

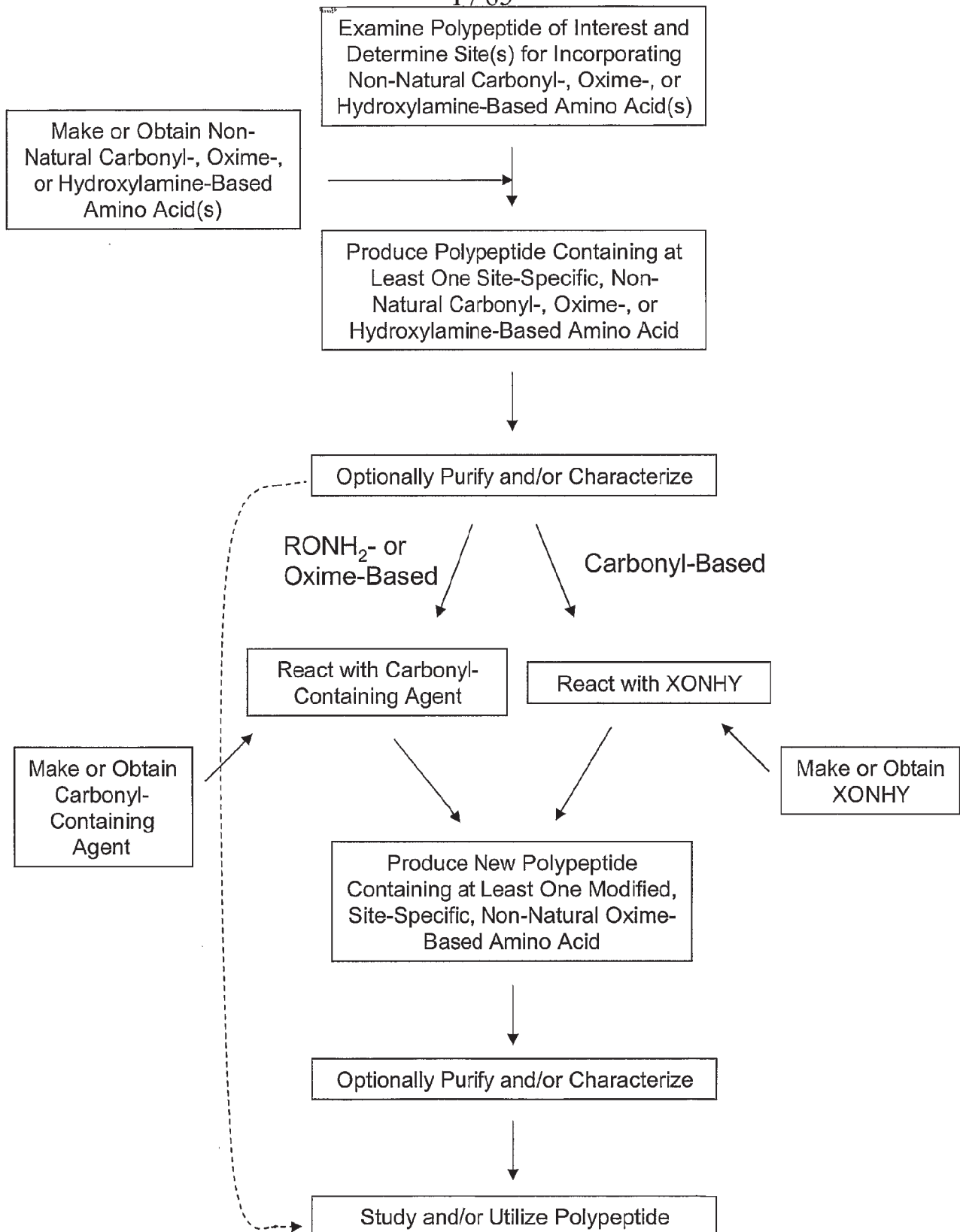
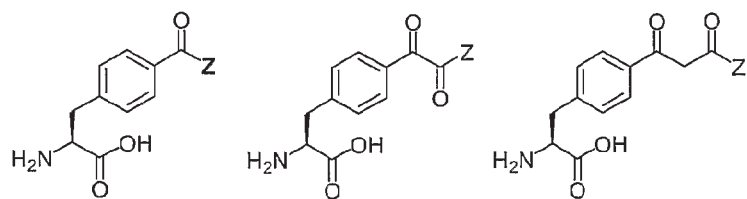
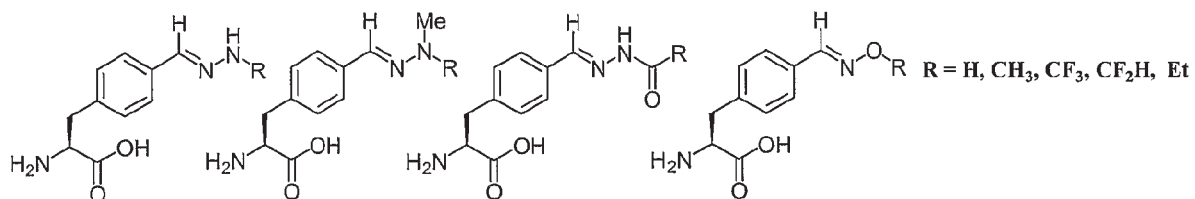


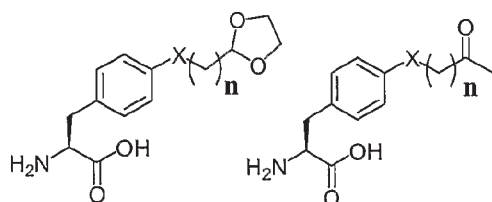
FIG. 1



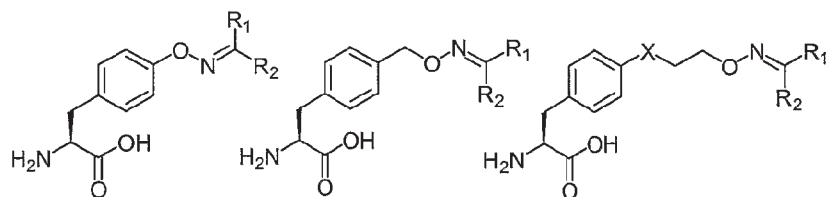
$Z = \text{CH}_3, \text{CF}_3, \text{CF}_2\text{H}, \text{CH}_2\text{Cl}, \text{CH}_2\text{OH}, \text{CH}_2\text{OMe}, \text{Et}, \text{iPrCH}_2\text{CN}$



$R = \text{H}, \text{CH}_3, \text{CF}_3, \text{CF}_2\text{H}, \text{Et}$

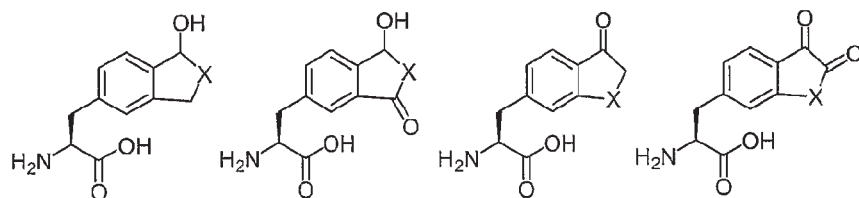


$n = 0-4; X = \text{O}, \text{S}, \text{NH}, \text{CH}_2, \text{CF}_2, \text{CO}$

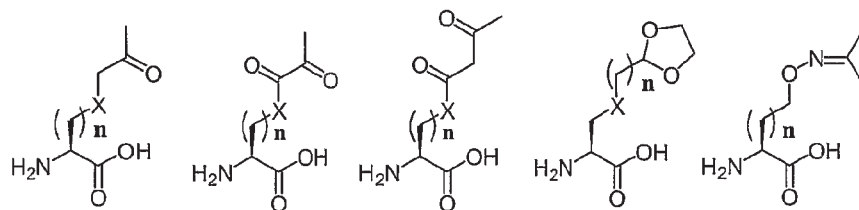


$R_1, R_2 = \text{H}, \text{CH}_3, \text{CF}_3, \text{CF}_2\text{H}, \text{Et}$

$X = \text{O}, \text{S}, \text{NH}, \text{CH}_2, \text{CF}_2, \text{CO}$



$X = \text{O}, \text{S}, \text{NH}, \text{CH}_2, \text{CF}_2, \text{CO}$



$n = 0-4; X = \text{O}, \text{S}, \text{NH}, \text{CH}_2, \text{CO}$

FIG. 2

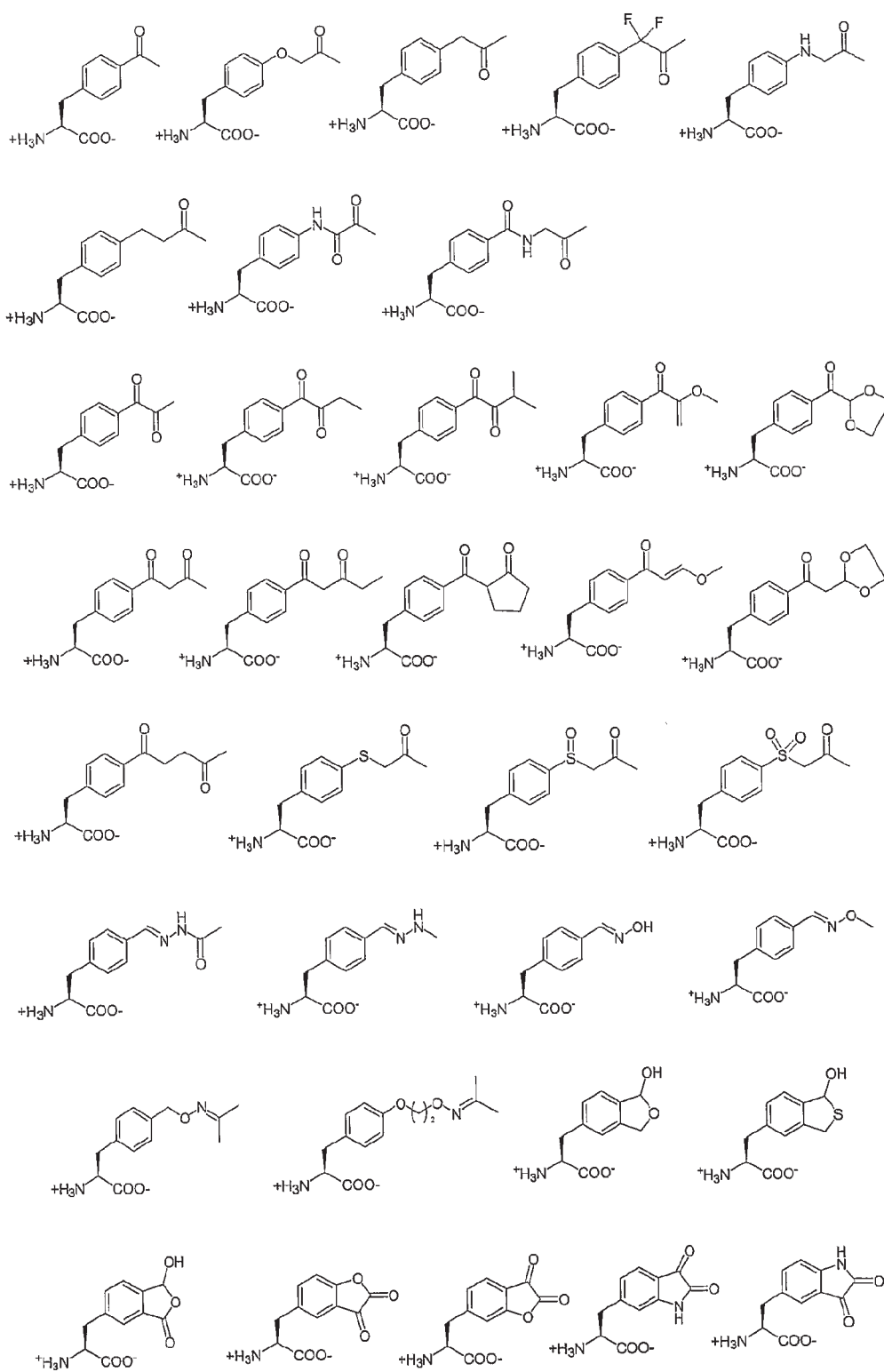


FIG. 3

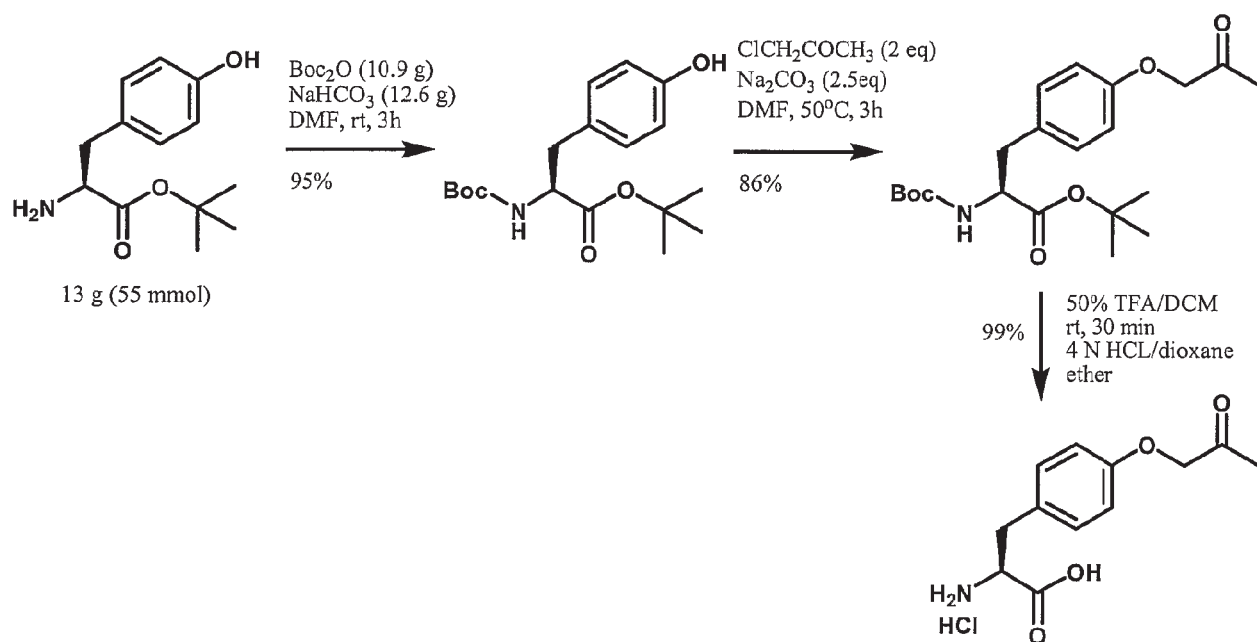


FIG. 4

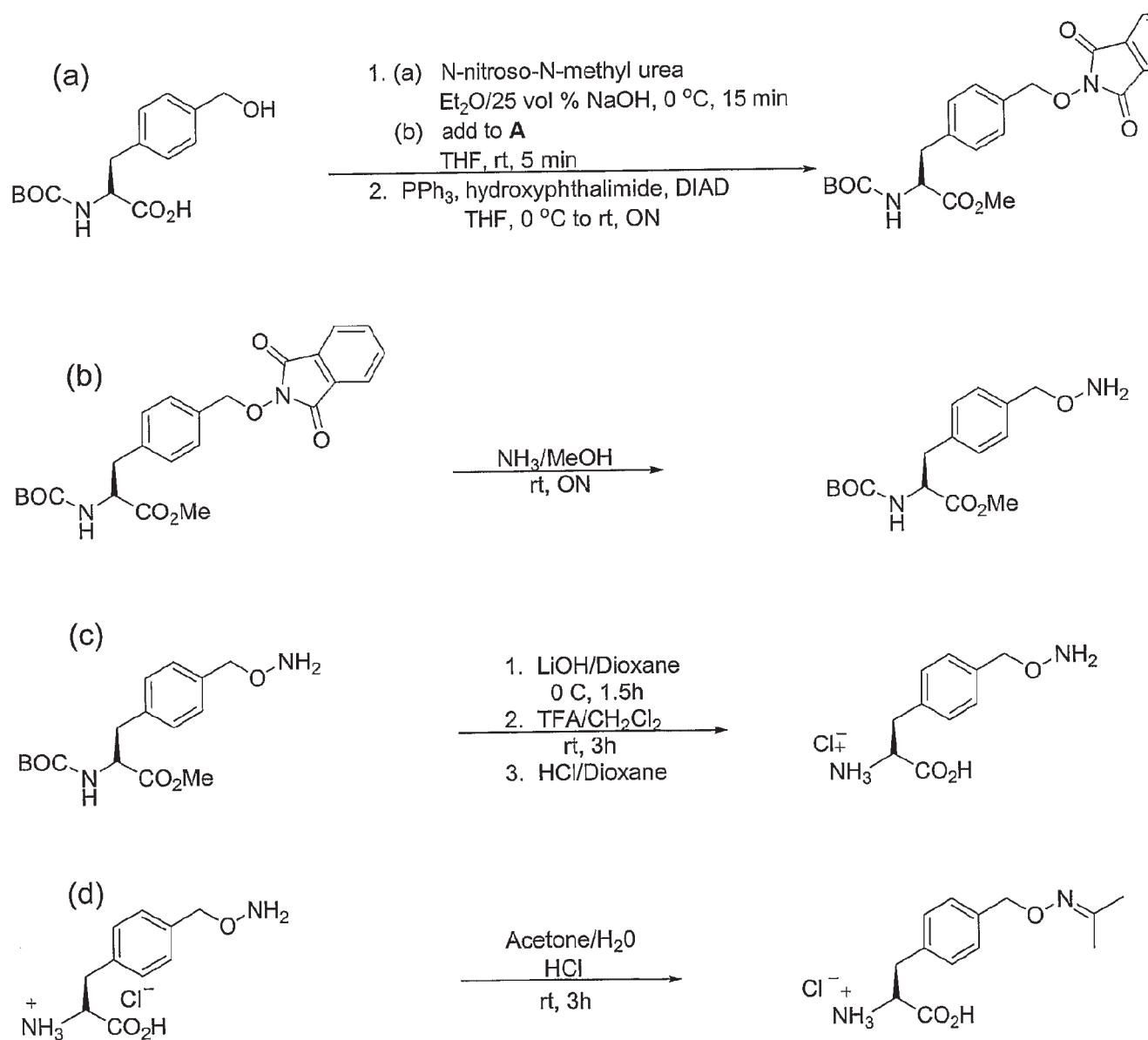


FIG. 5

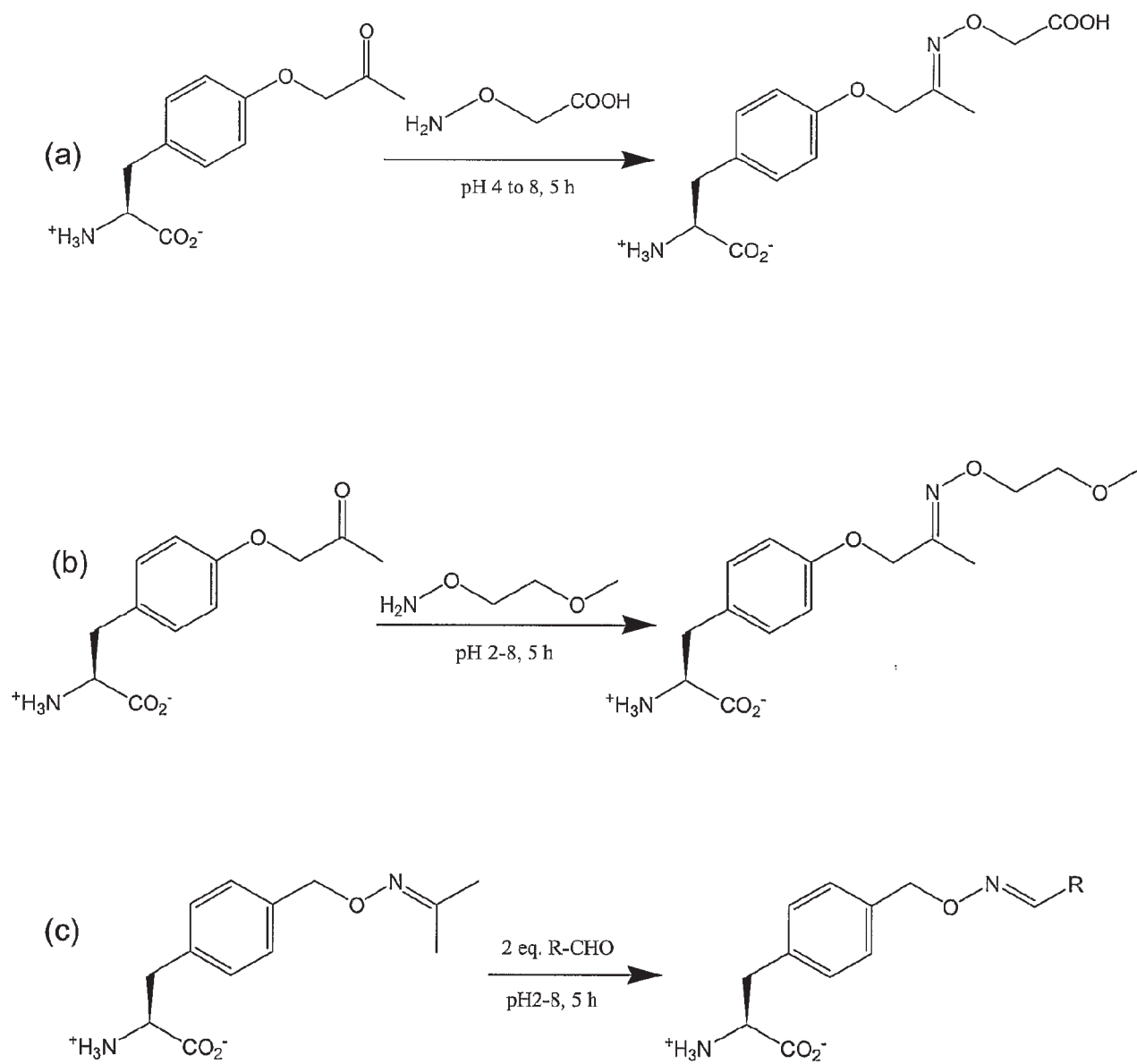
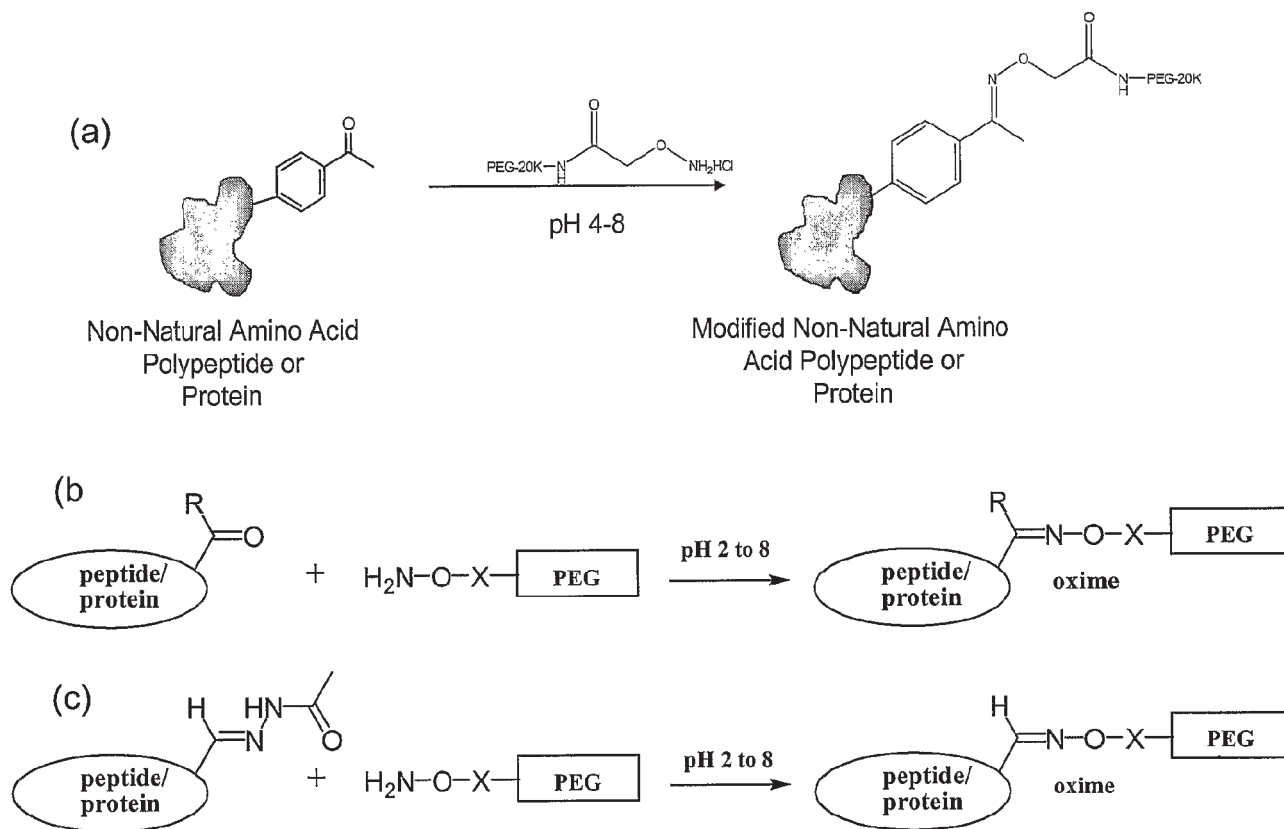


FIG. 6



R = H, (substituted) alkyl, (substituted) aryl;

X = linker

FIG. 7

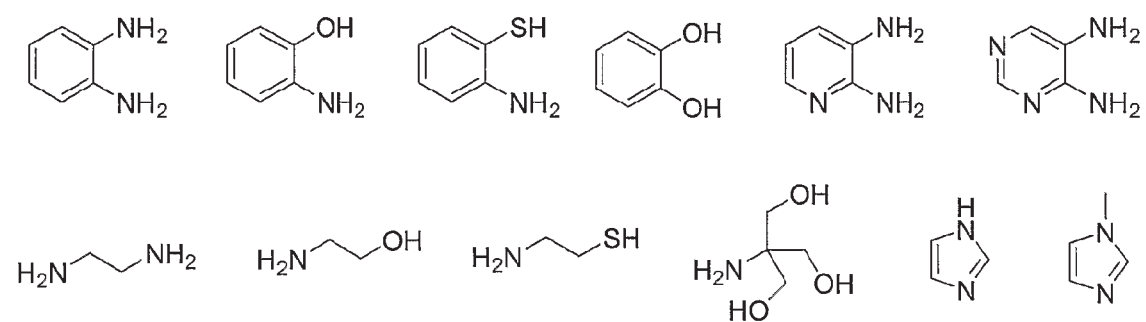


FIG. 8

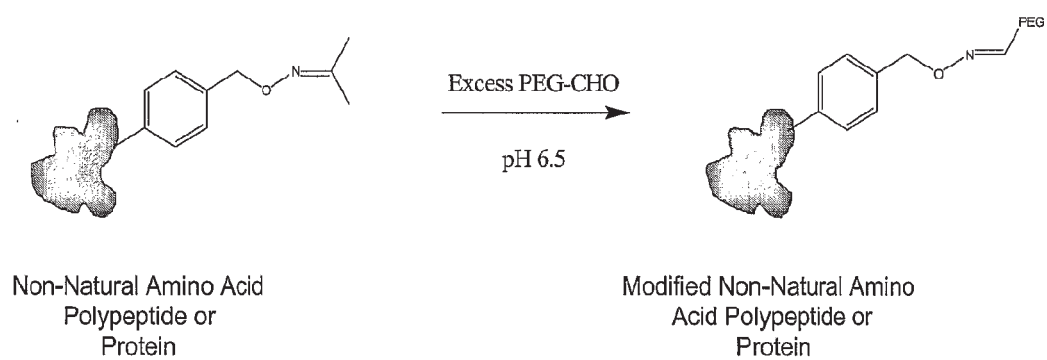
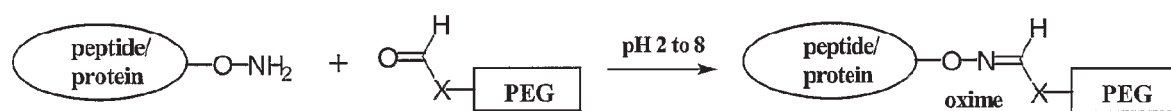


FIG. 9



R, R₁, R₂ = H, (substituted) alkyl, (substituted) aryl; X = linker

FIG. 10

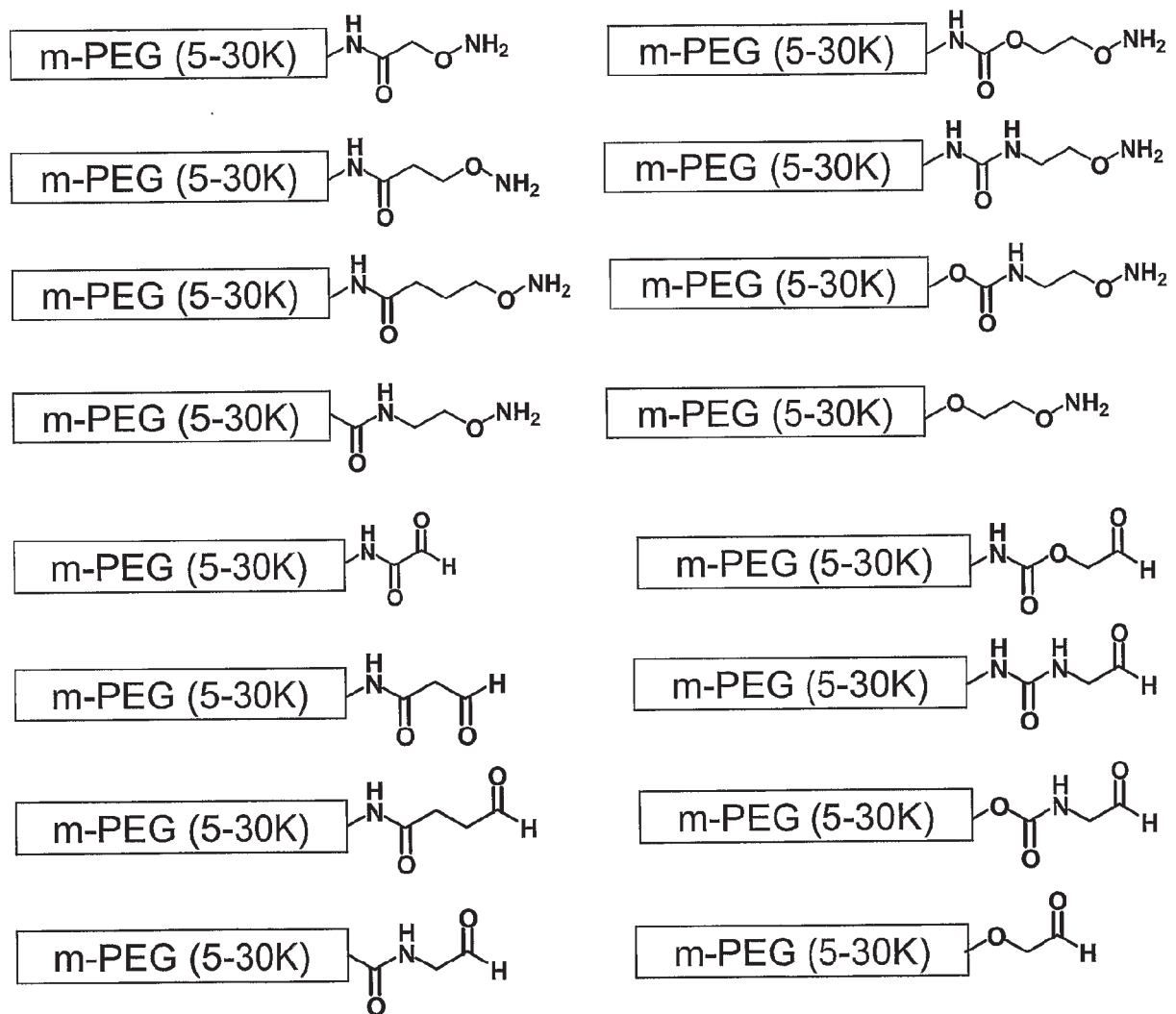


FIG. 11

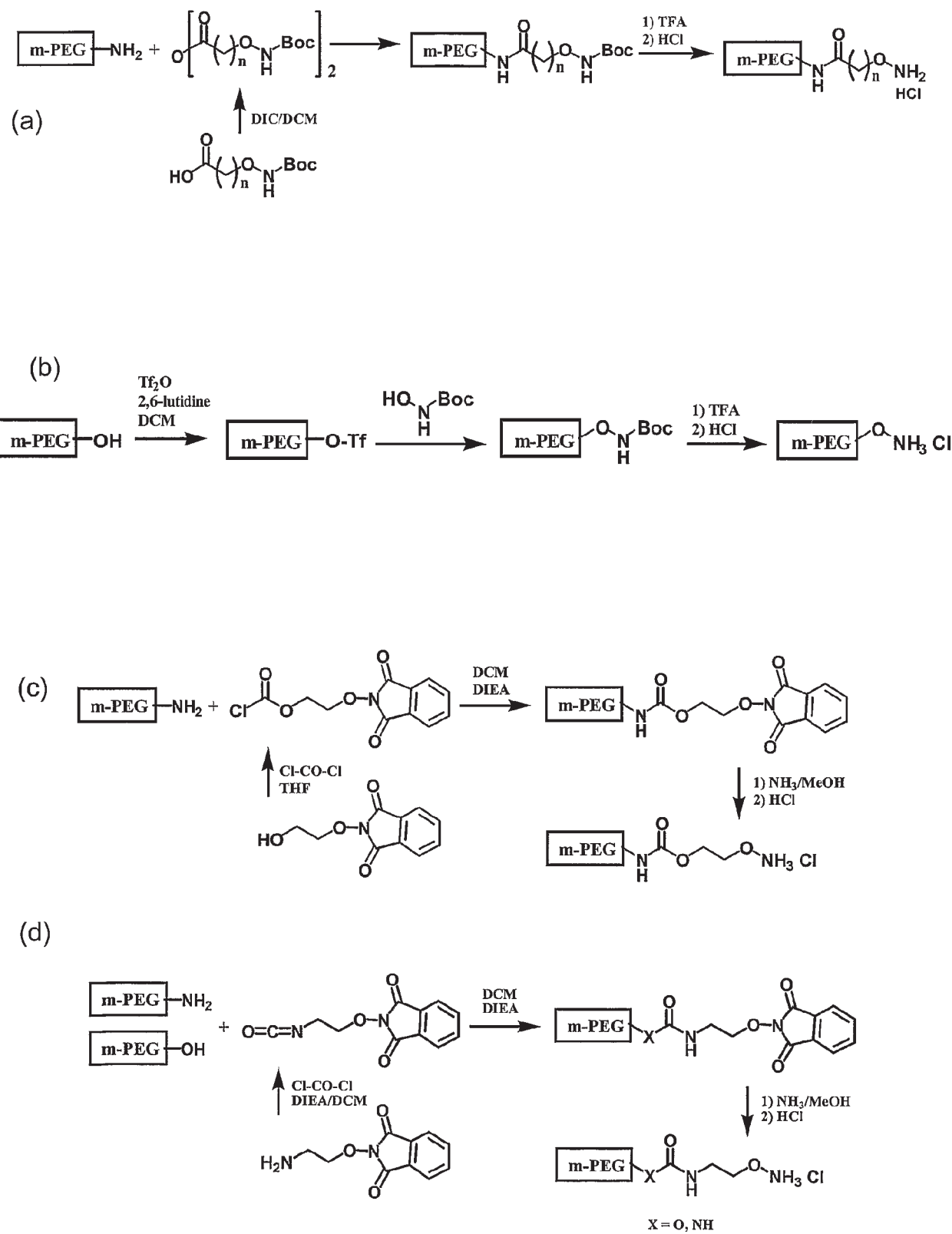


FIG. 12

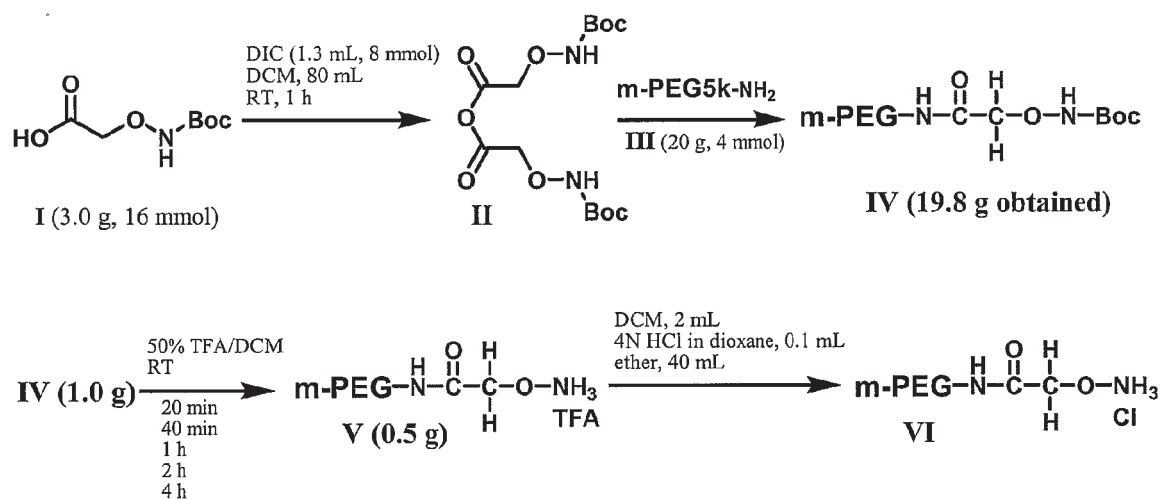
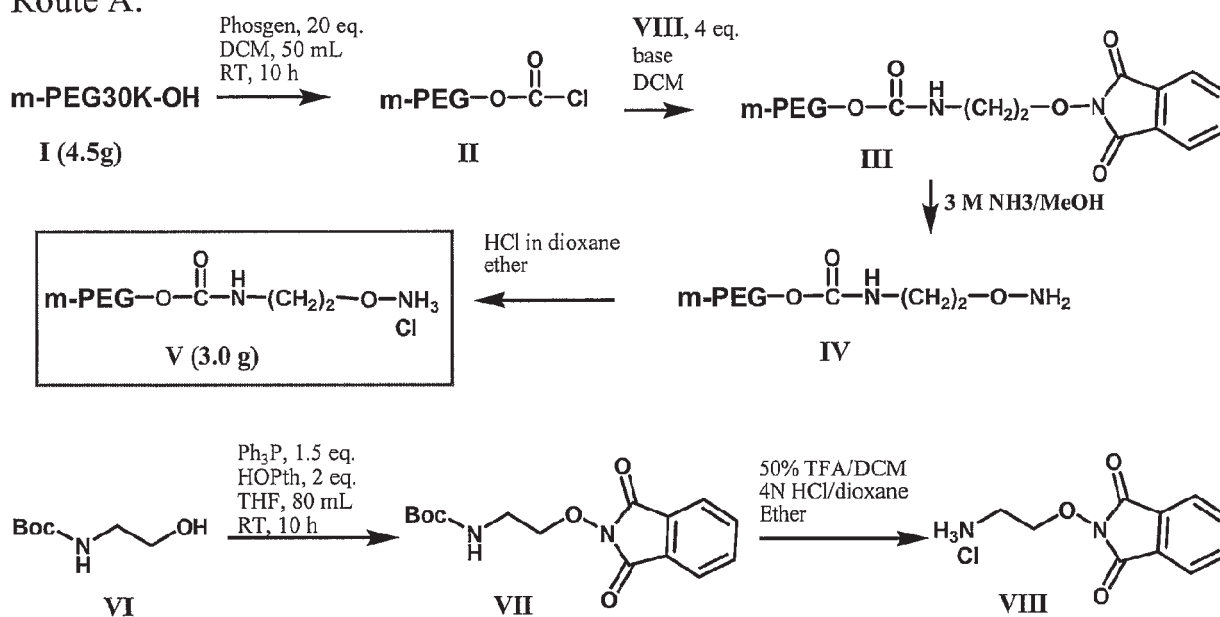


FIG. 13

Route A:



Route B:

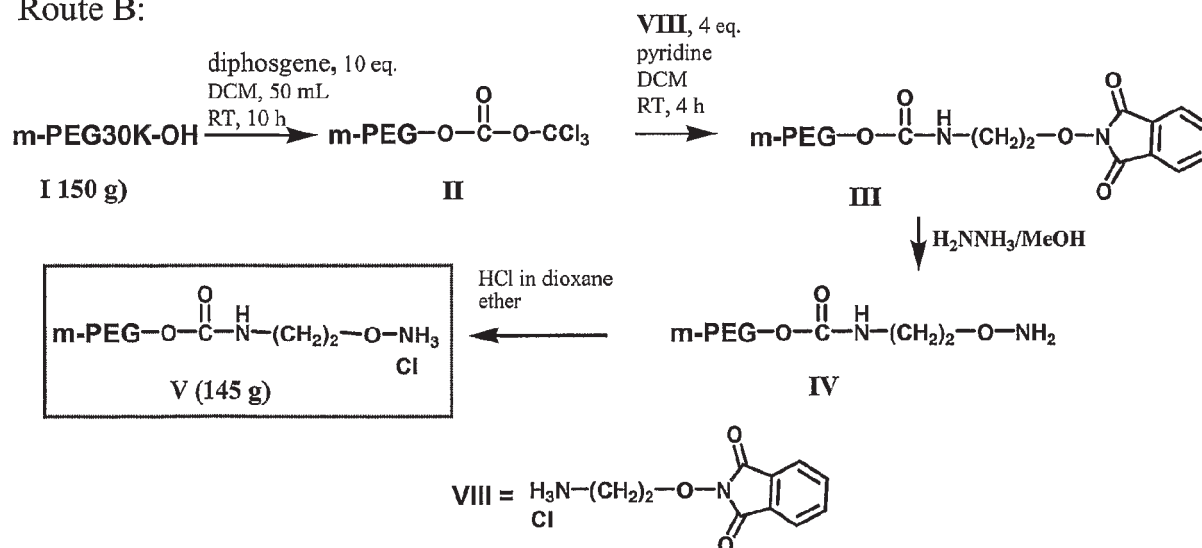
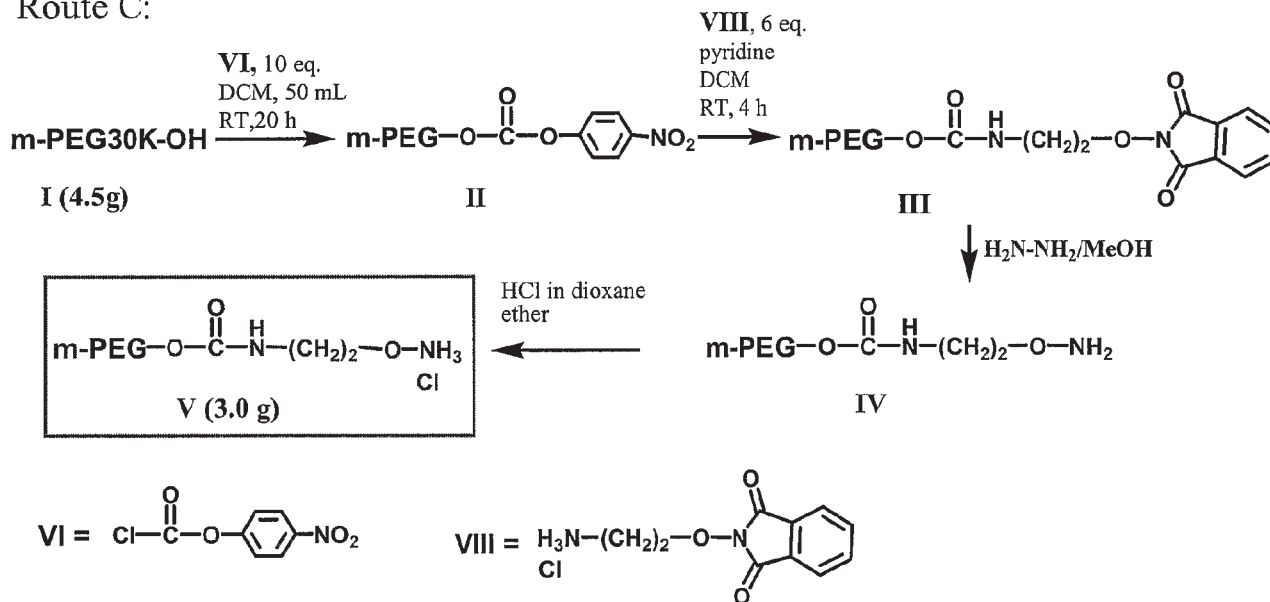


FIG. 14

Route C:



Route D:

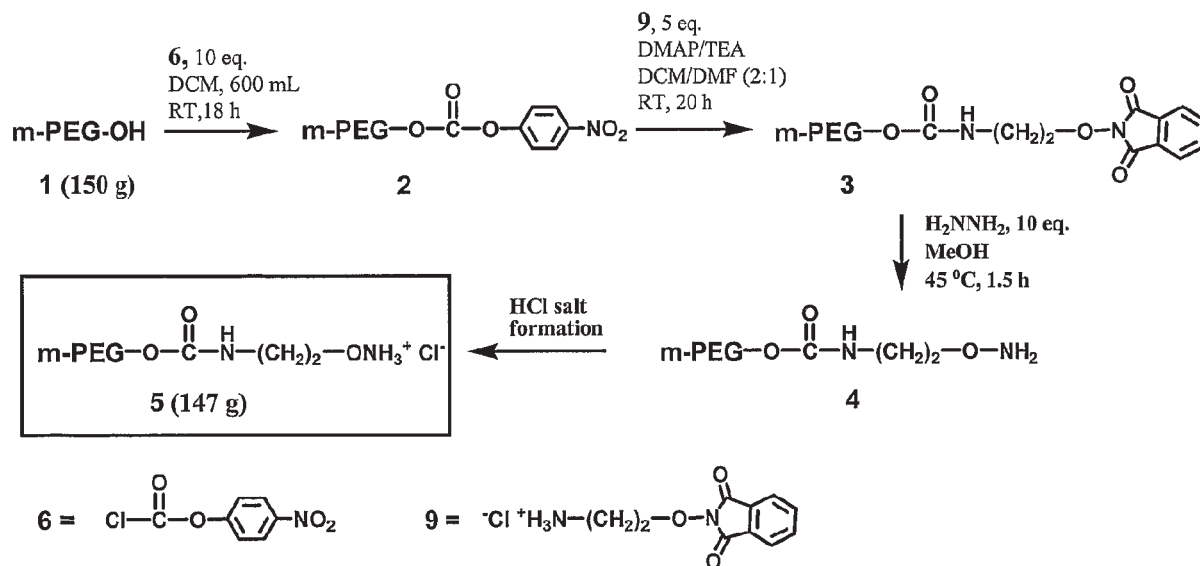


FIG. 15

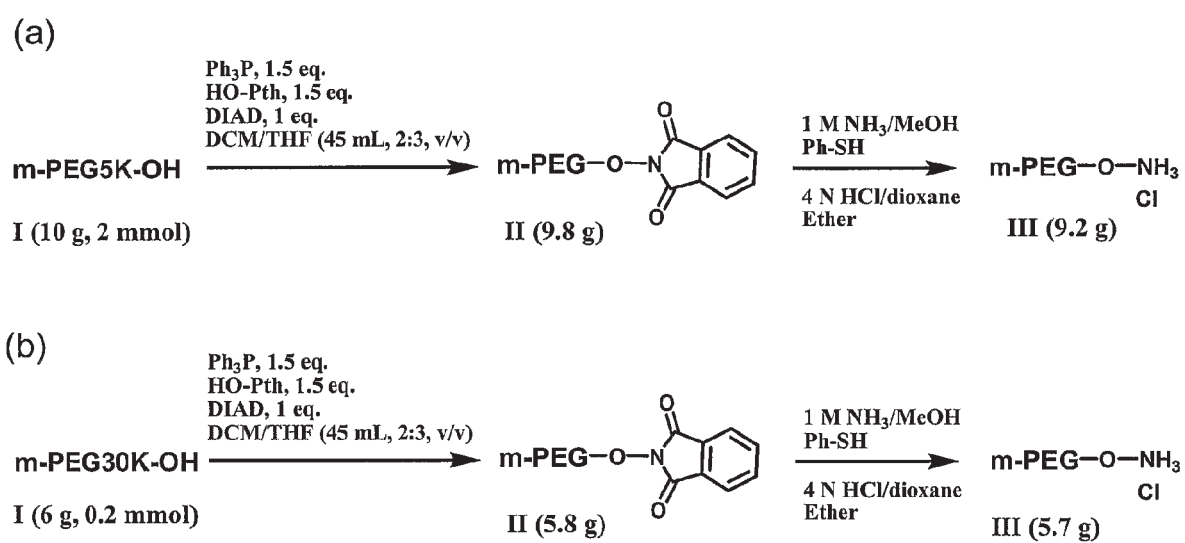
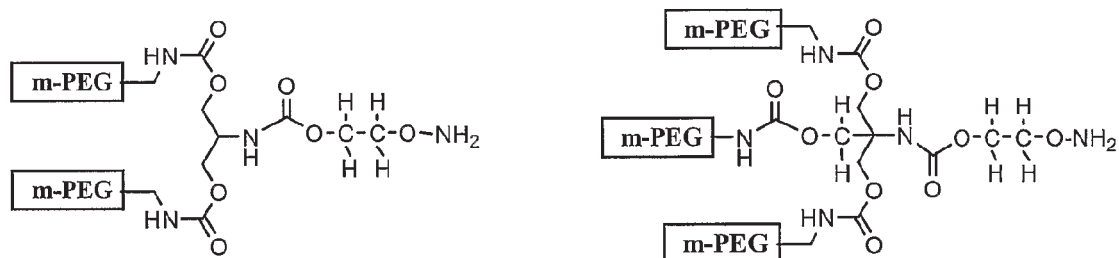
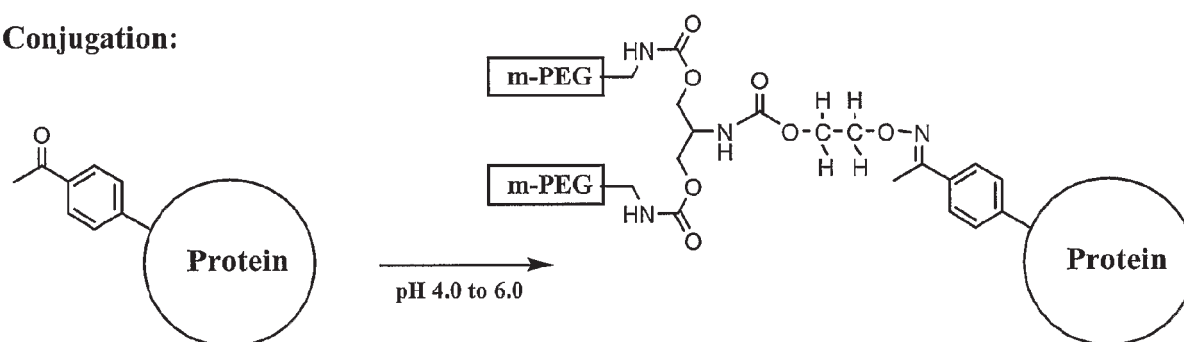
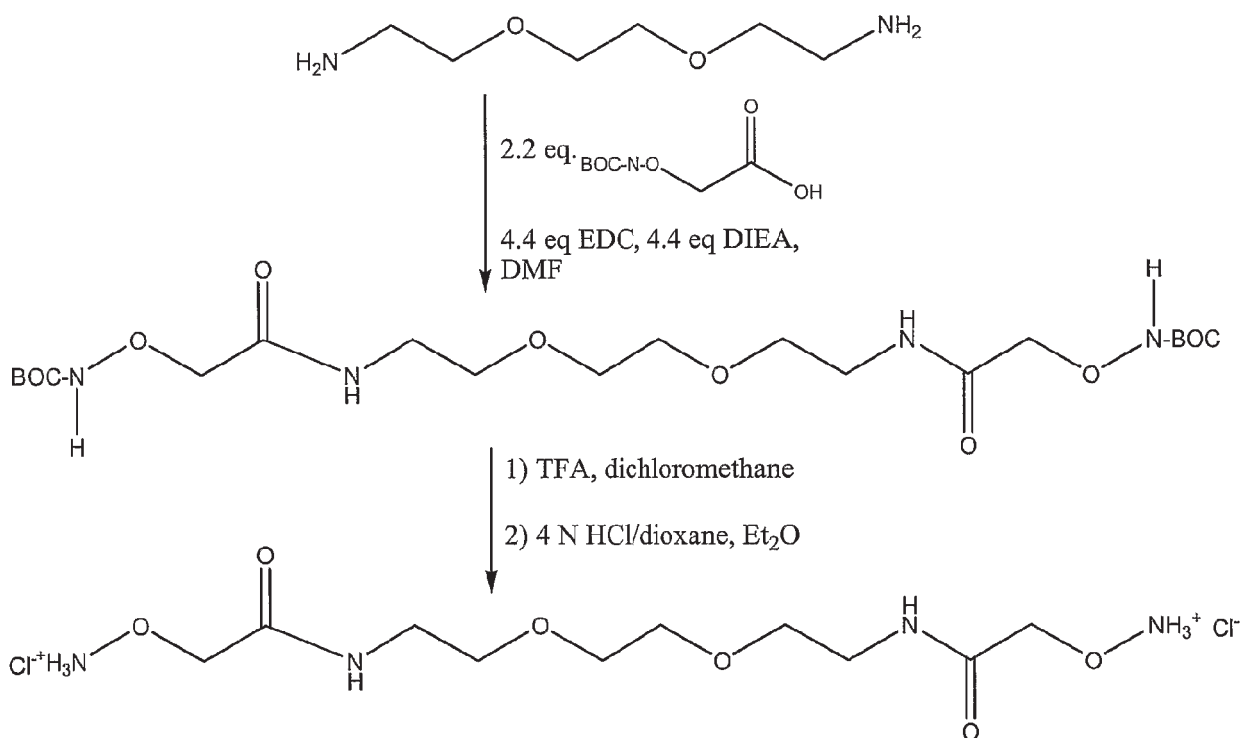


FIG. 16

Branched PEG:**Conjugation:****FIG. 17**

a



b

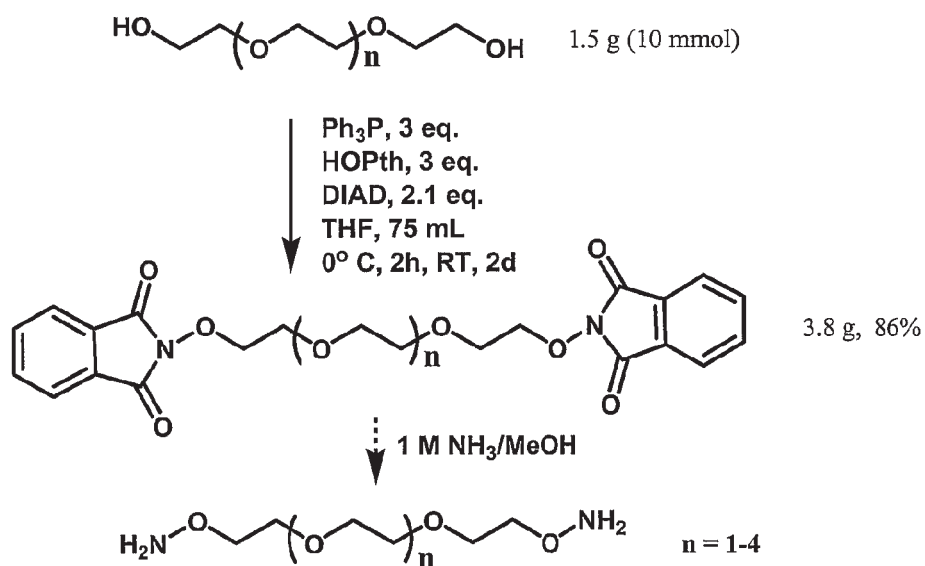


FIG. 18

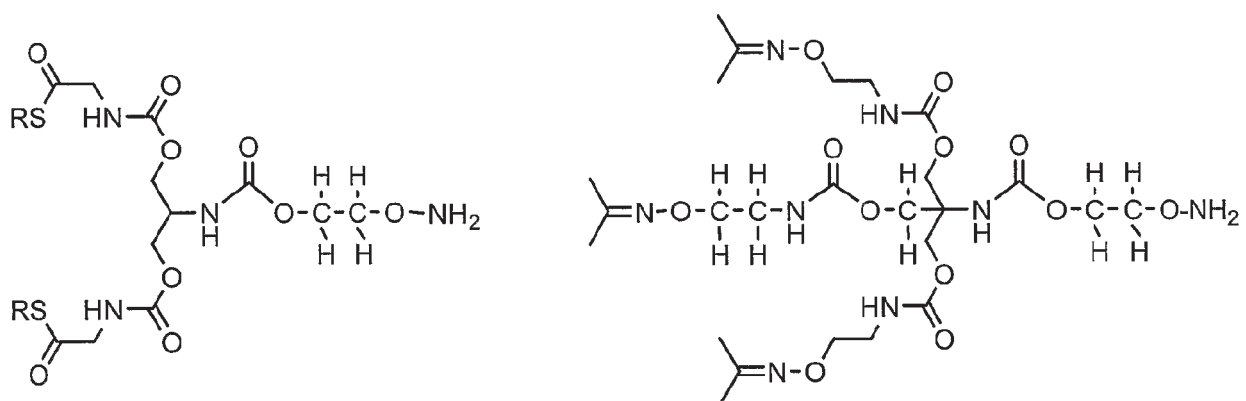


FIG. 19

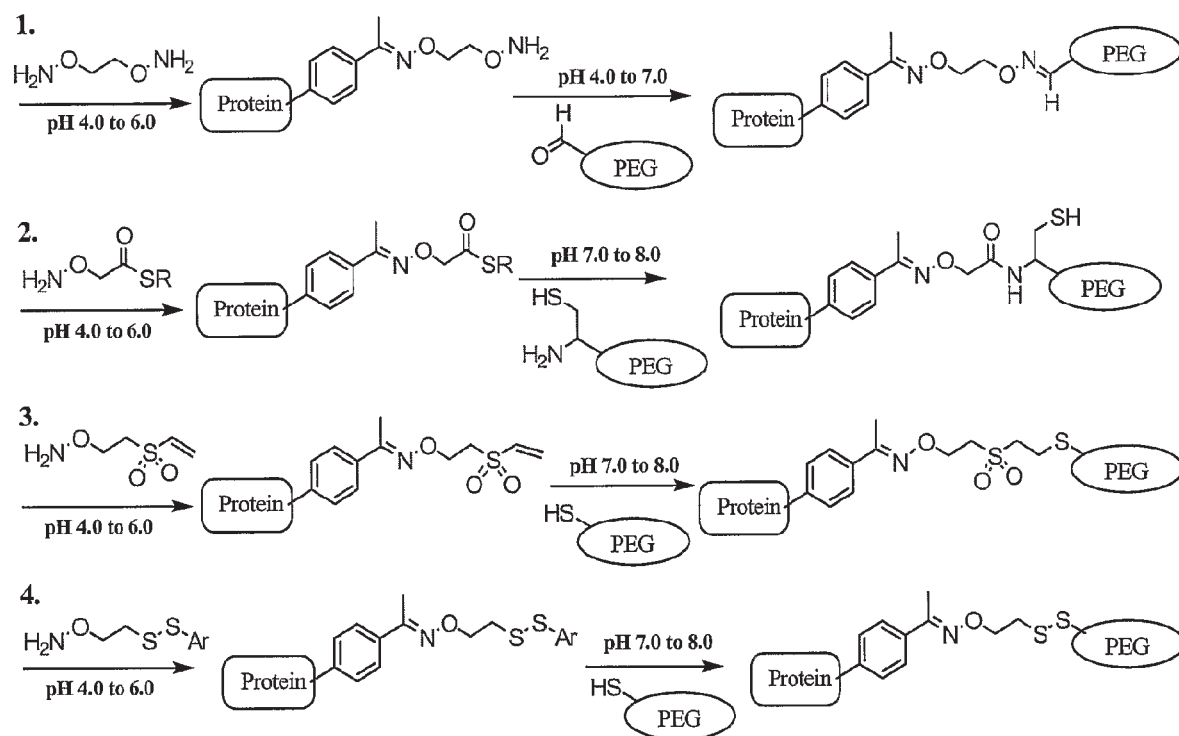


FIG. 21

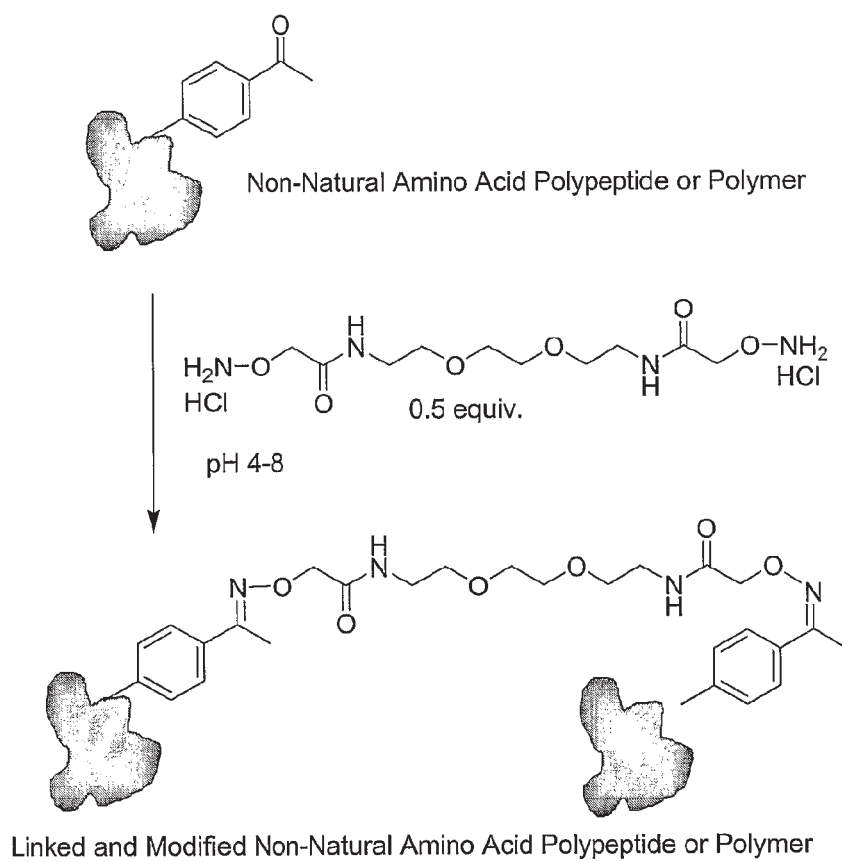


FIG. 22

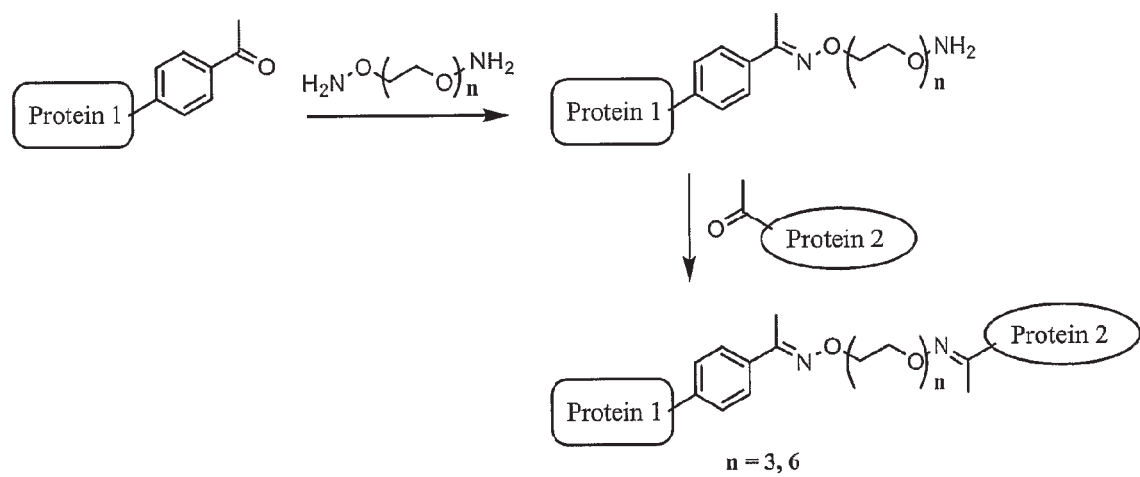


FIG. 23

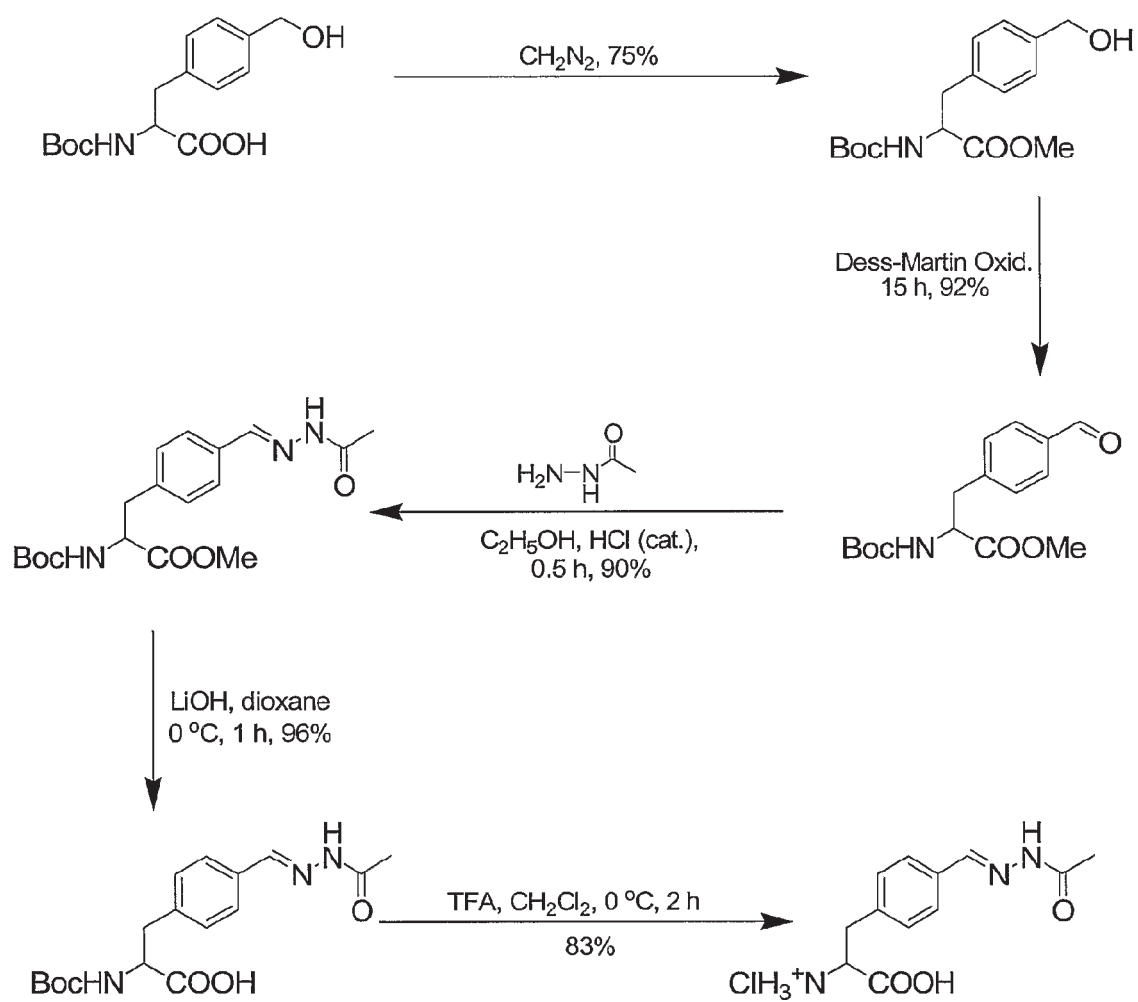


FIG. 24

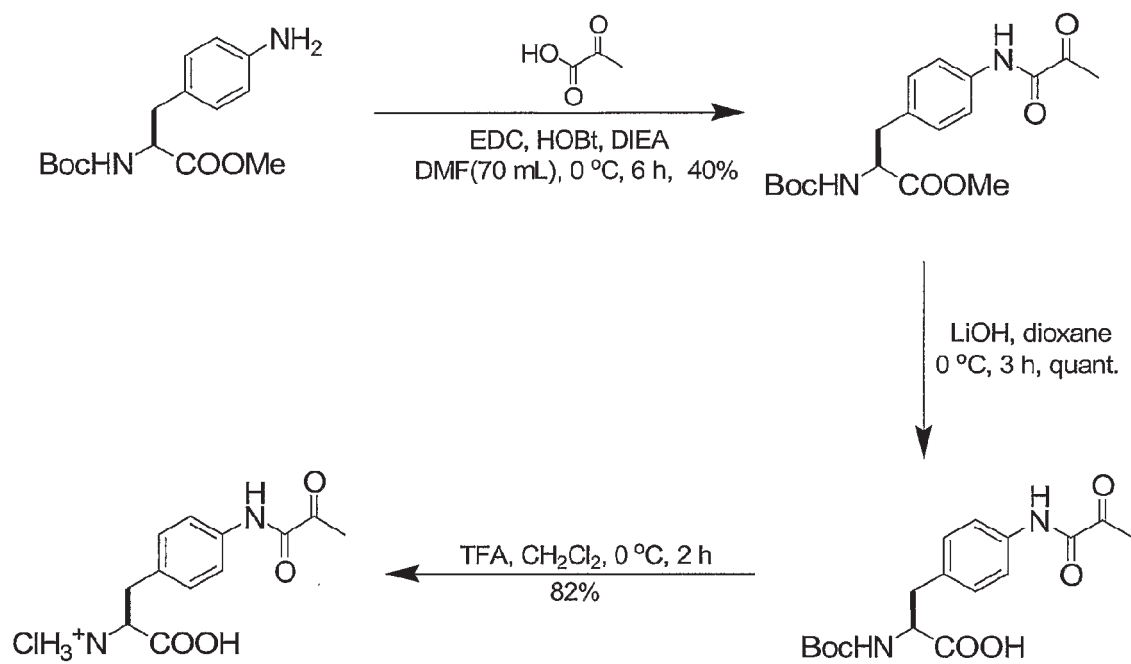


FIG. 25

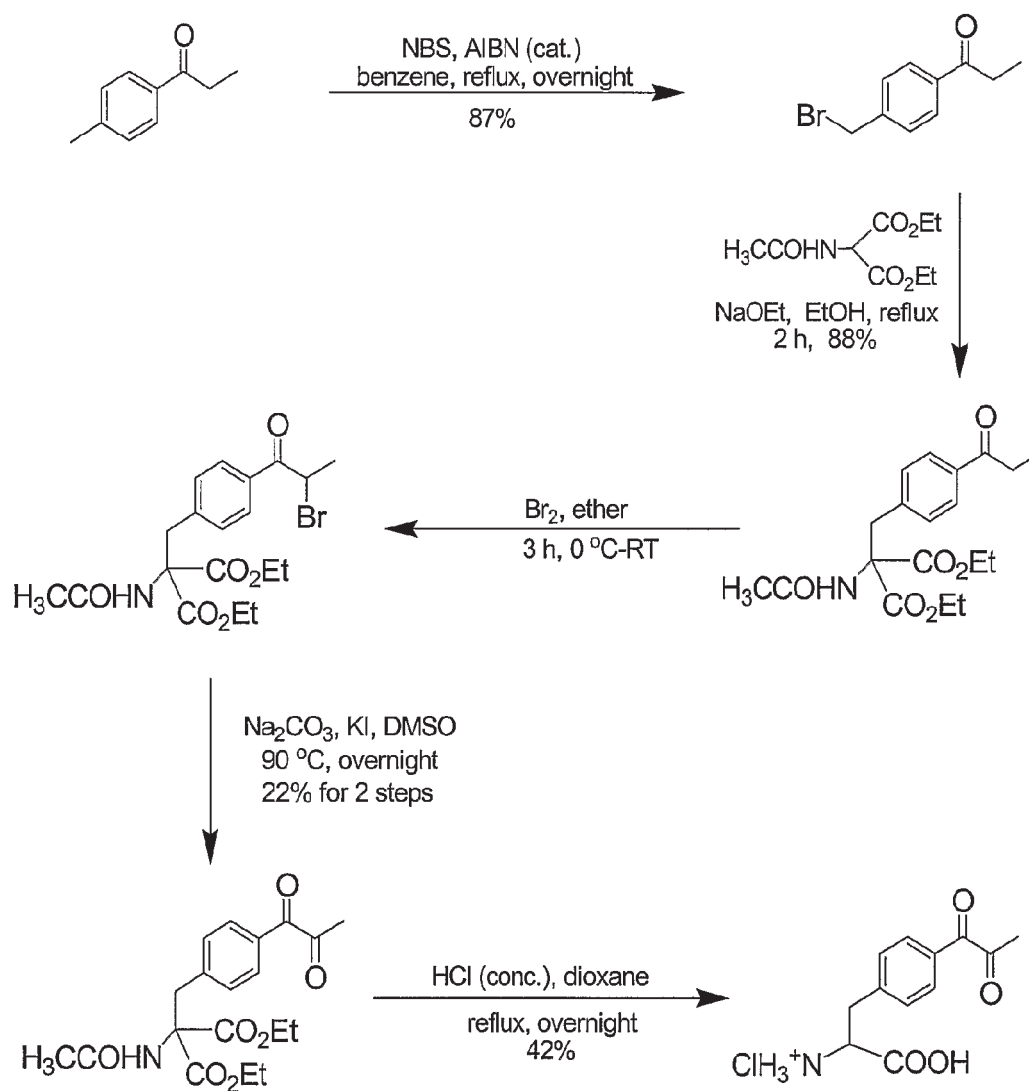


FIG. 26

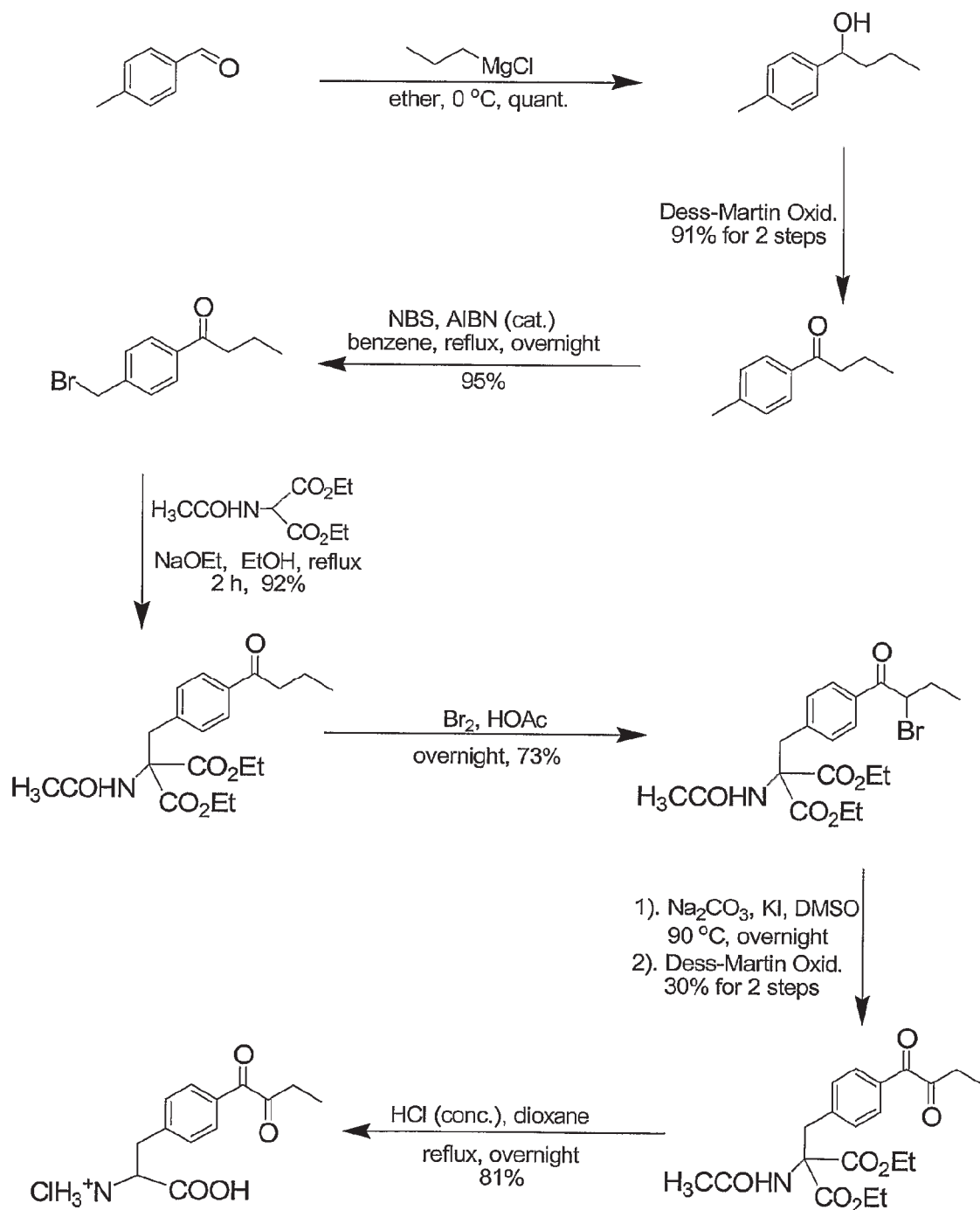


FIG. 27

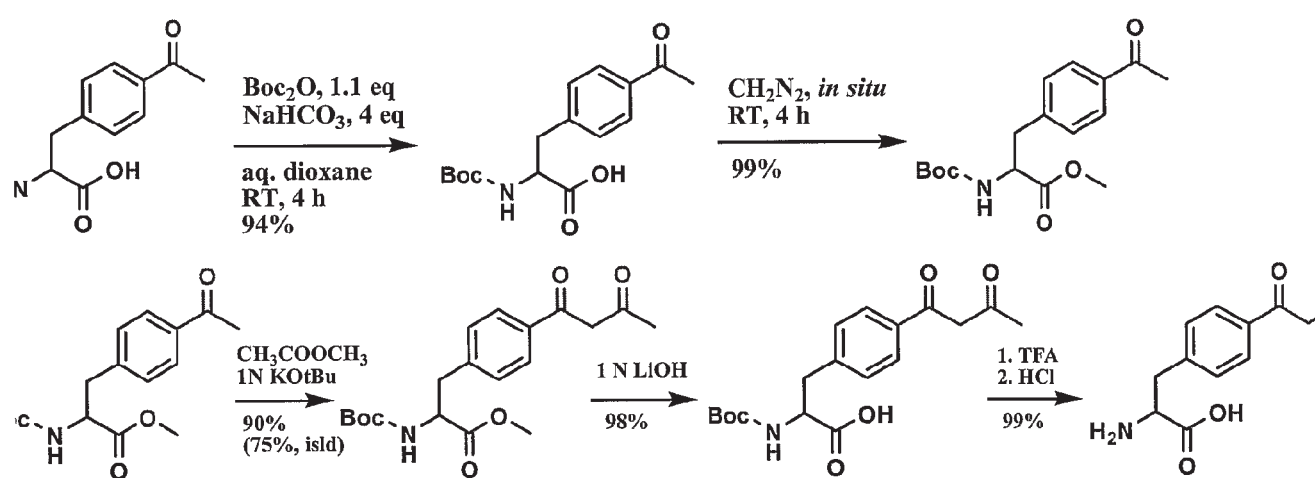


FIG. 28

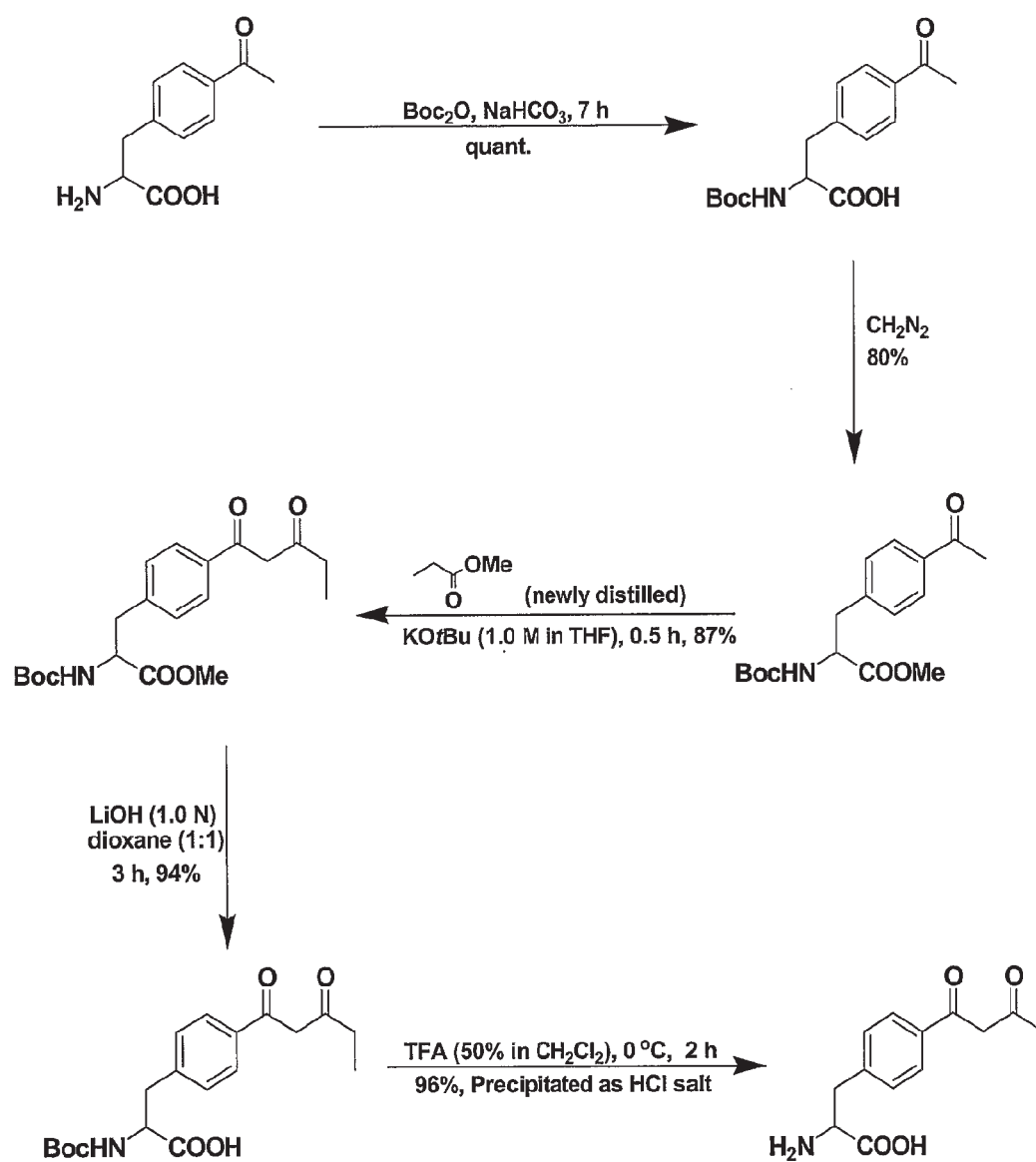


FIG. 29

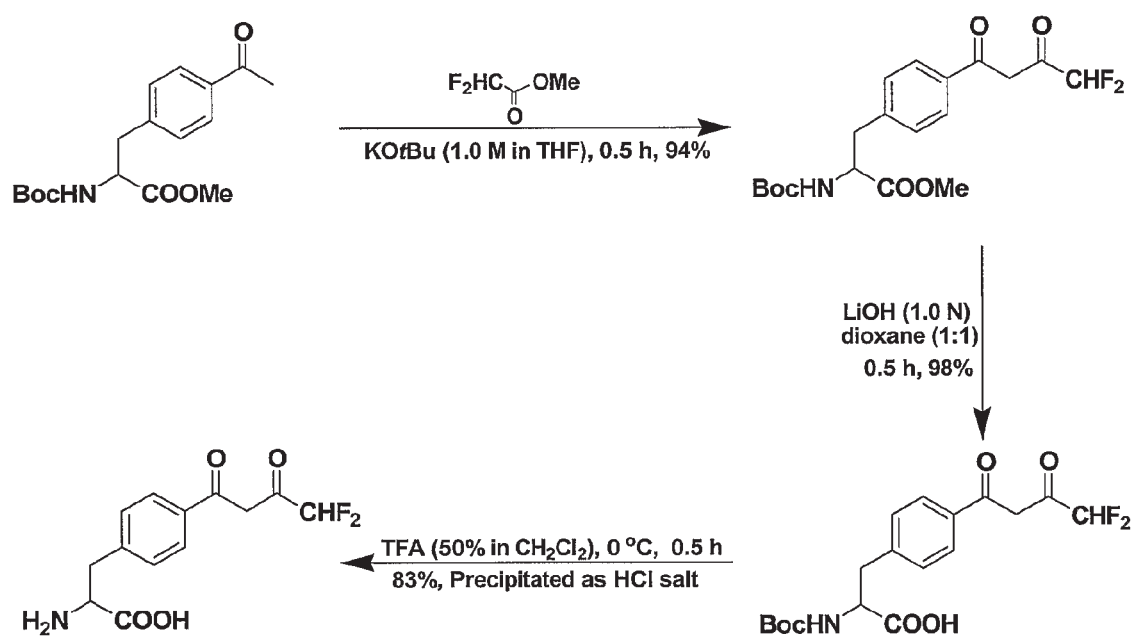


FIG. 30

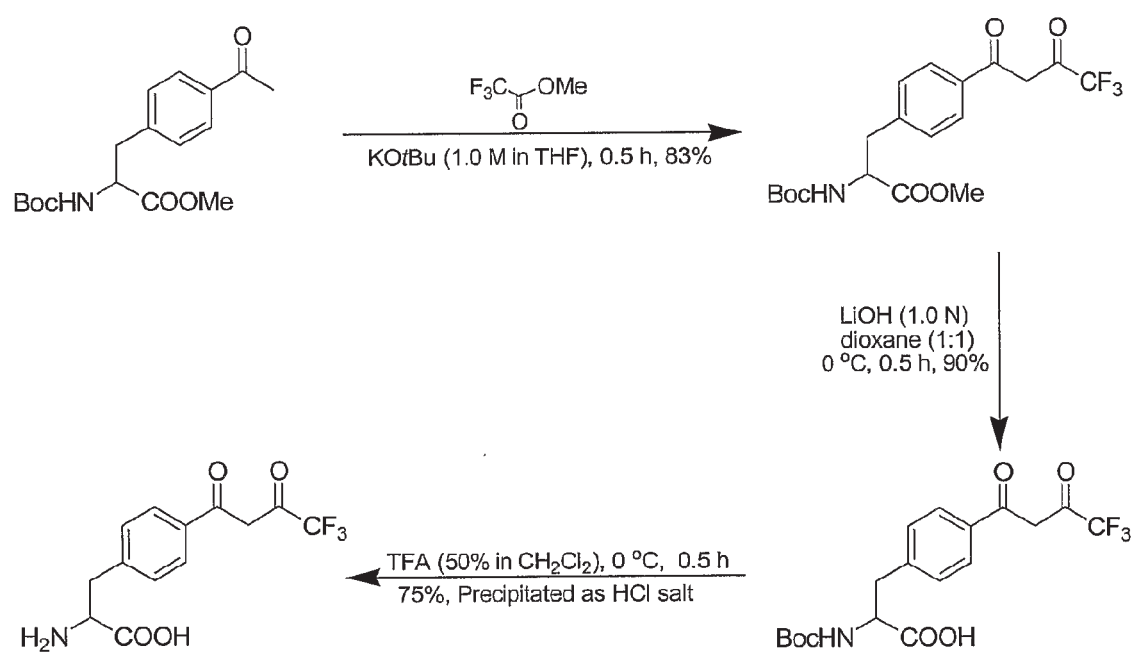


FIG. 31

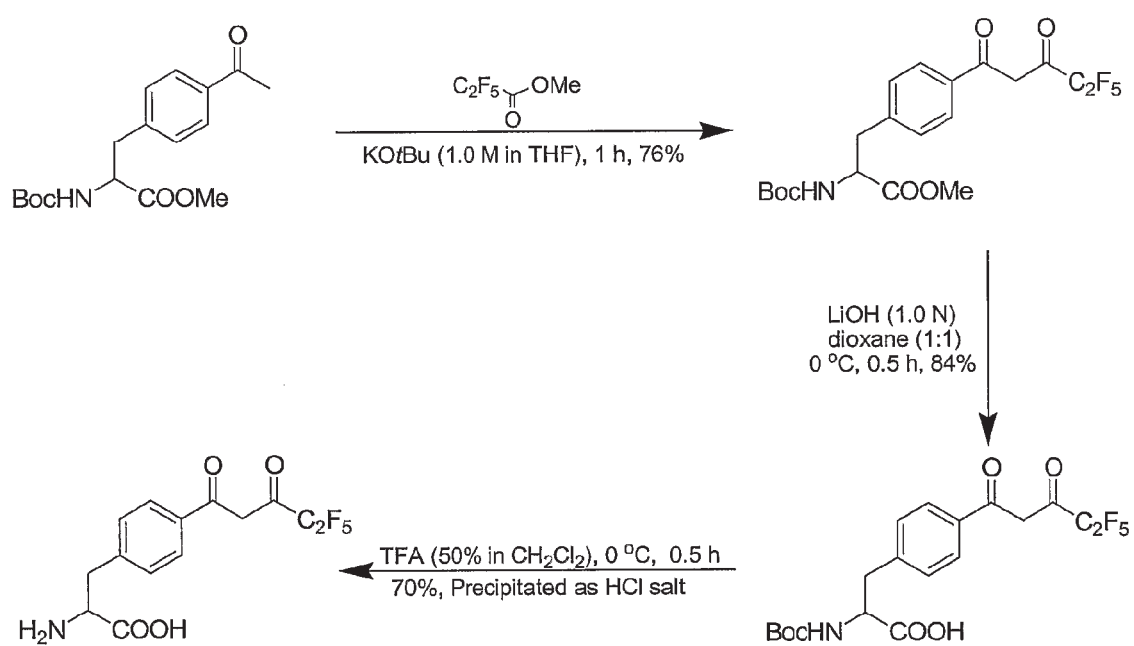


FIG. 32

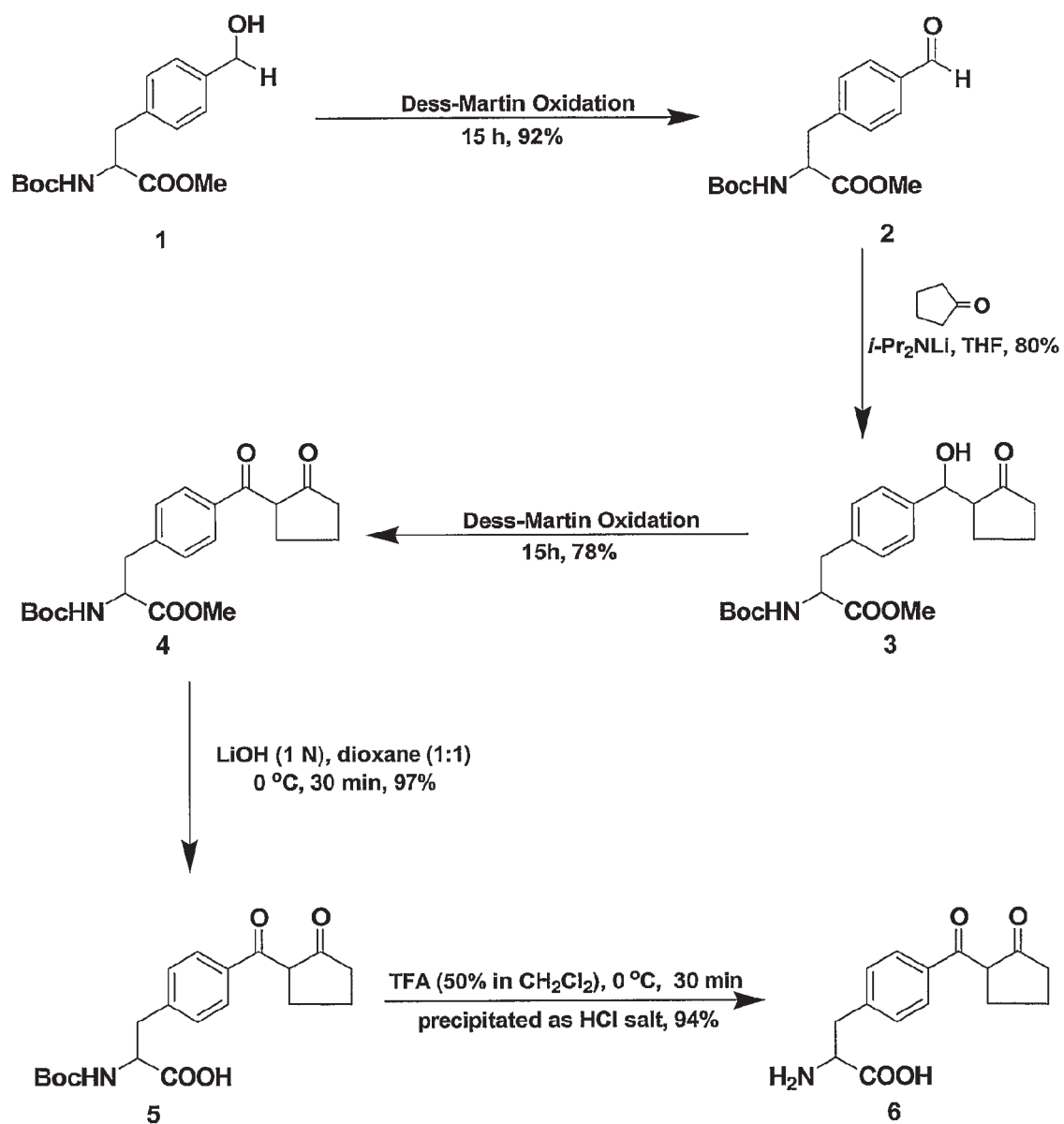


FIG. 33

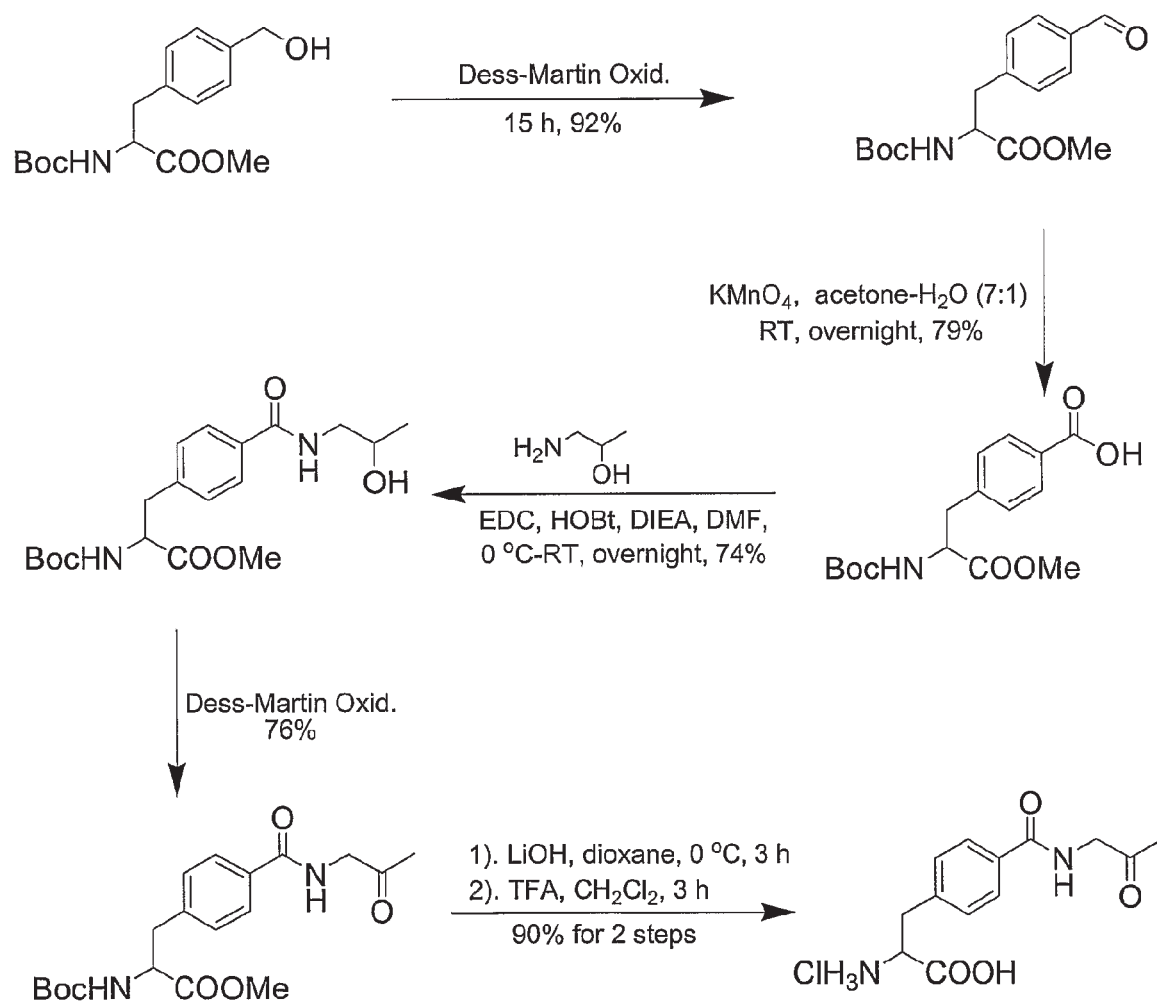


FIG. 34

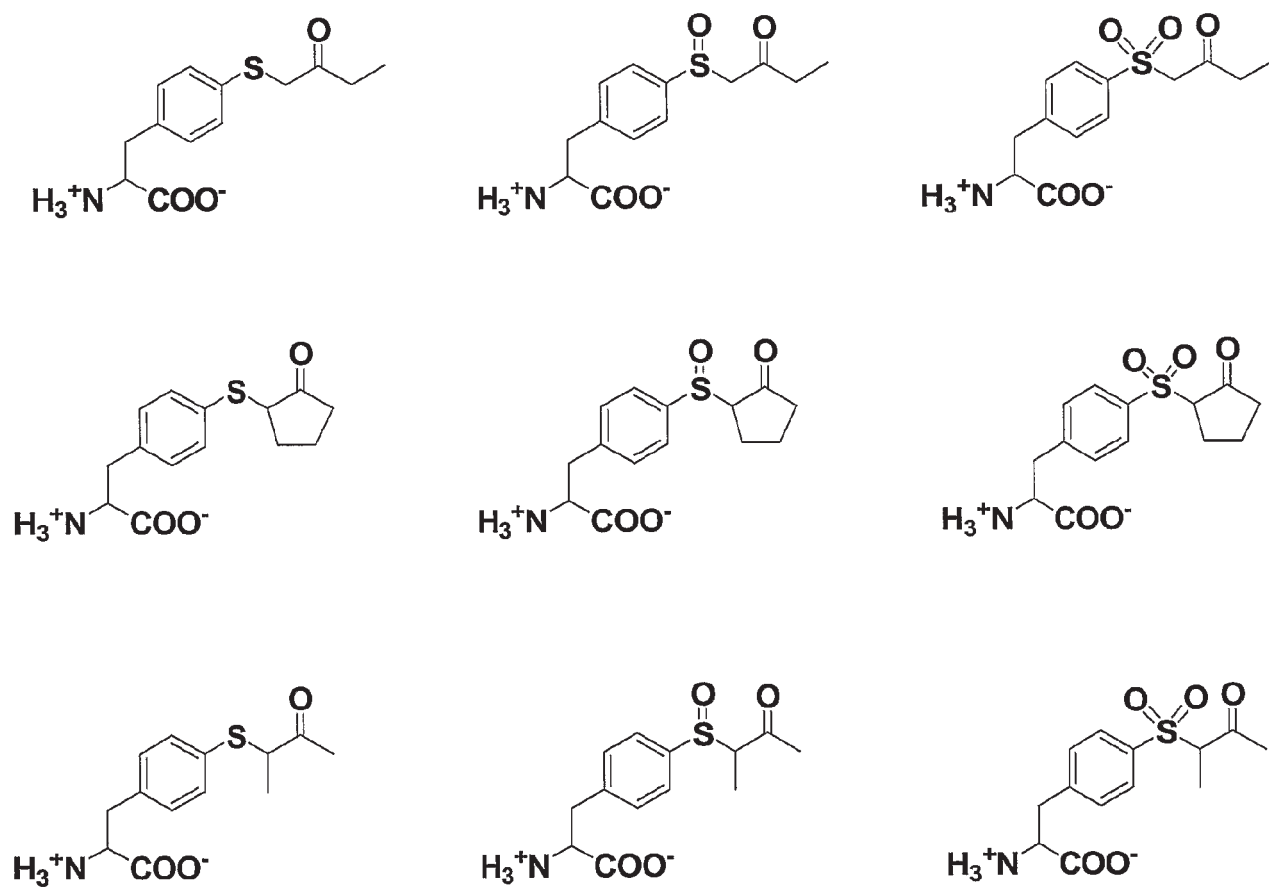


FIG. 35

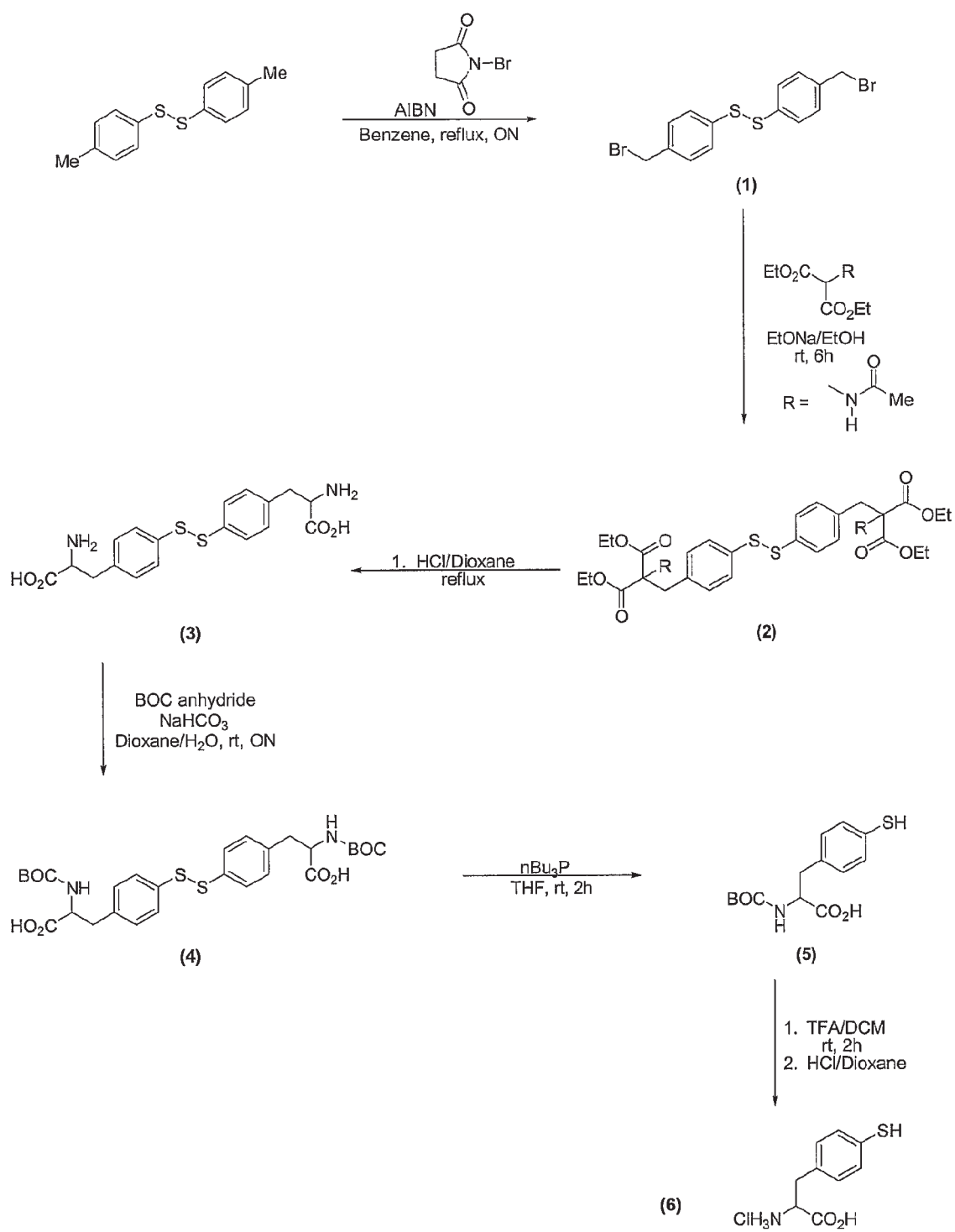


FIG. 36

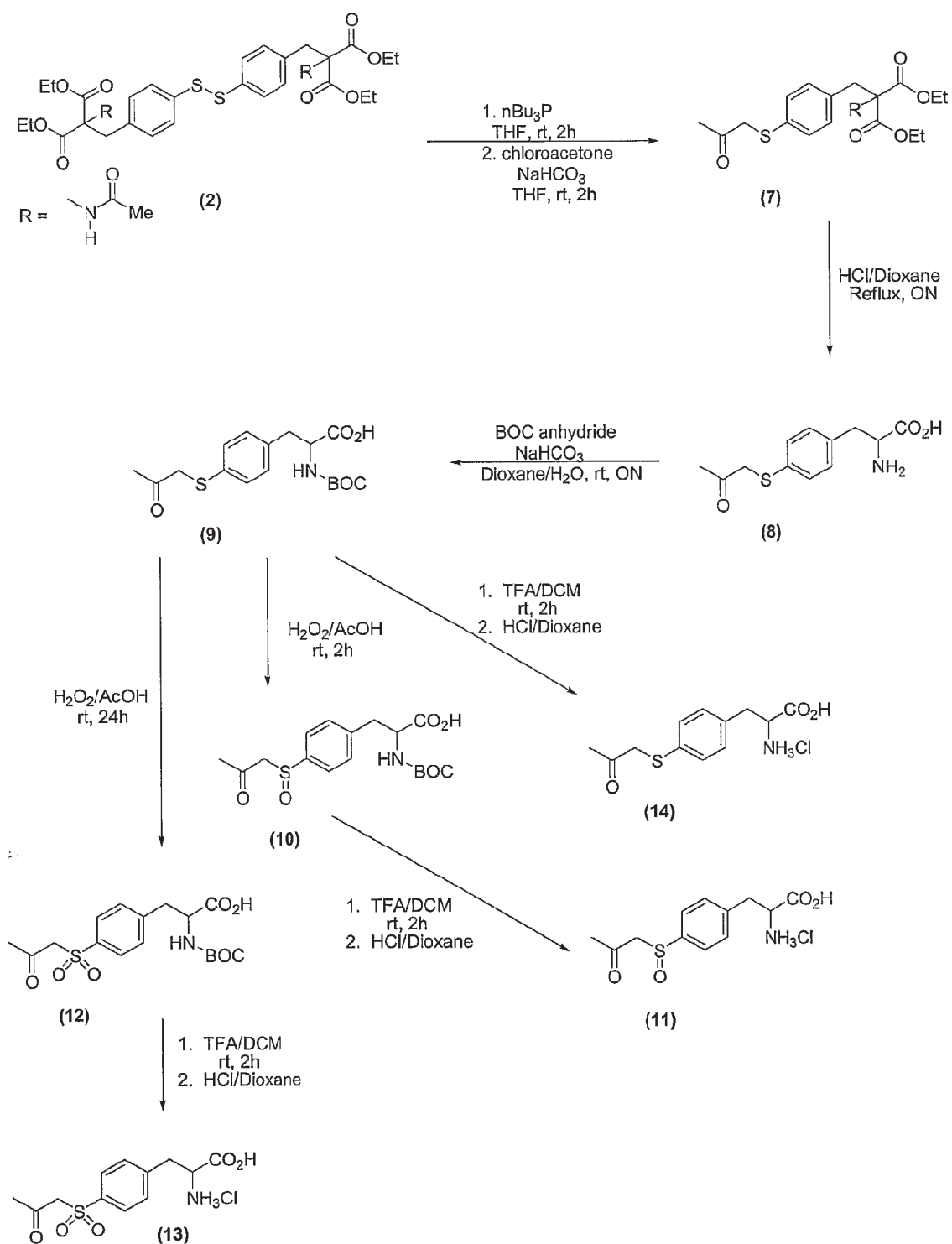


FIG. 37

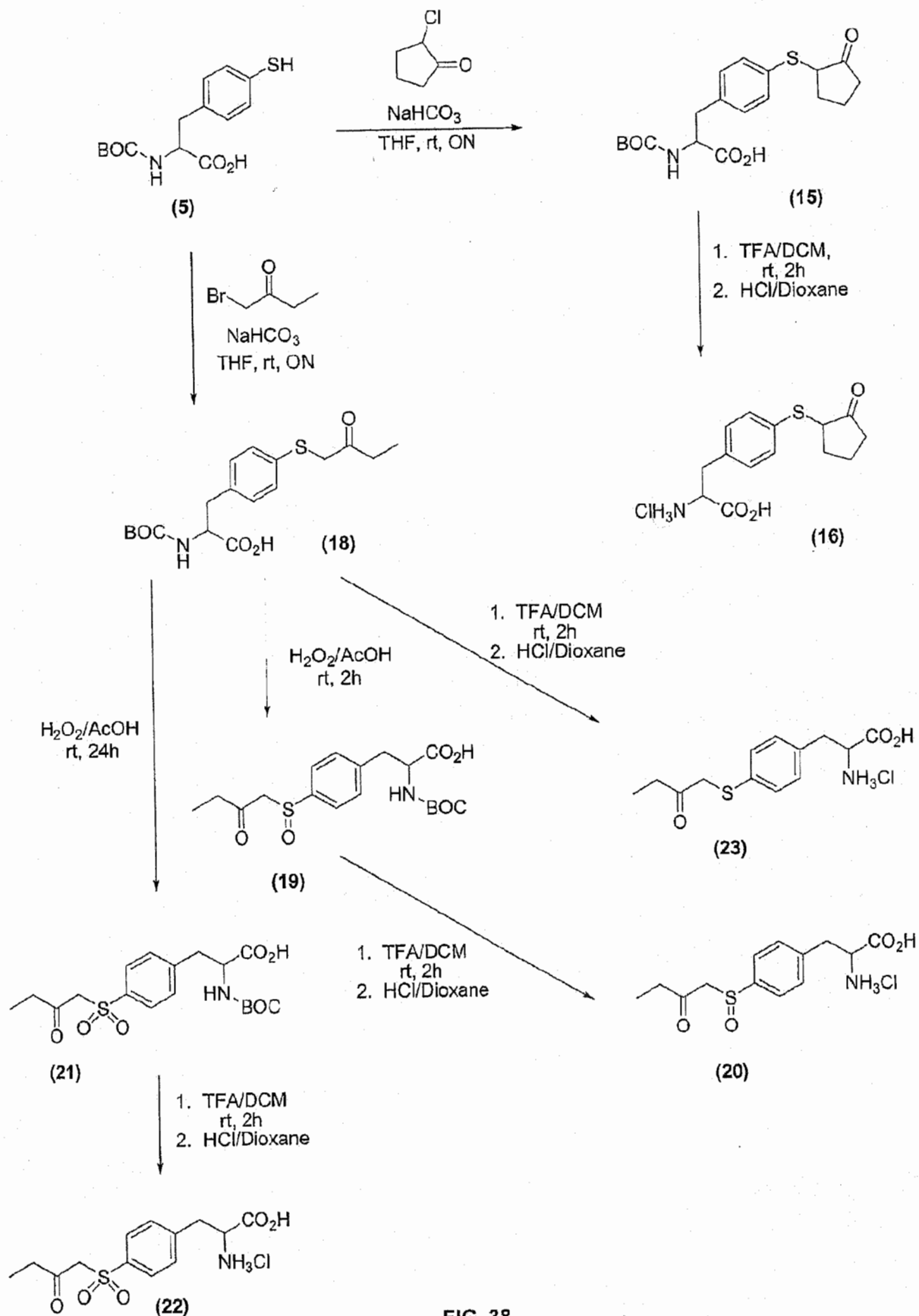


FIG. 38

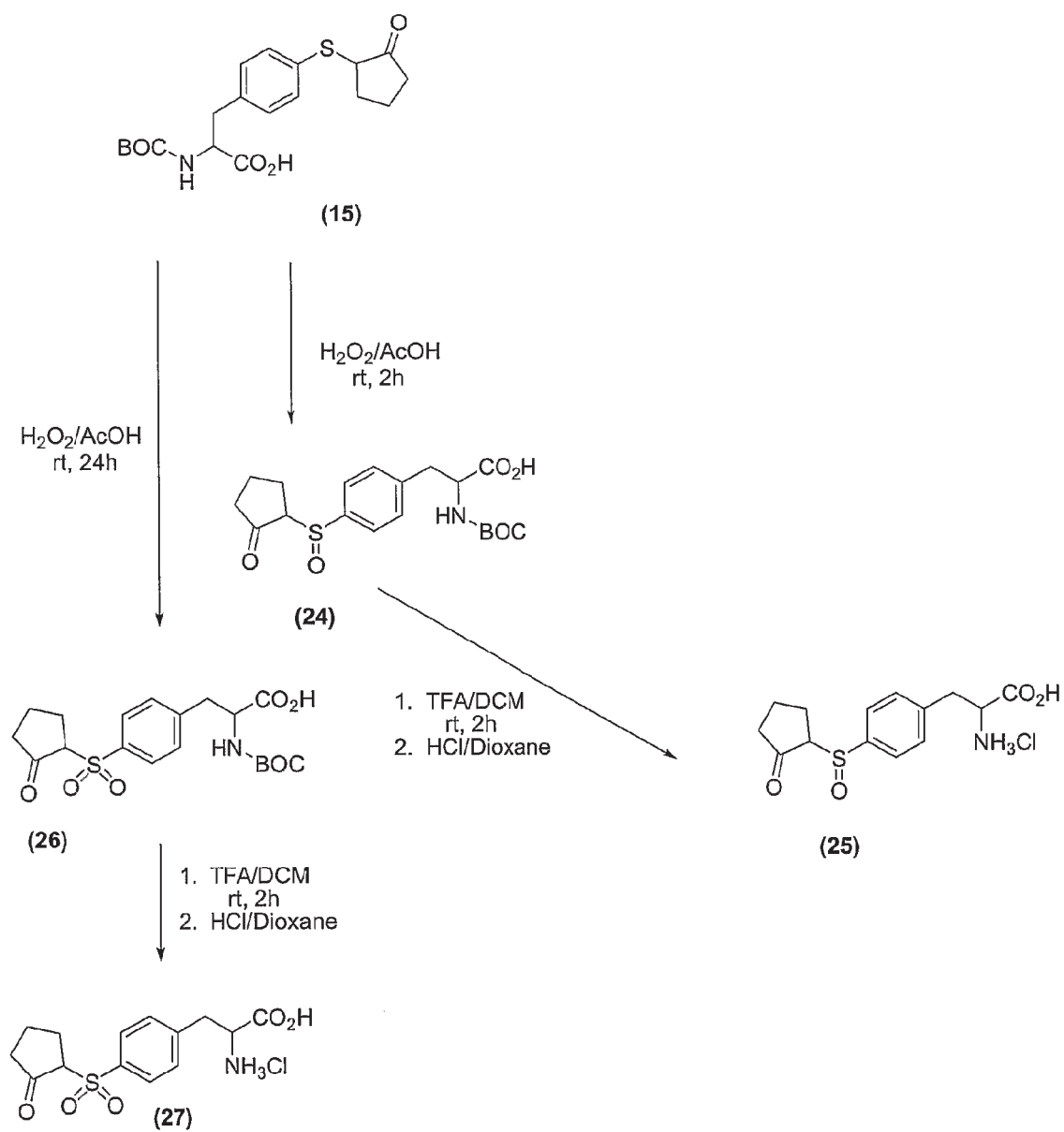


FIG. 39

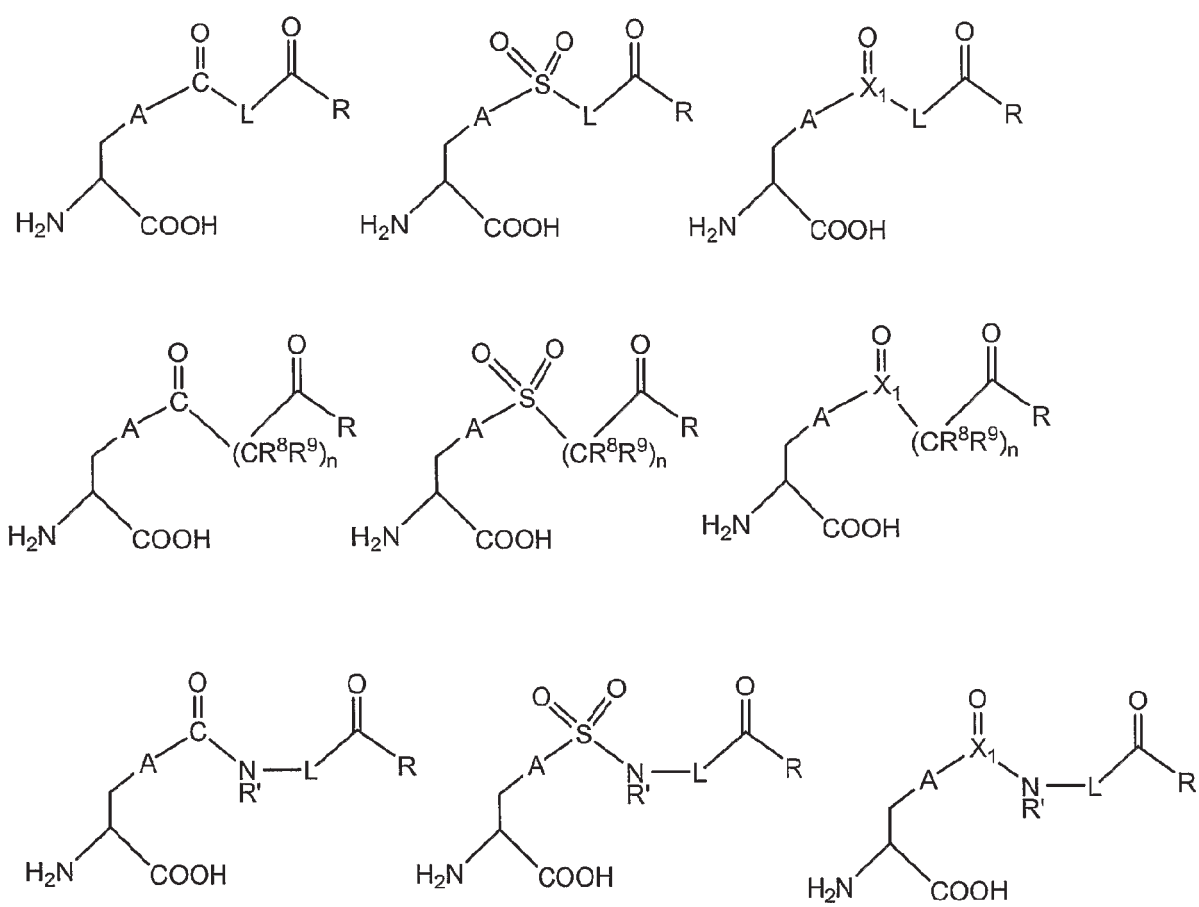


FIG. 40

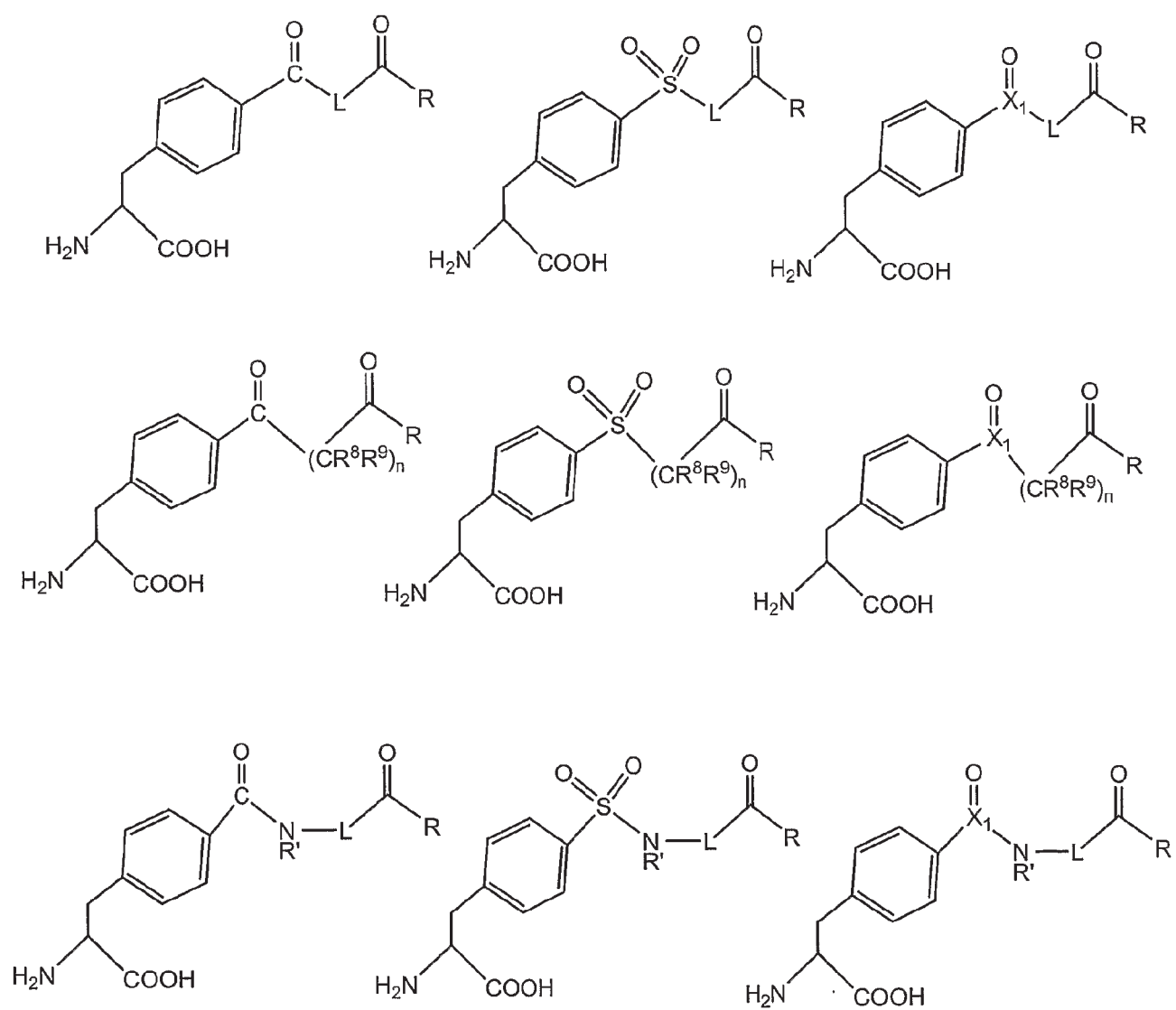
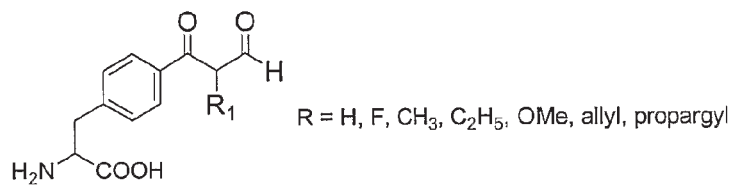
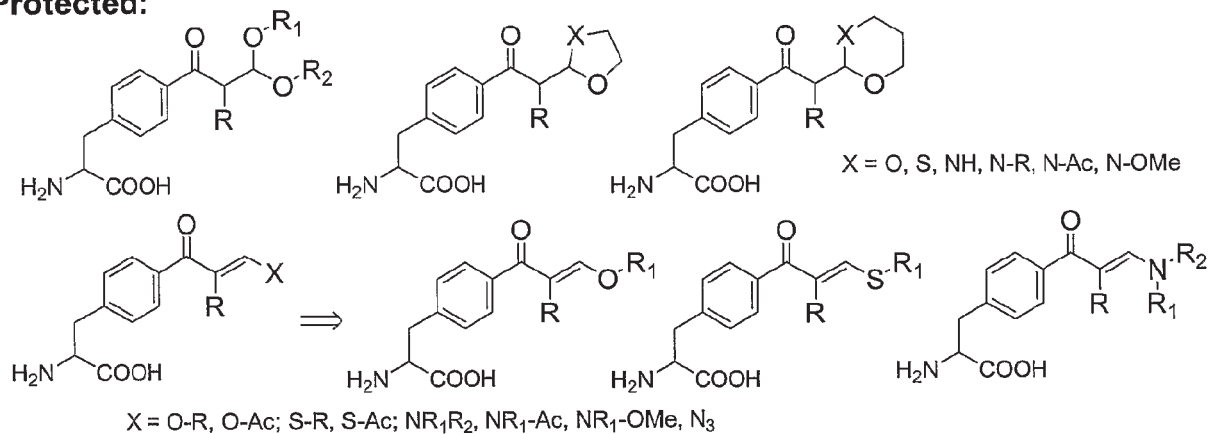


FIG. 41

Examples:



(a)

Unprotected**Protected:**

(b)

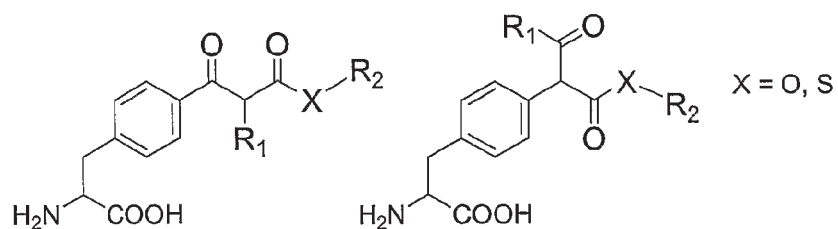
Structure:

FIG. 43

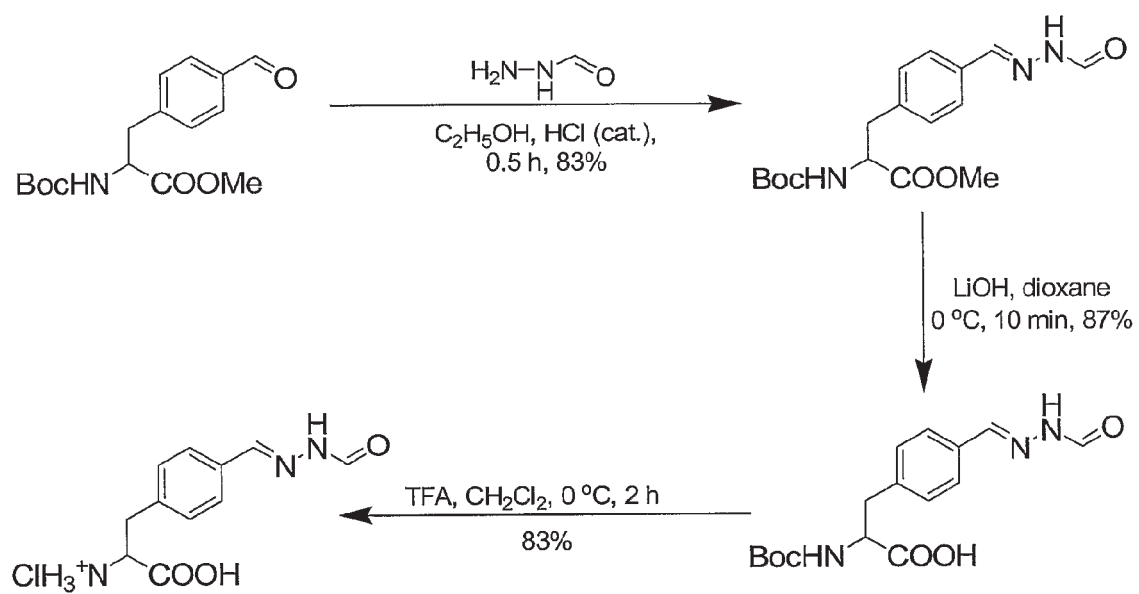


FIG. 44

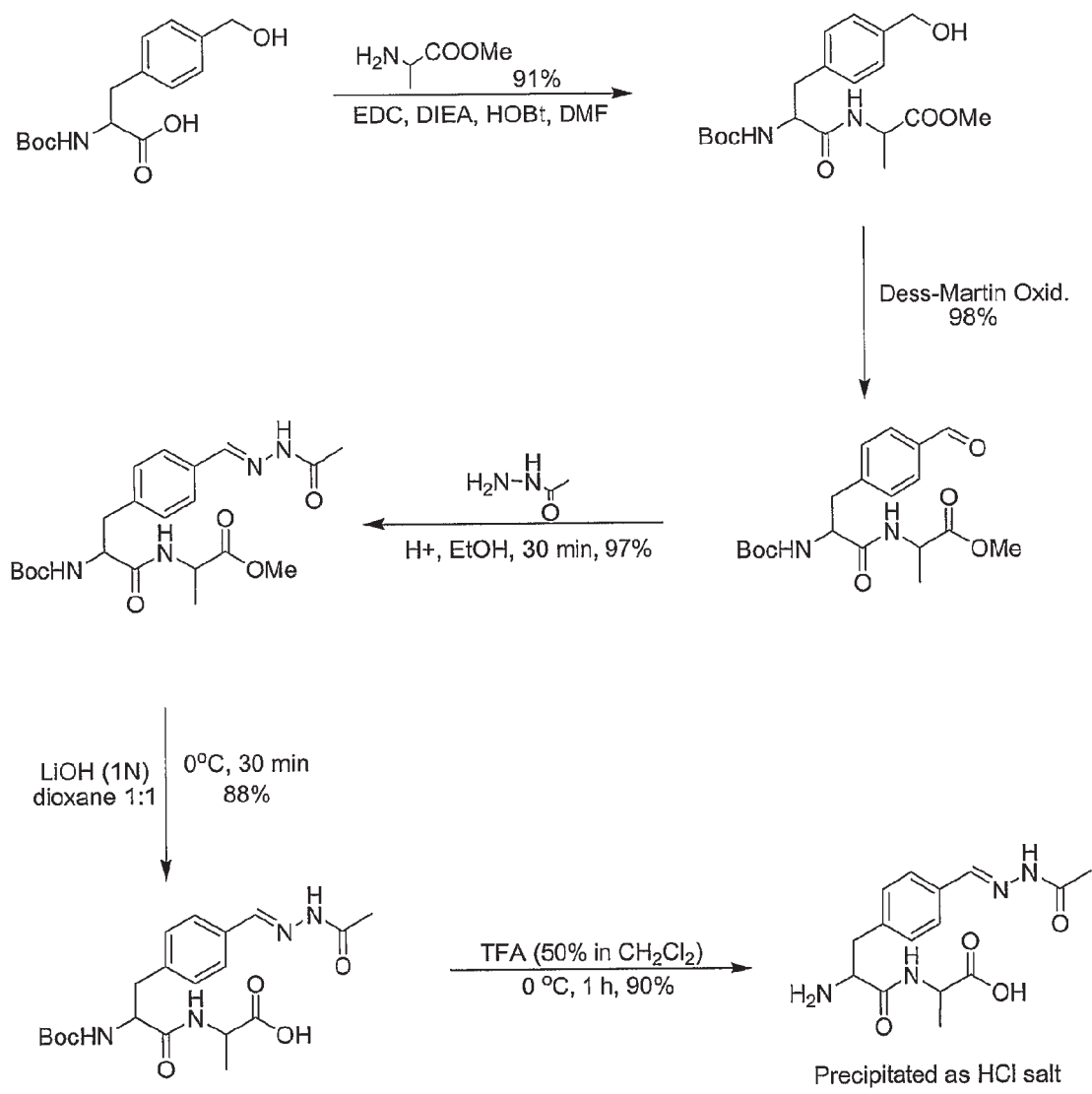


FIG. 45

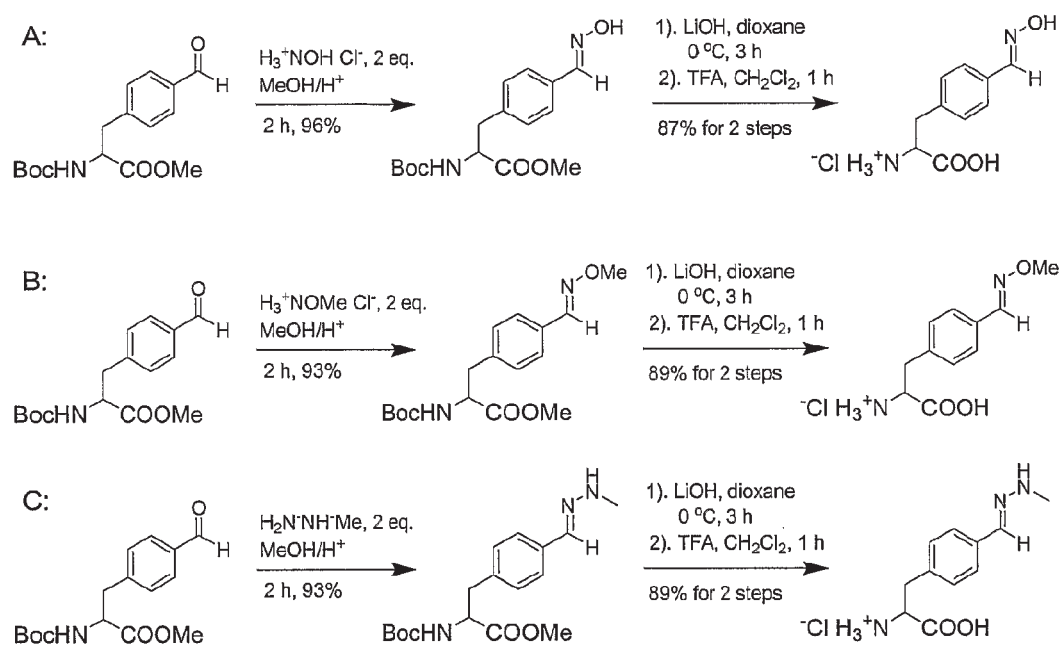
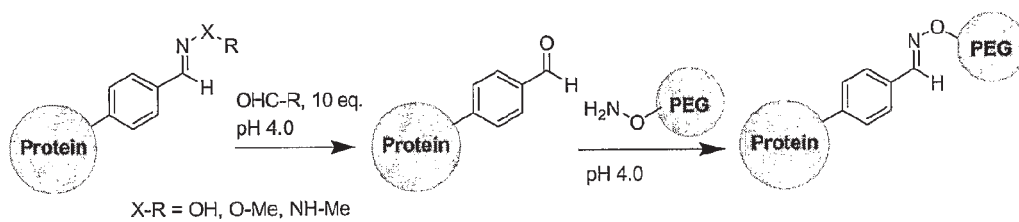
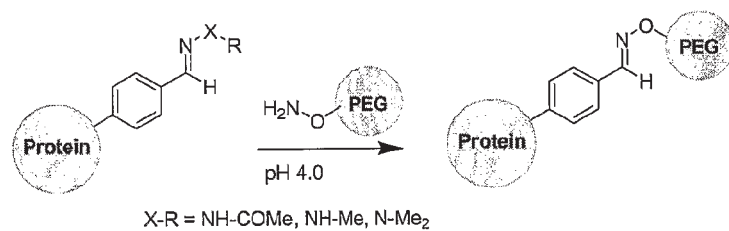
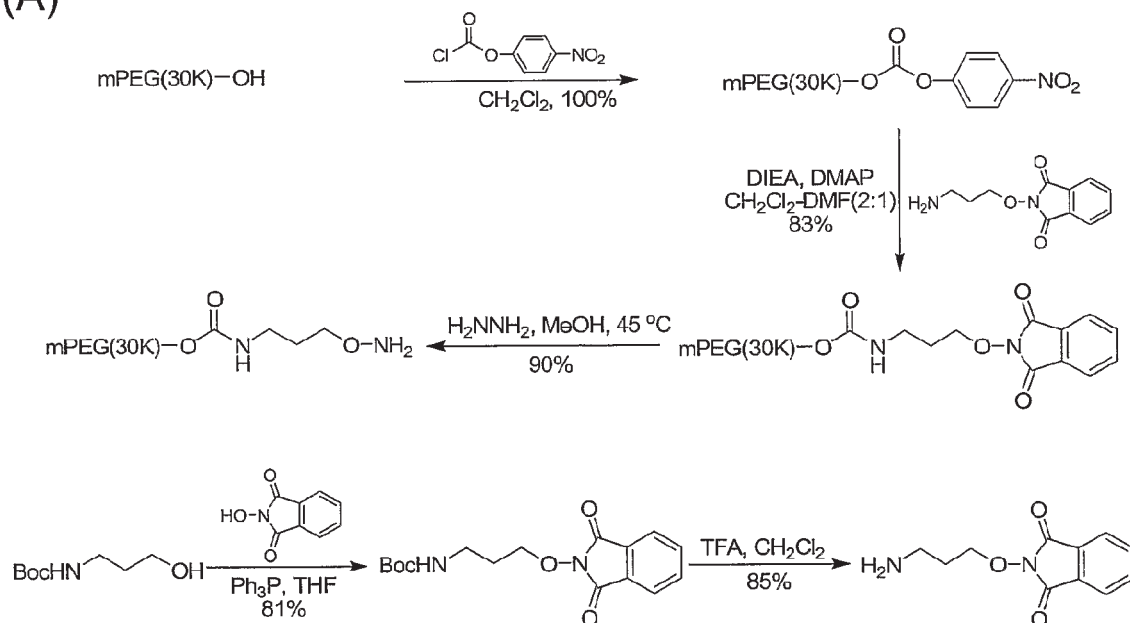


FIG. 46

Two-step conjugation:**One-step conjugation:****FIG. 47**

(A)



(B)

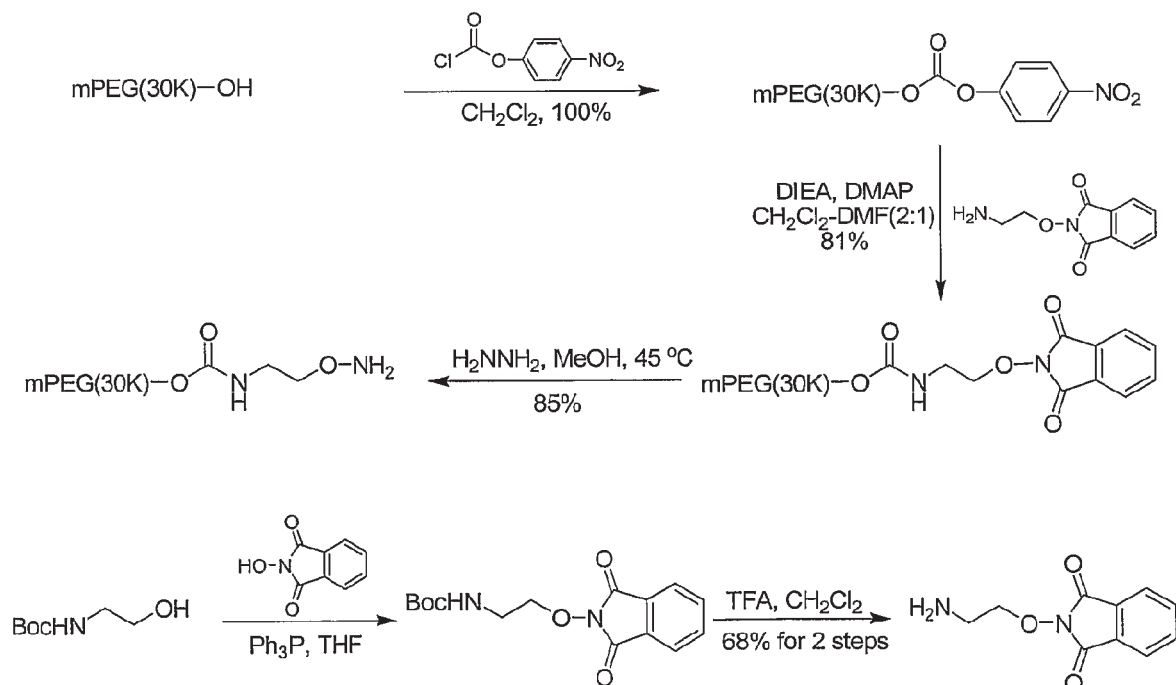
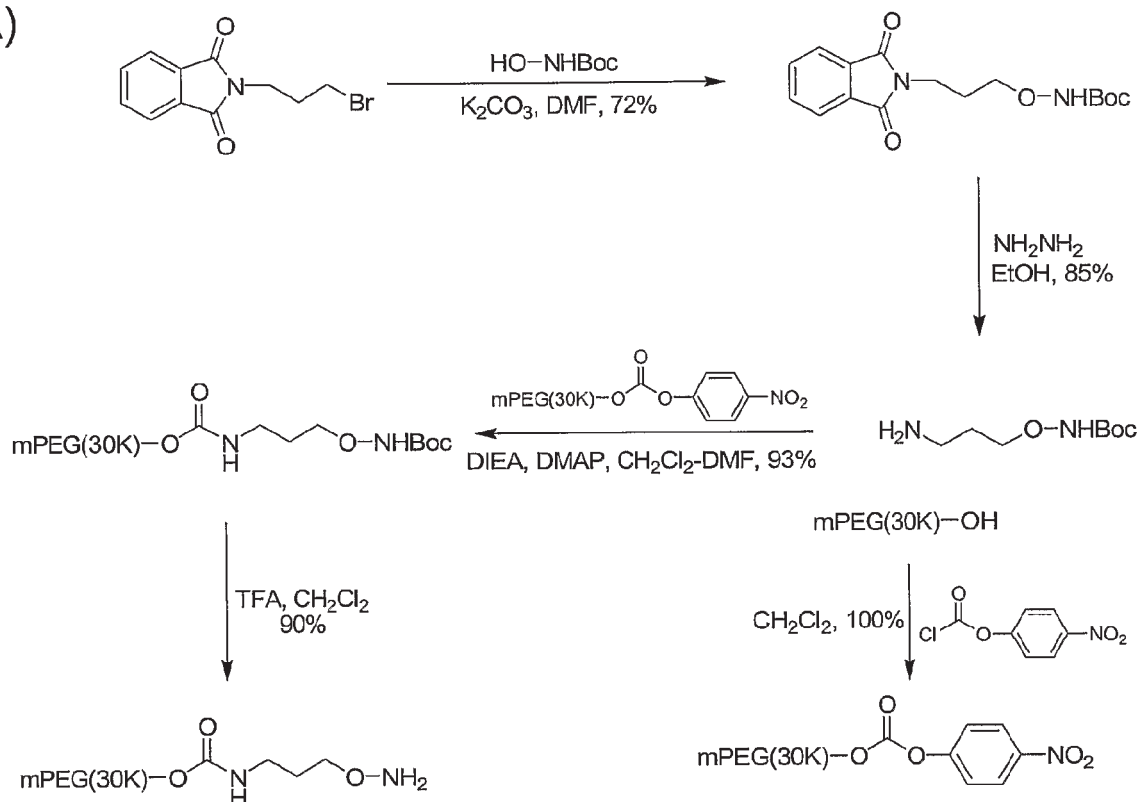


FIG. 48

(A)



(B)

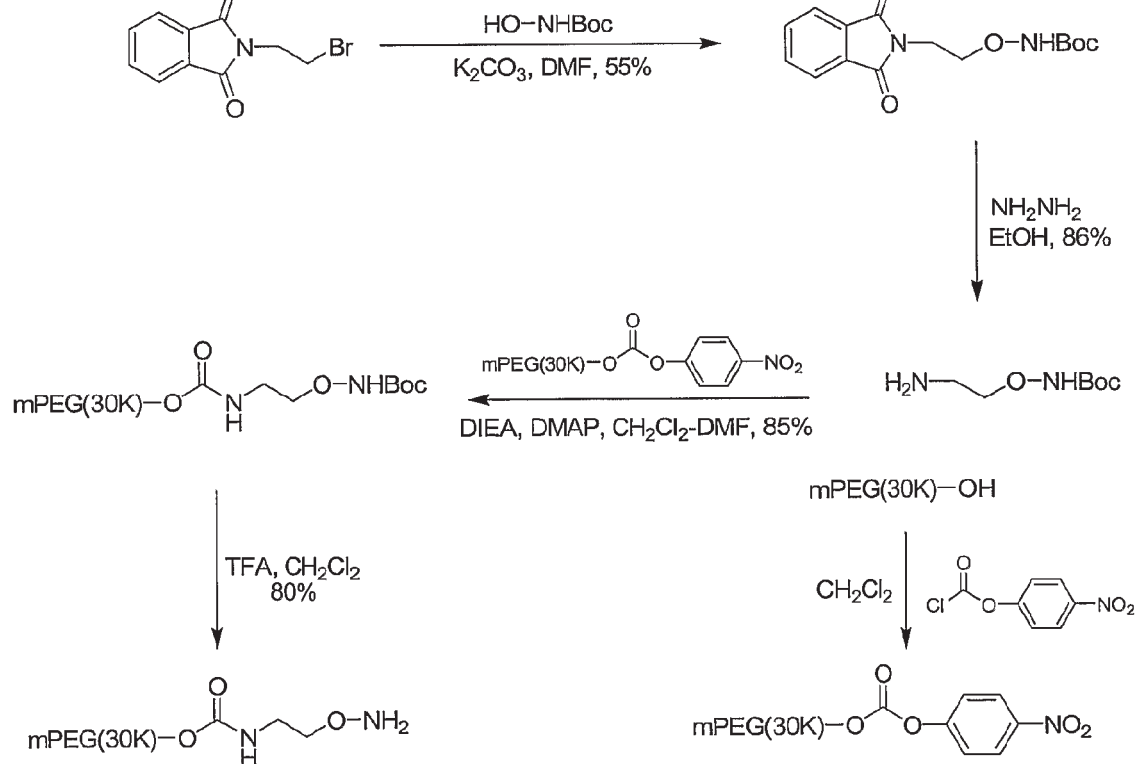


FIG. 49

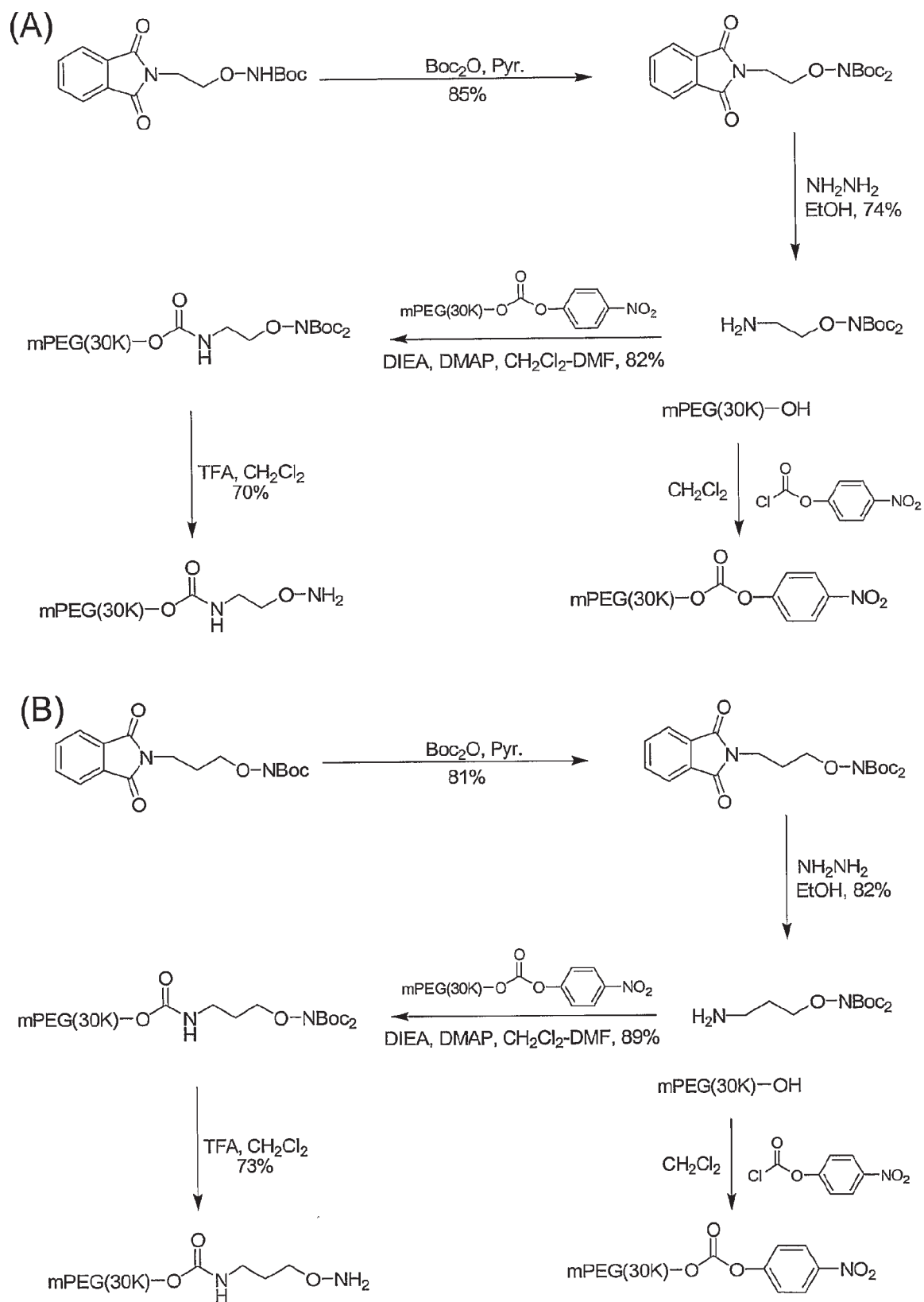
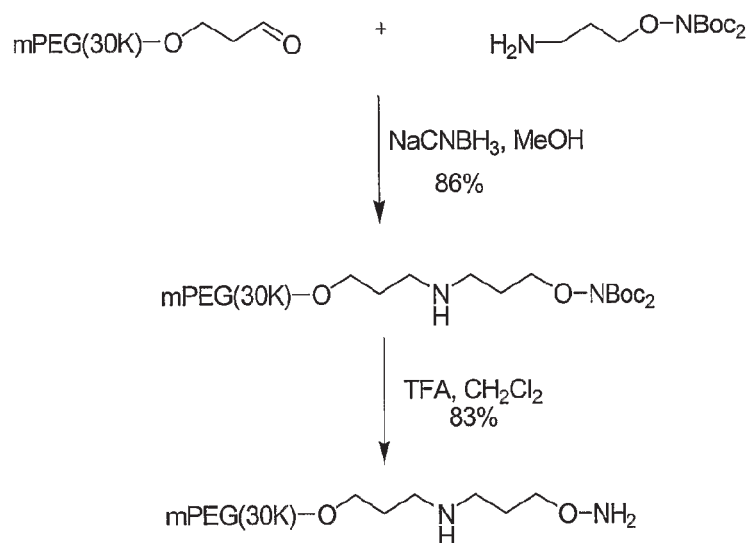


FIG. 50

(A)



(B)

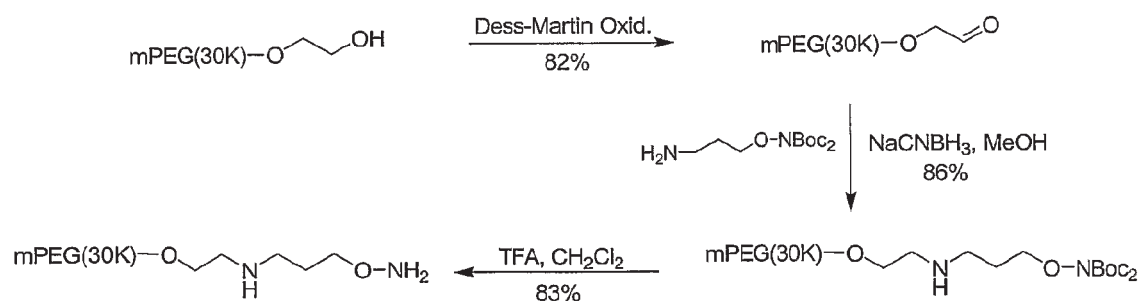
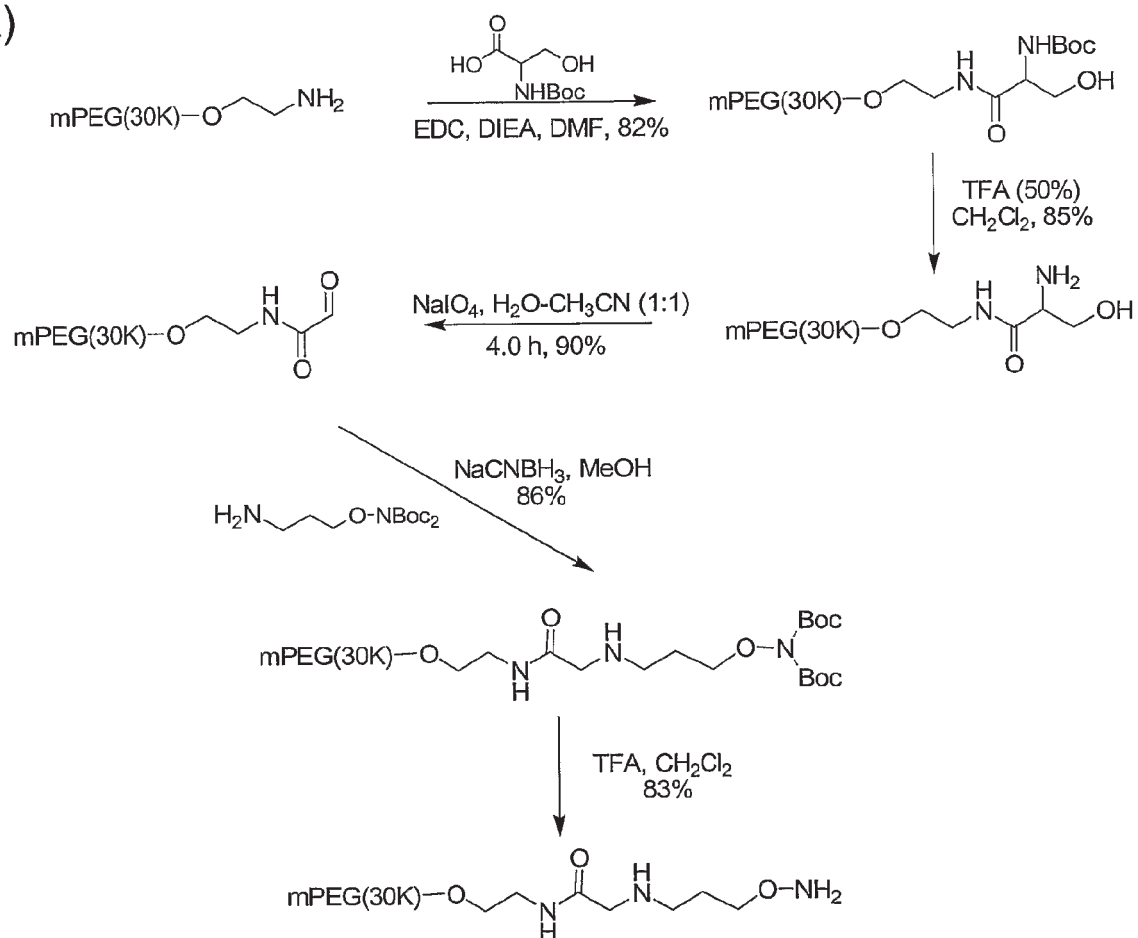


FIG. 51

(A)



(B)

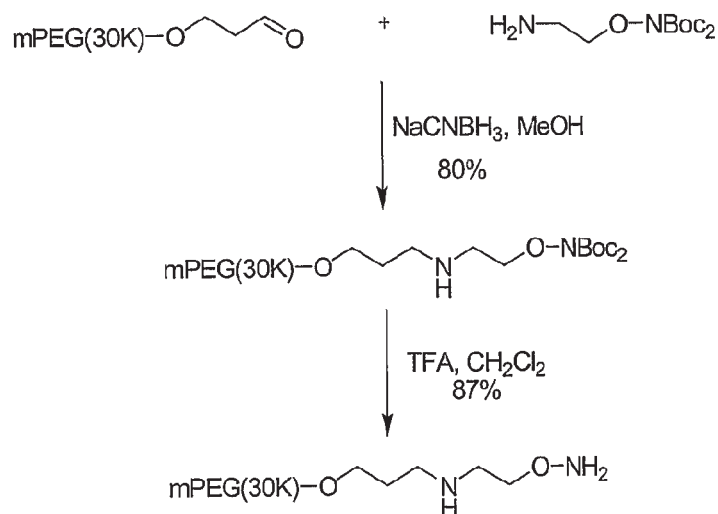
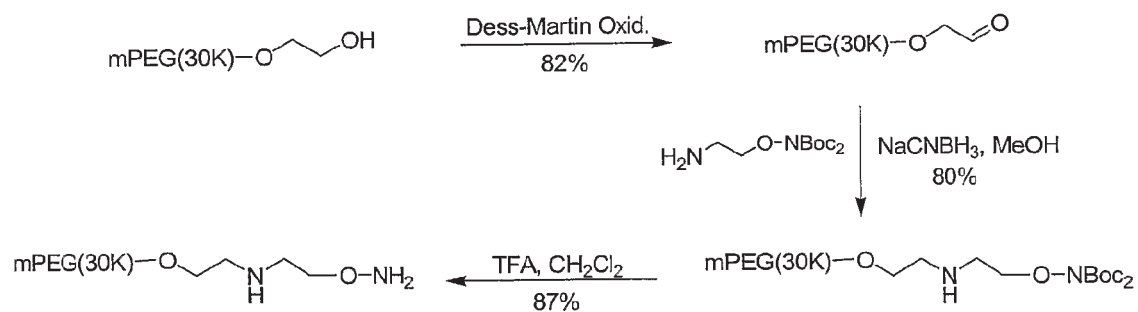


FIG. 52

(A)



(B)

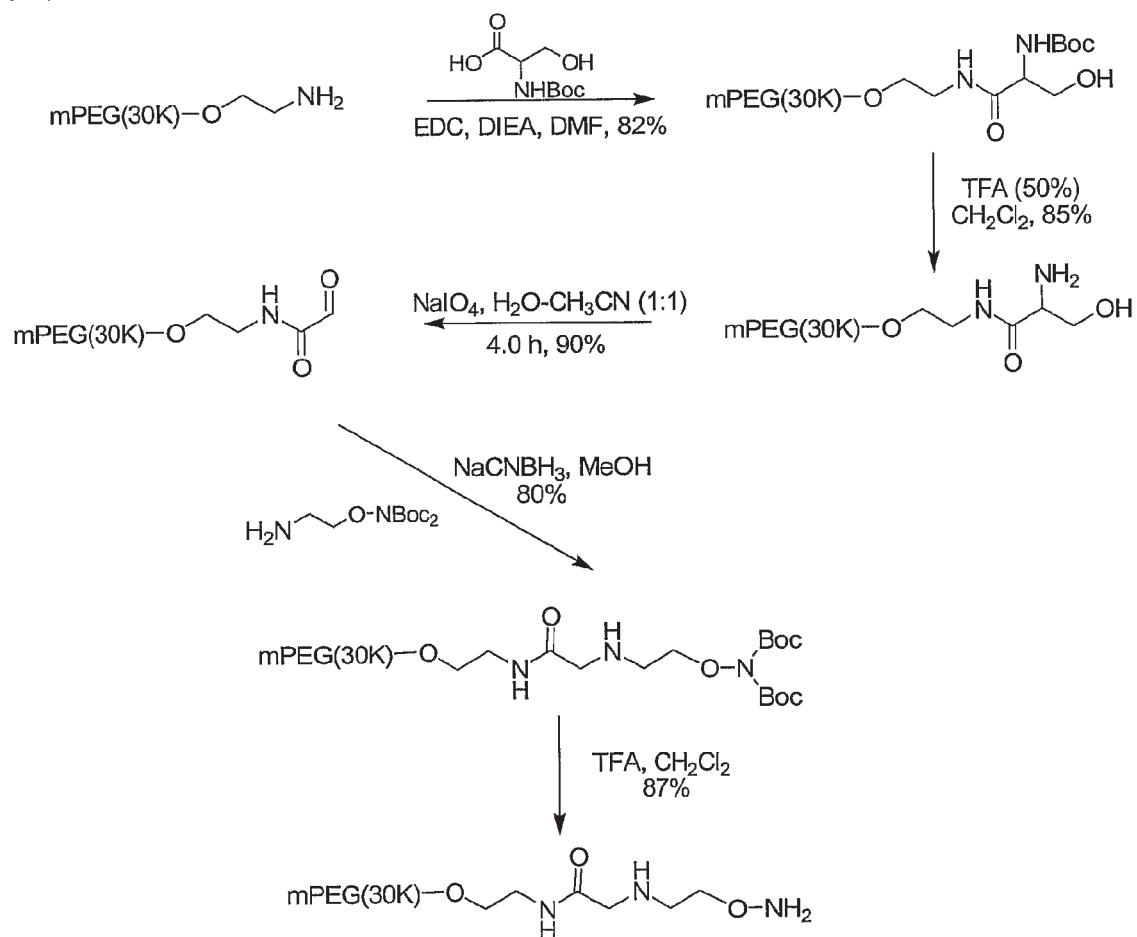
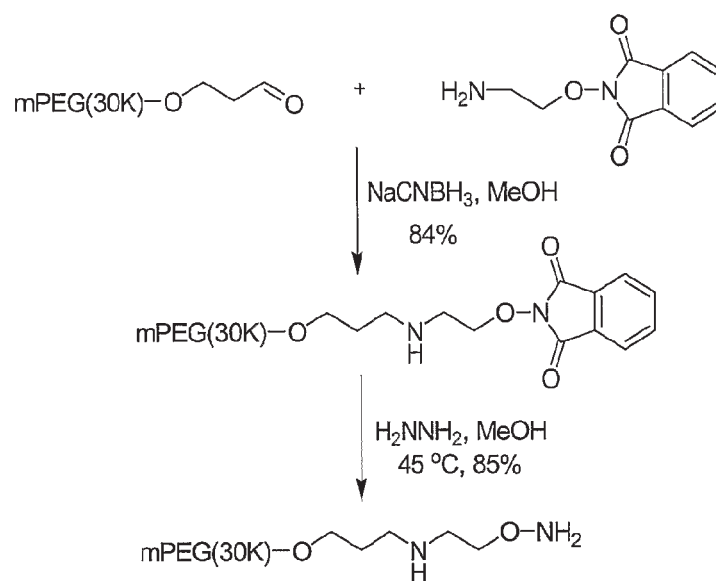


FIG. 53

(A)



(B)

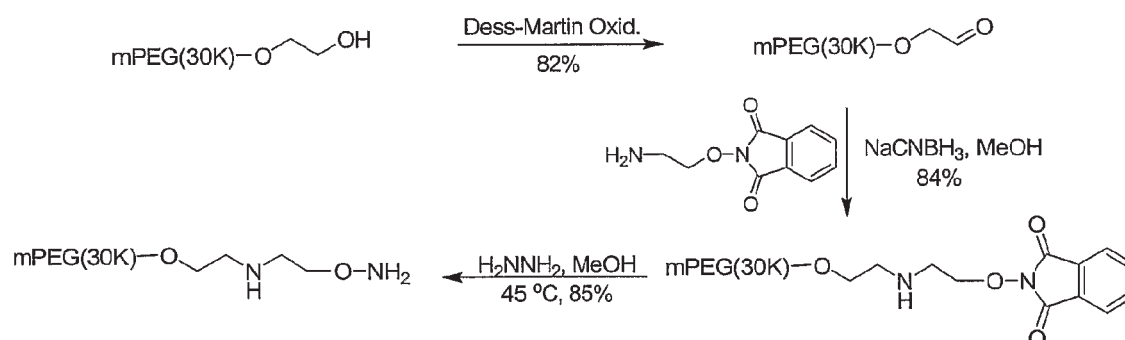


FIG. 54

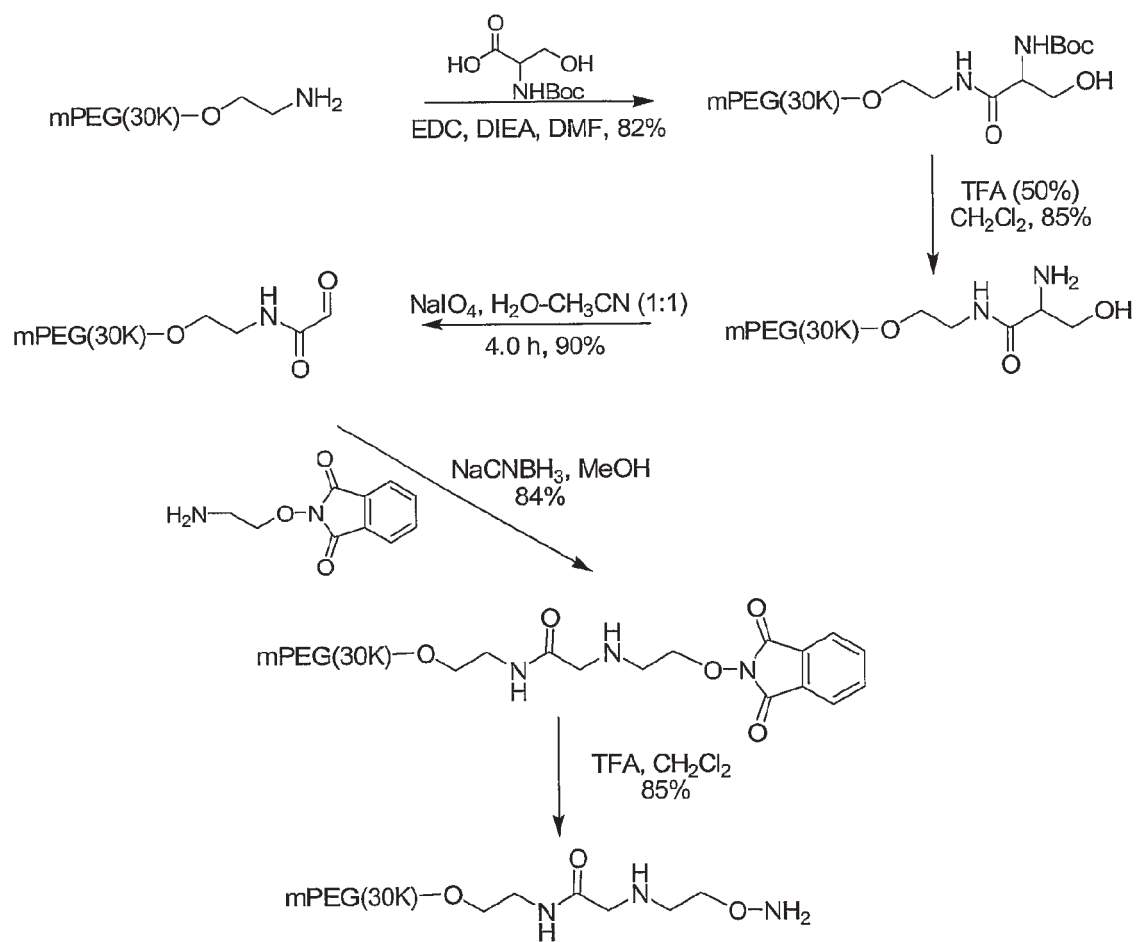
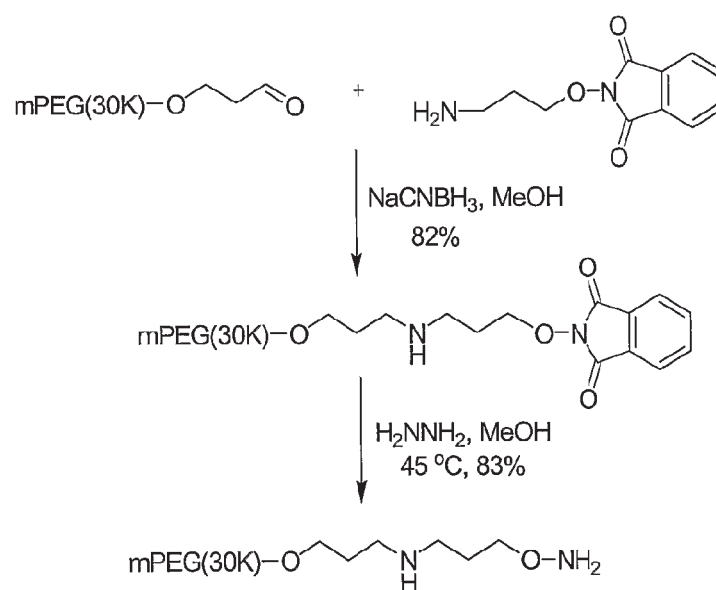


FIG. 55

(A)



(B)

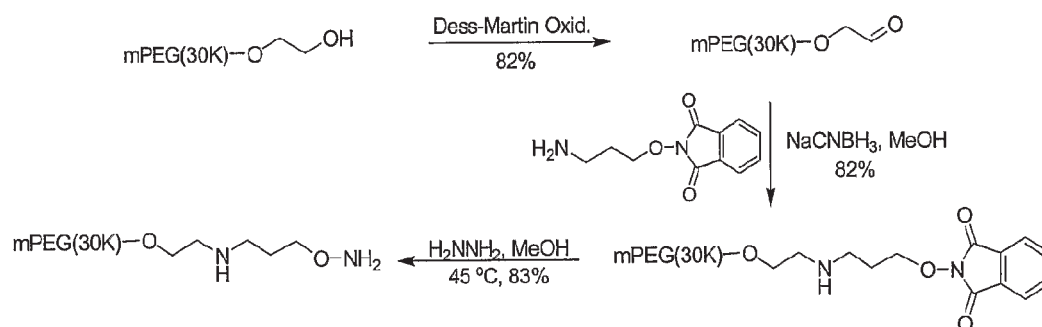


FIG. 56

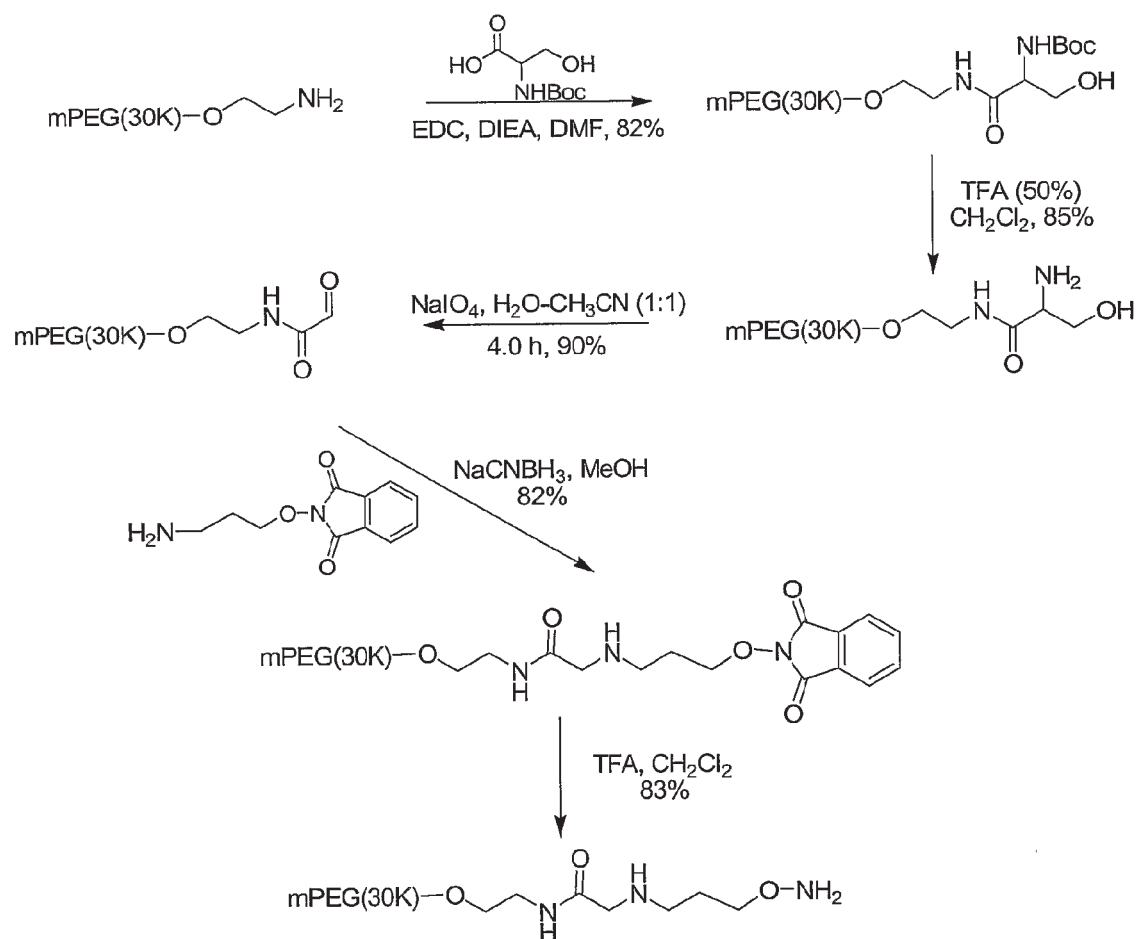
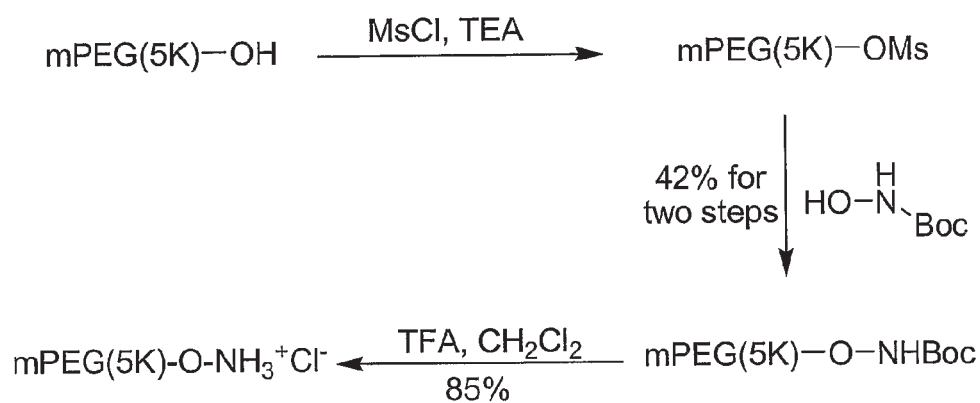


FIG. 57

(A)



(B)

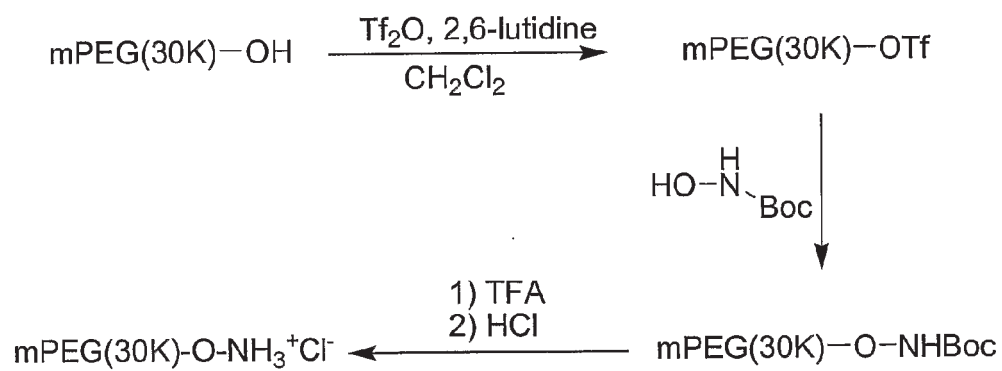
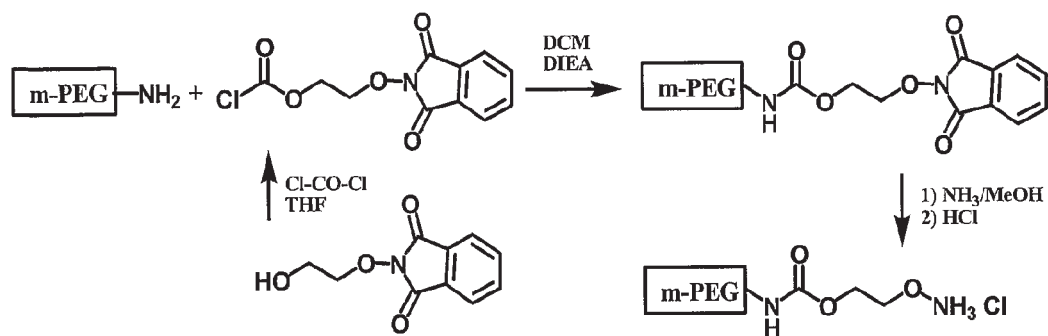


FIG. 58

(A)



(B)

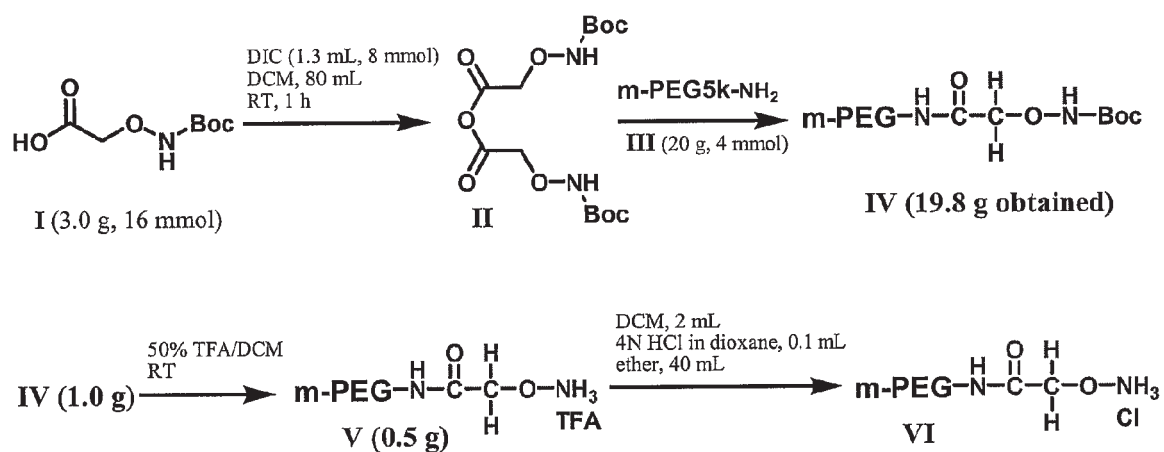
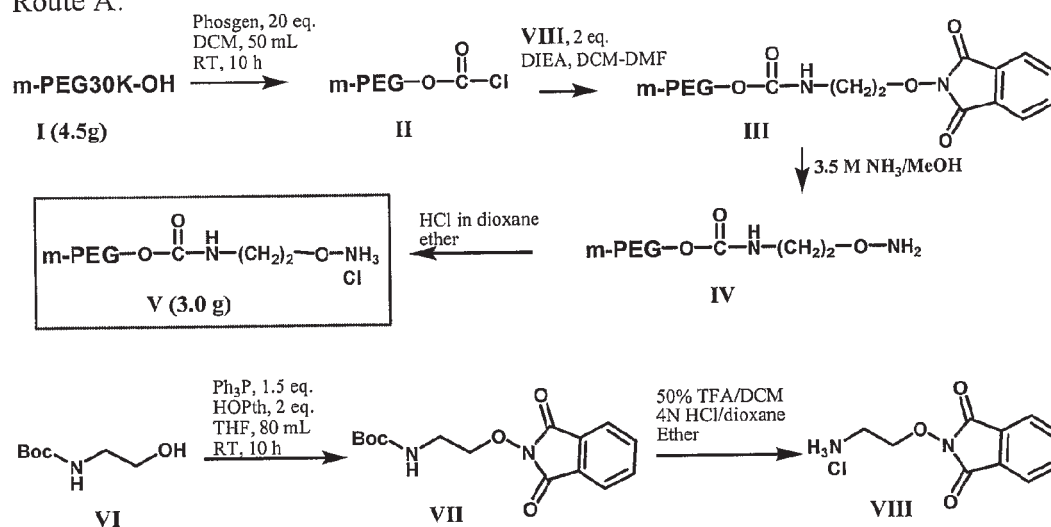


FIG. 59

(A) Route A:



(B)

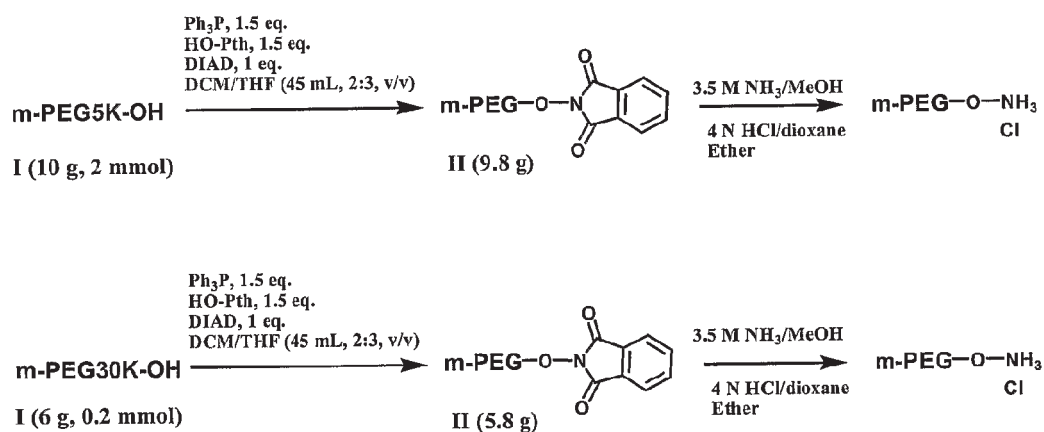
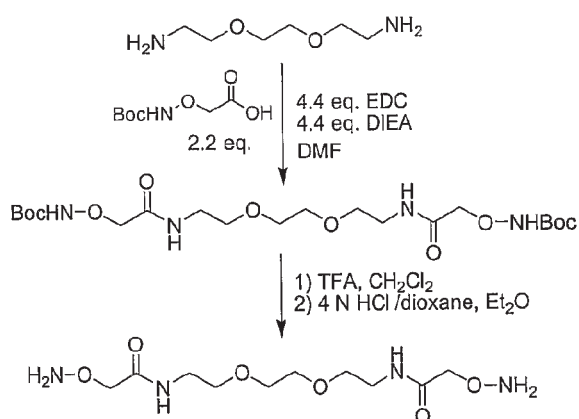
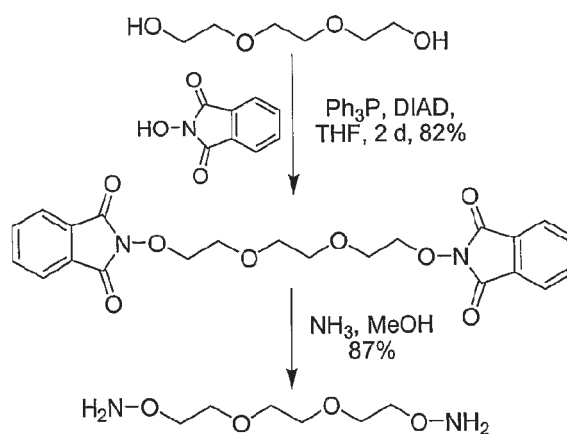


FIG. 60

(A)



(B)



(C)

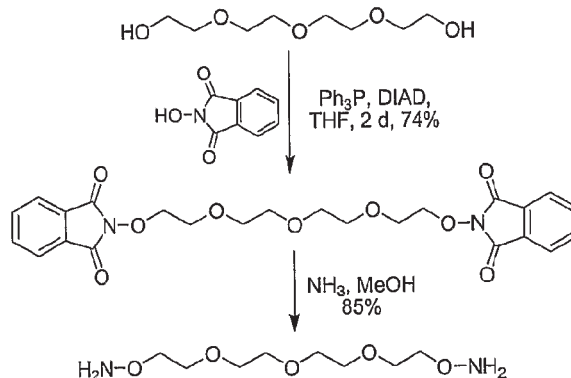
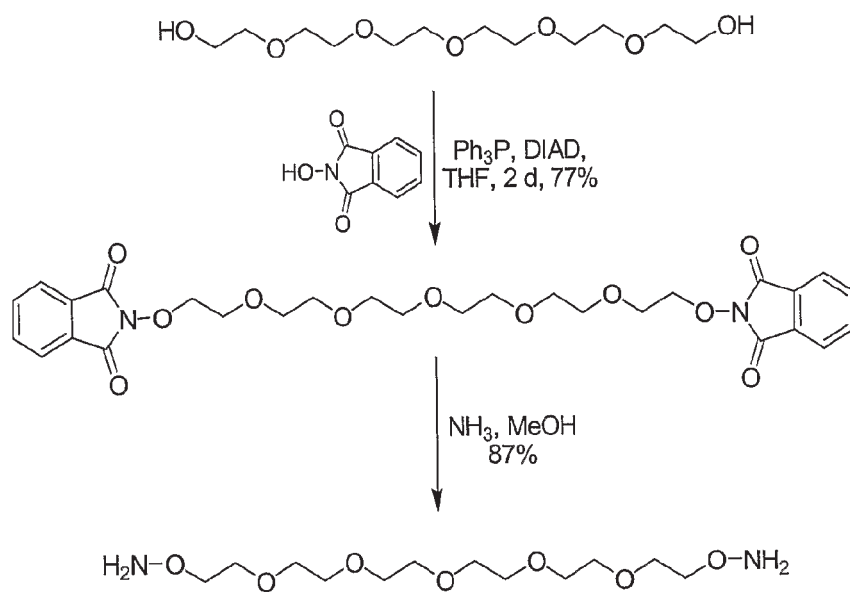


FIG. 61

(A)



(B)

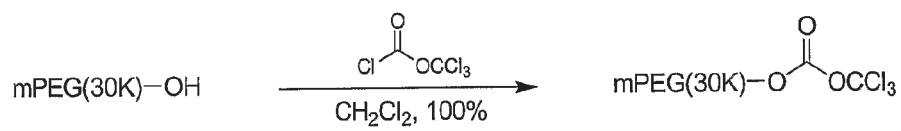
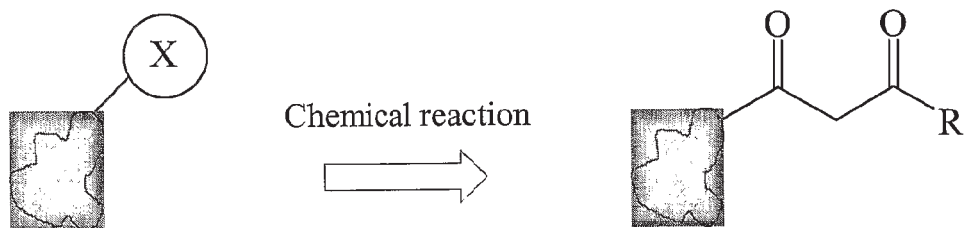


FIG. 62

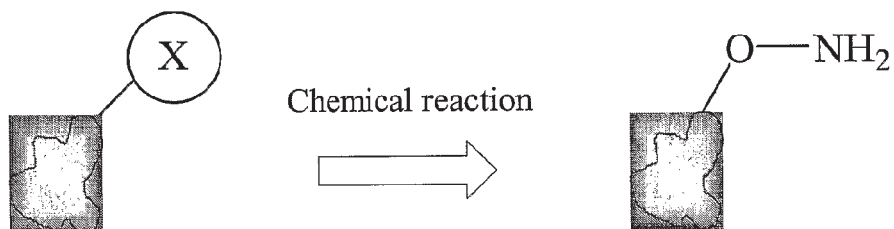
(A)



Non-Natural Amino
Acid, Polypeptide or Protein
convertible into a Dicarbonyl
Non-Natural Amino
Acid, Polypeptide or Protein

Dicarbonyl Non-Natural Amino
Acid, Polypeptide or Protein

(B)

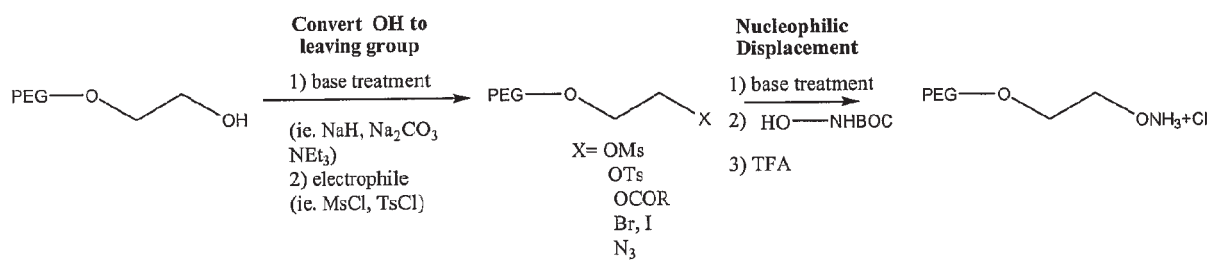


Non-Natural Amino
Acid, Polypeptide or Protein
convertible into a Hydroxylamine
Non-Natural Amino
Acid, Polypeptide or Protein

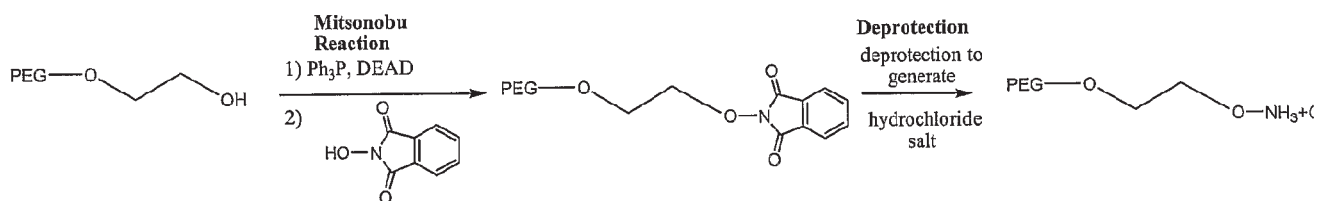
Hydroxylamine Non-Natural Amino
Acid, Polypeptide or Protein

FIG. 63

1) Synthesis based upon nucleophilic displacement



2) Synthesis based upon Mitsunobu reaction



3) Synthesis starting with PEG oxirane

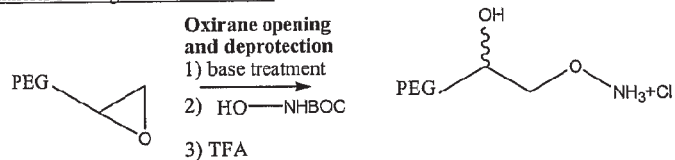
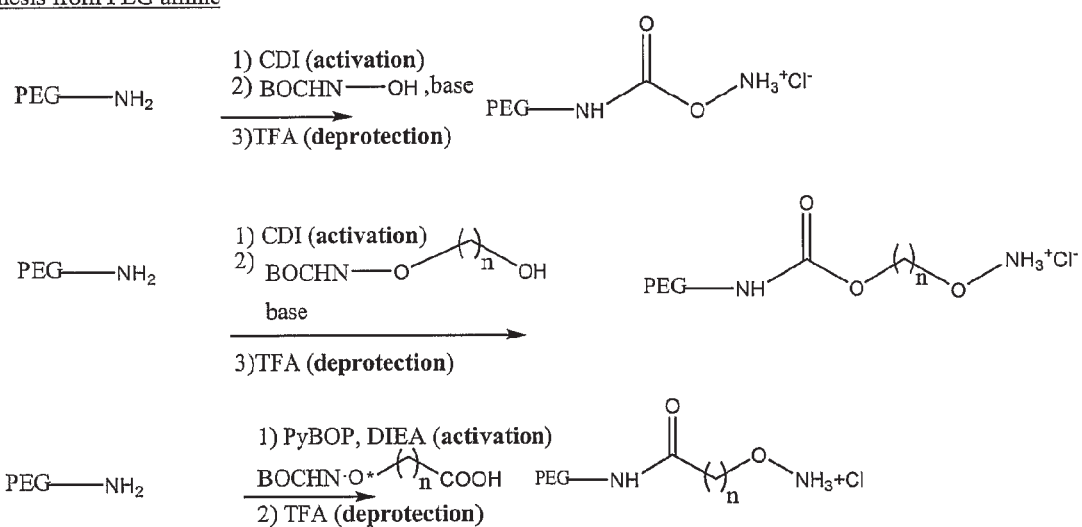


FIG. 64

4) Synthesis from PEG amine



5) Synthesis from PEG aldehyde

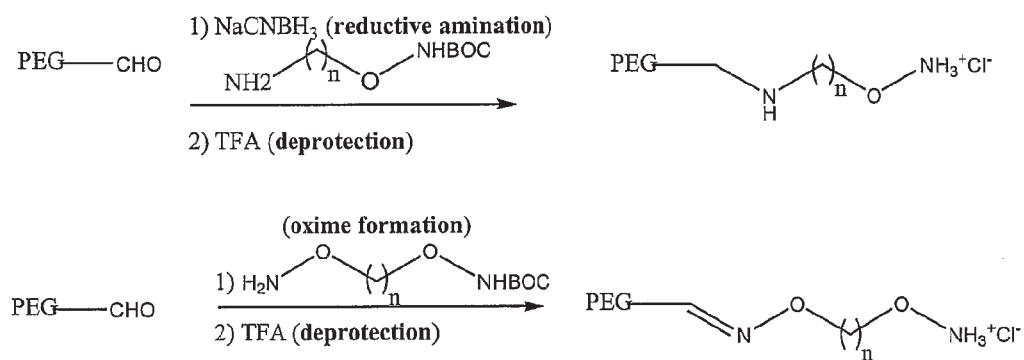


FIG. 65