Figures

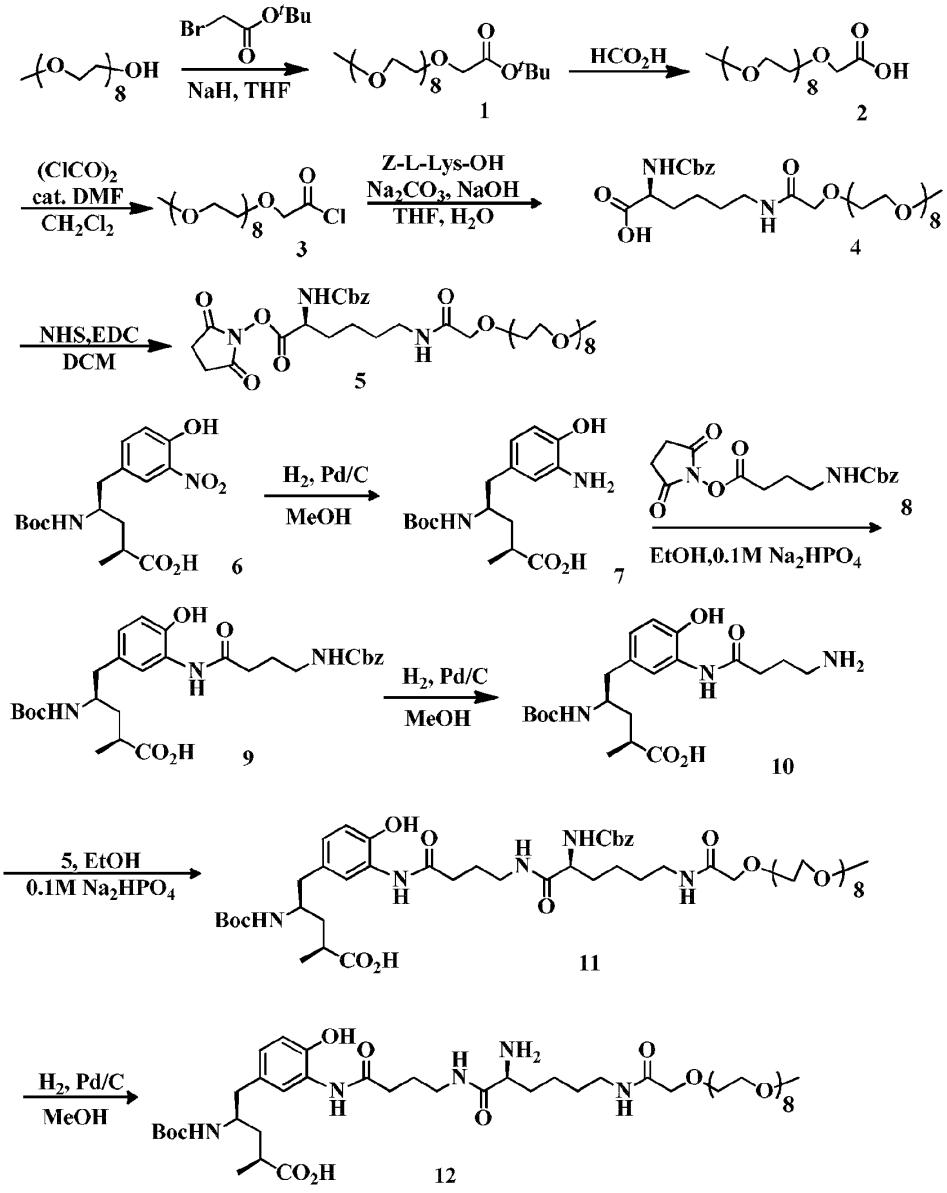


Fig .1

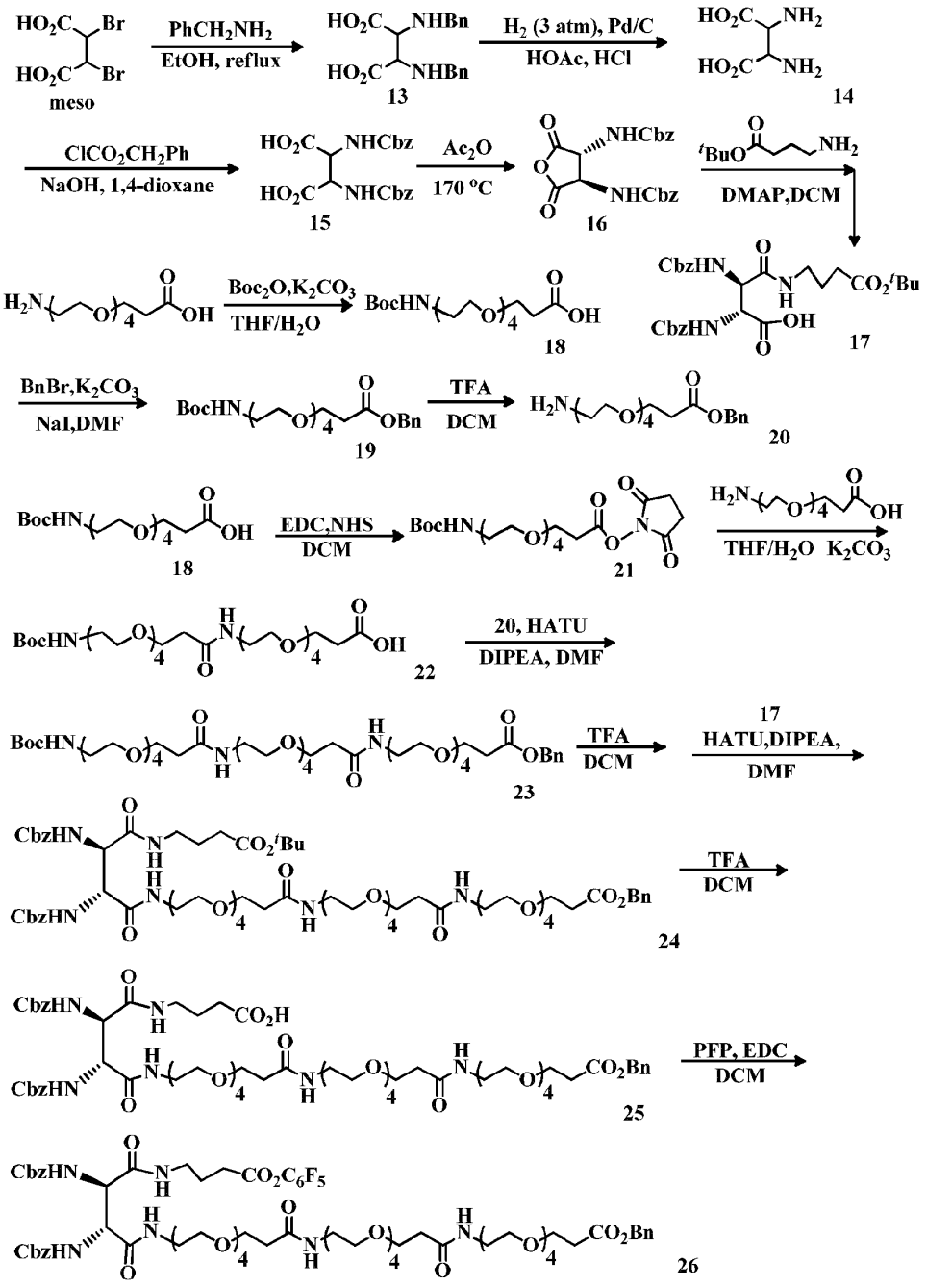


Fig. 2

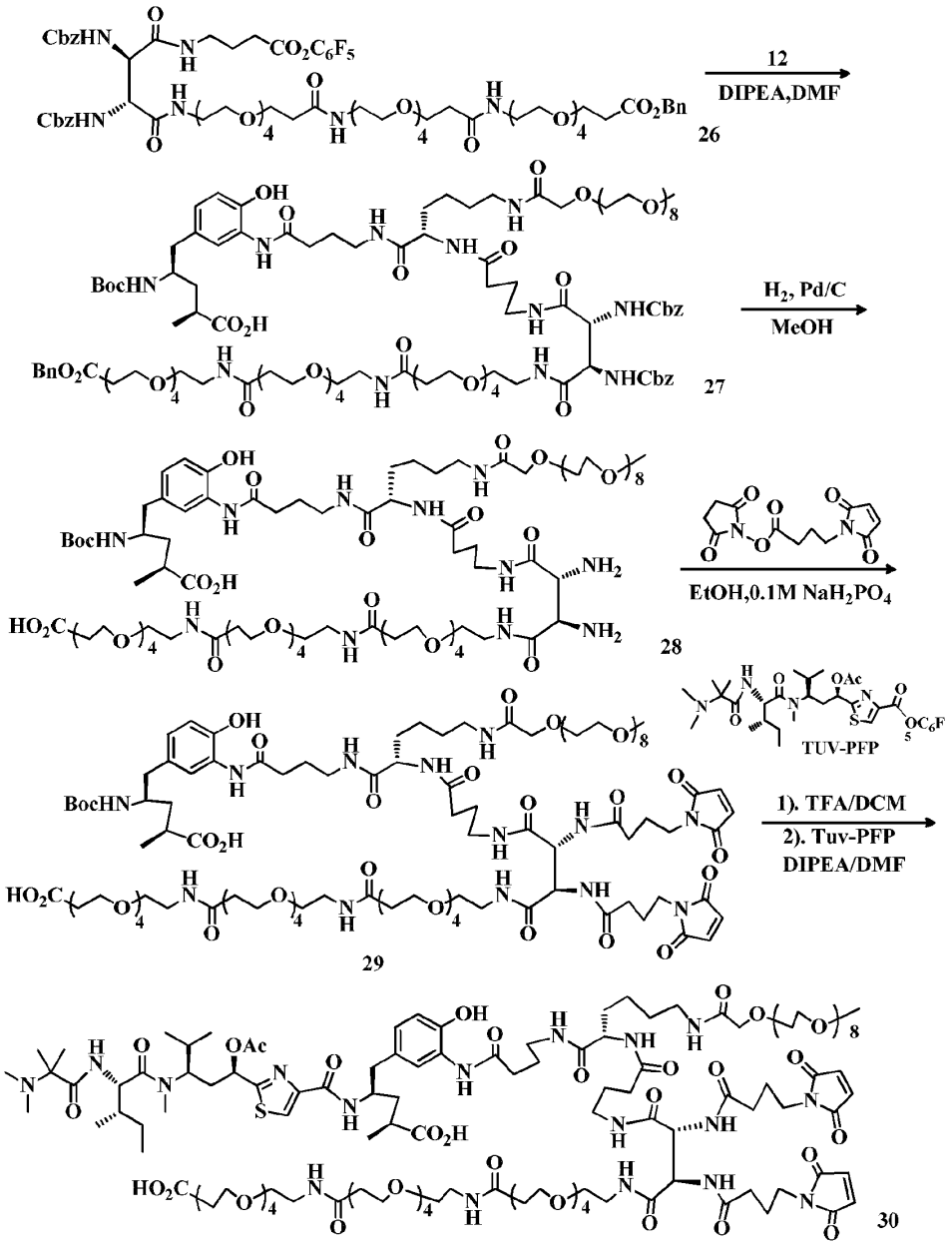

12
DIPEA,DMF
26
H2, Pd/C
MeOH
27
EtOH,0.1M NaH2PO4
28
TUV-PFP
1). TFA/DCM
2). Tuv-PFP
DIPEA/DMF
29
30

Fig. 3

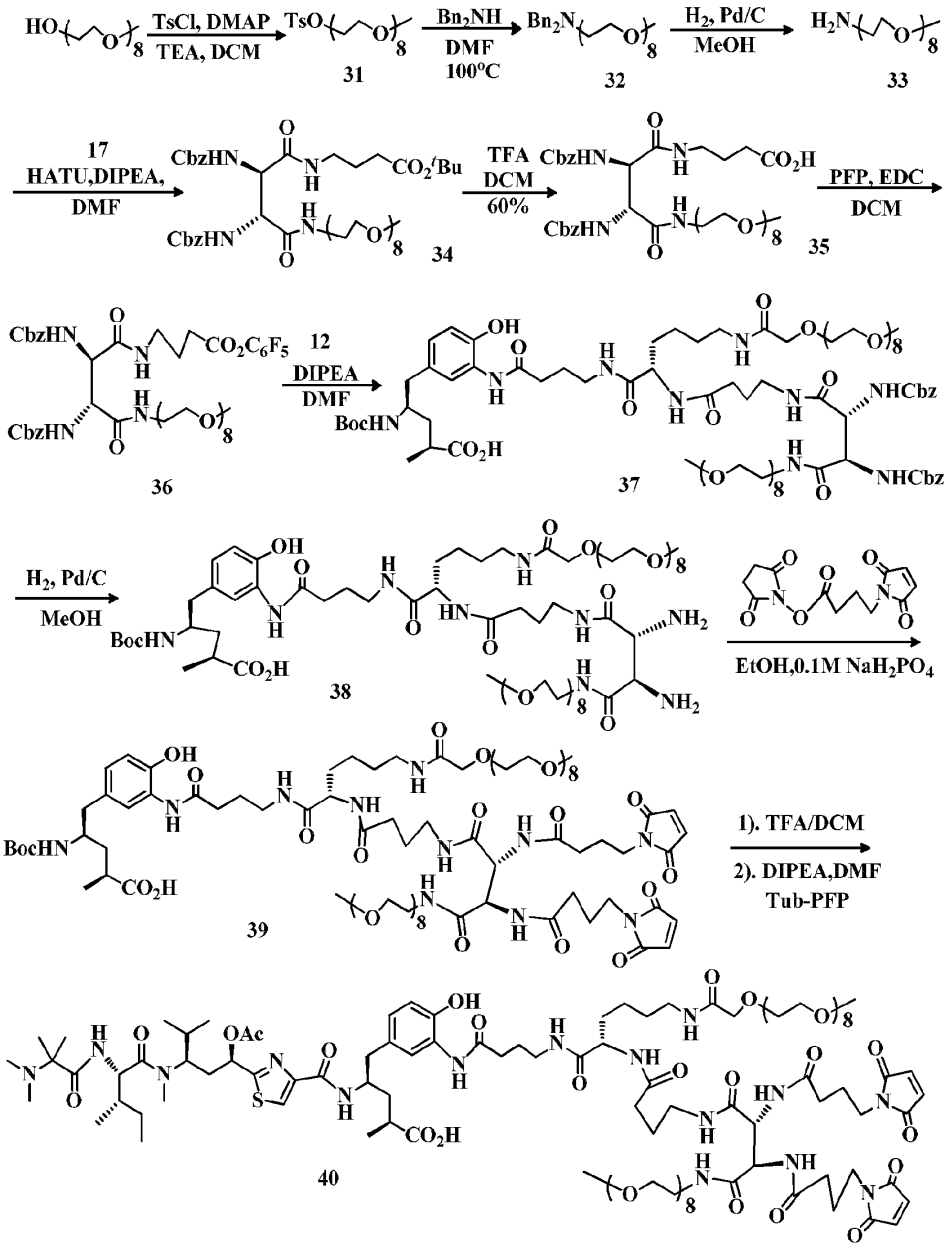

TsCl, DMAP
TEA, DCM
Bn2NH
DMF
100°C
H2, Pd/C
MeOH
31
32
33
17
HATU,DIPEA,
DMF
TFA
DCM
60%
PFP, EDC
DCM
34
35
12
DIPEA
DMF
36
37
H2, Pd/C
MeOH
38
EtOH,0.1M NaH2PO4
1). TFA/DCM
2). DIPEA,DMF
Tub-PFP
39
40

Fig. 4

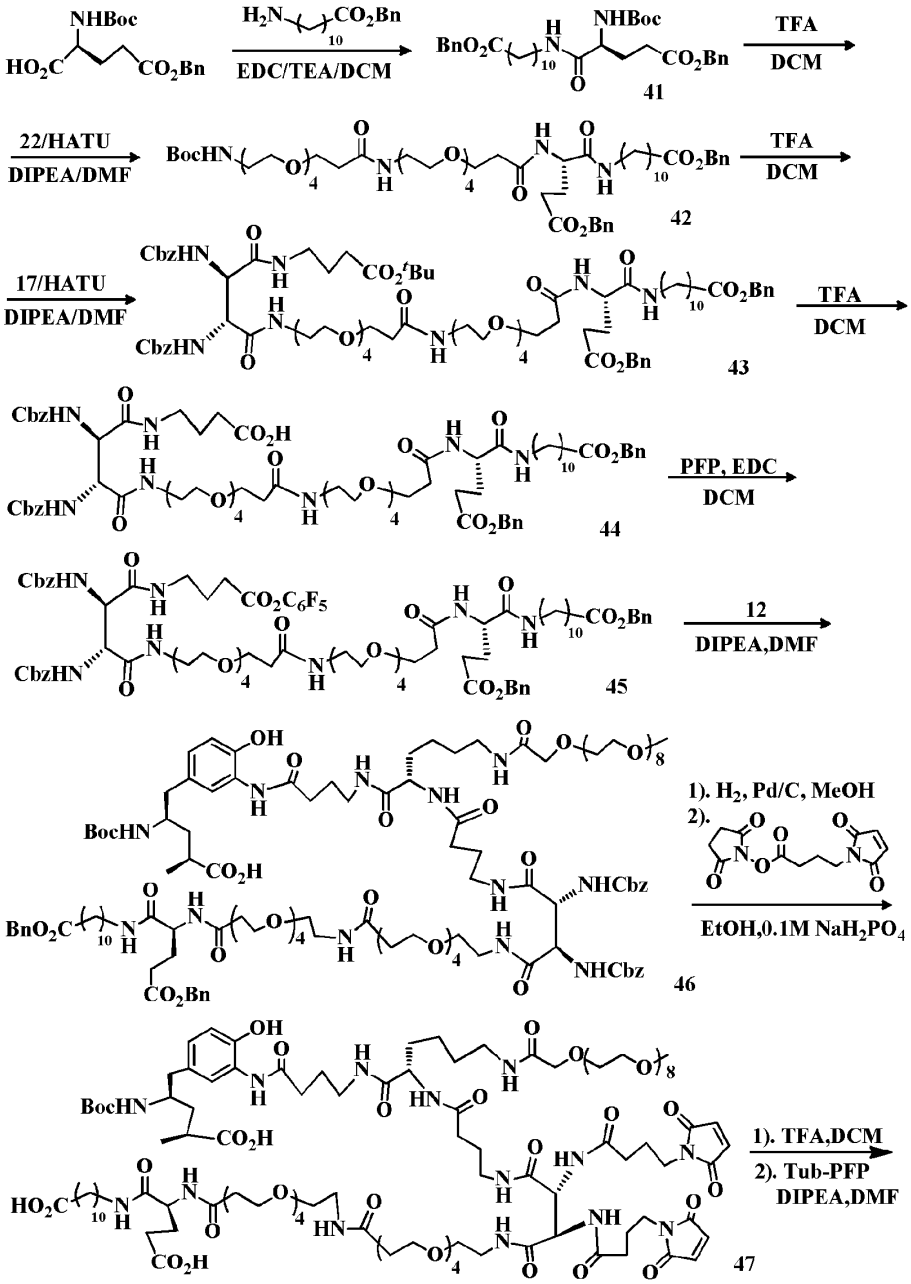
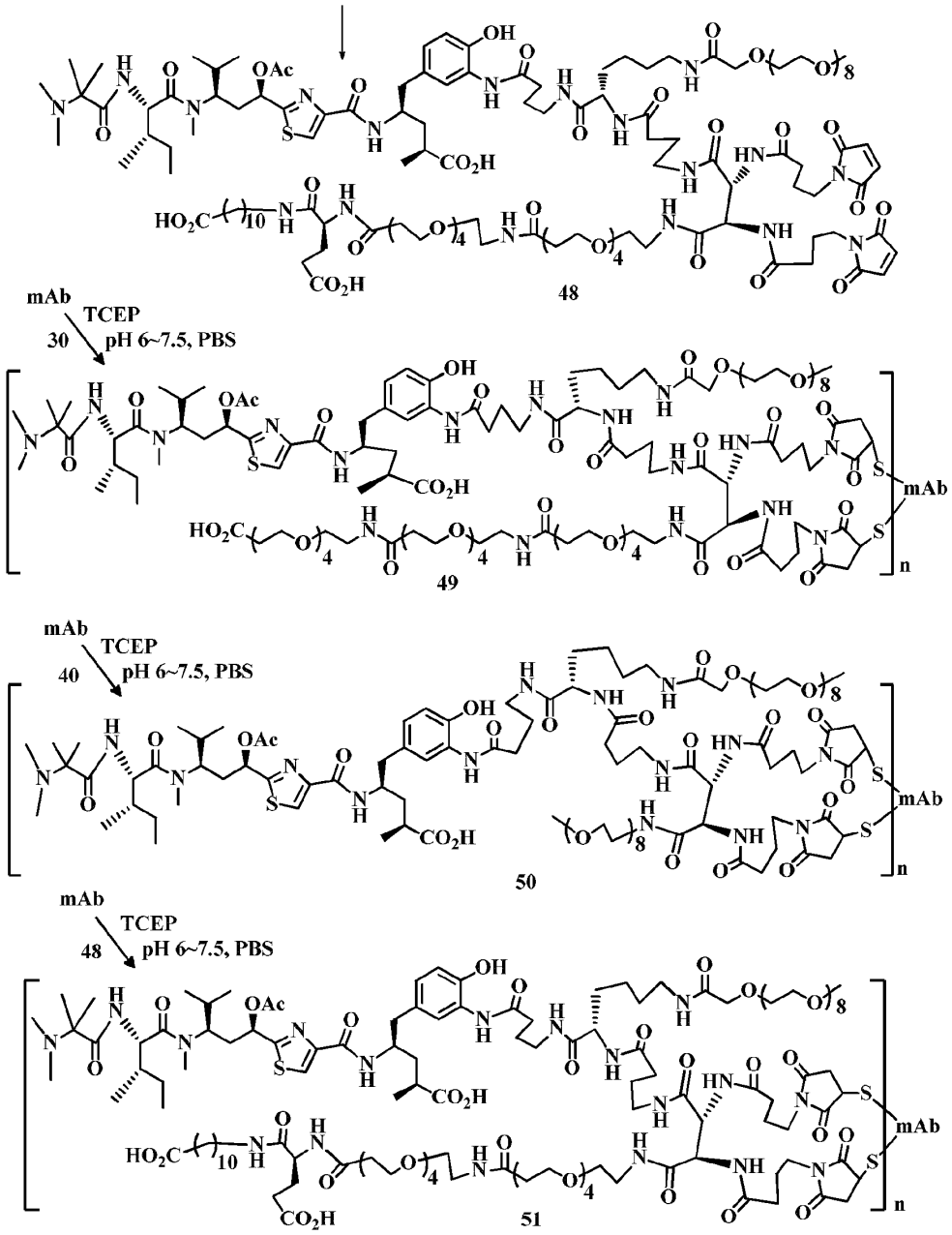

NHBoc
HO2C
CO2Bn
H2N
10
CO2Bn
EDC/TEA/DCM
BnO2C
NHBoc
41
TFA
DCM
22/HATU
DIPEA/DMF
BocHN
42
17/HATU
DIPEA/DMF
CbzHN
CO2tBu
43
PFP, EDC
DCM
CO2H
44
CO2C6F5
45
12
DIPEA,DMF
1). H2, Pd/C, MeOH
2).
EtOH,0.1M NaH2PO4
NHCbz
46
1). TFA,DCM
2). Tub-PFP
DIPEA,DMF
47

Fig. 5.



48 49 50 51

Fig. 6

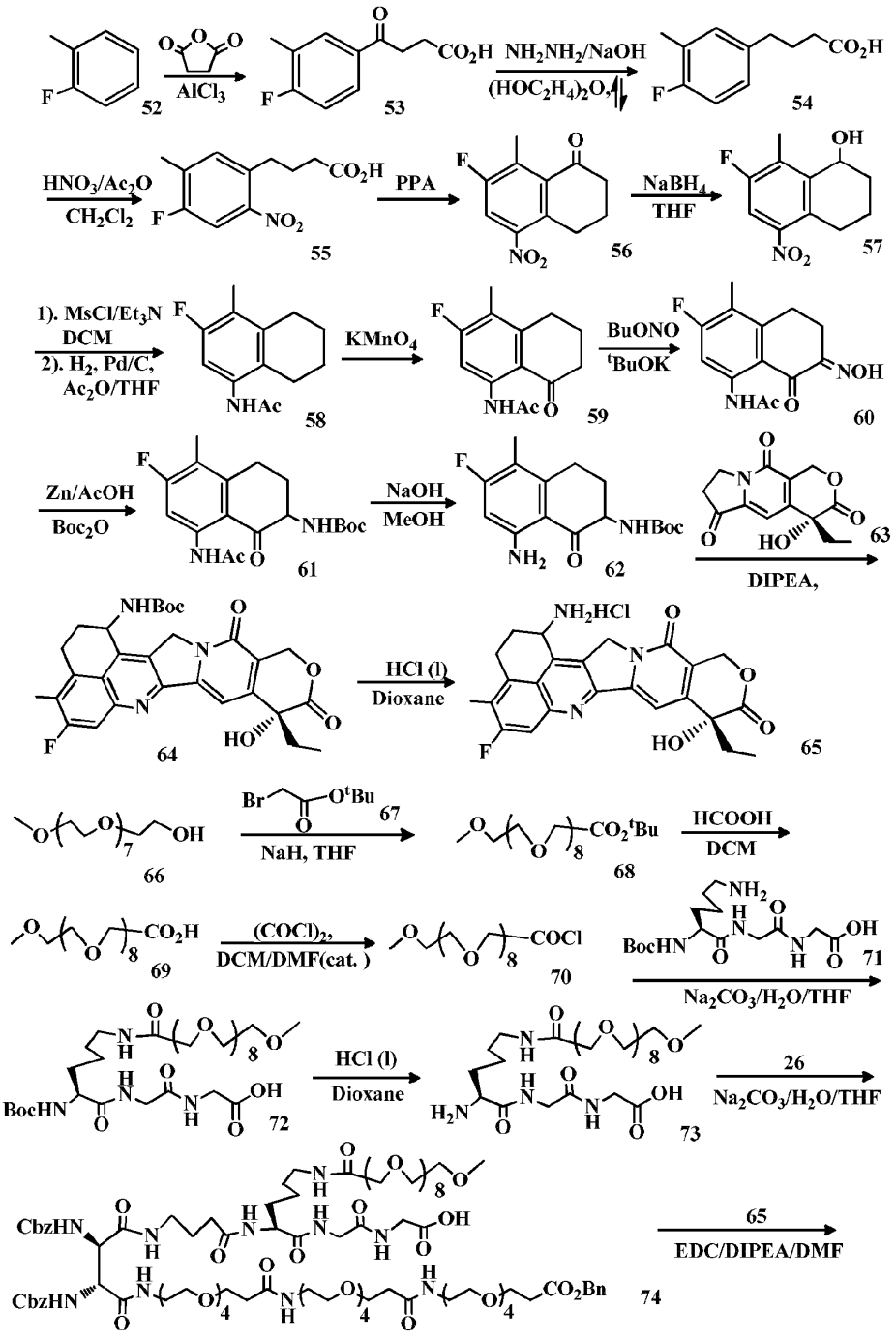

AlCl3
NH2NH2/NaOH
(HOC2H4)2O
HNO3/Ac2O
CH2Cl2
PPA
NaBH4
THF
1). MsCl/Et3N
DCM
2). H2, Pd/C,
Ac2O/THF
KMnO4
BuONO
tBuOK
Zn/AcOH
Boc2O
NaOH
MeOH
DIPEA,
HCl (l)
Dioxane
NaH, THF
HCOOH
DCM
(COCl)2,
DCM/DMF(cat.)
Na2CO3/H2O/THF
26
EDC/DIPEA/DMF

Fig. 7

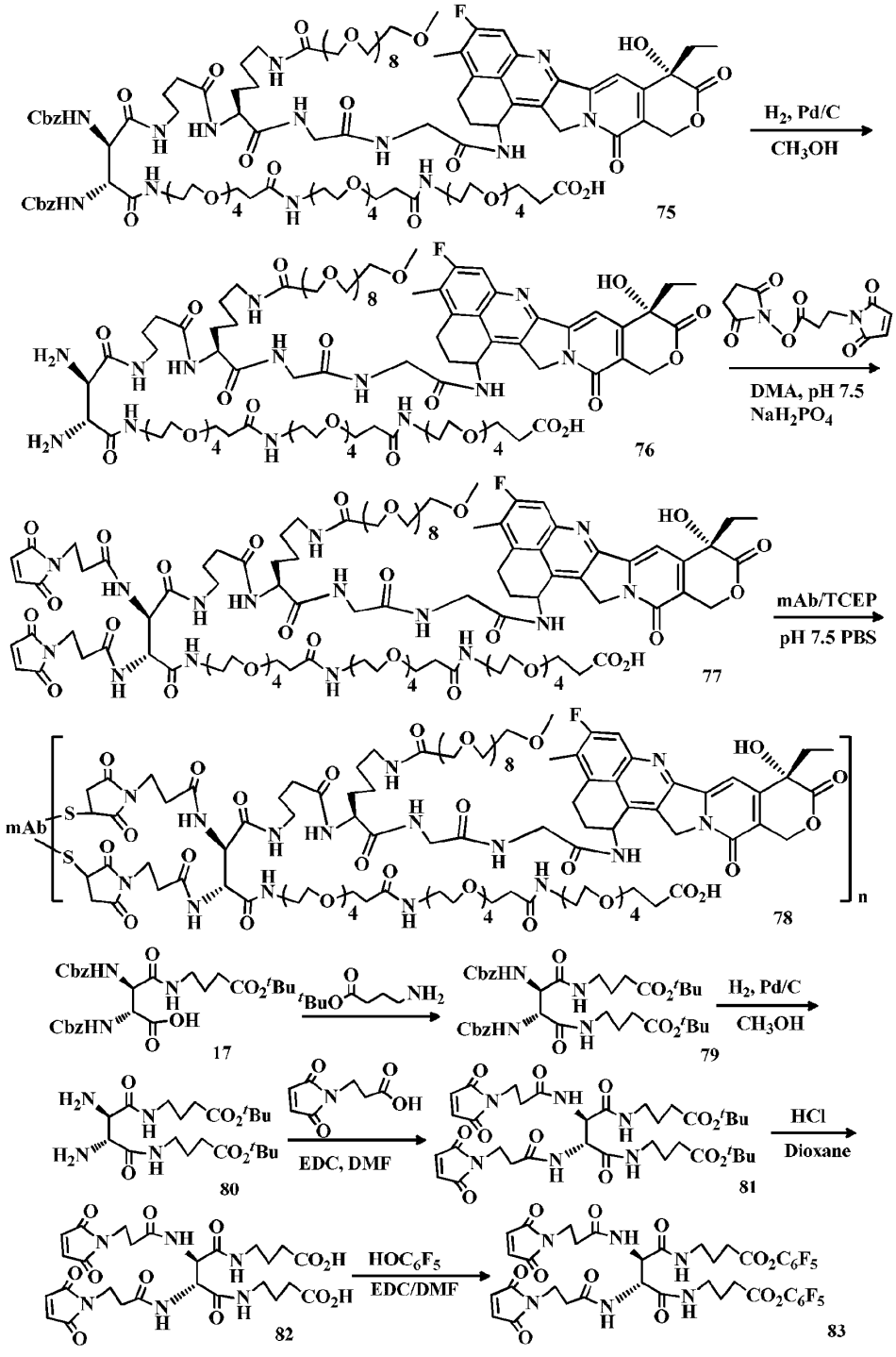

H2, Pd/C
CH3OH
DMA, pH 7.5
NaH2PO4
mAb/TCEP
pH 7.5 PBS
EDC, DMF
HCl
Dioxane
HOC6F5
EDC/DMF

Fig. 8

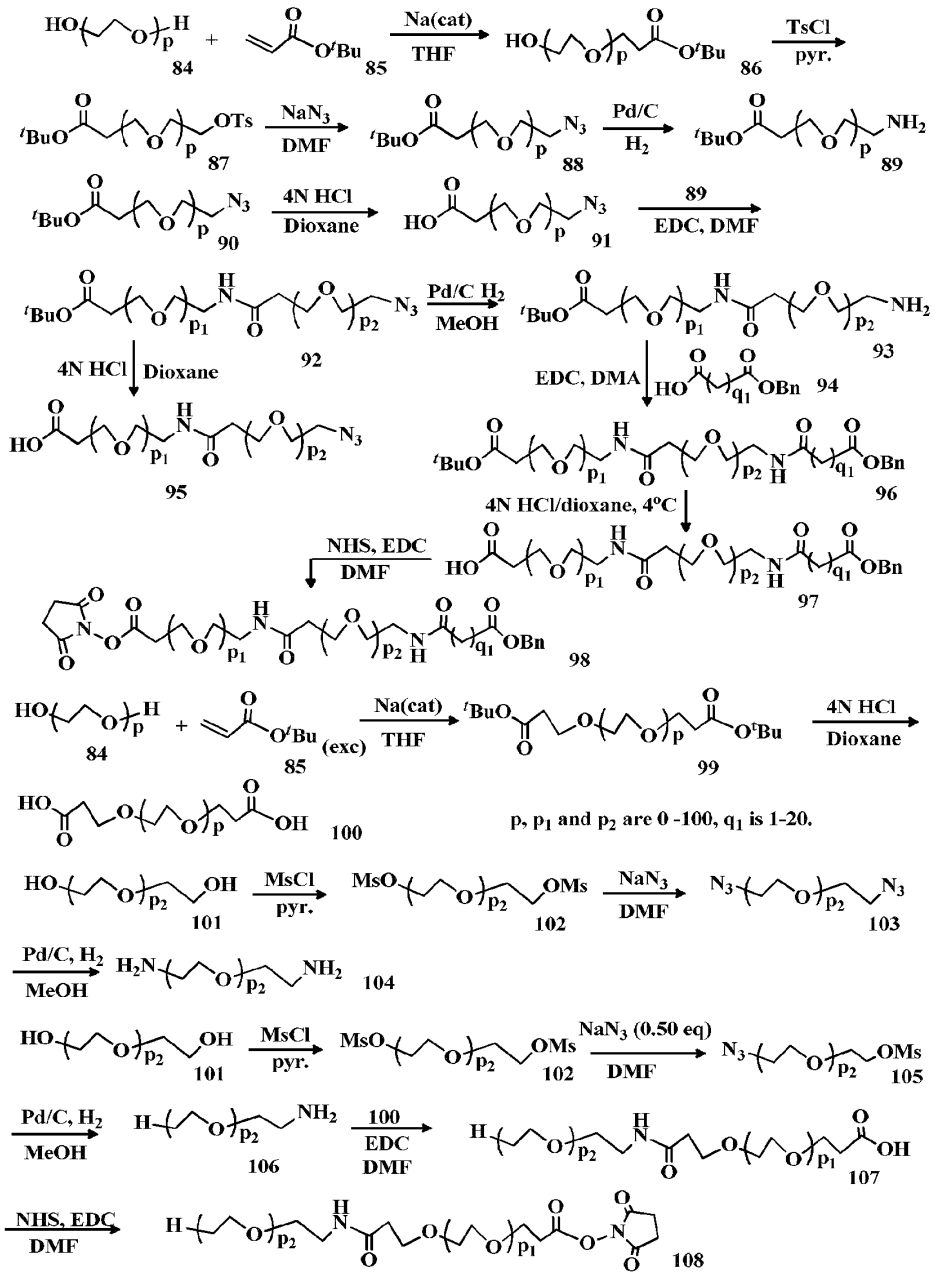

Na(cat)
THF
TsCl
pyr.
NaN3
DMF
Pd/C
H2
4N HCl
Dioxane
89
EDC, DMF
Pd/C H2
MeOH
EDC, DMA
4N HCl/dioxane, 4°C
NHS, EDC
DMF
(exc)
p, p1 and p2 are 0 -100, q1 is 1-20.
MsCl
pyr.
NaN3 (0.50 eq)
100
EDC
DMF

Fig. 9

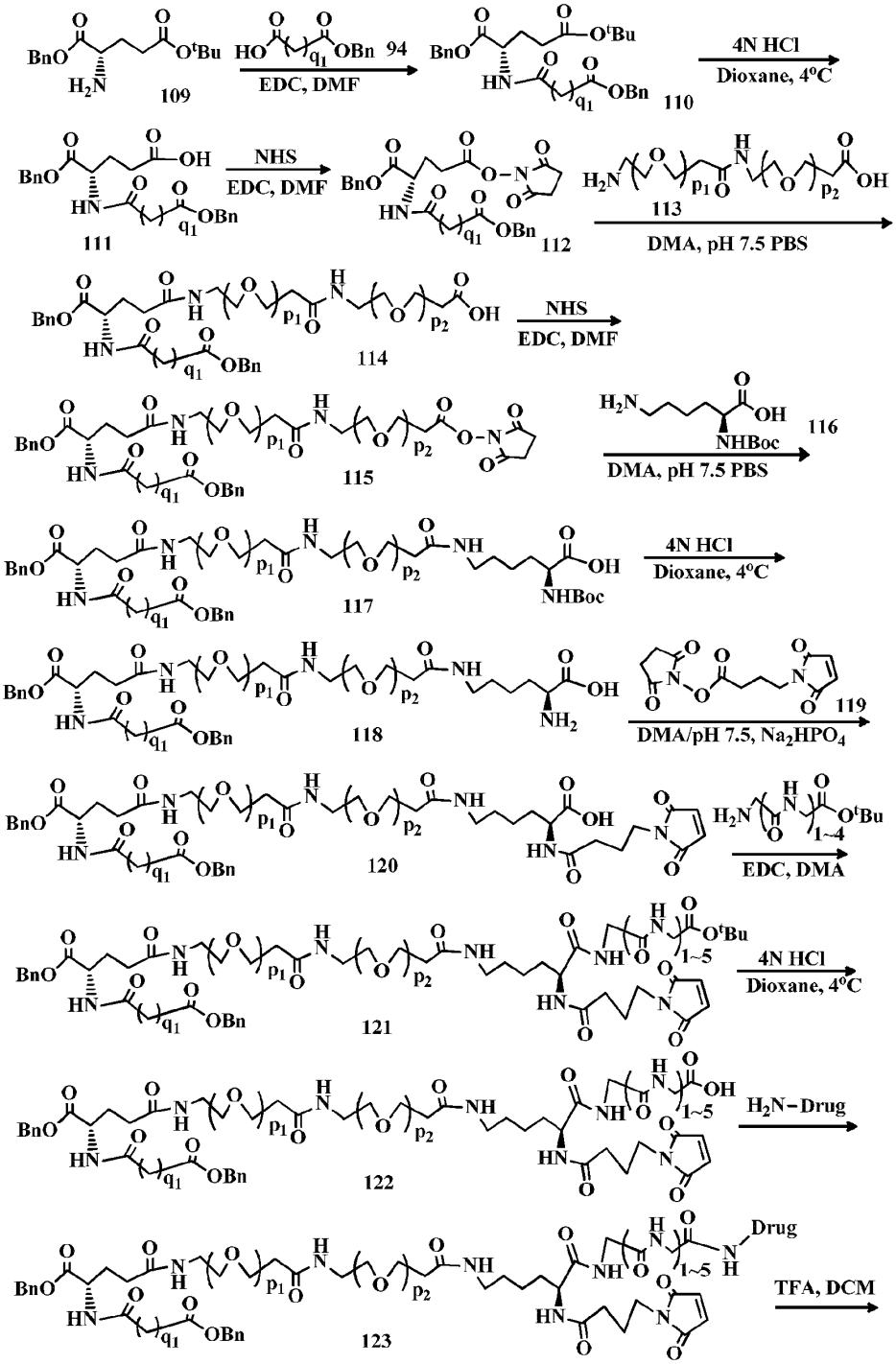

109
94
EDC, DMF
110
4N HCl
Dioxane, 4°C
111
NHS
EDC, DMF
112
113
DMA, pH 7.5 PBS
114
NHS
EDC, DMF
115
116
NHBoc
DMA, pH 7.5 PBS
117
4N HCl
Dioxane, 4°C
118
119
DMA/pH 7.5, Na2HPO4
120
1~4
EDC, DMA
121
1~5
4N HCl
Dioxane, 4°C
122
1~5
H2N−Drug
123
Drug
1~5
TFA, DCM

Fig. 10

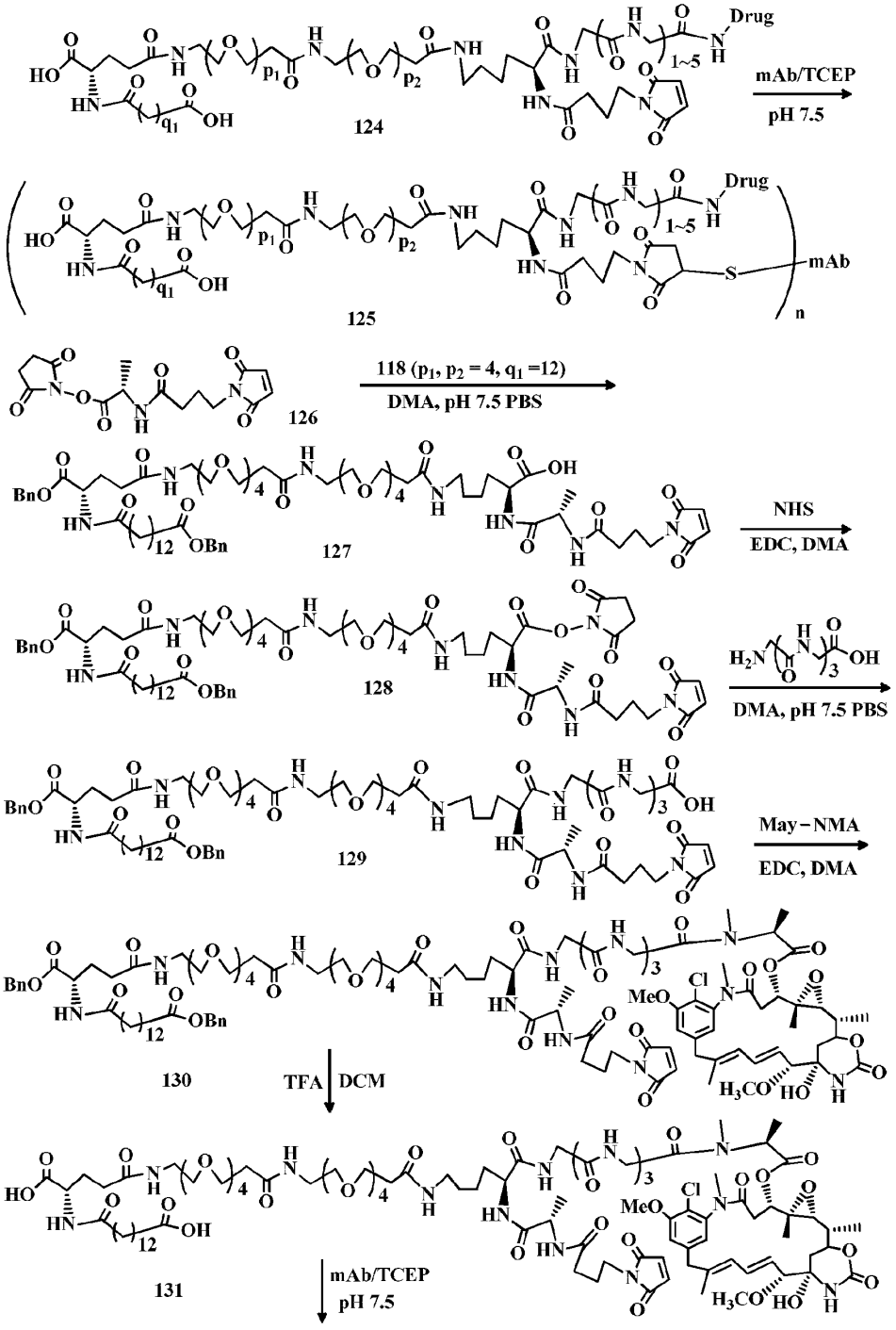

Drug
1~5
mAb/TCEP
pH 7.5
124
mAb
n
125
118 (p_1, p_2 = 4, q_1 =12)
DMA, pH 7.5 PBS
126
NHS
EDC, DMA
127
128
DMA, pH 7.5 PBS
129
May-NMA
EDC, DMA
130
TFA
DCM
131
mAb/TCEP
pH 7.5

Fig. 11

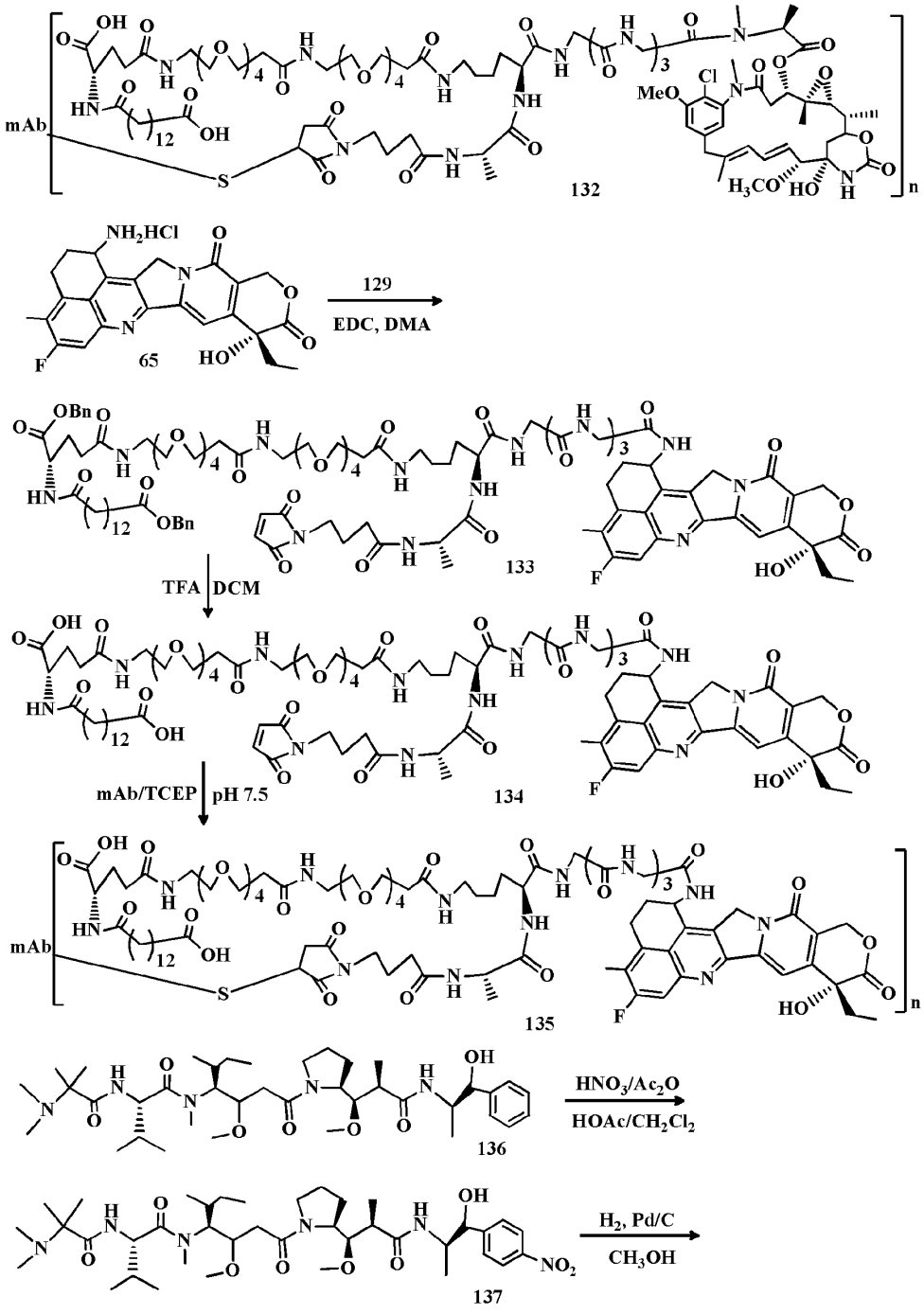

mAb
132
NH2HCl
65
129
EDC, DMA
133
TFA
DCM
134
mAb/TCEP
pH 7.5
135
HNO3/Ac2O
HOAc/CH2Cl2
136
H2, Pd/C
CH3OH
137

Fig. 12

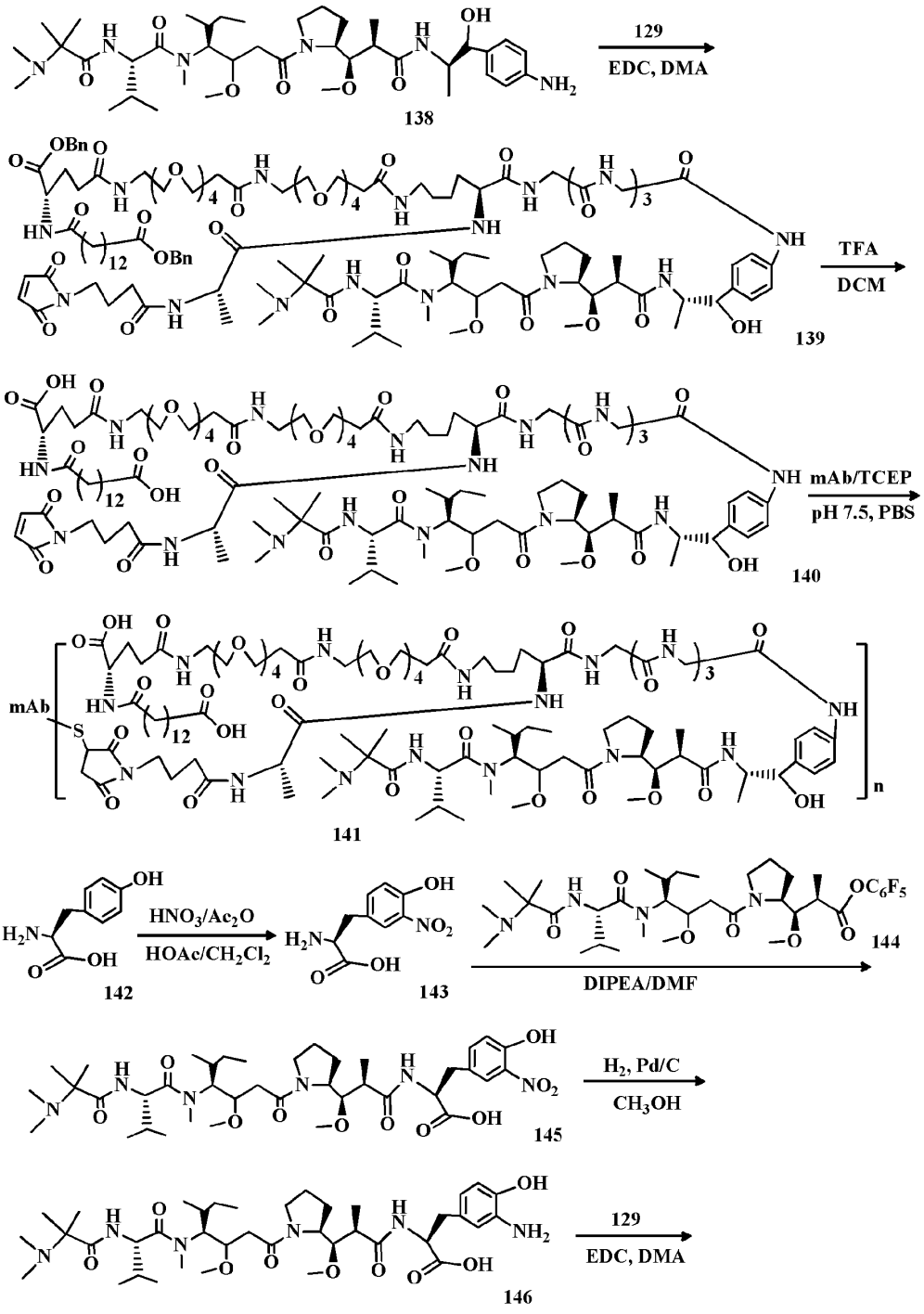

129
EDC, DMA
138
TFA
DCM
139
mAb/TCEP
pH 7.5, PBS
140
mAb
n
141
HNO3/Ac2O
HOAc/CH2Cl2
142
143
144
DIPEA/DMF
H2, Pd/C
CH3OH
145
129
EDC, DMA
146

Fig. 13

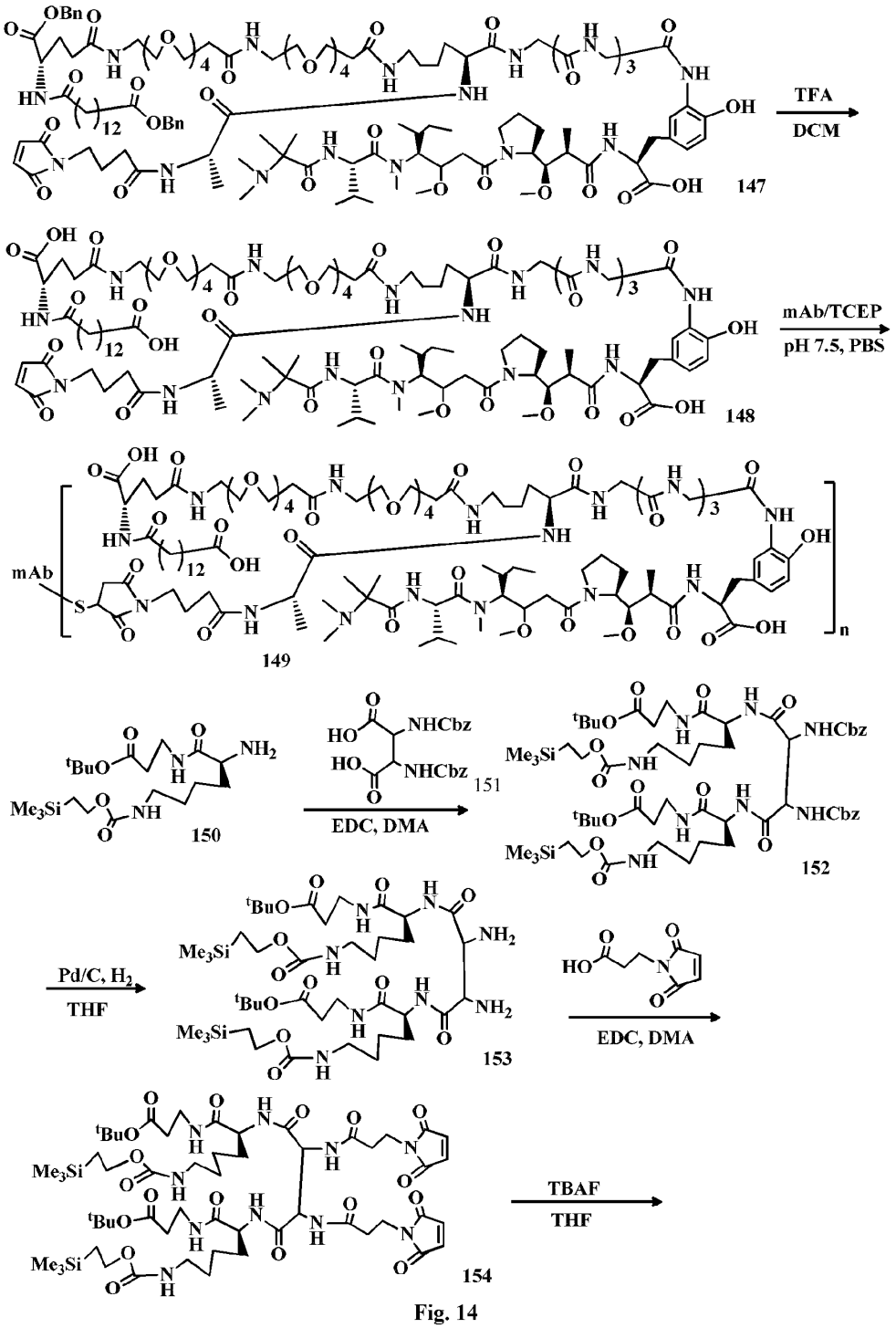

TFA
DCM
147
mAb/TCEP
pH 7.5, PBS
148
mAb
149
150
EDC, DMA
151
152
Pd/C, H2
THF
153
EDC, DMA
TBAF
THF
154

Fig. 14

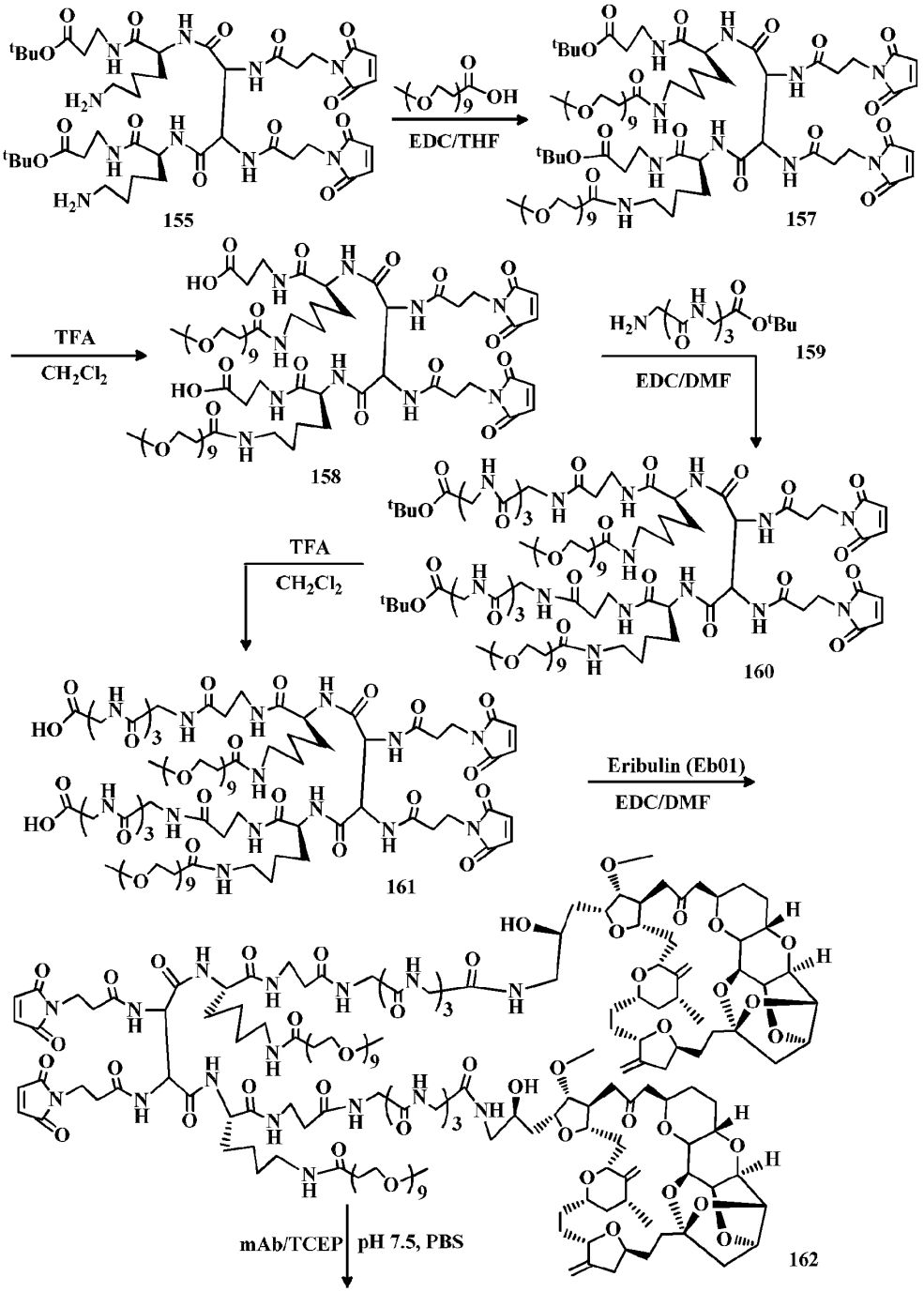

155
EDC/THF
157
TFA
CH2Cl2
158
159
EDC/DMF
160
TFA
CH2Cl2
161
Eribulin (Eb01)
EDC/DMF
mAb/TCEP
pH 7.5, PBS
162

Fig. 15

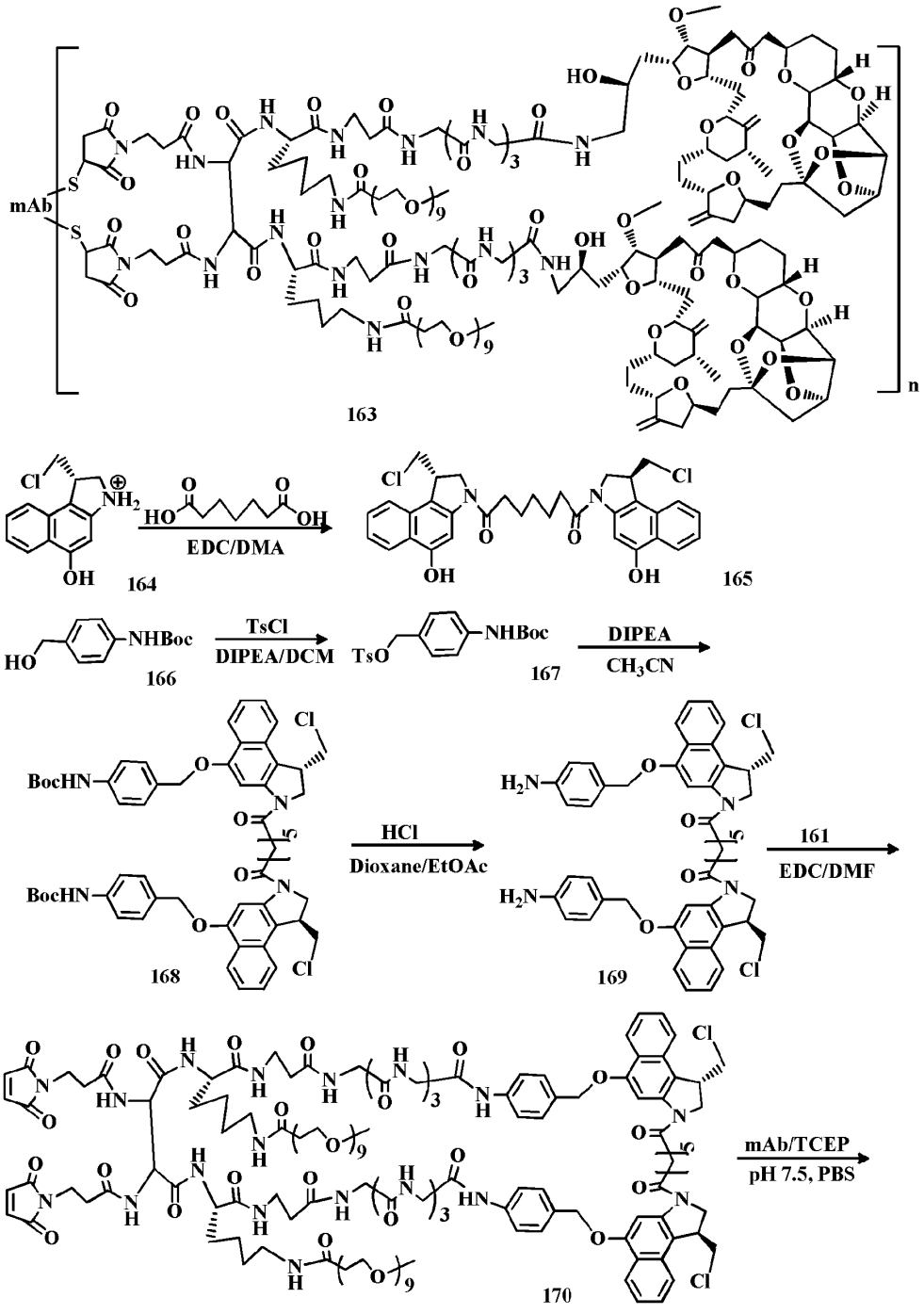

mAb
n
163
EDC/DMA
164
165
TsCl
DIPEA/DCM
166
167
DIPEA
CH3CN
BocHN
168
HCl
Dioxane/EtOAc
H2N
169
161
EDC/DMF
mAb/TCEP
pH 7.5, PBS
170

Fig. 16

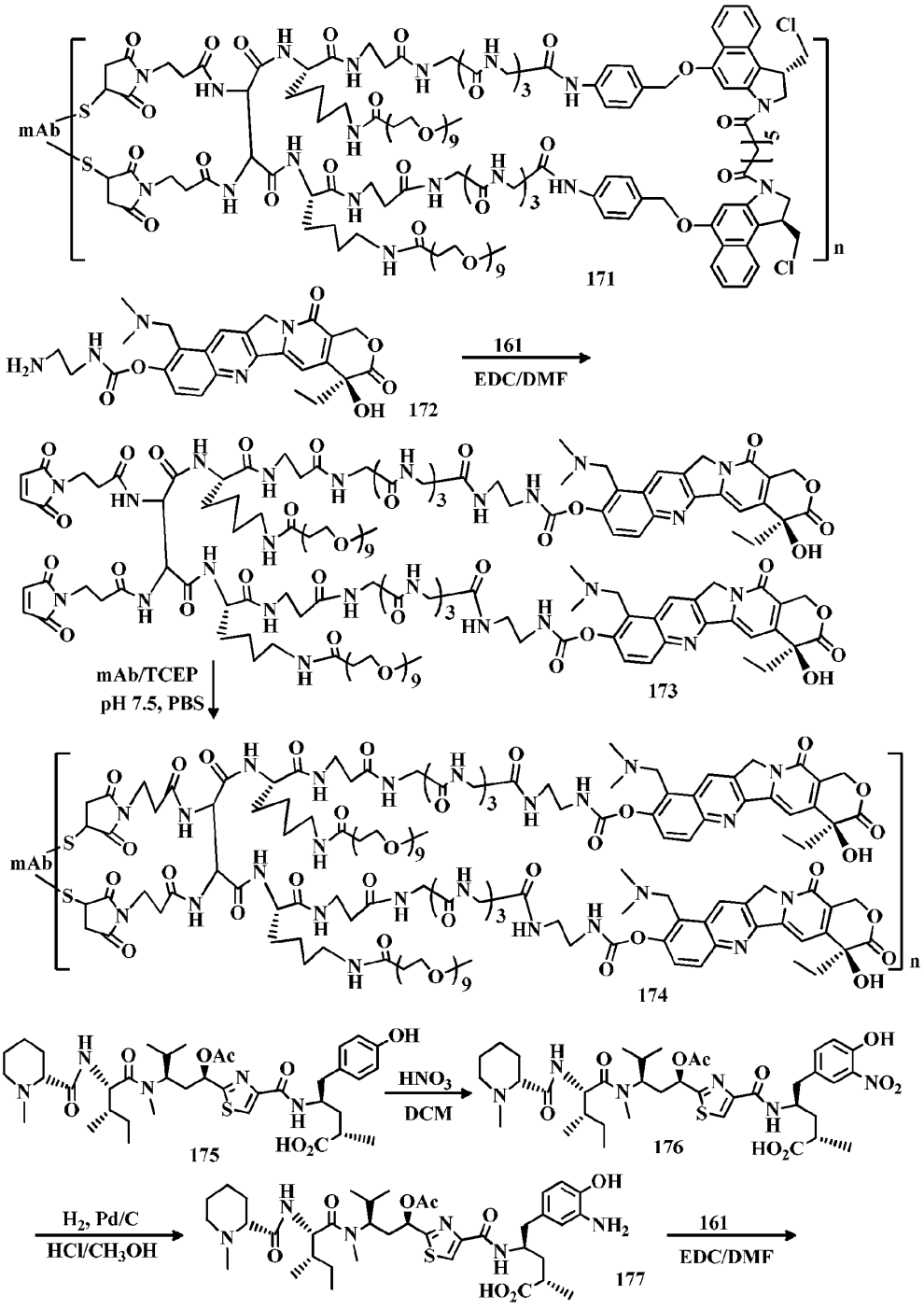

mAb
171
161
EDC/DMF
172
173
mAb/TCEP
pH 7.5, PBS
174
175
HNO3
DCM
176
H2, Pd/C
HCl/CH3OH
177
161
EDC/DMF

Fig. 17

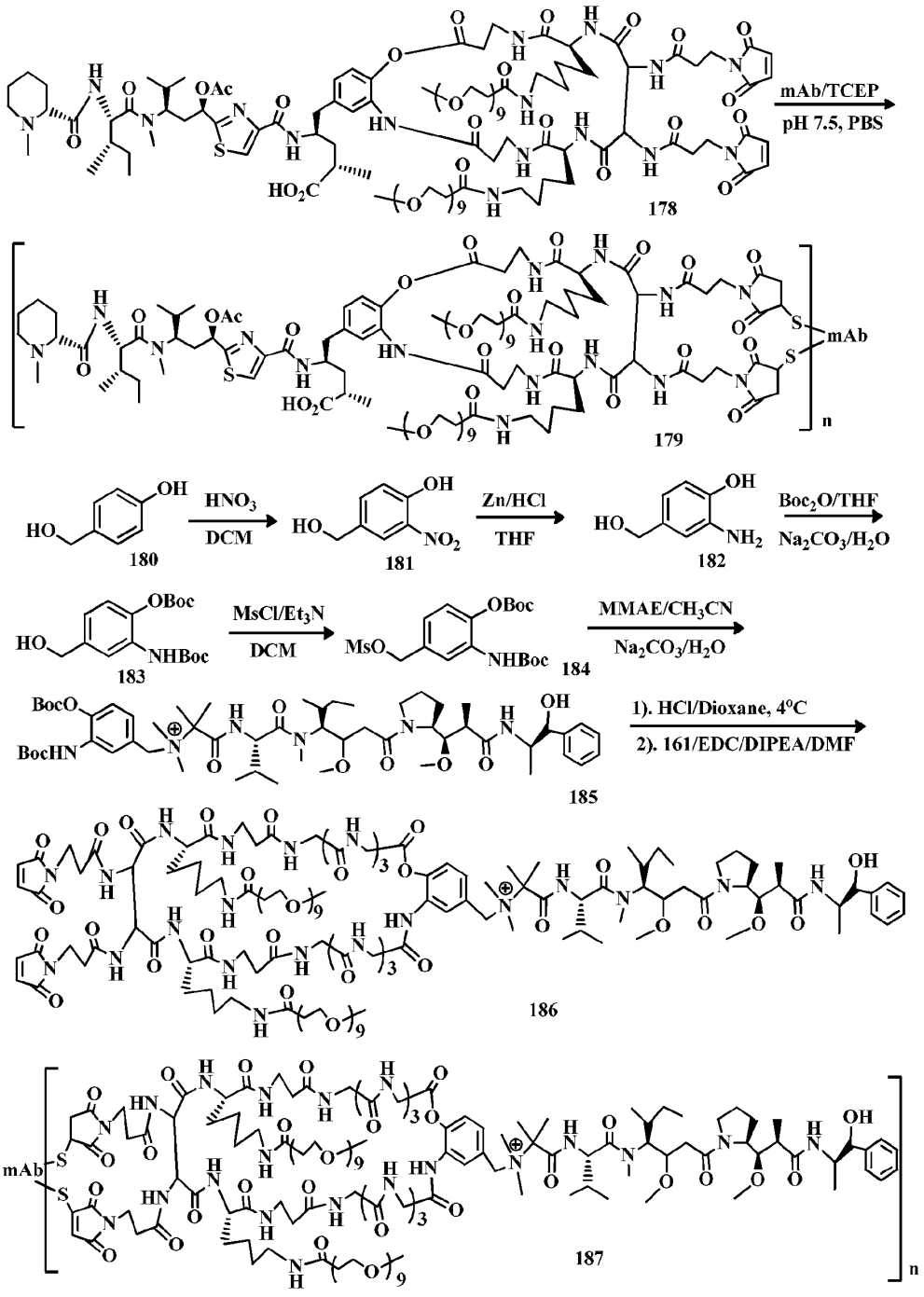

mAb/TCEP
pH 7.5, PBS
178
mAb
n
179
HNO3
DCM
Zn/HCl
THF
Boc2O/THF
Na2CO3/H2O
180
181
182
MsCl/Et3N
DCM
MMAE/CH3CN
Na2CO3/H2O
183
184
1). HCl/Dioxane, 4°C
2). 161/EDC/DIPEA/DMF
185
186
187

Fig. 18

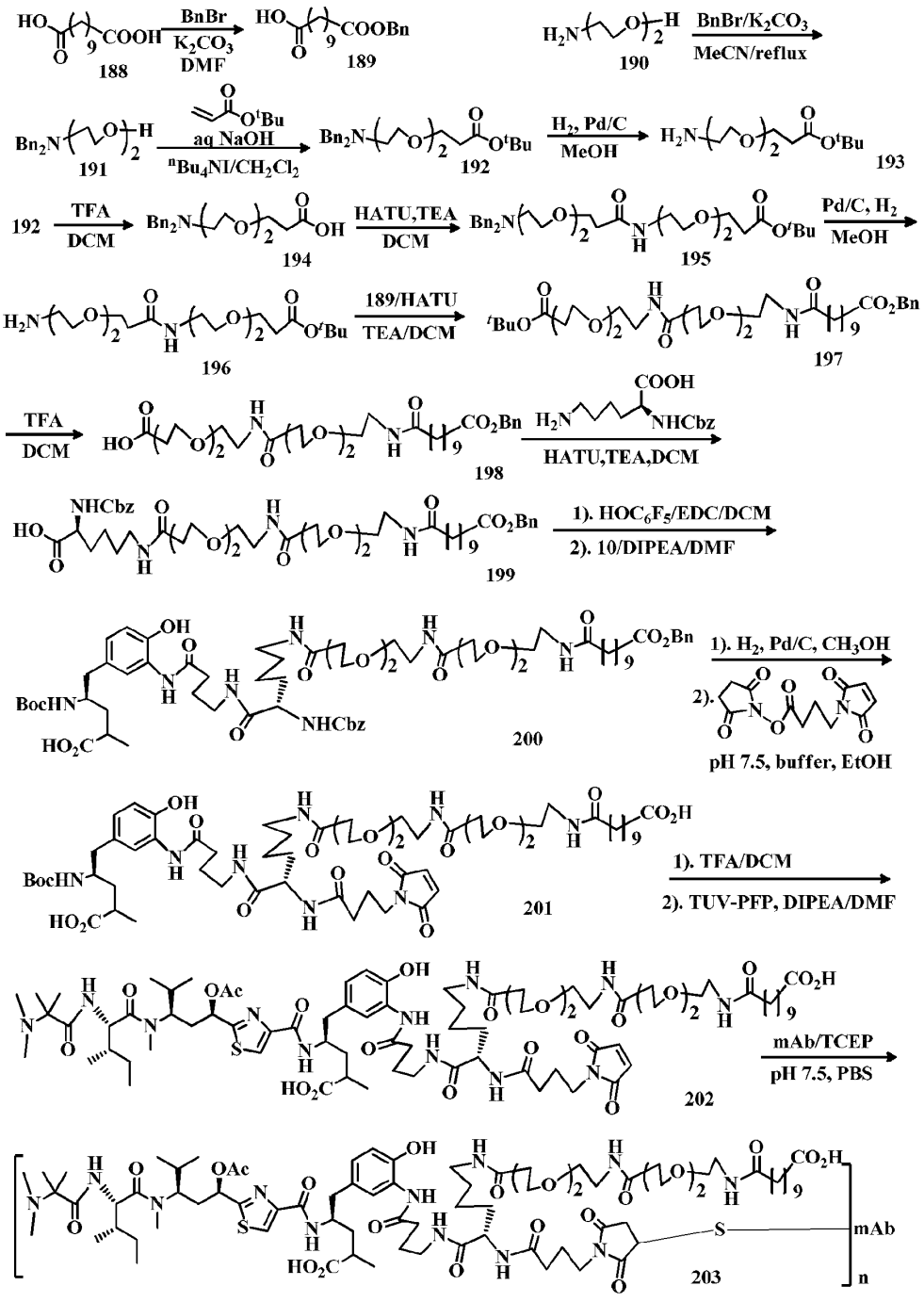

BnBr
K2CO3
DMF
188
189
BnBr/K2CO3
MeCN/reflux
190
aq NaOH
nBu4NI/CH2Cl2
191
192
H2, Pd/C
MeOH
193
TFA
DCM
194
HATU,TEA
DCM
195
Pd/C, H2
MeOH
189/HATU
TEA/DCM
196
197
TFA
DCM
198
HATU,TEA,DCM
1). HOC6F5/EDC/DCM
2). 10/DIPEA/DMF
199
200
1). H2, Pd/C, CH3OH
2).
pH 7.5, buffer, EtOH
201
1). TFA/DCM
2). TUV-PFP, DIPEA/DMF
202
mAb/TCEP
pH 7.5, PBS
203
mAb
n

Fig. 19

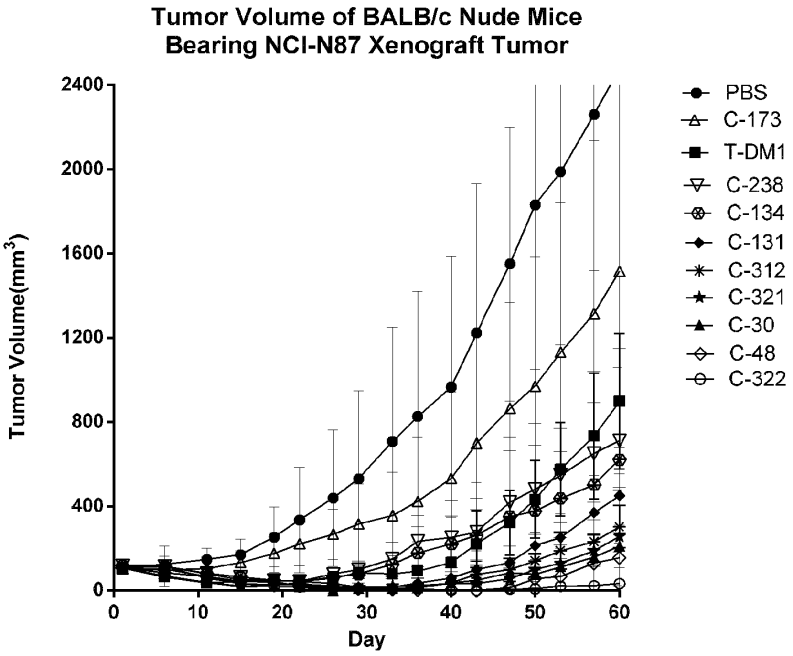

Tumor Volume of BALB/c Nude Mice
Bearing NCI-N87 Xenograft Tumor
Tumor Volume(mm3)
2400
2000
1600
1200
800
400
0
0
10
20
30
40
50
60
Day
PBS
C-173
T-DM1
C-238
C-134
C-131
C-312
C-321
C-30
C-48
C-322

Fig. 20

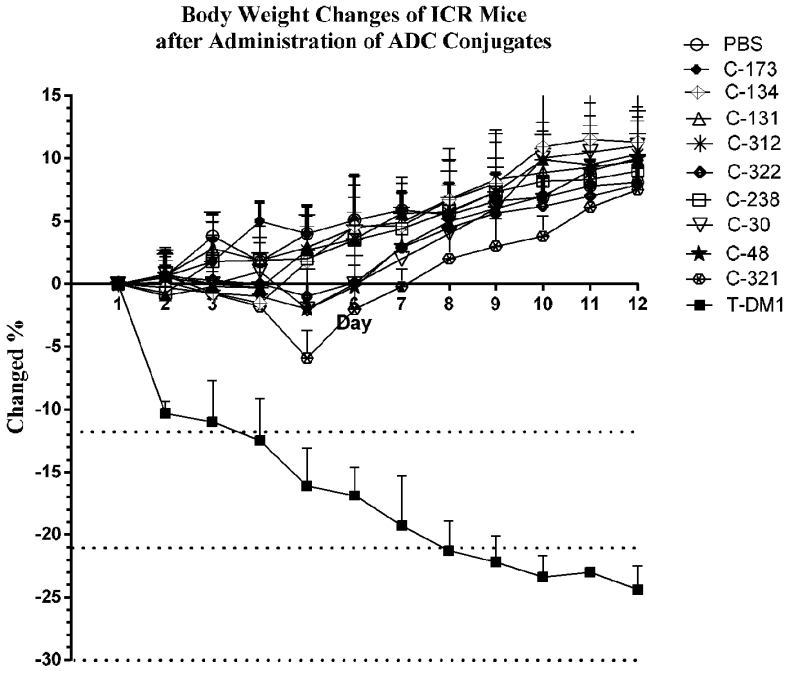

Body Weight Changes of ICR Mice
after Administration of ADC Conjugates
Changed %
15
10
5
0
-5
-10
-15
-20
-25
-30
1
2
3
4
7
8
9
10
11
12
Day
PBS
C-173
C-134
C-131
C-312
C-322
C-238
C-30
C-48
C-321
T-DM1

Fig. 21