



(12)发明专利

(10)授权公告号

(45)授权公告日

---

(21)申请号 201910374991.2

审查员

(22)申请日 2019.05.07

(65)同一申请的已公布的文献号  
申请公布号 CN 110015996 A

(43)申请公布日 2019.07.16

(73)专利权人  
地址 453000 46

(72)发明人

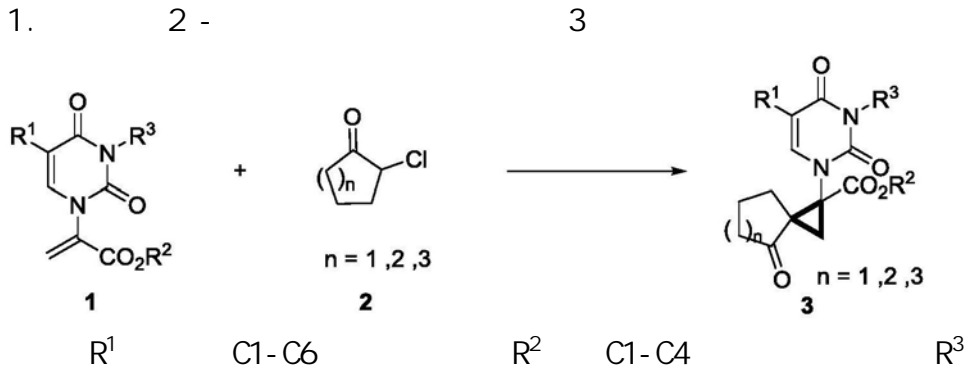
(74)专利代理机构  
( ) 51244  
代理人

(51)Int.Cl.  
C07D 239/54(2006.01)  
C07D 239/553(2006.01)

---

(54)发明名称  
2 -

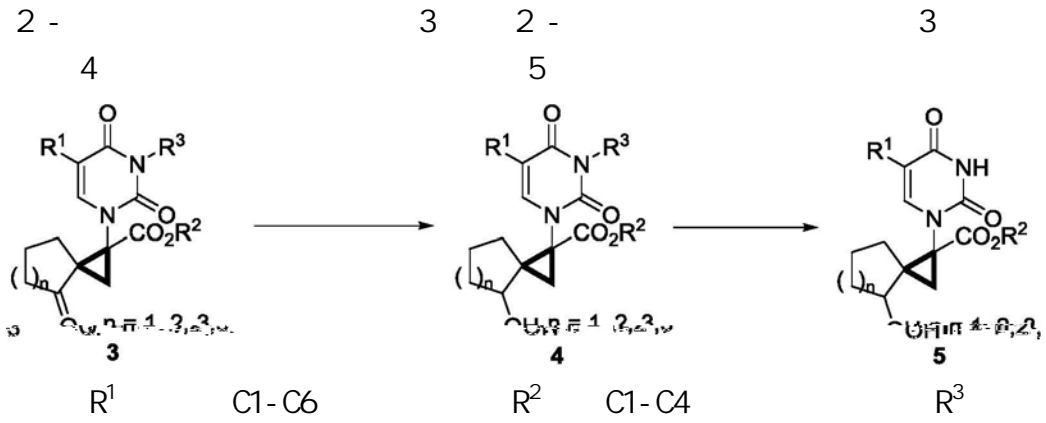
(57)摘要  
2 -



2. 1 2 - 3                      1 - 2                      3                      R<sup>1</sup>

3. 1 2 - 3                      1 - 2                      3                      -

4. 2 - 3                      2                      1: 1.5: 1.5                      5                      1



5. 4 2 - 5

/

一种合成2-螺环基取代三元碳环核苷的方法

技术领域

[0001]

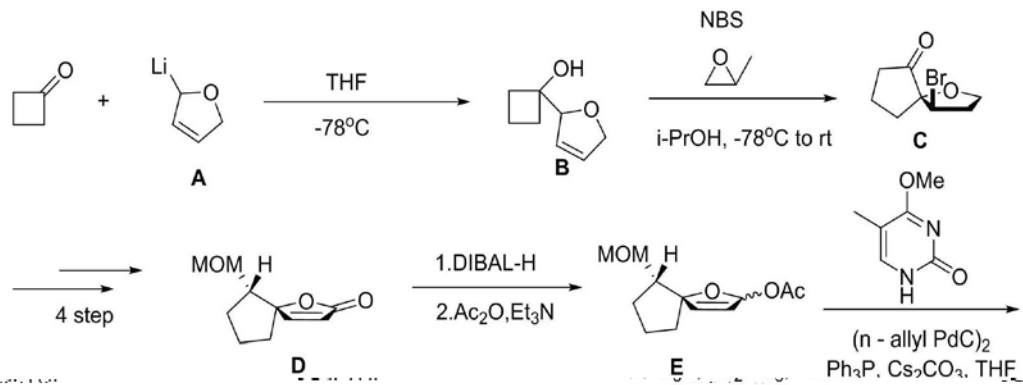
2 -

背景技术

[0002]

[0003] 4

[0003] 1 G F



[0004]

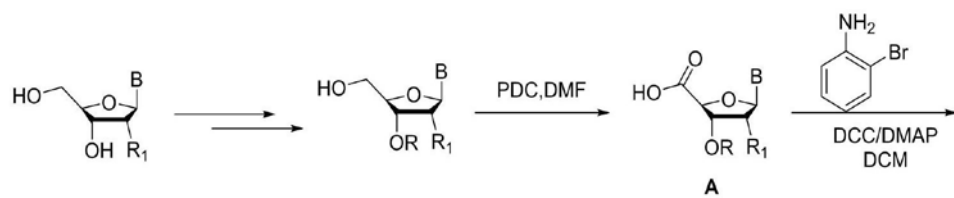


[0005]

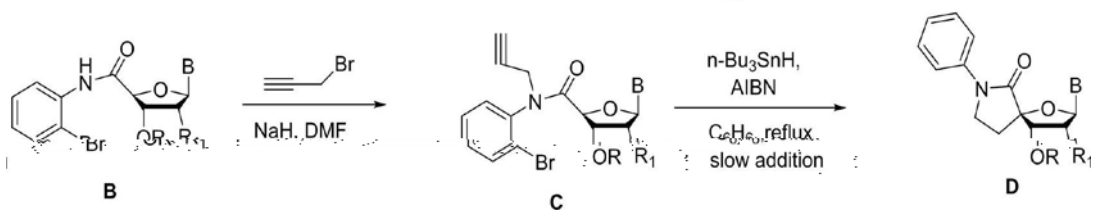
C-N

[0006] 2

D



[0007]



B = T, R = TBS, R<sub>1</sub> = H

[0008]

n-Bu<sub>3</sub>SnH

[0009]

## 发明内容

[0010]

2 -

[0011]

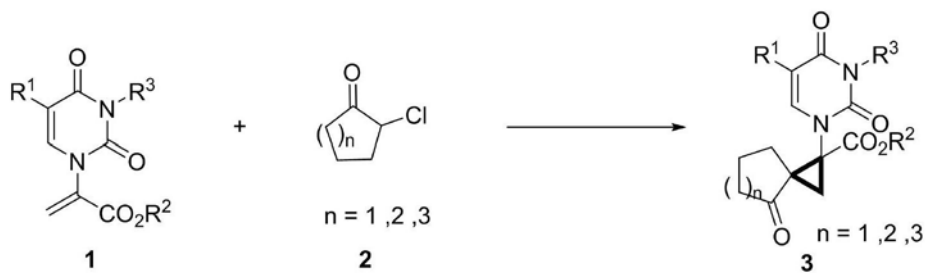
2 -

1 -

2

3

[0012]



[0013]

R<sup>1</sup>

C1-C6

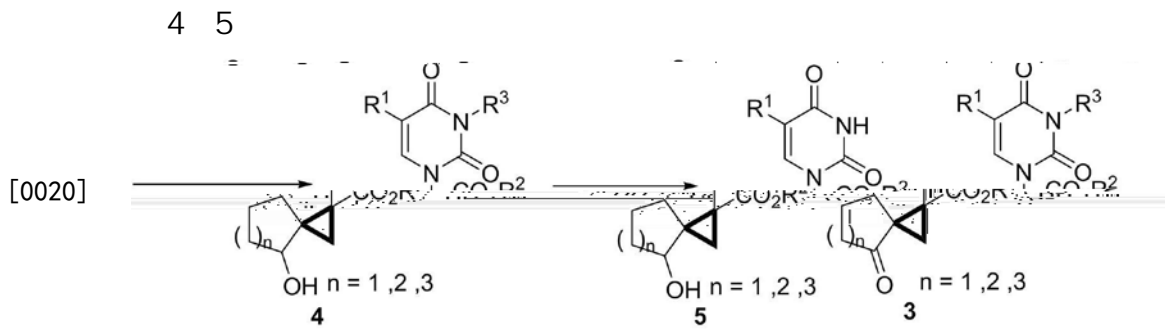
R<sup>2</sup>

C1-C4

R<sup>3</sup>

[0018]

[0019]



[0021]



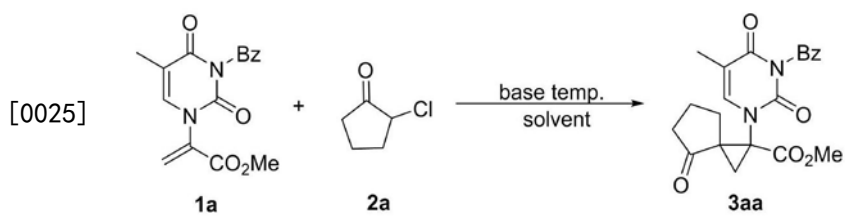
[0022]

[0023]

84

具体实施方式

[0024]



[0026]

[0027]

[0028] <sup>a</sup> 1a(0.1mmol) 2a(1.5equiv) (1.5equiv)  
<sup>b</sup> 5 (1.2equiv)<sup>d</sup> (2.0equiv)<sup>e</sup>1h<sup>f</sup>0.5h  
 [0029] (entries 1-6)

-20  
 [0030]  
 [0031] 1a(0.1mmol) 1.5eq(0.15mmol)  
 1mL -20 10 - 2a(0.15mmol)  
 0.5h TLC

3aa 83

[0032] 3aa: White solid, mp. 227.2-232.5 33mg, 83% yield

[0033] <sup>1</sup>H NMR(400MHz, CDCl<sub>3</sub>): 7.90-7.88(d, J = 8.0Hz, 2H), 7.62(d, J = 7.6Hz, 1H), 7.48(t, J = 8.0Hz, 2H), 7.06(d, J = 3.2Hz, 1H), 3.77(s, 3H), 2.44(m, 1H), 2.36-2.27(m, 1H), 2.27-2.17(m, 2H), 2.08(m, 2H), 2.01-1.95(m, 4H), 1.89(s, 1H). <sup>13</sup>C NMR(100MHz, CDCl<sub>3</sub>): 212.1, 167.7, 139.4, 135.0, 131.5, 130.7, 129.1, 111.5, 77.3, 53.6, 50.4, 42.6, 38.9,

28.5, 26.2, 20.2, 12.7. HRMS(ESI-TOF): exact mass calcd for  $C_{21}H_{20}N_2NaO_6(MNa)^+$  requires  $m/z$  419.1214, found  $m/z$  419.1206.

[0034] 2

[0035] 10mL - (3- -5- ) 1b 1.5eq  
 (O.15mmol) 1mL -20 10 - 2a  
 (O.15mmol) 0.5h TLC

3ba 85

[0036] 3

[0037] 10mL - (3- -5- ) 1c 1.5eq  
 (O.15mmol) 1mL -20 10 - 2a  
 (O.15mmol) 0.5h TLC

3ca 83

[0038] 4

[0039] 10mL - (3- -5- ) 1d 1.5eq  
 (O.15mmol) 1mL -20 10 - 2a  
 (O.15mmol) 0.5h TLC

3da 83

[0040] 5

[0041] 10mL - (3- -5- ) 1f 1.5eq  
 (O.15mmol) 1mL -20 10 - 2a  
 (O.15mmol) 0.5h TLC

3fa 79

[0042] 3fa: White solid, mp. 180.0-185.4 31mg, 79 yield

[0043]  $^1H$  NMR(600MHz,  $CDCl_3$ ): 6.94-6.92(m 1H), 3.74(s, 3H), 2.65-2.44(m 2H), 2.33-2.18(m 3H), 2.03(d, J = 4.8Hz, 1H), 1.93-1.92(m 3H), 1.89(d, J = 5.4Hz, 1H), 1.68(s, 1H), 1.56(s, 9H).  $^{13}C$  NMR(100MHz,  $CDCl_3$ ): 211.2, 167.8, 147.7, 139.0, 111.1, 86.5, 53.6, 50.6, 42.4, 38.8, 28.6, 27.5, 26.3, 20.2, 12.7. HRMS(ESI-TOF): exact mass calcd for  $C_{19}H_{24}N_2NaO_7(MNa)^+$  requires  $m/z$  415.1476, found  $m/z$  415.1471.

[0044] 6

[0045] 10mL - (3- -5- ) 1i 1.5eq  
 (O.15mmol) 1mL -20 10 -  
 2a(O.15mmol) 0.5h TLC

3ia 81

[0046] 3ia Colorless oil, 33mg, 81 yield

[0047]  $^1\text{H NMR}$ (400MHz,  $\text{CDCl}_3$ ): 7.88(d, J 7.6Hz, 2H), 7.61(d, J 7.2Hz, 1H), 7.47(d, J 7.6Hz, 2H), 6.98(s, 1H), 3.77(s, 3H), 2.47-2.37(m 3H), 2.35-2.18(m 3H), 2.14-2.08(m 2H), 1.96(d, J 5.2Hz, 1H), 1.90-1.85(m 1H), 1.17(t, J 7.2Hz, 3H).  $^{13}\text{C NMR}$ (100MHz,  $\text{CDCl}_3$ ): 212.1, 168.6, 167.7, 138.5, 135.0, 131.5, 130.6, 129.1, 117.1, 53.6, 50.5, 42.6, 38.9, 28.5, 26.2, 20.3, 20.1, 12.5. HRMS(ESI-TOF): exact mass calcd for  $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_6(\text{M}+\text{Na})^+$  requires  $m/z$  433.1370, found  $m/z$  433.1365.

[0048] 7

[0049] 10mL - (3- -5- ) 1j 1.5eq  
 (0.15mmol) 1mL -20 10 - 2a  
 (0.15mmol) 0.5h TLC

3j a 68

[0050] 8

[0051] 10mL - (3- -5- ) 1a 1.5eq  
 (0.15mmol) 1mL -20 10 - 2b  
 (0.15mmol) 12h TLC

3ab 66

[0052] 9

[0053] 10mL - (3- -5- ) 1a 1.5eq  
 (0.15mmol) 1mL -20 10 0.15mmol -  
 2c 0.5h TLC

3ac 72

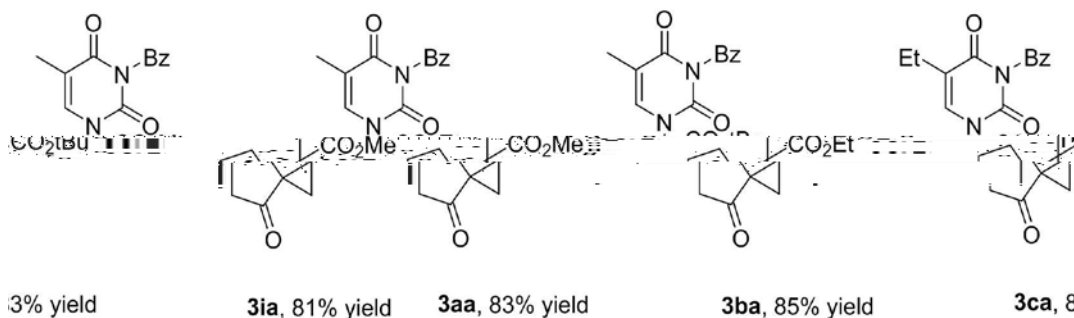
[0054] 3ac: White solid, mp. 213.0-218.4 31mg, 72% yield

[0055]  $^1\text{H NMR}$ (400MHz,  $\text{CDCl}_3$ ): 7.87(d, J 8.0Hz, 2H), 7.62(t, J 7.2Hz, 1H), 7.48(t, J 8.0Hz, 2H), 7.04(s, 1H), 3.76(s, 3H), 2.82(t, J 12.0Hz, 1H), 2.34-2.29(m 1H), 2.21-2.15(m 3H), 2.00-1.73(m 8H), 1.38-1.25(m 2H).  $^{13}\text{C NMR}$ (100MHz,  $\text{CDCl}_3$ ): 207.6, 168.4, 167.6, 150.5, 139.7, 135.0, 131.5, 130.6, 129.1, 111.4, 53.7, 51.3, 46.1, 44.0, 30.6, 27.5, 27.1, 26.4, 25.6, 12.6. HRMS(ESI-TOF): exact mass calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_2\text{NaO}_6(\text{M}+\text{Na})^+$  requires  $m/z$  447.1527, found  $m/z$  447.1532.

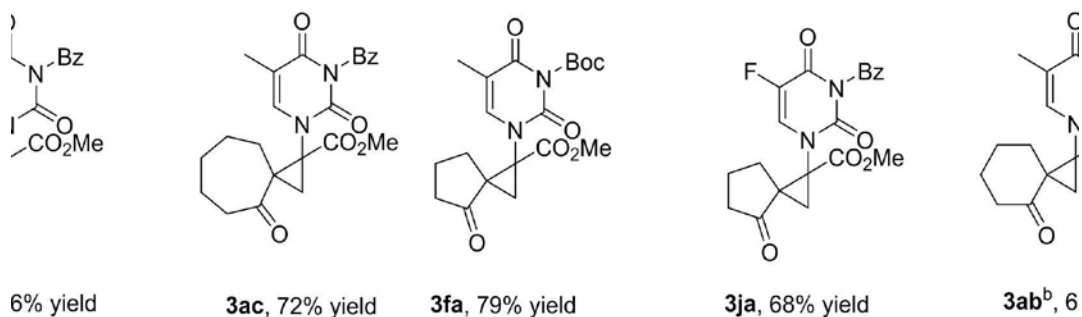
[0056] 10

[0057] 2-9





[0058]



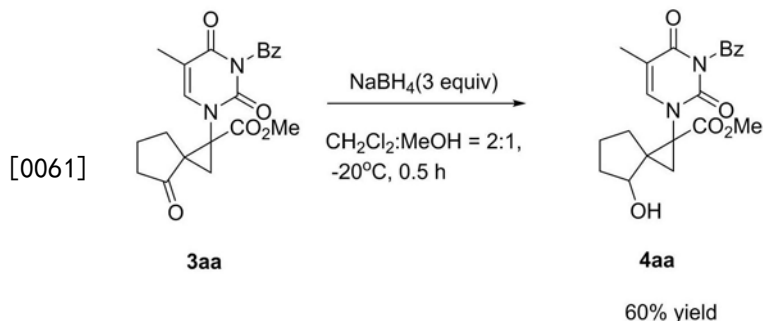
[0059]      11

[0060]      10mL      **3aa** (39.6mg, 0.1mmol)

2:1      1.5mL      -20      10

(11.3mg, 0.3mmol)      -20      30      TLC

0.5mL      **4aa** (24mg, 0.06mmol)

[0062]      **4aa**: White solid, mp. 175.5-180.1      24mg, 60 yield

[0063]      <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>): 7.97-7.95(m, 2H), 7.66-7.63(m, 1H), 7.50(t, J = 8.0Hz, 2H), 7.13(s, 1H), 3.74(s, 3H), 3.54(d, J = 3.2Hz, 1H), 2.30(s, 1H), 2.13-2.02(m, 1H), 1.99-1.94(m, 3H), 1.90-1.70(m, 6H), 1.34(d, J = 5.2Hz, 1H). <sup>13</sup>C NMR (150MHz, CDCl<sub>3</sub>): 169.2, 167.8, 153.5, 139.8, 135.3, 131.2, 130.5, 129.3, 112.8, 77.4, 53.3, 49.8, 47.0, 32.9, 27.9, 26.6, 20.9, 12.6. HRMS (ESI-TOF): exact mass calcd for C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>NaO<sub>6</sub> (MNa)<sup>+</sup> requires m/z 421.1370, found m/z 421.1366.

[0064]      12

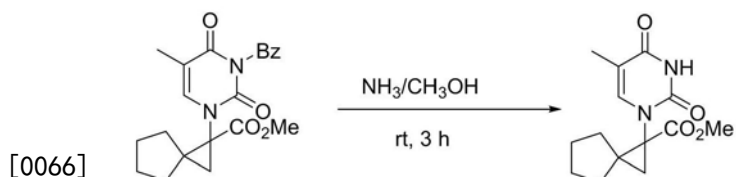
[0065]      10mL      **4aa** (39.8mg, 0.1mmol)

(      1mol /L) 1mL

/  
3

TLC

5aa (24mg, 0.08mmol)



[0067]

[0068] 5aa: White solid, mp. 233.0-238.4 26mg, 87% yield

[0069]  $^1\text{H NMR}$  (400MHz,  $\text{CDCl}_3$ ): 9.36(s, 1H), 7.00(s, 1H), 4.23(s, 1H), 3.71(s, 3H), 3.52(d, J = 3.2Hz, 1H), 2.38(s, 1H), 2.11(s, 1H), 1.95-1.72(m, 8H), 1.69(d, J = 5.3Hz, 1H), 1.27(d, J = 5.2Hz, 1H).  $^{13}\text{C NMR}$  (150MHz,  $\text{CDCl}_3$ ): 169.4, 163.4, 154.3, 140.1, 112.7, 77.2, 53.3, 49.3, 47.0, 32.8, 27.9, 26.9, 20.9, 12.5. HRMS (ESI-TOF): exact mass calcd for  $\text{C}_{14}\text{H}_{18}\text{N}_2\text{NaO}_5(\text{M}+\text{Na})^+$  requires  $m/z$  317.1108, found  $m/z$  317.1107.

[0070]