Lec 9 5th stage

# Organic Pharmaceutical Chemistry IV

2018-2019

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# Preparation of CPT-PEG-BH3

- Anticancer drug camptothecin (CPT) **as an apoptosis inducer.**

- Synthetic BCL2 homology 3 domain (BH3) peptide **as a suppressor of cellular antiapoptotic defense.**

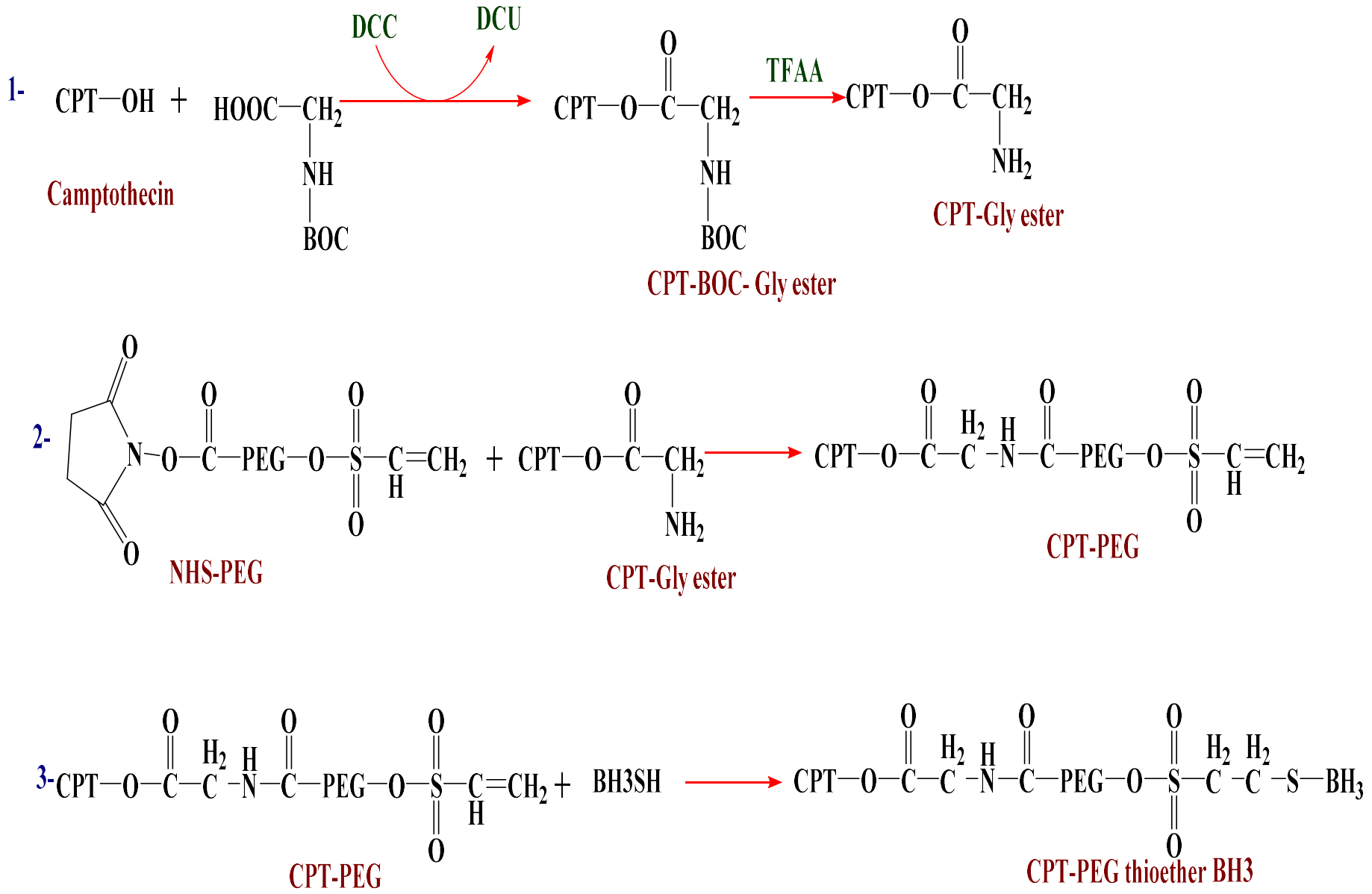
**BH3**

**Ac-Met-Gly-Gln-Val-Gly-Arg-Gln-Leu-Ala-Ile**

**Ile-Gly-Asp-Asp-Ile-Asn-Arg-Arg-Tyr-Cys-NH2**

**SH**

**Note: - The BCL2 protein family is characterized by specific regions of homology termed BCL2 homology (BH1, BH2, BH3, BH4) domains. These domains are critical to the functions of these proteins, including their impact on cell survival and their ability to interact with other family members and regulatory proteins. It was found that the BCL2 homology 3 (BH3) domain of proapoptotic proteins from the BCL2 family is responsible for the induction of apoptosis.**

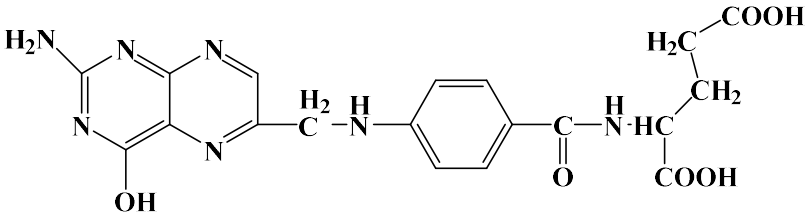



**This system showed its high potential to suppress cellular antiapoptotic defense and increase the anticancer efficacy of CPT.**

## Folate-receptor-targeted anti-cancer agent doxorubicin.

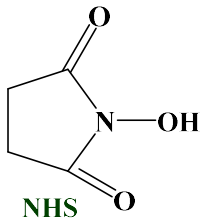
# Preparation of FOL-PEG-DOX

FOL and DOX were separately conjugated at a- and N-terminal end of a PEG chain to produce FOL–PEG–DOX. The FOL–PEG–DOX conjugate has a targeting moiety at one end and an anti-cancer drug moiety at the other end in a single flexible PEG chain structure.

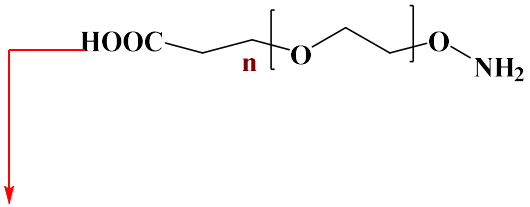


Folic acid (Vit B9)

DCC



NHS



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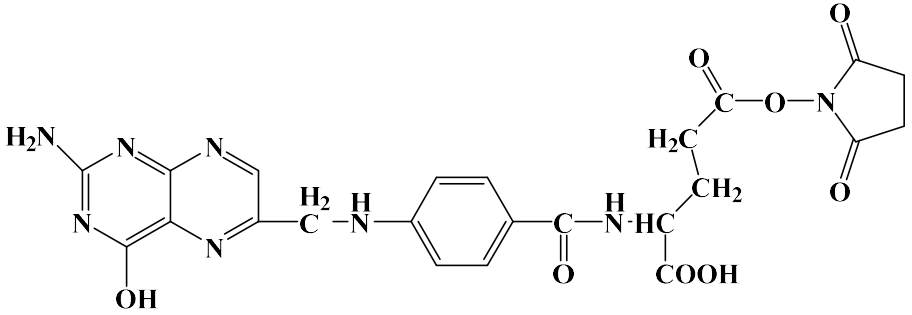
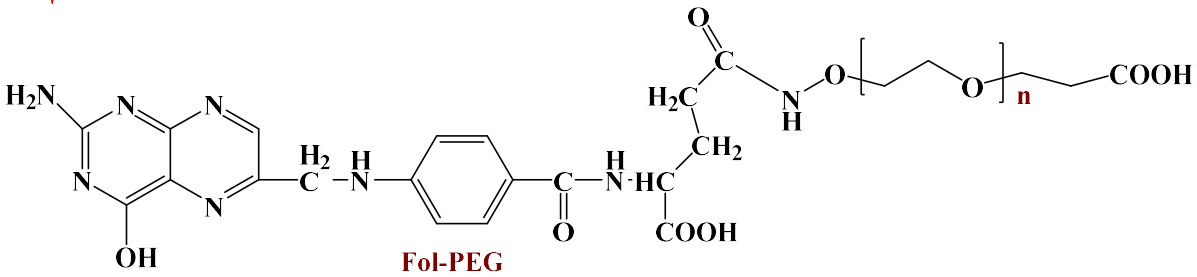
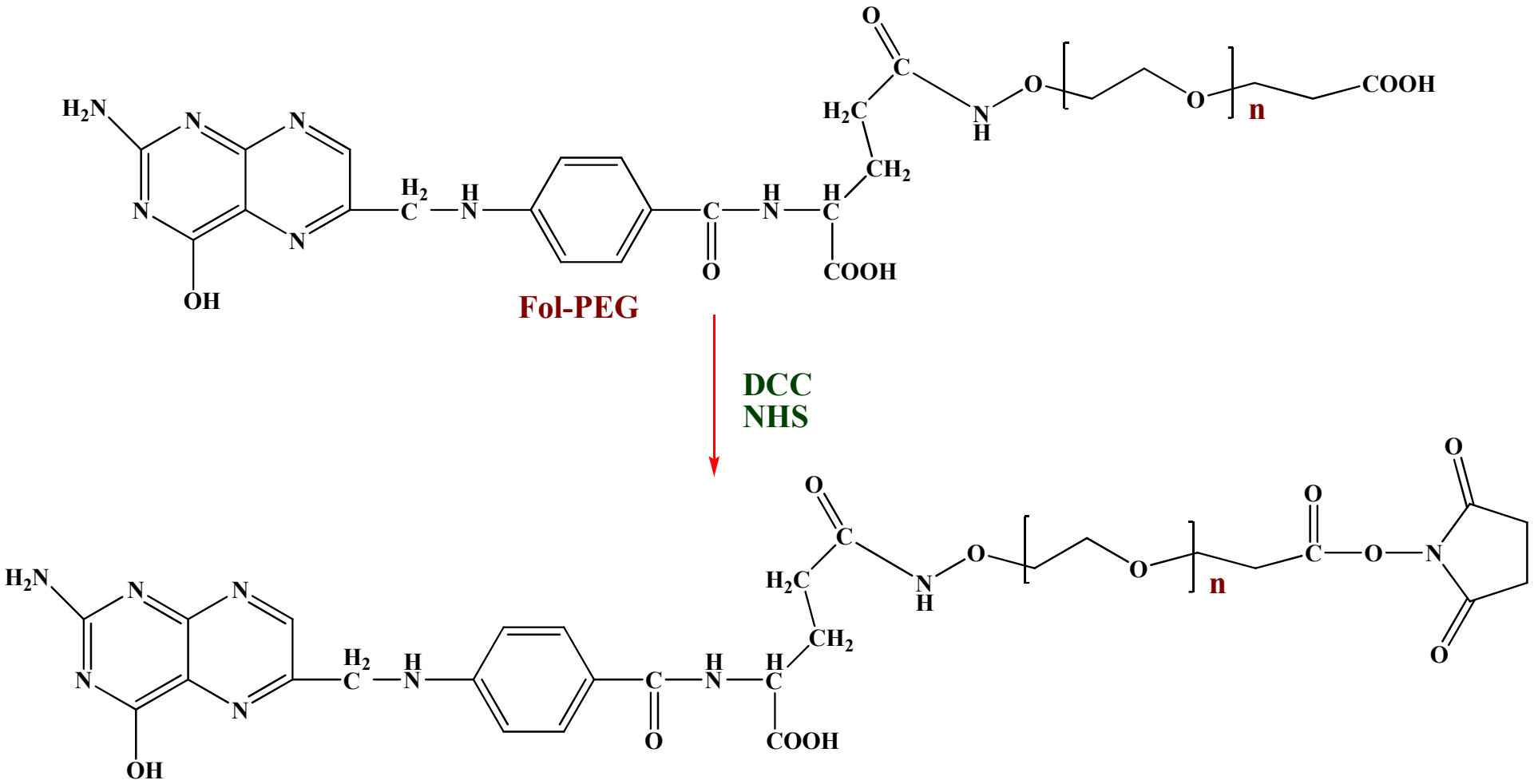
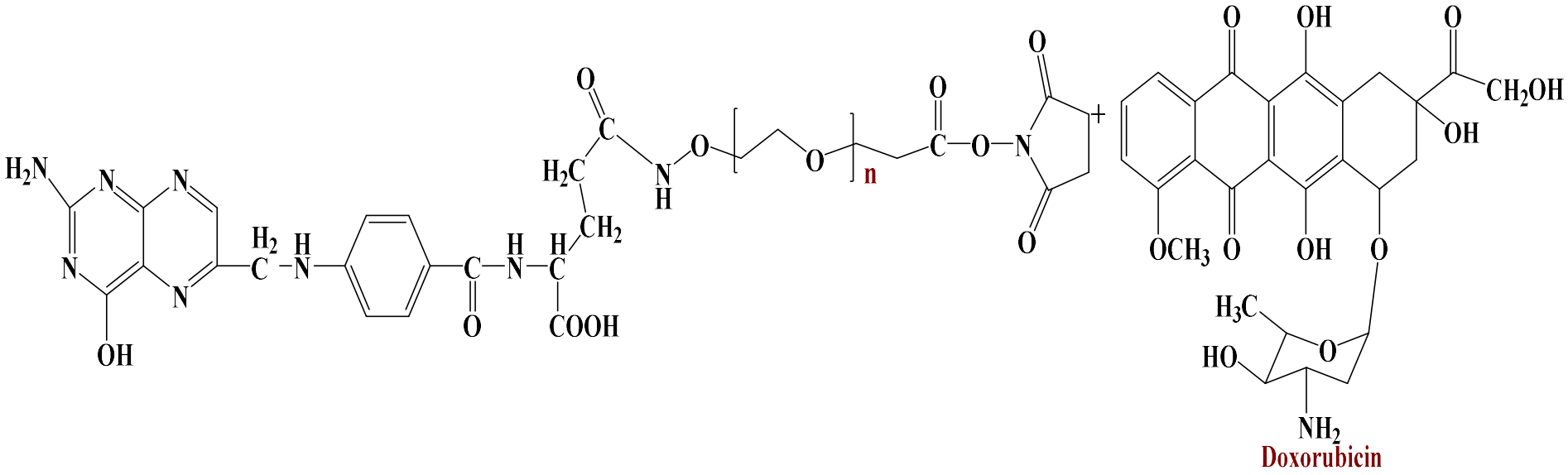


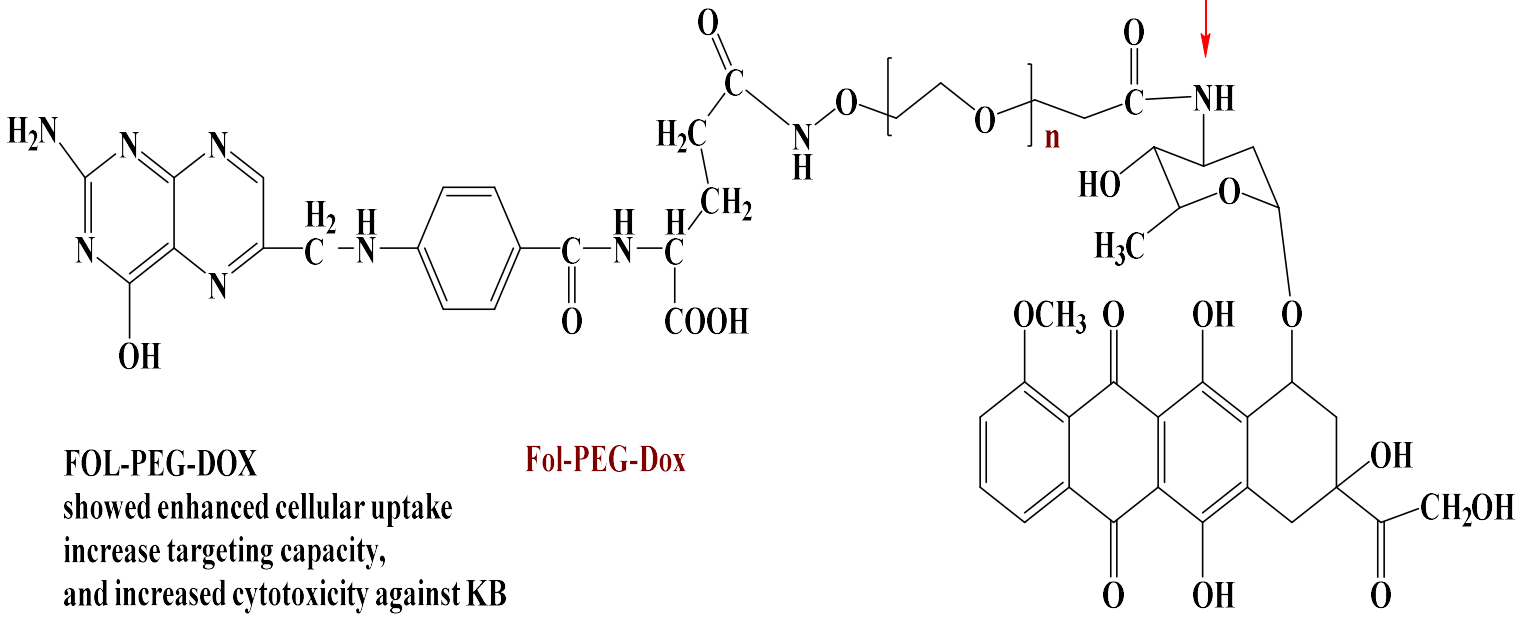


Fol-PEG


Fol-PEG
DCC
NHS



Doxorubicin



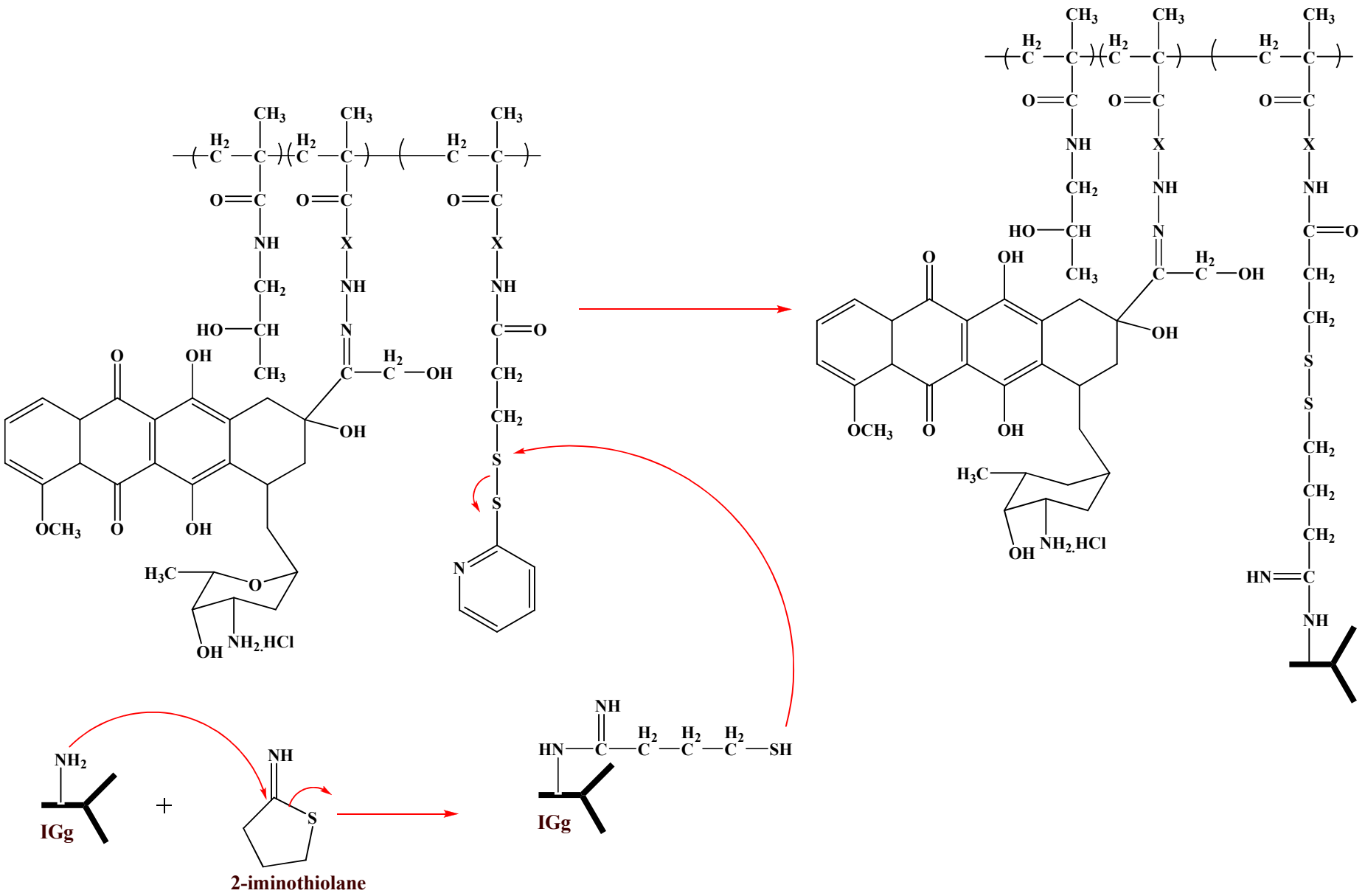
Fol-PEG-Dox

FOL-PEG-DOX
showed enhanced cellular uptake
increase targeting capacity,
and increased cytotoxicity against KB
cells over expressing folate receptors.

## Antibody-targeted polymer-doxorubicin conjugates designed as anticancer drugs.

Antibody-targeted conjugates with DOX bound via hydrazone bond exhibited even more extensive inhibition of the tumor growth with some long-term survivors. No survivors were observed after treatment of mice with free DOX or the nontargeted PHPMA-DOX conjugate.

HPMA hydrazide were modified by introduce the pyridyldisulfanyl group from N-succinimidyl-3(2-pyridyldisulfanyl) propanoate.


IGg
2-iminothiolane
IGg