Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

for

Regioselective Palladium-Catalyzed Intramolecular Oxidative Aminofluorination of Unactivated Alkenes

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General Procedures and New Compounds Characterization

Content:

1. General Considerations.

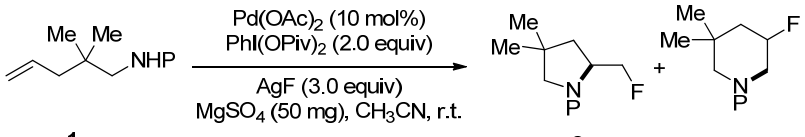
All commercially available compounds were used as received. ^{1}H and ^{13}C spectroscopy were recorded on a Varian Mercury-400 MHz (400 MHz for ^{1}H; 376 MHz for ^{19}F; 100 MHz for ^{13}C) or a Bucker Avance-300 MHz (300 MHz for ^{1}H; 282 MHz for ^{19}F; 75 MHz for ^{13}C) spectrometer. $CDCl_3$ was purchased from J&K. The chemical shifts (δ) are given in parts per million relative to internal standard TMS (0 ppm for ^{1}H), $CDCl_3$ (77.0 ppm for ^{13}C). Flash column chromatography was performed on silica gel 60 (particle size 200-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate. All solvents were dried and purified according to the procedure from 'Purification of Laboratory Chemicals book'. AgF was purchased from Aldrich. 1,1,1,3,3,3-hexafluoro-2-propanol(HFIP) was purchased from TCI. Compounds **1a-1i** (Table 2) and **4a-4m** (Table 3) were synthesized according to the reported procedures as below, and the NMR data were same with the reported literatures [S1][S2].

2. General Procedure for Aminofluorination of Substrates

2.1 Screening of Substrates bearing Different Protecting Group:

In a dry glass tube, $Pd(OAc)_2$ catalyst (2.4 mg, 0.01 mmol), AgF (39 mg, 0.3 mmol), oxidant (0.2 mmol), alkene **1** (0.1 mmol) and $MgSO_4$ (50 mg) were dissolved in 0.5 mL dry CH_3CN. The reaction mixture was stirred at room temperature for 24 h, then EtOAc (4.0 mL) was added and the mixture was stirred for ca.10 minutes, centrifuged and the filtrate was concentrated and analyzed by ^{1}H NMR and ^{19}F NMR with 2,2,2-trifluoro-*N*,*N*-dimethylacetamide as internal standard. The results were summarized in Table S1.

Table S1. Screening of Substrates.[a]



1 2 3

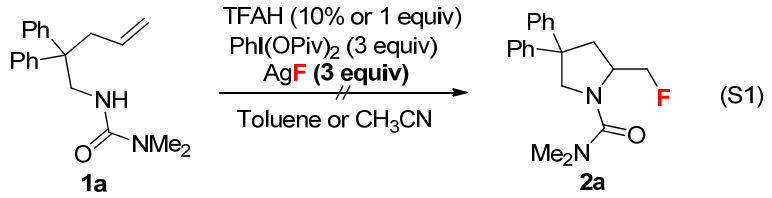
Entry	PG (substrate)	Yield[b] 2	Yield[b] 3
1	Ts(**S1a**)	0	84%
2	CH_3CO (**S1b**)	0	0
3	Boc (**S1c**)	0	0
4	Cbz (**S1d**)	0	0
5	$CONMe_2$ (**1a**)	12%	0

All the reactions were conducted in 0.1 mmol scale.

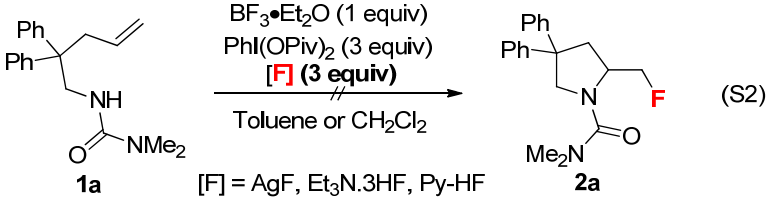
2.2 General Procedure for Screening of Reaction Conditions of Substrate 1a:

In a dry glass tube, Pd catalyst (0.005 mmol), AgF (39 mg, 0.3 mmol), oxidant (0.3 mmol) and alkene **1a** (32 mg, 0.1 mmol) were dissolved in 0.5 mL solvent. Other additives were added according to the superscripts in the table S2. The reaction mixture was stirred at room temperature for 24 h, then EtOAc (4.0 mL) was added and the mixture was stirred for ca.10 minutes, centrifuged and the filtrate was concentrated and analyzed by ^{1}H NMR and ^{19}F NMR with 2,2,2-trifluoro-*N*,*N*-dimethylacetamide as internal standard. The results were summarized in Table S2.

In order to test the possibility of Bronsted acid or Lewis acid promoted aminofluorination of alkene mediated by hypervalent iododine, substrate **1a** was treated by TFAH or BF3 • Et2O. However, no reaction occurred at all (see eq S1-2).

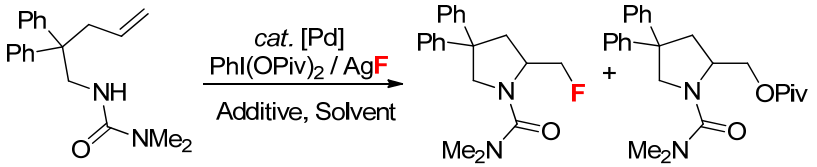


1a **2a** (S1)



1a [F] = AgF, $Et_3N.3HF$, Py-HF **2a** (S2)

Table S2. Screening of reaction conditions. [a]



1a **2a** **3a**

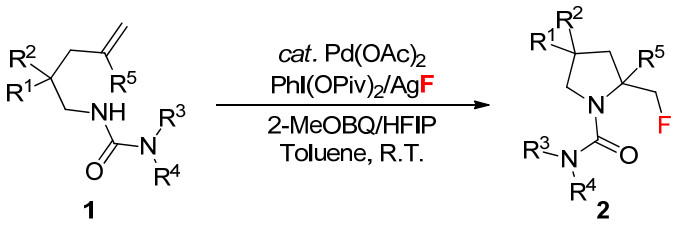
Entry	[Pd] (5 mol%)	Additive (equiv)	Solvent	Yield [b]	
				2a	**3a**
1	$Pd(OAc)_2$	–	CH_3CN	13%	26%
2	$Pd(OAc)_2$	–	EtOAc	19%	30%
3	$Pd(OAc)_2$	–	Benzene	49%	21%
4	$Pd(OAc)_2$	–	Toluene	51%	17%
5	$Pd(OAc)_2$	–	xylene	46%	23%
6	$PdCl_2(MeCN)_2$	–	Toluene	44%	18%
7	$PdCl_2(PhCN)_2$	–	Toluene	34%	13%
8	$Pd(dba)_2$	–	Toluene	50%	16%
9	–	–	Toluene	0	0
10[c]	$Pd(OAc)_2$	–	Toluene	12%	65%
11[d]	$Pd(OAc)_2$	–	Toluene	21%	43%
12[e]	$Pd(OAc)_2$	–	Toluene	0	0
13	$Pd(OAc)_2$	NaOPiv (1)	Toluene	13%	12%
14	$Pd(OAc)_2$	HOPiv (1)	Toluene	45%	34%
15	$Pd(OAc)_2$	$HOBu^t$ (1)	Toluene	60%	13%
16	$Pd(OAc)_2$	TFE (2.5)	Toluene	62%	6%
17	$Pd(OAc)_2$	HFIP (2.5)	Toluene	73%	trace
18[f]	**$Pd(OAc)_2$**	**HFIP (2.5)**	**Toluene**	**81%**	**trace**

[a] Reaction condition: **1a** (0.1 mmol), [Pd] (5 mol %), $PhI(OPiv)_2$ (3 equiv), AgF (3 equiv), solvent (0.5 mL), at *r.t.* for 24 hr. [b] ^1H NMR yield with CF_3-DMA as internal standard. [c] $PhI(OAc)_2$ (3 equiv). [d] $PhI(O_2CPh)_2$ (3 equiv). [e] 1-Acetoxy-1,2-benziodoxol-3-(1H)-one (3 equiv). [f] 2-MeOBQ (1 equiv).

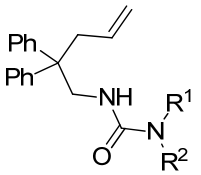
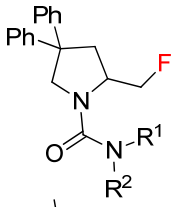
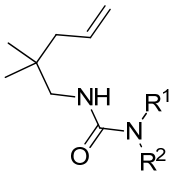
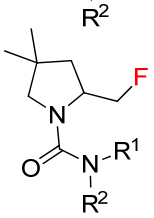
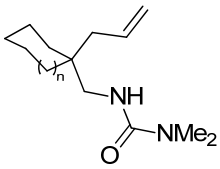
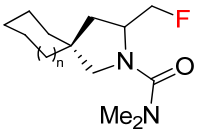
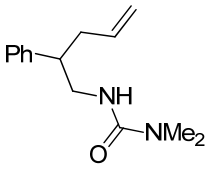
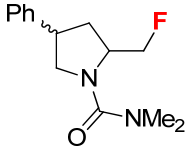
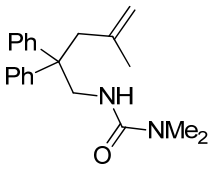
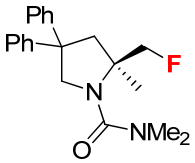
2.3 General Procedure for Aminofluorination of Substrates 1:

In a dry glass tube, $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), AgF (76 mg, 0.6 mmol), $PhI(OPiv)_2$ (245 mg, 0.6 mmol), 2-Me-BQ (27 mg, 0.2 mmol), $(CF_3)_2CHOH$ (HFIP) (55 μL, 0.5 mmol) and alkene **1** (0.2 mmol) were dissolved in 1.0 mL dry toluene. The reaction mixture was stirred at room temperature for 24 h, then filtered and the solid was washed by ethyl acetate. Combined filtrates were concentrated under vacuum. The residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether (or hexane) and ethyl acetate afforded the products **2**. The results were summarized in Table S3.

Table S3. Substrate scope of aminofluorination.[a]



1 **2**

Entry	Substrate	Product	Yield[b]
1 2	 **1a** $R^1 = R^2 =$ Me **1b** $R^1 = R^2 = {}^i$Pr	 **2a** **2b**	82% 78%
3 4 5	 **1c** $R^1 = R^2$ = Me **1d** $R^1 = R^2$ = Bn **1e** R^1 = Me, R^2 = Ph	 **2c** **2d** **2e**	53% 63% 61%
6 7	 **1f** n = 0 **1g** n = 1	 **2f** **2g**	47% 51%
8	 **1h**	 **2h**	50% (1/1)[c]
9	 **1i**	 **2i**	33%

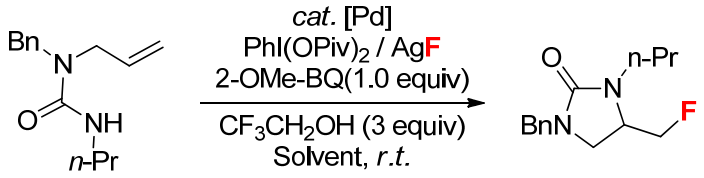
[a]All the reactions were conducted at 0.2 mmol scale, reaction condition is the same with entry 18 in table S2. [b]Isolated yield. [c]Diastereoselectivity.

2.4 General Procedure for Screening of Reaction Conditions of Substrate 4a:

In a dry glass tube, Pd catalyst (0.005 mmol), AgF (38 mg, 0.3 mmol), $PhI(OPiv)_2$ (124 mg, 0.3 mmol), 2-MeO-BQ (14 mg, 0.1 mmol), $(CF_3)_2CHOH$ (HFIP) (30 μL, 0.25 mmol) and alkene **4a** (24 mg, 0.1 mmol) were dissolved in 0.5 mL solvent. The reaction mixture was stirred at room temperature for 24 h, then EtOAc (4.0 mL) was added and the mixture was stirred for ca.10 minutes, centrifuged and the filtrate was

concentrated and analyzed by ^{1}H NMR and ^{19}F NMR with 2,2,2-trifluoro-*N*,*N*-dimethylacetamide as internal standard. The results were summarized in Table S4.

Table S4. Screening results of substrates **4a.**[a]



4a **5a**

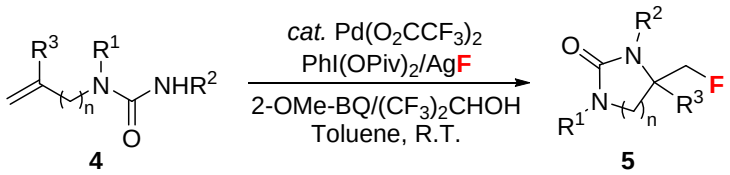
Entry	[Pd] (5 mol%)	Solvent	**5a**(Yield) [b]
1	$Pd(OAc)_2$	Toluene	61%
2	$Pd(OTFA)_2$	Toluene	72%
3	$PdCl_2(MeCN)_2$	Toluene	67%
4	$PdCl_2(PPh_3)_2$	Toluene	53%
5	$Pd(dba)_2$	Toluene	65%
6	$Pd(acac\text{-}F_6)_2$	Toluene	55%
7	--	Toluene	0
8	$Pd(OTFA)_2$	$CHCl_3$	61%
9	$Pd(OTFA)_2$	Dioxane	28%
10	$Pd(OTFA)_2$	EtOAc	43%
11	$Pd(OTFA)_2$	$ClCH_2CH_2Cl$	25%
12	$Pd(OTFA)_2$	MeCN	38%
13	$Pd(OTFA)_2$	C_6H_5OMe	61%

[a] Reaction condition: **4a** (0.1 mmol), [Pd] (5 mol %), $PhI(OPiv)_2$ (3 equiv), AgF (3 equiv), 2-Me-BQ (1 equiv) and HFIP (3 equiv) in solvent (0.5 mL), at *r.t.* for 24 hr.
[b] ^{1}H NMR yield with CF_3-DMA as internal standard.

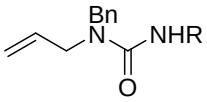
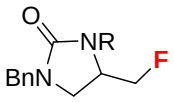
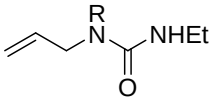
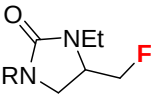
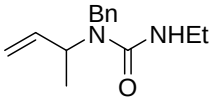
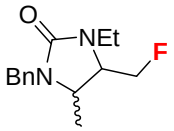
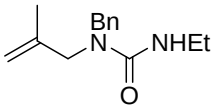
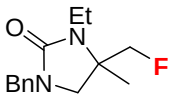
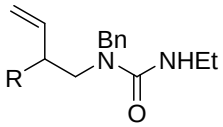
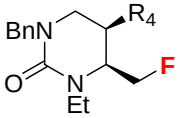
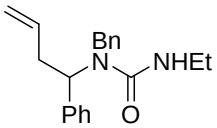
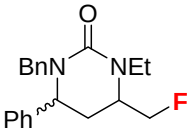
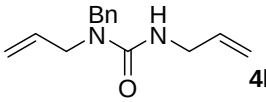
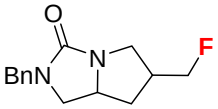
2.5 General Procedure for Aminofluorination of Substrates 4:

In a dry glass tube, $Pd(OTFA)_2$ (3.3 mg, 0.01 mmol), AgF (76 mg, 0.6 mmol), $PhI(OPiv)_2$ (125 mg, 0.6 mmol), 2-Me-BQ (28 mg, 0.2 mmol), $(CF_3)_2CHOH$ (HFIP) (55 μL, 0.5 mmol) and alkene **4** (0.2 mmol) were dissolved in 1.0 mL dry toluene. The reaction mixture was stirred at room temperature for 24 h, then filtered and the solid was washed by ethyl acetate. Combined filtrates were concentrated under vacuum. The residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether (or hexane) and ethyl acetate afforded the products **5**. The results were summarized in Table S5.

Table S5. The *exo*-aminofluoration of substrates **4.**[a]



4 **5**

Entry	Substrate		Product		Yield[b]
1		**4a** R = ^{n}Pr		**5a**	75%
2		**4b** R = Me		**5b**	72%
3		**4c** R = Et		**5c**	71%
4		**4d** R = Bn		**5d**	70%
5		**4e** R = Ph		**5e**	55%
6		**4f** R = *c*-C_5H_9		**5f**	58%
7		**4g**		**5g**	50% (2:1)[c]
8		**4h**		**5h**	56%
9		**4i** R = H		**5i**	80%
10		**4j** R = Me		**5j**	66%[d]
11		**4k**		**5k**	56% (2/1)[c]
12		**4l**		**5l**	35%

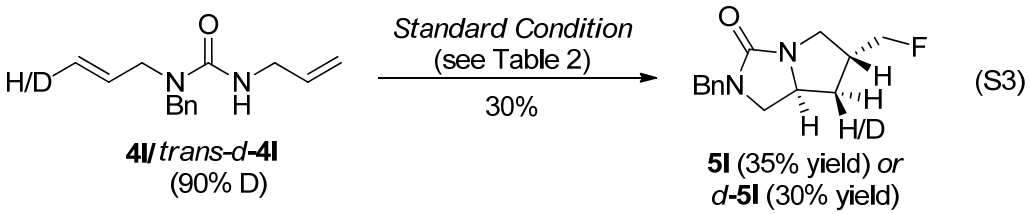
[a]Reaction condition: **4** (0.2 mmol), $Pd(O_2CCF_3)_2$ (5 mol %), $PhI(OPiv)_2$ (3 equiv), AgF (3 equiv), 2-MeO-BQ (1 equiv), $(CF_3)_2CHOH$ (3 equiv) in Toluene (1.0 mL) at r.t. for 24 hours. [b]Isolated yield. [c]Diastereoselectivity. [d]d.r value > 20:1

3. Mechanistic studies

3.1 Stereochemistry of Aminopalladation.

In order to get further mechanistic information of this transformation, diene substrate **4l** and the related deuterium labeled substrate *trans-d*-**4l** were synthesized (see Part **4.5**) and then applied it to the standard reaction condition as below: In a dry glass tube, $Pd(OTFA)_2$ (3.4 mg, 0.01 mmol), AgF (78 mg, 0.6 mmol), $PhI(OPiv)_2$ (245 mg, 0.6

mmol), 2-Me-BQ (28 mg, 0.2 mmol), $(CF_3)_2CHOH$ (HFIP) (56 μL, 0.5 mmol) and alkene **4l** (47 mg, 0.2 mmol) or *trans-d-***4l** (90% D, 49 mg, 0.2 mmol) were dissolved in 1.0 mL dry toluene. The reaction mixture was stirred at room temperature for 24 h, then filtered and the solid was washed by ethyl acetate. Combined filtrates were concentrated under vacuum. The residue was purified by column chromatography on silica gel with a gradient eluant of petroleum ether (or hexane) and ethyl acetate afforded the product **5l** 18 mg (35% yield) or *trans-d-***4l** 16 mg (30% yield). The results were summarized in eq S3.



4l/*trans-d-***4l**
(90% D)

5l (35% yield) *or*
*d-***5l** (30% yield)

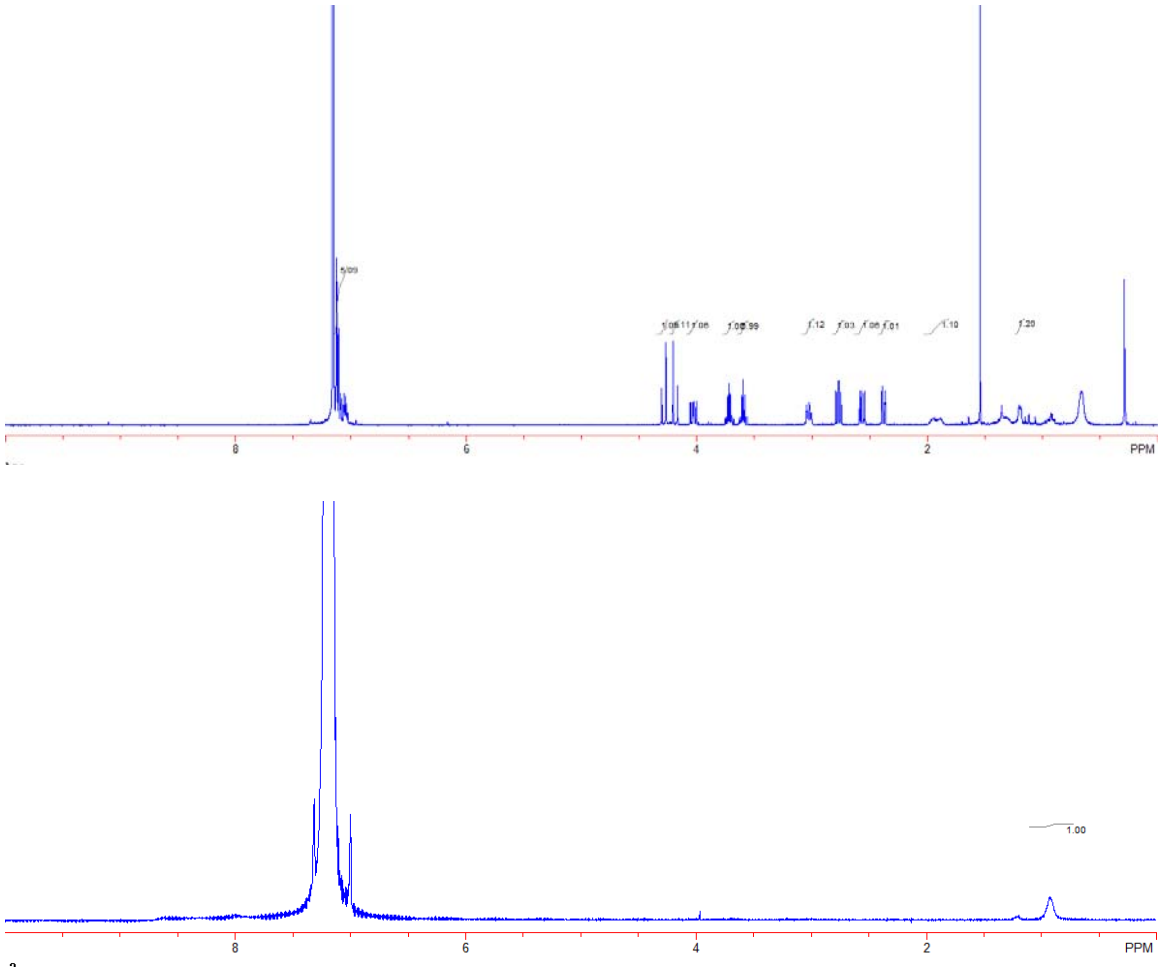


Figure S1. The ^{1}H NMR (top) and ^{2}D NMR (bottom) spectrum of profuct *d*-**5l.**

The characterization of compounds 5l and *d*-5l:

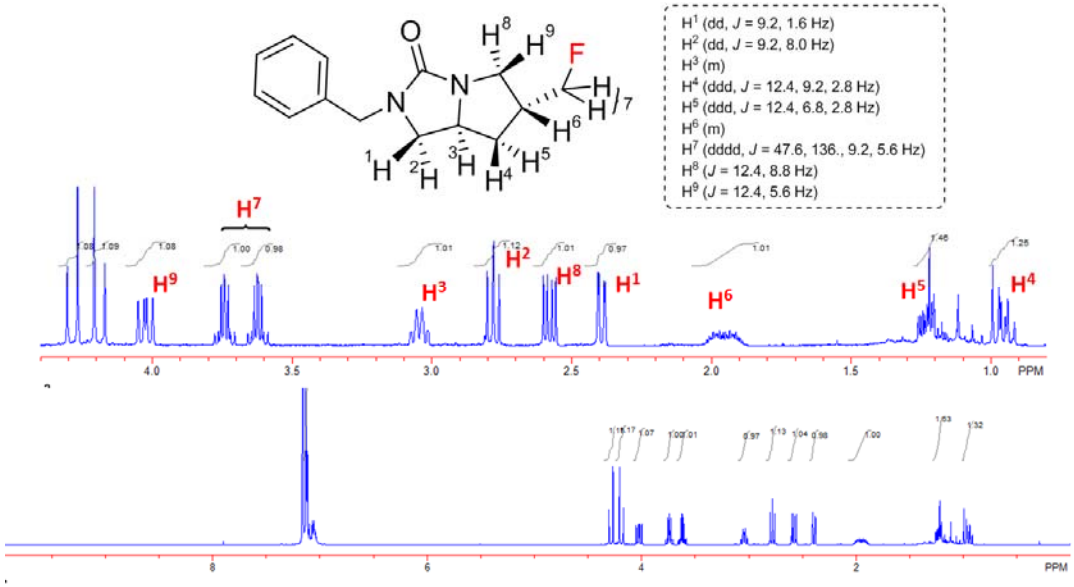
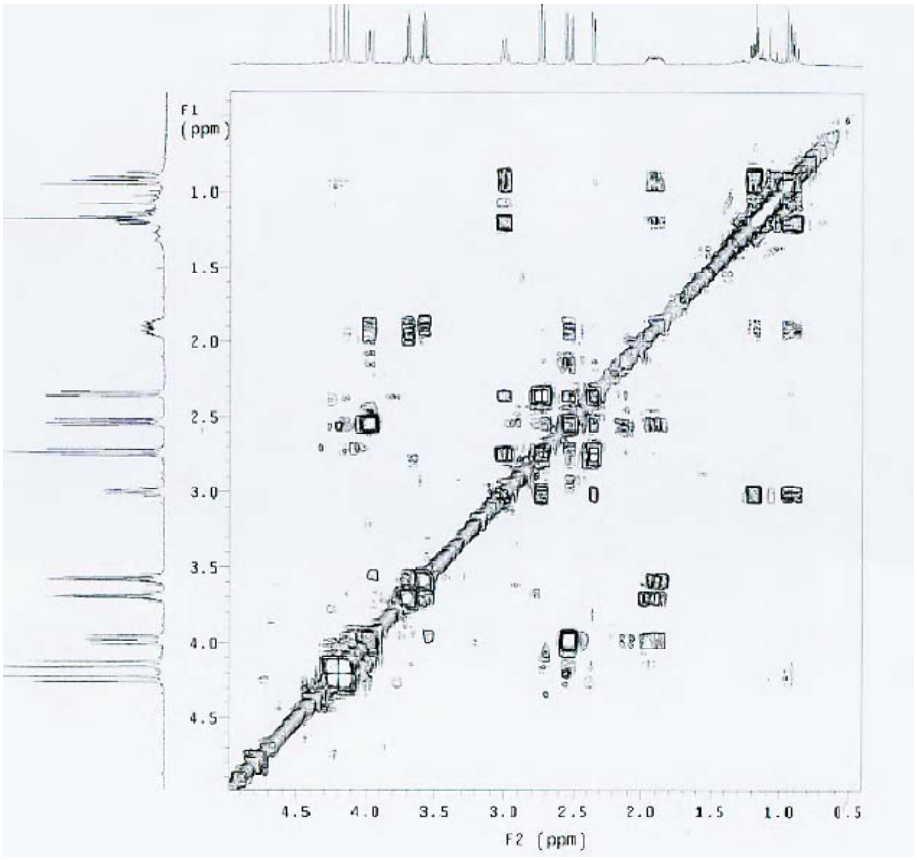
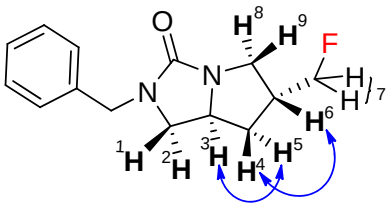


Figure S2. The ^{1}H NMR spectrum of profuct **5l.**



^{1}H-^{1}H NOSEY



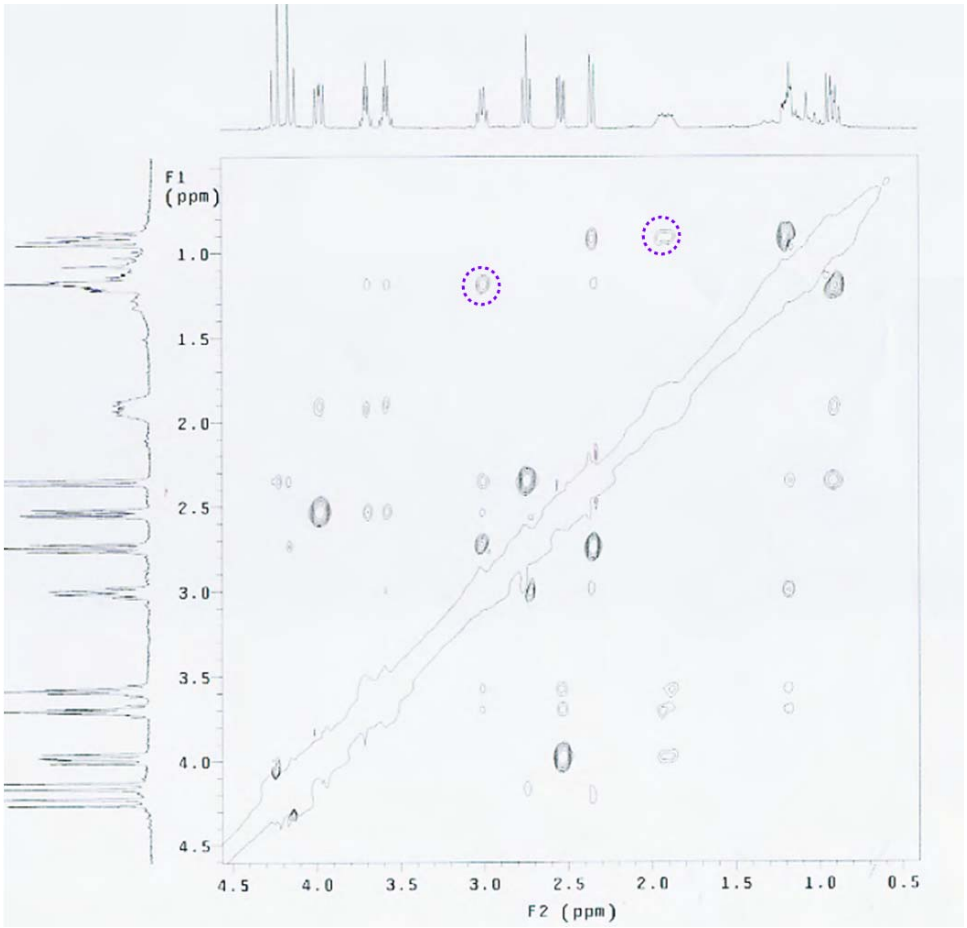
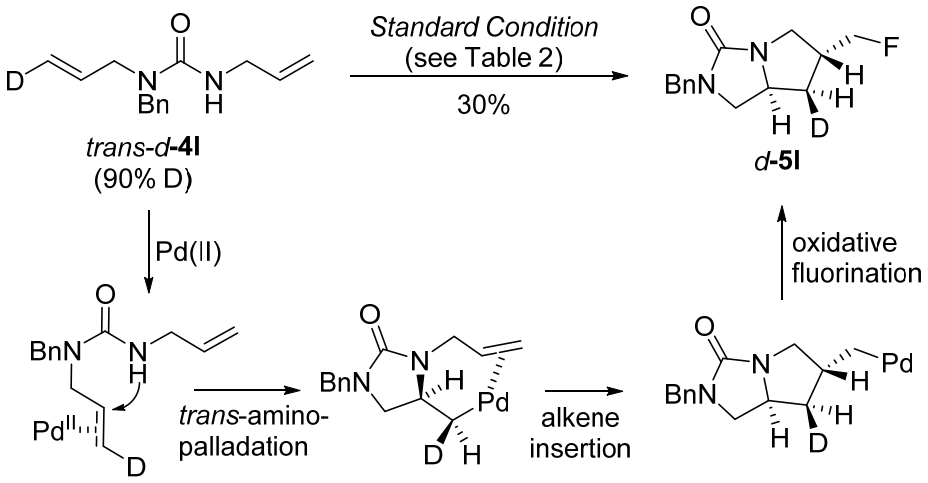


Figure S3. The ^{1}H-^{1}H COSY (top) and ^{1}H-^{1}H NOSEY (bottom)spectrum of profuct **5l.**

A possible catalytic cycle based on our above results is shown below: *trans*-aminopalladation of the alkene forms a primary sp^3 C–Pd bond, following subsequently second double bond insertion to generate a new sp^3 C–Pd bond. Finally, the oxidation of primary sp^3 C–Pd bond by PhI(OPiv)2/AgF to give C–F bond via a Pd(IV) intermediate.

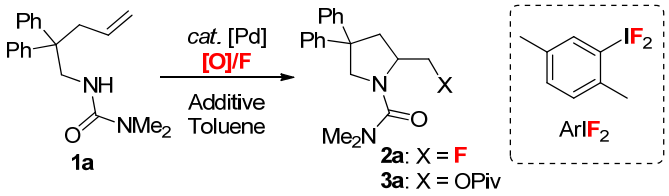


Scheme S1. The *exo*-aminofluorination of substrates *trans*-*d*-**4l** and the proposed mechanism for *exo*-aminofluorination of alkenes**.**

3.2 Controlling Experiment on the Aminofluorination with $ArIF_2$.

In order to test the reactivity of $ArIF_2$ in the aminofluorination of alkenes, $ArIF_2$ (Ar = 2,5-dimethylphenyl) was synthesized according to the literaure procedure.[S4] Then, substrate 1a was treated by using ArIF2 in the presence of palladium catalyst with following procedure: In a oven-dried glass Schlenk tube, $Pd(OAc)_2$ (1.2 mg, 0.005 mmol), $ArIF_2$ (54 mg, 0.2 mmol), AgOPiv (41.6 mg, 0.2 mmol), additives (2 equiv), and alkenes **1a** (0.1 mmol) were dissolved in dry toluene (1.0 mL). The reaction mixture was stirred at room temperature for 24 h, then the mixture was filtered and the solid was washed by CH_2Cl_2. Filtrates were combined and concentrated under vacuum. The residue was analyzed by ^1H NMR and ^{19}F NMR with 2,2,2-trifluoro-*N*,*N*-dimethylacetamide as internal standard. The results were summarized in Table S6.

Table S6. Pd-Catalyzed Aminofluorination with $ArIF_2$.[a]



Entry	[Pd]	[O]/F	Additive	**2a**	**3a**
1	$Pd(OAc)_2$	$ArIF_2$	--	0	0
2	--	$ArIF_2$	--	0	0
3	$Pd(OAc)_2$	$ArIF_2$/AgOPiv	--	13%	0
4	$Pd(OAc)_2$	$ArIF_2$/AgOPiv	HFIP	45%	0
5	--	$ArIF_2$/AgOPiv	HFIP	0	0

[a] Reaction condition: **1a** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), $ArIF_2$ (2 equiv), AgOPiv (2 equiv), Additive (2 equiv) in toluene (1 mL) at r.t. [b] NMR yield.

3.3 Experiment of $ArIF_2$ (Ar = 2,5-dimethylphenyl) with AgOPiv.

In a oven-dried glass NMR tube, $ArI(OPiv)_2$ (20.3 mg, 0.05 mmol), AgF (41.6 mg, 0.05 mmol), with or without $(CF_3)_2CHOH$ (5uL, 0.05 mmol) were added, then dry toluene (0.6 mL) was added, CF_3-DMA was added as internal standard.

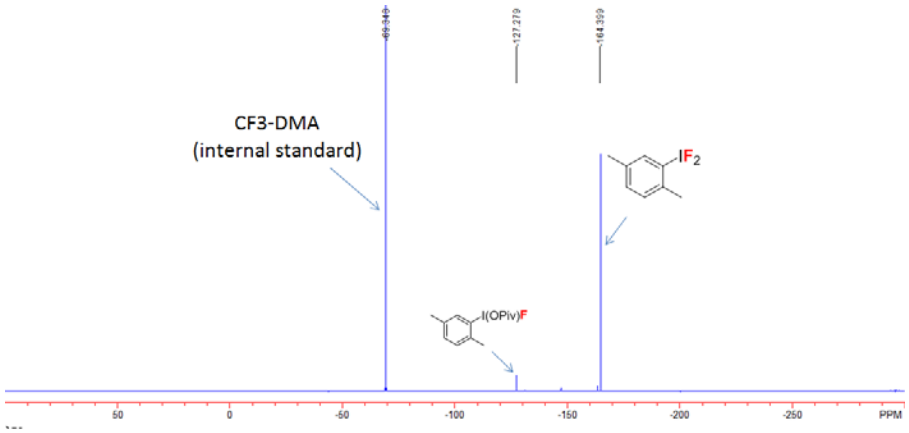


Figure S4. The FNMR of $ArIF_2$+AgOPiv.

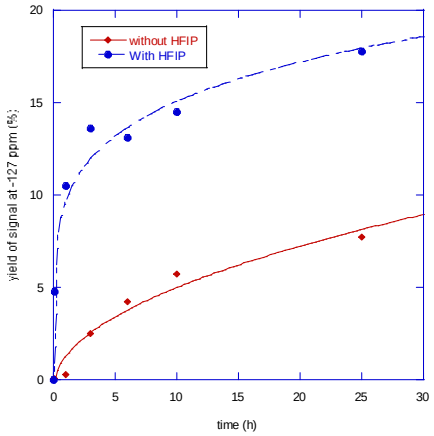
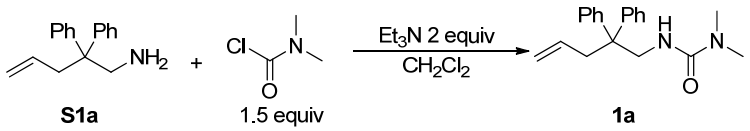


Figure S5. The effect of HFIP on the Transfermation from $ArIF_2$ to ArI(OPiv)F.

4 Procedure of Substrate Synthesis

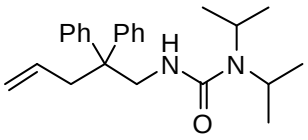
4.1 Typical procedures for the synthesis of substrate 1a:



S1a 1.5 equiv **1a**

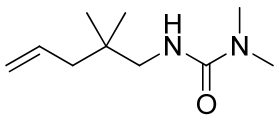
Substrate S**1a** was synthesized according to the previous literature.[S1d] The mixture of S**1a** (4.8 g, 20 mmol) and Et_3N (4.1 ml, 36 mmol, 1.8 equiv) in dry CH_2Cl_2 (50 mL) were placed in a three-necked 100 ml flask. The solution of *N*,*N*-dimethylcarbamic chloride (2.8 ml, 36 mmol, 1.8 equiv) in CH_2Cl_2 (10 mL)was added dropwisely at 0 ^oC. The resulting mixture was allowed to warm to room temperature and stirred over night. After reaction completed, water (20 mL) was added, and the mixtrue was extracted by CH_2Cl_2. The organic layer was combined and dried over $MgSO_4$. After removal solvent, the residue was purified through silical gel column chromatography (PE/EA = 3:1) to afford the desired product **1a** (5.54g, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 4H), 7.25-7.16 (m, 6H), 5.47 (m, 1H), 5.08-4.82 (m, 2H), 4.00-3.81 (m, 3H), 2.87 (d, *J* = 7.1 Hz, 2H), 2.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 145.6, 133.9, 128.2, 128.1, 126.4, 118.6, 50.5, 47.6, 42.1, 35.9; HRMS: m/z (ESI) calculated $[M+Na]^+$: 331.1781, measured: 331.1794.

Substrates **1b-1i** were synthesized with the same produce with **1a**,



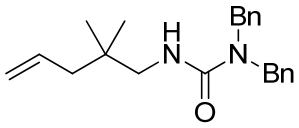
1b-

1b, yield: 75%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.24 (m, 4H), 7.25-7.17 (m, 6H), 5.47 (m, 1H), 5.12-4.83 (m, 2H), 3.97 (d, *J* = 5.4 Hz, 2H), 3.89-3.60 (m, 3H), 2.90 (d, *J* = 7.2 Hz, 2H), 0.99 (d, *J* = 6.9 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 145.7, 133.8, 128.2, 128.0, 126.3, 118.3, 50.0, 47.6, 44.4, 42.3, 21.1; HRMS: m/z (ESI) calculated $[M+Na]^+$: 387.2407, measured: 387.2422.



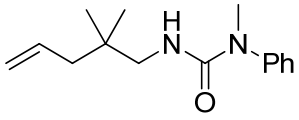
1c

1c, yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03-5.74 (m, 1H), 5.14-4.96 (m, 2H), 4.52 (br, 1H), 3.09 (d, *J* = 6.2 Hz, 2H), 2.91 (s, 6H), 1.98 (d, *J* = 8.8 Hz, 2H), 0.89 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 135.3, 117.0, 50.3, 44.6, 36.1, 34.6, 24.8. HRMS: m/z (ESI) calculated $[M+H]^+$: 185.1648, measured: 185.1648.



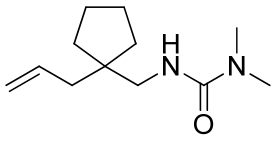
1d

1d, yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H), 5.71-5.65 (m, 1H), 4.93-4.90 (m, 2H), 4.35 (s, 4H), 4.38 (t, *J* = 5.6 Hz, 1H), 3.05 (d, *J* = 6.4 Hz, 2H), 1.72 (d, *J* = 7.6 Hz, 2H), 0.70 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 137.9, 135.0, 128.8, 127.5, 127.2, 117.1, 50.8, 50.3, 44.3, 34.6, 24.8. HRMS: m/z (ESI) calculated $[M+H]^+$: 337.2274, measured: 337.2273.



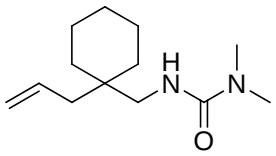
1e

1e, yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.26 (m, 5H), 5.77-5.67 (m, 1H), 4.88-4.76 (m, 2H), 4.37 (br, 1H), 3.27 (s, 3H), 3.01 (d, *J* = 6.4 Hz, 2H), 1.82 (d, *J* = 7.6 Hz, 2H), 0.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 143.5, 135.0, 130.0, 127.5, 127.3, 117.0, 50.0, 44.6, 37.0, 34.9, 24.9; HRMS: m/z (ESI) calculated $[M+H]^+$: 247.1805, measured: 247.1807.

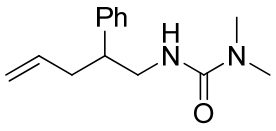


1f

1f, yield: 67%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99-5.78 (m, 1H), 5.07 (m, 2H), 4.52 (br, 1H), 3.16 (m, 2H), 2.9 (s, 6H), 2.18-2.01 (m, 2H), 1.76-1.51 (m, 4H), 1.52-1.27 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 136.4, 116.8, 47.7, 46.3, 43.2, 36.1, 35.1, 24.8. HRMS: m/z (ESI) calculated $[M+Na]^+$: 233.1624 measured: 233.1619.

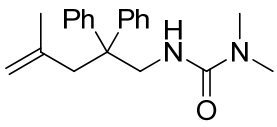


1g: yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08-5.76 (m, 1H), 5.21-4.95 (m, 2H), 4.47 (br, 1H), 3.17 (d, *J* = 6.4 Hz, 2H), 2.89 (s, 6H), 2.15-1.98 (m, 2H), 1.72-1.15 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 135.6, 116.8, 47.2, 41.5, 37.0, 36.2, 33.6, 26.2, 21.4. HRMS: m/z (ESI) calculated $[M+Na]^+$: 247.1781, measured: 247.1781.



1h

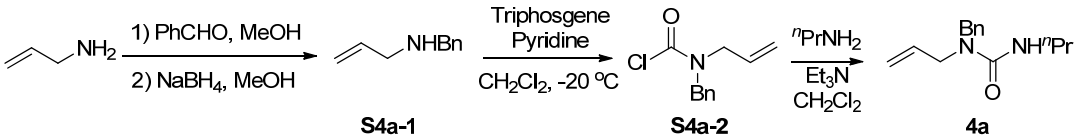
1h, yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.04 (m, 5H), 5.70 (ddt, *J* = 17.1, 10.2, 7.1 Hz, 1H), 5.12-4.88 (m, 2H), 4.20 (br, 1H), 3.73 (ddd, *J* = 13.0, 6.4, 4.2 Hz, 1H), 3.26-3.08 (m, 1H), 2.90 (m, 1H), 2.76 (s, 6H), 2.51-2.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 142.6, 136.2, 128.6, 127.8, 126.6, 116.4, 46.1, 45.8, 38.0, 36.0; HRMS: m/z (ESI) calculated $[M+Na]^+$: 255.1468, measured: 255.1469.



1i

1i, yield: 72%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.25 (m, 4H), 7.26-7.18 (m, 6H), 4.84 (s, 1H), 4.64 (s, 1H), 4.03-3.91 (d, *J* = 9.2 Hz, 2H), 3.85 (br, 1H), 2.87 (s, 2H), 2.69 (s, 6H), 1.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 146.0, 141.6, 128.2, 128.1, 126.4, 116.2, 50.1, 47.0, 44.9, 35.8, 24.3. H RMS: m/z (ESI) calculated $[M^+]$: 322.2045, measured: 322.2040.

4.2. Typical procedures for the synthesis of substrate 4a:



S4a-1 **S4a-2** **4a**

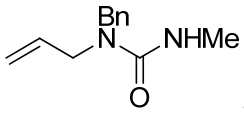
In a 100 ml round bottom flask, to a solution of allyl amine (1.7 g, 30 mmol) in

MeOH (40 ml), freshly distilled benzaldehyde (4.3 g, 40 mmol) was added. After the solution was stirred for 3 hours, $NaBH_4$ (1.52g, 40 mmol) was added in several portions. The mixture was stirred for another two hours, then brine was added to quench the reaction. After removal of solvent, the residue was extracted by diethyl ether (100 mL for twice). The organic layer wasdried over $MgSO_4$. After removal solvent, the residue was purified by column chromatography (PE/EA = 10:1) to afford product S**4a-1** (3.67g, 83%).

Pyridine (2 mL, 20 mmol) was added dropwisely to a solution of triphosgene (3 g, 10 mmol) in dry CH_2Cl_2 (20 mL) at -20 ^oC. Then, a solution of the secondary amine S**4a-1** (1.1 g, 7.8 mmol) in CH_2Cl_2 (10 mL) was added to the resulting suspension solution at the same temperature. The reaction was allowed to warn to room temperature and stirred for overnight. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with 0.1M HCl, water and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure to give the crude carbamoyl chloride which was used directly in the next step.

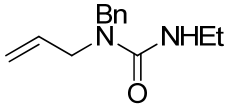
The solution of allyl(benzyl) carbamic chloride (20 mmol) in CH_2Cl_2 was added dropwisely to the solution of propylamine (1.2 g, 20 mmol) and Et_3N (4.1 ml, 36 mmol, 1.8 equiv) in CH_2Cl_2 (30 mL) at 0 ^oC. The resulting mixture was allowed to warm to room temperature and stirred over night. After the reaction was completed, water was added to quench the reaction and the mixture was abstracted by CH_2Cl_2. The organic layer was dried over $MgSO_4$. After removal solvent, the residue was purified by silical gel column chromatography (PE/EA = 6:1) to afford the desired product **4a** (2.94g, 80% yield). **4a:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 2H), 7.29-7.22 (m, 3H), 5.92-5.65 (m, 1H), 5.25-5.09 (m, 2H), 4.48 (s, 3H), 3.85 (d, J = 5.4 Hz, 2H), 3.27-3.09 (q, J = 7.4 Hz, 2H), 1.53-1.40 (m, 2H), 0.84 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 138.0, 133.9, 128.6, 127.2, 116.7, 50.1, 49.5, 42.5, 23.3, 11.2. HRMS: m/z (ESI) calculated $[M+Na]^+$: 255.1468, measured: 255.1469.

Substrates **4b-4e** was synthesized with the same procedure with **4a**,



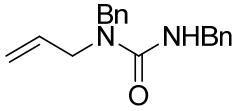
4b

4b: yield: 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 2H), 7.26 (m, 3H), 5.89-5.68 (m, 1H), 5.29-5.03 (m, 2H), 4.52 (br, 1H), 4.48 (s, 2H), 3.91-3.77 (m, 2H), 2.84-2.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 137.9, 133.7, 128.5, 127.2, 127.2, 116.7, 49.9, 49.3, 27.6. HRMS: m/z (ESI) calculated $[M+H]^+$: 205.1335, measured: 205.1336.



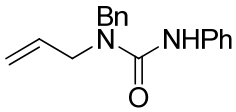
4c

4c: yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 7.29-7.21 (m, 3H), 5.87-5.68 (m, 1H), 5.27-5.09 (m, 2H), 4.48 (s, 2H), 4.40 (s, 1H), 3.84 (d, J = 5.3 Hz, 2H), 3.34-3.17 (m, 2H), 1.08 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 138.0, 133.9, 128.6, 127.3, 127.2, 116.7, 50.0, 49.4, 35.7, 15.5; HRMS: m/z (ESI) calculated $[M+Na]^+$: 241.1311, measured: 241.1311.



4d

4d: yield: 82%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.13 (m, 10H), 5.78 (m, 1H), 5.24-5.09 (m, 2H), 4.76 (br, 1H), 4.51 (s, 2H), 4.43 (d, J = 5.4 Hz, 2H), 3.88 (d, J = 5.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 139.4, 137.9, 133.7, 128.7, 128.5, 127.4, 127.3, 127.1, 116.9, 50.2, 49.5, 44.9; HRMS: m/z (ESI) calculated $[M+Na]^+$: 303.1468, measured: 303.1469.

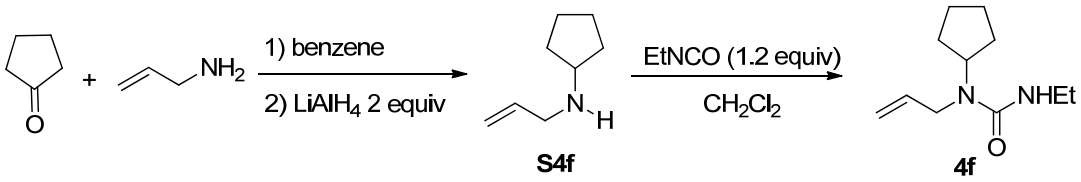


4e

4e: yield: 69%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.16 (m, 9H), 7.07-6.94 (m, 1H), 6.46 (d, J = 4.8 Hz, 1H), 5.86 (m, 1H), 5.40-5.16 (m, 2H), 4.59 (s, 2H), 4.08-3.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 139.0, 137.6, 133.8, 128.8, 128.8, 127.6,

127.5, 122.9, 119.6, 119.6, 117.4, 50.6, 50.0; HRMS: m/z (ESI) calculated $[M+Na]^+$: 289.1311, measured: 289. 1317.

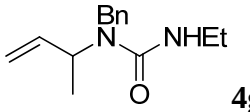
4.3 Typical procedures for the synthesis of substrate 4f:



S4f 4f

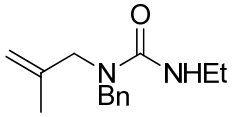
Substrate **S4f** was synthesized according to the previous literature.[S5] To a solution of **S4f** (0.58 g, 5 mmol) in 20ml CH_2Cl_2, EtNCO (0.48 ml, 6 mmol) was added dropwisely at 0 ^oC. The resulting mixture was allowed to warm to room temperature and stirred for overnight. After that, water was added to quench the reaction, and the mixture was extracted by CH_2Cl_2. The organic layer was dried over $MgSO_4$. After removal solvent, the residue was purified by silical gel column chromatography (PE/EA = 6:1) to afford the desired product **4f** (0.78 g, 80% yield). **4f:** ^1H NMR (400 MHz, $CDCl_3$) δ 5.97-5.68 (m, 1H), 5.36-5.07 (m, 2H), 4.79-4.59 (m, 1H), 4.35 (s, 1H), 3.75-3.58 (m, 2H), 3.31-3.07 (q, J = 7.2 Hz, 2H), 1.93-1.72 (m, 2H), 1.72-1.45 (m, 4H), 1.46-1.28 (m, 2H), 1.17-1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 135.8, 116.0, 55.8, 44.9, 35.5, 29.2, 23.7, 15.5; HRMS: m/z (ESI) calculated $[M+Na]^+$: 219.1468, measured: 219.1470.

Substrates **4g-4i, 4k** were synthesized with the above procedure.



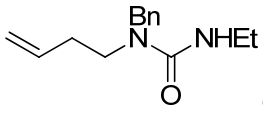
4g.

4g: yield: 72%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (q, J = 7.4 Hz, 2H), 7.31-7.21 (m, 3H), 5.91 (m, 1H), 5.26-5.10 (m, 2H), 5.01 (br, 1H), 4.39 (m, 1H), 4.31-4.13 (m, 2H), 3.30-3.03 (q, J = 7.2 Hz, 2H), 1.25 (d, J = 6.9 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 139.4, 138.6, 128.7, 127.2, 126.4, 115.6, 51.9, 46.7, 35.6, 16.5, 15.4; HRMS: m/z (ESI) calculated $[M+Na]^+$: 255.1468, measured: 255.1470.



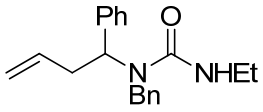
4h

4h: yield: 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 2H), 7.29-7.20 (m, 3H), 4.91 (m, 1H), 4.87 (s, 1H), 4.49 (s, 3H), 3.73 (s, 2H), 3.34-3.14 (m, 2H), 1.69 (s, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 141.3, 138.0, 128.5, 127.3, 127.1, 111.6, 52.4, 50.1, 35.6, 19.8, 15.4; HRMS: m/z (ESI) calculated $[M+Na]^+$: 255.1468, measured: 255.1471.



4i

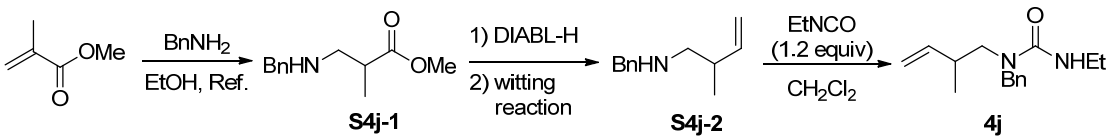
4i, yield: 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.31 (m, 2H), 7.31-7.16 (m, 3H), 5.91-5.64 (m, 1H), 5.07 (m, 2H), 4.47 (s, 2H), 4.32 (br, 1H), 3.34 (dd, *J* = 13.0, 5.6 Hz, 2H), 3.24 (q, *J* = 7.2 Hz, 2H), 2.42-2.23 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 137.9, 135.3, 128.7, 127.3, 126.8, 116.8, 50.5, 47.0, 35.6, 32.8, 15.5; HRMS: m/z (ESI) calculated $[M+Na]^+$: 255.1468, measured: 255.1473.



4k

4k, yield: 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-6.94 (m, 10H), 6.04-5.67 (m, 2H), 5.26-4.89 (m, 2H), 4.43-3.87 (m, 3H), 3.40-3.03 (m, 2H), 2.90-2.60 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 140.1, 137.8, 135.2, 128.6, 128.3, 128.1, 127.4, 127.2, 126.4, 117.2, 56.9, 46.7, 35.6, 35.4, 15.1; HRMS: m/z (ESI) calculated $[M+Na]^+$: 331.1781, measured: 331.1779.

4.4 Typical procedures for the synthesis of substrate 4j:



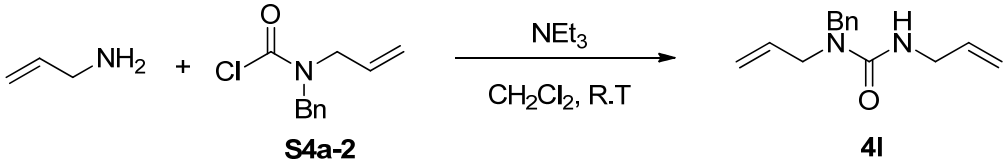
To a solution of benzylamine (2.2 g, 20 mmol) in anhydrous EtOH (20 mL), methyl methacrylate (2.4 g, 24 mmol) was added. The mixture was refluxed for 24 hours. After the evaporation of the solvent, the crude product **S4j-1** was obtained.

To a suspended solution of Ph_3PCH_3Br (15 mmol) in dry THF(30 mL), n-BuLi(16.5 mmol) was added dropwisely at 0 °C over 10 min, and the mixture was stirred at 0° C for another 30 min. Then this witting reagent was prepared.

To a solution of crude product S**4j-1** (2.1 g, 10 mmol) in dry THF (50 mL), DIBAL-H (10 mL, 1.0 M in hexane solution) was added dropwisely for 10 min at -78 °C. The solution was stirred for another 30 min at the same temperature. Then the freshly prepared Wittig reagent was added at -78 °C for more than 30 min. The mixture was allowed to warm to room temperature and stirred for 1 hour. After reaction finished, saturated NH_4Cl aqueous solution was added to quench the reaction. The mixture was extracred by diethyl ether. The organic layer was dried over $MgSO_4$. After removal solvent, the residue was purified by silical gel column chromatography (PE/EA = 10:1) to afford product S**4j-2** (1.1 g, 62%). The substrate **4j** was synthesized according to the procedure of **4i.**

4j: yield: 66%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.22 (m, 5H), 5.58-5.73 (m, 1H), 5.04 (dd, *J* = 17.7, 14.2 Hz, 2H), 4.48 (s, 2H), 4.25 (br, 1H), 3.26-3.16 (m, 4H), 2.56 (m, 1H), 1.04 (t, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 141.6, 137.8, 128.7, 127.3, 126.8, 114.7, 53.4, 51.0, 37.5, 35.7, 17.5, 15.5; HRMS: m/z (ESI) calculated $[M+Na]^+$: 269.1624, measured: 269.1627.

4.5 Typical procedures for the synthesis of substrate 4l and *trans-d*-4l:



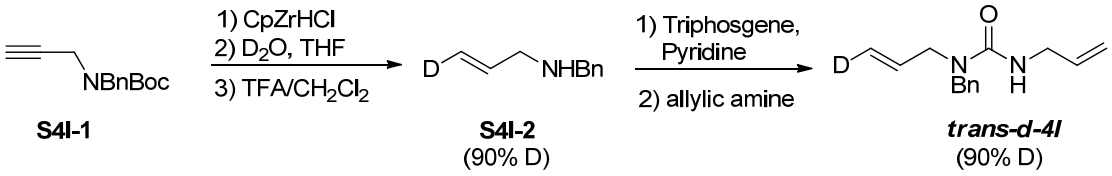
S4a-2 **4l**

Substrate **4l** can be synthesized with the same procedure of **4a**.

4l, yield: 63%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 2H), 7.29-7.25 (m, 3H),

5.92-5.70 (m, 2H), 5.26-5.14 (m, 2H), 5.14-5.00 (m, 2H), 4.50 (s, 3H), 3.94-3.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 137.8, 135.5, 133.7, 128.5, 127.2, 127.2, 116.8, 115.1, 50.0, 49.4, 43.2; HRMS: m/z (ESI) calculated [M^+]: 230.1419, measured: 230.1415.

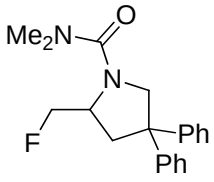
Procedures for the synthesis of substrate *trans-d-***4l**:



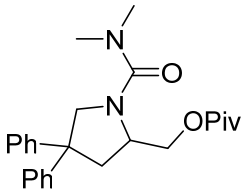
S4l-1 **S4l-2** (90% D) ***trans-d-4l*** (90% D)

Under N_2, To a suspended solution of CpZrHCl (1.1 g, 3 mmol) in dry THF (20 mL), a solution of alkyne **S4l-1** (720 mg, 2.8 mmol) in THF (3.0 mL) was added at room temperature. The mixture was stirred for 1 h, and then quenched by addition of D_2O (0.5mL). The mixture was stirred for 24 h, then was dried by anhydrous Na_2SO_4. After removal solvent, the residue was dissolved in CH_2Cl_2 (10 ml), then TFA (1.2 mL, 15mmol) was added and the mixture was stirred for 4h. After removal solvent, the residue was treated by 10% NaOH solution, and the mixture was extracted by diethyl ether. The organic layer was dried by Mg_2SO_4. After removal solvent, the residue was purified through silica gel flash column chromatography (eluents: hexanes / ethyl acetate = 10/1) to give compound **S4l-2** (90% D, 325 mg, 78% yield).[S2a] Finally, substrate ***trans-d-4l*** (90% D) was synthesized with the same procedure of **4a** in 55% yield.

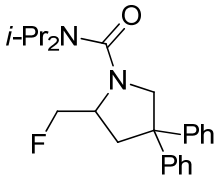
5 New product characterization



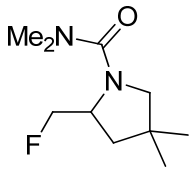
2a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.05 (m, 10H), 4.61 (ddd, *J* = 48.9, 9.6, 3.6 Hz, 1H), 4.42 (ddd, *J* = 46.5, 9.6, 2.3 Hz, 1H), 4.33-4.24 (m, 1H), 4.08-3.91 (m, 1H), 3.67 (d, *J* = 10.6 Hz, 1H), 2.91 (s, 6H), 2.78 (t, *J* = 11.6 Hz, 1H), 2.56 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 145.3, 144.6, 128.5, 128.4, 126.7, 126.5, 126.4, 126.3, 82.6 (d, *J* = 170.0 Hz), 60.1, 56.5 (d, *J* = 20.0 Hz), 53.5, 38.3 (d, *J* = 10.4 Hz), 38.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.8 (dt, *J* = 48.7, 25.2 Hz). HRMS: m/z (ESI) calculated [M^+]: 326.1794, measured: 326.1806.



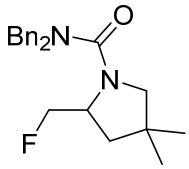
3a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.09 (m, 10H), 4.29 (m, 2H), 4.12 (m, 2H), 3.64 (d, *J* = 10.4 Hz, 1H), 2.89 (s, 6H), 2.57 (d, *J* = 8.8 Hz, 2H), 1.18 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 162.5, 145.5, 144.7, 128.5, 128.1, 128.0, 126.6, 126.5, 126.4, 63.9, 60.2, 55.5, 53.5, 39.7, 38.7, 38.1, 27.2. HRMS: m/z (ESI) calculated [M^+]: 408.2413, measured: 408.2402.



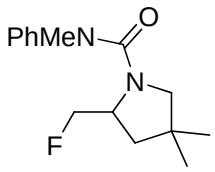
2b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-6.78 (m, 10H), 4.56 (ddd, *J* = 49.0, 9.6, 3.6 Hz, 1H), 4.46-4.29 (ddd, *J* = 49.0, 9.6, 3.6 Hz, 1H), 4.20 (t, *J* = 10.6 Hz, 1H), 4.06 (m, 1H), 3.65 (m, 3H), 2.71 (t, *J* = 11.6 Hz, 1H), 2.54 (m, 1H), 1.35 (d, *J* = 6.6 Hz, 6H), 1.32 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 145.7, 144.9, 128.5, 128.4, 126.9, 126.6, 126.5, 126.4, 83.2 (d, *J* = 170.0 Hz), 60.6, 56.1 (d, *J* =20.0 Hz), 53.6, 47.3, 38.3 (d, *J* = 4.6 Hz), 22.7, 21.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.3 (dt, *J* = 48.5, 25.6 Hz). HRMS: m/z (ESI) calculated [M^+]: 382.2420, measured: 382.2418.



2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.55 (ddd, *J* = 47.6, 9.4, 3.8 Hz, 1H), 4.51-4.32 (m, 1H), 4.30 (ddd, *J* = 47.6, 9.2, 2.6 Hz, 1H), 3.16 (d, *J* = 9.6 Hz, 1H), 3.00 (d, *J* = 9.6 Hz, 1H), 2.82 (s, 6H), 1.72 (m, 1H), 1.58-1.48 (m, 1H), 1.19 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 83.0 (d, *J* = 170.0 Hz), 63.8, 57.0 (d, *J* = 20.0 Hz), 39.9 (d, *J* = 4.0 Hz), 38.4, 38.0, 25.8, 25.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.2 (dt, *J* = 48.1, 25.2 Hz). HRMS: m/z (ESI) calculated [M^+]: 202.1481, measured: 202.1484.

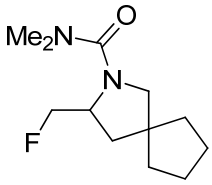


2d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4H), 7.32-7.25 (m, 2H), 7.25-7.16 (m, 4H), 4.67 (d, *J* = 15.4 Hz, 2H), 4.63-4.24 (m, 3H), 4.04 (d, *J* = 15.4 Hz, 2H), 3.22 (s, 2H), 1.87-1.68 (m, 2H), 1.13 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 137.6, 128.4, 127.7, 127.1, 83.4 (d, *J* = 170.8 Hz), 63.6, 57.0 (d, *J* = 20.1 Hz), 50.1, 39.7 (d, *J* = 4.0 Hz), 38.6, 25.6, 25.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -231.3 (m). HRMS: m/z (ESI) calculated [M^+]: 354.2107, measured: 354.2104.

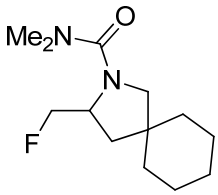


2e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.08 (m, 5H), 4.83 (ddd, *J* = 49.2, 9.2, 3.2 Hz, 1H), 4.34 (ddd, *J* = 49.2, 9.6, 2.0 Hz, 1H), 4.33 (m, 1H), 3.25 (s, 3H), 2.73 (d, *J* = 10.4 Hz, 1H), 2.25 (d, *J* = 10.0 Hz, 1H), 1.64 (d, *J* = 8.8 Hz, 2H), 0.92 (s, 3H), 0.90 (s,

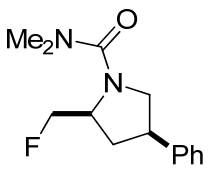
3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 145.7, 129.2, 124.6, 124.4, 82.5 (d, *J* = 170.1 Hz), 62.3, 57.0 (d, *J* = 19.7 Hz), 39.5 (d, *J* = 3.8 Hz), 39.0, 37.7, 25.7, 25.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -233.3 (ddd, *J* = 49.4, 46.3, 27.2 Hz). HRMS: m/z (ESI) calculated [M^+]: 264.1638, measured: 264.1631.



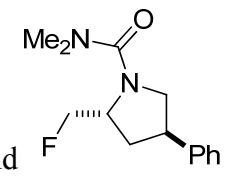
2f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56-4.22 (m, 3H), 3.24 (d, *J* = 9.6 Hz, 1H), 3.08 (d, *J* = 9.6 Hz, 1H), 2.83 (s, 6H), 1.89-1.77 (m, 2H), 1.73-1.53 (m, 6H), 1.50-1.35 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 83.5 (d, *J* = 169.0 Hz), 62.3, 57.2 (d, *J* = 21.0 Hz), 49.4, 38.7 (d, *J* = 4.1 Hz), 38.0, 37.2, 35.1, 24.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -231.9 (td, *J* = 47.7, 24.4 Hz). HRMS: m/z (ESI) calculated [M^+]: 228.1638, measured: 228.1640.



2g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.53-4.27 (m, 3H), 3.18 (d, *J* = 9.9 Hz, 1H), 3.08 (d, *J* = 9.9 Hz, 1H), 2.83 (s, 6H), 1.93 (dd, *J* = 12.4, 7.2 Hz, 1H), 1.64-1.54 (m, 1H), 1.54-1.35 (m, 6H), 1.32-1.28 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 83.7 (d, *J* =170.0 Hz), 56.1 (d, *J* = 20.0 Hz), 42.2, 38.0, 36.1, 33.6, 27.2, 26.1, 23.8, 22.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.1 (td, *J* = 48.1, 24.3 Hz). HRMS: m/z (ESI) calculated [M^+]: 242.1794, measured: 242.1800.



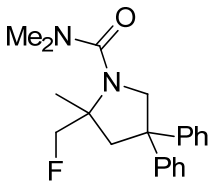
***cis*-2h** and



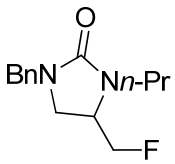
trans-2h

These two isomers can not be separated.

***cis*-2h:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.21 (m, 5H), 4.62-4.39 (m, 3H), 3.67 (t, *J* = 8.4 Hz, 1H), 3.371 (t, *J* = 9.2 Hz, 1H), 3.26 (m, 1H), 2.85 (s, 6H), 2.35 (m, 1H), 2.13 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 139.8, 128.5, 127.1, 126.6, 83.3 (d, *J* = 170.6 Hz), 58.0, 57.9 (d, *J* = 20.0 Hz), 44.1, 37.9, 33.4 (d, *J* = 4.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.2 (td, *J* = 47.7, 24.4 Hz). ***trans*-2h:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.12 (m, 5H), 4.54-4.36 (m, 3H), 3.89 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.51 (td, *J* = 12.0, 6.4 Hz, 1H), 3.37 (dd, *J* = 7.6, 6.8 Hz, 1H), 2.87 (s, 6H), 2.33 (m, 1H), 2.12 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 142.9, 128.6, 127.0, 126.5, 84.0 (d, *J* = 170.6 Hz), 56.8 (d, *J* = 20.5 Hz), 56.7, 43.3, 38.2, 34.2 (d, *J* = 3.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -230.8 (td, *J* = 47.0, 24.7 Hz). HRMS: m/z (ESI) calculated [M^+]: 250.1481, measured: 250.1475.

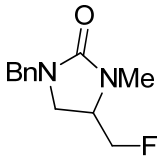


2i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.05 (m, 10H), 4.43 (dd, *J* = 48.0, 9.0 Hz, 1H), 4.29 (d, *J* = 10.7 Hz, 1H), 4.21 (dd, *J* = 48.0, 9.0 Hz, 1H), 4.02 (d, *J* =10.8 Hz, 1H), 3.19 (d, *J* = 12.4 Hz, 1H), 2.80 (s, 6H), 2.44 (d, *J* = 12.5 Hz, 1H), 1.17 (d, *J* = 2.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 145.7, 145.6, 128.6, 128.5, 126.7, 126.5, 126.4, 126.3, 85.4 (d, *J* = 172.0 Hz), 63.8 (d, *J* = 18.0 Hz), 58.9, 51.8, 46.3 (d, *J* = 4.0 Hz), 38.9, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -221.4 (t, *J* = 47.8 Hz). HRMS: m/z (ESI) calculated [M^+]: 340.1951, measured: 340.1946.

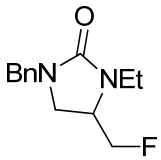


5a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.20 (m, 5H), 4.44 (d, *J* = 4.7 Hz, 1H), 4.36 (d, *J* = 4.6 Hz, 2H), 4.33 (d, *J* = 4.7 Hz, 1H), 3.89-3.73 (m, 1H), 3.49-3.36 (m, 1H),

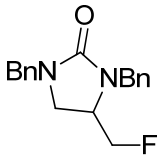
3.30 (m, 1H), 3.18-3.07 (m, 1H), 2.96 (dd, *J* = 9.0, 6.0 Hz, 1H), 1.72-1.47 (m, 2H), 0.92 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 136.9, 128.4, 127.9, 127.3, 82.8 (d, *J* = 174.0 Hz), 52.4 (d, *J* = 21.0 Hz), 47.9, 44.0, 43.9 (d, *J* = 8.0 Hz), 20.9, 11.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.5 (td, *J* = 47.0, 16.9 Hz). HRMS: m/z (ESI) calculated [M^+]: 250.1481, measured: 250.1479.



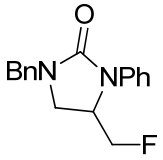
5b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.07 (m, 5H), 4.55-4.42 (m, 1H), 4.41-4.29 (m, 3H), 3.68 (m, 1H), 3.31 (m, 1H), 2.97-2.90 (m, 1H), 2.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 136.8, 128.5, 127.9, 127.4, 82.7 (d, *J* = 173.0 Hz), 54.9 (d, *J* = 21.0 Hz), 48.0, 43.7 (d, *J* = 7.0 Hz), 29.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.7 (td, *J* = 47.0, 17.4 Hz). HRMS: m/z (ESI) calculated [M^+]: 222.1168, measured: 222.1163.



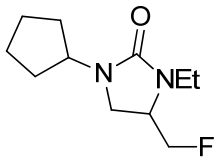
5c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.20 (m, 5H), 4.46 (d, *J* = 4.8 Hz, 1H), 4.37 (s, 2H), 4.32 (d, *J* = 4.8 Hz, 1H), 3.95-3.75 (m, 1H), 3.61-3.45 (m, 1H), 3.38-3.26 (m, 1H), 3.26-3.16 (m, 1H), 3.00-2.88 (m, 1H), 1.18-1.10 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 136.7, 128.5, 127.9, 127.3, 83.0 (d, *J* = 173.0 Hz), 52.0 (d, *J* = 21.0 Hz), 48.0, 44.0 (d, *J* = 7.0 Hz), 37.1, 12.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.3 (tdd, *J* = 46.9, 16.5, 3.4 Hz). HRMS: m/z (ESI) calculated [M^+]: 236.1325, measured: 236.1317.



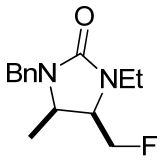
5d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 10H), 4.85 (d, *J* = 15.2 Hz, 1H), 4.45-4.33 (m, 2H), 4.40-4.33 (m, 1H), 4.28-4.21 (m, 1H), 4.22 (d, *J* = 15.2 Hz, 1H), 3.62 (m, 1H), 3.27 (t, *J* = 9.2 Hz, 1H), 2.97 (dd, *J* = 9.2, 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 137.1, 136.8, 128.6, 128.2, 128.2, 128.0, 127.5, 127.5, 82.7 (d, *J* = 173.0 Hz), 51.8 (d, *J* = 21.0 Hz), 48.1, 46.5, 43.8 (d, *J* = 7.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.6 (td, *J* = 46.9, 17.2 Hz). HRMS: m/z (ESI) calculated [M^+]: 298.1481, measured: 298.1475.



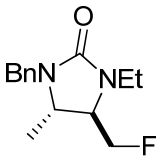
5e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.43 (m, 2H), 7.38-7.23 (m, 6H), 7.17-7.01 (m, 2H), 4.52-4.36 (m, 4H), 4.34 (d, *J* = 4.2 Hz, 1H), 3.48 (m, 1H), 3.38-3.27 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 138.2, 136.5, 129.0, 128.6, 128.1, 127.5, 124.1, 121.1, 81.0 (d, *J* = 174.0 Hz), 52.7 (d, *J* = 23.0 Hz), 47.84, 44.0 (d, *J* = 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -232.3 (m). HRMS: m/z (ESI) calculated [M^+]: 284.1325, measured: 284.1323.



5f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56-4.47 (m, 1H), 4.45-4.36 (m, 1H), 4.27-4.23 (m, 1H), 3.96-3.77 (m, 1H), 3.54-3.33 (m, 2H), 3.17 (m, 1H), 3.12-2.99 (m, 1H), 1.82-1.73 (m, 2H), 1.66-1.42 (m, 6H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 83.0 (d, *J* = 174.0 Hz), 53.49, 52.2 (d, *J* = 21 Hz), 40.3 (d, *J* =6.0 Hz), 37.0, 28.4, 28.1, 23.9, 12.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.4 (td, *J* = 47.0, 15.9 Hz). HRMS: m/z (ESI) calculated [M^+]: 214.1481, measured: 214.1477.



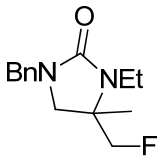
cis-5g and



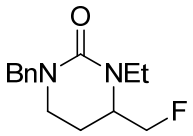
trans-5g

These two isomers cannot be separated.

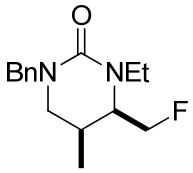
***cis*-5g:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H), 4.77 (d, *J* = 15.6 Hz, 1H), 4.42 (d, *J* = 4.8 Hz, 1H), 4.30 (d, *J* = 4.8 Hz, 1H), 4.02 (d, *J* = 15.6 Hz, 1H), 3.55 (m, 1H), 3.32 (m, 1H), 3.24-3.10 (m, 2H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 136.9, 128.4, 128.0, 127.8, 82.4 (d, *J* = 173.1 Hz), 60.0 (d, *J* = 20.2 Hz), 45.1, 40.0, 26.9, 18.2, 12.6 (d, *J* = 10.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.0 (td, *J* = 47.1, 17.3 Hz). ***trans*-5g:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.22 (m, 5H), 4.75 (d, *J* = 15.2 Hz, 1H), 4.17 (d, *J* = 4.4 Hz, 1H), 4.12 (d, *J* = 15.6 Hz, 1H), 3.97 (d, *J* = 4.8 Hz, 1H), 3.64 (m, 1H), 3.37 (td, *J* = 7.2, 4.4 Hz, 1H), 3.16-3.08 (m, 2H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 136.8, 128.4, 127.9, 127.1, 80.4 (d, *J* = 171.6 Hz), 55.3 (d, *J* = 20.4 Hz), 44.9 (d, *J* = 4.9 Hz), 36.7, 27.0, 18.0, 12.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -228.2 (td, *J* = 46.7, 19.0 Hz). HRMS: m/z (ESI) calculated [M^+]: 250.1481, measured: 250.1474.



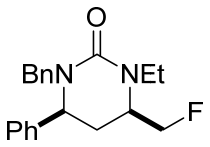
5h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.16 (m, 5H), 4.45-4.32 (m, 2H), 4.28 (dd, *J* = 22.9, 9.4 Hz, 1H), 4.16 (dd, *J* = 21.8, 8.6 Hz, 1H), 3.35-3.18 (m, 2H), 3.14 (dd, *J* = 8.8, 2.3 Hz, 1H), 2.87 (dd, *J* = 8.9, 1.9 Hz, 1H), 1.31-1.25 (m, 3H), 1.19 (t, *J* = 4.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 137.1, 128.5, 127.9, 127.3, 85.4 (d, *J* = 178.0 Hz), 57.6 (d, *J* =18.0 Hz), 51.6 (d, *J* = 4.0 Hz), 47.8, 34.72, 20.3, 15.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -224.7 (t, *J* = 47.2 Hz). HRMS: m/z (ESI) calculated [M^+]: 250.1481, measured: 250.1475.

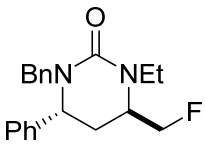


5i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 2H), 7.27-7.16 (m, 3H), 4.56 (s, 2H), 4.51-4.20 (m, 2H), 3.85-3.68 (m, 1H), 3.70-3.55 (m, 1H), 3.31-3.19 (m, 1H), 3.15 (dd, *J* = 13.9, 7.0 Hz, 1H), 3.11-3.02 (m, 1H), 2.10-1.82 (m, 2H), 1.18 (d, *J* = 4.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 138.1, 128.3, 127.6, 126.9, 81.9 (d, *J* = 175.0 Hz), 53.4 (d, *J* = 22.0 Hz), 51.1, 42.3, 41.2, 22.8 (d, *J* = 2.0 Hz), 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -224.0 (td, *J* = 46.9, 12.3 Hz). HRMS: m/z (ESI) calculated [M^+]: 250.1481, measured: 250.1480.



5j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 4.59 (d, *J* = 15.2 Hz, 1H), 4.49 (d, *J* = 15.2 Hz, 1H), 4.47-4.35 (m, 2H), 3.92-3.87 (m, 1H), 3.37 (dd, *J* = 12.4, 4.4 Hz, 1H), 3.28 (m, 1H), 3.02-2.97 (m, 1H), 2.78 (d, *J* =12.0 Hz, 1H), 2.12 (m, 1H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 138.1, 128.2, 127.8, 127.0, 82.6 (d, *J* = 174.8 Hz), 59.4 (d, *J* = 22.0 Hz), 51.1, 50.0, 42.0, 25.3, 17.3, 13.5 (d, *J* = 2.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -224.01 (td, *J* = 47.0, 12.1 Hz). HRMS: m/z (ESI) calculated [M+]: 264.1638, measured: 264.1637.



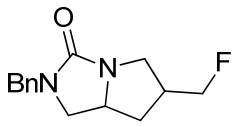
***cis*-5k** and 

***trans*-5k**

These two isomers can not be separated.

***cis*-5k:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.08 (m. 10H), 5.45 (d, *J* = 15.6 Hz, 1H), 4.41 (d, *J* = 5.2 Hz, 1H), 4.30 (d, *J* = 5.2 Hz, 1H), 4.29 (dd, *J* = 8.4, 5.2 Hz, 1H), 3.91

(tt, J = 14.0 Hz, 7.2 Hz, 1H), 3.56-3.46 (m, 1H), 3.48 (d, J = 15.2 Hz, 1H), 3.23 (dt, J = 14.0, 7.2 Hz, 1H), 2.28-2.19 (m, 1H), 2.07-1.98 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 140.7, 137.9, 128.7, 128.3, 128.0, 127.7, 127.0, 126.5, 82.8 (d, J = 175.0 Hz), 55.4, 51.5 (d, J = 21 Hz), 48.3, 41.3, 33.1 (d, J = 3.0 Hz), 13.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ-228.2 (td, J = 46.7, 19.0 Hz). ***trans*-5k:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.14 (m, 10H), 5.59 (d, J = 15.2 Hz, 1H), 4.46 (t, J = 4.4 Hz, 1H), 4.19-4.08 (m, 1H), 4.02-3.96 (m, 1H), 3.80-3.62 (m, 2H), 3.62 (d, J = 7.2 Hz, 2H), 3.38-3.30 (m, 1H), 2.24-2.20 (m, 1H), 2.05-1.97 (m, 1H), 1.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 140.4, 138.2, 128.8, 128.3, 127.7, 127.5, 126.7, 126.1, 84.2 (d, J = 171.0 Hz), 55.6, 54.4 (d, J = 22.0 Hz), 49.1, 42.3, 31.2, 13.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -227.0 (td, J = 47.1, 17.3 Hz). HRMS: m/z (ESI) calculated [M^+]: 326.1794, measured: 326.1793.



5l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 5H), 4.48 (dd, J = 11.4, 5.6 Hz, 1H), 4.40 (s, 2H), 4.31 (dd, J = 11.4, 5.6 Hz, 1H), 4.00 (dd, J = 12.2, 8.7 Hz, 1H), 3.80-3.63 (m, 1H), 3.41 (t, J = 8.6 Hz, 1H), 3.06 (d, J = 9.3 Hz, 1H), 2.86 (dd, J = 12.4, 5.5 Hz, 1H), 2.71-2.48 (m, 1H), 1.91 (ddd, J = 12.7, 6.6, 3.0 Hz, 1H), 1.56 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 136.8, 128.6, 127.9, 127.5, 85.0 (d, J = 169.0 Hz), 55.27, 47.8 (d, J = 7.0 Hz), 47.7, 46.8, 38.7 (d, J =18.0 Hz), 33.4 (d, J = 7.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -222.8 (td, J = 47.1, 23.7 Hz). HRMS: m/z (ESI) calculated [M^+]: 248.1325, measured: 248.1321.

6 References

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