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(12)

(10)

CN 108299285 B

(45)

2020.10.30

(21) &\$% %\$&\*, \$, - "

(56)

(22) &\$% "\$' "&-

7B %\$' % \$' &+ 5ž&\$% "\$\* "&\*

(65)

<i UbZYb[ ' >] Ub[ "7i ! 7UhU nmYX H\FYY!

7B %\$, &- -& ) ' 5

7cadcbYbh 7UgWUXY 5bbi `Uh] cb FYUW] cb. ' 5b

(43)

&\$% "\$+ "&\$

9bhf m hc : i bVh] cbU ] nYX Dmf ] X] bYg" >"

(73)

Cf[ " 7\Ya" "&\$% ž , \$ , +\*! , ++% "

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(72)

(74)

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(51) Int. Q .

007D 211/86f&\$\*\$ "\$%&

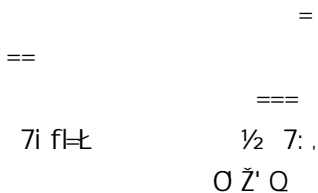
007D 409/04f&\$\*\$ "\$%&

1

15

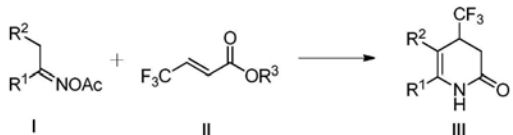
(54)

(57)

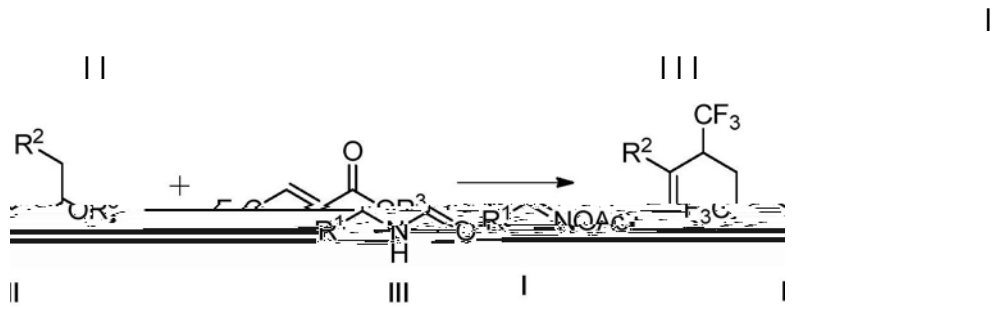


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CN 108299285 B



1. III



	R <sup>1</sup>	9H	2					
6,7,8	2				3,4			5, 3,4
				4 ( 0 )	4			4
4	4							
	R <sup>2</sup>						3	3
	R <sup>3</sup>							

2. 1 III  
CuCl CuBr CuI CuOAc

3. 1 III  
DMF DMSO

4. 1 III  
60 120

5. 1 III

1MHCl

III

[ 0001]

[ 0002]

[ 0003]

[ 0004]

C H C X( )

[ 0005]

[ 0006]

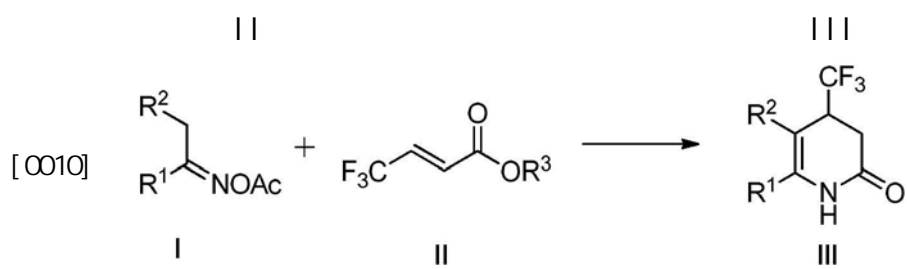
[ 0007]

[ 0008]

III

[ 0009]

I



[ 0011]

CN 108299285 B

[0012] R<sup>1</sup>

R<sup>2</sup> H

R<sup>3</sup>

[0013]

O

[0014]

R<sup>1</sup> C<sub>1</sub> rGI vÙd ` Q•• S`F rGI vÑ,, F Q•• SY,, ` rGI vÓ ` Q•• SdF  
C

[0031] I II 1:1 2  
 I II 1:1.1 1:2  
 [0032] 20mol 10mol 10 50mol  
 [0033] 25mol I  
 [0034] II I  
 III  
 [0035] I  
 (0.20mmol) II (0.2 0.4mmol) Cu<sup>I</sup> (0.02 0.04mmol, 10 20mol) Zn  
 (0.02 0.05mmol, 10 25mol) DMSO(2  
 3.5mL) 60 120 12 36  
 H<sub>2</sub>O(2.0mL) 1MHCl (aq, 3mL)  
 (4 10mL) (EA: PE 5: 1)  
 III  
 [0036] III  
 [0037] III  
 [0038] CF<sub>3</sub> [3+3] Cu(I)  
 4  
 4  
 [0039]  
 [0040]  
 [0041]  
 [0042]  
 [0043]

[0044] 1 30 1 20 1 15  
 1 10 1 6 1 4 1 3 1 2

(Me CH3) (Et CH2CH3)  
 (n Pr CH2CH2CH3) (i Pr CH(CH3)2) (n Bu CH2CH2CH2CH3)  
 (i Bu CH2CH(CH3)2) (s Bu CH(CH3)CH2CH3) (t Bu C(CH3)3)

2 3 2 2 3 2 3 1 2 1  
 2 3 2 2 3 2 4 2 3 3 2  
 3 2,3 2 3,3 2

[0045] 2 12 2 8 2 6 2 4  
 C C sp2

"E" "Z" ( CH CH2) ( CH2CH  
 CH2) ( CH2CH2CH CH2)

[0046] 2 12 2 8 2 6 2 4  
 C C sp

( C CH) ( CH2C CH)  
 F Cl Br I

[0047]  
 [0048] C1 20 C1 6  
 C1 4

[0049] C1 20 C1 6 C1 3  
 2 2,2

[0050] 6 14 6 12 6 10  
 3 7

[0051] 5 12 5 10 5 6  
 5 7  
 5 10

1 2 3 4 O S N

[0052]

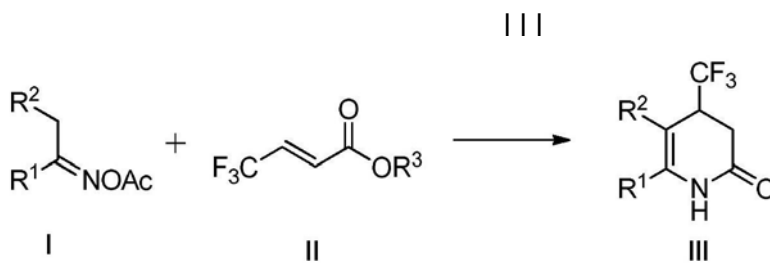
[0053]

(Z) (E) ) R S (Z) (E)

[0054]

[0055]

[0056]



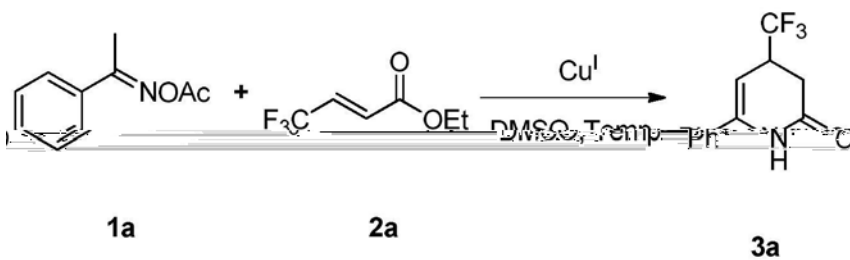
[0057]

I (0.20mmol) II (0.2 0.4mmol) CuCl  
 (0.02 0.04mmol, 10 20ml) Zn(0.02 0.05mmol, 10 25ml)  
 DMSO(2 3.5ml) 60 120 12 36  
 H<sub>2</sub>O(2.0ml)

1M HCl (aq, 3ml) (4 10ml)  
 (EA: PE 5: 1) III

[0058]

[0059]



[0060]

1a(0.20mmol) 2a(0.24mmol) CuCl (0.02mmol 10ml )  
 Zn(0.05mmol 25ml ) DMSO(3.5ml)  
 80 24  
 H<sub>2</sub>O(2.0ml) 1M HCl (aq, 3ml) (4 10ml)  
 (EA: PE 5: 1) 3a

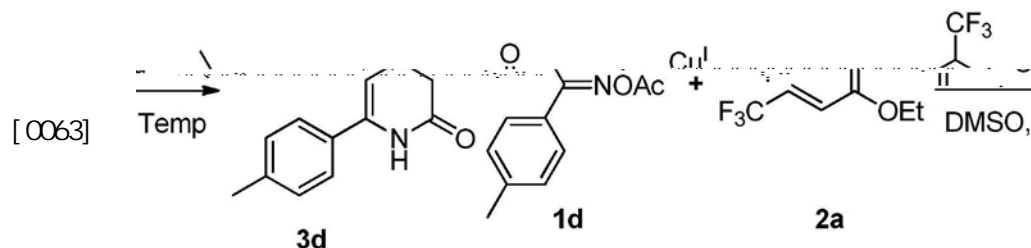
(35mg, 72 )

[0061]

mp 144 146 .<sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 7.82(s, 1H) , 7.48 7.41(m 5H) ,

5. 27(d, J 3.0 Hz, 1H), 3.45 3.34(m, 1H), 2.84 2.72(m, 2H).  $^{13}\text{C}$  NMR(100MHz,  $\text{CDCl}_3$ ) 168.7, 140.5, 134.0, 129.7, 129.0, 126.4(q, J 277.8 Hz), 125.4, 94.9(q, J 2.9 Hz), 37.9 (q, J 29.4 Hz), 29.8(q, J 2.5 Hz).  $^{19}\text{F}$  NMR(565MHz,  $\text{CDCl}_3$ ) 74.86(d, J 8.0 Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{11}\text{F}_3\text{NO}^+$ : 242.0787, found 242.0787.

[0062] 2



[0064] 1d(0.20mmol) 2a(0.4mmol) CuCl(0.03mmol) Zn(0.02mmol) DMSO(3ml)

100 14

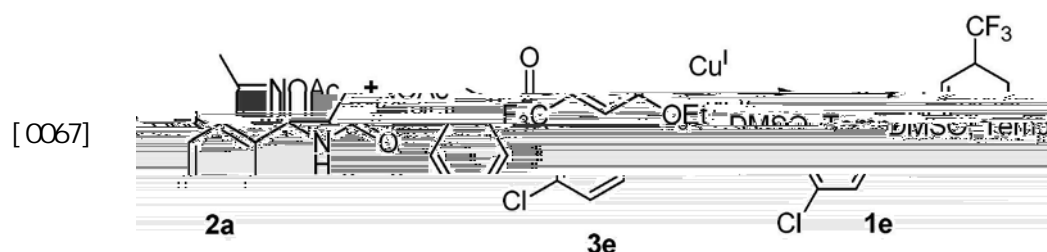
$\text{H}_2\text{O}$ (2.0ml) 1M HCl (aq, 3ml) (4 10ml)

(EA: PE 5:1)

3d(38mg, 75%)

[0065] mp 100-102.  $^1\text{H}$  NMR(400MHz,  $\text{CDCl}_3$ ) 7.92(s, 1H), 7.35(d, J 8.0 Hz, 2H), 7.22(d, J 8.0 Hz, 2H), 5.23(d, J 3.8 Hz, 1H), 3.41 3.34(m, 1H), 2.83 2.71(m, 2H), 2.38(s, 3H).  $^{13}\text{C}$  NMR(100MHz,  $\text{CDCl}_3$ ) 168.9, 140.5, 139.8, 131.2, 129.6, 126.5(q, J 277.7 Hz), 125.2, 94.1(q, J 2.9 Hz), 37.8(q, J 29.4 Hz), 29.8(q, J 2.5 Hz).  $^{19}\text{F}$  NMR(565MHz,  $\text{CDCl}_3$ ) 73.24(d, J 8.6 Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{13}\text{H}_{13}\text{F}_3\text{NO}^+$ : 256.0944, found 256.0946.

[0066] 3



[0068] 1e(0.20mmol) 2a(0.4mmol) CuCl(0.03mmol) Zn(0.02mmol) DMSO(3ml)

100 14

$\text{H}_2\text{O}$ (2.0ml) 1M HCl (aq, 3ml) (4 10ml)

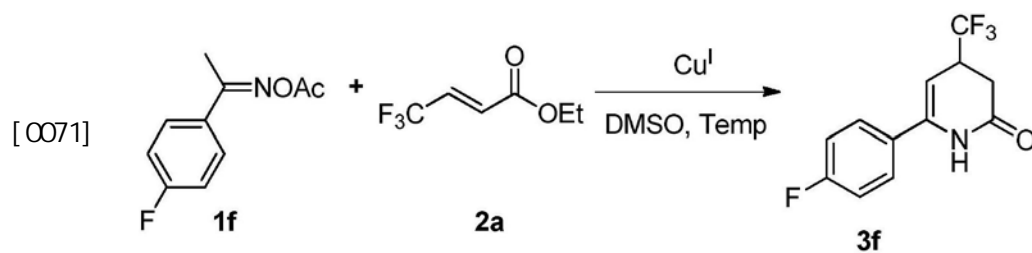
(EA: PE 5:1)

3e(39mg, 71%)

[0069] mp 196-198.  $^1\text{H}$  NMR(400MHz,  $\text{CDCl}_3$ ) 8.08(s, 1H), 7.43 7.38(m, 4H), 5.26(d, J 4.0 Hz, 1H), 3.44 3.33(m, 1H), 2.84 2.72(m, 2H).  $^{13}\text{C}$  NMR(100MHz,  $\text{CDCl}_3$ ) 168.9, 139.7, 135.8, 132.5, 129.3, 126.3(q, J 277.8 Hz), 126.8, 95.4(q, J 2.8 Hz), 37.9 (q, J 29.5 Hz), 29.7(q, J 2.5 Hz).  $^{19}\text{F}$  NMR(565MHz,  $\text{CDCl}_3$ ) 73.15(d, J 8.5 Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{10}\text{ClF}_3\text{NO}^+$ : 276.0398, found 276.0399.

[0070] 4





[0072] 1f (0.20mmol) 2a (0.4mmol) CuCl (0.03mmol) Zn (0.02mmol) DMSO (3mL)

100 14

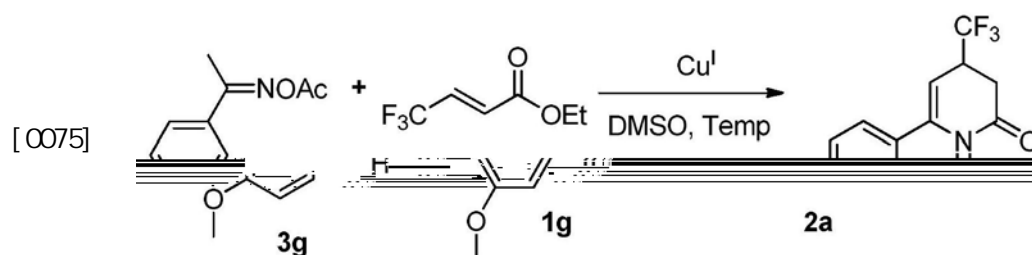
H<sub>2</sub>O (2.0mL) 1M HCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3f (36mg, 70%)

[0073] mp 122-124. <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) 8.09 (s, 1H), 7.48-7.44 (m, 2H), 7.13-7.09 (m, 2H), 5.21 (d, J = 3.6Hz, 1H), 3.44-3.32 (m, 1H), 2.83-2.71 (m, 2H). <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) 168.9, 163.5 (d, J = 250.1Hz), 139.8, 130.3 (d, J = 3.4Hz), 127.5 (d, J = 8.4Hz), 126.4 (q, J = 277.8Hz), 116.1 (d, J = 21.9Hz), 94.9 (q, J = 1.6Hz), 37.8 (q, J = 29.4Hz), 29.7 (q, J = 2.5Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.22 (s), 110.60 (m). HRMS: [M+H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>10</sub>F<sub>4</sub>NO<sup>+</sup>: 260.0693, found 260.0697.

[0074] 5



[0076] 1g (0.20mmol) 2a (0.4mmol) CuCl (0.03mmol) Zn (0.02mmol) DMSO (3mL)

100 14

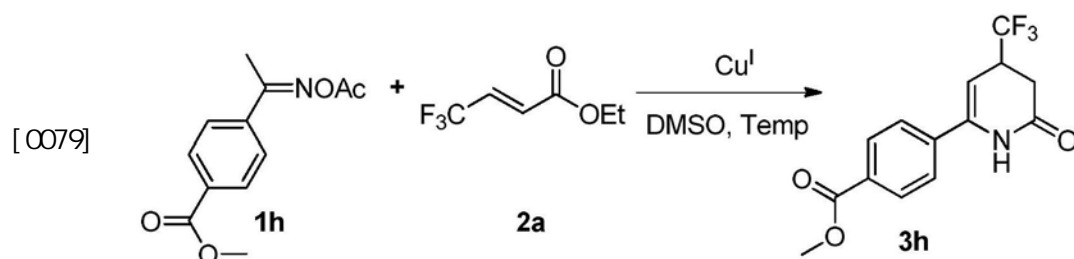
H<sub>2</sub>O (2.0mL) 1M HCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3g (41mg, 76%)

[0077] mp 96-98. <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) 7.76 (s, 1H), 7.40-7.38 (m, 2H), 6.94-6.92 (m, 2H), 5.17 (d, J = 4.1Hz, 1H), 3.82 (s, 3H), 3.43-3.31 (m, 1H), 2.83-2.71 (m, 2H). <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) 168.8, 160.7, 140.1, 126.7, 126.5, 126.4 (q, J = 277.7Hz), 114.3, 93.4 (q, J = 2.9Hz), 55.4, 37.8 (q, J = 29.4Hz), 29.9 (q, J = 2.5Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.28 (d, J = 6.8Hz). HRMS: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>NO<sup>+</sup>: 272.0893, found 272.0894.

[0078] 6



[0080] 1h (0.20mmol) 2a (0.4mmol) CuCl (0.02mmol) Zn (0.05mmol) DMSO (3mL)

100 24

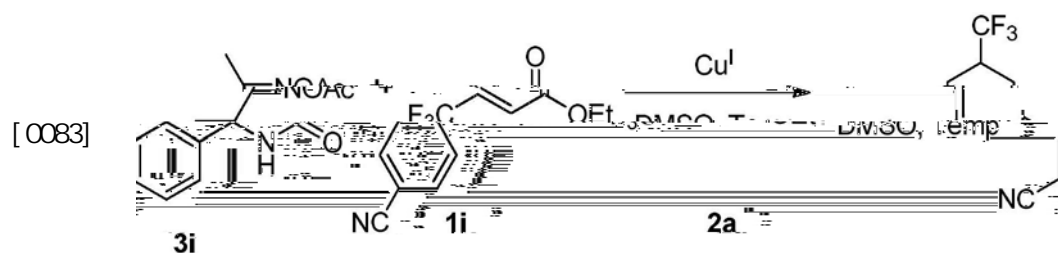
H<sub>2</sub>O (2.0mL) 1M HCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3h (45mg, 75%)

[0081] mp 122-124 °C. <sup>1</sup>H NMR (400MHz, CD<sub>3</sub>OD) 8.05 (d, J = 8.4Hz, 1H), 7.63 (d, J = 8.4Hz, 1H), 5.43 (d, J = 4.9Hz, 1H), 3.92 (s, 3H), 2.87 (dd, J = 16.8, 7.8Hz, 1H), 2.70 (dd, J = 16.8, 6.8Hz, 1H). <sup>13</sup>C NMR (100MHz, CD<sub>3</sub>OD) 171.2, 167.9, 142.2, 140.1, 132.0, 130.9, 128.2 (q, J = 277.3Hz), 127.2, 97.9 (q, J = 2.6Hz), 52.8, 38.6 (q, J = 29.2Hz), 30.5 (q, J = 2.4Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.45 (d, J = 8.8Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>13</sub>F<sub>3</sub>NO<sub>3</sub><sup>+</sup>: 300.0842, found 300.0845.

[0082] 7



[0084] 1i (0.20mmol) 2a (0.4mmol) CuCl (0.02mmol) Zn (0.05mmol) DMSO (3mL)

100 24

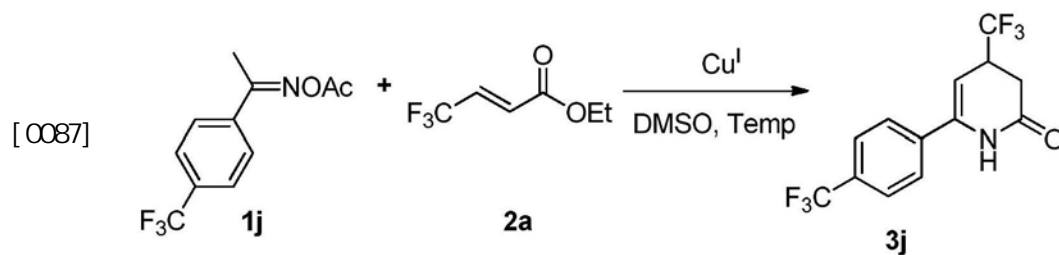
H<sub>2</sub>O (2.0mL) 1M HCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3i (30mg, 56%)

[0085] mp 148-150 °C. <sup>1</sup>H NMR (400MHz, CD<sub>3</sub>OD) 7.78 (d, J = 8.5Hz, 1H), 7.69 (d, J = 8.5Hz, 1H), 5.46 (d, J = 4.9Hz, 1H), 3.64 (s, 1H), 3.53 (m, 1H), 2.87 (dd, J = 16.9, 7.8Hz), 2.71 (dd, J = 16.9, 6.9Hz, 1H). <sup>13</sup>C NMR (100MHz, CD<sub>3</sub>OD) 169.7, 140.3, 138.7, 132.3, 126.8 (q, J = 277.5Hz), 117.9, 112.5, 97.4 (q, J = 2.7Hz), 37.2 (q, J = 29.3Hz), 29.1 (q, J = 2.5Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.58 (d, J = 8.8Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>N<sub>2</sub>O<sup>+</sup>: 267.0740, found 267.0736.

[0086] 8



[0088] 1j (0.20mmol) 2a(0.4mmol)  $\text{CuCl}$  (0.02mmol) Zn  
(0.04mmol) DMSO(3mL)

120 24

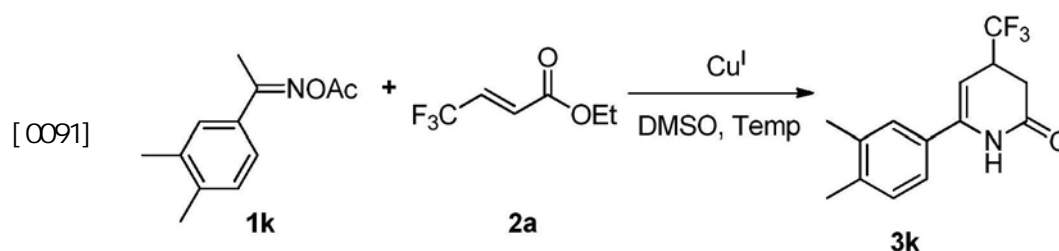
$\text{H}_2\text{O}$ (2.0mL) 1MHCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

**3j** (36mg, 56%)

[0089] mp 188-190.  $^1\text{H NMR}$ (400MHz,  $\text{CD}_3\text{OD}$ ) 7.74, 7.69(m, 4H), 5.43(d, J 4.9Hz, 1H), 3.64, 3.52(m, 1H), 2.88(dd, J 16.9, 7.8Hz, 1H), 2.71(dd, J 16.9, 6.9Hz, 1H).  $^{13}\text{C NMR}$ (100MHz,  $\text{CDCl}_3$ ) 169.8, 140.5, 138.1, 130.8(d, J 32.5Hz), 126.4, 126.8(q, J 277.3Hz), 125.3(q, J 3.8Hz), 124.0(q, J 266.0Hz), 96.6(q, J 2.6Hz), 37.2(q, J 29.2Hz), 29.1(q, J 2.3Hz).  $^{19}\text{F NMR}$ (565MHz,  $\text{CDCl}_3$ ) 63.23(s, 1H), 73.61(d, J 8.9Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{13}\text{H}_{10}\text{F}_6\text{NO}^+$ : 310.0661, found 310.0658.

[0090] 9



[0092] 1k(0.20mmol) 2a(0.4mmol)  $\text{CuCl}$  (0.02mmol) Zn  
(0.04mmol) DMSO(3mL)

120 24

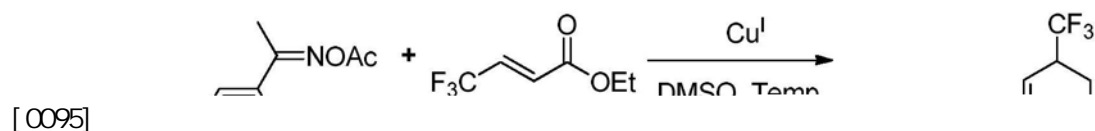
$\text{H}_2\text{O}$ (2.0mL) 1MHCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

**3k** (69mg, 74%)

[0093] mp 132-134.  $^1\text{H NMR}$ (400MHz,  $\text{CDCl}_3$ ) 7.68(s, 1H), 7.23, 7.16(m, 3H), 5.23(d, J 3.2Hz, 1H), 3.43, 3.32(m, 1H), 2.83, 2.71(m, 2H), 2.29, 3.28(m, 6H).  $^{13}\text{C NMR}$ (100MHz,  $\text{CDCl}_3$ ) 168.7, 140.4, 138.6, 137.4, 131.6, 130.2, 126.5(q, J 277.6Hz), 126.4, 122.6, 93.9(q, J 2.9Hz), 37.8(q, J 29.3Hz), 29.9(q, J 2.4Hz), 19.8, 19.6.  $^{19}\text{F NMR}$ (565MHz,  $\text{CDCl}_3$ ) 73.26(d, J 8.3Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{14}\text{H}_{15}\text{F}_3\text{NO}^+$ : 270.1100, found 270.1102.

[0094] 10



[0096] 1l (0.20mmol) 2a(0.4mmol) CuCl (0.02mmol) Zn  
(0.04mmol) DMSO(3mL)

100 20

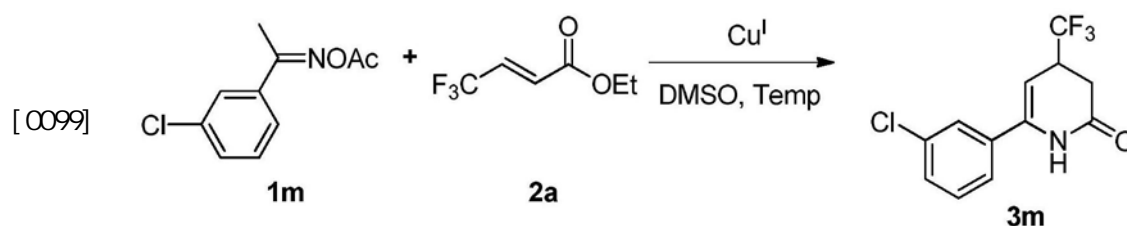
H<sub>2</sub>O(2.0mL) 1MHCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3l (45mg, 75 )

[0097] <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 8.05(s, 1H), 7.05 7.03(m, 1H), 6.96 6.95(m, 1H), 6.90 6.87(m, 1H), 5.19(d, J = 3.9Hz, 1H), 3.93(s, 1H), 3.90(s, 3H), 3.43 3.31(m, 1H), 2.82 2.70(m, 2H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 169.8, 150.3, 149.3, 140.4, 126.8, 126.5 (q, J = 277.7Hz), 118.1, 111.2, 108.5, 93.6(q, J = 2.6Hz), 56.0, 59.9, 37.8(q, J = 29.2Hz), 29.9(q, J = 2.2Hz). <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 73.22(d, J = 8.8Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>15</sub>F<sub>3</sub>NO<sub>3</sub><sup>+</sup>: 302.0999, found 302.0999.

[0098] 11



[0100] 1m(0.20mmol) 2a(0.3mmol) CuCl (0.03mmol) Zn  
(0.03mmol) DMSO(3mL)

100 22

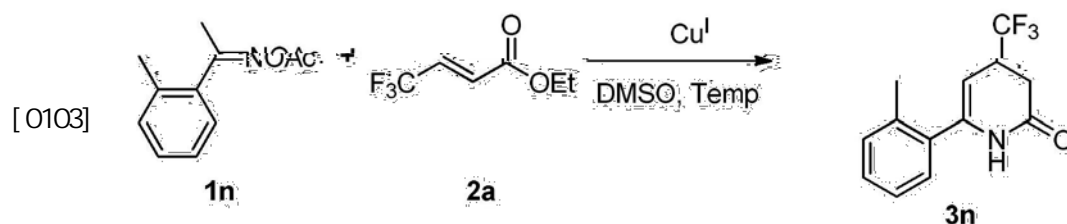
H<sub>2</sub>O(2.0mL) 1MHCl (aq, 3mL) (4 10mL)

(EA: PE 5: 1)

3m(39mg, 71 )

[0101] mp 128 130. <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 8.07(s, 1H), 7.47 7.46(m, 1H), 7.41 7.35(m, 3H), 5.29(d, J = 2.8Hz, 1H), 3.46 3.34(m, 1H), 2.84 2.72(m, 2H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 168.8, 139.5, 135.8, 135.1, 130.3, 129.8, 126.3(q, J = 277.7Hz), 125.8, 123.5, 96.0(q, J = 2.9Hz), 37.8(q, J = 29.5Hz), 29.7(q, J = 2.5Hz). <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 73.13(d, J = 8.7Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>10</sub>ClF<sub>3</sub>NO<sup>+</sup>: 276.0398, found 276.0394.

[0102] 12



[0104] 1n(0.20mmol) 2a(0.4mmol) CuCl(0.03mmol) Zn  
(0.03mmol) DMSO(3mL)

110 22

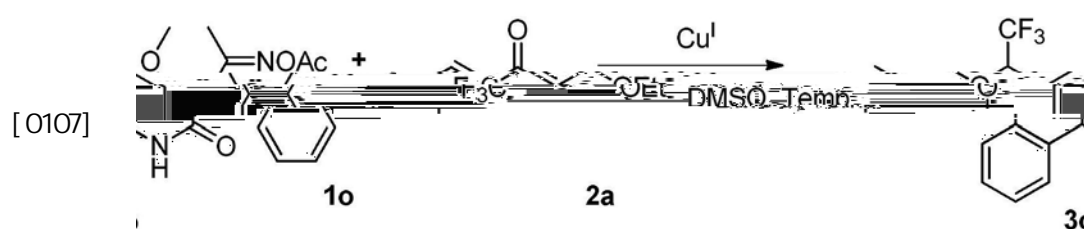
H<sub>2</sub>O(2.0mL) 1MHCl(aq, 3mL) (4 10mL)

(EA: PE 5:1)

3n(39mg, 76%)

[0105] mp 124-126 °C. <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 7.32-7.19(m, 1H), 7.16(s, 1H), 4.94(d, J = 3.8Hz, 1H), 3.42-3.30(m, 1H), 2.84-2.72(m, 2H), 2.35(s, 3H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 167.9, 140.7, 135.9, 134.4, 130.7, 129.5, 128.7, 126.5(q, J = 277.9Hz), 126.2, 96.6(q, J = 2.7Hz), 37.8(q, J = 29.3Hz), 29.6(q, J = 2.5Hz), 19.5. <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 73.22(d, J = 6.4Hz). HRMS: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>NO<sup>+</sup>: 256.0944, found 256.0948.

[0106] 13



[0108] 1o(0.20mmol) 2a(0.4mmol) CuCl(0.03mmol) Zn  
(0.04mmol) DMSO(3mL)

100 22

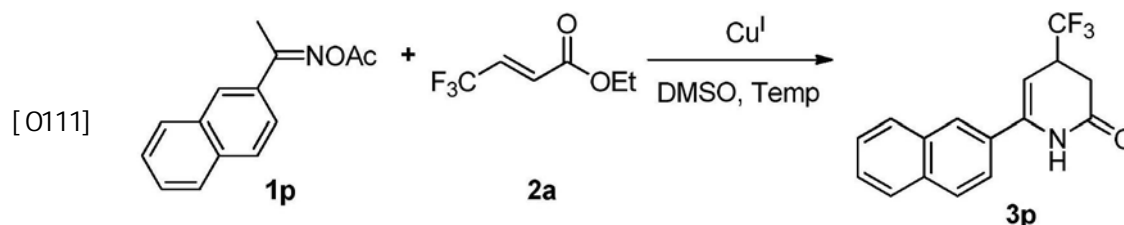
H<sub>2</sub>O(2.0mL) 1MHCl(aq, 3mL) (4 10mL)

(EA: PE 5:1)

3o(40mg, 74%)

[0109] <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 7.71(s, 1H), 7.35-7.31(m, 1H), 7.05-7.03(m, 1H), 6.98-6.94(m, 2H), 5.27(d, J = 2.9Hz, 1H), 3.84(s, 3H), 3.44-3.33(m, 1H), 2.84-2.72(m, 2H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 168.6, 160.0, 140.4, 135.5, 130.1, 126.4(q, J = 279.4Hz), 117.7, 115.4, 110.9, 95.0(q, J = 2.9Hz), 55.4, 37.9(q, J = 29.4Hz), 29.8(q, J = 2.5Hz). <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 73.22(d, J = 4.5Hz). HRMS: [M+H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>13</sub>F<sub>3</sub>NO<sub>2</sub><sup>+</sup>: 272.0893, found 272.0896.

[0110] 14



[0112] 1p(0.20mmol) 2a(0.4mmol) CuCl(0.03mmol) Zn  
(0.04mmol) DMSO(3mL)

100 22

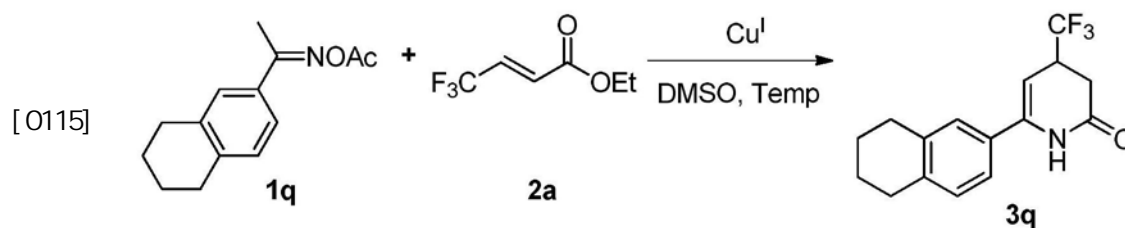
H<sub>2</sub>O(2.0mL) 1MHCl(aq, 3mL) (4 10mL)

(EA: PE 5:1)

3p(46mg, 79%)

[0113] mp 192-194.  $^1\text{H NMR}$  (400 MHz,  $\text{CD}_3\text{OD}$ ) 8.01 (s, 1H), 7.93-7.86 (m, 4H), 7.62-7.60 (m, 1H), 7.54-7.50 (m, 2H), 5.45 (d, J = 4.9 Hz, 1H), 3.62-3.51 (m, 1H), 2.90 (dd, J = 16.8, 7.8 Hz, 1H), 2.73 (dd, J = 16.8, 6.7 Hz, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CD}_3\text{OD}$ ) 171.4, 142.8, 135.1, 134.5, 132.9, 129.6, 129.5, 128.3 (q, J = 277.6), 128.7, 127.9, 127.7, 126.1, 124.6, 96.6 (q, J = 2.7 Hz), 38.6 (q, J = 29.0 Hz), 30.7 (q, J = 2.5 Hz).  $^{19}\text{F NMR}$  (565 MHz,  $\text{CDCl}_3$ ) 73.56 (d, J = 8.8 Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{14}\text{H}_{13}\text{F}_3\text{NO}^+$ : 268.0944, found 268.0945.

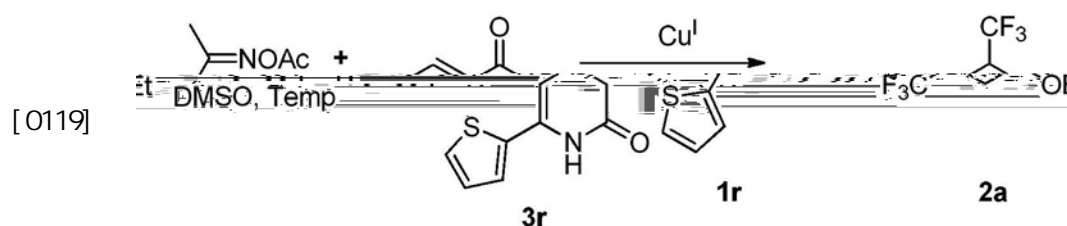
[0114]



[0116] 1q (0.20 mmol) 2a (0.3 mmol) CuCl (0.02 mmol) Zn (0.04 mmol) DMSO (3 mL)  
100 23  
 $\text{H}_2\text{O}$  (2.0 mL) 1M HCl (aq, 3 mL) (4 10 mL)  
(EA: PE 5:1) 3q (42 mg, 71%)

[0117] mp 188-190.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ) 7.56 (s, 1H), 7.17-7.15 (m, 2H), 7.11-7.09 (m, 1H), 5.22 (d, J = 3.3 Hz, 1H), 3.43-3.31 (m, 1H), 2.83-2.71 (m, 6H), 1.83-1.79 (m, 4H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ) 168.6, 140.5, 139.2, 138.0, 131.2, 129.8, 126.5 (q, J = 277.6), 125.9, 122.3, 93.9 (q, J = 2.8 Hz), 37.9 (q, J = 29.3 Hz), 29.9 (q, J = 2.6 Hz), 29.4, 29.2, 22.9 (d, J = 2.3 Hz).  $^{19}\text{F NMR}$  (565 MHz,  $\text{CDCl}_3$ ) 73.26 (d, J = 8.5 Hz). HRMS:  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{16}\text{H}_{17}\text{F}_3\text{NO}^+$ : 296.1257, found 296.1256.

[0118]



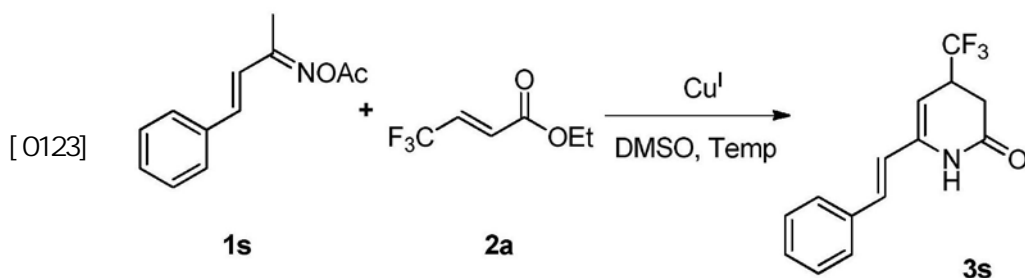
[0120] 1r (0.20 mmol) 2a (0.3 mmol) CuCl (0.02 mmol) Zn (0.04 mmol) DMSO (3 mL)  
100 24  
 $\text{H}_2\text{O}$  (2.0 mL) 1M HCl (aq, 3 mL) (4 10 mL)  
(EA: PE 5:1) 3r (28 mg, 57%)

[0121] mp 130-132.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ) 8.14 (s, 1H), 7.32-7.30 (m, 1H), 7.27-7.26 (m, 1H), 7.08-7.05 (m, 1H), 5.34 (d, J = 3.9 Hz, 1H), 3.42-3.35 (m, 1H), 2.86-2.73 (m, 2H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ) 168.6, 136.7, 134.8, 127.8, 126.3 (q, J = 277.6 Hz), 126.3, 124.4, 94.1 (q, J = 2.9 Hz), 37.8 (q, J = 29.6 Hz), 29.9 (q, J = 2.4 Hz).  $^{19}\text{F NMR}$

(565MHz, CDCl<sub>3</sub>) 73.11(d, J 8.1Hz). HRMS: [M-H]<sup>+</sup>calculated for C<sub>10</sub>H<sub>9</sub>F<sub>3</sub>NOS<sup>+</sup>: 248.0351, found 248.0350.

[0122]

17



[0124] 1s (0.20mmol) 2a (0.2mmol) CuCl (0.02mmol) Zn (0.04mmol) DMSO (3mL)

100

24

H<sub>2</sub>O (2.0mL)

1MHCl (aq, 3mL)

(4 10mL)

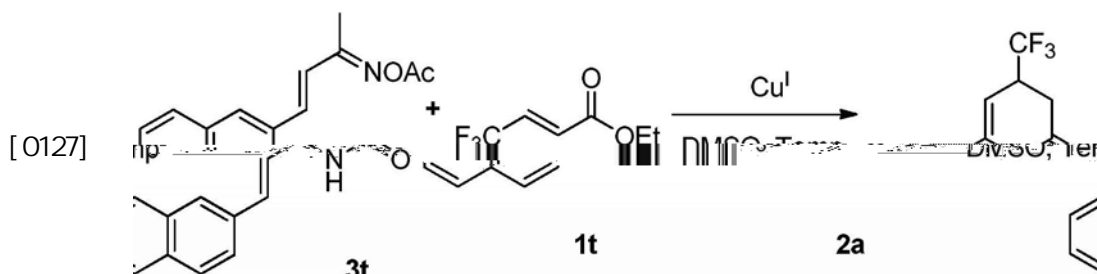
(EA: PE 5: 1)

3s (43mg, 81%)

[0125] mp 168-170. <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) 8.32(s, 1H), 7.46-7.44(m, 2H), 7.39-7.35(m, 2H), 7.32-7.29(m, 1H), 6.83(d, J 16.6Hz, 1H), 6.57(d, J 16.6Hz, 1H), 5.16(d, J 4.1Hz, 1H), 3.45-3.32(m, 1H), 2.84-2.72(m, 2H). <sup>13</sup>C NMR (100MHz, CDCl<sub>3</sub>) 168.7, 138.1, 135.6, 129.0, 128.8, 128.7, 126.8, 126.2 (q, J 277.9), 121.4, 99.2 (q, J 2.9Hz), 37.9 (q, J 29.5Hz), 30.0 (q, J 2.4Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.09 (d, J 7.8Hz). HRMS: [M-H]<sup>+</sup>calculated for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>NO<sup>+</sup>: 268.0944, found 268.0945.

[0126]

18



[0128] 1t (0.20mmol) 2a (0.25mmol) CuCl (0.02mmol) Zn (0.05mmol) DMSO (3.5mL)

80

24

H<sub>2</sub>O (2.0mL)

1MHCl (aq, 3mL)

(4 10mL)

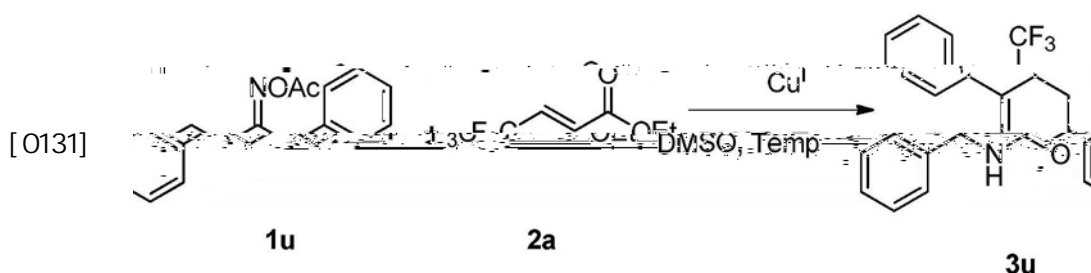
(EA: PE 5: 1)

3t (49mg, 77%)

[0129] mp 186-188. <sup>1</sup>H NMR (400MHz, (CD<sub>3</sub>)<sub>2</sub>CO) 8.77(s, 1H), 7.95-7.88(m, 4H), 7.80-7.78(m, 1H), 7.52-7.50(m, 2H), 7.35(d, J 16.7Hz, 1H), 6.99(d, J 16.6Hz, 1H), 5.32(d, J 4.4Hz, 1H), 3.68-3.58(m, 1H), 2.84(dd, J 15.6, 9.0Hz, 1H), 2.65(dd, J 16.7, 6.7Hz, 1H). <sup>13</sup>C NMR (100MHz, (CD<sub>3</sub>)<sub>2</sub>CO) 168.4, 140.4, 135.0, 134.7, 134.4, 129.9 (d, J 2.0Hz), 129.5, 129.1, 128.7, 128.2, 128.1 (q, J 277.2Hz), 127.5, 127.3, 124.4, 123.5 (q, J 5.3Hz), 99.5 (q, J 3.9Hz), 38.4 (q, J 28.6Hz), 30.7 (q, J 2.0Hz). <sup>19</sup>F NMR (565MHz, CDCl<sub>3</sub>) 73.72(s). HRMS: [M-H]<sup>+</sup>calculated for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>NO<sup>+</sup>: 318.1100, found

318.1101.

[0130] 19



[0132]                      1u(0.20mmol)                      2a(0.25mmol)    CuCl (0.02mmol)    Zn  
(0.05mmol)    DMSO(3.5mL)

80                      36

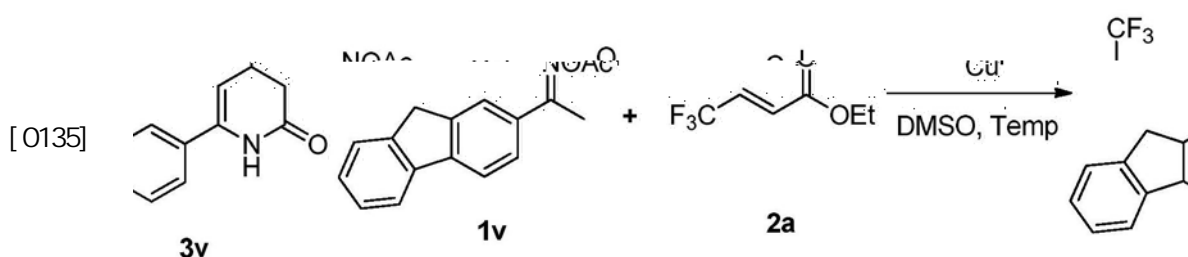
H<sub>2</sub>O(2.0mL)                      1MHCl (aq, 3mL)                      (4 10mL)

(EA: PE 5: 1)

3u(20mg, 31 %)

[0133]                      mp 142-144 °C. <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>) 7.26-7.25(m, 2H), 7.23(s, 1H), 7.16-7.13(m, 6H), 7.06-7.05(m, 2H), 3.55-3.46(m, 1H), 3.07-2.94(m, 2H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 167.8, 138.2, 138.0, 135.0, 129.8, 129.0, 128.7, 128.6, 128.2, 126.8(q, J = 265.1), 110.9, 108.6, 43.2(q, J = 27.8Hz), 30.8(q, J = 2.4Hz, 1H). <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 70.37(d, J = 8.6Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>18</sub>H<sub>15</sub>F<sub>3</sub>NO<sup>+</sup>: 318.1100, found 318.1098.

[0134] 20



[0136]                      1v(0.20mmol)                      2a(0.25mmol)    CuCl (0.02mmol)    Zn  
(0.05mmol)    DMSO(3.5mL)

80                      30

H<sub>2</sub>O(2.0mL)                      1MHCl (aq, 3mL)                      (4 10mL)

(EA: PE 5: 1)

3v(47mg, 75 %)

[0137]                      mp 180-182 °C. <sup>1</sup>H NMR(400MHz, DMSO) 9.88(s, 1H), 7.94-7.91(m, 2H), 7.77(s, 1H), 7.62-7.56(m, 2H), 7.42-7.32(m, 2H), 5.32(d, J = 4.8Hz, 1H), 3.94(s, 2H), 3.73-3.65(m, 1H), 2.82(dd, J = 16.6, 7.8Hz, 1H), 2.56(dd, J = 16.7, 6.4Hz, 1H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>) 168.3, 143.4, 143.2, 142.1, 141.6, 140.4, 132.5, 127.2, 127.1(q, J = 277.6), 126.9, 125.2, 124.7, 122.7, 120.4, 120.0, 93.6(q, J = 2.1Hz), 36.4, 36.3(q, J = 27.9Hz), 29.7(q, J = 1.8Hz). <sup>19</sup>F NMR(565MHz, CDCl<sub>3</sub>) 73.24(d, J = 8.9Hz). HRMS: [M-H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>15</sub>F<sub>3</sub>NO<sup>+</sup>: 330.1100, found 330.1101.

[0138] 21

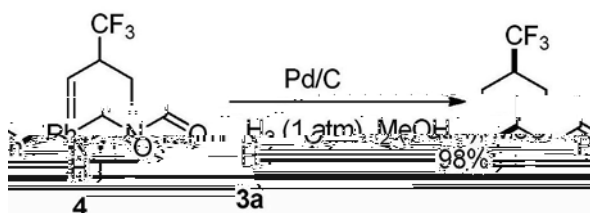


[0139]

3a

4

[0140]



[0141]

3a (0.2 mmol)

(30 mL)

10 Pd/C

(100 mg)

12 h.

4

[0142]

(45 mg, 98%) . mp 124-126 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 7.42-7.36 (m, 4H),

7.35-7.30 (m, 1H), 4.60 (dd, J = 11.6, 4.1 Hz, 1H), 3.03-2.96 (m, 1H), 2.64-2.58 (m, 1H),

2.51-2.43 (m, 1H), 2.27-2.23 (m, 1H), 1.67 (dd, J = 24.8, 12.7 Hz, 1H). <sup>13</sup>C NMR (100 MHz,CDCl<sub>3</sub>) 172.2, 142.9, 130.0, 129.3, 128.1 (q, J = 275.8 Hz), 127.5, 57.5, 38.6 (q, J28.6 Hz), 32.4 (d, J = 2.6 Hz), 30.9 (d, J = 2.4 Hz). HRMS: [M+H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>13</sub>F<sub>3</sub>NO

+: 244.0944, found 244.0945.

[0143]