



STATUS DECISION OF CONTROLLED AND NON-CONTROLLED SUBSTANCE(S)

Substances: Ajulemic acid, its formyl analogue, and its hydroxymethylpivalate analogue

Based on the current information available to the Office of Controlled Substances, it appears that the above substances are:

Controlled X
Not Controlled []

under the schedules of the Controlled Drugs and Substances Act (CDSA) for the following reason(s):

- The drug is currently not listed specifically on the CDSA.
Item 1 of Schedule II to the CDSA includes, "Cannabis, its preparations, derivatives and similar synthetic preparations." This item includes, in addition to the well known components of cannabis, other substances similar in structure to the classical cannabinoids. These include nabilone and DMHP.
A status decision was made by OCS on August 21, 2001 that made HU 210 (III) is a controlled substance by inclusion in item I of Schedule II. Therefore, ajulemic acid and its analogues (II) and (IV) being similar synthetic preparations of the cannabinoids, must be included in item I of Schedule II to the CDSA.

Supporting document(s) attached: X

Prepared by: TIANA BRANCH Date: 2005-07-28

Verified by: See email MICHAEL LEBELLE Date: 2005-07-27

Approved by: DIRECTOR, OFFICE OF CONTROLLED SUBSTANCES Date:

Drug Status Report

Drugs: Ajulemic acid, its formyl analogue (II), and its hydroxymethylpivalate analogue (IV).

Drug Name Status: Ajulemic acid is the common name.

This status decision was prompted by a request from a custom chemical synthesis company. The final product was ajulemic acid (I). During the synthetic process several intermediates are prepared. These include the formyl analogue (II), the hydroxymethyl analogue (III) and the hydroxymethylpivalate analogue (IV). The hydroxymethyl analogue (III) is known as HU 210 and was determined to be controlled on 2001-08-21.

Another series of derivatives of some of these substances is used in the synthesis. These are shown on the information from the company as OTBDMS. These are tertiarybutyldimethylsilyl derivatives that are commonly used in synthetic and analytical chemistry procedures. These derivatives are formed in solution usually to protect a sensitive functional group in a molecule and are seldom isolated. They have not been dealt with here for that reason.

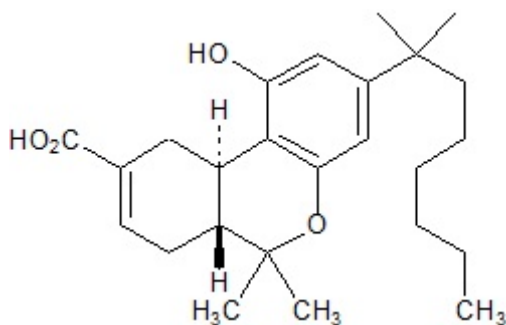
Chemical Names:

Ajulemic acid (I): (6aR,10aR)-3-(1,1-dimethylheptyl)-6a,7,10,10a-tetrahydro-1-hydroxy-6,6-dimethyl-6H-Dibenzo(b,d)pyran-9-carboxylic acid

(II): (6aR,10aR)-3-(1,1-dimethylheptyl)-9-formyl-6a,7,10,10a-tetrahydro-6,6-dimethyl-6H-dibenzo[b,d]pyran-1-ol

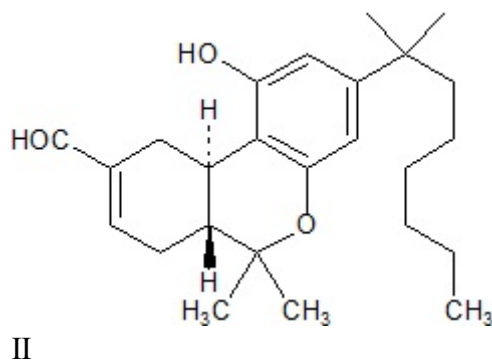
(III): (6aR,10aR)-3-(1,1-dimethylheptyl)-9-hydroxymethyl-6a,7,10,10a-tetrahydro-6,6-dimethyl-6H-dibenzo[b,d]pyran-1-ol

(IV): (6aR,10aR)-3-(1,1-dimethylheptyl)-9-(2,2-dimethyl-1-oxopropoxy)methyl-6a,7,10,10a-tetrahydro-6,6-dimethyl-6H-dibenzo[b,d]pyran-1-ol

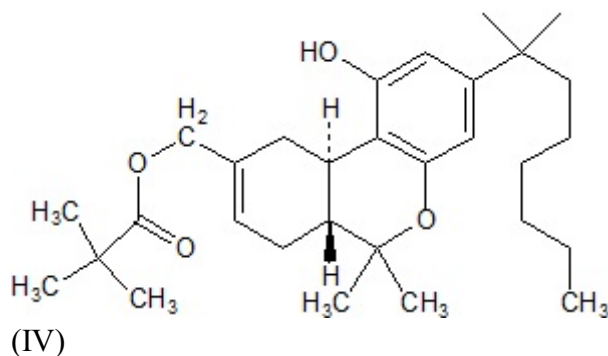
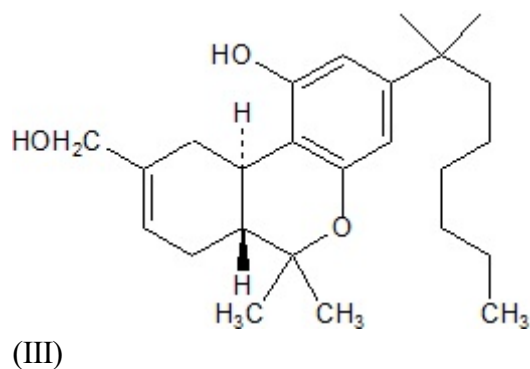


Ajulemic acid (I)

Chemical structures:



II



Molecular Formulas:

Ajulemic acid (I): $C_{25}H_{36}O_4$

(II): $C_{25}H_{36}O_3$

(III): $C_{25}H_{38}O_3$

(IV): $C_{30}H_{46}O_4$

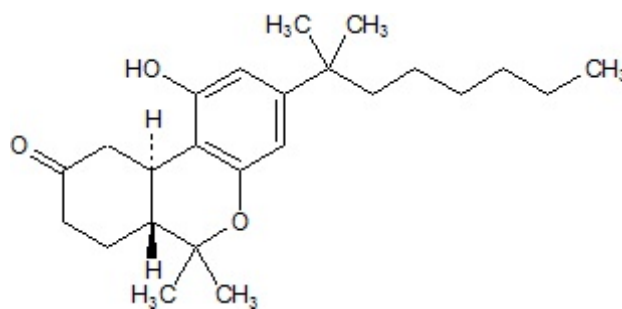
Pharmacological class / Application: cannabinoid

International status:

US: The drugs are not currently listed on the US Controlled Substances Act and are not mentioned on the DEA website. However, the tetrahydrocannabinols are listed on Schedule I to the CSA. The analogue provision of the CSA, "controlled substance analogue" means a substance- (i) the chemical structure of which is substantially similar to the chemical structure of a controlled substance in schedule I or II" therefore applies. The DEA would have to confirm the status of ajulemic acid under the CSA.

United Nations: The drug is not listed on the Yellow List - List of Narcotic Drugs under International Control. The drug is not listed on the Green List - List of Psychotropic Substances under International Control.

Canadian Status: The drug is currently not listed specifically on the CDSA. Item 1 of Schedule II to the CDSA includes, "Cannabis, its preparations, derivatives and similar synthetic



Nabilone

preparations.” This item includes, in addition to the well known components of cannabis, other substances similar in structure to the classical cannabinoids. These include nabilone and DMHP. A status decision was made by OCS on August 21, 2001 that made

HU 210 (III) a controlled substance by inclusion in item I of Schedule II.

For illustration, the structure of nabilone is given on the next page.

Therefore, ajulemic acid and its analogues (II) and (IV) being similar synthetic preparations of the cannabinoids, must be included in item I of Schedule II to the CDSA.

Recommendation: Ajulemic acid and (II) and (IV) are currently included in Schedule II to the CDSA and are controlled substances.