Data Base compiled

Didanosine

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About Didanosine

- Didanosine is a synthetic nucleoside analogue of the naturally occurring nucleosidedeoxyadenosine in which the 3'-hydroxyl group is replaced by hydrogen
- Didanosine is a nucleoside analogue and a highly potent nucleoside reverse transcriptase inhibitor, which has been used in the treatment of human immunodeficiency virus (HIV) infections

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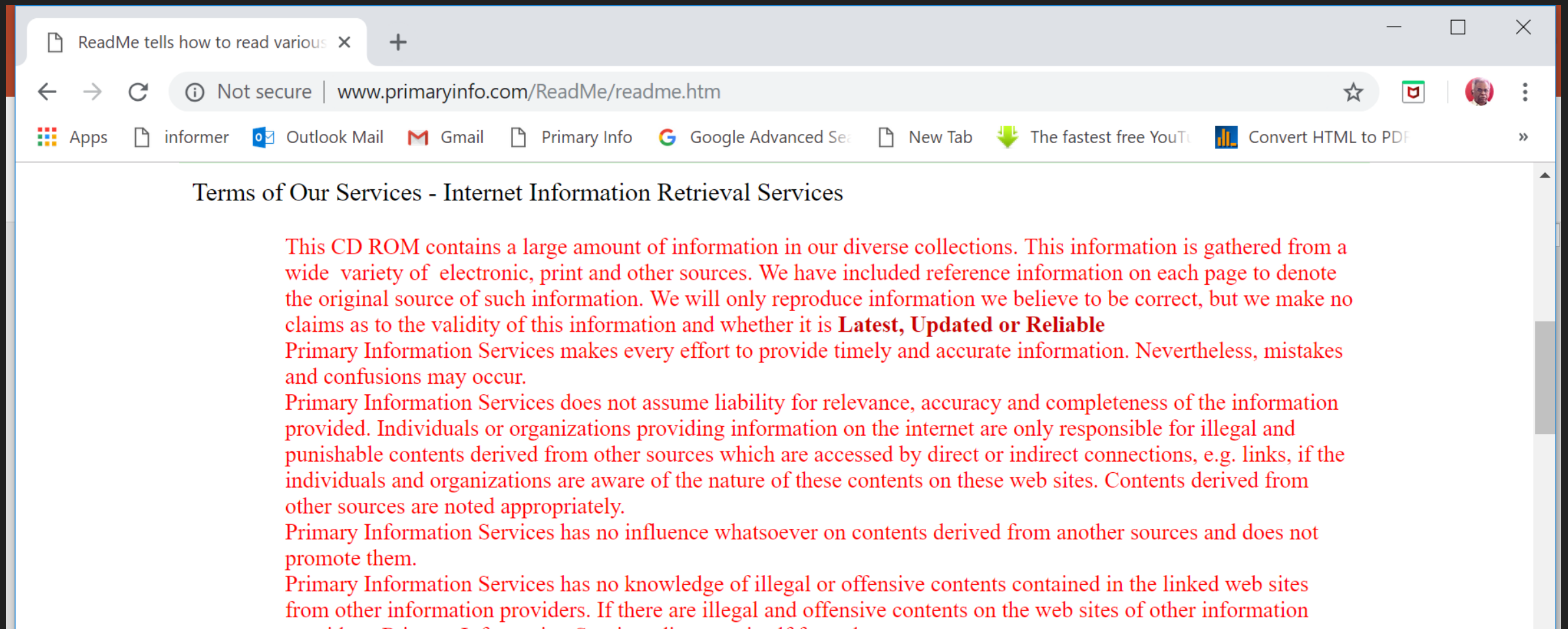

Didanosine can be synthesized from 2',3'-Dideoxyuridine or Adenosine. Synthesis from Dideoxyuridine is realized by use of organic reactions and compounds. Synthesis from Adenosine uses enzymes for selective catalysis. The enzymes are obtained from bateria cultures like E.Coli.

PATENT INFORMATION

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(54) **A PROCESS FOR PREPARING DIDANOSINE**

(57) This invention provides a method for preparing didanosine. The method comprises removing a protecting group in position 5' of compound II by hydrolysis under basic reaction conditions, and simultaneously enolizing of the carbonyl group of the purine ring to obtain a stable salt, and then producing the salt of 2',3-dideoxyinosine through catalytic hydrogenation, which salt is finally converted with acid to yield the finished product.

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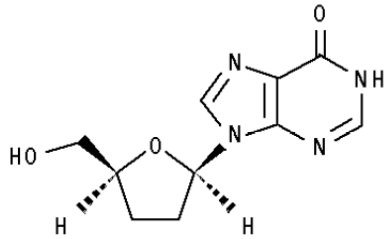
Didanosine is also available as an enteric-coated formulation (VIDEX® EC Delayed-Release Capsules). Please consult the prescribing information for VIDEX EC (didanosine). The chemical name for didanosine is 2',3'-dideoxyinosine. The structural formula is:



Didanosine is a white crystalline powder with the molecular formula $C_{10}H_{12}N_4O_3$ and a molecular weight of 236.2. The aqueous solubility of didanosine at 25°C and pH of approximately 6 is 27.3 mg/mL. Didanosine is unstable in acidic solutions. For example, at pH <3 and 37°C, 10% of didanosine decomposes to hypoxanthine in less than 2 minutes.

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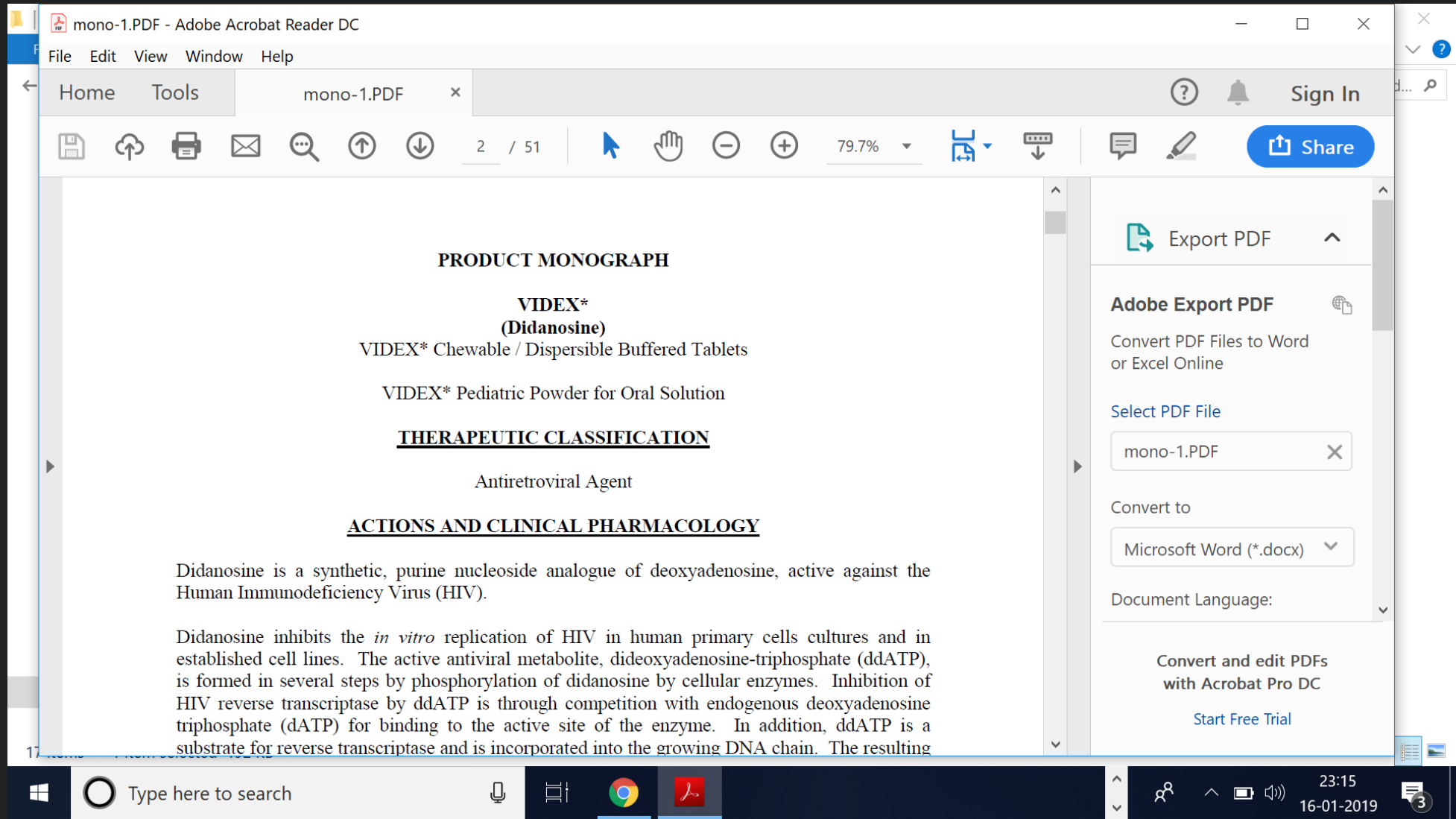

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Selective benzoylation of the 5′-hydroxyl group of 2′-deoxyinosine is achieved by dropwise addition of a pyridine solution of benzoyl chloride to 2′-deoxyinosine suspended in pyridine. The 5′-*O*-benzoyl-2′-deoxyinosine formed is then treated in one portion with 1,1′-thiocarbonyldiimidazole to form the thioimidazolide. Deoxygenation at the 3′ position of the thioimidazolide gives 5′-*O*-benzoyl-2′,3′-dideoxyinosine. Removal of the benzoate group by treatment with anhydrous methanol saturated with anhydrous ammonia at 0 °C yields didanosine in 90% yield (Nassar *et al.*, 1993).

Didanosine has also been prepared enzymatically by deamination of 2′,3′-dideoxyadenosine with adenosine deaminase at room temperature. Recrystallization

QUESTIONS?

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