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Synthesis of Prodrugs of Zidovudine

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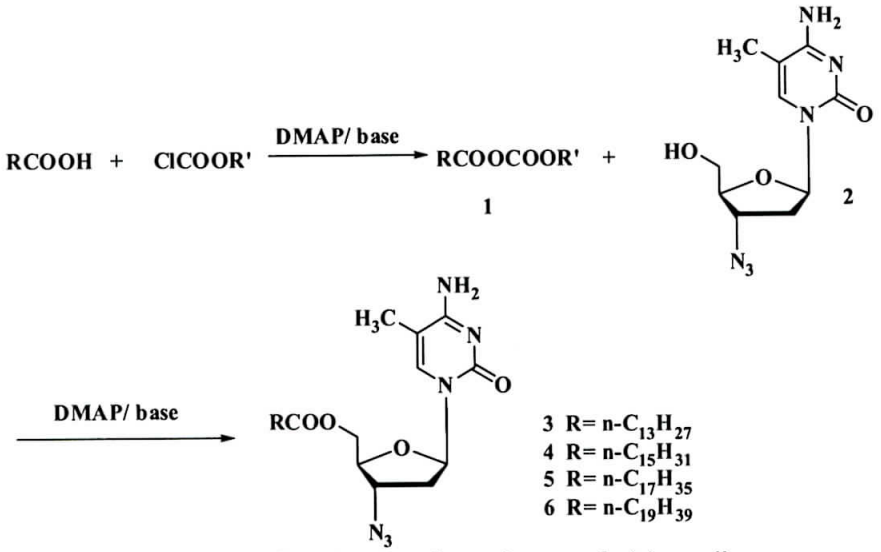
Abstract

Intensive efforts to develop new chemotherapeutic agents effective against the human immunodeficiency virus (HIV), the etiological agent of acquired immunodeficiency syndrome (AIDS). Zidovudine (3'-azido-2'3'-dideoxythymidine, AZT, azidothymidine) is the first FDA-approved drug available for the treatment of patients suffering from AIDS and AIDS-related complex. Treatment of AZT has led to a decrease in the mortality rate and frequency of opportunistic infections in AIDS patients[1]. But AZT has three disadvantages or side effects. They are (1) the short plasma half-life [2] (about 1 hour), (2) significant dose-related toxicity (bone marrow toxicity, severe anemia), (3) no ability to penetrate into brain. In attempts to overcome the problem of rapid elimination and decreased permeability of AZT through the blood brain barrier and to increase its therapeutic efficacy, we have synthesized a variety of 5'-ester of AZT [3]. Here we synthesize the 5'- arachidate of AZT for the first time. The synthesis of prodrugs of zidovudine was showed in Scheme 1. The further study on biological evaluation and pharmaceutical research of these compounds are carrying on.



Scheme 1. Synthesis of prodrugs of zidovudine