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Ethynylphosphonamidates for the Rapid and Cysteine-Selective Generation of Efficacious Antibody–Drug Conjugates
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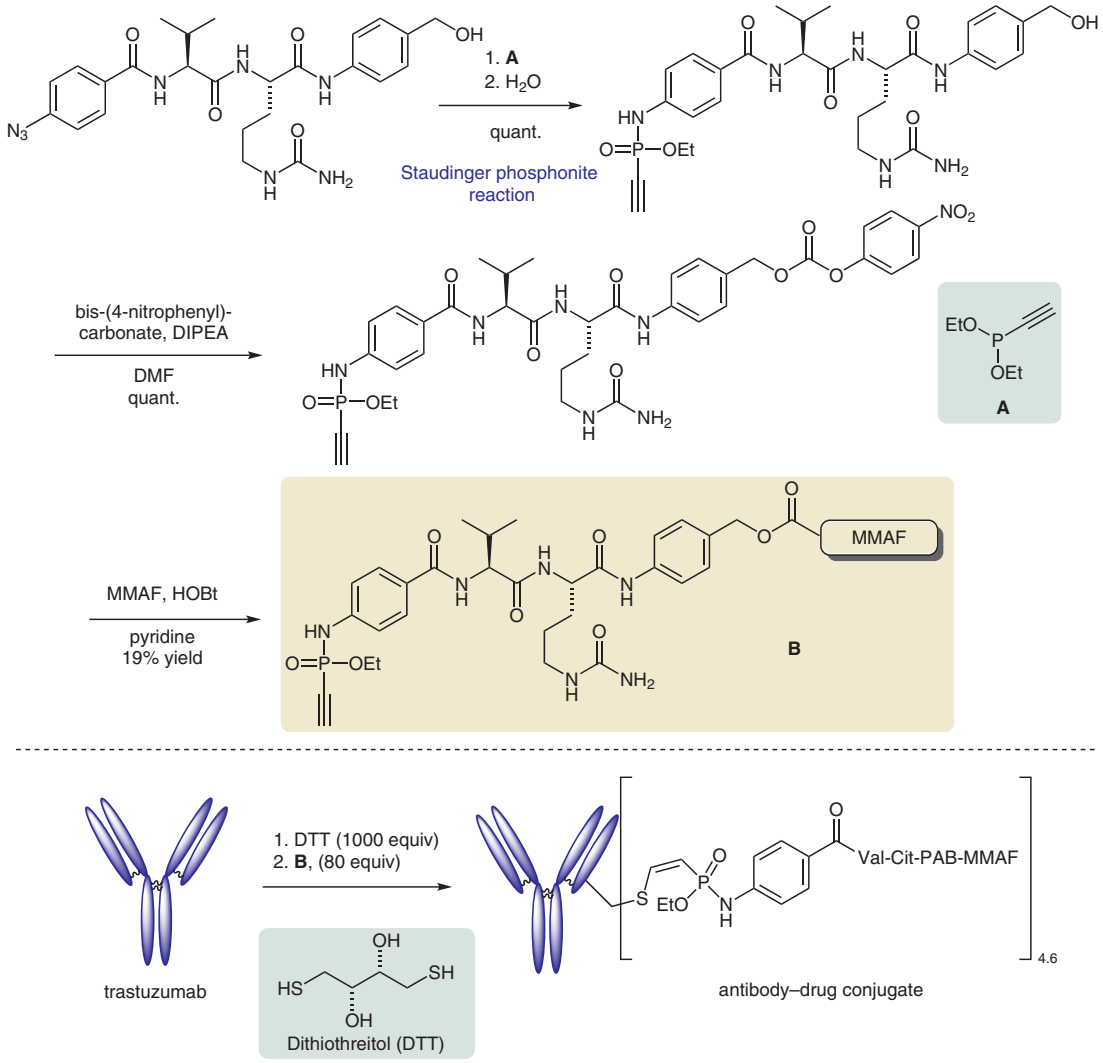
Ethynylphosphonamidates in the Synthesis of Antibody–Drug Conjugates



Significance: Antibody–drug conjugates (ADCs) have emerged as a new class of targeted therapeutics. They combine the high potency of cytotoxic drugs with the tumor specificity of monoclonal antibodies. However, the insufficient stability in serum and undesired aggregation often lead to off-target toxicity.

Comment: The researchers report the conjugation of antimitotic agent monomethyl auristantin F (MMAF) to the Her2-targeting antibody trastuzumab by using ethynylphosphonamidate functionalized linker **B**. The resulting ADC showed a drug-to-antibody ratio of 4.6. Furthermore, the use of a phosphonamidate linker bearing diethyleneglycol improved the polarity of the whole linker system. The ADCs had in vivo antitumor activity.

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Synfact of the Month