

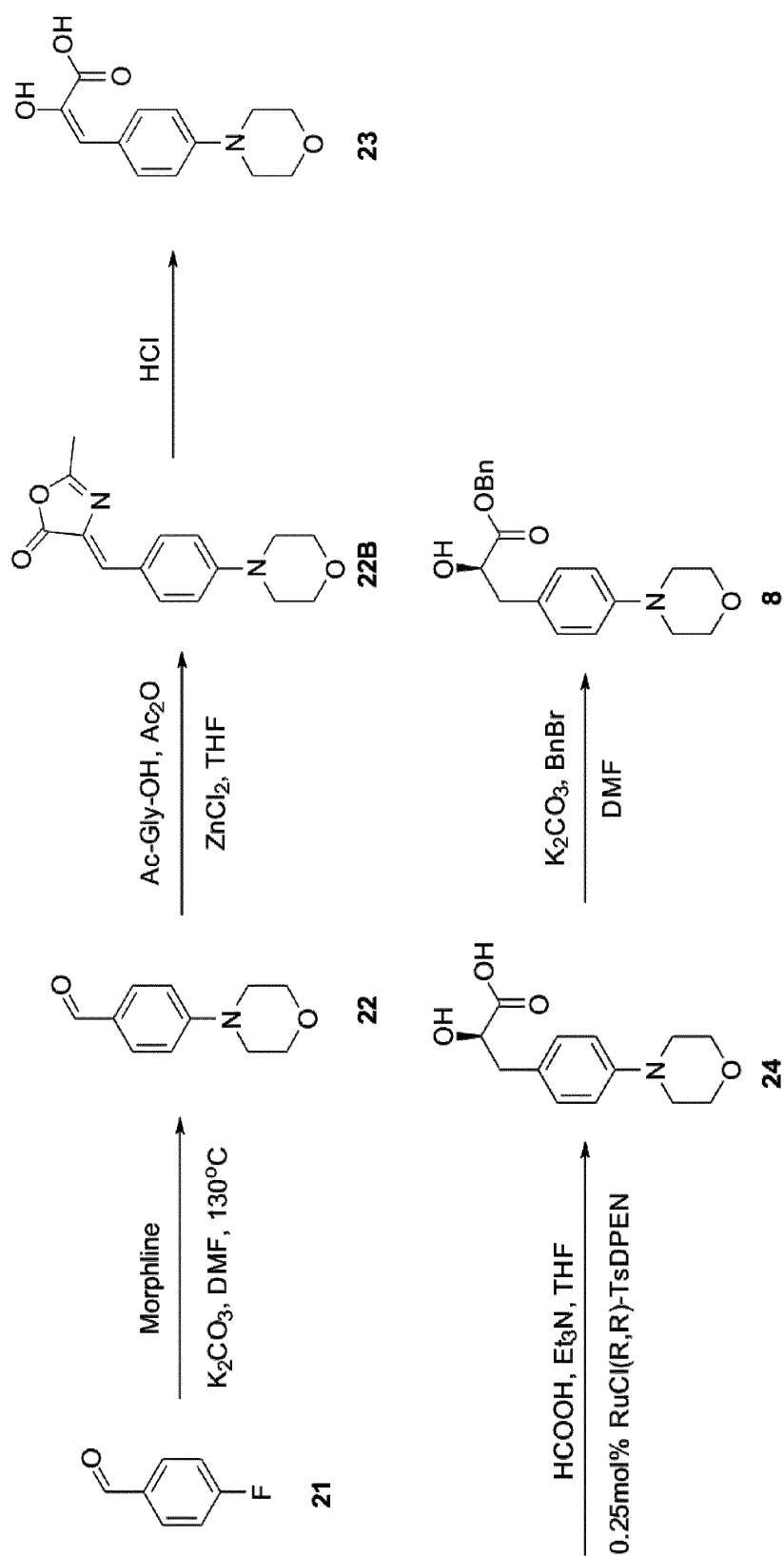


Fig. 1

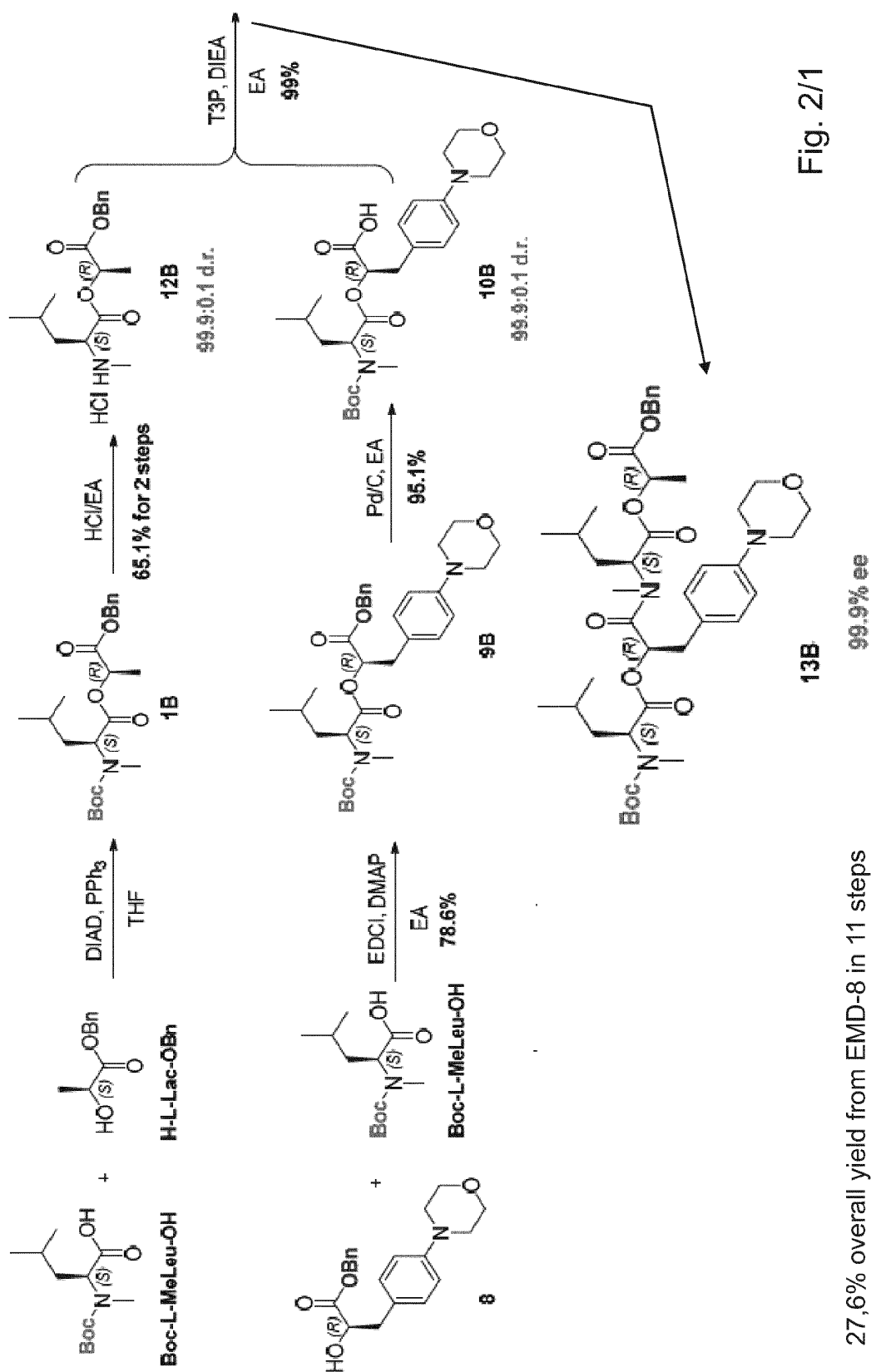


Fig. 2/1

27,6% overall yield from EMD-8 in 11 steps

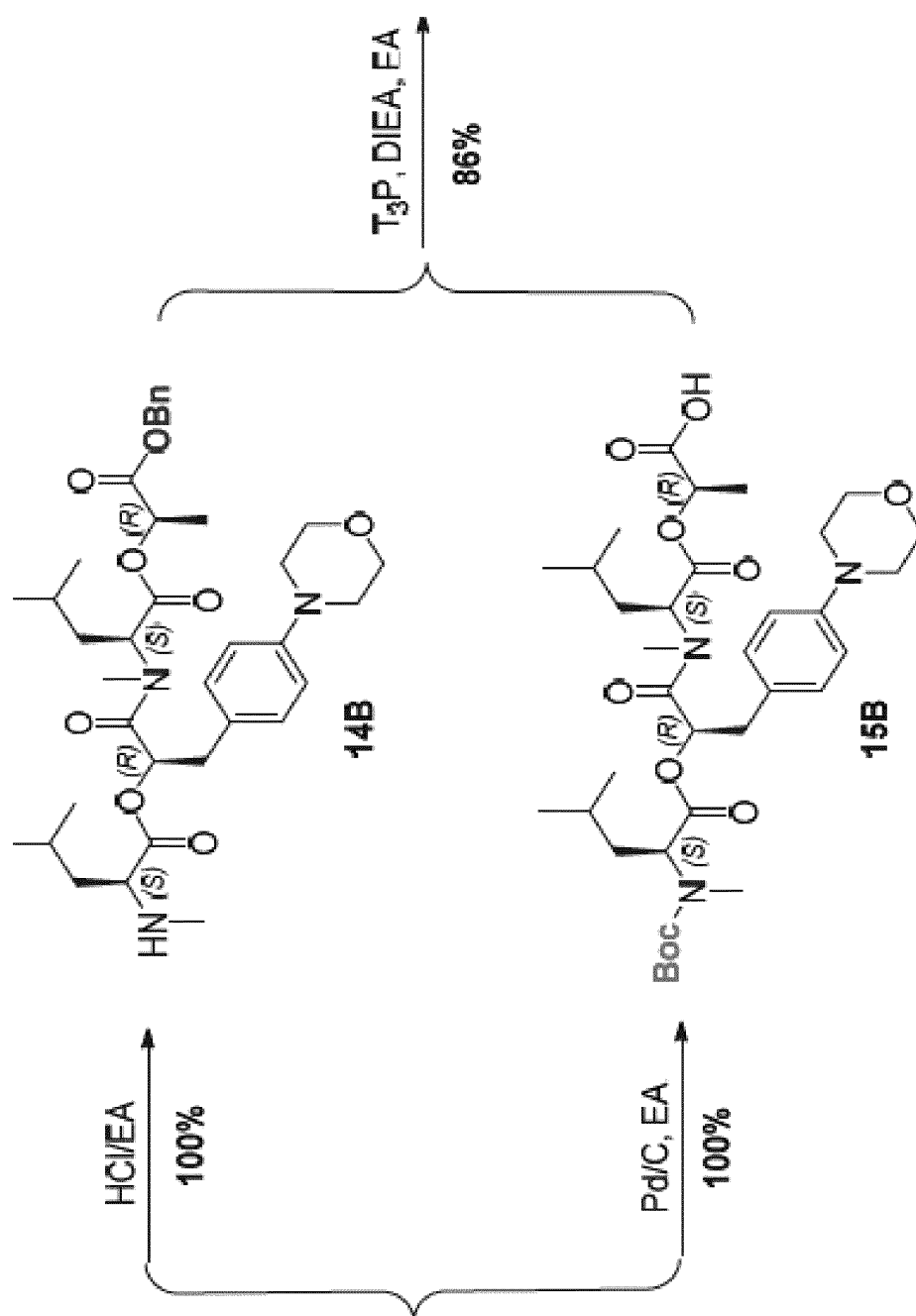


Fig. 2/2

27,6% overall yield from EMD-8 in 11 steps

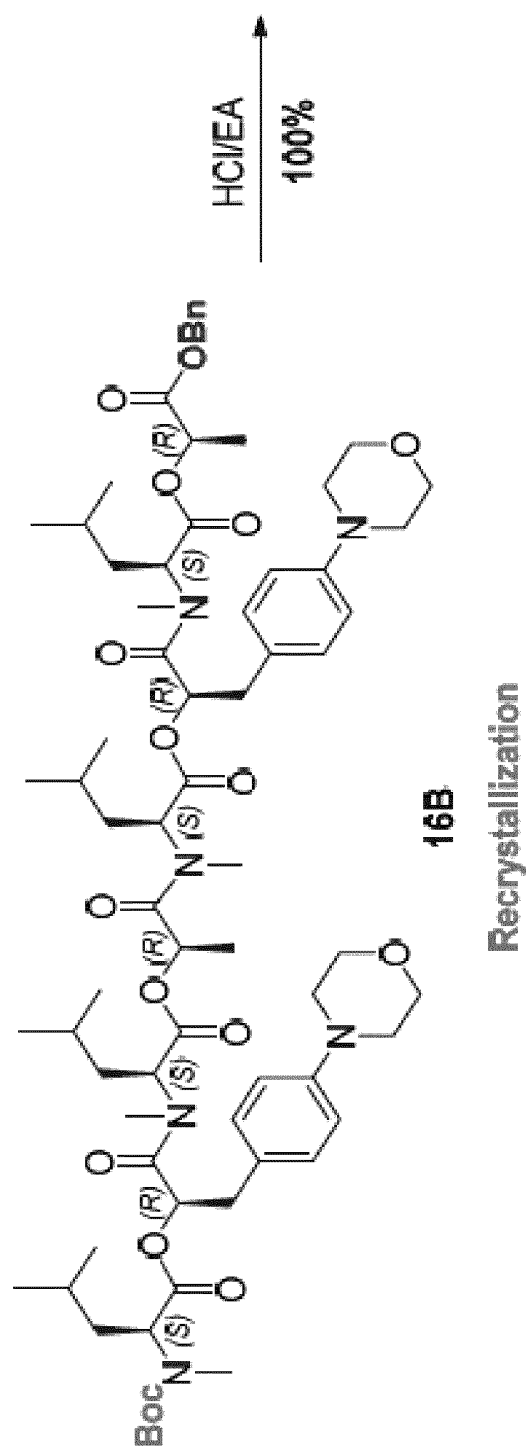


Fig. 2/3

27,6% overall yield from EMD-8 in 11 steps

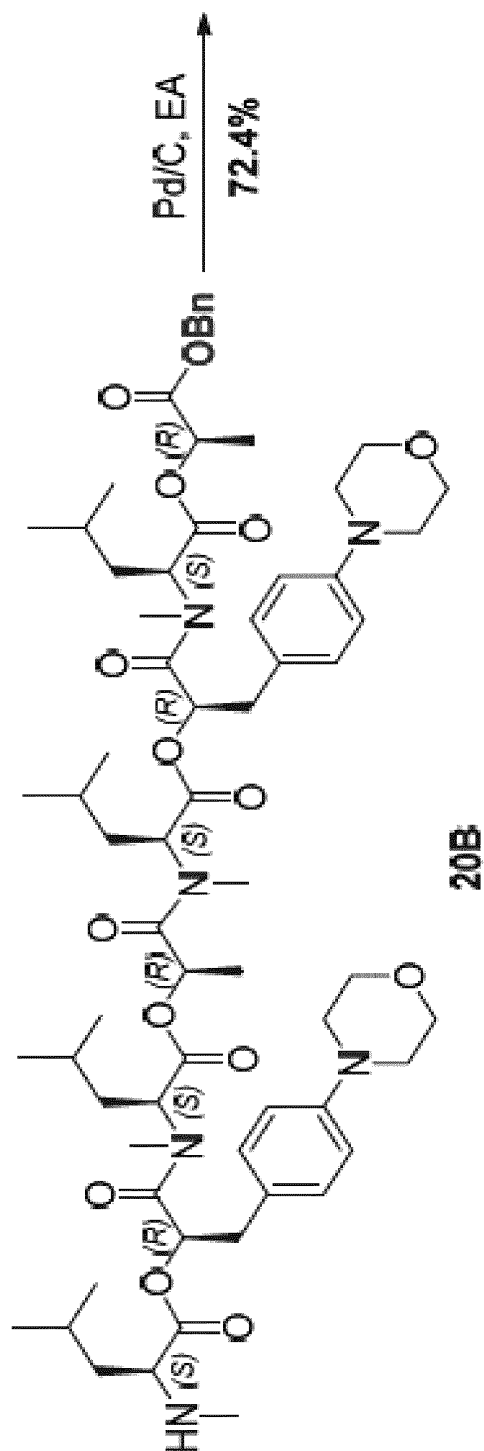


Fig. 2/4

27,6% overall yield from EMD-8 in 11 steps

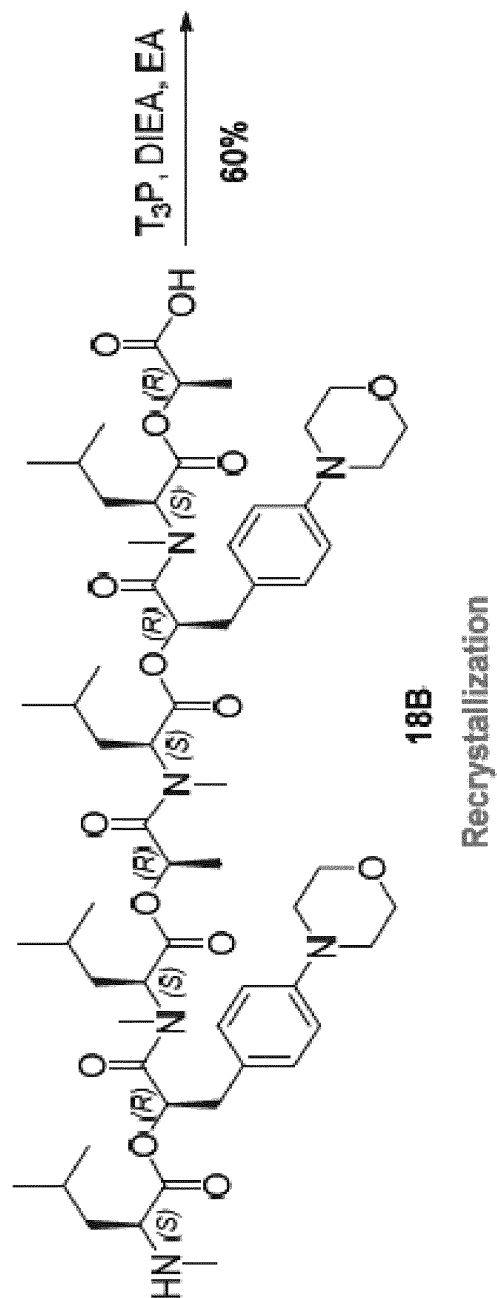
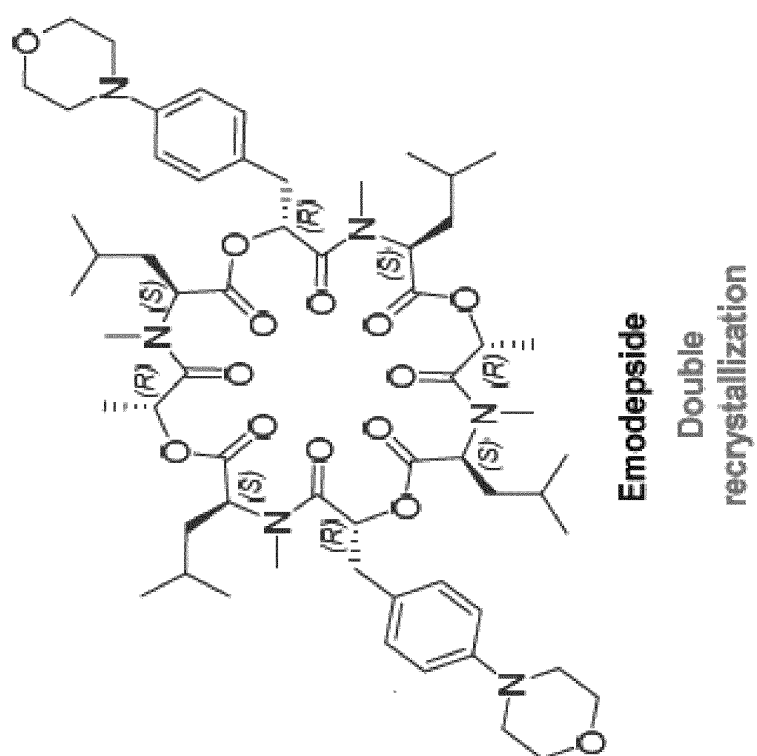


Fig. 2/5

27,6% overall yield from EMD-8 in 11 steps



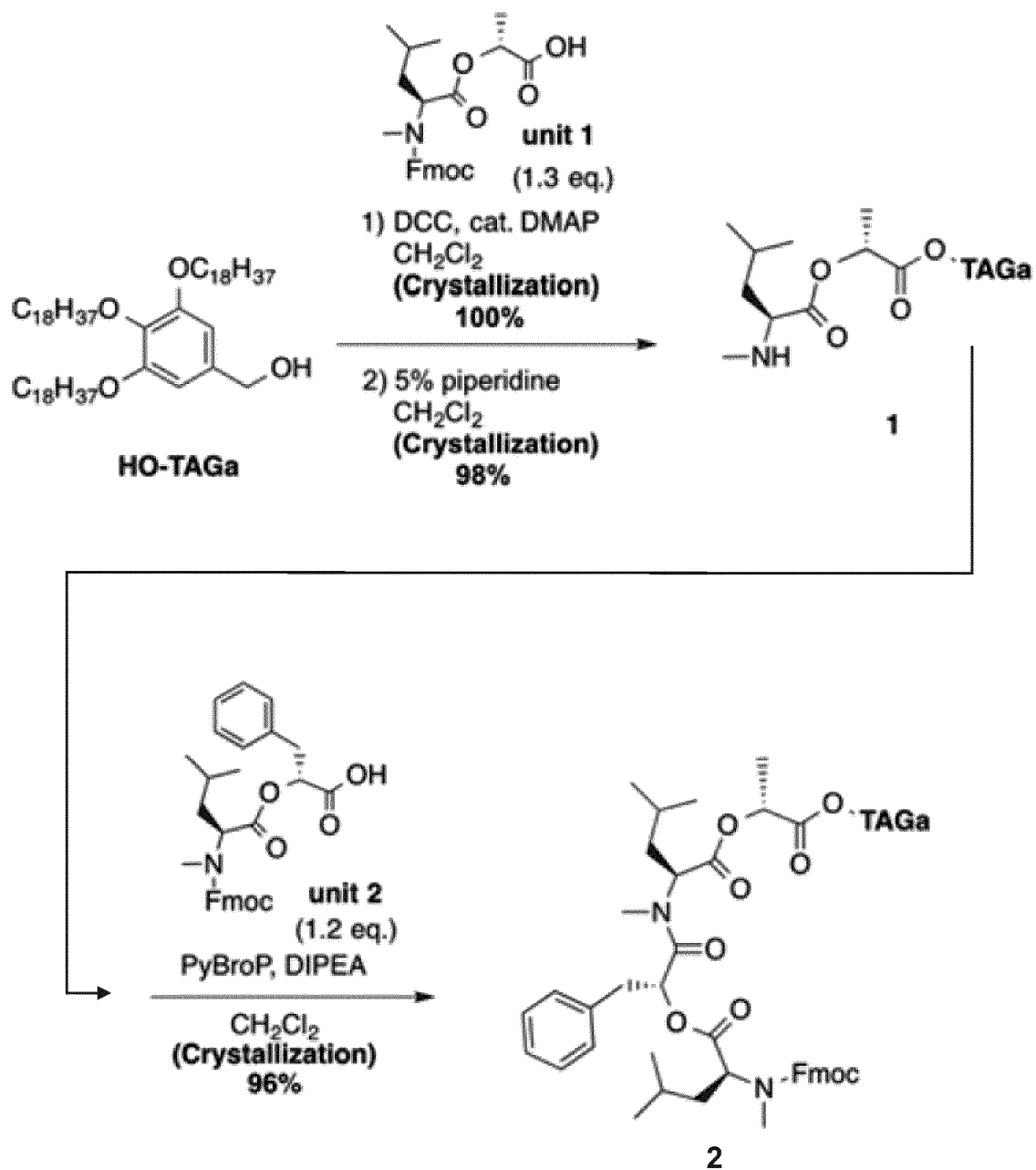


Fig. 3/1

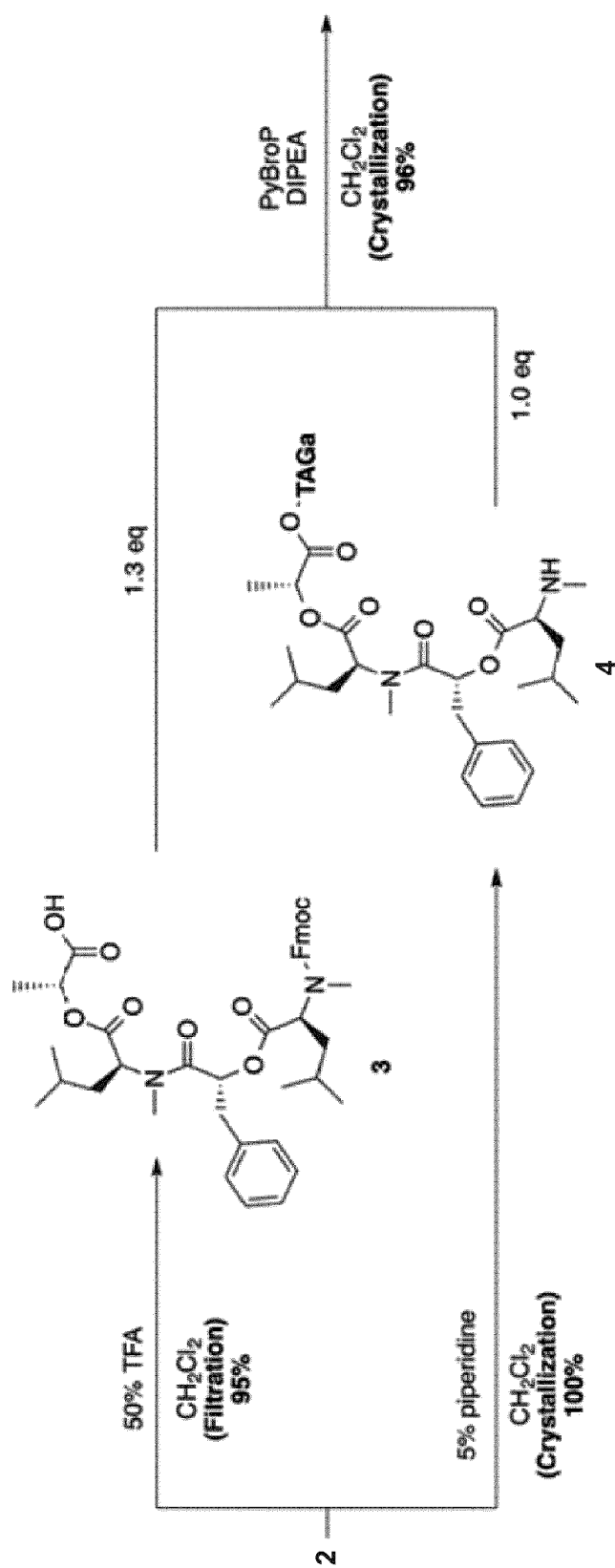
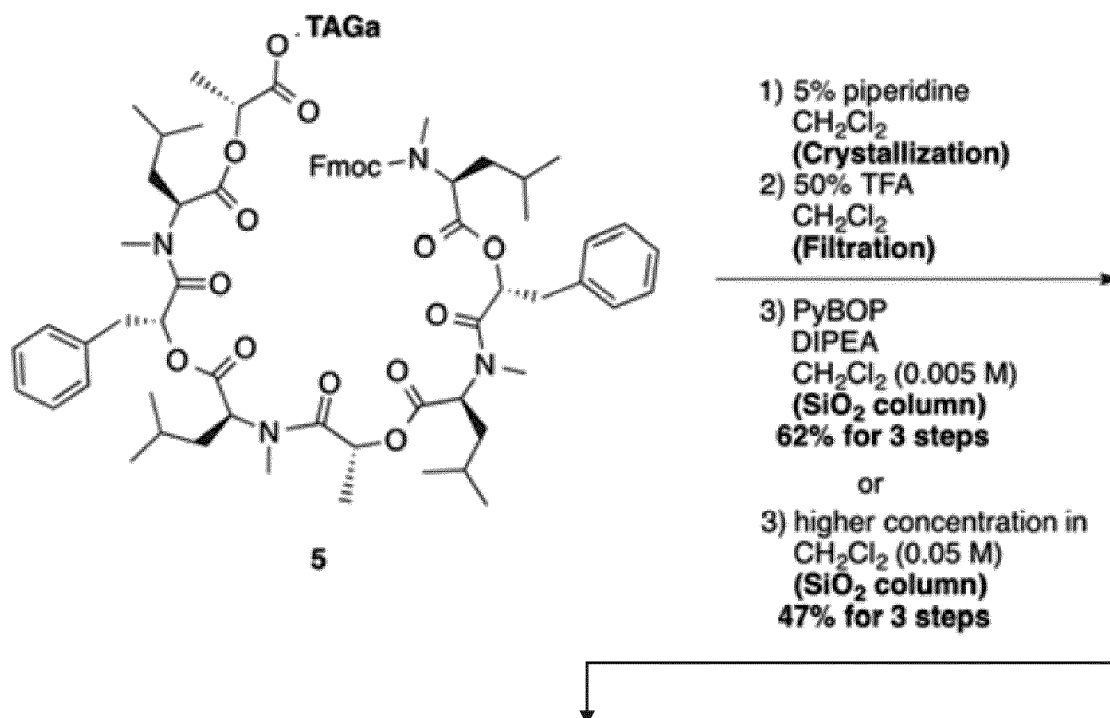


Fig. 3/2



PF1022A (8 steps for longest linear from HO-TAGa)

56% overall yield
(in case of diluted condition for last step)

43% overall yield
(in case of higher conc. condition for last step)

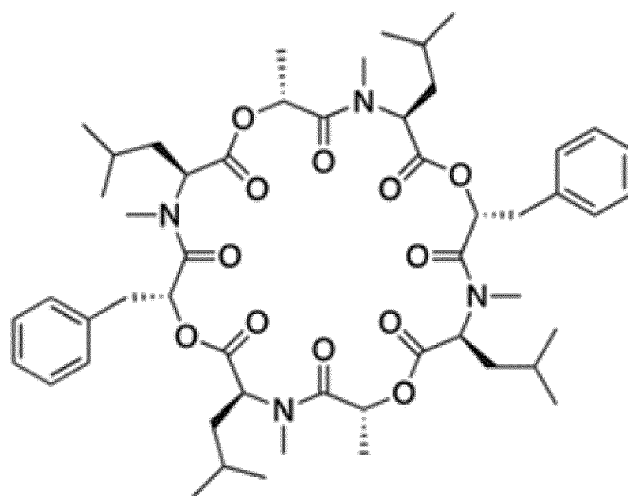


Fig. 3/3

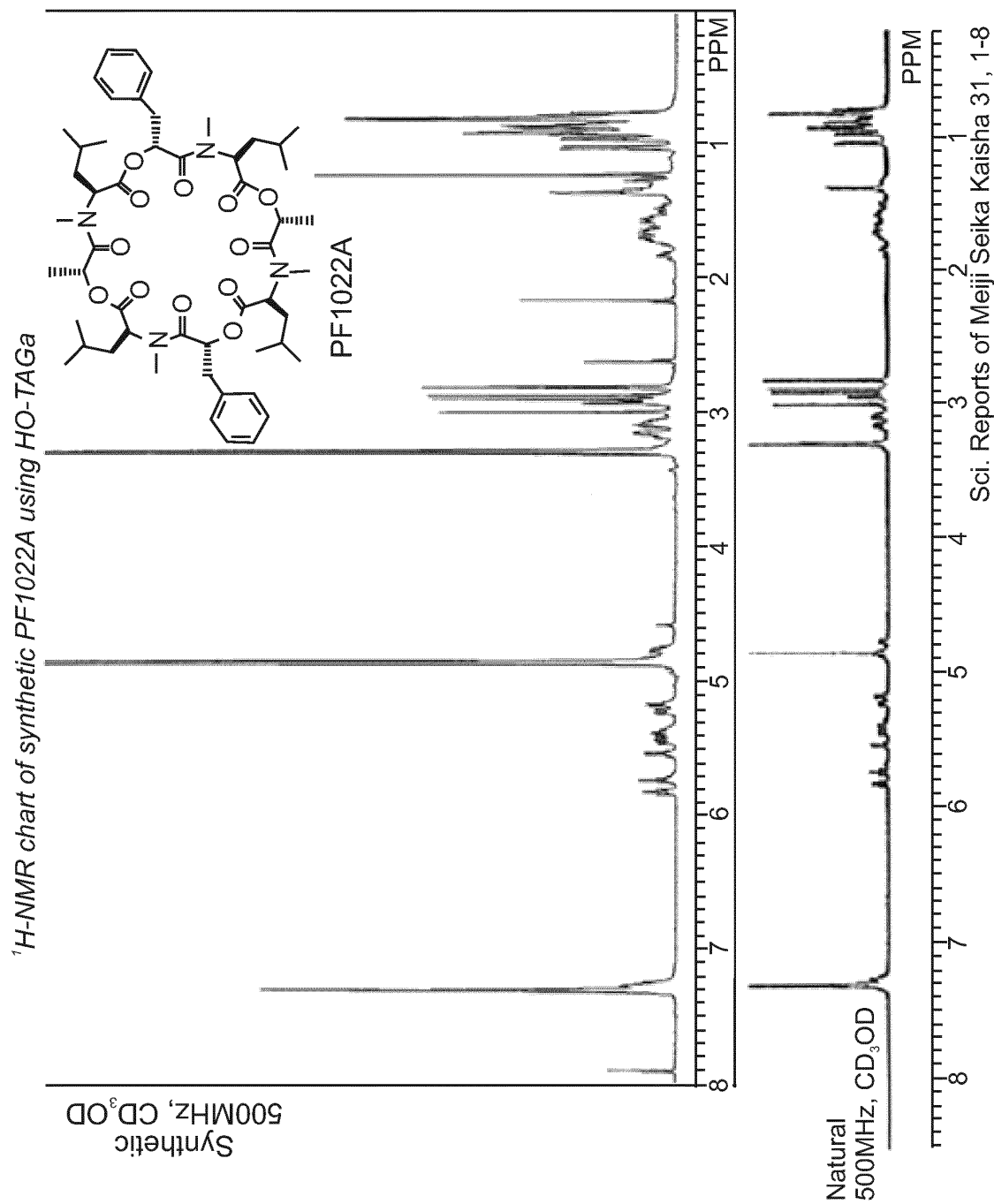


Fig. 4

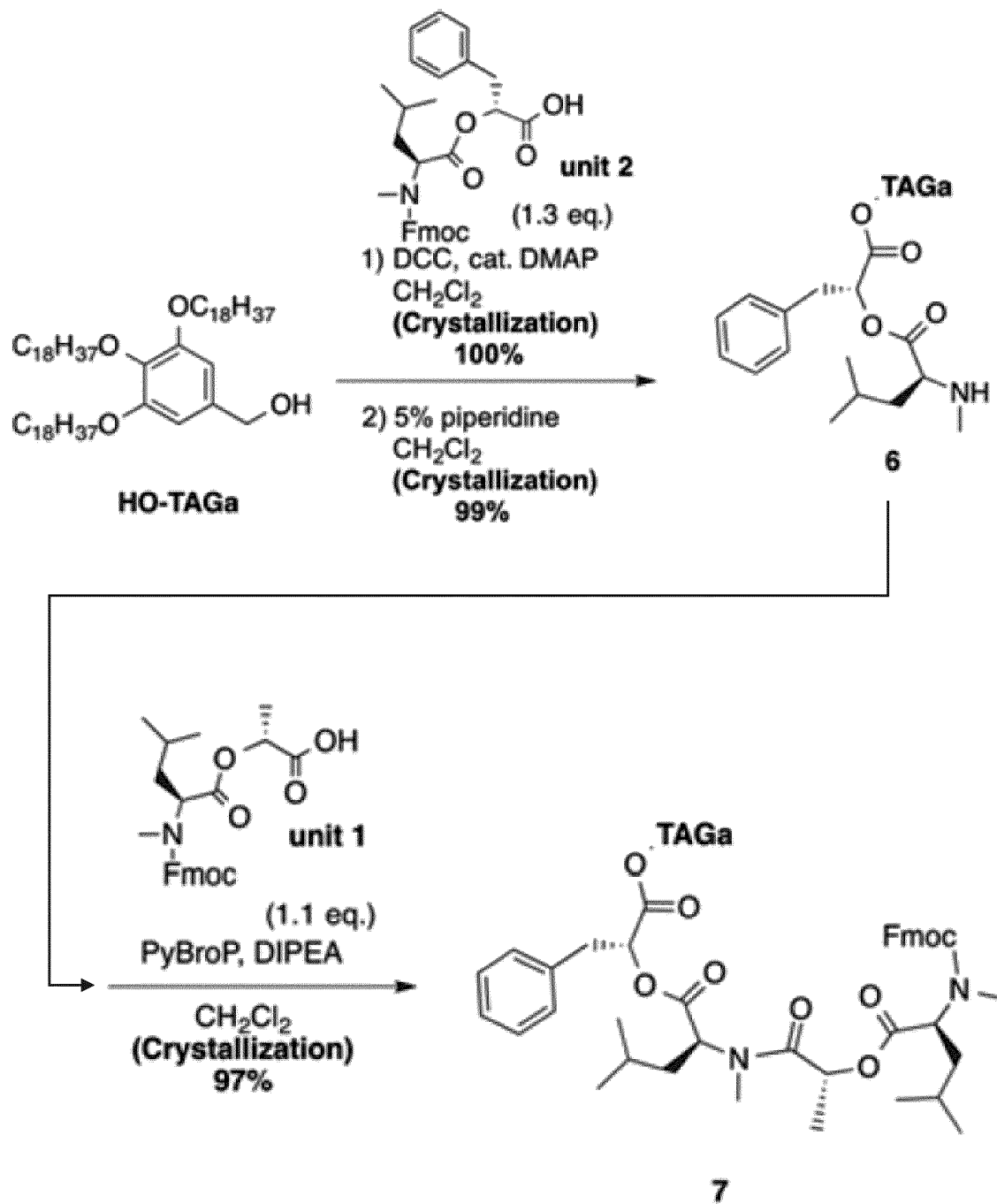


Fig. 5/1

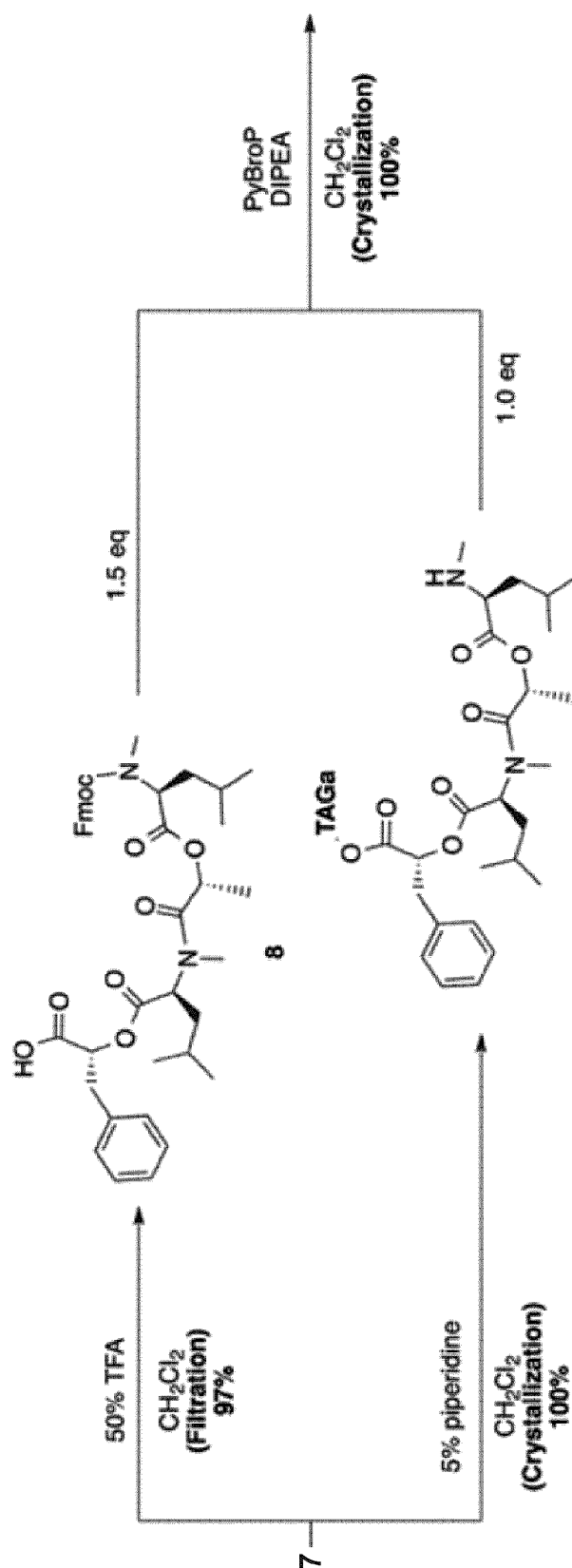
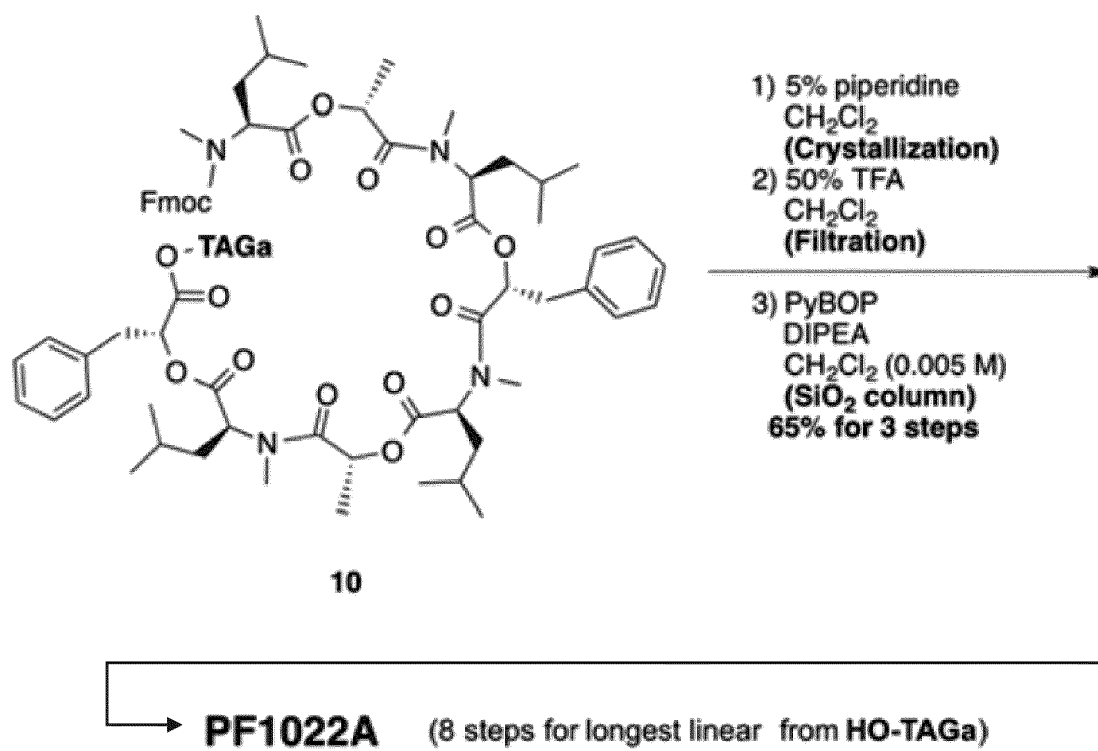


Fig. 5/2



62% overall yield

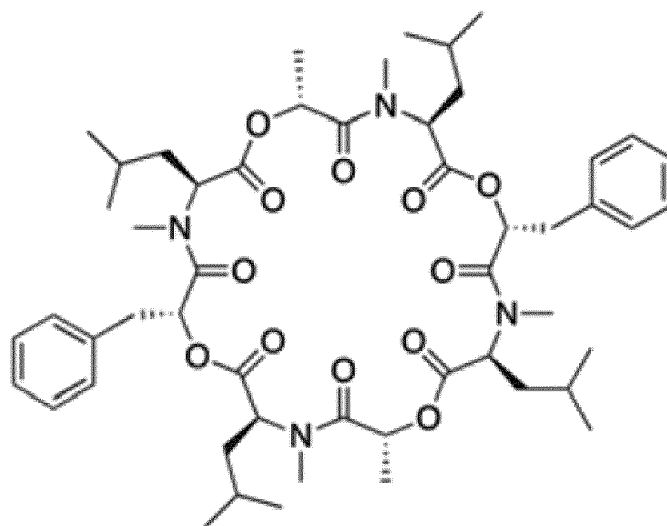


Fig. 5/3

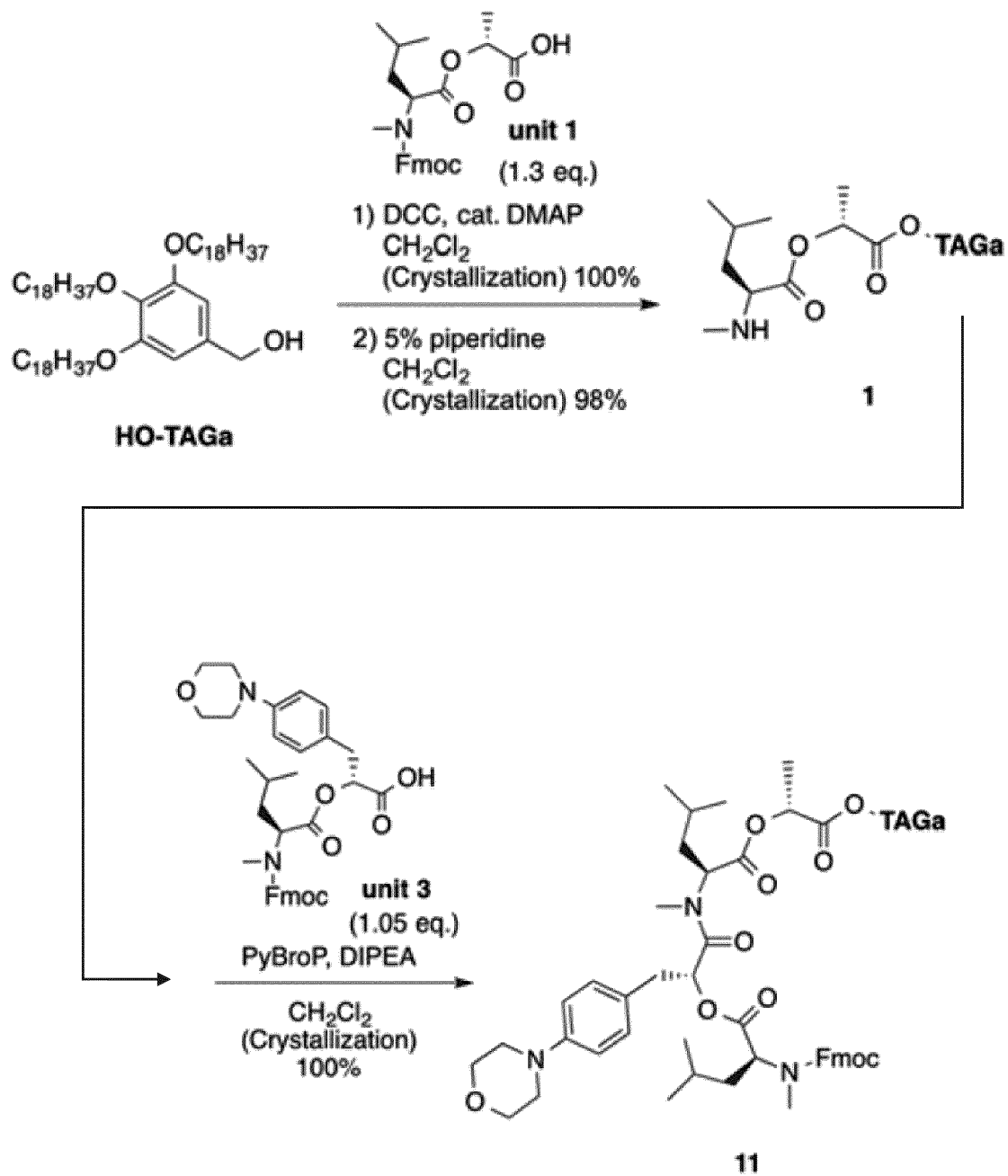


Fig. 6/1

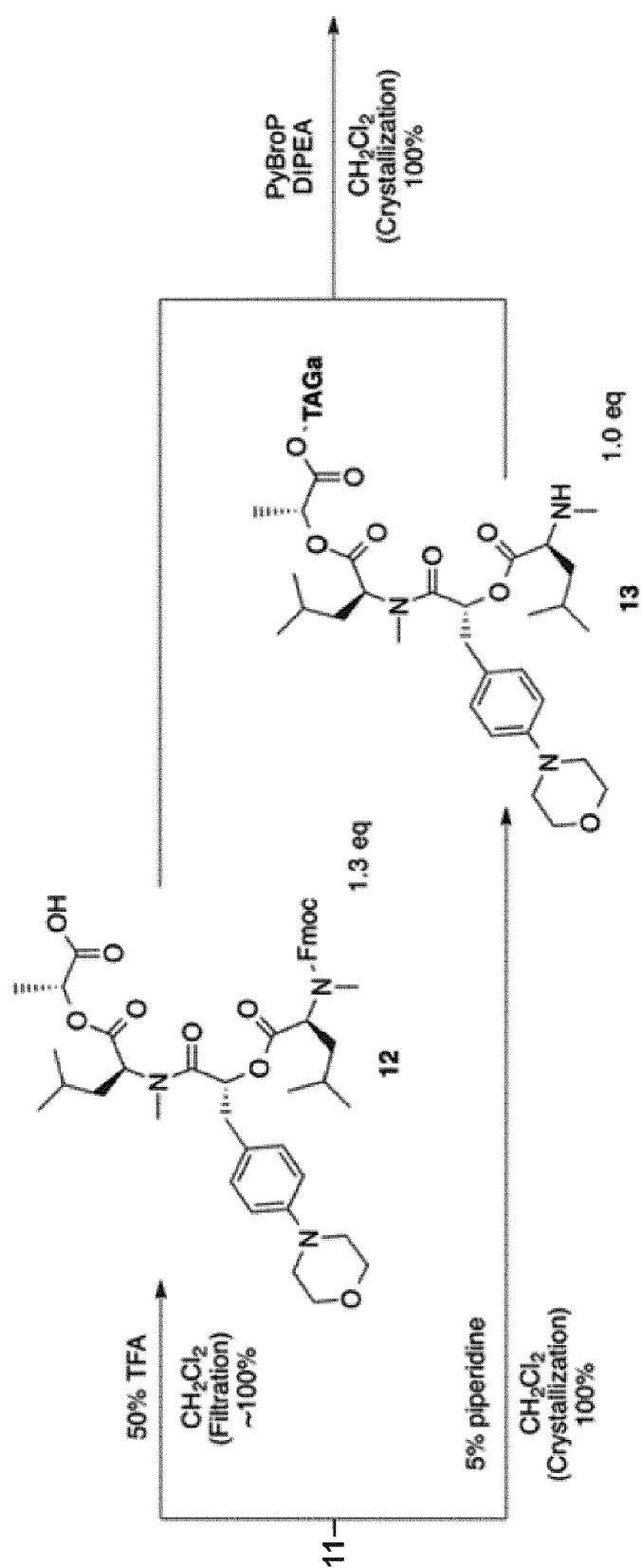
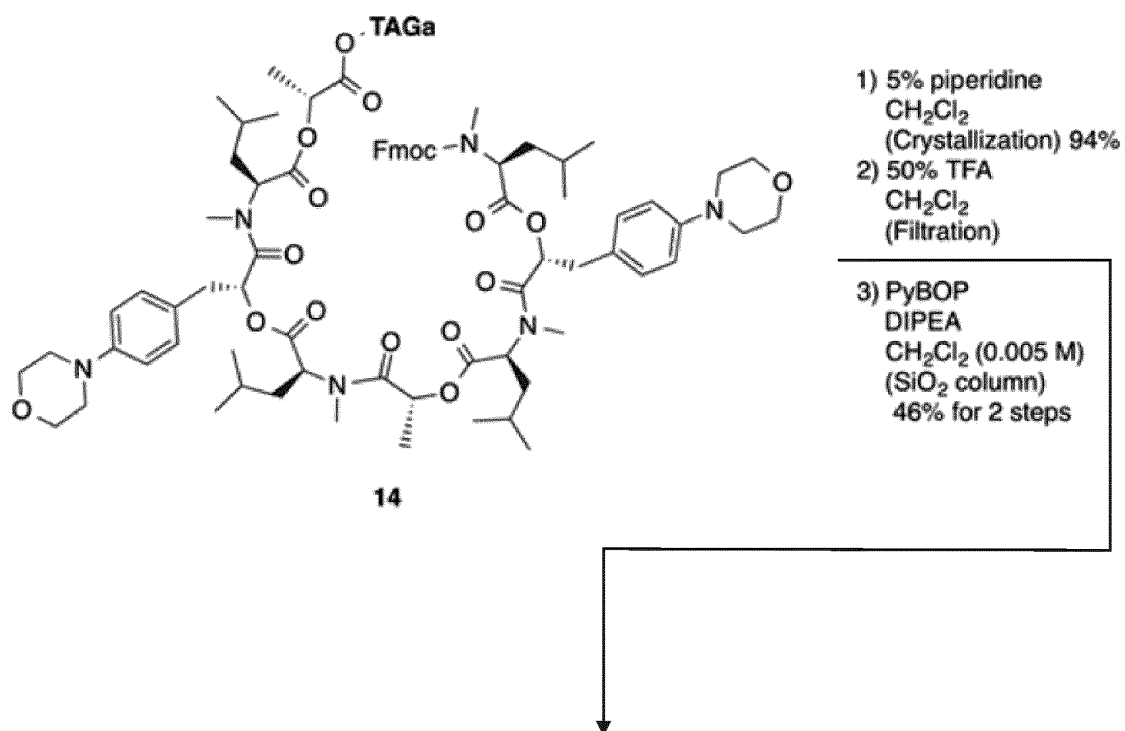


Fig. 6/2

**Emodepside**

(8 steps for longest linear from HO-TAGa)
42% overall yield from HO-TAGa

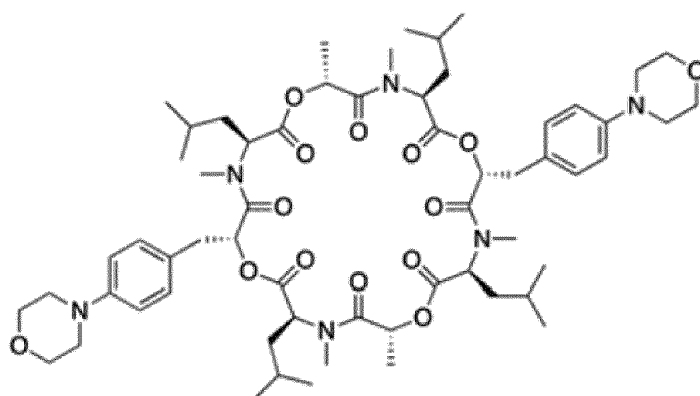
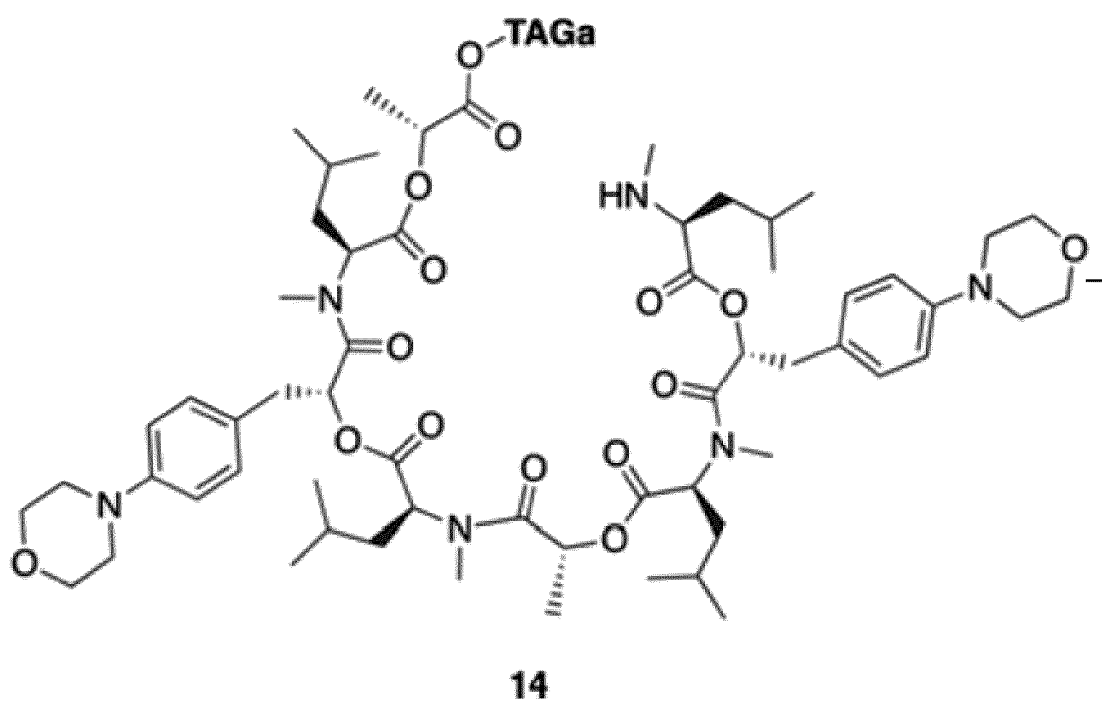


Fig. 6/3

Improved macrocyclization on Method 1



1) 50% TFA
CH₂Cl₂
(Filtration)

2) T₃P, DIPEA
CH₂Cl₂ (0.05 M),
r.t., 20 h
(SiO₂ column)
88% for 2 steps

Emodepside

(8 steps for longest linear from **HO-TAGa**)
85% overall yield from HO-TAGa

Fig. 6/4



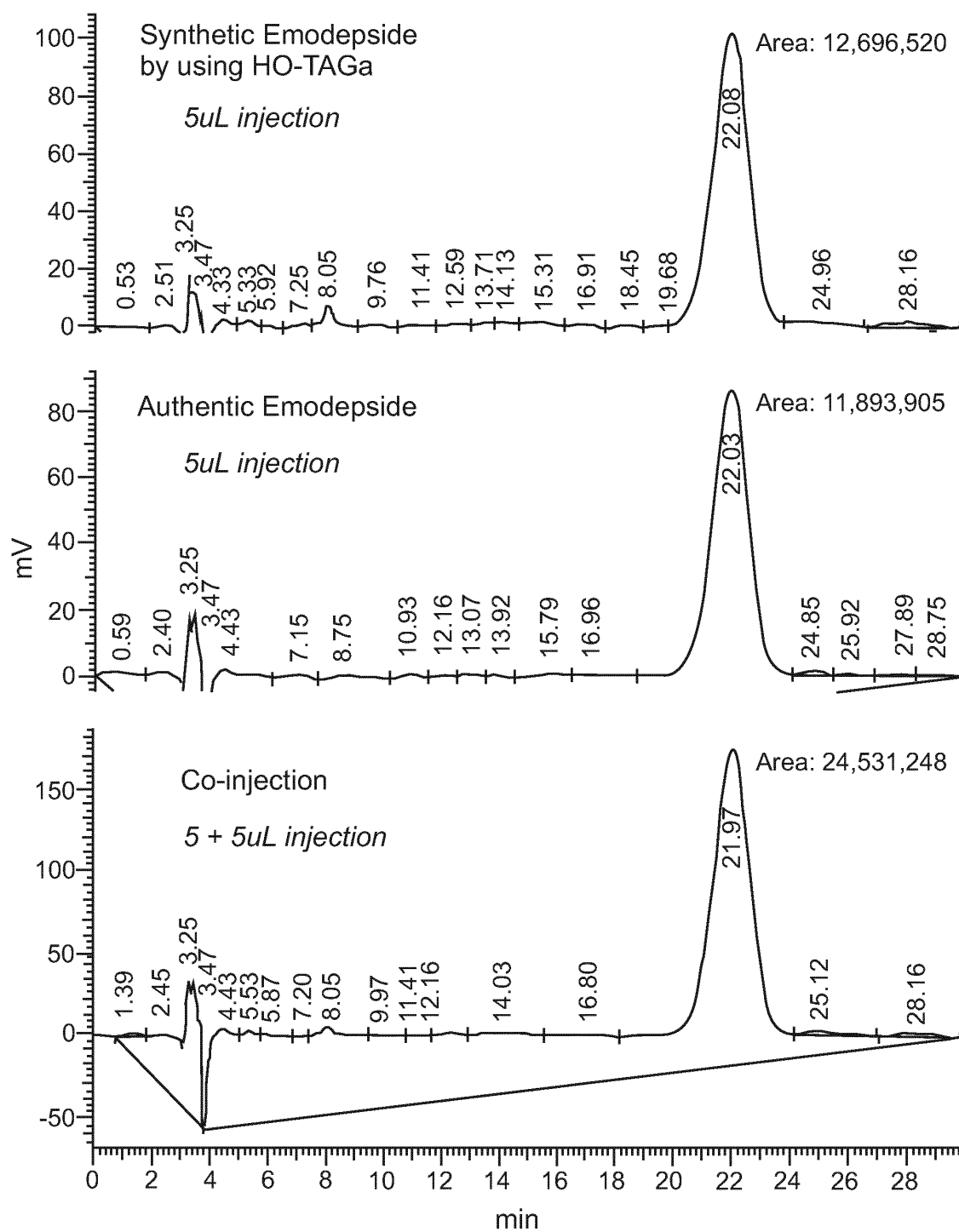


Fig. 8

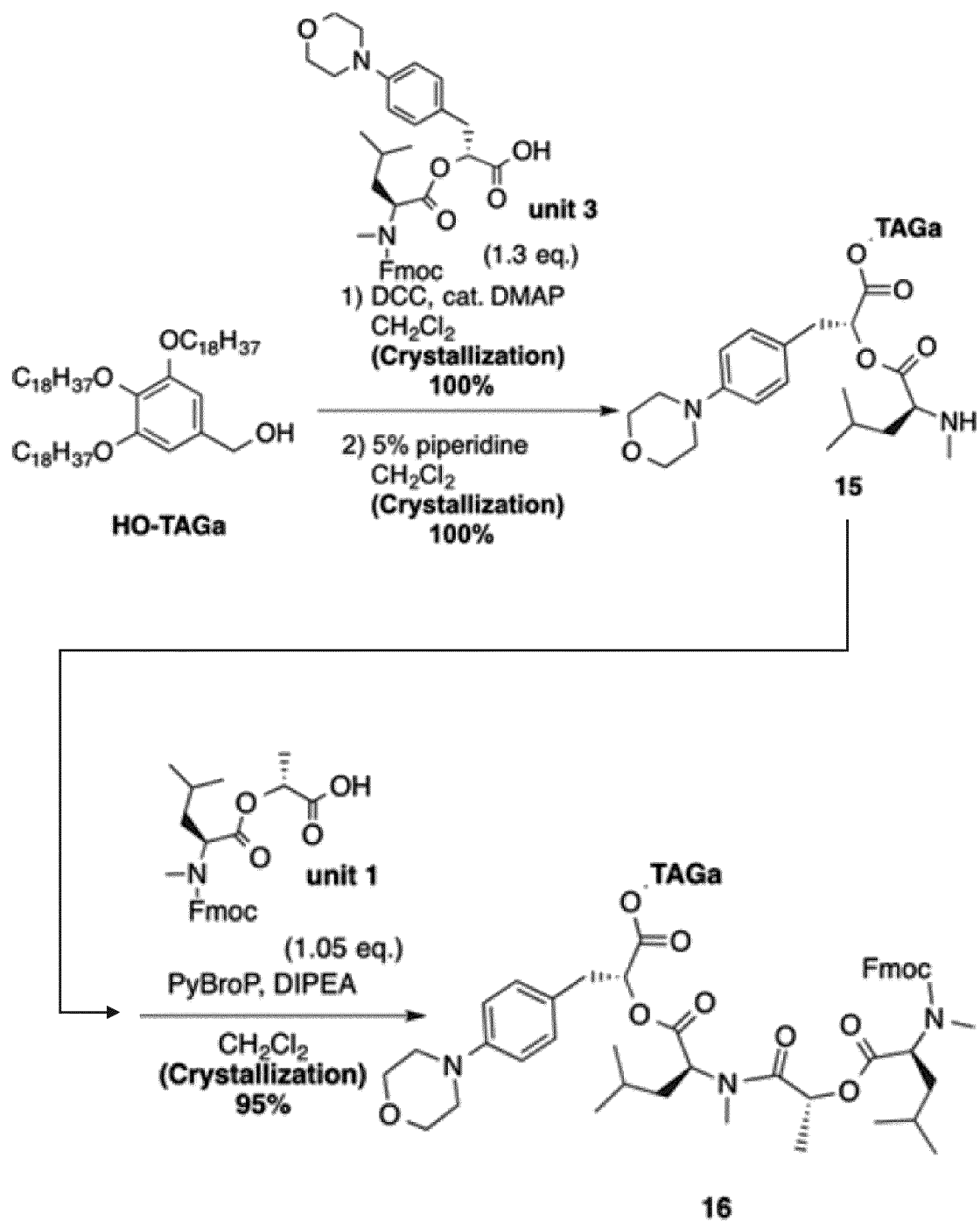


Fig. 9/1

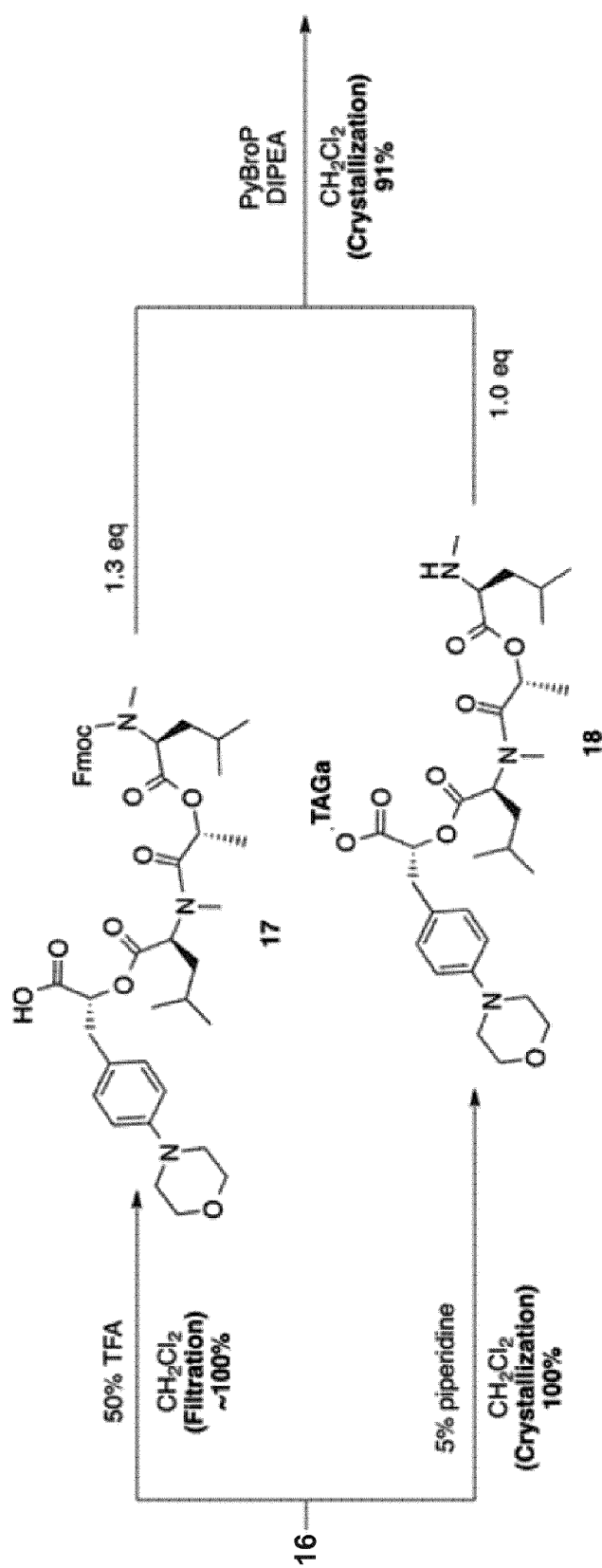
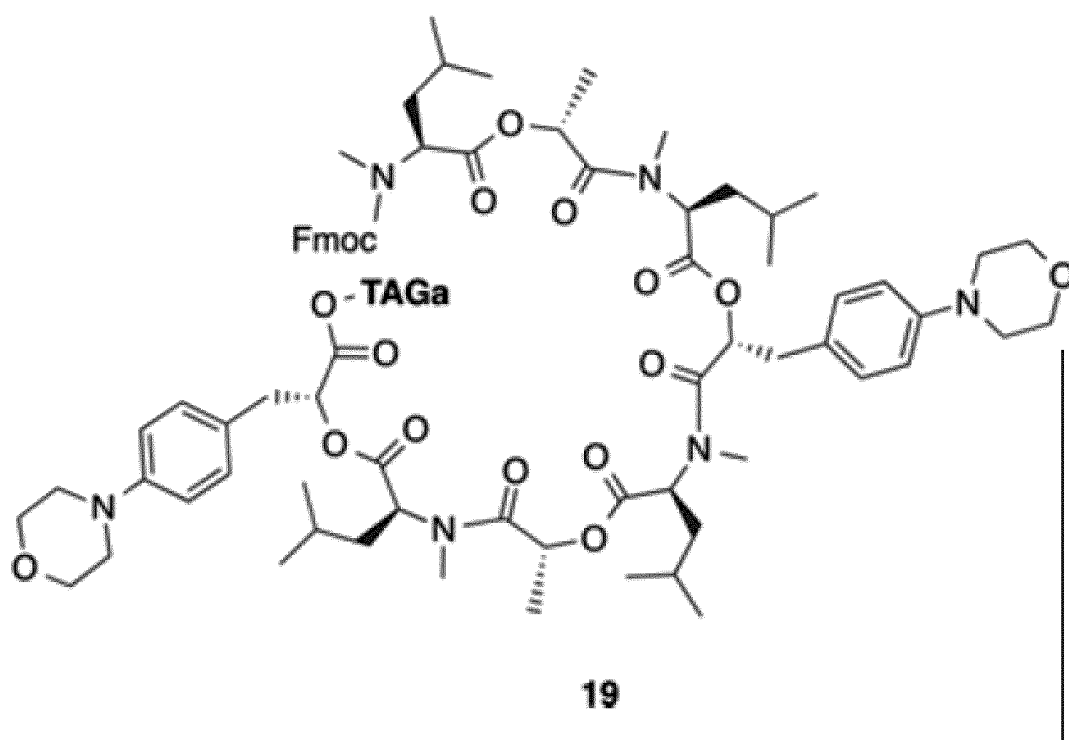


Fig. 9/2



- 1) 5% piperidine
CH₂Cl₂
(Crystallization) 100%
- 2) 50% TFA
CH₂Cl₂
(Filtration)

Emodepside

- 3) PyBOP
DIPEA
CH₂Cl₂ (0.005 M)
(SiO₂ column)
44% for 2 steps

(8 steps for longest linear from HO-TAGa)
38% overall yield from HO-TAGa

Fig. 9/3