Category

Chemistry in Medicine and Biology

Key words

antibodies

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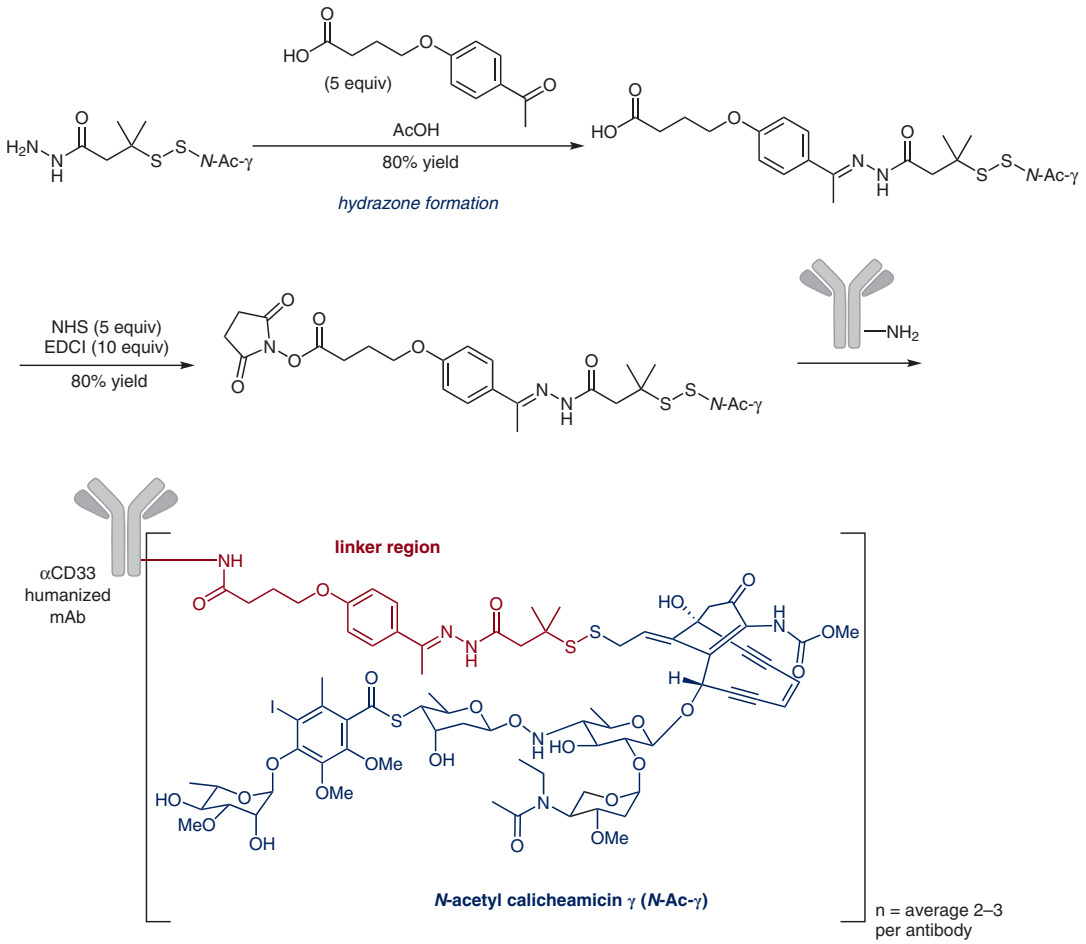
Gemtuzumab Ozogamicin, A Potent and Selective Anti-CD33 Antibody-Calicheamicin Conjugate for Treatment of Acute Myeloid Leukemia

Bioconjugate Chem. **2002**, *13*, 47–58.

The First FDA-Approved Antibody-Drug Conjugate



Significance: The enediyne-containing antitumor antibiotic calicheamicin induces double-stranded DNA breakage and is highly cell-toxic. Conjugation of calicheamicin to a humanized monoclonal antibody against CD33, an adhesion protein that is expressed on the cell surface of leucoblasts, allows its targeted delivery to the non-solid tumor acute myeloid lymphoma (AML). This construct was the first FDA-approved antibody-drug conjugate (ADC) and was marketed as Mylotarg. It was retracted in 2010; however, calicheamicin ADCs have now been re-evaluated as therapeutic.

Comment: *N*-Ac-γ was linked via a hydrazone to lysine residues on a humanized monoclonal antibody against the tumor antigen CD33 and succumbs to hydrolytic hydrazone cleavage upon endocytosis. The conjugation of calicheamicin to an antibody was previously reported (*Cancer Res.* **1993**, *53*, 3336) and, here, the authors investigate different linkers to produce a more potent and selective agent.

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