Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

Supporting Information

Quantitative and convenient real-time reaction monitoring using stopped-flow benchtop NMR.

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1. General Methods

a. Chemicals

Benzotrifluoride (BTF, **1**, 99%), trifluoroacetic acid (TFA, **2**, 99%), diisopropylethylamine (DIPEA, 99%), triethylamine (TEA, 99%), acetonitrile (MeCN), and methanol (MeOH) were purchased from Sigma-Aldrich. Sulfonyldiimidazole (SDI, **3**, 99%), 4-fluorobenzoic acid (**7**, 98%), and potassium fluoride (KF, 99%) were purchased from AK Scientific. Diphenylphosphoryl azide (DPPA, 99%) and hexafluoro-2-propanol (HFIPA, **12**, 99%) were purchased from Oakwood Chemicals. Lastly, toluene was purchased from Fischer Chemical. All reagents and solvents were used as received, unless otherwise stated. Silica was sourced from Silicycle (F60 60 Å, 230-400 mesh).

b. NMR data collection, processing, and analysis

Chemical shifts (δ) are reported in parts-per-million (ppm) and all NMR data were processed and analyzed with MestReNova (mnova) software. The following abbreviations were used to describe multiplicities of resonances: s = singlet, d = doublet, q = quartet, s = septet, br s = broad singlet, dd = doublet of doublets, m = multiplet. Additionally, all coupling constants (J) are provided in hertz (Hz).

LF ^{19}F NMR data were processed with baseline correction (zeroth-order polynomial fit) and auto phase correction (manual phase correction applied if additional correction necessary). Additionally, data were processed with applied exponential apodization of 2.0 Hz.

LF NMR data were collected with a Nanalysis NMReady-60PRO spectrometer (^{1}H 60.49 MHz and ^{19}F 56.91 MHz). All offline high-field (HF) NMR data were collected with a Bruker Avance 300 spectrometer (^{1}H 300.13 MHz, ^{13}C 75.48 MHz, ^{19}F 282.40 MHz, ^{31}P 121.49 MHz) and/or a Bruker Avance 400 spectrometer (^{1}H 400.13 MHz, ^{13}C 100.62 MHz, ^{31}P 161.97 MHz).

c. Hazards and experimental precautions

Reactions included in this work include hazardous material that must be taken under special consideration. Sulfuryl fluoride (SO_2F_2, **4**) is a toxic, electrophilic gas and must only be worked with in well ventilated conditions. The included reactions involving **4** additionally result in the formation of hydrofluoric acid (HF), highly corrosive and dangerous. The Curtius rearrangement work involves both gas formation and hazardous azide handling. Consideration to avoid over pressurization with either reaction system (venting and/or balloon) must be taken.

2. Stopped-flow LF NMR system details

a. General physical description

For a schematic of the stopped-flow system, please see **Figure 1** in main text. To facilitate stopped-flow LF NMR measurements, the NMR spectrometer was equipped with a

glass flow cell (Nanalysis), with a total internal volume of approximately 1.20 mL (~ 0.575 mL within the reading frame of the instrument). The internal diameter of the flow cell within the reading frame is the same as a 5 mm NMR tube as the flow cell is initially made from a 5 mm NMR tube. The NMR instrument was additionally placed on internally designed and 3D printed legs (**Figure S1**). These legs allowed for the vibration dampening feet, while also allowing for additional clearance for the flow cell between the bottom of the flow cell and the lab bench.

Figure S1. Close up picture displaying the utilized 3D printed legs, allowing for instrument to be slightly lifted (advantageous for flow cell) and use of the instrument's vibration dampening features.

To physically move solutions within the flow system, a Vapourtec (SF-10) peristaltic reagent pump was used within the system. Solutions were directed either to the spectrometer or back to the vial determined by the position of Vici 6-port valve (**Figure 1**). The hardware components of the flow system (pump, spectrometer, and valve) were connected by either ethylene tetrafluoroethylene (ETFE) tubing (1/16" O.D., 0.02" inner diameter I.D.) or polyether ether ketone (PEEK) tubing (1/16" O.D., 0.01" I.D.)). The identity and lengths of each segment of line is designated in **Figure S2**. In our experience the segments of smaller I.D. tubing were necessary to eliminate solvent cavitation, resulting from insufficient generation of backpressure. Further, the temperature of the reaction flask was further controlled using an oil bath on a hot plate, where appropriate and indicated. No temperature control is allowable with the NMR spectrometer itself (magnet internally controlled at constant 35° C) and the segments of ETFE and PEEK tubing were not thermally insulated.

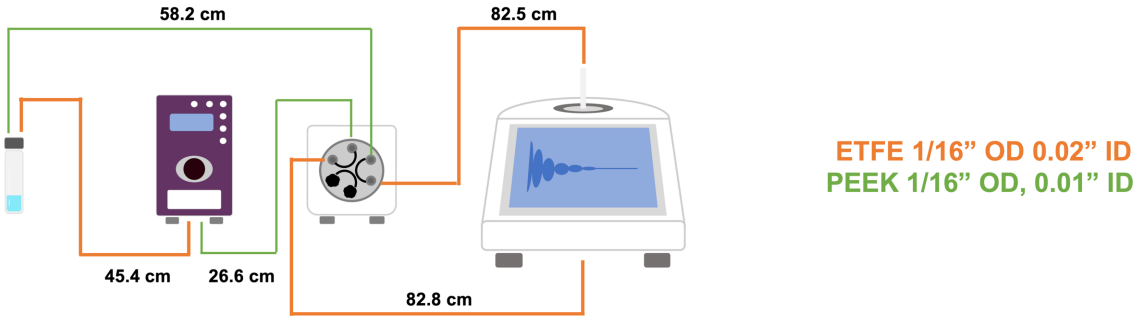


Figure S2. Colour designated identity (orange for ETFE or green for PEEK) and associated lengths of tubing for each segment of stopped-flow LF NMR system.

b. Description of workflow with Python script and stopped-flow NMR system

As described in the main text, the stopped-flow NMR system's hardware components are controlled remotely by a Python script. Prior to analysis, our work generally began by performing an autoshim with the spectrometer. This was generally performed on the reaction solvent (preferably on solution with starting material) until a linewidth $\leq$ 1.8 Hz was achieved, generally the case after a 'Medium' or 'Full' autoshim. Then the workflow began with designating the observed nucleus ('19F' for our ^{19}F NMR work), lock nucleus ('1H' for our work in protio solvent), the solvent (either 'Acetonitrile' or 'Toluene' in our included work), and the experiment ('1D' for our trials). By selecting 'Experiment Settings', the relevant acquisition parameters can be selected on the spectrometer (SW, d1, o1p, number complex data points, number transients, dummy scans, pulse angle, rg), thereby determining the overall NMR experiment time.

Then in the Python script (screenshot in **Figure S3**), the pre-magnetization time, pump flow rate, whether a spectrum at time zero (t=0 s) was desired, total number of spectra, and desired total time between spectra are denoted. This is considering that the spectrometer's IP address, COM port connected to valve, and valve serial number (turquoise arrows in **Figure S3**) are already inputted to script (this only needs to be done once considering these don't change). Further, we noticed that unless the pulse angle and fixed rg is explicitly fixed in the script itself, these values may default to another spectrometer determined value. These can be denoted where designated with dark blue arrows in **Figure S3**. Once the reaction of interest is ready to be initiated, the 'NMReady-CONNECT' feature on the spectrometer must be enabled to allow remote calls (done by going to 'Setup' -> 'System' -> 'Network' -> 'Remote' -> check box to enable 'NMReady-CONNECT'). Then the script is ready to be started.

Our reaction monitoring work generally began with acquiring a spectrum at t=0 s. Considering the valve in Position 'B' (our default position), once the script is started in PyCharm, the pump starts (at determined flow rate) and the valve instantly switches to position 'A'. Therefore, at this point the reaction solution is static in the flow cell (note, no new solution enters the flow cell once the script is initiated with these conditions). After waiting the designated pre-magnetization time allowing for sufficient polarization of the spins in the static sample prior to application of radiofrequency (rf) pulse, NMR data is acquired per the acquisition parameters denoted on the spectrometer (pulse angle/rg denoted in script). After data acquisition, the valve switches position (position 'B') and fresh solution flows through the NMR flow cell for the remainder of the denoted time between spectra. The process is then repeated until the desired number of spectra are acquired, with the pump turning off after the final NMR spectrum is acquired.

Figure S3. Screenshot of the Python script allowing for convenient and centralized control of the stopped-flow LF NMR system, with important designations for analysis annotated.

c. Calibration of system's peristaltic pump

The used Vapourtec SF-10 reagent pump was calibrated with the use of MeOH and five flow rates (later determined to be 0.7, 1.3, 2.2, 2.6, and 3.2 mL/min), with each flow rate analyzed in triplicate. To do so, three scintillation vials per flow rate were pre-weighed using an analytical balance. With the stopped-flow NMR system primed with MeOH and valve in position 'B' (**Figure 1**), MeOH was pumped through the flow system and collected into one of the pre-weighed scintillation vials at a single set flow rate (1.0, 2.0, 3.3, 4.0, and 5.0 mL/min flow set flow rates analyzed) for 2 minutes. The mass of MeOH pumped in this time interval was converted to a volume using the density of MeOH - allowing for the actual flow rate to be determined. Within the flow rate range analyzed, these data suggested a conversion factor of multiplying the set flow rate by 0.6495 to determine the actual flow rate (**Figure S4**).

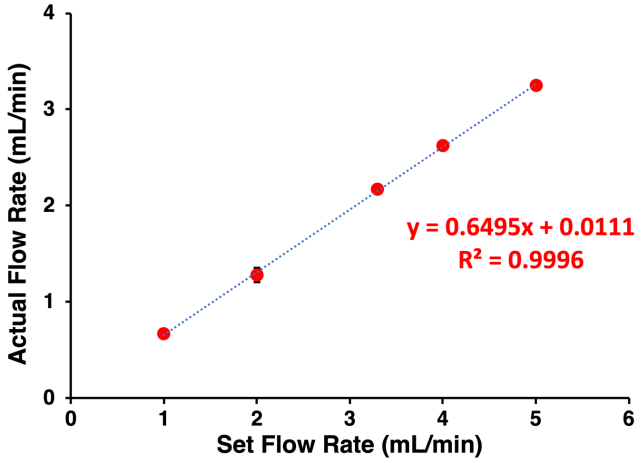


Figure S4. Calibration of Vapourtec SF-10 reagent pump used for LF NMR stopped-flow system.

d. Volume determination of LF NMR stopped-flow system

With no thermal control of reaction solution in the lines of the NMR stopped-flow system, nor of the solution in the NMR spectrometer, it was of keen interest to understand the volume of the stopped-flow NMR system. This information was of interest as this fraction of the solution is not necessarily exposed to conditions (such as mixing or temperature) of the remainder of the reaction solution at any given point of time.

To do measure this volume, a 0.32 M solution of **1** was prepared using a microsyringe, brought to 25.00 mL with MeCN in a volumetric flask, and thoroughly mixed. Using a volumetric pipet, 5.00 mL of this solution was transferred to a scintillation vial, equipped with a magnetic stir bar and fitted with a septum filled cap. About 19 mL of the remainder solution in the volumetric flask was flowed through the stopped-flow NMR system (2.14 mL/min per previous calibration, valve in position 'B' per **Figure 1**) and collected into a waste container, ensuring this solution was purely within the reading frame of the instrument. The pump was stopped and three ^{19}F NMR spectra ('pre' spectra) were acquired on the solution, each with the same acquisition parameters: four transients, zero dummy scans, 90° pulse, 44 db rg, 61.2 s d1, -50.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points).

Post data acquisition, the solution in the flow system was evacuated and fresh MeCN was flowed into the system (again, collecting into waste at 2.14 mL/min with valve in position 'B') for ~ 20 minutes. With the system primed with fresh MeCN, the inlet and outlet lines of the

system were transferred to the scintillation vial with the 5.00 mL of the **1** standard solution. On a magnetic stir plate, the solution in the vial was stirred (500 rpm) and the inlet line was placed well below the liquid level. The pump was then turned on (2.14 mL/min) and the solution was able to circulate and reach an equilibrium concentration over 20 minutes. After this time, the pump was turned off and three ^{19}F NMR spectra ('post' spectra) were acquired on the solution with the same acquisition parameters previously described for the 'pre' spectra.

The above procedure was completed in duplicate (six total spectra for 'pre' conditions and total spectra for 'post conditions'). Once spectra were imported and processed in mnova, the absolute integration of the trifluoromethyl resonance (δ_F -63.5 ppm) of **1** was determined. The average 'pre' integration (587.9545, 1.48% RSD) and average 'post' integration (433.7993, 2.81%) were used to determine the volume of the system based on a 5.00 mL 'pre' volume. Therefore, the system's volume (calculated 1.78 mL) was equal to the 'post' volume minus the 'pre' volume, with the 'post' volume equal to (('pre' integration * 'pre' volume) / 'post' integration).

e. Determination of flow rate for subsequent analyses with LF NMR stopped-flow system

Using too high of a flow rate (> 2.2 mL/min) with the utilized flow cell has shown eddying and mixing behaviours that are less than optimal for efficient emptying/filling with the flow system.[1] Therefore, we desired to use a medium flow rate to transfer reaction solution to the flow cell for analysis within a reasonable amount of time, without the introduction of behaviours that might be counterproductive for efficient filling/emptying.

Considering some factors that would fix the time that analyte solution is static in the valve and NMR loop (such as the pre-magnetization time just prior to data acquisition and the NMR data acquisition time itself), we desired to flow fresh solution at a rate of the system's volume per minute, for no more than four minutes. This was in effort to decrease time between subsequent data points without jeopardizing the integrity and representative nature of acquired qNMR data. To verify this timing scheme resulted in both sufficient mixing and a representative sample for analysis, a solution of **1** in MeCN was once again used. A 0.24 M solution of **1** was prepared in a 10.00 mL volumetric flask, using a microsyringe to measure and transfer **1**. This was then brought to 10.00 mL with fresh MeCN. Using a volumetric pipet, 5.00 mL was transferred to a scintillation vial that was configured with a magnetic stir bar and septum filled cap.

The NMR flow system was cleaned and primed with fresh MeCN (valve in position 'B' per **Figure 1**). On the spectrometer, ^{19}F NMR data acquisition parameters were designated: four transients, zero dummy scans, 90° pulse, 44 db rg, 61.2 s d1, -50.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). Relevant parameters were also designated in the Python script: collect spectrum at t=0, 15 s pre-magnetization time, 11 total time points after t=0, spectrum every 510 s, and a 1.78 mL/min pump flow rate. Then, with the inlet line placed well below the liquid level in the scintillation vial, stirring was initiated (500 rpm), and the spectrometer in 'Remote' mode, the script was initiated.

Once spectra were imported and processed in mnova, the absolute integration of the trifluoromethyl resonance (δ_F -63.5 ppm) of **1** was determined and monitored as a function of time. To our delight, this timing scheme (3.94 minutes of analyte flow between time points with a 1.78 mL/min flow rate) appeared to result in efficient transfer of analyte (**Figure S5**). This was concluded based on the first data point with **1** observed at the second overall timepoint, and the concentration of **1** remained constant over the duration of analysis. No oscillation in **1** concentration was observed until an equilibrium concentration was achieved, expected if either

the flow rate or time of flow needed to be adjusted to allow. Therefore, for all following stopped-flow analyses, this flow rate (1.78 mL/min) and time period of flow (3.94 min) was used.

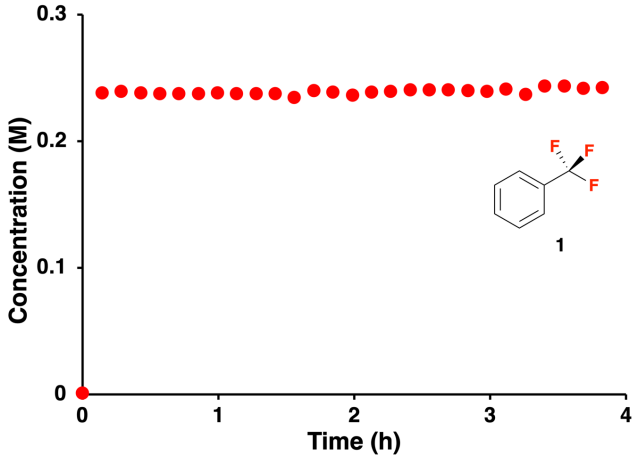


Figure S5. Verification of sufficient transfer and mixing of analyte with a 1.78 mL/min flow rate and 3.94 min. Determined by ^{19}F NMR (57 MHz) monitoring the trifluoromethyl resonance of **1** (δ_F -63.5 ppm), with the system initially primed with MeCN.

3. ^{19}F NMR data acquisition parameter selection

a. Radiofrequency (rf) pulse verification

To verify pulse excitation, a sample of lithium bis(fluorosulfonyl)imide (LiFSI) was gravimetrically prepared in a 50:50 mixture of H_2O:D_2O (0.26 M). ^{19}F NMR spectra were acquired (in triplicate) with four transients, zero dummy scans, 44.0 dB rg, 61 s d1, -60.0 ppm o1p, 219.6 ppm, and 2.79 AQ (34,816 complex data points). 16 pulse angles were analyzed from 0° to 372.5° (0.00°, 23.3°, 45.0°, 66.7°, 90.0°, 116.9°, 146.2°, 174.0°, 198.0°, 219.9°, 241.5°, 264.2°, 290.1°, 319.2°, 347.7°, and 372.5°) by changing the proportional pulse width. Once these data were acquired and processed, the integral area for the symmetrical sulfonyl fluoride peaks (δ_F -52.2 ppm) was monitored and plotted against anticipated pulse angle values. These data were compared expected sine function behaviour of relative resonance integration based on varying pulse angles (**Figure S6**).

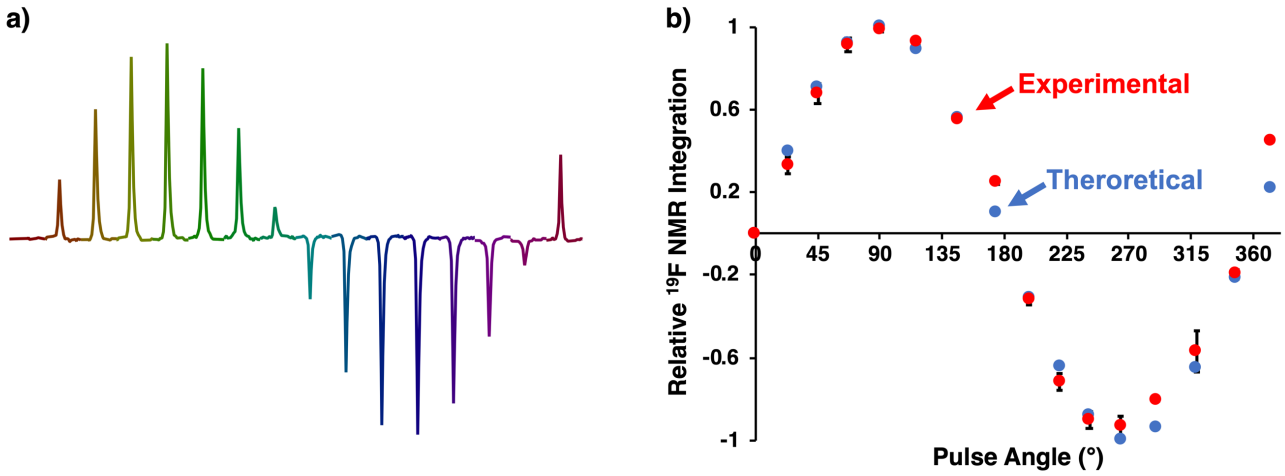


Figure S6. Results from ^{19}F NMR pulse calibration (57 MHz). These results are shown a) qualitatively with the LiFSI resonance (all spectra normalized to noise) and b) graphically with the relative ^{19}F NMR integration of the LiFSI compared to expected (a sinusoid).

b. Spin-lattice relaxation time (T_1) estimations

In effort to allow for sufficient relaxation (at least five times the longest T_1) between subsequent rf excitation to ensure quantitative NMR (qNMR) conditions, T_1 values for each of the major chemical species were estimated in effort to determine the longest T_1. To do so, the inversion recovery technique[2,3] was used.

To determine the T_1 of chemical species relevant to the sulfuryl fluoride work, a sample was prepared of the **7** (0.09 M) starting material in a 5 mL volumetric flask. An aliquot of this was transferred to a 5 mm NMR tube and ^{19}F spectra were acquired with four transients, zero dummy scans, 15 dB rg, 101 s d1, -20.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). The time between the 180° and 90° pulses (τ) was varied in 16 linearly spaced increments between τ_{start} (0.10 s) and τ_{stop} (16.0 s). Once processed in mnova, these data were analyzed by integrating the signal corresponding to the aryl fluoride peak (δ_F -107.9 ppm) and plotting this integration against τ. These data were fitted to a line of best fit in mnova, and a τ_{null} (τ where signal integration/intensity was equal to zero) was calculated. For results for this resonance, see **Figure S7**.

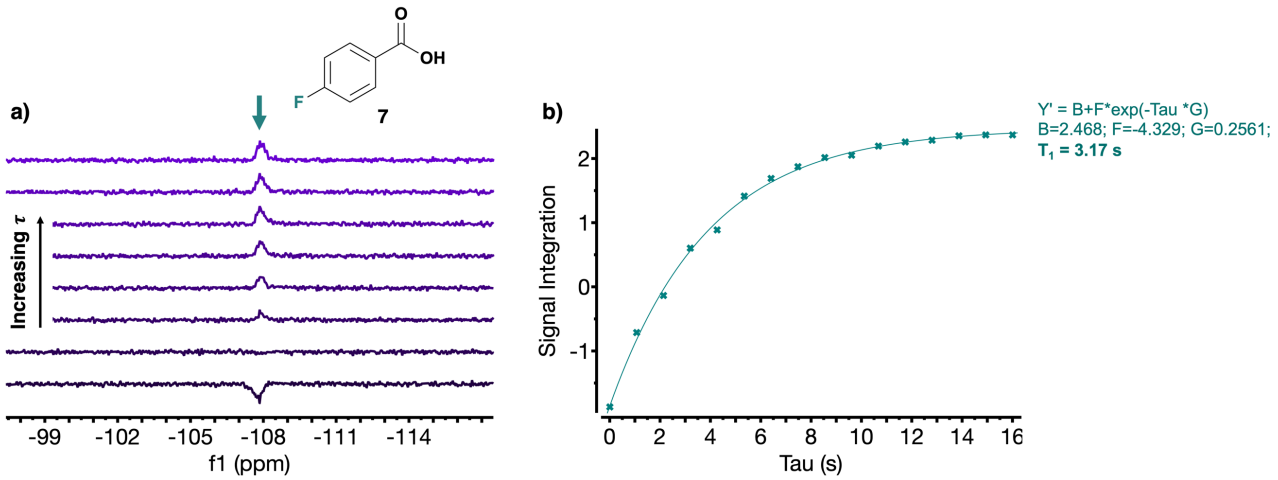


Figure S7. Results from application of the inversion recovery method for T_1 estimation of the aryl fluoride peak of **7** (57 MHz, 32° C). These results are shown a) qualitatively with the resonance of interest (decimated spectra, normalized to noise) and b) graphically with peak integration of the resonance graphed with application of various τ values. This line of best fit was used to determine a τ_{null} value and then T_1 as the $T_1 = \tau_{null} / \ln(2)$.

To determine the approximate T_1 of observed products of the activation reaction with **4**, an aliquot of a reaction mixture was analyzed. For this reaction, prior to the reaction commencing, a round-bottom flask ('vial 1') was equipped with a magnetic stir bar, KF (7.32 g, 126 mmol), **3** (8.92 g, 45.0 mmol), and water (10 mL). This 'vial' was connected to another round-bottom flask ('vial 2') *via* small segment of tubing. 'Vial 2' was equipped with an empty balloon, and **7** (1.26 g, 9.00 mmol), DIPEA (4.70 mL, 27.0 mmol), and MeCN were added. **1** (368 uL, 3.00 mmol) was also added to Vial 2 as an internal standard. The reaction was initiated by SO_2F_2 formation, initiated by slowly dosing **2** (306 mmol, 23.4 mL) into Vial 1 (over 10 minutes with the use of a New Era NE-1000 syringe pump).

After ~ 8 hours of reaction progress, an aliquot was transferred to a 5 mm NMR tube and the inversion recovery method was used. First, T_1 estimates for fluorosulfate (FSO_3^-, **5**, δ_F 37.3 ppm), acyl fluoride resonance of product **9** (δ_F 16.5 ppm), and **1** (δ_F -63.5 ppm) where calculated. This was achieved by collecting ^{19}F spectra with four transients, zero dummy scans, 15 dB rg, 51 s d1, -10.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). The time between the 180° and 90° pulses (τ) was varied in 35 linearly spaced increments between τ_{start} (0.01 s) and τ_{stop} (15.0 s). These data were fit to a trend and T_1 values were calculated consistent with previous analyses. The resonance consistent with **4** (δ_F 33.6 ppm) appeared to have a T_1 less than the acyl fluoride resonance of **7**, and as this resonance did not have the longest T_1, it was not calculated. Results for these resonances can be found in **Figure S8**. These results were additionally insightful and considered for the SO_2F_2 hydrolysis work.

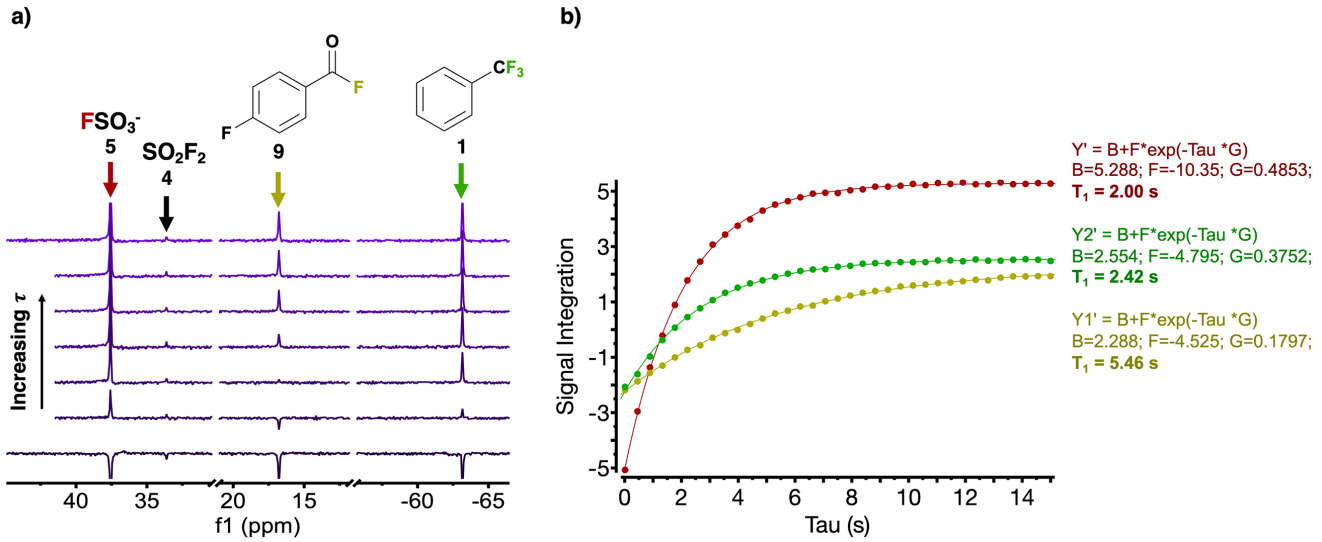


Figure S8. Results from application of the inversion recovery method for T_1 estimation of some of the products of the SO_2F_2 (**4**) activation reaction of interest (57 MHz, 32° C). These results are shown a) qualitatively with the resonances of interest (decimated spectra, normalized to noise) and b) graphically with peak integrations of each of the resonance graphed with application of various τ values. This line of best fit was used to determine a τ_{null} value and then T_1 as the $T_1 = \tau_{null} / \ln(2)$.

While this experiment was adequate to properly characterize the recovery of magnetization for the aforementioned product resonances with the used τ and d1 values, it appeared inadequate to properly characterize the z-magnetization recovery of **9**'s aryl fluoride resonance. Therefore, ^{19}F spectra with four transients, zero dummy scans, 15 dB rg, 102 s d1, -20.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points) were collected and the time between the 180° and 90° pulses (τ) was varied in 16 linearly spaced increments between τ_{start} (0.01 s) and τ_{stop} (90.0 s). These acquisition parameters allowed for the data to be fit to a trendline and T_1 values were calculated consistent with previous analyses. For results see **Figure S9**.

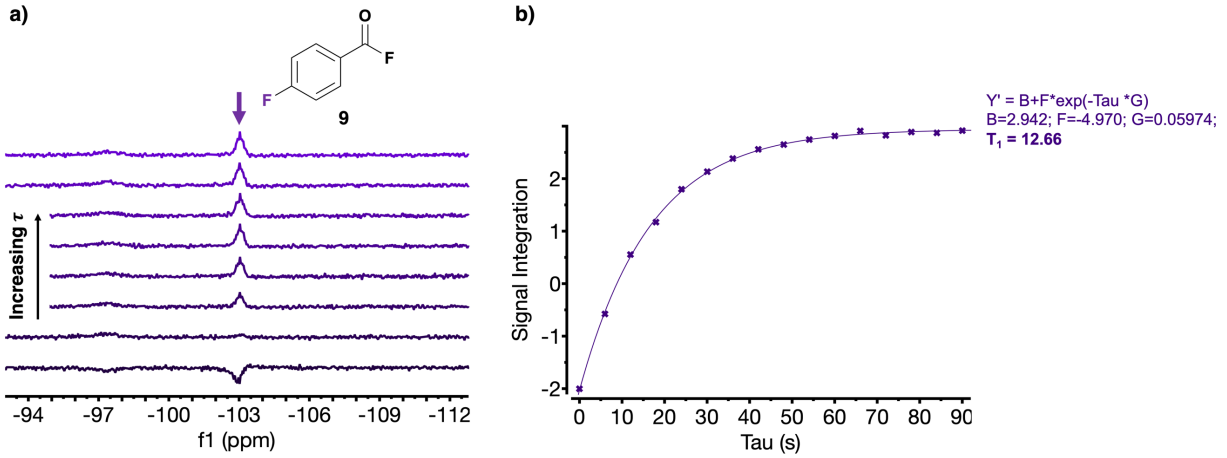


Figure S9. Results from application of the inversion recovery method for T_1 estimation of the aryl fluoride peak of the acyl fluoride product (**9**, 57 MHz, 32° C). These results are shown a) qualitatively with the resonance of interest (decimated spectra, normalized to noise) and b) graphically with peak integration of the resonance graphed with application of various τ values. This line of best fit was used to determine a τ_{null} value and then T_1 as the $T_1 = \tau_{null} / \ln(2)$.

To determine the approximate T_1 of relevant components of the Curtius rearrangement work, an aliquot of a reaction mixture was analyzed. The reaction mixture used for this analysis was the same solution that was analyzed overtime and showcased in **Figure 10** of the paper (details of procedure in section SI Section 4.d below). This sample, however, was analyzed significantly later after the time course data was acquired. The ^{19}F spectra were acquired with four transients, zero dummy scans, 15 dB rg, 61 s d1, -85.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). The time between the 180° and 90° pulses (τ) was varied in 16 linearly spaced increments between τ_{start} (0.001 s) and τ_{stop} (20.0 s). These acquisition parameters allowed for the data to be fit to a trendline and T_1 values were calculated consistent with previous analyses (**Figure S10**). The estimated T_1s of each compound of interest were all relatively short (less than 1.2 s) and, therefore, the resulting curves could be better characterized at lower τ values than the utilized experimental parameters. Nonetheless, these data provided confirmation that our utilized d1 for reaction monitoring fulfilled quantitative requirements.

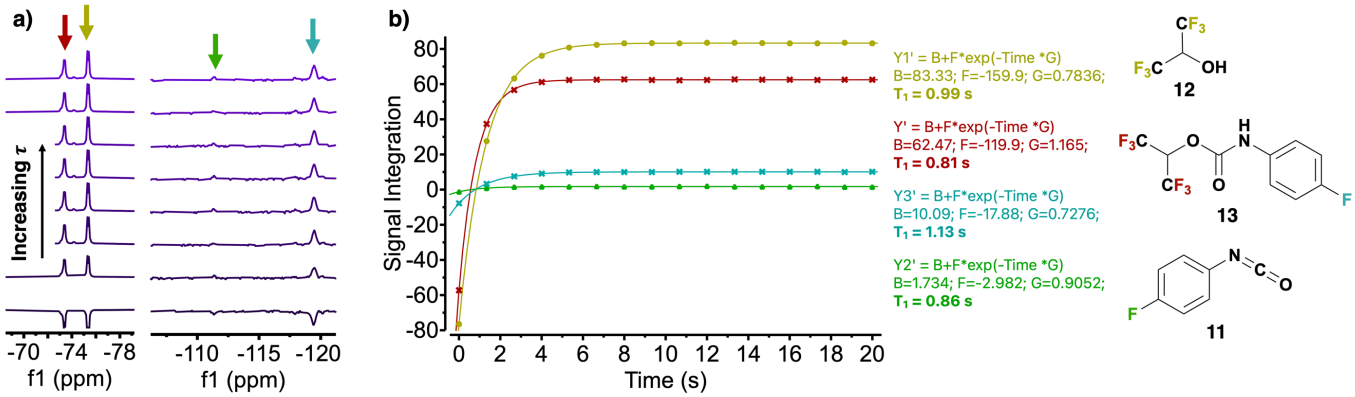


Figure S10. Results from application of the inversion recovery method for T_1 estimation of reaction species relevant to Curtius rearrangement work (57 MHz, 32° C). A reaction mixture (reaction shown in Figure 10) well past its end point was used for analysis. These results are shown a) qualitatively with the resonances of interest (decimated spectra, note left and right spectra are of different intensities) and b) graphically with peak integration of the resonance graphed with application of various τ values. This line of best fit was used to determine a τ_{null} value and then T_1 as the $T_1 = \tau_{null} / \ln(2)$.

c. Pulse excitation over 220 ppm spectral range

To observe uniform resonance excitation over the desired 220 ppm ^{19}F SW, a sample of **1** (0.63 M) was prepared by bringing **1** to 2 mL with MeCN in a volumetric flask. Once an aliquot was transferred to a 5 mm NMR tube, ^{19}F spectra were acquired in triplicate with four transients, zero dummy scans, 44 dB rg, 30 s d1, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). Spectral offsets were changed such that the resonance consistent with **1** (δ_F -63.5 ppm) changed its relative downfield spectral position (from 5% to 95% of the downfield spectrum edge) and the following offsets (o1p) were selected: -162.0, -151.0, -129.0, -107.0, -85.0, -63.0, -41.0, -19.0, 3.0, 25.0, and 36.0 ppm. Once the spectra were transferred and processed in mnova, the average absolute integration per resonance position was determined. The average integration was normalized and these were plotted against spectral position (**Figure 2**).

d. ^{19}F NMR concentration conversion factor determination and verification

To determine a CCF, **1** (0.67 M) was gravimetrically measured and brought to 5 mL in MeCN. The purity of **1** (99%) was considered for determining an accurate CCF. This stock solution was used in a 1:1 serial dilution with MeCN to prepare seven total samples. These samples were then analyzed *via* ^{19}F NMR, as spectra were acquired in triplicate with four transients, zero dummy scans, 90° pulse, 44 dB rg, 62 s d1, -60.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). These spectra were processed and the singlet resonance consistent with the trifluoromethyl substituent of **1** (δ_F -63.5 ppm) was integrated. The absolute integration was plotted against the concentrations. The inverse of this slope was divided by 3 and this represented the CCF per nuclide for a given resonance (**Figure 3a**).

This CCF was verified by preparing a stock solution of **2** in MeCN (0.38 M) gravimetrically and bringing this to 5 mL with MeCN. The purity of the **2** (99%) was also considered into account to accurately determine concentration of solution. This stock solution was used in a 1:1 serial dilution with MeCN to prepare four total samples. These samples were then analyzed *via* ^{19}F NMR, as spectra were acquired in triplicate with four transients, zero

dummy scans, 90° pulse, 44 dB rg, 62 s d1, -60.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). These spectra were processed and the singlet resonance consistent with **2** (δ_F -77.0 ppm) was integrated. The absolute integration and previously determined CCF were used to calculated concentrations. These concentrations calculated *via* ^{19}F qNMR were then graphed against the gravimetrically determined concentrations (**Figure 3b**).

e. Monitoring change in NMR response with differing ionic strength

A 0.20 M solution of **2** was prepared by transferring **2** *via* microsyringe to a volumetric flask and bringing to 25.00 mL with H_2O. After mixing this solution, 10.00 mL was transferred (*via* volumetric pipet) to a scintillation vial equipped with a septum filled cap and magnetic stir bar. This solution was then flowed through the stopped-flow system (cleaned and dried). Once the system was well primed, this solution was analyzed *via* ^{19}F NMR, as spectra were acquired in triplicate with four transients, zero dummy scans, 90° pulse, 44 dB rg, 62 s d1, -60.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points).

The system was evacuated of the solution, NaCl was added (0.3065 g) to prepare a 0.52 M solution and the solution was allowed to circulate through the system (~ 15 minutes). The pump was then halted and ^{19}F NMR spectra (in triplicate) were collected with the same acquisition parameters as previously listed. This process was repeated by adding 0.3208, 0.3062, 0.3248, and 0.3196 g NaCl sequentially, preparing 1.0, 1.6, 2.1, and 2.7 M solutions, respectively.

Once completed, these spectra were processed and analyzed with mnova. The singlet resonance consistent with the trifluoromethyl substituent of **2** (δ_F -77.0 ppm) was integrated. The average of the absolute integration was plotted against NaCl concentrations where a decrease in 2.8% integral area can be expected per 1.0 M increase in ionic strength (**Figure S11**).

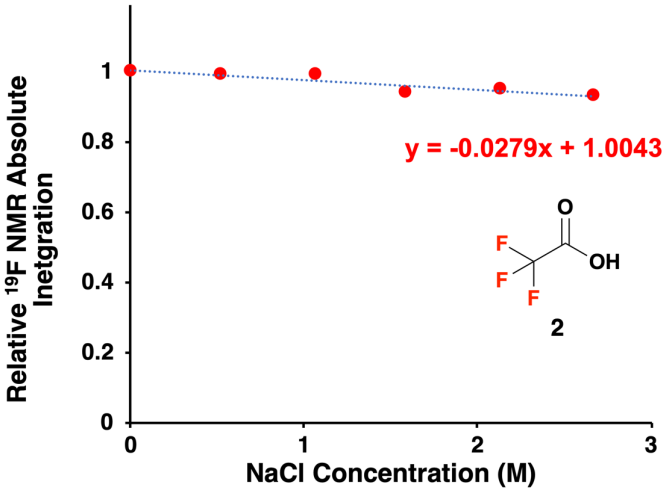


Figure S11. Effect of change in ionic strength (by altering NaCl concentrations) on the average ^{19}F NMR (57 MHz) integration of the resonance consistent with **2** (δ_F -77.0 ppm).

4. Reaction monitoring procedures

a. Capture and hydrolysis of SO_2F_2 (4)

Prior to the hydrolysis reaction commencing, a standard solution with **1** (0.19 M) was created in a volumetric flask, brought 25.00 mL with MeCN. After mixing this solution, 10.00 mL was transferred to a scintillation vial ('Vial 2') equipped with a magnetic stir bar and septum filled cap. The remainder was used to prime the stopped-flow system with this standard solution. When ~ 1 mL remained in the volumetric flask, the inlet and outlet lines of the stopped-flow system were transferred to Vial 2, ultimately increasing the volume of Vial 2 by 1.78 mL through adding the system's volume (see SI Section 2.d).

Next, a round-bottom flask ('Vial 1') was equipped with a magnetic stir bar, KF (2.5350 g, 44.1 mmol), **3** (3.5350 g, 17.6 mmol), and water (11.5 mL). Vial 1 was additionally fitted with a septum and connected to Vial 2 *via* PEEK tubing (~ 49 cm). Vial 2 was then placed in a heated water bath (40° C), fitted with a balloon, and stirring was applied to each vial. Once **2** (8.5 mL) was measured, a syringe pump (New Era NE-1000) was prepared to dose this reagent over 10 min into Vial 1. After the NMR spectrometer and Python script were configured with experimental parameters, the script was started. Immediately following, a small segment of PEEK tubing attached to the syringe to allow for **2** dosing was connected to Vial 1 and the syringe pump was started. After the 7th ^{19}F NMR spectrum was acquired, an equilibrium concentration of **4** (~ 0.1 M, 1 eq.) appeared to be reached. Therefore, once the 8th spectrum started to be acquired, the connecting line between Vial 1 and 2 was removed (Vial 2 was still septum capped) and both H_2O (0.08 mL, 2.4 eq.) and DIPEA (1.4 mL, 5.8 eq.) were dosed into Vial 2. Observation of this reaction mixture continued for the remainder of time points.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 26 s d1, -50.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 44 timepoints were collected every 366 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure 5** of the main text.

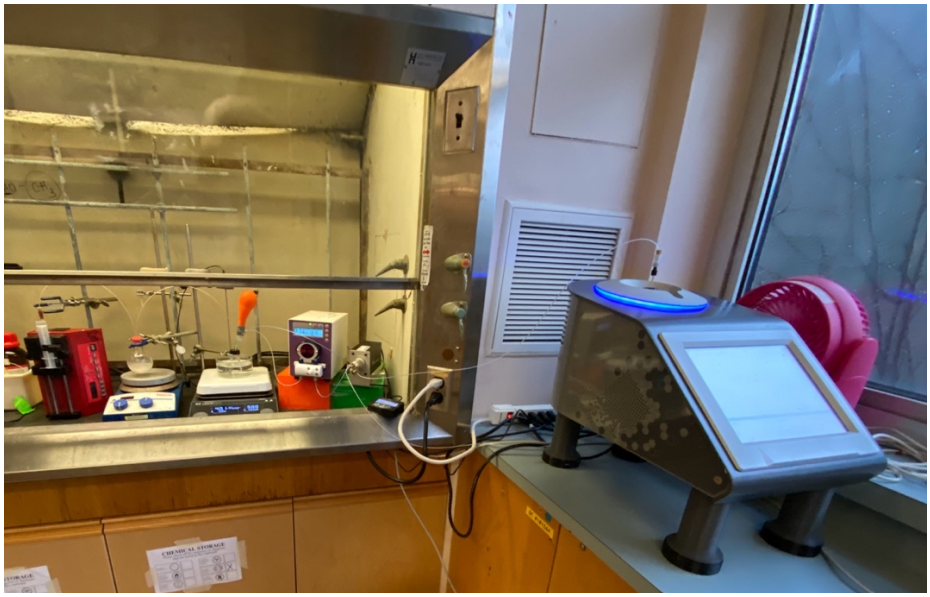


Figure S12. Picture of the experimental setup to study the hydrolysis of **4**. From left to right one can see the syringe pump dosing **2**, Vial 1 (round-bottom flask) connected to Vial 2 (scintillation vial), and the stopped-flow NMR system. Note of caution: this process involves the evolution and use of a toxic gas so special consideration to perform this work in a well-ventilated space must be done. Additionally, precautions to avoid over-pressurization of the system must be taken.

b. Activation of carboxylic acid to acyl fluoride with SO_2F_2

To a round-bottom flask ('Vial 1') a magnetic stir bar, KF (5.1239 g, 87.7 mmol), **3** (7.0250 g, 35.09 mmol), and water (24.0 mL), were added. Next, a standard solution was prepared in a volumetric flask by transferring DIPEA (6.30 mL, 35.8 mmol) and **1** (0.60 mL, 4.84 mmol), brought to 25.00 mL with MeCN. A portion of this solution (10.00 mL) was transferred to a scintillation vial ('Vial 2') with **7** (7.0250 g, 7.03 mmol, 1 eq.), a magnetic stir bar, and fitted with a septum filled cap.

The stopped-flow NMR system was cleaned and primed with MeCN, after which the inlet and outlet lines were connected to Vial 2 (inlet line below liquid level, system's volume (SI Section 2.d) added to the overall total volume in Vial 2, 11.78 mL total). Additionally, Vial 2 was connected to Vial 1 by a small segment of PEEK tubing (~ 49 cm), fitted with a balloon, and was lowered into a 40° C heated oil bath. **2** (17.0 mL) was then measured, and a syringe pump (New Era NE-1000) was prepared to dose this reagent over 10 min into Vial 1.

After the NMR spectrometer and Python script were configured with experimental parameters, the script was started. Immediately following, a small segment of PEEK tubing attached to the syringe to allow for dosing **2** was connected to Vial 1 and the syringe pump was started. Observation of this reaction mixture continued for the remainder of time points.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -40.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 33 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure 6** of the main text.

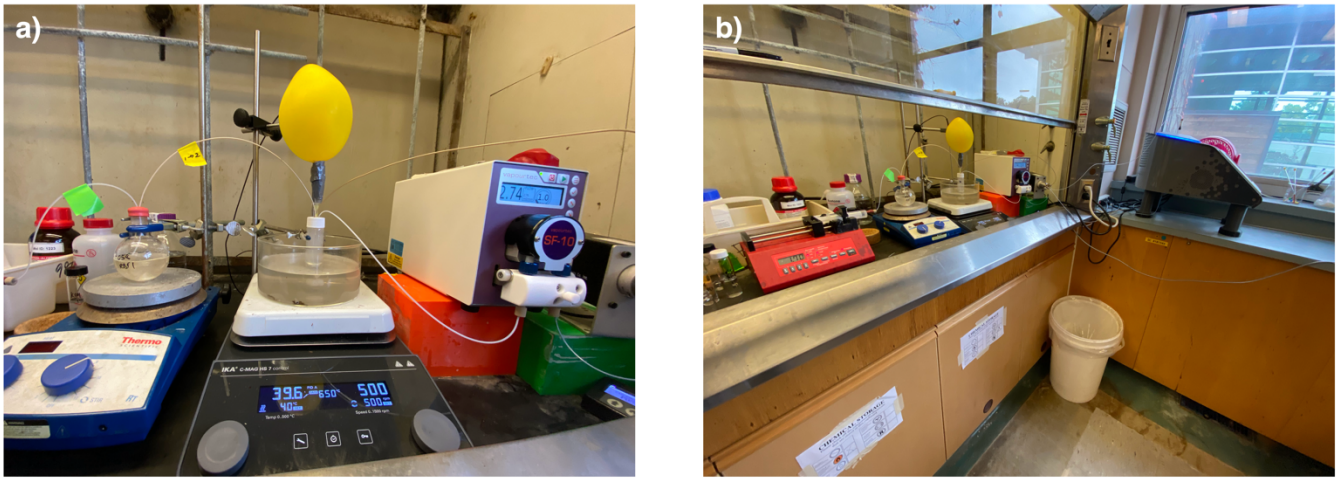


Figure S13. Picture of the experimental setup (a) up-close and b) of the entire stopped-flow system) to study the activation **7** with **4**. Note of caution: this process involves the evolution and use of a toxic gas so special consideration to perform this work in a well-ventilated space must be done. Additionally, precautions to avoid over-pressurization of the system must be taken.

c. Stepwise Curtius rearrangement and carbamate (13) formation - HFIPA (12) addition prior to heat

To a scintillation vial, **7** (1.0383 g, 7.34 mmol, 1 eq.), 10.00 mL toluene, TEA (1.1 mL, 1.1 eq.), and a magnetic stir bar were added prior to being fitted with a septum filled cap and venting needle. The stopped-flow NMR system was cleaned and primed with toluene, after which the inlet and outlet lines were connected to the vial (inlet line below liquid level). Therefore, the system's volume (see SI Section 2.d) was added to the overall total volume of toluene in the vial (now 11.78 mL). After the NMR spectrometer and Python script were configured with experimental parameters, the script was started.

Once the 4th ^{19}F NMR spectrum started acquisition, DPPA (1.8 mL, 1.1 eq.) was added. Then, **12** (0.84 mL, 1.1 eq.) was added to the reaction solution once the 12th spectrum started to be acquired as significant conversion from **7** to the corresponding acyl azide (**10**) was observed. This reaction solution remained untouched until after the 26th spectrum was acquired, when the reaction solution was lowered to a pre-heated oil bath (80 °C). The reaction was then monitored for the remaining time points as denoted with the script.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -90.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 174 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure 8** of the main text.

d. Curtius rearrangement and carbamate (13) formation - reagents added directly after one another to heated solution

To a scintillation vial, **7** (1.0335 g, 7.30 mmol, 1 eq.), 10.00 mL toluene, TEA (1.1 mL, 1.1 eq.), and a magnetic stir bar were added prior to being fitted with a septum filled cap and

venting needle. The stopped-flow NMR system was cleaned and primed with toluene, after which the inlet and outlet lines were connected to the vial (inlet line below liquid level). Therefore, the system's volume (see SI Section 2.d) was added to the overall total volume of toluene in the vial (now 11.78 mL). The vial was now lowered into a pre-heated oil bath (80 °C). After the NMR spectrometer and Python script were configured with experimental parameters, the script was started. Once the Python script was started, DPPA (1.8 mL, 1.1 eq.) and **12** (0.84 mL, 1.1 eq.) were added sequentially. The reaction was then monitored for the remaining time points as denoted with the script.

Note: the pump halted operation after the spectrum at the 5.24 h timepoint being acquired. Spectra were still collected, but of the halted reaction mixture in the instrument. These data were excluded from those shown in **Figure S14**. Despite losing insight into the reaction system between 5.24 and 8.39 h, pump operation was restored remotely allowing for the remainder of time points to be accurately acquired.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -90.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 144 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure S14** below.

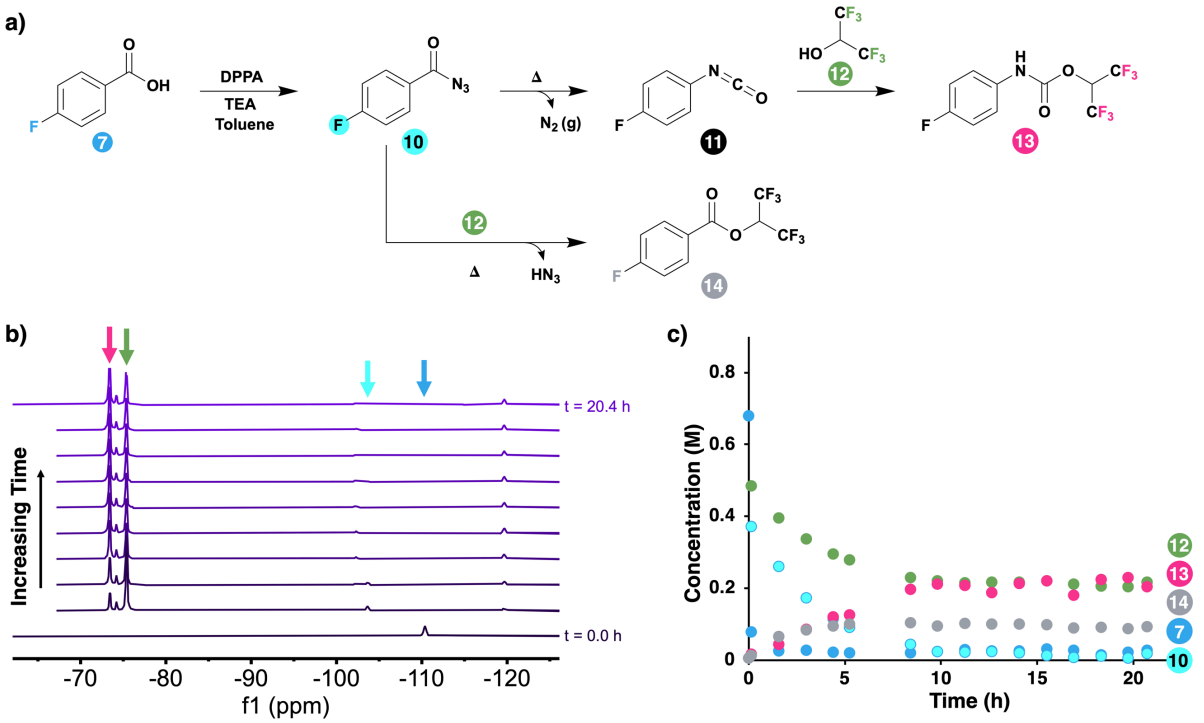


Figure S14. a) Reaction scheme for the carbamate forming modified Curtius rearrangement of **7** (0.68 M, toluene, 80° C) with TEA (1.1 eq.) DPPA (1.1 eq.) and **12** (1.1 eq.) and reagents added sequentially, directly after one another. b) Decimated stacked array of LF ^{19}F NMR spectra (57 MHz) acquired on the process, with increasing time from bottom to top. c) Concentration trends determined using resonance absolute integration and CCF of NMR system.

e. Stepwise Curtius rearrangement and carbamate (13) formation - heat prior to HFIPA (12) addition

To a scintillation vial, **7** (1.0363 g, 7.34 mmol, 1 eq.), 10.00 mL toluene, TEA (1.1 mL, 1.1 eq.), and a magnetic stir bar were added prior to being fitted with a septum filled cap and venting needle. The stopped-flow NMR system was cleaned and primed with toluene, after which the inlet and outlet lines were connected to the vial (inlet line below liquid level). Therefore, the system's volume (see SI Section 2.d) was added to the overall total volume of toluene in the vial (now 11.78 mL). After the NMR spectrometer and Python script were configured with experimental parameters, the script was started.

Once the 5th ^{19}F NMR spectrum started acquisition, DPPA (1.8 mL, 1.1 eq.) was added. Then, once the 14th spectrum started to be acquired, the reaction solution was lowered to a pre-heated oil bath (80 °C) as significant conversion of **7** to the corresponding **10** was observed. **12** (0.84 mL, 1.1 eq.) was added to the reaction solution once the 116th spectrum started to be acquired as significant conversion from the **10** to the corresponding isocyanate (**11**) was observed. The reaction was then monitored for the remaining time points as denoted with the script.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -90.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 136 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure 10** of the main text.

f. Mitsunobu type reaction between DPPA and HFIPA (12)

To a scintillation vial, 10.00 mL toluene, TEA (1.1 mL, 7.83 mmol, 1.0 eq.), and a magnetic stir bar were added prior to being fitted with a septum filled cap and venting needle. The stopped-flow NMR system was cleaned and primed with toluene, after which the inlet and outlet lines were connected to the vial (inlet line below liquid level). Therefore, the system's volume (see SI Section 2.d) was added to the overall total volume of toluene in the vial (now 11.78 mL). After the NMR spectrometer and Python script were configured with experimental parameters, the script was started.

Once the 2nd ^{19}F NMR spectrum started acquisition, DPPA (1.8 mL, 1.0 eq.) was added. Then, once the 4th spectrum started to be acquired, the reaction solution was lowered to a pre-heated oil bath (80 °C). **12** (0.84 mL, 1.0 eq.) was added to the reaction solution once the 7th spectrum started to be acquired. The reaction was then monitored for the remaining time points as denoted with the script.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -90.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 55 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure S15** below, with the significance shown in **Figure 11** of the main text.

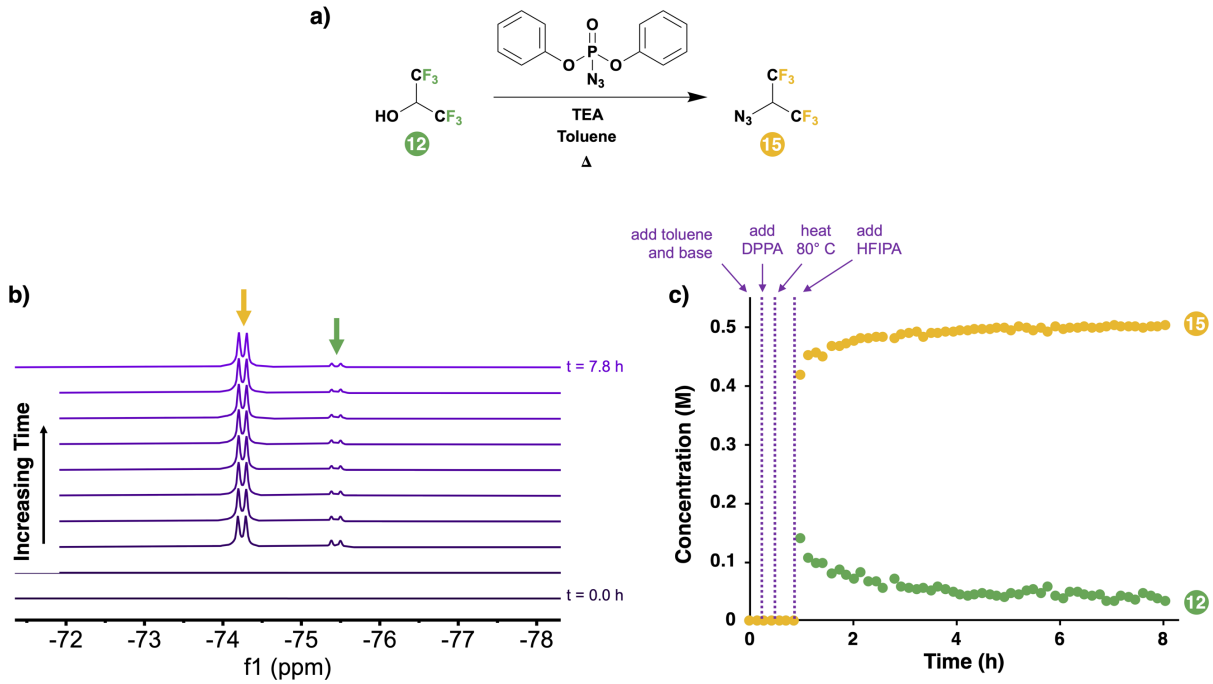


Figure S15. a) Reaction scheme for the Mitsunobu type reaction between DPPA and **12**, with reagents added stepwise, as indicated. b) Decimated stacked array of LF ^{19}F NMR spectra (57 MHz) acquired for the process, with increasing time from bottom to top. c) Concentration trends determined using resonance absolute integration and CCF of NMR system. ^{19}F NMR spectra zoomed into spectral region between δ_F -72 and -78 ppm.

5. Simultaneous reaction monitoring *via* stopped-flow ^{19}F NMR and ReactIR

a. Stopped-flow system configuration

With no thermal insulation of the lines of the stopped-flow NMR system, it is logical to question how representative NMR data acquired with this system are of a reaction that is heated well above ambient temperature (such as the studied Curtius rearrangement in this report). Therefore, to monitor a Curtius rearrangement reaction with conditions of heat prior to HFIPA (**12**) addition (analogous to reaction described in SI 4.e) simultaneously *via* benchtop LF ^{19}F NMR and ReactIR, a Mettler Toledo ReactIR (702L) equipped with a Mettler Toledo DS Micro Flow Cell was placed between the pump and valve in the flow system (**Figure S16**). This was completed with the same stopped-flow system as displayed in **Figure 1**, but with the PEEK line exiting the pump connected to the 'in' port of the flow ReactIR and a 29 cm segment of PEEK tubing (1/16" O.D., 0.01" I.D.) placed to connect the 'out' of the flow React IR to the valve. Applying the same procedure as described in SI 2.d, the volume of this system was determined to be 1.89 mL.

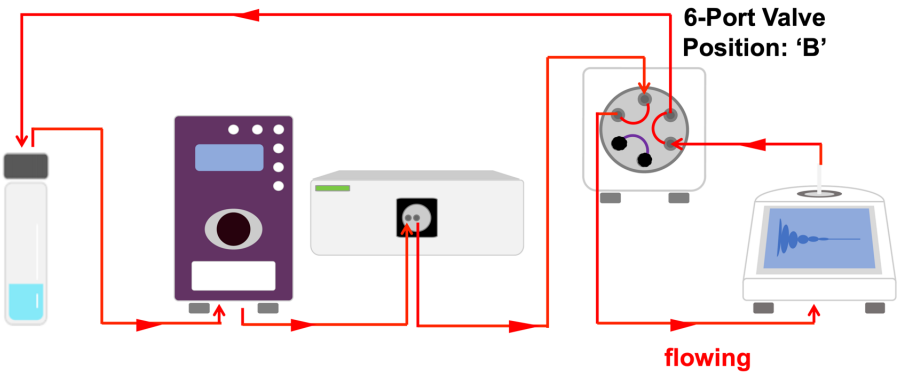


Figure S16. Schematic representation of the stopped-flow LF NMR system (shown in valve position B) with a Mettler Toledo ReactIR (702L) equipped with a Mettler Toledo DS Micro Flow Cell placed between the pump and valve, allowing for simultaneous monitoring of a reaction *via* ^{19}F NMR and IR.

b. Reaction monitoring procedure

Once the system was configured, the system was tested with the Curtius rearrangement process previously highlighted and with conditions analogously described in SI section 2.d. Therefore, 10.00 mL of toluene was added to a scintillation vial equipped with a magnetic stir bar and septum filled cap (with venting needle). With the stopped-flow system pumping fresh toluene (collecting into waste), the ReactIR was blanked on toluene and these 'in' and 'out' lines were connected to the scintillation vial (adding 1.89 mL toluene to overall volume). Next, TEA (1.1 mL, 1.0 eq.) was added to the vial and allowed to circulate. With the 'in' line pulled out of solution, **7** (1.0361 g, 7.32 mmol, 1 eq.) was added. Once the solution appeared homogeneous, the 'in' line was again placed well below the liquid level. After, the NMR spectrometer and Python script were configured with experimental parameters, the stopped-flow script was started and IR spectra began to be collected every minute using the iC IR software (Mettler Toledo).

Once the 5th ^{19}F NMR spectrum started acquisition, DPPA (1.8 mL, 1.1 eq.) was added. Then, once the 15th spectrum started to be acquired, the reaction solution was lowered to a pre-heated oil bath (80 °C) as significant conversion of **7** to the corresponding **10** was observed. **12** (0.84 mL, 1.1 eq.) was added to the reaction solution once the 135th spectrum started to be acquired as significant conversion from the **10** to the corresponding isocyanate (**11**) was observed. The reaction was then monitored for the remaining time points as denoted with the script.

For this trial, ^{19}F NMR spectra were acquired with four transients, zero dummy scans, 90° pulse, 44 dB rg, 61 s d1, -90.0 ppm o1p, 219.6 ppm SW, and 2.79 s AQ (34,816 complex data points). In the Python script, 170 timepoints were collected every 510 s, with a 15 s pause time, 1.78 mL/min calibrated pump rate, and an additional t=0 s spectrum collected.

Results from this reaction can be found summarized in **Figure S17** below.

c. Results of simultaneous reaction monitoring *via* ^{19}F and ReactIR

Monitoring the described process *via* LF ^{19}F NMR was again successful (**Figure S17**) and resulted in reaction trends previously observed (see **Figure 10** in main text) under these conditions.

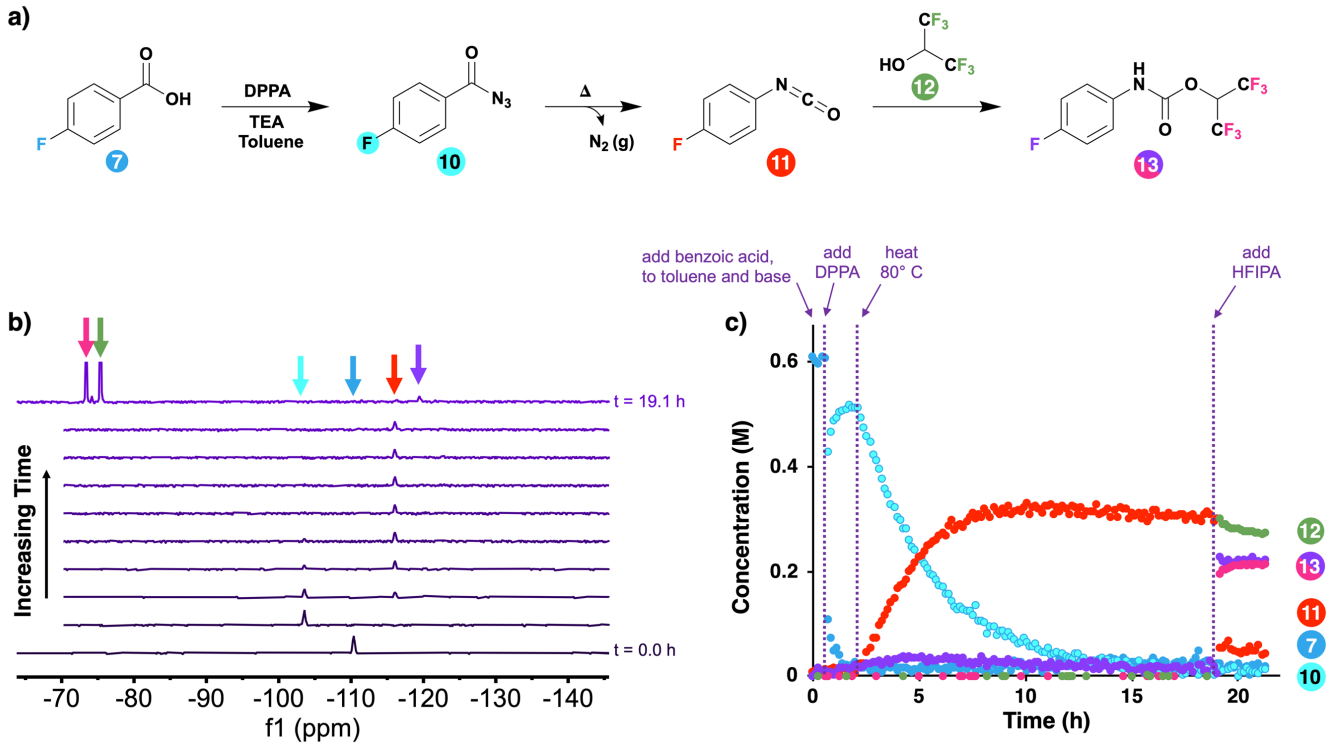


Figure S17. a) Reaction scheme for the carbamate forming modified Curtius rearrangement of **7** (0.61 M, toluene) with TEA (1.1 eq.), DPPA (1.1 eq.), heat (80° C) and **12** (1.1 eq.) added stepwise. b) Decimated stacked array of LF ^{19}F NMR spectra (57 MHz) acquired for the process, with increasing time from bottom to top. c) Concentration trends determined using resonance absolute integration and CCF of NMR system.

Monitoring the reaction *via* ReactIR (**Figure S18**), resulted in successful observation of some of the major reaction species. This includes the carboxylic acid starting material **7** (trended with peak at 1120 cm^{-1}), acyl azide intermediate **10** (trended with peak at 1696 cm^{-1}), isocyanate intermediate **11** (trended with peak at 2272 cm^{-1}), and desired carbamate product **13** (trended with peak at 1759 cm^{-1}). Data analysis was performed in the iC IR software on the double derivative of the resultant IR spectra (to assist in deconvolution of IR peaks).

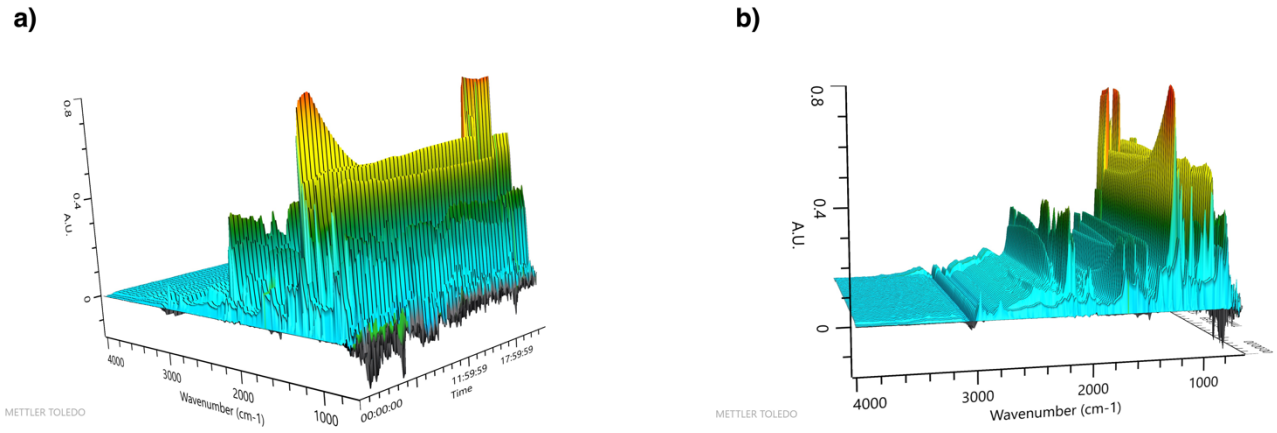


Figure S18. Full waterfall plots representing the ReactIR data acquired over the entire reaction course with a) allowing for better visualization of peaks with smaller wavenumbers and b) the same data but turned to allow for better visualization of peaks with larger wavenumbers.

Monitoring the previously denoted reaction species (**7**, **10**, **11**, **13**) by either orthogonal technique generally resulted in similar trends and are shown in **Figure S19**. The agreement provides evidence for the representative nature of the resulting ^{19}F NMR trends, even despite the non-insulated lines of the stopped-flow system when monitoring a heated process. The IR trend consistent with the intermediate isocyanate species (**11**) highlights the complex nature of IR data processing, as tracking the ^{19}F NMR resonance consistent with this species *via* LF NMR resulted in a cleaner and arguably more reasonable/representative trend. Additionally, the quantitative nature of the ^{19}F NMR trends further promotes the utility of LF NMR in such circumstance. Nonetheless, the general agreement of reaction trends (whether from ReactIR or LF NMR) provides validation of the representative nature of the discussed ^{19}F NMR trends with this stopped-flow system, even despite the lack of thermal insulation with the stopped-flow system.

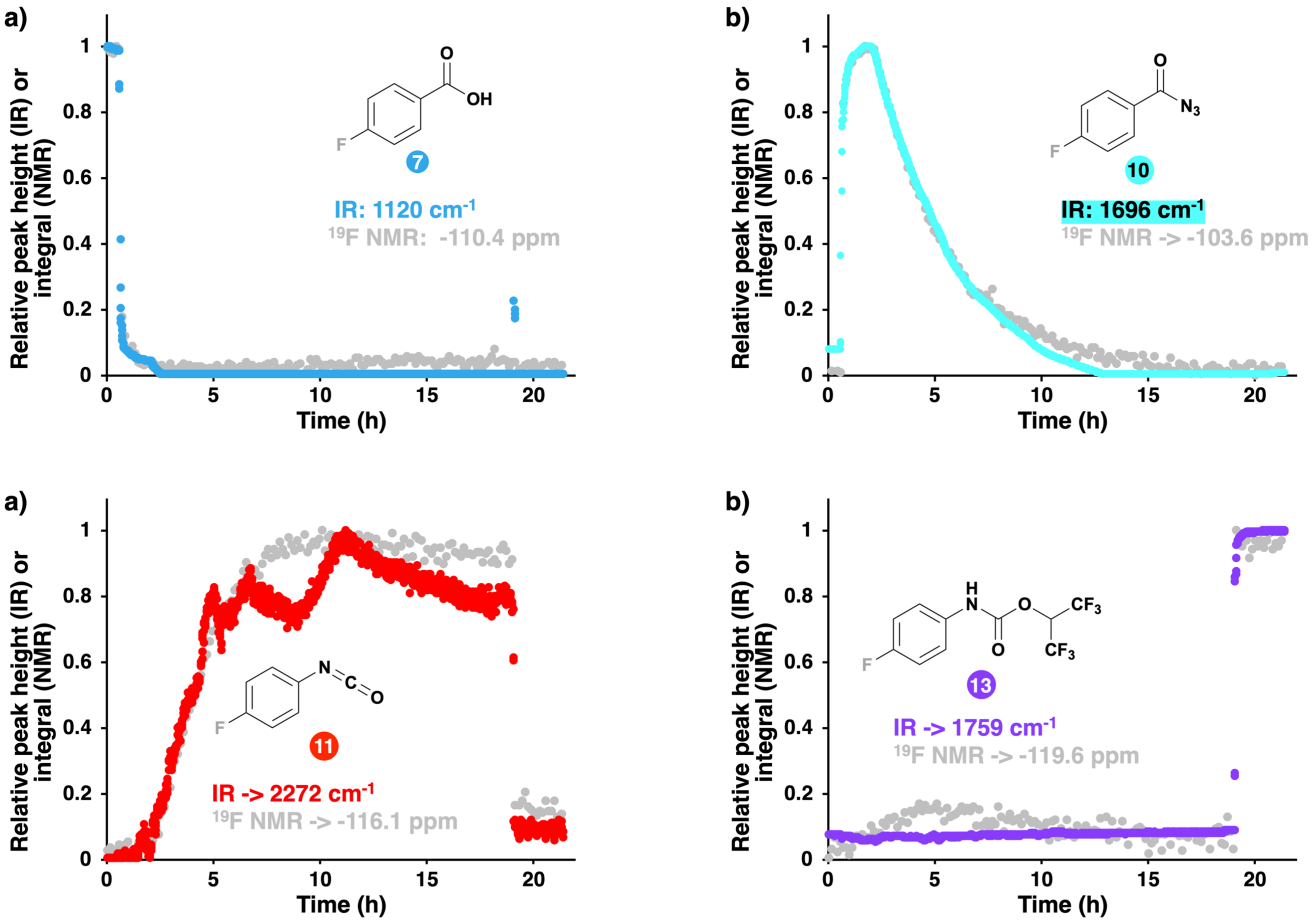
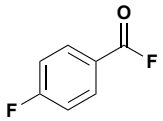


Figure S19. Comparison of some major reaction components monitored *via* ReactIR (coloured trends) and LF ^{19}F NMR (greyed trends). This includes a) carboxylic acid starting material **7**, b) acyl azide intermediate **10**, c) isocyanate intermediate **11**, and desired carbamate product **13**.

6. Product characterization

a. 4-fluorobenzoyl fluoride (9)

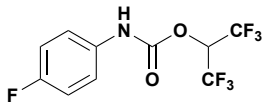
9 was synthesized from **7** and **4**, per SI Section 4.b. Isolation of this product was attempted to be isolated *via* silica gel column chromatography, but was unsuccessful (compound has been reported to be slightly unstable to silica gel[4]). Nonetheless, characterization was successful on the DMSO soluble components of the reaction mixture - resulting in data consistent with previously reported data.[4,5]



^{1}H NMR (300 MHz, DMSO-d6) δ_H 8.13 (m, 2H), 7.47 (m, 2H); **^{13}C{^{1}H}** (100 MHz, MeCN with 10% v/v MeCN-d3) δ_C 166.70 (d, *J* = 255.5 Hz), 156.15 (d, *J* = 342.4), 134.54 (dd, *J* = 10.3, 3.9 Hz), 120.78 (dd, *J* = 62.2 Hz, 2.8 Hz), 116.83 (dd, *J* = 22.9, 1.0 Hz); **^{19}F NMR** (282 MHz, DMSO-d6) δ_F 17.28 (s), -102.62 (m); **MS-EI** (m/z) 142.18 [M]+ (Calculated for $C_7H_4F_2O$, 142.02).

b. 1,1,1,3,3,3-hexafluoropropan-2-yl (4-fluorophenyl)carbamate (13)

13 was synthesized from **7** using DPPA and **12**, per protocols listed in SI Sections 4.c - 4.e (in varying yields depending on conditions). For successful isolation, reaction solution was extracted with hexanes (2 x 15 mL). Once combined, these hexanes layers were dried down *via* rotary evaporation and isolation was successful by silica gel column chromatography using hexanes. Product was obtained as white crystals.



^{1}H NMR (400 MHz, CD_2Cl_2) δ_H 7.40 (m, 2H), 7.13(br s, 2H), 7.08 (m, 2H), 5.83 (sep, 1H); **^{13}C{^{1}H}** (100 MHz, CD_2Cl_2) δ_C 160.23 (d, J = 244.0 Hz), 150.28, 132.78, 121.64 (d, J = 8.1 Hz), 121.01 (q, J = 281.8 Hz), 68.02 (sep, J = 281.8 Hz); **^{19}F NMR** (282 MHz, CD_2Cl_2) δ_F -73.94 (d, J = 6.2 Hz), -102.74 (m); **MS-EI** (m/z) 305.06 [M]+ (Calculated for $C_{10}H_6F_7NO_2$, 305.03).

7. References

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4. J. A. Birrell, J-N. Desrosiers, E. N. Jacobsen, *J. Am. Chem. Soc.*, 2011, **133**, 13872-13875.
5. Y. Liang, Z. Zhao, N. Shibata, *Commun. Chem.*, 2020, **3**, 59.

8. NMR spectra

a. NMR data for 4-fluorobenzoyl fluoride (9) characterization

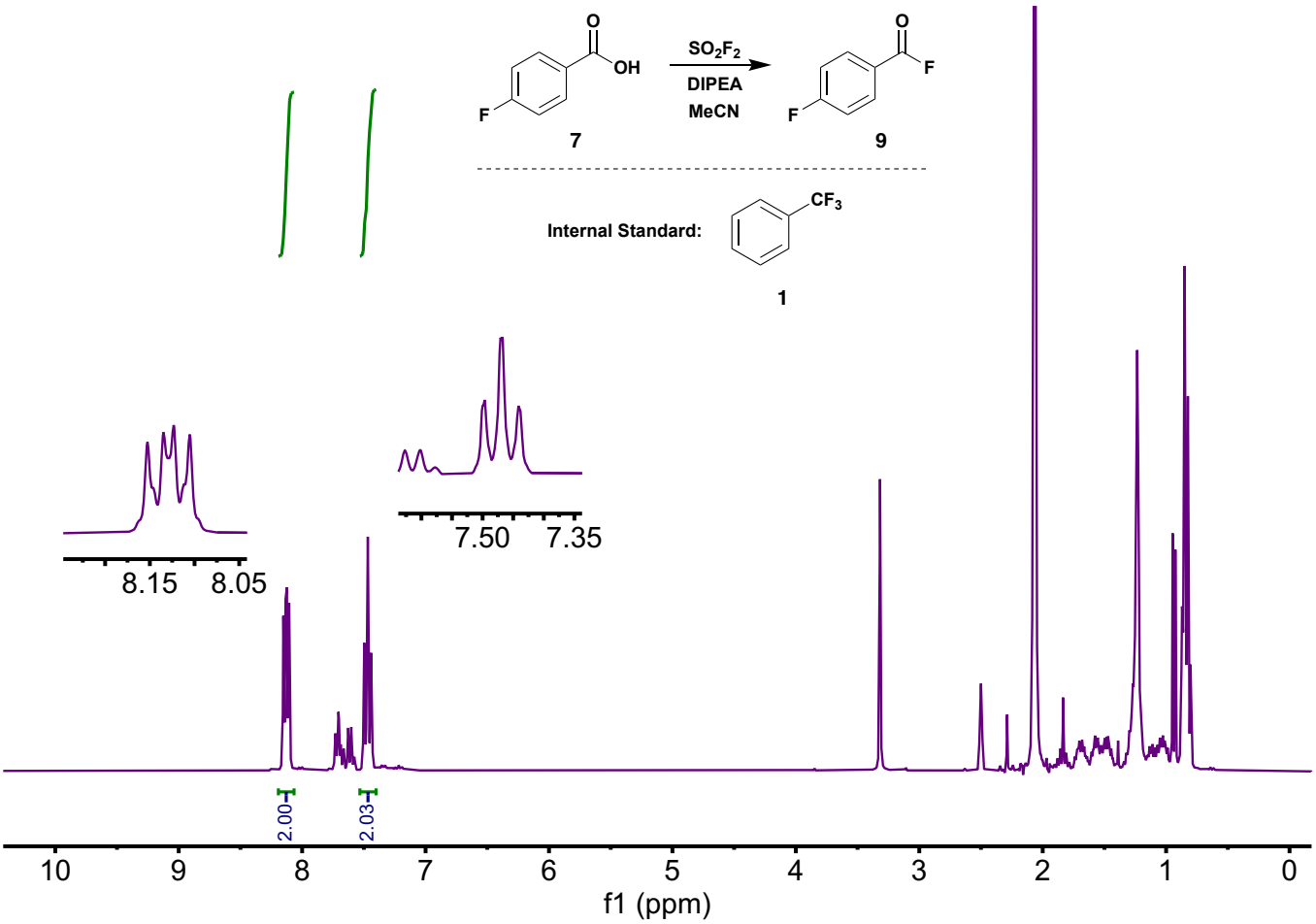

Figure S20. ^{1}H NMR spectrum (300 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

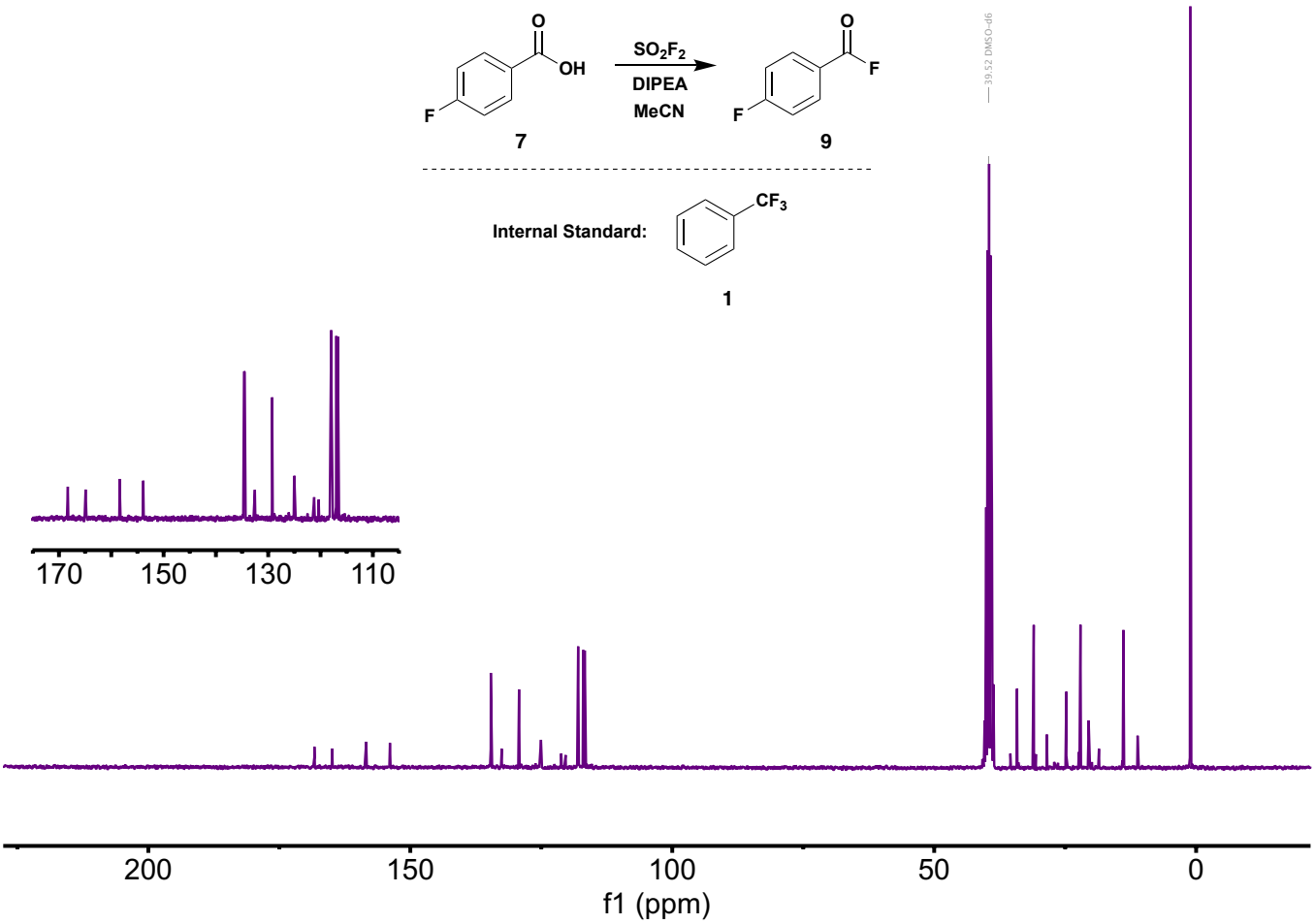

Figure S21. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

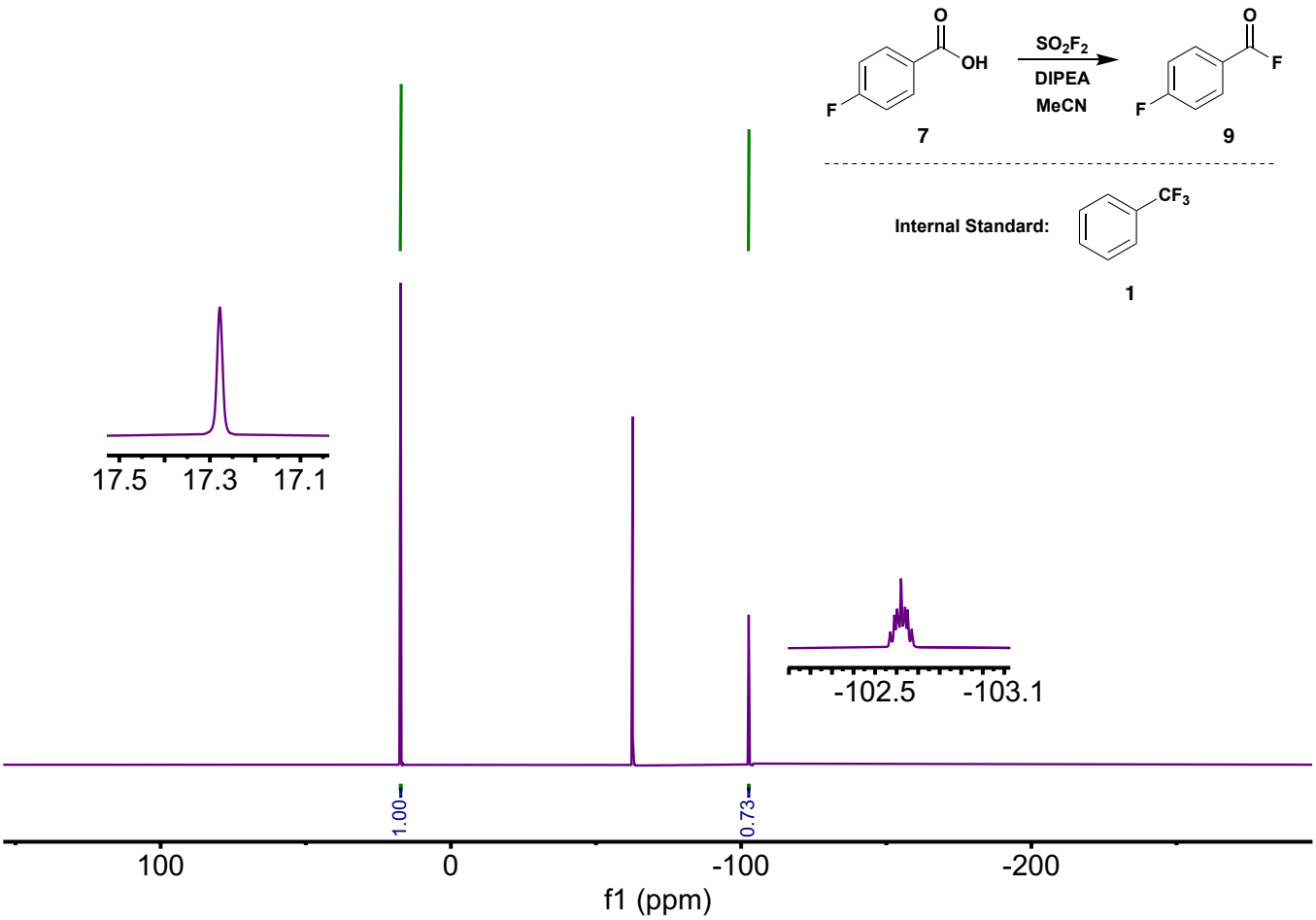

Figure S22. ^{19}F NMR spectrum (282 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

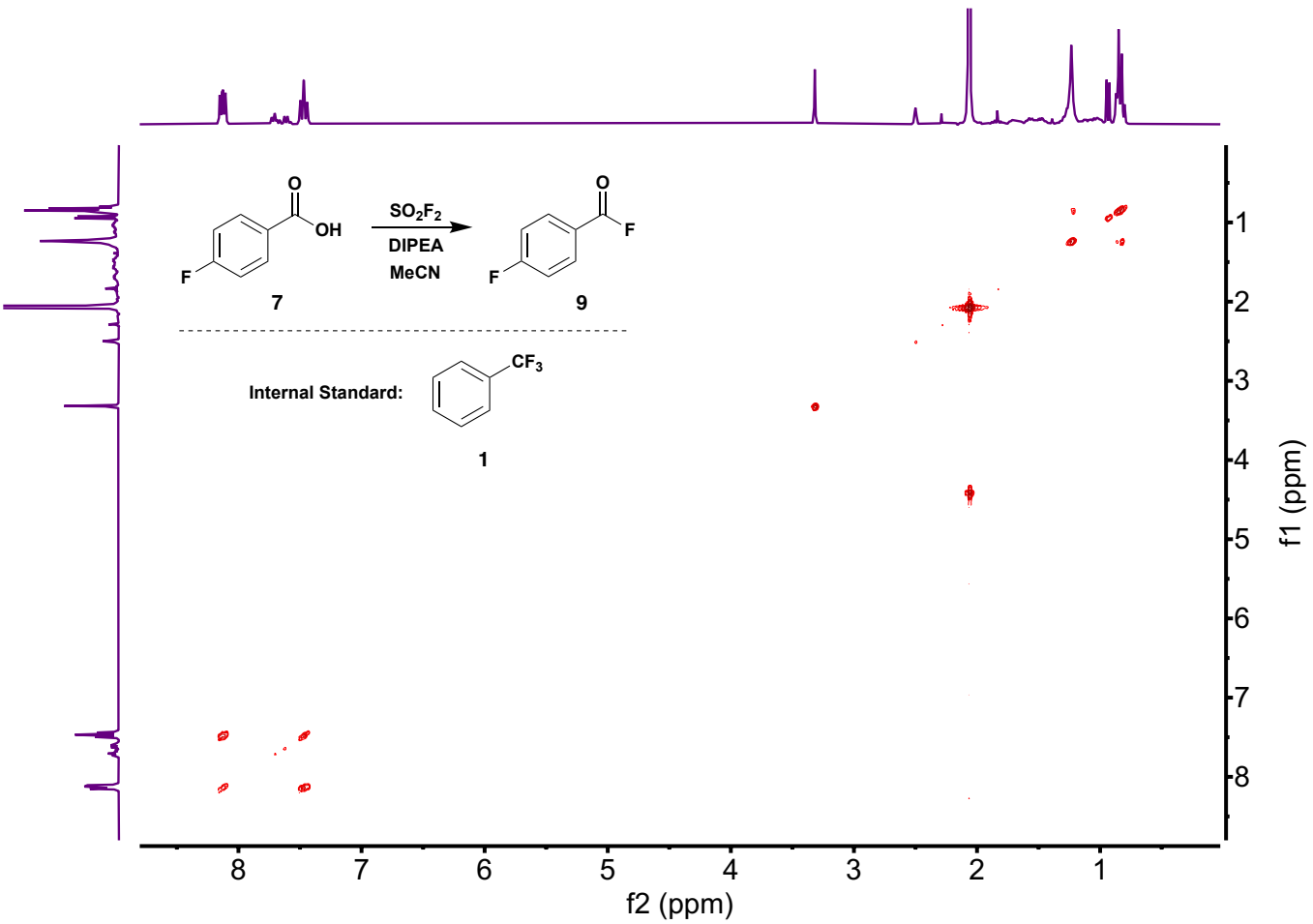

Figure S23. ^{1}H - ^{1}H COSY NMR spectrum (300 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

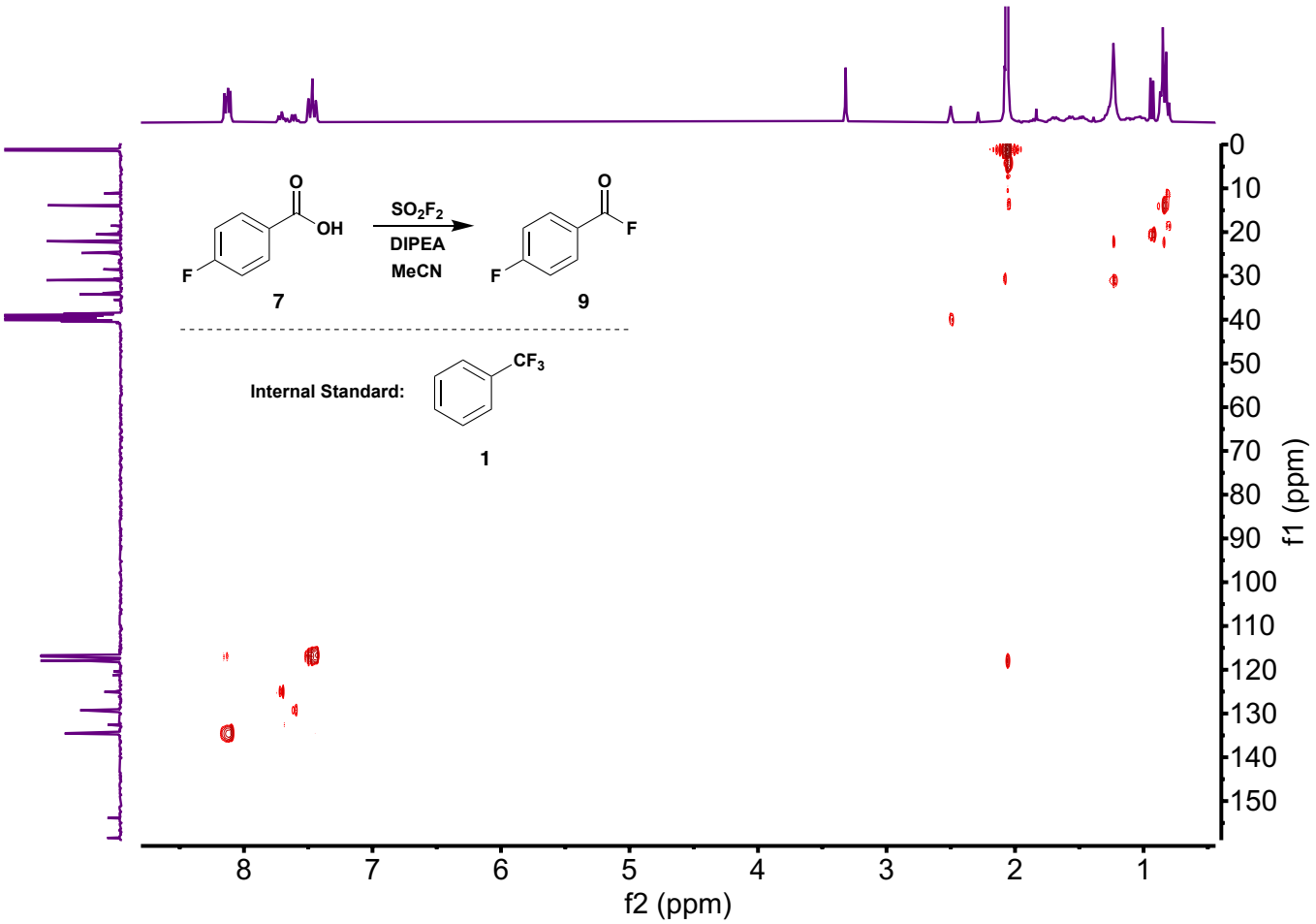

Figure S24. ^{1}H - ^{13}C HSQC NMR spectrum (300/75 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

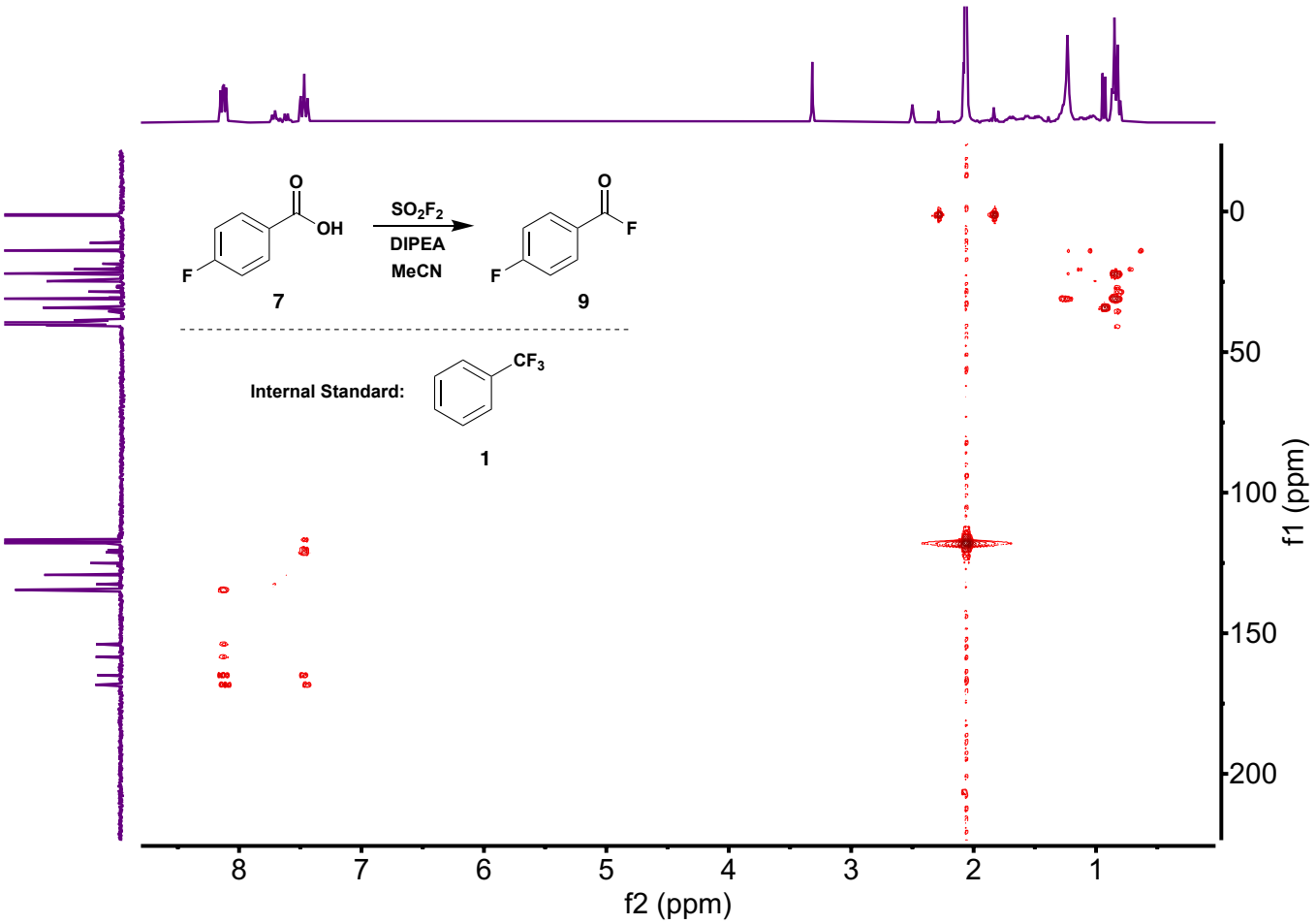

Figure S25. ^{1}H - ^{13}C HMBC NMR spectrum (300/75 MHz, DMSO-d6) of DMSO soluble reaction components, including **9**.

b. 1,1,1,3,3,3-hexafluoropropan-2-yl (4-fluorophenyl)carbamate (13) characterization NMR data

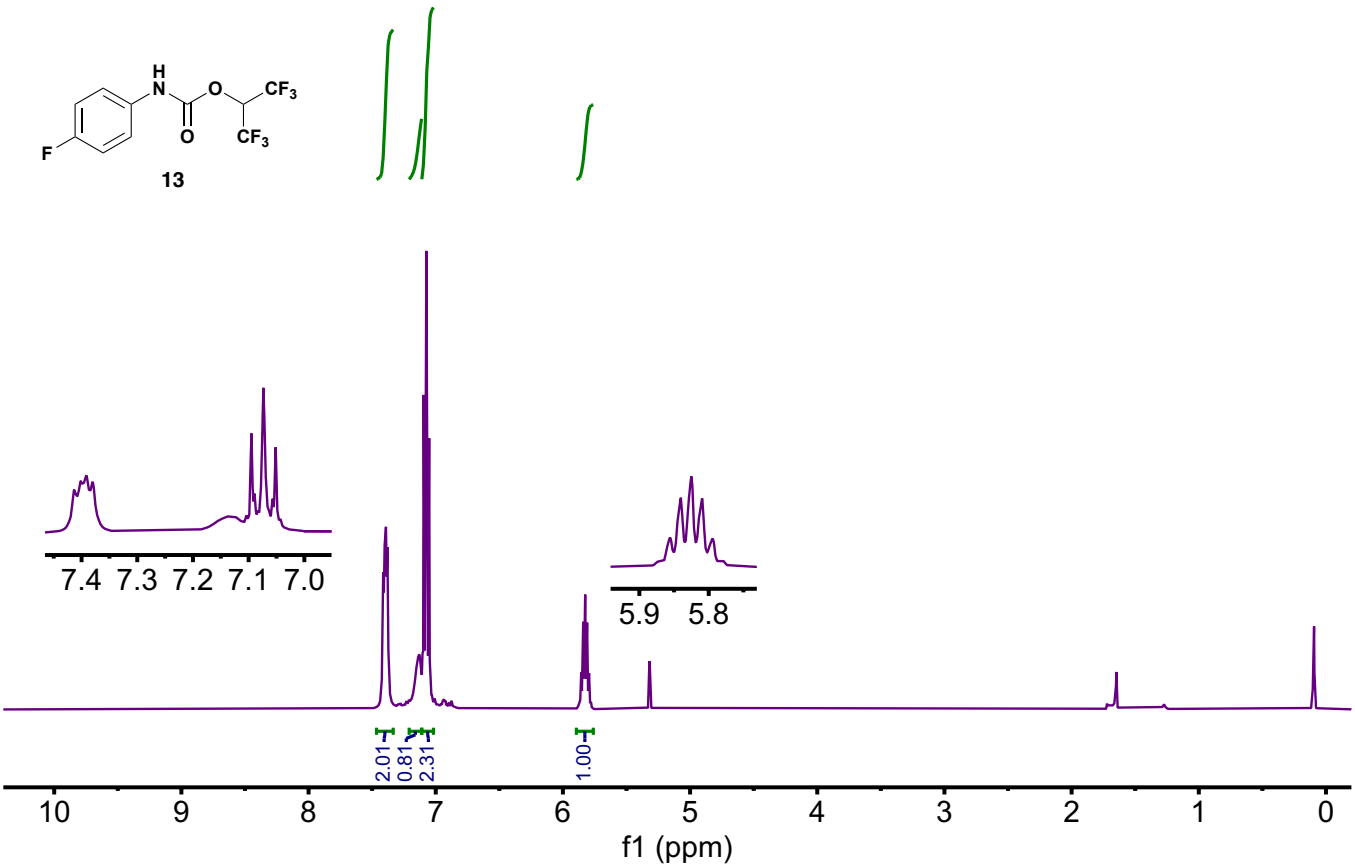

Figure S26. ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **13**.

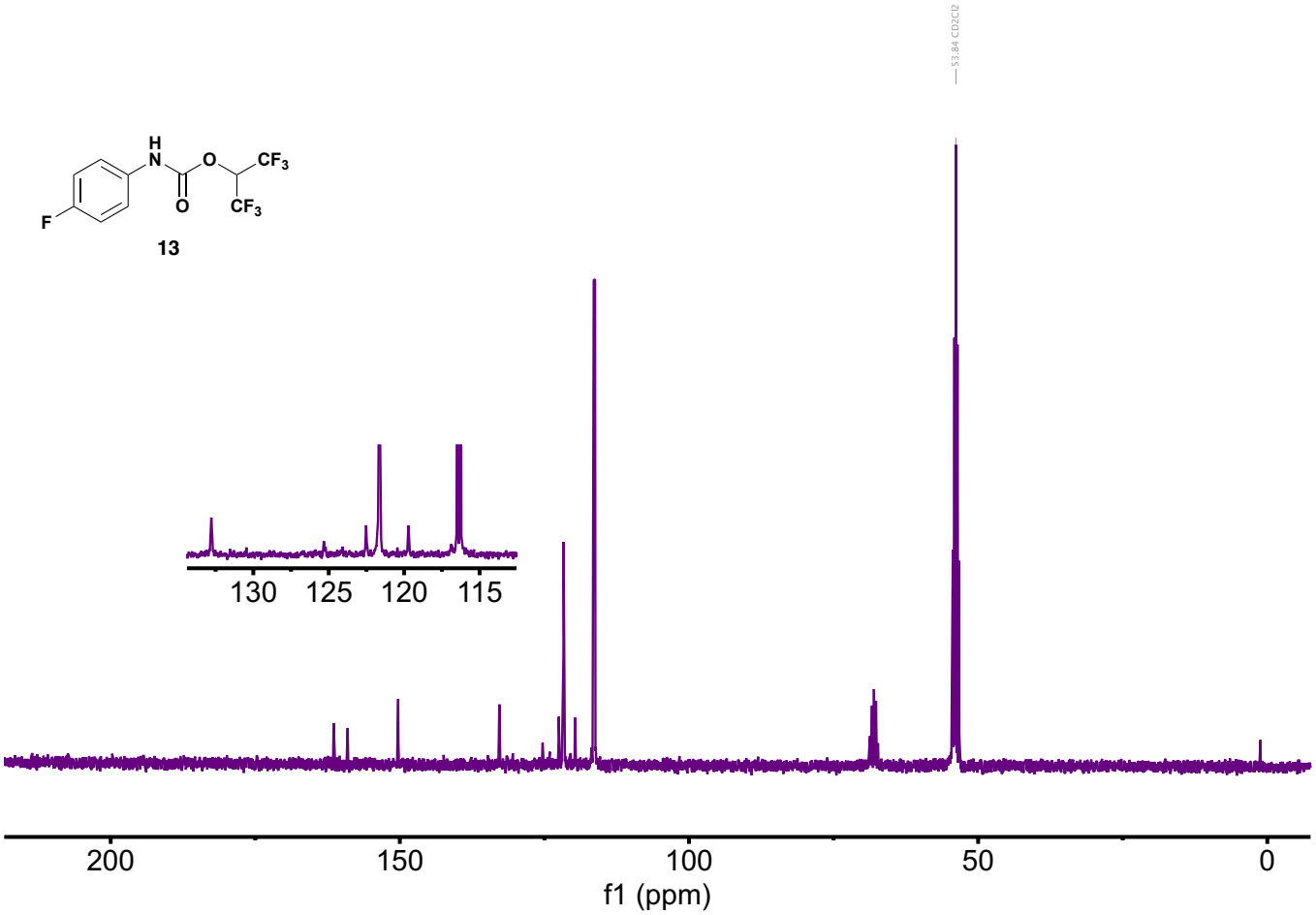

Figure S27. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_2Cl_2) of **13**.

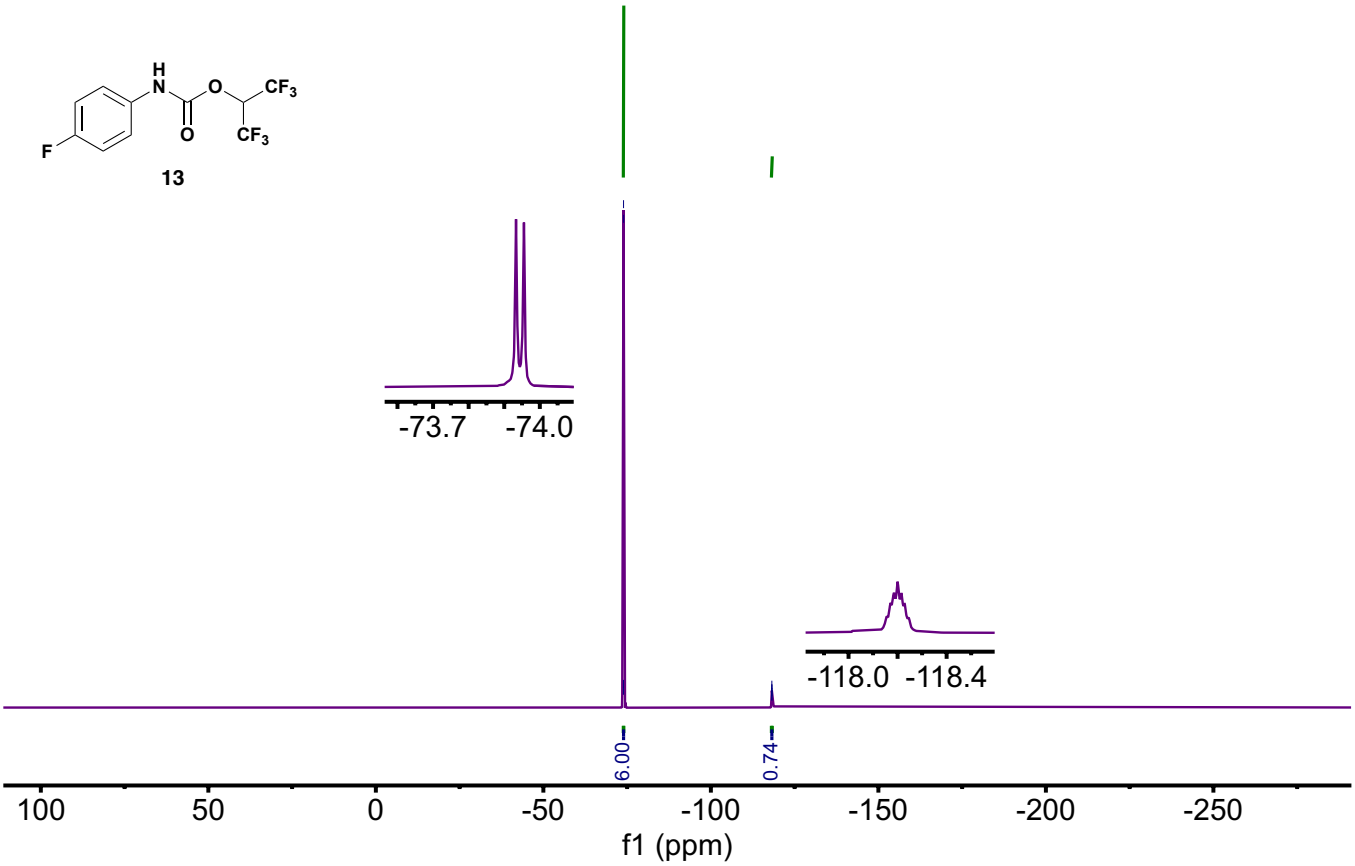

Figure S28. ^{19}F NMR spectrum (282 MHz, CD_2Cl_2) of **13**.

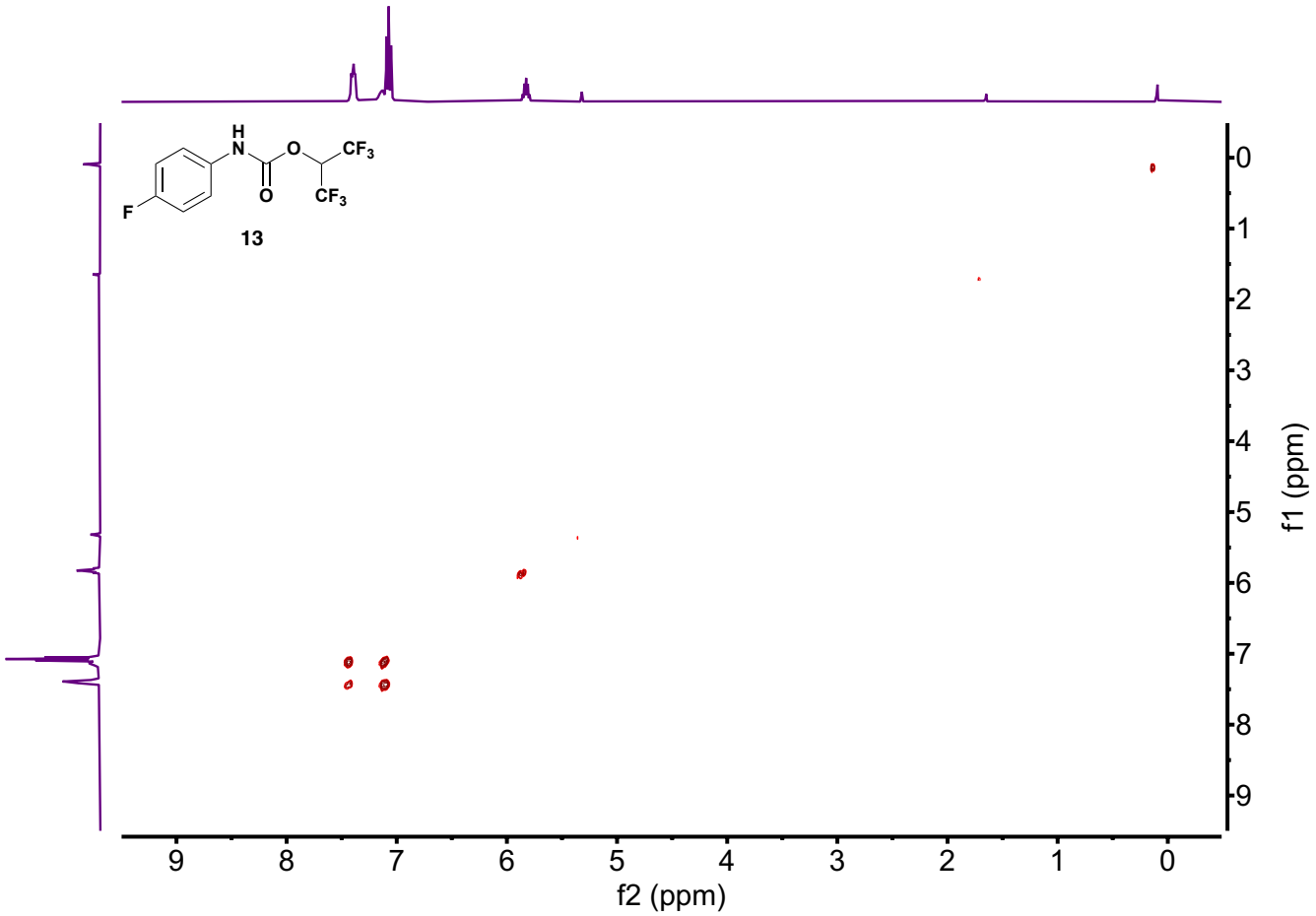

Figure S29. ^{1}H - ^{1}H COSY NMR spectrum (400 MHz, CD_2Cl_2) of **13**.

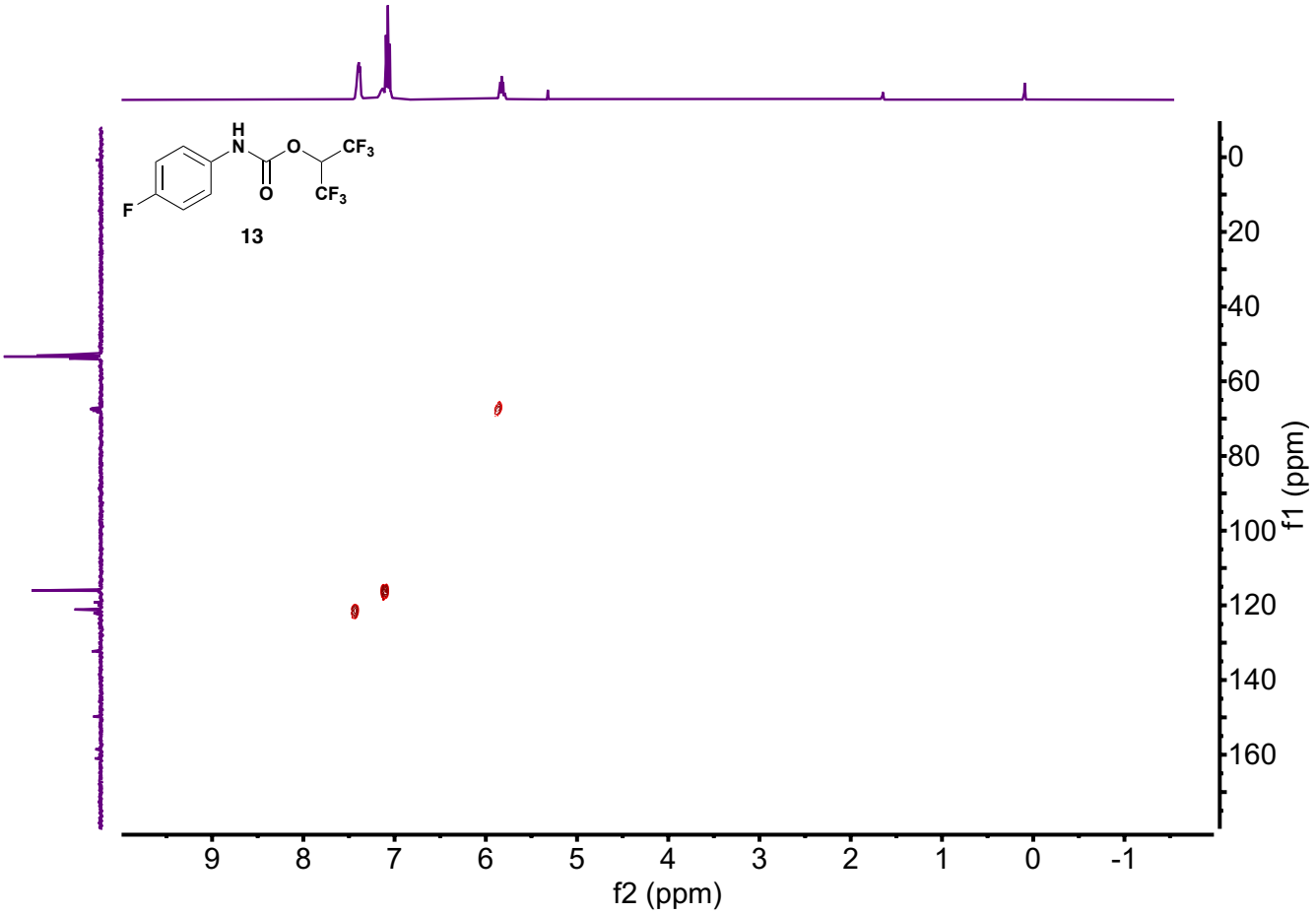

Figure S30. ^{1}H - ^{13}C HSQC NMR spectrum (400/101 MHz, CD_2Cl_2) of **13**.

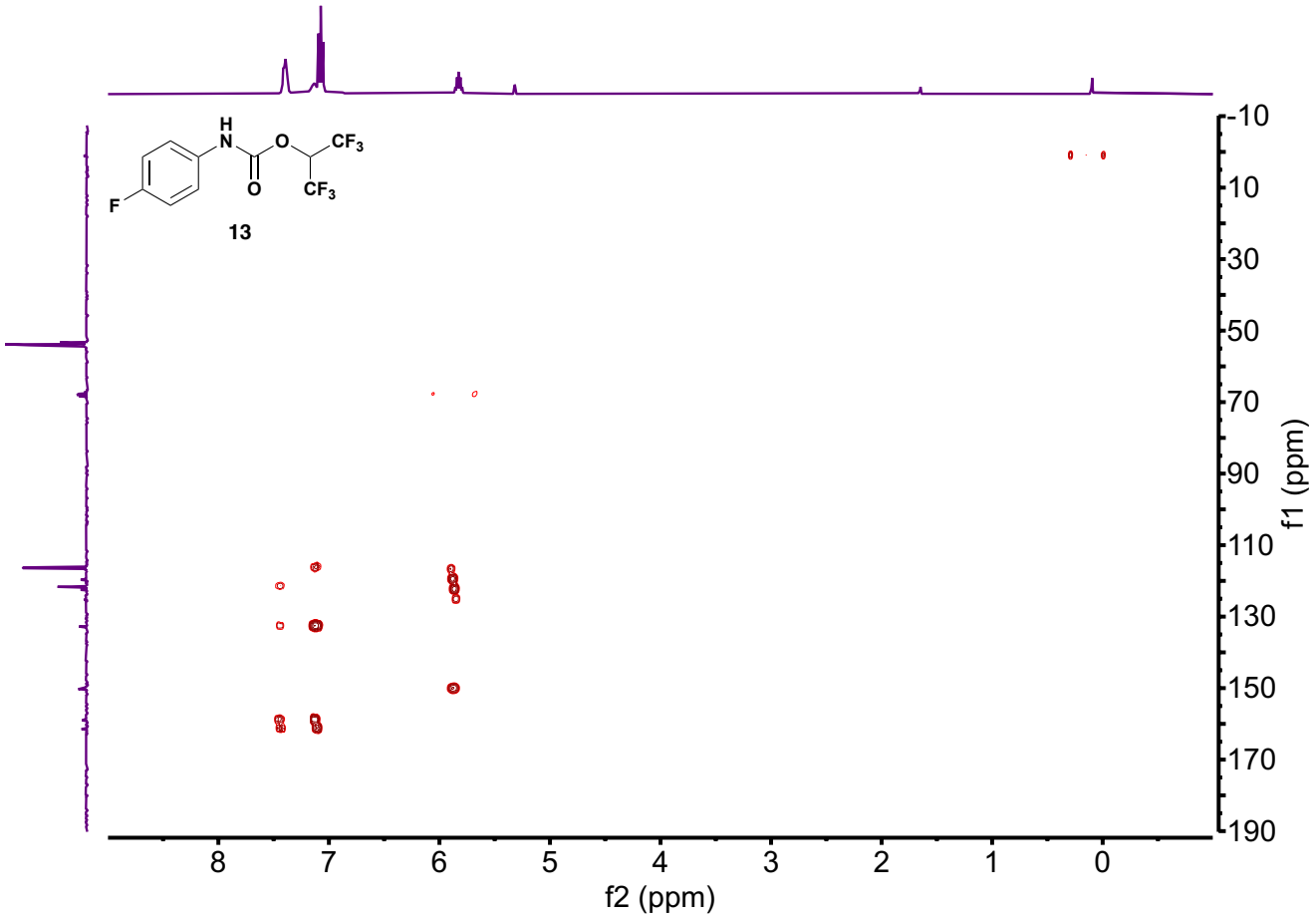

Figure S31. ^{1}H - ^{13}C HMBC NMR spectrum (400/101 MHz, CD_2Cl_2) of **13**.

c. End point NMR data of carbamate (13) forming reaction mixture, with all reagents added directly after one another to heated solution

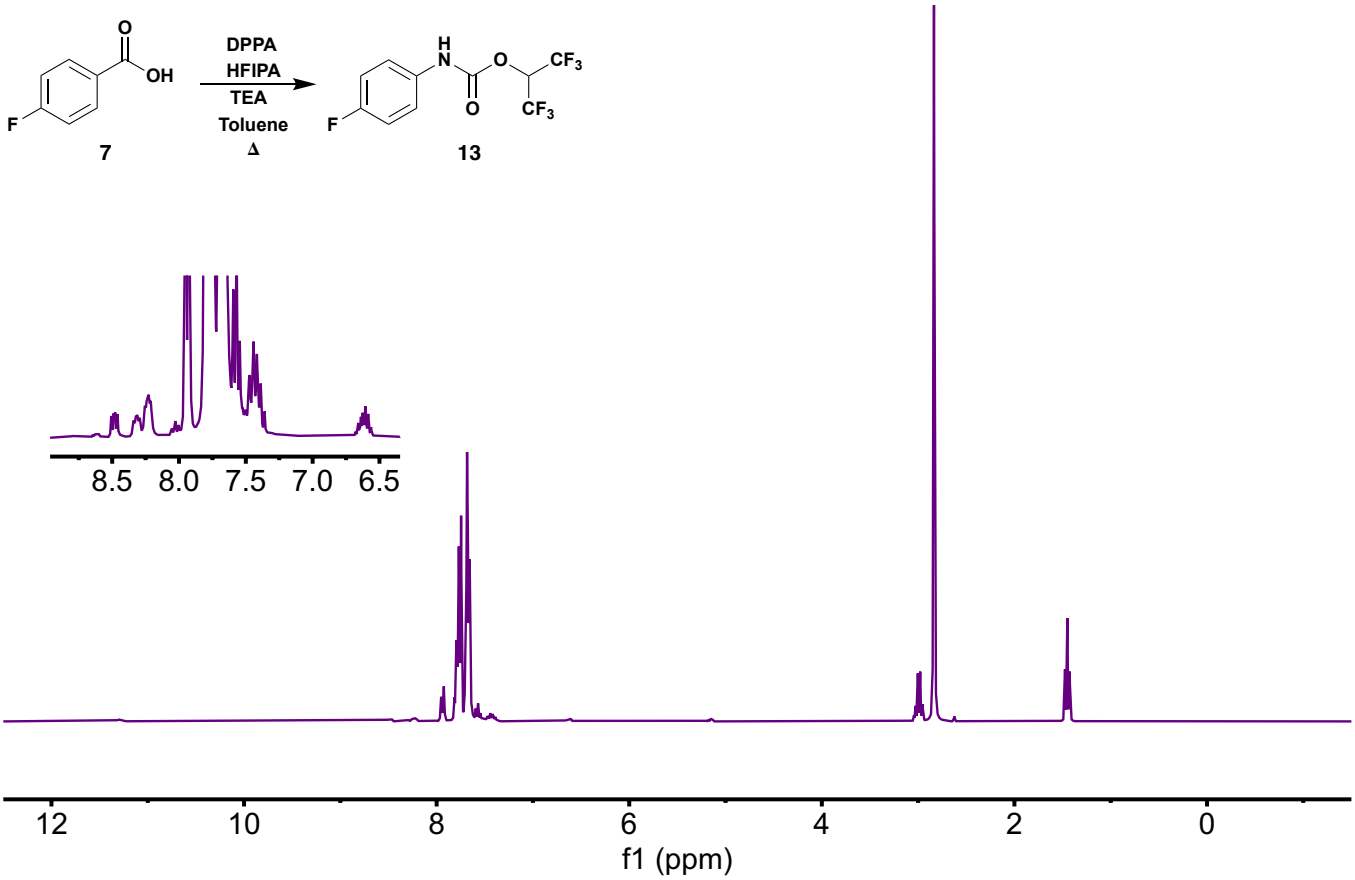

Figure S32. ^{1}H NMR spectrum (300 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

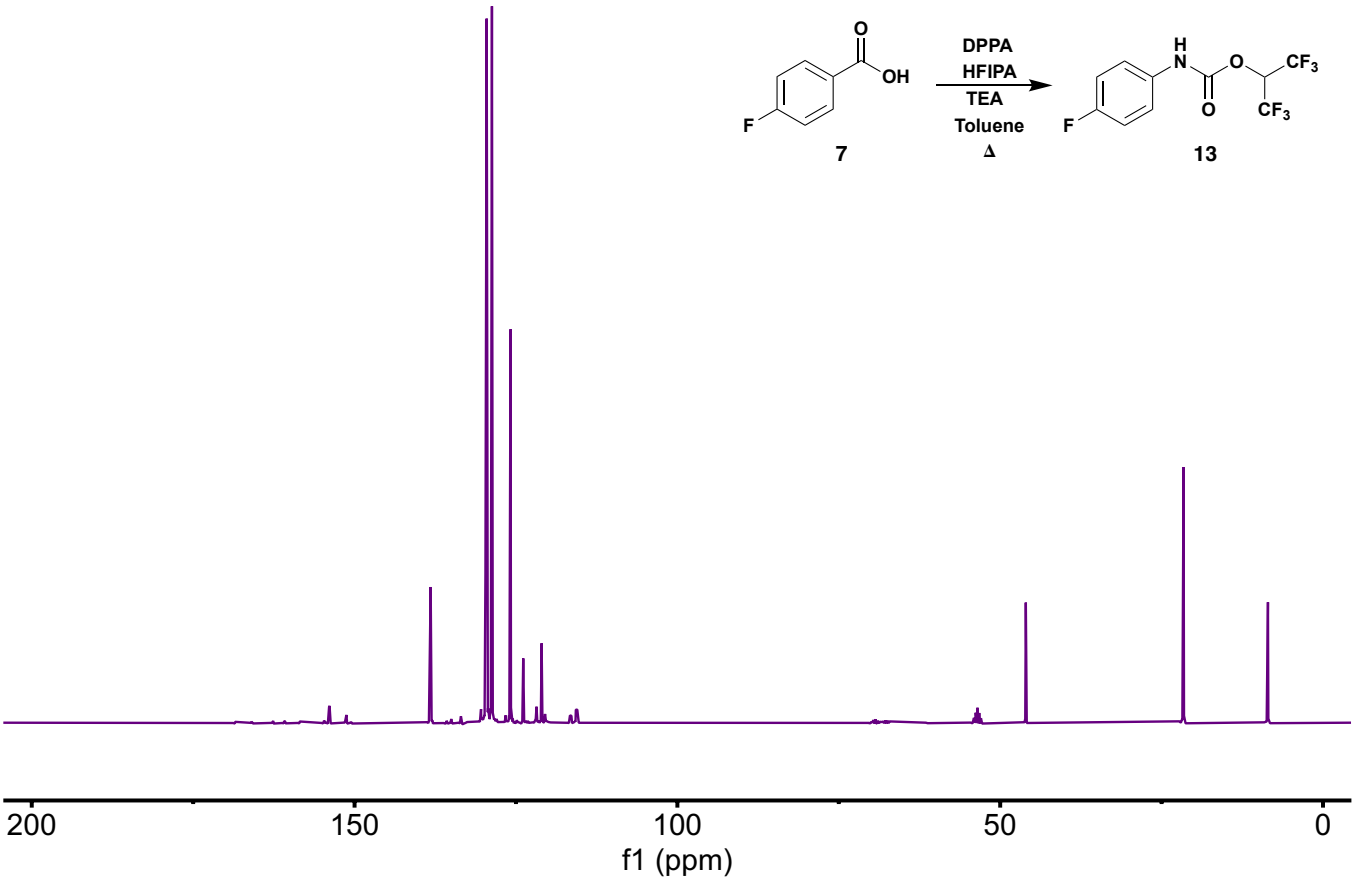

Figure S33. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

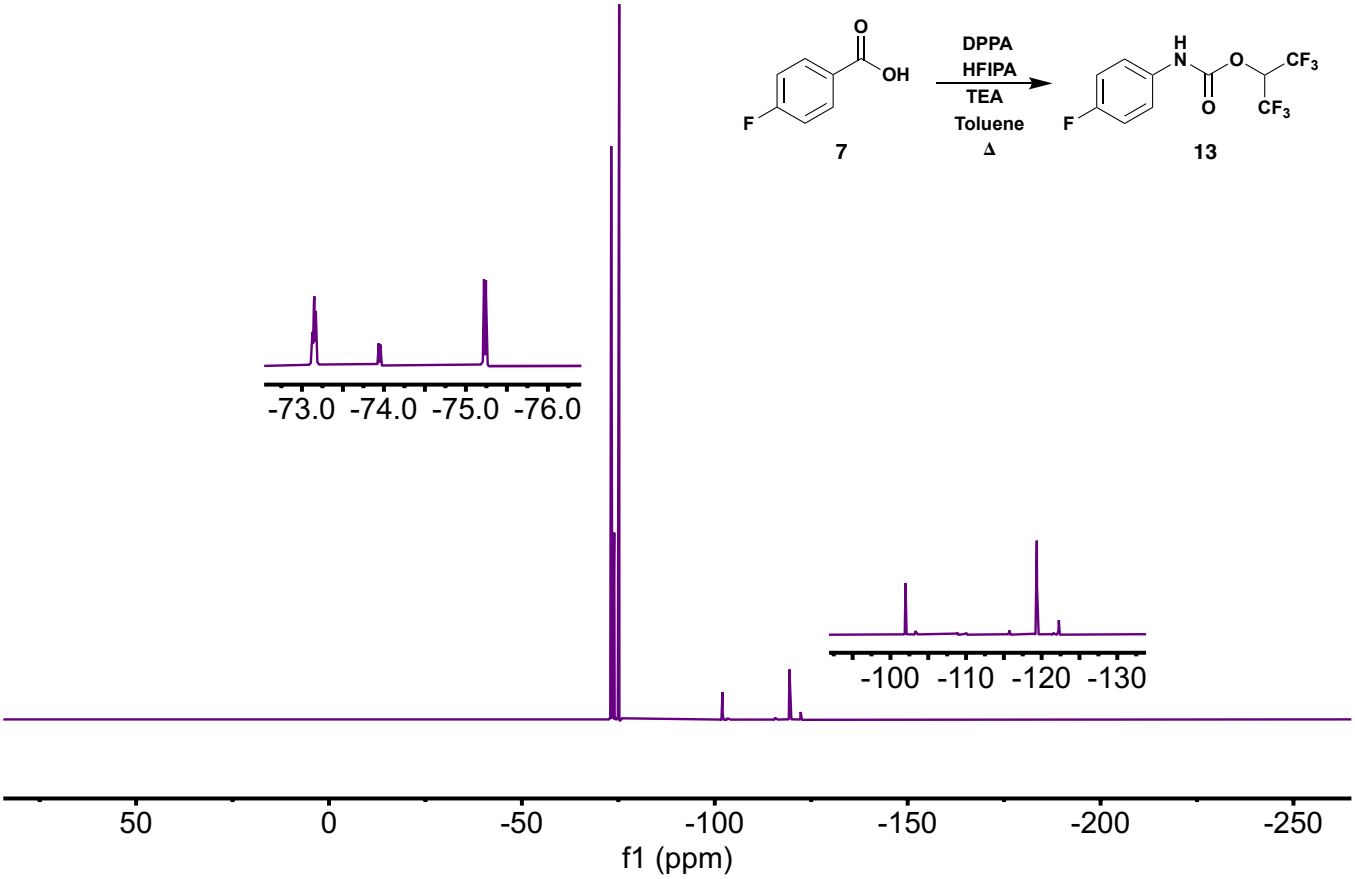

Figure S34. ^{19}F NMR spectrum (282 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

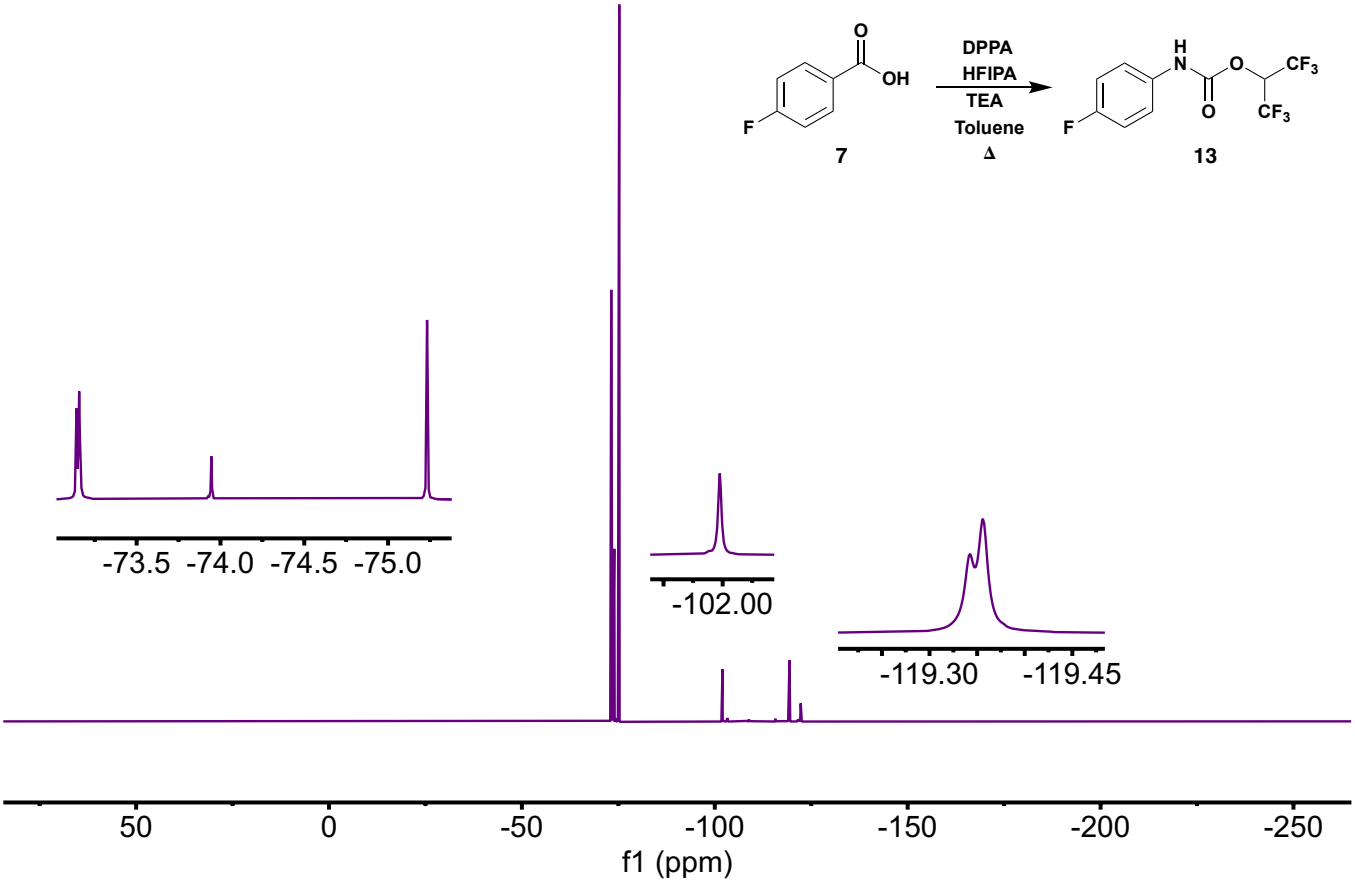

Figure S35. $^{19}F\{^{1}H\}$ NMR spectrum (282 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

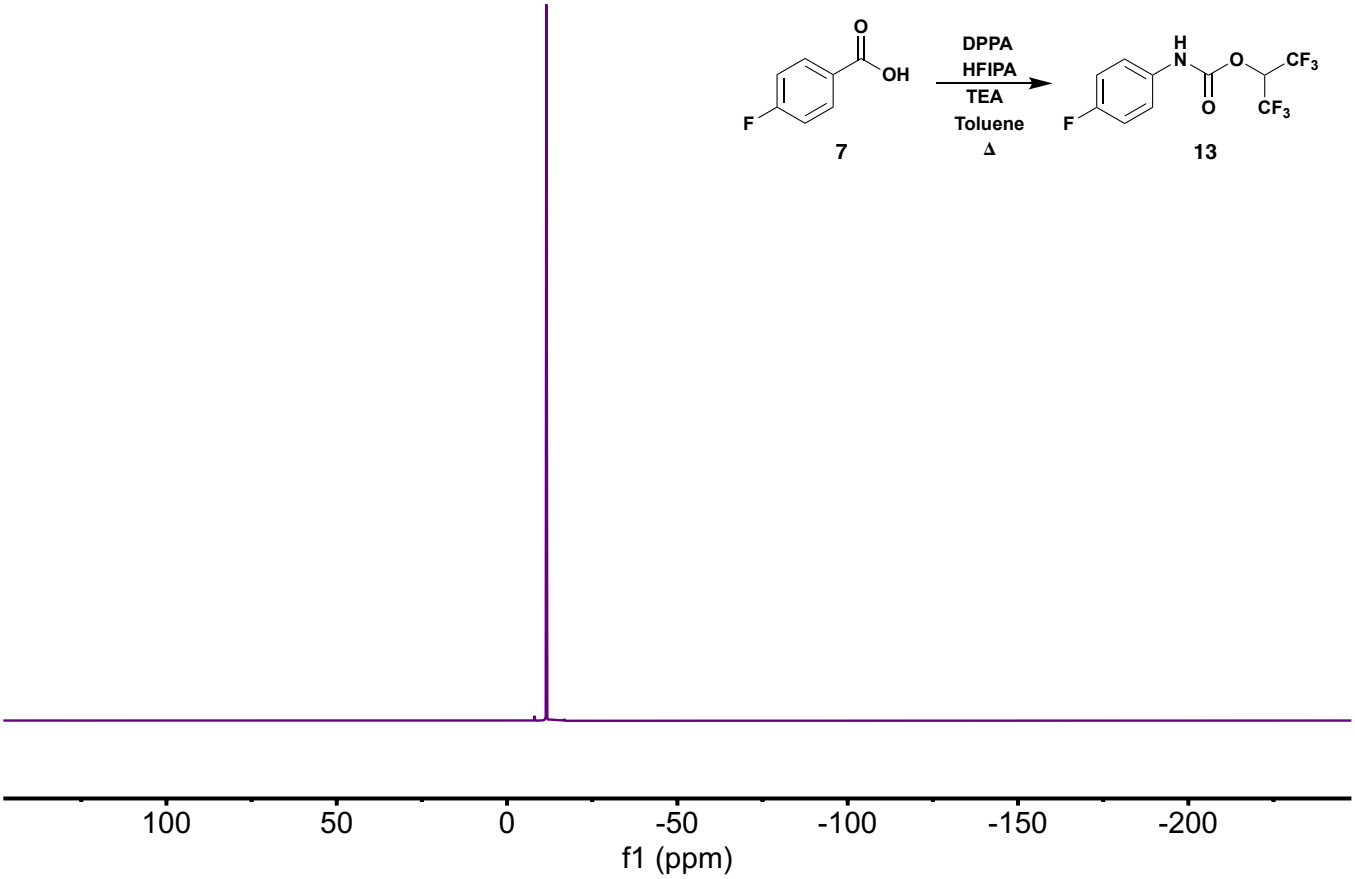

Figure S36. ^{31}P NMR spectrum (162 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

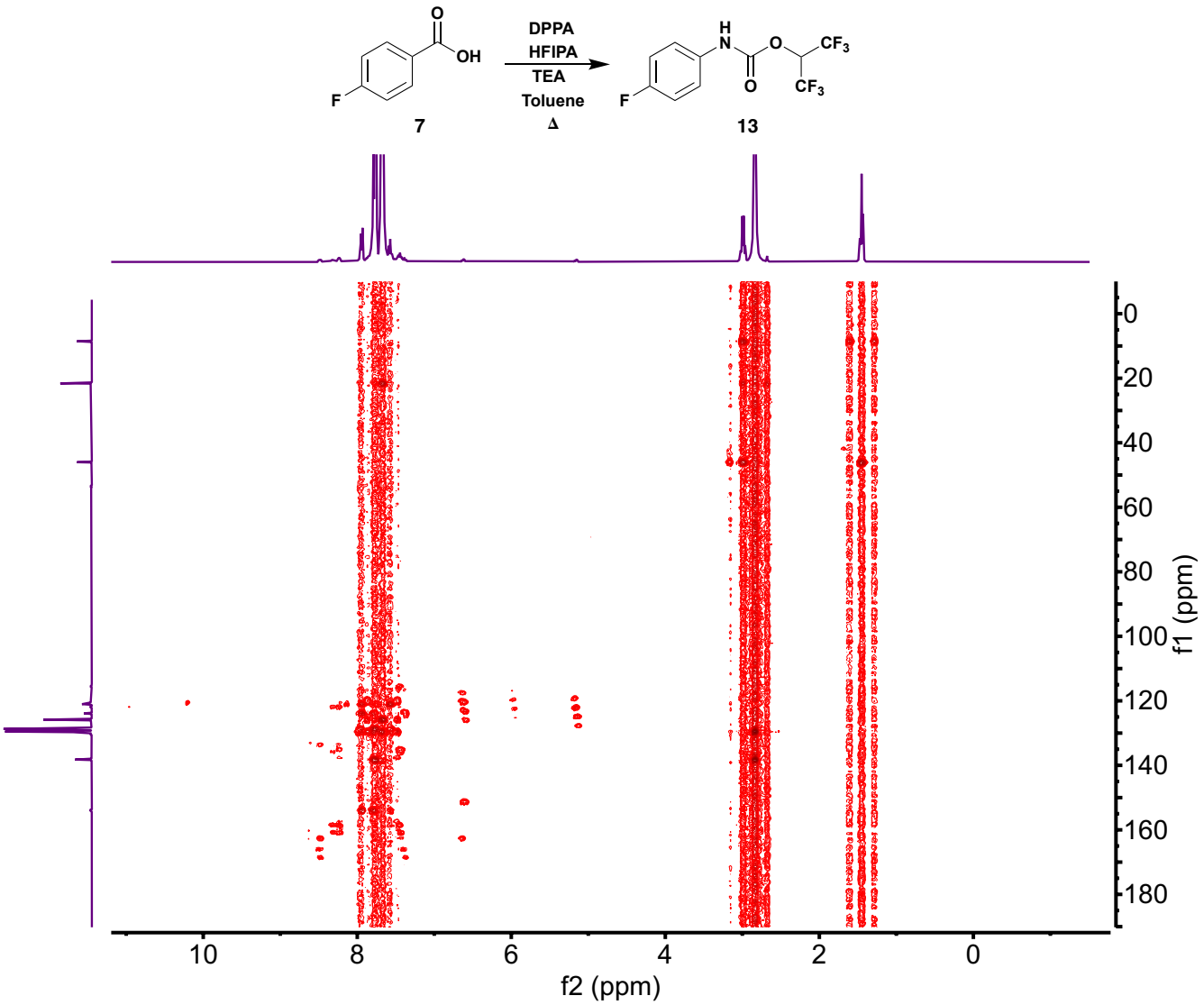

Figure S37. ^{1}H - ^{13}C HMBC NMR spectrum (400/101 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution. Please excuse excessive t1 noise, necessary to observe some key correlations (*i.e.* correlations consistent with ester byproduct).

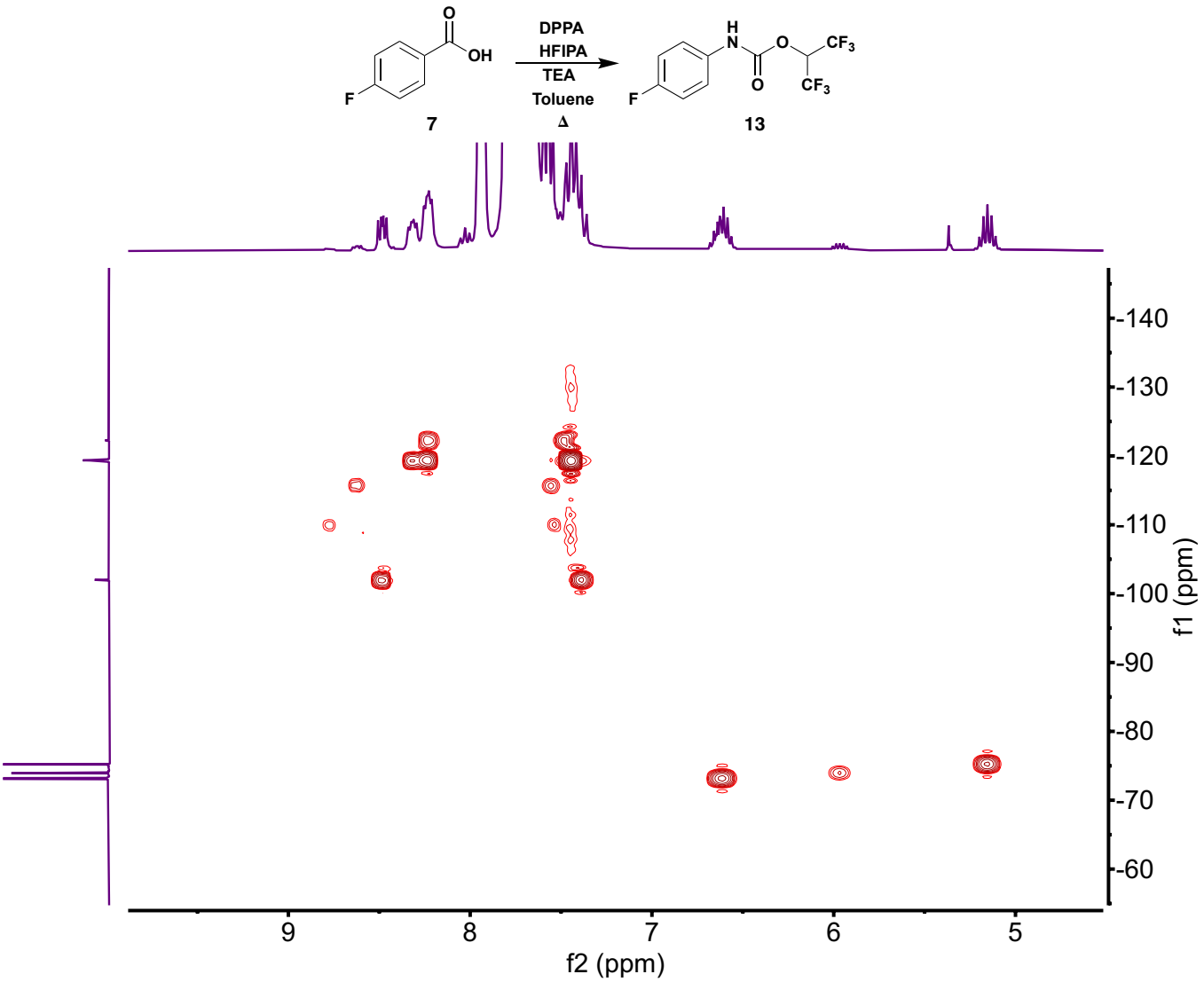

Figure S38. ^{1}H - ^{19}C HMBC NMR spectrum (300/282 MHz, CD_2Cl_2) of reaction mixture to form **13**, with all reagents added directly after one another to heated solution.

d. End point NMR data of carbamate (13) forming reaction mixture, with isocyanate (11) formation achieved prior to HFIPA (12) addition

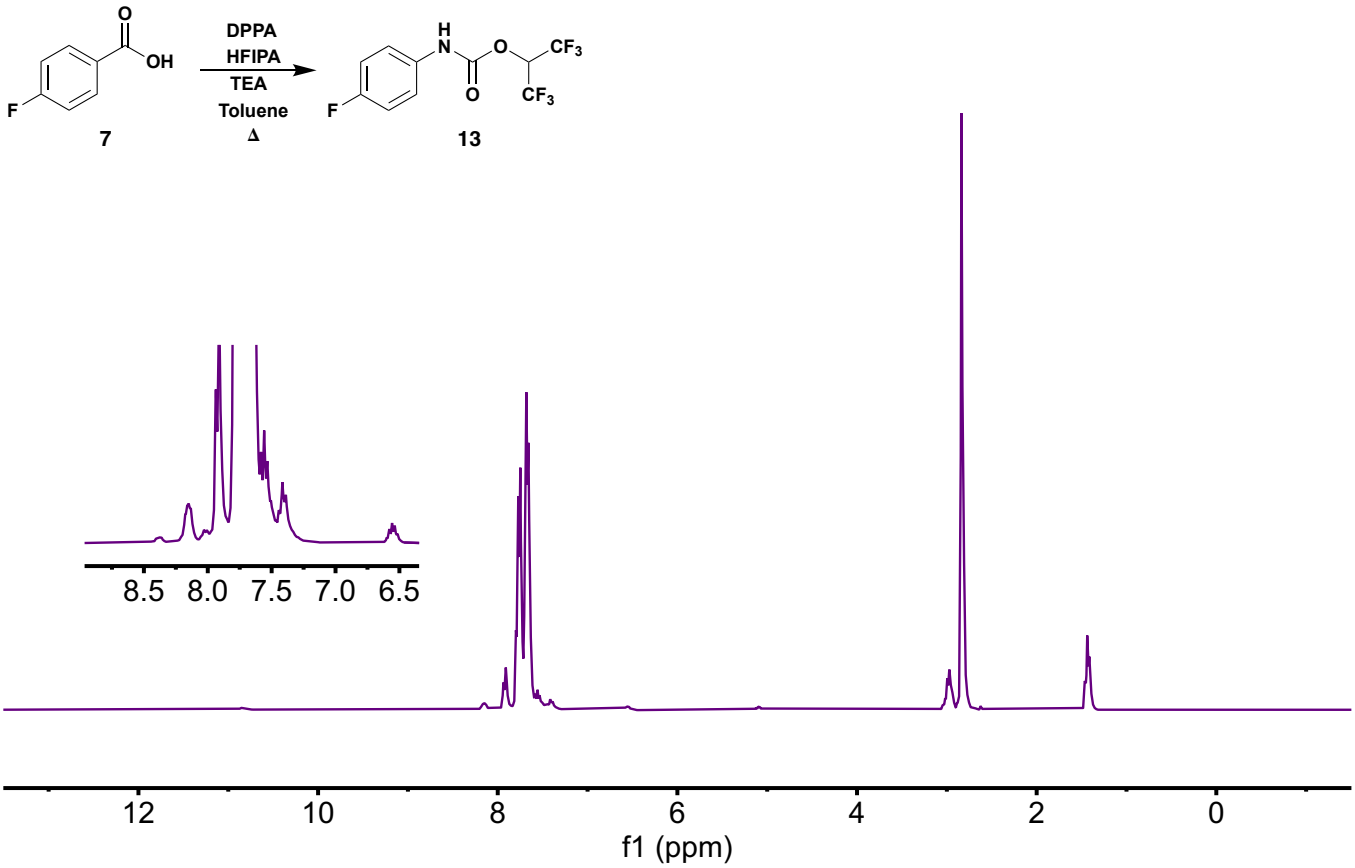

Figure S39. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

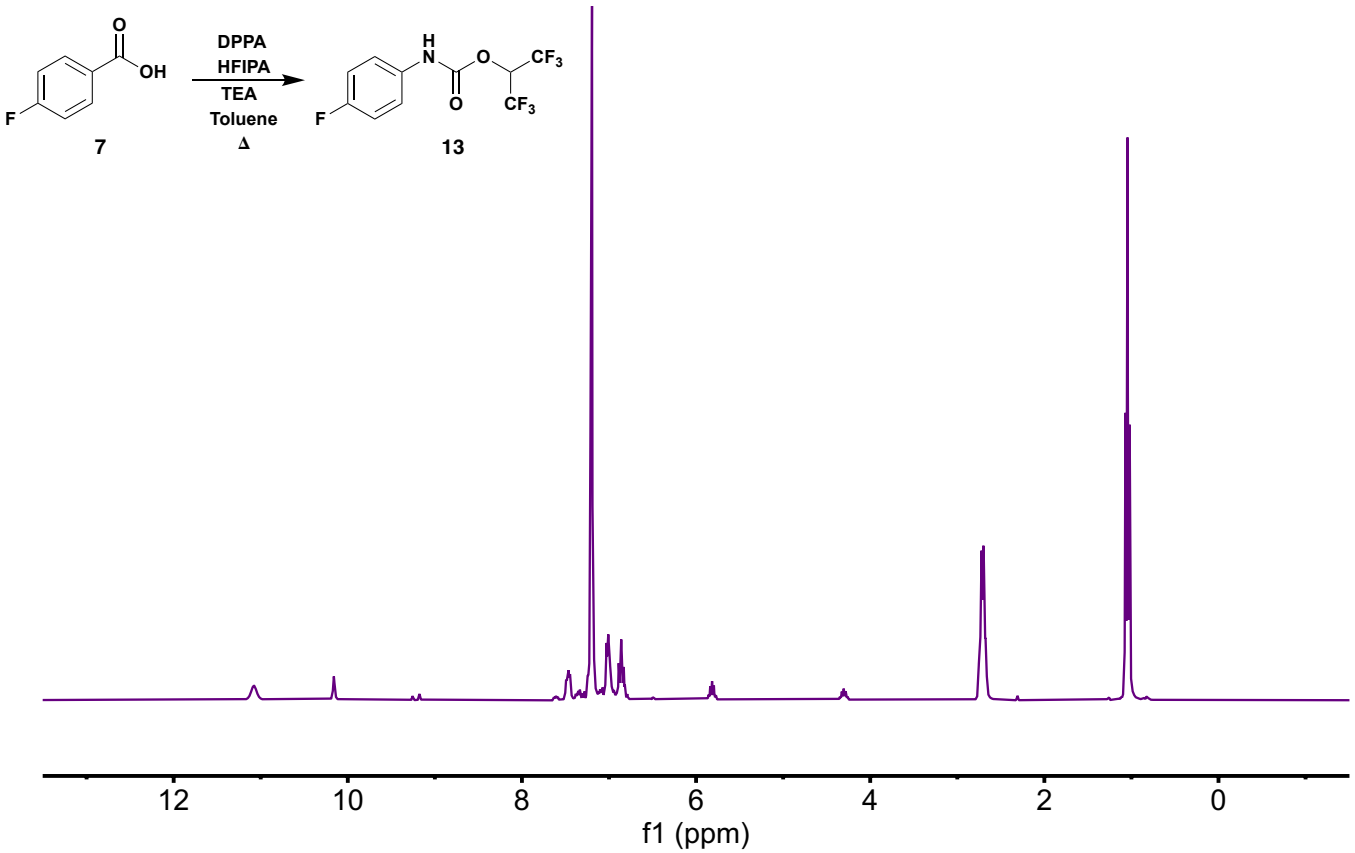

Figure S40. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of dried reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

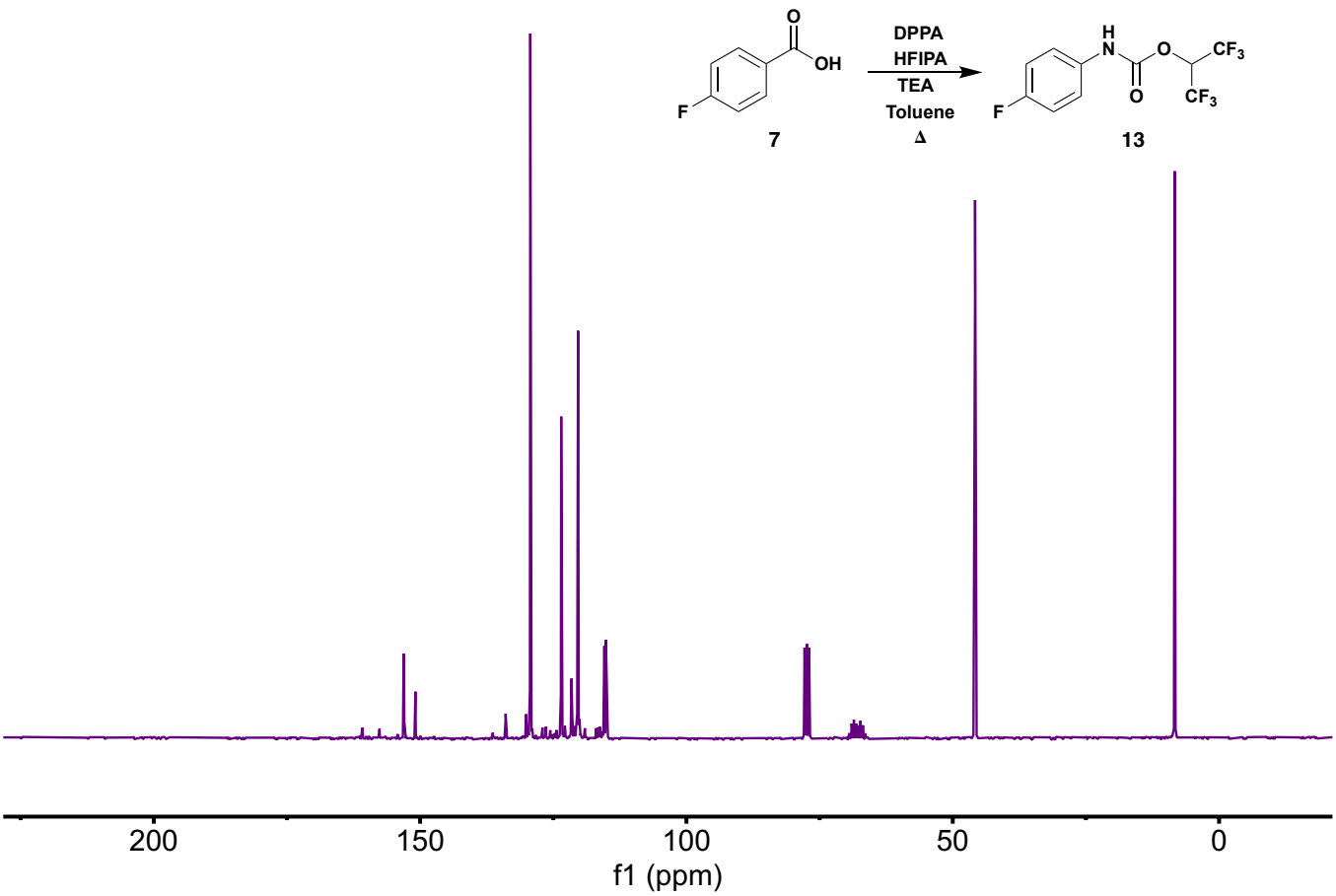

Figure S41. $^{13}C\{^{1}H\}$ NMR spectrum (75 MHz, $CDCl_3$) of dried reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

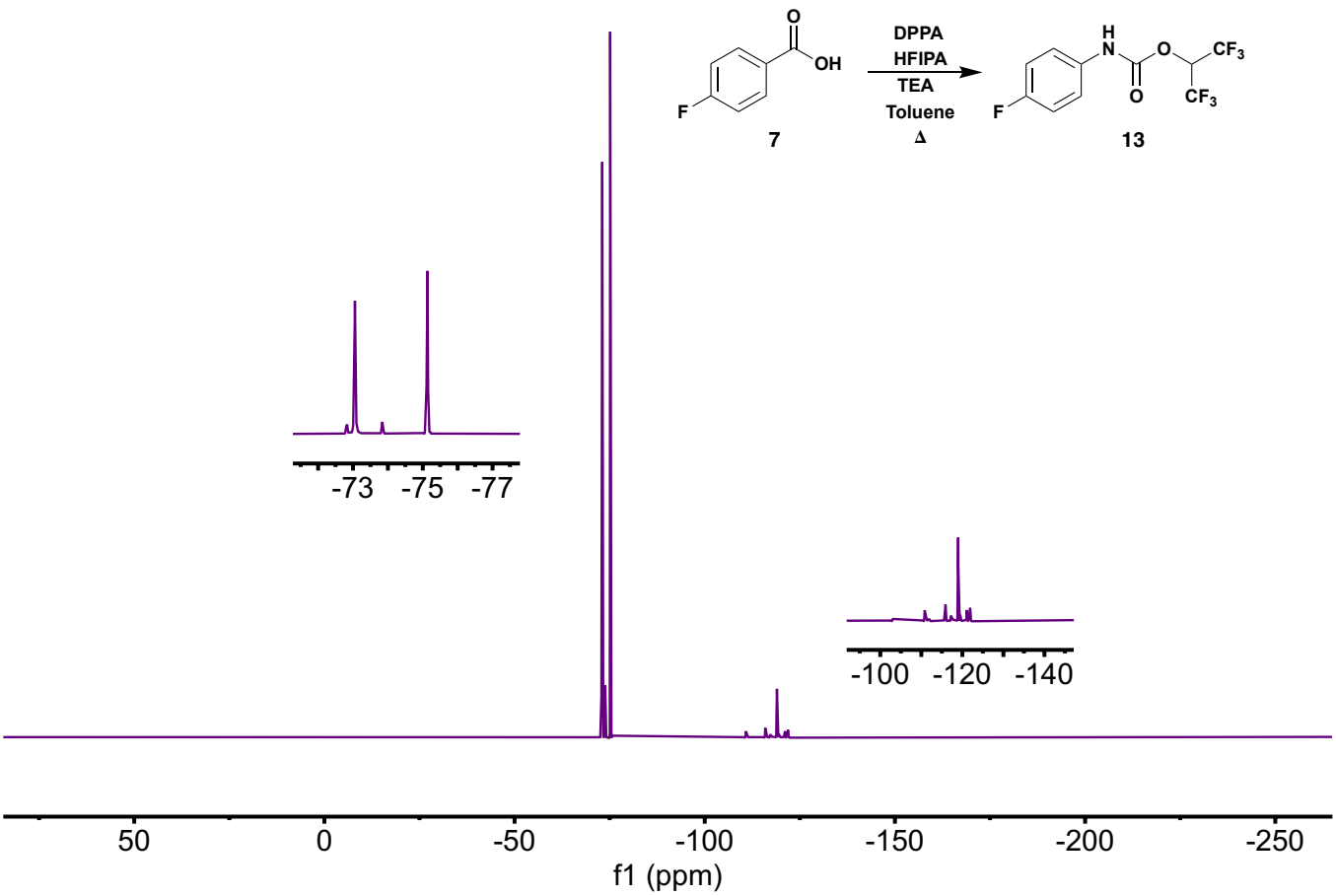

Figure S42. ^{19}F NMR spectrum (282 MHz, $CDCl_3$) of reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

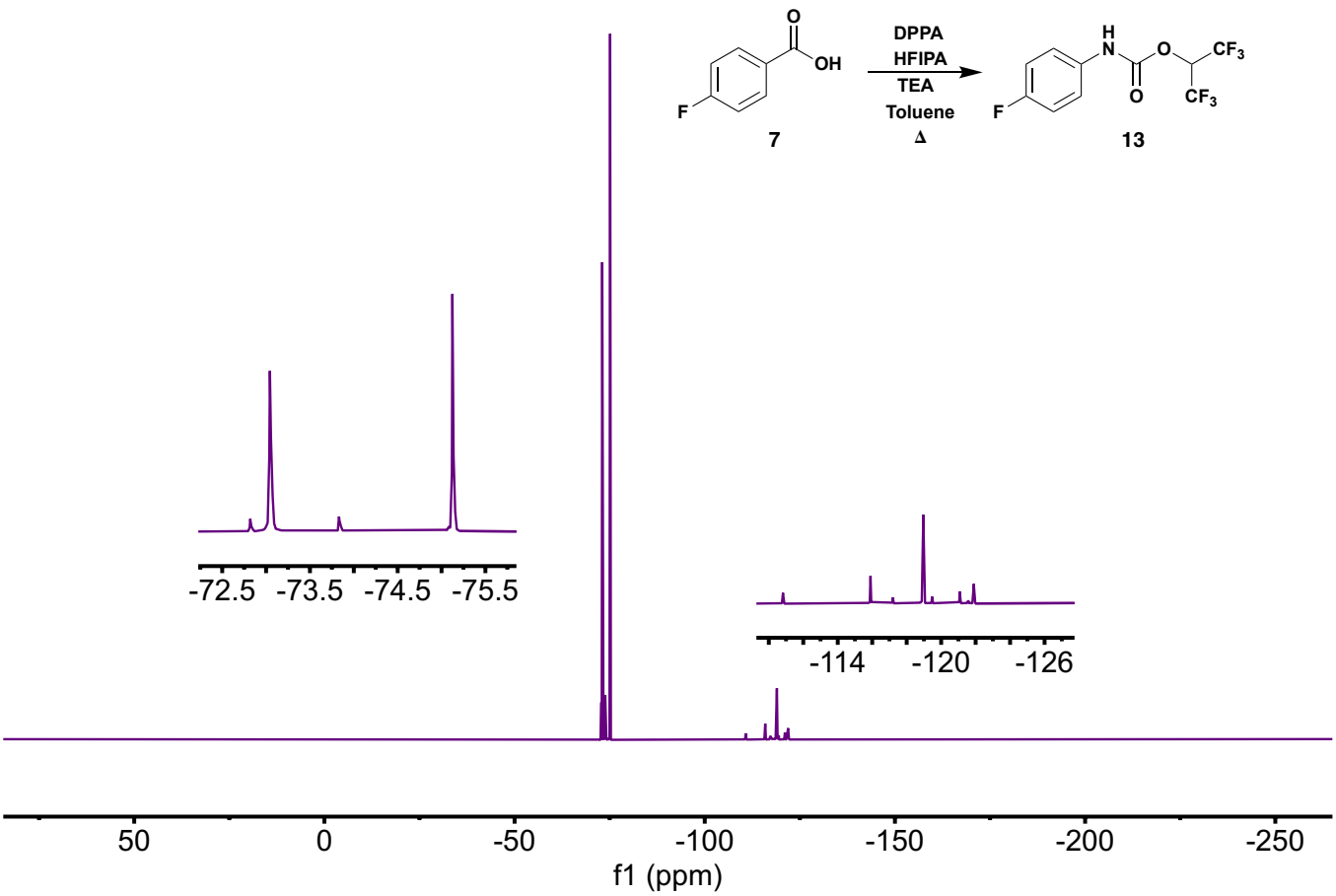

Figure S43. $^{19}F\{^{1}H\}$ NMR spectrum (282 MHz, $CDCl_3$) of reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

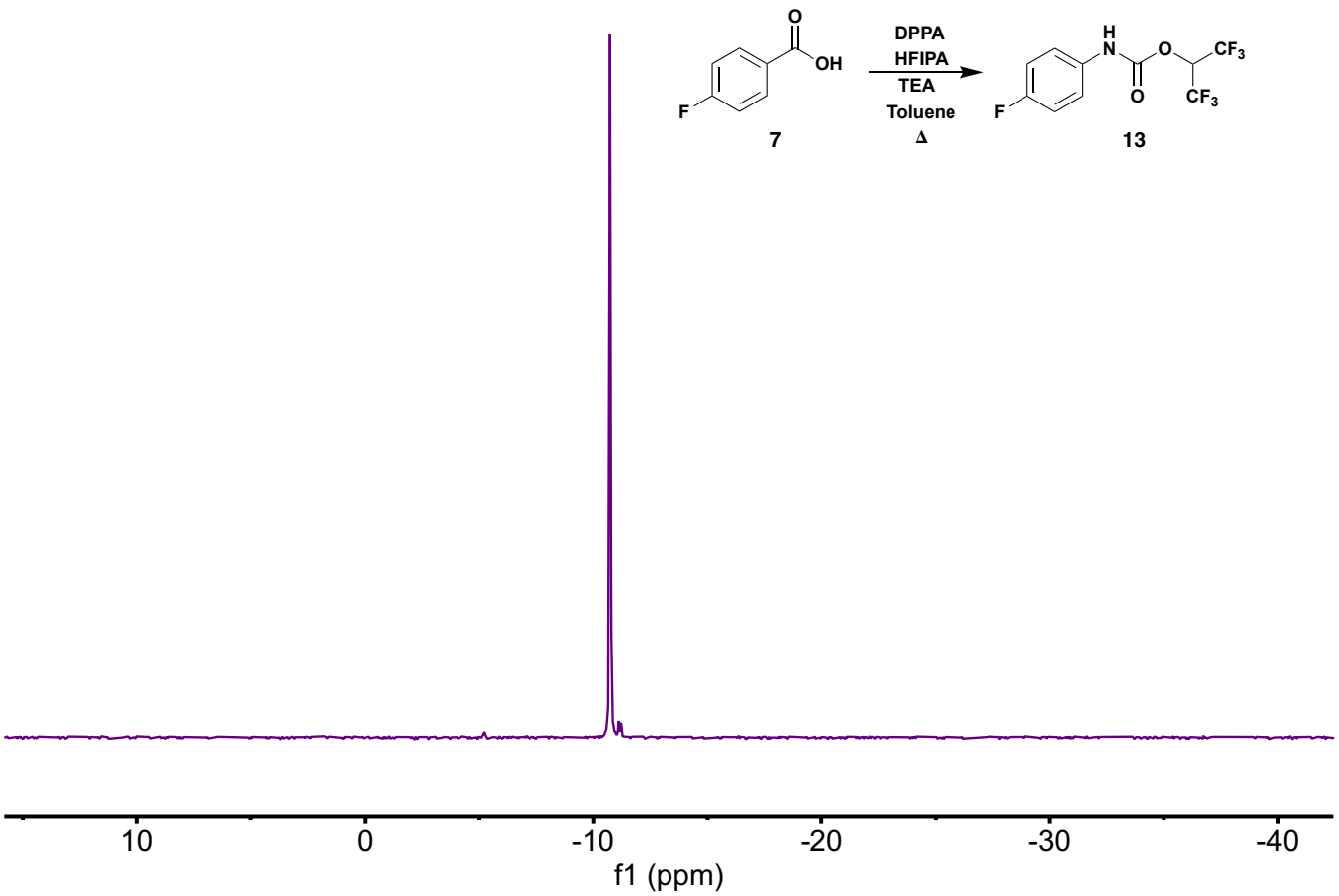

Figure S44. ^{31}P NMR spectrum (121 MHz, $CDCl_3$) of reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

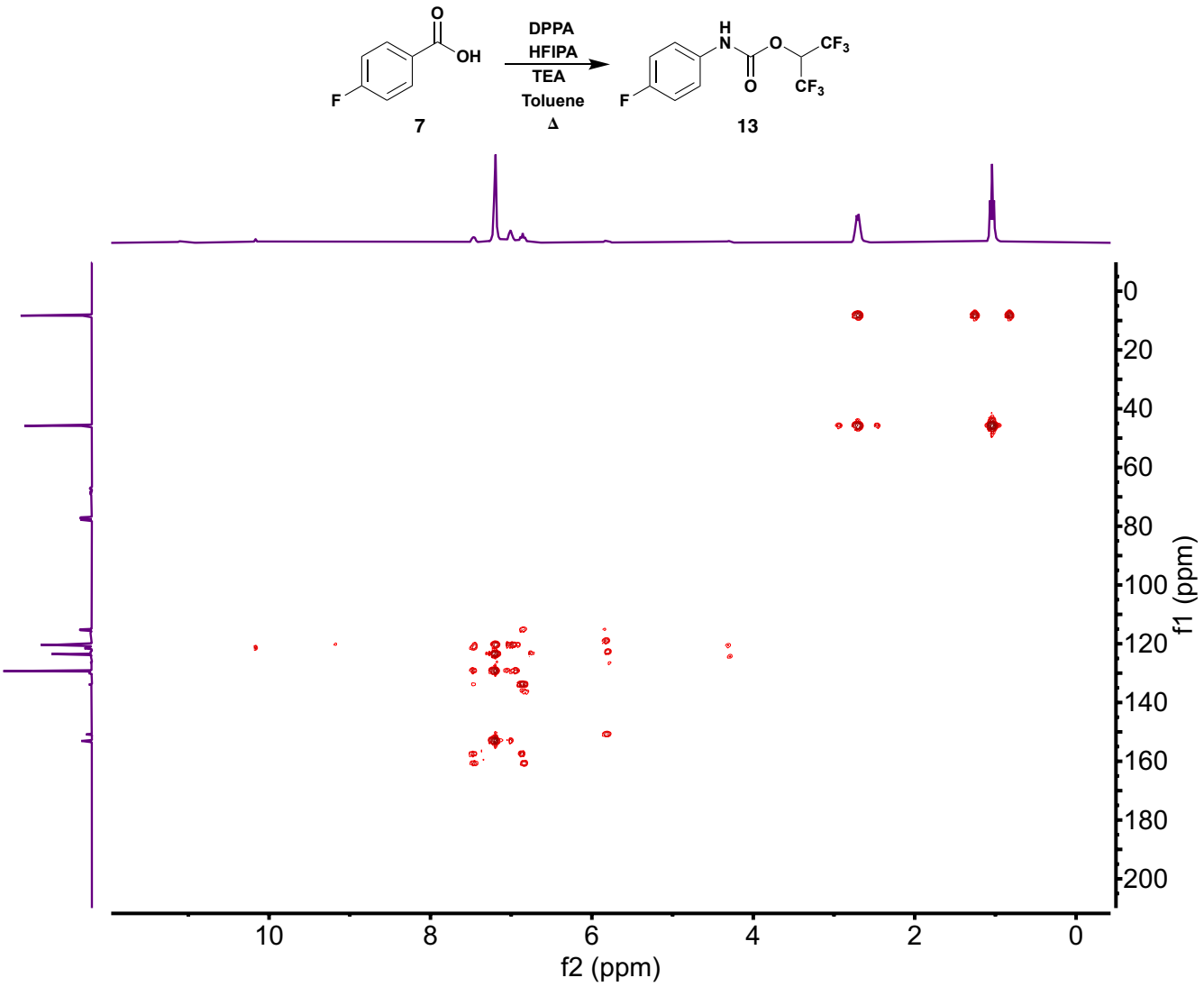

Figure S45. ^{1}H - ^{13}C HMBC NMR spectrum (300/75 MHz, $CDCl_3$) of dried reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.

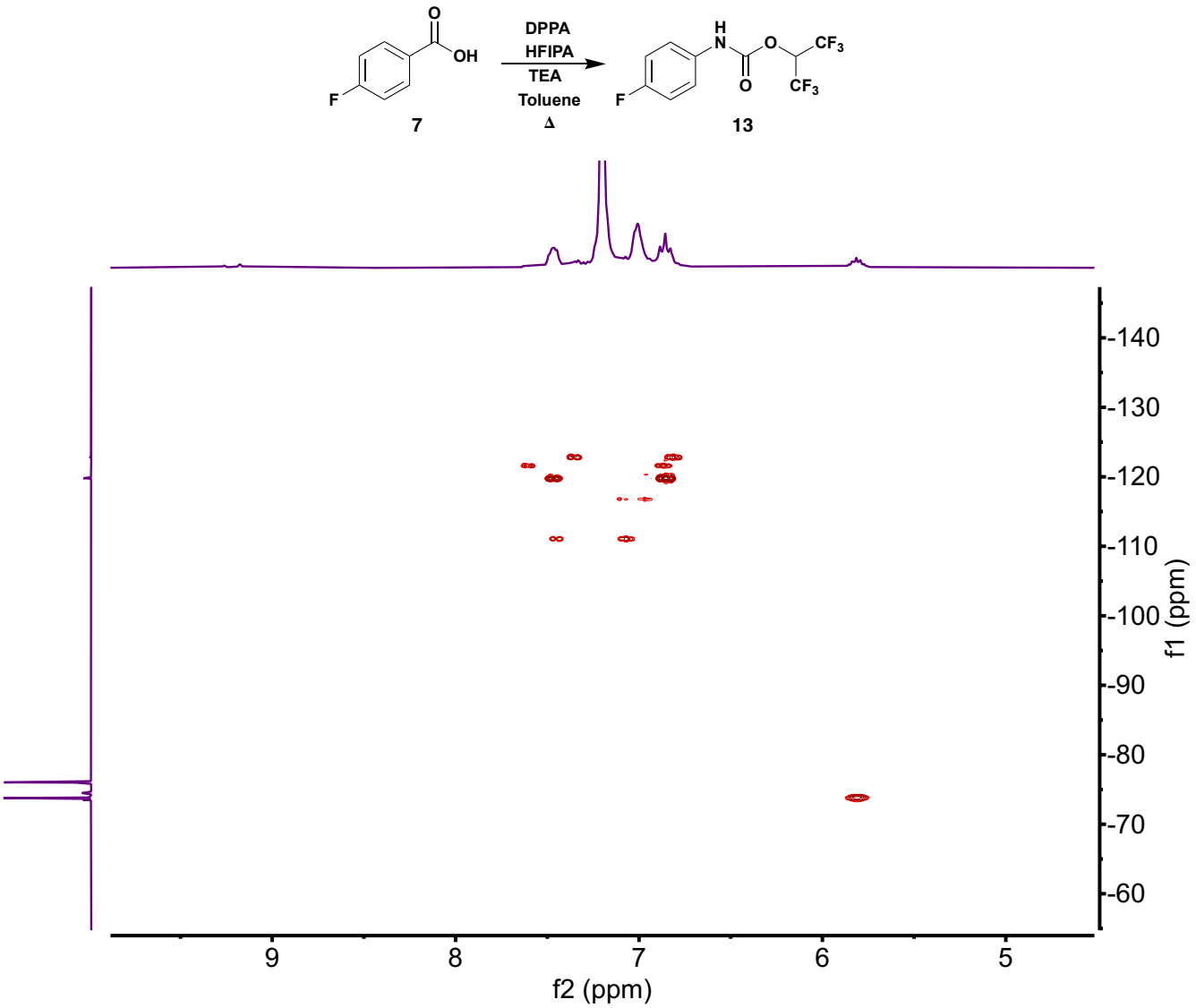

Figure S46. ^{1}H - ^{19}F HMBC NMR spectrum (300/75 MHz, $CDCl_3$) of dried reaction mixture to form **13**, with isocyanate (**11**) formation prior to addition of **12**.