ChemAxon

Dóra Barna

HOW TO REACH THE HIDDEN WORLD OF CHEMISTRY IN PATENTS

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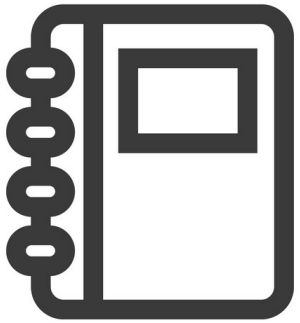
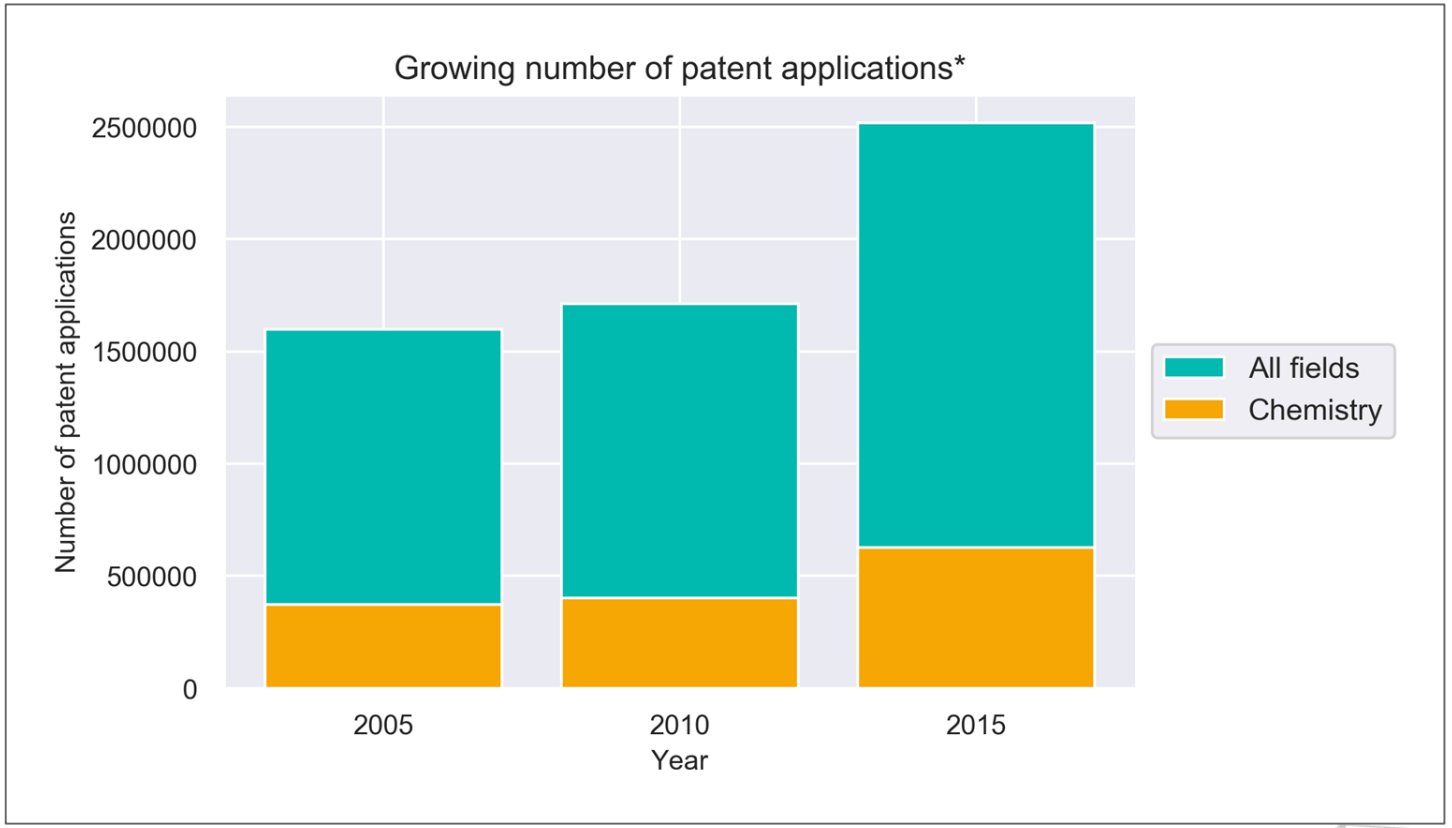
HOW TO REACH THE HIDDEN WORLD OF CHEMISTRY IN DOCUMENTS

THE PROBLEM





*World Intellectual Property Indicators 2017 Patents,
https://www.wipo.int/edocs/pubdocs/en/wipo_pub_941_2017-chapter2.pdf

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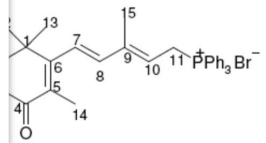
4–Oxo-β-ionylidene-ethyl-triphenylphosphonium bromide (38):

To a solution of PPh_3HBr (10.3 g, 28.6 mmol) in anhydrous methanol (100 mL) was added **36** (6.7 g, 28.6 mmol) in methanol (100 mL). After stirring for 75 h at room temp., the solvent was evaporated and **38** (10.57 g, 18.9 mmol, 66 %, lit.[30c] yield: 84 %) was obtained as a yellow solid. (m.p. 50 °C). The NMR spectra correspond to the



38

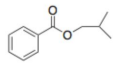
M⁺-Br].

cm⁻¹ (w), 1655 (s, C=O), 1588 (w),1480 (s), 1107 (s), 756

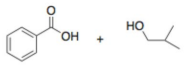
List of Schemes

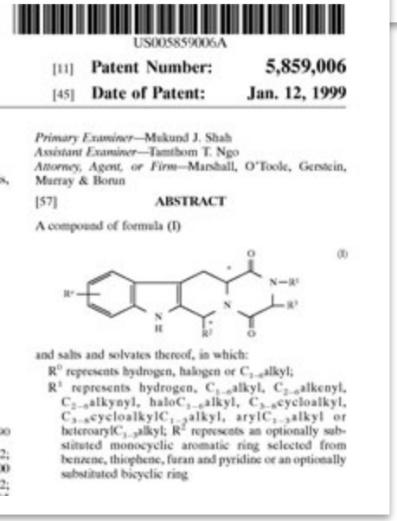
1 Background

Our research project requires a target ester, whose starting material requires 15 synthetic steps. We decided to optimize the conditions of this Fischer esterification by preparing a closely related analogue **3**. The starting materials in this model reaction is the readily available benzoic acid (**1**) and *i*-PrOH (**2**).



1





United States Patent [19]

[11] Patent Number: 5,859,006

[45] Date of Patent: Jan. 12, 1999

Primary Examiner—Mukund J. Shah
Assistant Examiner—Tamthom T. Ngo
Attorney, Agent, or Firm—Marshall, O'Toole, Gerstein, Murray & Borun

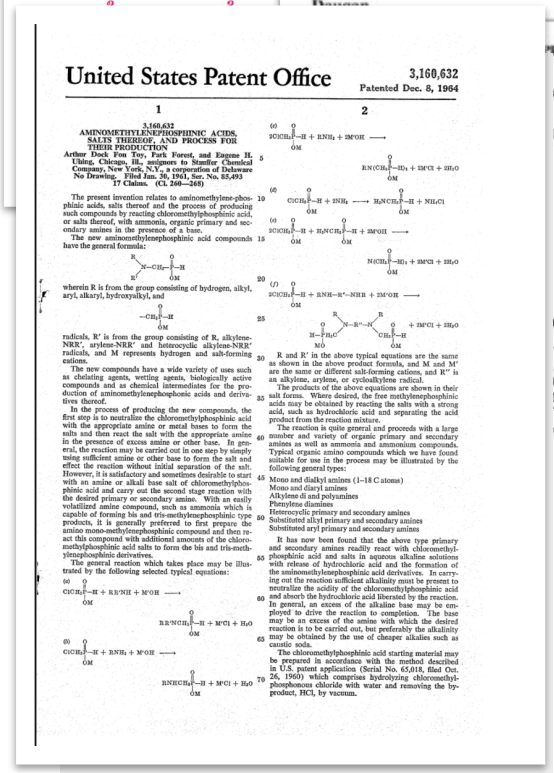
[57] ABSTRACT

A compound of formula (I)

and salts and solvates thereof, in which:

R^0 represents hydrogen, halogen or C_{1-6}alkyl;

R^1 represents hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, haloC_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-3}alkyl, arylC_{1-3}alkyl or heteroarylC_{1-3}alkyl; R^2 represents an optionally substituted monocyclic aromatic ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring



United States Patent Office 3,160,632 Patented Dec. 8, 1964

3,160,632
AMINOMETHYLENEPHOSPHINIC ACIDS, SALTS THEREOF, AND PROCESS FOR THEIR PRODUCTION
Arthur Dock Fox Toy, Park Forest, and Eugene H. Uhing, Chicago, Ill., assignors to Stauffer Chemical Company, New York, N.Y., a corporation of Delaware
No Drawing. Filed Jan. 26, 1961, Ser. No. 85,493
17 Claims. (Cl. 260—249)

The present invention relates to aminomethylene-phosphinic acids, salts thereof and the process of producing such compounds by reacting chloromethylphosphinic acid, or salts thereof, with ammonia, organic primary and secondary amines in the presence of a base.

The new aminomethylenephosphinic acid compounds have the general formula:

wherein R is from the group consisting of hydrogen, alkyl, aryl, alkaryl, hydroxyalkyl, and

radicals, R' is from the group consisting of R, alkylene-NRR', arylene-NRR' and heterocyclic alkylene-NRR' radicals, and M represents hydrogen and salt-forming cations.

The new compounds have a wide variety of uses such as chelating agents, wetting agents, biologically active compounds and as chemical intermediates for the production of aminomethylenephosphonic acids and derivatives thereof.

In the process of producing the new compounds, the first step is to neutralize the chloromethylphosphinic acid with the appropriate amine or metal bases to form the salts and then react the salt with the appropriate amine in the presence of excess amine or other base. In general, the reaction may be carried out in one step by simply using sufficient amine or other base to form the salt and effect the reaction without initial separation of the salt. However, it is satisfactory and sometimes desirable to start with an amine or alkali base salt of chloromethylphosphinic acid and carry out the second stage reaction with the desired primary or secondary amine. With an easily volatilized amine compound, such as ammonia which is capable of forming bis and tris-methylenephosphinic type products, it is generally preferred to first prepare the amino mono-methylenephosphinic compound and then react this compound with additional amounts of the chloromethylphosphinic acid salts to form the bis and tris-methylenephosphinic derivatives.

The general reaction which takes place may be illustrated by the following selected typical equations:

2

R and R' in the above typical equations are the same as shown in the above product formula, and M and M' are the same or different salt-forming cations, and R'' is an alkylene, arylene, or cycloalkylene radical.

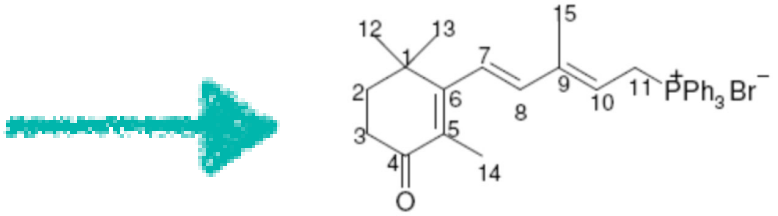
The products of the above equations are shown in their salt forms. Where desired, the free methylenephosphinic acids may be obtained by reacting the salts with a strong acid, such as hydrochloric acid and separating the acid product from the reaction mixture.

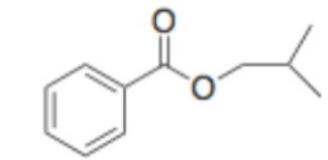
The reaction is quite general and proceeds with a large number and variety of organic primary and secondary amines as well as ammonia and ammonium compounds. Typical organic amino compounds which we have found suitable for use in the process may be illustrated by the following general types:

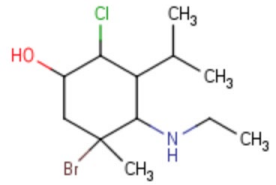
Mono and dialkyl amines (1–18 C atoms)
Mono and diaryl amines
Alkylene di and polyamines
Phenylene diamines
Heterocyclic primary and secondary amines
Substituted alkyl primary and secondary amines
Substituted aryl primary and secondary amines

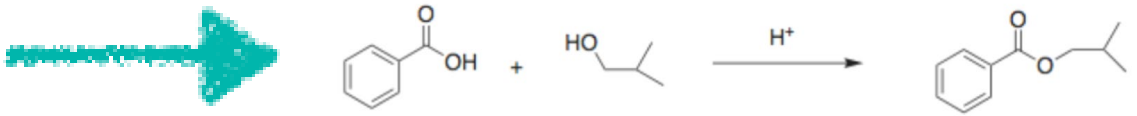
It has now been found that the above type primary and secondary amines readily react with chloromethylphosphinic acid and salts in aqueous alkaline solutions with release of hydrochloric acid and the formation of the aminomethylenephosphinic acid derivatives. In carrying out the reaction sufficient alkalinity must be present to neutralize the acidity of the chloromethylphosphinic acid and absorb the hydrochloric acid liberated by the reaction. In general, an excess of the alkaline base may be employed to drive the reaction to completion. The base may be an excess of the amine with which the desired reaction is to be carried out, but preferably the alkalinity may be obtained by the use of cheaper alkalies such as caustic soda.

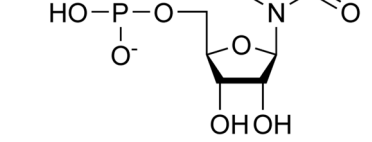
The chloromethylphosphinic acid starting material may be prepared in accordance with the method described in U.S. patent application (Serial No. 65,018, filed Oct. 26, 1960) which comprises hydrolyzing chloromethylphosphonous chloride with water and removing the by-product, HCl, by vacuum.











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UNSTRUCTURED → STRUCTURED

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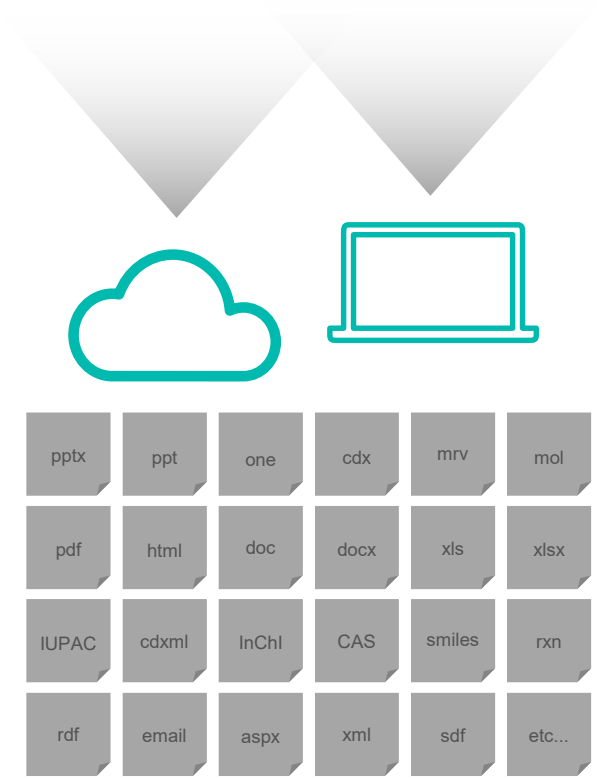
CHEMLOCATOR

Aspirin, also known as acetylsalicylic acid (ASA), is a medication used to treat pain, fever, or inflammation.[4] Specific inflammatory conditions in which aspirin is used include Kawasaki disease, pericarditis, and rheumatic fever.[4] Aspirin given …



ChemAxon Naming + Free text indexing + Semantic indexing

Chemical NER*

OCR

OSR

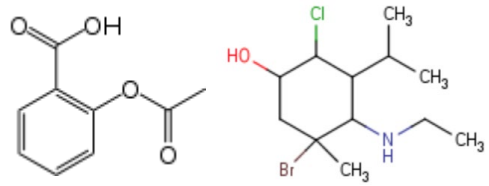
Metadata extraction

Tagging

Keywords

Biological NER

etc.



***NER:** Named Entity Recognition

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24,000 patent documents

- From the **USPTO** patent database
- Medicinal chemistry patents from 2015

AN EXPERIMENT

Processing

- Indexing time: 7.08 days
- Chemical database: 13.5 GB
- Elastic database: 25 GB

771,000 unique molecules

- exact molecules: 740,000
- fragments: 23,000
- generic structures: 8,800

3.1 million molecules in total

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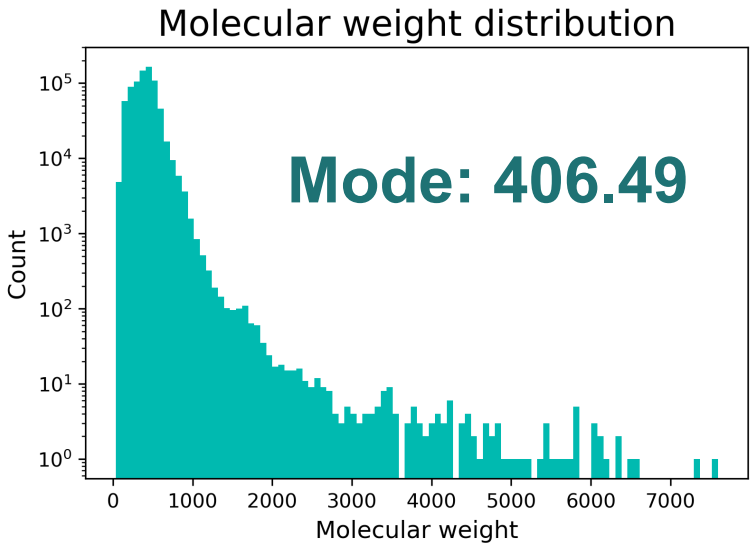
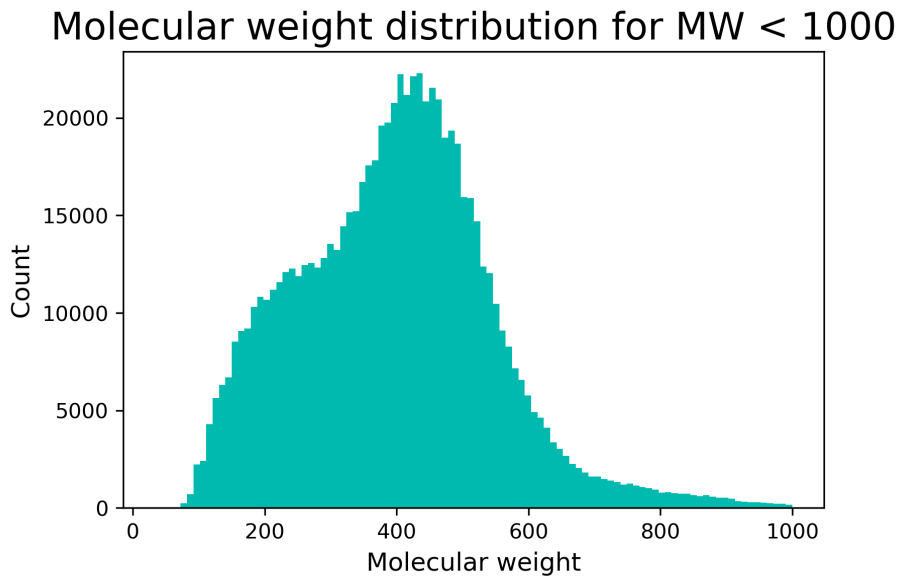
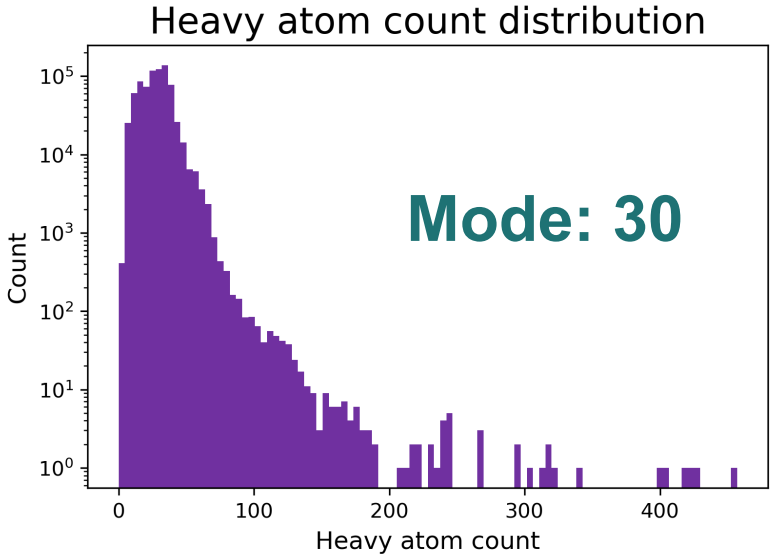
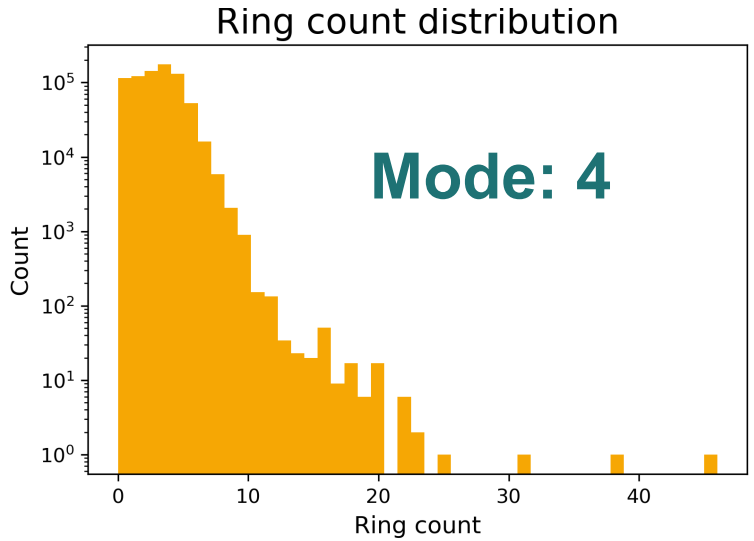
CHEMICAL SPACE – BASIC PROPERTIES



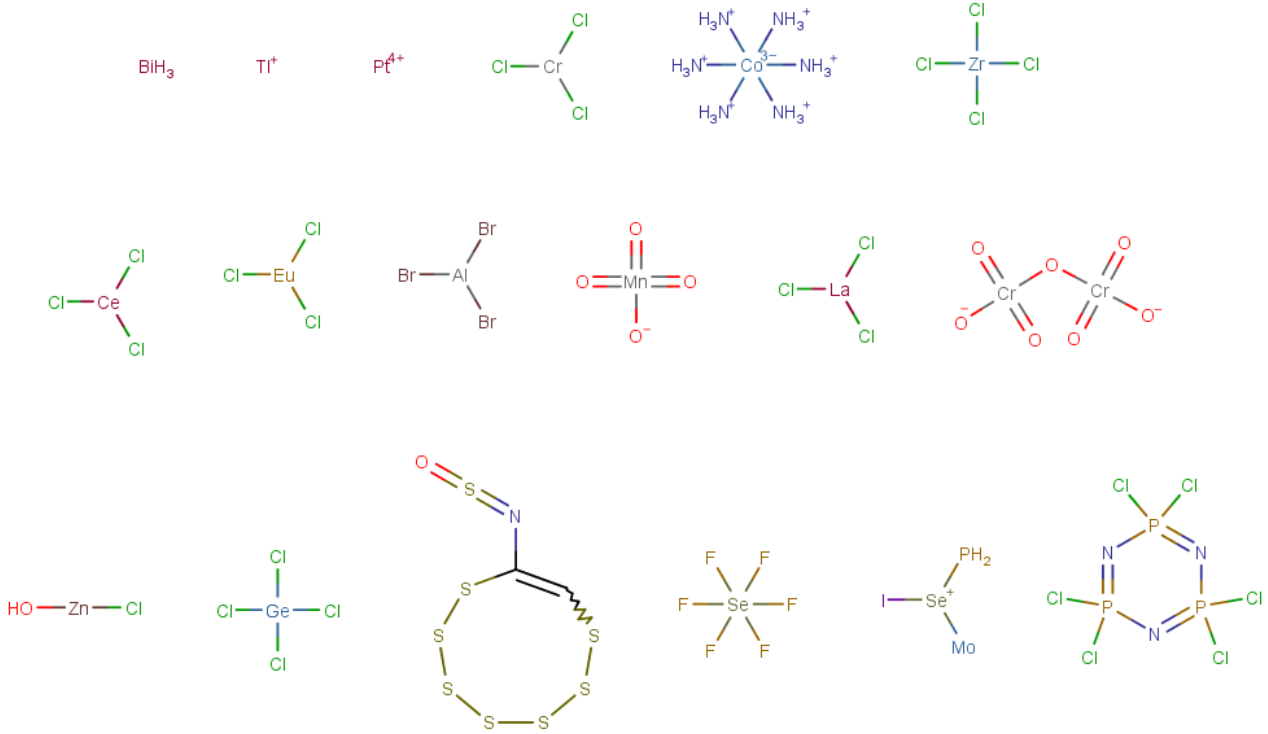


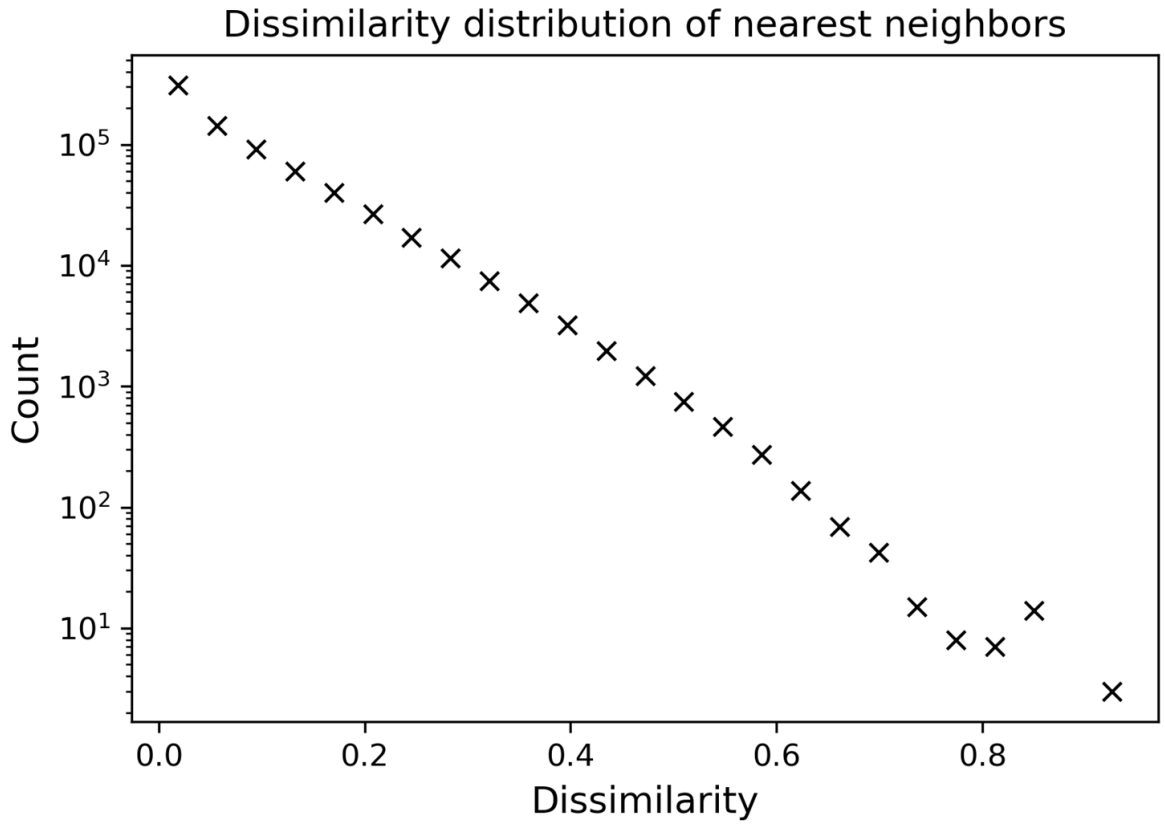




CHEMICAL SPACE – STRUCTURAL SIMILARITY

- 50% of the molecules had its most similar pair within 0.05 dissimilarity;
- Molecules that are very different from their nearest neighbors:





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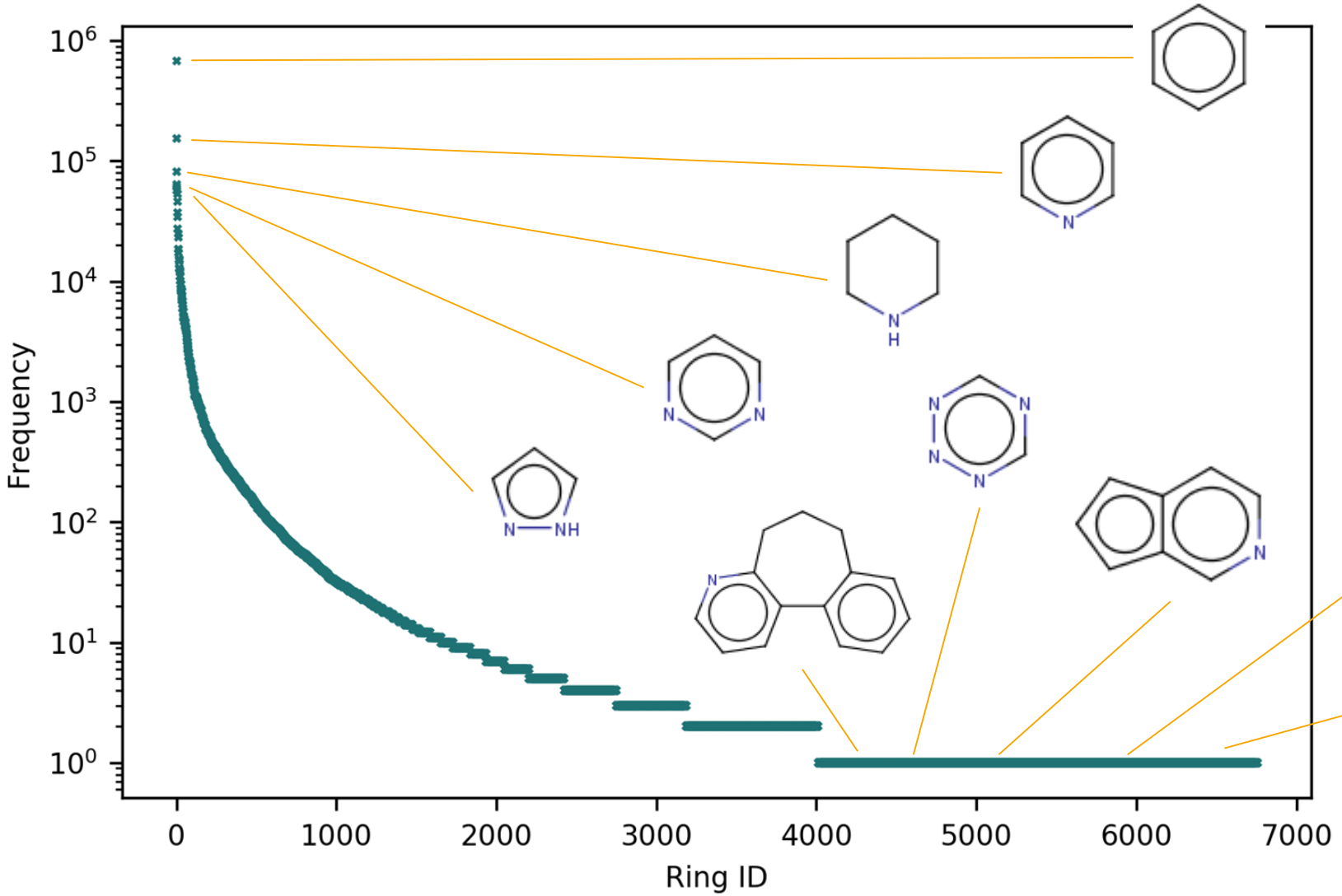
CHEMICAL SPACE – TYPICAL RING SYSTEMS



- 6756 different ring systems;
- 2745 rings occur only once;

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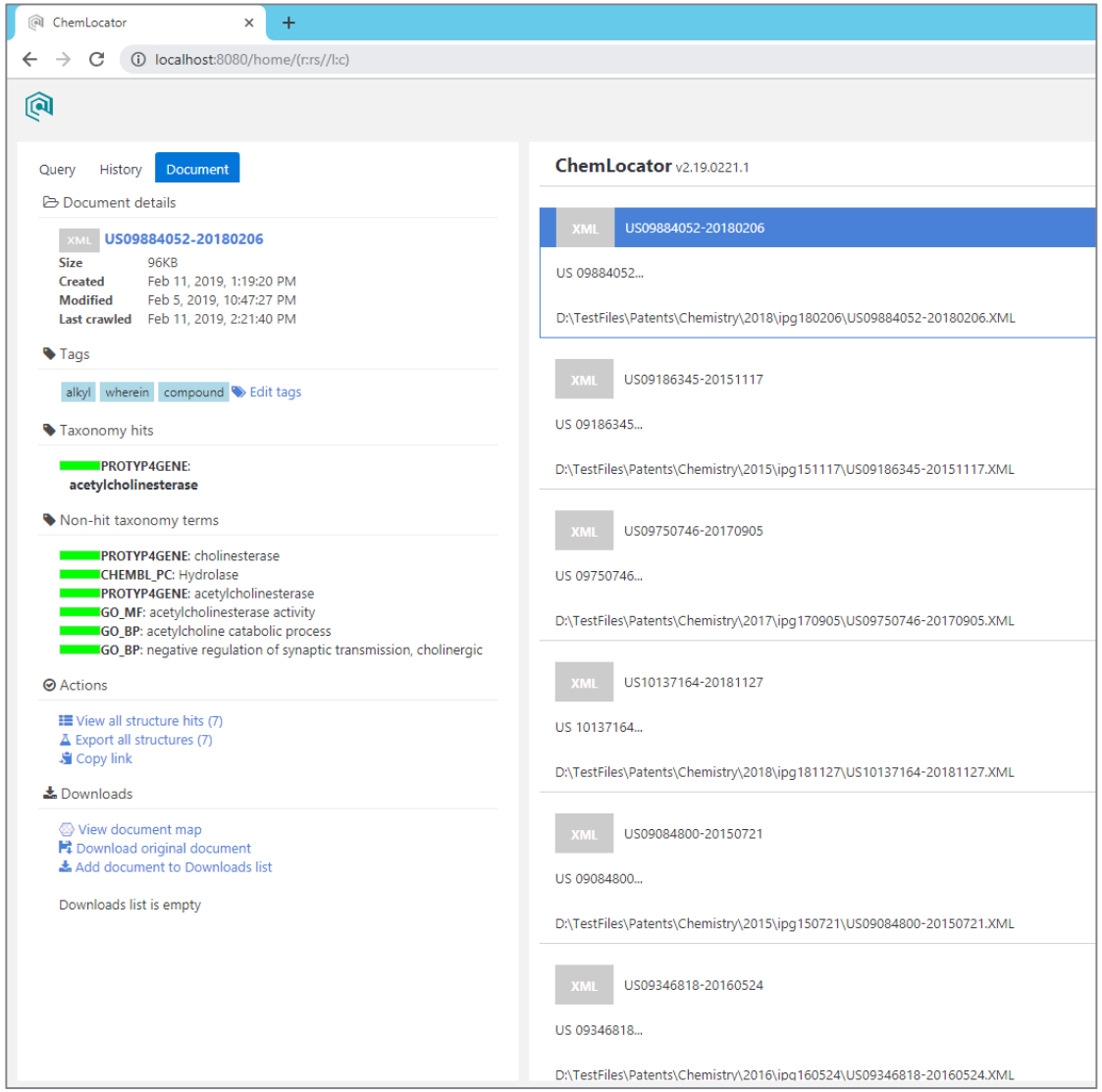
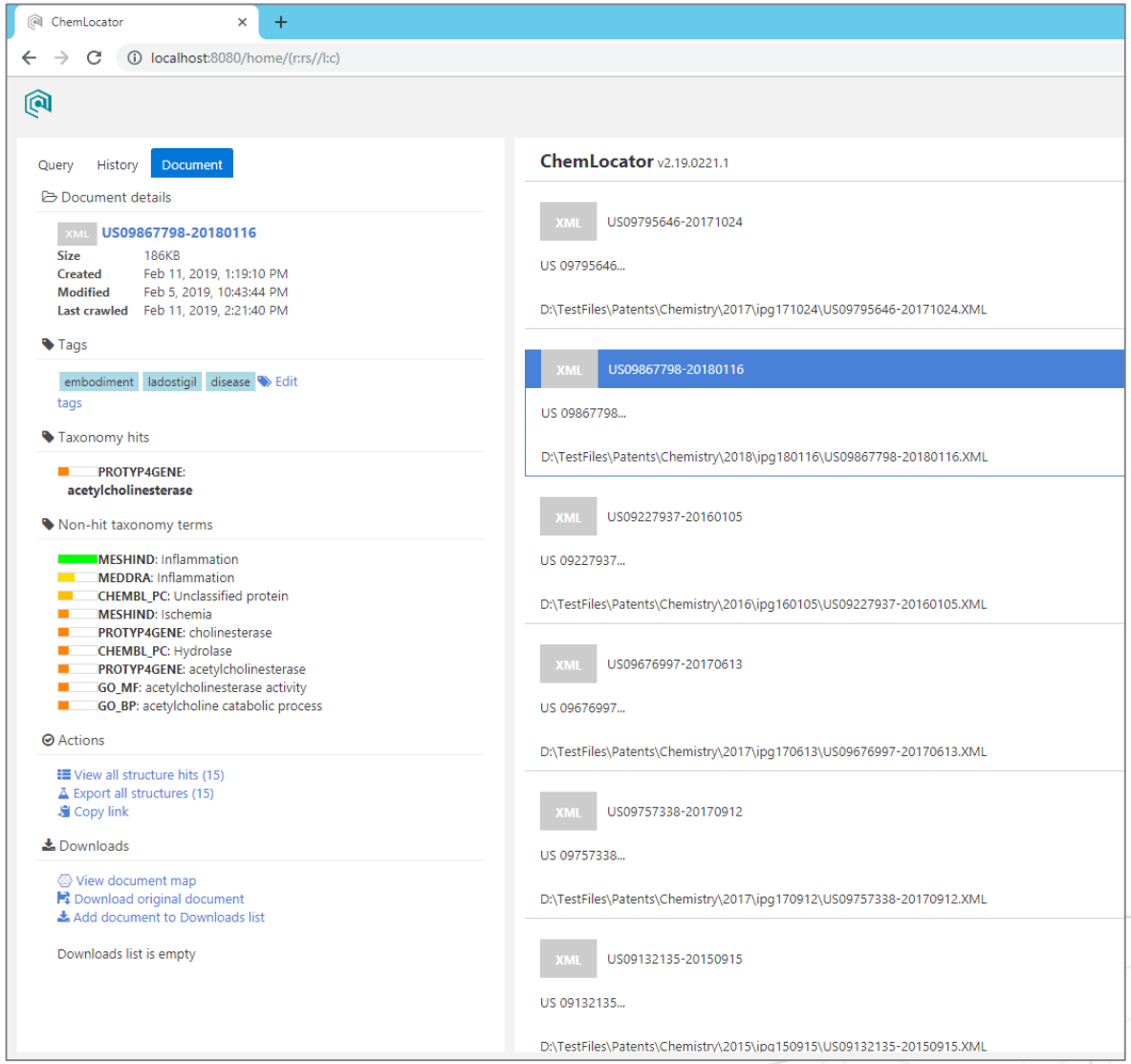
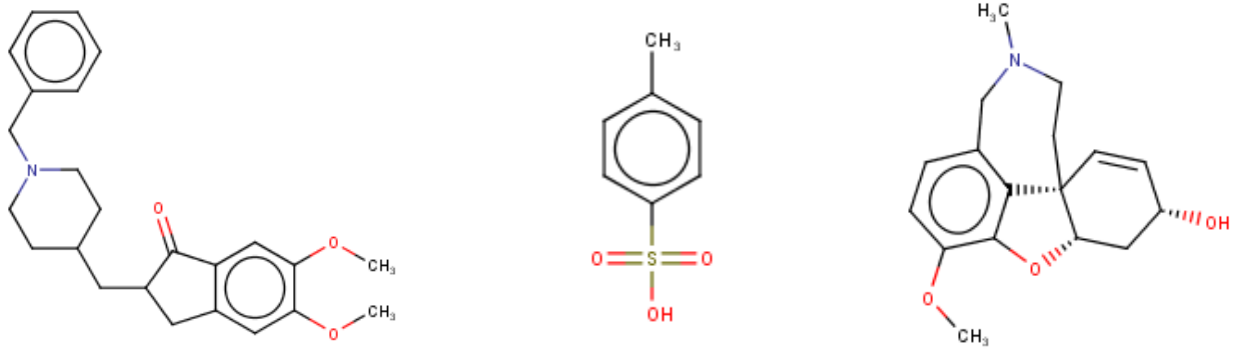
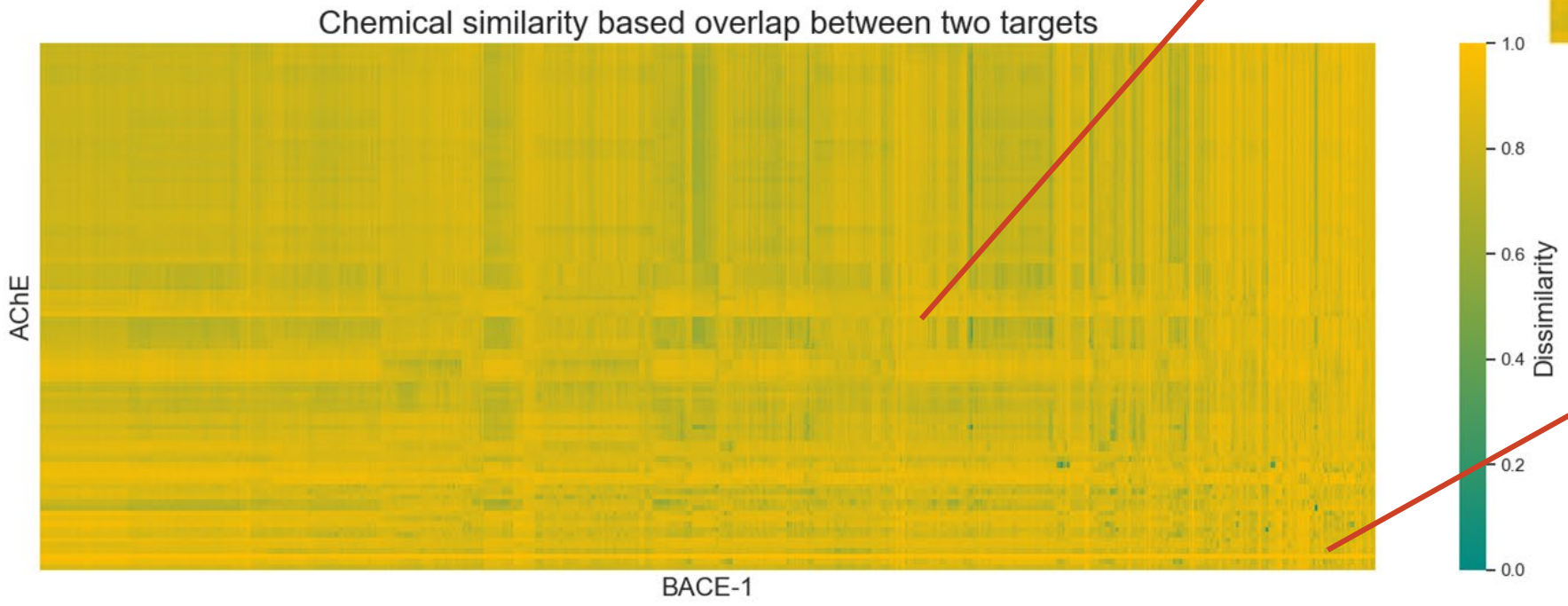
CHEMICAL SPACE OVERLAP OF TWO TARGETS 1.

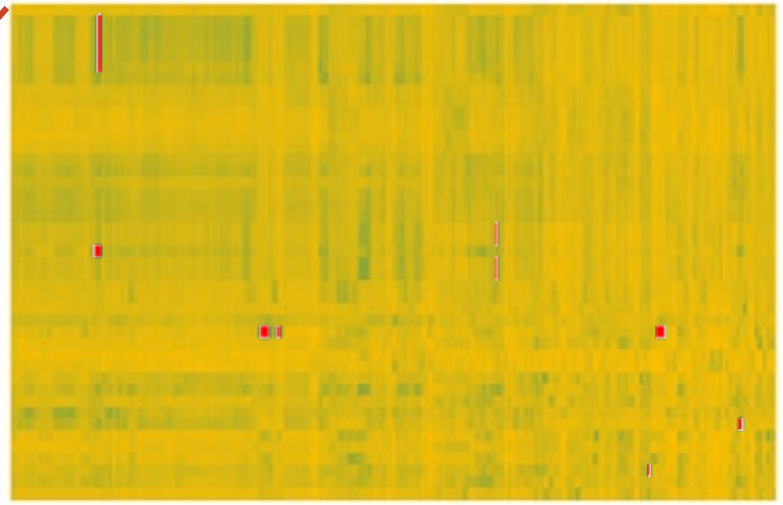




CHEMICAL SPACE OVERLAP OF TWO TARGETS 2.







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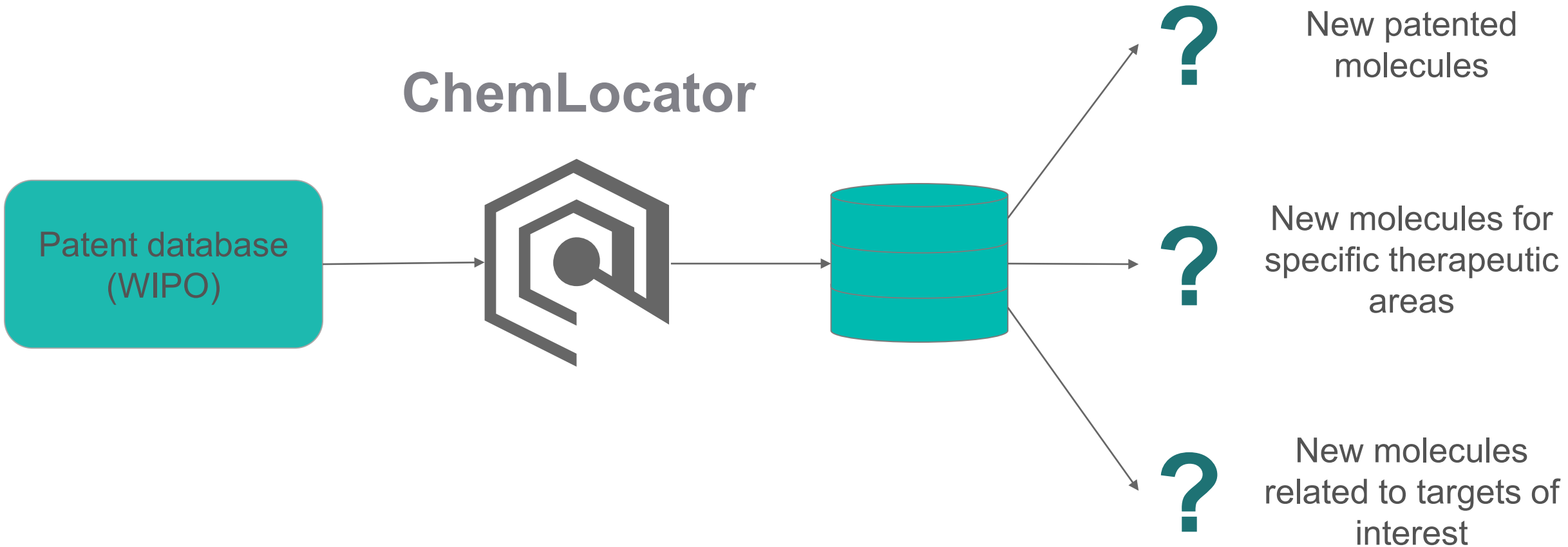
UP-TO-DATE INFORMATION AUTOMATICALLY



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Thank you

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