BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

Supporting Information

for

Polarity effects in 4-fluoro- and 4-(trifluoromethyl)prolines

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Data on acid–base transition and amide bond isomerism and NMR characterization of compounds 1–7

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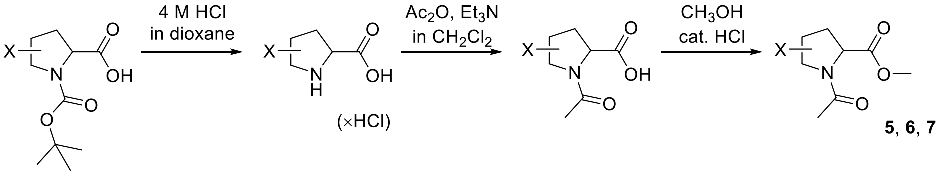
Experimental description

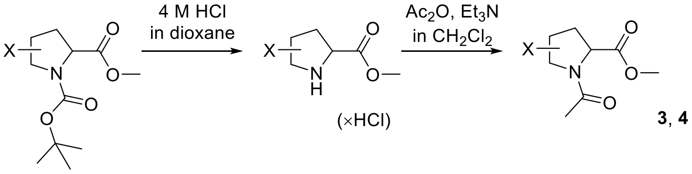
Sample preparation

Pure enantiomeric (2*S*,4*S*)- and (2*S*,4*R*)-fluoroprolines were obtained from commercial sources and processed as described.[S1] The methyl ester of *N*-Boc-(2*S*,4*S*)-trifluoromethylproline was obtained as described.[S2] Its partial epimerization at position 2 was received in an attempt to saponificate the material with an excess of 1 M NaOH in methanol under overexposure. The non-converted methyl ester was recovered in about 0.33 g amount with the ratio of the (2*S*,4*S*) and (2*R*,4*S*) isomers of about 3:2. This material was processed towards the model compounds **3**, and **4** that were eventually separated on a silica gel column (ethyl acetate/methanol 40:1 to 20:1, **4** eluted first). Commercial (5-(*tert*-butoxycarbonyl)-1,1-difluoro-5-azaspiro[2.4]heptane-6-carboxylic acid was purchased from a commercial supplier. The ratio of the diastereomers (3*R*,6*S*):(3*R*,6*R*) was about 2:1 according to the report of their synthesis from the company.[S3] The diastereomers were separated using preparative reversed phase HPLC (C18 column) with water/acetonitrile gradient elution (no ion-pairing additives). Resulting species were enriched to about 80% of pure diastereomers. Their further assignment was achieved by $^{1}H^{19}F$ HOESY experiments (mixing time 500 ms). The compounds were processed towards the model compounds **5** and **6**. Final purification on a silica gel column (ethyl acetate/methanol 40:1 to 20:1) allowed complete separation of the diastereomers in pure forms, while compound **5** eluted first. Finally, (*6S*)-(5-(*tert*-butoxycarbonyl)-5-azaspiro[2.4]heptane-6-carboxylic acid was obtained from commercial sources.

The synthesis of the model compounds **3–7** was performed on 0.2–0.1 g scales using the following general schemes:



5, **6**, **7**



3, **4**

All manipulations were performed at room temperature under air atmosphere. An *N*-Boc amino acid was treated with an excess of 4 M hydrogen chloride in dioxane for 90–120 min. The solvent was removed under reduced pressure, the residue dissolved in water and freeze-dried. To the residue anhydrous dichloromethane was added, followed by acetic anhydride (2–5 equiv), and trimethylamine (2–5 equiv). The resulting mixture was stirred for about 1 hour. The solvent was removed under reduced pressure, the residue dissolved in water and freeze-dried. The resulting mixture was dissolved in water and filtered through a short cation exchange column. The acidic fractions were collected and freeze-dried. The *N*-acetylated compound obtained in this way was dissolved in methanol (≈ 1–2 mL) and trimethylsilane (≈ 0.1–0.2 mL) was added to acidify the mixture. The mixture was stirred for several hours, the solvent was removed under reduced pressure, and the residue purified on a short silica gel column using ethyl acetate/methanol 40:1 to 20:1 gradient elution. The compounds **3–7** were obtained as colorless oils.

NMR experiments

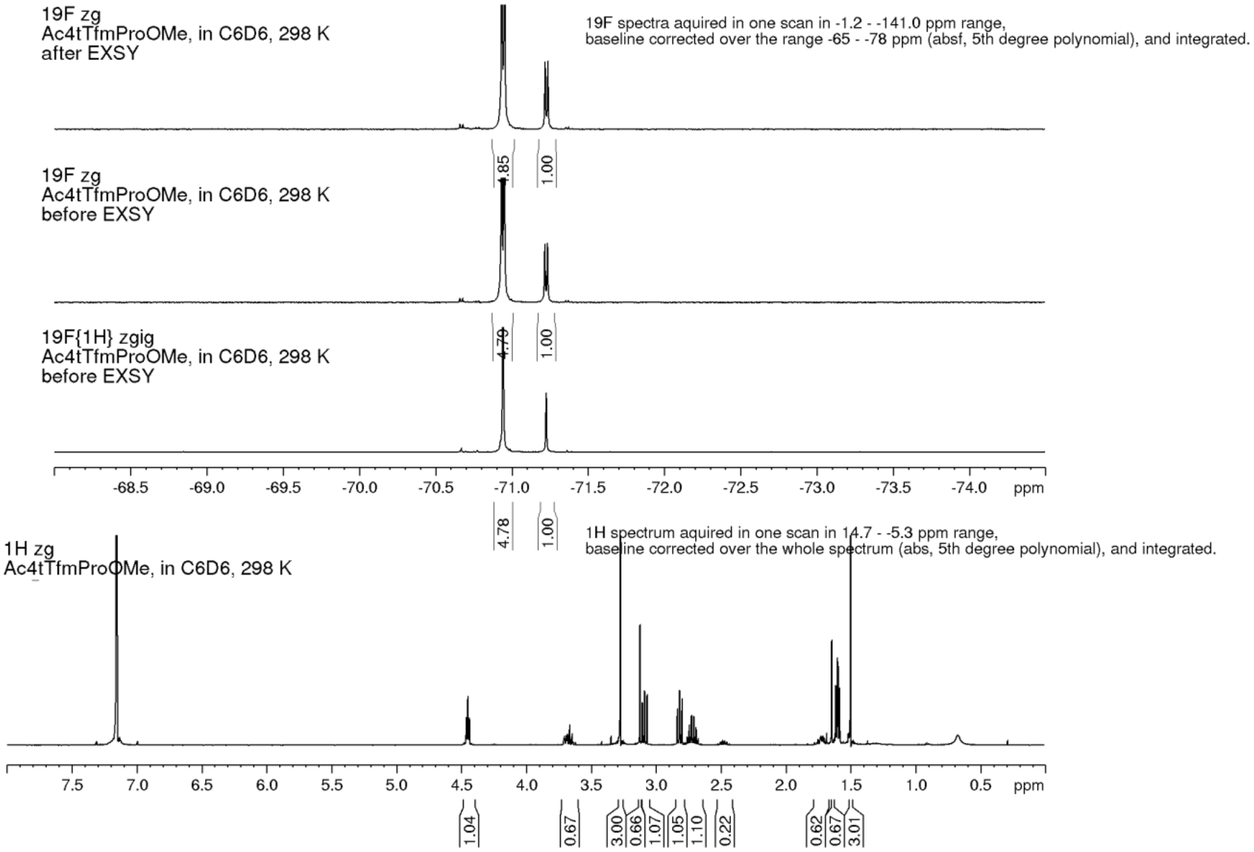
NMR experiments were performed with spectrometers operating at 500 and 700 MHz proton frequency. The variable temperature unit was calibrated according to conventional methanol standard. The pK_a values were obtained from analytical samples according to the detailed protocols described earlier.[S1,S4] The samples were titrated at 295–298 K, and the measurements were performed at 298 K. The lipophilicity measurements were performed as described.[S1] A compound (4–6 mg) was shaken with deionized water and octan-1-ol (1.00 mL each) for about 24 hours at 295–298 K. Then, 0.30 mL of each phase were taken in NMR tubes and diluted with 0.30 mL of acetonitrile-d_3. The measurements were performed with either ^{1}H or ^{19}F detection using datasets with identical settings. The equilibrium ratio (P) was determined as the ratio between absolute integral values from the octanol and water samples. The measurements were performed in triplicate.

For the amide isomerism measurements 4–6 mg of an analyte (**1–7**) was dissolved in a solvent (0.53 mL) in a standard 5 mm NMR tube. The ^{1}H and ^{19}F NMR measurements were performed manually in one scan in order to enable complete prerelaxation of the nuclei. The ratios between equivalent integrals originating from rotameric species were taken as the equilibrium constants (K). The value was averaged from few different resonances, few different spectra, ^{1}H and ^{19}F measurements.

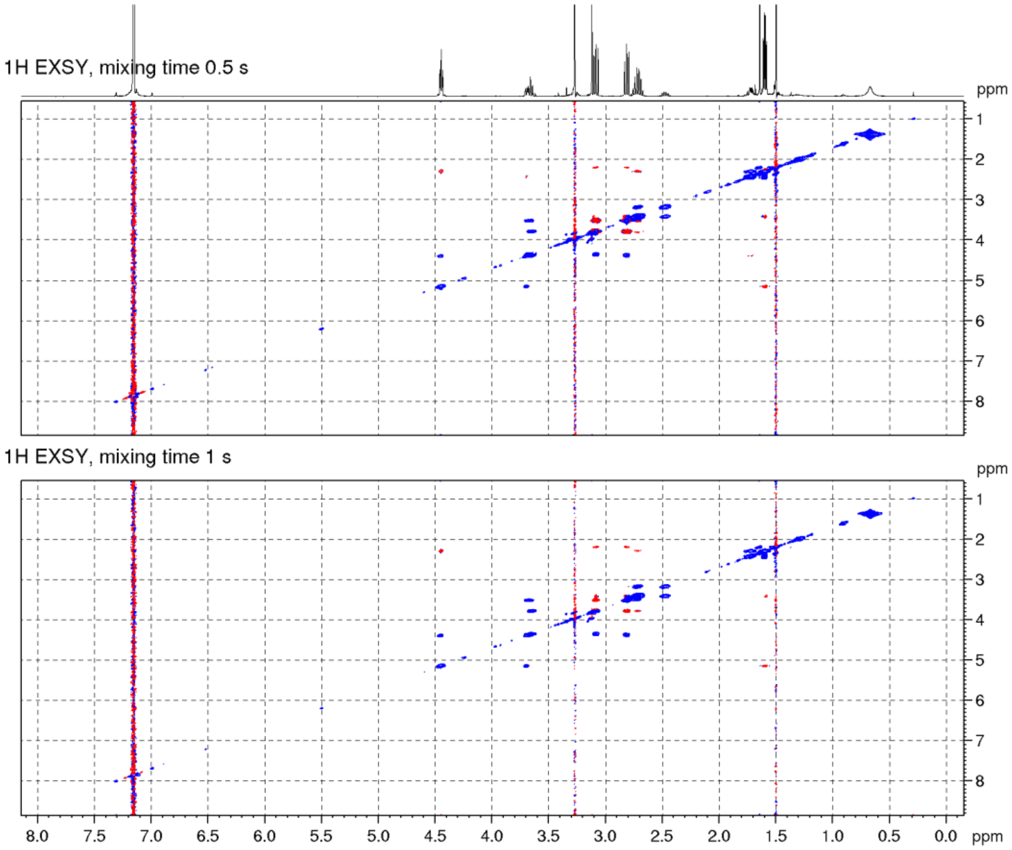
The rotation velocities were measured in 2D cross-relaxation pulse sequences with z gradients: ^{1}H EXSY (for all samples), ^{19}F EXSY (for **3** and **4**) and ^{19}F{^{1}H} EXSY with proton decoupling during evolution, mixing and detection (for **1** and **2**). The measurements in aqueous samples (D_2O) were performed at 310 K, the measurements in benzene (C_6D_6), and dichloromethane (CD_2Cl_2) were performed at 298 K. The frequency domains were zoomed to the regions of interest, and the experiments were performed with standard settings and prolonged recycling delays ($\geq 3 \cdot t_1$ of the analyzed resonances). The frequency domain spectra were baseline corrected and integrated. The exchange rate matrices were calculated using EXSYCalc freeware (Mestrec). A detailed description is provided below.

EXSY procedure description

For the compound/solvent combination **4**/C_6D_6, first the $K_{trans/cis}$ was identified from the 1D ^{1}H and ^{19}F NMR spectra as 4.69 ± 0.14:



Then, ^{1}H EXSY were acquired with mixing times 0.5 and 1 s, with the parameters as outlined below:



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PROCNO               1

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PROBHD   Z119470_0029 (
PULPROG       noesygpph
TD                 2048
SOLVENT            C6D6
NS                    2
DS                   16
SWH         4152.824 Hz
FIDRES      4.055492 Hz
AQ        0.2465792 sec
RG                   64
DW         120.400 usec
DE           14.20 usec
TE              298.0 K
D0       0.00010321 sec
D1      12.00000000 sec
D8       0.50000000 sec
D16      0.00020000 sec
IN0      0.00024080 sec
TDav                  1
SFO1     500.2519984 MHz
NUC1                 1H
P1           13.50 usec
P2           27.00 usec
PLW1     15.00000000 W
GPNAM[1]     SMSQ10.100
GPZ1            40.00 %
P16        1000.00 usec

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SW            8.301 ppm
FnMODE       States-TPPI

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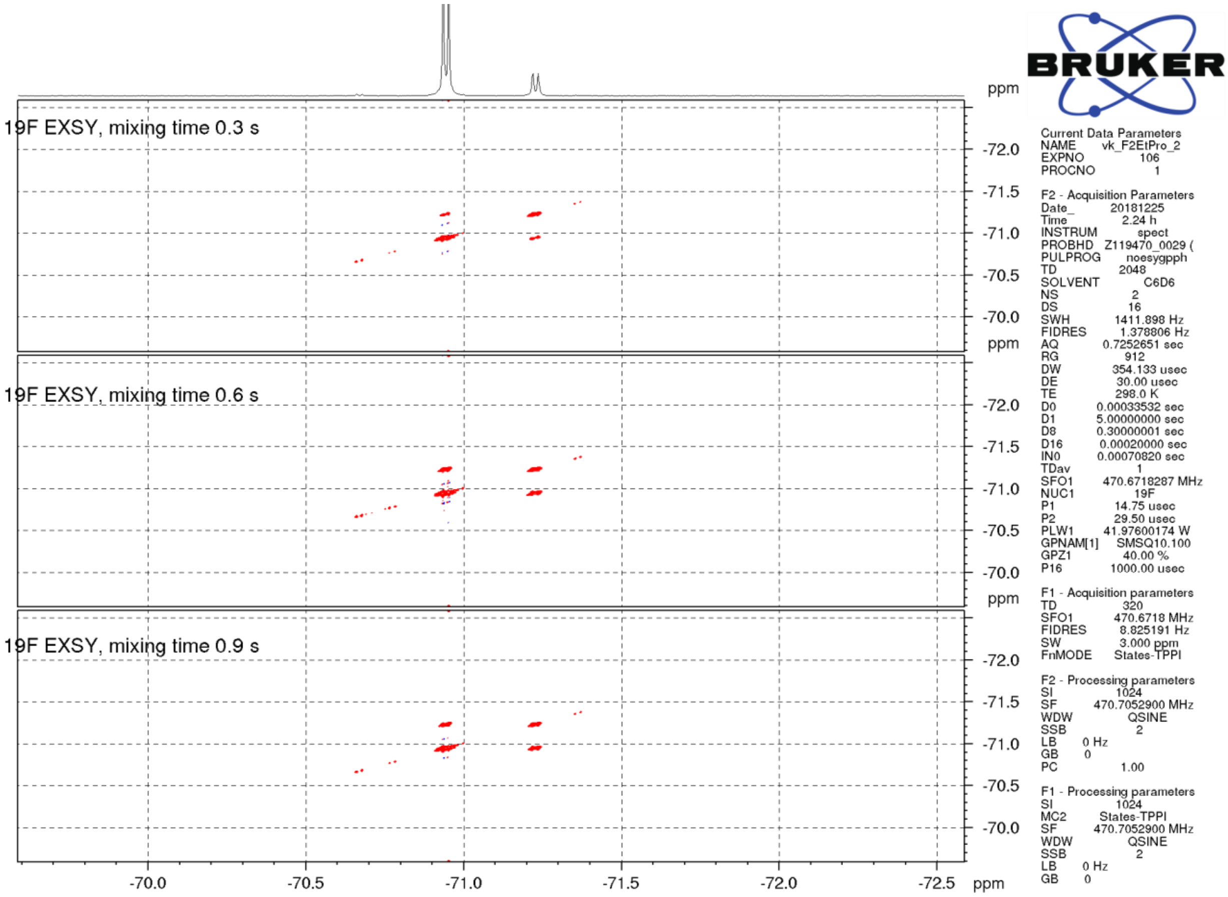
WDW               QSINE
SSB                   2
LB       0 Hz
GB       0
PC                 1.00

F1 - Processing parameters
SI                 1024
MC2         States-TPPI
SF      500.2500000 MHz
WDW               QSINE
SSB                   2
LB       0 Hz
GB       0
```

Note prolonged recycling delay (d1). According to our experience, a prolonged recycling delay does not change the final exchange rate, but it substantially improves the agreement between the rate constants derived from analysis of individual resonances. Effectively, this helps to reduce the standard deviation in the final value.

There is also a relatively high number of data points in the indirect dimension (TD1 512). This enables suppression of truncation artifacts in the indirect dimension, and effectively the sharp CH_3-group resonances could be integrated and analyzed.

^{19}F EXSY spectra were acquired with mixing times 0.3, 0.6, and 0.9 s with the parameters as shown below:



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PROCNO               1

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NS                   2
DS                  16
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FIDRES     1.378806 Hz
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RG                 912
DW        354.133 usec
DE          30.00 usec
TE             298.0 K
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D1      5.00000000 sec
D8      0.30000001 sec
D16     0.00020000 sec
IN0     0.00070820 sec
TDav                 1
SFO1    470.6718287 MHz
NUC1               19F
P1          14.75 usec
P2          29.50 usec
PLW1    41.97600174 W
GPNAM[1]    SMSQ10.100
GPZ1           40.00 %
P16       1000.00 usec

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FIDRES     8.825191 Hz
SW           3.000 ppm
FnMODE     States-TPPI

F2 - Processing parameters
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WDW              QSINE
SSB                  2
LB      0 Hz
GB      0
PC                1.00

F1 - Processing parameters
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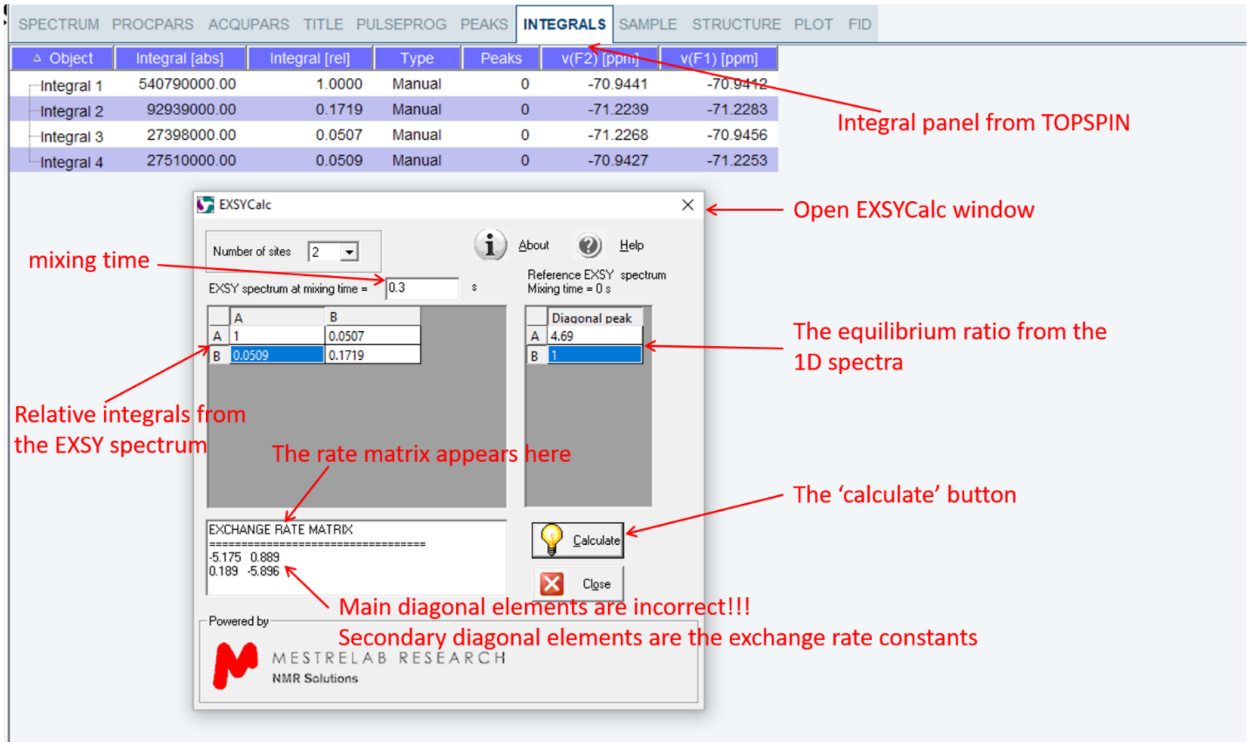
MC2        States-TPPI
SF     470.7052900 MHz
WDW              QSINE
SSB                  2
LB      0 Hz
GB      0
```

Here, prolonged recycling was also applied. The t_1 value was estimated as ≈ 1.4 s according to an inversion recovery experiment. Hence, the spin recycling aq+d1 = 5.7 s ≥ $4 \cdot t_1$. Interestingly, the inversion recovery showed that the t_1 for the s-*cis* resonance is slightly longer.

The frequency domain spectra were phased in direct and baseline corrected in both dimensions. In the ^{1}H EXSY, the CH_3O and acetyl CH_3 resonances were integrated. In the ^{19}F EXSY, the fluorine resonance was integrated. Relative integrals were input into EXSYcalc as shown:



Object	Integral [abs]	Integral [rel]	Type	Peaks	v(F2) [ppm]	v(F1) [ppm]
Integral 1	540790000.00	1.0000	Manual	0	-70.9441	-70.9412
Integral 2	92939000.00	0.1719	Manual	0	-71.2239	-71.2283
Integral 3	27398000.00	0.0507	Manual	0	-71.2268	-70.9456
Integral 4	27510000.00	0.0509	Manual	0	-70.9427	-71.2253

Number of sites: 2

EXSY spectrum at mixing time = 0.3 s

	A	B
A	1	0.0507
B	0.0509	0.1719

Reference EXSY spectrum
Mixing time = 0 s

	Diagonal peak
A	4.69
B	1

```
EXCHANGE RATE MATRIX
====================================
-5.175  0.889
0.189  -5.896
```

Integral panel from TOPSPIN

Open EXSYCalc window

mixing time

The equilibrium ratio from the 1D spectra

Relative integrals from the EXSY spectrum

The rate matrix appears here

The 'calculate' button

Main diagonal elements are incorrect!!!

Secondary diagonal elements are the exchange rate constants

The exchange rate matrix is defined as:

$$\begin{bmatrix} -R_1 - k_1 & k_{-1} \\ k_1 & -R_2 - k_{-1} \end{bmatrix}$$

The main diagonal elements contain the relaxation terms (R_1 and R_2) that are incorrect in the current treatment. To obtain a fully correct exchange rate matrix, a reference EXSY spectrum with zero mixing time should be acquired, and absolute integral values should be inserted into the EXSYCalc. With the existed method, only the secondary diagonal elements that represent the exchange rates are correct.

In the current example (**4**/C_6D_6), the following exchange rates were obtained:

	^{1}H EXSY				^{19}F EXSY		
	mix 0.5 s		mix 1 s		mix 0.3 s	mix 0.6 s	mix 0.9 s
	CH_3O	Ac	CH_3O	Ac			
k_{-1}, Hz	0.829	0.872	0.823	0.811	0.889	0.879	0.886
k_1, Hz	0.182	0.175	0.179	0.170	0.189	0.190	0.188

The rates were averaged to deliver the final value that is presented in Table S2. The standard deviation values were also calculated from the measured values.

Results: $k_{trans\text{-}to\text{-}cis} = 0.182 \pm 0.007$ Hz; $k_{cis\text{-}to\text{-}trans} = 0.855 \pm 0.031$ Hz

Molecular modeling

The molecular modeling was performed with compounds **1–4** using Scigress Modelling Suite (Fujitsu, Poland). Dipole calculations were performed after geometry optimization using the PM6 Hamiltonian included in the MOPAC package.

The C^4-*exo/endo* conformations were extracted from dynamic simulations of potential energy map generated in MM3 force field. The dihedral angles H–C^2–C^3–H were estimated from resulting conformations. The experimental $^{2}J_{HCCH}$ were then converted to dihedral angles using MestReJ freeware (Mestrec) with the following substitutes: S1=NRC(=O)R(s-cis), S2=COOR, S3,S4=H/CHClMe as the closest ones from the existing list. The conformations were readjusted to fit both dihedral angles within ± 10° accuracy. The ranges for the dihedral angles in the C^4-*endo* and C^4-*exo* conformations were estimated from the ones obtained in the simulation run before and after the adjustments. The estimated dihedral angle ranges were then converted to the *J* value ranges. These are shown in Figure 4.

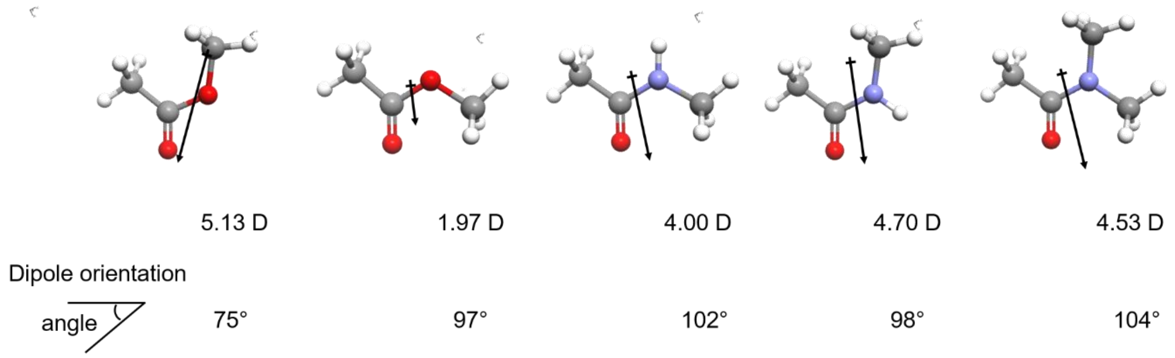
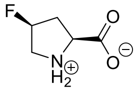
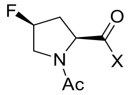
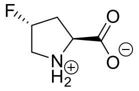
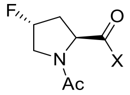
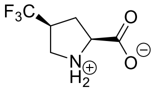
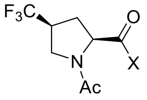
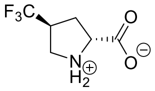
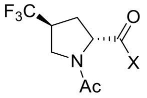
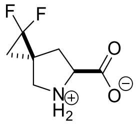
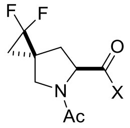
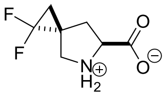
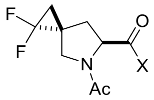
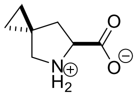
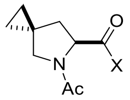


Figure S1 Dipole size and orientation in methyl acetate and *N*-methyl- and *N*,*N*-dimethylacetamides. The simulations were done using PM6 Hamiltonian from MOPAC package.

Extended physicochemical data

Table S1 Acid–base transition

compound	pK_a	compound	X = OH				X = O$^-$	ΔpK_a*
			rotamer		ΔpK_a	$K_{trans/cis}$	$K_{trans/cis}$	
			s-*cis*	s-*trans*				
	9.10±0.10		2.87	3.39	0.52	2.27±0.02	0.68±0.04	0.52
	9.10±0.10		2.37	3.19	0.82	5.30±0.20	0.91±0.02	0.77
	8.42±0.05		2.60	3.18	0.58	3.53±0.06	0.89±0.02	0.60
	8.43±0.05		2.55	3.15	0.60	2.86±0.04	0.75±0.02	0.58
	9.06±0.06		2.64	3.18	0.54	3.13±0.09	0.76±0.01	0.61
	9.05±0.12		2.73	3.30	0.57	2.65±0.10	0.67±0.02	0.60
	10.59±0.10		2.96	3.57	0.61	3.14±0.15	0.80±0.01	0.59

The ΔpK_a values are obtained according to the equation:

$$\Delta pK_a = pK_a(s - trans) - pK_a(s - cis)$$

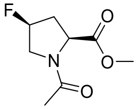
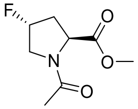
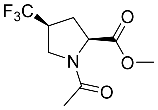
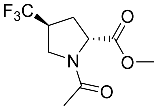
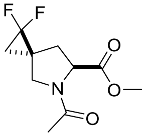
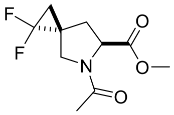
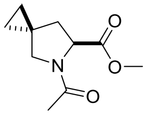
The ΔpK_a* values are obtained according to the equation[S4]:

$$\Delta pK_a^* = log_{10} \frac{K_{trans/cis}(X = OH)}{K_{trans/cis}(X = O^-)}$$

Thus, the first value is obtained from the titration experiments, while the second is obtained from equilibrium measurements at extreme pH. In principle, both values (columns highlighted in yellow) should be equal within the accuracy of the experimental determination.

The values for fluoroproline derivatives are from reference.[S4]

Table S2 Amide bond isomerism

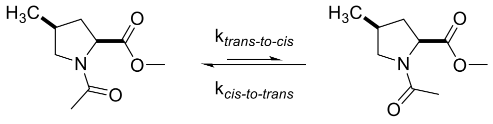
compound	$K_{trans/cis}$			k, Hz						E$^{\neq}$, kJ mol^{-1}					
				cis-to-*trans*			*trans*-to-*cis*			*cis*-to-*trans*			*trans*-to-*cis*		
	in C_6D_6	in CD_2Cl_2	in D_2O	in C_6D_6	in CD_2Cl_2	in D_2O	in C_6D_6	in CD_2Cl_2	in D_2O	in C_6D_6	in CD_2Cl_2	in D_2O	in C_6D_6	in CD_2Cl_2	in D_2O
	2.09±0.03	1.71±0.07	2.57±0.08	0.463±0.034	0.187±0.003	0.041±0.004	0.223±0.008	0.109±0.002	0.016±0.002	74.9±0.2	77.1±0.1	84.3±0.2	76.6±0.1	78.5±0.1	86.7±0.3
	5.38±0.22	4.64±0.10	7.08±0.27	0.556±0.027	0.220±0.016	0.087±0.009	0.103±0.004	0.049±0.005	0.012±0.002	74.4±0.2	76.7±0.2	82.3±0.3	78.6±0.1	80.5±0.2	87.4±0.5
	5.39±0.09	3.22±0.06	4.36±0.11	2.44±0.07	0.690±0.019	0.131±0.008	0.453±0.011	0.211±0.003	0.031±0.002	70.8±0.1	73.9±0.1	81.3±0.1	74.9±0.1	76.8±0.2	85.0±0.1
	4.69±0.14	2.66±0.11	3.57±0.13	0.855±0.031	0.265±0.007	0.060±0.006	0.182±0.007	0.098±0.009	0.018±0.002	73.4±0.1	76.3±0.1	83.3±0.3	77.2±0.1	78.7±0.3	86.4±0.3
	4.05±0.03	3.13±0.07	3.94±0.03	0.854±0.025	0.287±0.007	0.085±0.011	0.209±0.004	0.093±0.002	0.020±0.001	73.4±0.1	76.1±0.1	82.4±0.4	76.9±0.1	78.9±0.1	86.1±0.1
	3.23±0.05	2.47±0.02	3.15±0.05	0.620±0.025	0.188±0.007	0.038±0.004	0.189±0.003	0.074±0.003	0.011±0.002	74.2±0.1	77.1±0.1	84.5±0.2	77.1±0.1	79.4±0.1	87.6±0.6
	4.13±0.04	3.35±0.02	3.92±0.04	0.264±0.010	0.080±0.004	0.024±0.008	0.062±0.002	0.023±0.002	0.006±0.001	76.3±0.1	79.2±0.2	85.6±1.1	79.9±0.1	82.3±0.3	89.2±0.5

The equilibrium $K_{trans/cis}$ values were determined at 298 K. The rotation velocities k were determined at 298 K for benzene and dichloromethane solutions, and at 310 K for aqueous solutions. The activation energies were calculated using the Eyring equation:

$$E^{\neq} = -RT\left(ln\frac{k}{T} - 23.76\right),$$

where R – gas constant, T – absolute temperature. The standard deviation takes into account discrepancies between the measurements (different mixing times, ^{1}H, ^{19}F detection), and do not take into account the temperature error.

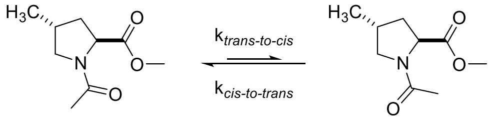
For 4-methylproline derivatives[S1] the rotation velocities were determined in deuterium oxide buffered by a phosphate buffer to pH 7, at 310 K:



$K_{trans/cis}$ (298 K) = 8.05 ± 0.13

$k_{cis\text{-}to\text{-}trans}$ = 0.041 ± 0.011 $E^{\neq}$ = 84.3 ± 0.7 kJ mol^{-1}

$k_{trans\text{-}to\text{-}cis}$ = 0.004 ± 0.001 $E^{\neq}$ = 90.3 ± 0.7 kJ mol^{-1}

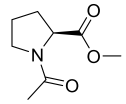
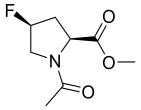
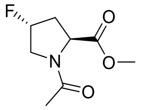
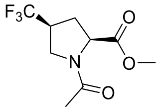
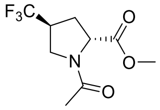
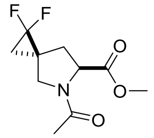
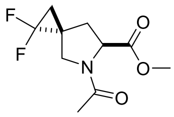
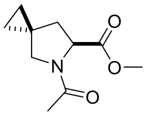


$K_{trans/cis}$ (298 K) = 4.67 ± 0.14

$k_{cis\text{-}to\text{-}trans}$ = 0.020 ± 0.003 $E^{\neq}$ = 86.1 ± 0.4 kJ mol^{-1}

$k_{trans\text{-}to\text{-}cis}$ = 0.005 ± 0.001 $E^{\neq}$ = 89.7 ± 0.6 kJ mol^{-1}

Table S3 Chemical shifts for the 2-CH resonances in ^1H NMR spectra

compound	in D_2O		in CD_2Cl_2		in C_6D_6	
	s-*trans*	s-*cis*	s-*trans*	s-*cis*	s-*trans*	s-*cis*
	4.36	4.62	4.42	4.40	4.34	3.68
	4.68	4.84	4.72	4.54	4.64	3.72
	4.50	4.84	4.52	4.60	4.62	4.04
	4.49	4.81	4.49	4.52	4.25	3.65
	4.56	4.82	4.63	4.56	4.45	3.69
	4.58	4.87	4.62	4.59	4.57	3.77
	4.64	4.82	4.67	4.55	4.66	3.84
	4.55	4.75	4.58	4.52	4.70	3.93

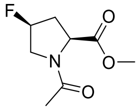
Note that the chemical shifts were read out from the ^1H NMR spectra acquired at 298 K. The spectra were referenced according to the conventional deuterium lock referencing (Bruker Avance III console, for solvent details see command 'edlock' in Topspin). No additional referencing was applied.

NMR data for compounds 1–7

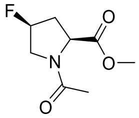
For earlier characterization of compounds see: **1**, **2**[S1,S5,S6], **3**[S1,S2].

Methyl (*2S,4S*)-1-acetyl-4-fluoroprolinate (**1**)

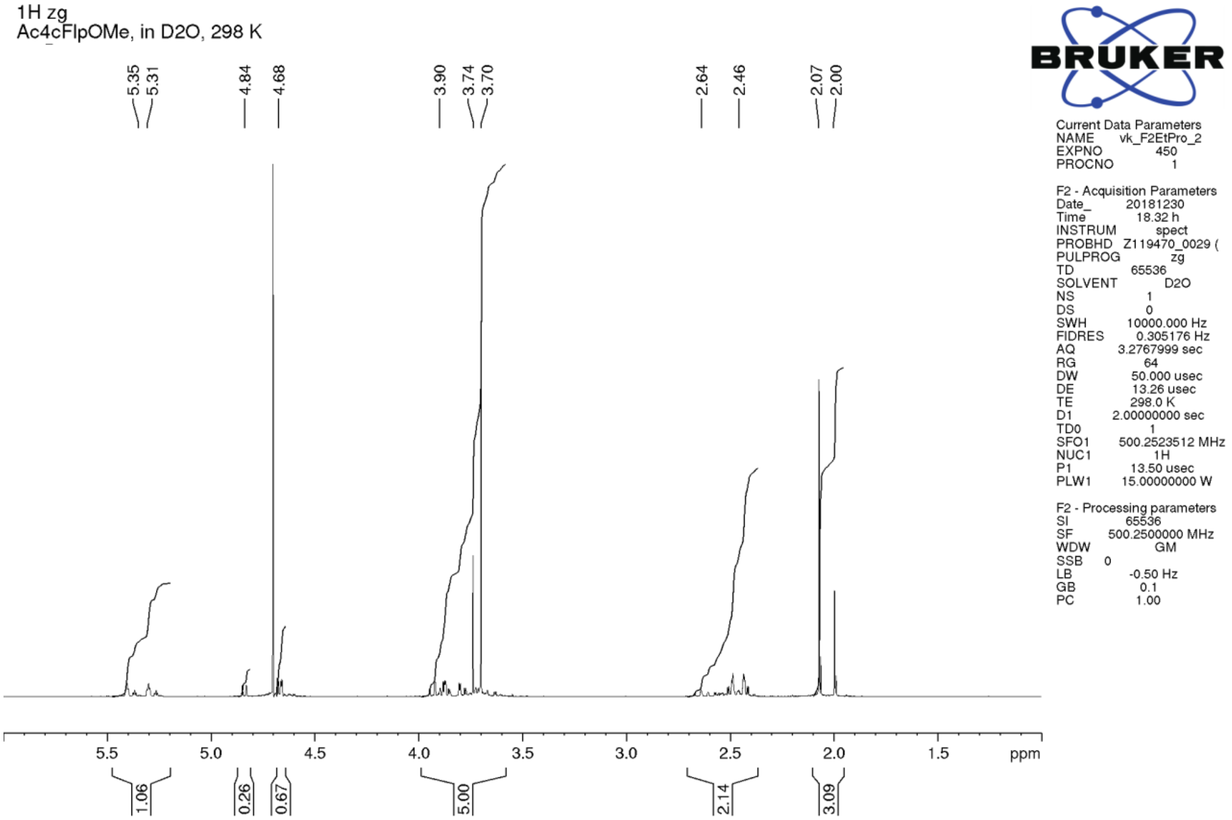
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 2.57 ± 0.08



s-*trans*: 5.35 (dtd, *J* = 52, 3.2, 1.4 Hz, 1H, γ-CH), 4.67 (dd, *J* = 8.8, 2.9 Hz, 1H, α-CH), 3.91 (ddd, *J* = 25, 13.3, 1.1 Hz, 1H, δ-CH), 3.85 (ddd, *J* = 39, 13.1, 3.6 Hz, 1H, δ-CH), 3.70 (s, 3H, CH_3O), 2.46 (m, 2H, β-CH_2), 2.07 (s, 3H, Ac);



s-*cis*: 5.32 (dt, *J* = 52, 3.4 Hz, 1H, γ-CH), 4.84 (d, *J* = 9.6 Hz, 1H, α-CH), 3.74 (s, 3H, CH_3O), 3.70 (ddd, *J* = 28, 14.8, 1.6 Hz, 1H, δ-CH), 3.67 (ddd, *J* = 38, 14.5, 4.0 Hz, 1H, δ-CH), 2.64 (tm, *J* = 16.0 Hz, 1H, β-CH), 2.51 (m, 1H, β-CH), 2.00 (s, 3H, Ac).



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Current Data Parameters
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EXPNO              450
PROCNO               1

F2 - Acquisition Parameters
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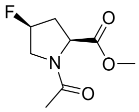
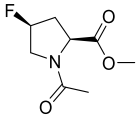
INSTRUM           spect
PROBHD   Z119470_0029 (
PULPROG              zg
TD               65536
SOLVENT             D2O
NS                   1
DS                   0
SWH         10000.000 Hz
FIDRES       0.305176 Hz
AQ         3.2767999 sec
RG                  64
DW          50.000 usec
DE          13.26 usec
TE             298.0 K
D1        2.00000000 sec
TD0                  1
SFO1     500.2523512 MHz
NUC1                1H
P1          13.50 usec
PLW1     15.00000000 W

F2 - Processing parameters
SI               65536
SF       500.2500000 MHz
WDW                 GM
SSB    0
LB            -0.50 Hz
GB                 0.1
PC                1.00
```

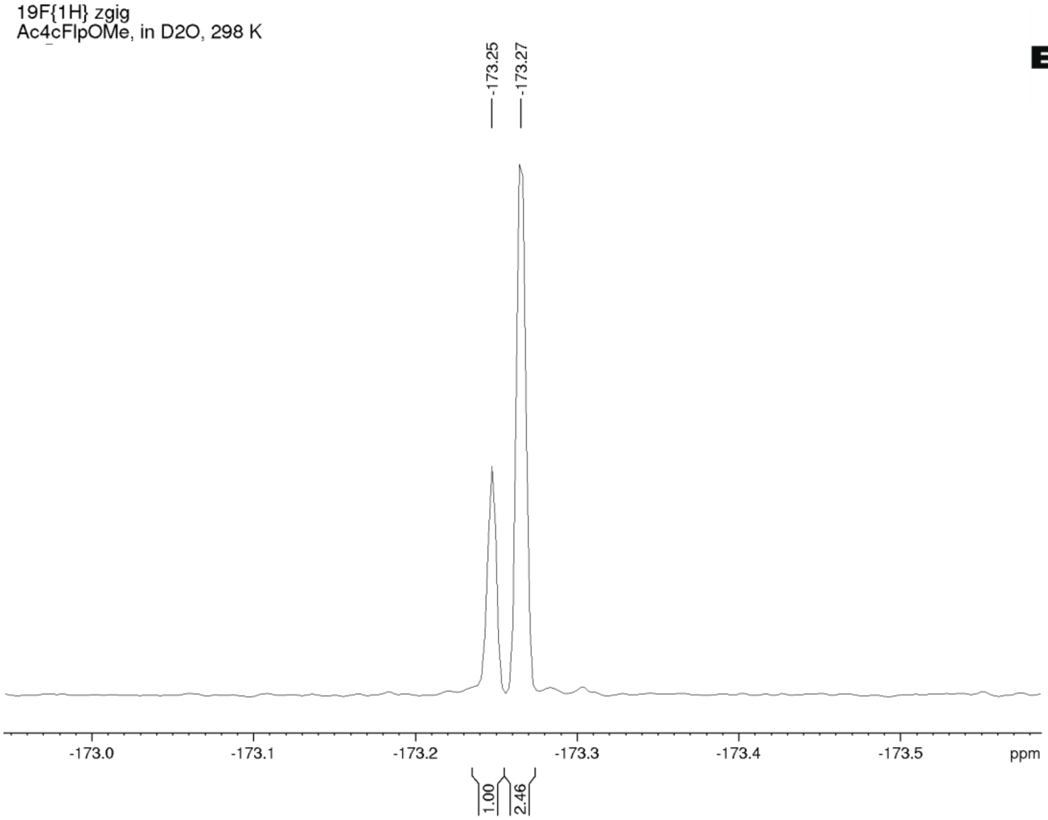
$^{19}F\{^{1}H\}$ NMR (471 MHz, D_2O):



s-*trans*: −173.27 (s);



s-*cis*: −173.25 (s).



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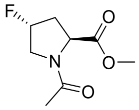
Current Data Parameters
NAME      vk_F2EtPro_2
EXPNO            451
PROCNO             1

F2 - Acquisition Parameters
Date_       20181230
Time          18.32 h
INSTRUM         spect
PROBHD   Z119470_0029 (
PULPROG          zgig
TD          135168
SOLVENT          D2O
NS               1
DS               0
SWH        65789.477 Hz
FIDRES      0.973447 Hz
AQ         1.0272768 sec
RG             256
DW            7.600 usec
DE           10.00 usec
TE           298.0 K
D1        1.00000000 sec
D11       0.03000000 sec
TD0              1
SFO1      470.6237412 MHz
NUC1             19F
P1           14.75 usec
PLW1      41.97600174 W
SFO2      500.2525013 MHz
NUC2              1H
CPDPRG[2      waltz16
PCPD2          80.00 usec
PLW2      14.99699974 W
PLW12      0.42706001 W

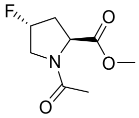
F2 - Processing parameters
SI           65536
SF        470.7052900 MHz
WDW              GM
SSB    0
LB           -1.00 Hz
GB            0.05
PC           10.00
```

Methyl (*2S,4R*)-1-acetyl-4-fluoroprolinate (**2**)

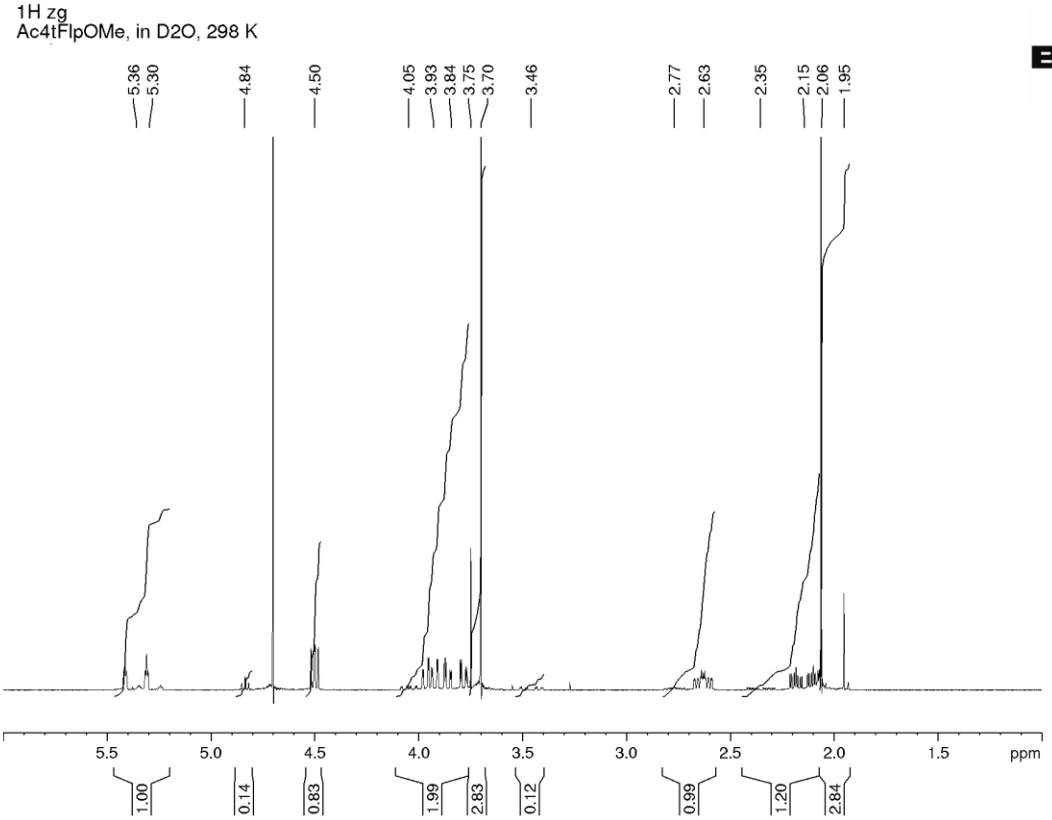
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 7.08 ± 0.27



s-*trans*: 5.36 (dt, *J* = 52, 3.4 Hz, 1H, γ-CH), 4.50 (dd, *J* = 10.0, 7.8 Hz, 1H, α-CH), 3.94 (ddd, *J* = 22, 13.1, 2.3 Hz, 1H, δ-CH), 3.83 (ddd, *J* = 38, 13.4, 3.3 Hz, 1H, δ-CH), 3.70 (s, 3H, CH_3O), 2.63 (m, 1H, β-CH), 2.14 (dddd, J = 42, 14.2, 10.2, 3.8 Hz, 1H, β-CH), 2.06 (s, 3H, Ac);



s-*cis*: 5.30 (dt, *J* = 52, 3.9 Hz, 1H, γ-CH), 4.84 (t, *J* = 8.4 Hz, 1H, α-CH), 4.03 (ddd, *J* = 21, 13.6, 2.6 Hz, 1H, δ-CH), 3.75 (s, 3H, CH_3O), 3.46 (ddd, *J* = 38, 14.3, 3.5 Hz, 1H, δ-CH), 2.77 (m, 1H, β-CH), 2.36 (m, 1H, β-CH), 1.95 (s, 3H, Ac).



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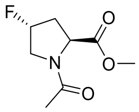
Current Data Parameters
NAME      vk_F2EtPro_2
EXPNO              460
PROCNO               1

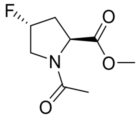
F2 - Acquisition Parameters
Date_         20181231
Time           17.17 h
INSTRUM          spect
PROBHD   Z119470_0029 (
PULPROG             zg
TD              65536
SOLVENT            D2O
NS                   1
DS                   0
SWH        10000.000 Hz
FIDRES      0.305176 Hz
AQ        3.2767999 sec
RG                  64
DW          50.000 usec
DE           13.26 usec
TE             298.0 K
D1       2.00000000 sec
TD0                  1
SFO1     500.2523512 MHz
NUC1                1H
P1           13.50 usec
PLW1     15.00000000 W

F2 - Processing parameters
SI              65536
SF       500.2500000 MHz
WDW                 GM
SSB     0
LB            -0.50 Hz
GB                 0.1
PC                1.00
```

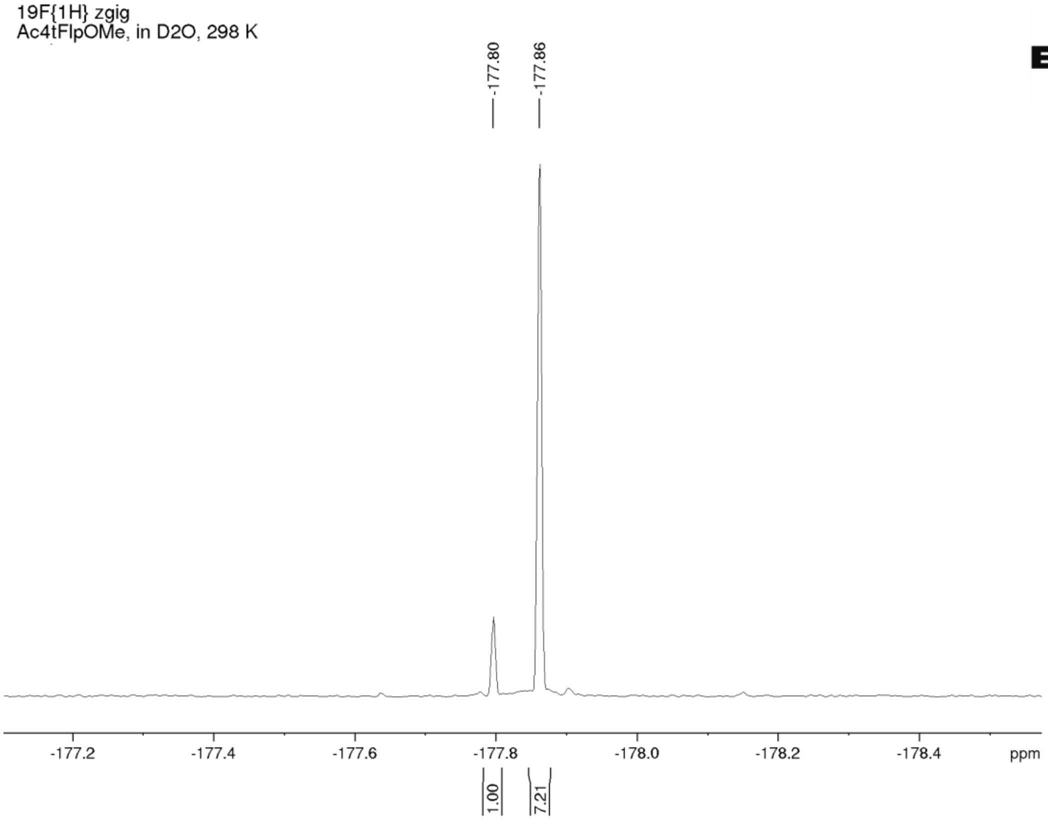
$^{19}F\{^1H\}$ NMR (471 MHz, D_2O):



s-*trans*: −177.86 (s);



s-*cis*: −177.80 (s).



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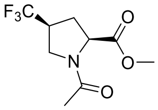
Current Data Parameters
NAME      vk_F2EtPro_2
EXPNO           461
PROCNO            1

F2 - Acquisition Parameters
Date_       20181231
Time          17.18 h
INSTRUM          spect
PROBHD   Z119470_0029 (
PULPROG          zgig
TD            135168
SOLVENT           D2O
NS                 1
DS                 0
SWH       65789.477 Hz
FIDRES     0.973447 Hz
AQ        1.0272768 sec
RG               256
DW           7.600 usec
DE           10.00 usec
TE           298.0 K
D1       1.00000000 sec
D11      0.03000000 sec
TD0                1
SFO1     470.6237412 MHz
NUC1             19F
P1           14.75 usec
PLW1      41.97600174 W
SFO2     500.2525013 MHz
NUC2              1H
CPDPRG[2       waltz16
PCPD2        80.00 usec
PLW2      14.99699974 W
PLW12      0.42706001 W

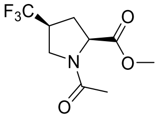
F2 - Processing parameters
SI             65536
SF       470.7052900 MHz
WDW               GM
SSB      0
LB            -1.00 Hz
GB              0.05
PC             10.00
```

Methyl (*2S,4S*)-1-acetyl-4-trifluoromethylprolinate (**3**)

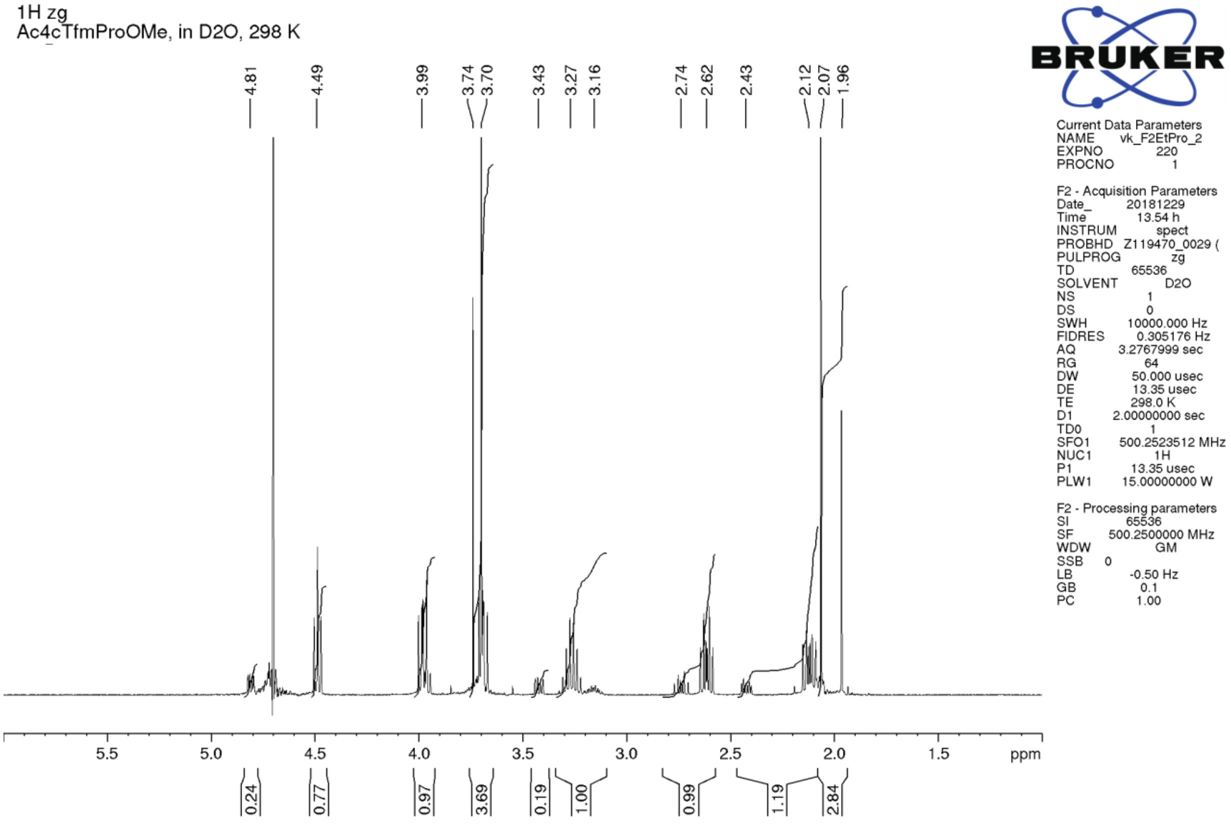
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 4.36 ± 0.11



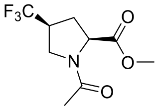
s-*trans*: 4.49 (t, *J* = 8.3 Hz, 1H, α-CH), 3.99 (dd, *J* = 11.0, 8.4 Hz, 1H, δ-CH), 3.70 (s, 3H, CH_3O), 3.69 (dd, *J* = 11.0, 9.1 Hz, 1H, δ-CH), 3.27 (m, 1H, γ-CH), 2.62 (dt, *J* = 13.4, 8.4 Hz, 1H, β-CH), 2.13 (dt, *J* = 13.4, 8.4 Hz, 1H, β-CH), 2.06 (s, 3H, Ac);



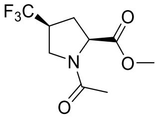
s-*cis*: 4.81 (dd, *J* = 9.9, 4.1 Hz, 1H, α-CH), 3.97 (m, 1H, δ-CH), 3.74 (s, 3H, CH_3O), 3.43 (dd, *J* = 12.8, 6.4 Hz, 1H, δ-CH), 3.16 (m, 1H, γ-CH), 2.74 (dt, *J* = 14.5, 9.5 Hz, 1H, β-CH), 2.43 (dt, *J* = 14.3, 4.5 Hz, 1H, β-CH), 1.96 (s, 3H, Ac).



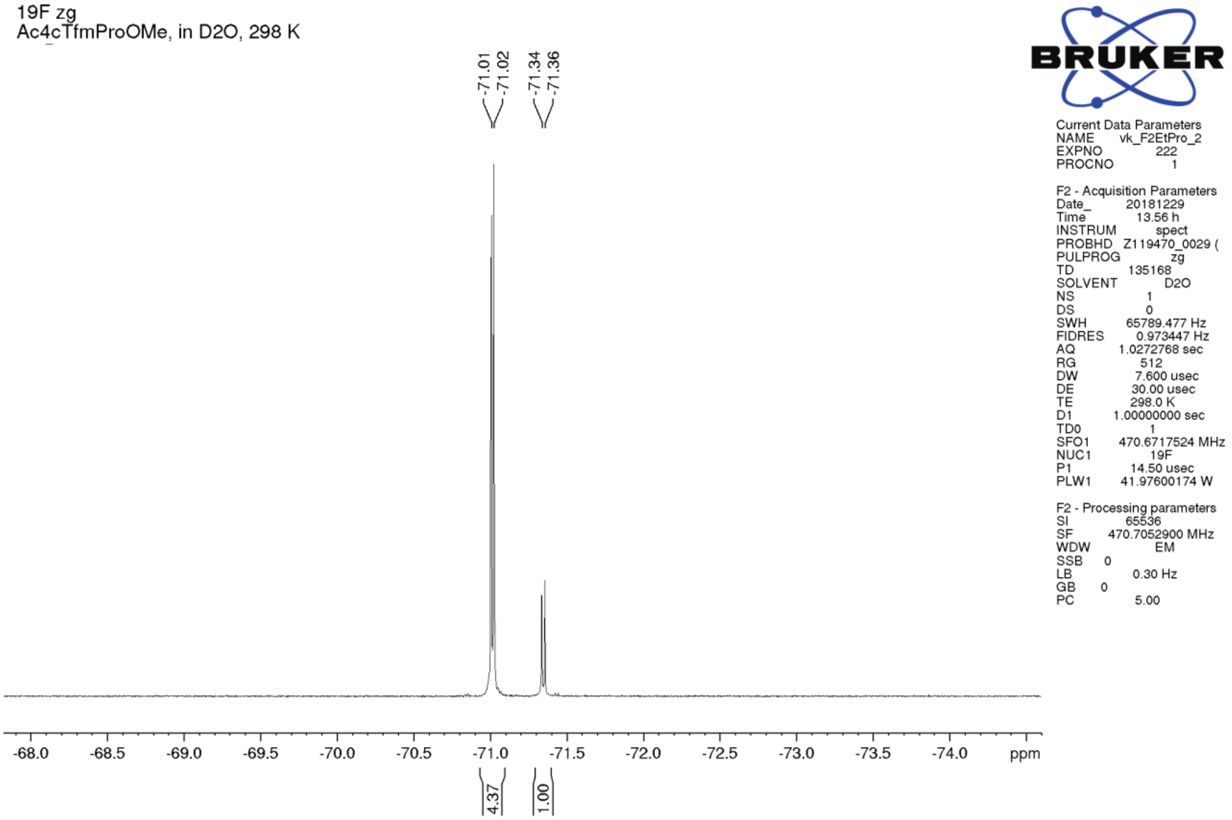
^{19}F NMR (471 MHz, D_2O):



s-*trans*: −71.01 (d, *J* = 8 Hz);



s-*cis*: −71.35 (d, *J* = 10 Hz).



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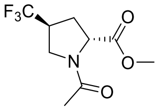
Current Data Parameters
NAME     vk_F2EtPro_2
EXPNO             222
PROCNO              1

F2 - Acquisition Parameters
Date_        20181229
Time          13.56 h
INSTRUM         spect
PROBHD   Z119470_0029 (
PULPROG            zg
TD             135168
SOLVENT           D2O
NS                  1
DS                  0
SWH      65789.477 Hz
FIDRES    0.973447 Hz
AQ      1.0272768 sec
RG                512
DW          7.600 usec
DE          30.00 usec
TE            298.0 K
D1     1.00000000 sec
TD0                 1
SFO1   470.6717524 MHz
NUC1              19F
P1          14.50 usec
PLW1     41.97600174 W

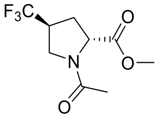
F2 - Processing parameters
SI              65536
SF     470.7052900 MHz
WDW                EM
SSB    0
LB            0.30 Hz
GB     0
PC               5.00
```

Methyl (*2R,4S*)-1-acetyl-4-trifluoromethylprolinate (**4**)

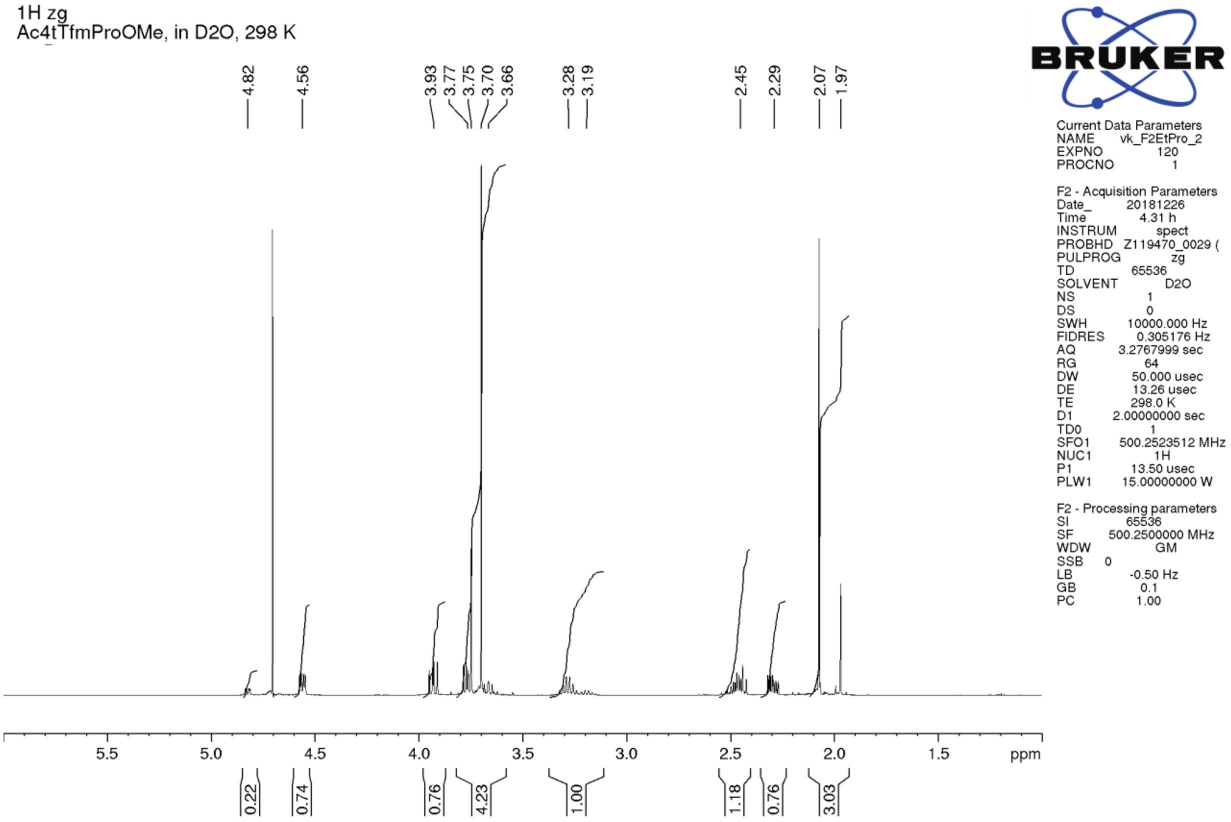
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 3.57 ± 0.13



s-*trans*: 4.56 d, *J* = 9.2, 4.0 Hz, 1H, α-CH), 3.93 (dd, *J* = 11.1, 8.3 Hz, 1H, δ-CH), 3.70 (s, 3H, CH_3O), 3.69 (dd, *J* = 11.1, 9.0 Hz, 1H, δ-CH), 3.27 (m, 1H, γ-CH), 2.62 (dt, *J* = 13.4, 8.4 Hz, 1H, β-CH), 2.12 (dt, *J* = 13.4, 8.6 Hz, 1H, β-CH), 2.06 (s, 3H, Ac);



s-*cis*: 4.81 (dd, *J* = 8.6, 2.6 Hz, 1H, α-CH), 3.75 (s, 3H, CH_3O), 3.66 (m, *2*H, δ-CH_2), 3.19 (m, 1H, γ-CH), 2.50 (m, *2*H, β-CH_2), 1.97 (s, 3H, Ac).

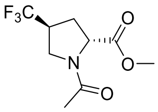


```
Current Data Parameters
NAME      vk_F2EtPro_2
EXPNO              120
PROCNO               1

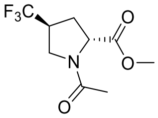
F2 - Acquisition Parameters
Date_         20181226
Time            4.31 h
INSTRUM          spect
PROBHD   Z119470_0029 (
PULPROG             zg
TD               65536
SOLVENT            D2O
NS                   1
DS                   0
SWH       10000.000 Hz
FIDRES     0.305176 Hz
AQ       3.2767999 sec
RG                  64
DW          50.000 usec
DE          13.26 usec
TE             298.0 K
D1      2.00000000 sec
TD0                  1
SFO1    500.2523512 MHz
NUC1                1H
P1          13.50 usec
PLW1     15.00000000 W

F2 - Processing parameters
SI               65536
SF      500.2500000 MHz
WDW                 GM
SSB    0
LB            -0.50 Hz
GB                 0.1
PC                1.00
```

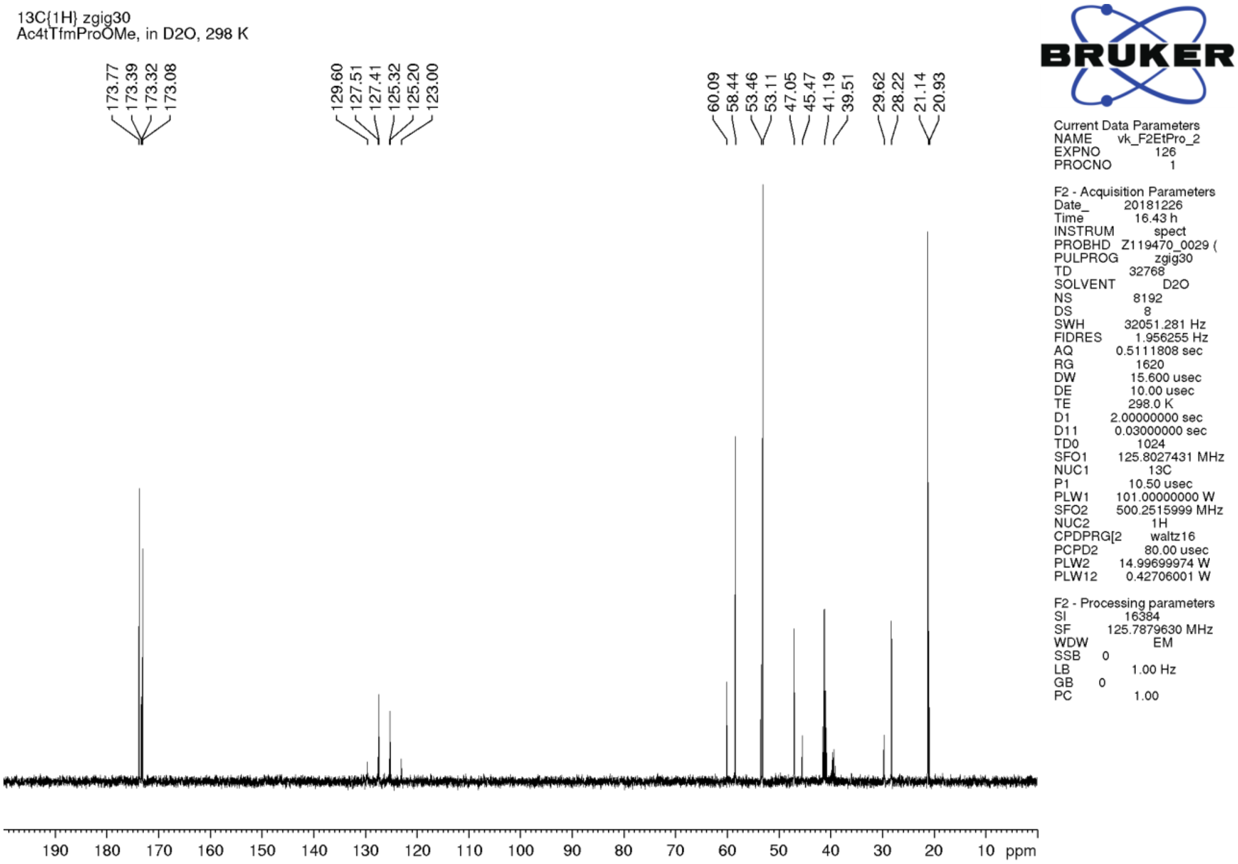
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O):



s-*trans*: 173.8 (s, CO_2Me), 173.1 (s, C(=O)N), 126.3 (q, J = 278 Hz, CF_3), 58.4 (s, α-CH), 53.1 (s, CH_3O), 47.0 (d, J = 4 Hz, δ-CH_2), 41.2 (q, J = 29 Hz, γ-CH), 28.2 (s, β-CH_2), 21.1 (s, Ac);



s-*cis*: 173.4 (s, C(=O)N), 173.3 (s, CO_2Me), 126.4 (q, J = 276 Hz, CF_3), 60.1 (s, α-CH), 53.4 (s, CH_3O), 45.5 (d, J = 4 Hz, δ-CH_2), 39.5 (q, J = 29 Hz, γ-CH), 29.6 (s, β-CH_2), 20.9 (s, Ac).

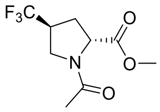


Current Data Parameters
NAME vk_F2EtPro_2
EXPNO 126
PROCNO 1

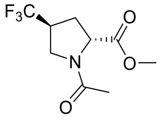
F2 - Acquisition Parameters
Date_ 20181226
Time 16.43 h
INSTRUM spect
PROBHD Z119470_0029 (
PULPROG zgig30
TD 32768
SOLVENT D2O
NS 8192
DS 8
SWH 32051.281 Hz
FIDRES 1.956255 Hz
AQ 0.5111808 sec
RG 1620
DW 15.600 usec
DE 10.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1024
SFO1 125.8027431 MHz
NUC1 13C
P1 10.50 usec
PLW1 101.00000000 W
SFO2 500.2515999 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 14.99699974 W
PLW12 0.42706001 W

F2 - Processing parameters
SI 16384
SF 125.7879630 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

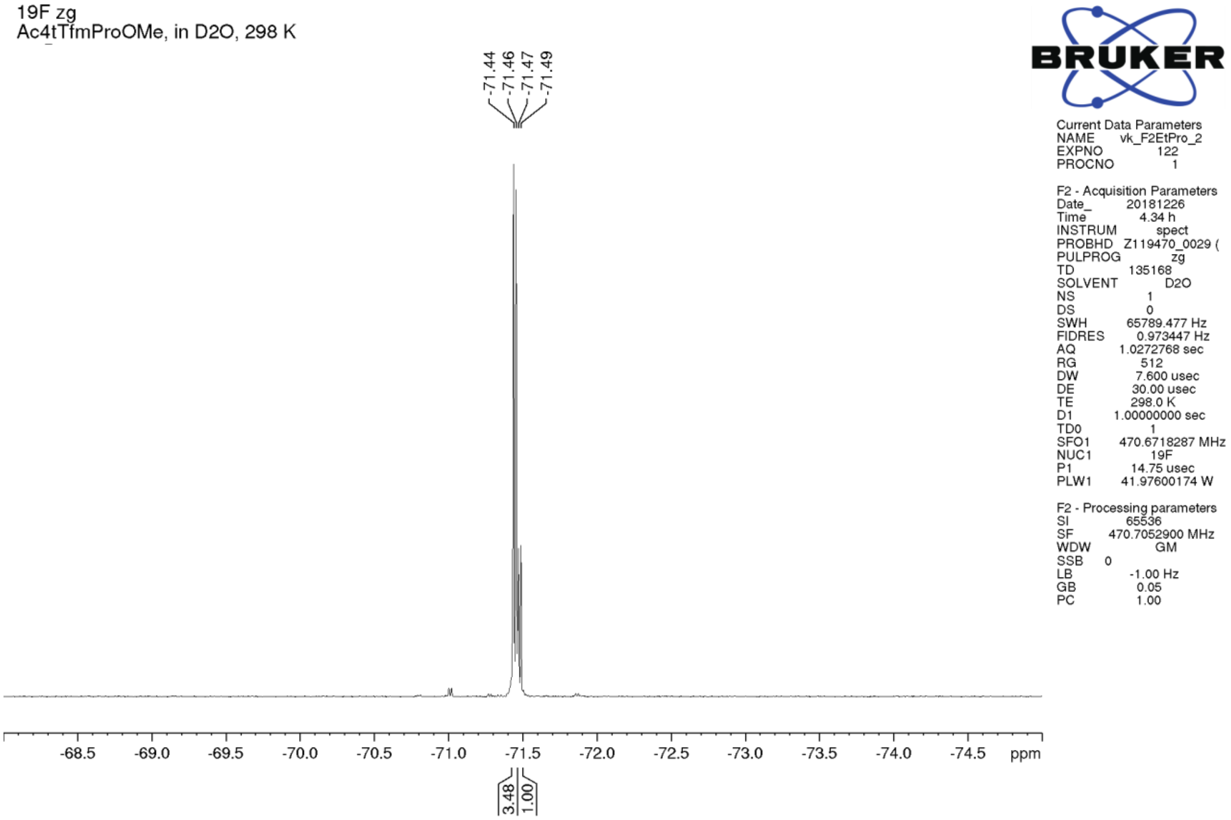
^{19}F NMR (471 MHz, D_2O):



s-*trans*: −71.44 (d, *J* = 9 Hz);

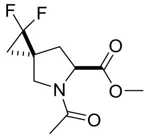


s-*cis*: −71.48 (d, *J* = 8 Hz).

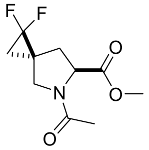


Methyl (*3r,6s*)-5-acetyl-1,1-difluoro-5-azaspiro[2.4]heptane-6-carboxylate (**5**)

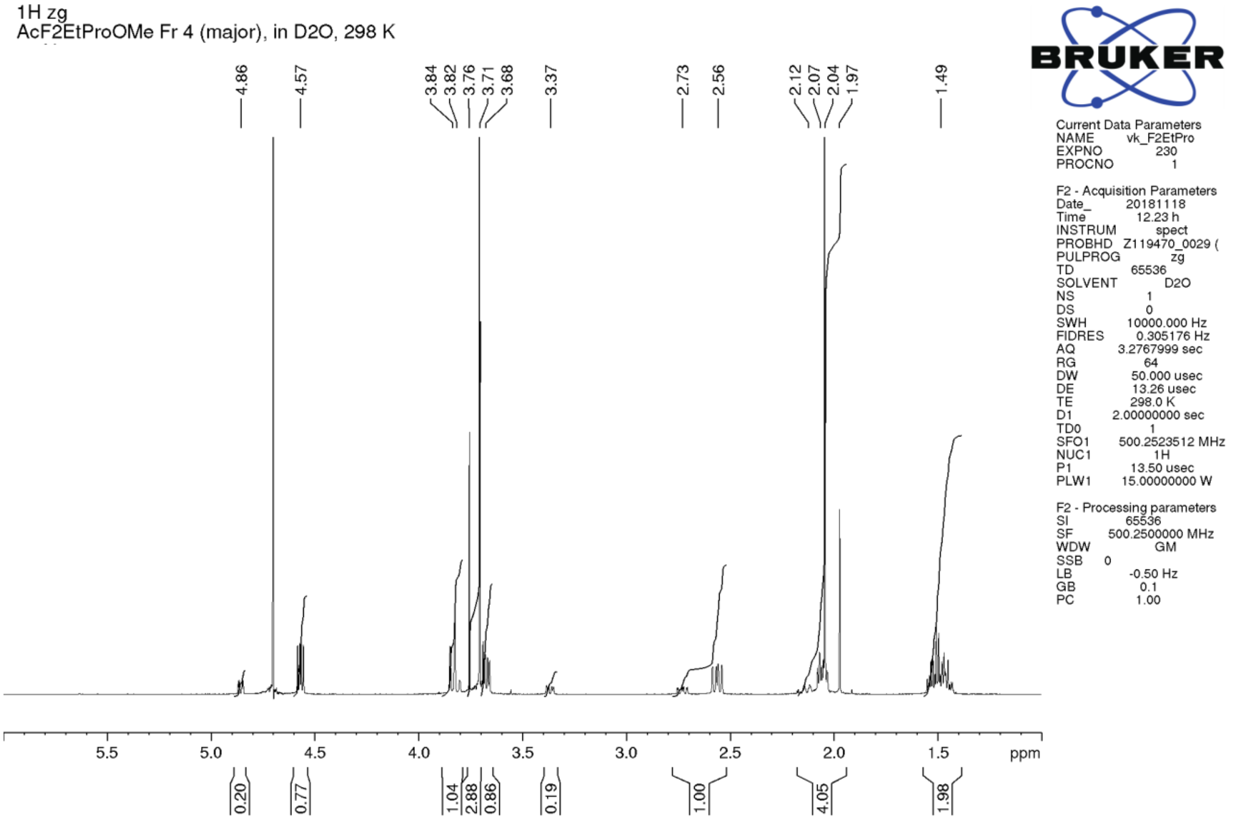
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 3.94 ± 0.03



s-*trans*: 4.57 (dd, *J* = 8.8. 5.0 Hz, 1H, α-CH), 3.84 (dd, *J* = 11.1, 1.4 Hz, 1H, δ-CH), 3.71 (s, 3H, CH_3O), 3.68 (dd, *J* = 11.1, 4.8 Hz, 1H, δ-CH), 2.56 (ddd, *J* = 13.6, 9.0, 1.0 Hz, 1H, β-CH), 2.06 (dt, *J* = 13.9, 4.8 Hz, β-CH), 2.04 (s, 3H, Ac), 1.50 (m, 2H, CH_2);



s-*cis*: 4.86 (dd, J= 8.7, 2.8 Hz, 1H, α-CH), 3.81 (dd, *J* = 12.3, 2.0 Hz, δ-CH), 3.76 (s, 3H, CH_3O), 3.37 (dd, *J* = 12.2, 4.3 Hz, 1H, δ-CH), 2.73 (ddd, *J* = 13.7, 8.8, 2.0 Hz, 1H, β-CH), 2.12 (dt, *J* = 13.6, 2.6 Hz, 1H, β-CH), 1.97 (s, 3H, Ac), 1.45 (m, 2H, CH_2).



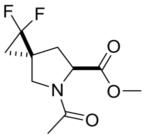
```
1H zg
AcF2EtProOMe Fr 4 (major), in D2O, 298 K
```

```
Current Data Parameters
NAME        vk_F2EtPro
EXPNO              230
PROCNO               1

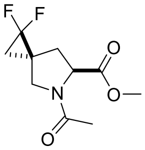
F2 - Acquisition Parameters
Date_         20181118
Time           12.23 h
INSTRUM          spect
PROBHD  Z119470_0029 (
PULPROG             zg
TD              65536
SOLVENT            D2O
NS                   1
DS                   0
SWH      10000.000 Hz
FIDRES    0.305176 Hz
AQ       3.2767999 sec
RG                 64
DW         50.000 usec
DE          13.26 usec
TE             298.0 K
D1      2.00000000 sec
TD0                  1
SFO1    500.2523512 MHz
NUC1               1H
P1          13.50 usec
PLW1    15.00000000 W

F2 - Processing parameters
SI              65536
SF      500.2500000 MHz
WDW                GM
SSB    0
LB            -0.50 Hz
GB                0.1
PC               1.00
```

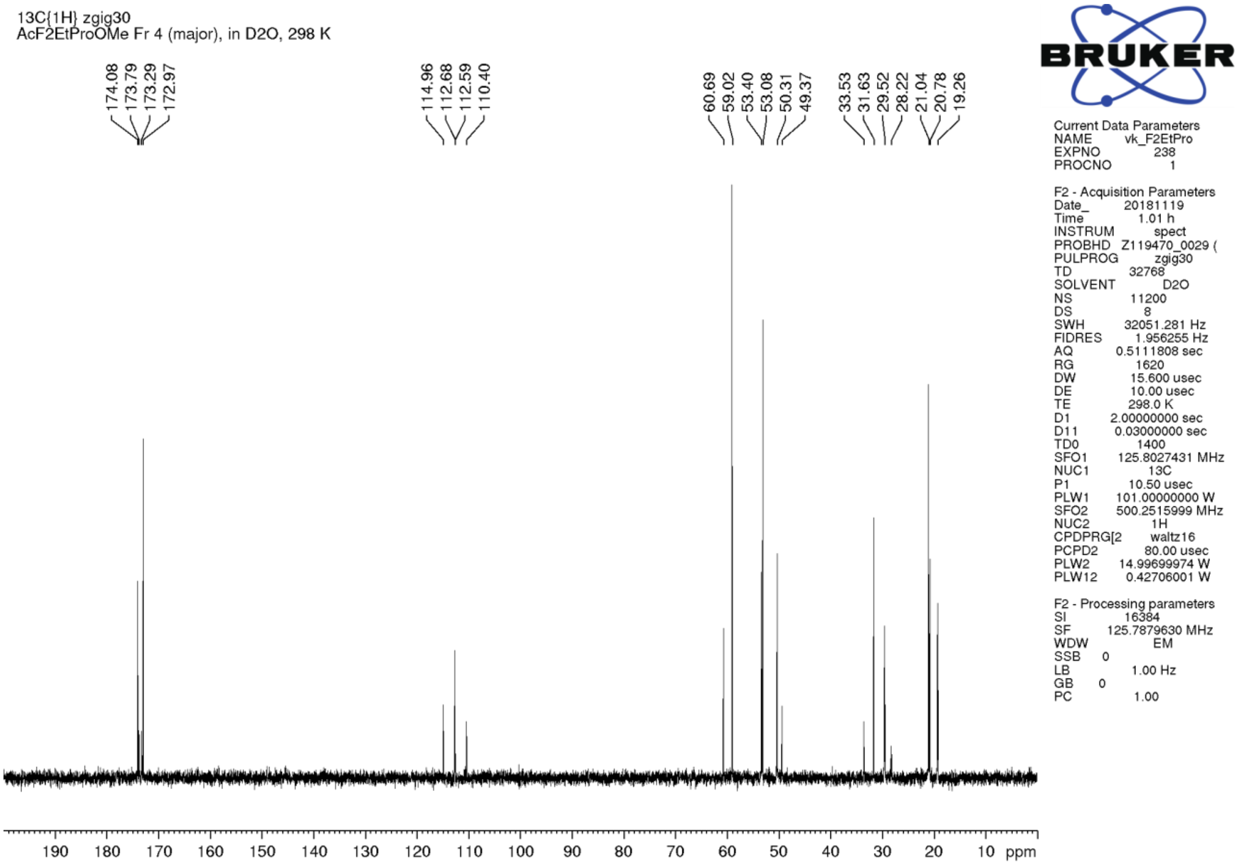
$^{13}C\{^1H\}$ NMR (126 MHz, D_2O):



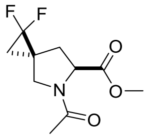
s-*trans*: 174.1 (s, CO_2Me), 173.0 (s, C(=O)N), 112.7 (t, CF_2, J = 287 Hz), 59.0 (s, α-CH), 53.1 (s, CH_3O), 50.3 (d, J = 6 Hz, δ-CH_2), 31.6 (d, J = 4 Hz, β-CH_2), 29.5 (t, J = 10 Hz, γ-C), 21.0 (s, Ac), 19.3 (t, J = 10 Hz, CH_2);



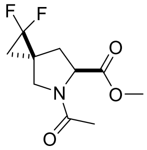
s-*cis*: 173.8 (s, CO_2Me), 173.3 (s, C(=O)N), 112.6 (t, CF_2, J = 287 Hz), 60.7 (s, α-CH), 53.4 (s, CH_3O), 49.4 (d, J = 4 Hz, δ-CH_2), 33.5 (s, β-CH_2), 28.2 (t, J = 12 Hz, γ-C), 20.8 (s, Ac), 20.8 (m, CH_2).



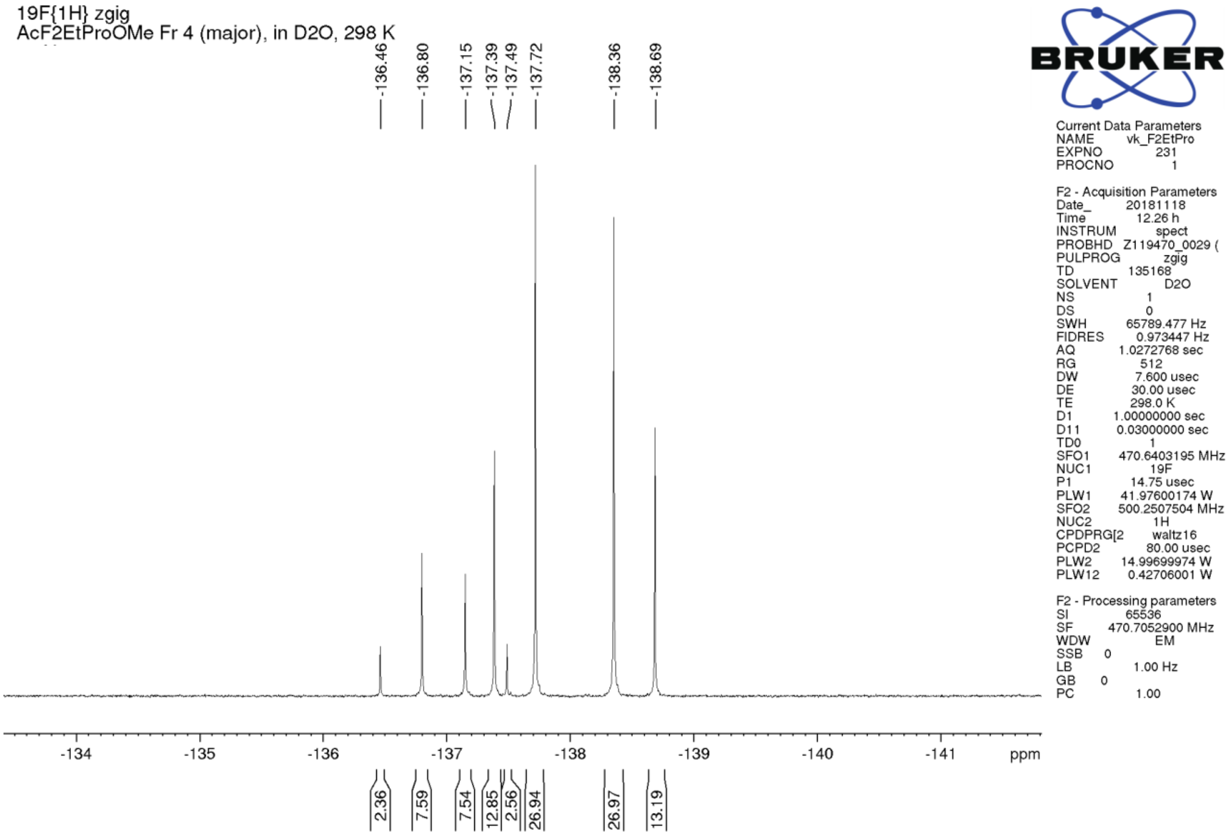
$^{19}F\{^{1}H\}$ NMR (471 MHz, D_2O):



s-*trans*: −137.6 (d, *J* = 157 Hz), −138.5 (d, *J* = 157 Hz);



s-*cis*: −136.6 (d, *J* = 159 Hz), −137.3 (d, *J* = 159 Hz).



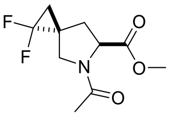
```
Current Data Parameters
NAME        vk_F2EtPro
EXPNO              231
PROCNO               1

F2 - Acquisition Parameters
Date_         20181118
Time            12.26 h
INSTRUM           spect
PROBHD   Z119470_0029 (
PULPROG            zgig
TD              135168
SOLVENT             D2O
NS                   1
DS                   0
SWH        65789.477 Hz
FIDRES      0.973447 Hz
AQ        1.0272768 sec
RG                  512
DW           7.600 usec
DE           30.00 usec
TE              298.0 K
D1       1.00000000 sec
D11      0.03000000 sec
TD0                  1
SFO1     470.6403195 MHz
NUC1                19F
P1           14.75 usec
PLW1      41.97600174 W
SFO2     500.2507504 MHz
NUC2                 1H
CPDPRG[2        waltz16
PCPD2        80.00 usec
PLW2      14.99699974 W
PLW12      0.42706001 W

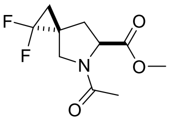
F2 - Processing parameters
SI                65536
SF       470.7052900 MHz
WDW                  EM
SSB     0
LB              1.00 Hz
GB      0
PC                 1.00
```

Methyl (*3r,6r*)-5-acetyl-1,1-difluoro-5-azaspiro[2.4]heptane-6-carboxylate (**6**)

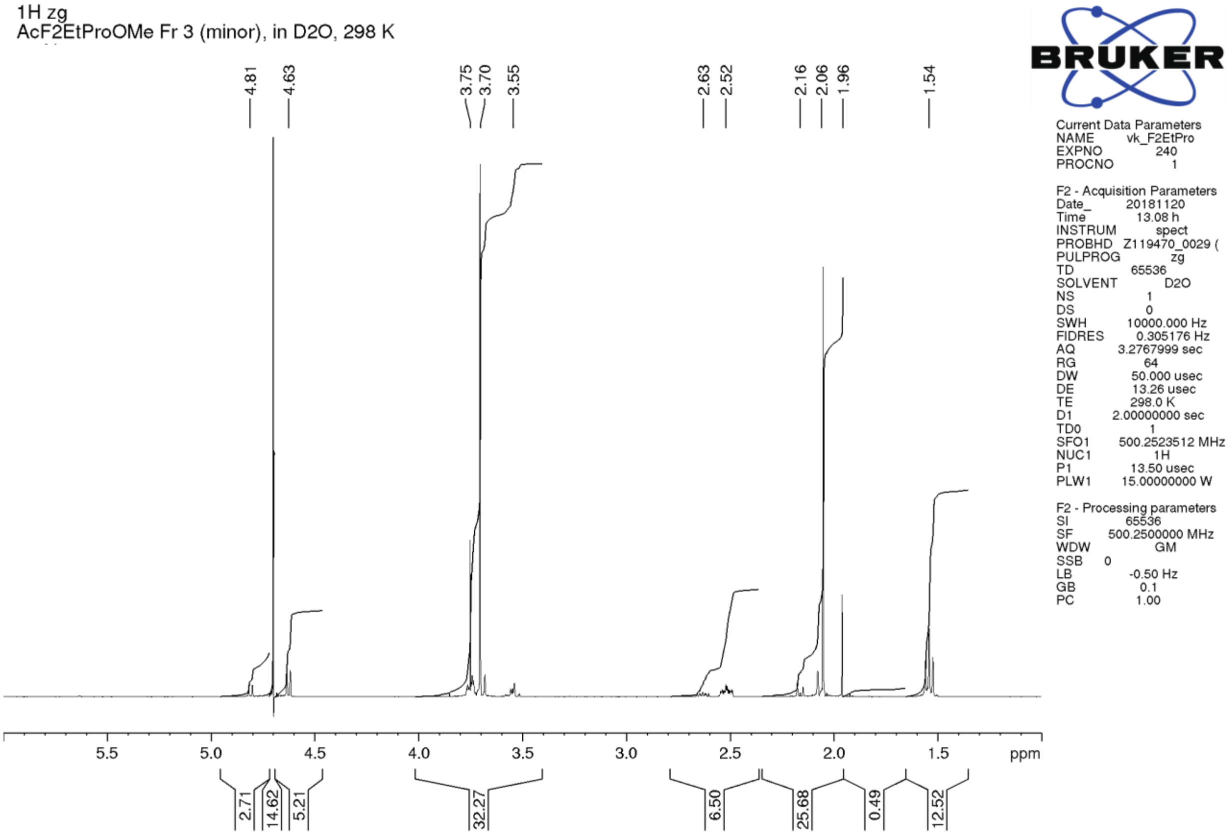
^{1}H NMR (500 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 3.15 ± 0.05



s-*trans*: 4.63 (dd, *J* = 9.1. 1.2 Hz, 1H, α-CH), 3.75 (ddd, *J* = 10.9, 3.8, 2.3 Hz, 1H, δ-CH), 3.70 (s, 3H, CH_3O), 3.69 (d, *J* = 10.5 Hz, 1H, δ-CH), 2.52 (ddm, *J* = 13.9, 9.2 Hz, 1H, β-CH), 2.06 (d, *J* = 14.6 Hz, 1H, β-CH), 2.05 (s, 3H, Ac), 1.54 (t, *J* = 9.0 Hz, 2H, CH_2);



s-*cis*: 4.81 (d, *J* = 8.6 Hz, 1H, α-CH), 3.75 (s, 3H, CH_3O), 3.57 (d, *J* = 12.1 Hz, δ-CH), 3.53 (d, *J* = 12.2, 1H, δ-CH), 2.63 (ddd, *J* = 13.7, 8.8, 6.0 Hz, 1H, β-CH), 2.16 (d, *J* = 13.9 Hz, 1H, β-CH), 1.96 (s, 3H, Ac), 1.54 (m, 2H, CH_2).

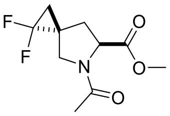


```
Current Data Parameters
NAME        vk_F2EtPro
EXPNO              240
PROCNO               1

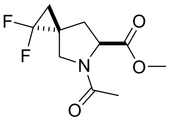
F2 - Acquisition Parameters
Date_        20181120
Time          13.08 h
INSTRUM         spect
PROBHD   Z119470_0029 (
PULPROG            zg
TD              65536
SOLVENT           D2O
NS                  1
DS                  0
SWH        10000.000 Hz
FIDRES      0.305176 Hz
AQ         3.2767999 sec
RG                 64
DW            50.000 usec
DE            13.26 usec
TE             298.0 K
D1        2.00000000 sec
TD0                 1
SFO1     500.2523512 MHz
NUC1               1H
P1            13.50 usec
PLW1      15.00000000 W

F2 - Processing parameters
SI              65536
SF       500.2500000 MHz
WDW                GM
SSB     0
LB           -0.50 Hz
GB               0.1
PC              1.00
```

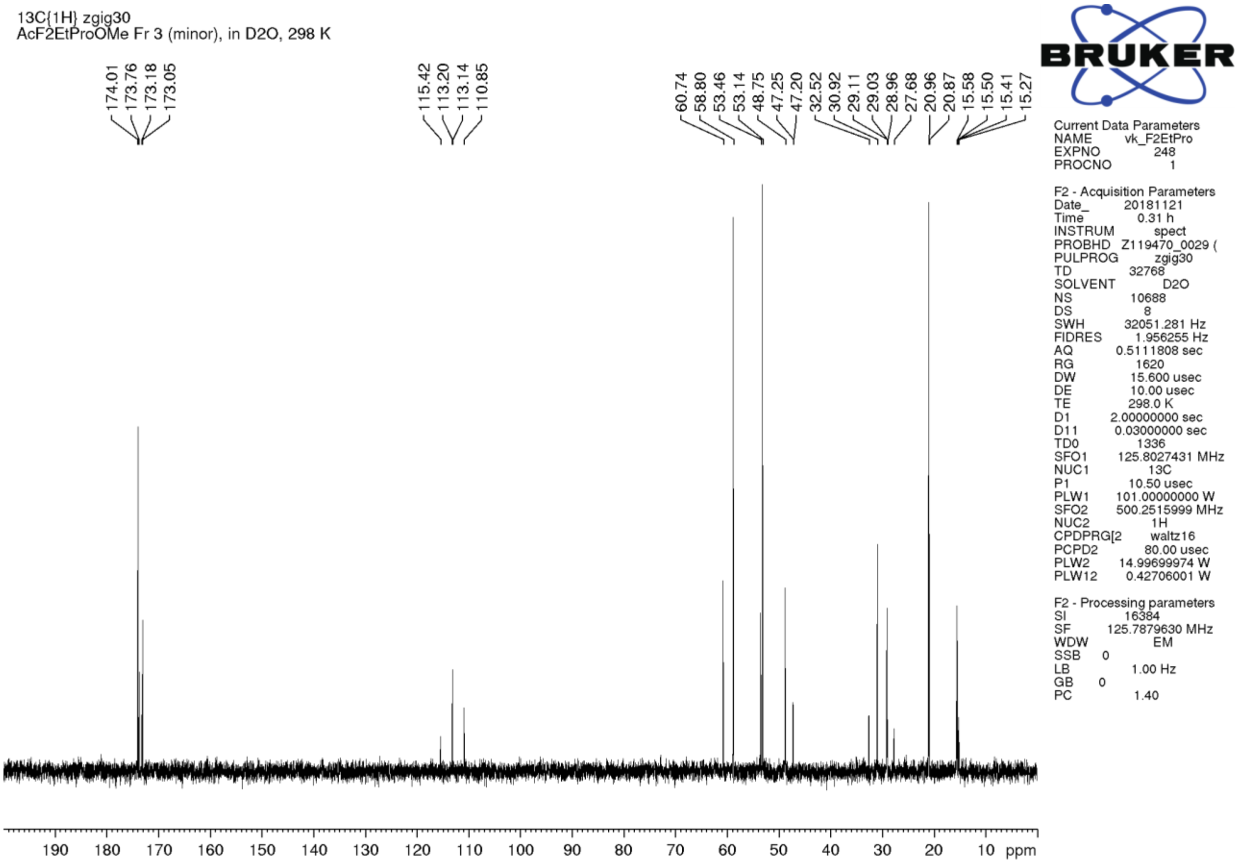
$^{13}C\{^{1}H\}$ NMR (126 MHz, D_2O):



s-*trans*: 174.0 (s, CO_2Me), 173.1 (s, C(=O)N), 113.2 (t, CF_2, *J* = 288 Hz), 58.8 (s, α-CH), 53.1 (s, CH_3O), 48.8 (d, *J* = 4 Hz, δ-CH_2), 30.9 (s, β-CH_2), 29.0 (t, *J* = 10 Hz, γ-C), 21.0 (s, Ac), 15.5 (t, *J* = 11 Hz, CH_2);



s-*cis*: 173.8 (s, CO_2Me), 173.2 (s, C(=O)N), 113.2 (t, CF_2, *J* = 287 Hz), 60.7 (s, α-CH), 53.5 (s, CH_3O), 47.2 (d, *J* = 6 Hz, δ-CH_2), 32.5 (d, *J* = 5 Hz, β-CH_2), 27.7 (t, *J* = 10 Hz, γ-C), 20.9 (s, Ac), 15.2 (t, *J* = 12 Hz, CH_2).

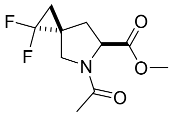

13C{1H} zgig30
AcF2EtProOMe Fr 3 (minor), in D2O, 298 K

```
Current Data Parameters
NAME       vk_F2EtPro
EXPNO             248
PROCNO              1

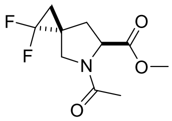
F2 - Acquisition Parameters
Date_        20181121
Time           0.31 h
INSTRUM         spect
PROBHD   Z119470_0029 (
PULPROG        zgig30
TD              32768
SOLVENT           D2O
NS              10688
DS                  8
SWH        32051.281 Hz
FIDRES      1.956255 Hz
AQ         0.5111808 sec
RG               1620
DW             15.600 usec
DE              10.00 usec
TE              298.0 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0              1336
SFO1      125.8027431 MHz
NUC1              13C
P1              10.50 usec
PLW1     101.00000000 W
SFO2      500.2515999 MHz
NUC2               1H
CPDPRG[2       waltz16
PCPD2           80.00 usec
PLW2      14.99699974 W
PLW12      0.42706001 W

F2 - Processing parameters
SI              16384
SF        125.7879630 MHz
WDW                EM
SSB     0
LB               1.00 Hz
GB      0
PC               1.40
```

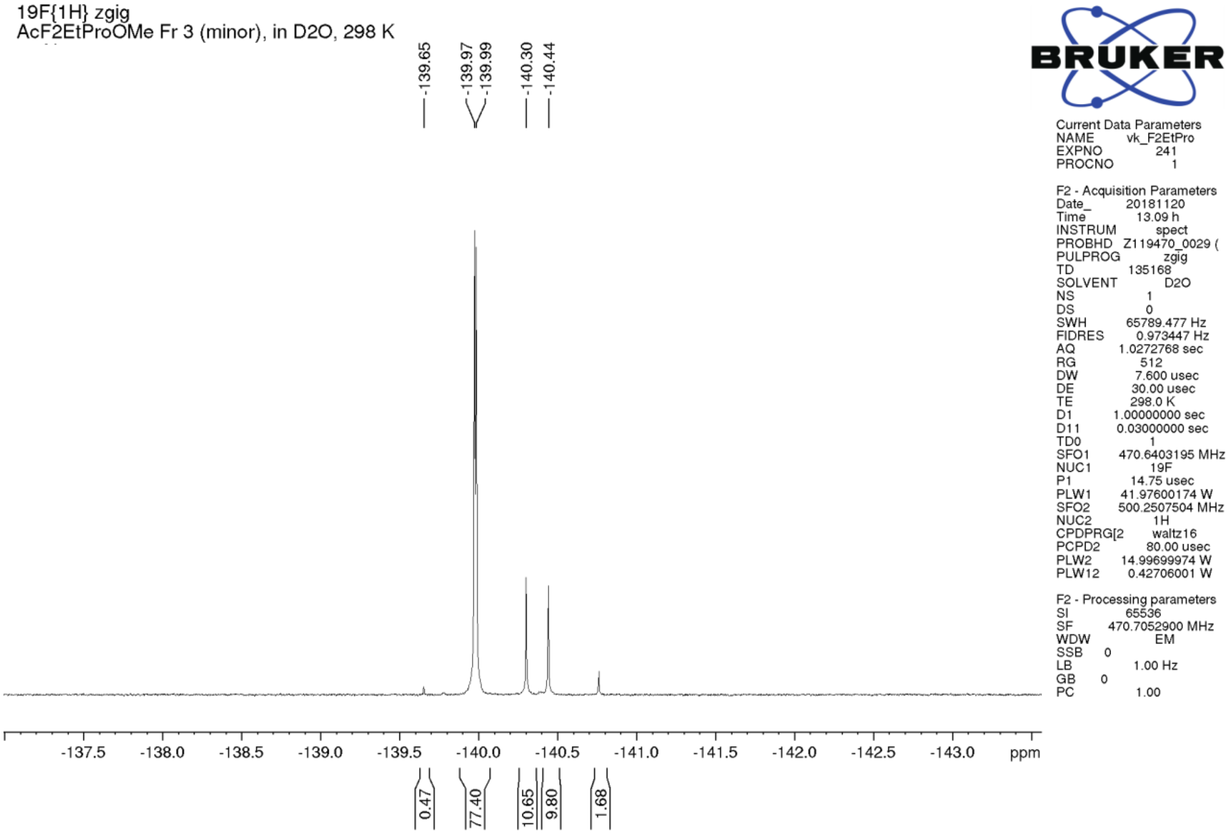
$^{19}F\{^1H\}$ NMR (471 MHz, D_2O):



s-*trans*: −139.9 (d, *J* = 152 Hz), −140.1 (d, *J* = 150 Hz);



s-*cis*: −140.3 (d, *J* = 150 Hz), −140.5 (d, *J* = 151 Hz).



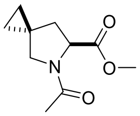
```
Current Data Parameters
NAME        vk_F2EtPro
EXPNO              241
PROCNO               1

F2 - Acquisition Parameters
Date_         20181120
Time           13.09 h
INSTRUM          spect
PROBHD   Z119470_0029 (
PULPROG           zgig
TD              135168
SOLVENT            D2O
NS                   1
DS                   0
SWH        65789.477 Hz
FIDRES      0.973447 Hz
AQ        1.0272768 sec
RG                 512
DW           7.600 usec
DE          30.00 usec
TE             298.0 K
D1       1.00000000 sec
D11      0.03000000 sec
TD0                  1
SFO1    470.6403195 MHz
NUC1               19F
P1          14.75 usec
PLW1      41.97600174 W
SFO2    500.2507504 MHz
NUC2                1H
CPDPRG[2       waltz16
PCPD2       80.00 usec
PLW2      14.99699974 W
PLW12      0.42706001 W

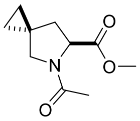
F2 - Processing parameters
SI               65536
SF      470.7052900 MHz
WDW                 EM
SSB     0
LB              1.00 Hz
GB      0
PC                1.00
```

Methyl (*6S*)-5-acetyl-5-azaspiro[2.4]heptane-6-carboxylate (**7**)

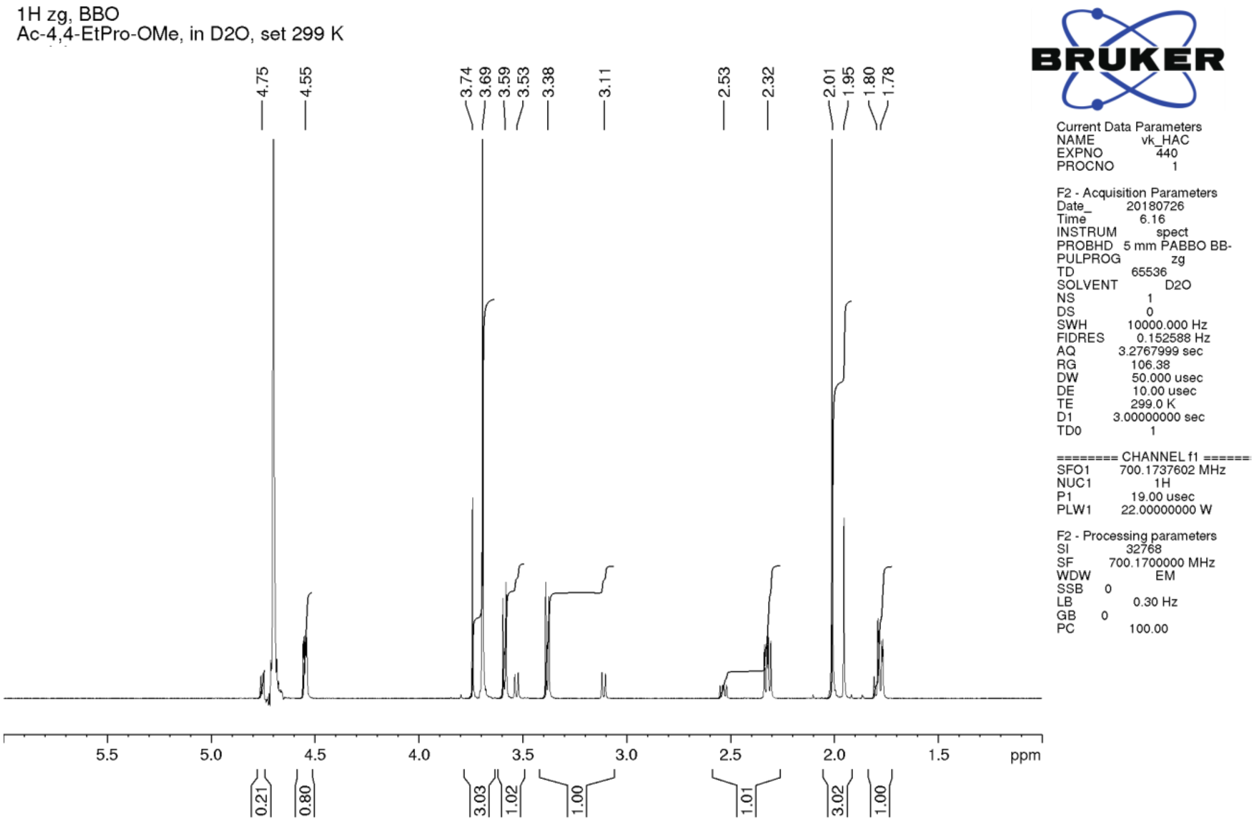
^{1}H NMR (700 MHz, D_2O), two rotamers, $K_{trans/cis}$ = 3.92 ± 0.04



s-*trans*: 4.55 (dd, *J* = 8.8. 3.6 Hz, 1H, α-CH), 3.69 (s, 3H, CH_3O), 3.59 (d, *J* = 10.3 Hz, 1H, δ-CH), 3.38 (d, *J* = 10.3 Hz, 1H, δ-CH), 2.32 (dd, *J* = 13.0, 8.8 Hz, 1H, β-CH), 2.01 (s, 3H, Ac), 1.78 (dd, *J* = 13.1, 3.8 Hz, 1H, β-CH), 0.60-0.40 (m, 4H, $2xCH_2$);



s-*cis*: 4.75 (d, *J* = 8.4 Hz, 1H, α-CH), 3.74 (s, 3H, CH_3O), 3.53 (d, *J* = 11.2 Hz, δ-CH), 3.11 (d, *J* = 11.5, 1H, δ-CH), 2.53 (dd, *J* = 12.9, 8.6 Hz, 1H, β-CH), 1.95 (s, 3H, Ac), 1.80 (d, *J* = 13.8 Hz, 1H, β-CH), 0.60-0.40 (m, 4H, $2xCH_2$).



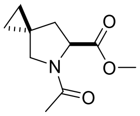
```
Current Data Parameters
NAME          vk_HAC
EXPNO            440
PROCNO             1

F2 - Acquisition Parameters
Date_       20180726
Time            6.16
INSTRUM        spect
PROBHD  5 mm PABBO BB-
PULPROG           zg
TD             65536
SOLVENT          D2O
NS                 1
DS                 0
SWH        10000.000 Hz
FIDRES      0.152588 Hz
AQ         3.2767999 sec
RG            106.38
DW            50.000 usec
DE             10.00 usec
TE             299.0 K
D1        3.00000000 sec
TD0                1

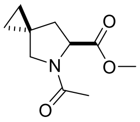
======== CHANNEL f1 =======
SFO1      700.1737602 MHz
NUC1              1H
P1             19.00 usec
PLW1     22.00000000 W

F2 - Processing parameters
SI             32768
SF        700.1700000 MHz
WDW               EM
SSB     0
LB              0.30 Hz
GB      0
PC            100.00
```

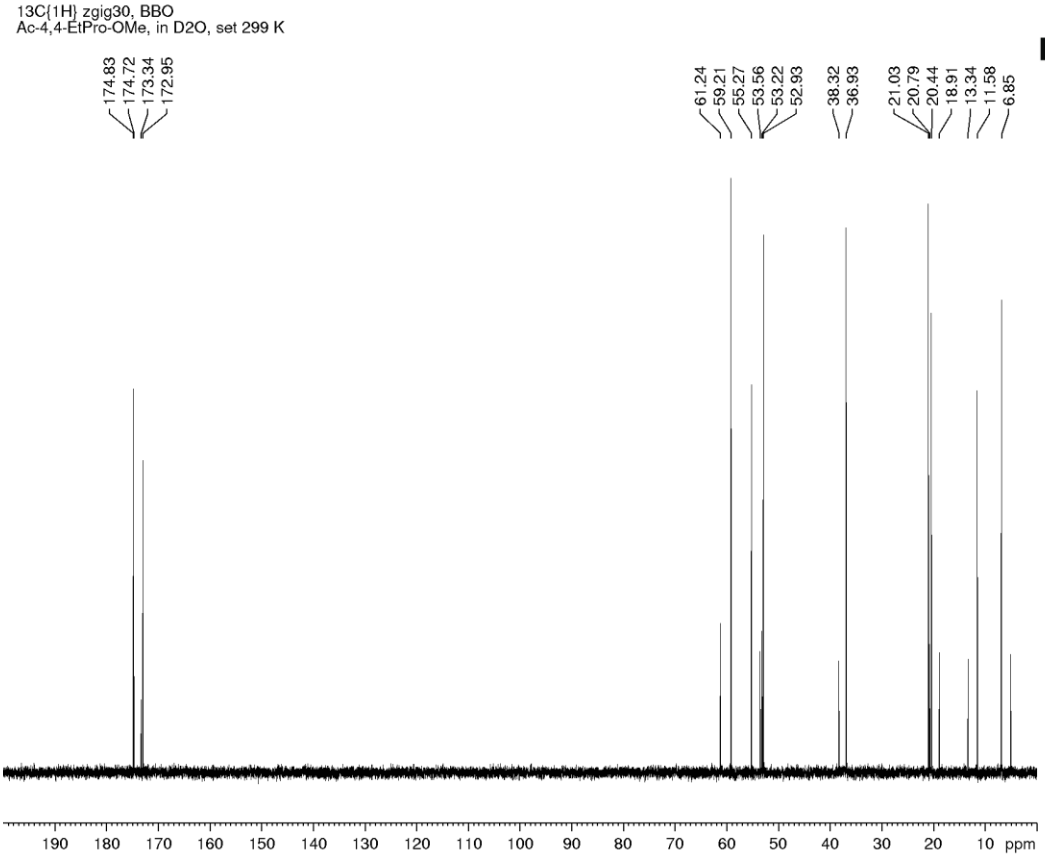
$^{13}C\{^1H\}$ NMR (176 MHz, D_2O):



s-*trans*: 174.8 (s, CO_2Me), 173.0 (s, C(=O)N), 59.2 (s, α-CH), 55.3 (s, δ-CH_2), 52.9 (s, CH_3O), 36.9 (s, β-CH_2), 21.0 (s, Ac), 20.4 (s, γ-C), 11.6 (s, CH_2), 6.9 (s, CH_2);



s-*cis*: 174.7 (s, CO_2Me), 173.3 (s, C(=O)N), 61.2 (s, α-CH), 53.6 (s, δ-CH_2), 53.2 (s, CH_3O), 38.3 (s, β-CH_2), 20.8 (s, Ac), 18.9 (s, γ-C), 13.3 (s, CH_2), 5.1 (s, CH_2).



```
Current Data Parameters
NAME          vk_HAC
EXPNO            445
PROCNO             1

F2 - Acquisition Parameters
Date_        20180726
Time            19.58
INSTRUM         spect
PROBHD   5 mm PABBO BB-
PULPROG        zgig30
TD             32768
SOLVENT           D2O
NS              6002
DS                 8
SWH        40760.871 Hz
FIDRES      1.243923 Hz
AQ         0.4019541 sec
RG              2050
DW            12.267 usec
DE            10.00 usec
TE             299.1 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0             1024

======== CHANNEL f1 =======
SFO1       176.0763711 MHz
NUC1             13C
P1              11.50 usec
PLW1       67.00000000 W

======== CHANNEL f2 =======
SFO2       700.1728007 MHz
NUC2              1H
CPDPRG[2        waltz16
PCPD2           65.00 usec
PLW2       22.00000000 W
PLW12       1.41760004 W

F2 - Processing parameters
SI             32768
SF         176.0578870 MHz
WDW               EM
SSB     0
LB              1.00 Hz
GB      0
PC              5.00
```

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