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Supporting Information

Evidence and exploitation of dicationic ammonium-nitrilium superelectrophiles: direct synthesis of unsaturated piperidinones

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1. General Informations

Solvents: All anhydrous solvents were purchased from Acros and used as received.

Reagents: All commercially available reagents were used as purchased. HF was purchased from Air Liquide and SbF_5 from ARC (USA) and used as received.

Reactions: The authors draw the reader's attention to the dangerous features of superacidic chemistry. Handling of hydrogen fluoride and antimony pentafluoride must be done by experienced chemists with all the necessary safety arrangements in place. Reactions performed in superacid were carried out in a sealed Teflon® flask with a magnetic stirrer. No further precautions have to be taken to prevent mixture from moisture (test reaction worked out in anhydrous conditions leads to the same results as expected). Yields refer to isolated pure products.

Chromatography: All flash chromatography were carried out using Merck 9385 Kieselgel 60 silica gel under air atmosphere or using puriFlash® columns (30 µm) on a CombiFlash® apparatus from Teledyne. Thin layer chromatography were carried out on Merck Kieselgel 60 F_{254} 0.2 mm plates. Visualization was accomplished using ultraviolet light (254 nm) and chemical staining with a solution of phosphomolybdic acid in EtOH as appropriate.

Data Collection: ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on an Avance Nandbay 400 MHz spectrometer using $CDCl_3$ as solvent and C_6F_6 as external reference. Chemical shifts (δ) are quoted in parts per million (ppm) relative to residual solvent ($CHCl_3$: δ_H = 7.26 ppm for ^{1}H and $CDCl_3$: δ_C = 77.16 ppm for ^{13}C). Coupling constants (*J*) are quoted to the nearest 0.1 Hz. The following abbreviations are used to indicate the multiplicity of the signals: s = singlet; d = doublet; t = triplet; q = quartet; quint = quintet; sep = septet; m = multiplet; br. = broad; app. = apparent; and associated combinations, e.g. dd = doublet of doublets. The temperature of the acquisition of the NMR spectra was 298 ± 3 K. DEPT 135 and 2-dimensional experiments (COSY, HSQC, HMBC and NOESY) were used to support assignments where appropriate but are not included in this document. High resolution mass spectra (HRMS) were recorded on a Bruker Q-TOF Impact HD apparatus using a positive electrospray (ESI) ionization source. Optical rotations were measured in $CHCl_3$ on an Anton Paar MCP 100 Polarimeter using a sodium lamp (λ 589 nm, D-line). $[\alpha]_D$ values are reported at a given temperature (°C) in 10^{-1} degrees $cm^2.g^{-1}$ with concentration in g/100mL. HPLC analyses for the determination of enantiomeric excesses were performed on a VWR LaChromElite apparatus equipped with a Hitachi Diode Array L-2455, a Hitachi L-2130 pump and an AutoSampler Hitachi L-2200, or on a Waters alliance system, consisting of a Separation Module 2695 (degasser, pump, oven and autosampler) and a UV/Visible Detector 2489, using Chiralpak AD-H (5 µm, 4.6 x 250 mm) or OJ-RH (5 µm, 4.6 x 150 mm). Melting points (Mp) were recorded using Büchi Melting Point B-545 apparatus.

2. Mechanistic study

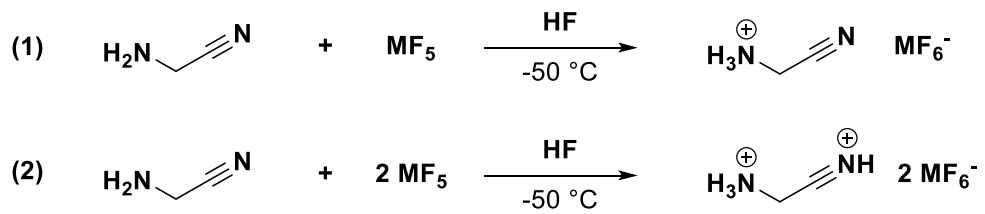
2.1. Crystal structure analyses

2.1.1. Apparatus and Materials

Syntheses were performed by standard Schlenk technique using a stainless-steel vacuum line. The used reaction vessels (FEP/PFA) were closed with stainless-steel valve. All reaction vessels were dried with fluorine prior to use. For IR measurements, a cooled cell with single-crystal CsBr plate was used. The IR spectra were recorded at a temperature of -196 °C with a Bruker Vertex 70 V FTIR spectrometer. Raman spectra were recorded at a Bruker MultiRAM FT-Raman spectrometer with ND:YAG laser excitation (λ = 1064 nm). The measurements were carried out in a cooled glass cell in vacuo at -196 °C. The low-temperature X-Ray diffraction was performed (at a temperature of 123(2) K) with an Oxford XCalibur3 diffractometer equipped with a Spellman generator (voltage 50 kV, current 40 mA) and a KappaCCD detector, operating with Mo-K_α radiation (λ = 0,7107 Å). For the data collection the CrysAlis CCD software and for its reduction the CrysAlis RED software was employed.[1] The solution as well as the refinement were carried out with the programs SHELXS-97[2] and SHELXL-97[3] implemented in the WinGX software package[4] and subsequently validated with PLATON software.[5] The absorption correction was performed with the SCALE3 ABSPACK multi-scan method.[6]

2.1.2. Syntheses of crystals

The salts were obtained using the superacidic systems HF/AsF_5 and HF/SbF_5 according to the equations (1) and (2):



Initially the superacidic media HF/SbF_5 were prepared using a large excess of HF. After homogenizing the reaction mixture at 10 °C, glycinonitrile hydrochloride was added under nitrogen atmosphere at -196 °C and then warmed up to -50 °C whilst the glycinonitrilium salts were formed. After removing the excess of HF in vacuo over night at -78 °C, the salts $[NH_3CH_2CN][AsF_6]$ (**A_1'**), $[NH_3CH_2CN][SbF_6]$ (**A_2'**), $[NH_3CH_2CNH][AsF_6]_2$ (**A_1**) and $[NH_3CH_2CNH][SbF_6]_2$ (**A_2**) were obtained in quantitative yield. All salts are air-sensitive, **A_1'** and **A_2'** are stable up to -40 °C, **A_1** is stable up to -35 °C and **A_2** is stable up to -25 °C. The deuterium isotopomers $[ND_3CH_2CND][AsF_6]_2$ (**A_{1D}**) were prepared using DF instead of HF for vibrational spectroscopic studies.

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[1] *CrysAlisRED*, Version 1.171.35.11 (release 16–05–**2011** CrysAlis 171.NET), Oxford Diffraction Ltd. **2011**.
[2] G. Sheldrick, *SHELXS-97*, *Program for Crystal Structure Solution*, University of Göttingen (Germany), **1997**.
[3] G. Sheldrick, *SHELXL-97*, *Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, **1997**.
[4] L. Farrugia, *J. Appl. Crystallogr*. **1999**, *32*, 837–838.
[5] A. Spek, PLATON, *A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht (The Netherlands), **1999**.
[6] SCALE3 ABSPACK – *An Oxford Diffraction program, Oxford Diffraction Ltd.*

2.1.3. Crystal structure of $[NH_3CH_2CN][SbF_6]$ A_2'

Monoprotonated glycinonitrile $[NH_3CH_2CN][SbF_6]$ **A_2'** crystallizes in the monoclinic space group *P2(1)/c* with four formula units per unit cell. A view of the asymmetric unit is illustrated in Figure 1. Table 1 contains selected geometric parameters together with quantum chemically calculated data which are discussed later.

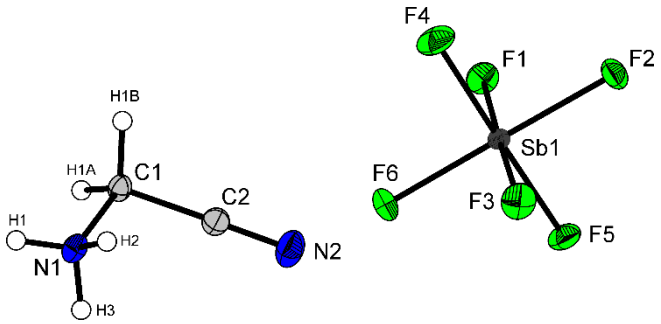


*Figure 1 : Asymmetric unit of $[NH_3CH_2CN][SbF_6]$ **A_2'** (50% probability displacement ellipsoids)*

The bond lengths and angles in the $[NH_3CH_2CN]^+$ cation show no particularities and are comparable to $[NH_3CH_2CN]^+$ cations known in the literature.[7,8,9] The C-NH_3 bond length is 1.490(6) Å and in the regular range of a formal CN single bond (1.47 Å). The C-C bond distance is 1.460(6) Å and is slightly shorter than a formal single C-C bond (1.54 Å). The CN bond length of 1.141(6) Å is in the regular range of a formal CN triple bond (1.11 Å).[10]

*Table 1 : Selected experimental and calculated bond lengths (in Å) and angles (in deg) of **A_2'** and selected experimental interatomic distances with estimated standard deviations in parentheses; Symmetry codes: i = x, 1+y, z; ii = 2−x, 1−y, −z; iii = 1−x, 1−y, −z.*

Bond length			
N1-C1	1.490(6)	N1-C1 $_{calc.}$ [a)]	1.506
C1-C2	1.459(6)	C1-C2 $_{calc.}$ [a)]	1.449
C2-N2	1.141(6)	C2-N2 $_{calc.}$ [a)]	1.148
Bond angles			
C2-C1-N1	110.3(4)	C2-C1-N1$_{calc.}$ [a)]	109.1
N2-C2-C1	179.3(5)	N2-C2-C1$_{calc.}$ [a)]	177.4
Interatomic distances			
N1-(H2)···F1*i*	2.846(5)	N1-(H3)···F5*ii*	2.896(5)
N1-(H2)···F2*iii*	2.941(5)		

a) Calculated at the PBE1PBE/6-311G++(3df,3pd) level of theory

[7] Han, M. T.; Zhang, Y. *Acta. Cryst. E* **2010**, *66* (8), o1941.
[8] Quan, J. *Acta. Cryst. E* **2012**, *68* (12), o3480.
[9] Wishkerman, S.; Bernstein, J. *CrystEngComm* **2006**, *8* (3), 245–249.
[10] Wiberg, N.; Holleman, A. F.; Wiberg, E. *Lehrbuch der Anorganischen Chemie*; Walter De Gruyter: Berlin, **2007**; Vol. 102.

The anion $[SbF_6]^-$ has regular Sb-F bond lengths between 1.865(3) and 1.881(2) Å which are in the regular range of typical Sb-F bond distances.[11,12,13] The ideal octahedral geometry of the $[SbF_6]^-$ anion is slightly distorted due to the Sb-F1 (1.872(3) Å), Sb-F2 (1.880(3) Å) and Sb-F5 (1.881(2) Å) bonds which are involved in the hydrogen bonds N1-(H2)···F1, N1-(H2)···F2 and N1-(H3)···F5. Cations and anions are connected *via* the hydrogen bonds N1-(H2)···F2 (2.941(5) Å) and N1-(H3)···F5 (2.896(5) Å) along the a axis which are of moderate strength.[14] A projection of the interionic contacts along the a axis of **A_2'** is illustrated in Figure 2. The protons were found in the difference Fourier synthesis and were refined isotropically.

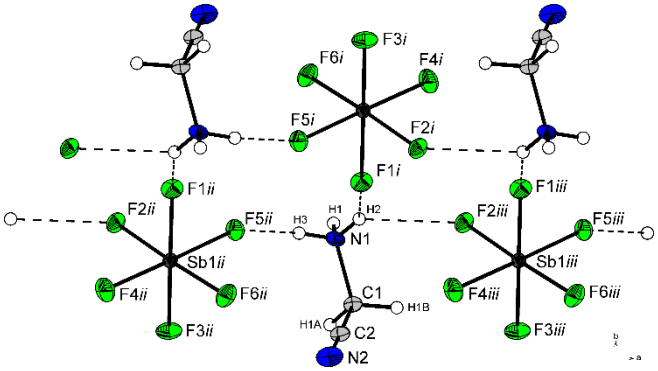


*Figure 2 : Projection of the interionic contacts in the **A_2'** crystal (50% probability displacement ellipsoids). Symmetry codes: i = x, 1+y, z; ii = 2−x, 1−y, −z; iii = 1−x, 1−y, −z.*

[11] Minkwitz, R.; Nowicki, G.; Preut, H. *Z. Anorg. Allg. Chem.* **1992**, *611* (5), 23–27.
[12] Minkwitz, R.; Preut, H.; Seifert, M.; Lamek, D. *Z. Naturforsch., B: Chem. Sci.* **1993**, *48*, 1241–1247.
[13] Minkwitz, R.; Seelbinder, R.; Schöbel, R. *Angew. Chem. Int. Ed.* **2002**, *41* (1), 111–114.
[14] Steiner, T. *Angew. Chem. Int. Ed.* **2002**, *41* (1), 48–76.

2.1.4. Crystal structure of $[NH_3CH_2CNH][SbF_6]_2 \cdot HF$ A_2

The salt of diprotonated glycinonitrile $[NH_3CH_2CNH][SbF_6]_2 \cdot HF$ **A_2** crystallizes in the orthorhombic space group *Pbca* with eight formula units per unit cell. A view of the asymmetric unit is illustrated in Figure 3. Table 2 contains selected geometric parameters. The bond lengths and angles of the dication $[NH_3CH_2CNH]^{2+}$ do not differ significantly from the bond lengths and angles of the monocation $[NH_3CH_2CN]^{+}$.

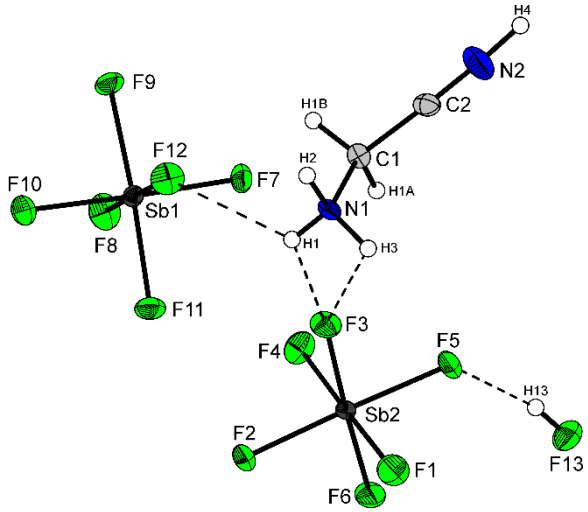


*Figure 3 : Asymmetric unit of **A_2** (50% probability displacement ellipsoids).*

*Table 2 : Selected experimental and calculated bond lengths (in Å) and angles (in deg) of **A_2** and selected experimental interatomic distances with estimated standard deviations in parantheses; Symmetry codes: i = 1/2−x, 1−y, 1/2+z; ii = −x, 1/2+y, 1/2−z; iii = 1/2+x, 3/2−y, −z; iv = x, 1+y, z; v = 1/2−x, 1/2+y, z; vi = −x, 1−y, z.*

Bond length			
N1-C1	1.486(6)	N1-C1 $_{calc.}$ [a)]	1.495
C1-C2	1.449(6)	C1-C2 $_{calc.}$ [a)]	1.464
C2-N2	1.120(6)	C2-N2 $_{calc.}$ [a)]	1.132
Bond angles			
C2-C1-N1	111.3(3)	C2-C1-N1$_{calc.}$ [a)]	114.1
N2-C2-C1	177.2(5)	N2-C2-C1$_{calc.}$ [a)]	175.8
Interatomic distances			
N1-(H2)···F6*i*	2.809(5)	N1-(H3)···F2*v*	2.912(5)
N1-(H2)···F9*ii*	2.900(4)	F13-(H13)···F5	2.599(4)
N1-(H1)···F3	2.703(4)	F13-(H13)···F9*vi*	2.929(4)
N1-(H1)···F12	2.984(5)	N2-(H4)···F8*iv*	2.623(6)
N1-(H3)···F11*v*	2.812(4)	N2-(H4)···F1*iii*	2.680(5)

a) Calculated at the PBE1PBE/6-311G++(3df,3pd) level of theory.

The C-NH_3 bond length (1.486(5) Å) and the C-C bond length (1.449(6) Å) are comparable with the C-NH_3 bond length (1.490(6) Å) and the C-C bond length (1.459(6) Å) of the monocation $[NH_3CH_2CN]^{+}$.

The slightly distorted anion $[SbF_6]^-$ has regular Sb-F bond lengths between 1.860(3) and 1.889(3) Å which are in the regular range of typical Sb-F bond distances.

In the crystal structure, the ions are connected by a three dimensional network of N···F and F···F hydrogen bonds. An image of the interionic contacts is illustrated in Figure 4. The cations and anions along the a axis are connected *via* the hydrogen bonds N1-(H3)···F11v (D-A: 2.812(4) Å) and N1-(H2)···F9ii (D-A: 2.900(4) Å), along the b axis *via* the hydrogen bonds N2-(H4)···F8iv (D-A: 2.623(6) Å) and N1-(H1)···F12 (D-A: 2.984(5) Å) and along the c axis *via* the hydrogen bonds N1-(H3)···2v (D-A: 2.921(5) Å) and N1-(H2)···F6i (D-A: 2.809(5) Å). All hydrogen bonds are of moderate strength.

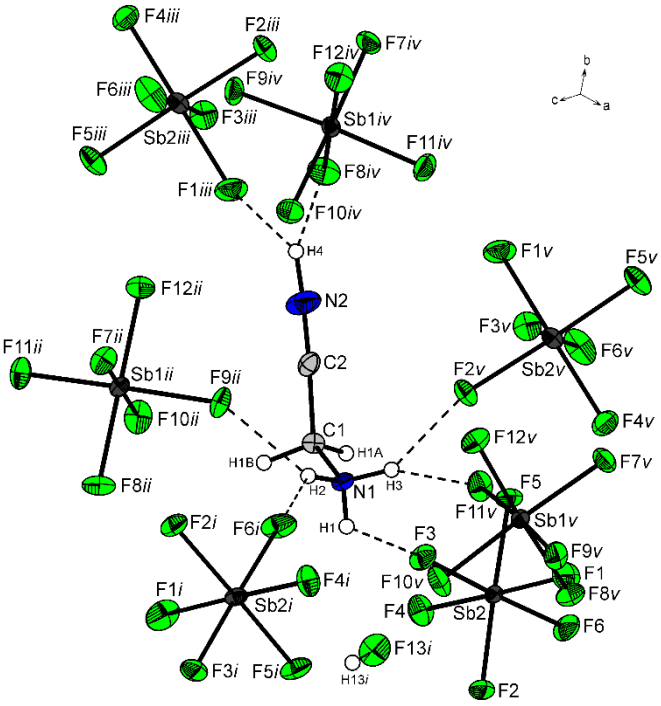


*Figure 4 : Projection of the interionic contacts in the **A_2** crystal (50% probability displacement ellipsoids). Symmetry codes: i = 1/2−x, 1−y, 1/2+z; ii = −x, 1/2+y, 1/2−z; iii = 1/2+x, 3/2−y, −z; iv = x, 1+y, z; v = 1/2−x, 1/2+y, z.*

2.1.5. Vibrational spectra of A_1', A_{1D}' and A_2'

The infrared and Raman spectra of the $[NA_3CH_2CN]^+$ salts and the Raman spectrum of glycinonitrile hydrochloride are shown in Figure 5. A complete table of all observed and quantum chemically calculated frequencies is summarized in Table 4.

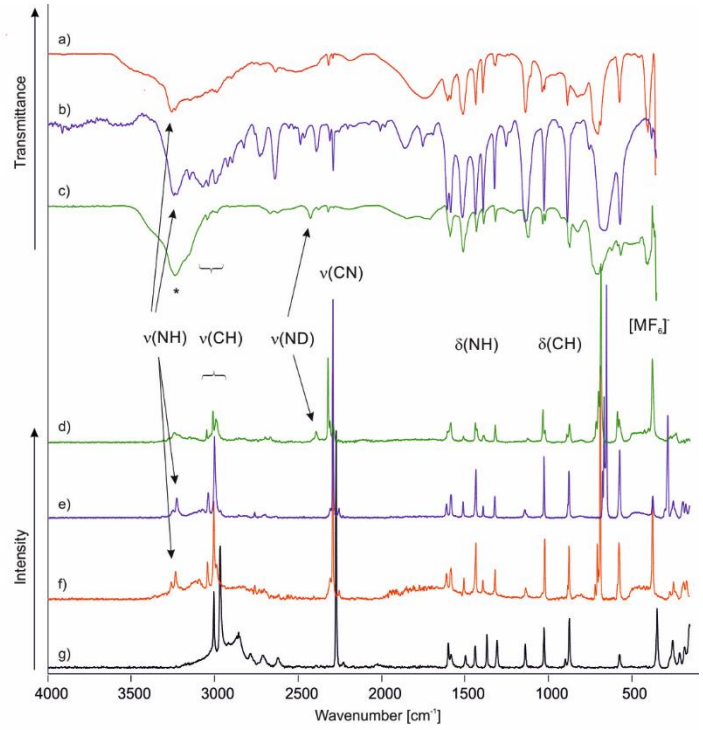


*Figure 5 : Low temperature infrared spectra of $[NH_3CH_2CN][AsF_6]$ (**A_1'**, a), $[NH_3CH_2CN][SbF_6]$ (**A_2'**, b), $[ND_3CH_2CN][AsF_6]$ (**A_{1D}'**, c), low temperature Raman spectra of $[ND_3CH_2CN][AsF_6]$ (**A_{1D}'**, d), $[NH_3CH_2CN][SbF_6]$ (**A_2'**, e), $[NH_3CH_2CN][AsF_6]$ (**A_1'**, f), and Raman spectrum of glycinonitrile hydrochloride (g); Ice band is marked with (*).*

For the $[NA_3CH_2CN]^+$ cation (A = H, D) with C_s symmetry, 21 fundamental vibrations are expected which are all Raman and Infrared active. Compared to the starting material glycinonitrile hydrochloride the spectra of $[NA_3CH_2CN][AsF_6]$ (H = **A_1'**, D = **A_{1D}'**) and $[NH_3CH_2CN][SbF_6]$ (**A_2'**) show, as expected, no significant differences except of the additional vibrations of the $[AsF_6]^-$ and $[SbF_6]^-$ anions.[15] Compared to the CN stretching vibration of the neutral molecule glycinonitrile (2194 cm^{-1}),[16] the CN stretching vibration in the monocation $[NH_3CH_2CN]^+$ is blue-shifted to 2270 (IR) and 2272 (Raman) in glycinonitrile hydrochloride and to 2290 (IR) and 2291 (Raman) in **A_1'** and **A_2'** and 2322 (IR/Raman) in **2**.

For the anions $[MF_6]^-$ (M = As, Sb) with ideal octahedral symmetry, two bands in the infrared spectrum and three lines in the Raman spectrum are expected. In both salts more than five vibrations are observed, which indicates a lower symmetry.

[15] S. Wishkerman, J. Bernstein, *CrystEngComm* **2006**, *8*, 245-249.
[16] G. M. Chaban, *J. Phys. Chem. A* **2004**, *108*, 4551-4556.

Table 3 : Experimental vibrational frequencies (cm^{-1}) of $[NH_3CH_2CN][AsF_6]$, $[NH_3CH_2CN][SbF_6]$ and $[ND_3CH_2CN][AsF_6]$ and calculated vibrational frequencies (cm^{-1}) of $[NH_3CH_2CN]^+$ and $[ND_3CH_2CN]^+$.

$[NH_3CH_2CN]^+$	$[NH_3CH_2CN][AsF_6]$		$[NH_3CH_2CN][SbF_6]$		$[ND_3CH_2CN]^+$	$[ND_3CH_2CN][AsF_6]$		assignment [b]
calc. [a] (IR/Ra)	IR	Ra	IR	Ra	calc. [a] (IR/Ra)	IR	Ra	
3498 (131/39)		3362 (1)	3336 (vw)	3315 (1)	2581 (68/20)			$\nu_{as}(NA_3)$
3487 (135/19)	3258 (s)	3260 (3)	3246 (s)	3251 (1)	2573 (66/11)	2428 (w)		$\nu_{as}(NA_3)$
3411 (66/93)	3236 (s)	3234 (9)	3230 (s)	3229 (8)	2444 (38/48)	2378 (vw)		$\nu_{s}(NA_3)$
	3143 (m)		3152 (m)					$2\delta_{as}(NA_3)$
		3092 (4)	3078 (s)	3077 (2)				$2\delta_{s}(NA_3)$
3156 (11/42)	3047 (m)	3042 (10)	3039 (s)	3040 (9)	3157 (14/40)	3049 (w)	3051 (5)	$\nu_{as}(CH_2)$
3099 (5/110)	3001 (m)	3004 (41)	2999 (s)	3003 (34)	3100 (6/123)	3024 (vw)	3013 (18)	$\nu_{s}(CH_2)$
	2764 (vw)	2759 (4)	2730 (m)	2761 (2)				$\delta_{as}(NA_3)+\rho(NA_3)$
	2723 (w)	2702 (3)	2718 (m)	2698 (2)				$\delta_{as}(NA_3)+\rho(NA_3)$
2405 (14/79)	2290 (vw)	2291 (95)	2290 (m)	2291 (95)	2405 (15/76)	2322 (w)	2322 (48)	$\nu(CN)$
		2253 (3)	2254 (vw)	2254 (4)				$2(\rho(NA_3), \tau(CH_2))$
	1741 (m)		1752 (m)					$2(\rho(NA_3), \rho(CH_2))$
1660 (37/3)	1600 (m)	1607 (6)	1604 (s)	1609 (5)	1194 (17/1)	1207 (vw)		$\delta_{as}(NA_3)$
1651 (50/4)	1582 (m)	1580 (12)	1584 (s)	1582 (10)	1186 (22/1)			$\delta_{as}(NA_3)$
1528 (134/1)	1508 (m)	1502 (7)	1513 (s)	1510 (7)	1176 (74/1)	1118 (m)	1123 (2)	$\delta_{s}(NA_3)$
1474 (18/6)	1431 (m)	1431 (23)	1435 (s)	1433 (21)	1474 (16/6)	1431 (m)	1437 (11)	$\delta_{s}(CH_2)$
1408 (20/3)	1389 (m)	1389 (6)	1389 (s)	1389 (5)	1395 (10/3)	1388 (m)	1386 (3)	$\omega(CH_2)$
1332 (8/2)	1314 (w)	1316 (11)	1320 (m)	1319 (9)	1295 (0.5/3)	1317 (m)	1319 (10)	$\tau(CH_2)$
1119 (28/2)								$\rho(NA_3)$
1117 (6/0.1)	1134 (m)	1132 (4)	1138 (s)	1139 (3)				$\rho(NA_3)$, $\tau(CH_2)$
					1050 (0.3/0.05)	1018 (w)	1020 (3)	$\rho(NA_3)$, $\rho(CH_2)$
997 (13/4)	1032 (m), 1019 (m)	1017 (26)	1023 (s)	1023 (27)	1017 (15/2)	1033 (w)	1032 (18)	$\nu(CN)$, $\nu(CC)$
869 (14/0.4)	881 (m)	871 (23)	863 (s)	874 (20)	719 (7/0.2)	619 (m)		$\rho(NA_3)$, $\rho(CH_2)$
					942 (4/5)	919 (vw)	888 (2)	$\nu(CN)$
867 (2/8)	819 (m)	798 (2)	752 (w)		760 (1/5)	823 (m)		$\rho(NA_3)$, $\nu(CN)$, $\nu(CC)$
555 (9/1)	568 (m)		567 (s)		524 (6/1)	565 (m)	574 (5)	$\delta(N\text{-}CC)$, $\delta(CC{\equiv}N)$
365 (0.1/2)		371 (42)	378 (s)	371 (9)	360 (0.05/2)	370 (s)	375 (47)	$\tau(NA_3)$, $\rho(CH_2)$, $\delta(CCN)$
211 (0.5/0.3)		243 (7)		247 (7)	156 (1/0.3)		232 (5)	$\tau(NA_3)$
194 (16/3)		183 (4), 166 (7)		189 (7), 172 (4)	183 (14/2)		125 (4)	$\delta(CC{\equiv}N)$
		715 (5)				712 (vs)	712 (4)	$[AsF_6]^-$
	699 (vs)	702 (17)				700 (vs)	698 (9)	$[AsF_6]^-$
	682 (s)	694 (4)				679 (vs)	683 (100)	$[AsF_6]^-$
		684 (100)				582 (w)	584 (17)	$[AsF_6]^-$
		571 (25)				411 (w)	422 (2)	$[AsF_6]^-$
	398 (s)	371 (42)				400 (s)	375 (47)	$[AsF_6]^-$
				672 (13)				$[SbF_6]^-$
				663 (36)				$[SbF_6]^-$
				657 (2)				$[SbF_6]^-$
			656 (vs)	649 (100)				$[SbF_6]^-$
				569 (29)				$[SbF_6]^-$
				280 (44)				$[SbF_6]^-$

a) Calculated at the PBE1PBE/6-311G++(3df,3pd) level of theory. IR intensity in $km.mol^{-1}$ and Raman intensity in $Å^4.\mu^{-1}$. Abbreviations for IR intensities: v = very, s = strong, m = medium, w = weak, br = broad. Raman activities are stated to a scale of 0 to 100; b) A = H, D.

2.1.6. Vibrational spectra of A_1, A_{1D} and A_2

Table 4 : Experimental vibrational frequencies /cm^{-1} of $[NH_3CH_2CNH][AsF_6]_2$, $[NH_3CH_2CNH][SbF_6]_2$ and $[ND_3CH_2CND][AsF_6]_2$ and calculated vibrational frequencies /cm^{-1} of $[NH_3CH_2CNH]^{2+}$ and $[ND_3CH_2CND]^{2+}$.

$[NH_3CH_2CNH]^{2+}$	$[NH_3CH_2CNH][AsF_6]_2$		$[NH_3CH_2CNH][SbF_6]_2$		$[ND_3CH_2CND]^{2+}$	$[ND_3CH_2CND][AsF_6]_2$		assignment [b]
calc. [a] (IR/Ra)	*IR*	*Ra*	*IR*	*Ra*	*calc. [a] (IR/Ra)*	*IR*	*Ra*	
3543 (842/19)	3554 (w)				2816 (440/9)	2519 (m)	2525 (5)	ν(NA)
3430 (191/18)	3457 (w)		3448 (m)		2532 (91/10)	2408 (m)		$\nu_{as}(NA_3)$
3409 (190/24)	3329 (w)		3317 (w)		2513 (99/13)			$\nu_{as}(NA_3)$
3355 (176/82)	3253 (w)				2407 (82/41)	2354 (m)	2362 (2)	$\nu_{s}(NA_3)$
	3197 (m)	3201 (5)	3212 (s)	3200 (3)				$2\delta_{as}(NA_3)$
	3163 (s)	3172 (1)	3165 (s)	3170 (1)				$\delta_{as}(NA_3)+\delta_{as}(NA_3)$
	3142 (m)	3141 (1)	3141 (s)	3141 (1)				$2\delta_{as}(NA_3)$
	3031 (m)		3025 (s)	3026 (2)				$\omega(CH_2)+\delta_{s}(CH_2)$
3094 (65/35)	3003 (m)	3006 (9)	3010 (s)	3012 (5)	3094 (70/34)	3003 (w)	3006 (10)	$\nu_{as}(CH_2)$
3043 (80/96)	2962 (m)	2964 (39)	2975 (s)	2976 (16)	3044 (58/97)	2962 (w)	2964 (40)	$\nu_{s}(CH_2)$
		2827 (2)	2816 (s)	2832 (1)				$2\omega(CH_2)$
		2759 (3)		2755 (1)				$\delta_{as}(NA_3)+\omega(CH_2)$
	2694 (m)	2698 (2)	2697 (s)	2703 (1)				$\delta_{as}(NA_3)+\rho(NA_3)$
	2626 (m)							$2\tau(CH_2)$
	2381 (w)		2362 (s)	2329 (3)				ν(CN)+$\tau(CH_2)$
2426 (1/88)	2244 (m), 2214(m)	2246 (3), 2218 (8)	2251 (s), 2215 (s)	2269 (4), 2221 (1)	2207 (60/71)	1809 (m)	1824 (5)	ν(C≡N(A))
1652 (57/4)	1632 (m), 1601 (m)	1600 (4)	1636 (w), 1597 (s)		1186 (25/1)			$\delta_{as}(NA_3)$
1645 (45/3)	1578 (m)	1579 (14)	1582 (s)	1582 (3)	1186 (25/1)			$\delta_{as}(NA_3)$
1568 (127/1)	1508 (s)	1506 (5)	1529 (s), 1510 (s)	1503 (2)	1207 (54/1)			$\delta_{s}(NA_3)$
1431 (37/5)			1426 (s)	1426 (10)	1431 (34/6)	1417 (m)	1418 (28)	$\delta_{s}(CH_2)$
1416 (11/2)	1417 (s)	1418 (28)	1412 (s)	1415 (1)	1408 (2/3)	1388 (w)	1390 (4)	$\omega(CH_2)$
1339 (7/2)	1315 (m)	1320 (12)	1314 (m)	1316 (2)	1308 (0.3/3)	1317 (w)	1320 (10)	$\tau(CH_2)$
1130 (6/0.03)	1124 (s)	1127 (2)	1142 (s)	1144 (2)				$\rho(NA_3)$
1127 (22/1)			1117 (s)					$\rho(NA_3)$, $\delta(CH_2)$
					1036 (0.4/0.3)	1035 (w)	1036 (28)	$\rho(NA_3)$, $\rho(CH_2)$
1033 (3/6)	1037 (m)	1038 (34)	1043 (s)	1041 (6)	996 (0.1/3)	878 (m)	879 (3)	ν(C-N)
					967 (3/4)	841 (m)	841 (12)	δ(CCN), $\rho(ND_3)$
			942 (m)					δ(C≡NA)+($\rho(CH_2)$, δ(CC≡N))
871 (21/0.4)	878 (s)	881 (2)	875 (s)	891 (2)				$\rho(CH_2)$
835 (8/4)	847 (s)	849 (12)	852 (s)	853 (2)	744 (6/3)	747 (s)	743 (1)	$\rho(NA_3)$, ν(C-N), ν(CC)
					737 (13/0.2)	621 (m)		$\rho(CH_2)$, $\rho(ND_3)$
729 (120/0.1)	787 (m)	785 (9)			595 (30/1)	575 (m)	577 (7)	δ(C≡NA)
670 (131/0.05)	576 (s)	579 (13)	581 (vs)		526 (49/1)	518 (m)	521 (20)	δ(C≡NA)
560 (13/1)	543 (vs), 531 (vs)	530 (21)	532 (vs)		502 (34/1)	486 (w)		δ(CC≡N), δ(CC-N)
389 (11/1)	371 (s)	376 (70)	366 (w), 355 (m)	372 (2)	367 (18/1)		387 (3), 376 (70)	$\rho(CH_2)$, δ(CC≡N)
		310 (7)		301 (3)			310 (14)	?
		273 (10)		277 (4)			271 (6)	?
224 (8/2)		190 (21)			160 (1/0.3)		190 (23)	δ(CC≡N)
216 (2/0.3)		169 (18)		167 (2)	203 (5/2)		169 (49)	$\tau(NA_3)$
	713 (vs)	723 (46)				714 (vs)	723 (57)	$[AsF_6]^-$
		701 (100)				696 (vs)	702 (89)	$[AsF_6]^-$
		686 (54)					686 (54)	$[AsF_6]^-$
		680 (6)				675 (vs)	679 (12)	$[AsF_6]^-$
		674 (14)					626 (6)	$[AsF_6]^-$
		599 (11)					609 (8)	$[AsF_6]^-$
		589 (4)					597 (7)	$[AsF_6]^-$
		562 (3)				583 (m)	588 (3)	$[AsF_6]^-$
		519 (s)					577 (9)	$[AsF_6]^-$
		486 (m)				544 (m)	539 (2)	$[AsF_6]^-$
	398 (vs)	398 (6)					442 (100)	$[AsF_6]^-$
						396 (vs)	398 (7)	$[AsF_6]^-$
		388 (3)					376 (70)	$[AsF_6]^-$
							243 (27)	$[AsF_6]^-$
							234 (3)	$[AsF_6]^-$
							157 (15)	$[AsF_6]^-$
			670 (vs)	659 (100)				$[SbF_6]^-$
				569 (14)				$[SbF_6]^-$

	521 (5)				$[SbF_6]^-$
	442 (96)				$[SbF_6]^-$
	423 (10)				$[SbF_6]^-$
		286 (15)			$[SbF_6]^-$

a) Calculated at the PBE1PBE/6-311G++(3df,3pd) level of theory. IR intensity in $km.mol^{-1}$ and Raman intensity in $Å^4.\mu^{-1}$. Abbreviations for IR intensities: v = very, s = strong, m = medium, w = weak, br = broad. Raman activities are stated to a scale of 0 to 100; b) A = H, D.

2.1.7. X-ray data and parameters of A_2' and A_2

*Table 5 : X-ray data and parameters of **A_2'** and **A_2***

	[NH₃CH₂CN][SbF₆]	***[NH₃CH₂CNH][SbF₆]₂·HF***
formula	$C_2H_5F_6N_2Sb$	$C_2H_7F_{13}N_2Sb_2$
M_r [g.mol^{-1}]	292.83	549.60
crystal size [mm^3]	0.19 x 0.16 x 0.09	0.49 x 0.23 x 0.18
crystal system	monoclinic	orthorhombic
space group	*P 21/c*	*Pbca*
a [Å]	7.7291(3)	14.8174(8)
b [Å]	9.3482(4)	10.5692(8)
c [Å]	10.1754(4)	15.6490(9)
α [deg]	90.0	90.0
β [deg]	97.481(4)	90.0
γ [deg]	90.0	90.0
V [Å^3]	728.95(5)	2450.8(3)
Z	4	8
ρ_{calcd}, [g.cm^{-3}]	2.668	2.979
μ(MoK_α) [cm^{-1}]	0.71073	0.71073
μ [mm^{-1}]	3.838	4.562
F(000)	544	2016
T [K]	143(2)	143(2)
hkl range	-9:10;-12:6;-13:13	-19:20;-10:14;-15:21
refl. measured	3830	9231
refl. unique	1957	3287
R_{int}	0.0254	0.0329
parameters	112	192
R(F)/wR(F^2)[a] (all reflexions)	0.0379 / 0.0663	0.0397 / 0.0701
weighting scheme[b]	0.0140 / 1.7329	0.0313 / 2.6671
S (GoF)[c]	1.178	1.016
Residual density [e.Å^{-3}]	1.196 / -1.182	1.283 / -1.707
device type	Oxford XCalibur	Oxford XCalibur
solution	SHELXS-97	SHELXS-97
refinement	SHELXL-97	SHELXL-97
CCDC	1857302	1857303

[a] $R_1 = \Sigma||F_0|-|F_c||/\Sigma|F_0|$; [b] $wR_2 = [\Sigma[w(F_0^2-F_c^2)^2]/\Sigma[w(F_0)^2]]^{1/2}$; $w = [\sigma_c^2(F_0^2)+(xP)^2+yP]^{-1}$; $P = (F_0^2+2F_c^2)/3$; [c] GoF = $\{\Sigma[w(F_o^2-F_c^2)^2]/(n-p)\}^{1/2}$ (n = number of reflections; p = total number of parameters).

2.1.8. Theoretical calculations

Quantum chemical calculations were carried out using the DFT hybrid method PBE1PBE with the basis set 6-311G++(3df,3pd).[17,18] A view of the calculated structure of the $[NH_3CH_2CN]^+$ cation with selected bond lengths and angles together with the experimentally determined cation from the crystal structure analysis of **A_2'** is illustrated in Figure 6 with its cartesian coordinates in Table 6, a view of the calculated structure of the $[NH_3CH_2CNH]^{2+}$ cation with selected bond lengths and angles together with the experimentally determined cation from the crystal structure analysis of **A_1'** is illustrated in Figure 7 with its cartesian coordinates in Table 7.

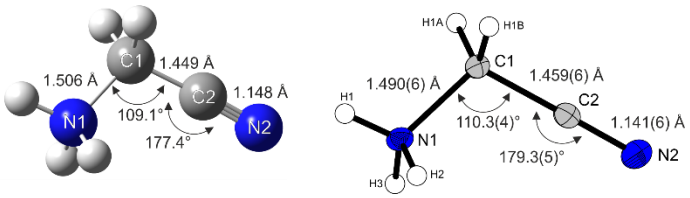


*Figure 6 : Calculated structure of the monoprotonated glycinonitrile cation $[NH_3CH_2CN]^+$ (left) and the monoprotonated glycinonitrile cation of the single-crystal X-ray structure of **A_2'** (right).*

Table 6. Cartesian coordinates of calculated minimum structures of the monoprotonated glycinonitrile cation A2' at the PBE1PBE/6-311G++(3df,3pd) level.

Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.501951	0.673966	0.000000
H	0.650484	1.273609	0.873651
H	0.650483	1.273609	-0.873651
N	1.462934	-0.438424	0.000000
H	1.324117	-0.998839	-0.816495
H	2.394294	-0.074325	-0.000002
C	-0.932343	0.113253	0.000000
N	-2.000240	-0.304224	0.000000
H	1.324120	-0.998837	0.816498

E(RBBE1PBE) = -188.26713645 Hartree

[17] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Wallingford CT, **2009**.

[18] a) J. P. Perdew, K. Burke, and M. Ernzerhof, *Phys. Rev. Lett.*, 77 (1996) 3865-68; b) J. P. Perdew, K. Burke, and M. Ernzerhof, *Phys. Rev. Lett.*, 78 (1997) 1396.

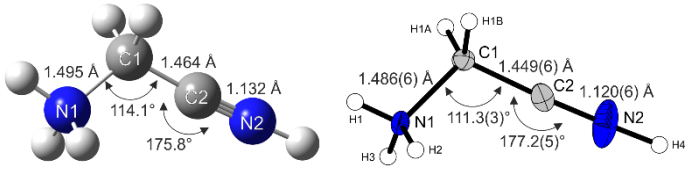


*Figure 7 : Calculated structure of the diprotonated glycinonitrile cation $[NH_3CH_2CNH]^{2+}$ (left) and the diprotonated glycinonitrile cation of the single-crystal X-ray structure of **A_1'** (right).*

The geometric parameters of both the mono- and the dication are in good agreement with the one experimentally found in the crystal structures. The vibrational frequencies satisfactorily agree with the experimental results except of overestimation of the N-*A* (*A* = H, D) stretching vibrations due to hydrogen bonds in the solid state which are not considered in the calculated gas phase structures.

Table 7. Cartesian coordinates of calculated minimum structures of the diprotonated glycinonitrile cation A1' at the PBE1PBE/6-311G++(3df,3pd) level.

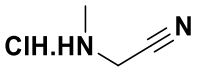
Atomic Type	Coordinates (Angstroms) X	Y	Z
C	0.578776	0.672770	0.000000
H	0.718240	1.274586	0.873652
H	0.718240	1.274587	-0.873651
C	-0.846892	0.090470	0.000000
N	-1.908366	-0.343078	0.000000
N	1.556440	-0.424988	0.000000
H	2.479233	-0.049512	-0.086433
H	1.483480	-0.936331	0.856274
H	1.371684	-1.035896	-0.769843
H	-2.698703	0.269593	-0.000008

E(RBBE1PBE) = -188.41277311 Hartree

2.2. *In situ* NMR analysis

2.2.1. Starting materials

Compound 1a': *methylaminoacetonitrile hydrochloride*

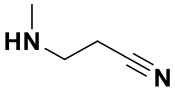


This compound was commercially available (CAS number: 25808-30-4).

^{1}H NMR (400 MHz, Acetone-*d6*) δ (ppm) 2.80 (t, *J* = 6.6 Hz, 2H), 2.56 (t, *J* = 6.6 Hz, 2H), 2.37 (s, 3H).

^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 118.8 (CN), 39.2 (CH_2), 35.3 (CH_3).

Compound 1b': *3-(methylamino)propionitrile*

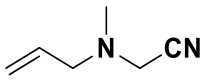


This compound was commercially available (CAS number: 693-05-0).

^{1}H NMR (400 MHz, Acetone-*d6*) δ (ppm) 3.59 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 120.0 (CN), 48.1 (CH_2), 36.0 (CH_3), 18.5 (CH_2).

Compound 1a: *2-(allyl(methyl)amino)acetonitrile*



N-methylallylamine (1 mL, 10.5 mmol, 1.0 equiv.) was added over K_2CO_3 (2.00 g, 14.5 mmol, 1.4 equiv.) dissolved in 20 mL of acetonitrile. Chloroacetonitrile (0.66 mL, 10.5 mmol, 1.0 equiv.) was added to the mixture and the medium was refluxed for 3 h. The solvent was evaporated under reduced pressure and the crude was taken up in water and extracted three times with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate, filtered and evaporated under reduced pressure. The reaction crude was purified by flash chromatography using dichloromethane as eluent. 1.07 g (93%) of compound **1a** were obtained as a yellow liquid. The spectroscopic data correspond to those previously described in the literature.[19]

Rf: 0.63 (Eluent: DCM/MeOH 99/1)

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.75 (ddt, *J* = 17.0, 10.1, 6.6 Hz, 1H), 5.28 (app. ddd, *J* = 17.0, 2.9, 1.4 Hz, 1H), 5.20 (dm, *J* = 10.1 Hz, 1H), 3.51 (s, 2H), 3.07 (d, *J* = 6.6 Hz, 2H), 2.36 (s, 3H).

[19] Liu, F.; Martin-Mingot, A.; Jouannetaud, M.-P.; Karam, O.; Thibaudeau, S. *Org. Biomol. Chem.* **2009**, *7* (22), 4789.

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 134.1 (CH), 119.4 (CH_2), 114.6 (CN), 59.0 (CH_2), 44.3 (CH_2), 42.1 (CH_3).

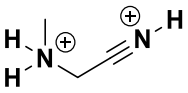
2.2.2. *In situ* NMR typical procedure

The substrate was added to a magnetically stirred solution of HF/SbF_5 in a Teflon® flask equipped with a Teflon® magnetic stirrer and maintained at the temperature of the reaction. The reaction mixture was stirred for a short period and an aliquot was taken, which was transferred into a Teflon® NMR tube that was inserted into a classical glass NMR tube containing acetone-*d6* as external standard. The ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Avance Nandbay 400 MHz spectrometer.

On ^{1}H NMR spectra, the two pics between 8 and 10 ppm are attributed to superacidic proton species.

2.2.3. Spectra of 1,4 ammonium-nitrilium dication

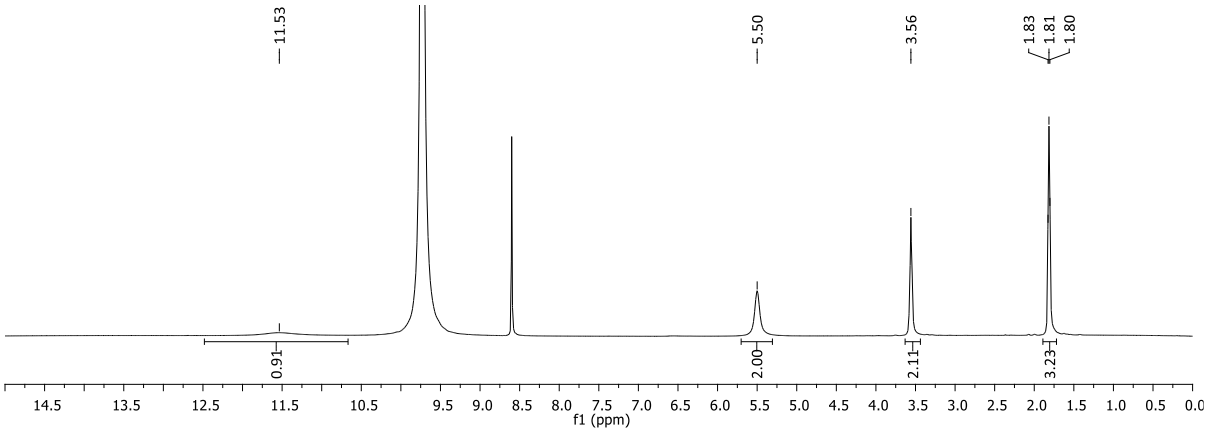
*Spectra of a solution of methylaminoacetonitrile **1a'** (100 mg, 1.3 mmol) in HF/SbF_5 (2 mL, 22 mol%) at -20 °C with acetone-d6 as external reference*



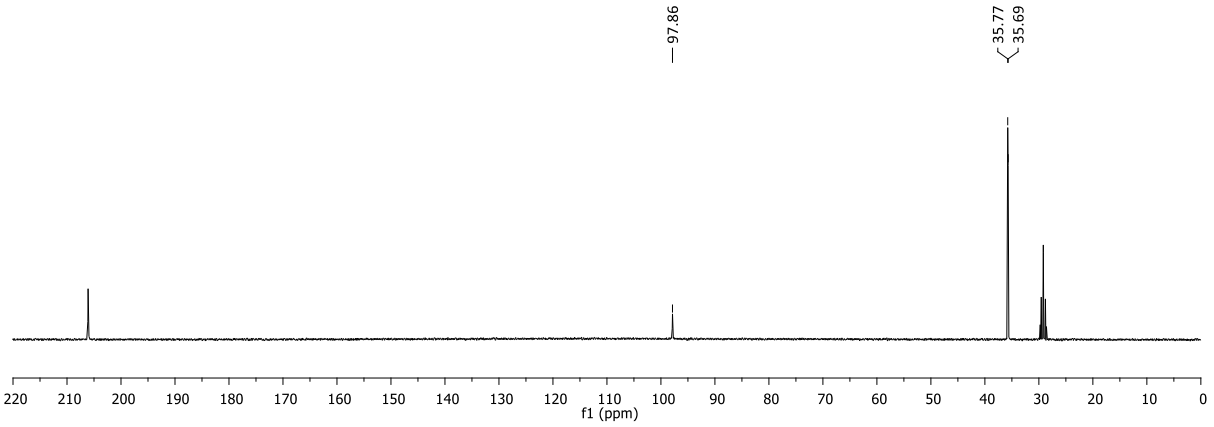
^{1}H NMR (400 MHz, Acetone-*d6*) δ (ppm) 11.53 (sl, 1H, CNH^+), 5.50 (s, 2H, NH_2^+), 3.56 (s, 2H, CH_2), 1.81 (t, 3H, *J* = 4.8 Hz, CH_3).

^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 97.9 (CN), 35.8 (CH_2), 35.7 (CH_3).

^{1}H NMR (400 MHz, Acetone-*d6*)

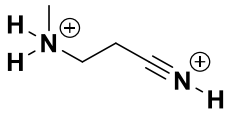


^{13}C NMR (101 MHz, Acetone-*d6*)



2.2.4. Spectra of 1,5 ammonium-nitrilium dication

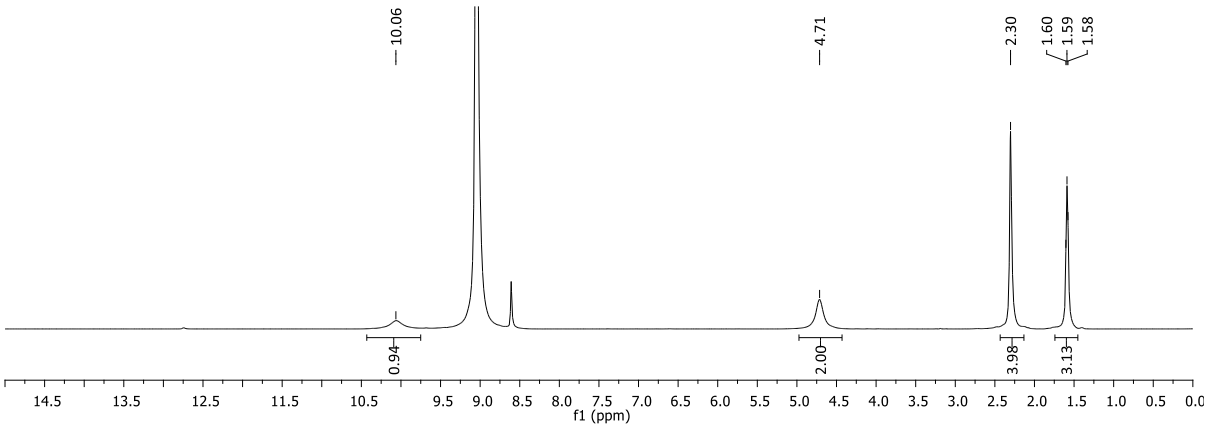
*Spectra of a solution of 3-(methylamino)propionitrile **1b'** (100 mg, 1.2 mmol) in HF/SbF_5 (2 mL, 22 mol%) at -20 °C with acetone-d6 as external reference*



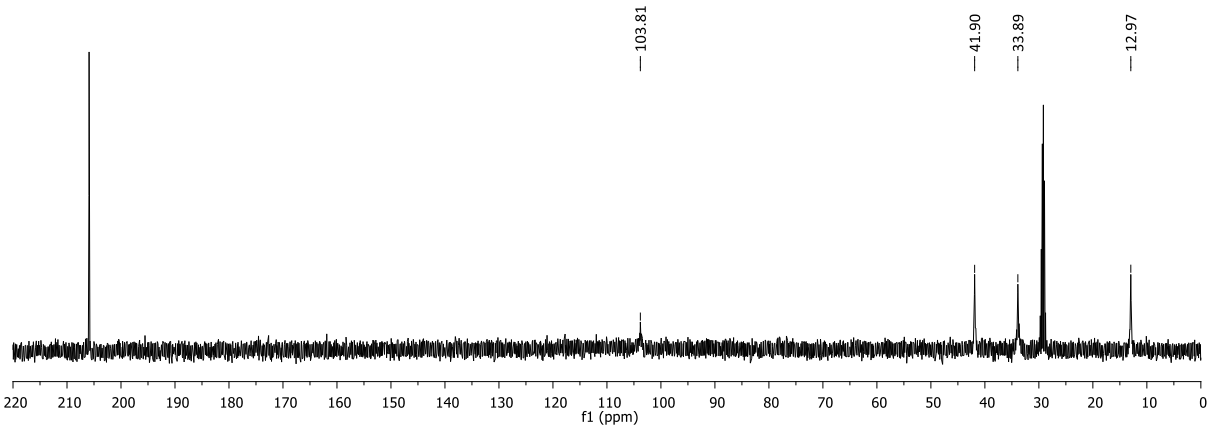
^{1}H NMR (400 MHz, Acetone-*d6*) δ (ppm) 10.06 (sl, 1H, CNH^+), 4.71 (s, 2H, NH_2^+), 3.30 (s, 4H, 2 CH_2), 1.59 (t, 3H, *J* = 4.8 Hz, CH_3).

^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 103.8 (CN), 41.9 (CH_2), 33.9 (CH_3), 13.0 (CH_2).

^{1}H NMR (400 MHz, Acetone-*d6*)



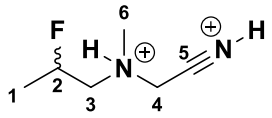
^{13}C NMR (101 MHz, Acetone-*d6*)



2.2.5. Spectra of intermediate **C**

*Spectra of a solution of compound **1a** (80 mg, 0.7 mmol) in HF/SbF_5 (2 mL, 4 mol%) at -20 °C with acetone-d6 as external reference*

Ion **C** was obtained in a mixture of two diastereomers (d.r. 1:2, ^{1}H NMR analysis), with the formation of two ammonium ions.

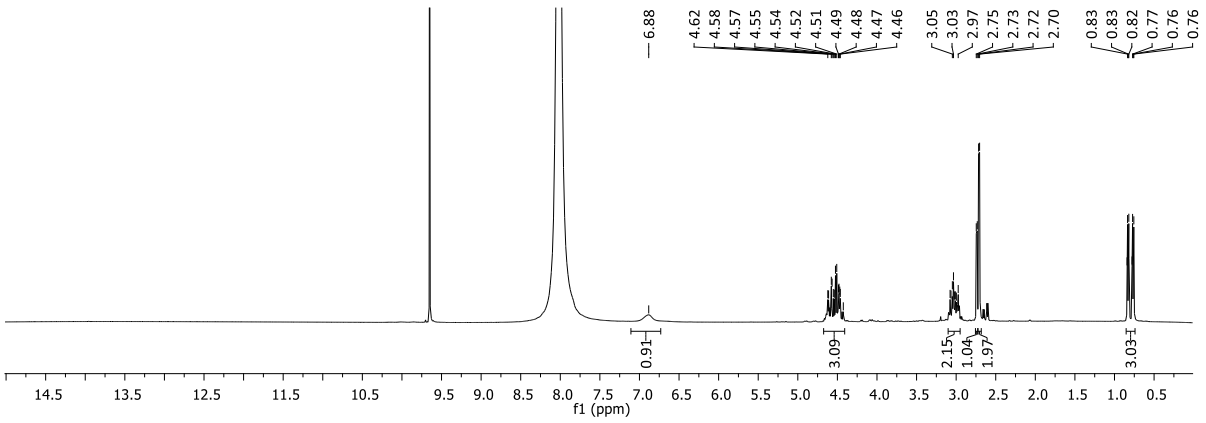


^{1}H NMR (400 MHz, Acetone-*d6*) δ (ppm) 6.88 (sl, 1H, NH^+), 4.62-4.43 (m, 3H, H_2 et H_3), 3.03 (m, 2H, H_4), 2.74 (d, *J* = 5.2 Hz, 1H, H_6), 2.71 (d, *J* = 5.2 Hz, 2H, H_6), 0.80 (2 dd, *J* = 25.2, 6.4 Hz, 3H, H_1).

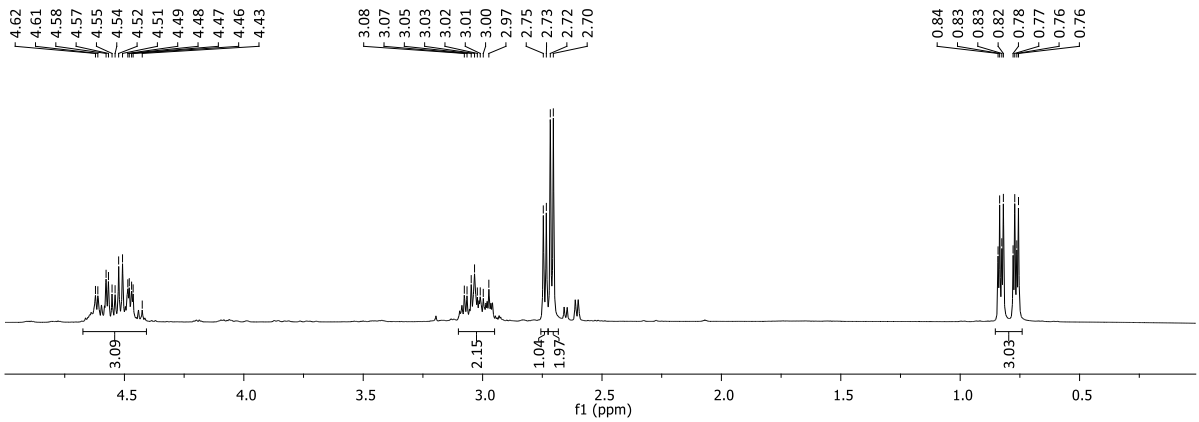
^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 98.3 (C_5), 84.8 (d, *J* = 167 Hz, C_2), 83.9 (d, *J* = 167 Hz, C_2), 62.6 (d, *J* = 20 Hz, C_3), 62.1 (d, *J* = 20 Hz, C_3), 43.8 (C_4), 43.1 (C_6), 15.0 (d, *J* = 21 Hz, C_1), 14.8 (d, *J* = 21 Hz, C_1).

^{19}F {^{1}H} NMR (376 MHz, Acetone-*d6*) δ (ppm) -180.5, -183.1.

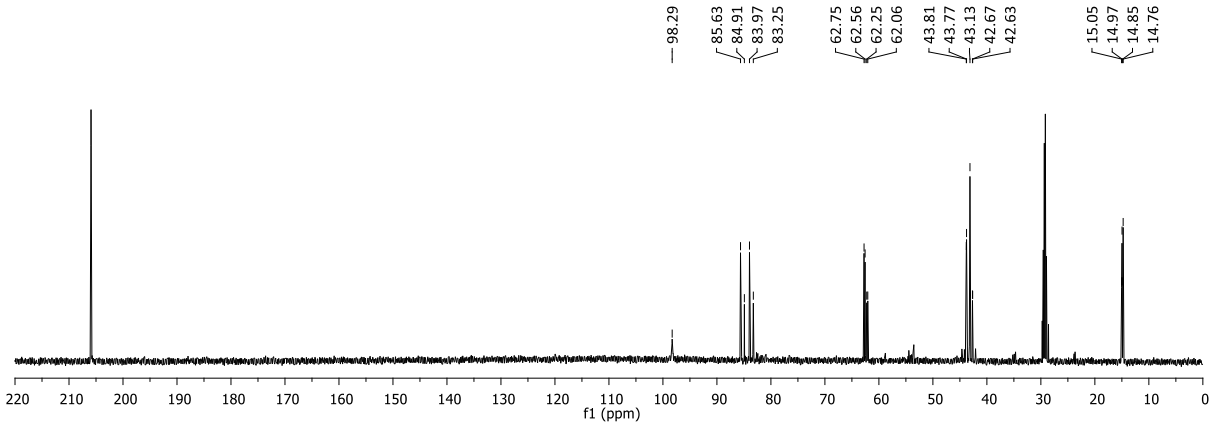
^{1}H NMR (400 MHz, Acetone-*d6*)



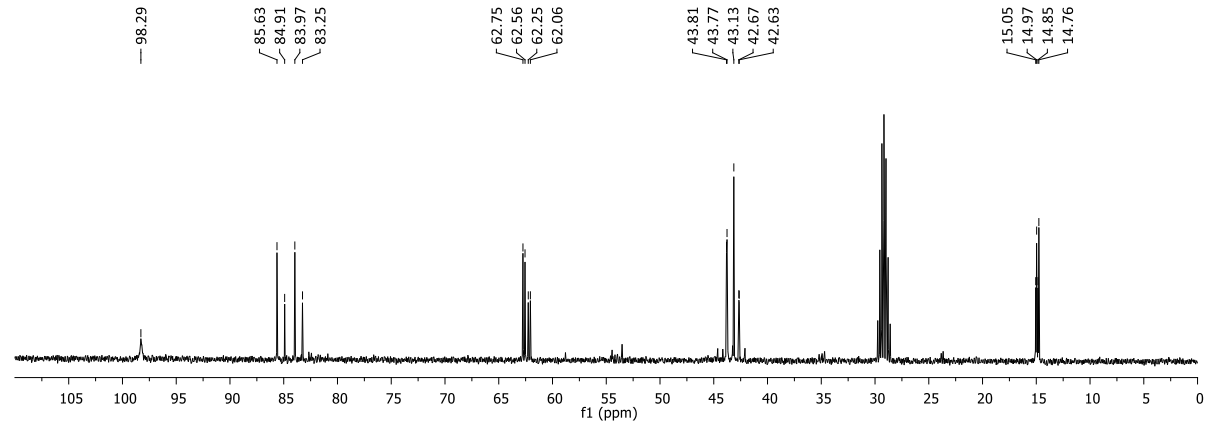
Zoom between 5.0 and 0.0 ppm



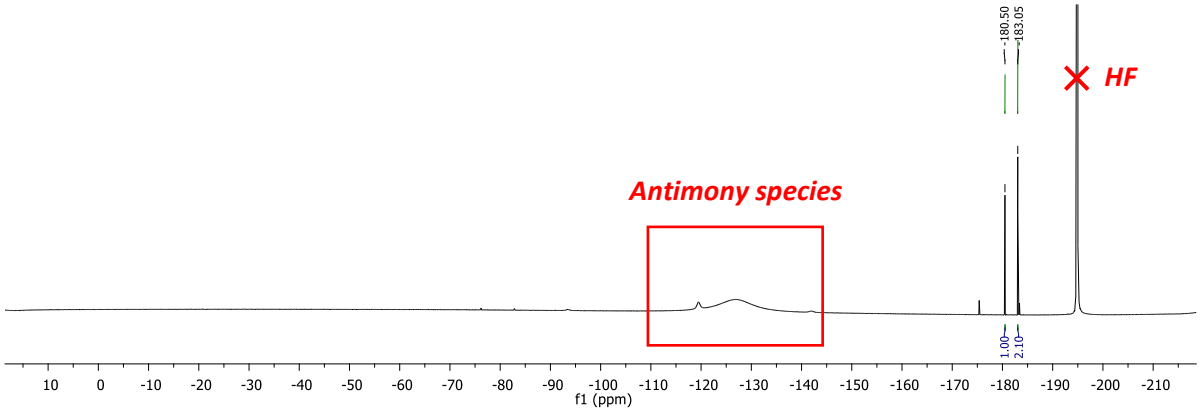
^{13}C NMR (101 MHz, Acetone-*d6*)



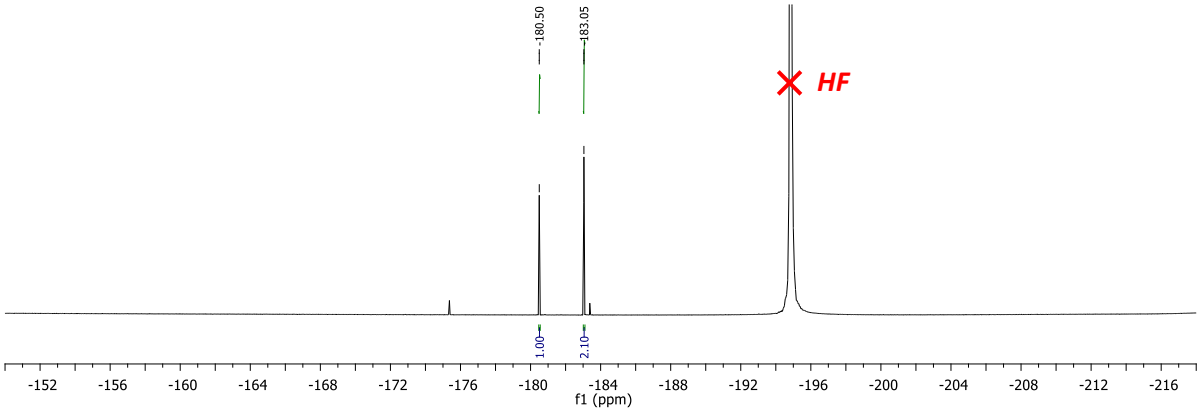
Zoom between 110.0 and 0.0 ppm



^{19}F {^{1}H} NMR (376 MHz, Acetone-*d6*)



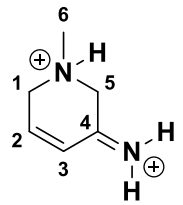
Zoom between -150.0 and -218.0 ppm



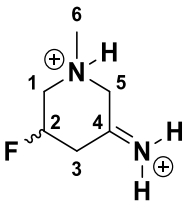
2.2.6. Spectrum of intermediates F and G

*Spectrum of a solution of compound **1a** (85 mg, 0.7 mmol) in HF/SbF_5 (2 mL, 22 mol%) at 0 °C with acetone-d6 as external reference after 2 h at 0 °C*

A mixture of ions **F** and **G** was obtained and two diastereomers of ion **F** was observed.

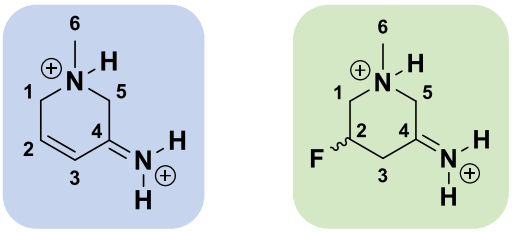


^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 172.6 (C_4), 153.0 (C_2), 119.4 (C_3), 53.9 (C_1), 53.0 (C_5), 44.0 (C_6).

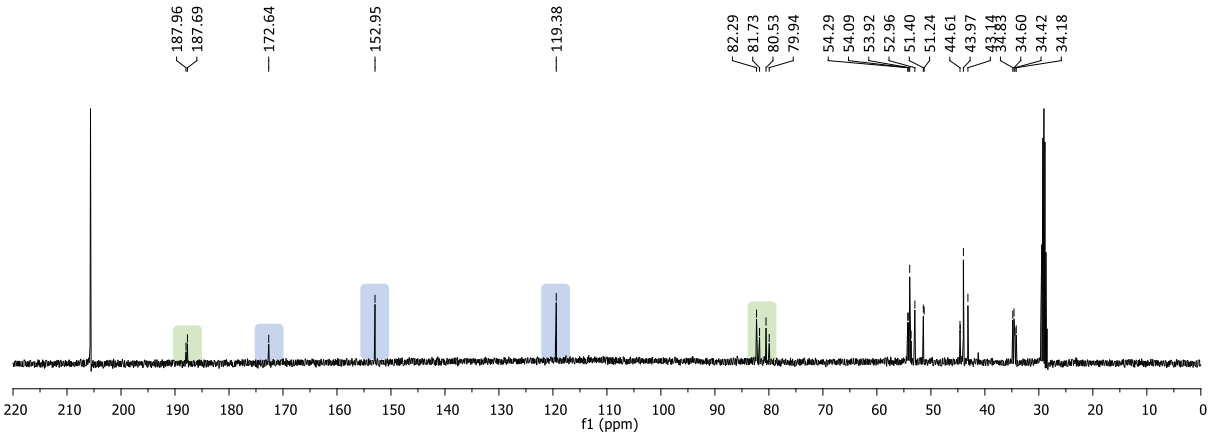


^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 188.0 (C_4), 187.7 (C_4), 81.4 (d, $J_{C\text{-}F}$ = 176 Hz, C_2), 80.9 (d, $J_{C\text{-}F}$ = 176 Hz, C_2), 54.2 (d, J = 19 Hz, C_1), 53.8 (d, J = 19 Hz, C_1), 53.3 (C_5), 44.6 (C_6), 43.1 (C_6), 34.7 (d, J = 23 Hz, C_3), 34.3 (d, J = 23 Hz, C_3).

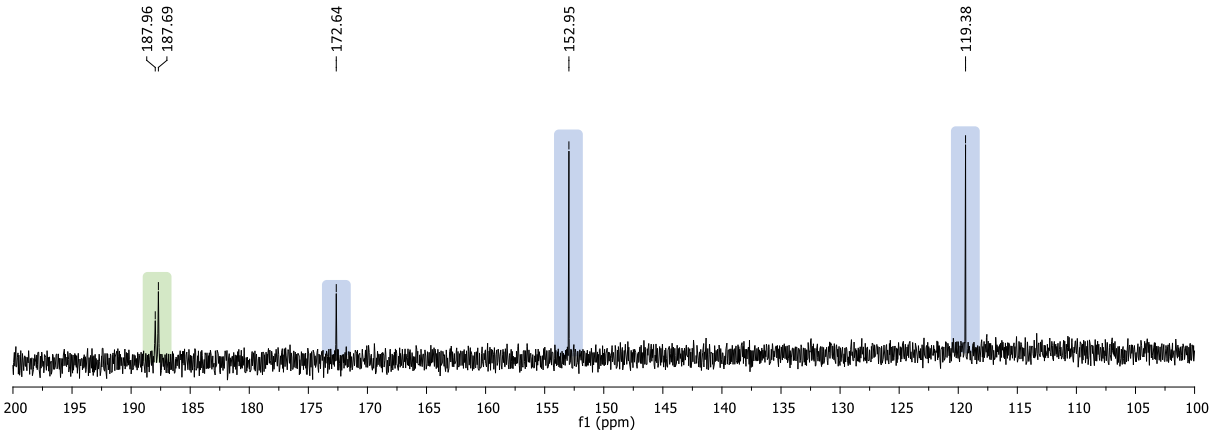
^{19}F {^{1}H} NMR (376 MHz, Acetone-*d6*) δ (ppm) -174.2, -183.3.



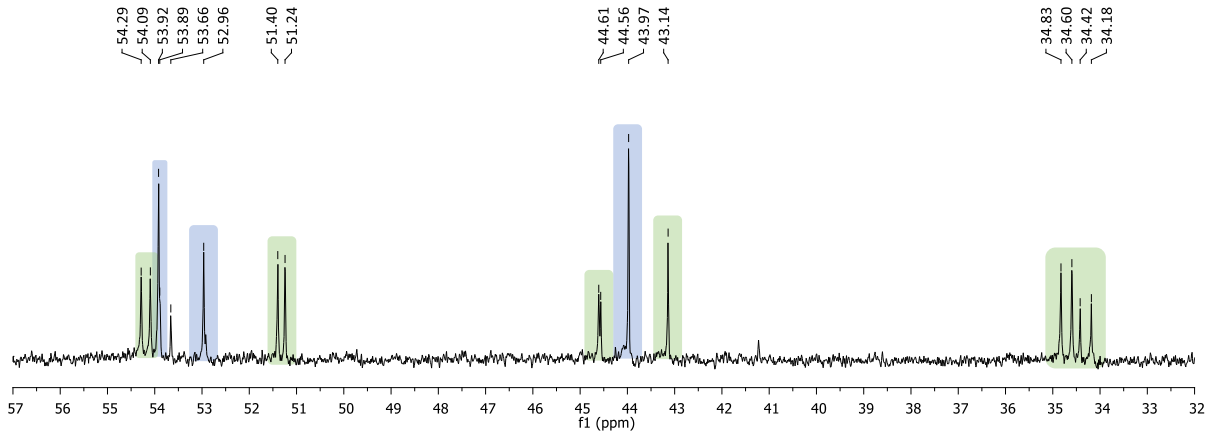
^{13}C NMR (101 MHz, Acetone-*d6*)



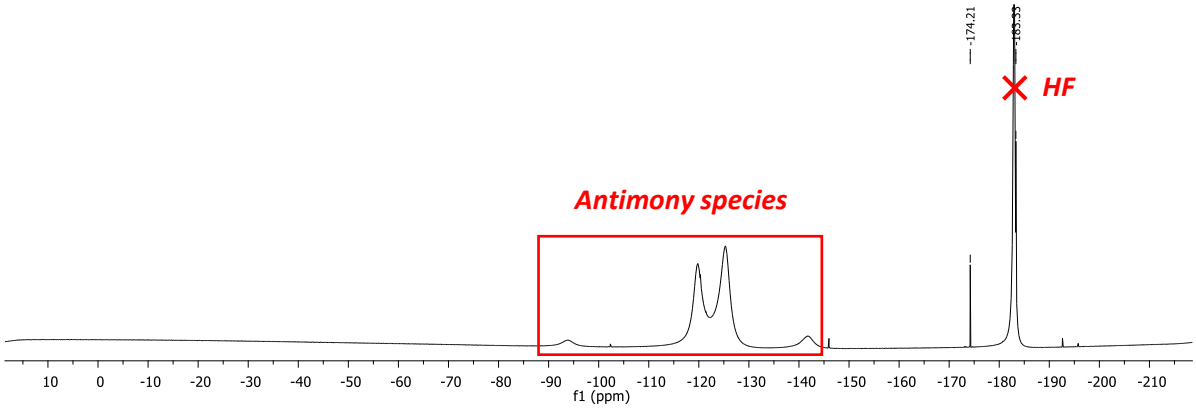
Zoom between 200.0 and 100.0 ppm



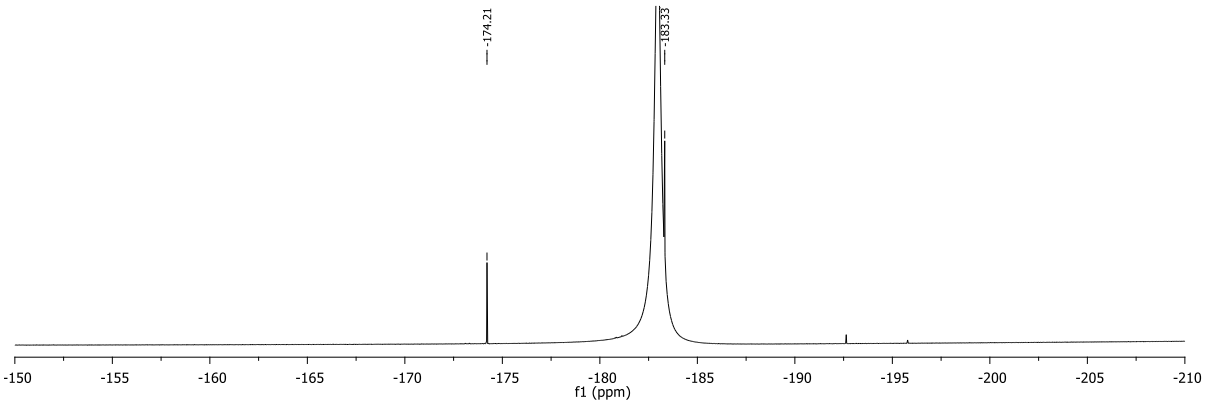
Zoom between 57.0 and 32.0 ppm



^{19}F {^{1}H} NMR (376 MHz, Acetone-*d6*)



Zoom between -150.0 and -210.0 ppm



2.3. Suggested mechanism for the formation of 2a from 1a

The formation of the cyclic compound **2a** first passes through the formation of the fluorinated intermediate **C**. Indeed, the C-F bond can be activated (by protonation or complexation) and this species is in equilibrium with the carbenium form **B** in this medium (Figure 8). The alkene resulting from an elimination reaction is in equilibrium with the fluorinated form and irreversibly traps the nitrilium ion **A**. The thermodynamic equilibrium is therefore shifted towards the formation of the cyclic product.

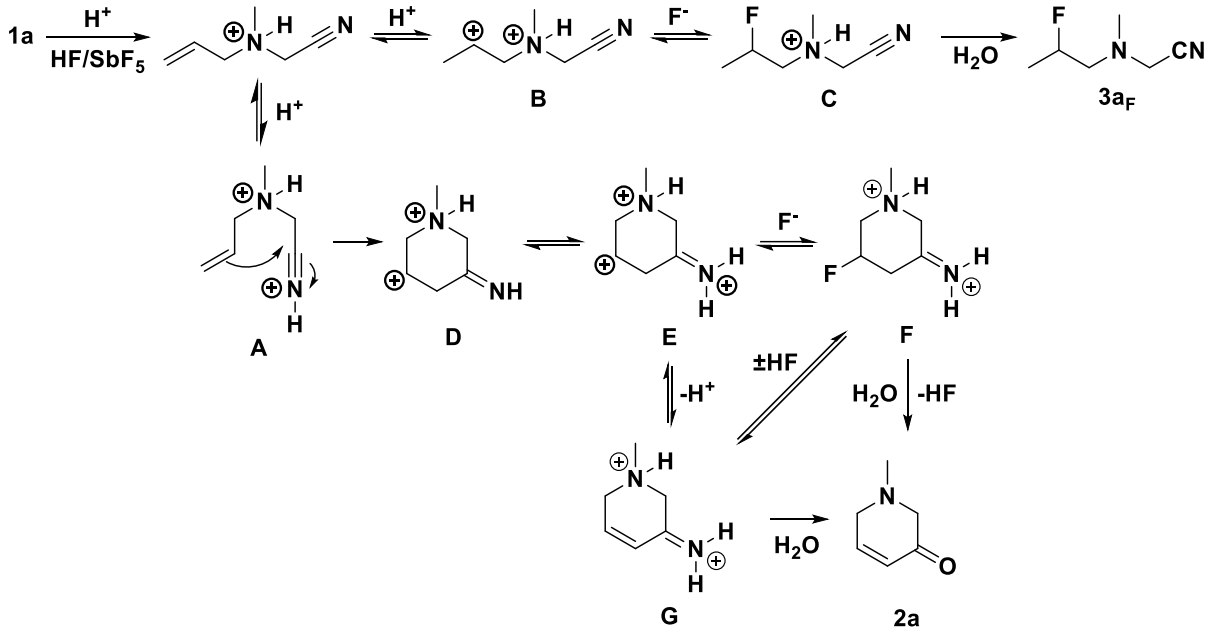


Figure 8 : Suggested mechanism

In order to verify this hypothesis, the fluorinated product **3a$_F$** was synthesized and subjected to the superacidic medium under cyclization conditions (22 mol% SbF_5, 0 °C, 2 h). The cyclic product **2a** was obtained with 80% yield. In addition, product **2a** was subjected to the same superacidic conditions at 0 °C for 2 hours and remains inert in the medium thus confirming the non-reversibility of the cyclization reaction (Figure 9).

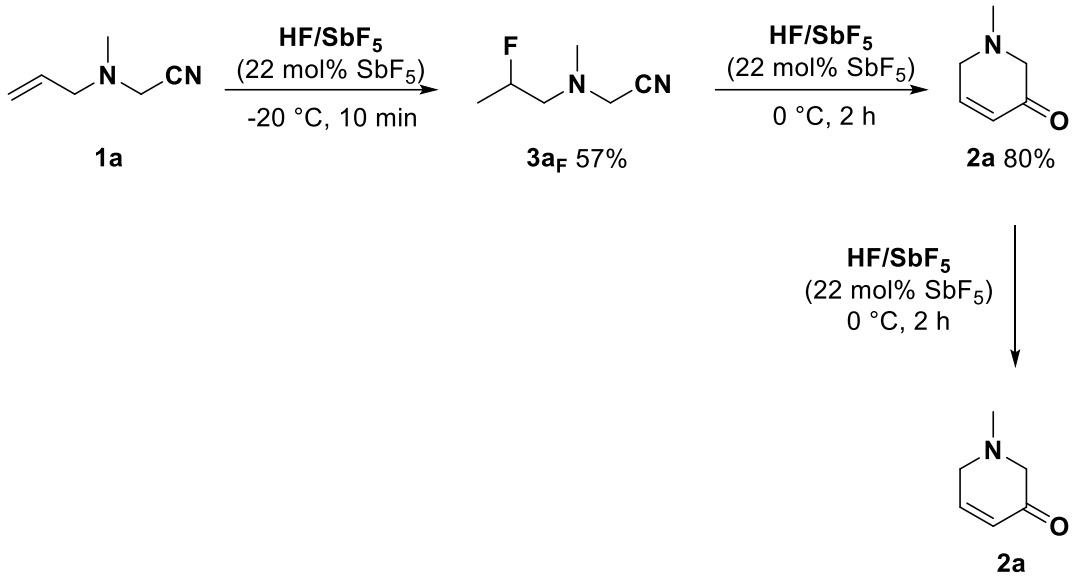
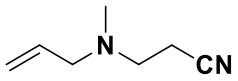


Figure 9 : Evidence of thermodynamic equilibrium

3. Experimental procedures and characterization data

3.1. Synthesis of starting materials

Compound 1b: *3-(allyl(methyl)amino)propanenitrile*



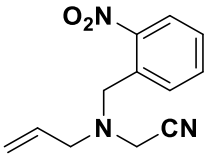
1.0 equiv. of *N*-methylallylamine was added to 1.4 equiv. of K_2CO_3 in solution in 20 mL of acetonitrile. 1.0 equiv. of corresponding alkyl bromide was added to the mixture and the medium was refluxed for 3 h. The solvent was evaporated under reduced pressure and the crude was taken up in water and extracted three times with dichloromethane. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude reaction product was purified by flash chromatography using a mixture of EtOAc/PE as eluent. The compound **1b** was obtained with 84% yield (brown oil). The spectroscopic data correspond to those previously described in the literature.[18]

Rf: 0.43 (Eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.79 – 5.89 (m, 1H), 5.22 – 5.07 (m, 2H), 3.01 (d, *J* = 6.4 Hz, 2H), 2.66 (t, *J* =7.0 Hz, 2H), 2.44 (t, *J* = 7.0 Hz, 2H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, Acetone-*d6*) δ (ppm) 136.7 ($CH_{C=C}$), 119.8 (CN), 117.6 ($CH_{2C=C}$), 60.8 (CH_2), 52.9 (CH_2), 41.7 (CH_3), 16.4 (CH_2).

Compound 1c: *2-(allyl(2-nitrobenzyl)amino)acetonitrile*



N-allylaminoacetonitrile (0.30 g, 3.12 mmol) was added to 2-nitrobenzyl bromide (0.67 g, 3.12 mmol, 1.0 equiv.) and K_2CO_3 (0.47 g, 3.43 mmol, 1.1 equiv.) in 45 mL of acetonitrile. After 5 days of reaction at room temperature, the reaction medium was filtered on pad of celite. The reaction crude was purified by flash chromatography with EtOAc/PE (5/95 to 2/8) as eluent to obtain 463 mg (65%) of compound **1c** as a yellow solid.

Rf: 0.23 (Eluent: EtOAc/PE 2/8).

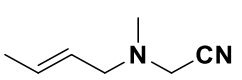
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.82 (d, *J* = 8.0 Hz, 1H), 7.44-7.58 (m, 3H), 5.70 (ddt, *J* = 16.9, 10.1, 6.5 Hz, 1H), 5.27 (dm, *J* = 17.2 Hz, 1H), 5.20 (dm, *J* = 10.1 Hz, 1H), 4.02 (s, 2H), 3.45 (s, 2H), 3.16 (d, *J* = 8.0 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 149.8 (C_{aro}), 133.6 (CH), 132.8 (CH_{aro}), 132.2 (C_{aro}), 131.4 (CH_{aro}), 129.0 (CH_{aro}), 125.0 (CH_{aro}), 119.9 (CH_2), 114.7 (CN), 56.9 (CH_2), 55.5 (CH_2), 41.4 (CH_2).

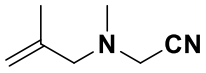
HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 232.1078, calc'd $C_{12}H_{14}N_3O_2$ requires 232.1086.

Mp: 84-85 °C.

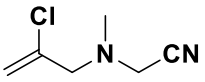
The following substrates were prepared by allylation of *N*-methylaminoacetonitrile with the corresponding allyl bromide according to the general procedure **A**.



1d



1e

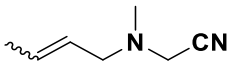


1f

General procedure **A**:

1.1 equiv. of the corresponding allyl bromide were added on 1.0 equiv. of hydrochloride *N*-methylaminoacetonitrile and 2.5 equiv. of K_2CO_3 dissolved in 15 mL of acetonitrile. The reaction mixture was refluxed for 15 h and then evaporated under reduced pressure. The crude was taken up in water and extracted three times with dichloromethane. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The reaction crude was purified by flash chromatography (EtOAc/PE or DCM/MeOH).

Compound 1d: *(E)-2-(but-2-en-1-yl(methyl)amino)acetonitrile*



The compound **1d** was synthesized following the general procedure **A** with 49% yield (colorless oil). Two isomers were obtained with a 9/1 molar ratio.

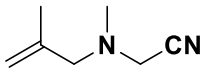
Rf: 0.17 (Eluent: EtOAc/PE 1/9).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.68 – 5.77 (m, 1H), 5.36 – 5.44 (m, 1H), 3.52 (s, 0.2H), 3.50 (s, 1.8H), 3.10 (dm, *J* = 7.2 Hz, 0.2H), 3.00 (dm, *J* = 6.8 Hz, 1.8H), 2.37 (s, 0.4H), 2.34 (s, 2.6H), 1.70 (dm, *J* = 8.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 130.9 (CH_{maj}), 129.5 (CH_{min}), 126.7 (CH_{maj}), 125.8 (CH_{min}), 114.7 (CN), 58.2 (CH_{2maj}), 52.1 (CH_{2min}), 44.2 (CH_{2min}), 44.0 (CH_{2maj}), 42.2 (CH_{3min}), 42.1 (CH_{3maj}), 17.9 (CH_{3maj}), 13.3 (CH_{3min}).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 125.1074, calc'd $C_7H_{13}N_2$ requires 125.1080.

Compound 1e: *2-(methyl(2-methylallyl)amino)acetonitrile*



The compound **1e** was synthesized following the general procedure **A** with 50% yield (colorless oil).

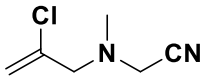
Rf: 0.63 (Eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.95 (s, 1H), 4.90 (s, 1H), 3.46 (s, 2H), 2.96 (s, 2H), 2.33 (s, 3H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 141.5 (C), 114.9 (CH_2), 114.7 (CN), 62.7 (CH_2), 44.2 (CH_2), 42.2 (CH_3), 20.5 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 125.1072, calc'd $C_7H_{13}N_2$ requires 125.1079.

Compound 1f: *2-((2-chloroallyl)(methyl)amino)acetonitrile*



The compound **1f** was synthesized following the general procedure **A** (use of allyl chloride and addition of KI in catalytic amount) with 52% yield (colorless oil).

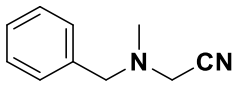
Rf: 0.80 (Eluent: EtOAc/PE 2/8).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.48 (d, *J* = 1.2 Hz, 1H), 5.41 (d, *J* = 1.2 Hz, 1H), 3.58 (s, 2H), 3.27 (s, 2H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 137.8 (CCl), 116.6 (CH_2), 114.3 (CN), 62.2 (CH_2), 44.1 (CH_2), 41.8 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 145.0538, calc'd $C_6H_{10}ClN_2$ requires 145.0533.

Compound 1g: *2-(benzyl(methyl)amino)acetonitrile*



1.30 mL (10.0 mmol) of *N*-methylbenzylamine were added over K_2CO_3 (1.66 g, 12.0 mmol, 1.2 equiv.) dissolved in 15 mL of acetone. Chloroacetonitrile (0.76 mL, 12.0 mmol, 1.2 equiv.) was added to the mixture and the medium was stirred for 24 h at room temperature. The reaction medium was filtered over celite pad and evaporated under reduced pressure. The reaction crude was purified by flash chromatography (EtOAc/PE 1/9). 1.07 g (93%) of compound **1g** were obtained as a yellow liquid. The spectroscopic data correspond to those previously described in the literature.[20]

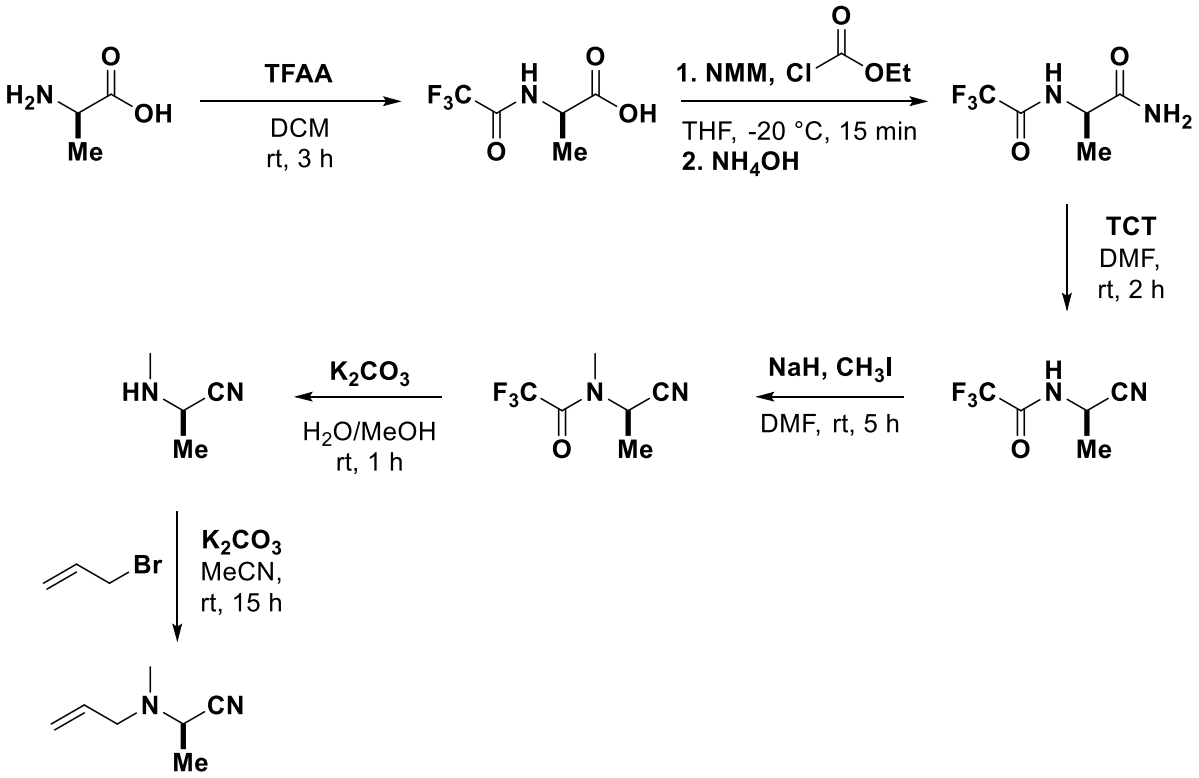
[20] Adolph, C. M.; Werth, J.; Selvaraj, R.; Wegener, E. C.; Uyeda, C. *J. Org. Chem.* **2017**, *82* (11), 5959–5965.

Rf: 0.35 (Eluent: EtOAc/PE 1/9).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.37 – 7.27 (m, 5H), 3.62 (s, 2H), 3.46 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 136.9 (C_{aro}), 129.1 (CH_{aro}), 128.7 (CH_{aro}), 127.9 (CH_{aro}), 114.5 (CN), 60.1 (CH_2), 44.1 (CH_2), 42.4 (CH_3).

Chiral aminonitriles **1h** and **1i** were synthetized following a multi-step synthesis:



General procedure **B**:

Trifluororacetic anhydride (2.0 mL, 14.6 mmol, 1.3 equiv.) was added dropwise to a suspension of aminoacid (1.00 g, 11.2 mmol, 1.0 equiv.) in 40 mL of dichloromethane. The reaction mixture was stirred 3 hours at room temperature and concentrated under vacuo. A white solid was obtained after coevaporation with toluene.[21]

The protected aminoacid (1.80 g, 9.7 mmol, 1.0 equiv.) was dissolved in tetrathydrofuran (23 mL) and cool down to -20 °C. *N*-methylmorpholine (1.07 mL, 9.7 mmol, 1.0 equiv.) and iso-butyle chloroformate (0.93 mL, 9.7 mmol, 1.0 equiv.) were added dropwise successively at -20 °C. The mixture was stirred 15 min and aqueous ammoniaque (4.70 mL, 48.5 mmol, 5.0 equiv., 32%w) was added at -20 °C. The reaction medium was stirred at room temperature for 18 hours and hydrolysed with 10% aqueous $KHSO_4$ until pH 2. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with a saturated aqueous solution of Na_2CO_3 and brine. Then the organic layer was dried over $MgSO_4$, filtered and evaporated to obtain a white solid.[22]

[21] Giordano, O. S.; Pestchanker, M. J.; Guerreiro, E.; Saad, J. R.; Enriz, R. D.; Rodriguez, A. M.; Jauregui, E. A.; Guzman, J.; Maria, A. O. M.; Wendel, G. H. *J. Med. Chem.* **1992**, *35* (13), 2452–2458.
[22] Löser, R.; Frizler, M.; Schilling, K.; Gütschow, M. *Angew. Chem. Int. Ed.* **2008**, *47* (23), 4331–4334.

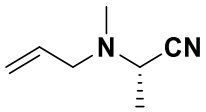
Trichlorotriazine (0.80 g, 4.3 mmol, 0.5 equiv.) was added in one portion to a solution of amide (1.60 g, 8.7 mmol, 1.0 equiv.) in 20 mL of DMF at room temperature. The mixture was stirred 1 hour at room temperature and hydrolysed with water. The aqueous layer was extracted 4 times with EtOAc/Toluene (2/1). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ and brine. Organic layer was dried over $MgSO_4$, filtered and evaporated to obtain the nitrile (white solid).[23]

NaH (0.41 g, 10.3 mmol, 1.2 equiv., 60% in mineral oil) was added at 0 °C to a solution of nitrile (1.43 g, 8.6 mmol, 1.0 equiv.) in 30 mL of THF. After stirring 15 min at 0 °C, CH_3I (1.07 mL, 17.2 mmol, 2.0 equiv.) was added and the mixture was stirred 16 h at room temperature. The reaction medium was hydrolysed with water and extracted 3 times with DCM. The combined organic layers were washed with brine and dried over $MgSO_4$, filtered and evaporated. The crude was purified by flash chromatography (EtOAc/PE).

The protecting group was removed by the addition of K_2CO_3 (0.36 g, 2.6 mmol, 1.0 equiv.) to a solution of amide (0.47 g, 2.6 mmol, 1.0 equiv.) in 26 mL of MeOH/H_2O (9/1; v/v). The reaction was stirred 2 h at room temperature and concentrated under vacuo. The crude was dissolved in a minimum amount of water and extracted 3 times with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated to obtain an oil.[24]

The aminonitrile (173 mg, 2.06 mmol, 1.0 equiv.) was diluted in 5 mL of acetonitrile and K_2CO_3 (426 mg, 3.08 mmol, 1.5 equiv.), allyl bromide (0.27 mL, 3.08 mmol, 1.5 equiv.) and KI (catalytic amount) were added successively. The reaction was stirred 24 h at room temperature and concentrated under vacuo. The residue was diluted with water and extracted 3 times with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude was purified by flash chromatography (EtOAc/PE) to afford the desired chiral aminonitrile.

Compound 1h: *(S)-2-(allyl(methyl)amino)propanenitrile*



The compound **1h** was synthesized following the general procedure **B** with 18% yield (yellow oil).

The corresponding enantiomer **1i** was obtained following the same procedure starting from *D*-alanine in 22% yield.

Rf: 0.65 (Eluent: EtOAc/PE 3/7).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.77 (dddd, *J* = 17.3, 10.1, 7.4, 5.7 Hz, 1H), 5.27 (ddd, *J* = 17.3, 3.0, 1.3 Hz, 1H), 5.19 (ddd, *J* = 10.1, 2.5, 1.3 Hz, 1H), 3.76 (q, *J* = 7.2 Hz, 1H), 3.20 (ddm, *J* = 13.4, 5.7 Hz, 1H), 2.98 (ddm, *J* = 13.4, 7.4 Hz, 1H), 2.28 (s, 3H), 1.44 (d, *J* = 7.2 Hz, 3H).

[23] Maetz, P.; Rodriguez, M. *Tetrahedron Lett.* **1997**, *38* (24), 4221–4222.
[24] Bergeron, R. J.; McManis, J. S. *J. Org. Chem.* **1988**, *53* (13), 3108–3111.

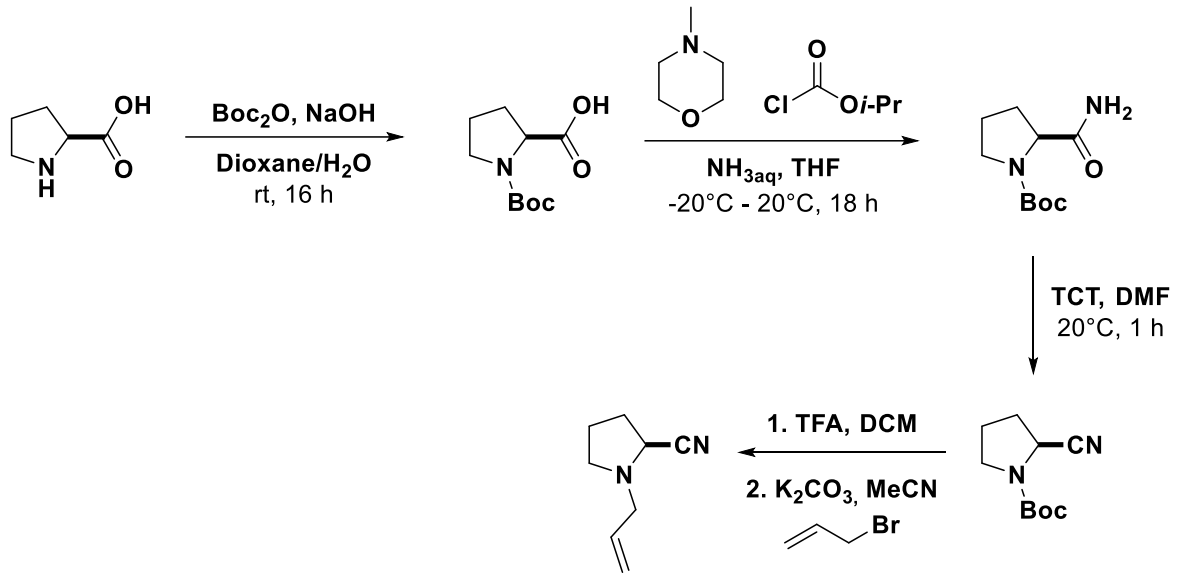
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 134.5 ($CH_{C=C}$), 119.1 ($CH_{2C=C}$), 117.6 (CN), 58.7 (CH_2), 50.8 (CH), 37.6 (CH_3), 17.8 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 125.1079, calc'd $C_7H_{13}N_2$ requires 125.1086.

$[\alpha]_D^{20}$ -45.1 (c = 0.11, $CHCl_3$).

HPLC analysis: (Chiralpak OD-H, Hexane/isopropanol 98/2, 1 mL/min, 20 °C, 215 nm) indicated >99% e.e., t_r (min) = 8.23 min, t_r (maj) = 9.27 min.

Chiral aminonitriles **1j** and **1k** were synthetized following a multi-step synthesis:



General procedure **C**:

Proline (2.00 g, 17.4 mmol, 1.0 equiv.) was solubilized in 30 mL of H_2O/Dioxane (1/2; v/v) and NaOH (1.00 g, 26.1 mmol, 1.5 equiv.) and Boc_2O (5.70 g, 26.1 mmol, 1.5 equiv.) were added successively. After stirring overnight at room temperature, the reaction mixture was washed 2 times with petroleum ether. The aqueous layer was acidified with $KHSO_4$ until pH 2 and extracted 3 times with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. A white solid was obtained and used without purification.

The protected aminoacid (3.50 g, 16.5 mmol, 1.0 equiv.) was dissolved in tetrathydrofuran (30 mL) and cool down to -20 °C. *N*-methylmorpholine (1.80 mL, 16.5 mmol, 1.0 equiv.) and iso-butyle chloroformate (1.60 mL, 16.5 mmol, 1.0 equiv.) were added dropwise successively at -20 °C. The mixture was stirred 15 min and aqueous ammoniaque (4.70 mL, 82.5 mmol, 5.0 equiv., 32%w) was added at -20 °C. The reaction medium was stirred at room temperature for 18 hours and hydrolysed with 10% aqueous $KHSO_4$ until pH 2. The aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with a saturated aqueous solution of Na_2CO_3 and brine. Then the organic layer was dried over $MgSO_4$, filtered and evaporated to obtain a white solid.

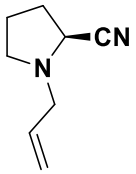
Trichlorotriazine (1.24 g, 6.7 mmol, 0.5 equiv.) was added in one portion to a solution of amide (2.84 g, 13.3 mmol, 1.0 equiv.) in 30 mL of DMF at room temperature. The mixture was stirred 1 hour at room temperature and hydrolysed with water. The aqueous layer was extracted 4 times with

EtOAc/Toluene (2/1). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$, filtered and evaporated to obtain the nitrile (colorless oil).

Boc-protecting group was removed in acidic medium. The carbamate (0.60 g, 3.0 mmol) was dissolved in dry dichloromethane (30 mL) and trifluoroacetic acid (10 mL) was added dropwise at 0 °C. The mixture was stirred 1 h at 0 °C and the solvents were evaporated under vacuo. The residue was precipitated with Et_2O to give the ammonium salt as a white solid.

The ammonium salt (0.62 g, 3.0 mmol, 1.0 equiv.) was dissolved in 15 mL of acetonitrile and K_2CO_3 (1.25 g, 9.0 mmol, 3.0 equiv.), allyl bromide (0.32 mL, 3.6 mmol, 1.2 equiv.) and KI (cat.) were added successively. After 24 h stirring at room temperature, the reaction was hydrolysed with water and extracted 3 times with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The crude was purified by flash chromatography (EtOAc/PE) to give the chiral aminonitrile as an oil.

Compound 1j: *(S)-1-allylpyrrolidine-2-carbonitrile*



The compound **1j** was synthesized following the general procedure **C** with 27% yield (yellow oil).

The corresponding enantiomer **1k** was obtained following the same procedure starting from *D*-proline in 23% yield.

Rf: 0.50 (Eluent: EtOAc/PE 2/8).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.85 (dddd, *J* = 17.2, 10.1, 7.3, 5.8 Hz, 1H), 5.31 (ddd, *J* = 17.2, 3.0, 1.5 Hz, 1H), 5.17 (dm, *J* = 10.1, 1H), 3.79 (dd, *J* = 7.4, 2.8 Hz, 1H), 3.36 (ddm, *J* = 13.3, 5.8 Hz, 1H), 3.18 (ddm, *J* = 13.3, 7.3 Hz, 1H), 2.91 (ddd, *J* = 9.5, 8.1, 4.5 Hz, 1H), 2.54 (m, 1H), 2.26-2.04 (m, 2H), 2.04-1.79 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 134.4 ($CH_{C=C}$), 118.6 ($CH_{2C=C}$), 118.1 (CN), 55.5 (CH_2), 53.3 (CH), 51.3 (CH_2), 29.7 (CH_2), 22.0 (CH_2).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 137.1072, calc'd $C_8H_{13}N_2$ requires 137.1075.

$[\alpha]_D^{20}$ -31.9 (c = 0.13, $CHCl_3$).

HPLC analysis: (Chiralpak OD-H, Hexane/isopropanol 99/1, 1 mL/min, 20 °C, 215 nm) indicated >98% e.e., t_r (min) = 6.97 min, t_r (maj) = 8.39 min.

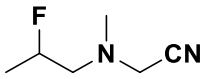
3.2. Superacidic reactions

Synthesis of products **3a$_F$** to **2g** were performed following the general procedure **D**.

General procedure **D**:

To a chosen HF/SbF_5 mixture at desired temperature was added the aminonitrile derivative. The mixture was magnetically stirred at the same temperature and then neutralized with water/ice/Na_2CO_3 up to pH 10 and extracted with dichloromethane (x3). The combined organic phases were dried over magnesium sulfate, filtered and concentrated in vacuo. The reaction crude was purified over silica gel to obtain the desired compound.

Compound 3a$_F$: *2-(N-(2-fluoropropyl)-N-methylamino)acetonitrile*



Aminonitrile **1a** (95 mg, 0.86 mmol), hydrofluoric acid (3.5 mL) and antimony pentafluoride (0.5 mL) were used. The reaction was carried out for 10 min at -20 °C. The fluorinated compound **3a$_F$** (62 mg, 55%, colorless oil) was obtained after purification by flash chromatography (DCM). The spectroscopic data correspond to those previously described in the literature.[18]

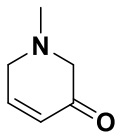
Rf: 0.8 (eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.80 (dm, *J* = 49.6 Hz, 1H), 3.64 (d, *J*= 17.3 Hz, 1H), 3.58 (d, *J* = 17.2 Hz, 1H), 2.70 (ddd, *J* = 18.5, 14.1, 7.7 Hz, 1H), 2.58 (ddd, *J* = 30.1, 14.1, 2.6 Hz, 1H), 2.44 (s, 3H), 1.34 (dd, *J* = 23.7, 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 114.9 (CN), 89.4 (d, $J_{C\text{-}F}$ = 168 Hz, CHF), 60.8 (d, $J_{C\text{-}F}$ = 20 Hz, CH_2), 46.0 (CH_2), 43.2 (CH_3), 19.0 (d, $J_{C\text{-}F}$ = 22 Hz, CH_3).

^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ (ppm) -176.1.

Compound 2a: *1-methyl-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1a** (168 mg, 1.5 mmol), hydrofluoric acid (2 mL) and antimony pentafluoride (2 mL) were used. The reaction was started at -20 ° C and then carried out for 2 hours at 0 °C. Compound **2a** (120 mg, 71%) was obtained as an yellow oil after purification over silica gel (DCM/MeOH(NH_3) 99/1).

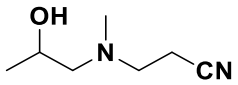
Rf: 0.25 (Eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.03 (dt, *J* = 10.1, 3.6 Hz, 1H), 6.10 (dt, *J* = 10.1, 2.1 Hz, 1H), 3.22 (m, 2H), 3.11 (s, 2H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.0 (CO), 148.6 ($CH_{C=C}$), 127.9 ($CH_{C=C}$), 63.3 (CH_2), 53.9 (CH_2), 45.0 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 112.0785, calc'd $C_6H_{10}NO$ requires 111.0789.

Compound $3b_{OH}$: *3-((2-hydroxypropyl)(methyl)amino)propanenitrile*



Aminonitrile **1b** (140 mg, 1.13 mmol), hydrofluoric acid (2 mL) and antimony pentafluoride (2 mL) were used. The reaction was carried out for 10 min at 0 °C. The product **$3b_{OH}$** (31 mg, 20%, yellow oil) was obtained after purification by flash chromatography (DCM/PE 5/5 to 1/0).

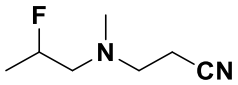
Rf: 0.85 (Eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.10 – 3.95 (m, 1H), 2.81 (t, *J* = 6.9 Hz, 2H), 2.72 (dd, *J* = 13.3, 6.8 Hz, 1H), 2.58 (dd, *J* = 13.3, 6.8 Hz, 1H), 2.49 (t, *J* = 6.8 Hz, 2H), 2.36 (s, 3H), 1.53 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 118.8 (CN), 65.5 (CH_2), 55.2 (CH), 53.6 (CH_2), 42.3 (CH_3), 23.2 (CH_3), 16.6 (CH_2).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 126.1151, calc'd $C_7H_{14}N_2$ requires 126.1162.

Compound $3b_F$: *3-((2-fluoropropyl)(methyl)amino)propanenitrile*



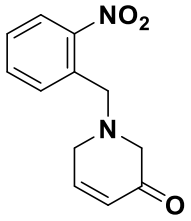
Aminonitrile **1b** (140 mg, 1.1 mmol), hydrofluoric acid (2 mL) and antimony pentafluoride (2 mL) were used. The reaction was started at -20 °C and then carried out for 10 min at 0 °C. Compound **$3b_F$** (22 mg, 14%) was obtained as a colorless oil after purification over silica gel (DCM/MeOH 99/1). The spectroscopic data correspond to those previously described in the literature.[18]

Rf: 0.43 (Eluent: DCM/MeOH 99/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 4.81 (dm, *J* = 49.4 Hz 1H), 2.82 (t, *J* = 6.9 Hz, 2H), 2.65 (m, 2H), 2.48 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H), 1.32 (dd, *J* = 23.8, 6.3 Hz, 3H).

^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ (ppm) -175.1.

Compound 2c: *1-(2-nitrobenzyl)-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1c** (89 mg, 0.38 mmol), hydrofluoric acid (2 mL) and antimony pentafluoride (2 mL) were used. The reaction was carried out for 30 min at 0 °C. The product **2c** (42 mg, 48%, yellow oil) was obtained after purification by flash chromatography (EtOAc/PE 2/8). The product was found contaminated by around 10%mol of 2-(4-methyl-8-nitro-3,4-dihydroisoquinolin-2(1H)-yl)acetonitrile (Friedel-Crafts reaction).

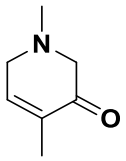
Rf: 0.28 (Eluent: EtOAc/PE 2/8).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.88 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.54 – 7.59 (m, 2H), 7.43 (td, *J* = 8.0, 2.0 Hz, 1H), 7.00 (dt, *J* = 10.0, 3,6 Hz, 1H), 6.11 (dt, *J* = 10.0, 2.0 Hz, 1H), 3.98 (s, 2H), 3.33 (m, 2H), 3.16 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 195.5 (CO), 149.6 (C_{aro}), 148.3 (CH), 133.0 (CH_{aro}), 132.5 (C_{aro}), 131.0 (CH_{aro}), 128.6 (CH_{aro}), 128.0 (CH), 125.0 (CH_{aro}), 61.0 (CH_2), 57.8 (CH_2), 52.3 (CH_2).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 232.0918, calc'd $C_{12}H_{13}N_2O_3$ requires 232.0935.

Compound 2d: *1,4-dimethyl-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1d** (72 mg, 0.58 mmol), hydrofluoric acid (1 mL) and antimony pentafluoride (1 mL) were used. The reaction was carried out for 10 min at 0 °C. The compound **2d** was obtained without purification because it's not stable under silica.

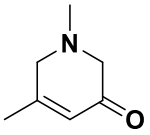
Rf: 0.30 (Eluent: DCM/MeOH 98/2).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.60 (qt, *J* = 7.2, 2.5 Hz, 1H), 3.52 – 3.47 (m, 2H), 3.10 (s, 2H), 2.48 (s, 3H), 1.79 (dt, *J* = 7.2, 1.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 201.6 (CO), 136.6 ($C_{C=C}$), 131.0 ($CH_{C=C}$), 63.8 (CH_2), 56.1 (CH_2), 43.1 (CH_3), 15.4 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 126.0914, calc'd $C_7H_{12}NO$ requires 126.0913.

Compound 2e: *1,5-dimethyl-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1e** (68 mg, 0.55 mmol), hydrofluoric acid (1 mL) and antimony pentafluoride (1 mL) were used. The reaction was carried out for 10 min at 0 °C. The product **2e** (58 mg, 85%, yellow oil) was obtained after purification by flash chromatography (DCM/MeOH(NH_3) 98/2).

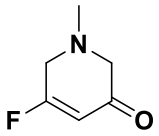
Rf: 0.30 (Eluent: DCM/MeOH 98/2).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.99 – 5.92 (m, 1H), 3.12 (s, 2H), 3.05 (s, 2H), 2.40 (s, 3H), 1.97 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.0 (CO), 160.8 ($C_{C=C}$), 124.9 ($CH_{C=C}$), 62.4 (CH_2), 58.5 (CH_2), 44.9 (CH_3), 21.8 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 126.0916, calc'd $C_7H_{12}NO$ requires 126.0913.

Compound 2f$_F$: *5-fluoro-1-methyl-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1f** (68 mg, 0.47 mmol), hydrofluoric acid (1 mL) and antimony pentafluoride (1 mL) were used. The reaction was carried out for 10 min at 0 ° C. The compound **2f$_F$** (27 mg, 45%) was obtained in the form of a colorless oil after purification by flash chromatography (EtOAc/PE 0/1 to 3/7).

Rf: 0.25 (Eluent: EtOAc/PE 3/7).

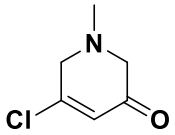
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.80 (dt, J = 13.6, 1.1 Hz, 1H), 3.45 – 3.35 (m, 2H), 3.12 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.2 (d, $J_{C\text{-}F}$ = 17 Hz, CO), 177.7 (d, $J_{C\text{-}F}$ = 293 Hz, CF), 108.2 (d, $J_{C\text{-}F}$ = 9 Hz), 62.0 (CH_2), 53.4 (d, $J_{C\text{-}F}$ = 28 Hz, CH_2), 44.5 (d, $J_{C\text{-}F}$ = 2 Hz, CH_3).

^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$) δ (ppm) -81.95.

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 130.0659, calc'd C_6H_9FNO requires 130.0674.

Compound $2f_{Cl}$: *5-chloro-1-methyl-1,6-dihydropyridin-3(2H)-one*



Aminonitrile **1f** (68 mg, 0.47 mmol), hydrofluoric acid (1 mL) and antimony pentafluoride (1 mL) were used. The reaction was carried out for 10 min at 0 °C. The compound **$2f_{Cl}$** (14 mg, 20%) was obtained in the form of a colorless oil after purification by flash chromatography (EtOAc/PE 0/1 to 3/7).

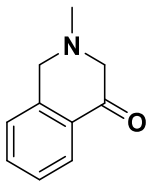
Rf: 0.35 (Eluent: EtOAc/PE 3/7).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.29 (s, 1H), 3.46 (s, 2H), 3.16 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 193.8 (CO), 155.7 (CCl), 126.7 ($CH_{C=C}$), 61.7 (CH_2), 59.6 (CH_2), 44.2 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 146.0373, calc'd C_6H_9ClNO requires 146.0367.

Compound 2g: *2-methyl-2,3-dihydroisoquinolin-4(1H)-one*



Aminonitrile **1g** (89 mg, 0.56 mmol), hydrofluoric acid (1 mL) and antimony pentafluoride (1 mL) were used. The reaction was carried out for 1 h at 0 °C. The compound **2g** (41 mg, 45%) was obtained in the form of a yellow oil after purification by flash chromatography (EtOAc/PE 0/1 to 1/1).

Rf: 0.30 (Eluent: EtOAc/PE 3/7).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.03 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.51 (td, *J* = 7.5, 1.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 3.75 (s, 2H), 3.33 (s, 2H), 2.49 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.8 (CO), 142.4 (C_{aro}), 133.9 (CH_{aro}), 130.4 (C_{aro}), 127.5 (CH_{aro}), 126.8 (CH_{aro}), 126.5 (CH_{aro}), 64.6 (CH_2), 57.5 (CH_2), 45.5 (CH_3).

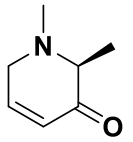
HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 162.0914, calc'd $C_{10}H_{12}NO$ requires 162.0919.

Synthesis of chiral products **2h** to **2k** were performed following the general procedure **E**.

General procedure **E**:

To a HF/SbF_5 mixture (2 mL, 22 mol% SbF_5) at -20 °C was added the chiral aminonitrile (0.3 mmol). The mixture was magnetically stirred at 0 °C for 2 h, then neutralized with water/ice/Na_2CO_3 up to pH 10 and extracted with dichloromethane (x3). The combined organic phases were dried over magnesium sulfate, filtered and concentrated in vacuo. The reaction crude was purified over silica gel to obtain the chiral unsaturated piperidinone.

Compound 2h: *(S)-1,2-dimethyl-1,6-dihydropyridin-3(2H)-one*



The compound **2h** (15 mg, 40%) was synthesized following the general procedure **E** starting from **1h** (36 mg, 0.30 mmol).

The corresponding (*R*)-enantiomer **2i** (9 mg, 26%) was synthesized following the general procedure **E** starting from **1i** (35 mg, 0.28 mmol).

Rf: 0.25 (Eluent: DCM/MeOH 98/2).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.96 (dt, *J* = 10.1, 3.6 Hz, 1H), 6.07 (dt, *J* = 10.1, 2.0 Hz, 1H), 3.45 (ddd, *J* = 19.3, 3.6, 2.0 Hz, 1H), 3.23 (dddd, *J* = 19.3, 3.6, 2.0, 1.6 Hz, 1H), 3.08 (qd, *J* = 6.8, 1.6 Hz, 1H), 2.43 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 4H).

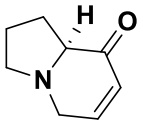
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.5 (CO), 147.2 ($CH_{C=C}$), 127.0 ($CH_{C=C}$), 65.0 (CH), 52.0 (CH_2), 41.8 (CH_3), 11.0 (CH_3).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 126.0912, calc'd $C_7H_{12}NO$ requires 126.0913.

$[\alpha]_D^{20}$ -25.6 (c = 0.10, $CHCl_3$).

HPLC analysis: (Chiralpak OD-H, Hexane/isopropanol 95/5, 1 mL/min, 20 °C, 215 nm) indicated >98% e.e., t_r (min) = 5.72 min, t_r (maj) = 7.33 min.

Compound 2j: *(S)-1,2,3,8a-tetrahydroindolizin-8(5H)-one*



The compound **2j** (14 mg, 19%) was synthesized following the general procedure **E** starting from **1j** (75 mg, 0.55 mmol).

The corresponding (*R*)-enantiomer **2k** (12 mg, 20%) was synthesized following the general procedure **E** starting from **1k** (62 mg, 0.45 mmol).

Rf: 0.30 (Eluent: DCM/MeOH 98/2).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.98 (ddd, *J* = 10.0, 5.0, 1.8 Hz, 1H), 6.08 (ddd, *J* = 10.0, 2.9, 1.4 Hz, 1H), 3.70 (ddd, *J* = 18.7, 5.0, 1.4 Hz, 1H), 3.22-3.09 (m, 2H), 2.88-2.72 (m, 1H), 2.42 (app. q, *J* = 8.7 Hz, 1H), 2.06-1.92 (m, 2H), 1.85-1.69 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.1 (CO), 147.8 ($CH_{C=C}$), 128.2 ($CH_{C=C}$), 68.2 (CH), 53.7 (CH_2), 51.7 (CH_2), 24.3 (CH_2), 21.1 (CH_2).

HRMS-ESI$^+$ (m/z): found $[M+H]^+$ 136.0757, calc'd $C_8H_{10}NO$ requires 136.0757.

$[\alpha]_D^{20}$ -22.4 (c = 0.14, $CHCl_3$).

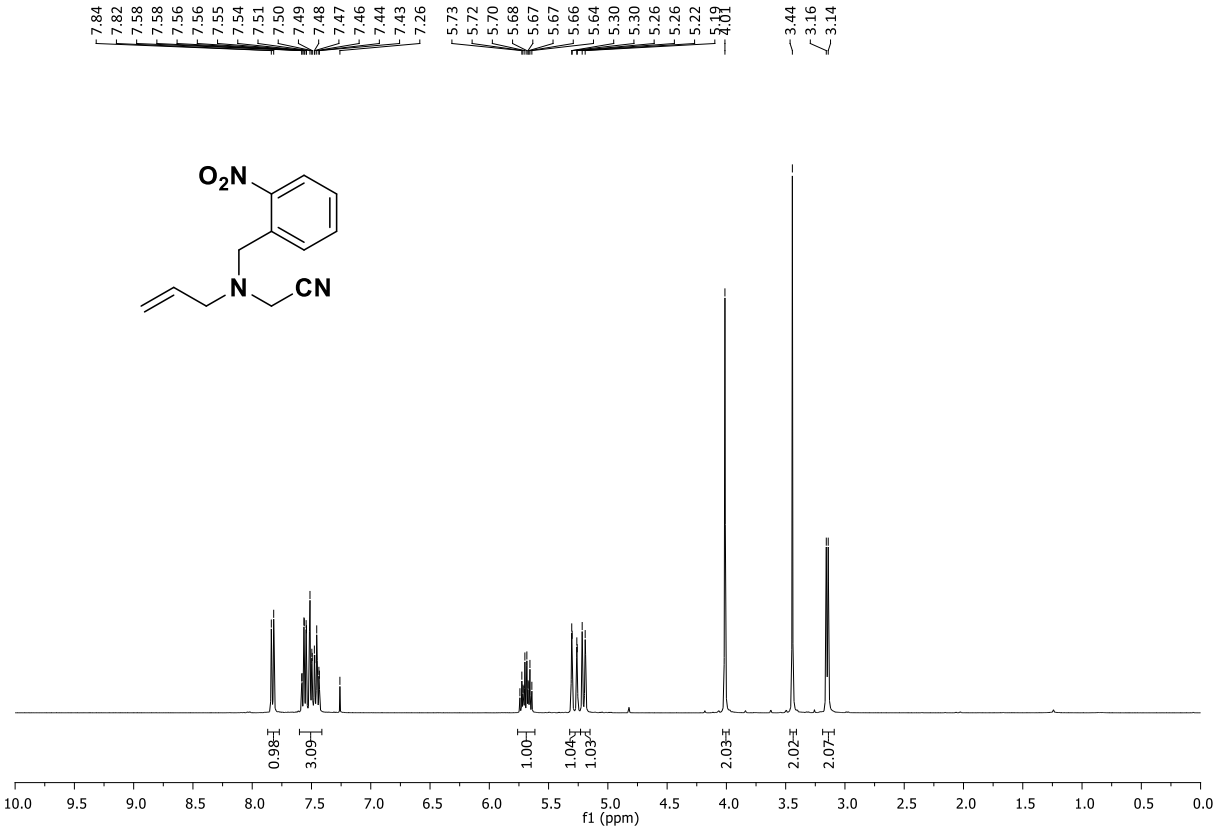
HPLC analysis: (Chiralpak OD-H, Hexane/isopropanol 95/5, 1 mL/min, 20 °C, 215 nm) indicated 97% e.e., t_r (min) = 6.97 min, t_r (maj) = 8.39 min.

4. NMR spectra of new compounds

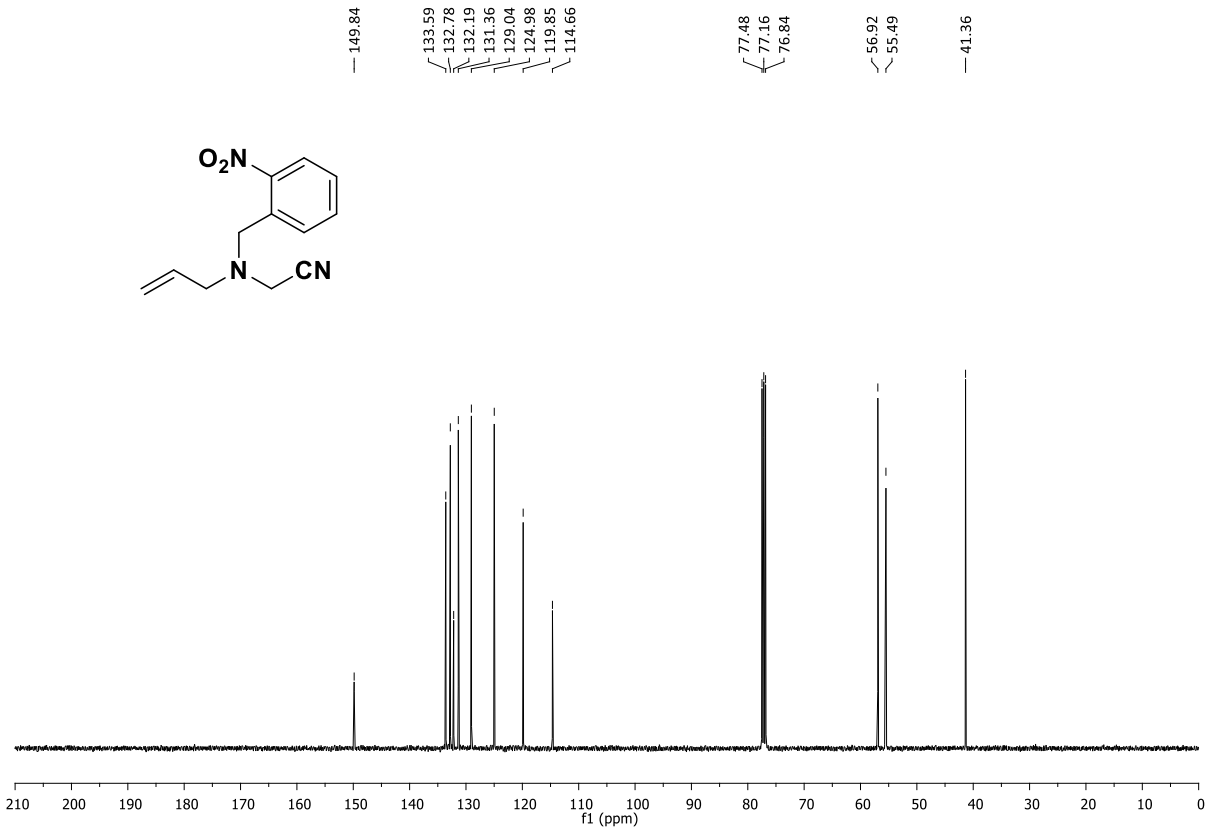
- Compound **1c**
- Compound **1d**
- Compound **1e**
- Compound **1f**
- Compound **1h**
- Compound **1j**
- Compound **2a**
- Compound **3b$_{OH}$**
- Compound **2c**
- Compound **2d**
- Compound **2e**
- Compound **2f$_{F}$**
- Compound **2f$_{Cl}$**
- Compound **2g**
- Compound **2h**
- Compound **2j**

Compound 1c: *2-(allyl(2-nitrobenzyl)amino)acetonitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

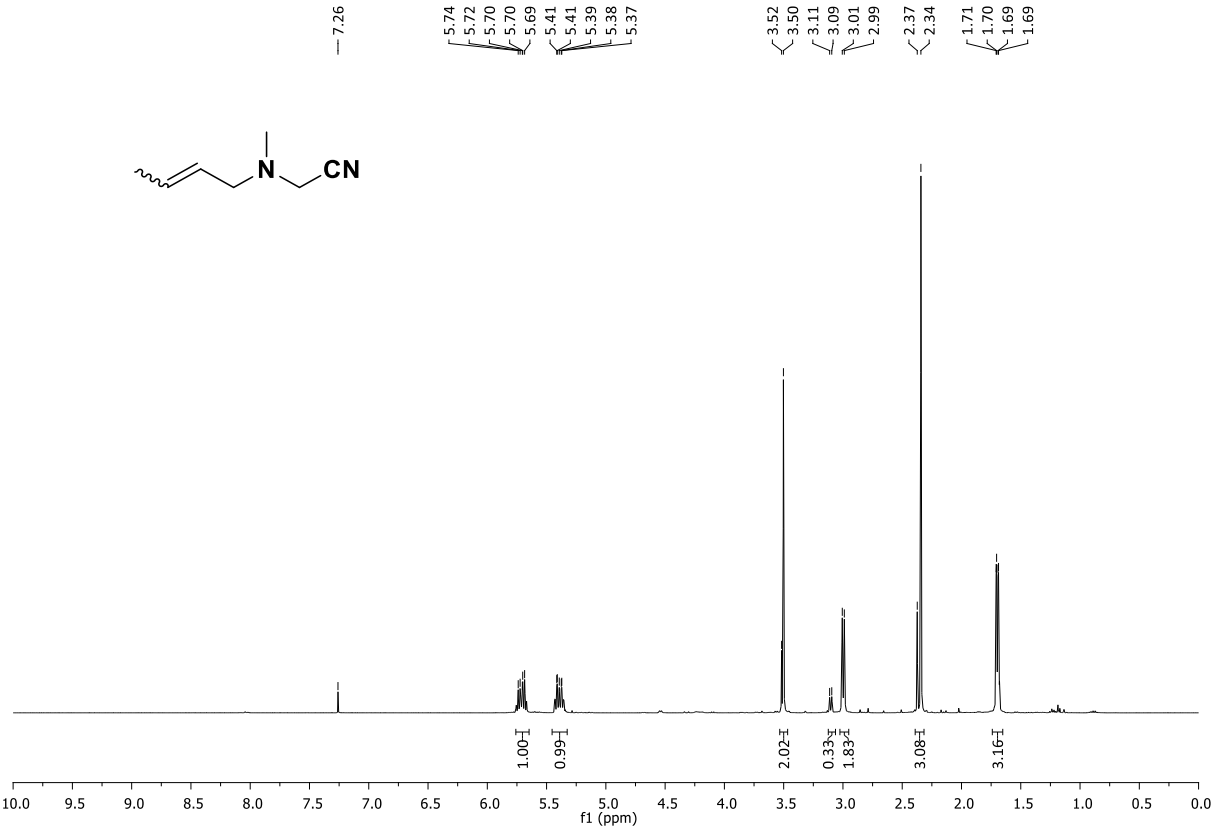


^{13}C NMR (101 MHz, $CDCl_3$)

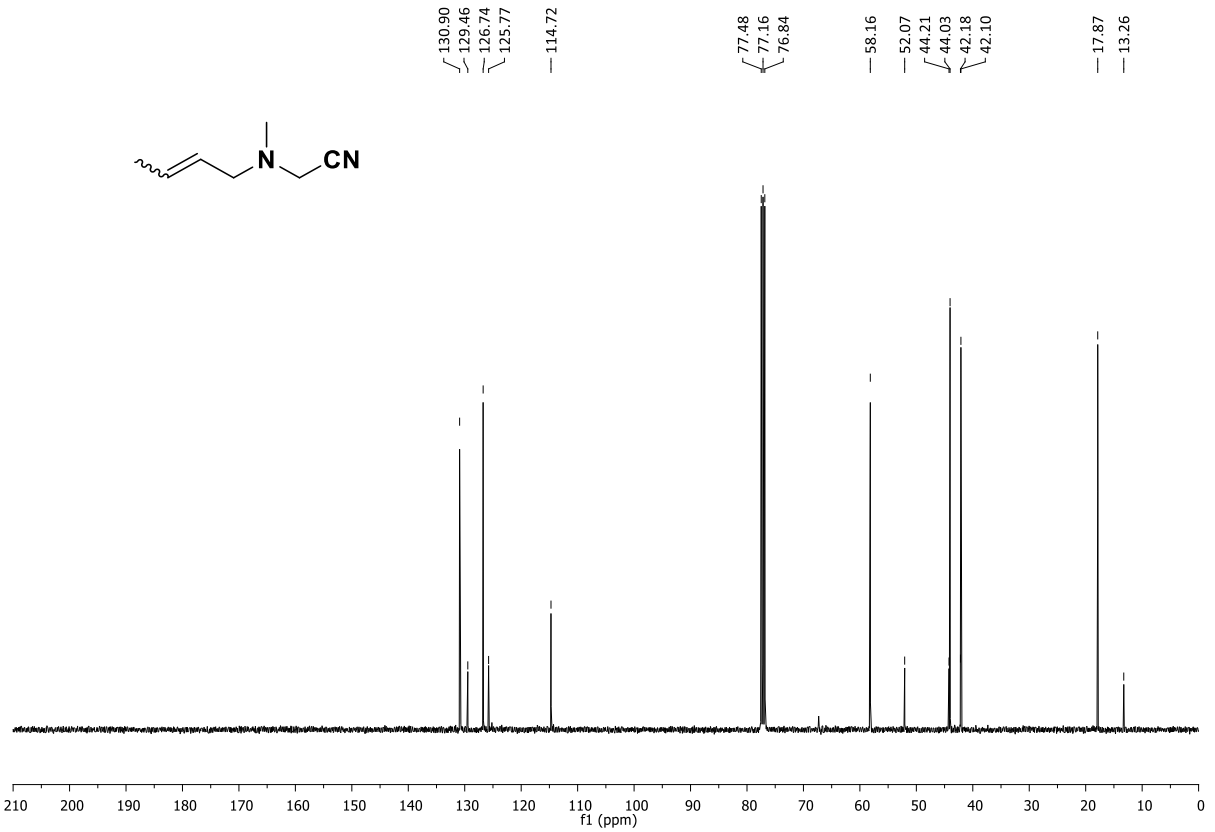


Compound 1d: *(E)-2-(but-2-en-1-yl(methyl)amino)acetonitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

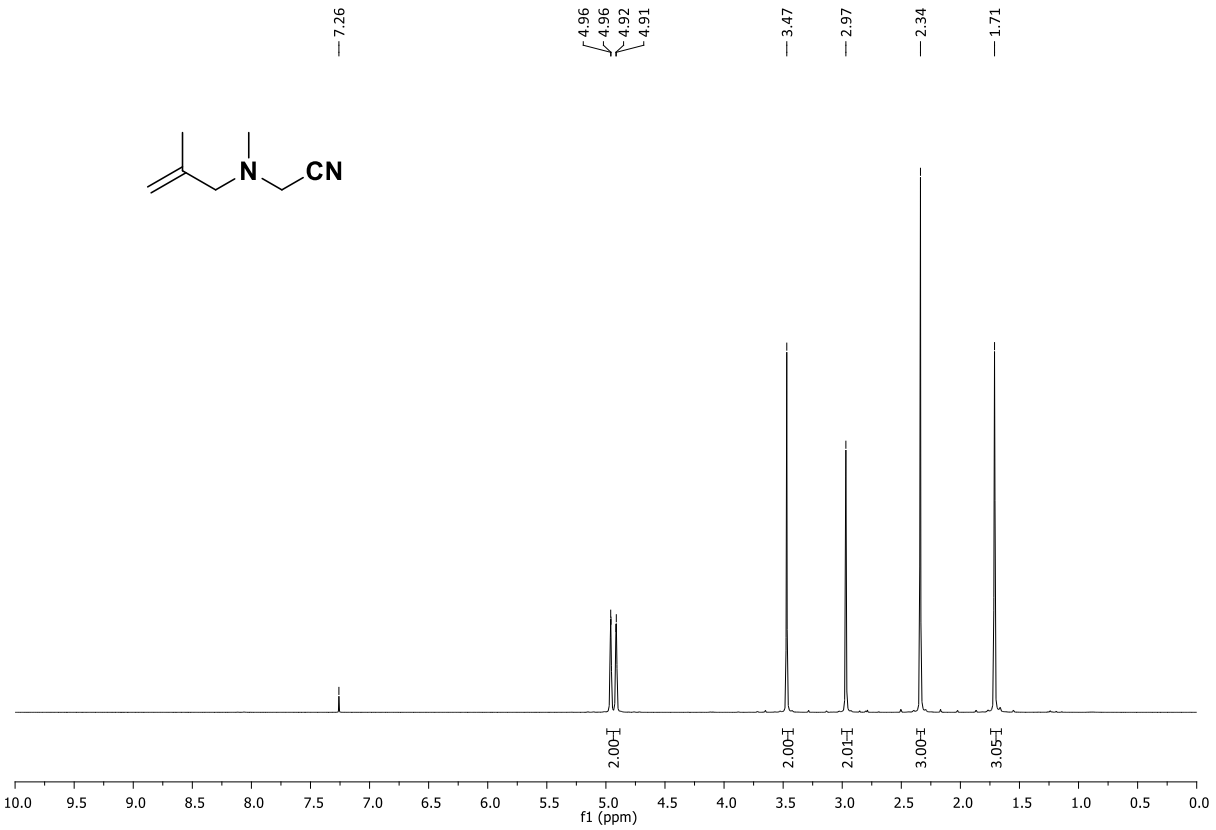


^{13}C NMR (101 MHz, $CDCl_3$)

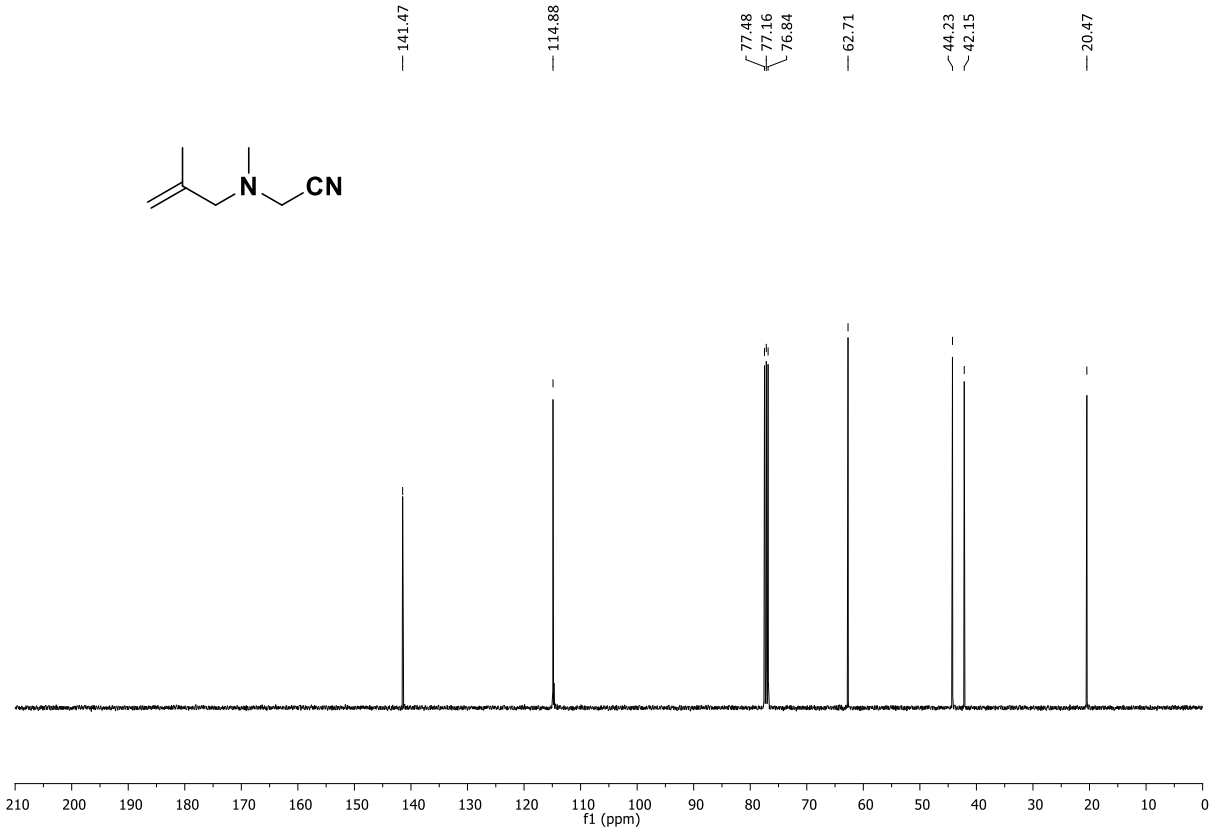


Compound 1e: *2-(methyl(2-methylallyl)amino)acetonitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

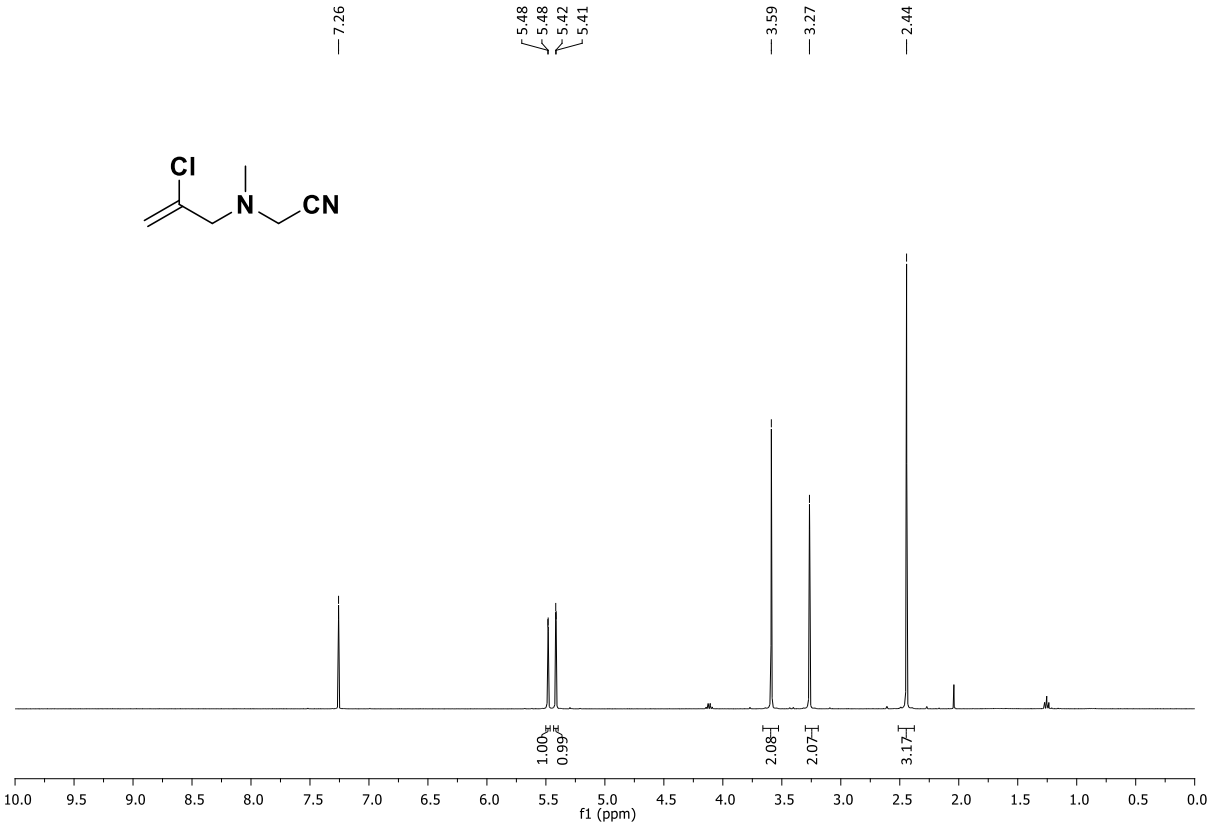


^{13}C NMR (101 MHz, $CDCl_3$)

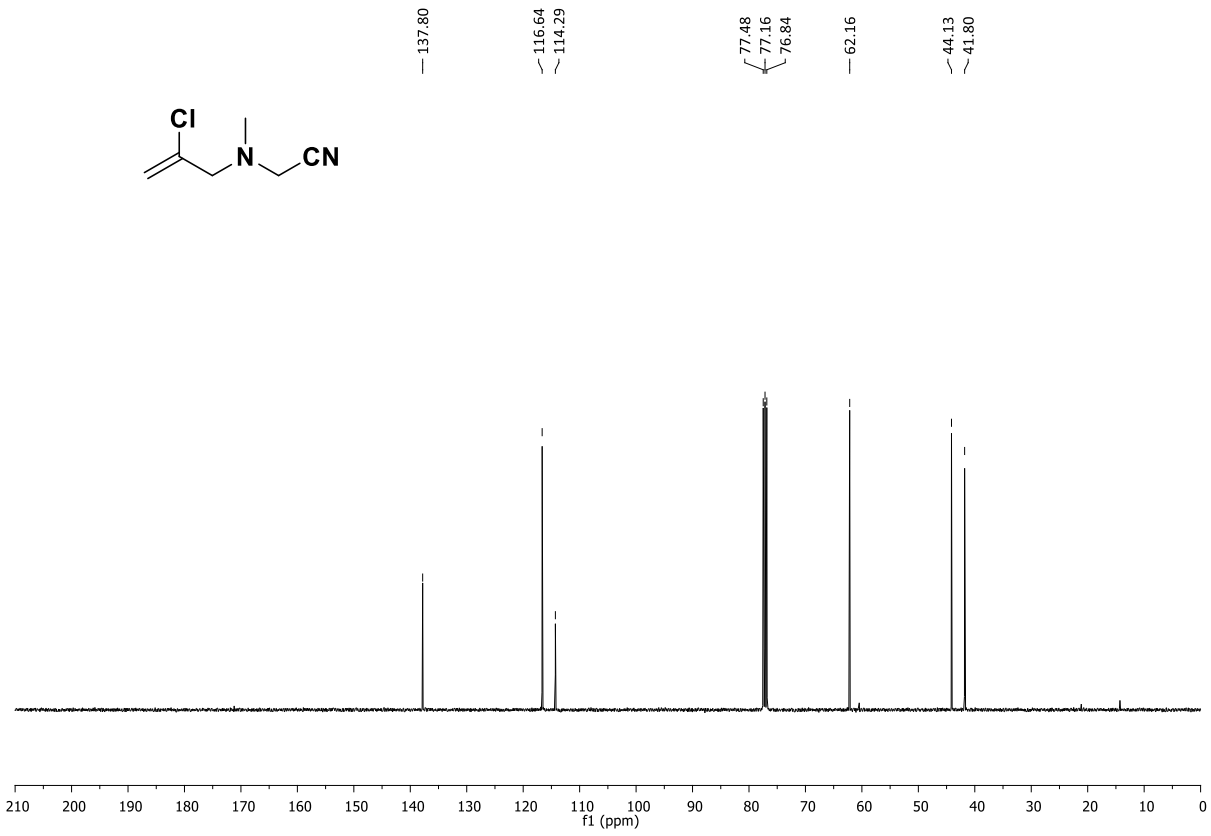


Compound 1f: *2-((2-chloroallyl)(methyl)amino)acetonitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

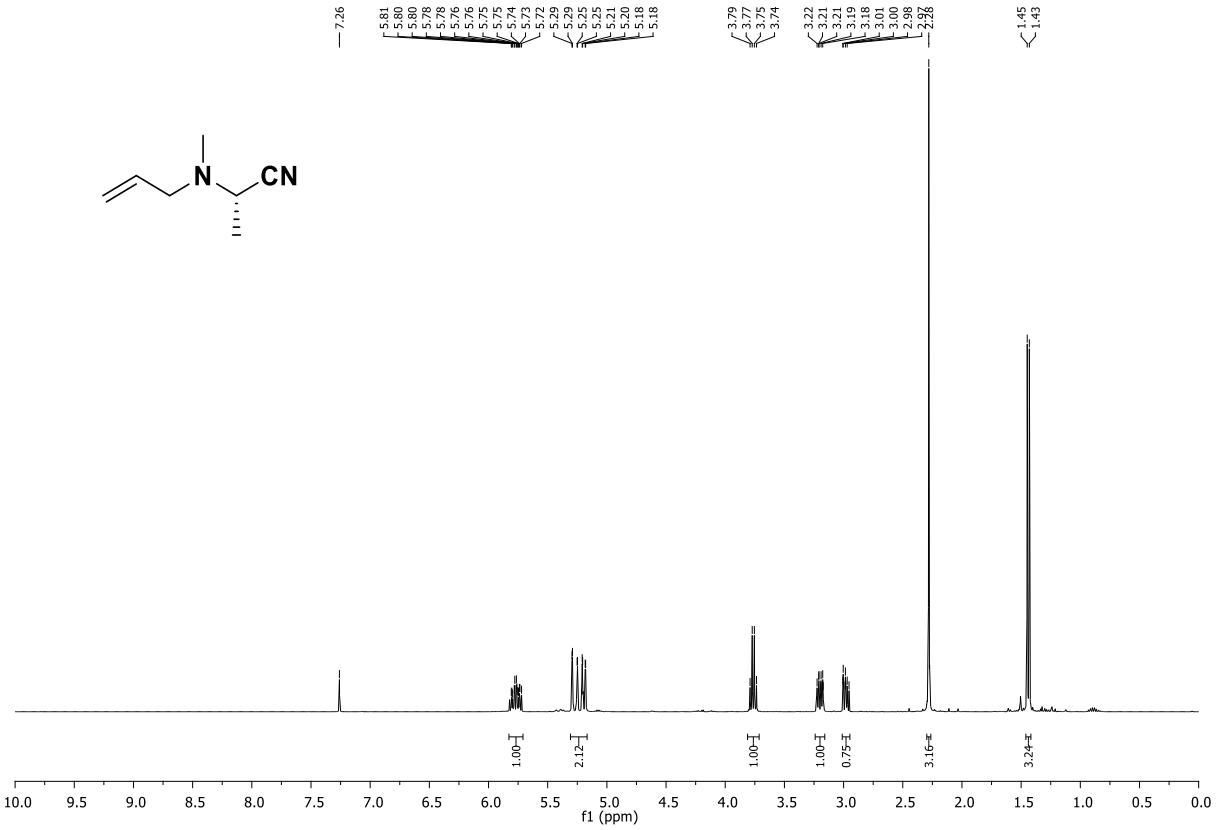


^{13}C NMR (101 MHz, $CDCl_3$)

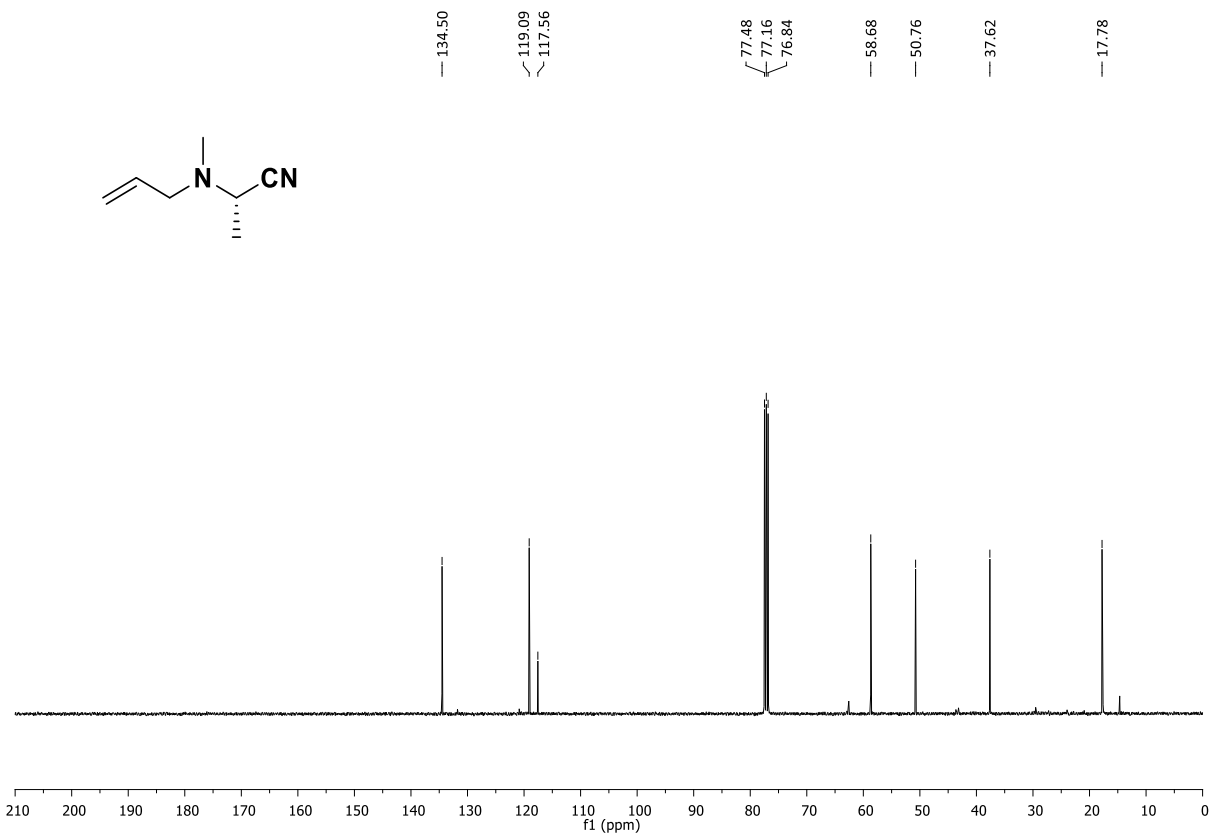


Compound 1h: *(S)-2-(allyl(methyl)amino)propanenitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

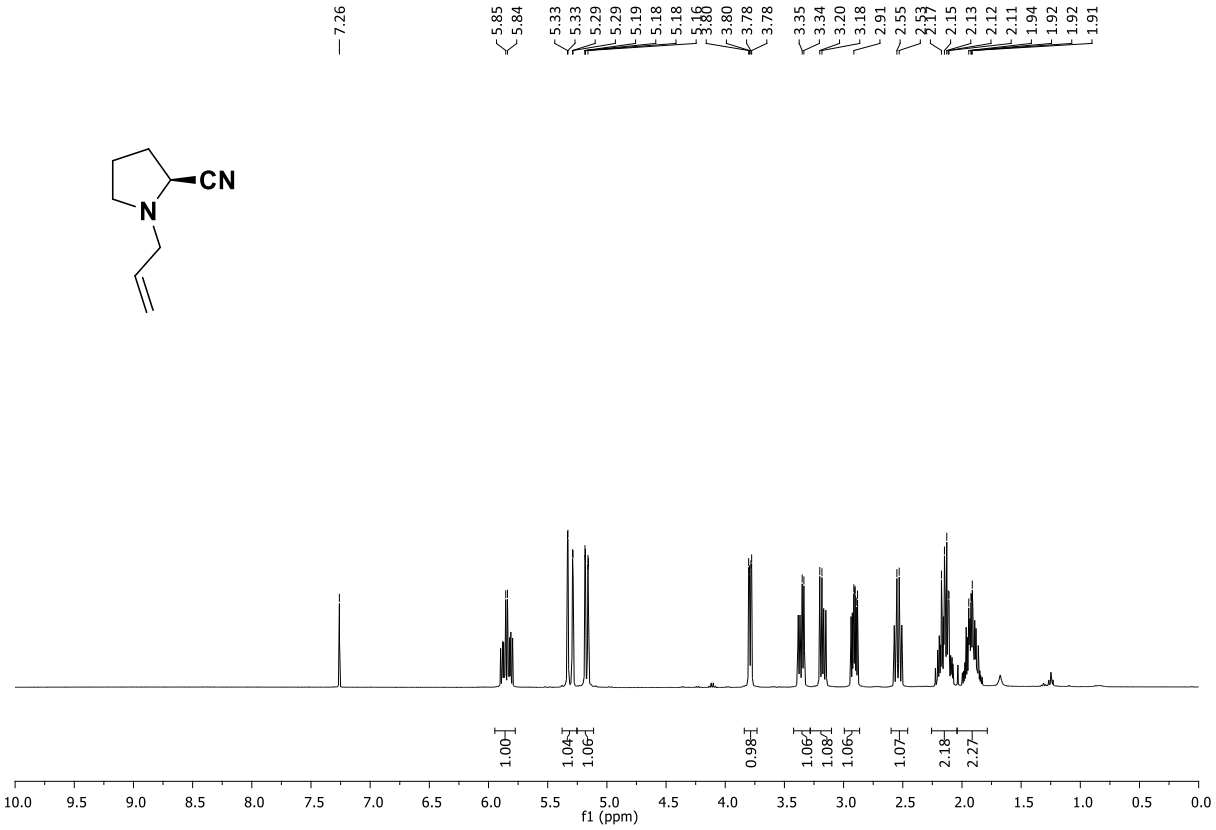


^{13}C NMR (101 MHz, $CDCl_3$)

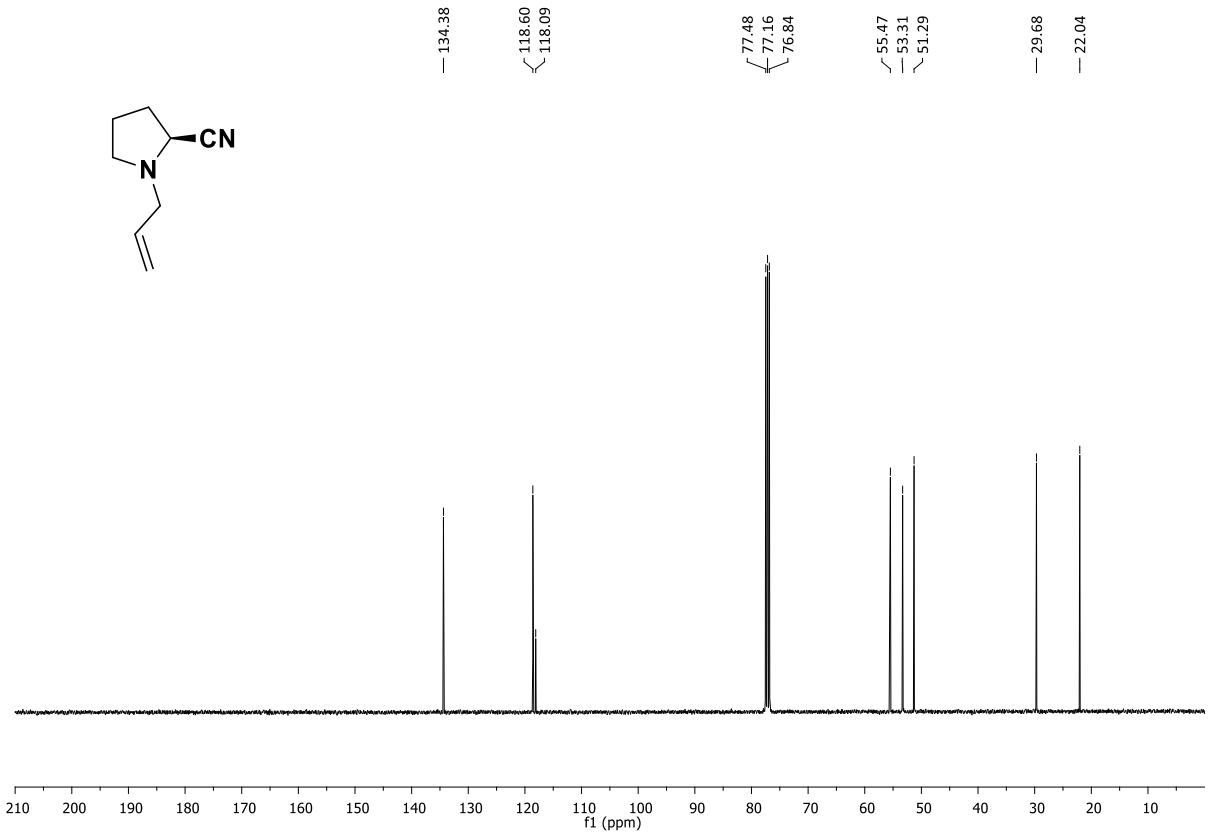


Compound 1j: *(S)-1-allylpyrrolidine-2-carbonitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

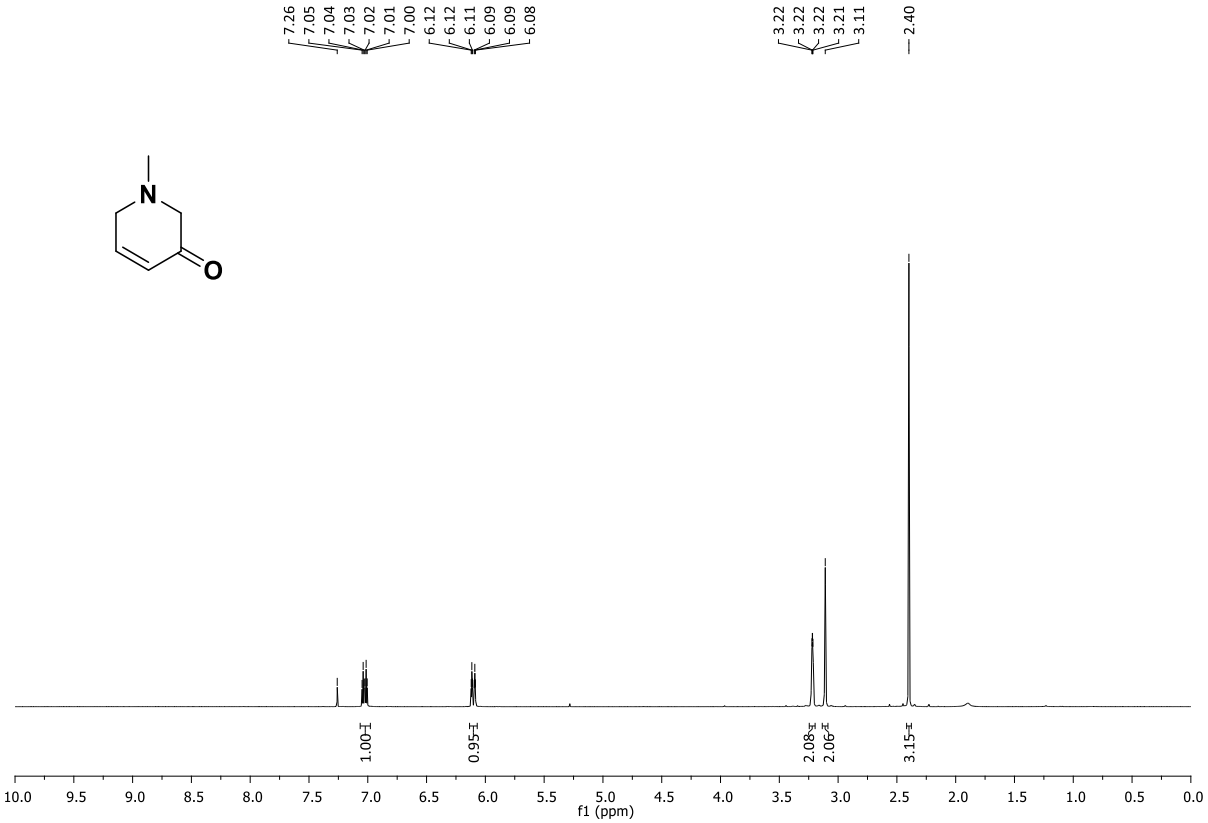


^{13}C NMR (101 MHz, $CDCl_3$)

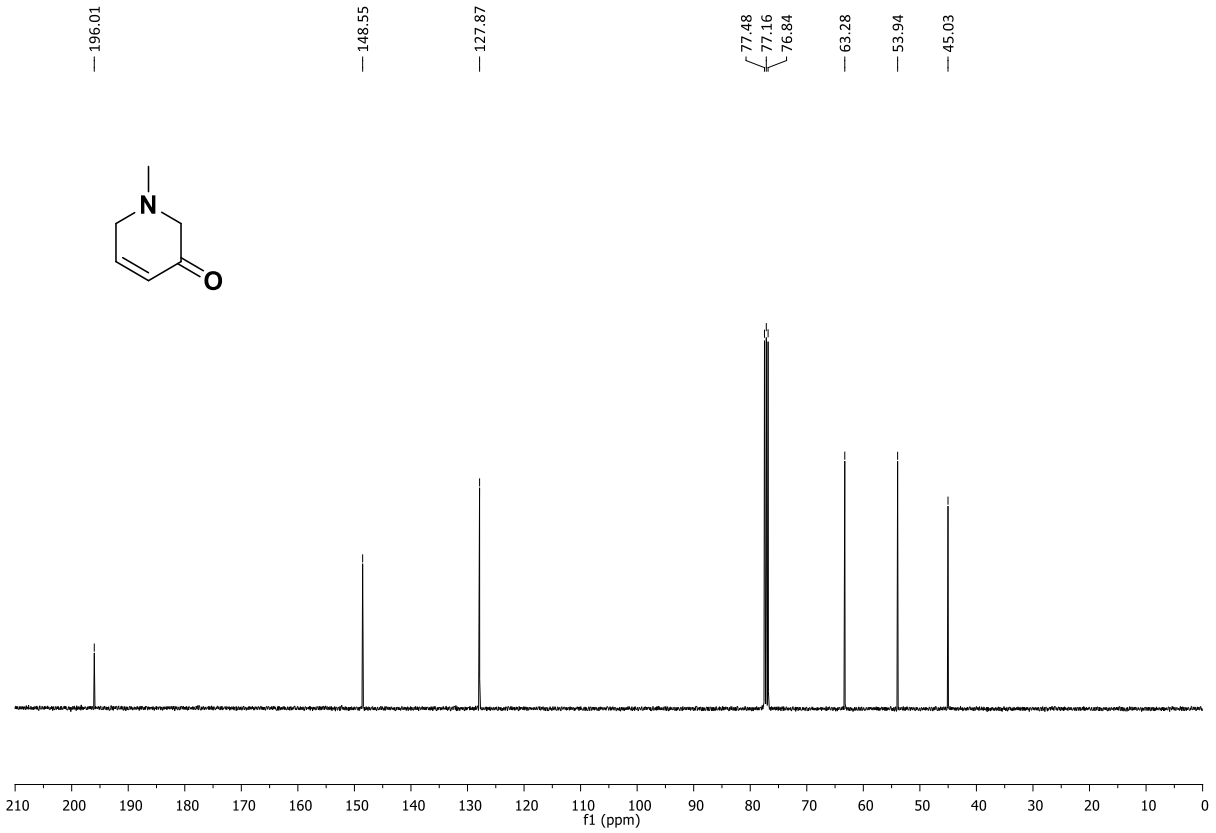


Compound 2a: *1-methyl-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

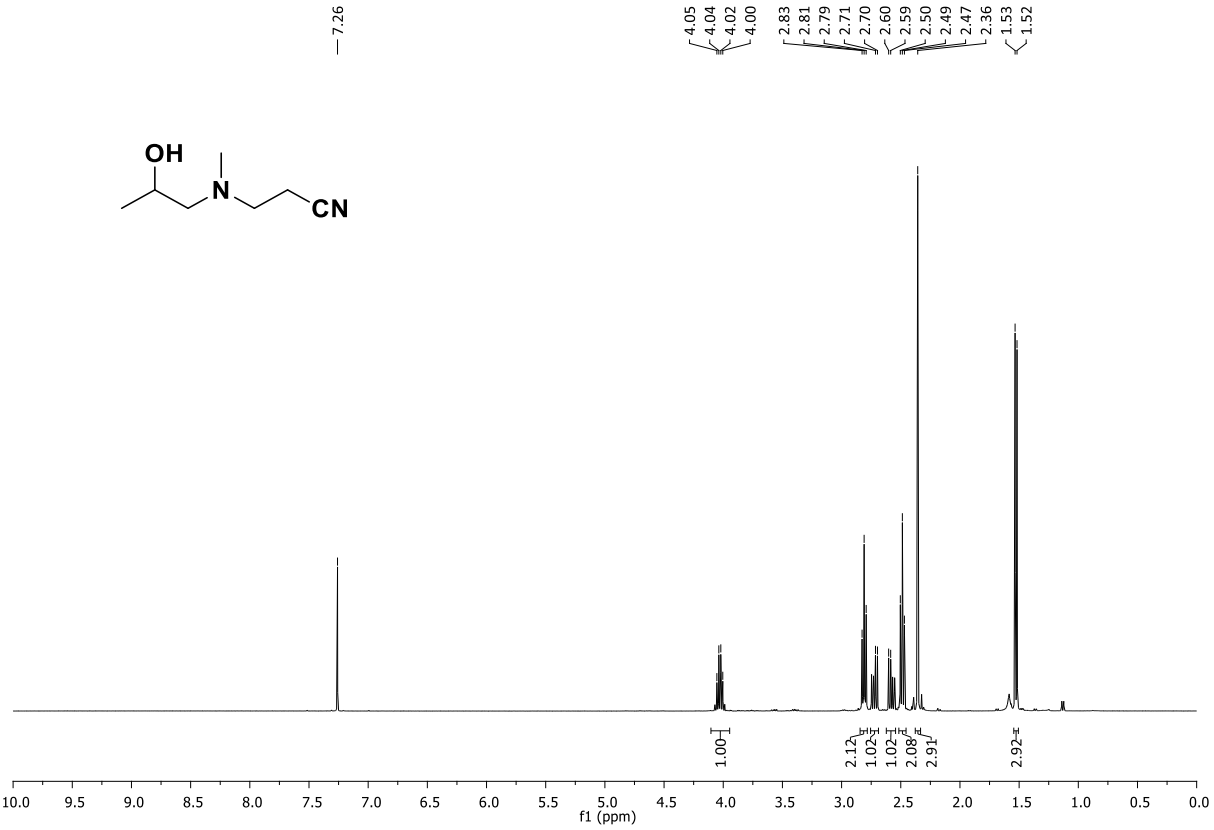


^{13}C NMR (101 MHz, $CDCl_3$)

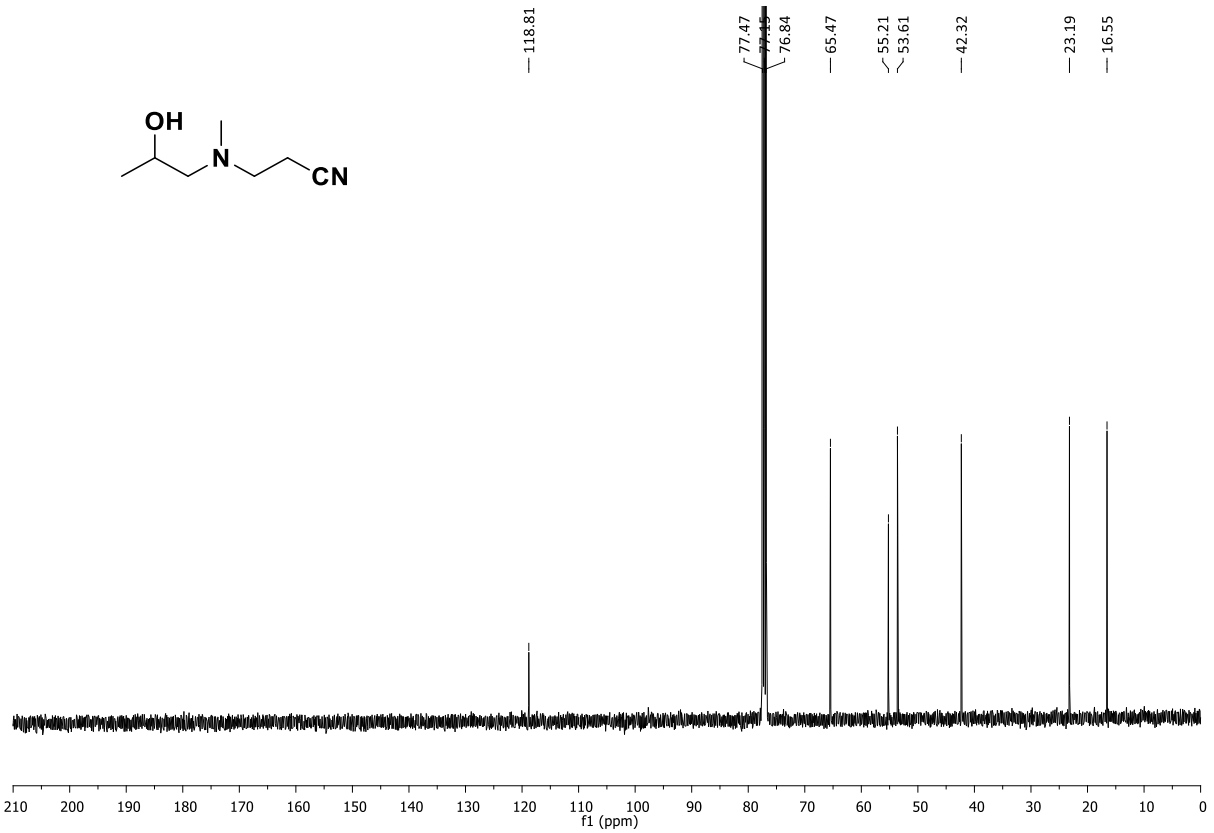


Compound $3b_{OH}$: *3-((2-hydroxypropyl)(methyl)amino)propanenitrile*

^{1}H NMR (400 MHz, $CDCl_3$)

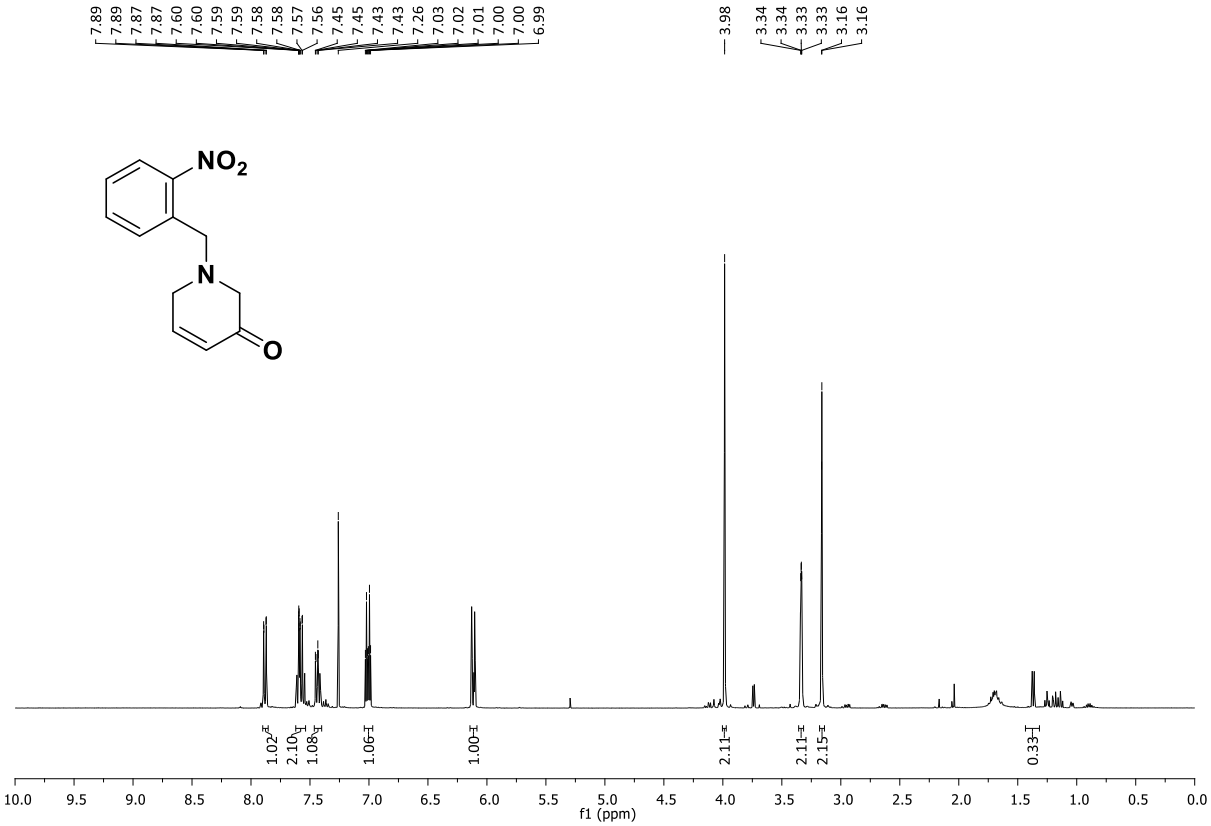


^{13}C NMR (101 MHz, $CDCl_3$)

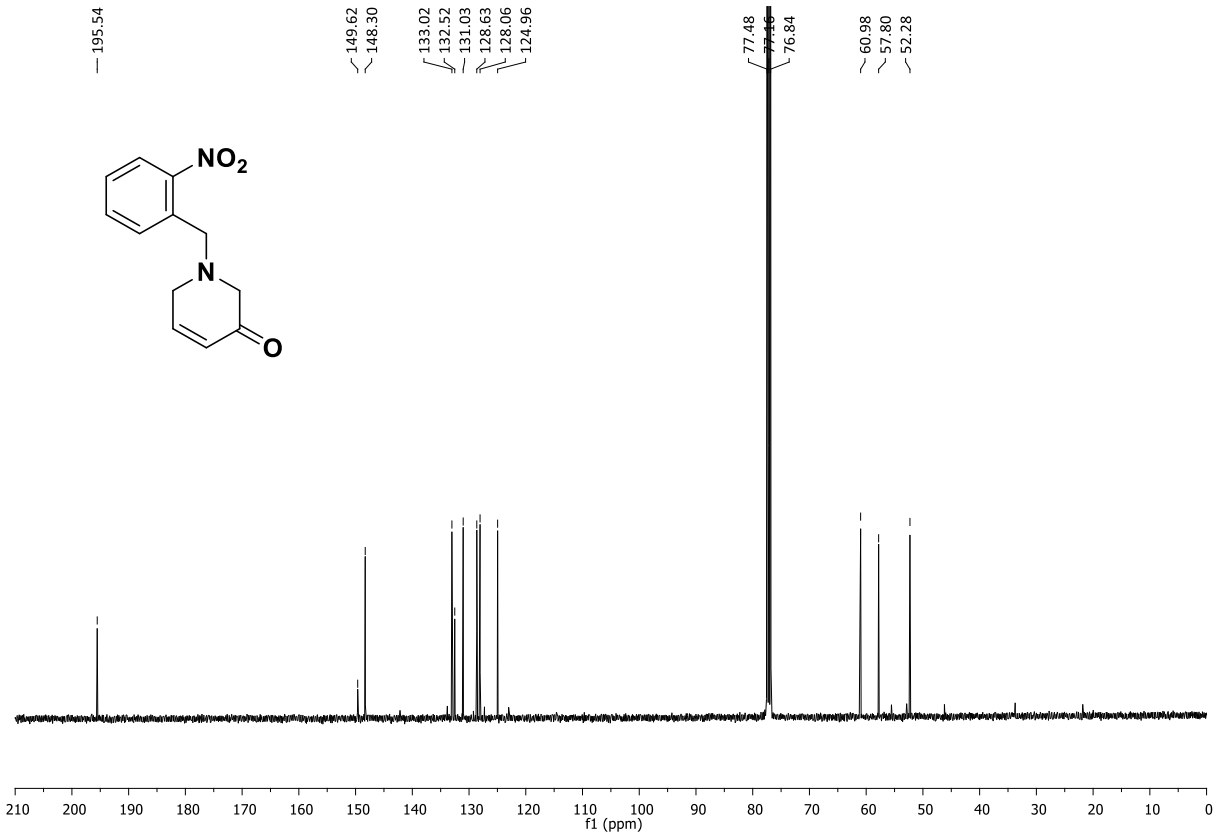


Compound 2c: *1-(2-nitrobenzyl)-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

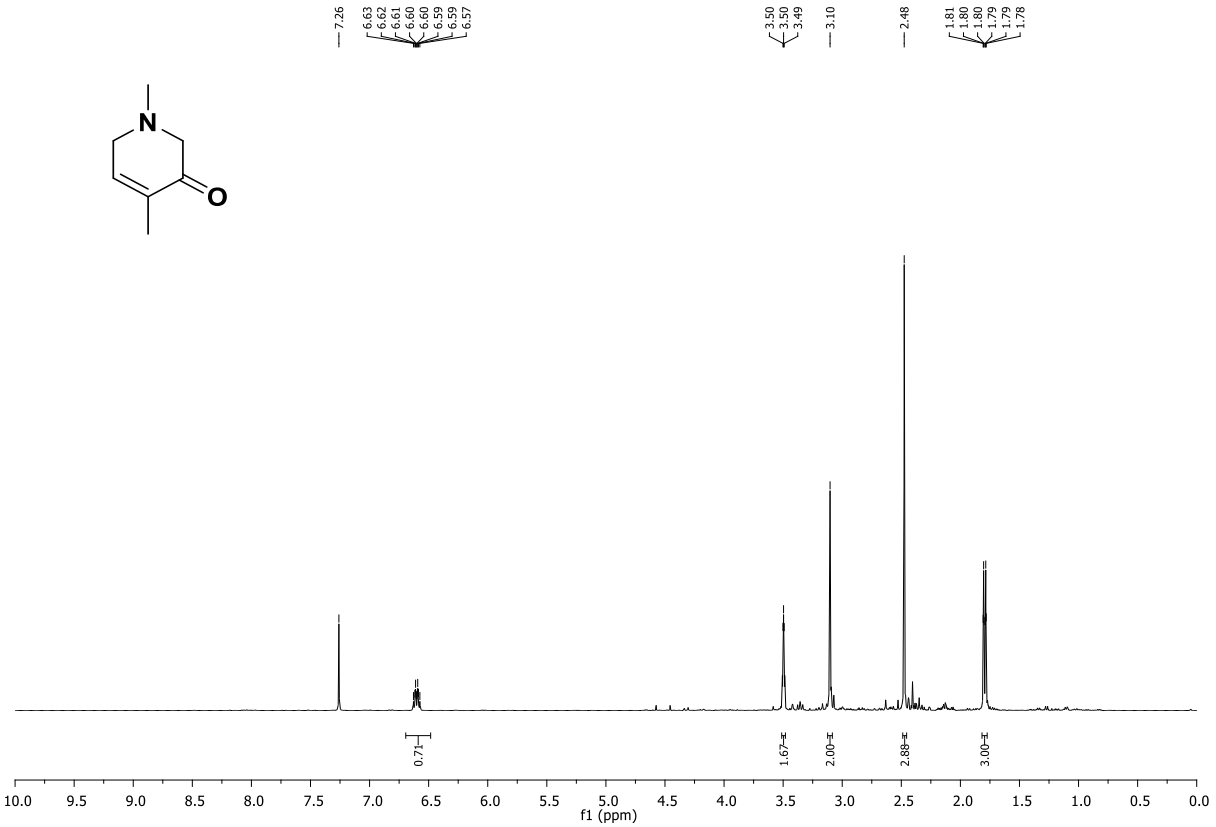


^{13}C NMR (101 MHz, $CDCl_3$)

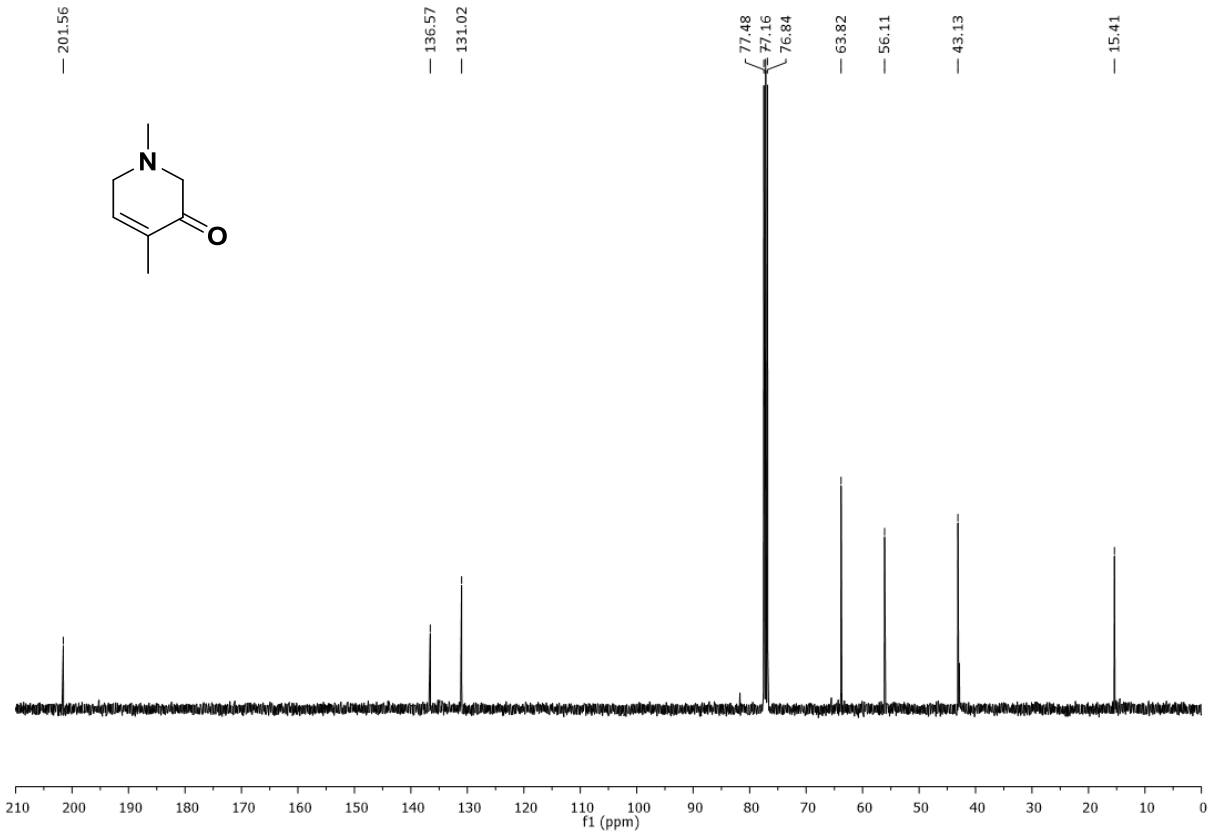


Compound 2d: *1,4-dimethyl-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

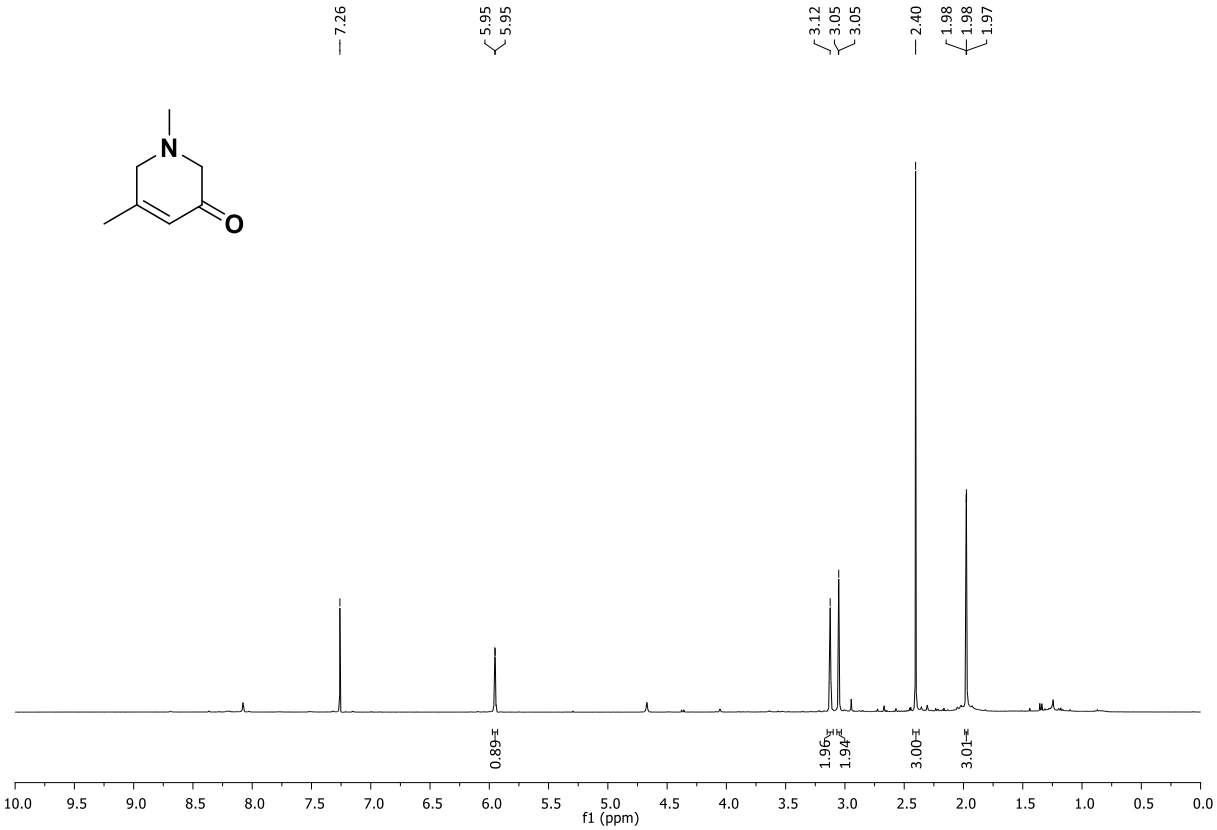


^{13}C NMR (101 MHz, $CDCl_3$)

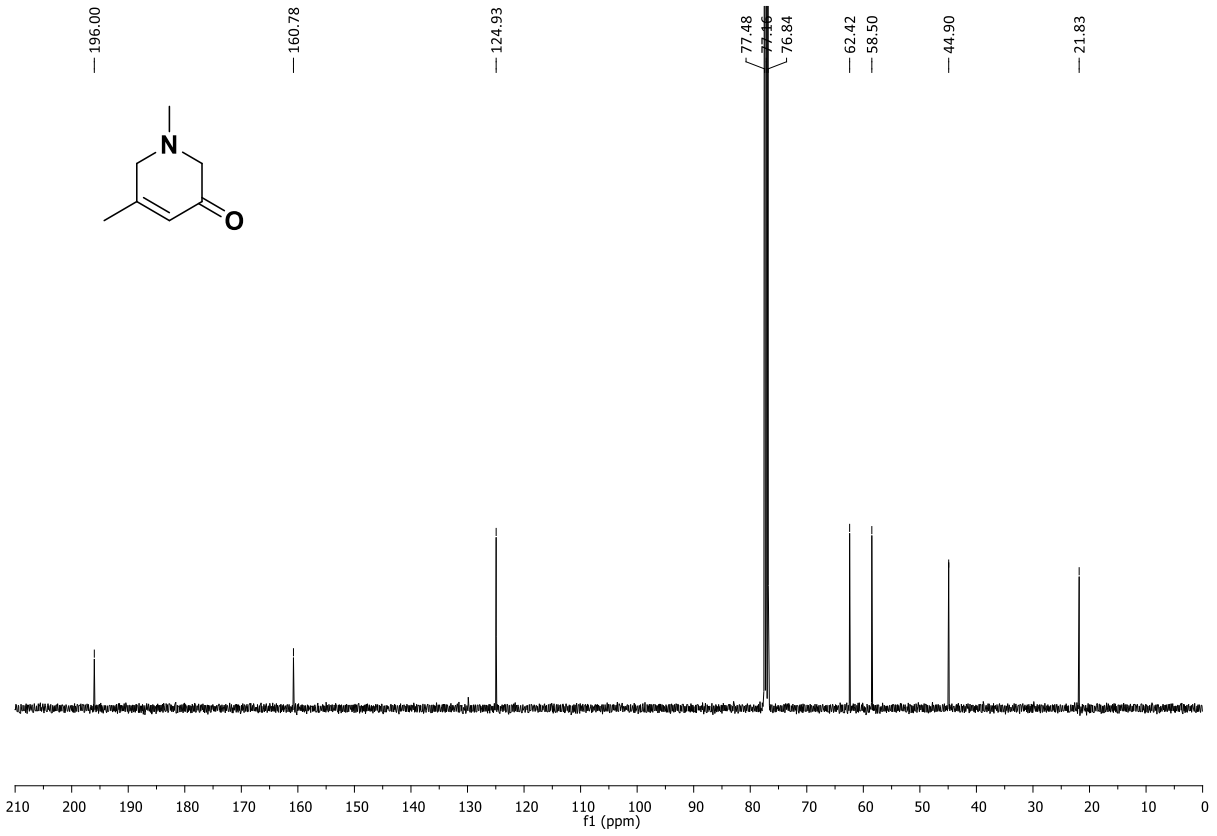


Compound 2e: *1,5-dimethyl-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

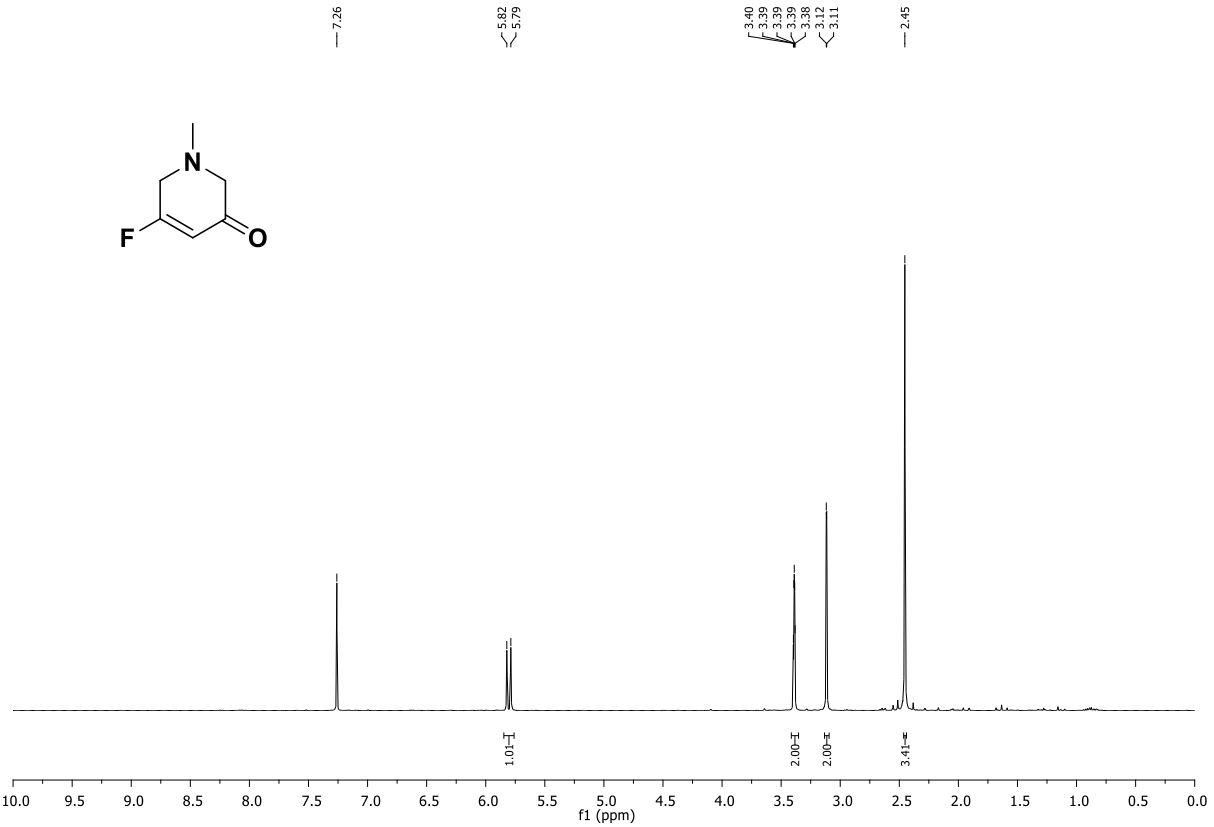


^{13}C NMR (101 MHz, $CDCl_3$)

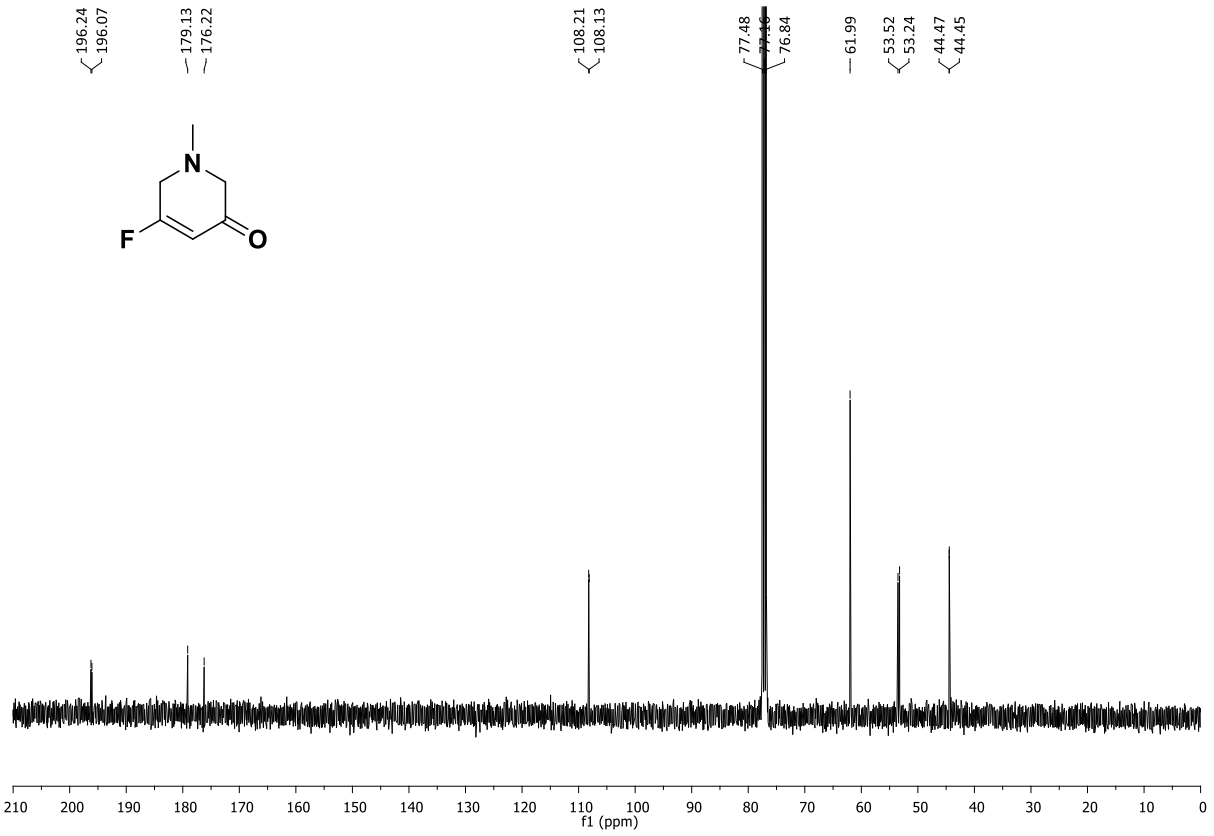


Compound 2f$_F$: *5-fluoro-1-methyl-1,6-dihydropyridin-3(2H)-one*

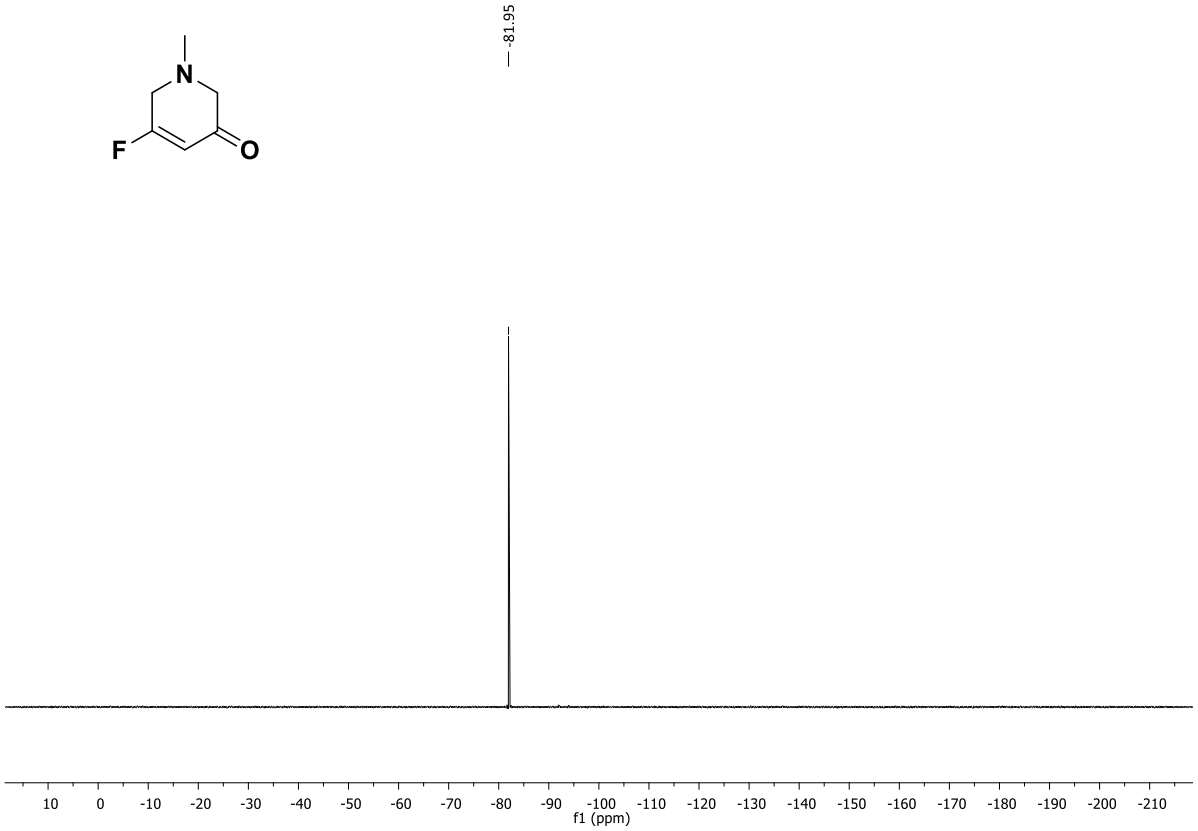
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

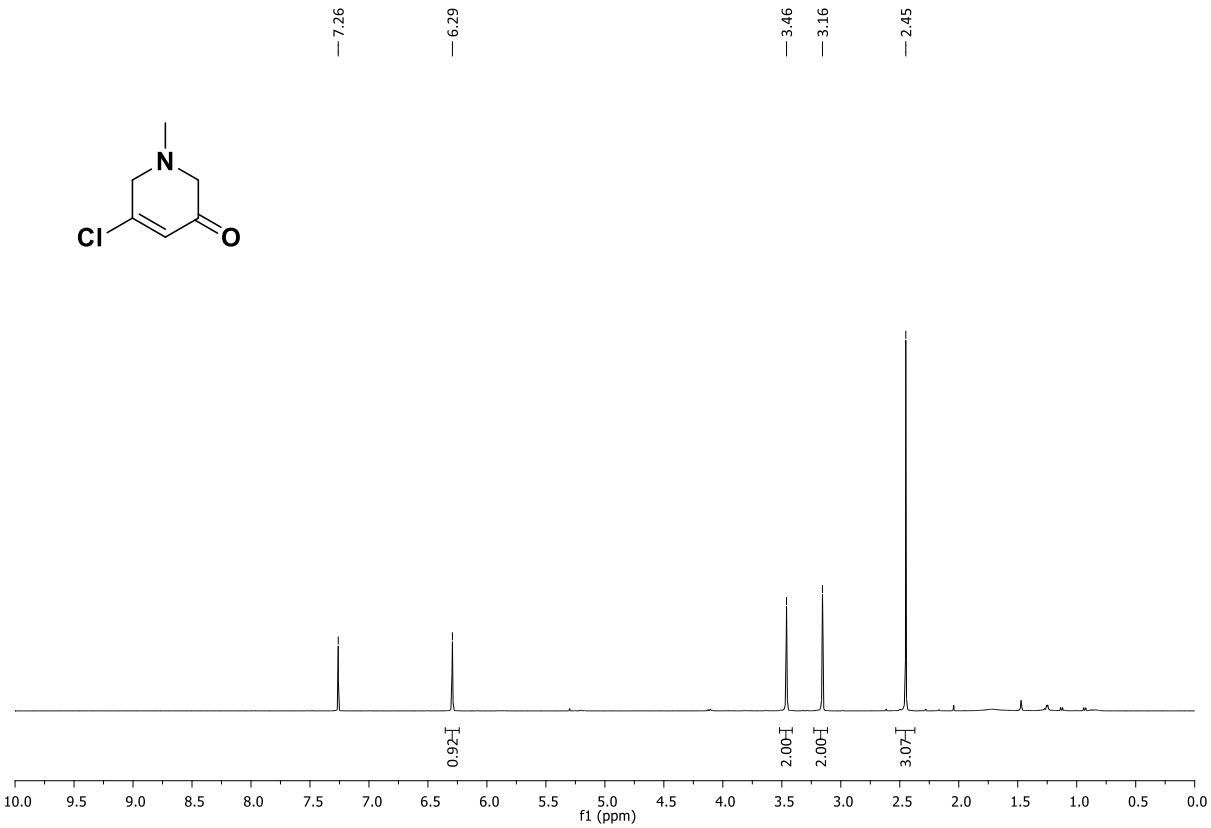


^{19}F {^{1}H} NMR (376 MHz, $CDCl_3$)

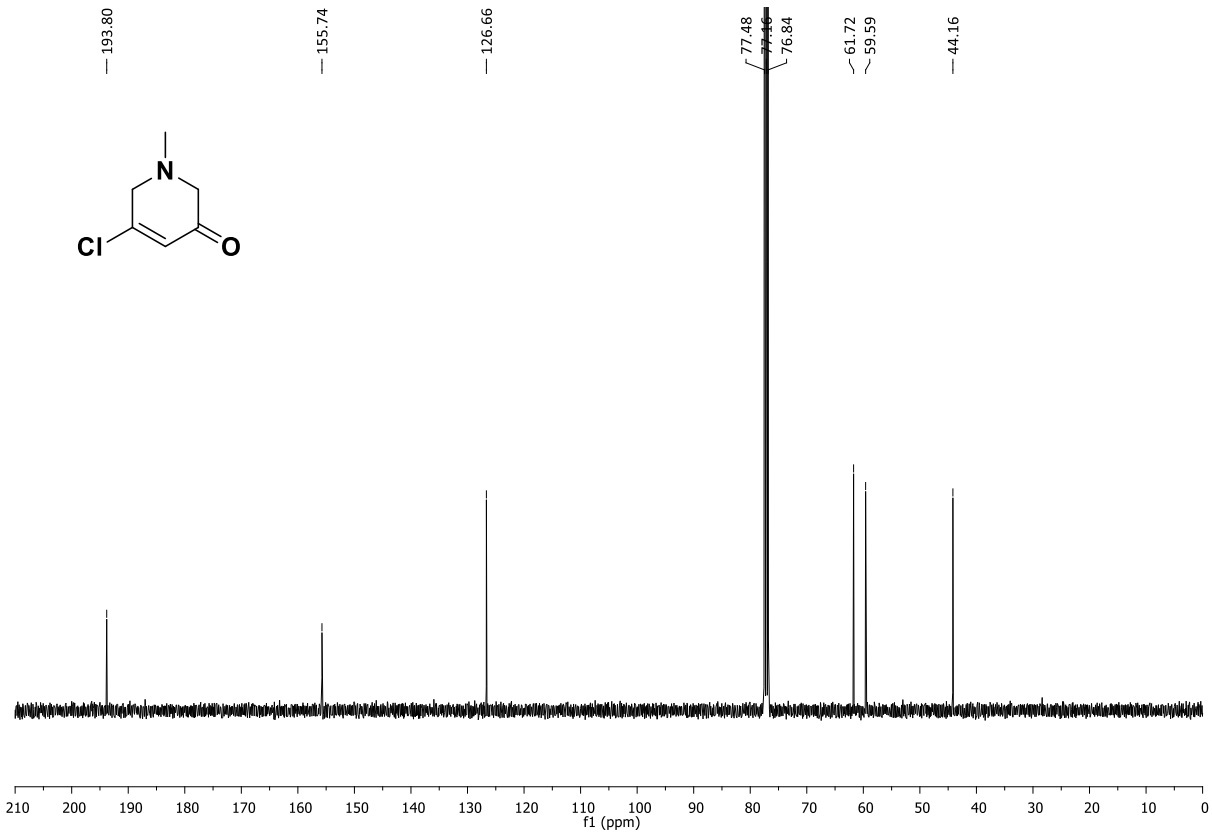


Compound 2f$_{Cl}$: *5-chloro-1-methyl-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

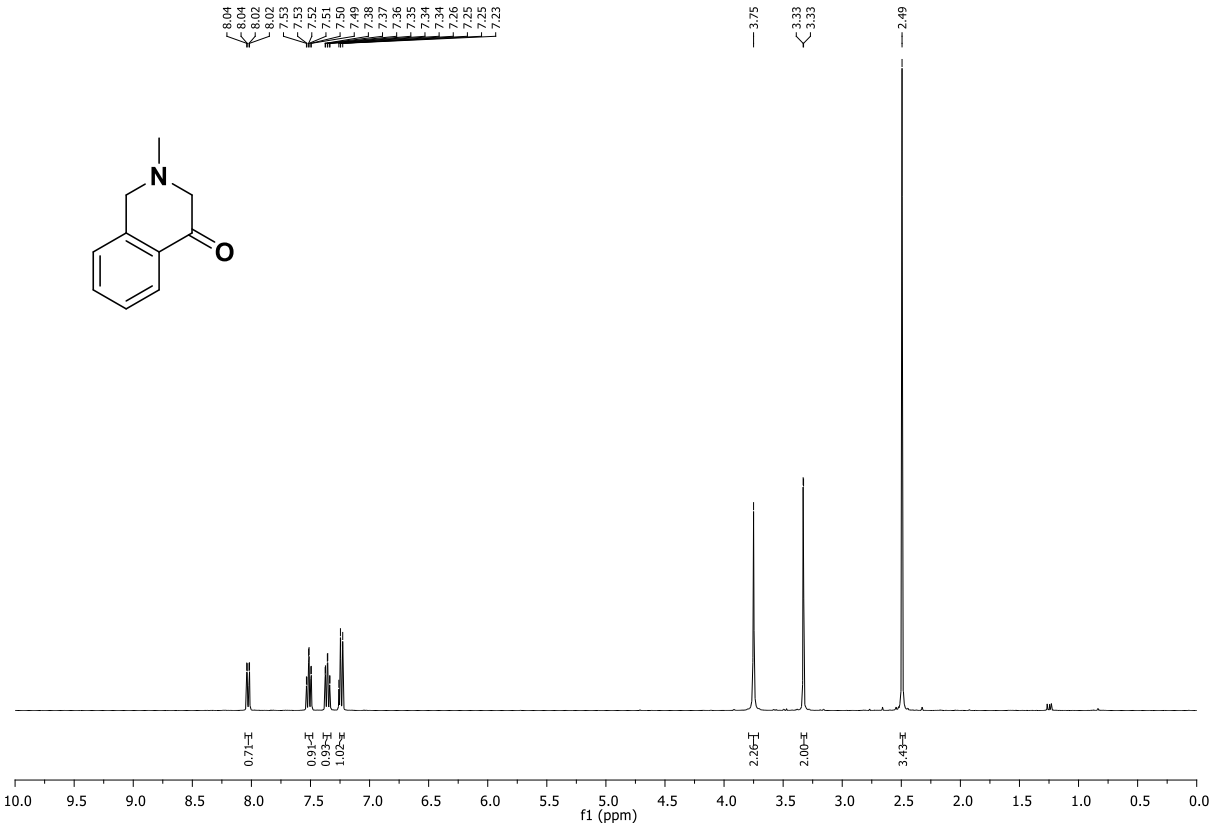


^{13}C NMR (101 MHz, $CDCl_3$)

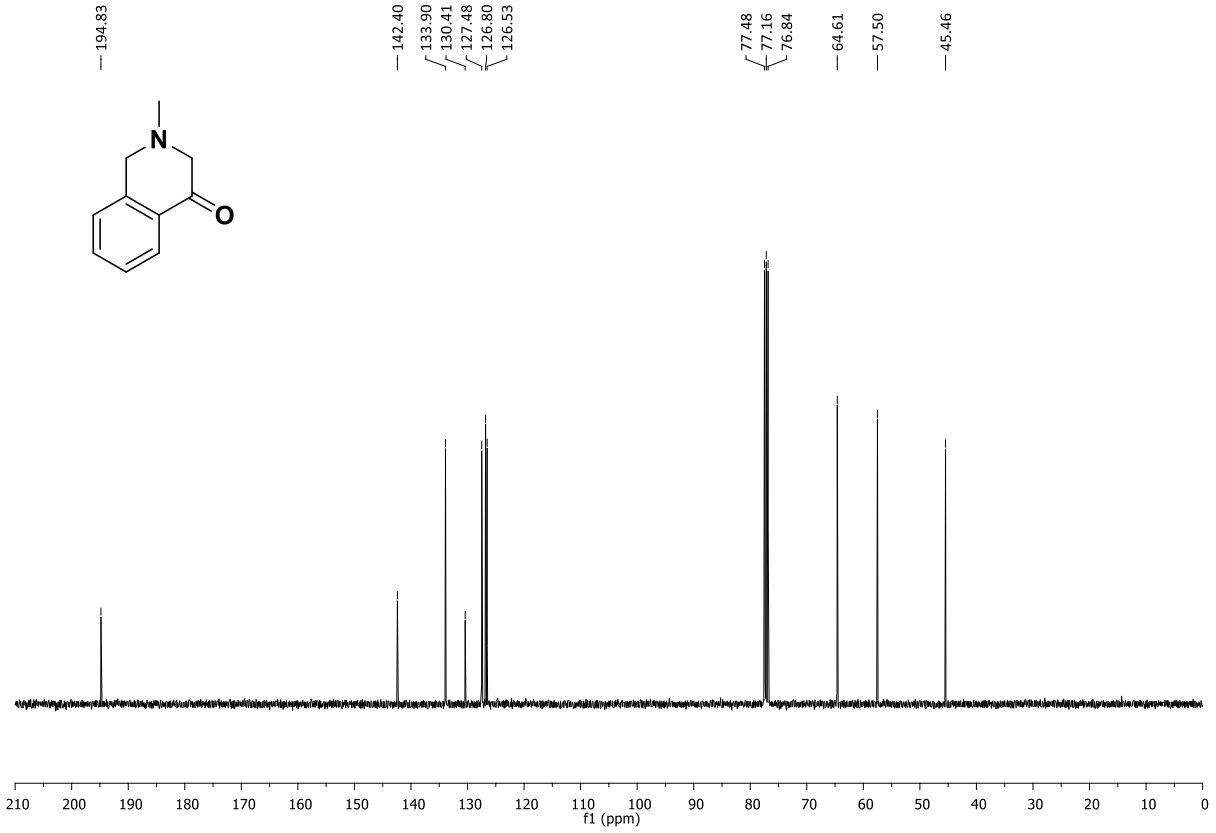


Compound 2g: *2-methyl-2,3-dihydroisoquinolin-4(1H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

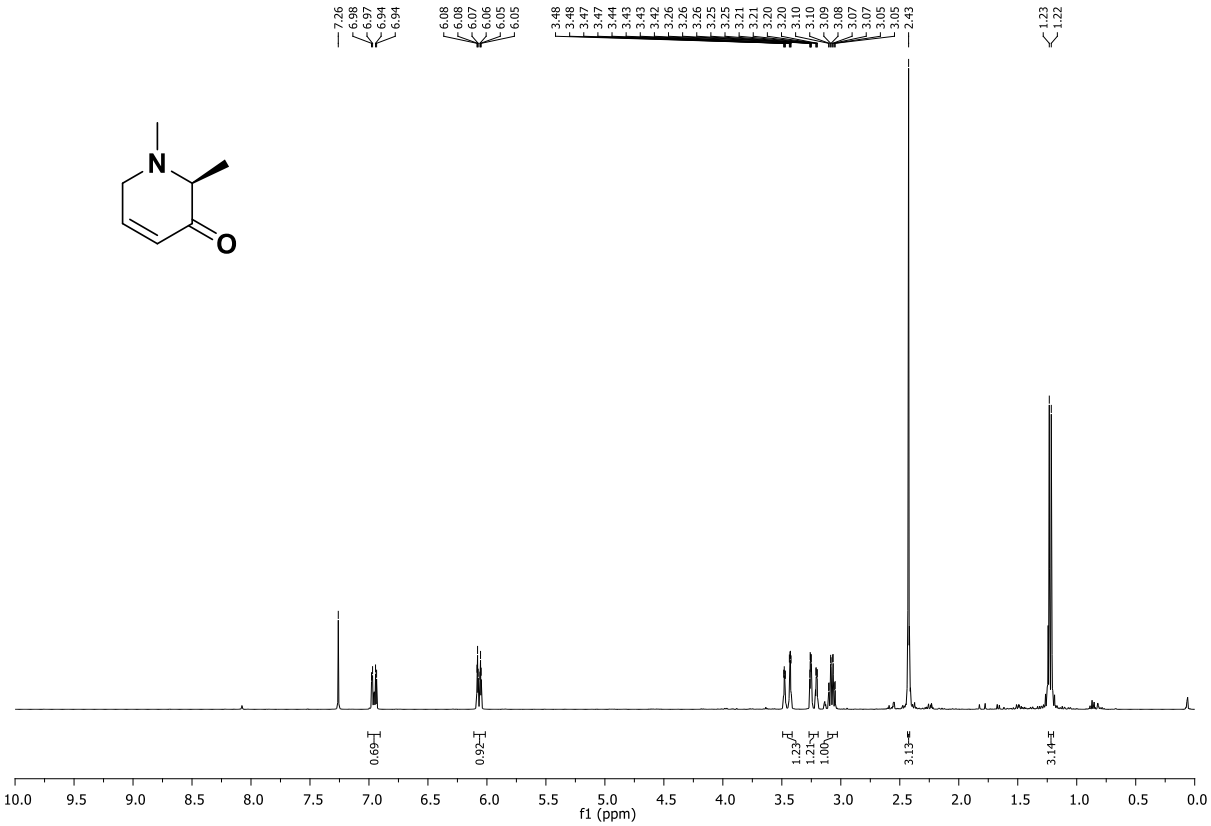


^{13}C NMR (101 MHz, $CDCl_3$)

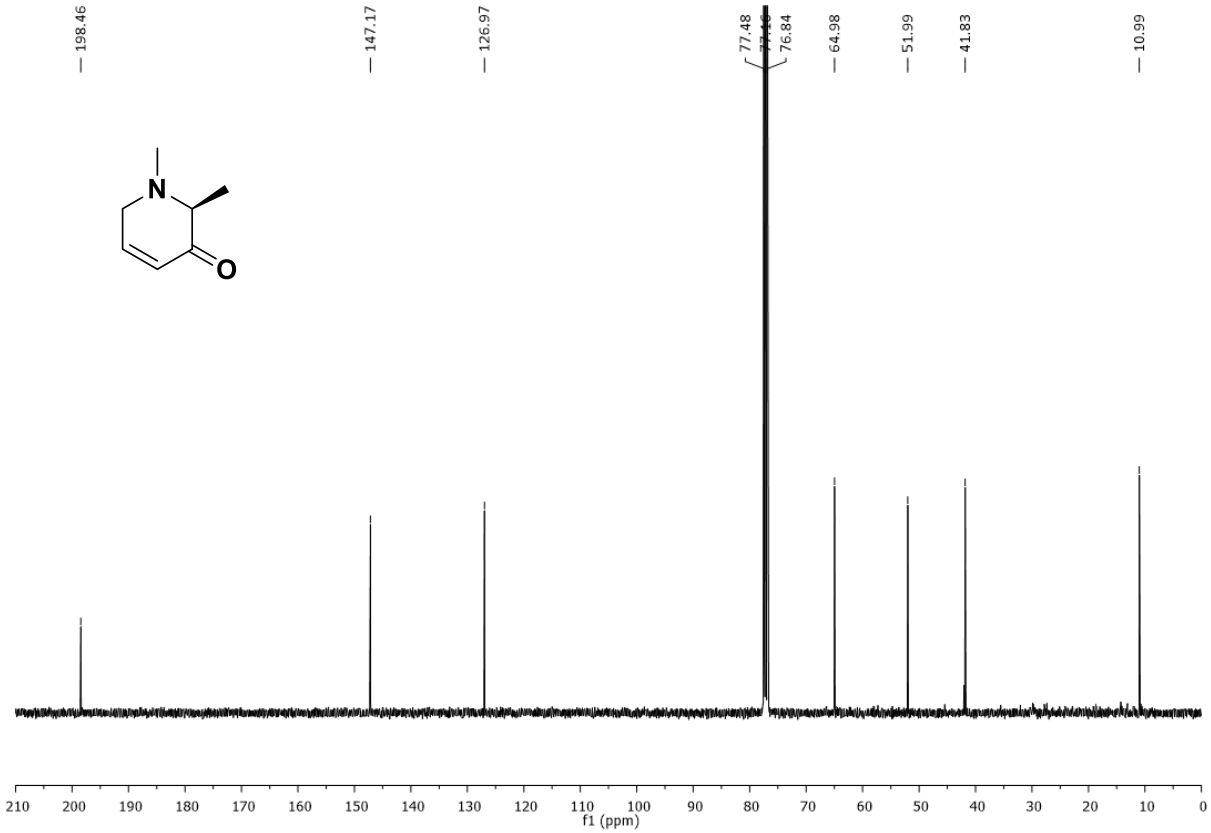


Compound 2h: *(S)-1,2-dimethyl-1,6-dihydropyridin-3(2H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)

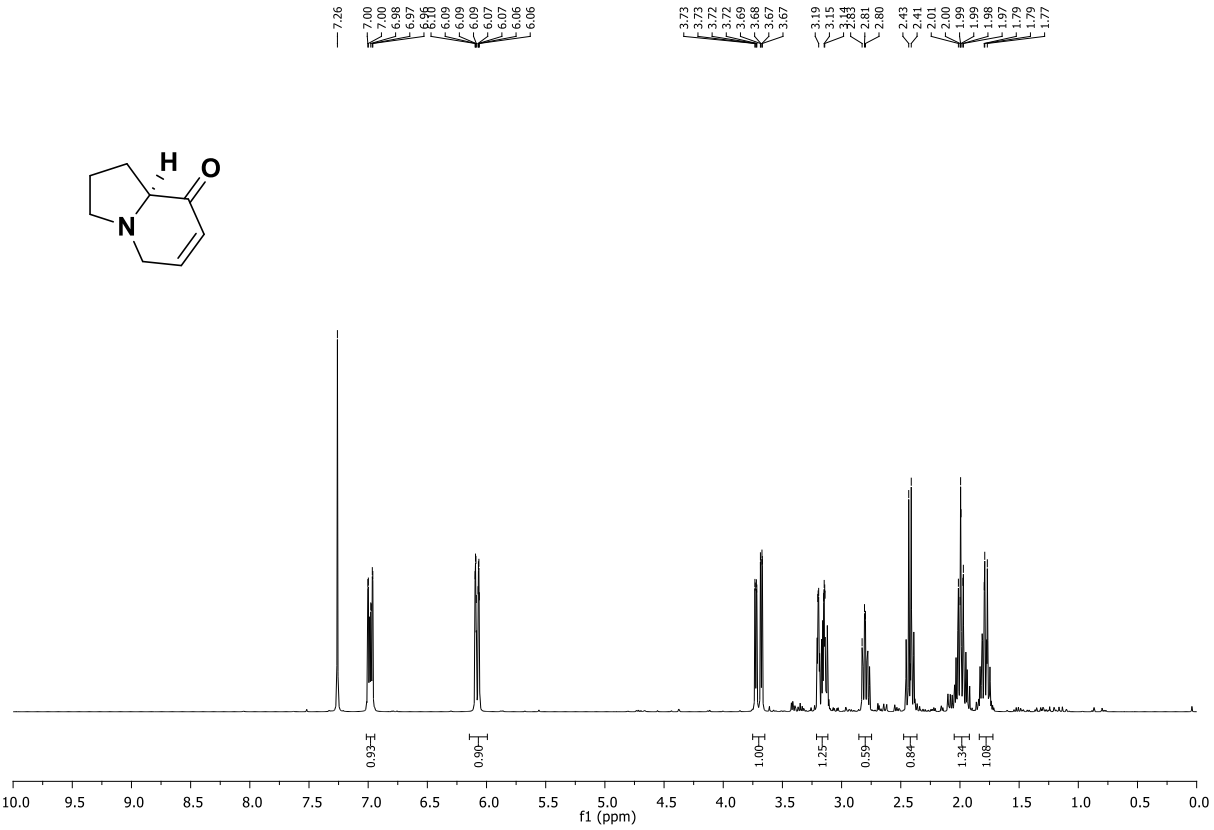


^{13}C NMR (101 MHz, $CDCl_3$)

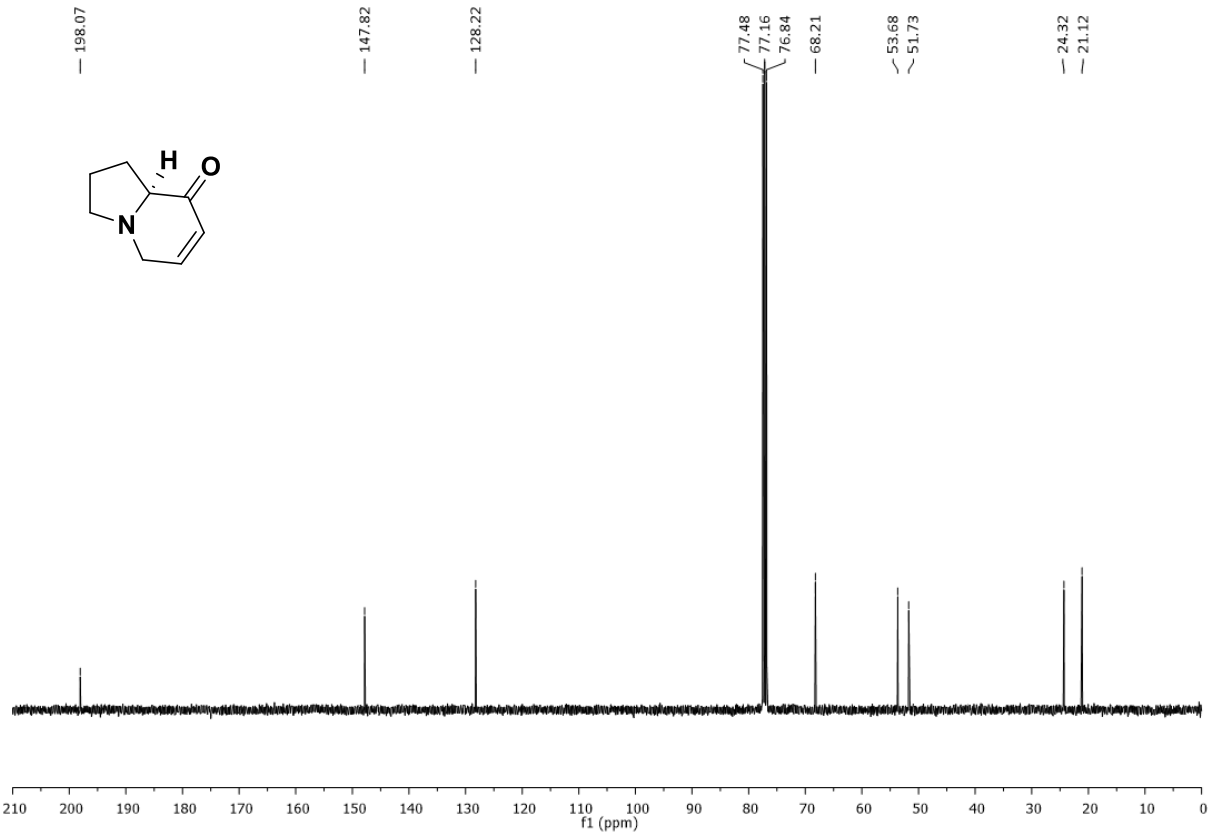


Compound 2j: *(S)-1,2,3,8a-tetrahydroindolizin-8(5H)-one*

^{1}H NMR (400 MHz, $CDCl_3$)



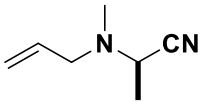
^{13}C NMR (101 MHz, $CDCl_3$)



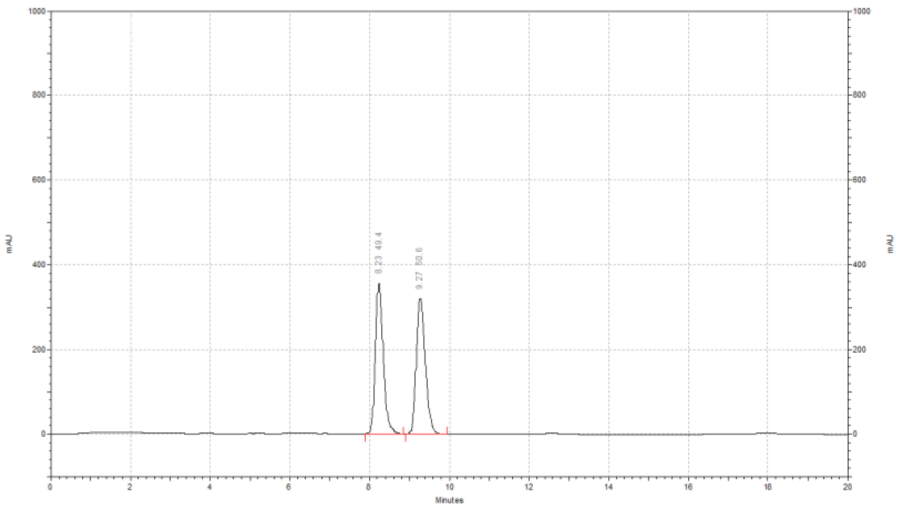
5. HPLC traces

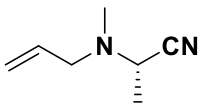
(S)-2-(allyl(methyl)amino)propanenitrile **1h**

HPLC conditions: Chiralpak OD-H, Hexane/isopropanol 98/2, 1 mL/min, 20 °C, 215 nm, t_r1 = 8.23 min, t_r2 = 9.27 min.

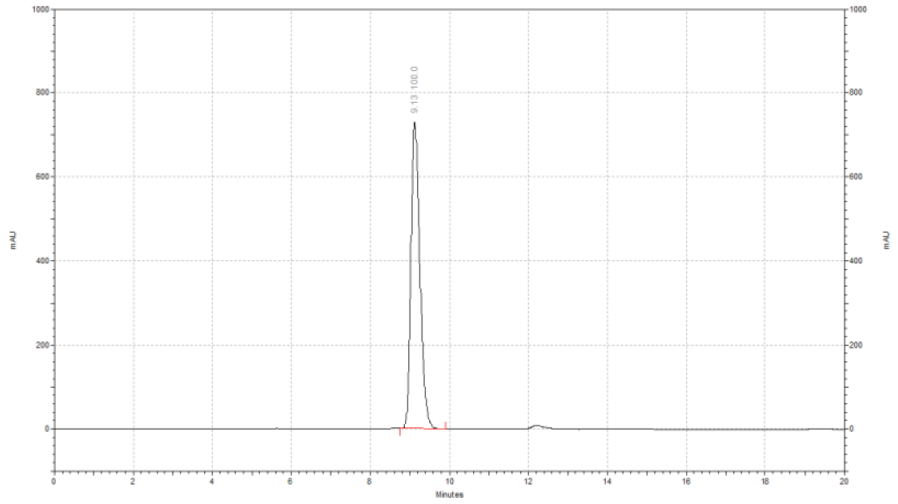


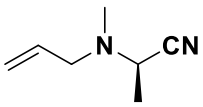
rac



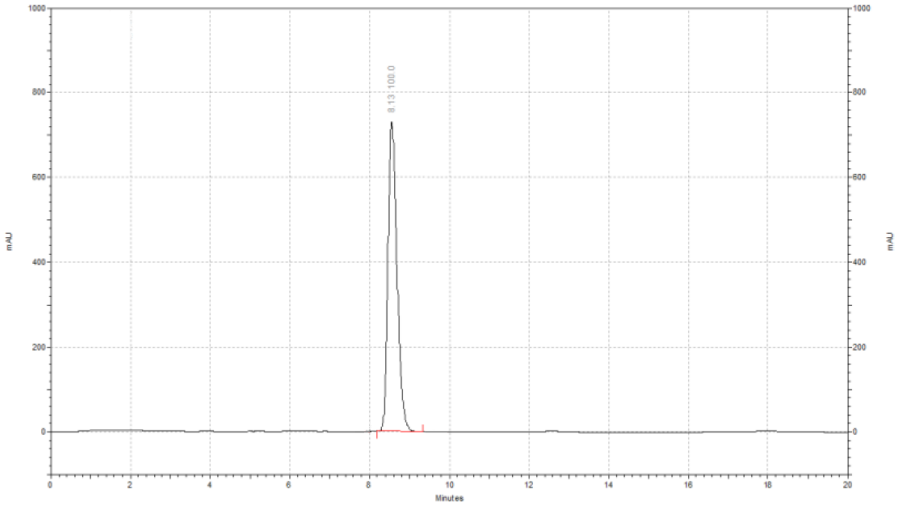


1h, >99% ee



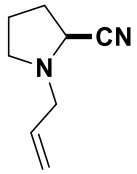


1i, >99% ee

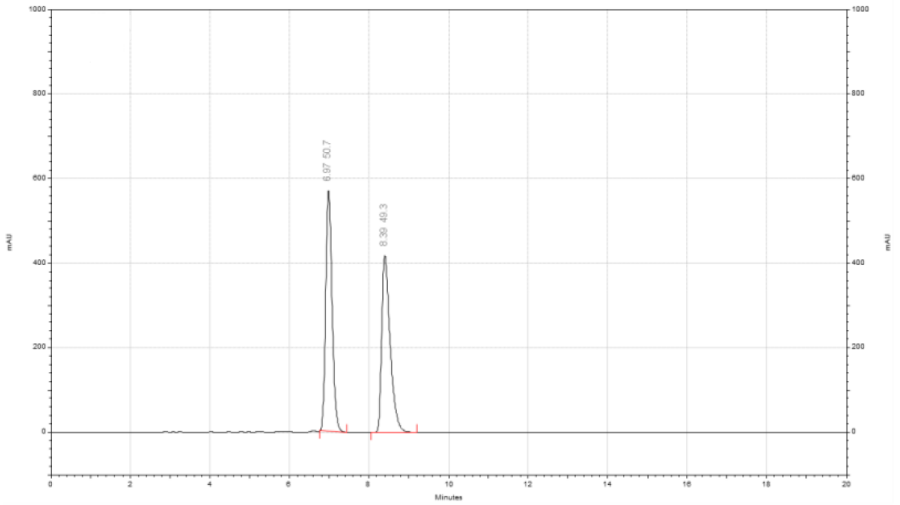


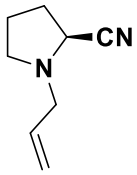
(S)-1-allylpyrrolidine-2-carbonitrile **1j**

HPLC conditions: Chiralpak OD-H, Hexane/isopropanol 99/1, 1 mL/min, 20 °C, 215 nm, t_r1 = 6.97 min, t_r2 = 8.39 min.

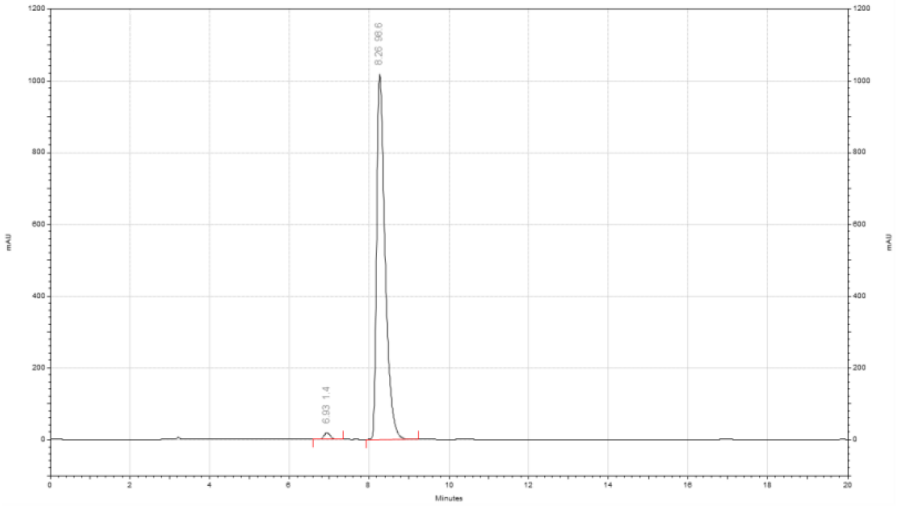


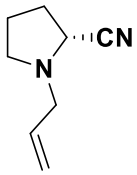
rac



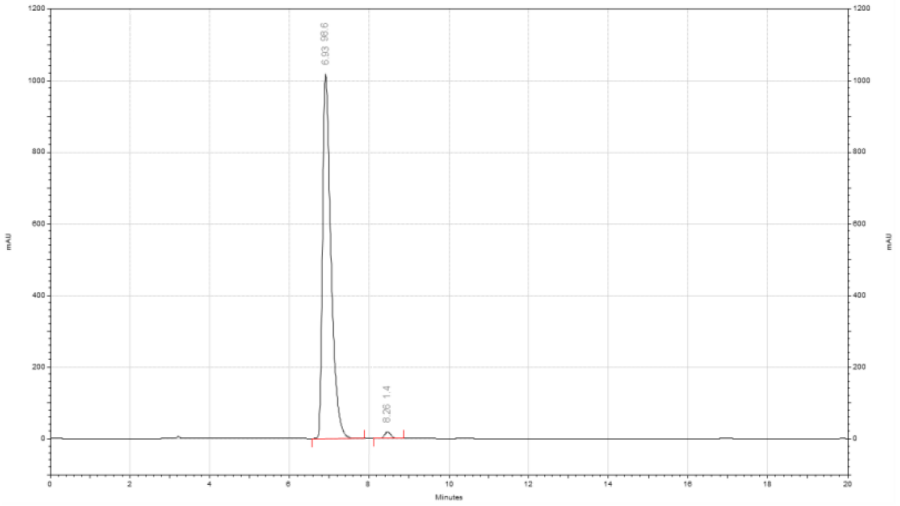


1j, >98% ee



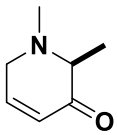


1k, >98% ee

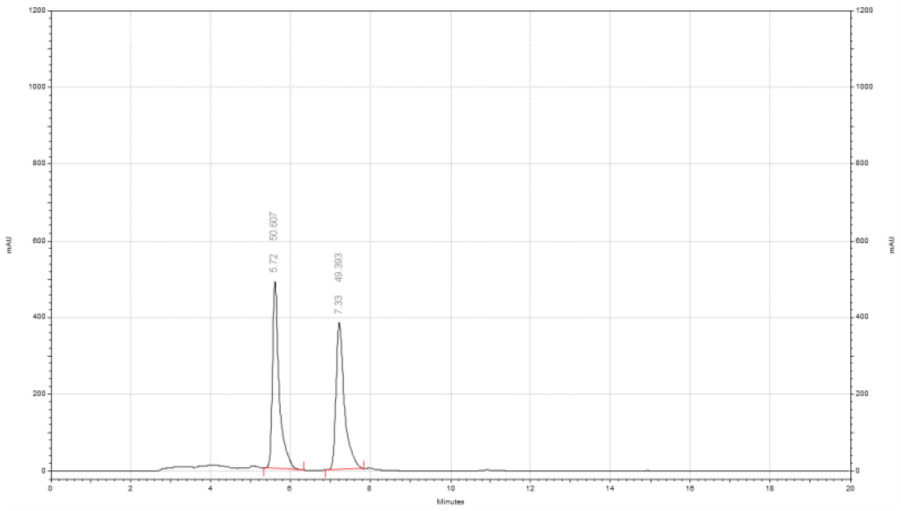


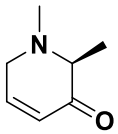
(S)-1,2-dimethyl-1,6-dihydropyridin-3(2H)-one **2h**

HPLC conditions: Chiralpak OD-H, Hexane/isopropanol 95/5, 1 mL/min, 20 °C, 215 nm, t_r1 = 5.72 min, t_r2 = 7.33 min.

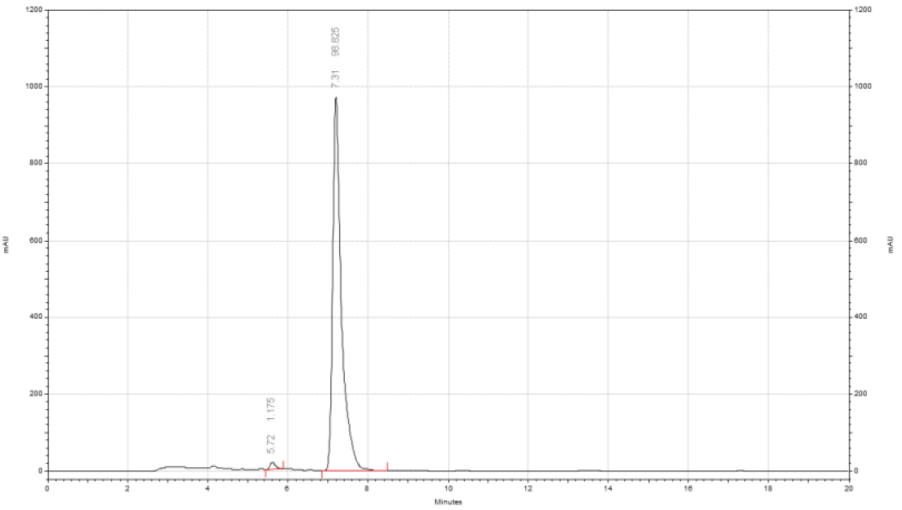


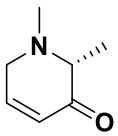
rac



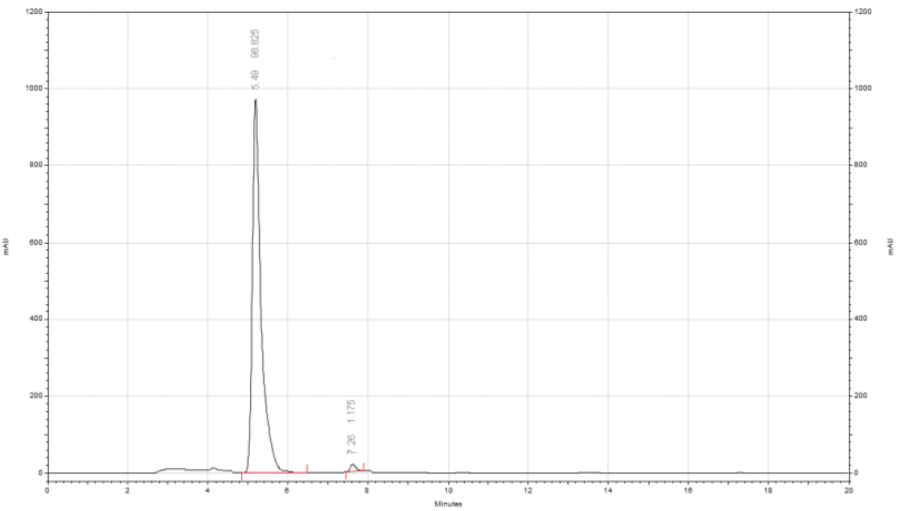


2h, >98% ee



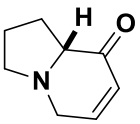


2i, >98% ee

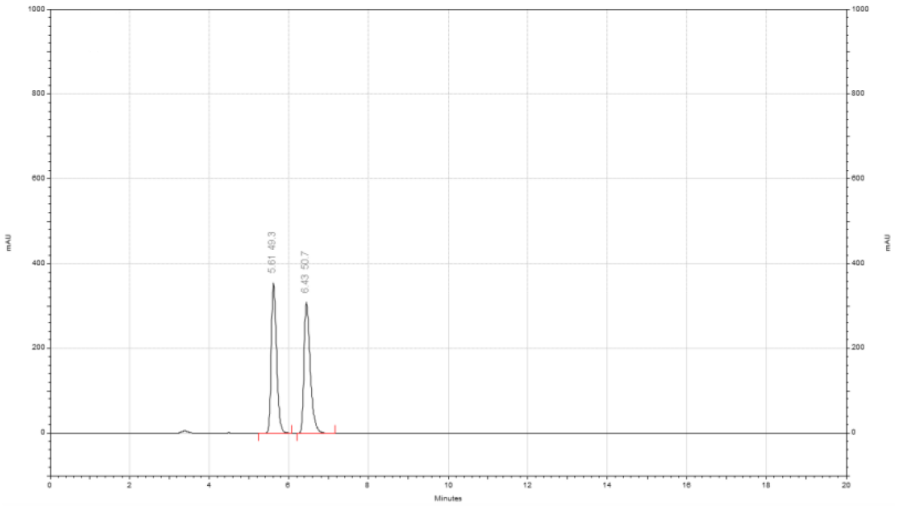


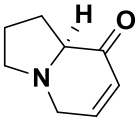
(S)-1,2,3,8a-tetrahydroindolizin-8(5H)-one **2j**

HPLC conditions: Chiralpak OD-H, Hexane/isopropanol 95/5, 1 mL/min, 20 °C, 215 nm, t_r1 = 6.97 min, t_r2 = 8.39 min.

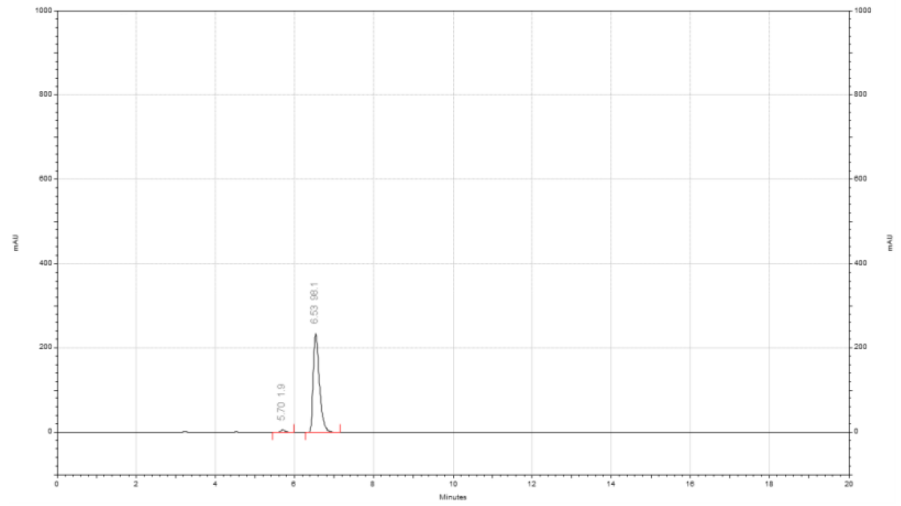


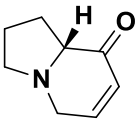
rac



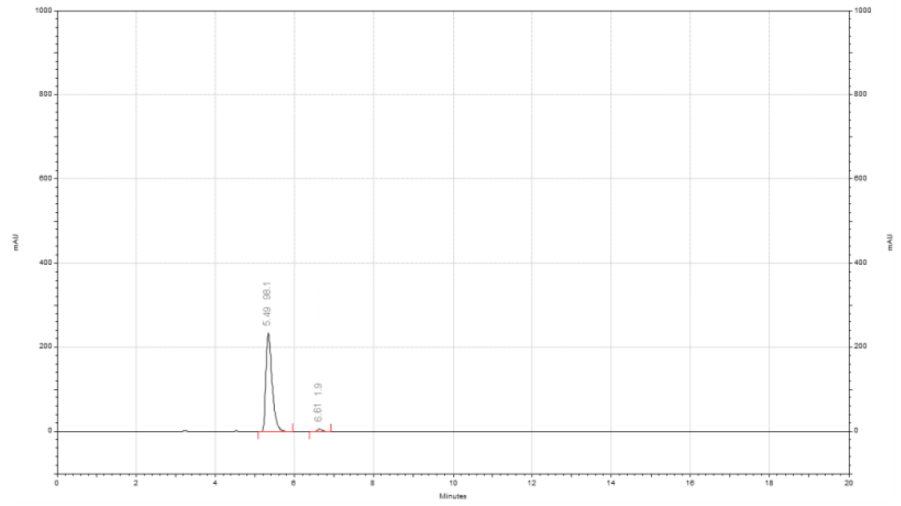


2j, 97% ee





2k, 96% ee



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