Patents and Small Molecules

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Technology Transfer: Health Science Center (Memphis) Office

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1. Patent Basics
2. Anatomy of a Patent Application
3. Prior Art Searching

Patent Basics

What is patentable?

YES	NO
Process	Laws of nature
Machine	Physical phenomena
Article of manufacture	Abstract ideas
Composition of matter	Literary, dramatic, musical, and artistic works
Improvement of any of the above	

US Supreme Court (ruling in 1980 that genetically engineered bacteria could be patented) : "…anything under the sun that is made by man [is patentable subject matter]."

What are the legal requirements?

- Useful
- Novel (not previously known)
  - U.S. PTO provides one year grace period after public disclosure.
  - Most foreign countries require absolute novelty = no public disclosures.
- Non-obvious
- Reduced to Practice
  - Actual
  - Conceptual (or constructive)

Public Disclosure

Public disclosure can include:

- Publications in open literature (includes internet)
- Poster Sessions & Abstracts
- Presentations to open forum
- Personal communications without expectation of confidentiality
- Anything catalogued in a library

Primary discriminators are:

- Good faith attempt to maintain secrecy
- Substantiality of material disclosed

Novelty: Assess Prior Art

- Invention must be new.

- Need to check if:
  - The invention is described in a printed publication anywhere, including published patent applications.

Description Requirement

Description requirements for U.S. patent application:

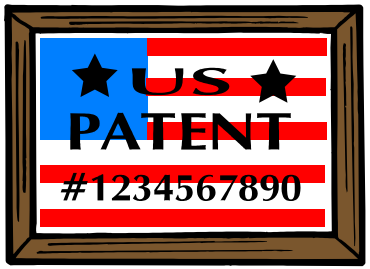
- *the application must contain a written description of the invention*
- *the description must be sufficient to enable any person skilled in the art to which it pertains to make and use the same*
- *the description must set forth the best mode contemplated by the inventor of carrying out his or her invention*

Publication Date

All U.S. patent applications are published by the PTO approximately 18 months after the application filing date.

Patent Term

The patent term begins on the date of issue but ends 20 years from the effective filing date.



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The U.S. Provisional Application

- The provisional application is not examined for patentability by the PTO and expires after 1 year.
- It is not published.
- Like a regular U.S. patent application, it must provide a description of invention.
- Within 1 year of filing a provisional application:
  - the inventor must file a regular application for the same invention as described in the provisional application
  - The inventors can add supporting data but not new matter

U.S. Provisional – Intent

- The intent behind the provisional application is to make it possible for an inventor to lock in an application filing date at a *lower cost* and with *less effort* than would be required in the preparation and filing of a regular U.S. patent application

Typical Route to U.S.Issuance

1. Provisional Application Filed
2. U.S. Application Filed
3. Patent Published
4. Examination of Applications
    - Office Action
    - Reply to Office Action
    - Second Office Action
    - Reply
    - Final Action
    - Notice of Allowance

Patent Cooperation Treaty (PCT)

- Created to achieve a unified procedure for filing patent applications.
- As of 2005, has 128 member countries.
- A patent application filed under the PCT is called an international application, or PCT application.
- At 30 months from the filing date of the international application or from the earliest priority date, the international phase ends and the international application enters in national and regional phase.

How to search, find and download Patents?

- United States Patent and Trademark Office (USPTO) database
  - *www.**uspto**.gov*
  - Good for searching whether a patent is issued or published
  - Good for searching a particular inventor
  - Public PAIR – patent application information retrieval
    - provides status of patent applications
- Google patents
  - *www.**google**.com/**patents***
  - Great for downloading pdf versions of patents
- Patent Lens
  - *www.Patentlens.net*
  - Great for downloading pdf versions of patents

Anatomy of a Patent Application

US 20090286824A1

(19) **United States**

(12) **Patent Application Publication**

Moore, II et al.

(10) **Pub. No.: US 2009/0286824 A1**

(43) **Pub. Date: Nov. 19, 2009**

(54) **PYRIDINE CLASSICAL CANNABINOID COMPOUNDS AND RELATED METHODS OF USE**

(76) Inventors: **Bob M. Moore, II**, Nesbit, MS (US); **Steven Gurley**, Memphis, TN (US); **Suni Mustafa**, Memphis, TN (US)

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(21) Appl. No.: **12/468,773**

(22) Filed: **May 19, 2009**

Related U.S. Application Data

(60) Provisional application No. 61/128,160, filed on May 19, 2008.

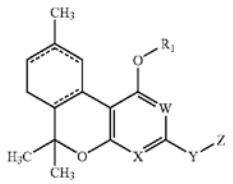
Publication Classification

(51) **Int. Cl.**
A61K 31/436 (2006.01)
C07D 491/052 (2006.01)
A61P 35/00 (2006.01)

(52) **U.S. Cl.** **514/291**; 546/89

(57) **ABSTRACT**

Disclosed are compounds of the formula I:



wherein R_1, R_2, V, W, X, Y and Z can be as defined herein. The compounds can be used in the treatment of disorders mediated by the cannabinoid receptors.

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Patent numbers

- **U.S. Application Number:**
  - Given to a patent application when filed in U.S.
  - 99999999 or 99/999999
- **U.S. Patent Number:**
  - Given to a patent application upon issuance in U.S.
  - 9,999,999
- **U.S. Publication Number:**
  - Given to a patent when published
  - US YYYY-9999999 A9 or 9999-9999999
- **PCT Number:**
  - Given to a patent application when filed as a PCT
  - PCT/CCYY/99999 or PCT/CCYYYY/999999
- **WO (PCT) Number**:
  - Given to a PCT patent application when published
  - WOYYYYUS99999

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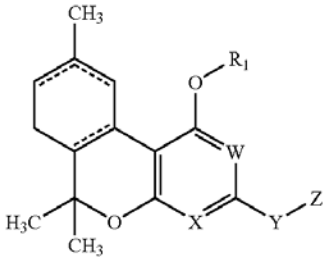

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(12) **United States Patent**
Shukla et al.

(10) **Patent No.: US 6,960,346 B2**
(45) **Date of Patent: Nov. 1, 2005**

(54) **VEHICLES FOR DELIVERY OF BIOLOGICALLY ACTIVE SUBSTANCES**

(75) Inventors: **Atul J. Shukla**, Cordova, TN (US); **James R. Johnson**, Germantown, TN (US); **Yichun Sun**, Germantown, TN (US); **Robert Cooper**, Starkville, MS (US); **Gregg Boring**, Starkville, MS (US); **Dan Scruggs**, Starkville, MS (US)

(73) Assignee: **University of Tennessee Research Foundation**, Knoxville, TN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 420 days.

(21) Appl. No.: **10/143,144**

(22) Filed: **May 9, 2002**

(65) **Prior Publication Data**

US 2003/0211123 A1 Nov. 13, 2003

(51) **Int. Cl.**[7] **A61K 9/02**; A61K 9/08; A61K 9/70; A61K 13/02; A61F 2/02

(52) **U.S. Cl.** **424/400**; 424/423; 424/443; 424/434; 424/78.04; 424/437

(58) **Field of Search** 424/400, 423, 424/443, 434, 78.04, 437

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Primary Examiner—Carlos A. Azpuru
(74) *Attorney, Agent, or Firm*—Howard Eisenberg, Esq.

(57) **ABSTRACT**

A formulation containing one or more biologically active substances dissolved, dispersed, emulsified, or suspended within a vehicle of one or more citric acid esters and/or citric acid ethers. Methods for making and using are disclosed, as are kits for administration of the pharmaceutical formulation.

80 Claims, 1 Drawing Sheet

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The Patent Application

- Title
- Field of Invention
- Background of Invention
- Summary of the Invention
- Brief Description of the Drawings
- Detailed Description of the Invention
  - Includes experimental examples
- What is claimed (a list of Claims)

Anatomy of a Patent Application

- Title
- Field of Invention
- Background of Invention
- Summary of the Invention
- Brief Description of the Drawings
- Detailed Description of the Invention
  - Includes experimental examples
- What is claimed (a list of Claims)

Specification – a written description of the invention

Specification

- **A general explanation of the invention and how to practice it.**
  - The invention is described in its broadest sense.
  - Preferred embodiments of the invention are described.
  - Definitions of key terms are provided and are extremely important in interpreting the scope of the claims.
- **Specific examples of how to practice the invention.**
  - A patent application does not require examples, however in practice, examples can often assist in showing patentability (e.g., enablement).
  - "Working" examples present completed undertakings.
  - "Prophetic" examples are hypothetical undertakings.

Patent Claims

- Claims define the scope of protection granted by the patent
- Claims describe the property, referred to as intellectual property (IP), and set the value of a patent
- The issued claims prevents others from using, producing or selling a product that uses the same idea as what is penned in the patent claims

Claims – Types

- There are two basic types of claims:
  - **independent claims**, which stand on their own
  - **dependent claims**, which depend on a single claim or on several claims

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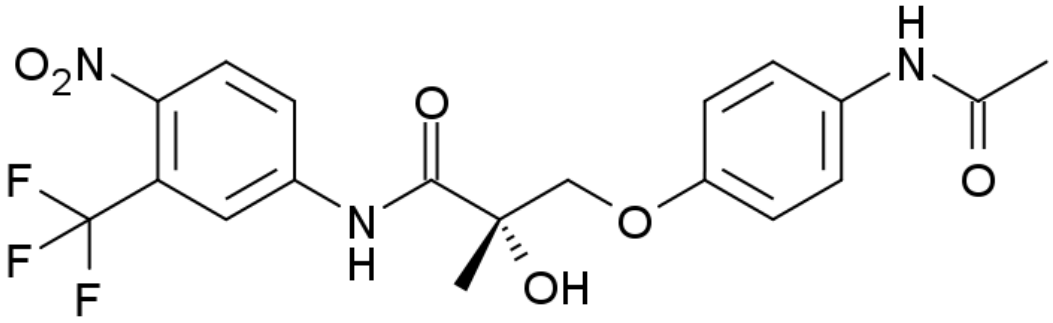
Broad claims ⟶ *Narrow claims*

Small molecule example

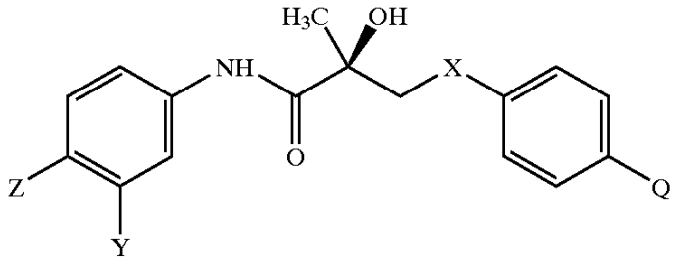


Andarine™

Selective androgen receptor modulator (SARM)

Small molecule example

1. A composition comprising a selective androgen receptor modulator (SARM) compound having in-vivo androgenic and anabolic activity of a nonsteroidal ligand for the androgen receptor, said compound represented by the structure of formula (I):



wherein
X is a O;
Z is NO_2, CN, COR, or CONHR;
Y is I, CF_3, Br, Cl, or SnR_3;
R is an alkyl group or OH; and
Q is acetamido or trifluroacetamido.

2. The composition according to claim **1**, wherein Z is NO_2.

3. The composition according to claim **1**, wherein Y is CF_3.

4. The composition according to claim **1**, wherein Q is $NHCOCH_3$.

5. The composition according to claim **1**, wherein Z is NO_2, Y is CF_3, and Q is $NHCOCH_3$.

US Patent 6,569,896

Independent (broadest) claim

Description of genus

Definition of species

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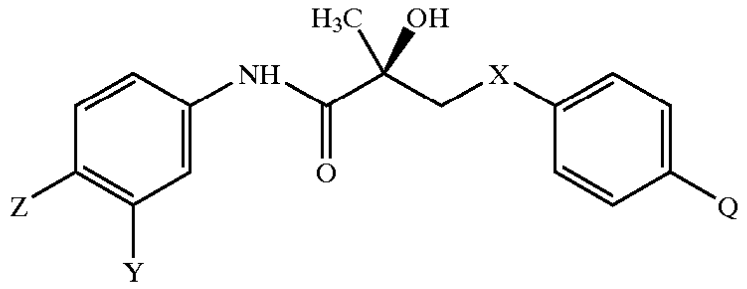
US Patent 6,569,896

1. A composition comprising a selective androgen receptor modulator (SARM) compound having in-vivo androgenic and anabolic activity of a nonsteroidal ligand for the androgen receptor, said compound represented by the structure of formula (I):



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Any compound described in this broadest claim (Claim 1) is considered prior art

Prophetic compounds will not appear when doing a simple Scifinder ® structure search

Small molecule patent claims

- Will include compounds synthesized and compounds closely related but not synthesized (prophetic examples)

- The compounds described in the claims must be “enabled” (how to make and use the compounds must be in the specification).

Claims – Defined words

- In a claim, an inventor may use a common word or phrase that is defined in the specification.

- That word or phrase must be interpreted in light of the definitions provided in the specification of a patent.
  - Examples: “alkyl”, “aryl”, “heteroaryl”, “substituent”

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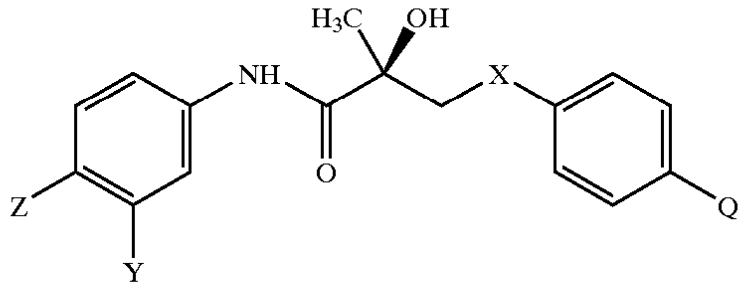
1. A composition comprising a selective androgen receptor modulator (SARM) compound having in-vivo androgenic and anabolic activity of a nonsteroidal ligand for the androgen receptor, said compound represented by the structure of formula (I):



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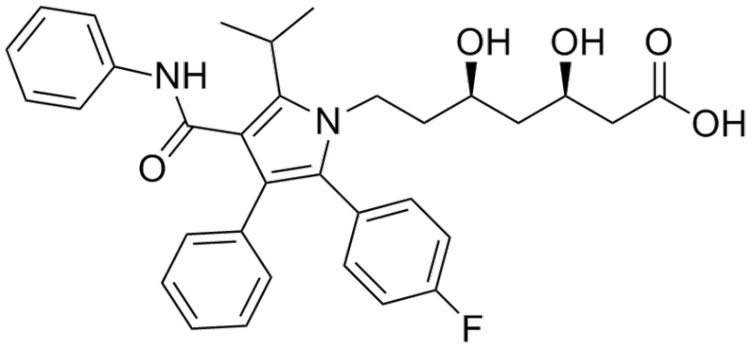
What does “alkyl” mean?
Straight chain? Branched?
Limited to how many carbons?

“Aryl” Definition example

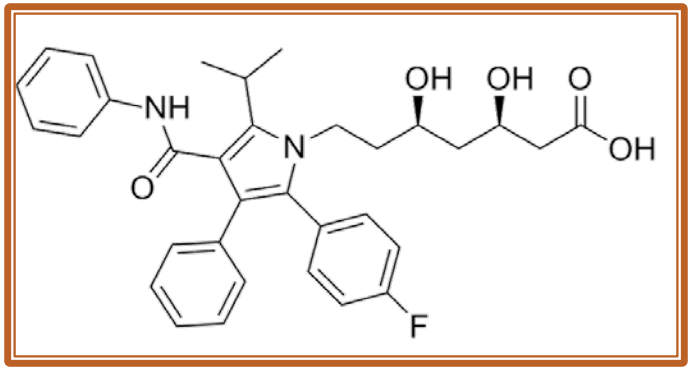
- The term aryl refers to an unsaturated, aromatic monocyclic ring of 6 carbon members or to an unsaturated, aromatic polycyclic ring of from 10 to 14 carbon members. Examples of such aryl rings include, and are not limited to, phenyl, naphthalenyl or anthracenyl. Preferred aryl groups are phenyl and naphthalenyl .

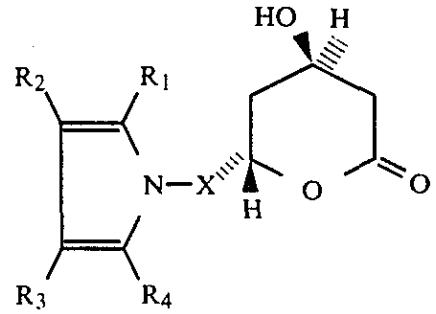
Lipitor

- What does the broadest claim look like?



Lipitor Patent 4,681,893





I

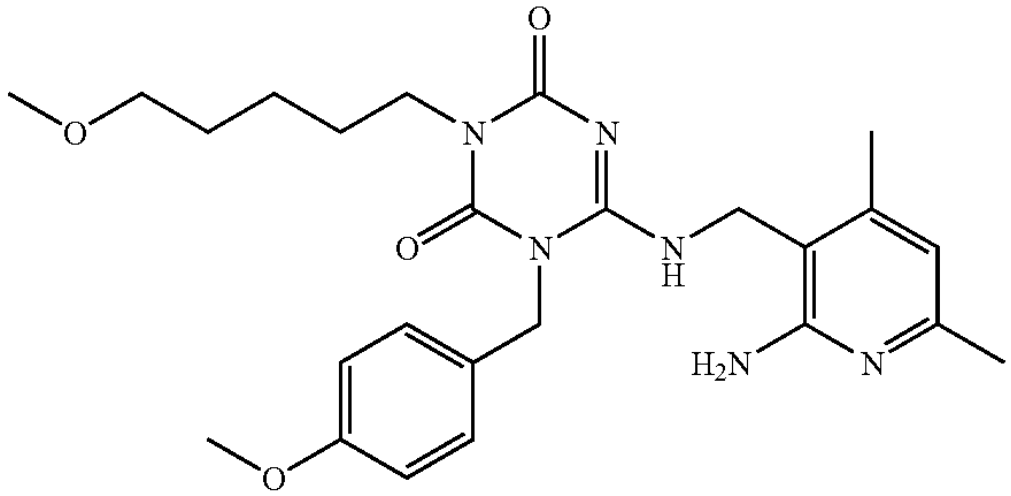
wherein

X is —CH_2—, —CH_2CH_2—, —$CH_2CH_2CH_2$—, or —$CH_2CH(CH_3)$—;

R_1 is

1-naphthyl;
2-naphthyl;
cyclohexyl;
norbornenyl;
phenyl;
phenyl substituted with
fluorine,
chlorine,
bromine,
hydroxyl,
trifluoromethyl,
alkyl of from one to four carbon atoms,
alkoxy of from one to four carbon atoms, or
alkanoyloxy of from two to eight carbon atoms;

Another example – PK1 receptor antagonists

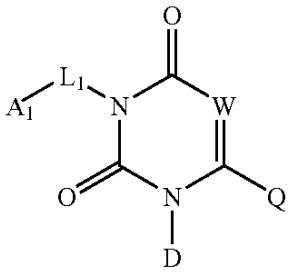


Cpd 252

A more complicated example – broadest claim 1 goes for 2.5 pages

1. A compound of Formula (I):

Formula (I)



wherein:

A_1 is CF_3, C_{1-4}alkoxy, aryl, aryloxy, benzofused heterocyclyl, or heteroaryl; wherein aryl, aryloxy, and heteroaryl are optionally substituted with pyrazol-1-yl or [1,2,3] thiadiazol-4-yl; or aryl, aryloxy, the benzo portion of benzofused heterocyclyl, and heteroaryl are optionally substituted with one to three substituents independently selected from the group consisting of C_{1-6}alkyl, hydroxy(C_{1-6})alkyl, C_{1-6}alkoxy, halogen, nitro, halogenated C_{1-6}alkyl, halogenated C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkoxycarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, cyano, hydroxy, aminocarbonyl, C_{1-6}alkylaminocarbonyl, di(C_{1-6}alkyl)aminocarbonyl, C_{1-6}alkoxycarbonylamino, C_{1-6}alkylcarbonyl, C_{1-6}alkylthiocarbonyl, formyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, aminosulfonyl, C_{1-6}alkylaminosulfonyl, and di(C_{1-6}alkyl)aminosulfonyl; provided that A_1 is other than 3,5-di-t-butyl-phenyl;

L_1 is —$(CH_2)_r$—, —CH_2C_{2-4}alkenyl-, or —$CH_2CH_2X(CH_2)_s$—, wherein L_1 is optionally substituted with one to two substituents independently selected from the group consisting of C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and halogen; and, r is an integer of 1 to 5; such that r is greater than or equal to 4 when A_1 is C_{1-4}alkoxy;

s is an integer of 1 to 3;

X is O or S;

D is —P-A_2;

wherein P is —$(CH_2)_{1-2}$— or —$CH_2CH{=}CH$— when A_2 is phenyl, benzofused heterocyclyl, heteroaryl, or C_{3-8}cycloalkyl; alternatively, P is —$(CH_2)_3$— when A_2 is hydrogen, C_{1-4}alkoxy, or C_{1-4}alkoxycarbonyl; and wherein P is optionally substituted with one to two substituents independently selected from the group consisting of C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and halogen;

A_2 is hydrogen, C_{1-4}alkoxy, C_{1-4}alkoxycarbonyl, phenyl, benzofused heterocyclyl, heteroaryl, tetrahydro-pyranyl, piperidinyl, or C_{3-8}cycloalkyl; wherein phenyl, heteroaryl, the benzo portion of benzofused heterocyclyl, and C_{3-8}cycloalkyl are optionally substituted with one to three substituents independently selected from the

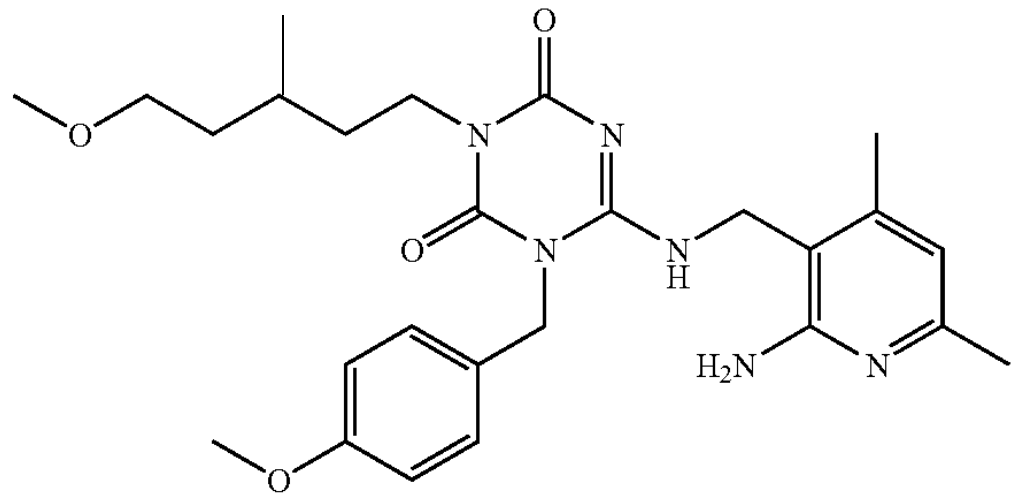
Small molecules and searching

- Scifinder® is the best database to search for small molecules
- Prior art can be compounds found in patents, publications, presentations.
- Prophetic compounds – compounds not synthesized in a patent but covered in a claim – is considered prior art.
- Compounds listed in the specification but not in the claims are considered prior art.

SciFinder® Markush searching

- SciFinder® Markush searching provides the capability to find additional patent documents containing prophetic structures.
- Searches are *not intended to be comprehensive*, but to provide relevant, focused answers that can be used for a preliminary assessment of the patent landscape.

Search example



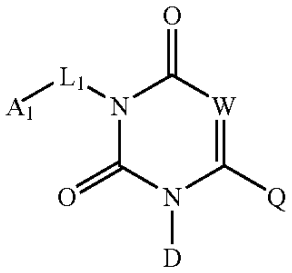
Cmpd 1

Exact structure search? No hits
Markush search? No hits

Compound 1 is known!

1. A compound of Formula (I):

Formula (I)



wherein:

A_1 is CF_3, C_{1-4}alkoxy, aryl, aryloxy, benzofused heterocyclyl, or heteroaryl; wherein aryl, aryloxy, and heteroaryl are optionally substituted with pyrazol-1-yl or [1,2,3] thiadiazol-4-yl; or aryl, aryloxy, the benzo portion of benzofused heterocyclyl, and heteroaryl are optionally substituted with one to three substituents independently selected from the group consisting of C_{1-6}alkyl, hydroxy(C_{1-6})alkyl, C_{1-6}alkoxy, halogen, nitro, halogenated C_{1-6}alkyl, halogenated C_{1-6}alkoxy, C_{1-6}alkylthio, C_{1-6}alkoxycarbonyl, amino, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, cyano, hydroxy, aminocarbonyl, C_{1-6}alkylaminocarbonyl, di(C_{1-6}alkyl)aminocarbonyl, C_{1-6}alkoxycarbonylamino, C_{1-6}alkylcarbonyl, C_{1-6}alkylthiocarbonyl, formyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, aminosulfonyl, C_{1-6}alkylaminosulfonyl, and di(C_{1-6}alkyl)aminosulfonyl; provided that A_1 is other than 3,5-di-t-butyl-phenyl;

L_1 is —$(CH_2)_r$—, —CH_2C_{2-4}alkenyl-, or —$CH_2CH_2X(CH_2)_s$—, wherein L_1 is optionally substituted with one to two substituents independently selected from the group consisting of C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and halogen; and, r is an integer of 1 to 5; such that r is greater than or equal to 4 when A_1 is C_{1-4}alkoxy;

s is an integer of 1 to 3;

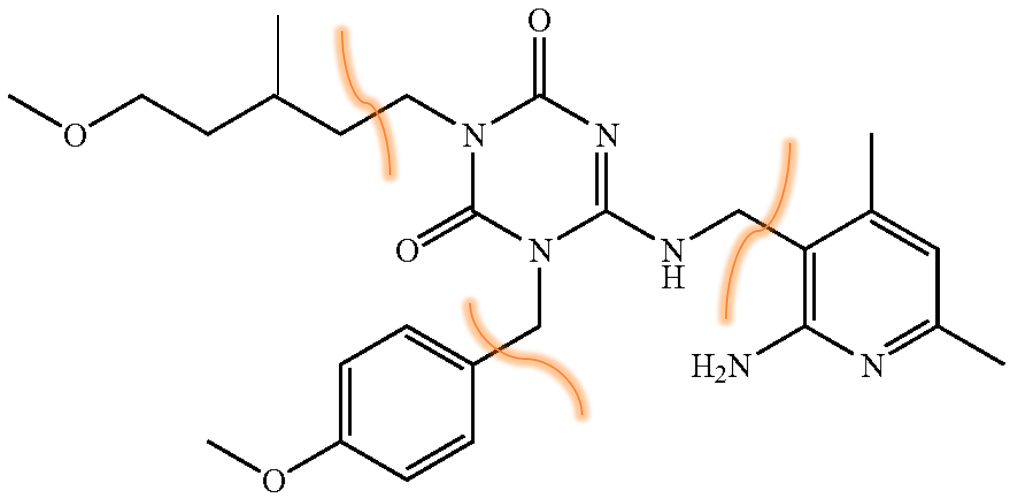
X is O or S;

D is —P-A_2;

wherein P is —$(CH_2)_{1-2}$— or —$CH_2CH{=}CH$— when A_2 is phenyl, benzofused heterocyclyl, heteroaryl, or C_{3-8}cycloalkyl; alternatively, P is —$(CH_2)_3$— when A_2 is hydrogen, C_{1-4}alkoxy, or C_{1-4}alkoxycarbonyl; and wherein P is optionally substituted with one to two substituents independently selected from the group consisting of C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, and halogen;

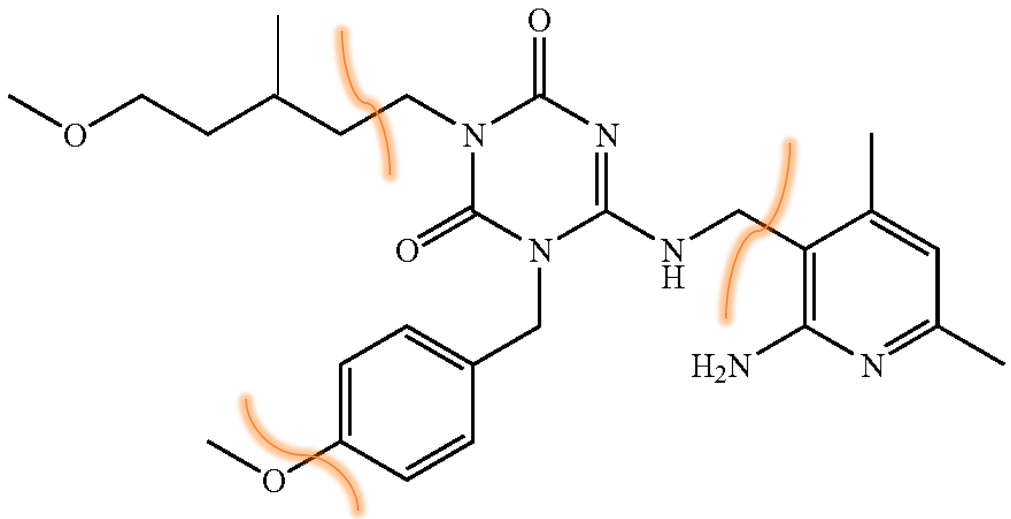
A_2 is hydrogen, C_{1-4}alkoxy, C_{1-4}alkoxycarbonyl, phenyl, benzofused heterocyclyl, heteroaryl, tetrahydro-pyranyl, piperidinyl, or C_{3-8}cycloalkyl; wherein phenyl, heteroaryl, the benzo portion of benzofused heterocyclyl, and C_{3-8}cycloalkyl are optionally substituted with one to three substituents independently selected from the

Truncate the scaffold



Cmpd 1

Do a variety of abbreviations



Cmpd 1

When designing compounds:

- Prior Art
  - Are my exact compounds known?
  - If not, are my compounds covered in a patent as prophetic examples?
  - If not, are my compounds obvious to one skilled in the art?
- Patent space
  - Are there an extremely large number of patents around my scaffold?
  - Will I be able to synthesize and patent a large number and diverse set of compounds?

Other thoughts:

- Search a number of abbreviated scaffolds
- If there are patent issues, think about structures that will create more novelty
  - Bioisosteres
  - Changes in ring size
  - New linkers
- Think about your scaffold and how it may be represented in a patent
  - A phenyl group – substituents are probably going to be covered

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