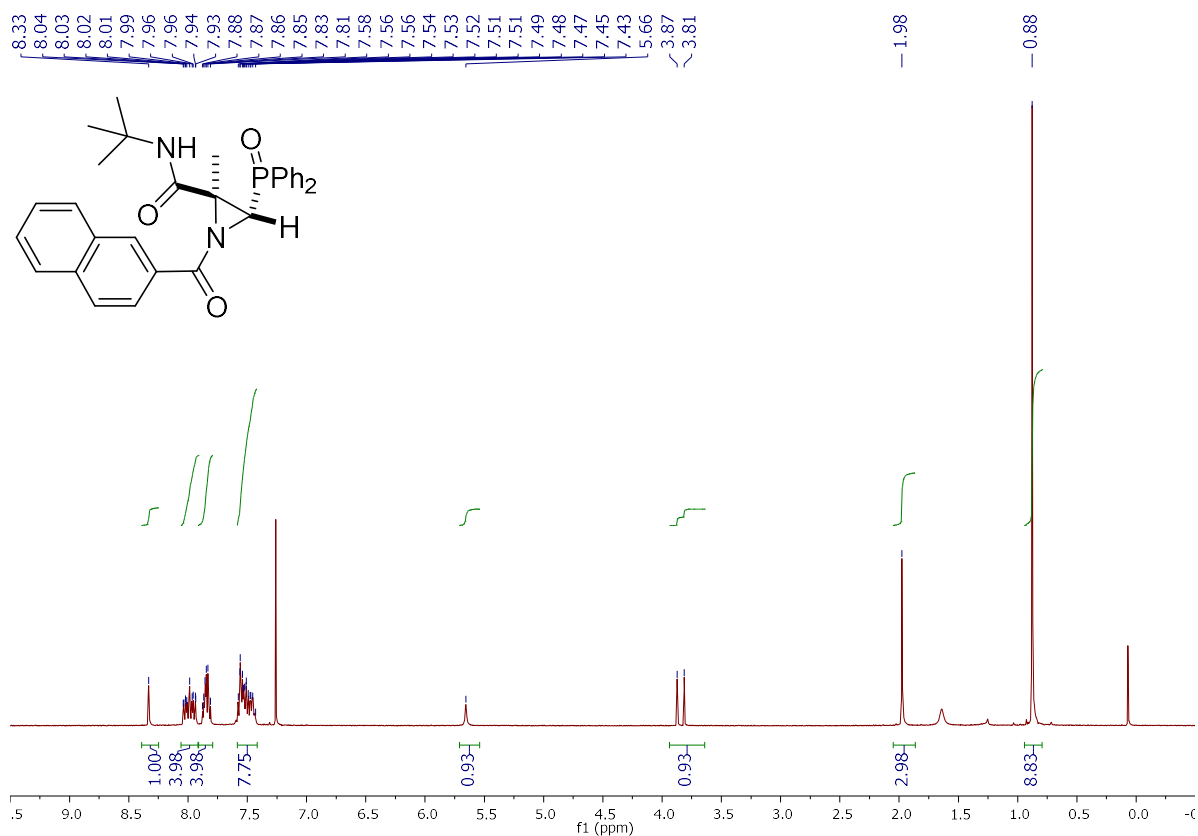
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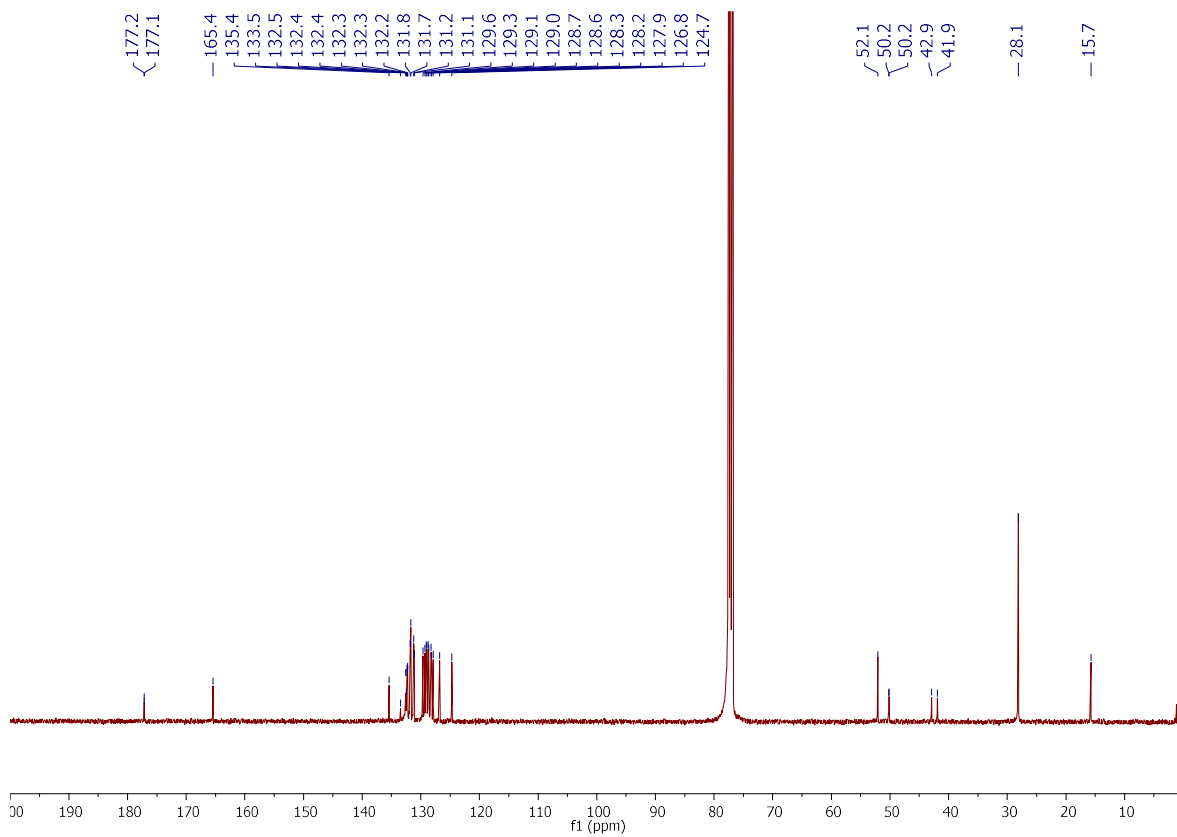
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4k**

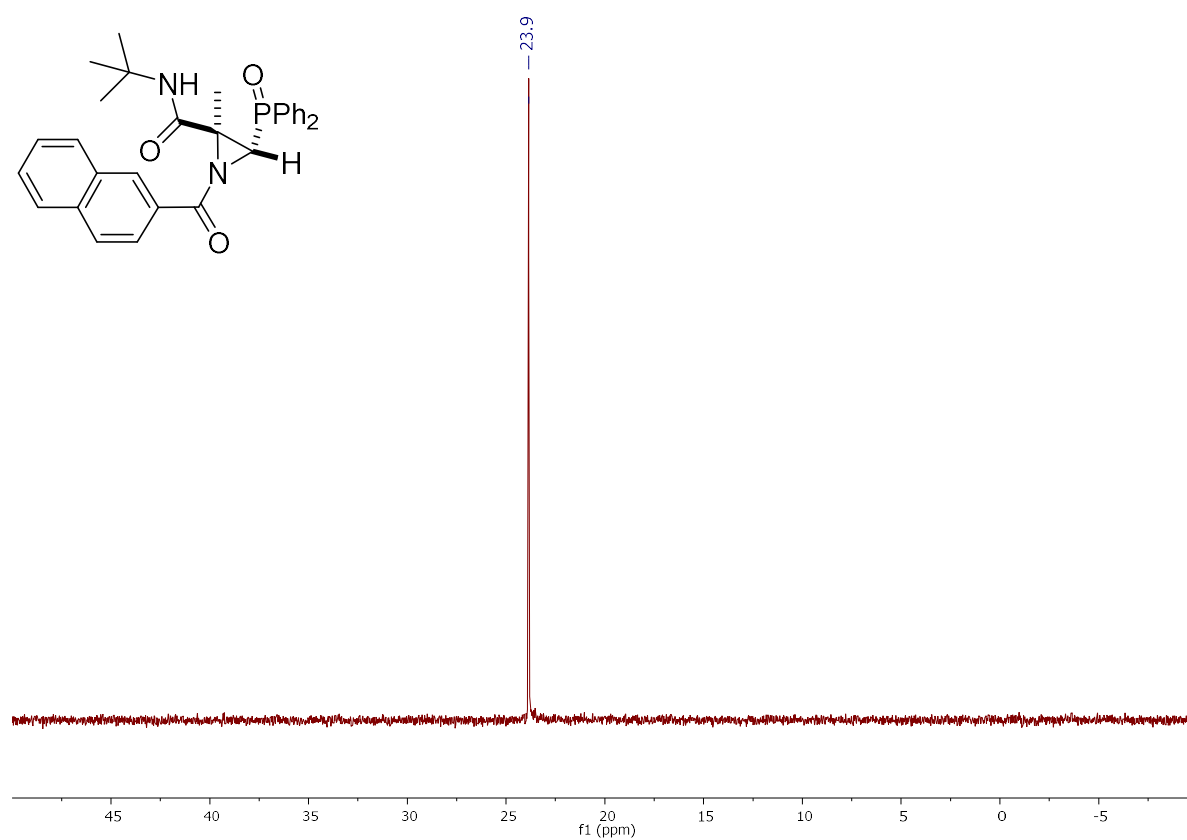


^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4I**

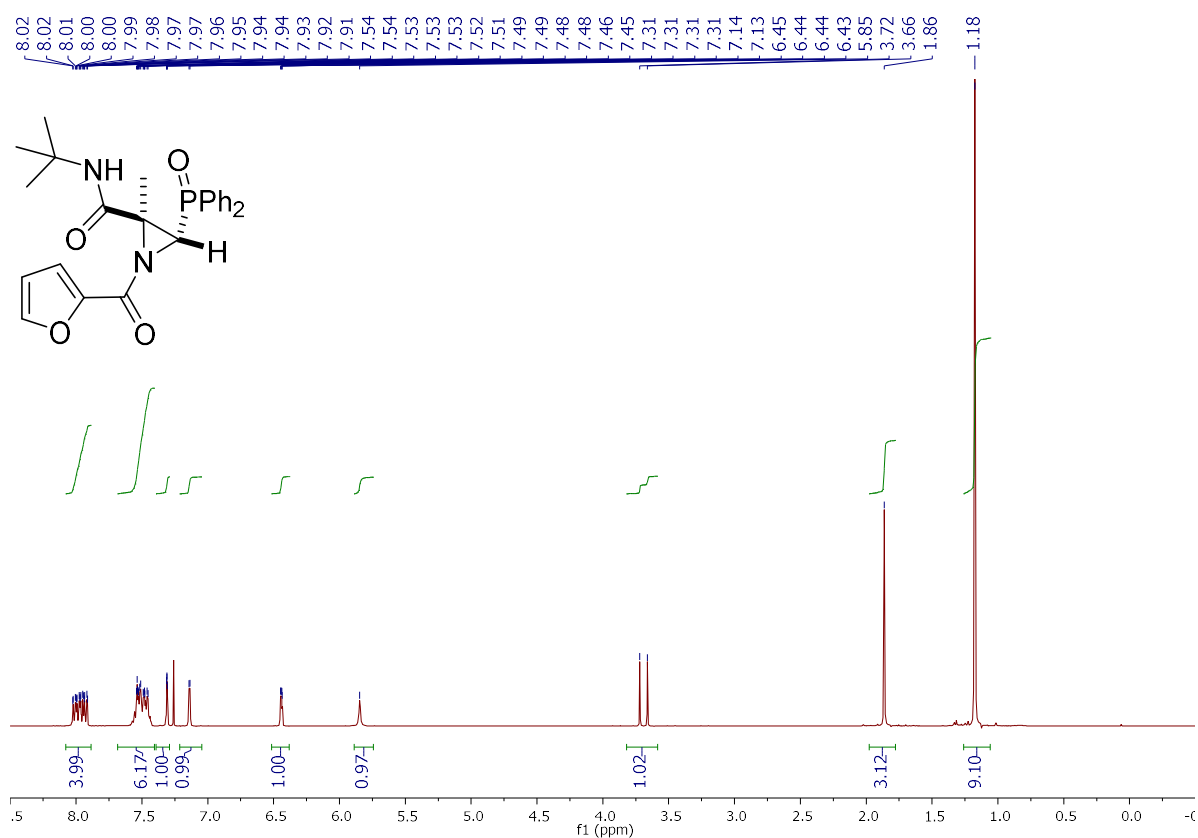


^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4I**

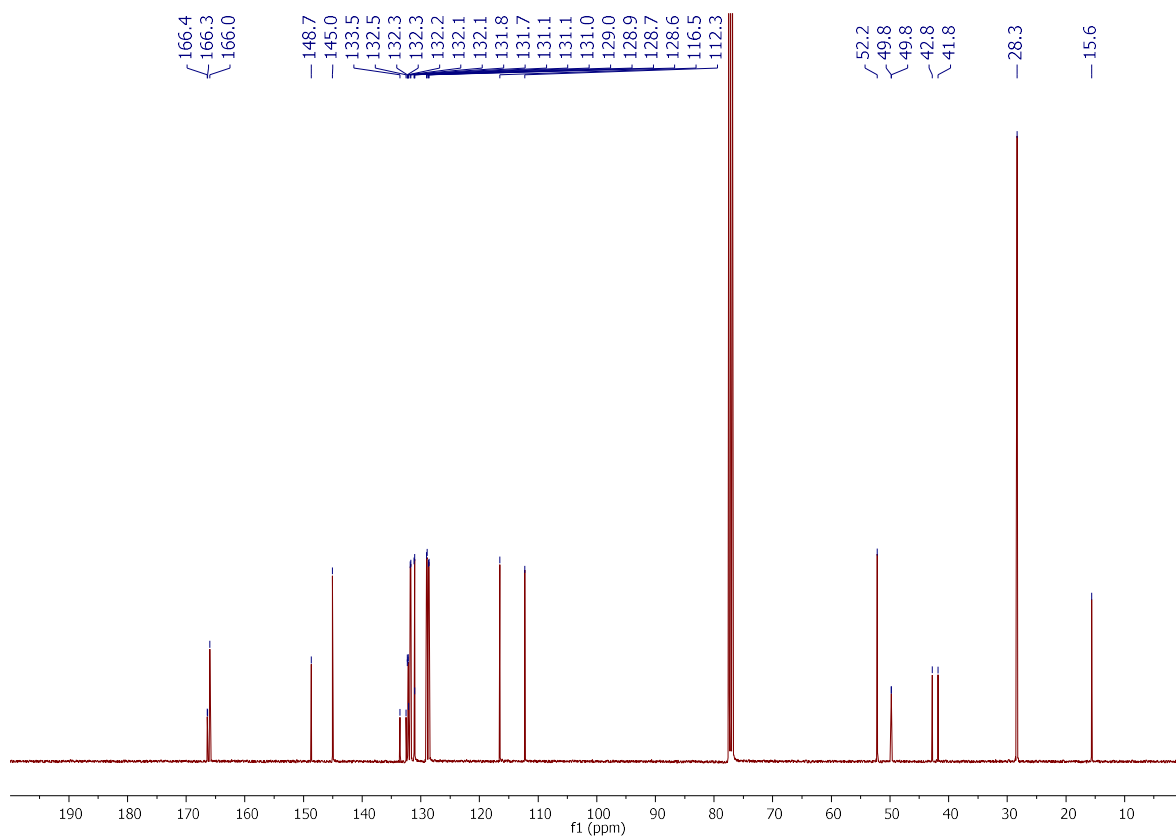


³¹P (160 MHz, CDCl₃) of *N*-Acylaziridine Phosphine Oxide **4l**

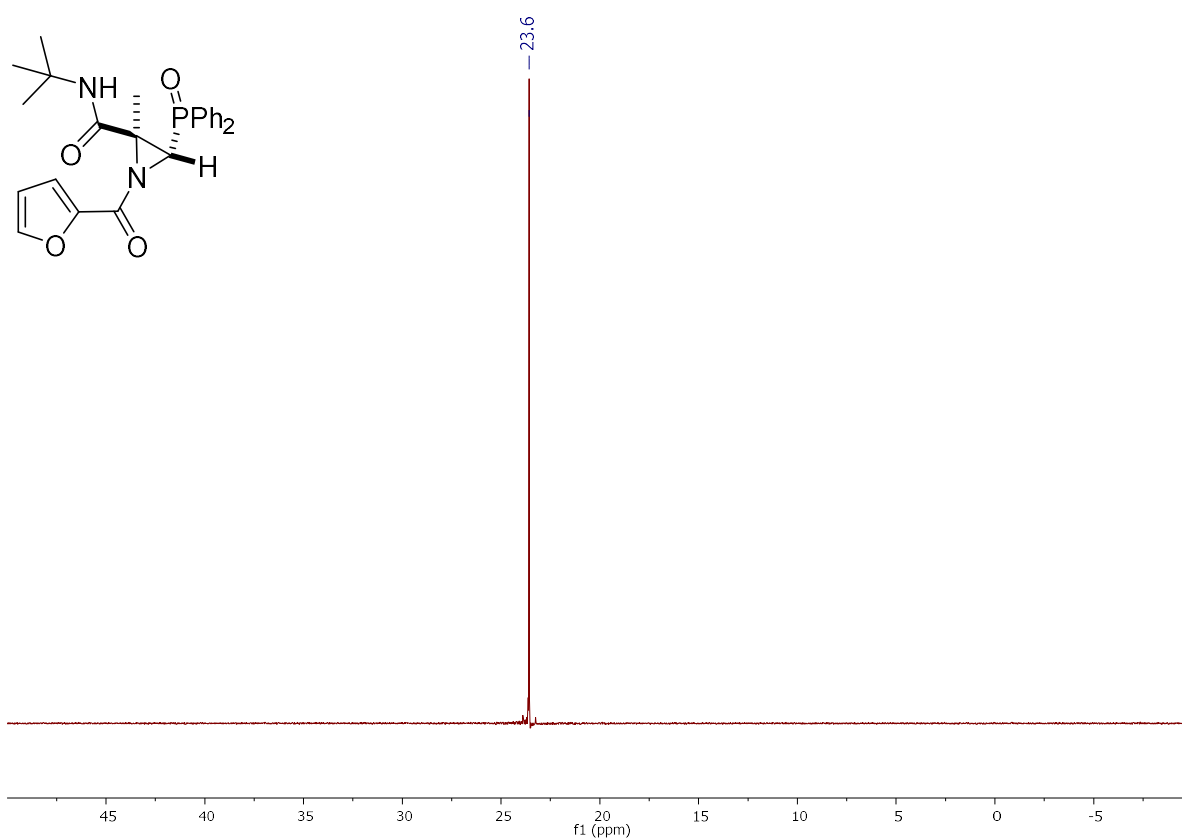
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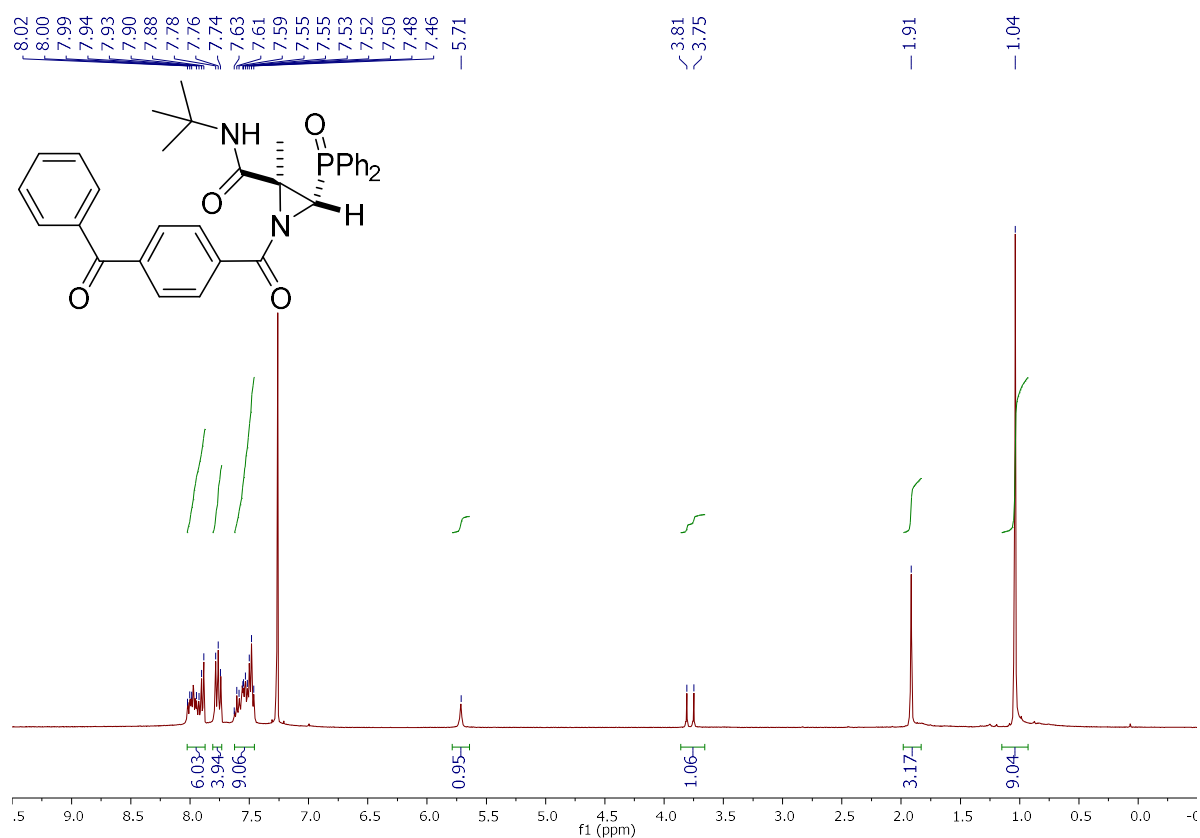
¹³C {¹H} NMR (100 MHz, CDCl₃) of *N*-Acylaziridine Phosphine Oxide **4m**



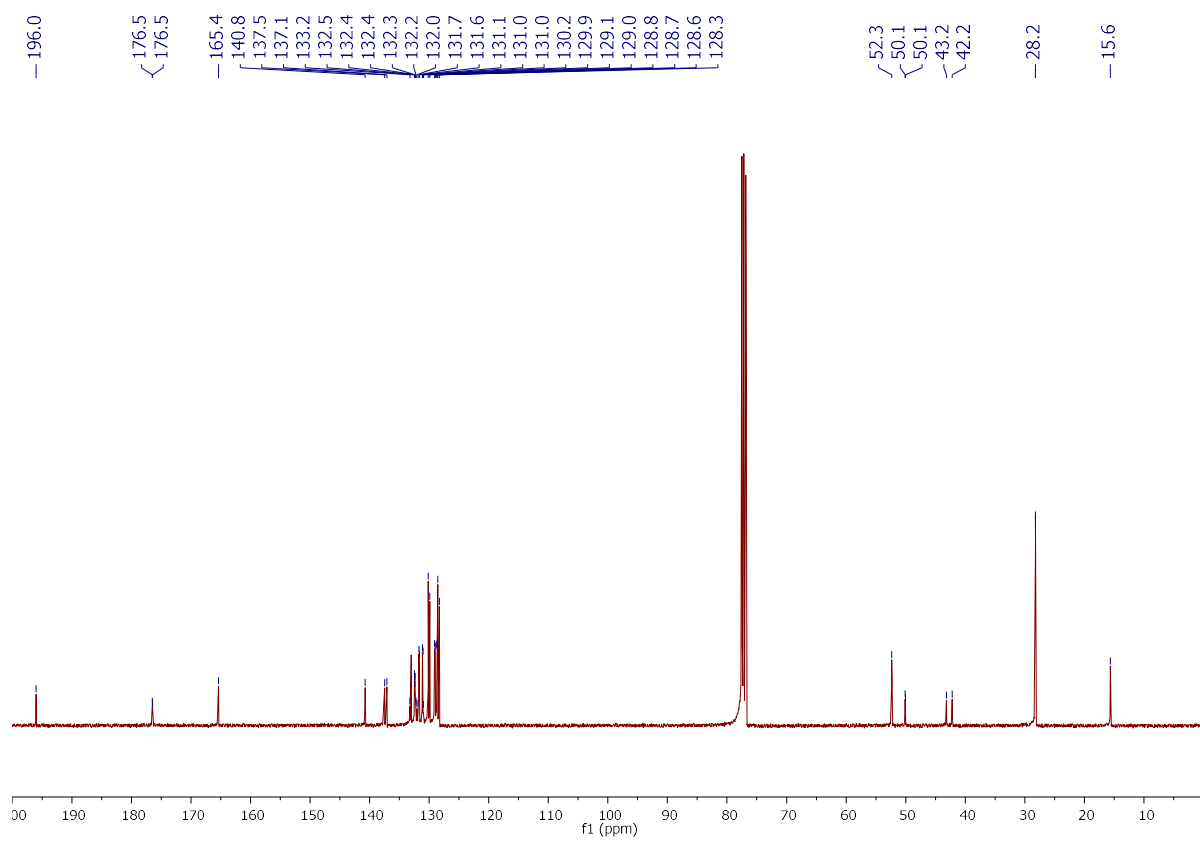
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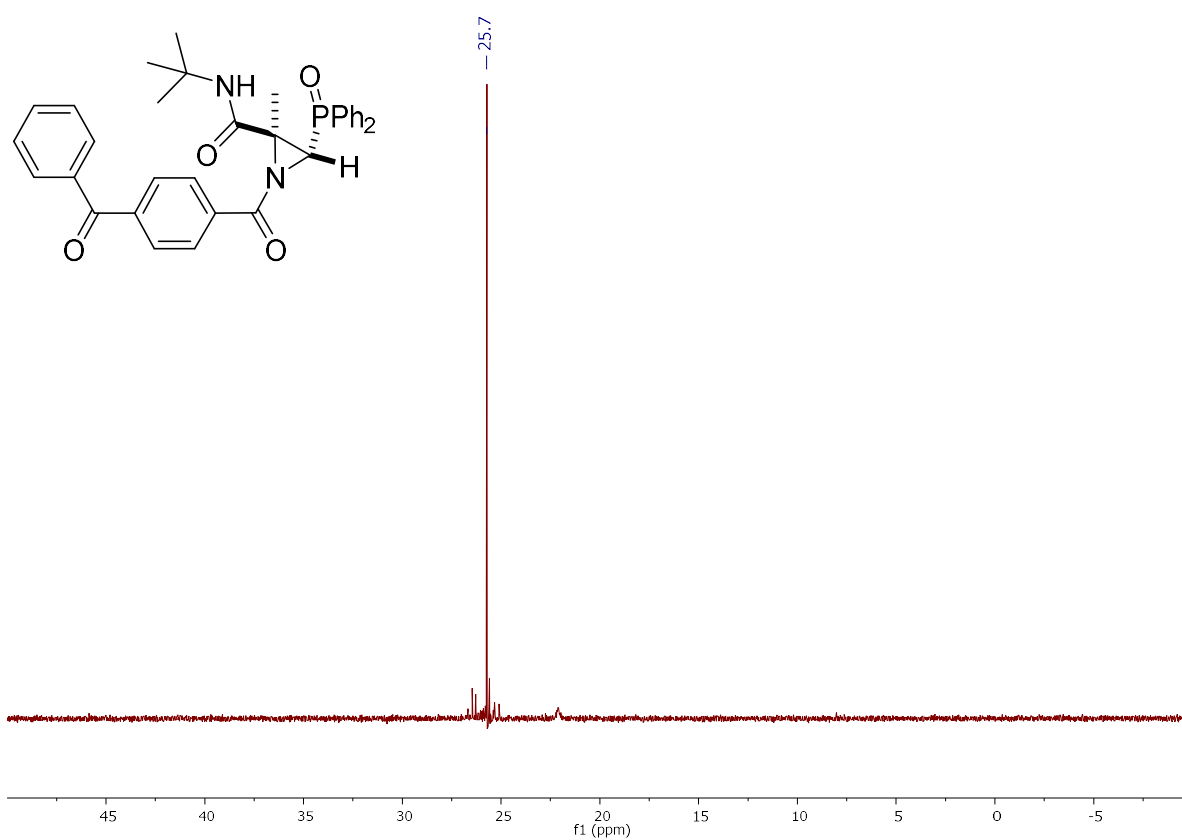
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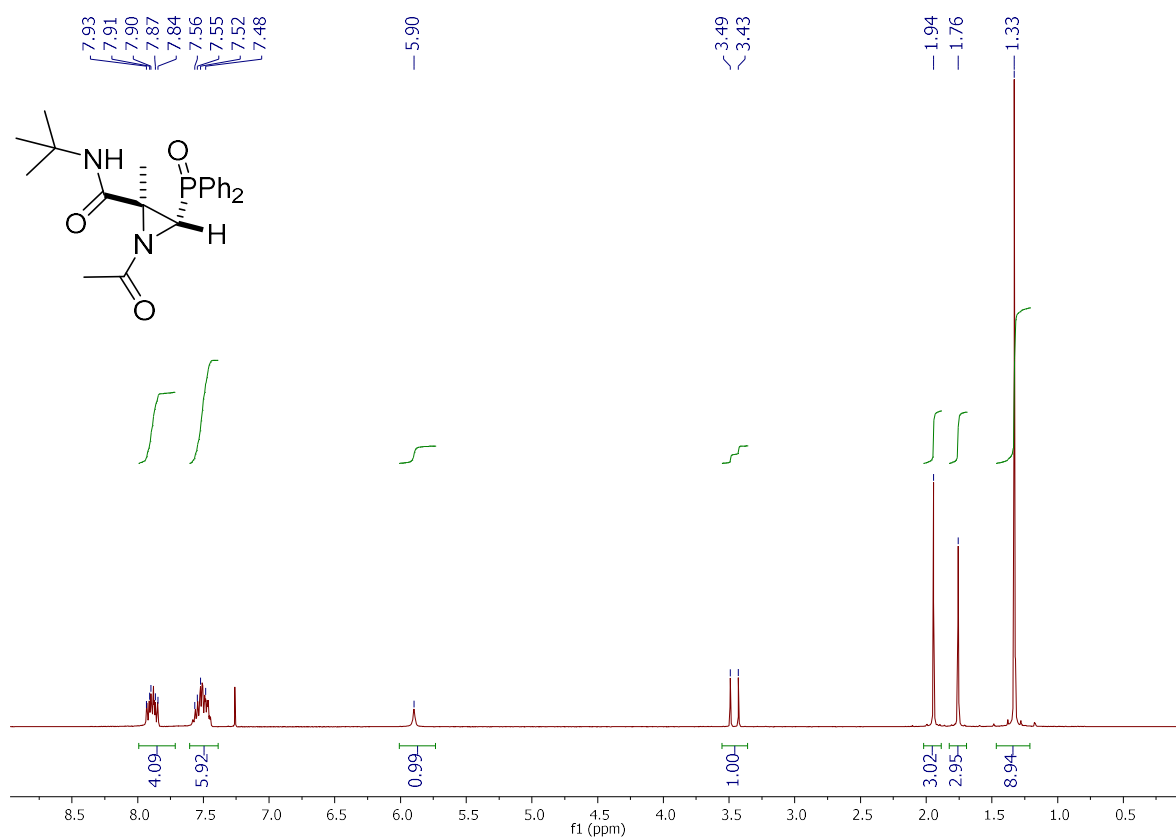
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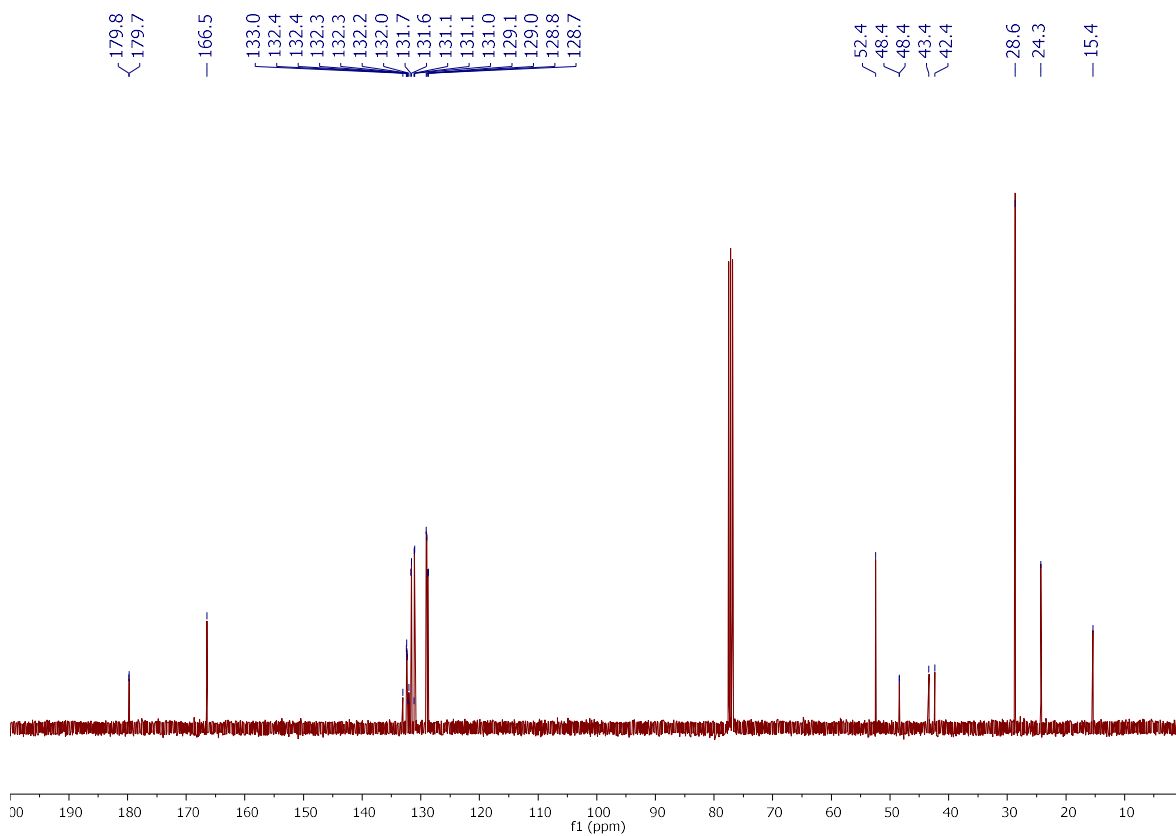
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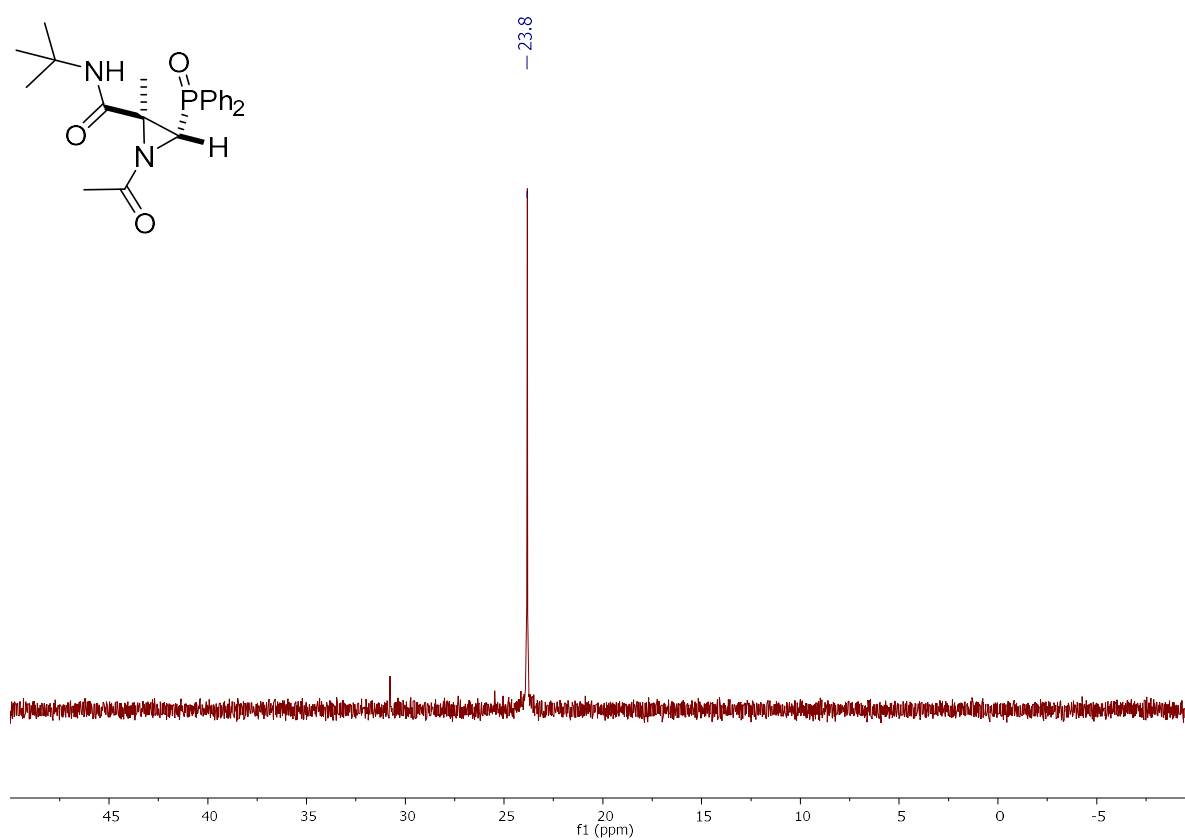
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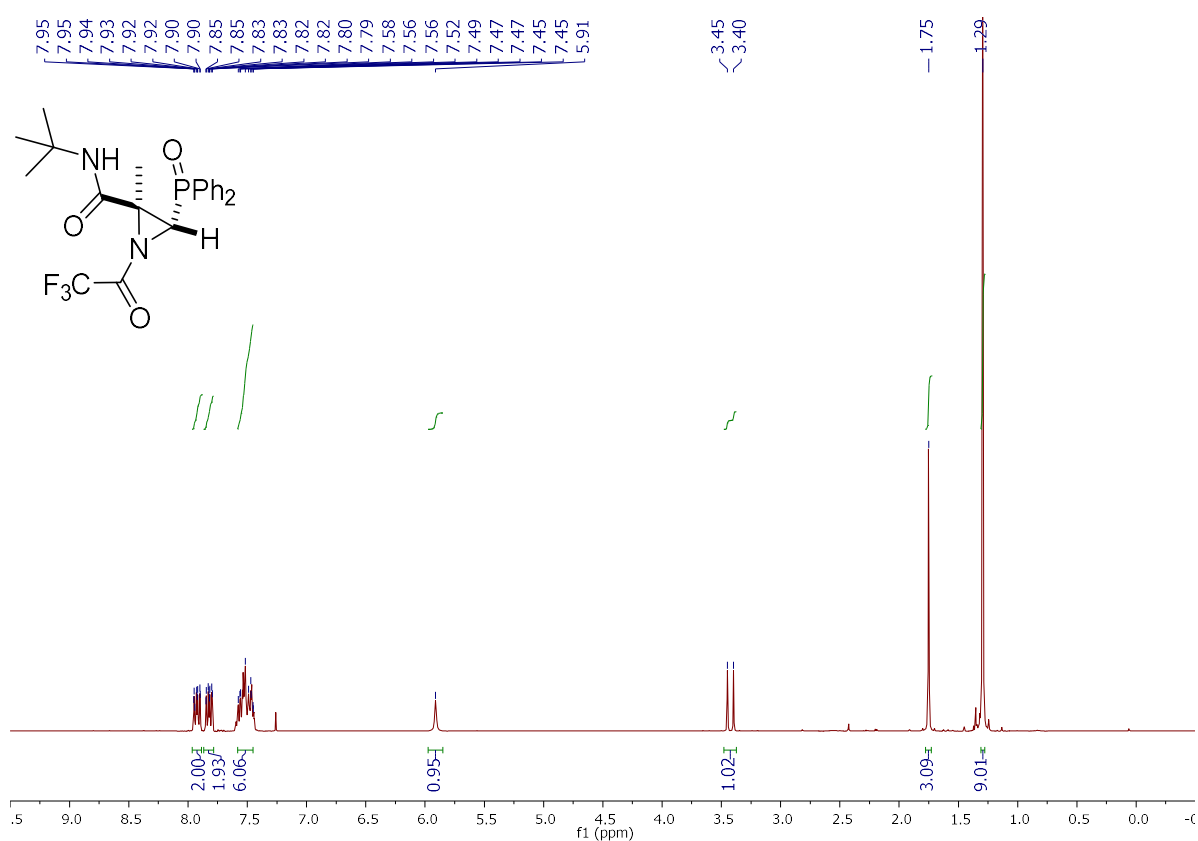
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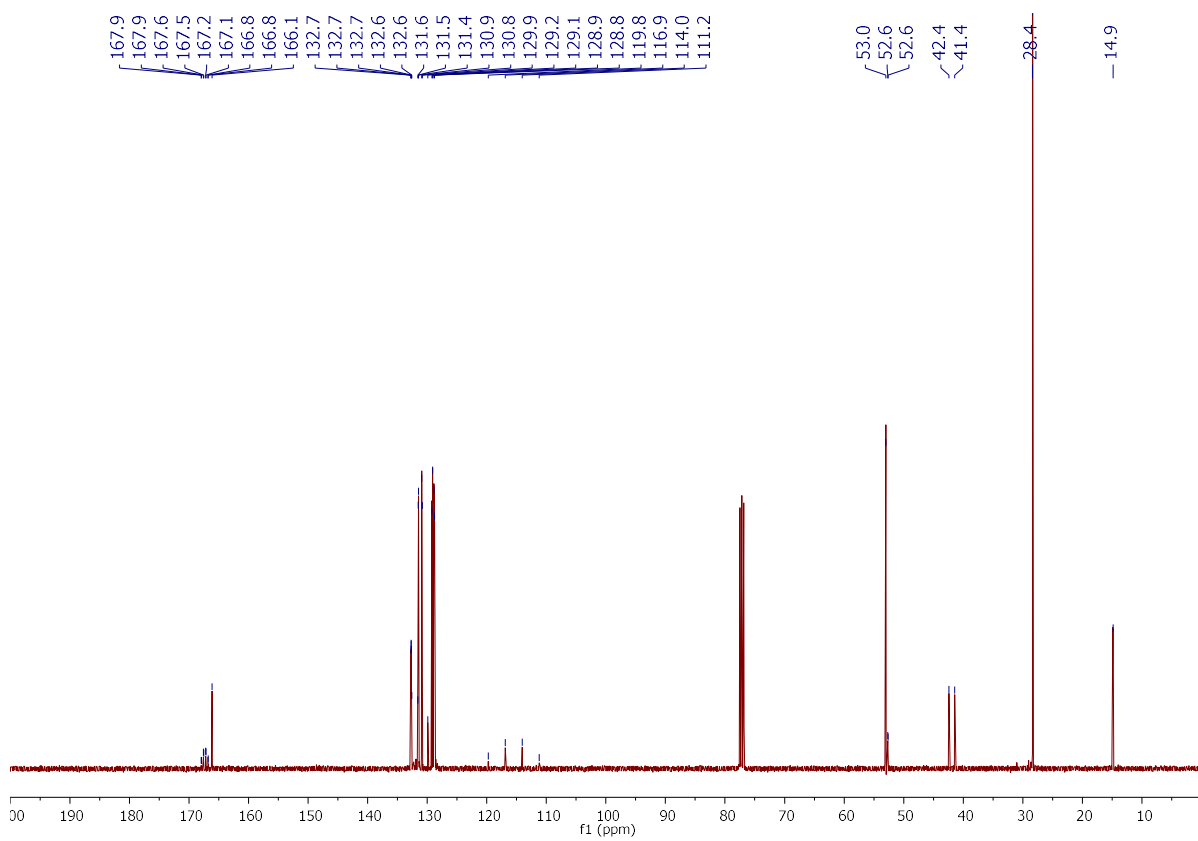
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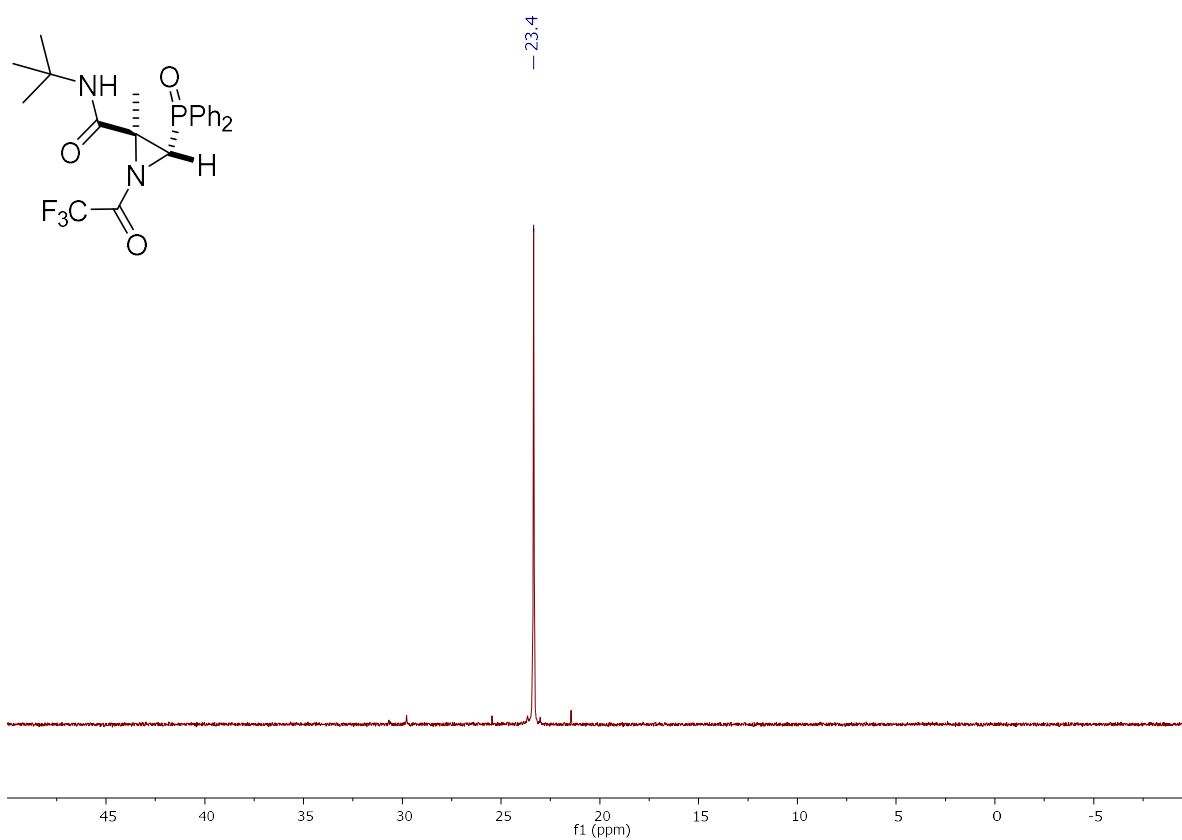
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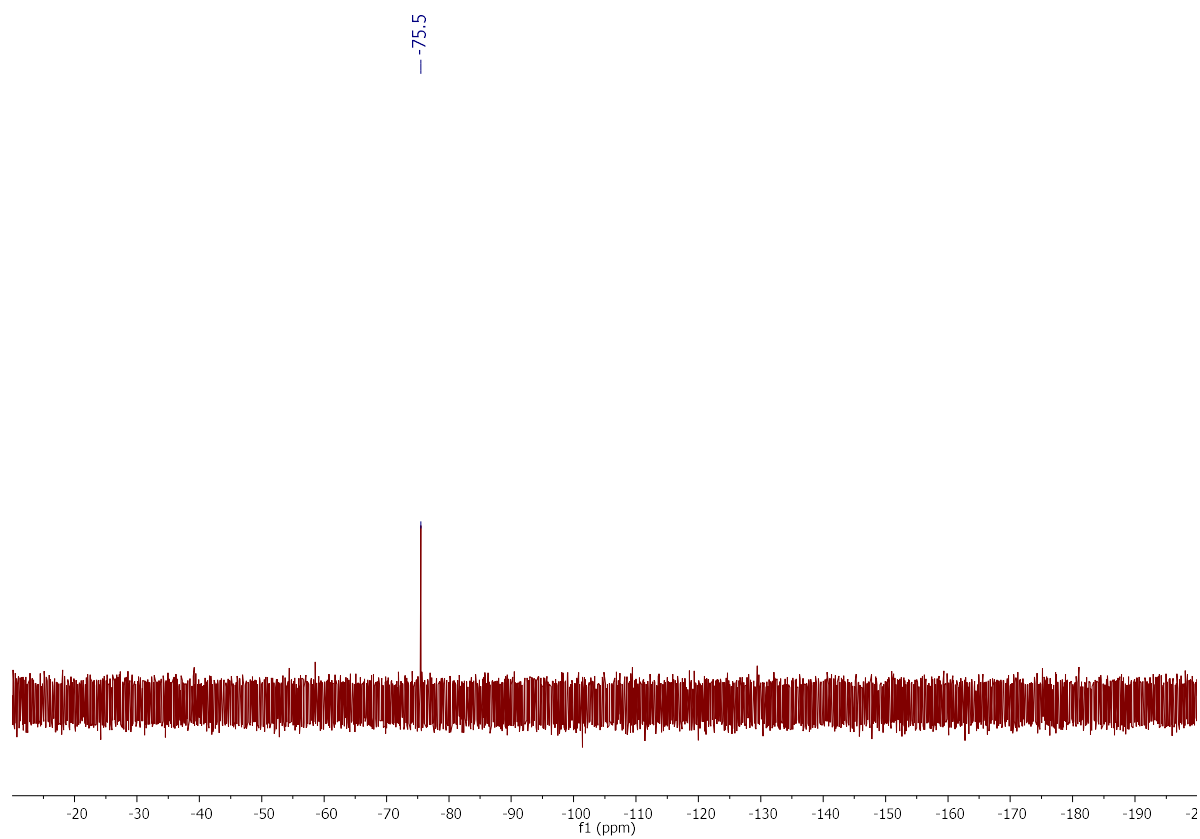
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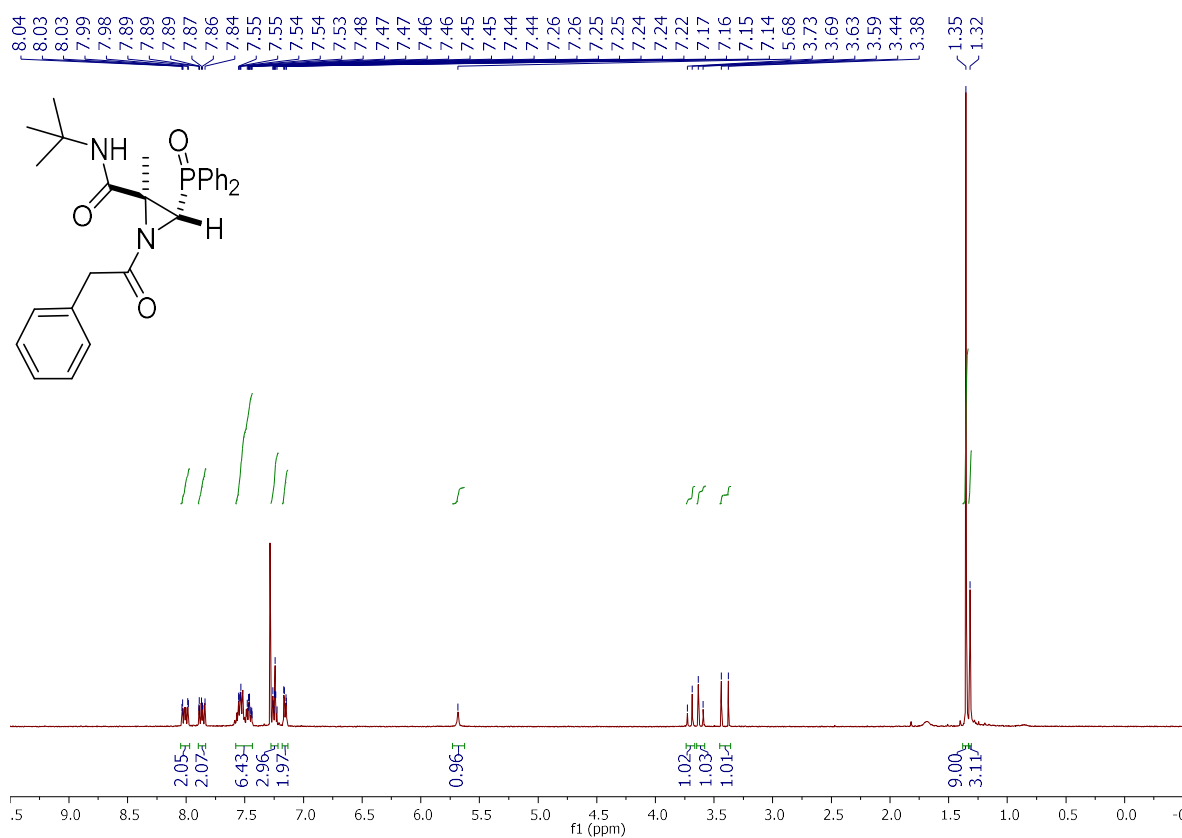
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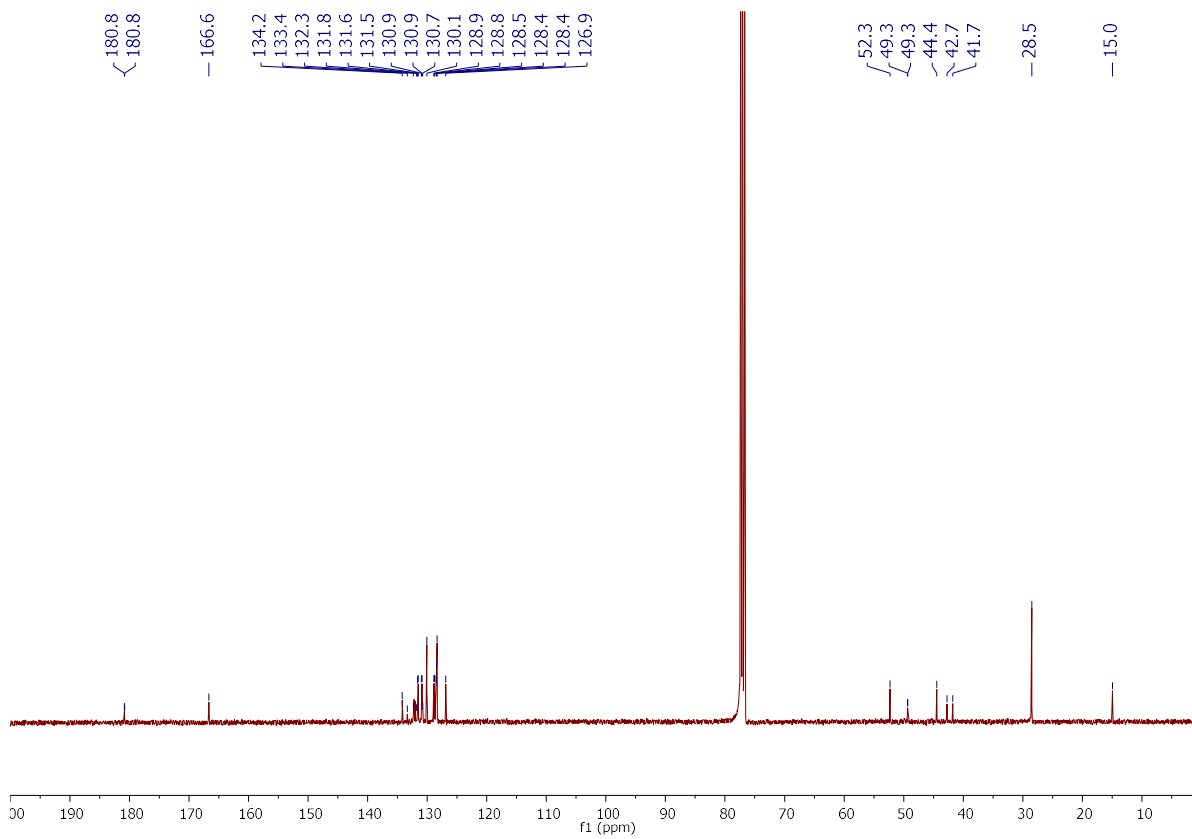
^{19}F (376 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4p**



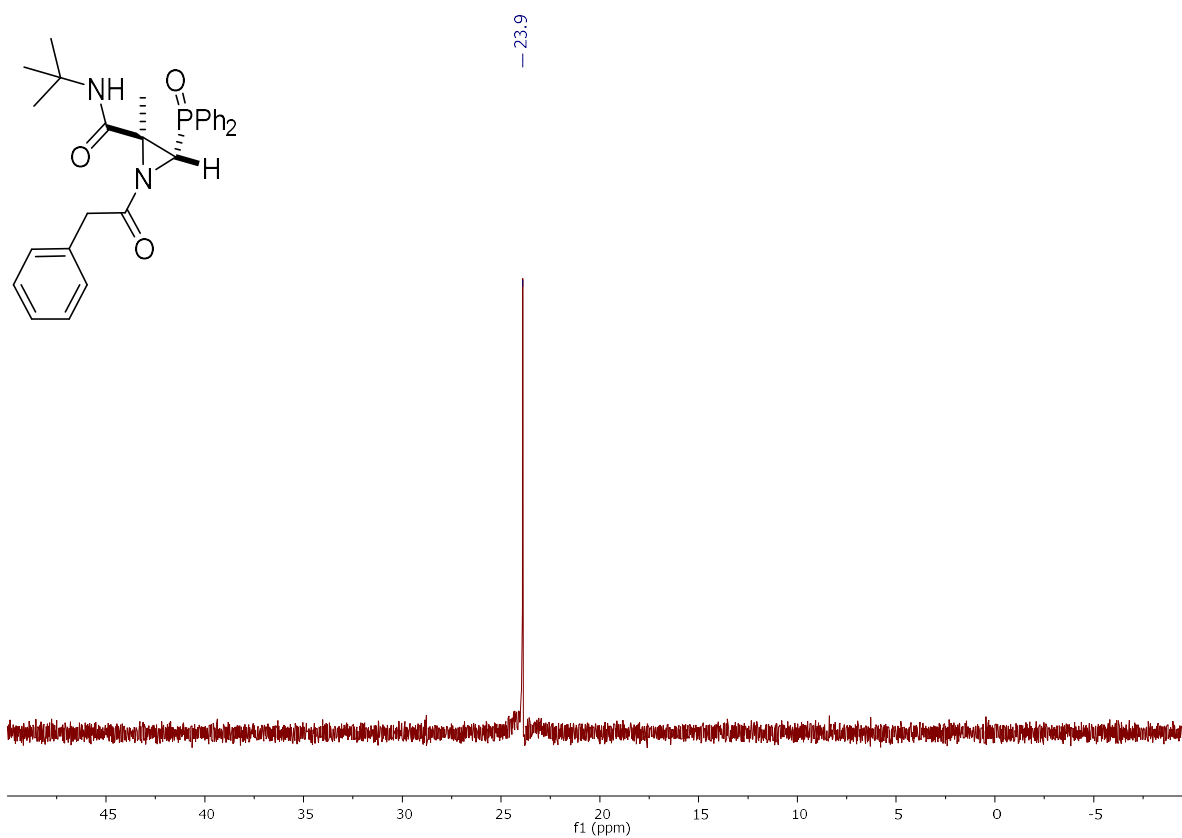
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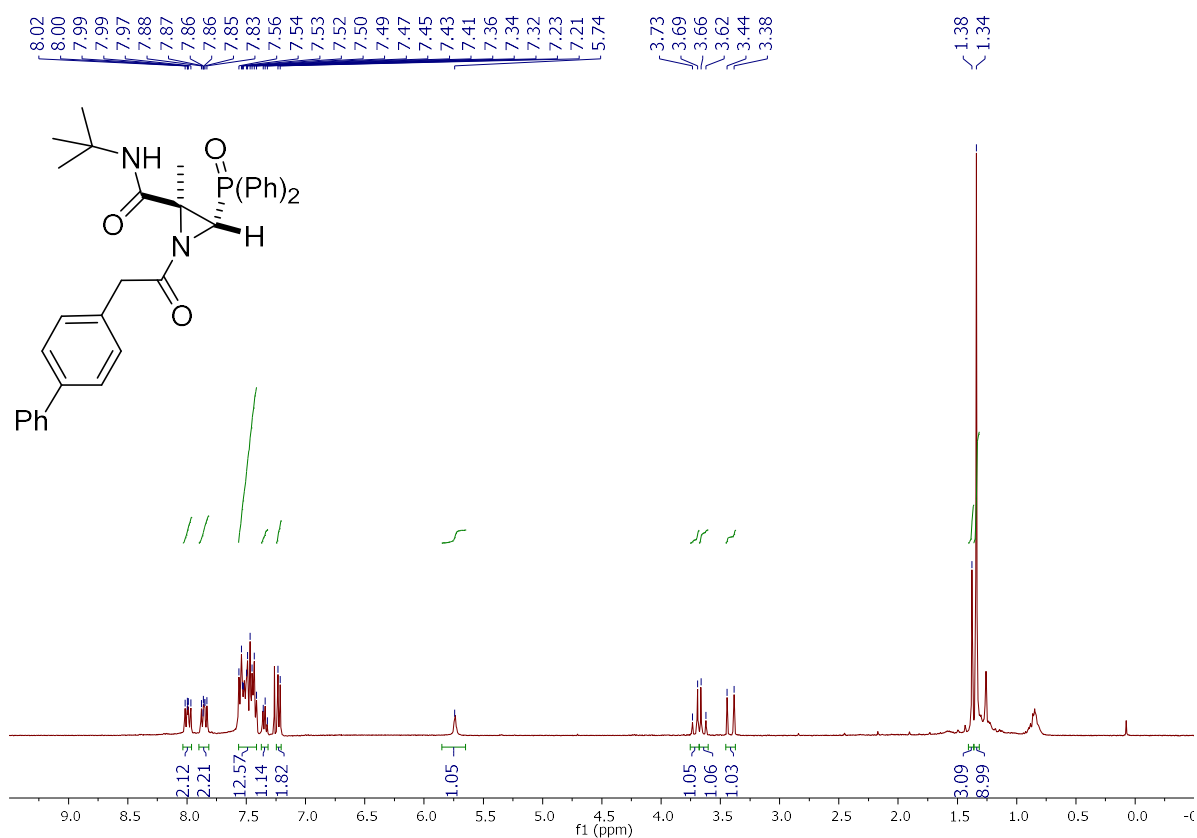
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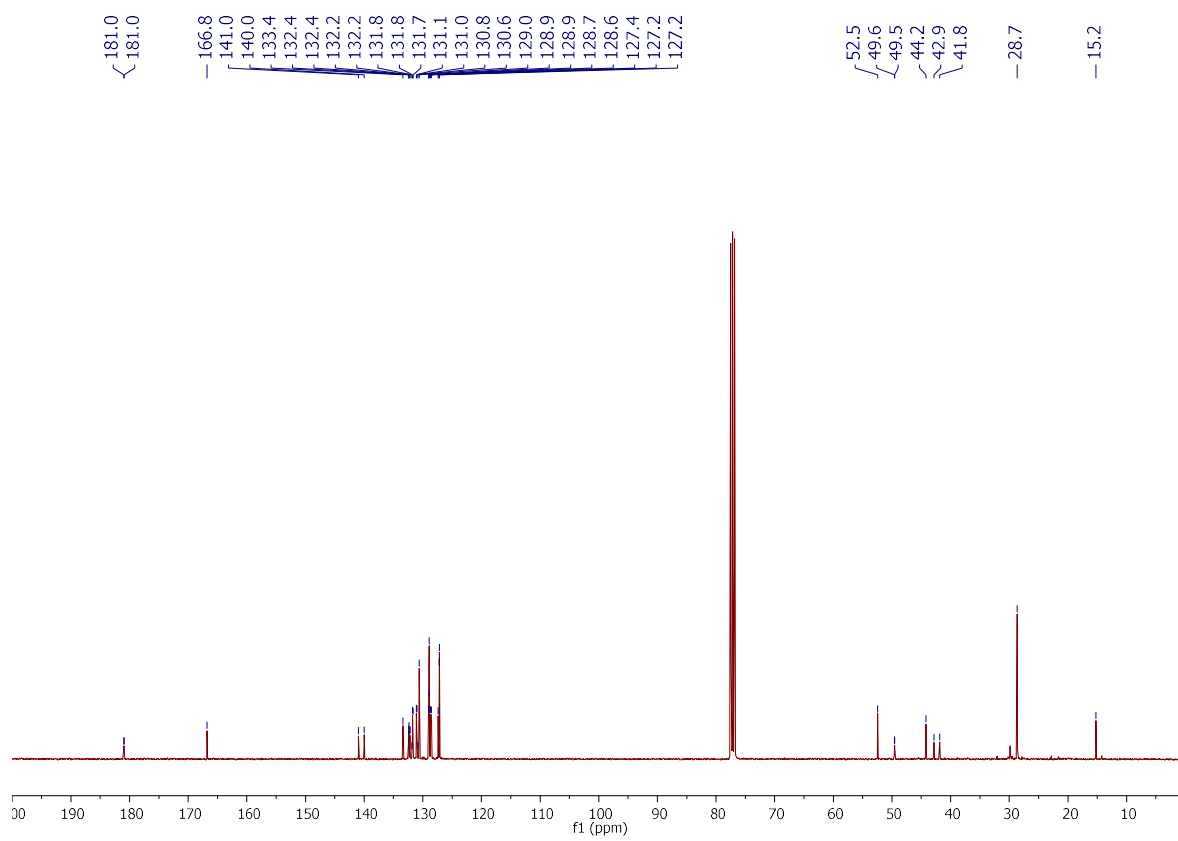
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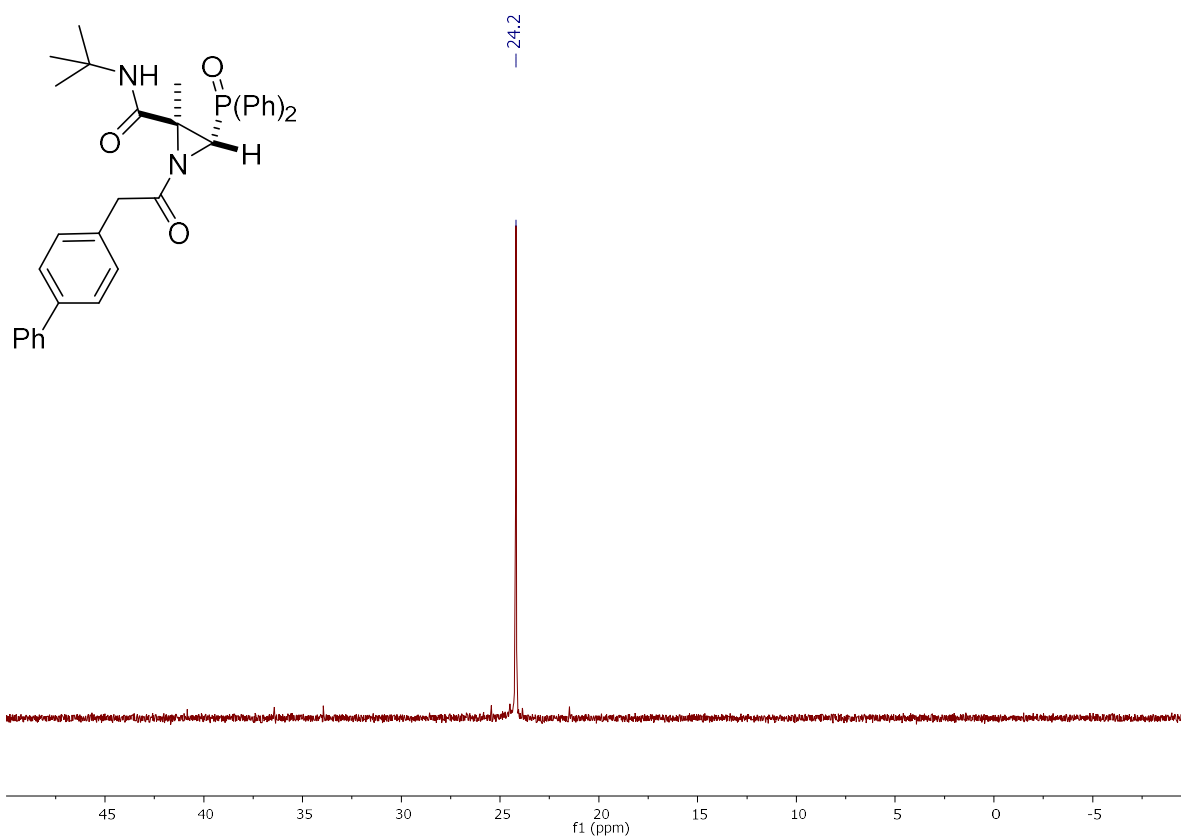
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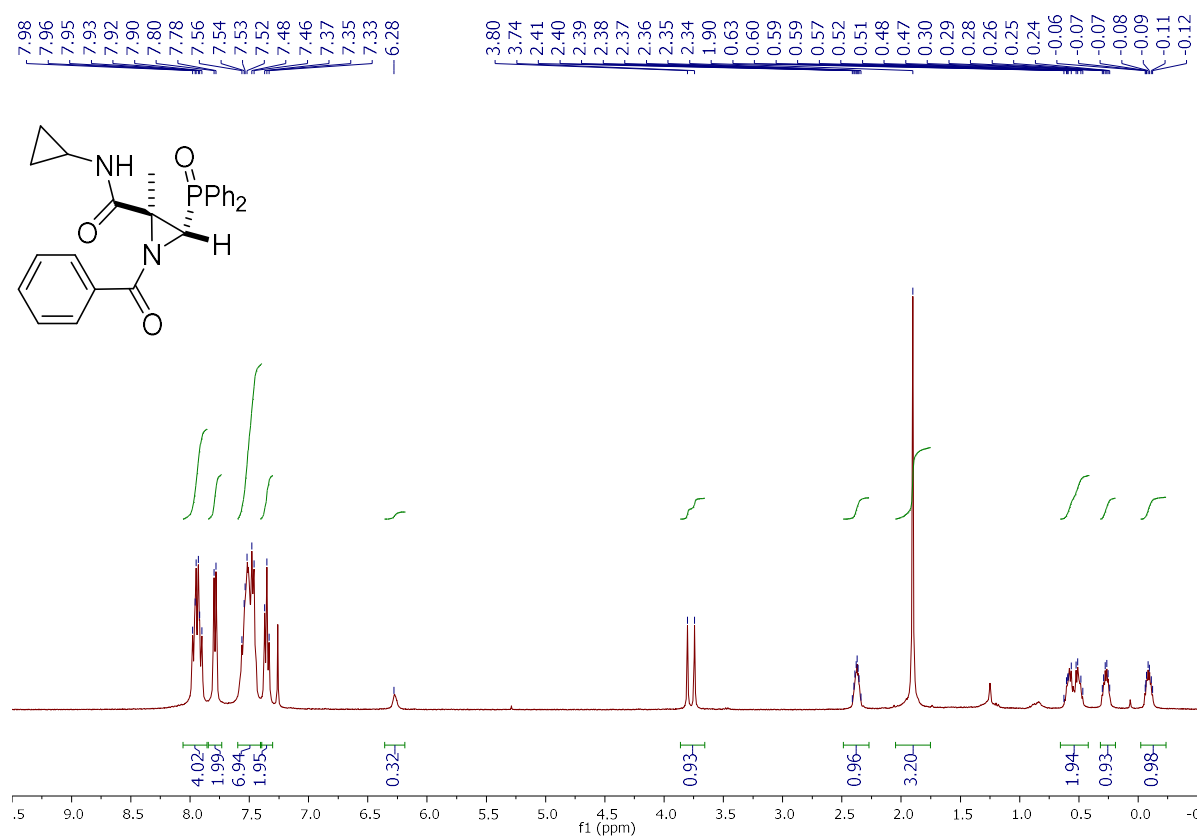
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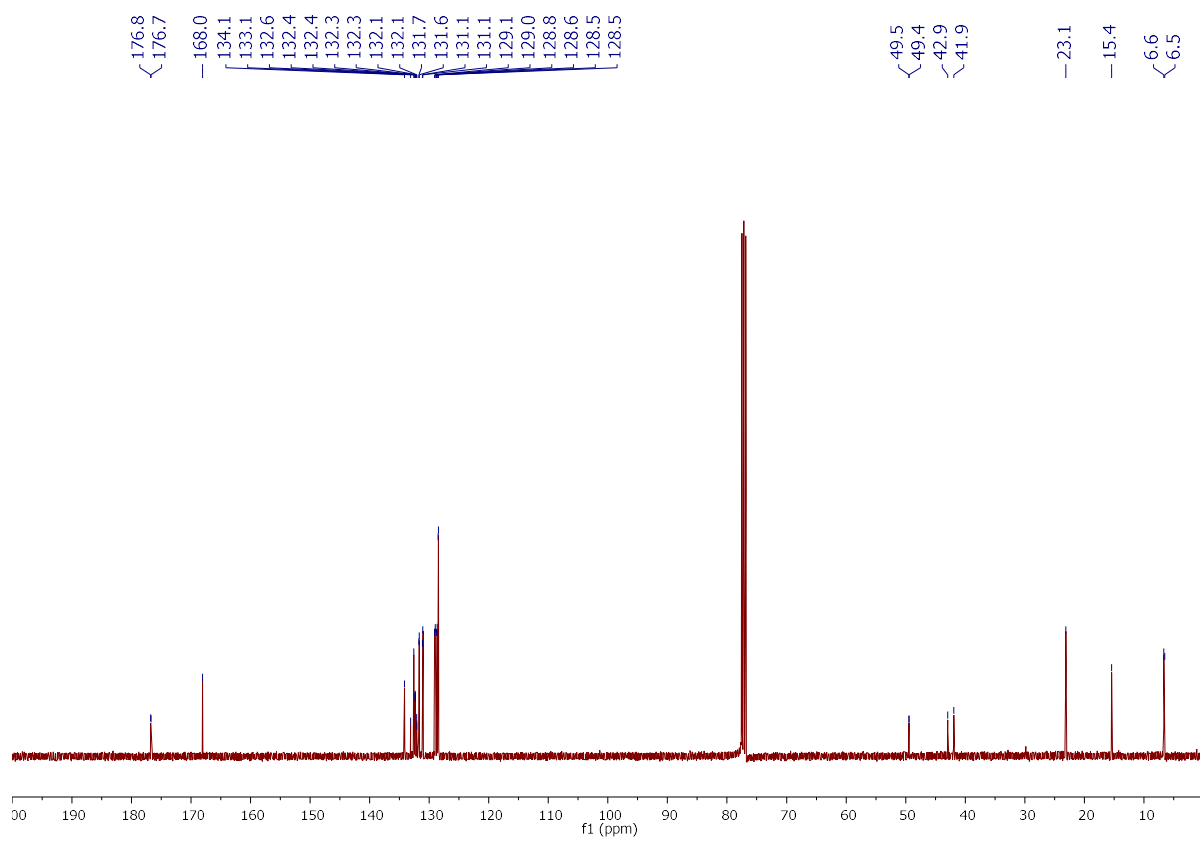
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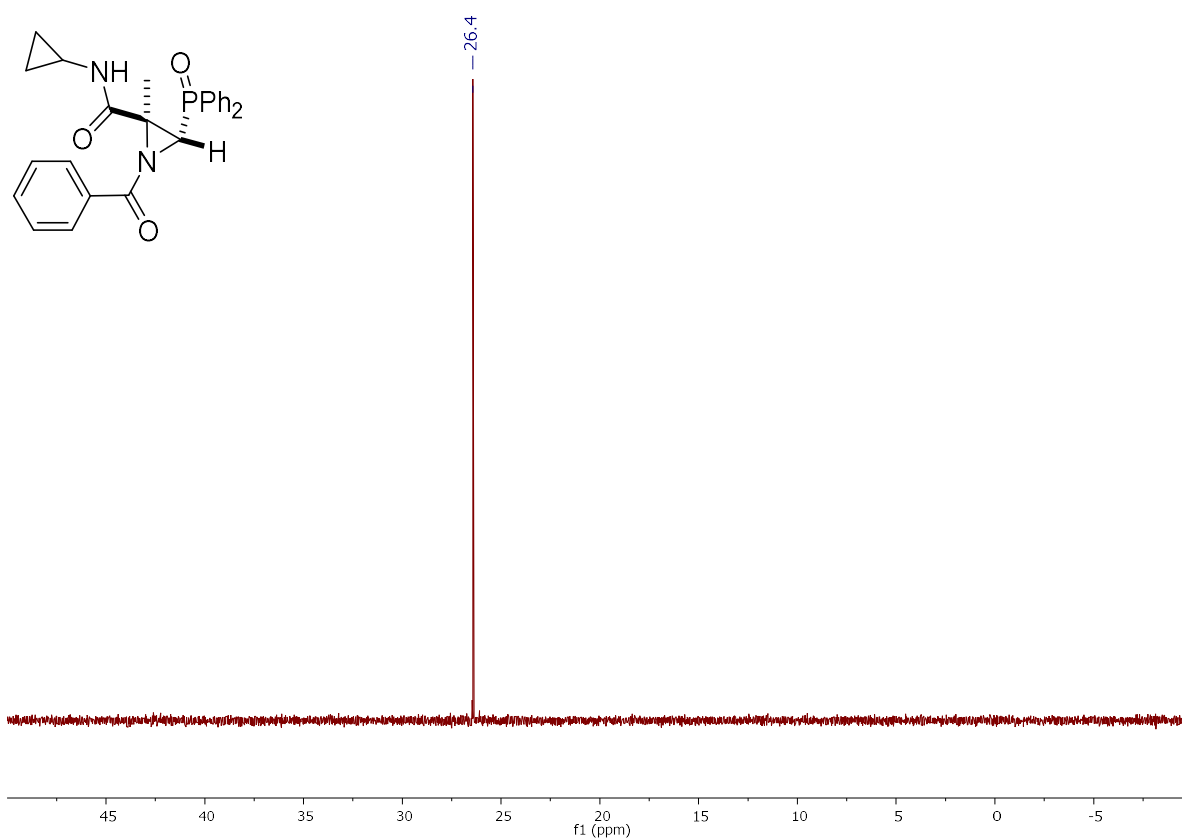
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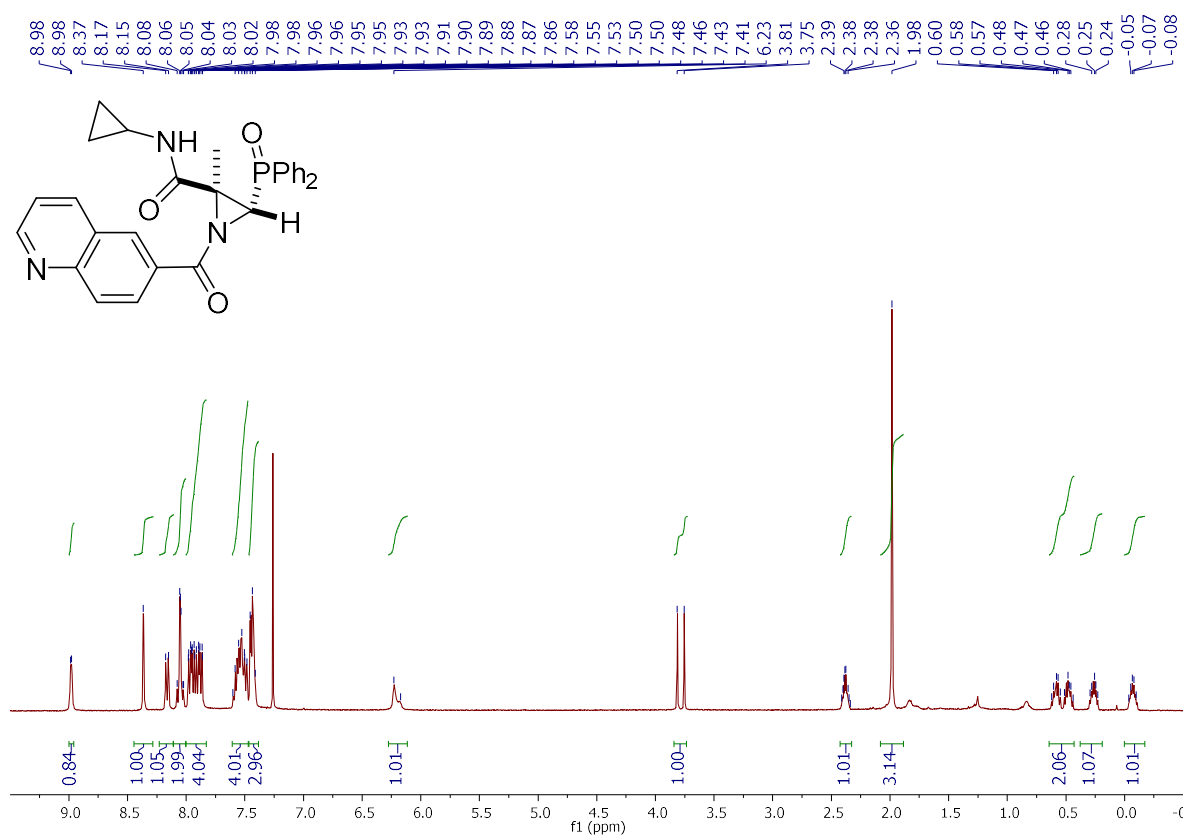
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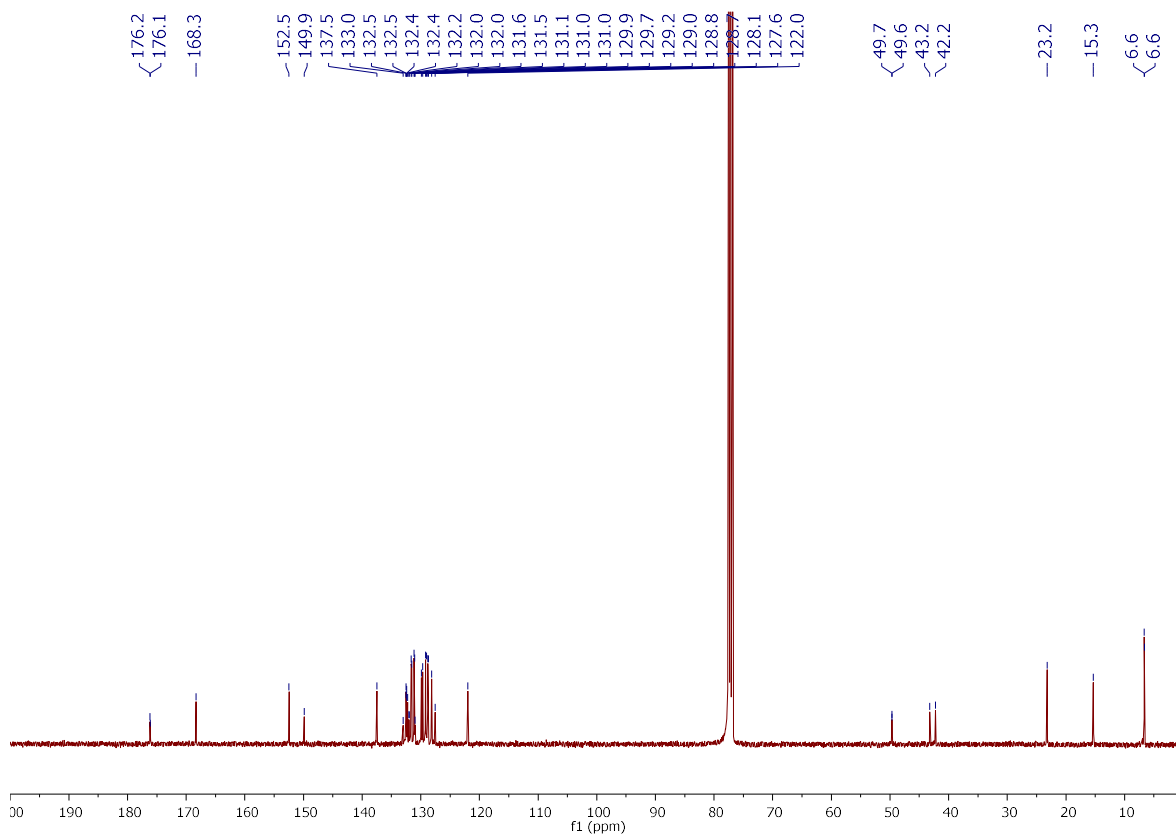
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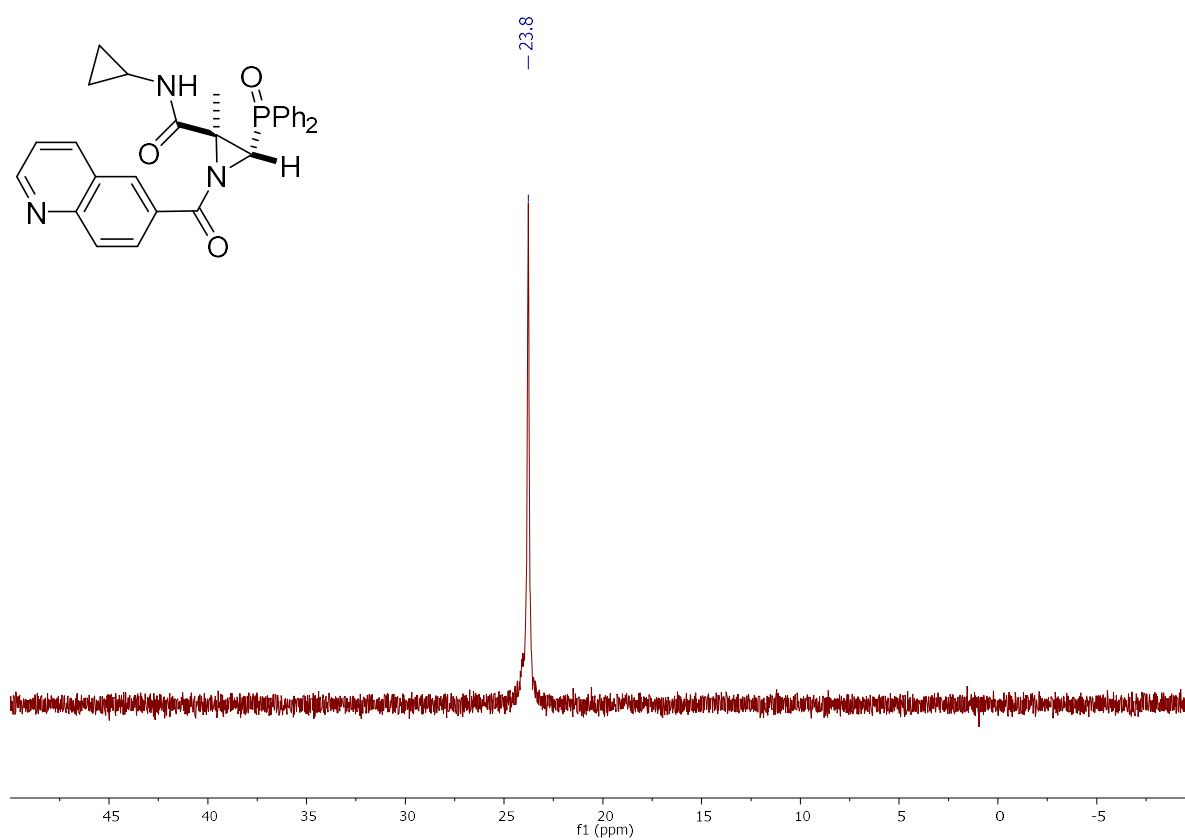
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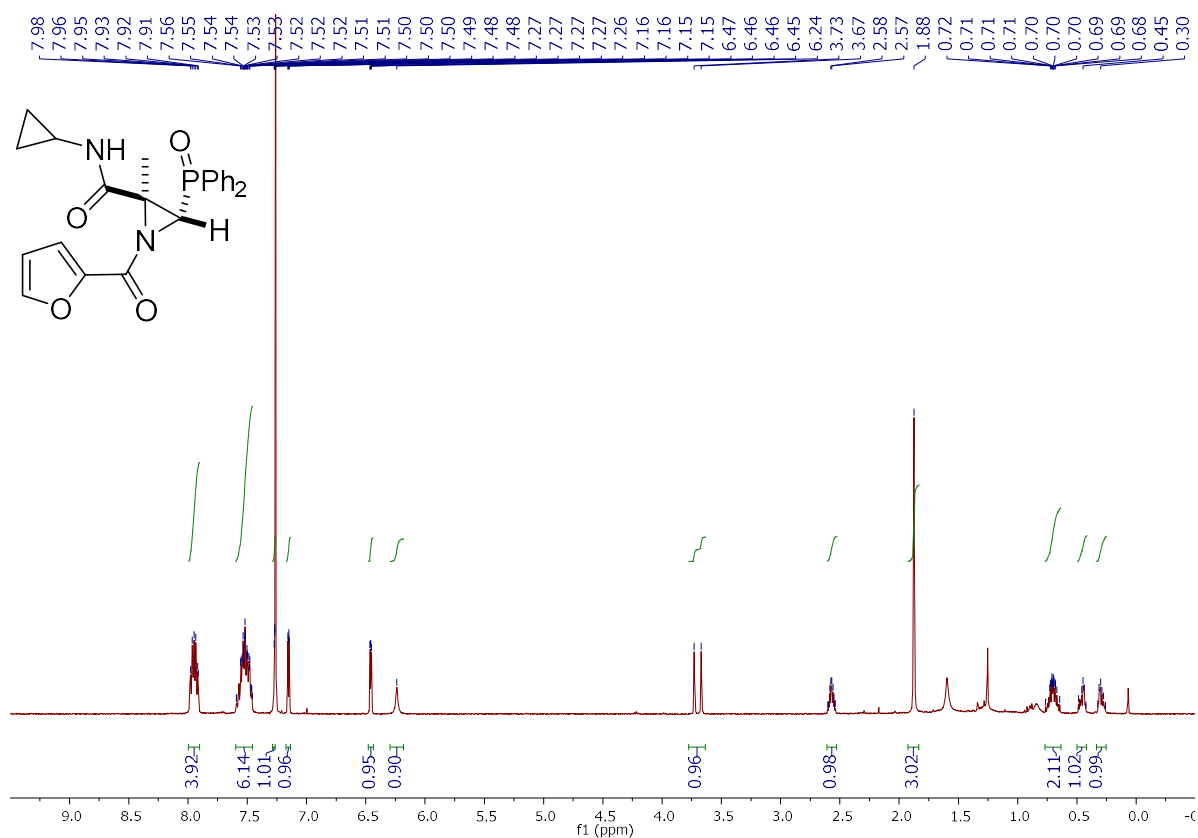
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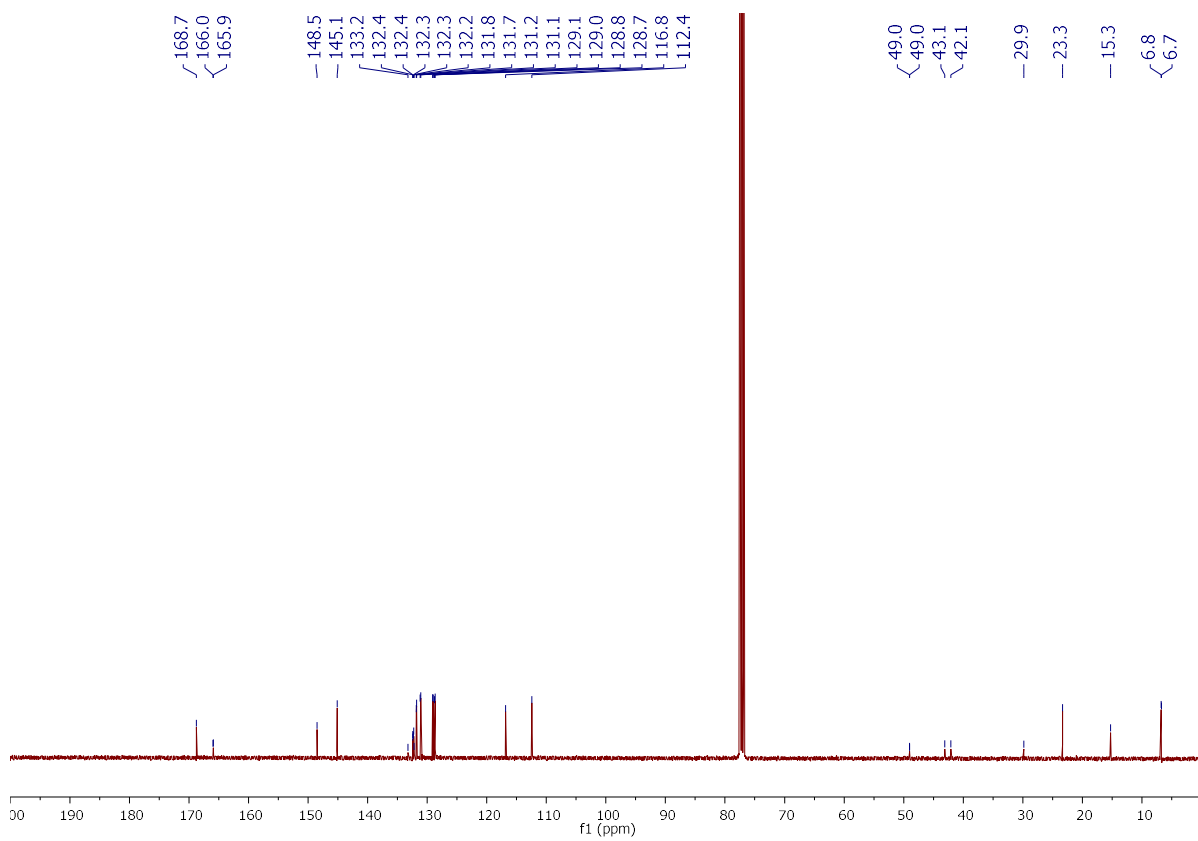
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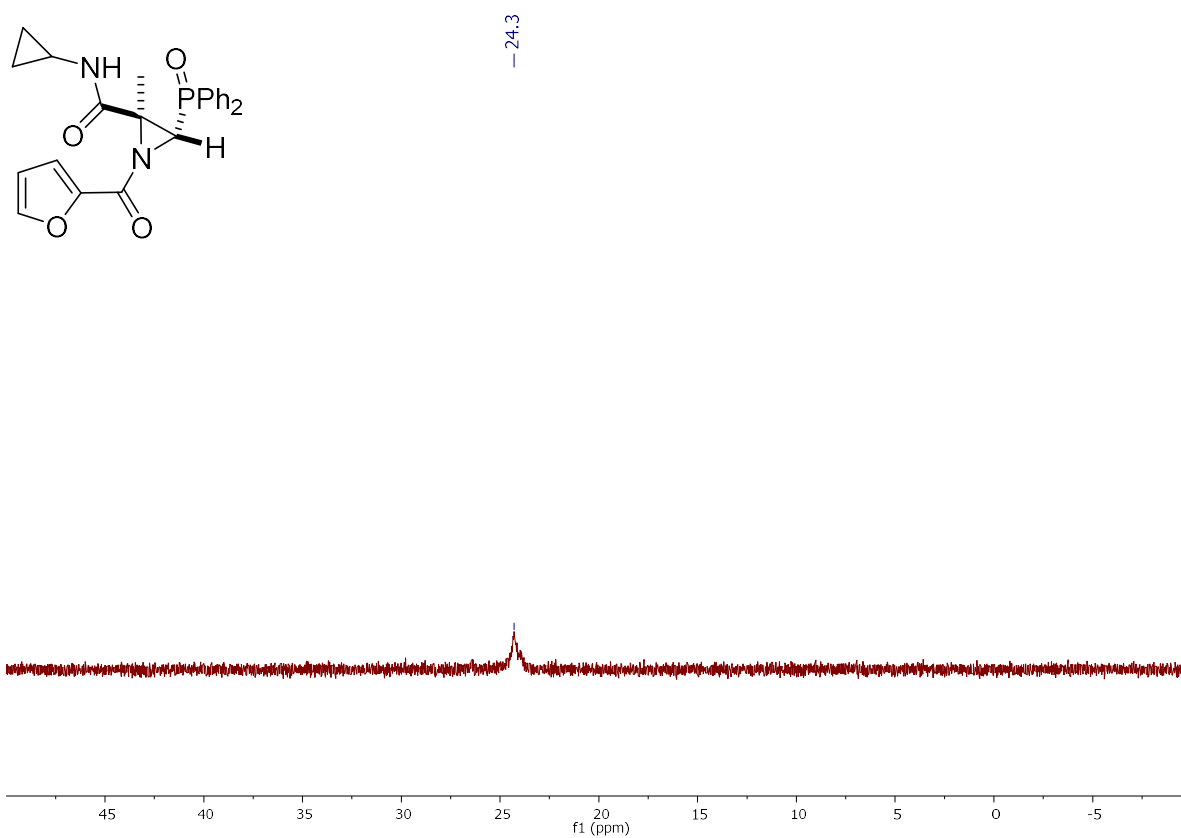
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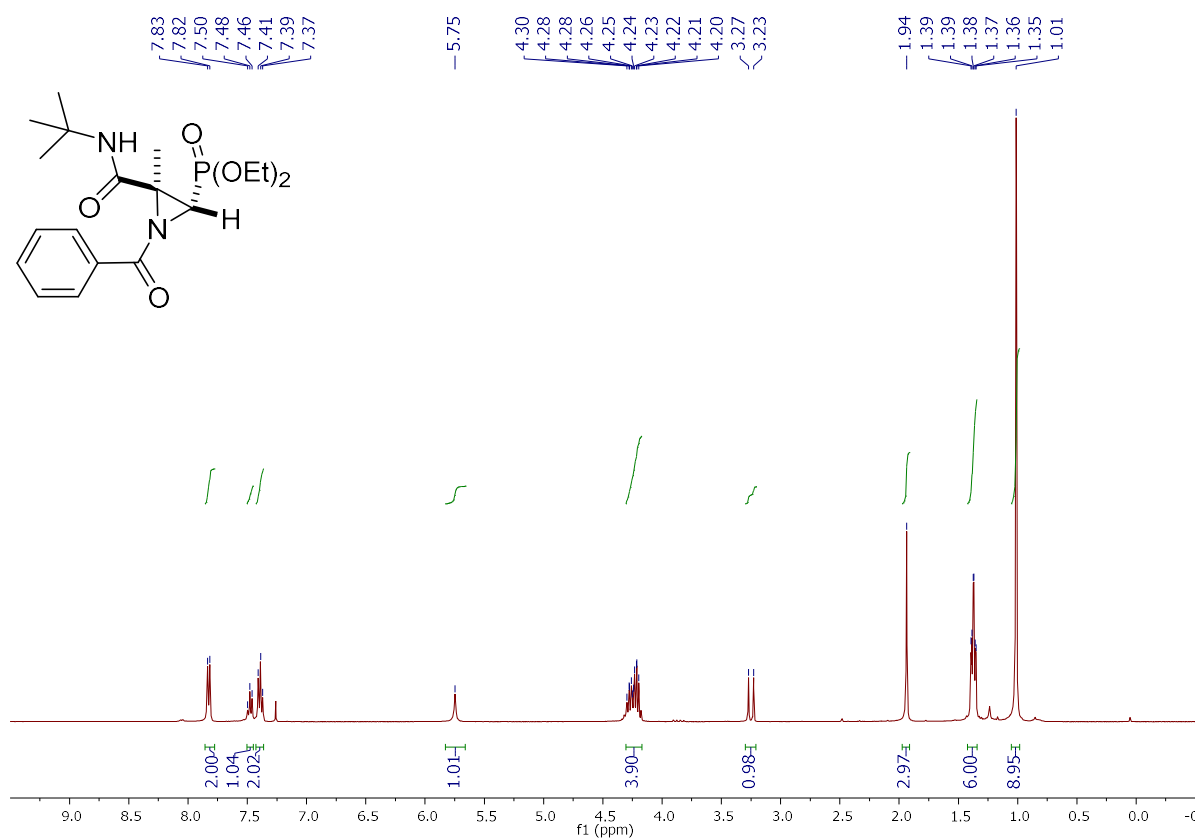
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4u**



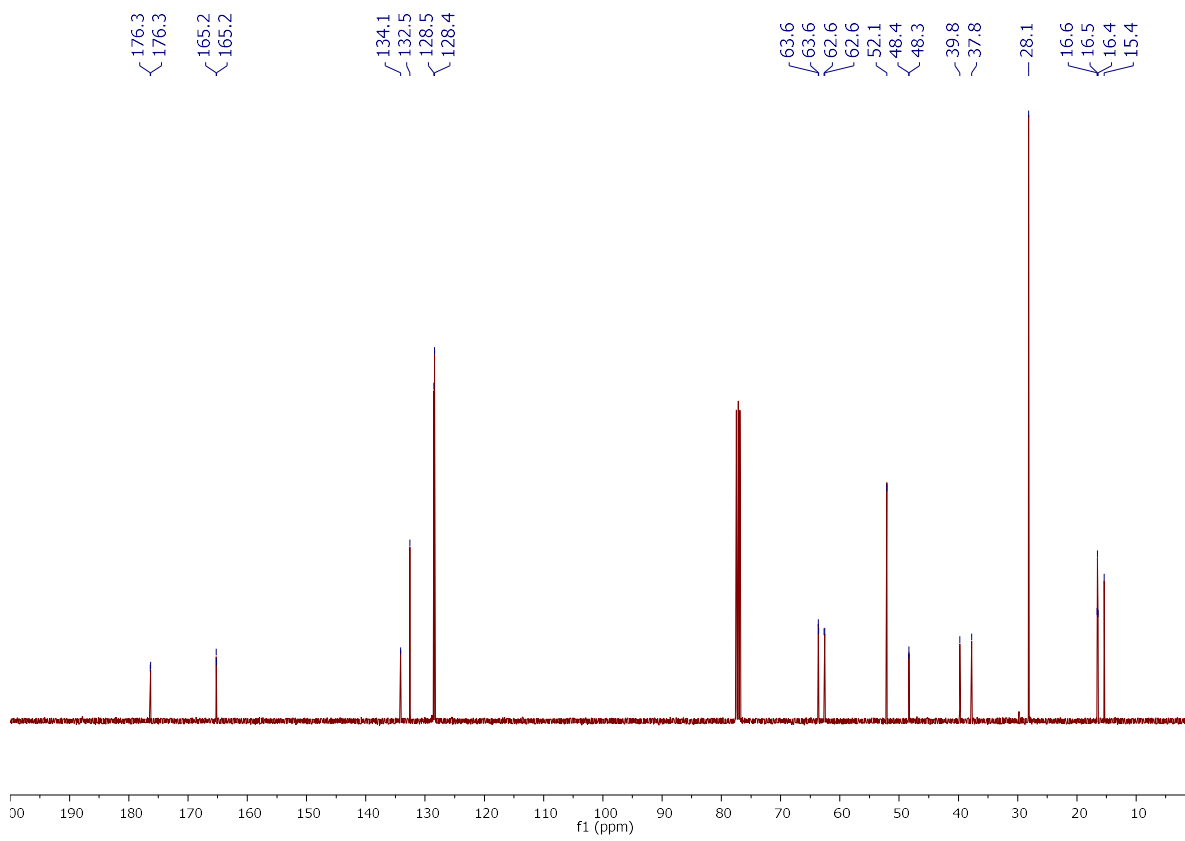
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphine Oxide **4u**



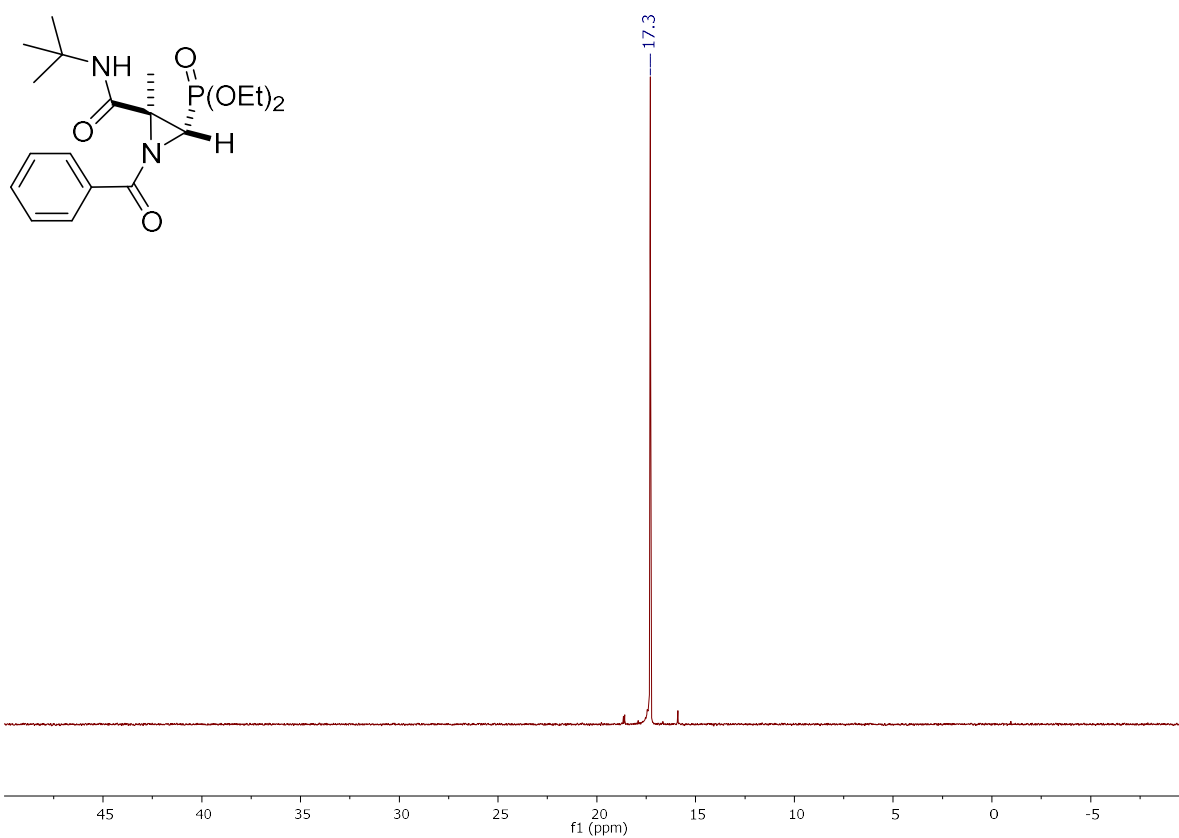
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5a**



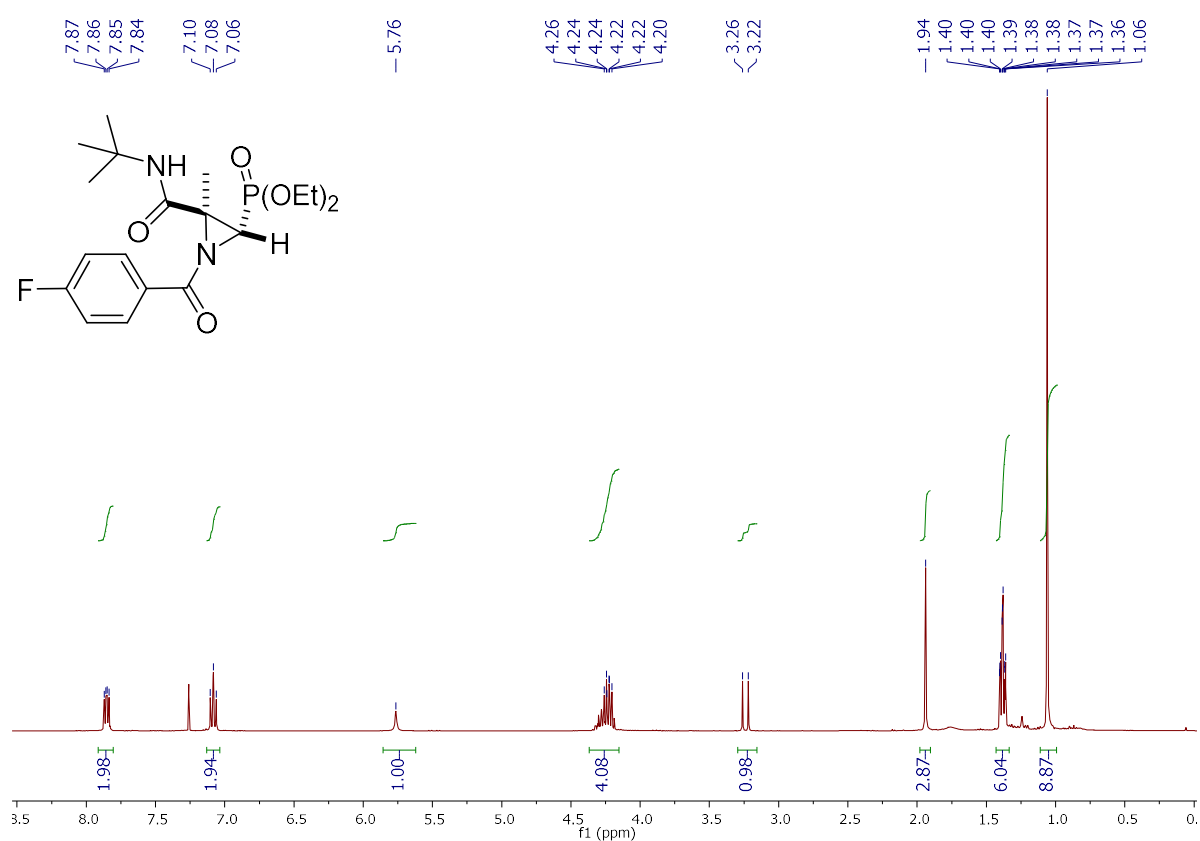
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5a**



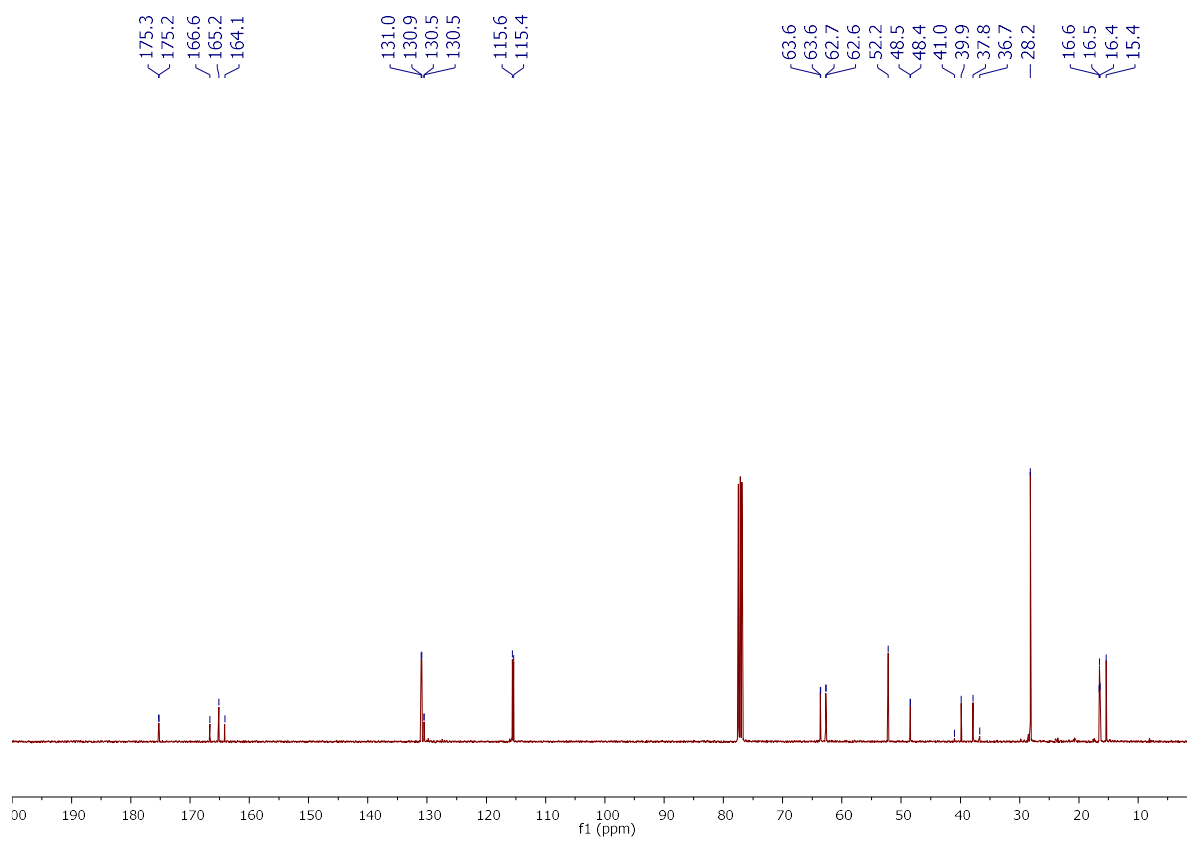
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5a**



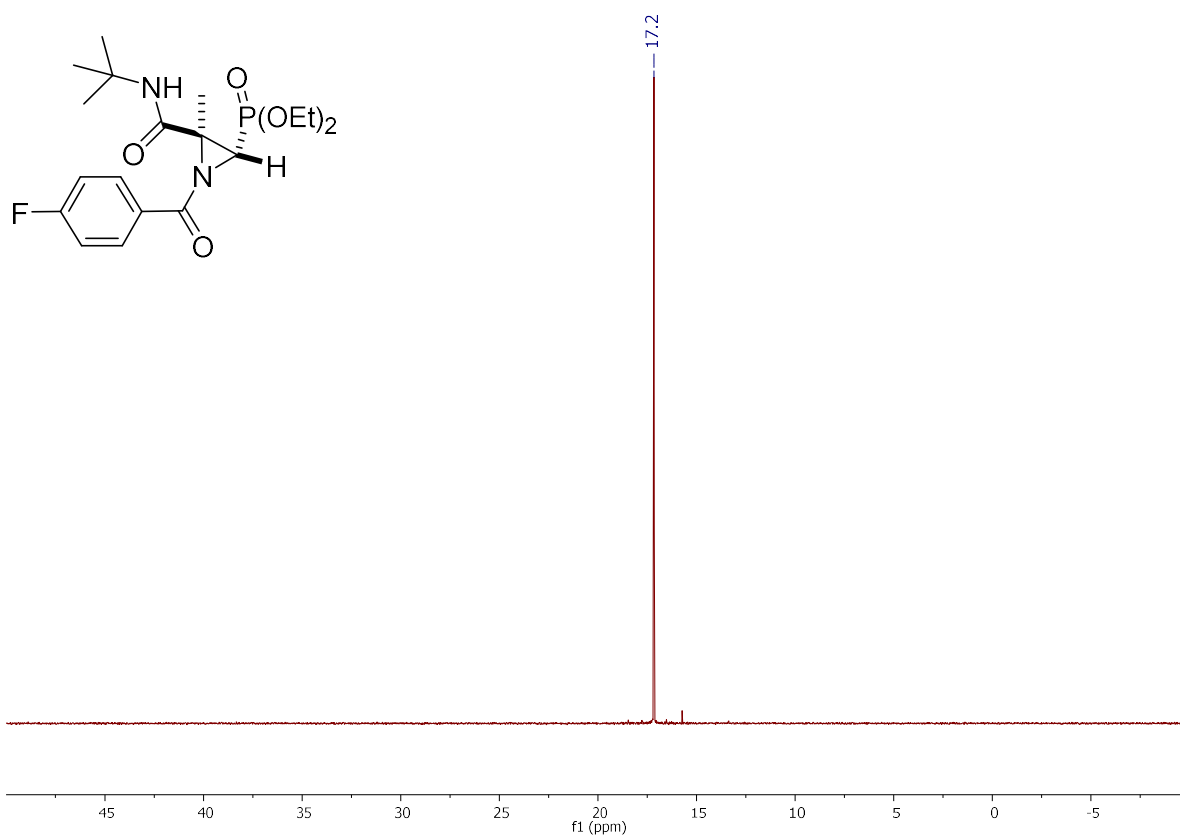
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5b**



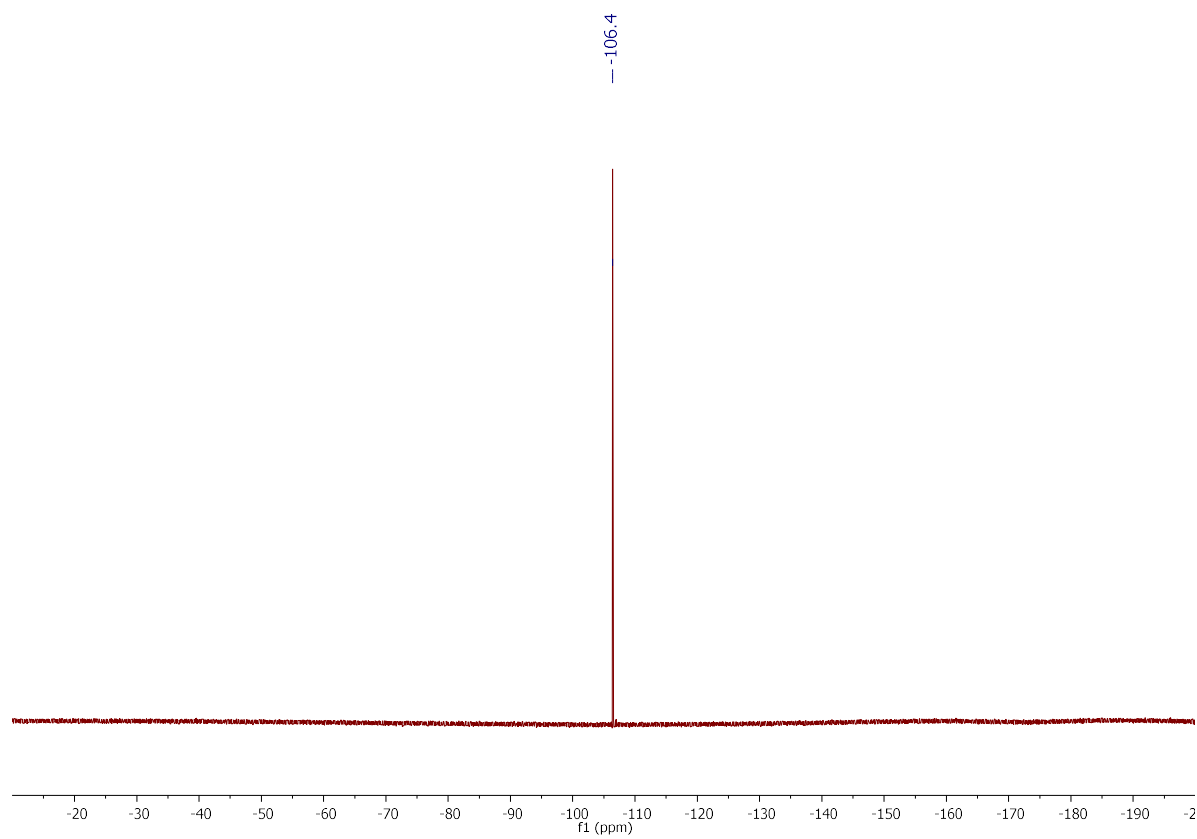
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5b**



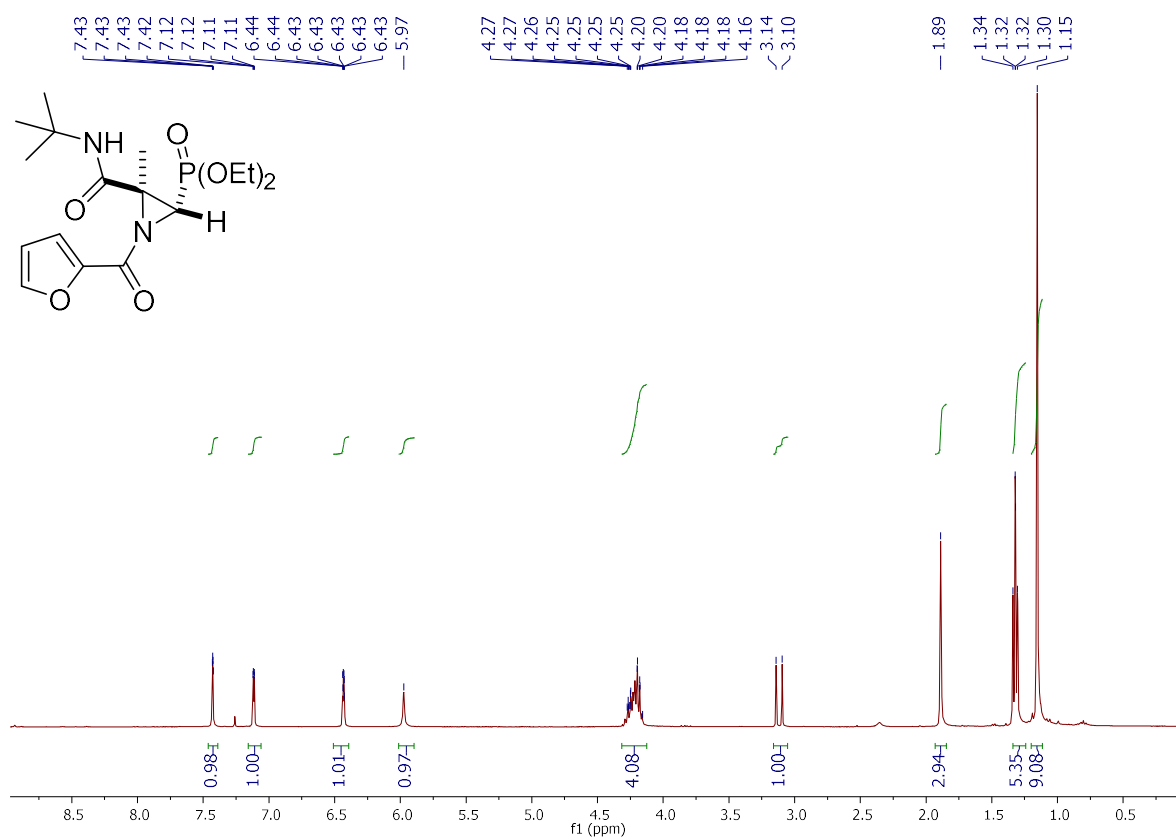
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5b**



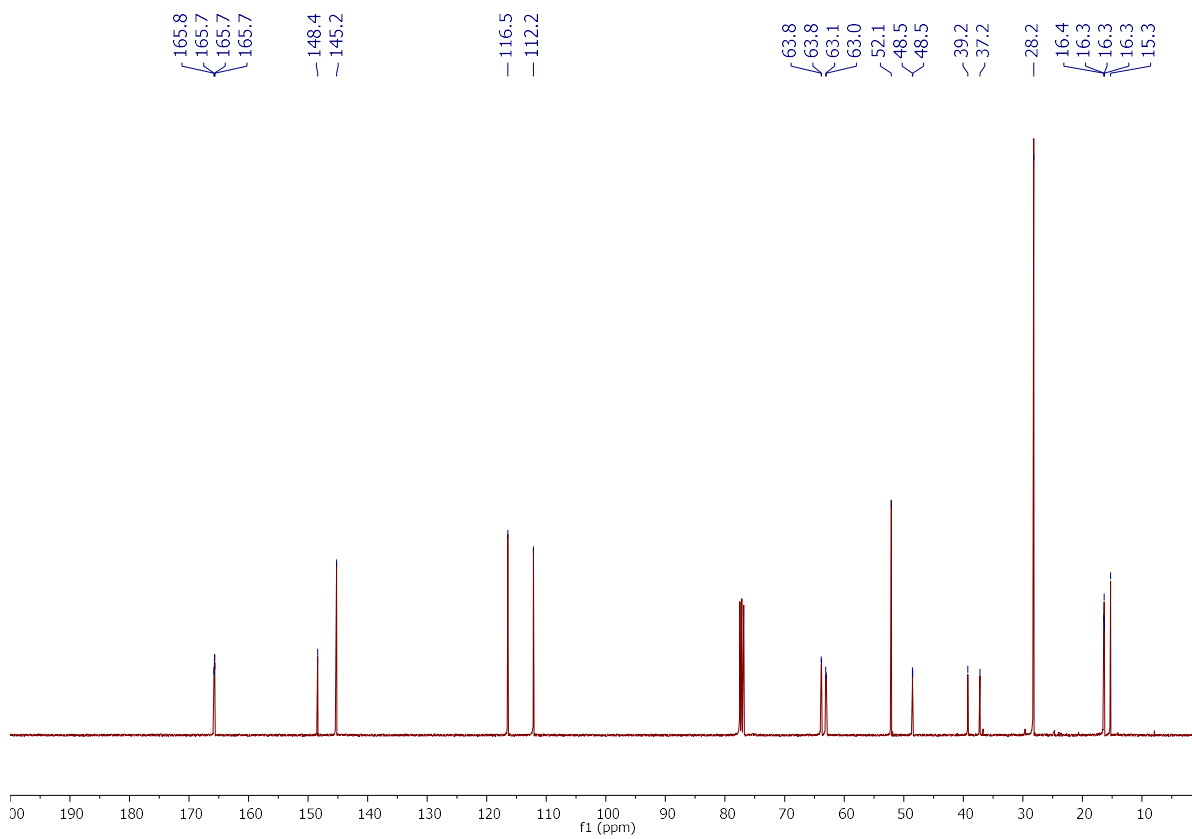
^{19}F (376 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5b**



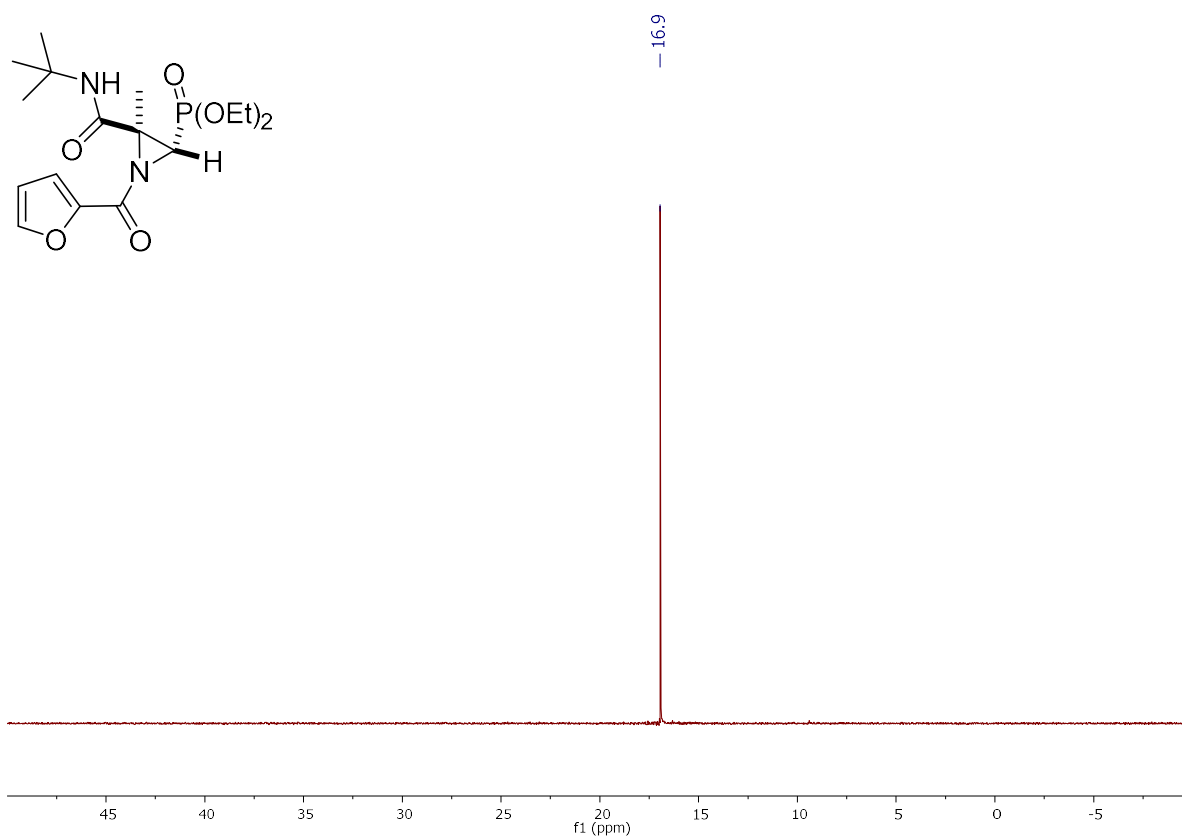
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5c**



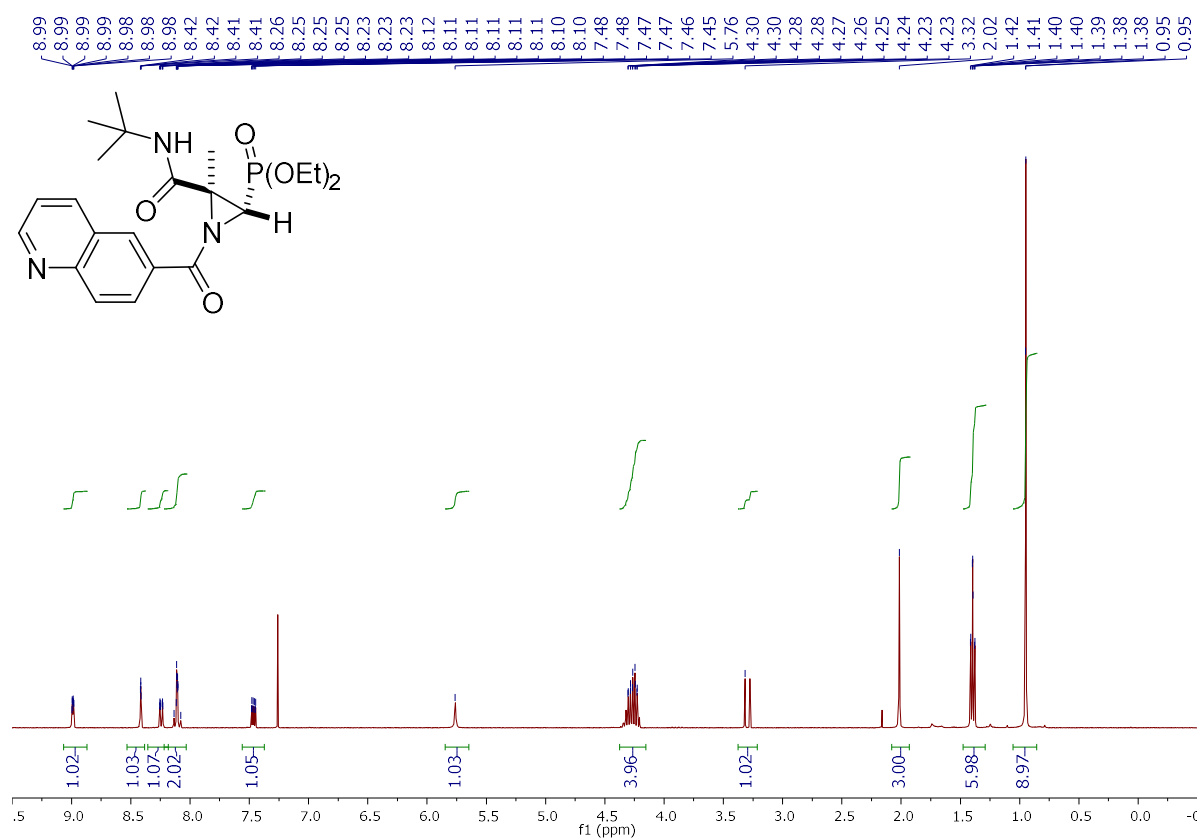
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5c**



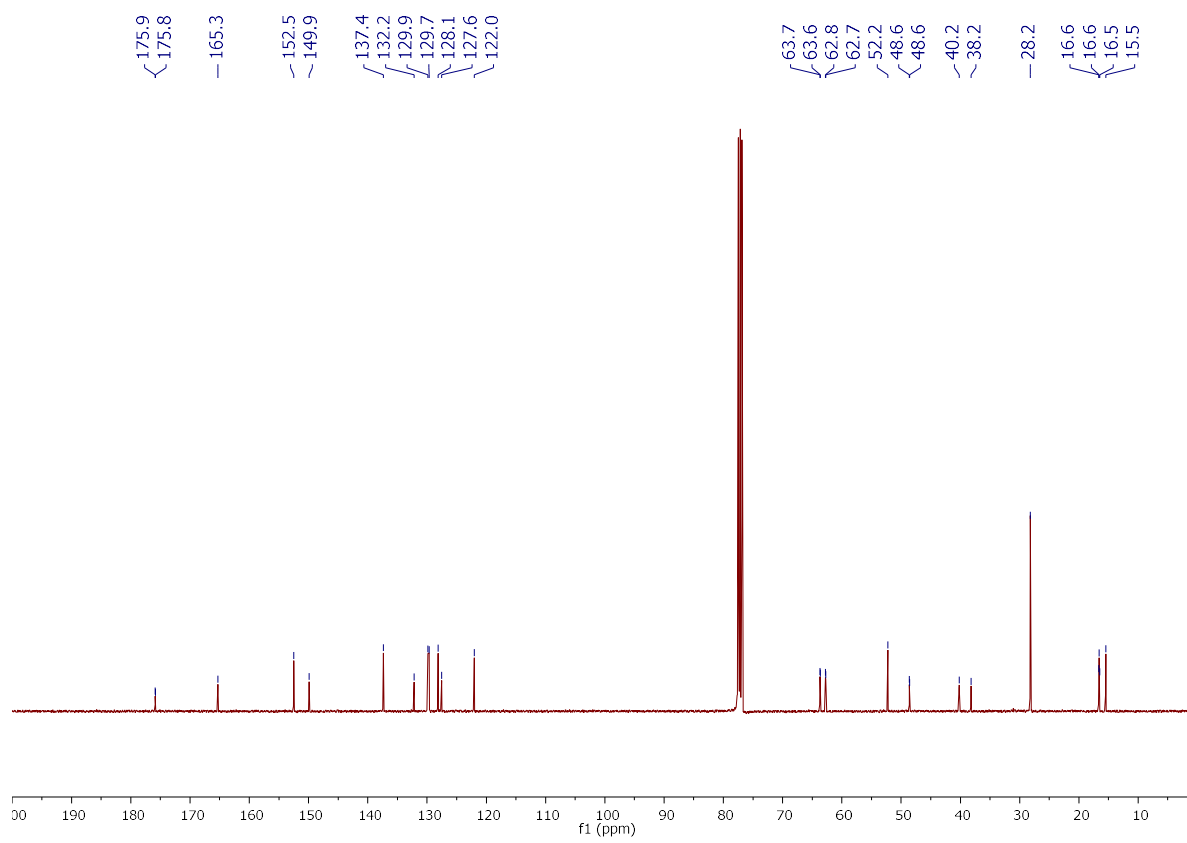
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5c**

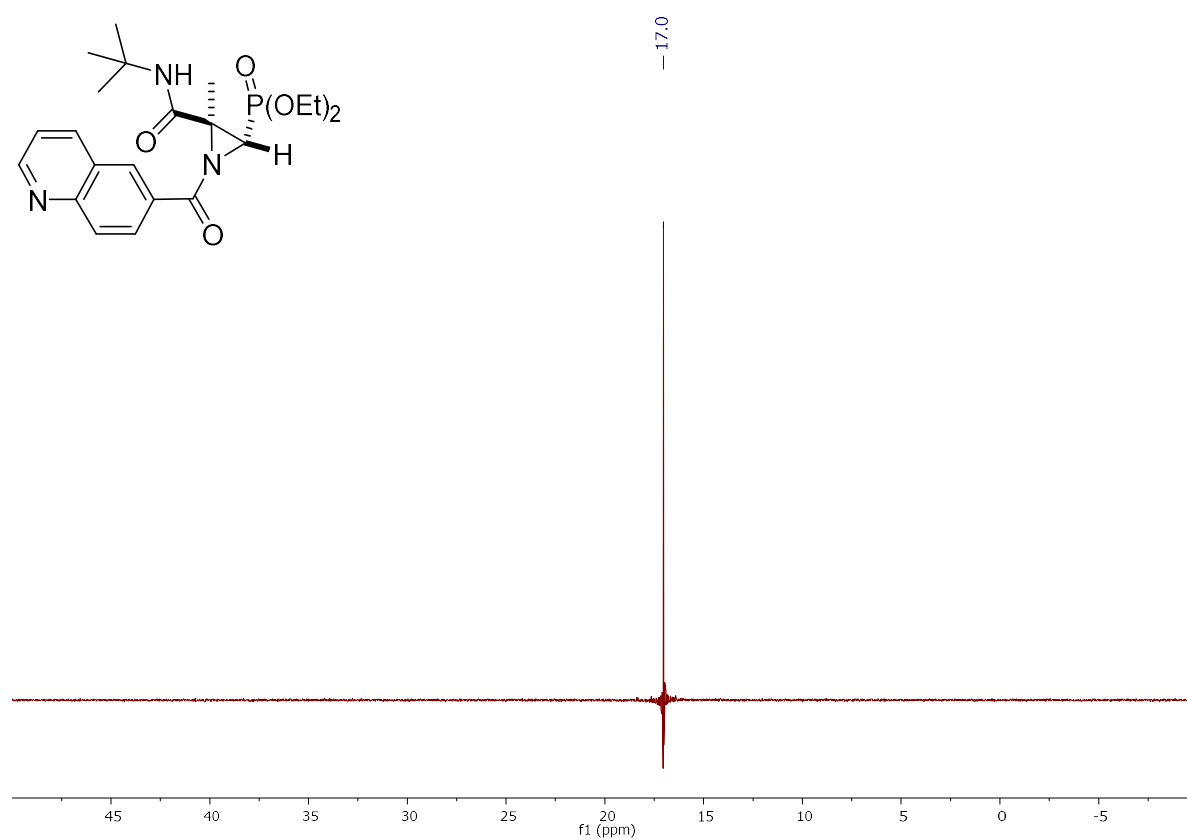


¹H NMR (400 MHz, CDCl₃) of *N*-Acylaziridine Phosphonate **5d**

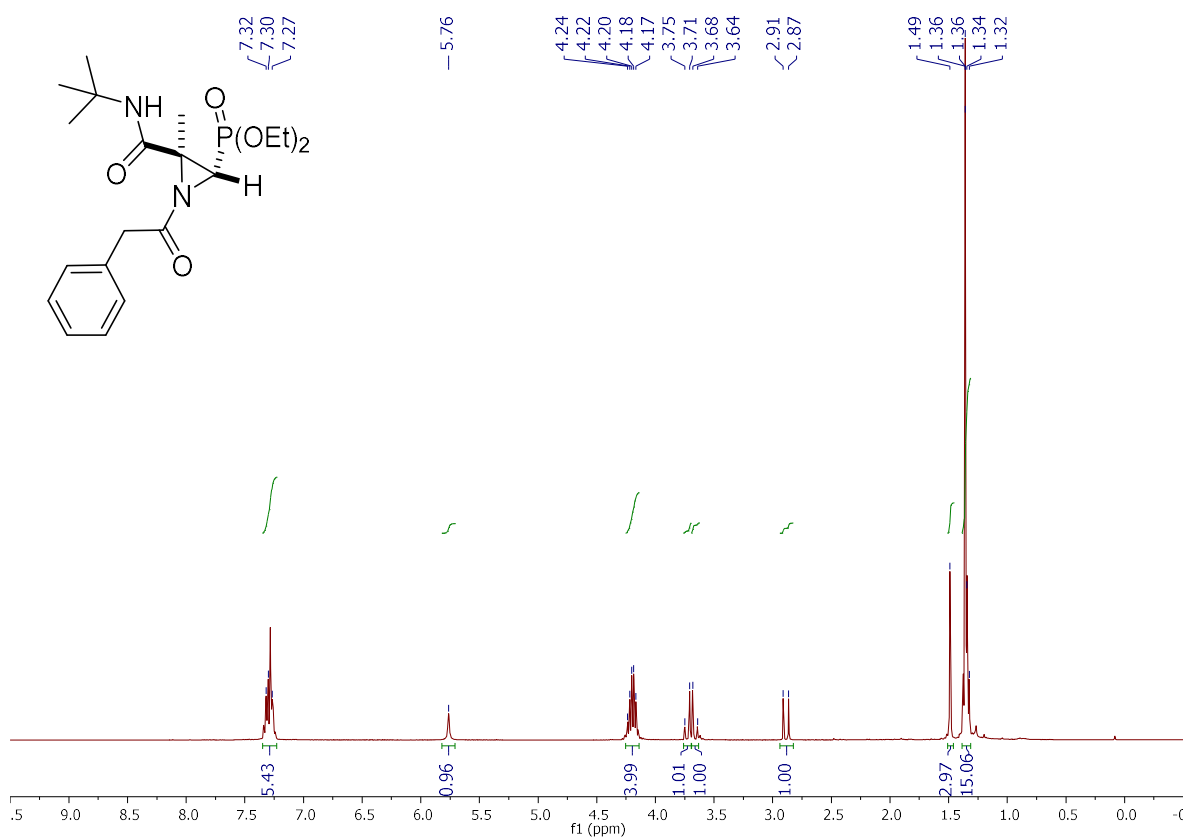


¹³C {¹H} NMR (100 MHz, CDCl₃) of *N*-Acylaziridine Phosphonate **5d**

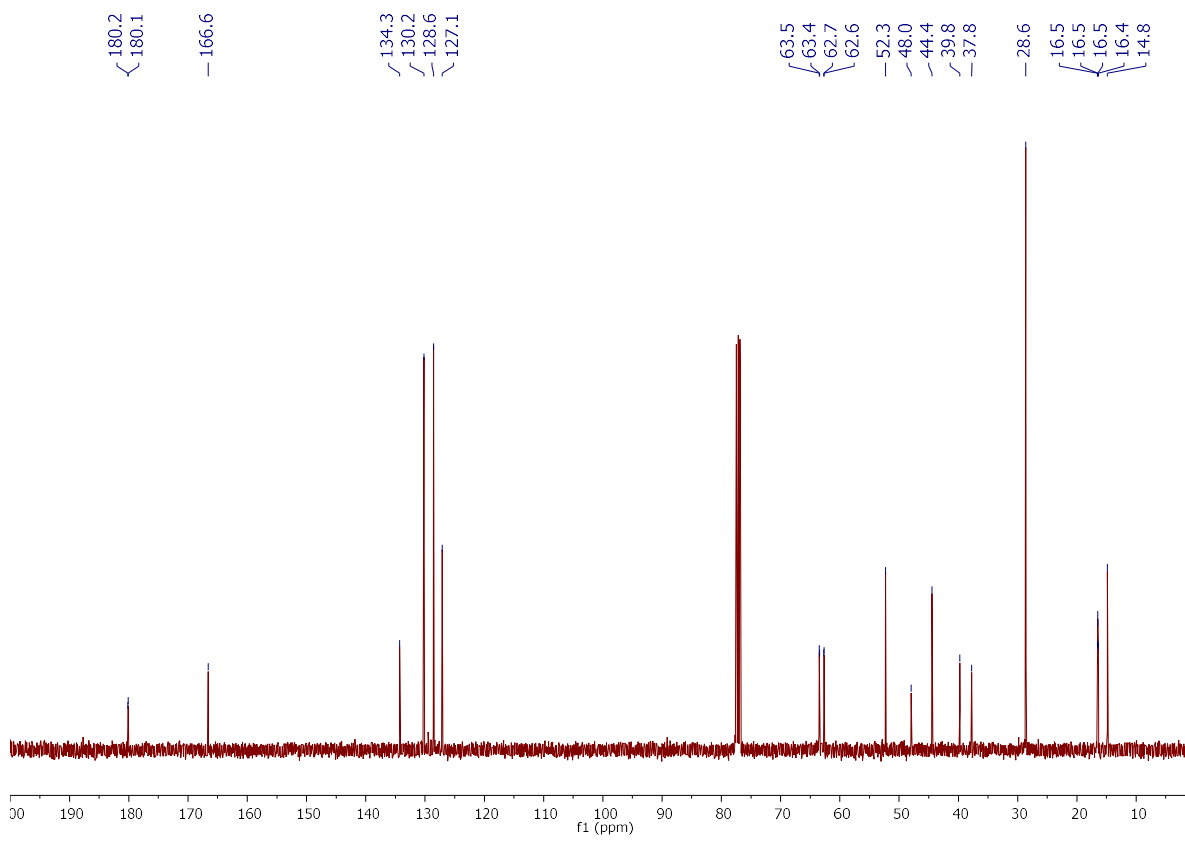


³¹P (160 MHz, CDCl₃) of *N*-Acylaziridine Phosphonate **5d**

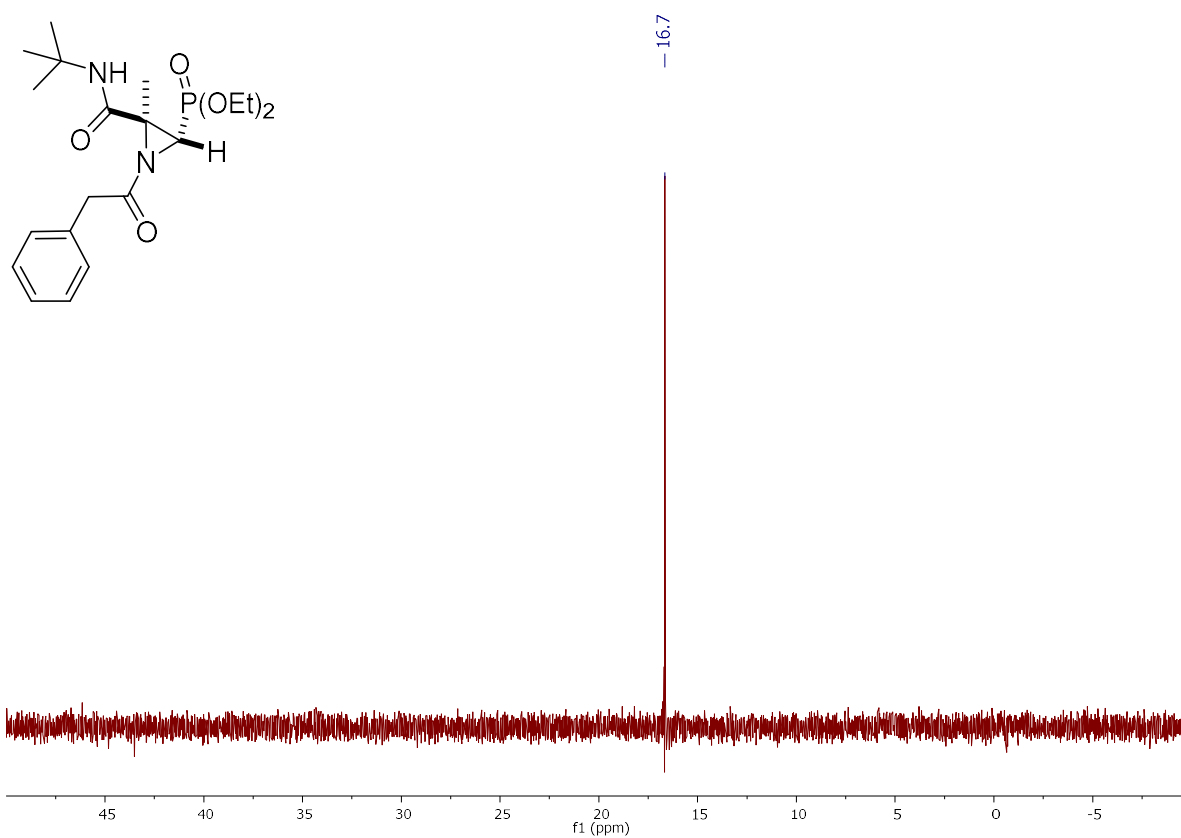
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5e**



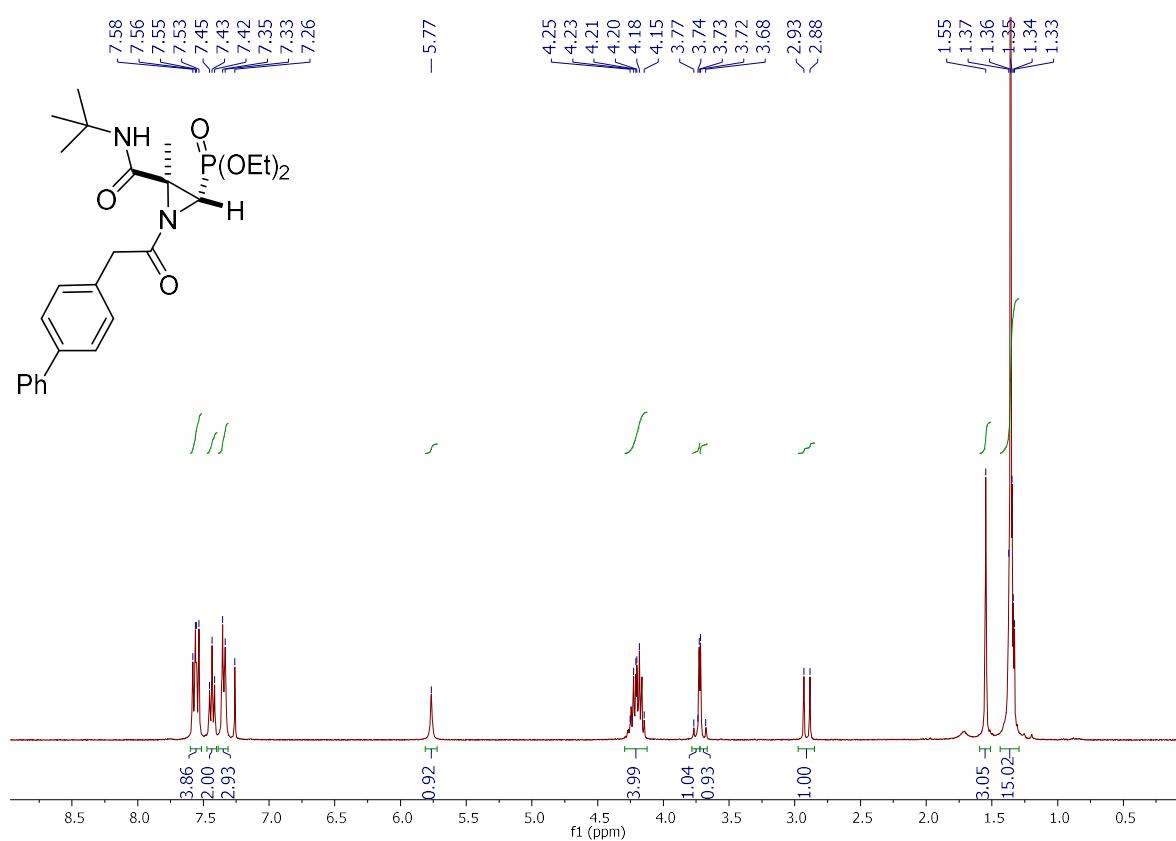
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5e**



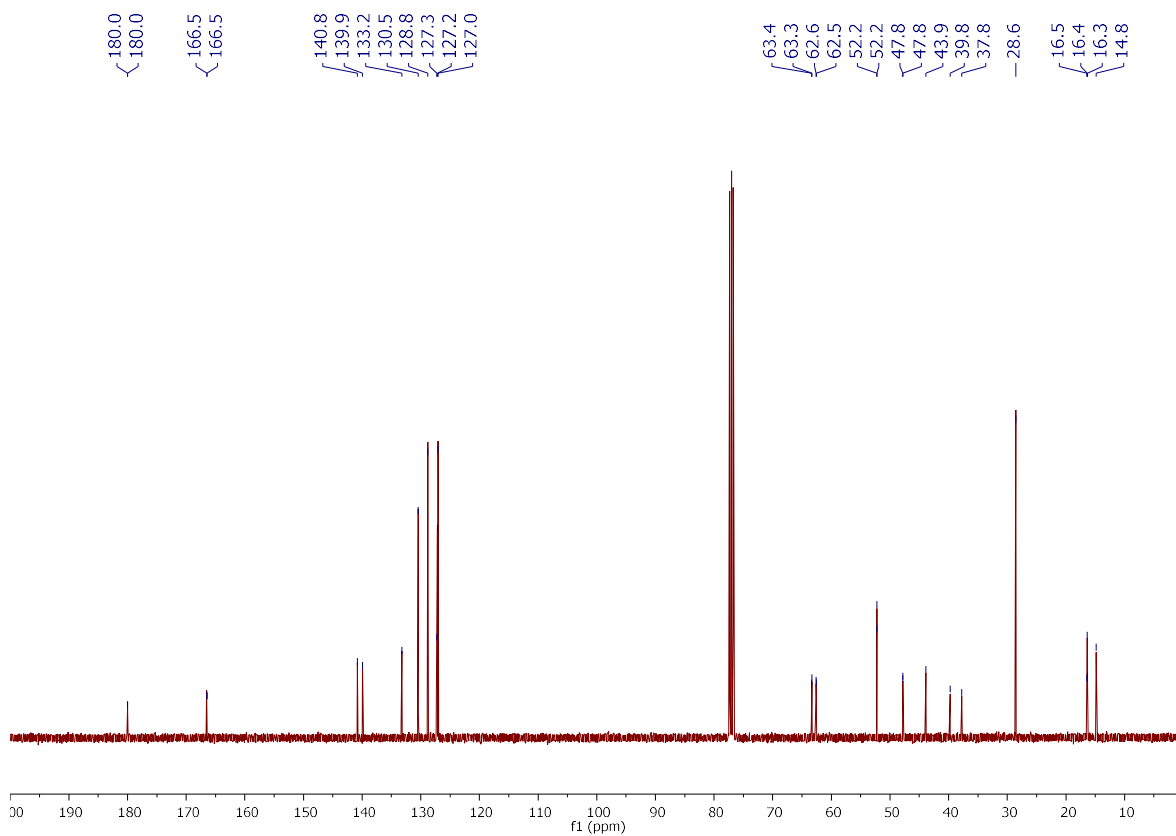
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5e**



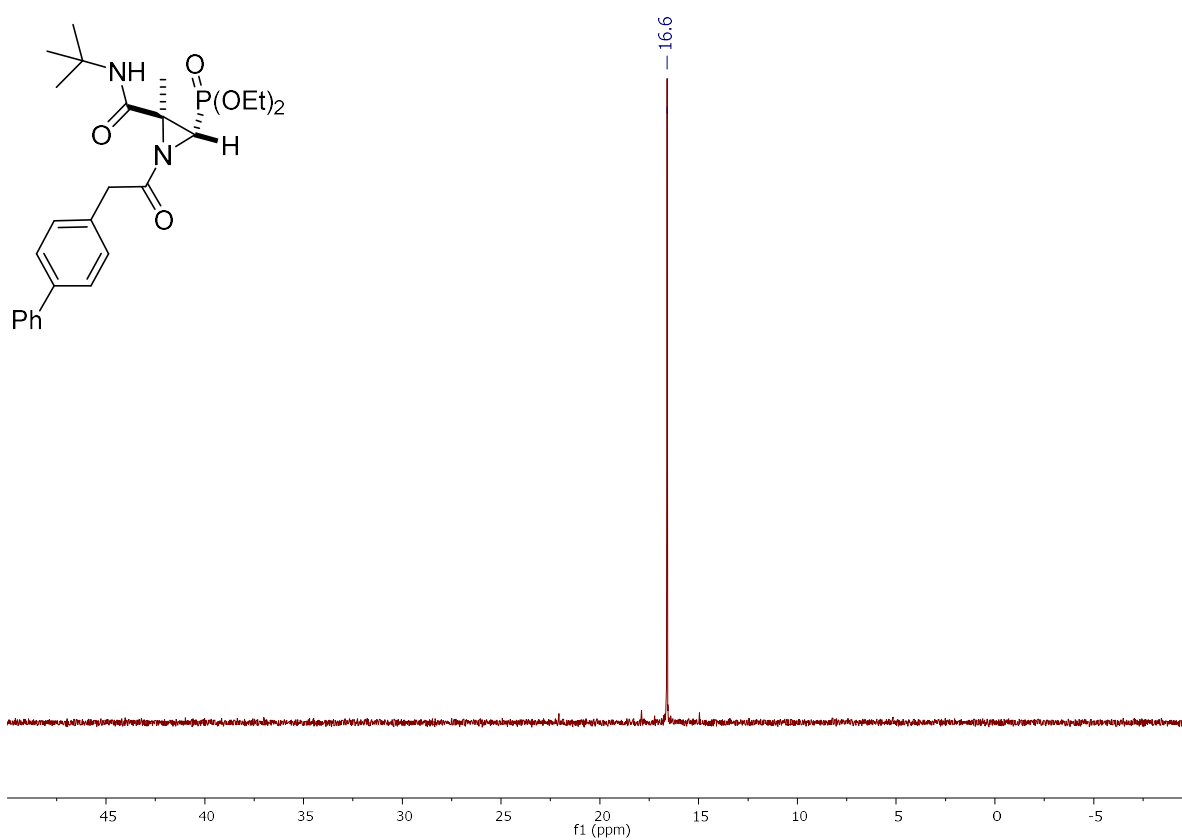
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5f**



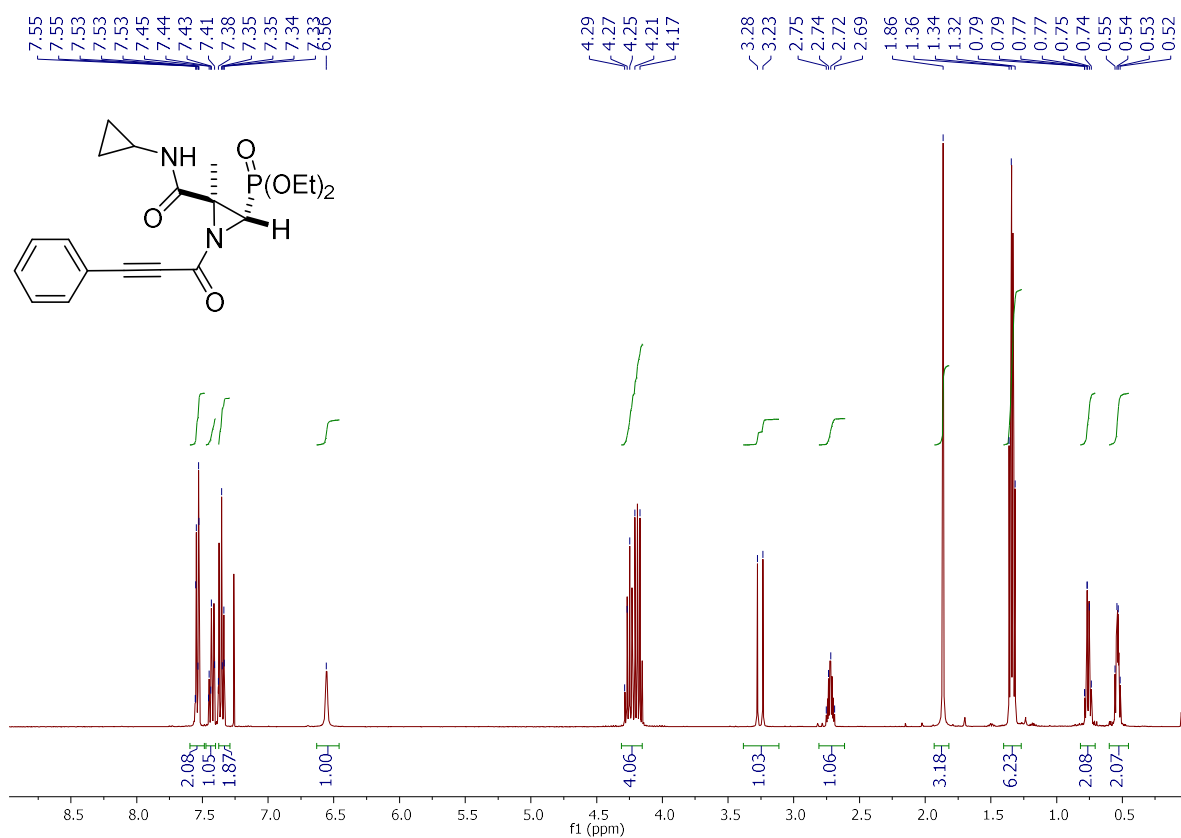
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5f**



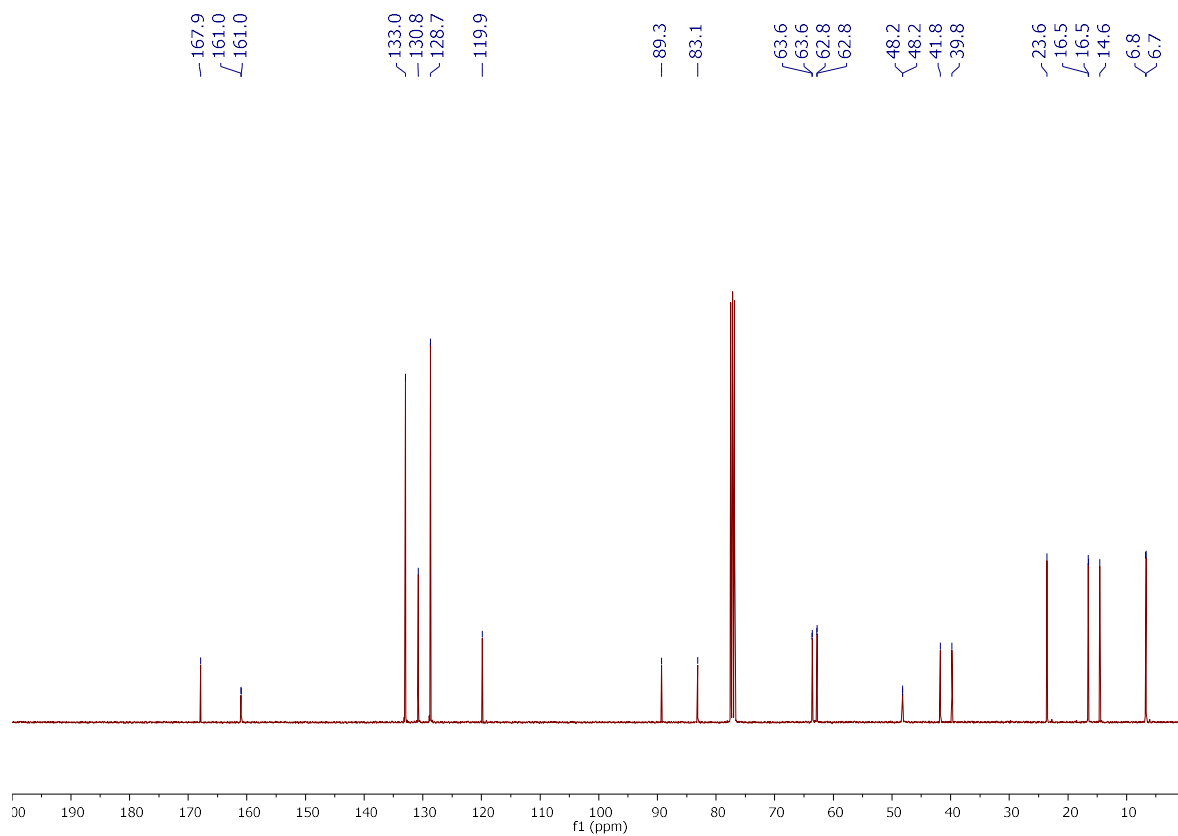
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5f**



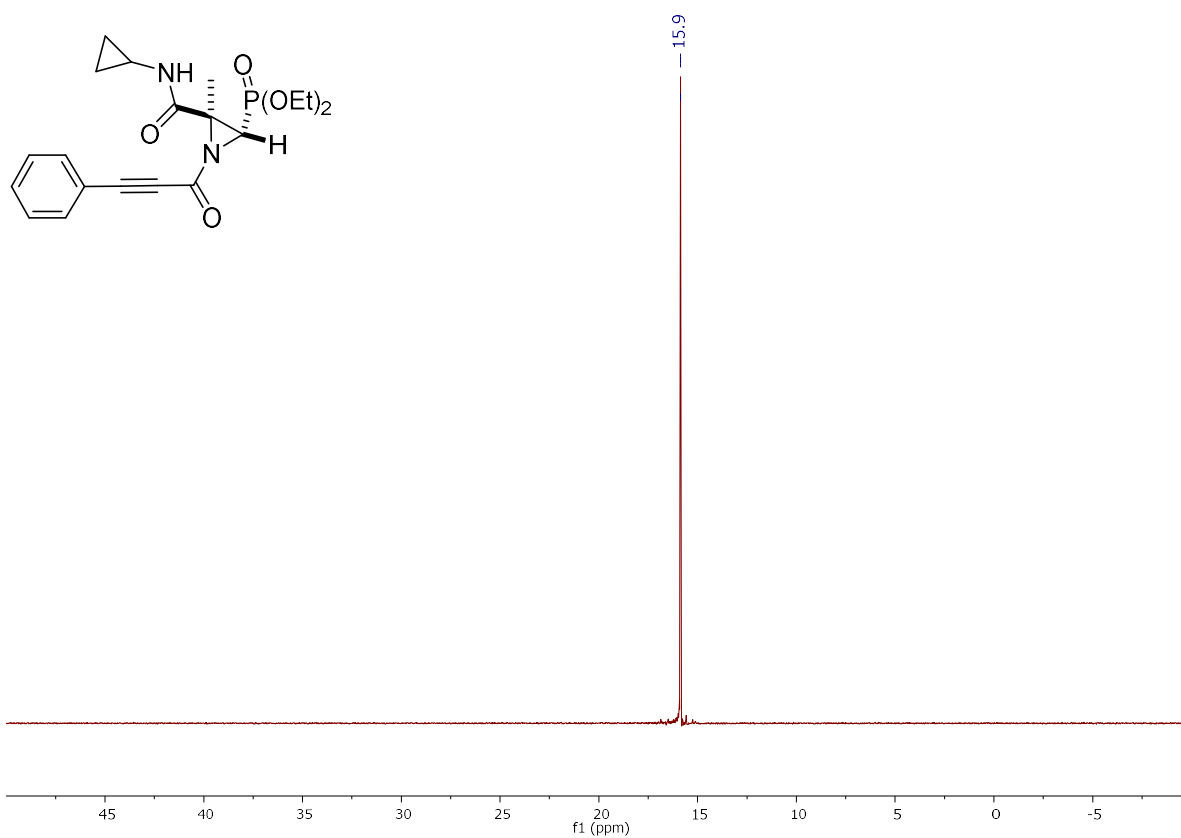
¹H NMR (400 MHz, CDCl₃) of *N*-Acylaziridine Phosphonate **5g**



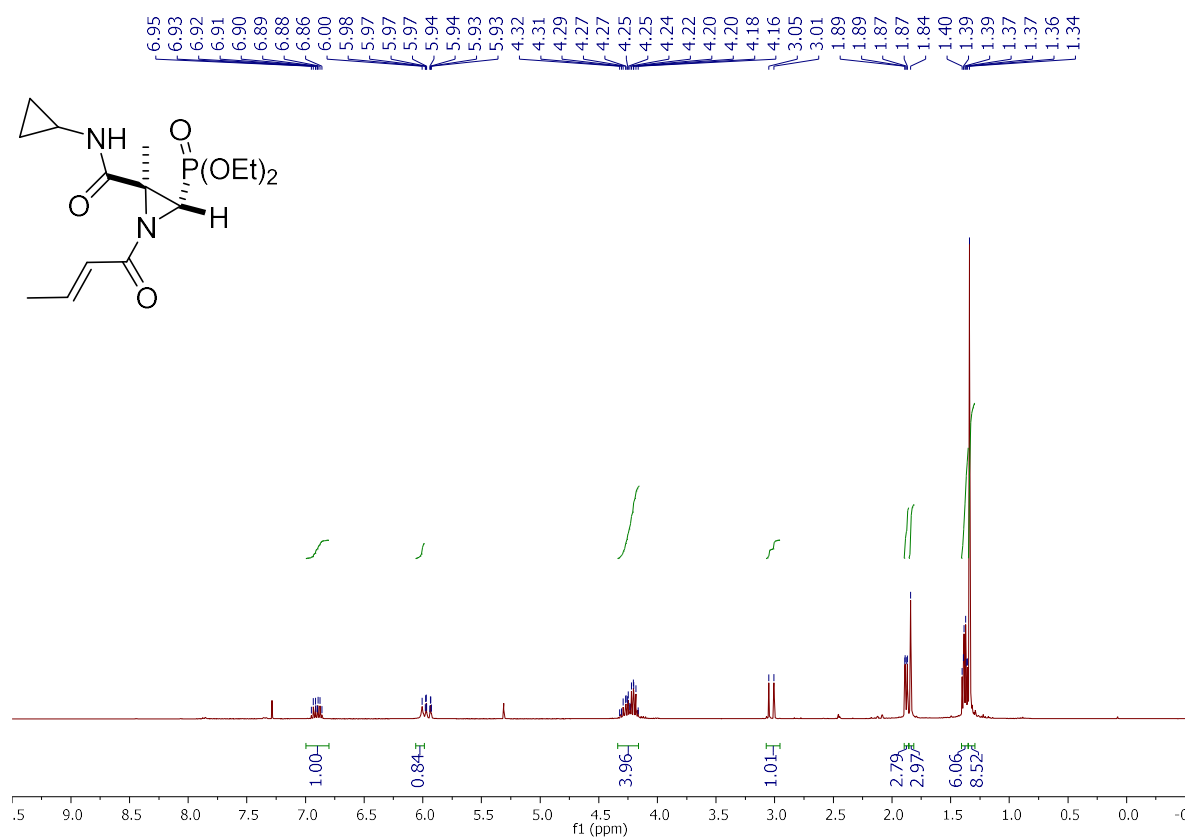
¹³C {¹H} NMR (100 MHz, CDCl₃) of *N*-Acylaziridine Phosphonate **5g**



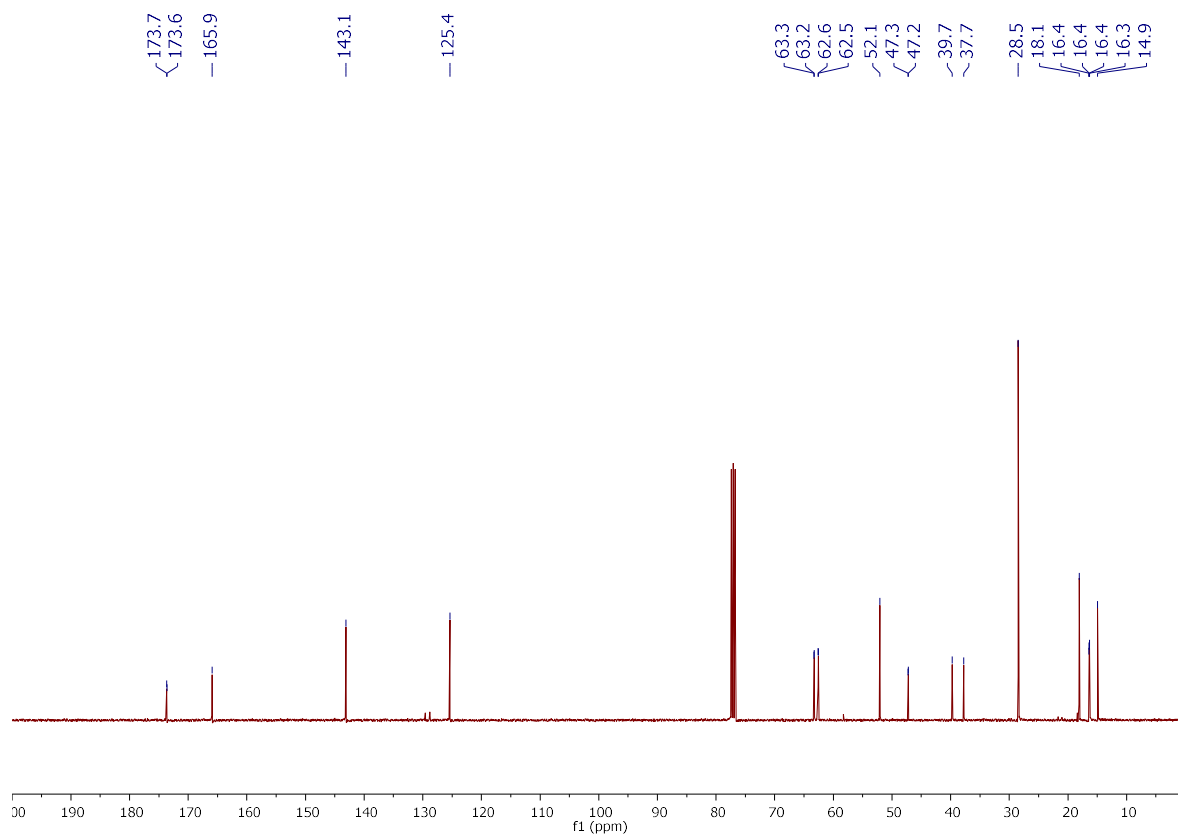
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5g**



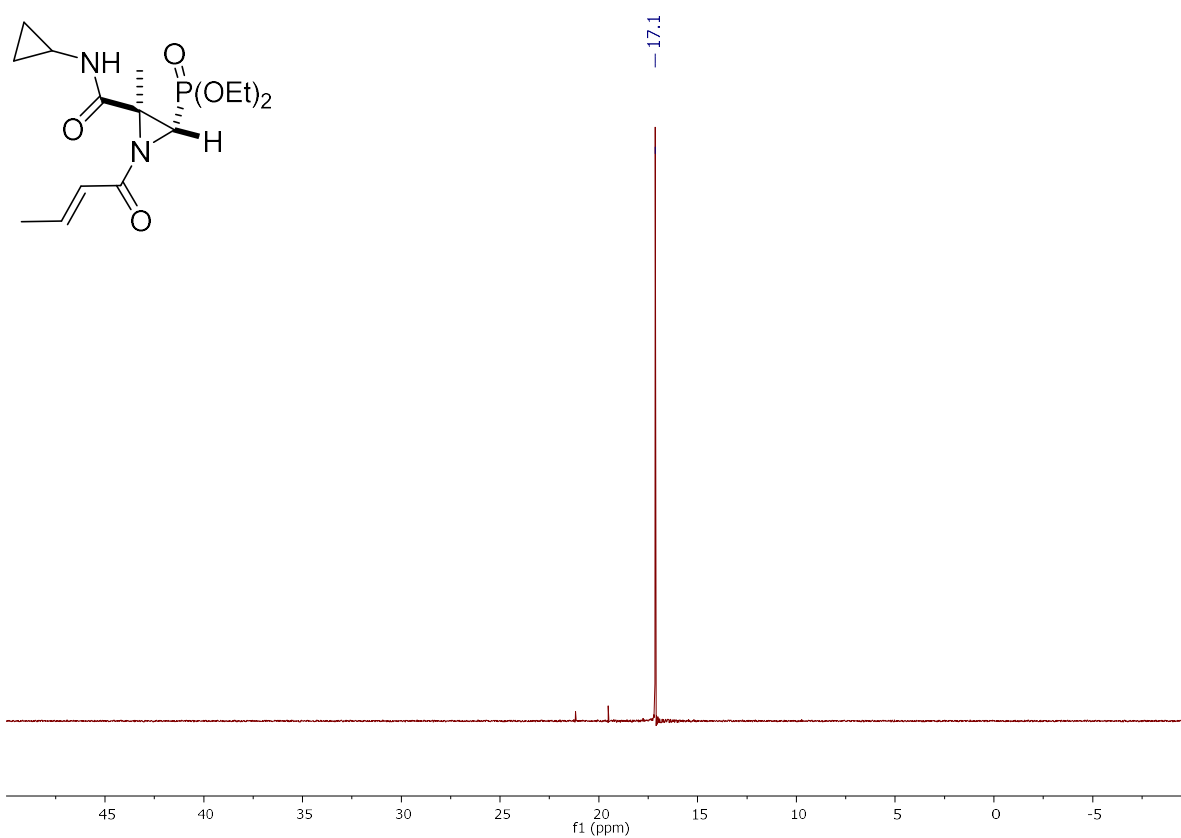
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5h**



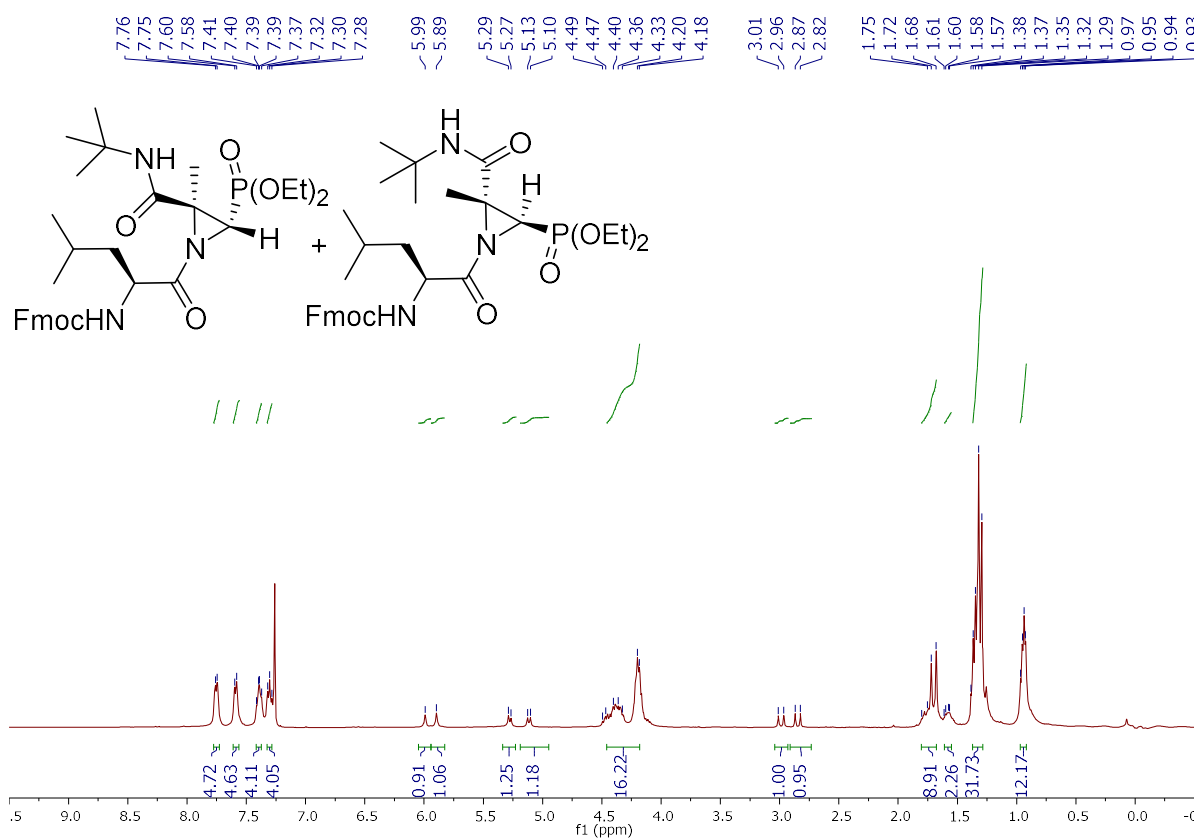
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5h**



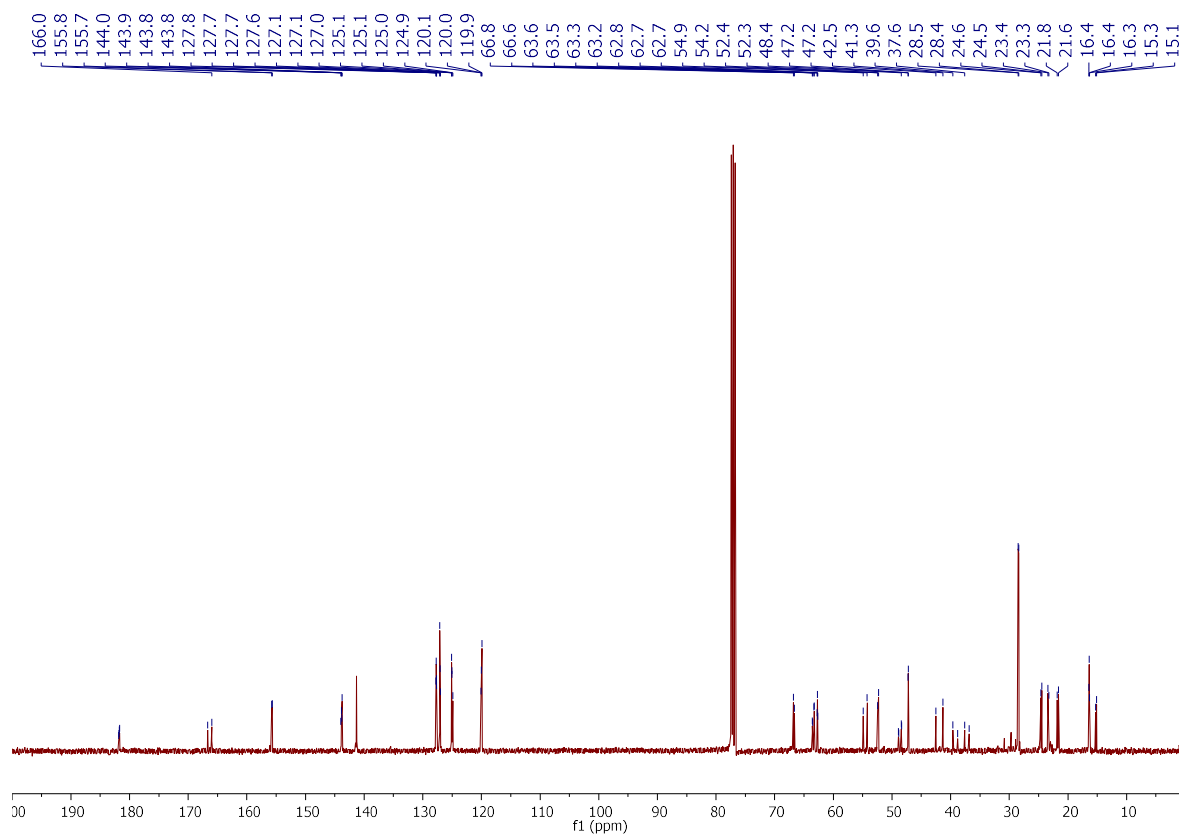
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Phosphonate **5h**



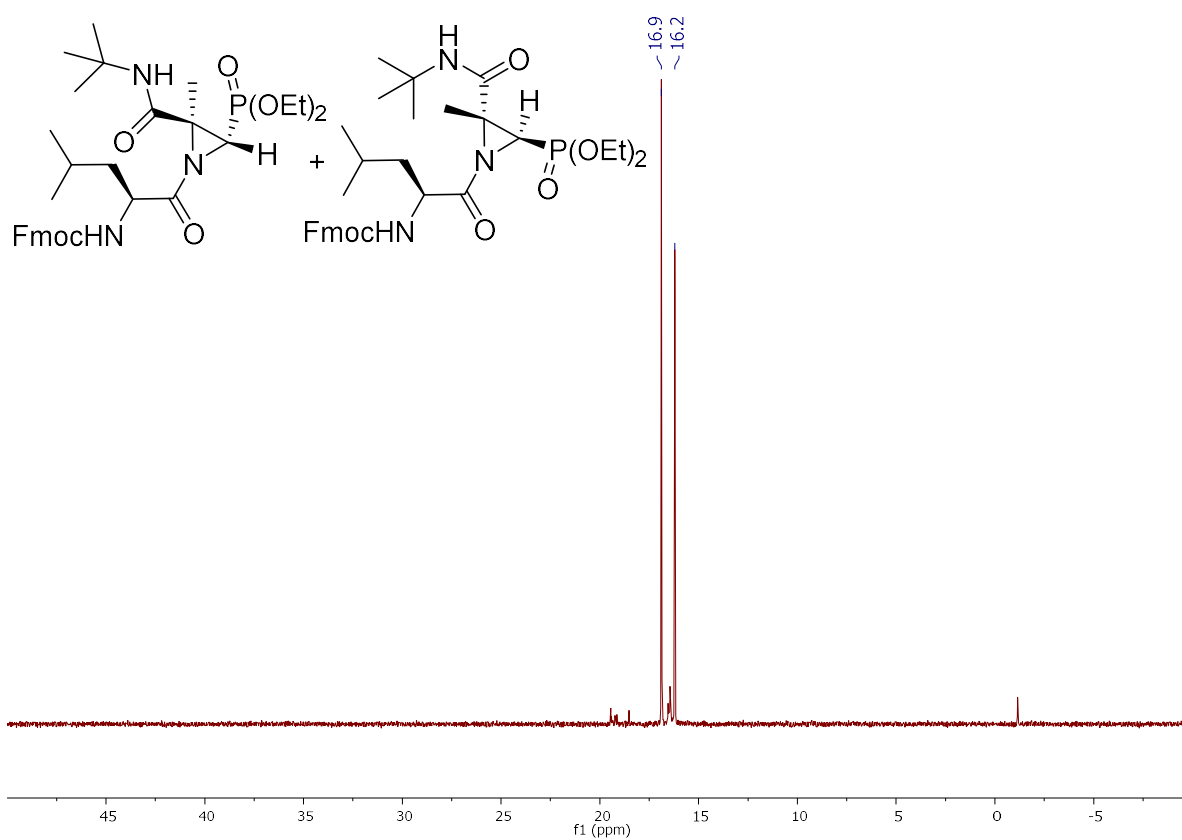
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6a**



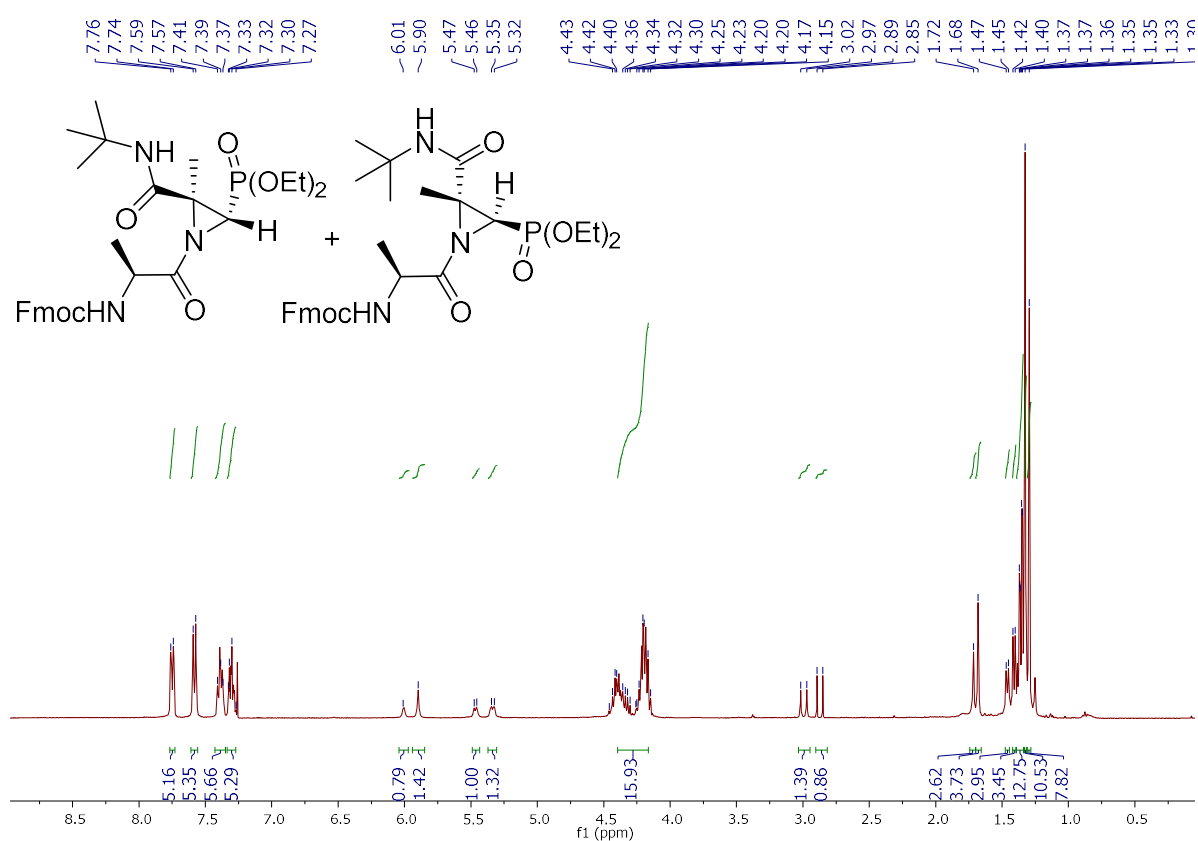
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6a**



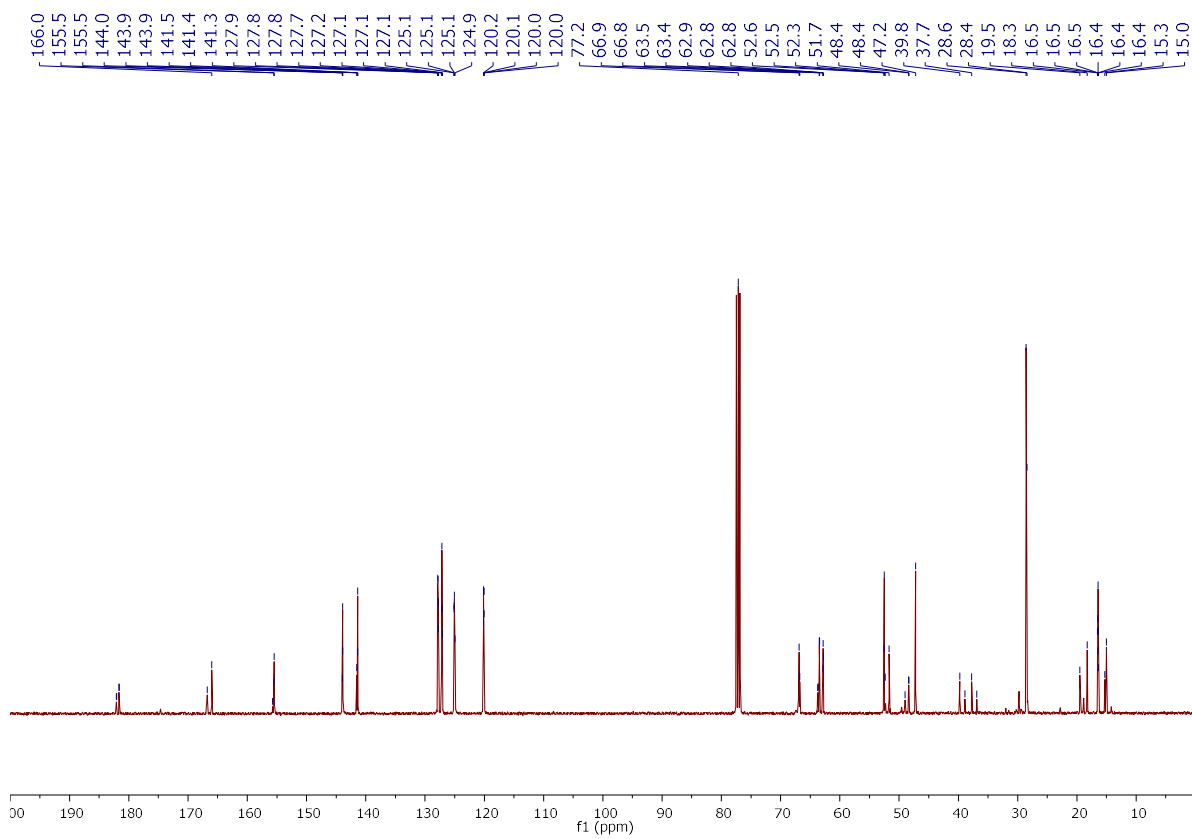
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6a**



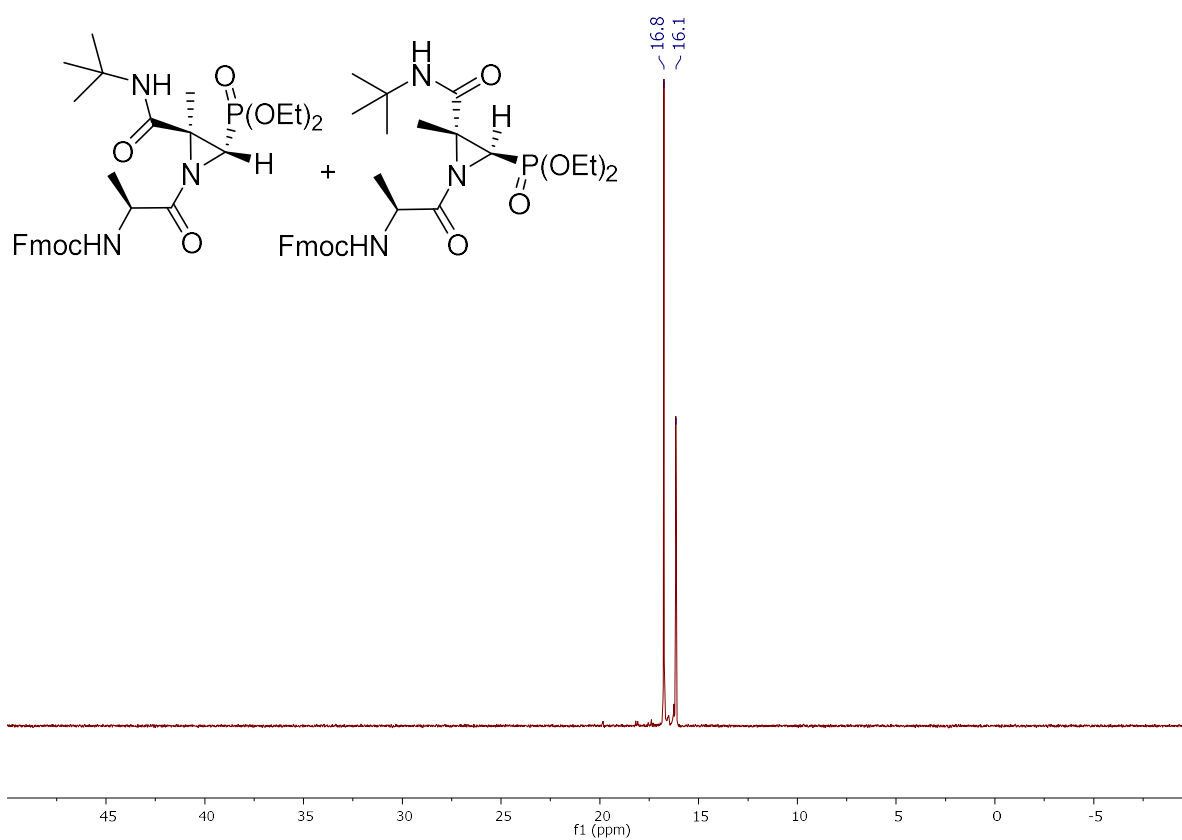
^1H NMR (400 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6b**



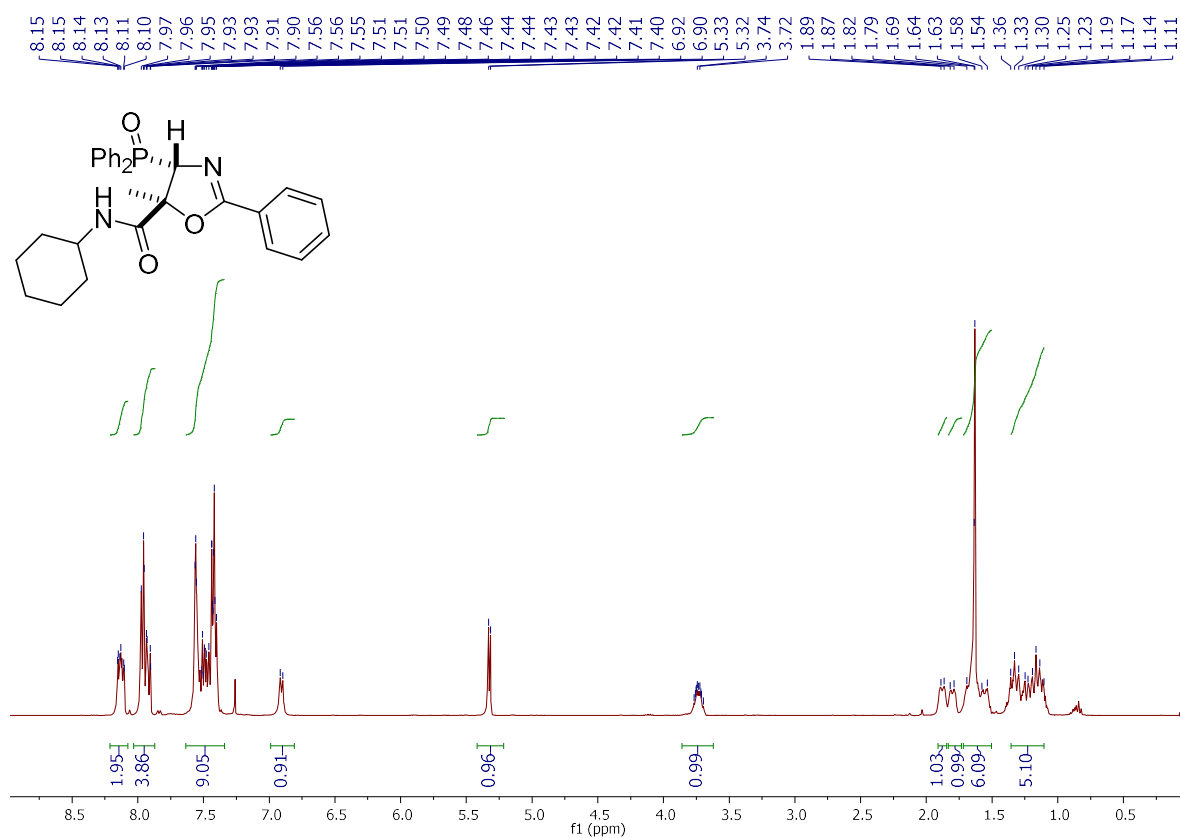
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6b**



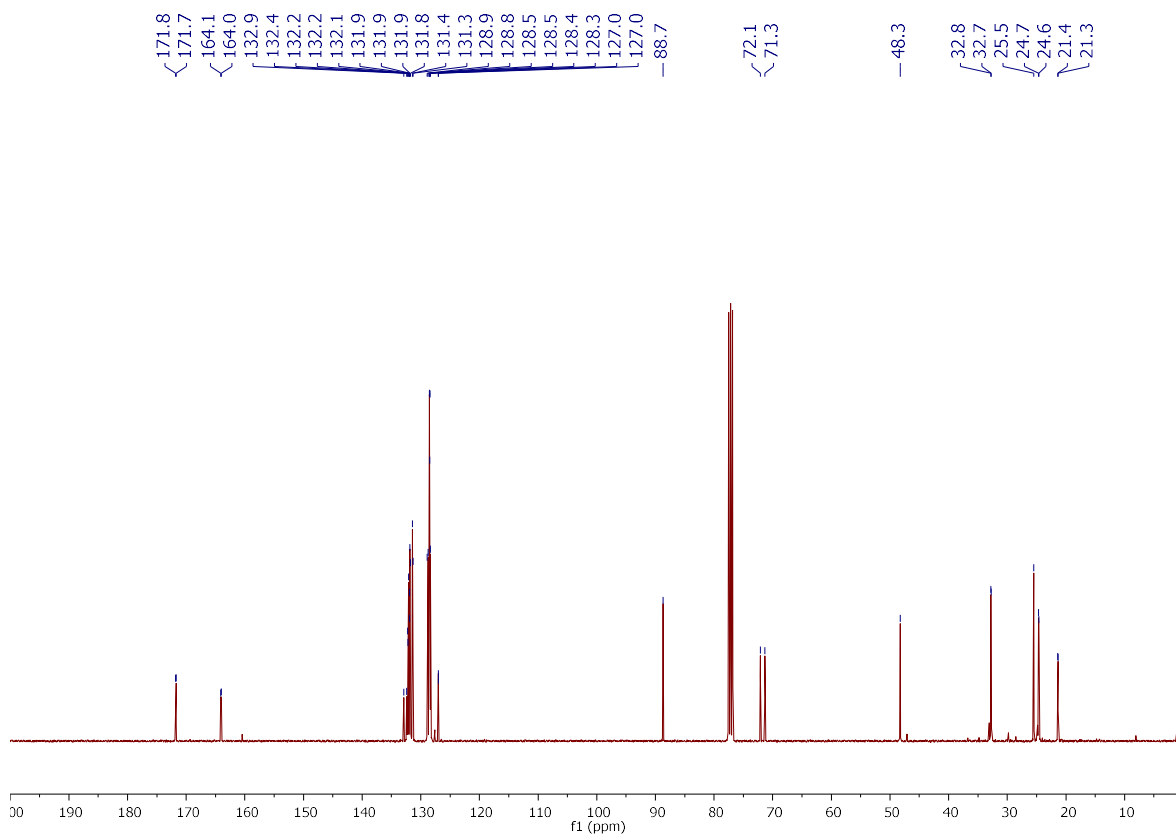
^{31}P (160 MHz, CDCl_3) of *N*-Acylaziridine Peptidomimetic **6b**



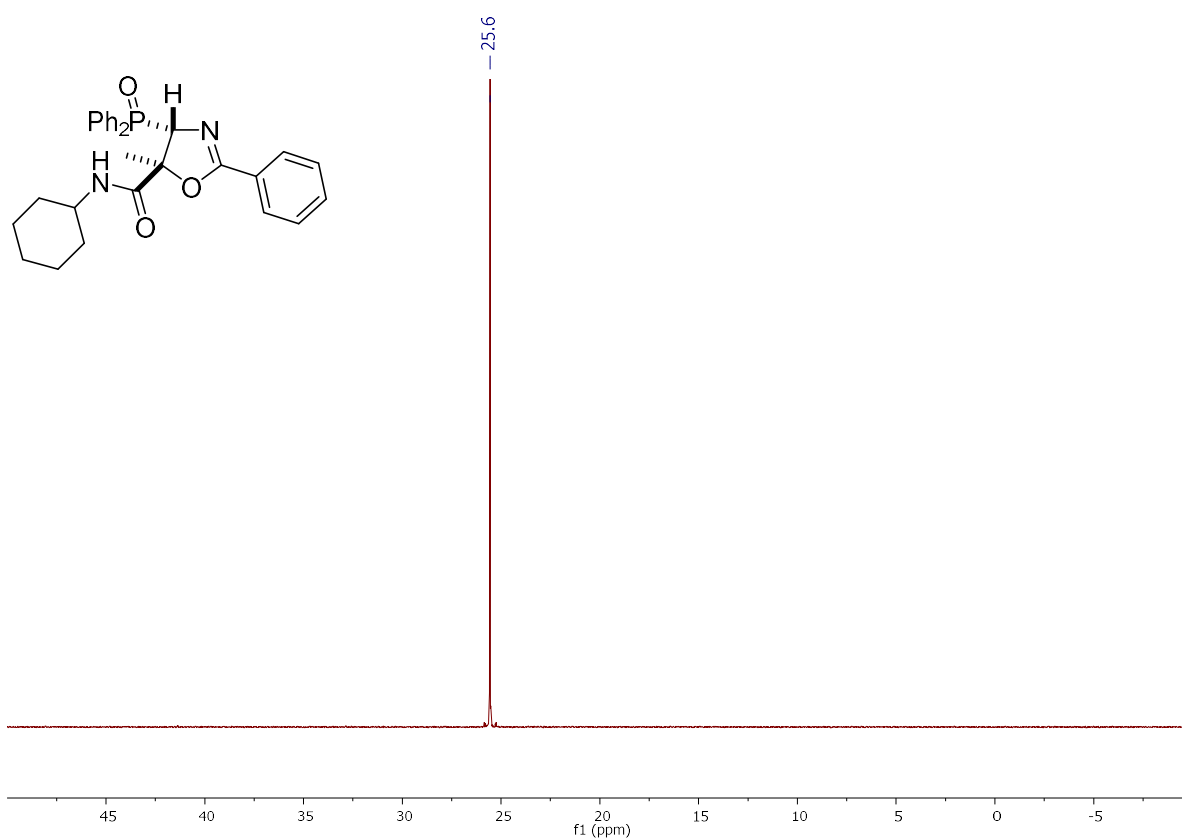
^1H NMR (400 MHz, CDCl_3) of Oxazole Derivative **7a**



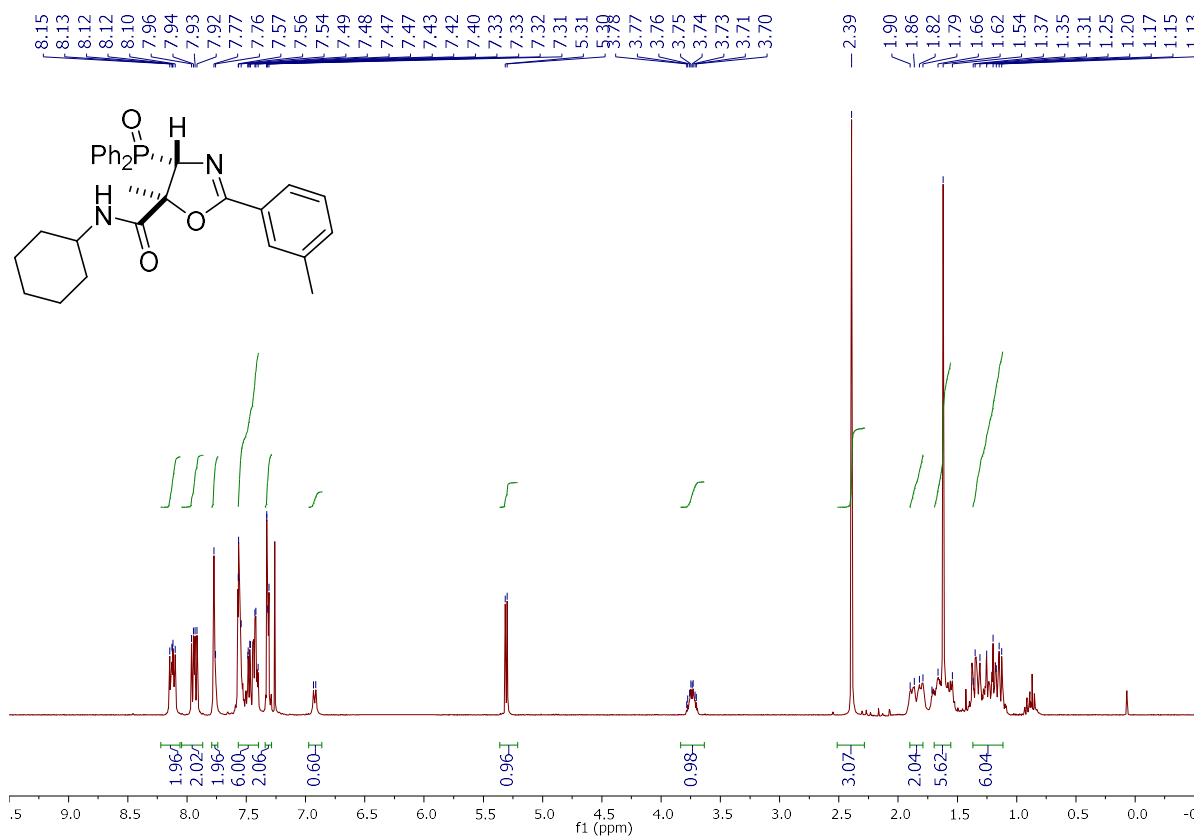
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of Oxazole Derivative **7a**



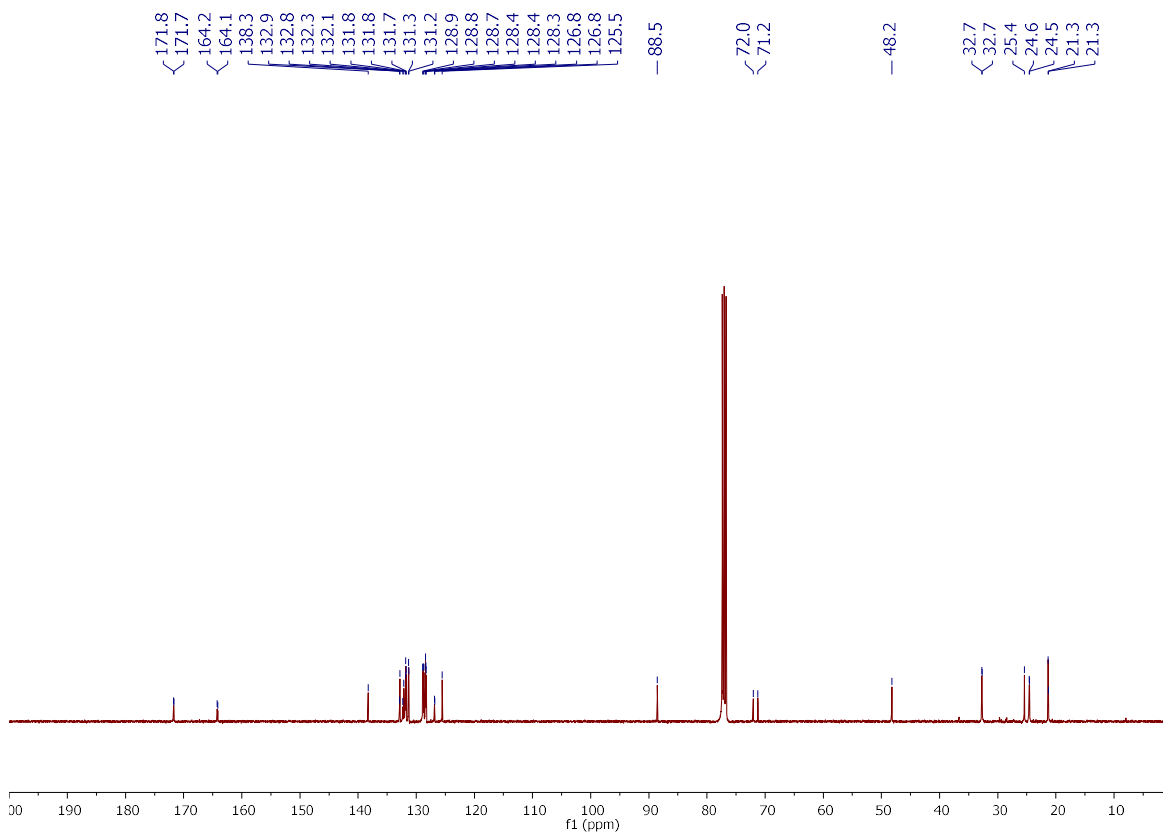
^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7a**



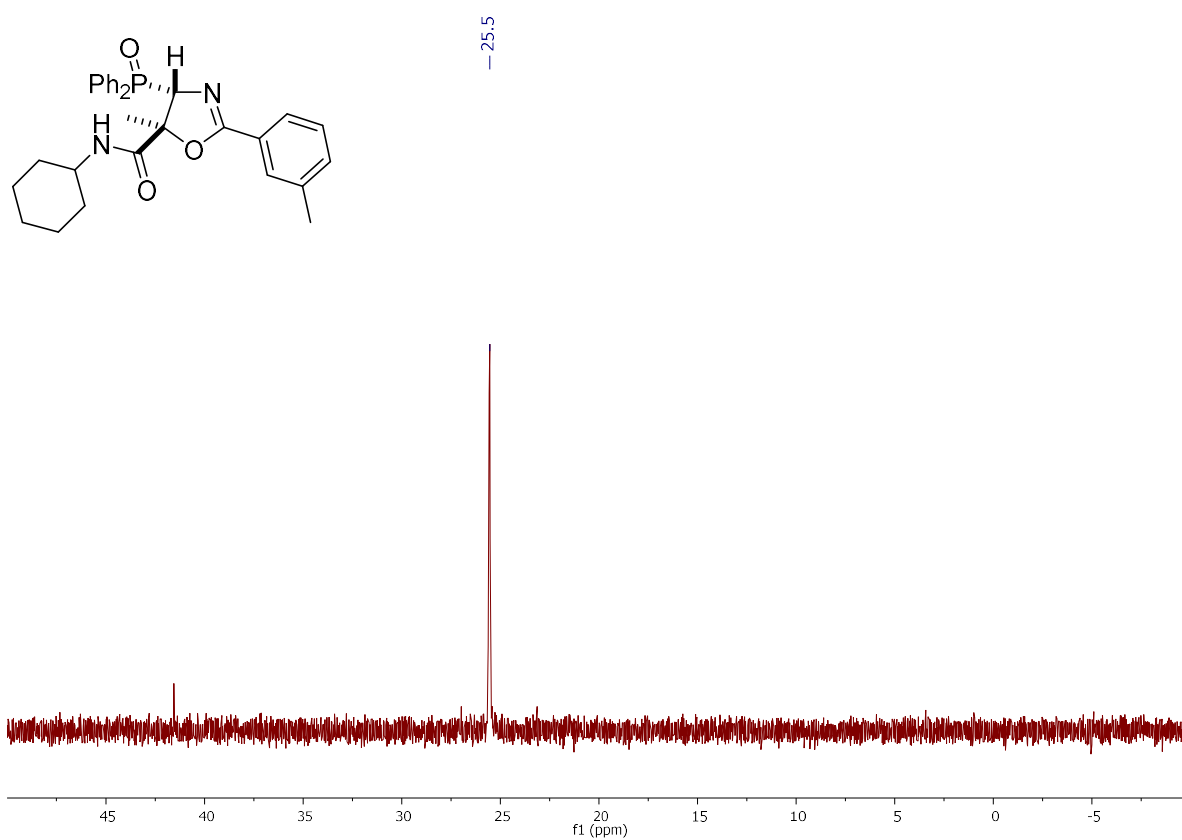
¹H NMR (400 MHz, CDCl₃) of Oxazole Derivative **7b**



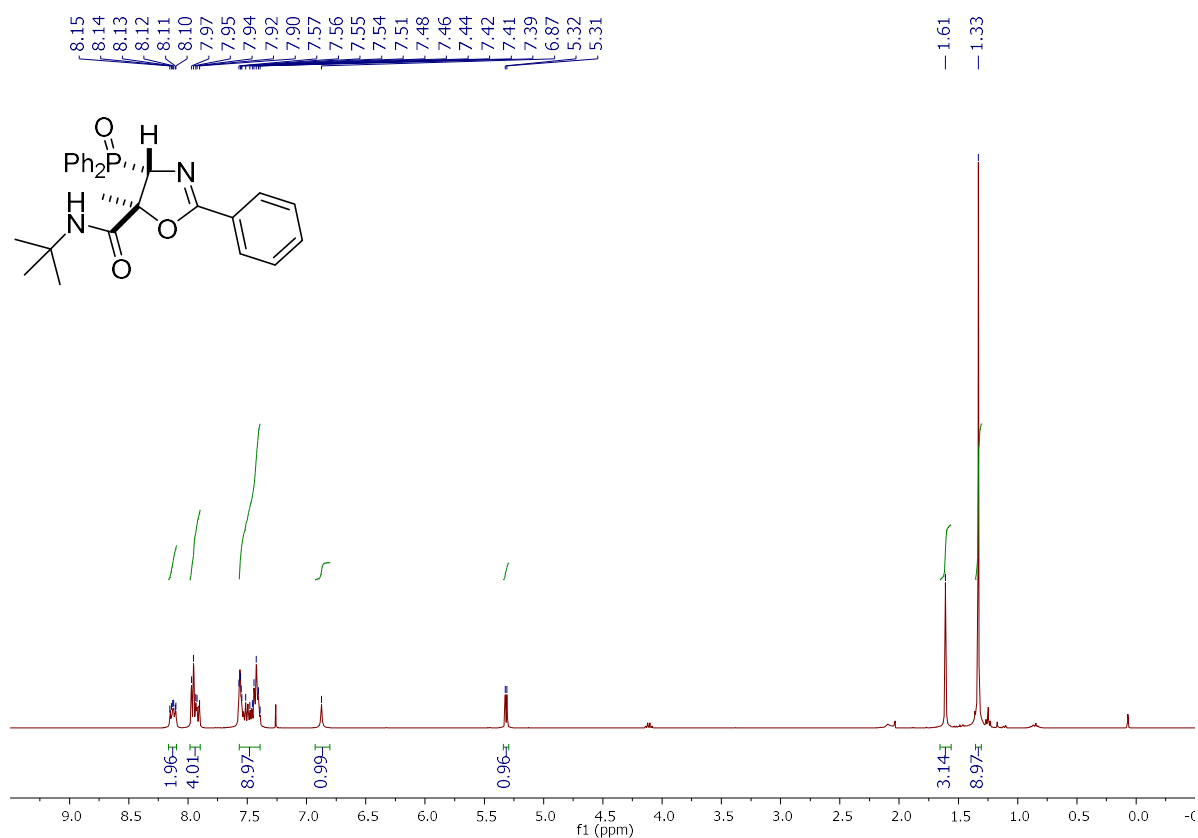
¹³C {¹H} NMR (100 MHz, CDCl₃) of Oxazole Derivative **7b**



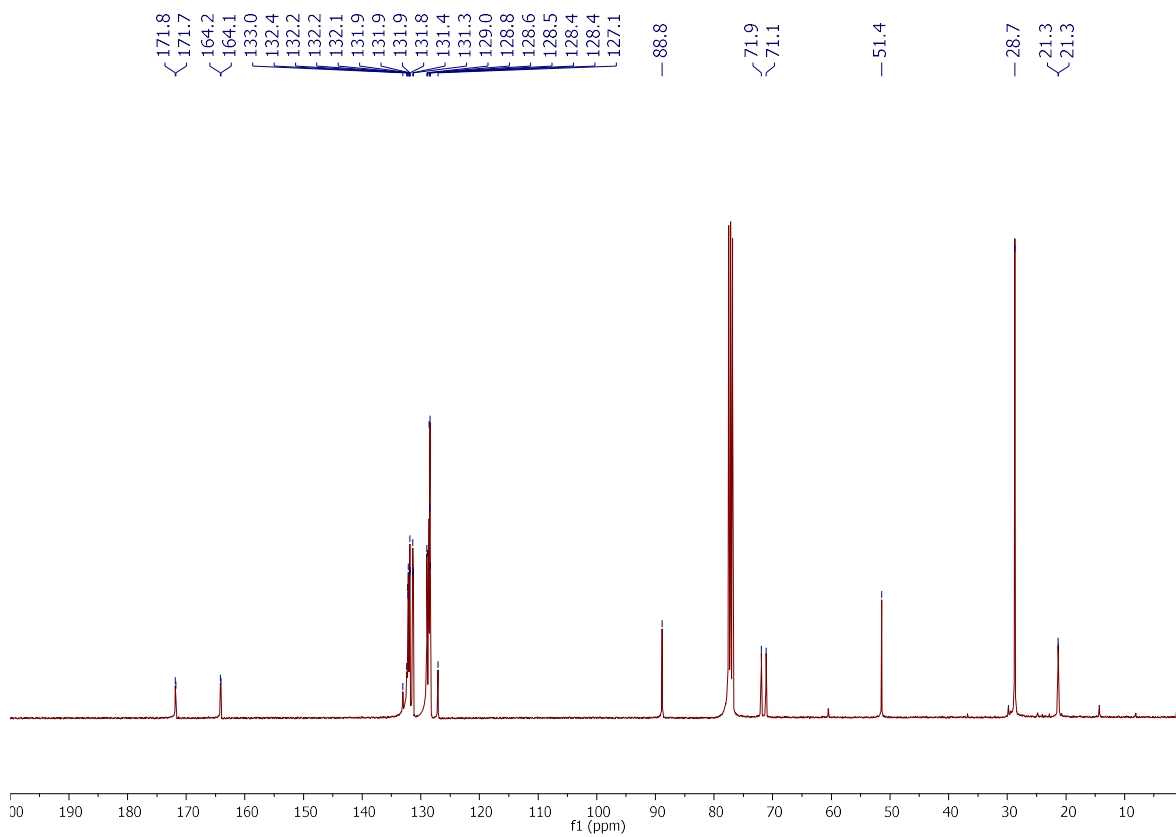
^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7b**



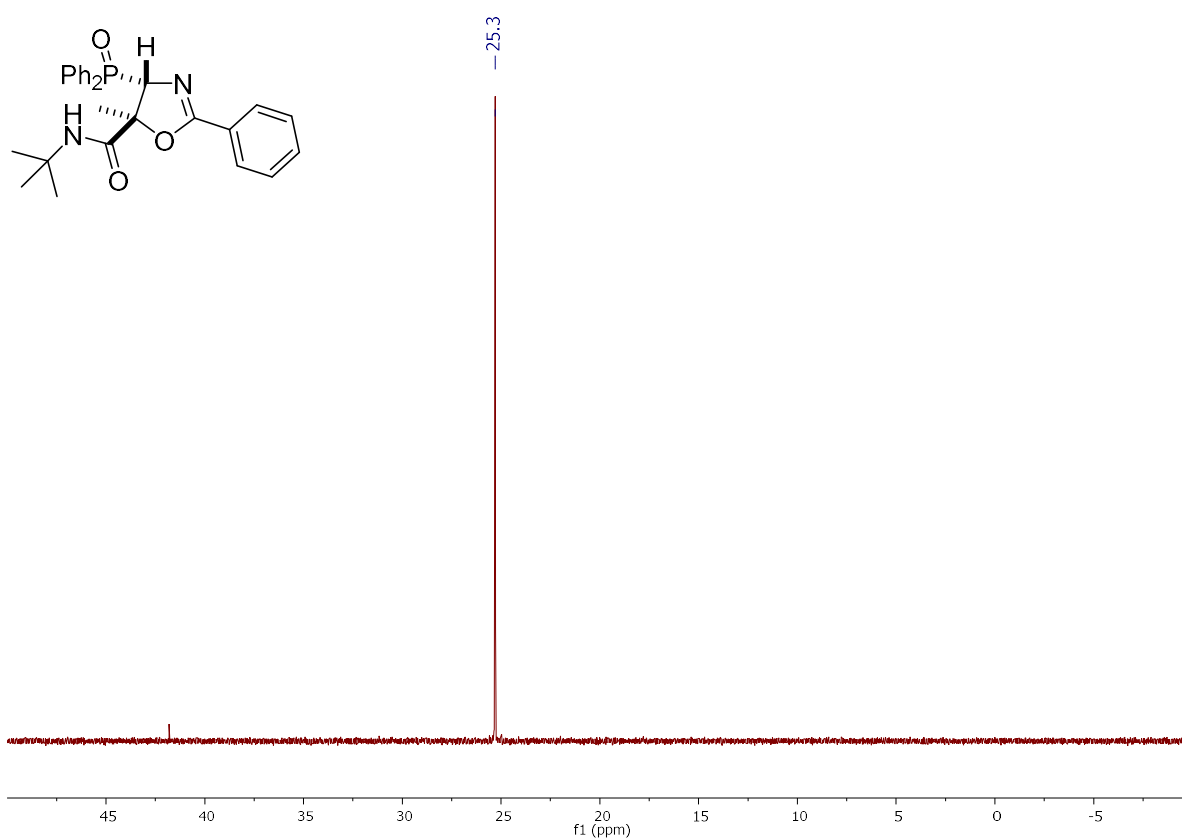
^1H NMR (400 MHz, CDCl_3) of Oxazole Derivative **7c**



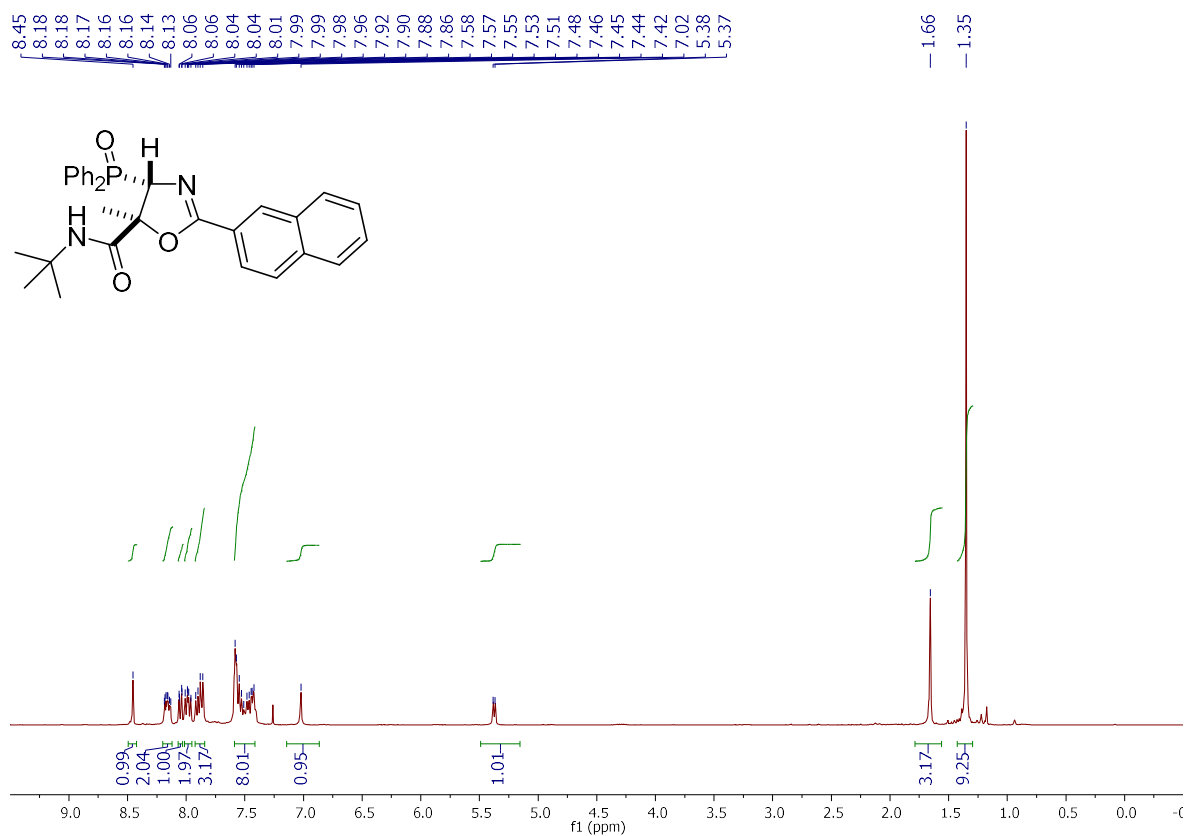
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of Oxazole Derivative **7c**



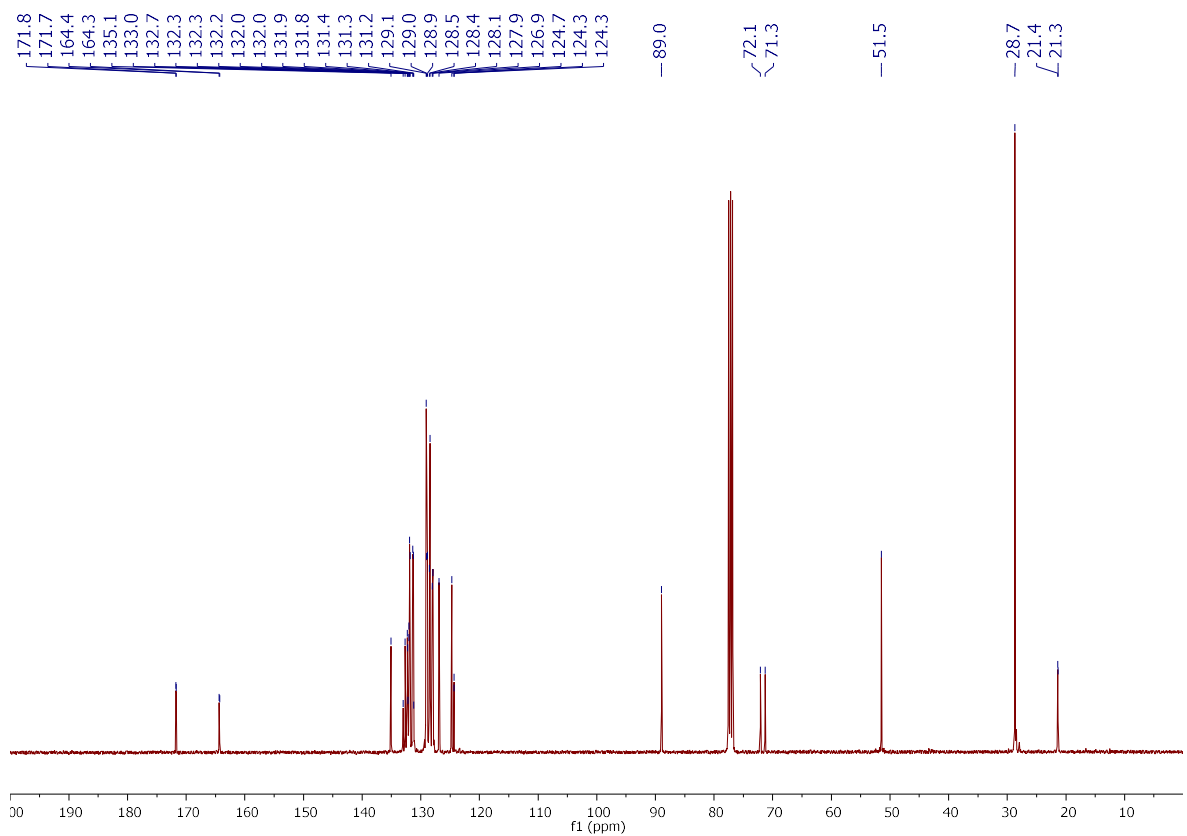
^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7c**



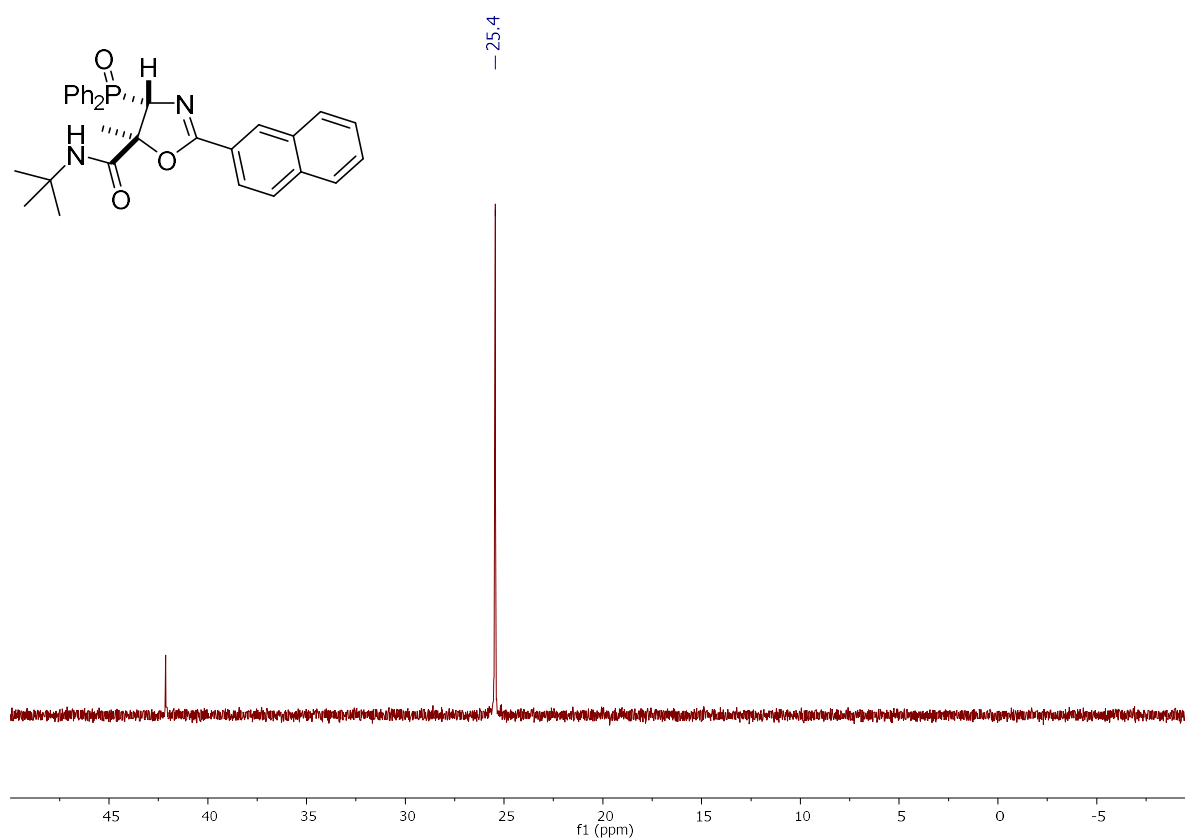
^1H NMR (400 MHz, CDCl_3) of Oxazole Derivative **7d**



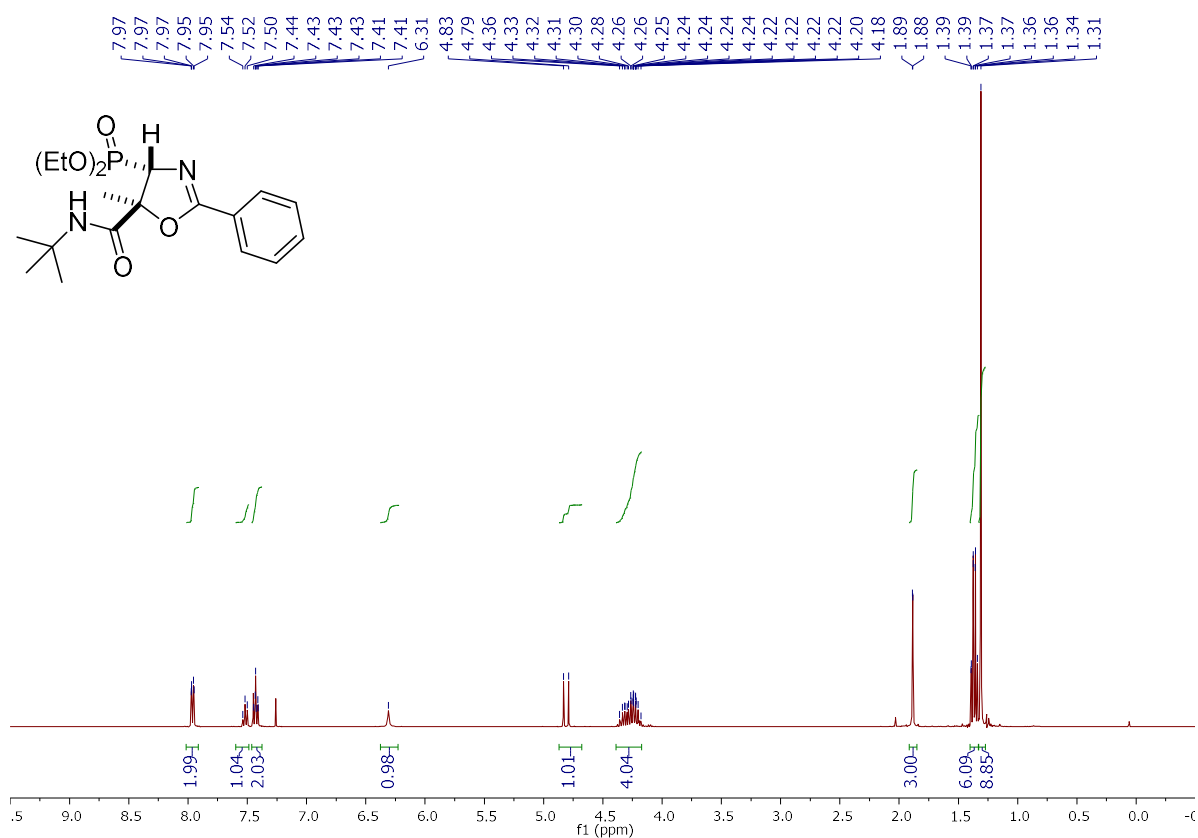
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of Oxazole Derivative **7d**



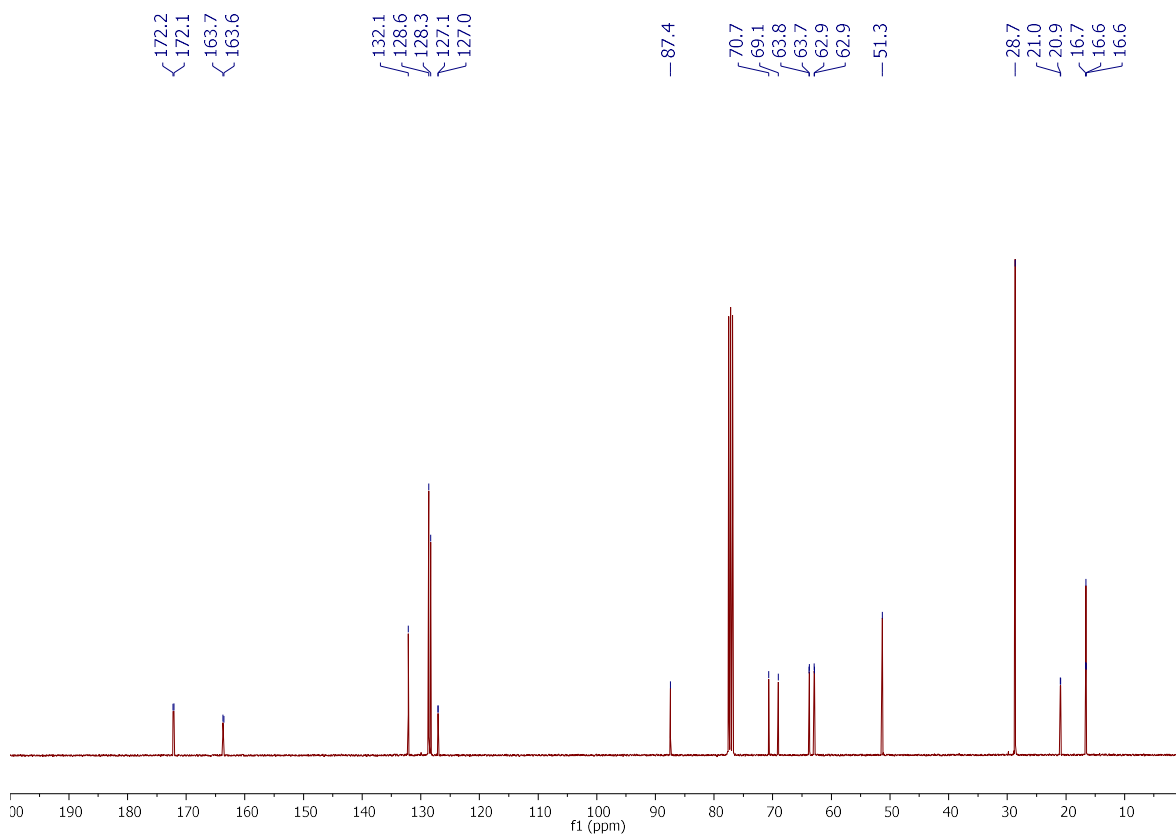
^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7d**



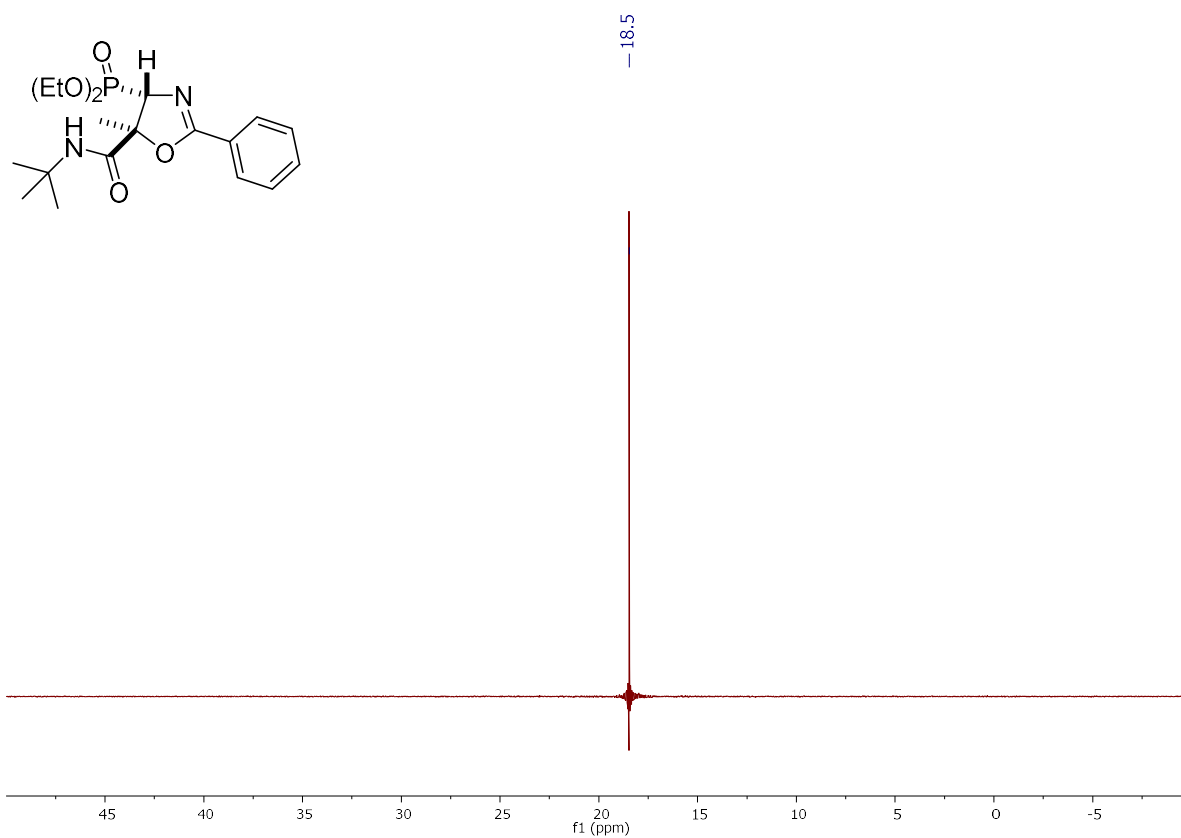
^1H NMR (400 MHz, CDCl_3) of Oxazole Derivative **7e**



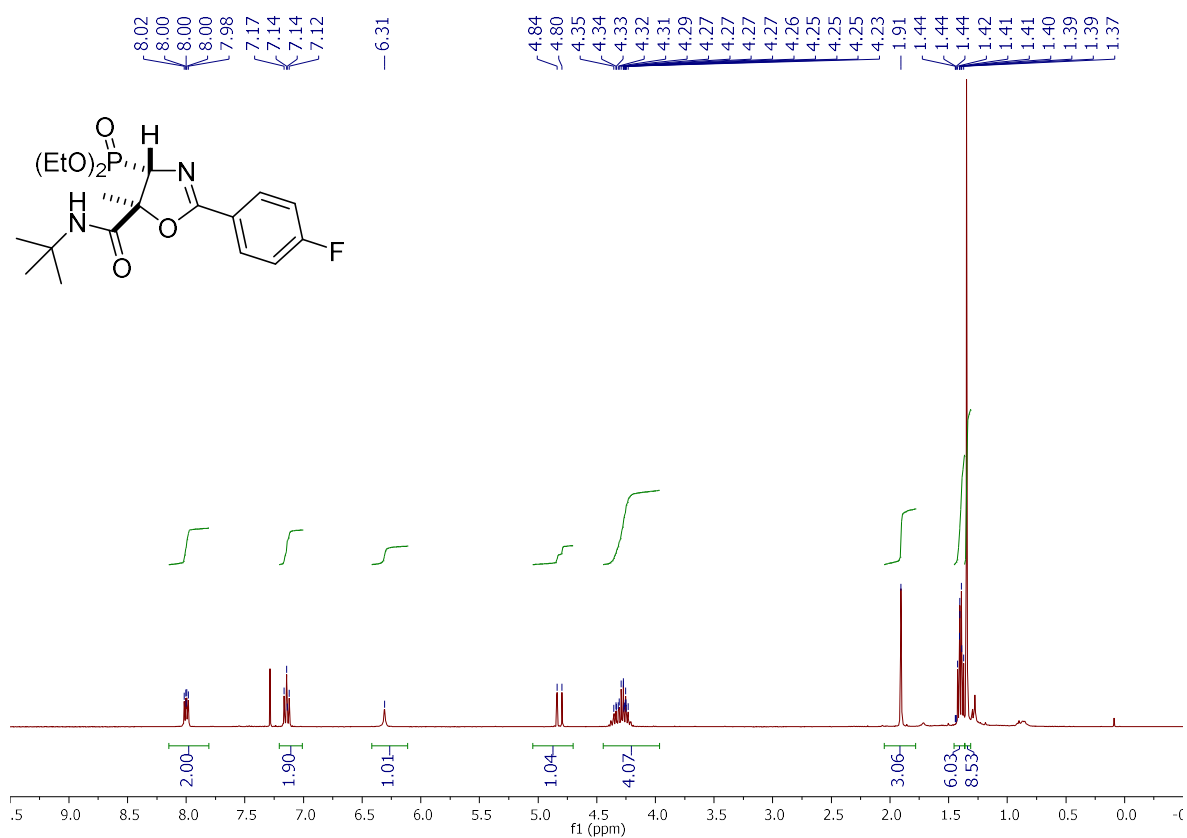
^{13}C { ^1H } NMR (100 MHz, CDCl_3) of Oxazole Derivative **7e**



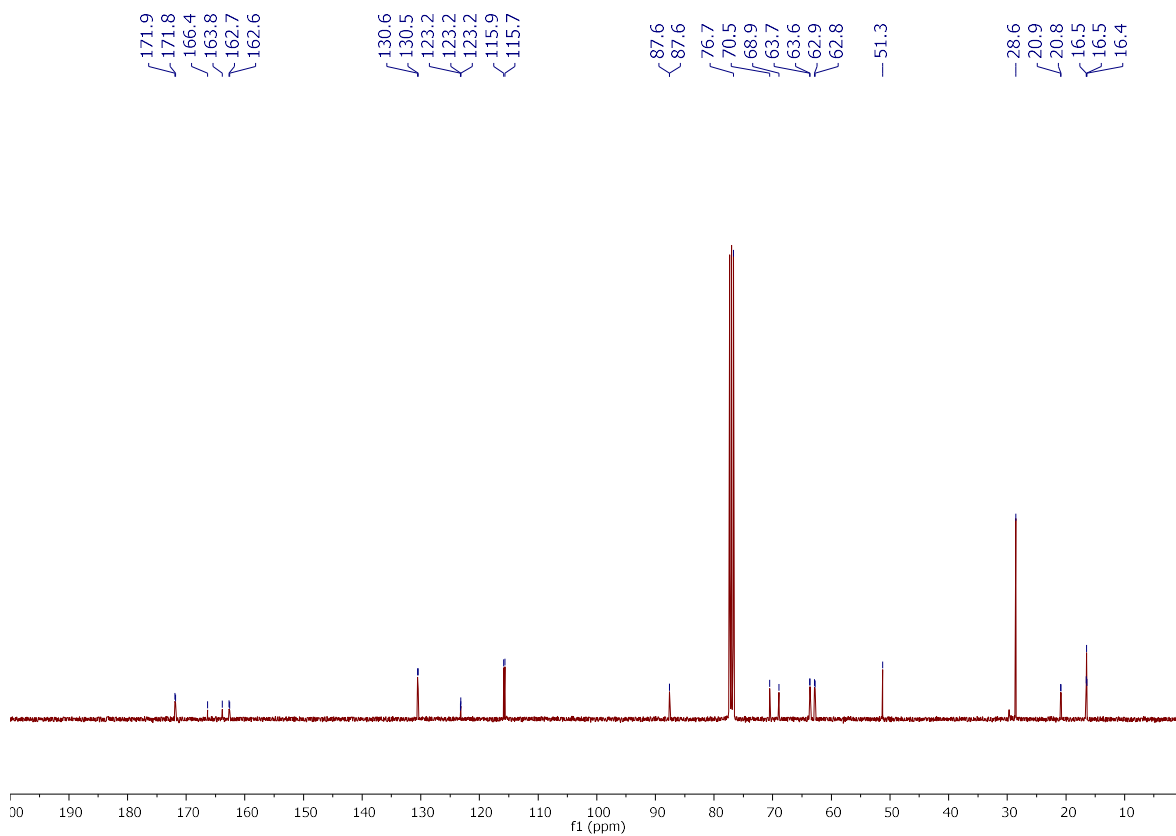
^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7e**



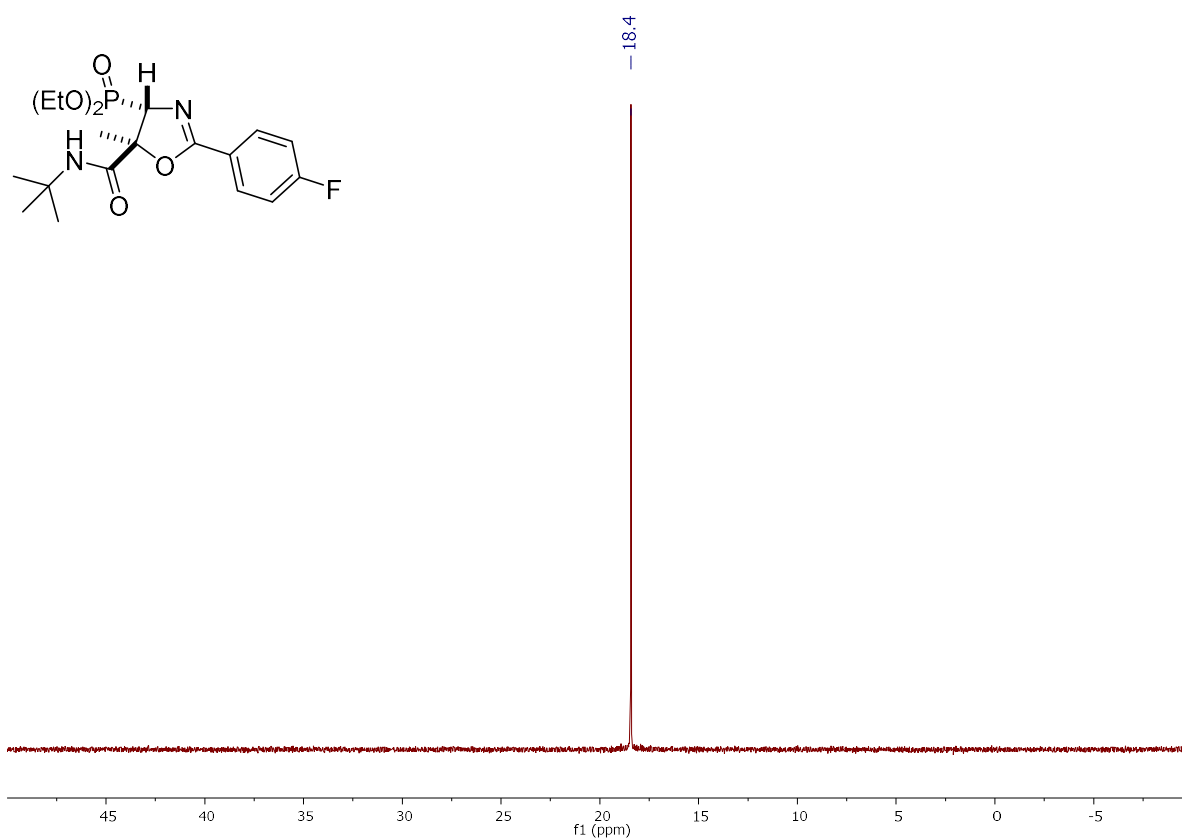
^1H NMR (400 MHz, CDCl_3) of Oxazole Derivative **7f**



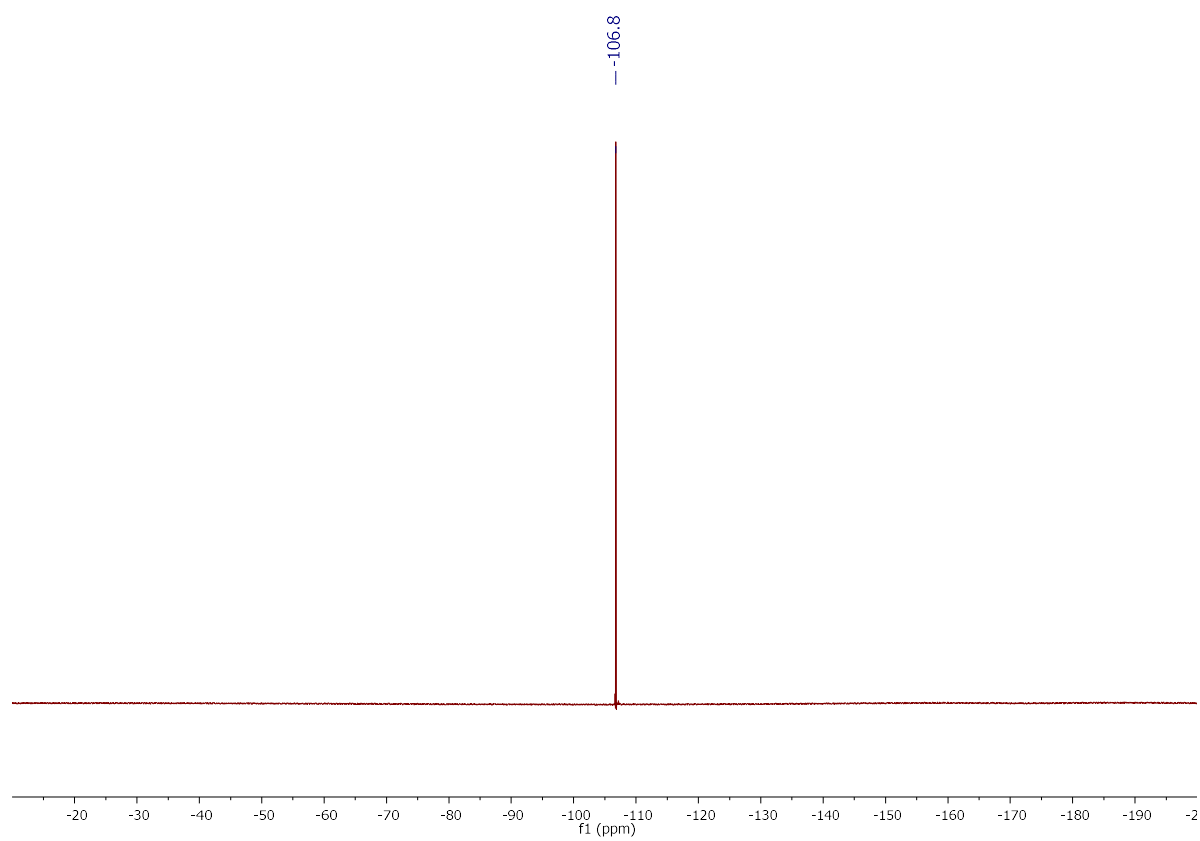
^{13}C $\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of Oxazole Derivative **7f**



^{31}P (160 MHz, CDCl_3) of Oxazole Derivative **7f**



^{19}F (376 MHz, CDCl_3) of Oxazole Derivative **7f**



2. ORTEP view and X-ray crystallographic statistics for compounds **4i** and **7a**

N-Acylaziridine Phosphine Oxide **4i**

(CCDC deposition number 2304039)

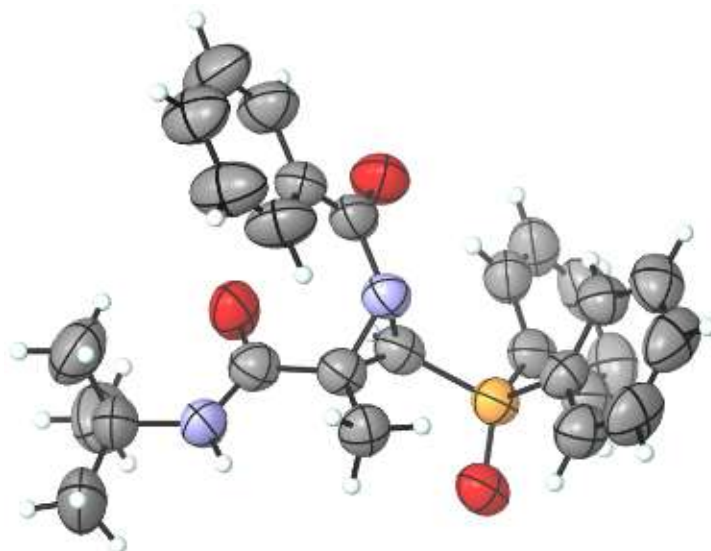


Figure S1. ORTEP diagram of compound **4i** with thermal displacement parameters drawn at 50% probability.

Single crystals of $C_{27}H_{29}N_2O_3P$ [**4i**] were obtained. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, HyPix diffractometer. The crystal was kept at 170.01(10) K during data collection. Using Olex2,¹ the structure was solved with the ShelXS² structure solution program using Intrinsic Phasing and refined with the ShelXL³ refinement package using Least Squares minimization.

Table S1. Crystal data and structure refinement for **4i**.

Empirical formula	C ₂₇ H ₂₉ N ₂ O ₃ P
Formula weight	460.49
Temperature/K	170.01(10)
Crystal system	monoclinic
Space group	Pc
a/Å	14.3797(5)
b/Å	18.5342(9)
c/Å	9.2763(3)
$\alpha/^\circ$	90.0
$\beta/^\circ$	99.780(3)
$\gamma/^\circ$	90.0
Volume/Å ³	2436.35(17)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.255
μ/mm^{-1}	1.247
F(000)	976.0
Crystal size/mm ³	0.255 × 0.133 × 0.118
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	6.238 to 138
Index ranges	-17 ≤ h ≤ 17, -22 ≤ k ≤ 20, -11 ≤ l ≤ 11
Reflections collected	43034
Independent reflections	8983 [R_{int} = 0.1481, R_{sigma} = 0.0972]
Data/restraints/parameters	8983/14/603
Goodness-of-fit on F ²	1.032
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0819, wR_2 = 0.2127
Final R indexes [all data]	R_1 = 0.1062, wR_2 = 0.2367
Largest diff. peak/hole / e Å ⁻³	0.51/-0.43
Flack parameter	0.04(4)
Bijvoet Pairs Covarage	98%
Hooft y	0.02(3)
P3 false	≤10 ⁻⁹⁹

Oxazole Derivative **7a**

(CCDC deposition number 2304041)

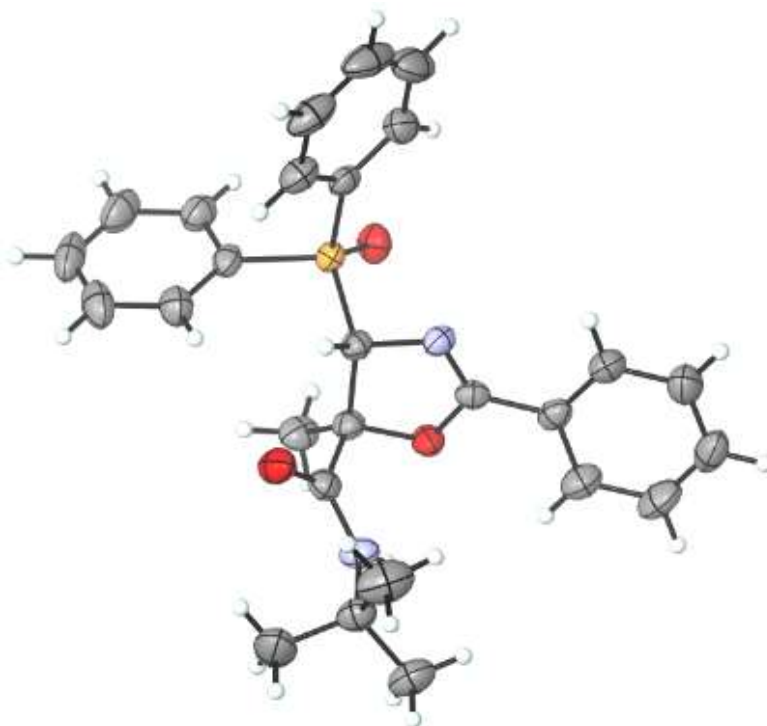


Figure S2. ORTEP diagram of compound **7a** with thermal displacement parameters drawn at 50% probability.

Single crystals of $C_{27}H_{29}N_2O_3P$ [**7a**] were obtained. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, HyPix diffractometer. The crystal was kept at 170.01(10) K during data collection. Using Olex2,¹ the structure was solved with the ShelXS² structure solution program using Intrinsic Phasing and refined with the ShelXL³ refinement package using Least Squares minimization.

Table S2. Crystal data and structure refinement for **7a**.

Empirical formula	C ₂₇ H ₂₉ N ₂ O ₃ P
Formula weight	460.49
Temperature/K	170.00(10)
Crystal system	monoclinic
Space group	P21/n
a/Å	12.87200(8)
b/Å	10.12924(7)
c/Å	18.65780(11)
$\alpha/^\circ$	90.0
$\beta/^\circ$	90.2466(5)
$\gamma/^\circ$	90.0
Volume/Å ³	2432.65(3)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.257
μ/mm^{-1}	1.247
F(000)	976.0
Crystal size/mm ³	0.559 × 0.26 × 0.126
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	8.328 to 137.96
Index ranges	-15 ≤ h ≤ 15, -12 ≤ k ≤ 12, -22 ≤ l ≤ 22
Reflections collected	44390
Independent reflections	4528 [R_{int} = 0.0611, R_{sigma} = 0.0264]
Data/restraints/parameters	4528/0/302
Goodness-of-fit on F ²	1.044
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0342, wR_2 = 0.0901
Final R indexes [all data]	R_1 = 0.0356, wR_2 = 0.0914
Largest diff. peak/hole / e Å ⁻³	0.27/-0.43

3. References

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- ¹ Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339–341.
 - ² Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112–122.
 - ³ Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3–8.