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Supporting Information for

Catalytic Hydrogenative Dechlorination Reaction for Efficient Synthesis of a Key Intermediate of SDHI Fungicides under Continuous-flow Conditions

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S1. General Information

Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECX-600 or ECA-500 spectrometer, operating at 600 MHz or 500 MHz for ^{1}H, 150 MHz for ^{13}C NMR in $CDCl_3$ unless otherwise noted. Tetramethylsilane (TMS) served as the internal standard ($\delta = 0$) for ^{1}H NMR, $CDCl_3$ ($\delta = 77.0$) was used as the internal standard for ^{13}C NMR. Gas chromatography (GC) was recorded on a Shimadzu GC-2030AF, 100V spectrometer using SH-Rtx-5 Amine column (30 m, 0.25 mmID, 0.25 μm df). Inductively coupled plasma-atomic emission spectrometry (ICP-AES) analysis was performed on a Shimadzu ICPS-7510 equipment. STEM/EDS images were obtained using a JEOL JEM-2100F instrument operated at 200 kV. All STEM specimens were prepared by placing a catalyst directly on carbon-coated copper grids. X-ray photoelectron spectroscopy (XPS) was measured using a JEOL JPS-9010MC equipment. High-pressure hydrogenation reactions under batch conditions were carried out using a Tokyo Rikakikai (EYELA) Co., Ltd. ChemiStation™ (PPV-CTRL1) equipment. For apparatuses for flow systems, a plunger pump (FLOM, UI-22-110P), a column heater (Tokyo Rikakikai Co., Ltd., LCR-1300), a back pressure regulator (DFC Co., Ltd., FC-BPV-100) and a stainless column with column ends were used. Preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F from Wako Pure Chemical Industries, Ltd. High Resolution Mass Spectra (HRMS) were recorded using a JEOL JMS-T100TD (DART) spectrometer. THF and toluene were purchased from FUJIFILM Wako Pure Chemical Co. Ltd. as dried solvents and were used directly. Other organic solvents used were commercially available dry solvents, which were distilled appropriately under an argon atmosphere or were stored over molecular sieves prior to use. Ethyl 3-(chlorodifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**5**) and Ethyl 3-(trifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**12**) were prepared following the literatures.[9, 17] Ethyl 4-(chlorodifluoromethyl)-2-phenylpyrimidine-5-carboxylate was prepared following the literature.[9] Tetrabutylammonium acetate was purchased from Tokyo Chemical Industry Co., Ltd. or Sigma-Aldrich Co. LLC and was used directly. Activated carbon and calcium phosphate were purchased from FUJIFILM Wako Pure Chemical Co. Ltd. and used directly. Dimethylpolysilane was purchased from Nippon Soda Co. Ltd. Polycarbosilane was purchased from JGC Catalysts and Chemicals Ltd.

The parameter SV_{mol} value in this article was calculated by the following equation.

SV_{mol} [h^{-1}] =

[Conc. of chlorodifluoro-substrate (mmol/mL)] x [Flow rate (mL/min)] x 60 (min/h)

/ [Pd (mmol) in the column]

S2. General Procedure for Catalyst Preparation

S2-1. Preparation of catalysts: DMPSi-Pd/Supports

Dimethylpolysilane-modified Pd on support catalysts were prepared according to our previous work[10a] with small modifications. Following is for an example of representative DMPSi-Pd/AC catalyst; to a suspension of 4.5 g of activated carbon in toluene (50 mL), THF (50 mL) solution of $Pd(OAc)_2$ (112.4 mg, 0.5 mmol) was added dropwise. After stirring for 30 min, polycarbosilane (250 mg), a reductant, was added portionwise and after completion of addition, the mixture was heated to 80 ℃ for 1 h in an oil bath. The resulting mixture was cooled to room temperature, and dimethylpolysilane (0.5 g), toluene (25 mL), and MeOH (25 mL) was added to the mixture and stirred overnight at 80 °C. After the completion of the above operation, the solution was then cooled to room temperature and a black solid material was filtered. This material was washed with acetone and water, and at 80 ℃ under reduced pressure for 15 h to give 0.1 mmol/g DMPS-Pd/AC catalyst.

S2-2. Preparation of catalyst; DMPSi-PD/AC-CP

Dimethylpolysilane-modified Pd on composite support catalysts were also prepared according to our previous work[10a] with small modifications. Following is for an example of representative DMPSi-Pd/AC-CP(3) catalyst; to a suspension of 3.38 g of activated carbon in toluene (50 mL), THF (50 mL) solution of $Pd(OAc)_2$ (112.4 mg, 0.5 mmol) was added dropwise. After stirring for 30 min, polycarbosilane (250 mg), a reductant, was added portionwise and after completion of addition, the mixture was heated to 80 ℃ for 1 h in an oil bath. The resulting mixture was cooled to room temperature, $Ca_3(PO_4)_2$ (1.13 g) and dimethylpolysilane (0.5 g) were successively added in this order at room temperature with an interval of 30 minutes, then toluene (25 mL) and MeOH (25 mL) was added to the mixture and stirred overnight at 80 °C. After the completion of the above operation, the solution was then cooled to room temperature and a black solid material was filtered. This material was washed with acetone and water, and at 80 ℃ under reduced pressure for 15 h to give 0.1 mmol/g DMPS-Pd/AC-CP catalyst.

S3. Typical Experimental Procedure of Hydrodechlorination under Batch and Flow Conditions

S3-1. Hydodechlorination of CDFMMP 5 under batch conditions

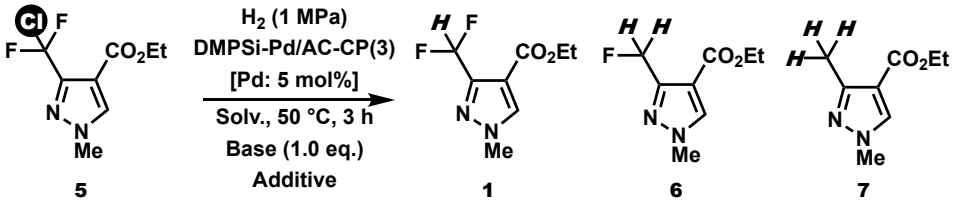
A mixture of ethyl 3-(chlorodifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**1**: CDFMMP) (23.2 mg, 0.10 mmol), DMPSi-Pd/AC-CP(3:1) (51.0 mg, Pd: 0.005 mmol) and tetrabutylammonium acetate (30.1 mg, 0.10 mmol) in THF (5 mL) was put in a stainless autoclave reactor. Then, the reactor was set to ChemiStation™ and filled with 1 MPa of H_2. After stirring at 50 °C for 3 h at 900 rpm, the reaction mixture was opened to air and vacuum filtrated with celite, washed with EtOH. The mixture was then analyzed by GC using decane as an internal standard. After that, solvent of collected sample was removed under reduced pressure and the residue was purified by preparative TLC (*n*-hexane/EtOAc = 2/1) to give ethyl 3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**1**: DFMMP) (7.2 mg, 35% yield) as white solid.

S3-2. Hydodechlorination of CDFMMP 5 under continuous-flow conditions

DMPS-Pd/AC-CP(1:1) (0.1 mmol/g, 1.20 g) was mixed well with celite 545® (3.0 g) in a screw vial and filled in a 10 mm (id) x 100 mm (L) stainless pipe with stainless filters on the both column ends. On the top of the reactor, tube-in-tube type column head was mounted for independent feeding of liquid (inside) and hydrogen gas (outside), respectively. The other column end was sealed with an appropriate one-way column cap. Before starting the reactions, liquid (solvent) and hydrogen gas flow were stabilized at required column temperature, gas flow, and back pressure for at least 1 h. The substrate THF solution of required concentration of the substrate **5** containing tetrabutylammonium acetate was then provided at 0.2 mL/min of flow rate. After stabilization of the continuous-flow conditions, resulting solution (1.0 mL) was collected and yields of products were analyzed by GC using decane as an internal standard.

S4. Additional Information for Reaction Conditions under Batch Conditions

Table S1 Additional information for base, solvent, and additive under batch conditions.



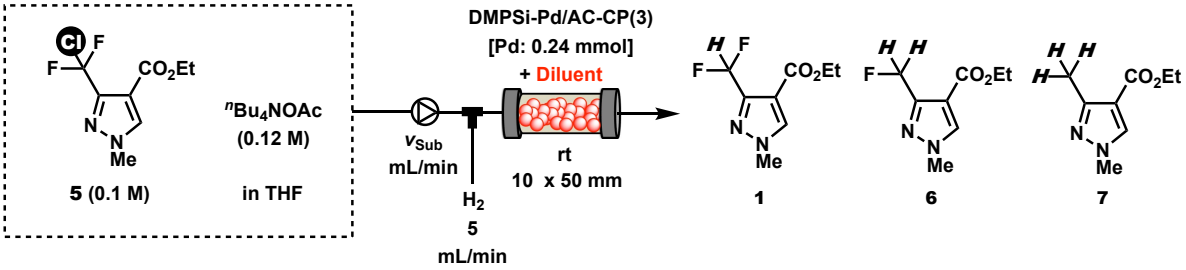
Run	Base	Solvent	Additive ([eq.])	Conv.[%]	Yield [%][a]		
					1	**6**	**7**
A1	Cs_2CO_3	THF+H_2O (12 μL)	No	>99	81	1	11
A2	Cs_2CO_3	THF+H_2O (18 μL)	No	>99	77	10	13
A3	Cs_2CO_3	THF+H_2O (9:1)[b]	No	24	10	3	11
A4	Cs_2CO_3	THF+H_2O (4:1)[c]	No	19	9	2	8
A5	Cs_2CO_3	Diox[d]+H_2O (18 μL)	No	92	76	9	9
A6	Cs_2CO_3	Tol+H_2O (18 μL)	No	86	47	10	29
A7	Cs_2CO_3	EtOH	No	>99	46	15	40
A8	Cs_2CO_3	EtOH	CsF (0.2)	>99	50	16	36
A9	Cs_2CO_3	EtOH	CsF (1.0)	>99	47	16	39
A10	No	EtOH	CsF (1.0)	77	56	10	11
A11	Cs_2CO_3	EtOH	^{n}Bu$_4$NF (0.5)	>99	42	15	43
A12	CsOAc	EtOH	No	87	57	12	18
A13	^{n}Bu$_4$NOAc	THF	No	41	40	1	Trace
A14	^{n}Bu$_4$NCl	THF	No	<1	Trace	Trace	Trace
A15	BnMe$_3$NOH	THF	No	15	6	5	4
A16	BnMe$_3$NOAc	THF	No	13	8	3	2
A17	CsOPiv	THF+EtOH (10:1)[e]	No	64	43	9	12
A18	$CsOCOC_5H_{11}$	THF+EtOH (10:1)[e]	No	65	45	9	12
A19	$CsOCOC_{17}H_{35}$	THF+EtOH (10:1)[e]	No	85	55	12	18
A20	Et_3N	THF	No	<1	Trace	Trace	Trace
A21	DBU	THF	No	14	7	2	5
A22	2,6-(^{t}Bu)$_2$-Py[f]	THF	No	<1	Trace	Trace	Trace
A23	1,2,2,6,6-(Me)$_6$-Piperidine[g]	THF	No	<1	Trace	Trace	trace

[a] Determined by ^{1}H-NMR analysis. [b] H_2O, 0.5 mL. [c] H_2O, 1.0 mL. [d] 1,4-Dioxane. [e] EtOH, 0.45 mL. [f] 2,6-di-*tert*-butyl pyridine. [g] 1,2,2,6,6-pentamethyl piperidine.

S5. Additional Information to Optimize Continuous-flow Reaction Conditions

S5-1. Effect of Diluents

In Figures S1-3, three additional results of continuous-flow hydrodechlorination reaction of **5** are summarized. Details data were displayed in Table S2.



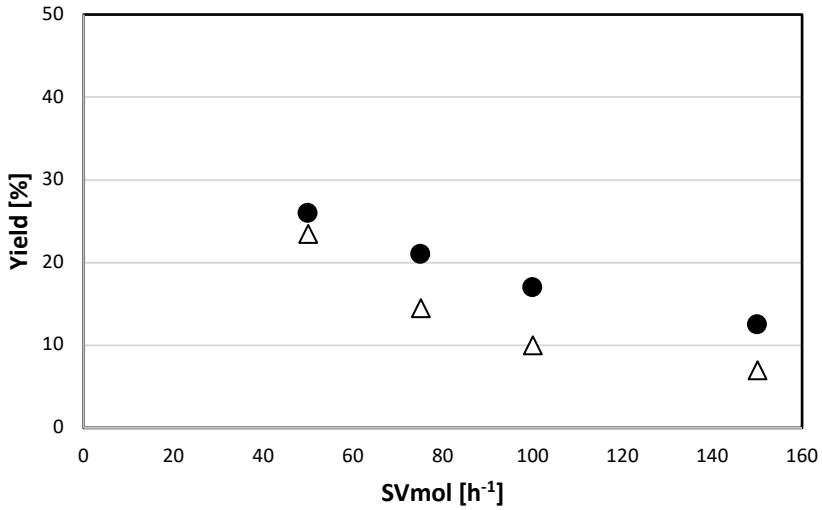


Figure S1 Flow reaction with celite (as a diluent).
Closed circle: Yield of **1**, *Open triangle*; Sum of the yield of **6** and **7.**
Average values of two samples are plotted.

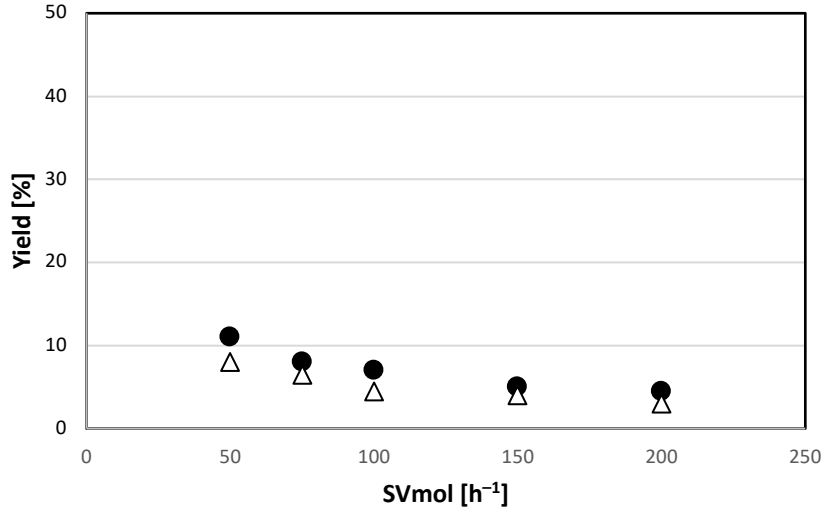


Figure S2 Flow reaction with powdered cellulose (as a diluent).
Closed circle: Yield of **1**, *Open triangle*; Sum of the yield of **6** and **7**
Average values of two samples are plotted.

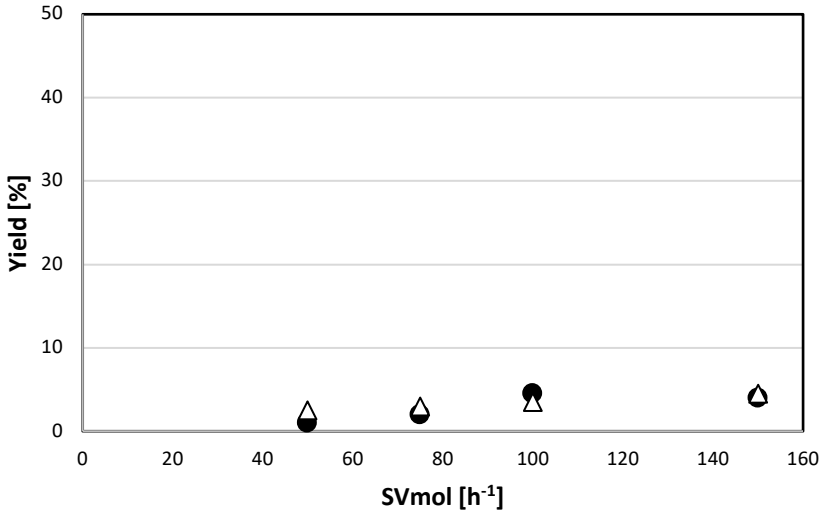


Figure S3 Flow reaction with activated carbon (as a diluent).
Closed circle: Yield of **1**, *Open triangle*; Sum of the yield of **6** and **7**
Average values of two samples are plotted.

Table S2 Details of the continuous-flow reactions shown in Figures S1~S3

Run	Diluent	v_{Sub} [mL/min]	SV_{mol} [h^{-1}]	t_R [min][a]	Conv.[%]	Yield [%][b]		
						1	**6**	**7**
A24-1-1	Celite	0.2	50	14.0	49	26	6	18
A24-1-2	Celite	0.2	50	14.0	49	26	5	18
A24-2-1	Celite	0.3	75	9.3	35	21	3	11
A24-2-2	Celite	0.3	75	9.3	36	21	3	12
A24-3-1	Celite	0.4	100	7.0	27	17	2	8
A24-3-2	Celite	0.4	100	7.0	26	17	2	8
A24-4-1	Celite	0.6	150	4.7	19	13	1	6
A24-4-2	Celite	0.6	150	4.7	19	12	1	6
A25-1-1	Cellulose	0.2	50	16.1	19	11	1	7
A25-1-2	Cellulose	0.2	50	16.1	19	11	1	7
A25-2-1	Cellulose	0.3	75	10.7	14	8	1	5
A25-2-2	Cellulose	0.3	75	10.7	14	8	1	6
A25-3-1	Cellulose	0.4	100	8.1	12	7	0	5
A25-3-2	Cellulose	0.4	100	8.1	12	7	0	4
A25-4-1	Cellulose	0.6	150	5.4	10	5	0	4
A25-4-2	Cellulose	0.6	150	5.4	9	5	0	4
A25-5-1	Cellulose	0.8	200	4.0	8	4	0	3
A25-5-2	Cellulose	0.8	200	4.0	8	5	0	3
A26-1-1	Carbon	0.2	50	14.0	3	1	0	2
A26-1-2	Carbon	0.2	50	14.0	4	1	0	3
A26-2-1	Carbon	0.3	75	9.3	5	2	0	3
A26-2-2	Carbon	0.3	75	9.3	5	2	0	3
A26-3-1	Carbon	0.4	100	7.0	8	4	Trace	3
A26-3-2	Carbon	0.4	100	7.0	8	5	Trace	4
A26-4-1	Carbon	0.6	150	4.7	8	4	0	4
A26-4-2	Carbon	0.6	150	4.7	9	4	Trace	5

[a] Residence time, estimated by; Void volume of reactors/v_{Sub}. Void volumes for the each reactor; 2.79 mL (celite), 3.22 mL (cellulose), and 2.80 mL (activated carbon). [b] Determined by ^{1}H-NMR analysis.

To avoid undesirable pressure-loss and clogging of flow systems, we usually use inert material as a diluent, and fulfill reactor with the catalysts. As demonstrated in Figures S1~S3 (Table S2), celite was a suitable diluent for the present reaction and thus hereafter we used this material as a general diluent.

S5-2. Details for reaction optimization

In Table S3, details of reaction optimization (composed Figure 2 in the main text) were displayed.

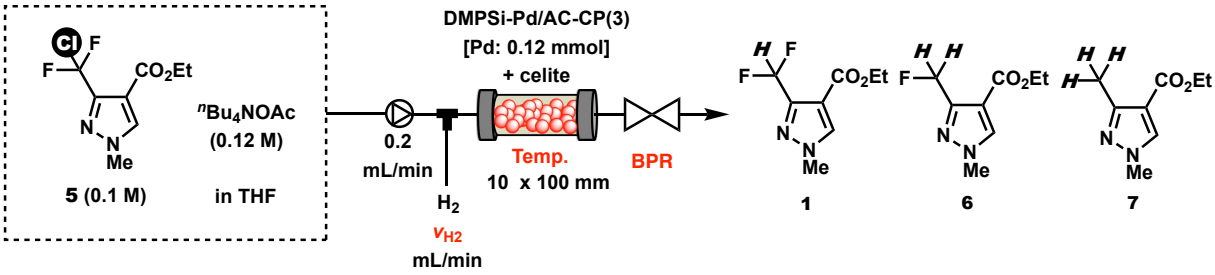


Table S3 Details of the continuous-flow reactions shown in Figures 2 of the main text

Run	Back Pressure [MPa]	Temp. [°C]	v_{H2} [mL/min]	Conv. [%]	Yield [%][a]		
					1	**6**	**7**
A27-1-1	0.2	70	10	61	40	1	0
A27-1-2	0.2	70	10	60	58	1	1
A27-2-1	0.2	90	10	83	79	3	1
A27-2-2	0.2	90	10	83	79	3	1
A27-3-1	0.2	110	10	80	75	2	2
A27-3-2	0.2	110	10	79	75	2	2
A28-1-1	0.4	70	10	37	37	0	0
A28-1-2	0.4	70	10	41	41	0	0
A28-2-1	0.4	90	10	77	74	2	1
A28-2-2	0.4	90	10	81	79	2	1
A28-3-1	0.4	110	10	77	74	2	2
A28-3-2	0.4	110	10	80	77	2	1
A29-1-1	0.6	70	10	57	54	1	1
A29-1-2	0.6	70	10	59	57	1	1
A29-2-1	0.6	90	10	75	73	2	1
A29-2-2	0.6	90	10	76	74	2	1
A29-3-1	0.6	110	10	82	79	2	1
A29-3-2	0.6	110	10	82	79	2	1
A30-1-1	0.2	90	10	78	74	2	1
A30-1-2	0.2	90	10	77	74	2	1
A30-2-1	0.2	90	20	82	79	2	1
A30-2-2	0.2	90	20	77	75	2	1
A30-3-1	0.2	90	30	68	66	1	2
A30-3-2	0.2	90	30	67	64	1	2

[a] Determined by GC analysis.

In Figure 2 of the main text, the above results were summarized by 3-D bar charts by using the average value of yields.

S5-3. Details for extended-time operation

In Table S4, details of extended-time operation (composed Figure 3 in the main text) were displayed.

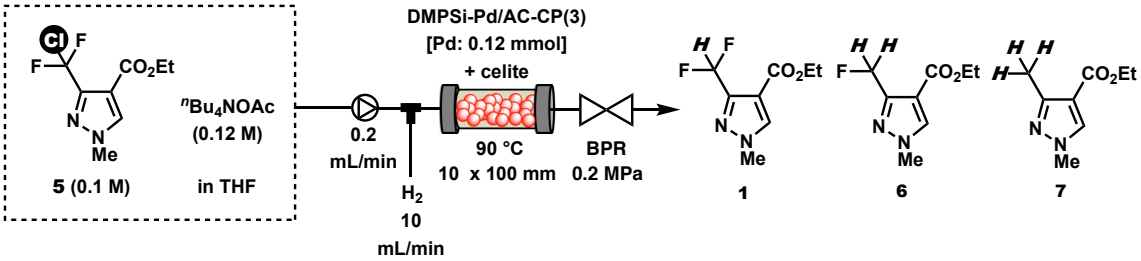


Table S4 Details of the continuous-flow reactions shown in Figures 3 of the main text

Run	Time[a] [min]	Total **5** Dosage [mmol]	**5**$_{total}$ / Pd [mmol/mmol]	Conv. [%]	Yield [%][b]		
					1	**6**	**7**
A31-1	90	1.9	15.8	41	38	1	1
A31-2	270	5.5	45.8	52	50	1	1
A31-3	330	6.7	55.8	72	69	2	1
A31-4	390	7.9	65.8	71	66	3	1
A31-5	480	9.7	80.8	71	68	2	1
A31-6	570	11.5	95.8	70	67	2	1
A31-7	660	13.3	110.8	69	66	2	2
A31-8	750	15.1	125.8	66	66	0	0
A31-9	840	16.9	140.8	67	67	0	0
A31-10	1020	20.5	170.8	80	76	1	3
A31-11	1080	22.0	183.3	78	72	0	6

[a] Operation time. Samples were taken for 10 minutes each time. [b] Determined by GC analysis.

S5-4. Details for catalysts comparison

As mentioned in the main text, we have compared the effects of catalyst especially derived from the difference in support materials. In Table S5, details of this investigation (composed Figure 4 in the main text) were displayed.

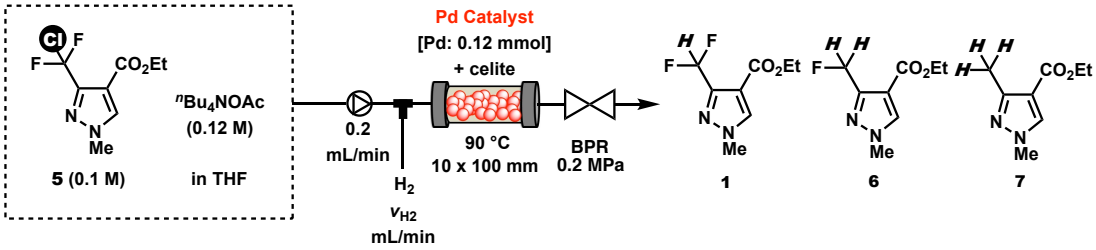


Table S5 Details of catalysts comparison under continuous-flow conditions shown in Figures 2

Run	Catalyst	v_{H2} [mL/min]	Conv. [%]	Yield [%][a]				TOF[h^{-1}] for **1**
				1	Select.	**6**	**7**	
A32-1-1	5wt% Pd/C	10	59	57	96	1	1	5.7
A32-1-2	5wt% Pd/C	10	57	55	96	1	1	5.5
A32-2-1	5wt% Pd/C	20	46	45	98	1	0	4.5
A32-2-2	5wt% Pd/C	20	45	44	98	1	0	4.4
A33-1-1	DMPSi-Pd/AC	10	72	69	96	2	1	6.9
A33-1-2	DMPSi-Pd/AC	10	71	68	96	2	1	6.8
A33-2-1	DMPSi-Pd/AC	20	70	68	98	2	1	6.8
A33-2-2	DMPSi-Pd/AC	20	67	66	99	2	1	6.6

A34-1-1	DMPSi-Pd/AC-CP (1)	10	80	77	96	2	1	7.7
A34-1-2	DMPSi-Pd/AC-CP (1)	10	81	77	95	2	1	7.7
A34-2-1	DMPSi-Pd/AC-CP (1)	20	84	81	93	2	1	8.1
A34-2-2	DMPSi-Pd/AC-CP (1)	20	84	81	93	2	1	8.1
A30-1-1	DMPSi-Pd/AC-CP (3)	10	78	74	95	2	1	7.4
A30-1-2	DMPSi-Pd/AC-CP (3)	10	77	74	96	2	1	7.4
A30-2-1	DMPSi-Pd/AC-CP (3)	20	82	79	96	2	1	7.9
A30-2-2	DMPSi-Pd/AC-CP (3)	20	77	75	97	2	1	7.5
A35-1-1	DMPSi-Pd/AC-CP (0.3)[b]	10	11	10	91	0	0	1.0
A35-1-2	DMPSi-Pd/AC-CP (0.3)[b]	10	9	8	89	0	0	0.8
A35-2-1	DMPSi-Pd/AC-CP (0.3)[b]	20	7	7	>99	0	0	0.7
A35-2-2	DMPSi-Pd/AC-CP (0.3)[b]	20	8	7	88	0	0	0.7
A36	DMPSi-Pd/CP	10	2	2	>99	0	0	0.2
A37-1-1	DMPSi-Pd/Al_2O_3	10	15	14	93	1	0	1.4
A37-1-2	DMPSi-Pd/Al_2O_3	10	13	12	92	1	0	1.2
A37-2-1	DMPSi-Pd/Al_2O_3	20	5	4	80	0	0	0.4
A37-2-2	DMPSi-Pd/Al_2O_3	20	4	3	75	0	0	0.3
A38-1-1	DMPSi-Pd/SiO_2	10	15	13	87	1	1	1.3
A38-1-2	DMPSi-Pd/SiO_2	10	13	12	92	1	1	1.2
A38-2-1	DMPSi-Pd/SiO_2	20	20	19	95	1	1	1.9
A38-2-2	DMPSi-Pd/SiO_2	20	19	18	95	1	0	1.8

[a] Determined by GC analysis. [b] DMPSi-Pd/AC-CP (1:3).

In Figure 4 of the main text, yields and selectivities for the target **1** were shown as bar charts by using the average value of yields at v_{H2} =20 mL/min.

S6. Additional Information of Continuous-flow Hydrodechlorination

S6-1. Continuous-flow Hydrodechlorination Reaction Using Commercially Available Pd/C Catalyst

According to the above catalyst screening experiments in ***S5-4***, commercially available (Fujifilm Wako Pure Chemical Co.) also exhibited potential possibility as a convenient catalyst. We pursued its feasibility in the following investigation.

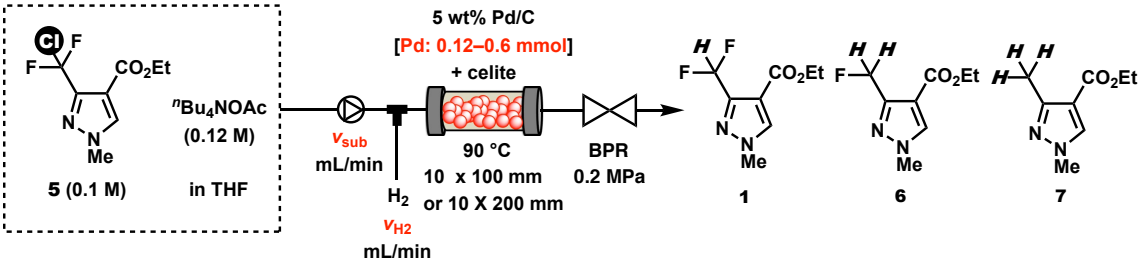


Table S6 Continuous-flow hydrodechlorination using Pd/C catalyst[a]

Run	Pd in Reactor [mmol]	v_{sub} [mL/min]	v_{H2} [mL/min]	SVmol [h^{-1}]	Conv. [%]	Yield [%][b]		
						1	**6**	**7**
A32-1-1	0.12	0.2	20	10	46	45	1	0
A32-1-2	0.12	0.2	20	10	45	44	1	0
A32-2-1	0.12	0.4	20	20	24	24	0	0
A32-2-2	0.12	0.4	20	20	21	21	0	0
A33-1-1	0.24	0.2	10	5	68	64	1	2
A33-1-2	0.24	0.2	10	5	67	64	2	1
A33-2-1	0.24	0.2	20	5	67	65	2	1
A33-2-2	0.24	0.2	20	5	68	65	2	1
A33-3-1	0.24	0.4	20	10	41	40	1	0
A33-3-2	0.24	0.2	20	10	36	35	1	0
A34-1-1	0.60	0.2	10	2	80	77	2	1
A34-1-2	0.60	0.2	10	2	83	80	2	1
A34-2-1	0.60	0.4	10	4	72	66	2	5
A34-2-2	0.60	0.4	10	4	71	66	1	4
A34-3-1	0.60	0.2	5	2	84	82	1	1
A34-3-2	0.60	0.2	5	2	82	79	1	1
A34-4-1	0.60	0.1	5	2	89	86	1	1
A34-4-2	0.60	0.1	5	2	91	89	1	1
A35-1-1	0.60	0.4	5	4	73	68	2	4
A35-1-2	0.60	0.4	5	4	73	69	2	2
A35-2-1	0.60	0.2	5	2	88	85	1	1
A35-2-2	0.60	0.2	5	2	89	86	2	1
A35-3-1	0.60	0.2	3	2	84	81	2	1
A35-3-2	0.60	0.2	3	2	82	80	2	1
A35-4-1	0.60	0.1	3	1	91	88	1	1
A35-4-2	0.60	0.1	3	1	92	89	2	1
A36-1-1	0.60[a]	0.4	10	4	84	82	1	1
A36-1-2	0.60[a]	0.4	10	4	84	82	1	1
A36-2-1	0.60[a]	0.2	10	2	93	91	1	1
A36-2-2	0.60[a]	0.2	10	2	94	92	1	1

[a] 10 x 100 mm Stainless column was used as reactor except for Runs A36. For Runs A36, 10 x 200 mm column was used. [b] Determined by GC analysis.

Table S6 indicated the commercially available 5wt% Pd/C also exhibited high catalytic activity at

low SV_{mol} of less than 2 h^{-1}.

S6-2. Effect of Acetic Acid

In this reaction performing with $^{n}Bu_4NOAc$ as a base, it presumed to be generated acetic acid as ca co-product form the base. To identify the effect of acetic acid, we performed several control experiments under batch conditions as shown in Table S7.

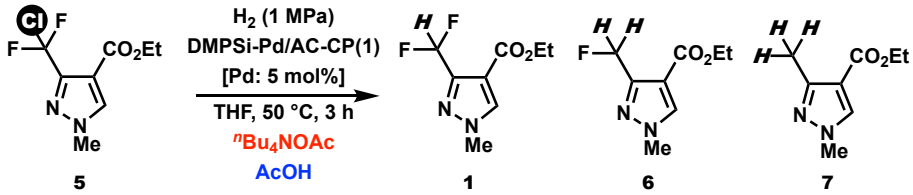


Table S7 Effect of acetic acid

Run	$^{n}Bu_4NOAc$ [eq.]	AcOH [eq.]	Conv. [%]	Yield [%][a]		
				1	**6**	**7**
A37	1.0	No	45	43	1	1
A38	2.0	No	54	53	1	1
A39	1.0	1.0	17	16	1	Trace
A40	2.0	1.0	31	30	1	Trace

[a] Determined by GC analysis.

Under batch reaction conditions, acetic acid generated during the reaction would be stayed till stopping the reaction, and this obviously prevented progress of the reaction. Under continuous-flow reaction, on the other hand, acetic acid will pass through the reactor with a stream. This will be beneficial for the present catalysis, and be an appearance of advantage of the present continuous-flow reaction.

S7. Additional Information of Continuous-flow Hydrodechlorination of the Pyrimidine Substrate

Additional data for optimization of selective hydrochlorination of the chlorodifluoropyrimidine substrate **8** were shown in Table S8.

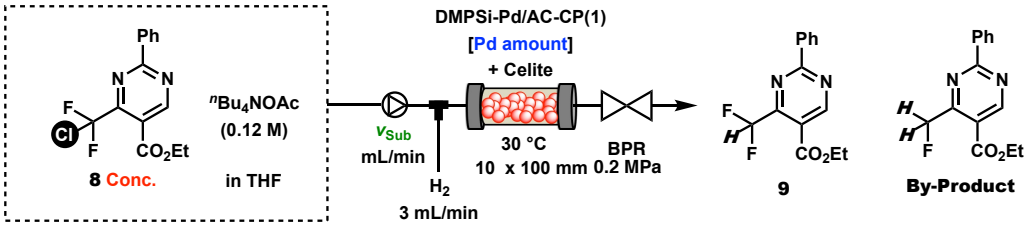


Table S8 Hydrodechlorination of pyrimidine derivative **8.**

Run	Conc. of **8** [M]	v_{sub} [mL/min]	Pd in Reactor [mmol]	SV_{mol} [h^{-1}]	Conv. [%]	Yield [%][a]	
						9	**By-Prod.**
A41[b, c]	0.03	0.1	0.12	1.5	>99	17	15[d]
A42[b]	0.03	0.2	0.12	3.0	>99	36	61
A43	0.03	0.3	0.12	4.5	>99	75	2
A44	0.03	0.3	0.06	9.0	>99	77	11
A45	0.03	0.4	0.06	12.0	>99	73	6
A46	0.05	0.3	0.06	15.0	99	75	2
A47	0.05	0.4	0.06	20.0	97	73	2
A48	0.05	0.5	0.06	25.0	93	73	2
A49	0.05	0.3	0.03	30.0	95	59	9
A50	0.05	0.4	0.03	40.0	92	58	13
A51	0.05	0.5	0.03	50.0	81	49	3

Low SVmol value resulted in less-selective formation of the target **9** accompanying several unidentified product including defluorinated products and others. Contrary, by increasing SVmol value by changing either decreasing Pd amount, increasing v_{sub} or increasing concentration gave better selectivity of **9** especially at the range of 4.5 < SVmol < 25.0. In the main text, we showed the result of Run A44 as an optimal to attain the highest yield.

S8. Effect of Pd Loading Concentration

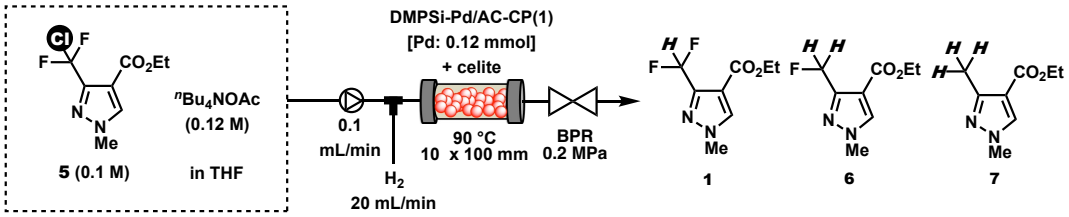


Table S9 Effect of loading concentration (v_{H_2} = 20 mL/min)**.**

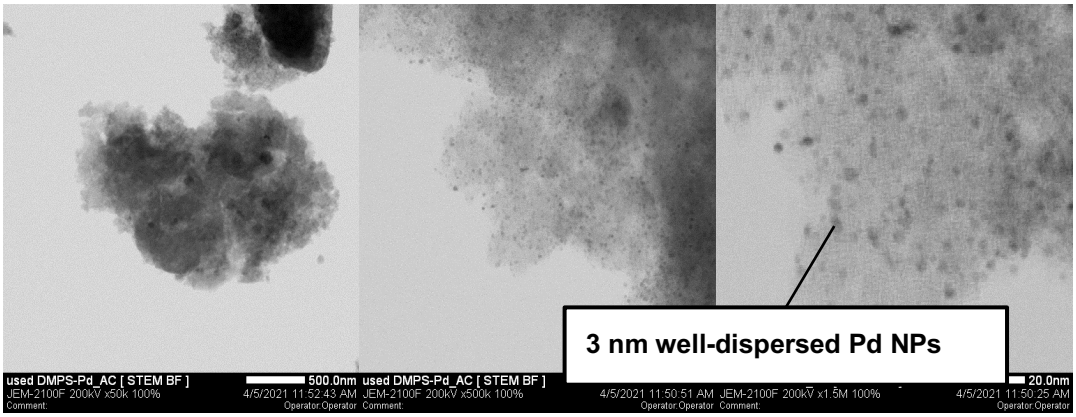
Run	Loading Concentration of Pd [mmol/g]	Amount of Catalyst in Reactor [g]	Conv. [%]	Yield [%][a]	
				1	**6** + **7**
A52	0.05	2.4	86	82	2
A53	0.10	1.2	91	88	3
A54	0.20	0.6	82	84	3

[a] Determined by GC analysis.

Here we investigated effect of loading concentration of Pd on an AC-CP=1:1 composite. Under standard continuous-flow conditions using 0.12 mmol Pd for each catalyst with different loading concentration, all catalysts gave the desired **1** in 82–88% yield with 82–91% conversion. While clear difference could not be identified, the catalyst of 0.1 mmol/g loading concentration exhibited the highest conversion and yield.

S9. Additional STEM and EDX Images of Catalysts

In addition to STEM and EDX images of DMPSi-Pd/AC-CP(1) shown in Figure 6 of the main text, here we provide additional data for DMPSi-Pd/AC, DMPSi-Pd/AC-CP(3), DMPSiPd/AC-CP(0.3), and DMPSi-Pd/CP. Images of the recovered samples for DMPSi-Pd/AC-CP(1) and DMPSi-Pd/AC are also provided.



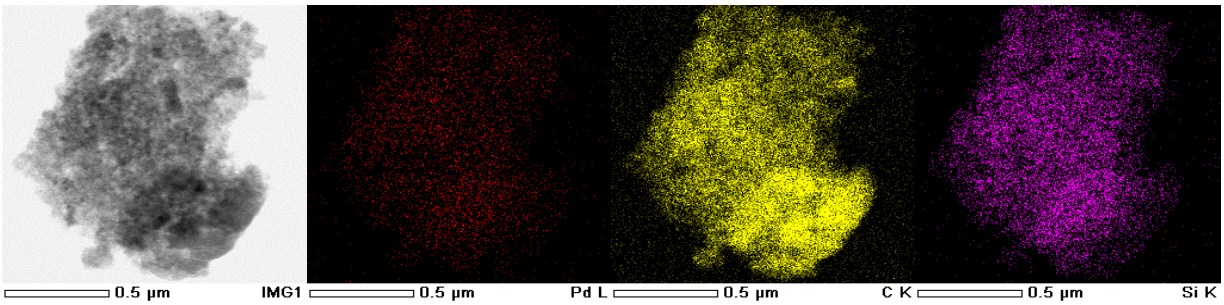


Figure S4 STEM and EDX mapping images of DMPSi-Pd/AC

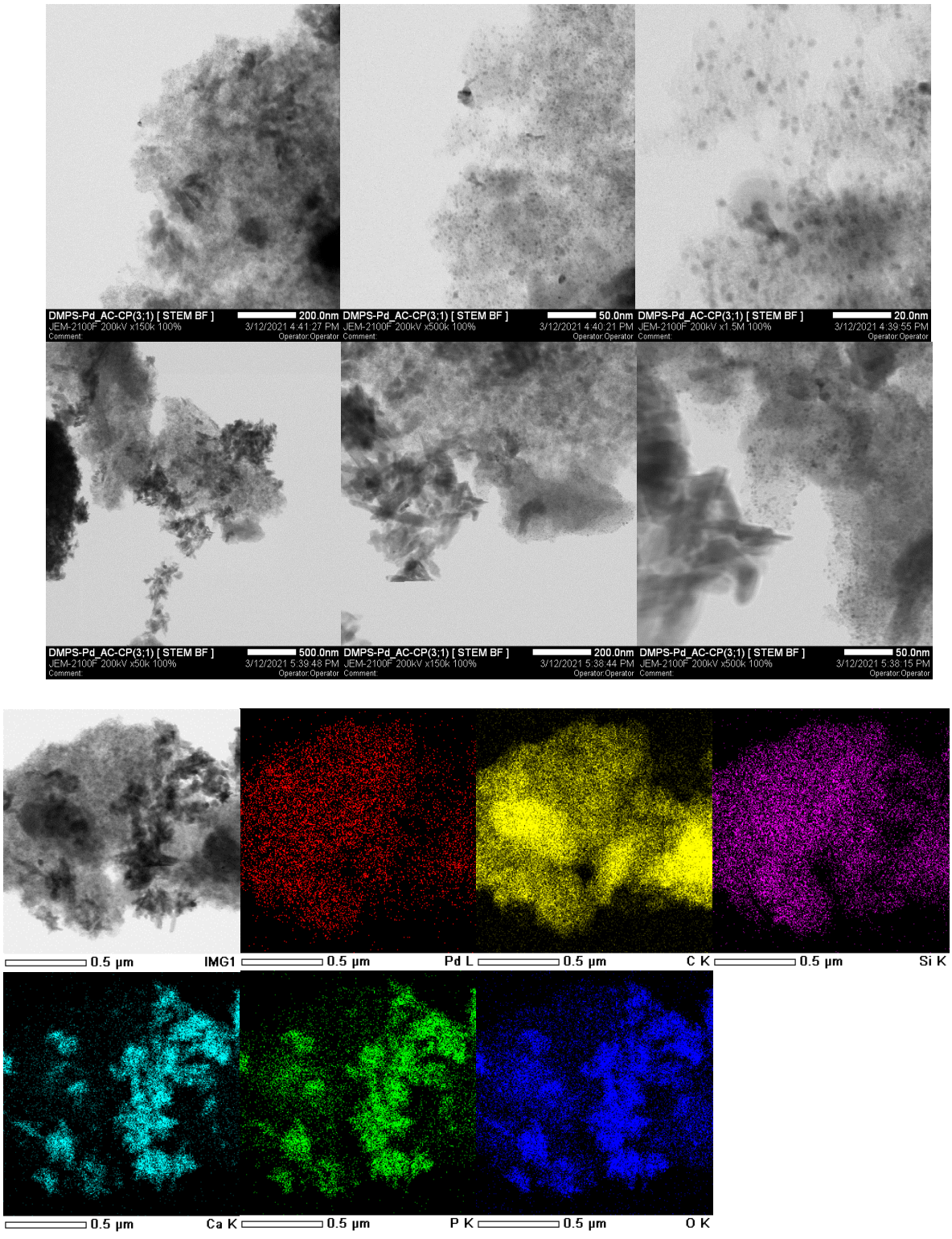


Figure S5 STEM and EDX mapping images of DMPSi-Pd/AC-CP(3)

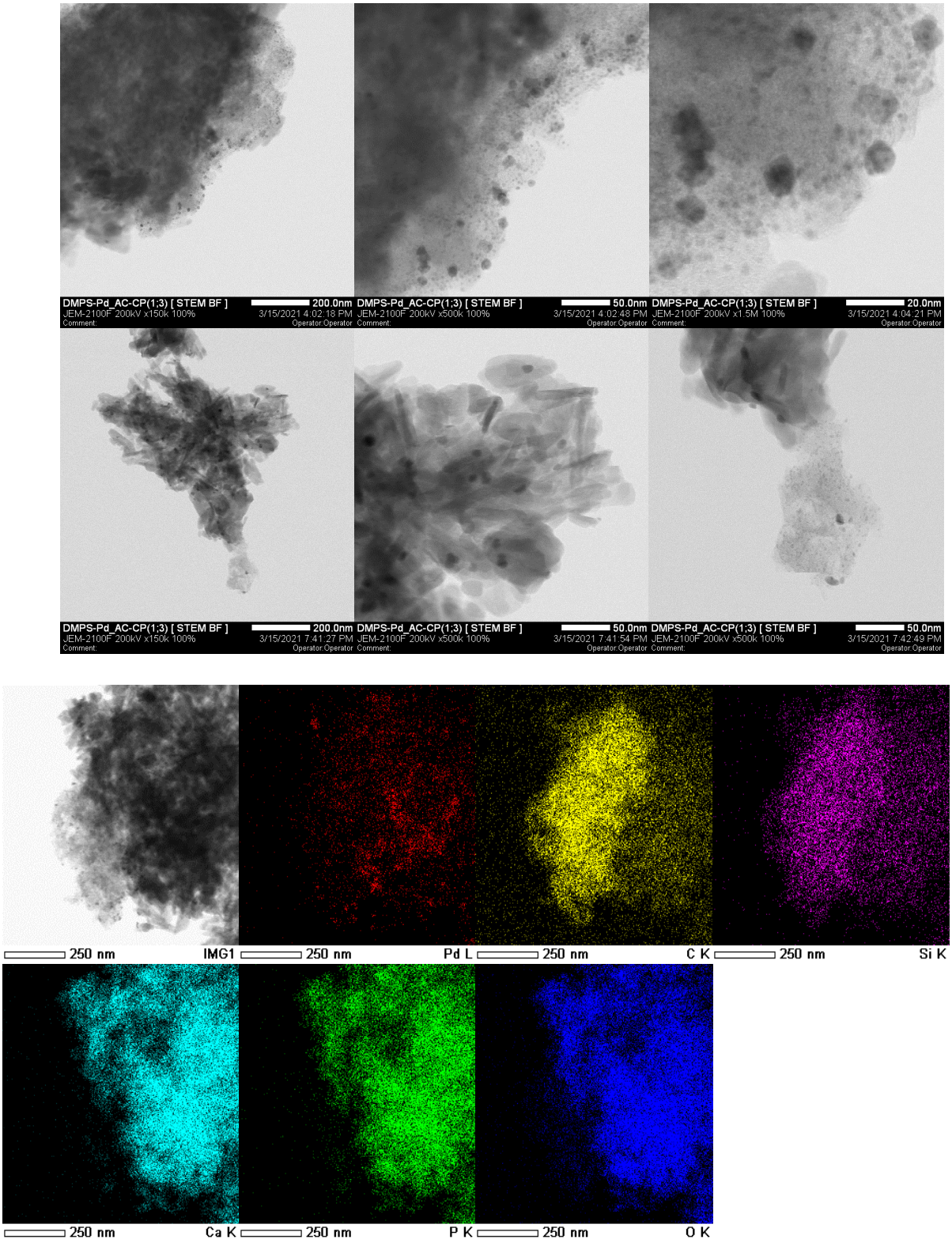


Figure S6 STEM and EDX mapping images of DMPSi-Pd/ AC-CP(0.3)

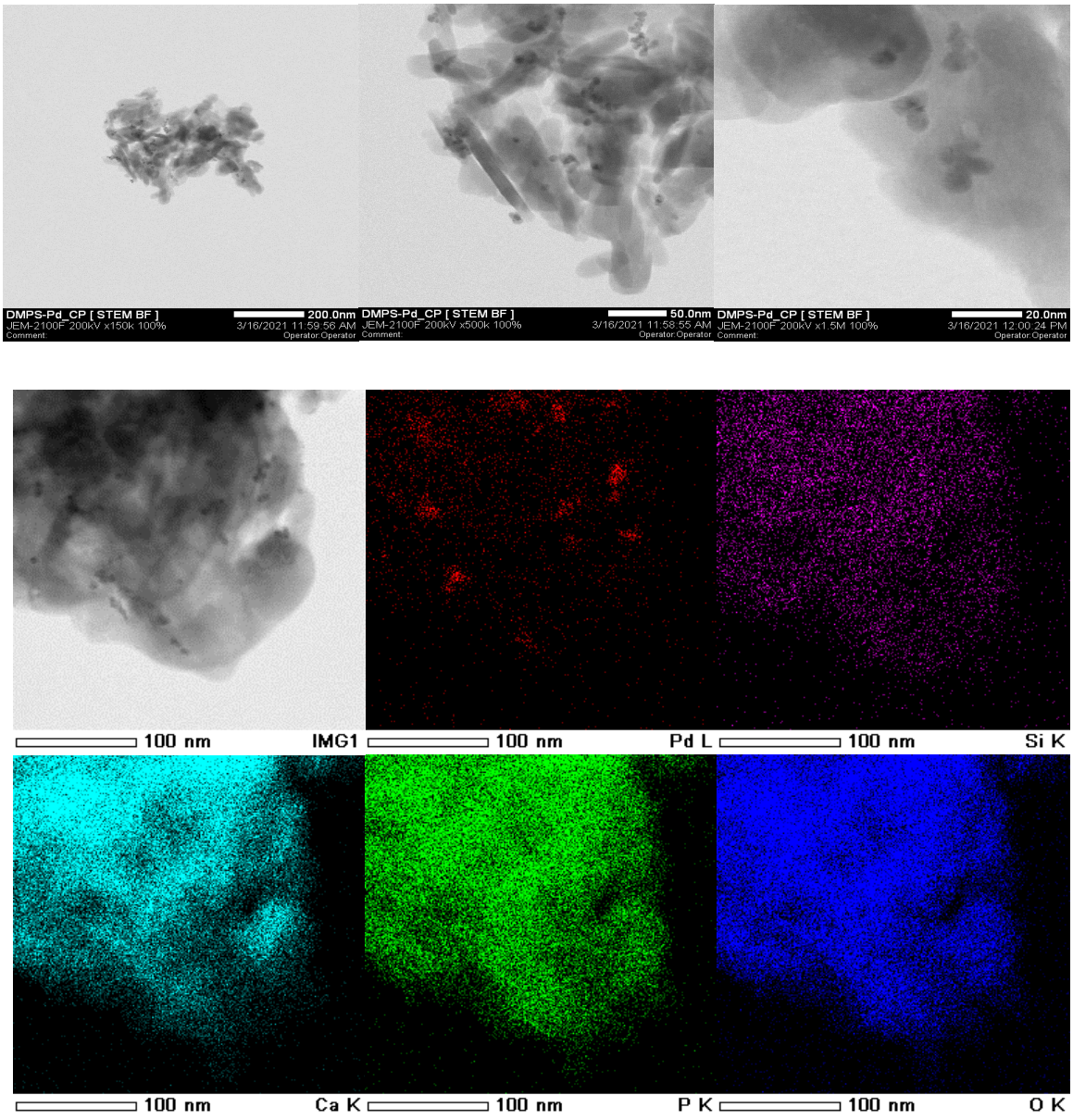
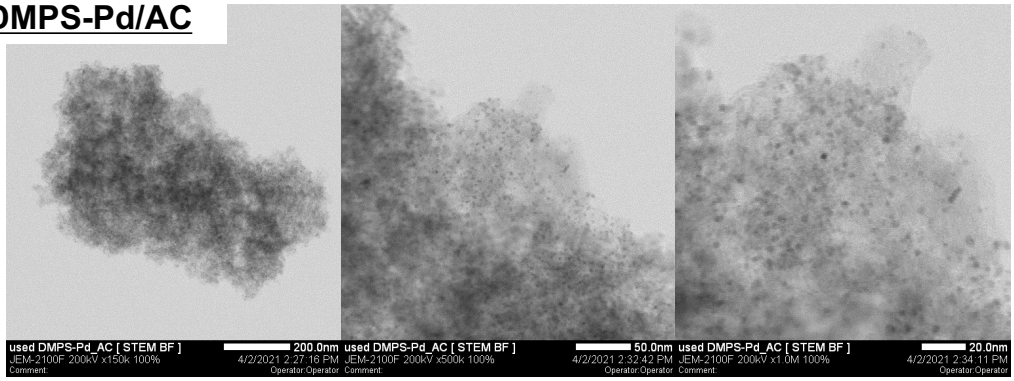
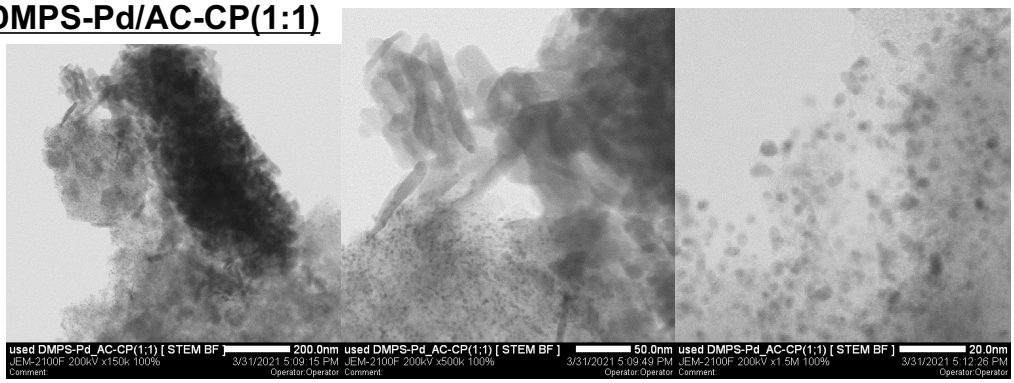


Figure S7 STEM and EDX mapping images of DMPSi-Pd/ CP(0.3)

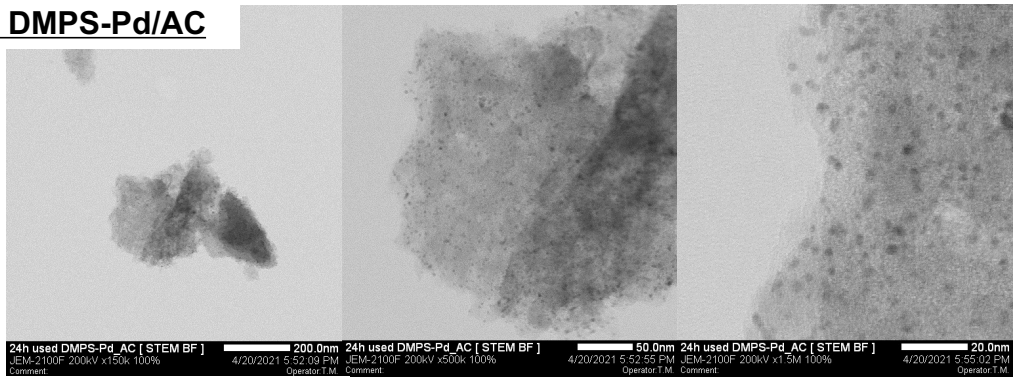
➢ **DMPS-Pd/AC**



➢ **DMPS-Pd/AC-CP(1:1)**



➢ **DMPS-Pd/AC**



➢ **DMPS-Pd/AC-CP(1:1)**

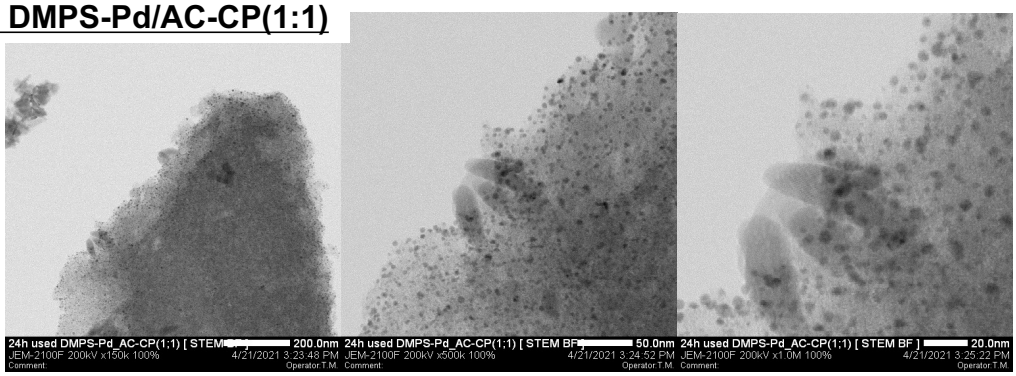
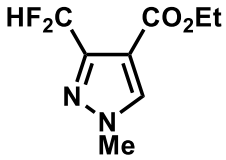


Figure S8 STEM images of recovered DMPSi-Pd/AC and DMPSi-Pd/AC-CP(1) from batch hydrodechlorination reactions for 6 h (top 2 sets) and for 24 h (bottom 2 sets).

S10. Spectral Information of Products

Ethyl 3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (1)[1]

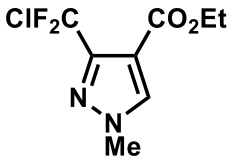


white solid

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.2 Hz, 3H), 3.97 (s, 3H), 4.32 (q, *J* = 7.1 Hz, 2H), 7.10 (t, $^2J_{H\text{-}F}$ = 54.0, 1H), 7.90 (s, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.2, 39.7, 60.7, 109.3 (t, $^1J_{C\text{-}F}$ = 237 Hz), 113.4, 134.9, 146.3, 161.8.

Ethyl 3-(chlorodifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (5)[1]

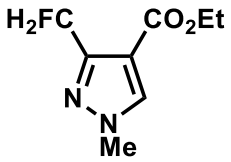


pale yellow oil

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.2 Hz, 3H), 3.96 (s, 3H), 4.32 (q, *J* = 7.3 Hz, 2H), 7.95 (s, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 39.8, 60.9, 112.5, 121.9 (t, $^1J_{C\text{-}F}$ = 288 Hz), 136.5, 146.1, 160.8.

Ethyl 3-(fluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (6)



pale yellow oil

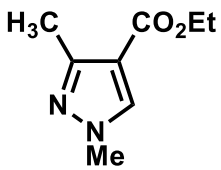
^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3H), 3.84 (s, 3H), 4.21 (q, *J* = 7.0 Hz, 2H), 5.51 (d, $^2J_{H\text{-}F}$ = 47.6 Hz, 2H), 7.80 (s, 1H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.0, 39.1, 60.0, 75.9, 112.8, 134.7, 148.3 (d, $^1J_{C\text{-}F}$ = 19 Hz), 162.3.

IR (neat, cm^{-1}): 3138, 2983, 1705, 1545, 1255, 1101, 977, 781, 764.

HRMS (DART): calcd for $C_8H_{12}FN_2O_2$ $[M+H]^+$ 187.08773, found 187.08797.

Ethyl 1,3-dimethyl-1*H*-pyrazole-4-carboxylate (7)[1]

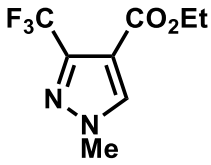


white solid

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.34 (t, *J* = 6.9 Hz, 3H), 2.45 (s, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 7.79

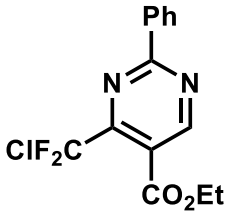
(s, 1H).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.4, 14.4, 39.0, 59.8, 112.4, 134.6, 151.3, 163.7.

Ethyl 3-(trifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (10) [2]



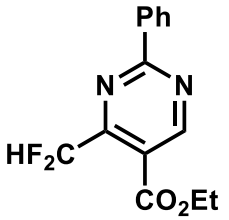
white solid
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.2 Hz, 3H), 3.97 (s, 3H), 4.31 (q, *J* = 7.1 Hz, 2H), 7.98 (s, 1H).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.0, 39.7, 60.8, 113.3, 120.3 (q, $^{1}J_{C\text{-}F}$ = 269 Hz), 136.2, 141.4, 160.7.

Ethyl 4-(chlorodifluoromethyl)-2-phenylpyrimidine-5-carboxylate (8)



white solid; m.p. 64 ℃
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.35 (t, *J* = 7.2 Hz, 3H), 4.39 (q, *J* = 7.1 Hz, 2H), 7.43-7.50 (m, 3H), 8.46 (d, *J* = 7.6 Hz, 2H), 9.10 (s, 1H).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 13.9, 62.8, 120.4, 122.9 (t, $^{1}J_{C\text{-}F}$ = 291 Hz), 128.8, 129.1, 132.4, 135.4, 157.3 (t, $^{2}J_{C\text{-}F}$ = 30 Hz), 160.0, 164.0, 165.8.
IR (neat, cm^{-1}): 2992-2856, 1721, 1574, 1428, 1367, 1324, 1314, 1301, 1275, 1250, 1177, 1134, 1063, 1013, 937, 861, 797, 767, 754, 711, 695, 664.
HRMS (DART): calcd for $C_{14}H_{12}ClF_2N_2O_2$ $[M+H]^+$ 313.05499, found 313.05491.

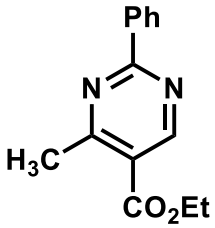
Ethyl 4-(difluoromethyl)-2-phenylpyrimidine-5-carboxylate (9)



white solid; m.p. 129-130 ℃
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.2 Hz, 3H), 4.45 (q, *J* = 7.1 Hz, 2H), 7.40 (t, $^{2}J_{H\text{-}F}$ = 54.0 Hz, 1H), 7.49-7.55 (m, 3H), 8.56 (d, *J* = 4.1 Hz, 2H), 9.36 (s, 1H).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 62.4, 109.8 (t, $^{1}J_{C\text{-}F}$ = 243 Hz), 120.0, 128.8, 129.3, 132.4, 135.8, 159.7, 160.4, 163.4, 166.8.

IR (neat, cm^{-1}): 2989, 1713, 1569, 1546, 1428, 1368, 1282, 1201, 1091, 1048, 783, 744, 695.
HRMS (DART): calcd for $C_{14}H_{13}F_2N_2O_2$ $[M+H]^+$ 279.09396, found 279.09411.

Ethyl 4-methyl-2-phenylpyrimidine-5-carboxylate[1]



The representative by-product which could be isolated in investigations shown in **S7**. white solid
^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.2 Hz, 3H), 2.86 (s, 3H), 4.39 (q, *J* = 7.1 Hz, 2H), 7.45-7.49 (m, 3H), 8.48-8.50 (m, 2H), 9.18 (s, 1H).
^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.2, 24.7, 61.4, 120.9, 128.6, 128.8, 131.4, 136.7, 159.1, 165.0, 165.5, 168.8.

S11. NMR Spectra

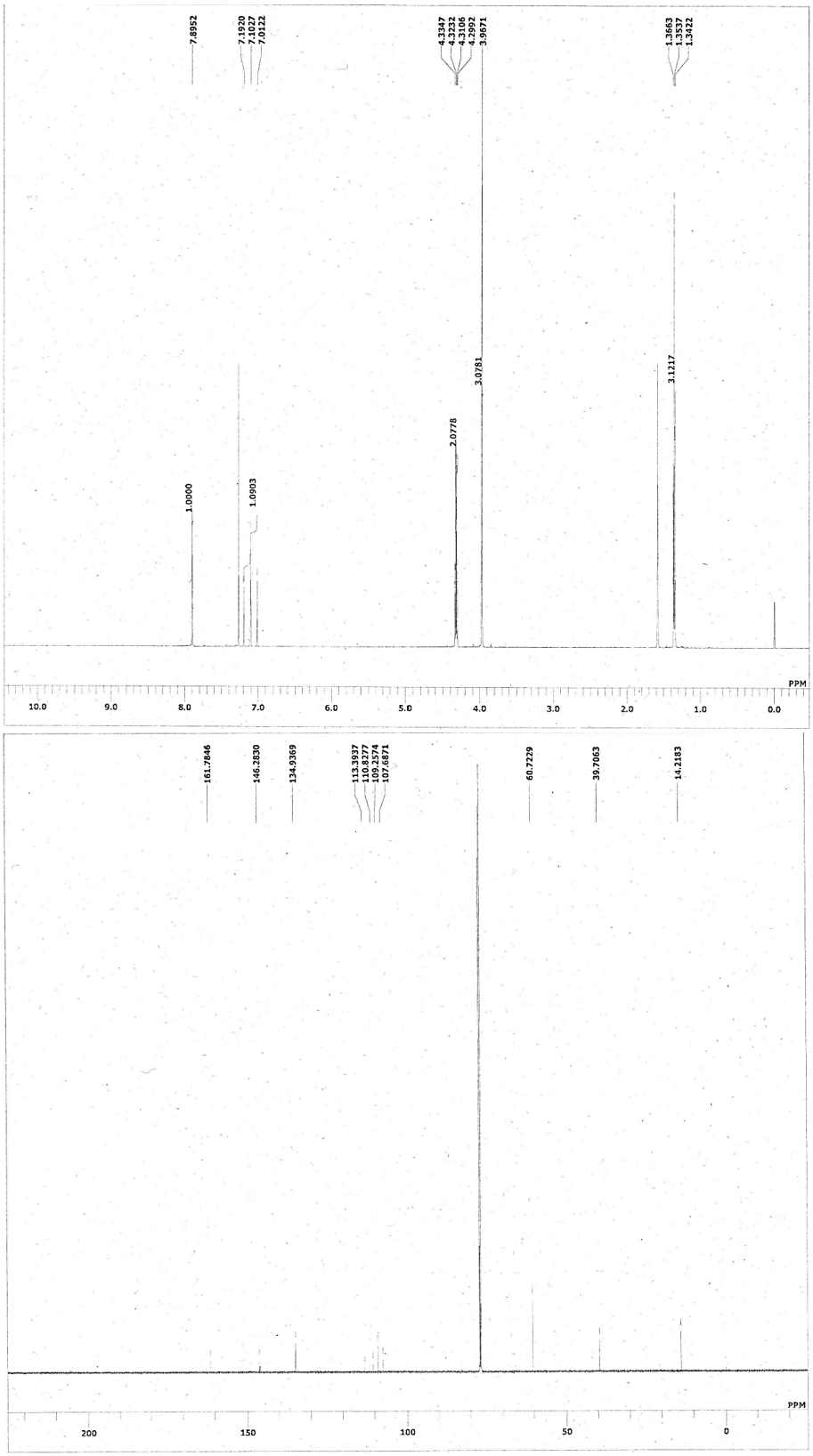


Figure S9 ^{1}H and ^{13}C NMR spectra of ethyl 3-(difluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**1**)

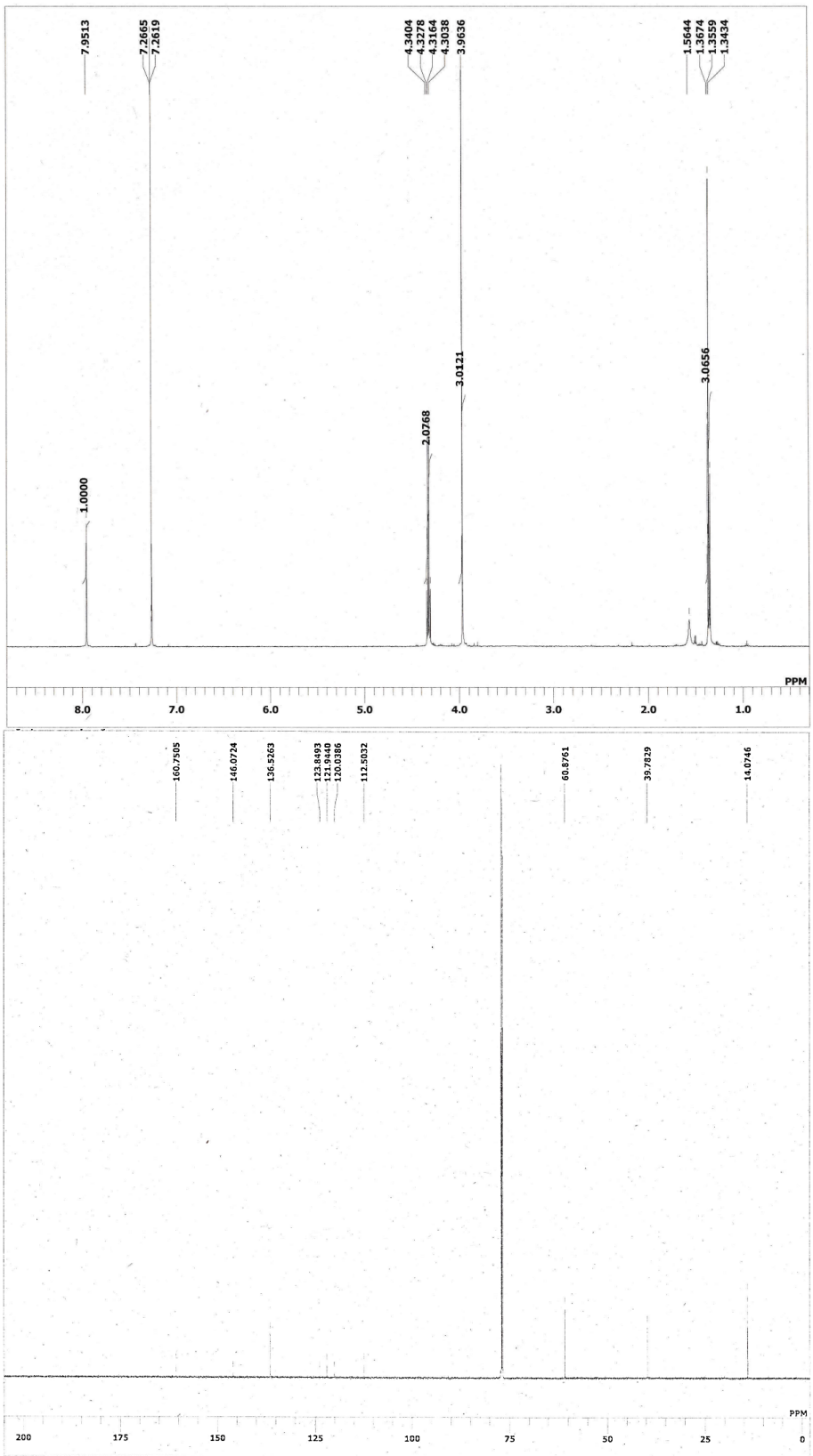


Figure S10 ^{1}H and ^{13}C NMR spectra of ethyl 3-(chlorodifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**5**)

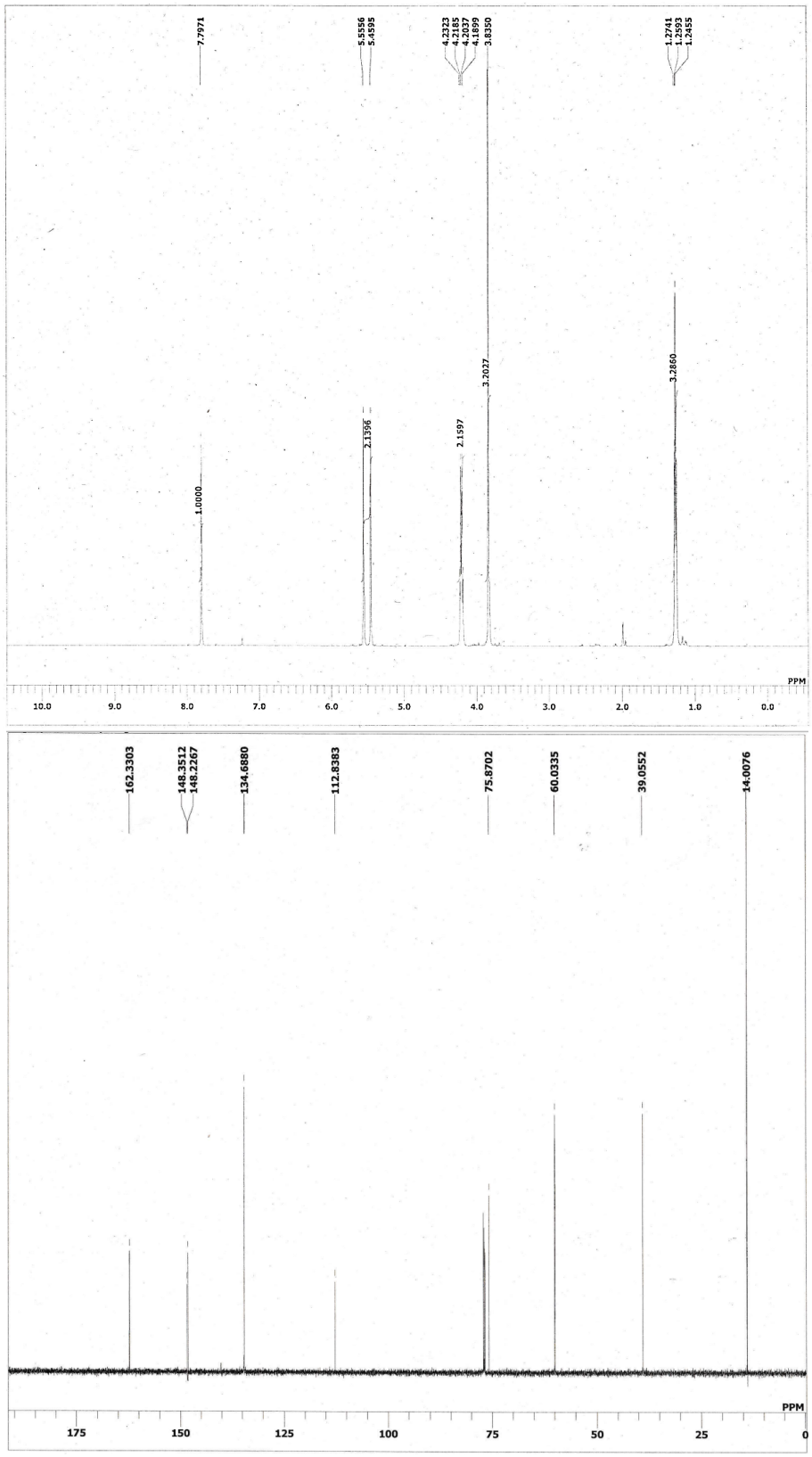


Figure S11 ^{1}H and ^{13}C NMR spectra of ethyl 3-(fluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**6**)

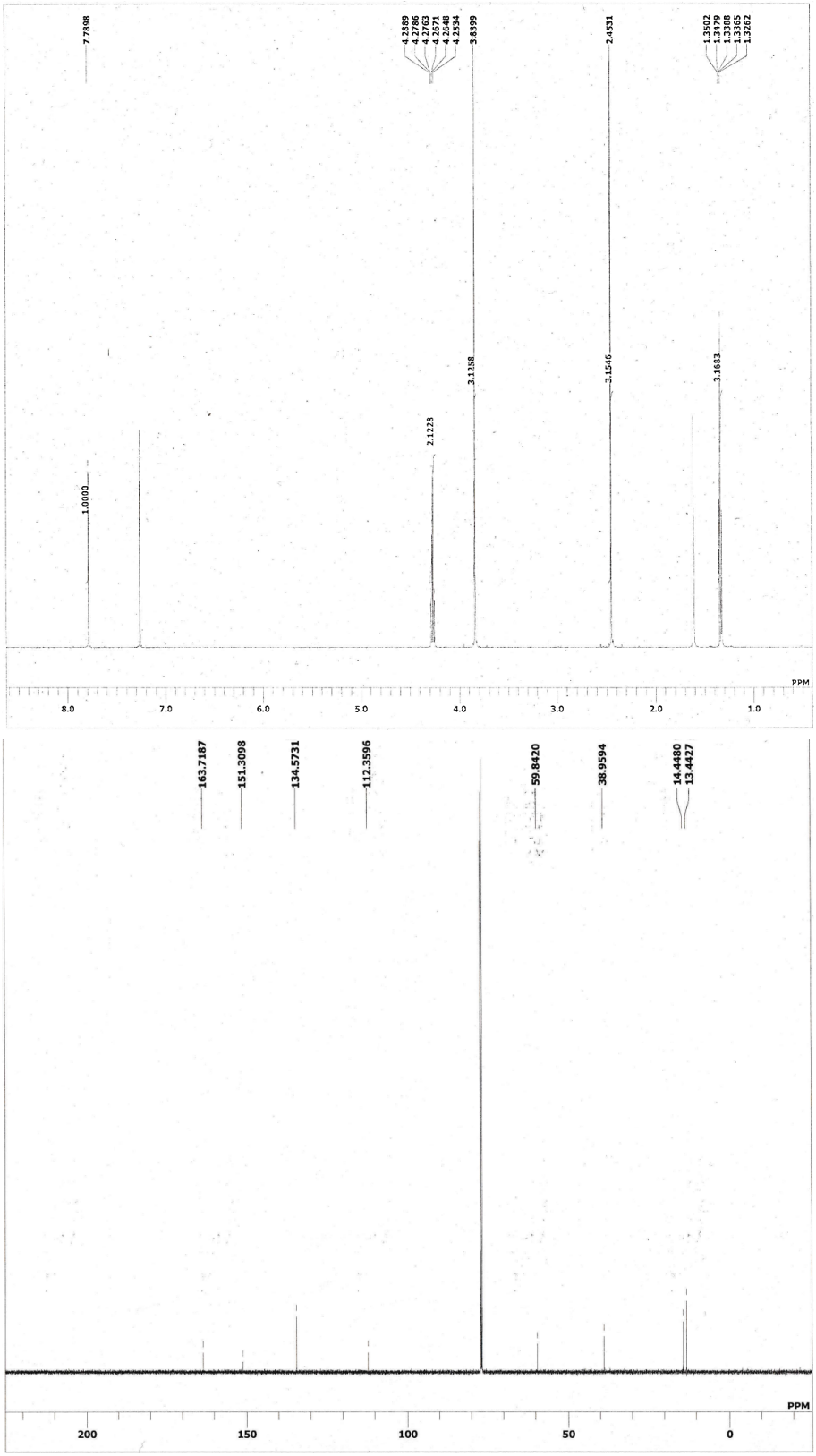


Figure S12 ^{1}H and ^{13}C NMR spectra of ethyl 1,3-dimethyl-1*H*-pyrazole-4-carboxylate (**7**)

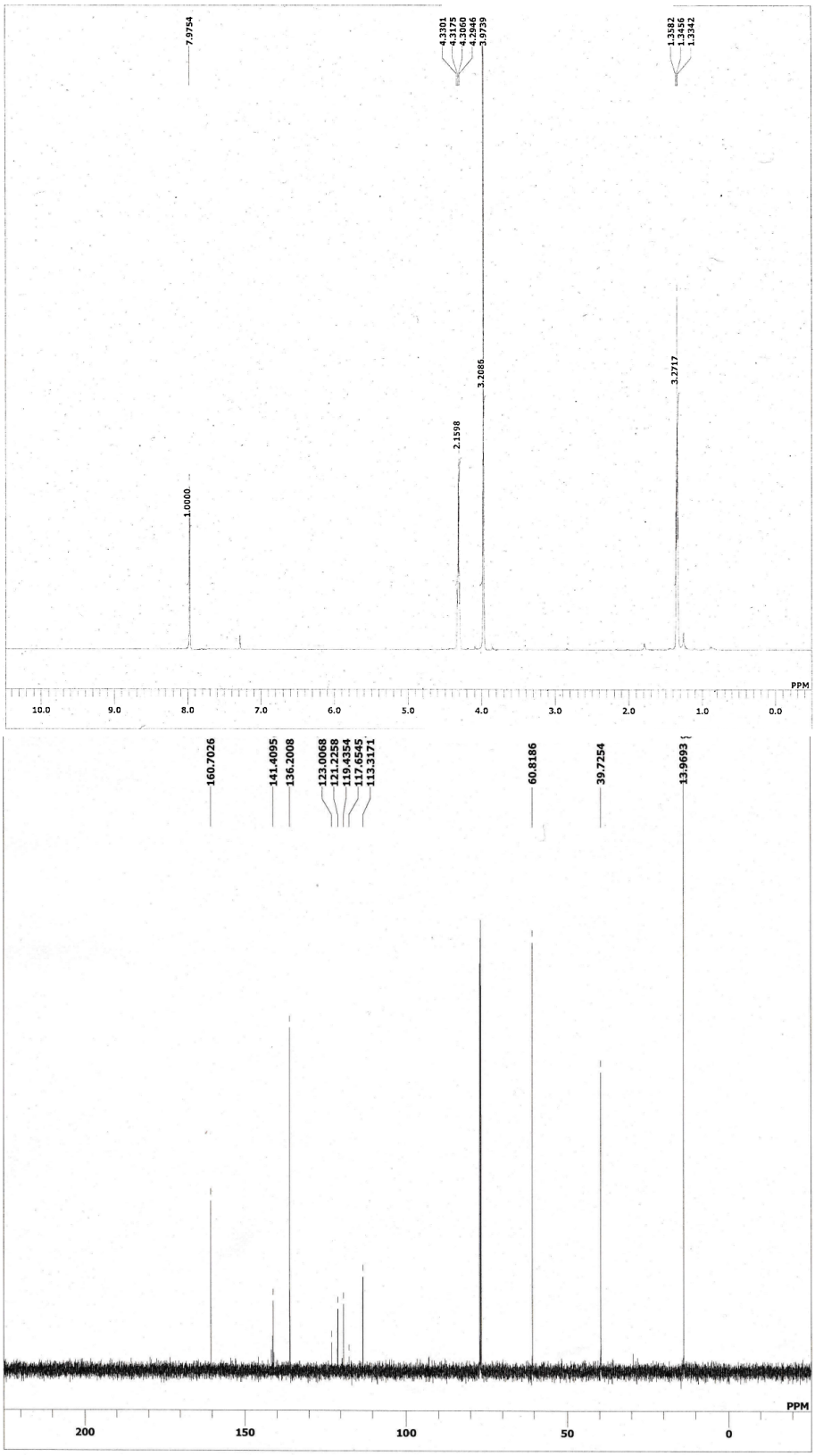


Figure S13 ^{1}H and ^{13}C NMR spectra of ethyl 3-(trifluoromethyl)-1-methyl-1*H*-pyrazole-4-carboxylate (**10**)

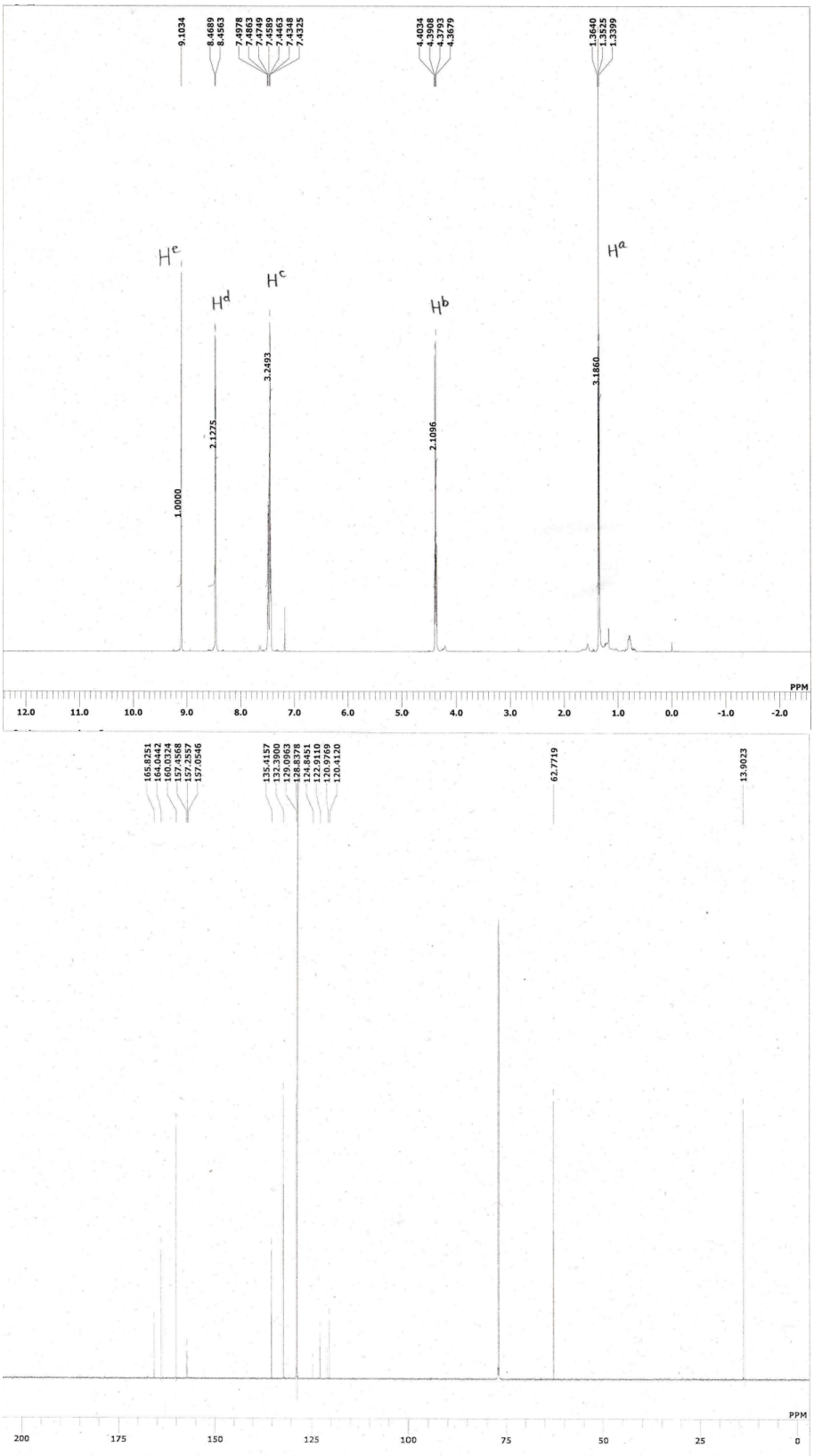


Figure S14 ^{1}H and ^{13}C NMR spectra of ethyl 4-(chlorodifluoromethyl)-2-phenylpyrimidine-5-carboxylate (**8**)

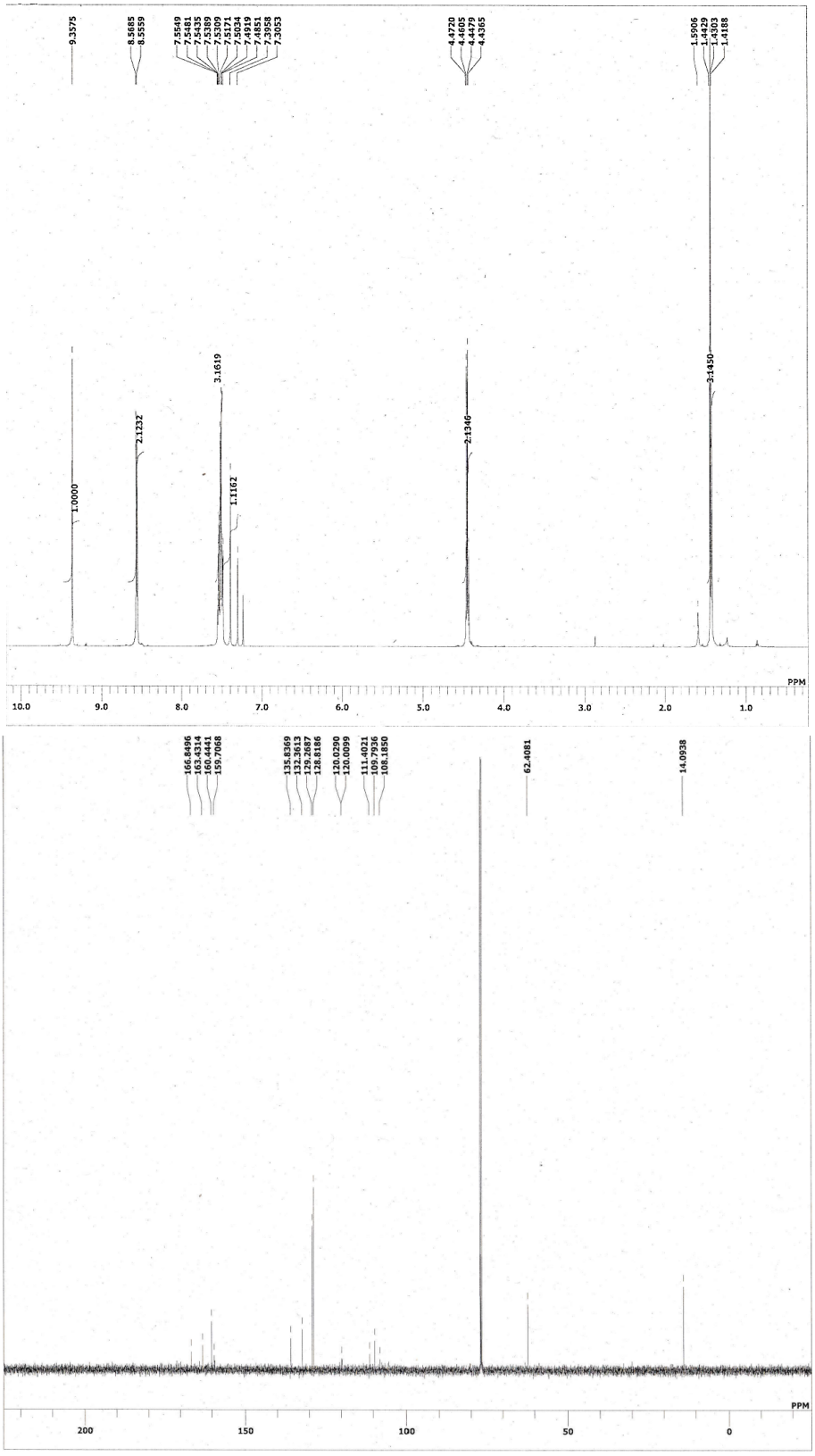


Figure S15 ^{1}H and ^{13}C NMR spectra of ethyl 4-(difluoromethyl)-2-phenylpyrimidine-5-carboxylate (**9**)

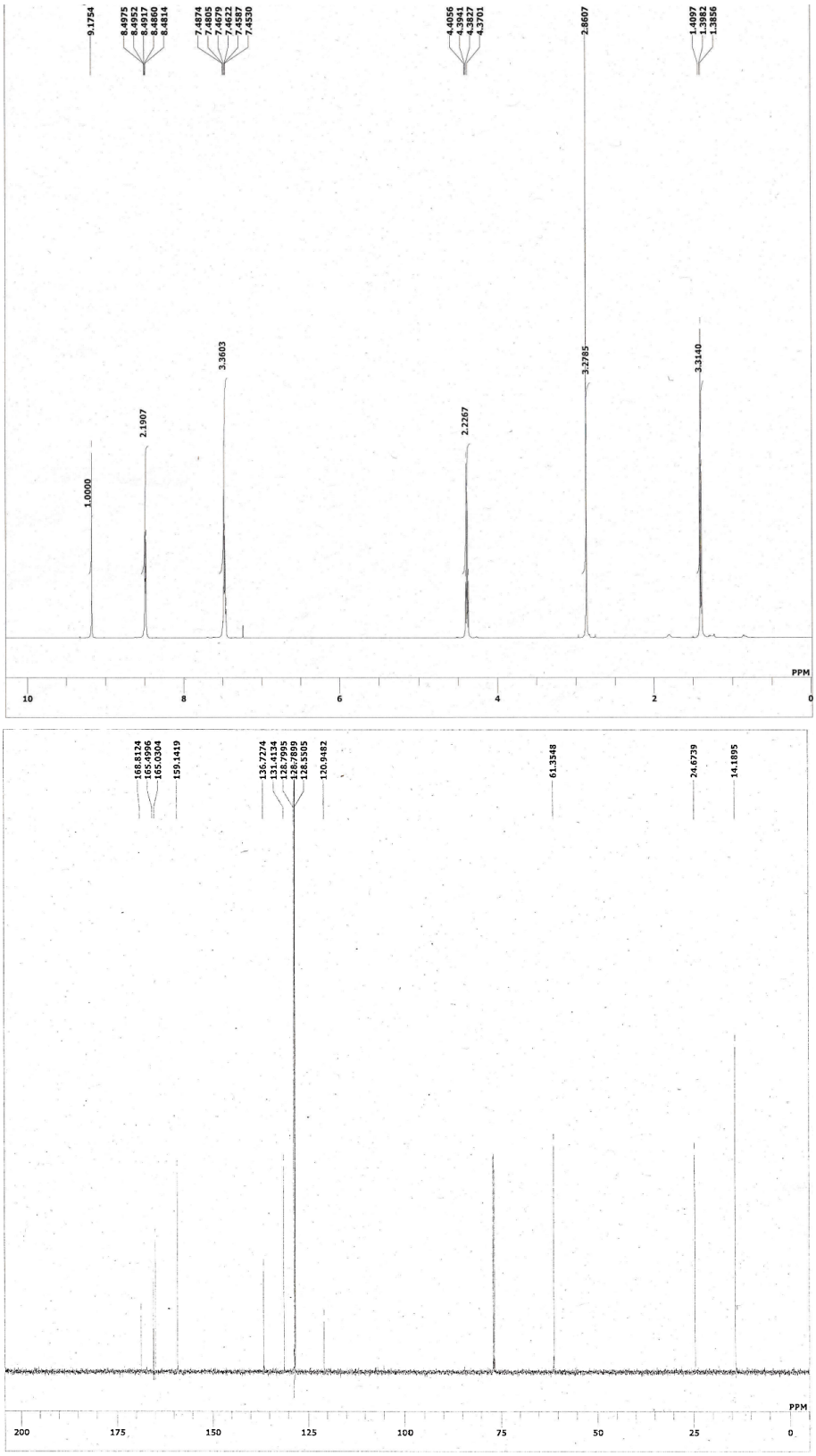


Figure S16. ^{1}H and ^{13}C NMR spectra of ethyl 4-methyl-2-phenylpyrimidine-5-carboxylate

S12. References

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