

1 / 65

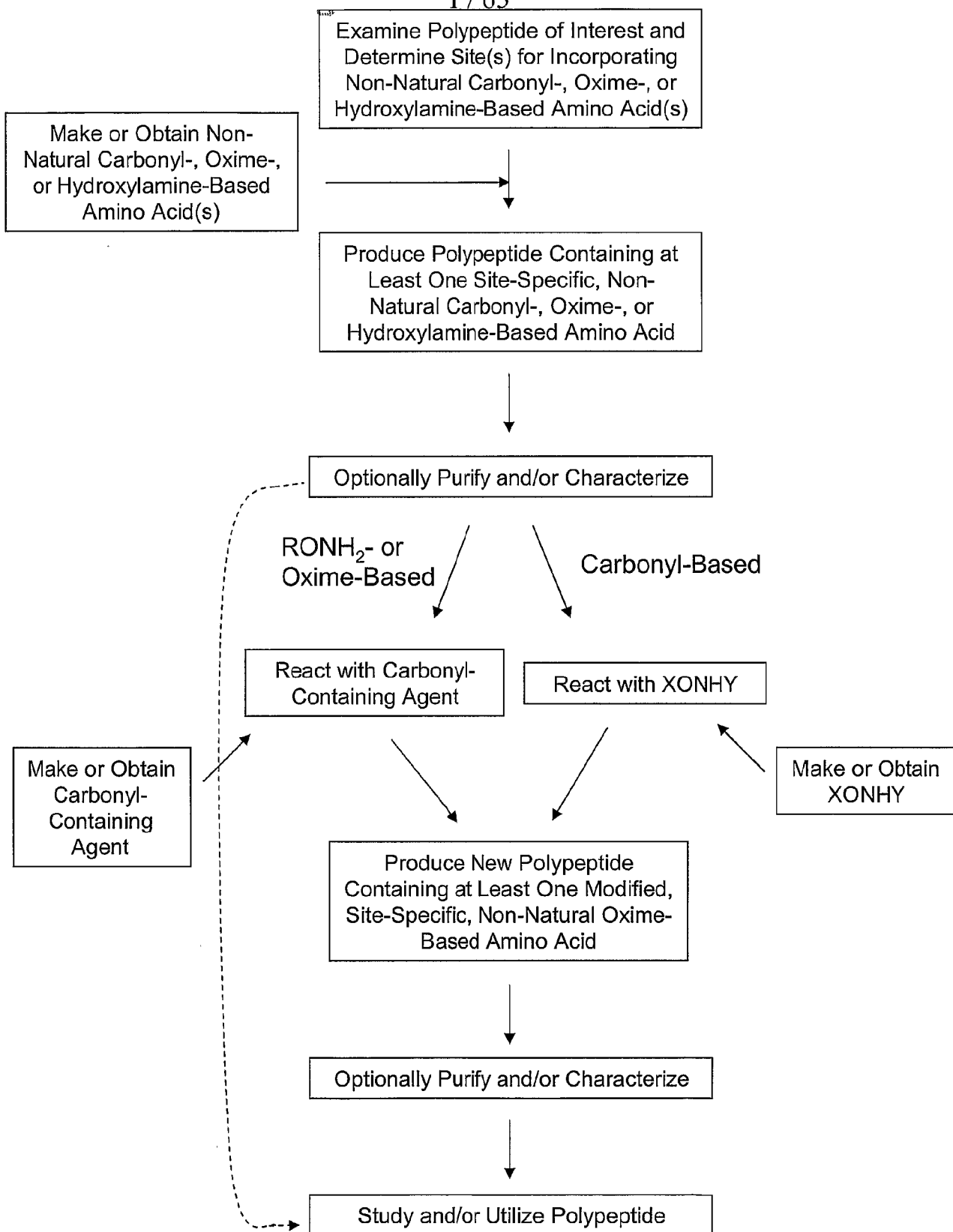
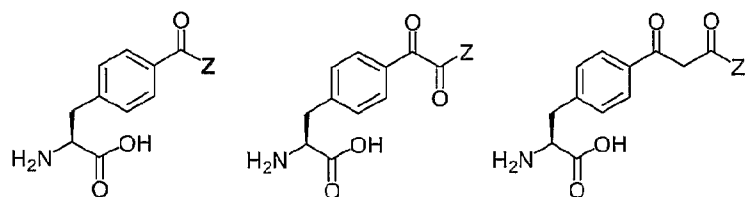
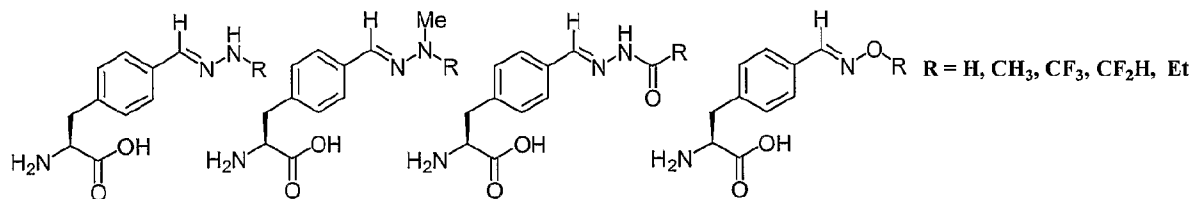


FIG. 1

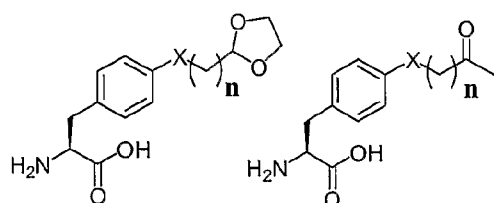
2 / 65



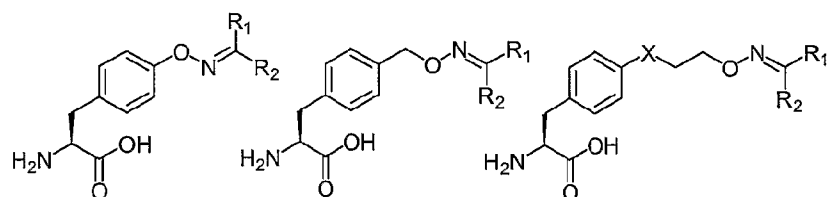
$Z = \text{CH}_3, \text{CF}_3, \text{CF}_2\text{H}, \text{CH}_2\text{Cl}, \text{CH}_2\text{OH}, \text{CH}_2\text{OMe}, \text{Et}, \text{iPrCH}_2\text{CN}$



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

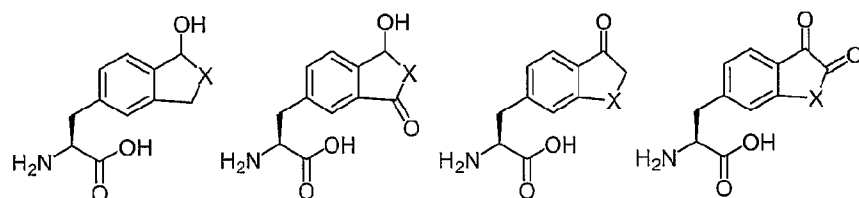


$n = 0-4; X = \text{O}, \text{S}, \text{NH}, \text{CH}_2, \text{CF}_2, \text{CO}$

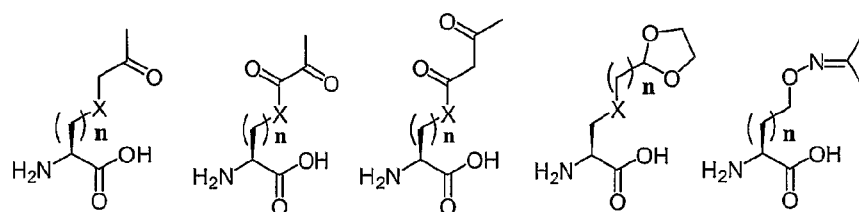


$R_1, R_2 = \text{H}, \text{CH}_3, \text{CF}_3, \text{CF}_2\text{H}, \text{Et}$

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



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



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

FIG. 2

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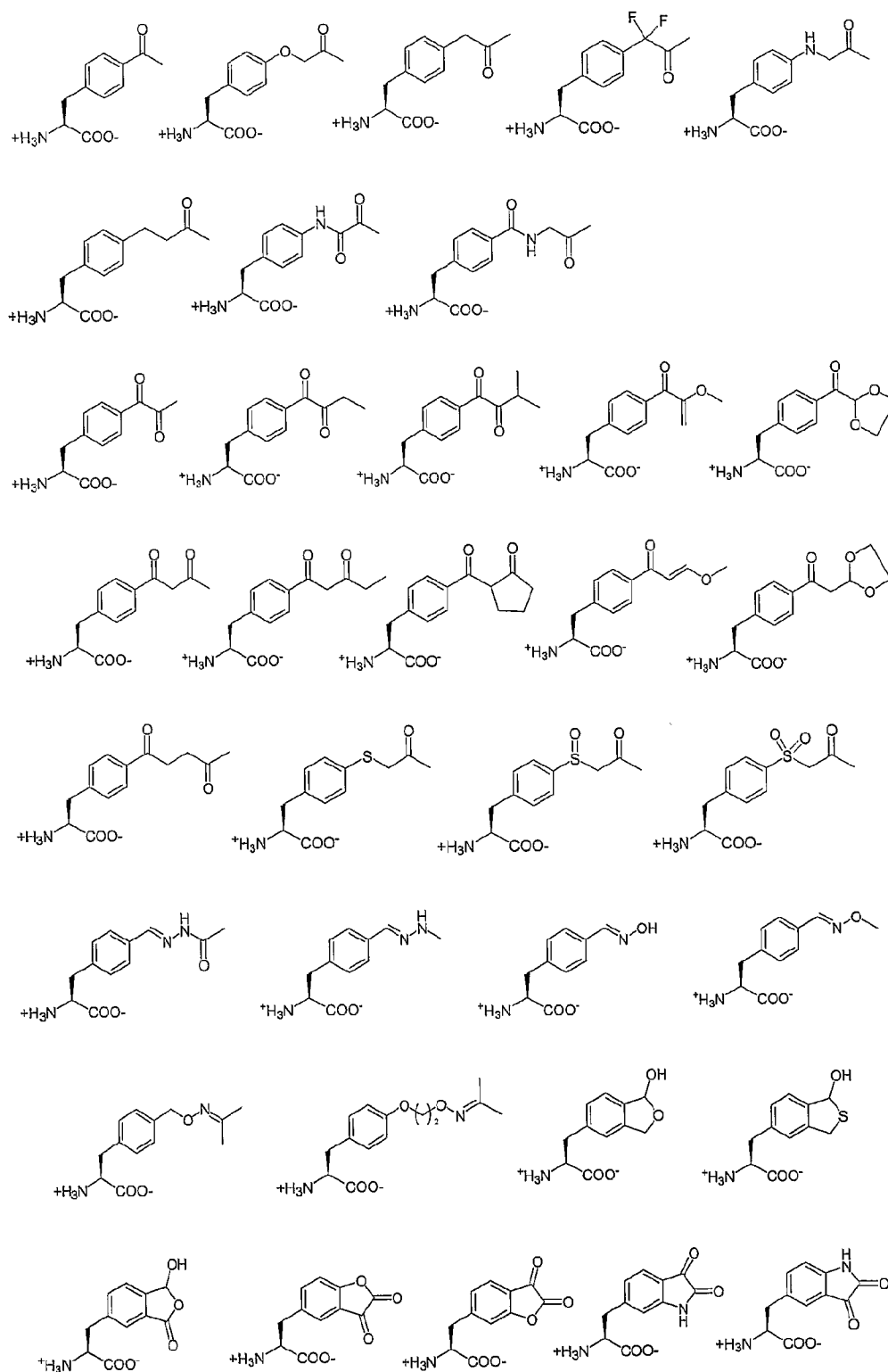


FIG. 3

4 / 65

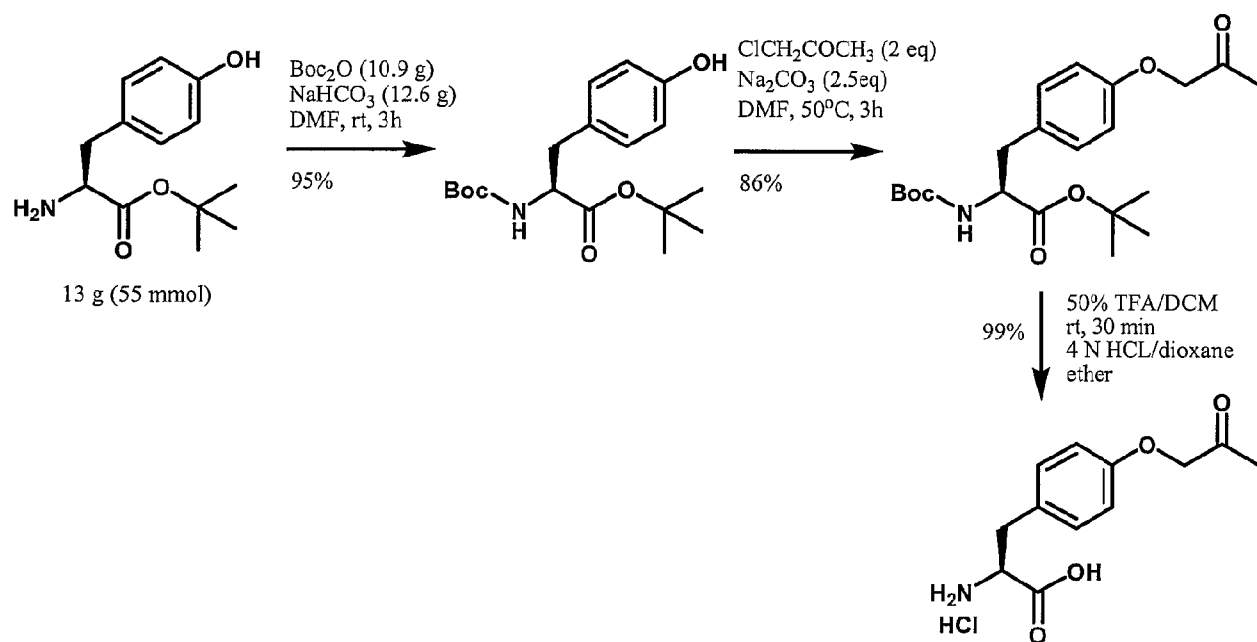


FIG. 4

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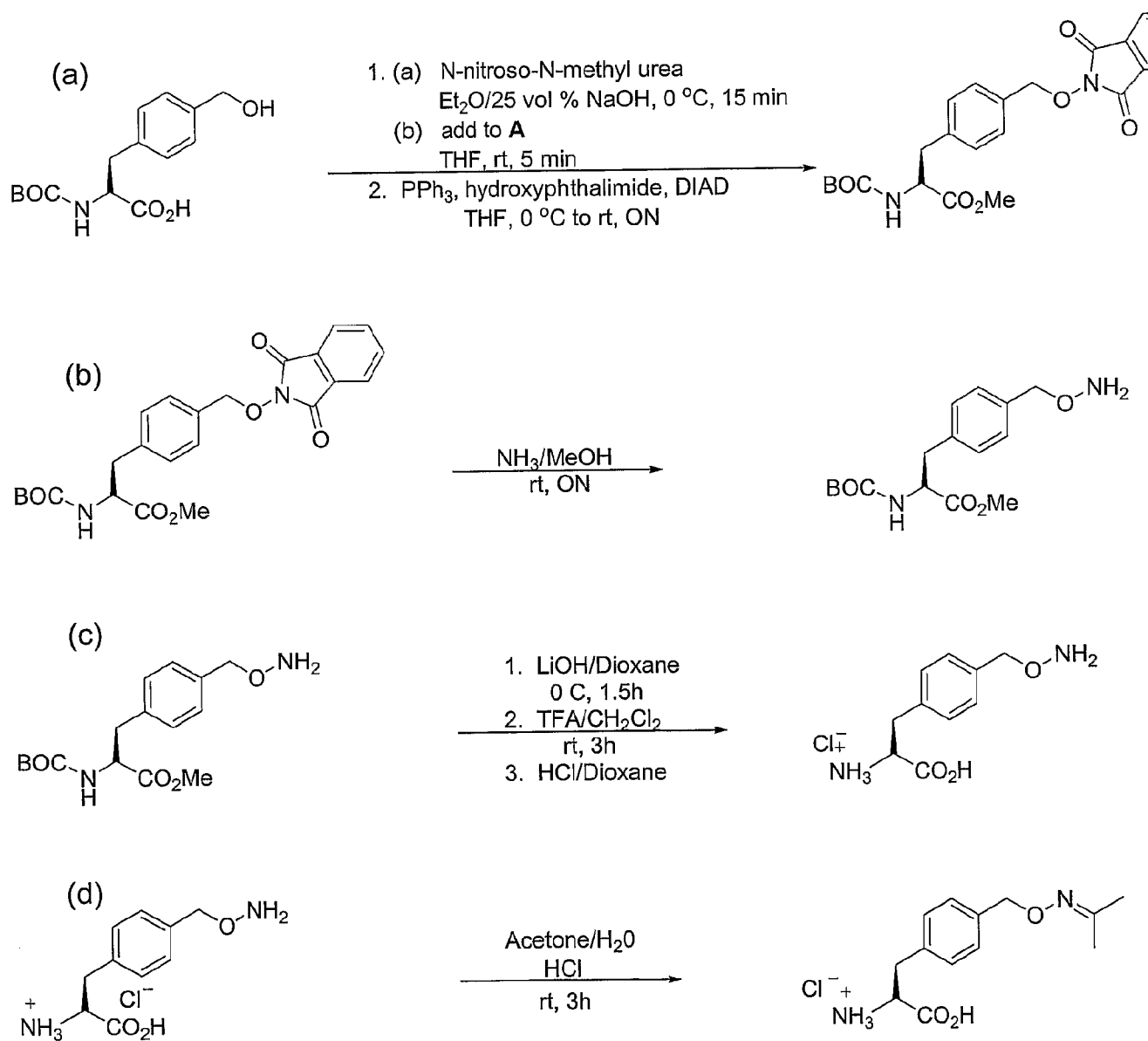


FIG. 5

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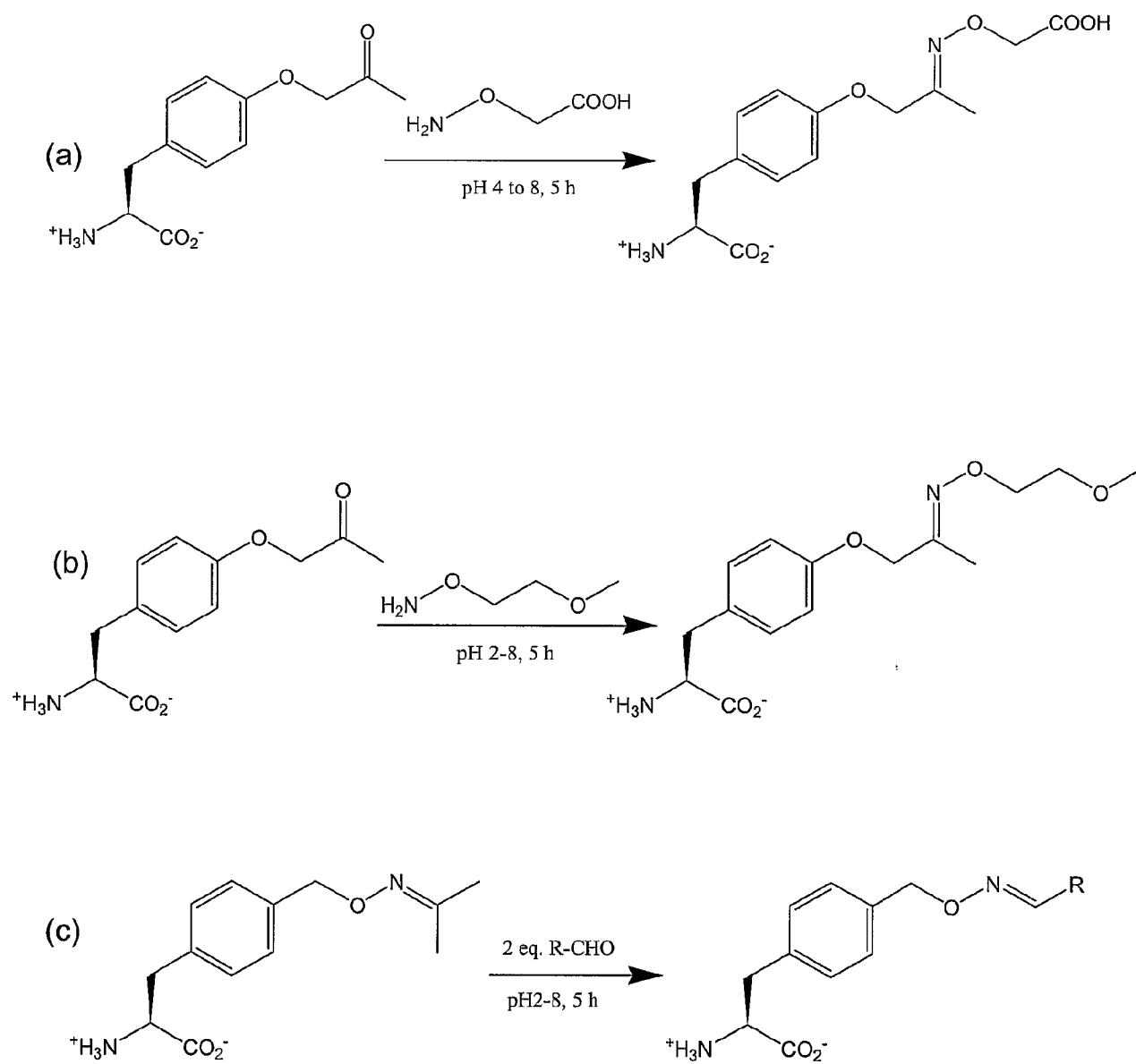
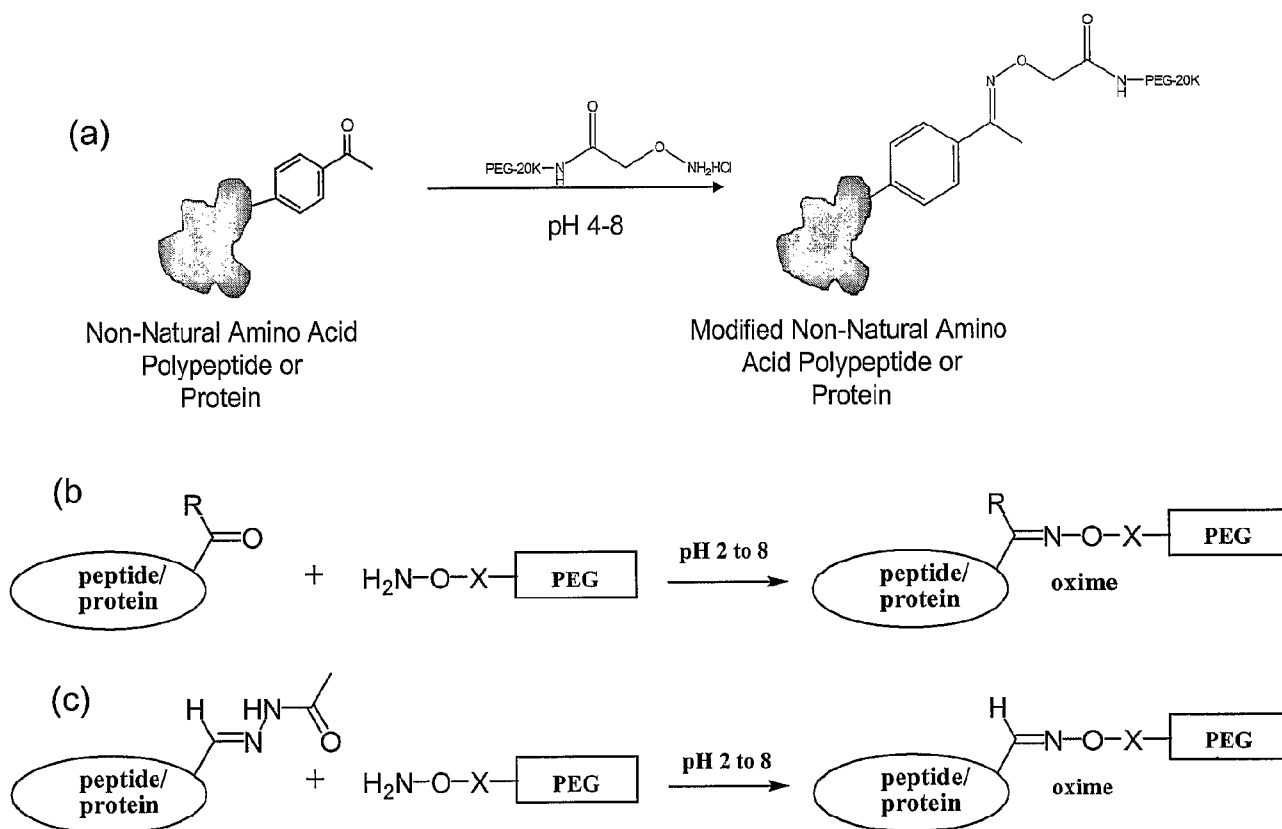


FIG. 6

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

X = linker

FIG. 7

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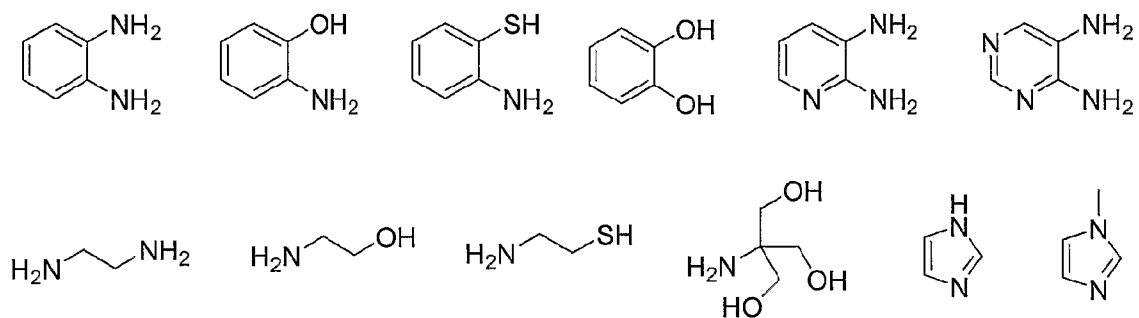


FIG. 8

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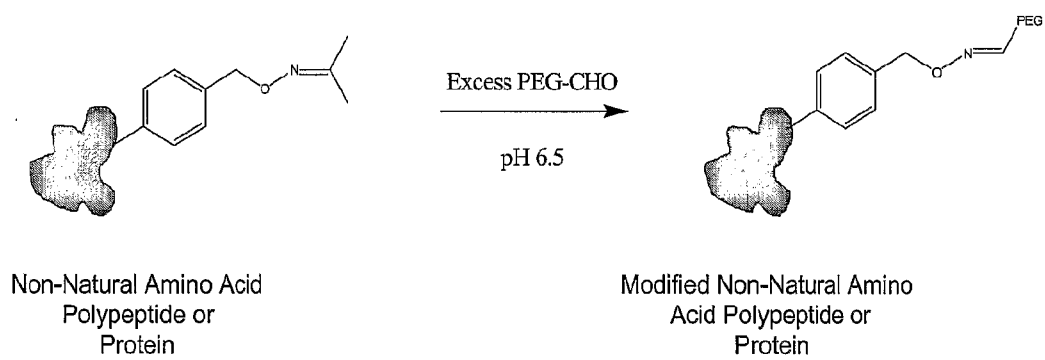
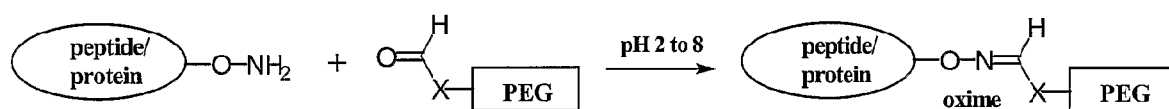


FIG. 9

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

FIG. 10

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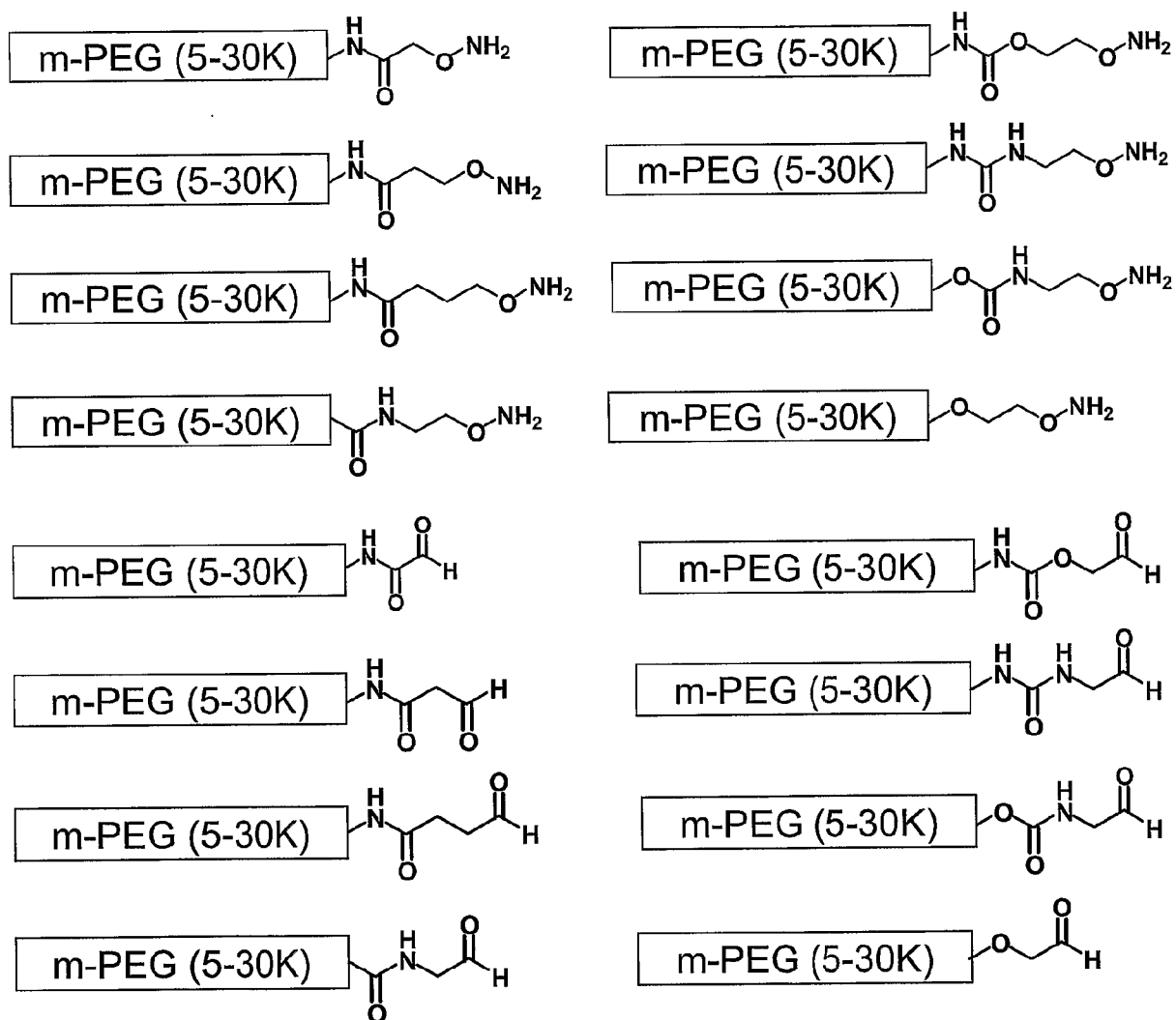


FIG. 11

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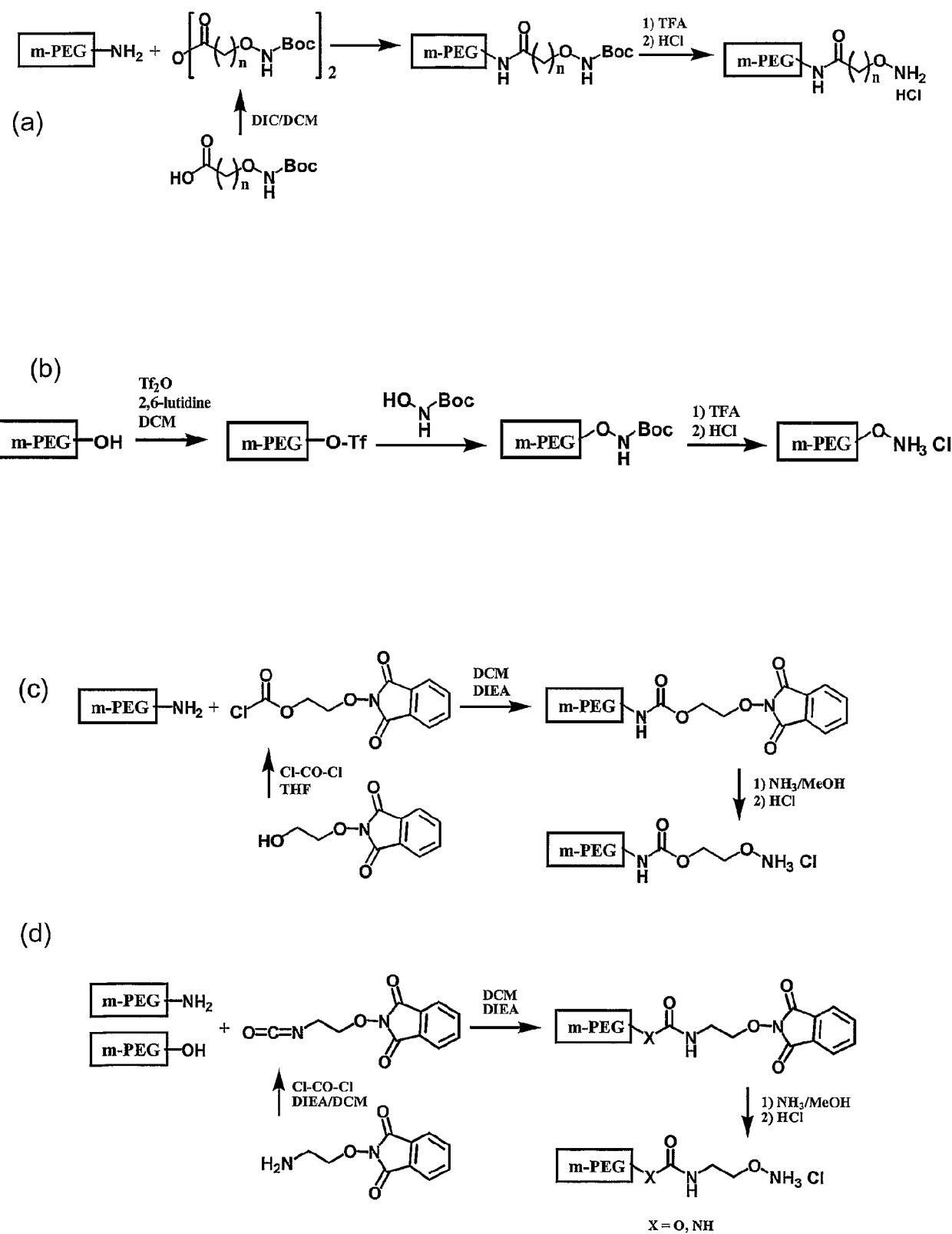
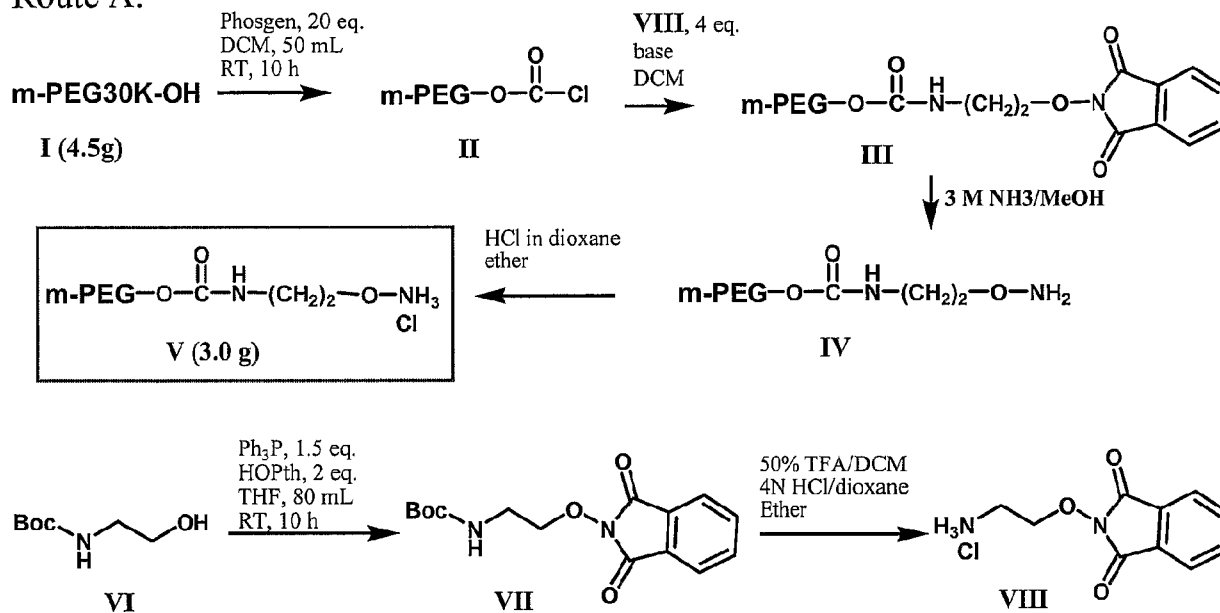


FIG. 12

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Route A:



Route B:

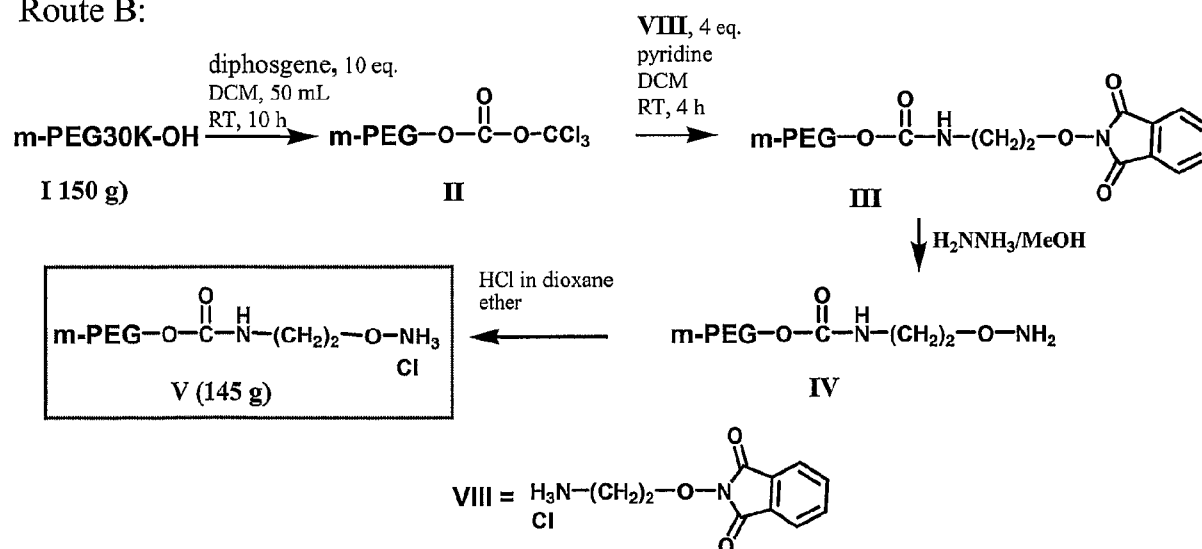
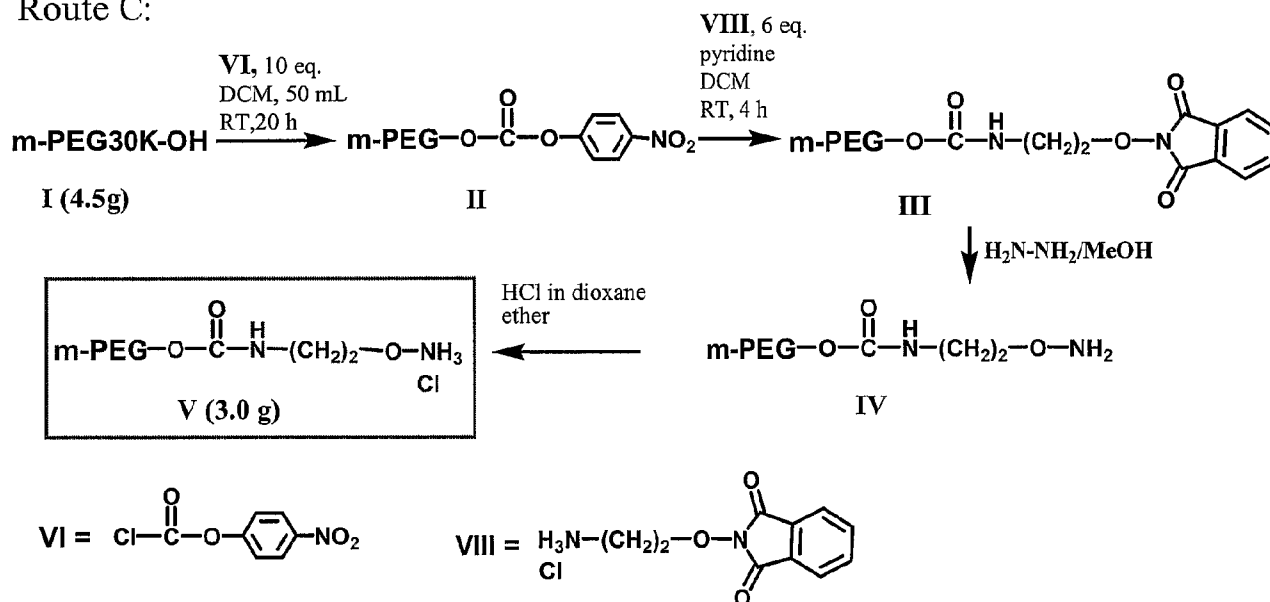


FIG. 14

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Route C:



Route D:

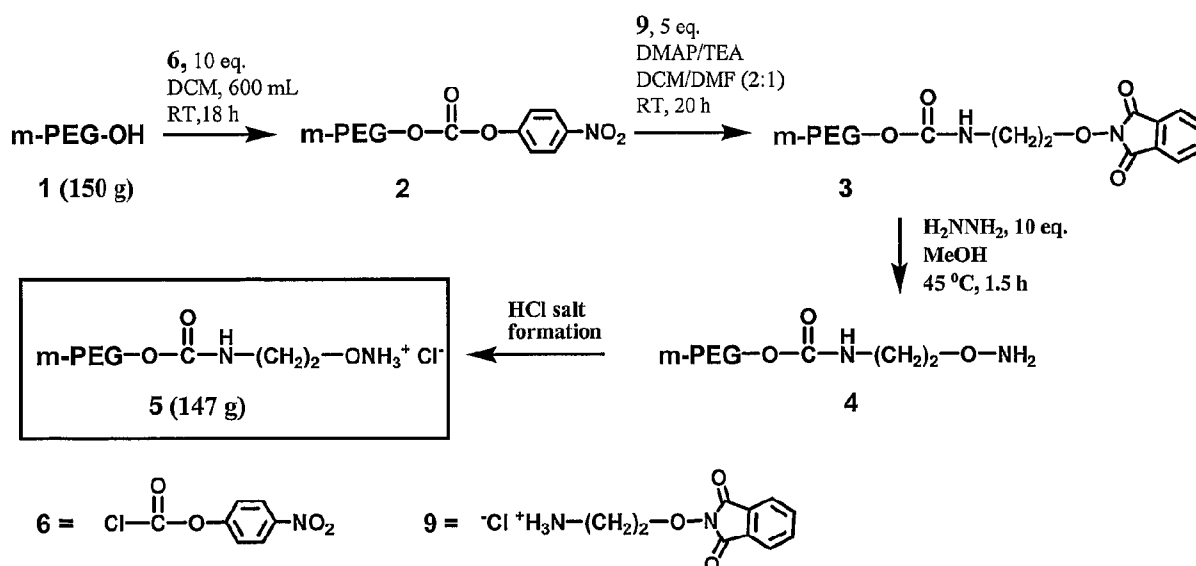


FIG. 15

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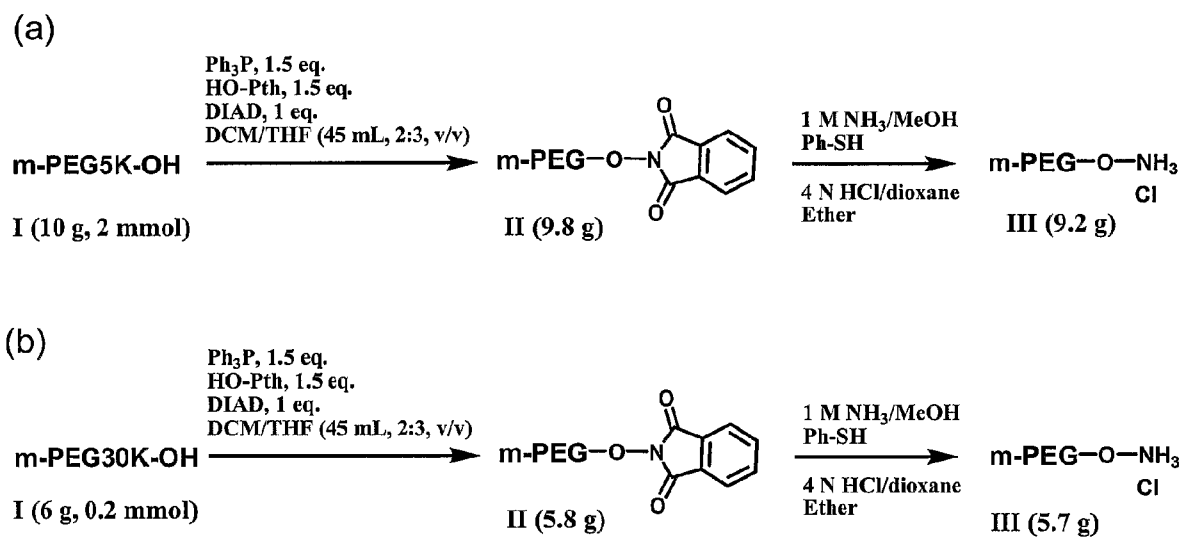
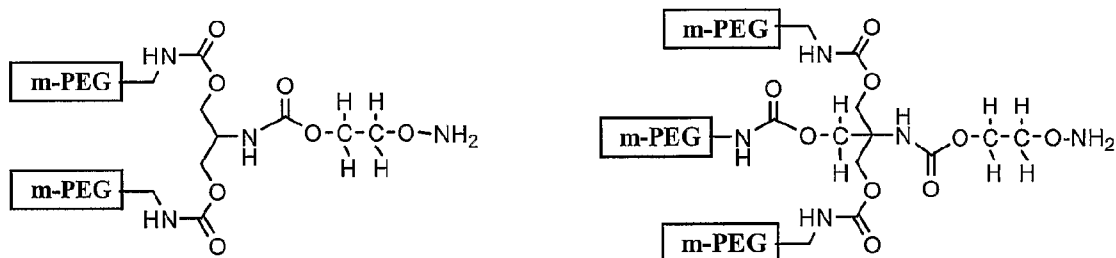
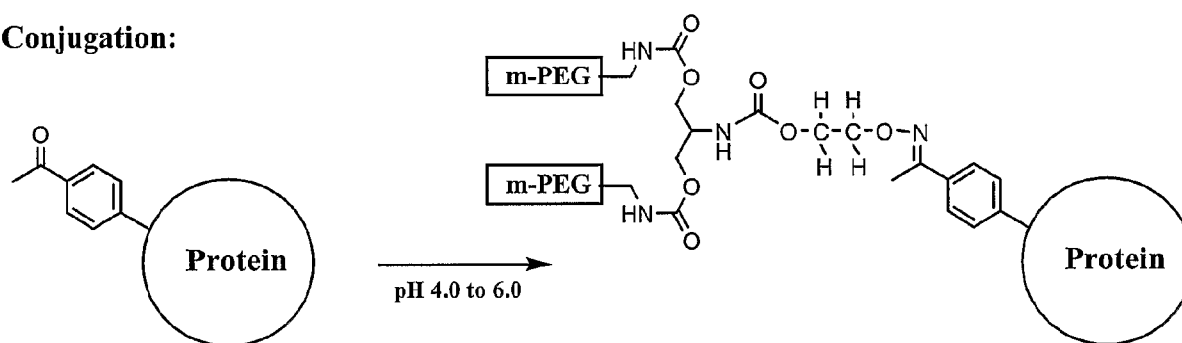


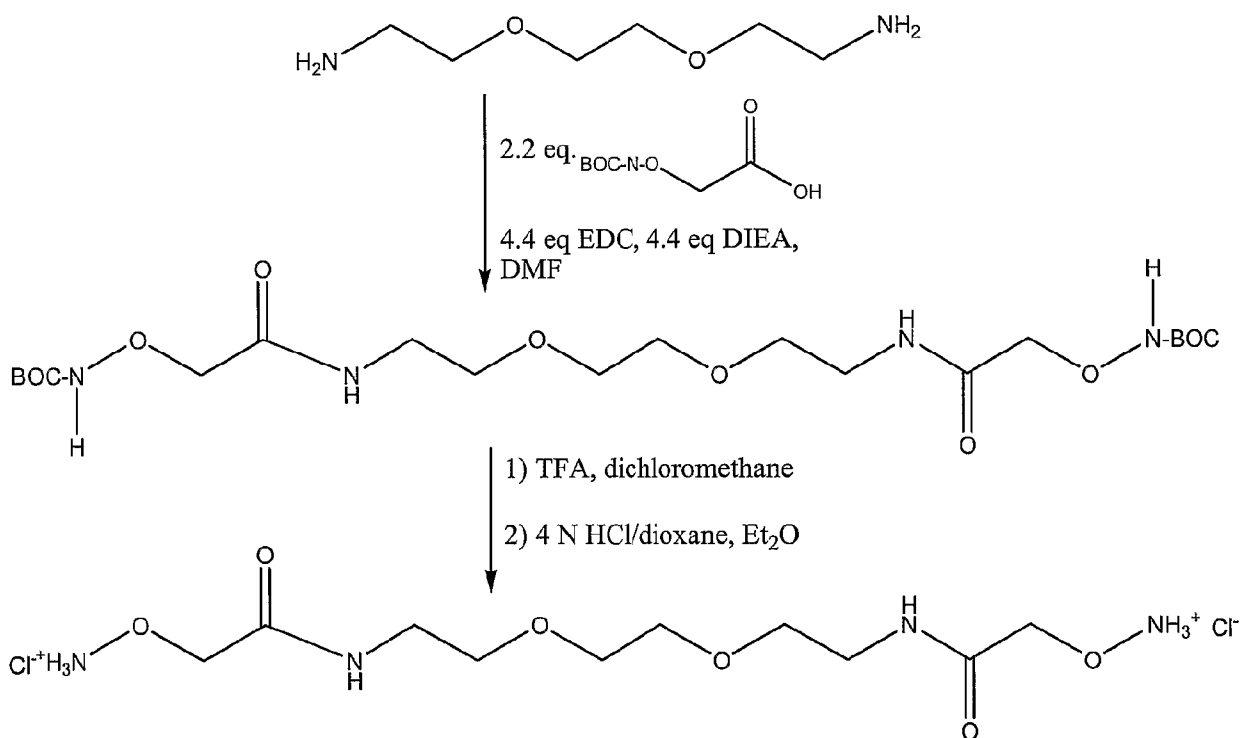
FIG. 16

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

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a



b

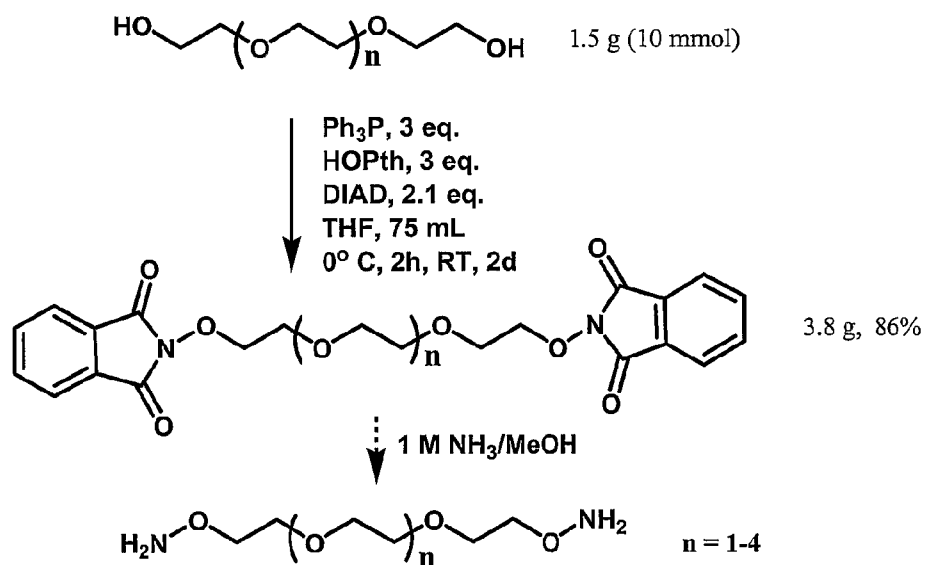


FIG. 18

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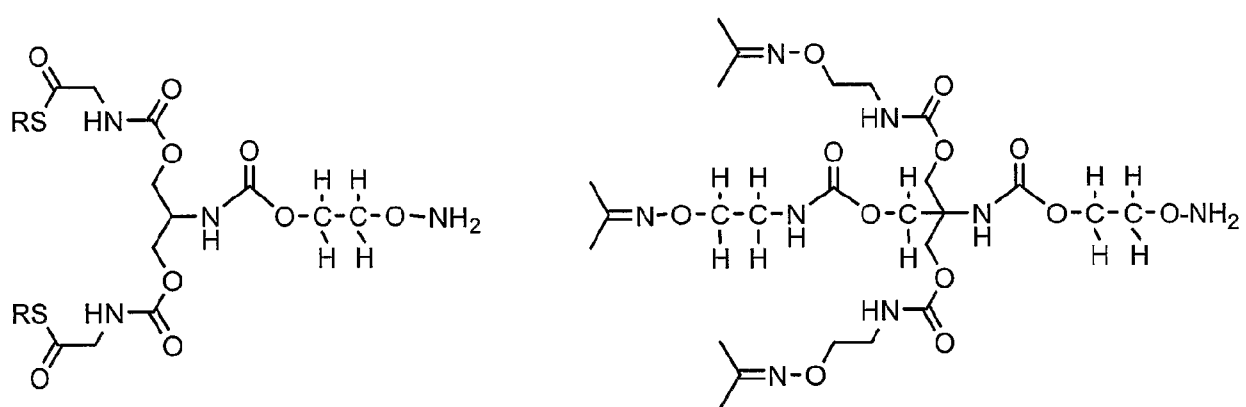


FIG. 19

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Bifunctional linker: $\text{H}_2\text{N}-\text{O}-\text{CH}_2-\text{[linker]}-\text{CH}_2-\text{[hexagon]}$

Scheme:

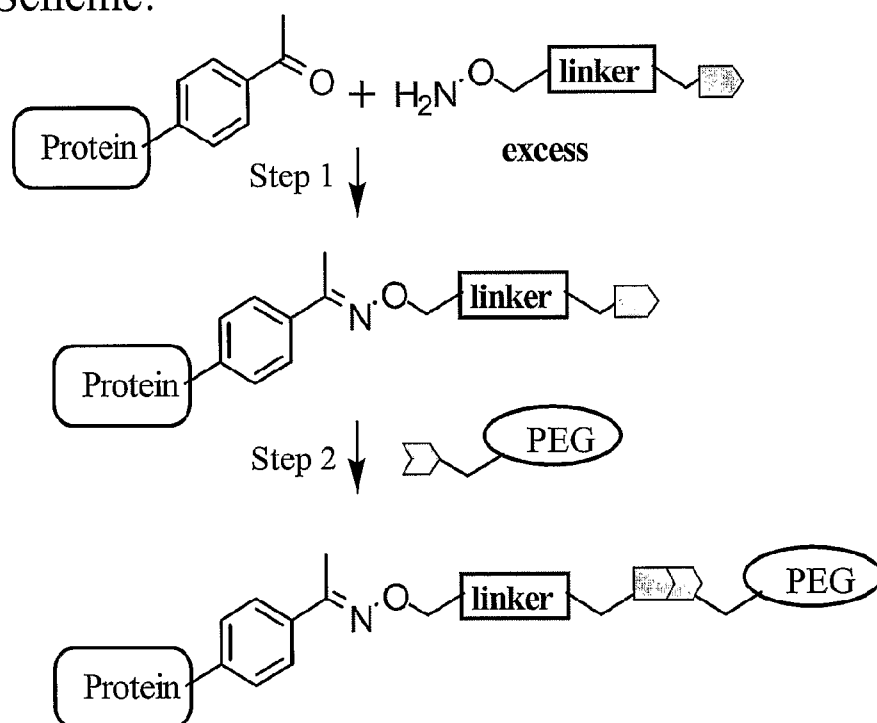


FIG. 20

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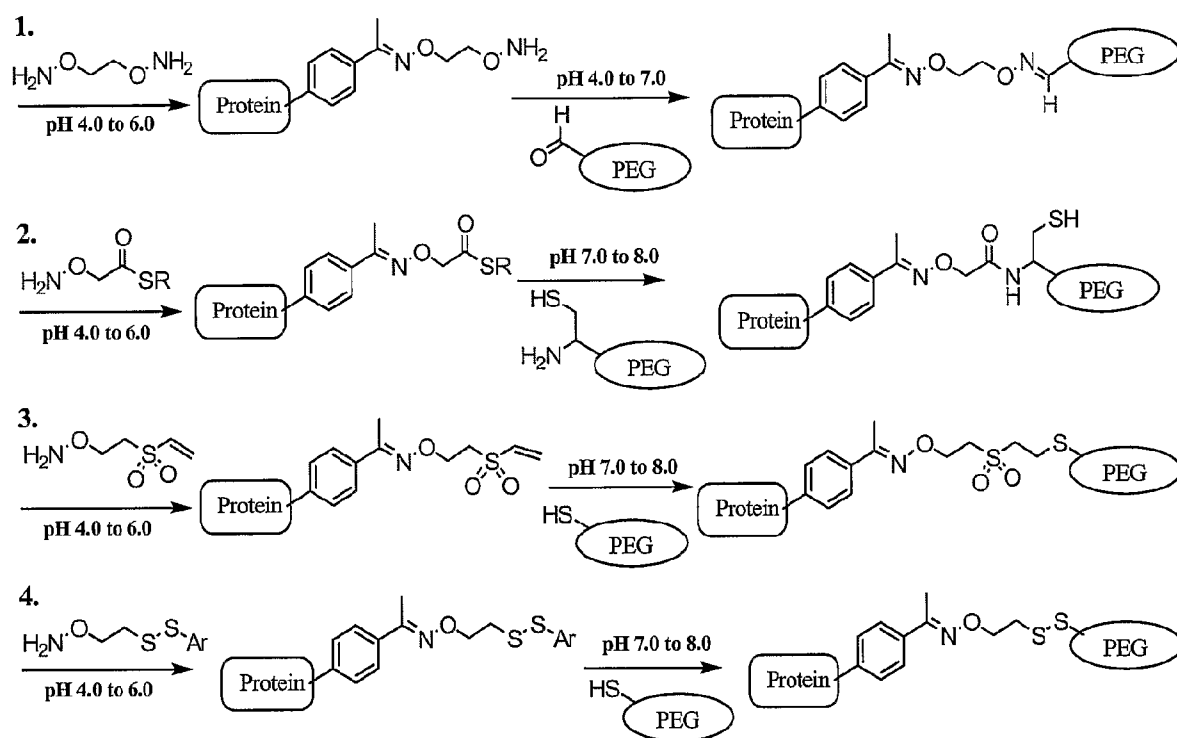


FIG. 21

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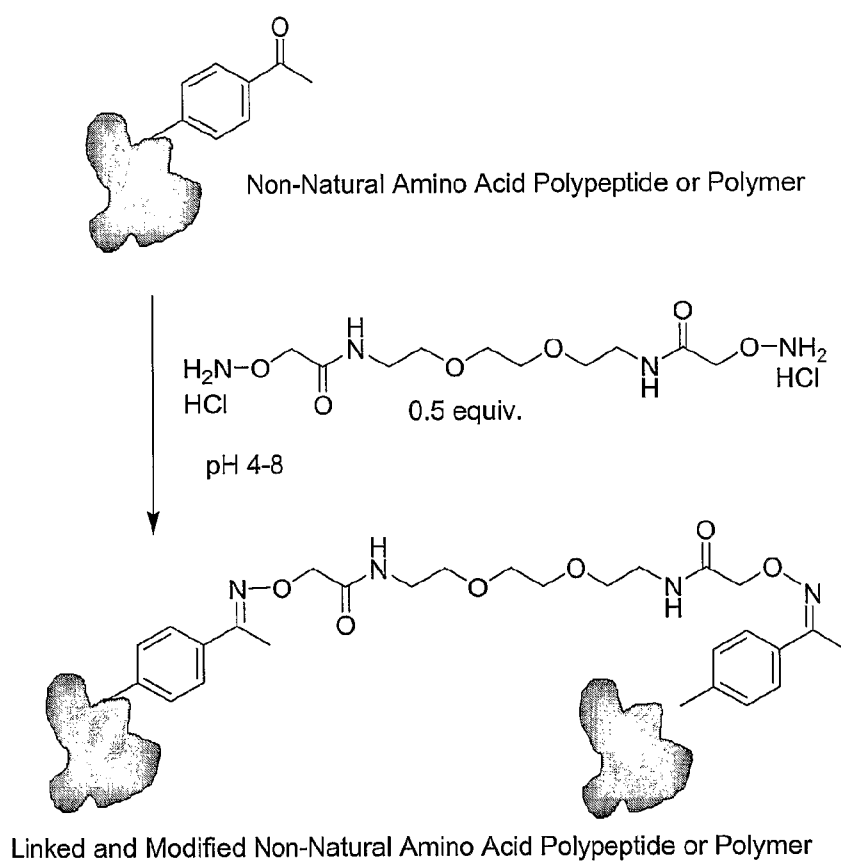


FIG. 22

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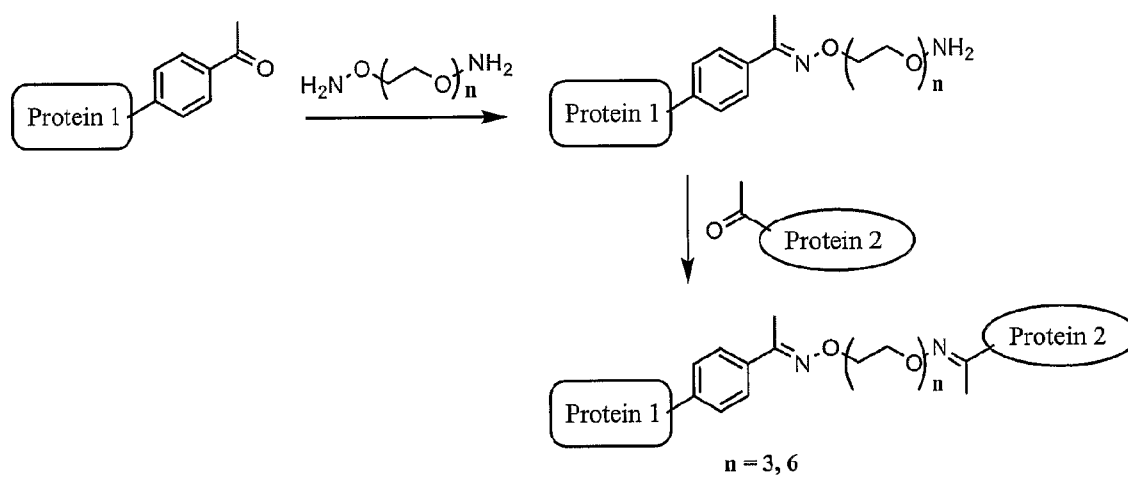


FIG. 23

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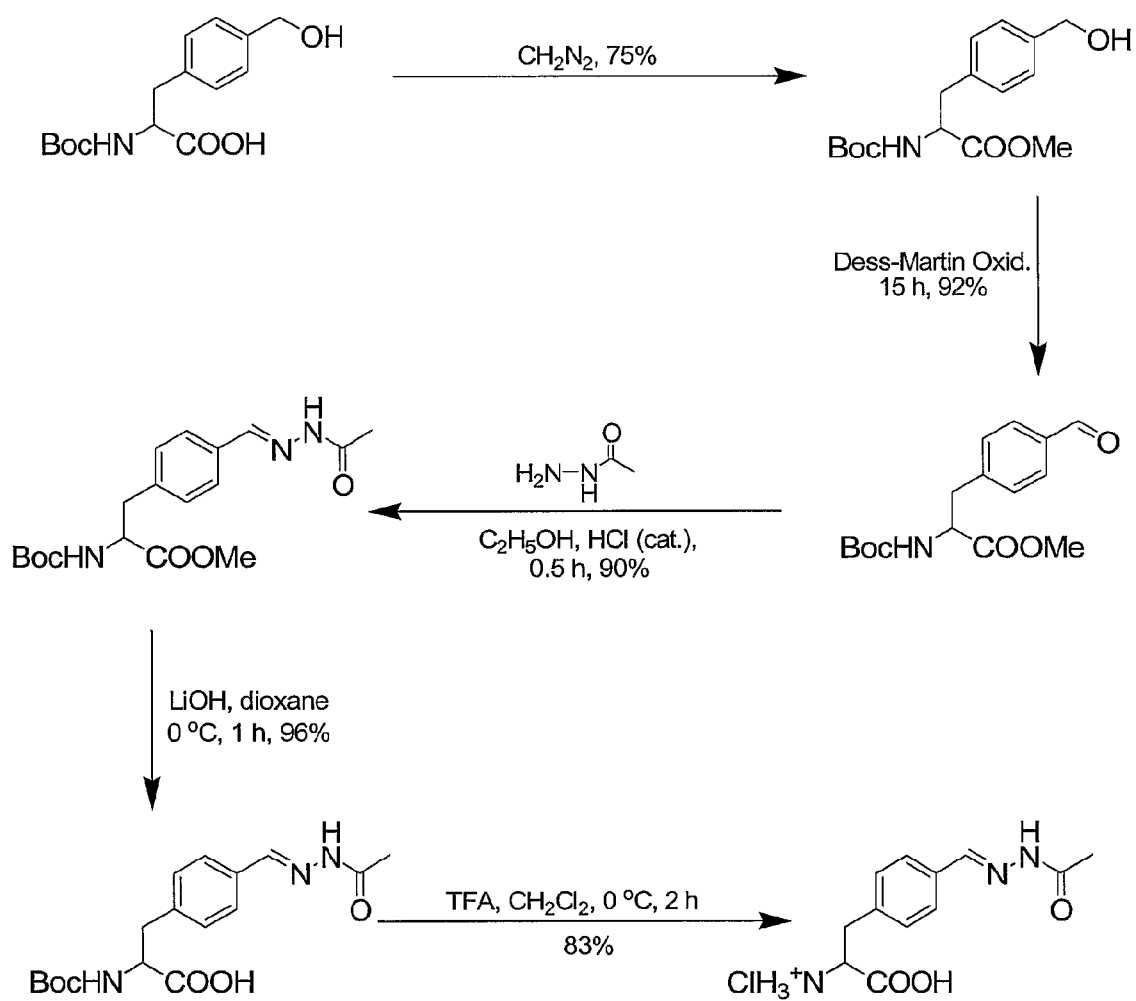


FIG. 24

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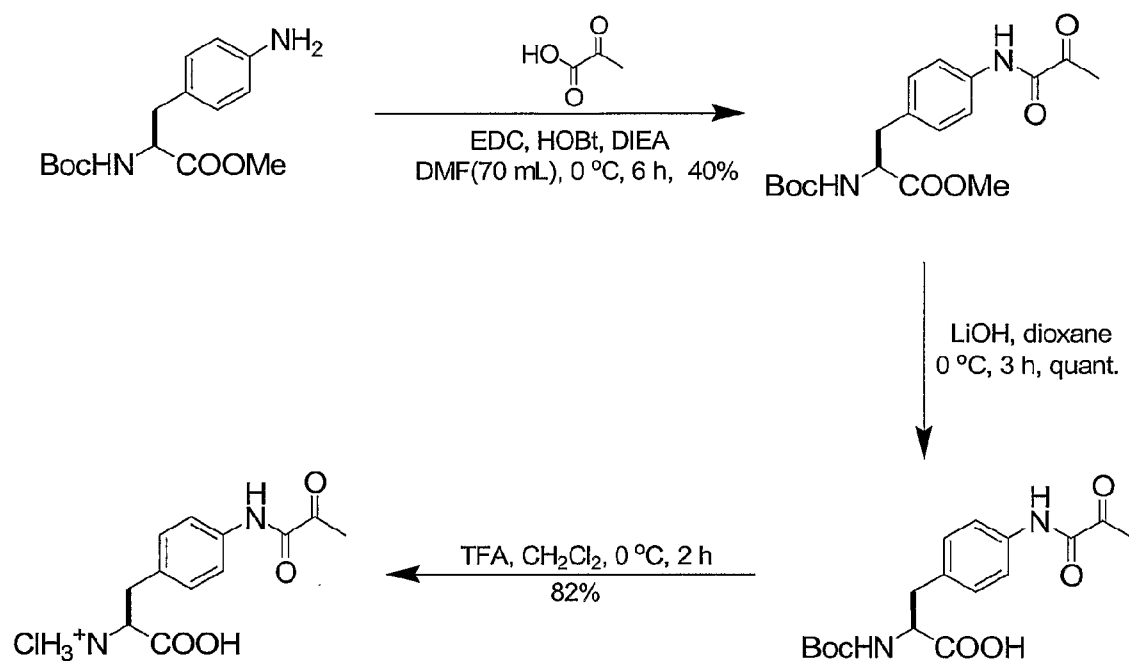


FIG. 25

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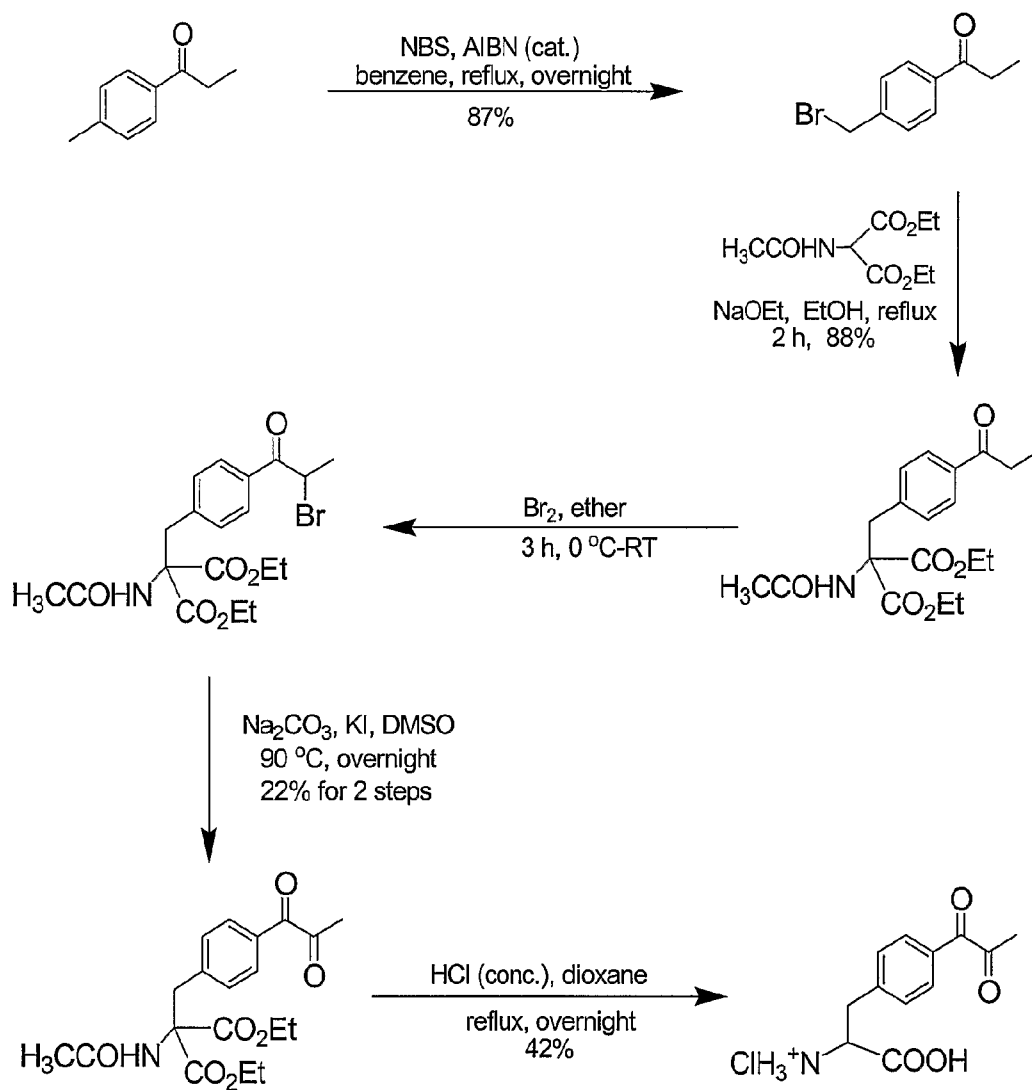


FIG. 26

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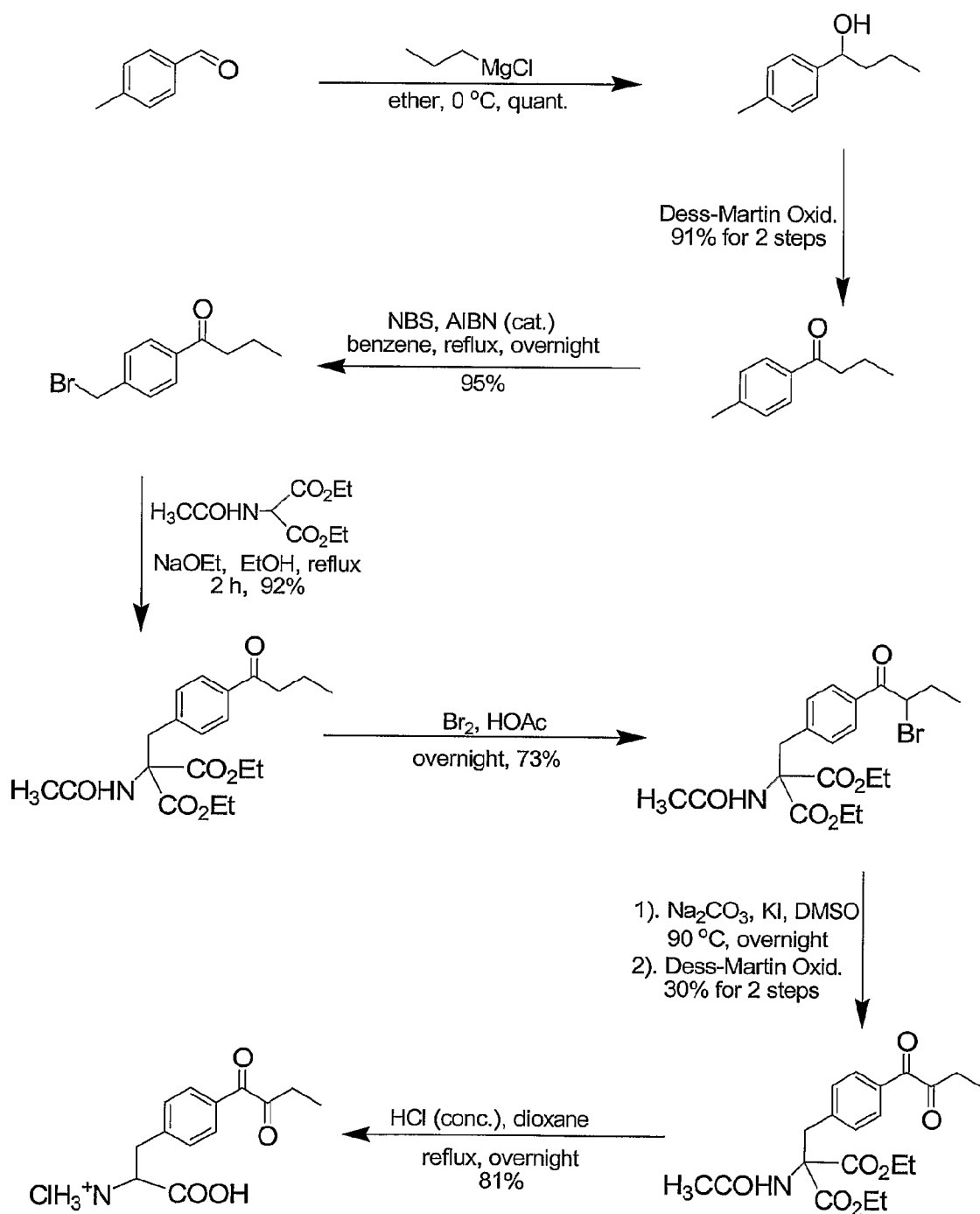


FIG. 27

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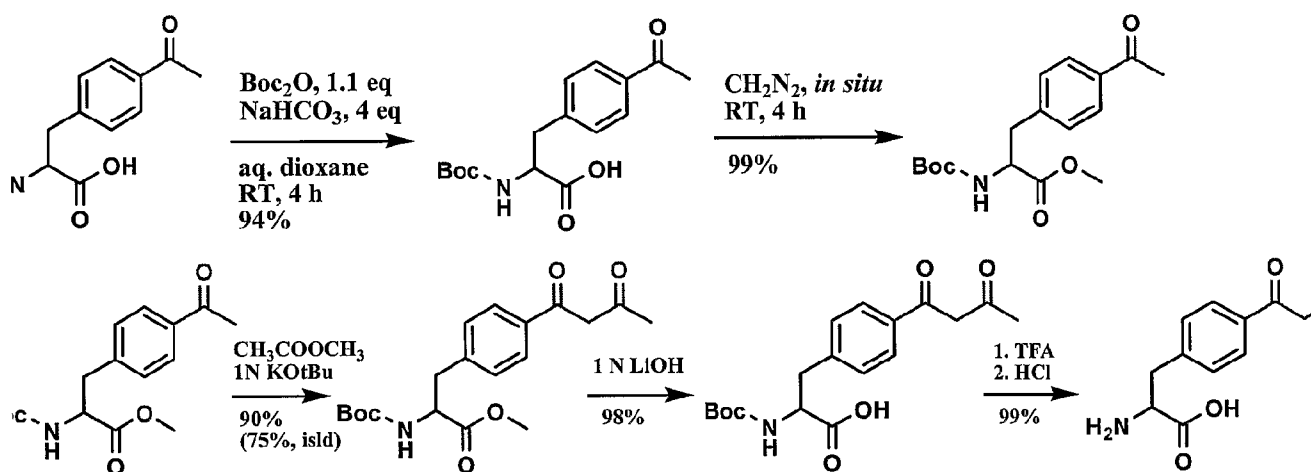


FIG. 28

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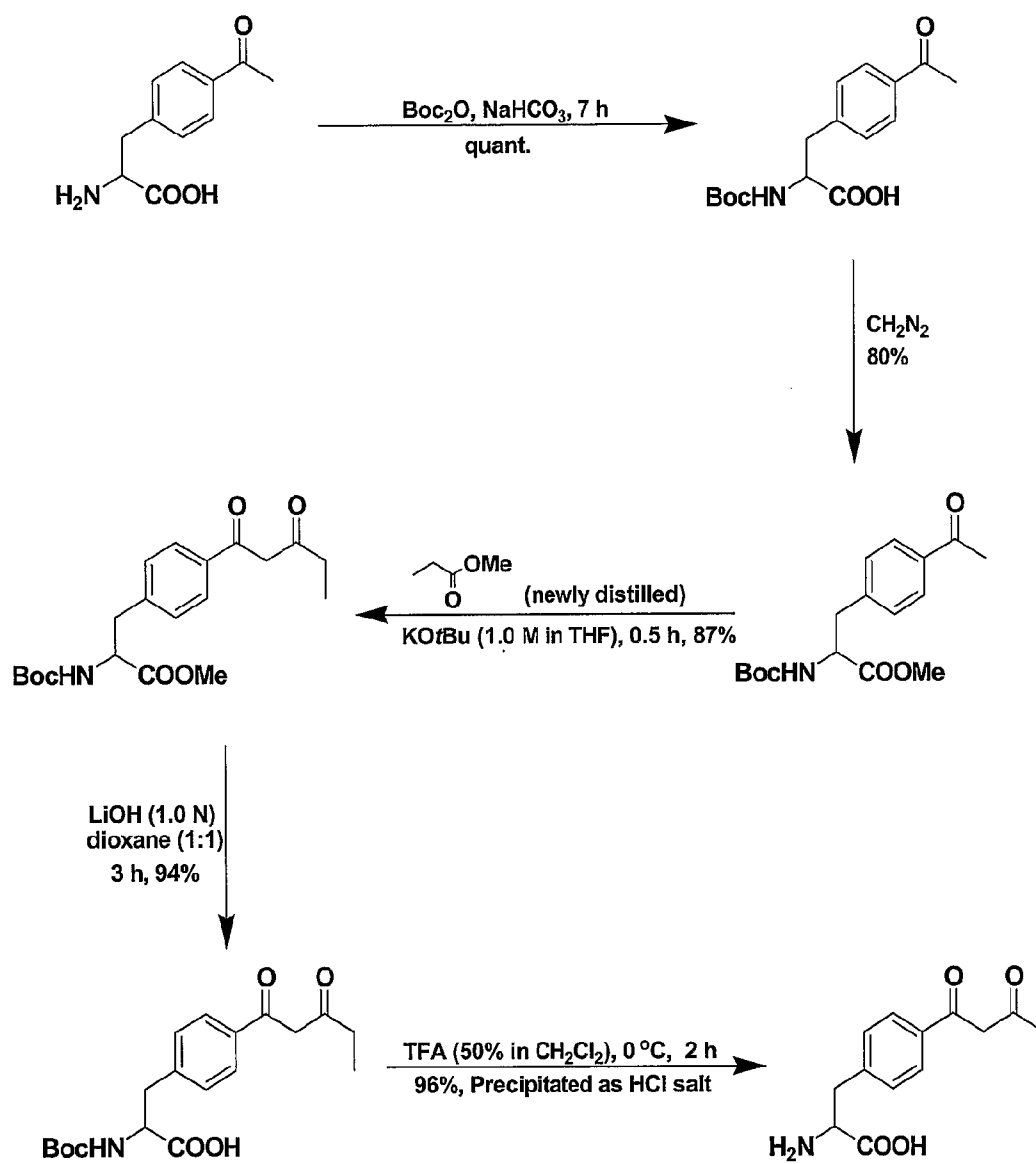


FIG. 29

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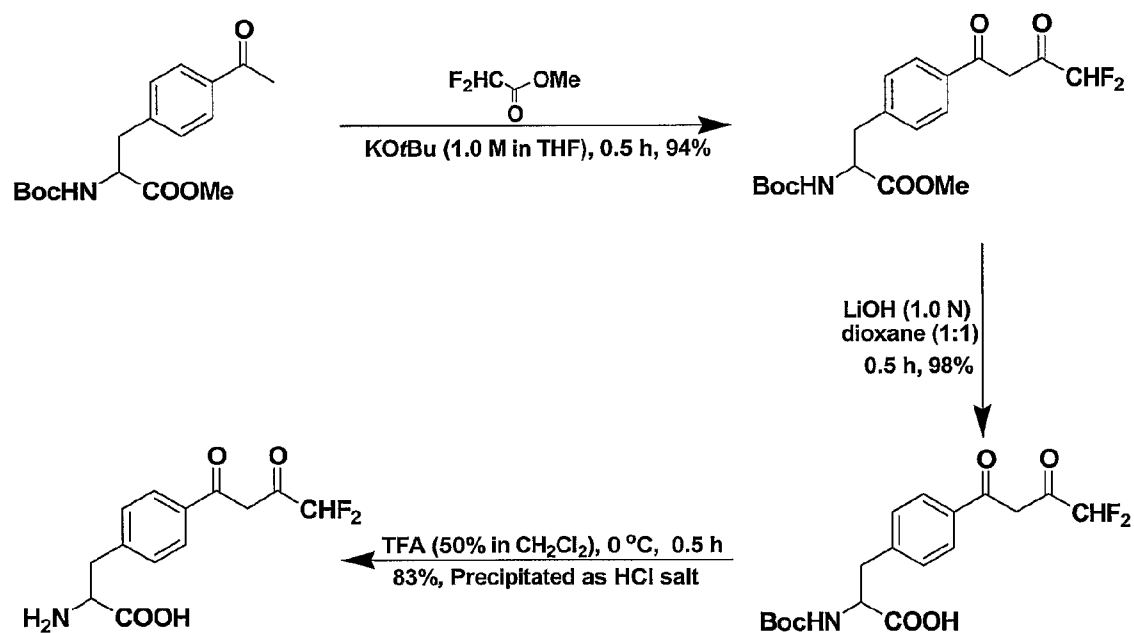


FIG. 30

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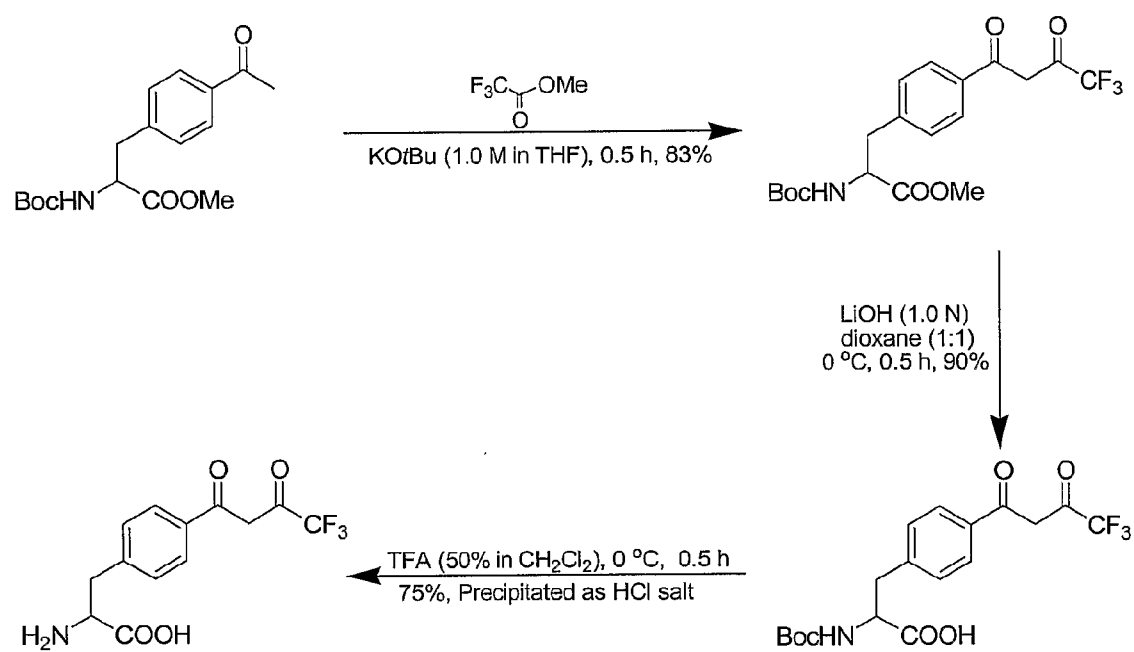


FIG. 31

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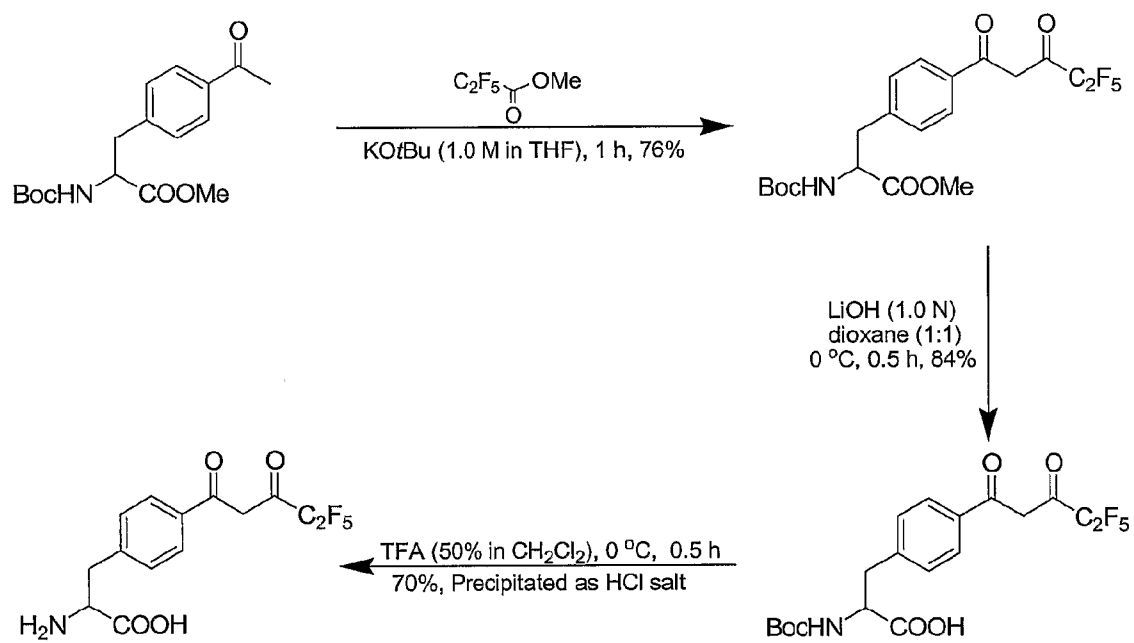


FIG. 32

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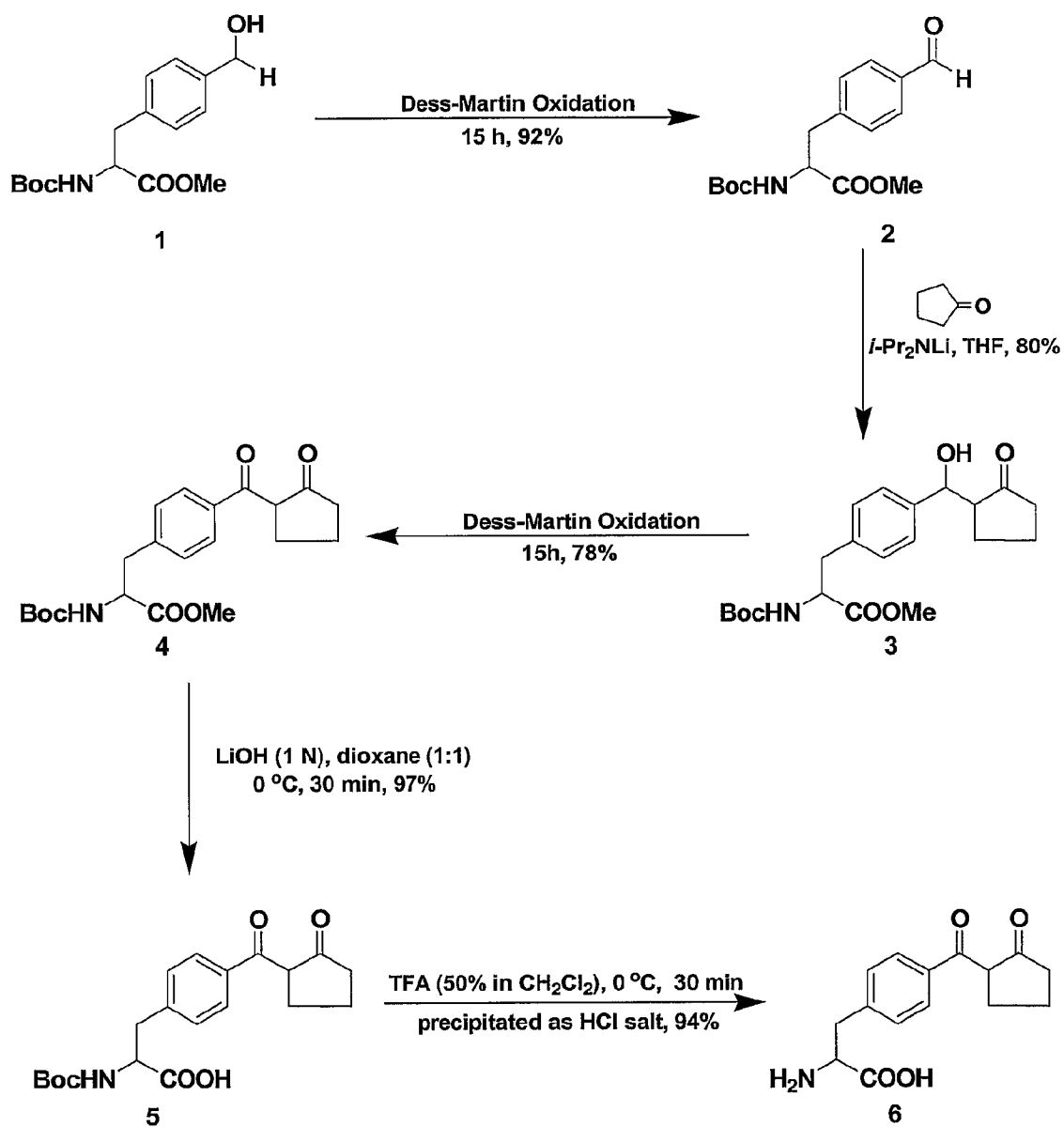


FIG. 33

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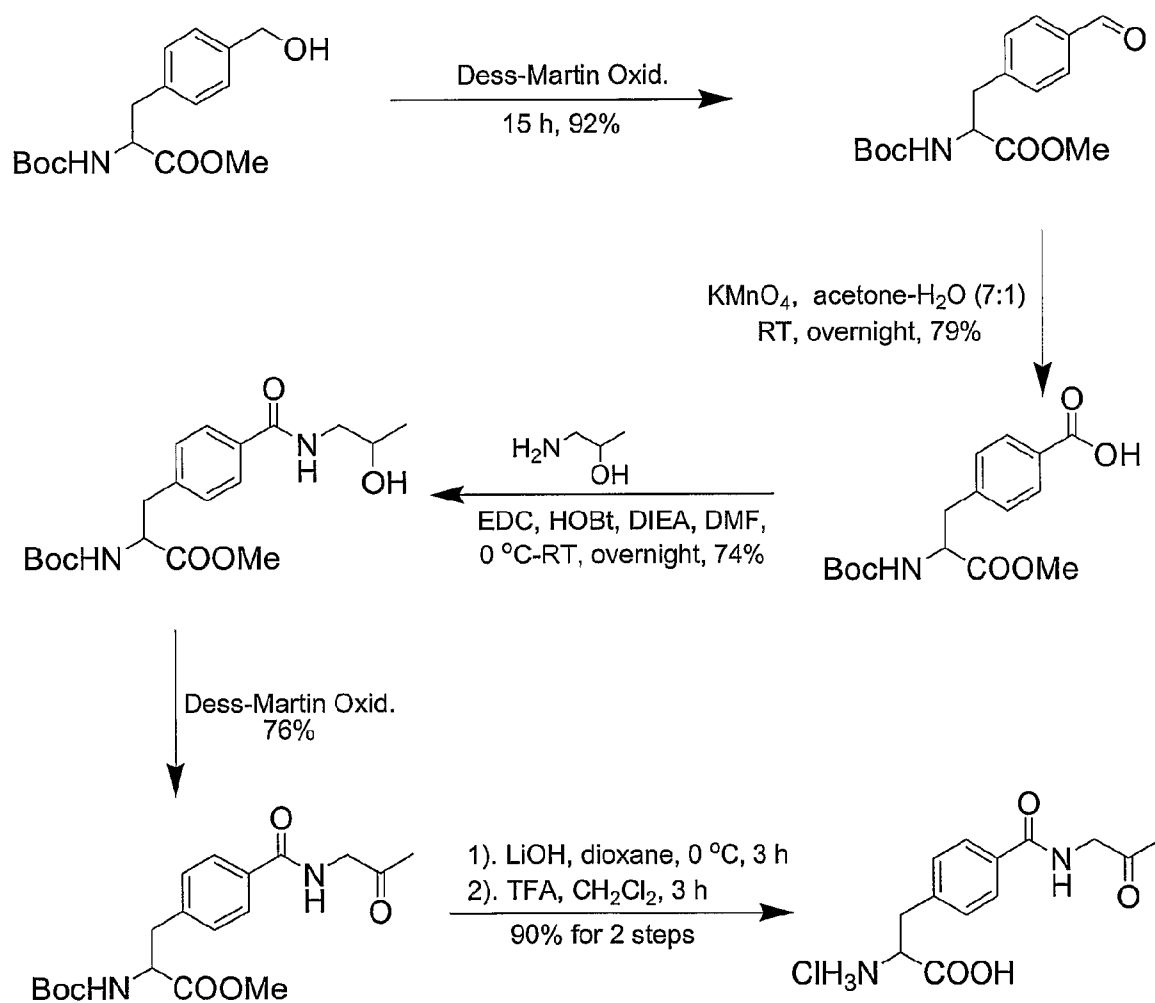


FIG. 34

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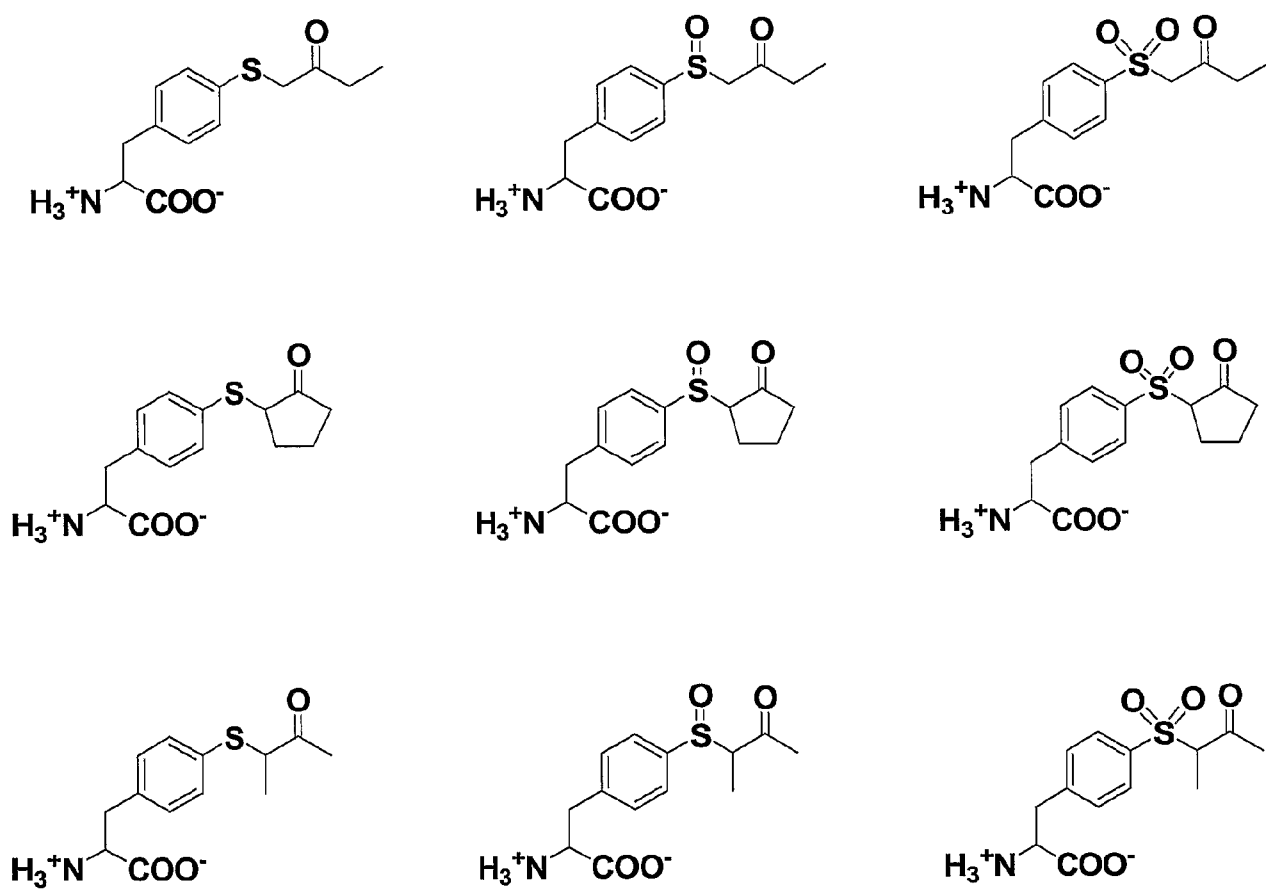


FIG. 35

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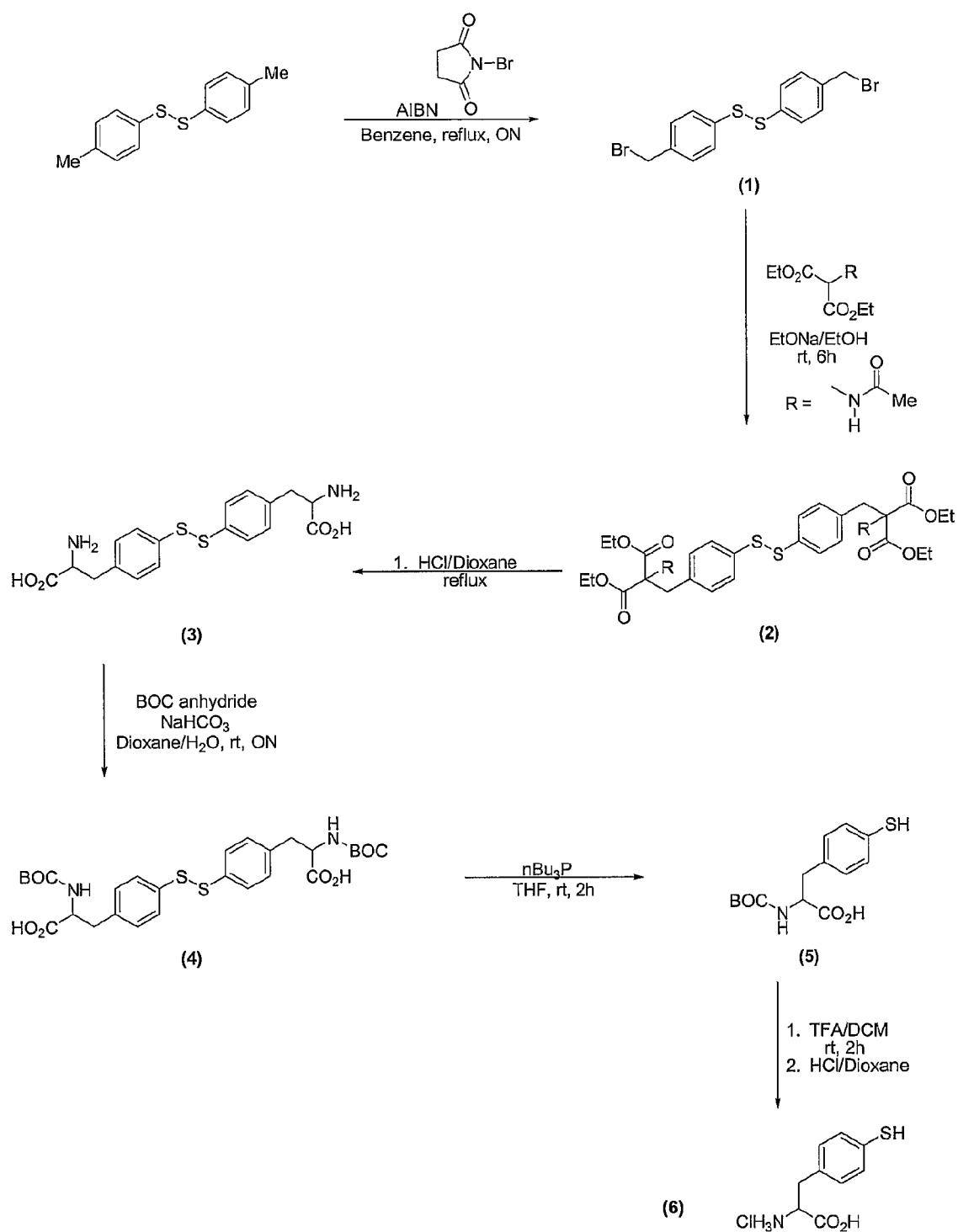


FIG. 36

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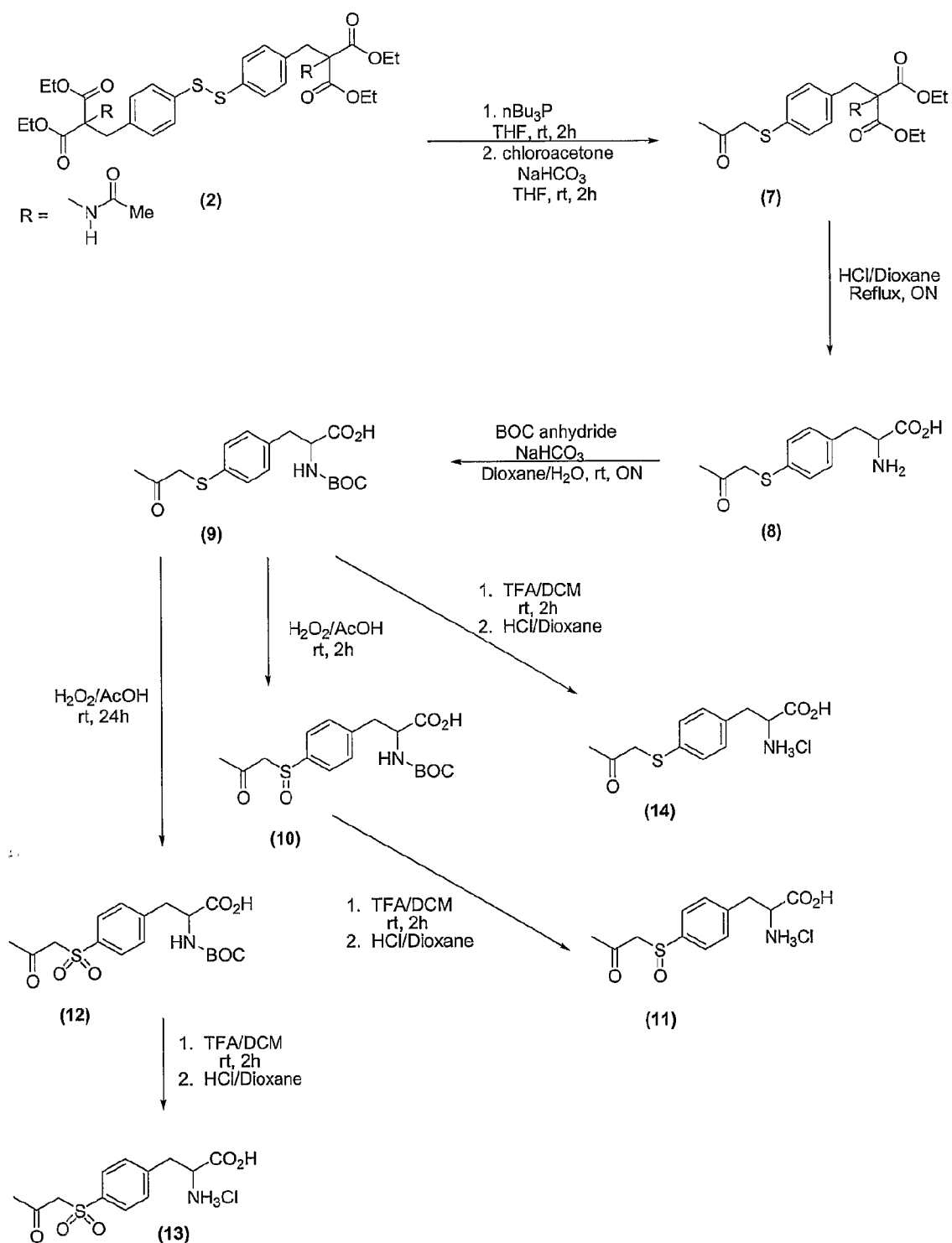


FIG. 37

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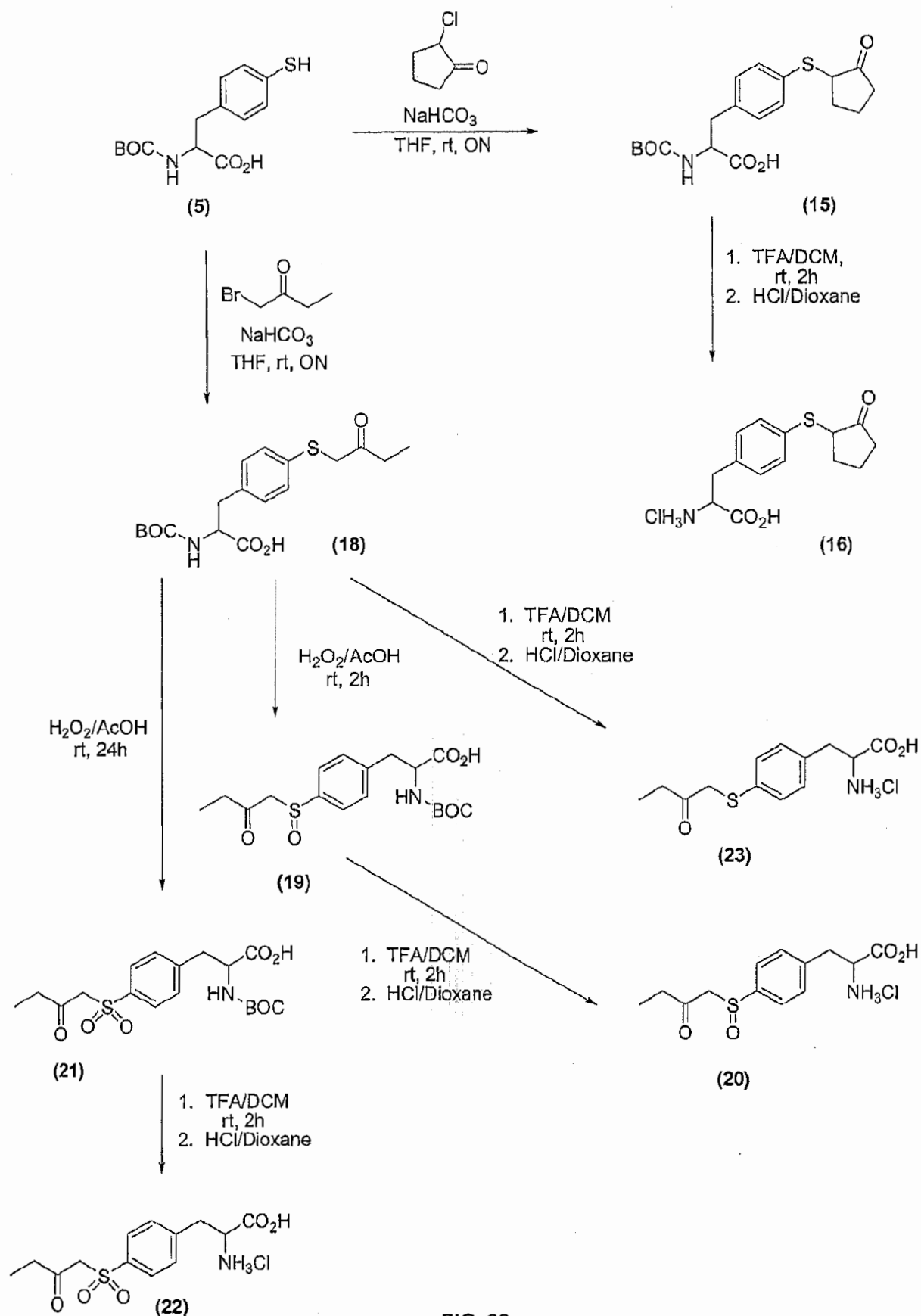


FIG. 38

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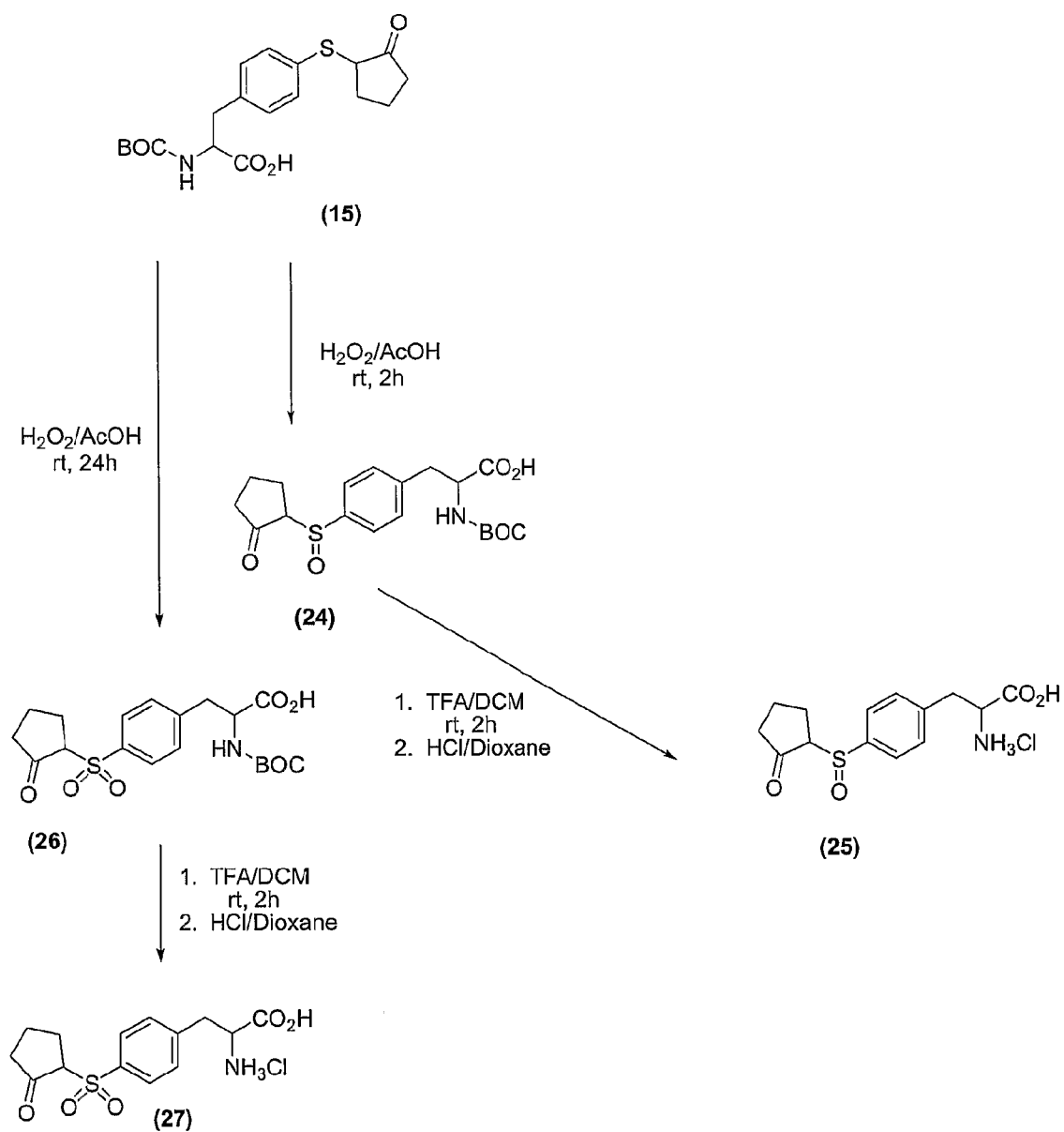


FIG. 39

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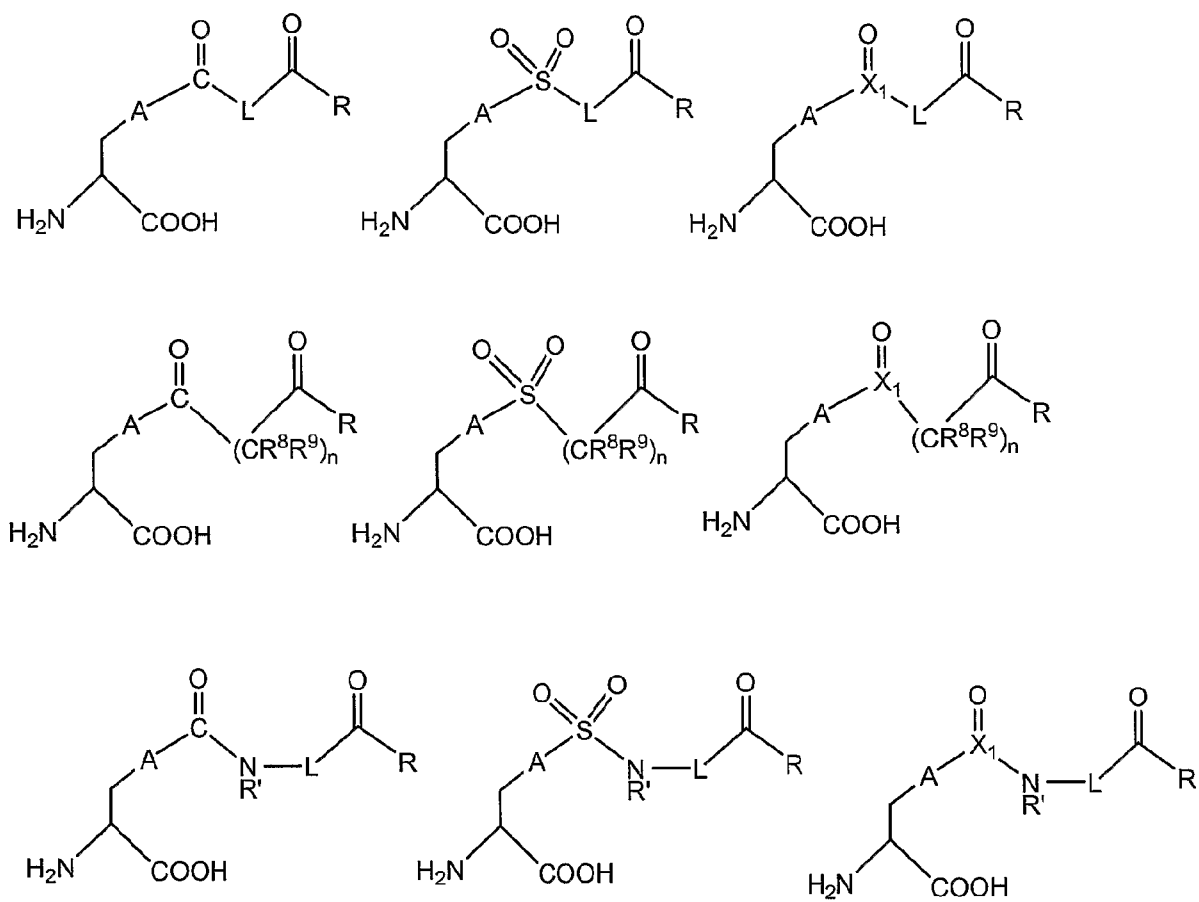


FIG. 40

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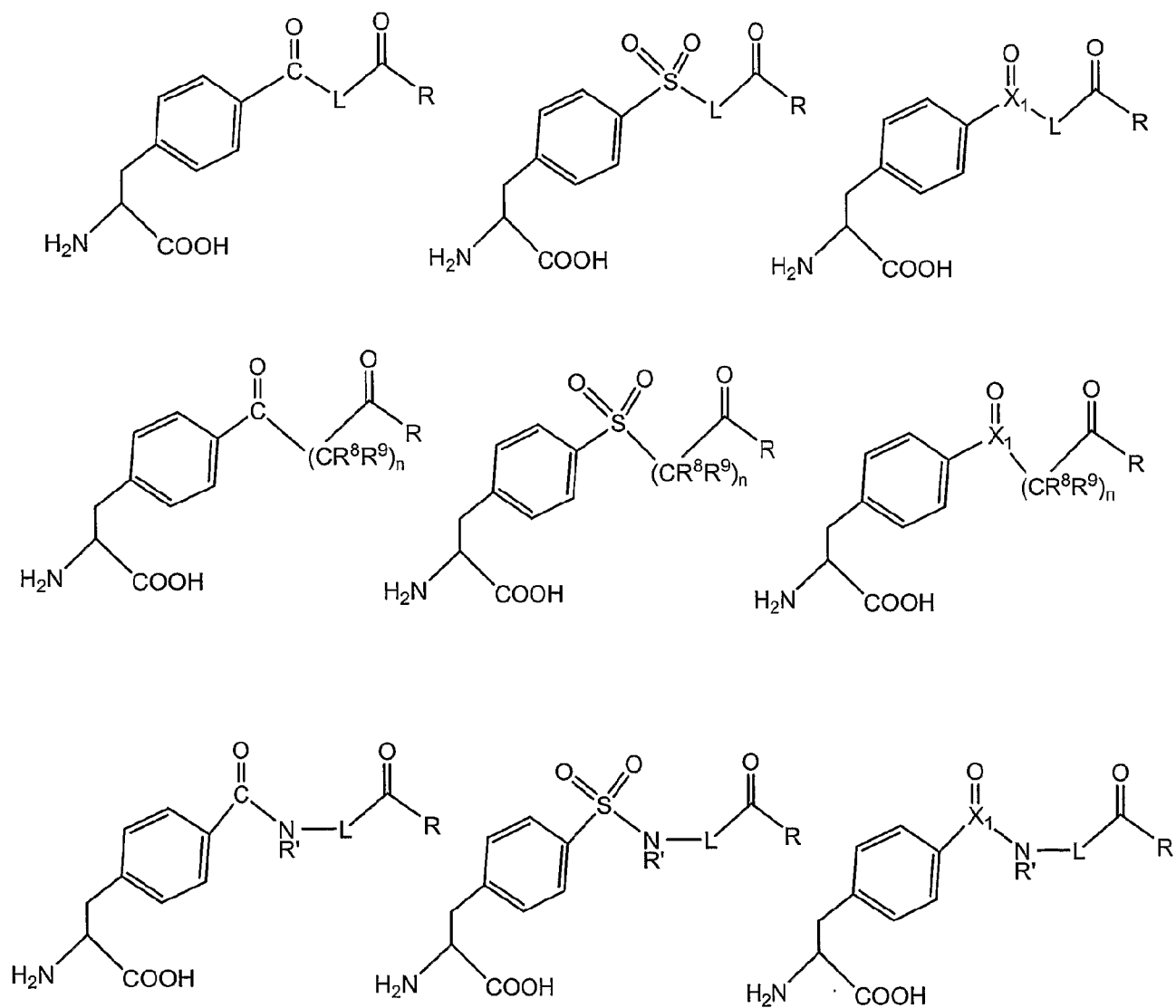
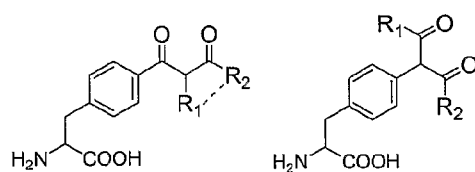


FIG. 41

General structure:



Examples:

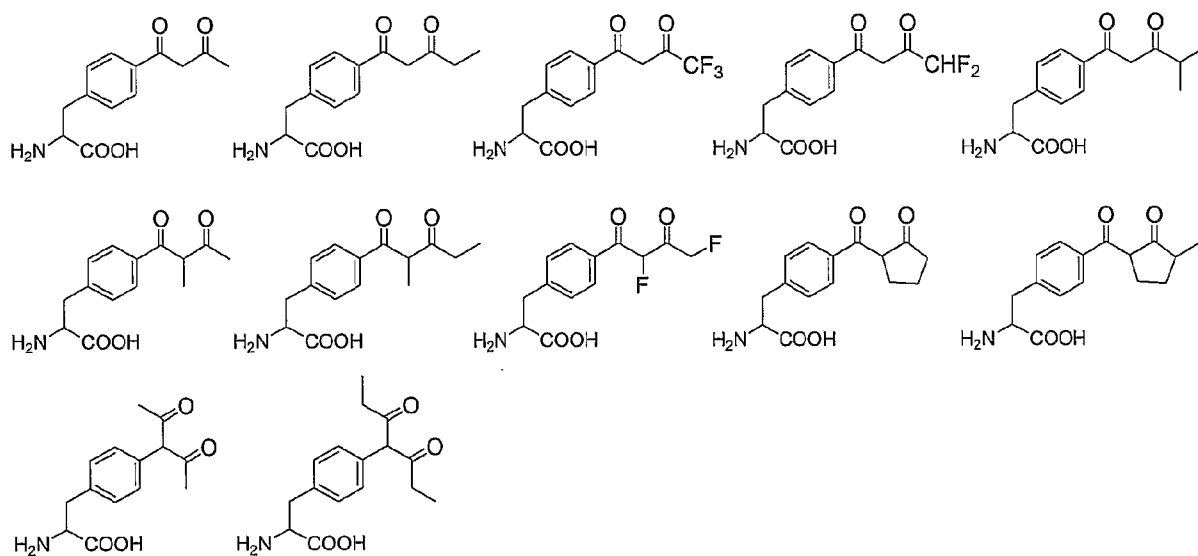
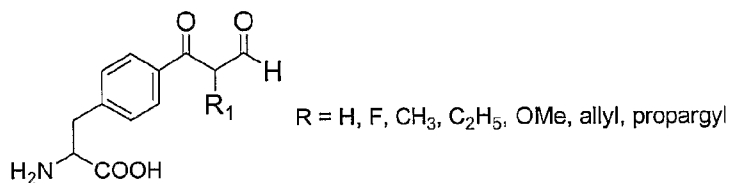
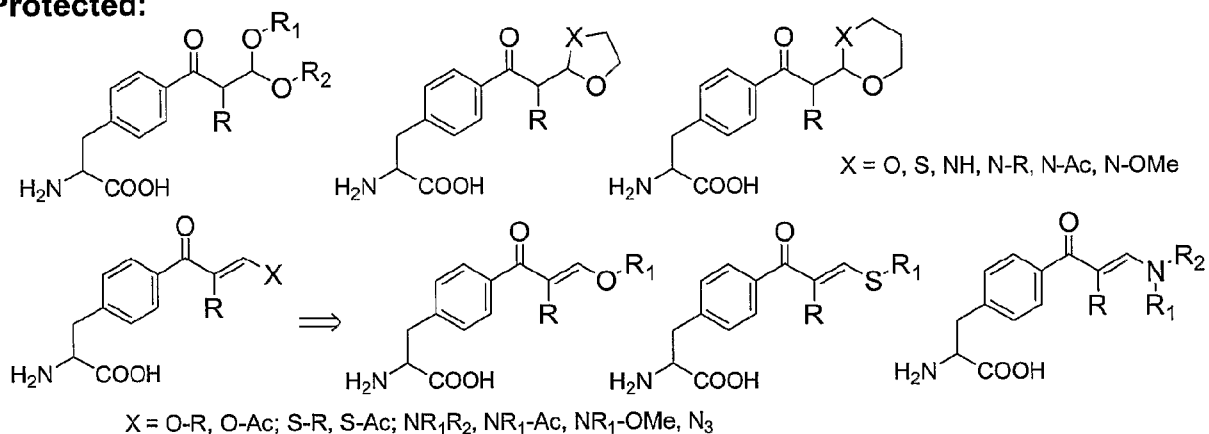


FIG. 42

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(a)

Unprotected**Protected:**

(b)

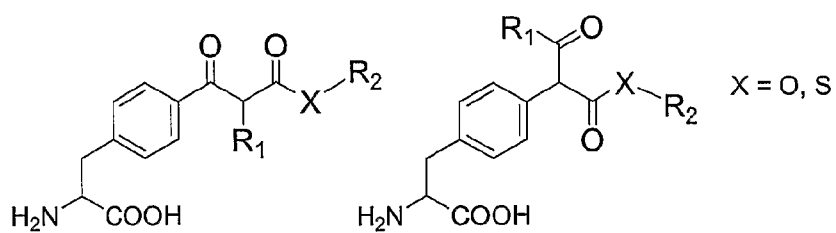
Structure:

FIG. 43

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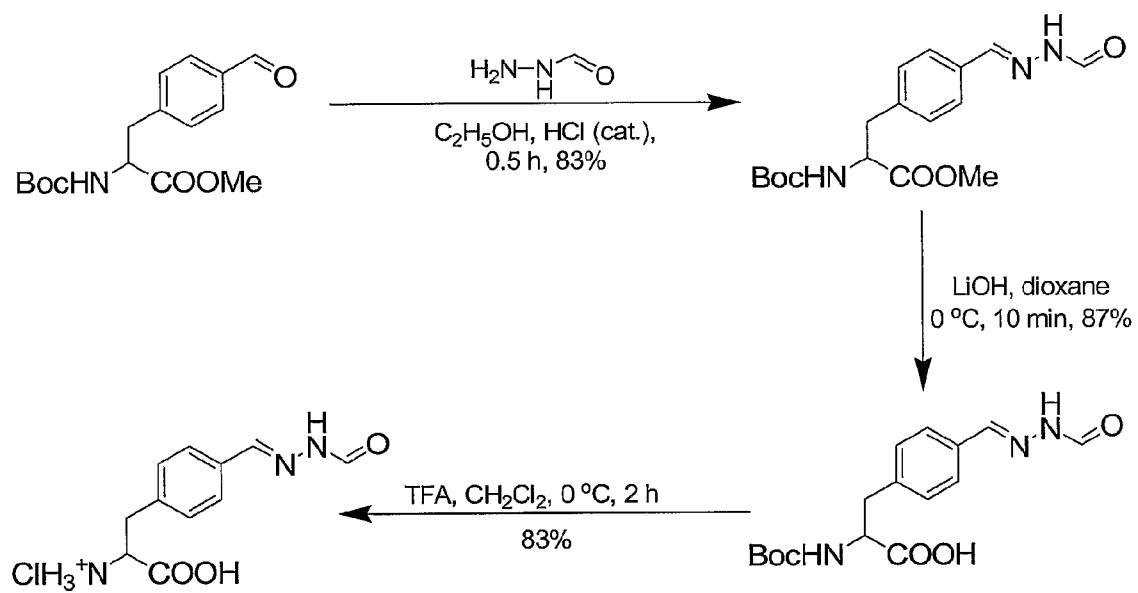


FIG. 44

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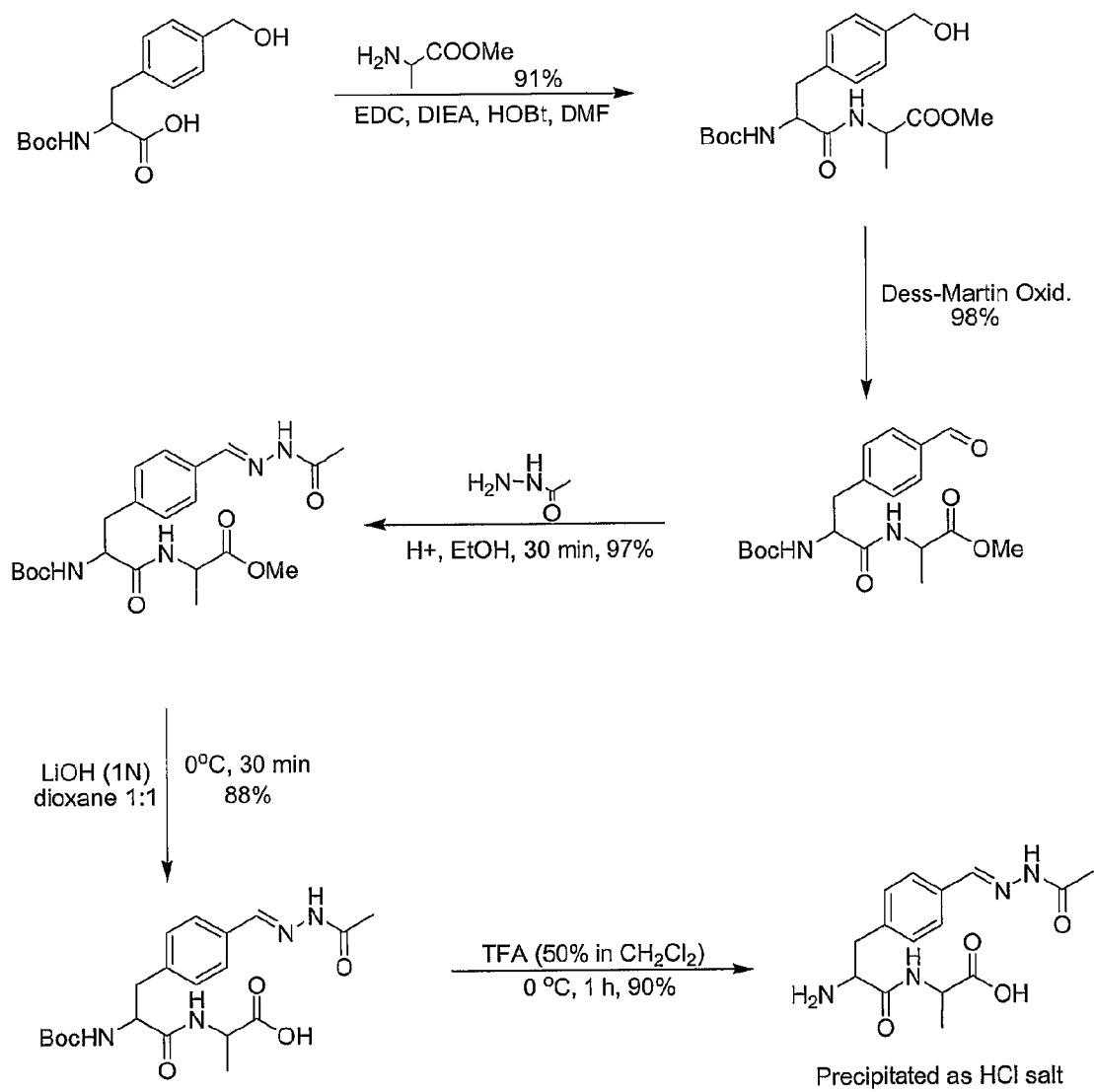


FIG. 45

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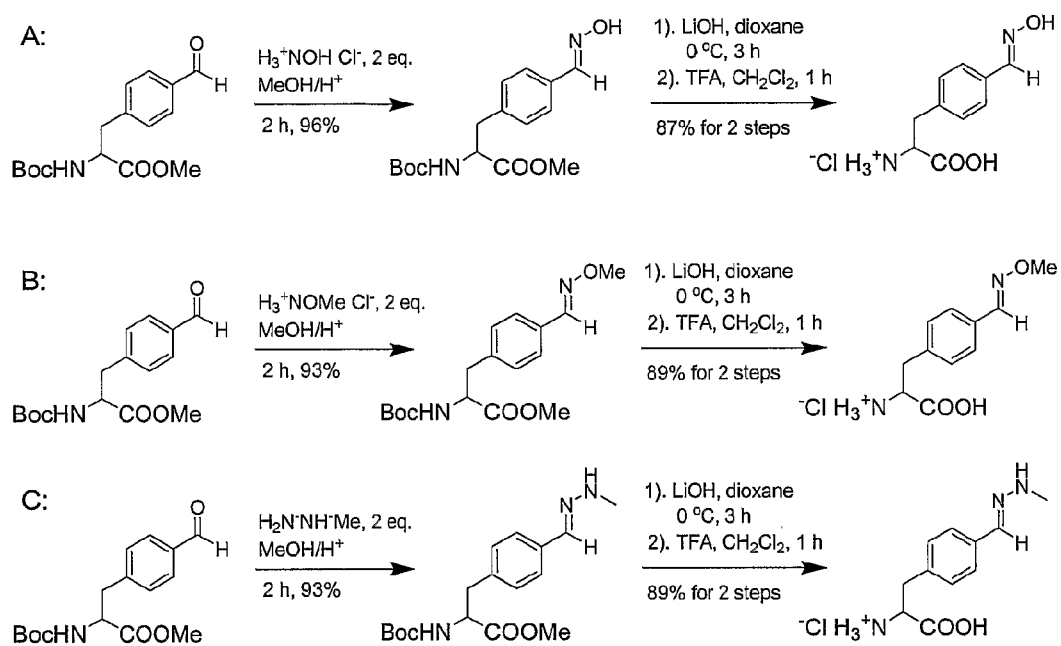
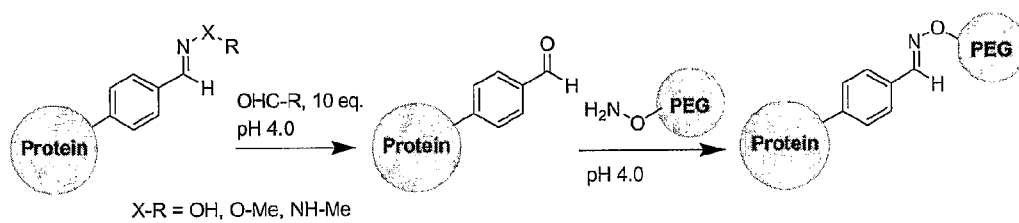
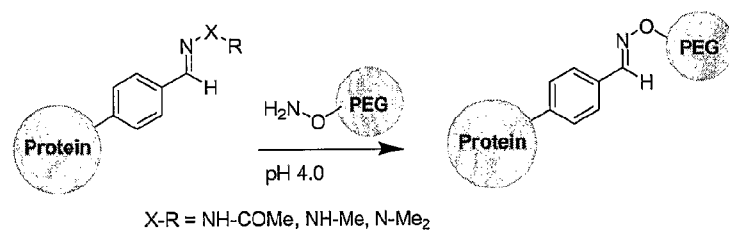


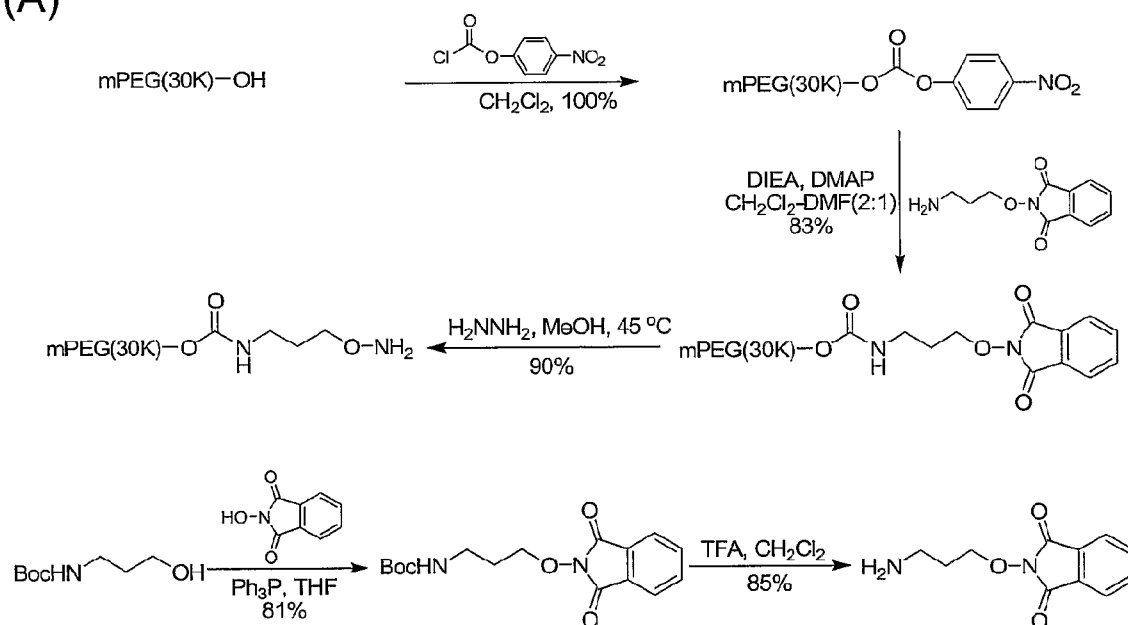
FIG. 46

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

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(A)



(B)

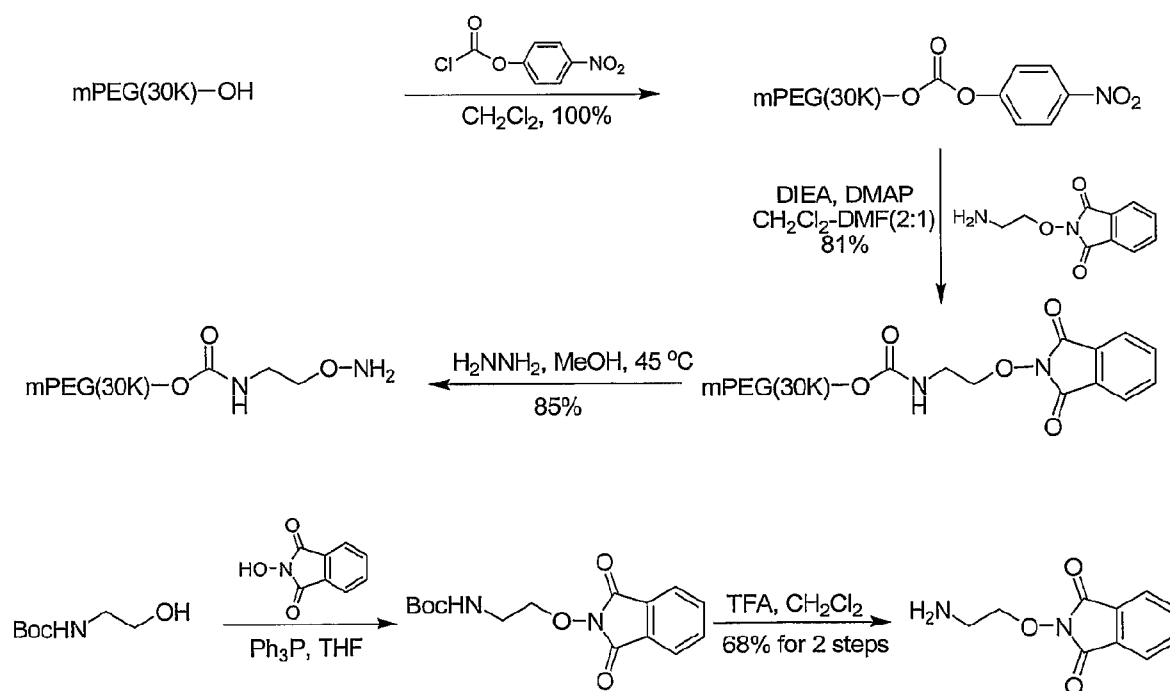
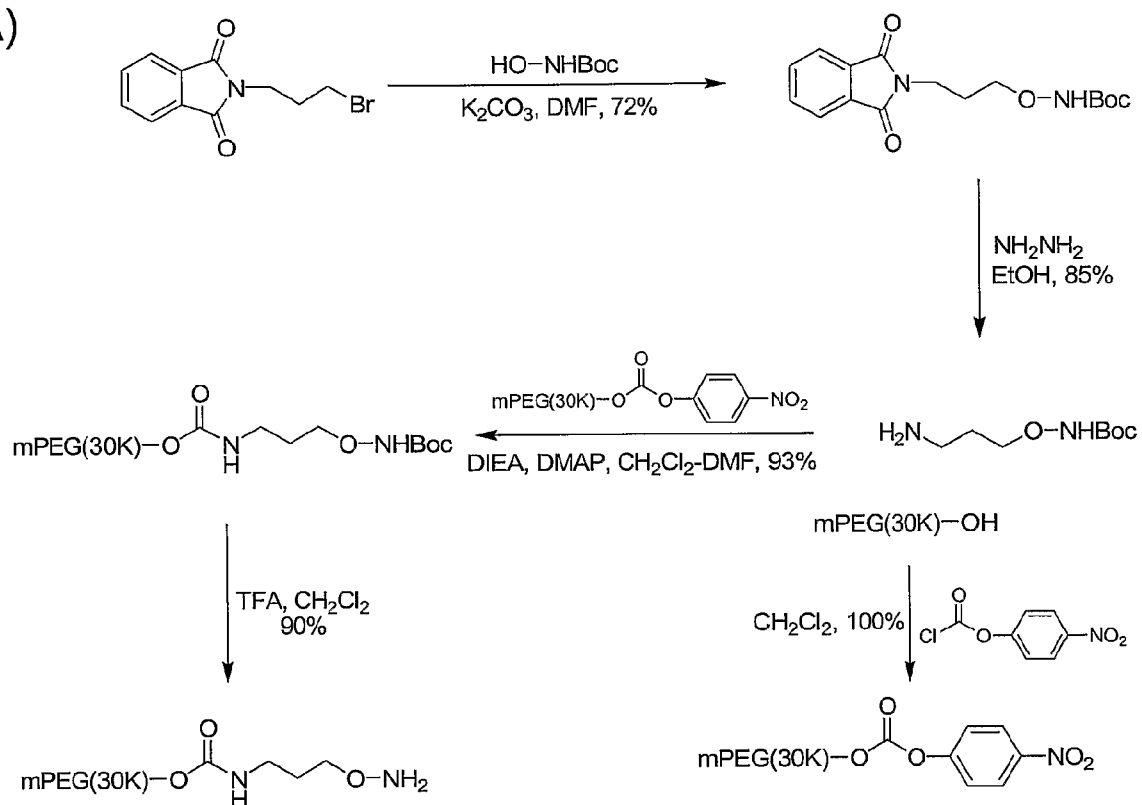


FIG. 48

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(A)



(B)

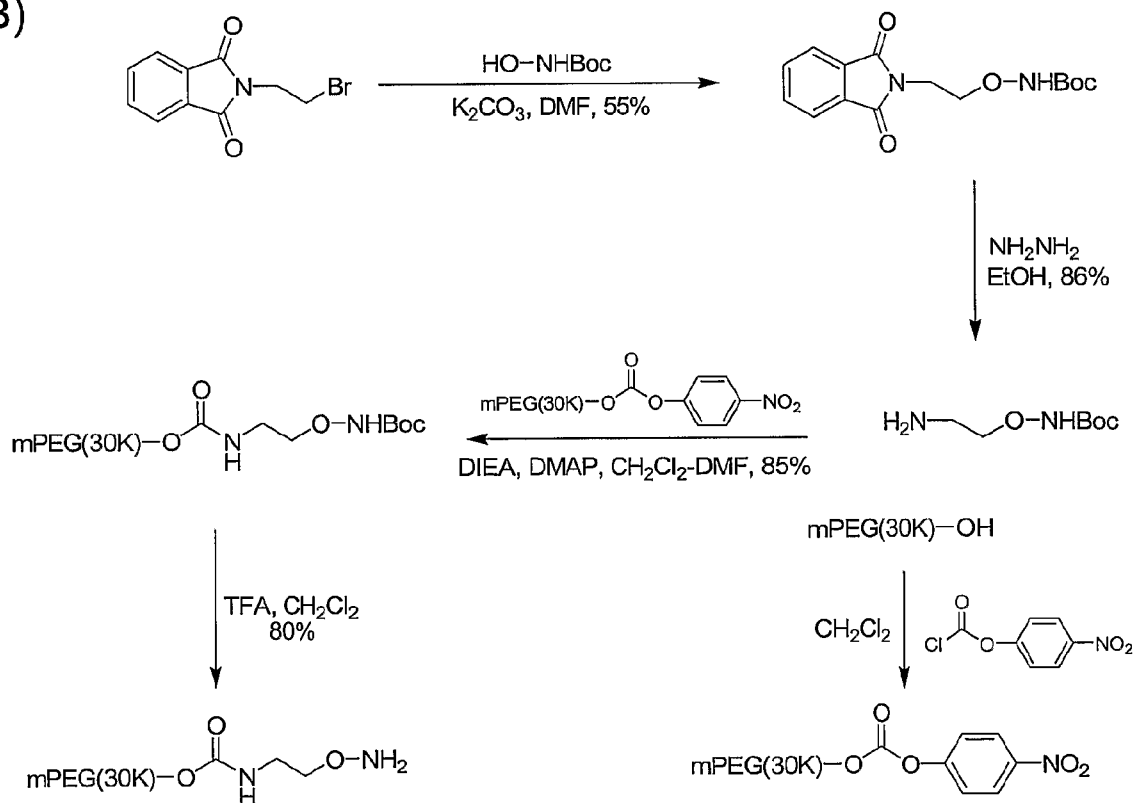


FIG. 49

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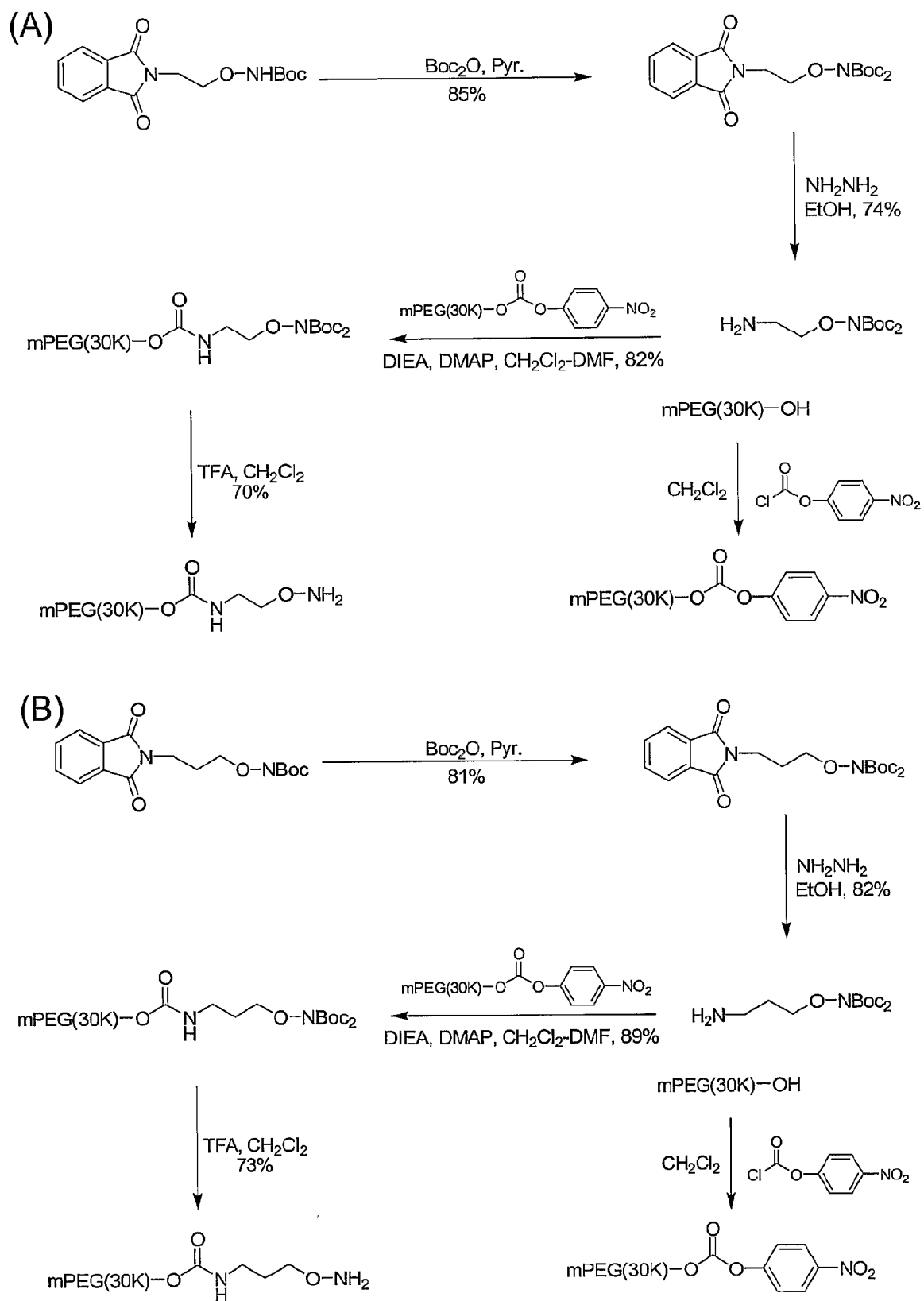
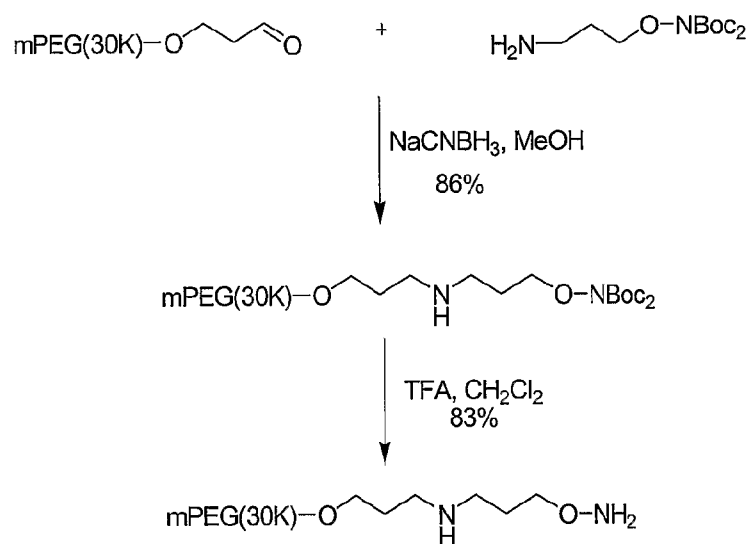


FIG. 50

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(A)



(B)

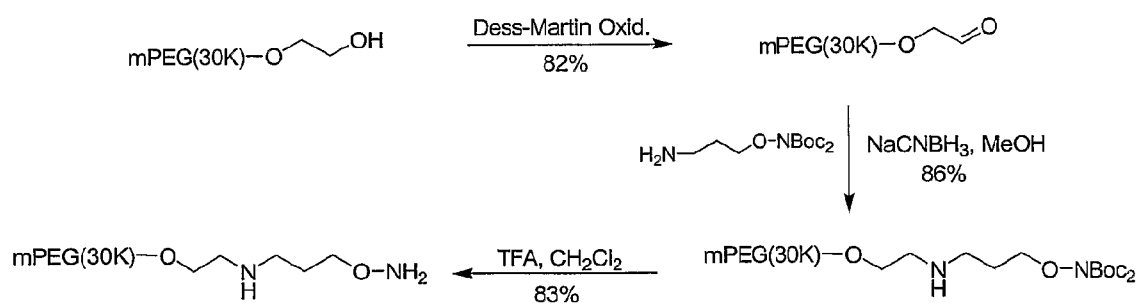
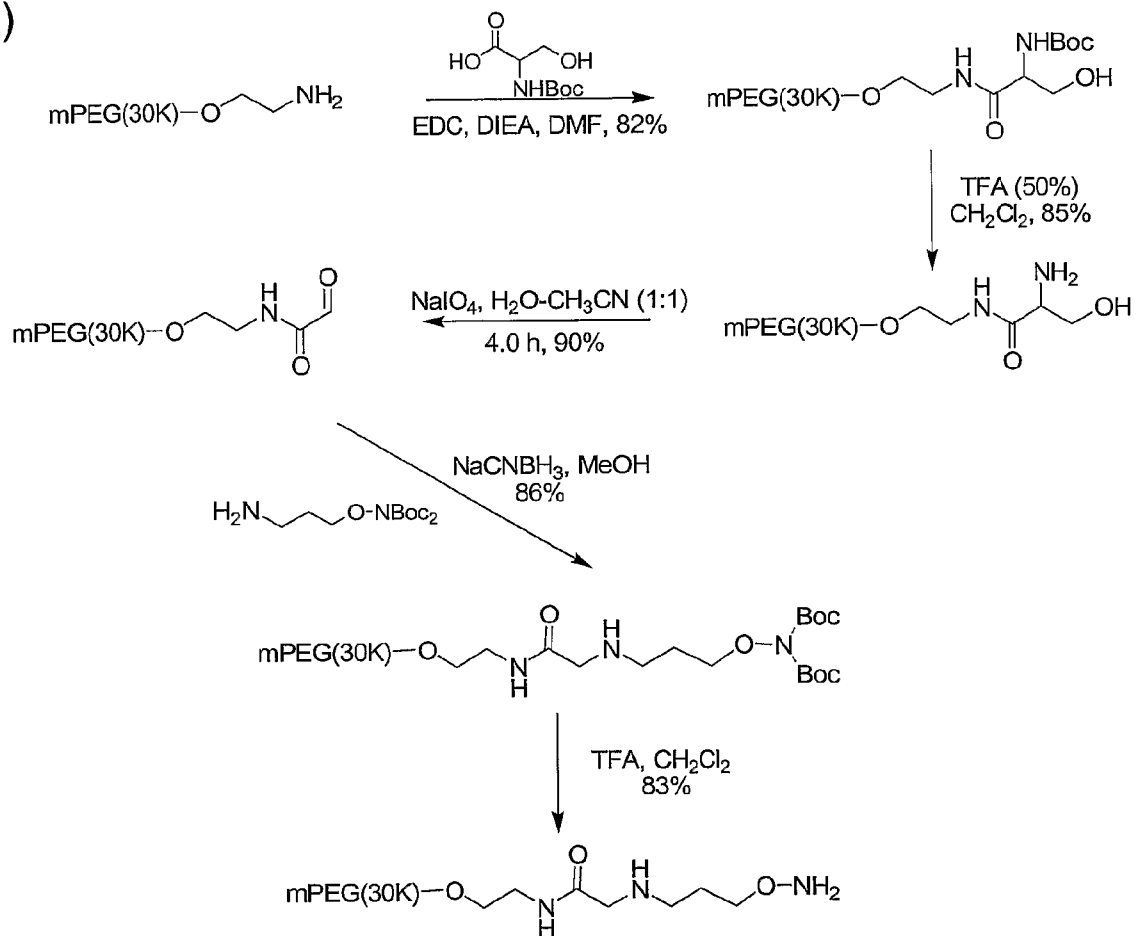


FIG. 51

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(A)



(B)

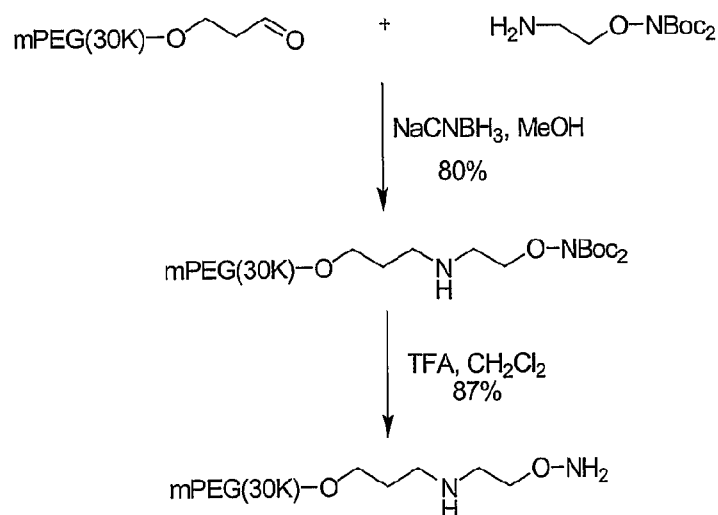
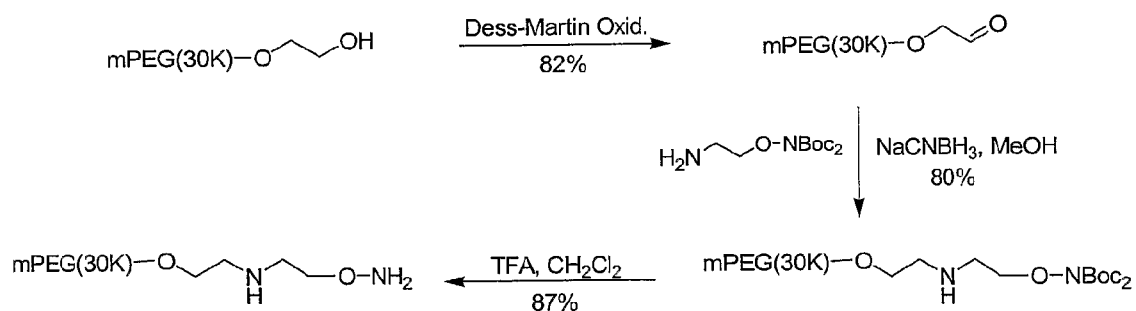


FIG. 52

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(A)



(B)

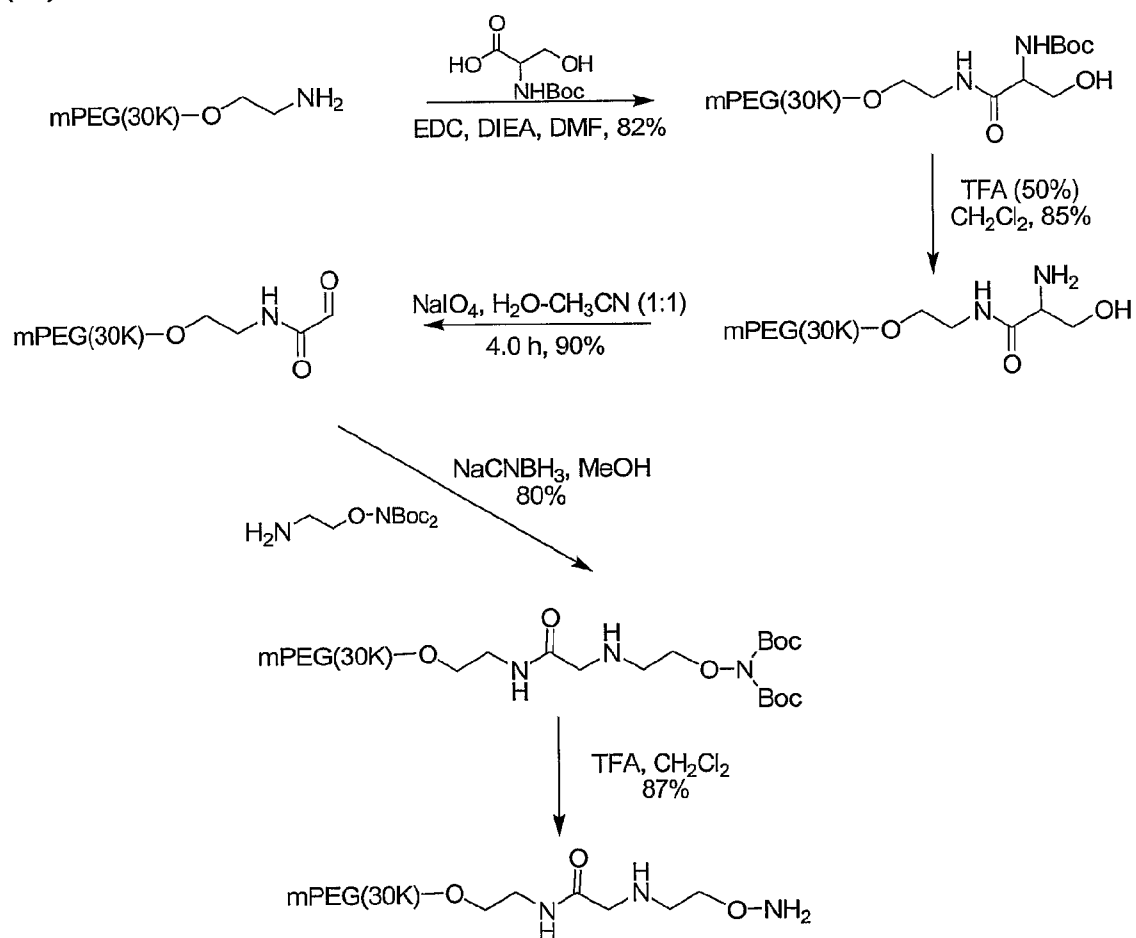
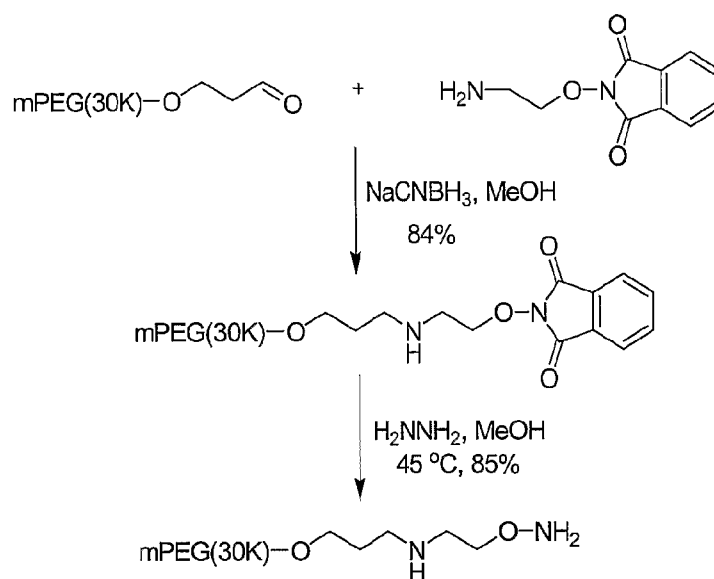


FIG. 53

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(A)



(B)

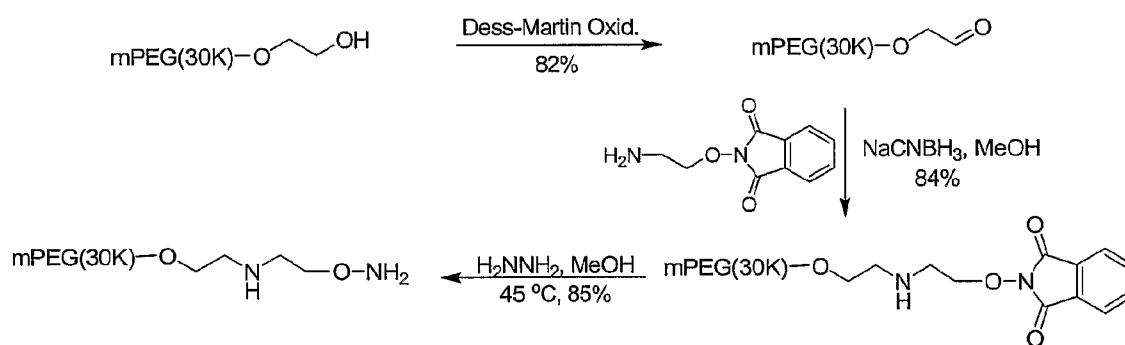


FIG. 54

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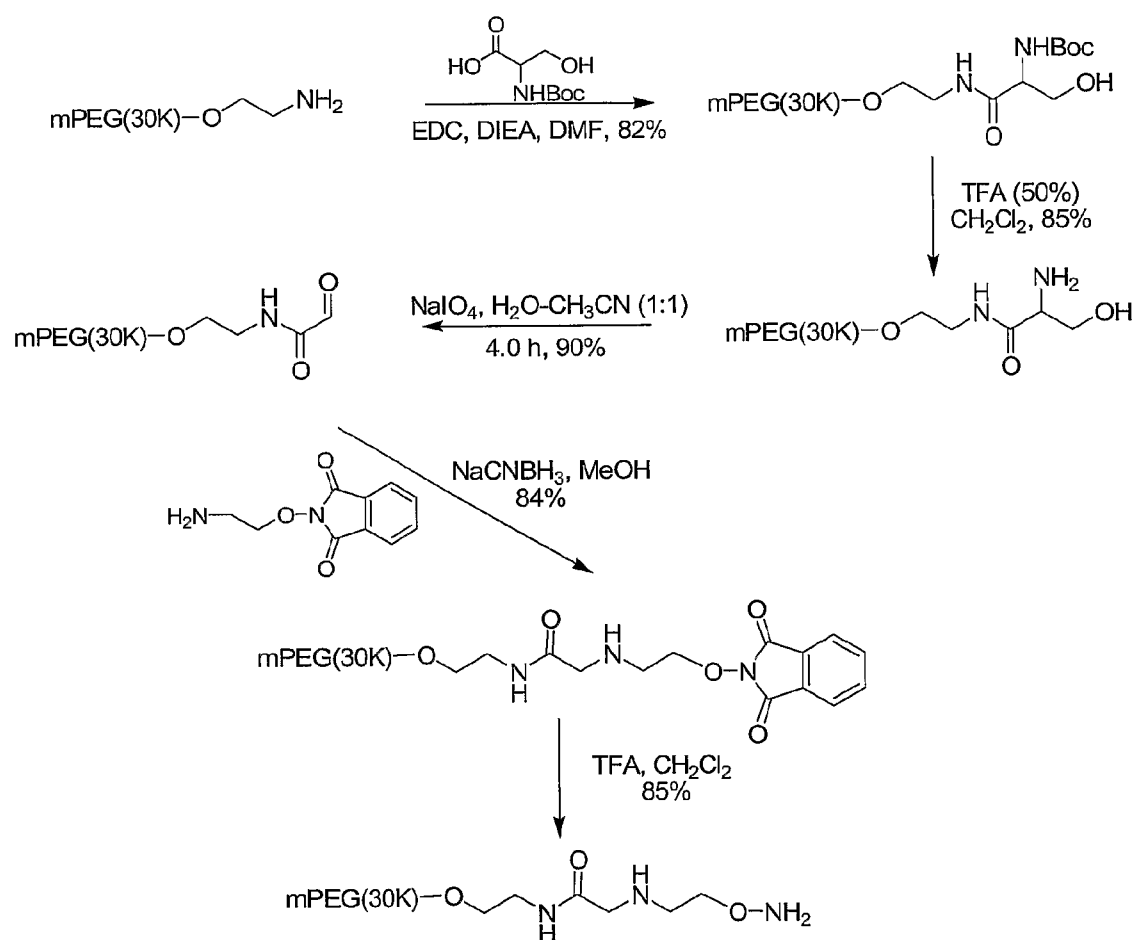
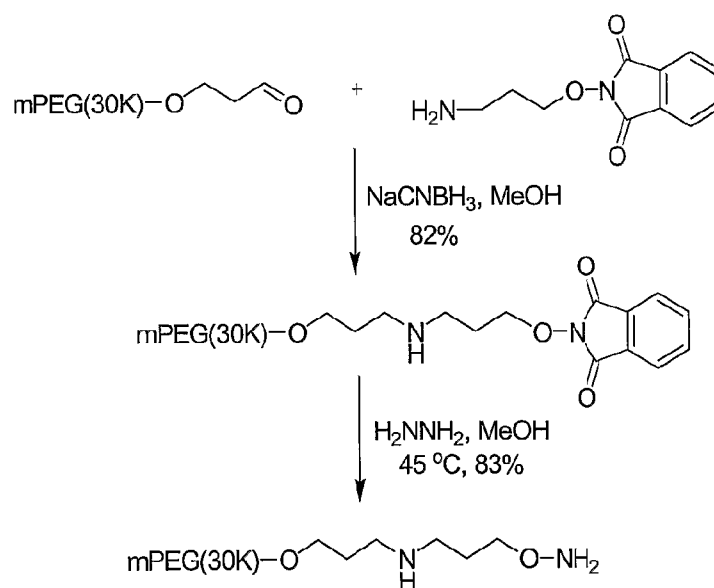


FIG. 55

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(A)



(B)

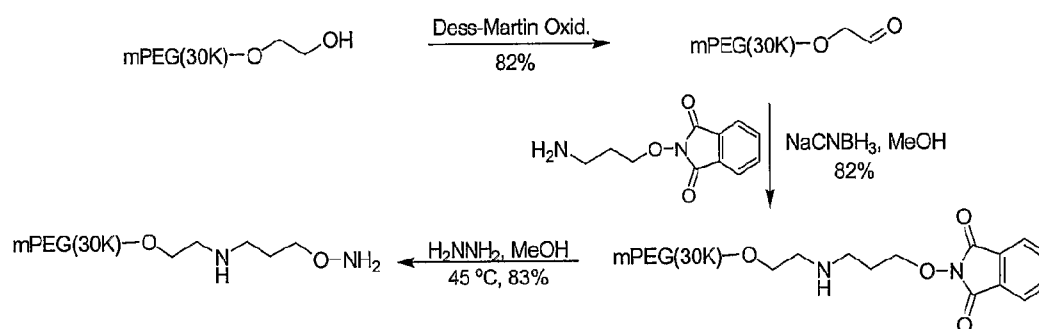


FIG. 56

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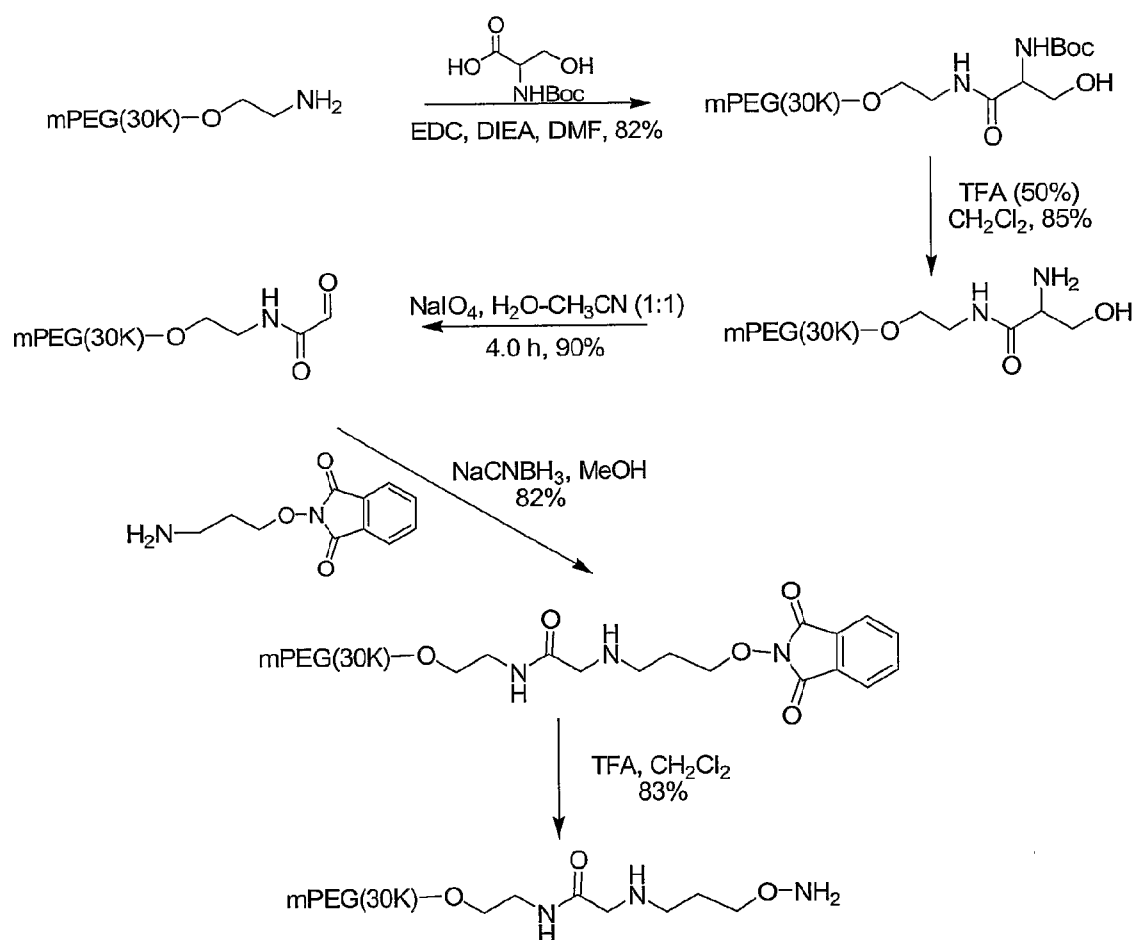
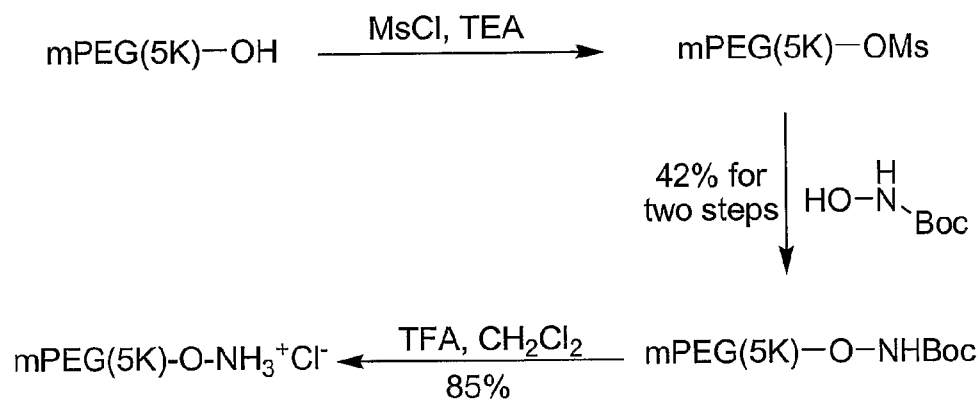


FIG. 57

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(A)



(B)

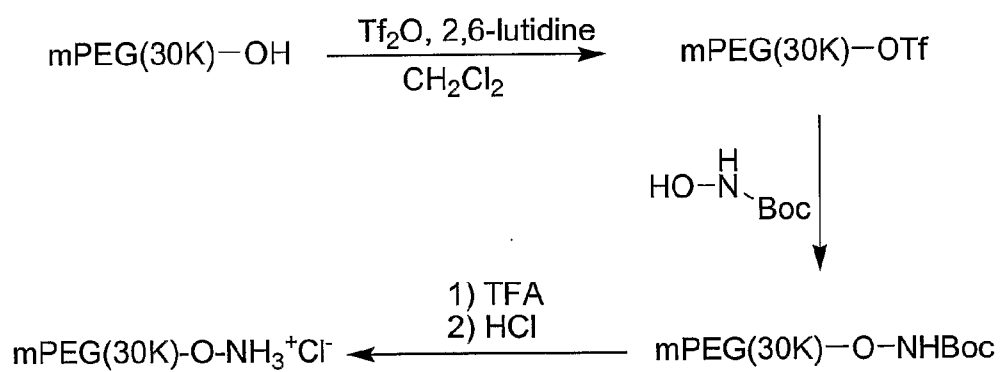
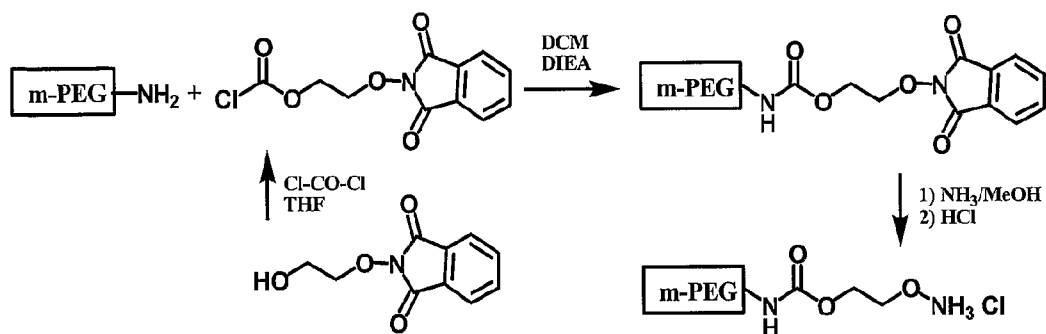


FIG. 58

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(A)



(B)

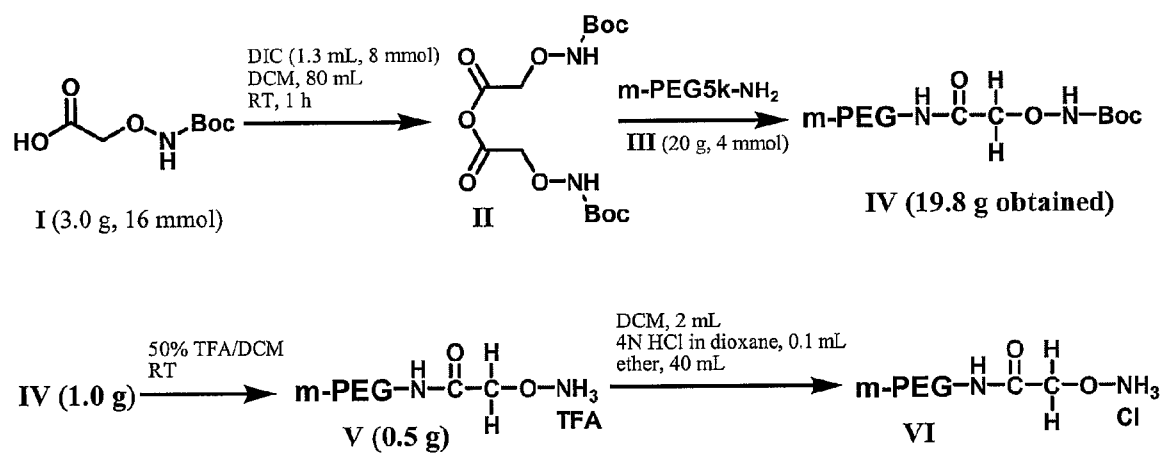
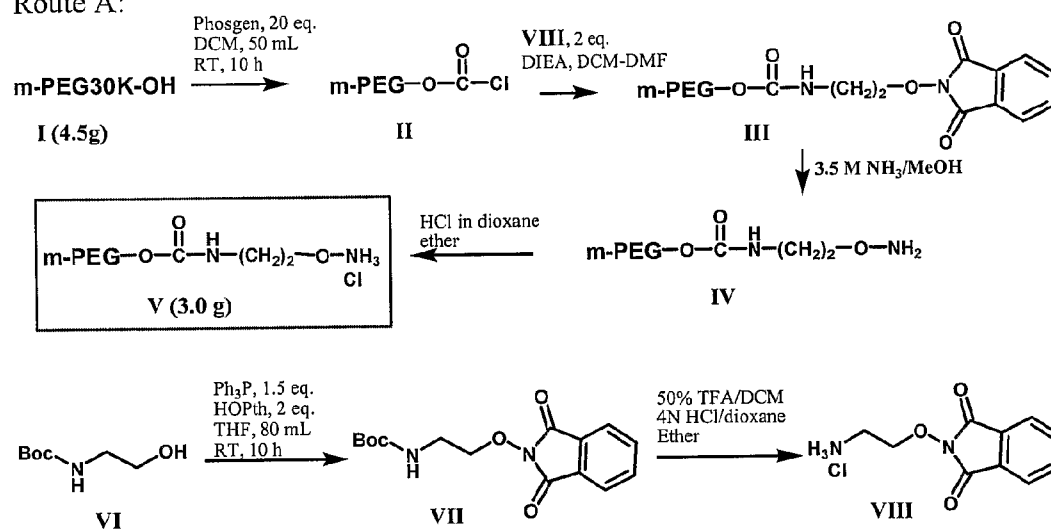


FIG. 59

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(A) Route A:



(B)

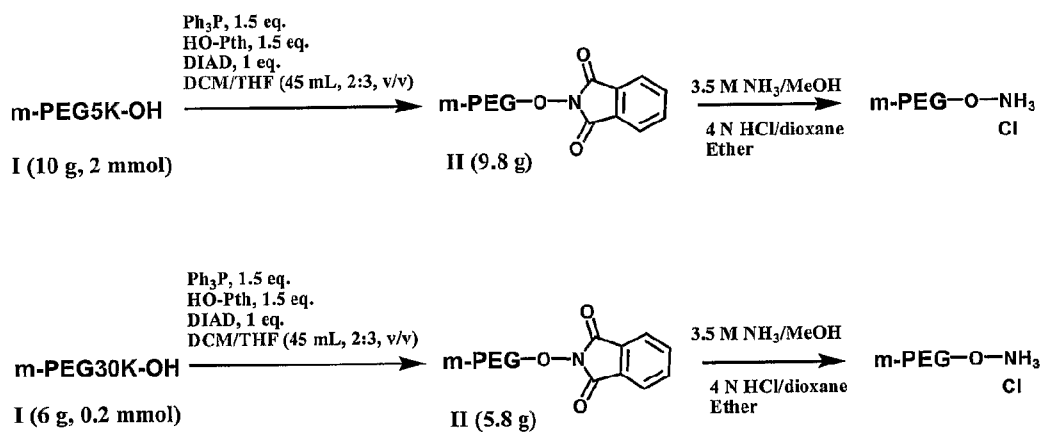
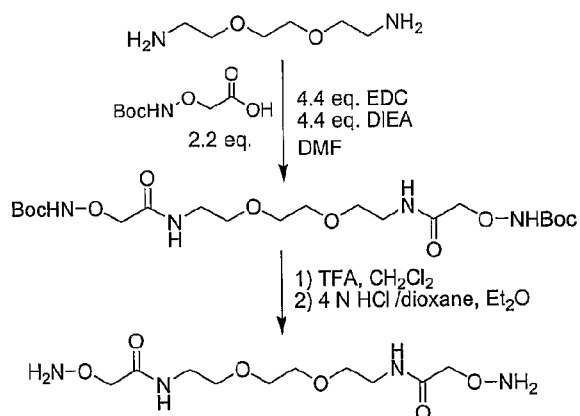


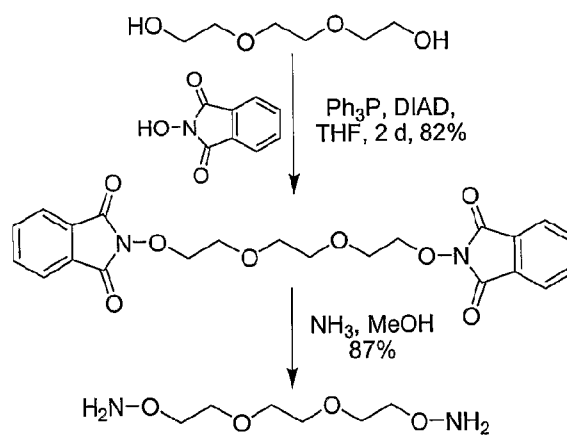
FIG. 60

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(A)



(B)



(C)

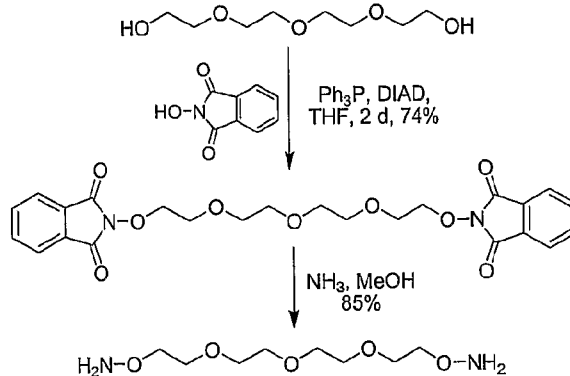
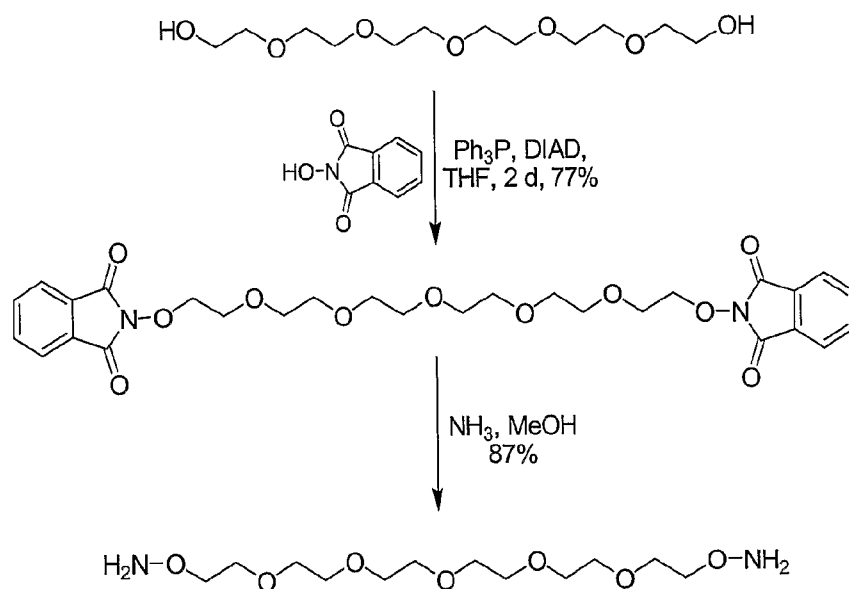


FIG. 61

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(A)



(B)

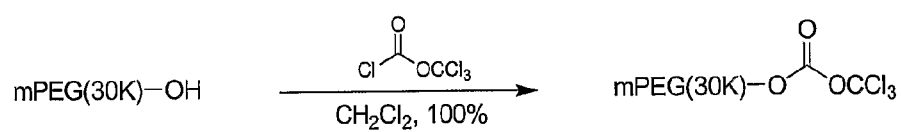


FIG. 62

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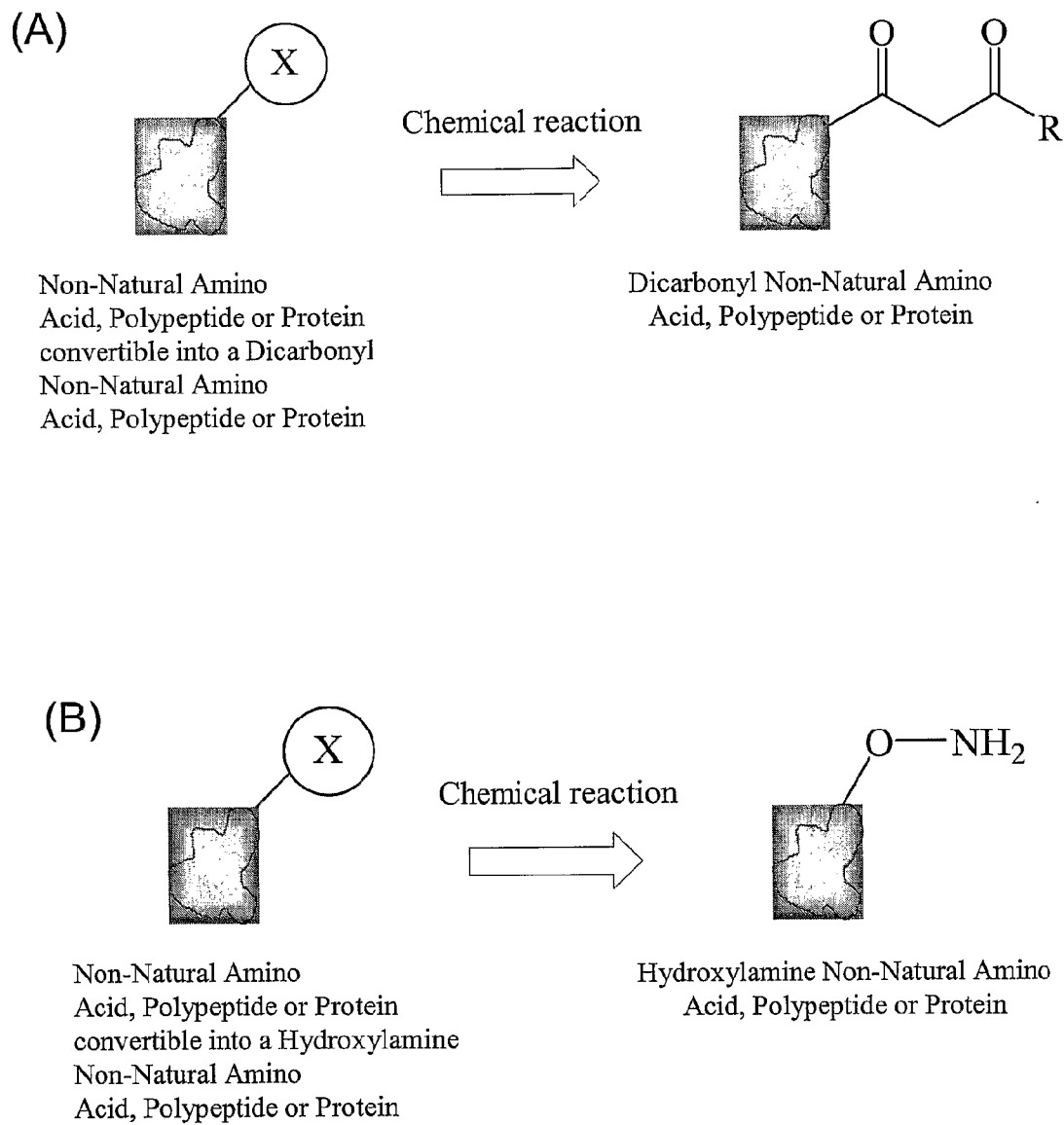


FIG. 63

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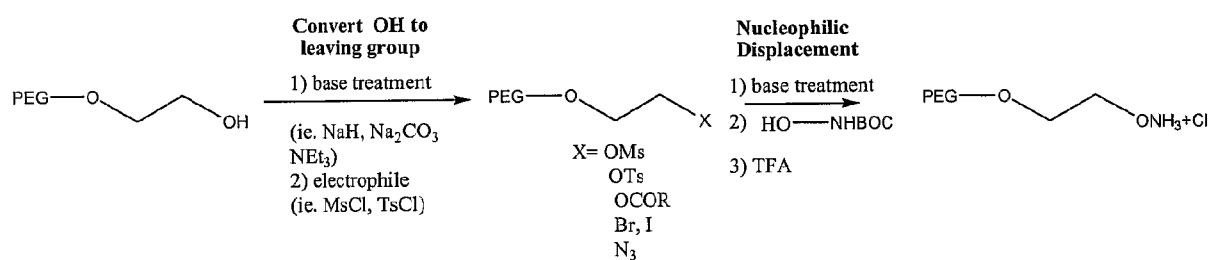
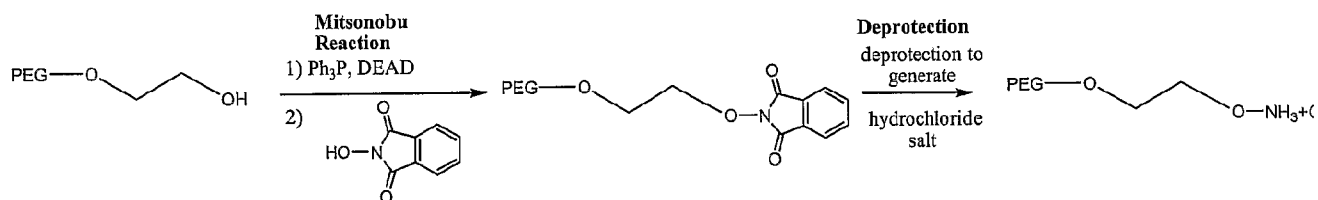
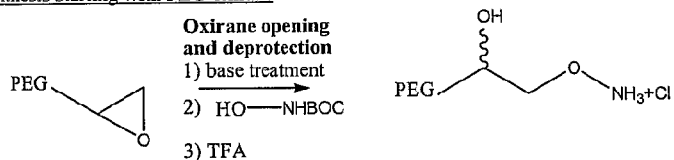
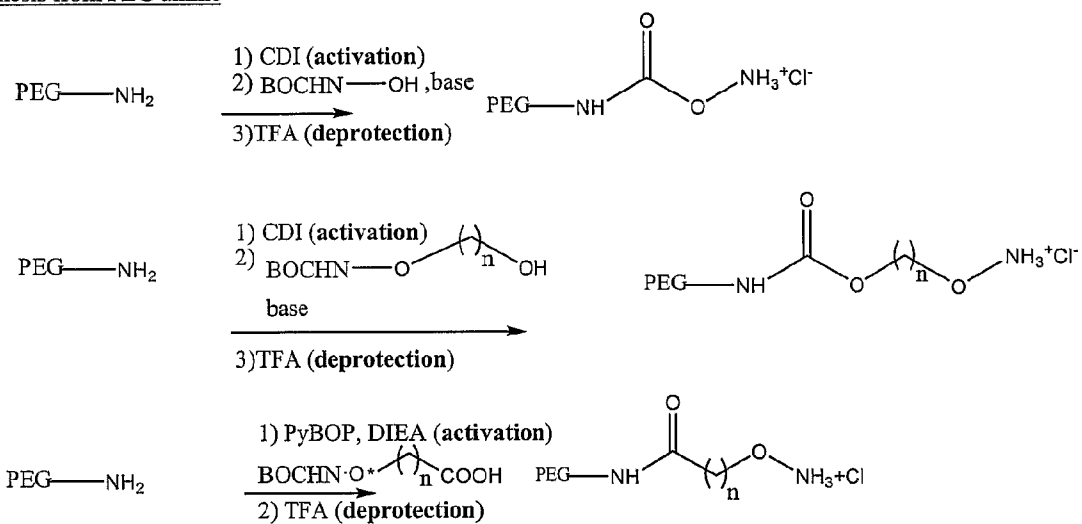
1) Synthesis based upon nucleophilic displacement2) Synthesis based upon Mitsunobu reaction3) Synthesis starting with PEG oxirane

FIG. 64

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4) Synthesis from PEG amine



5) Synthesis from PEG aldehyde

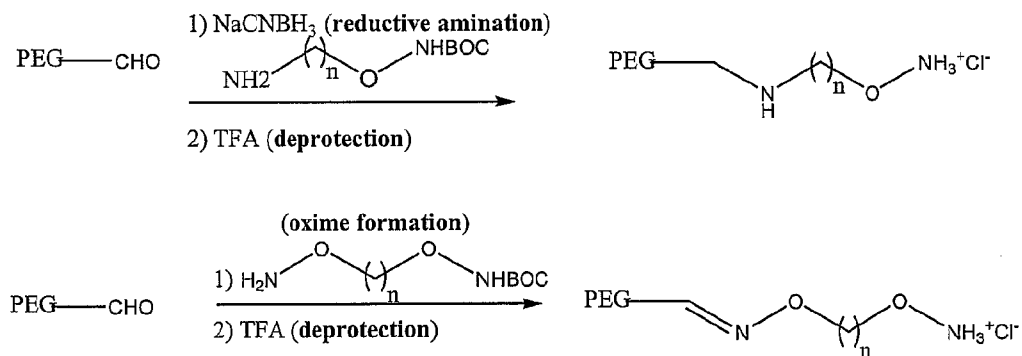


FIG. 65