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IT SOLUTIONS

Classifying Compounds in Public Databases

ACS San Diego, March 15, 2016

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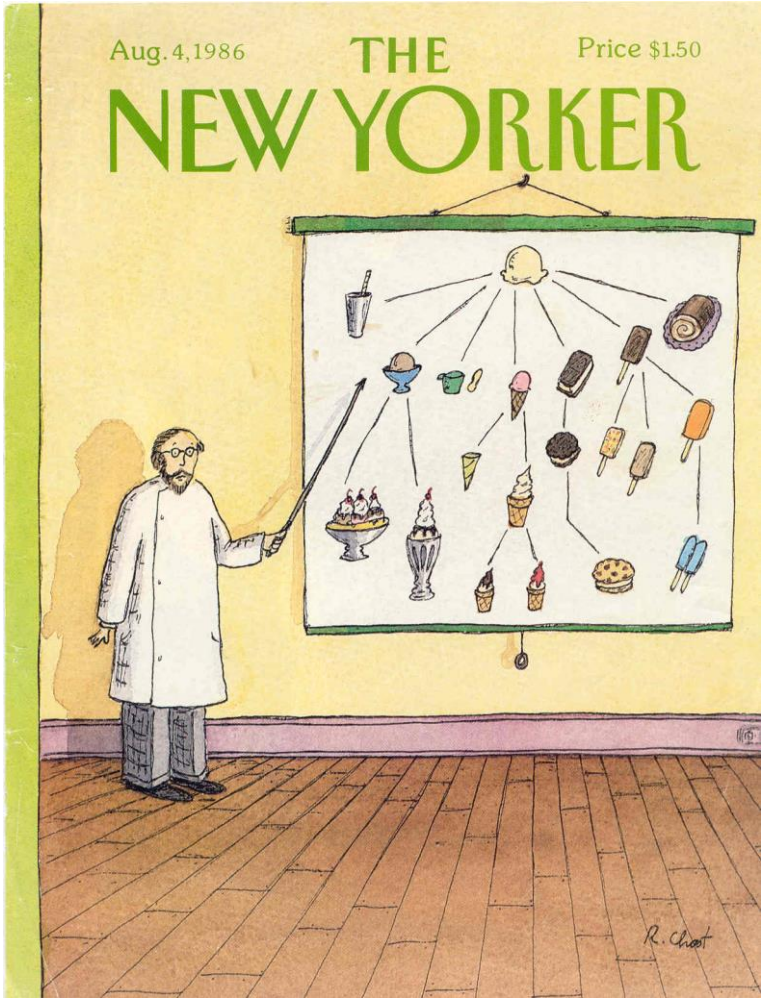
Background

Ontology… *is a formal naming and definition of the types, properties, and relationships of the entities for a particular domain of discourse.*



http://www.cse.buffalo.edu/~rapaport/676/F01/icecreamontology.jpg
William J. Rapaport

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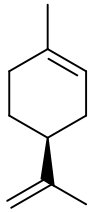
Ontology...

Why in chemistry ?

Organizing knowledge

e.g. terpenes are made of x times 5 carbon isoprene units



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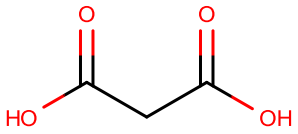
Ontology...

Why in chemistry ?

Organizing knowledge

Conserving old knowledge

what are dicarboxylic acids?



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Ontology...

Why in chemistry ?

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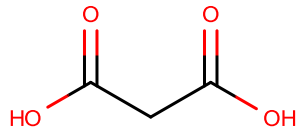
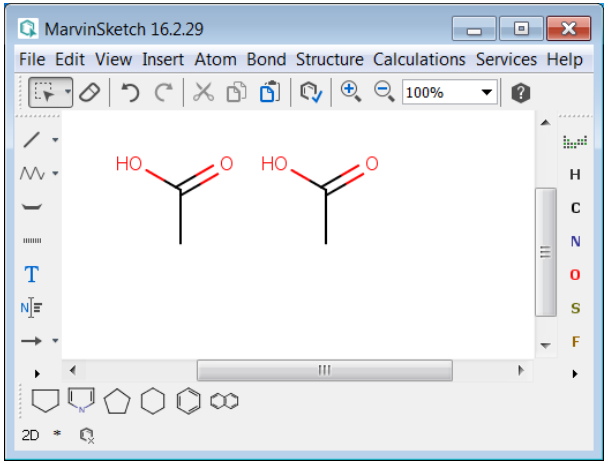
what are dicarboxylic acids?



is_a: dicarboxylic acid

ontology



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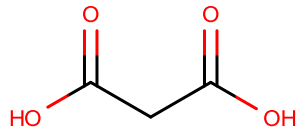
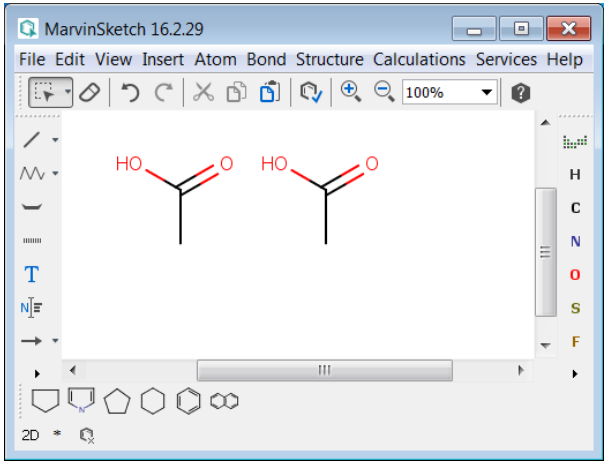
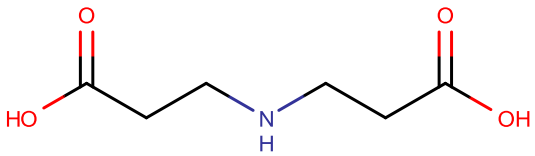


is_a: dicarboxylic acid

ontology





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Ontology...

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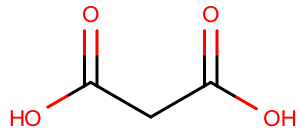
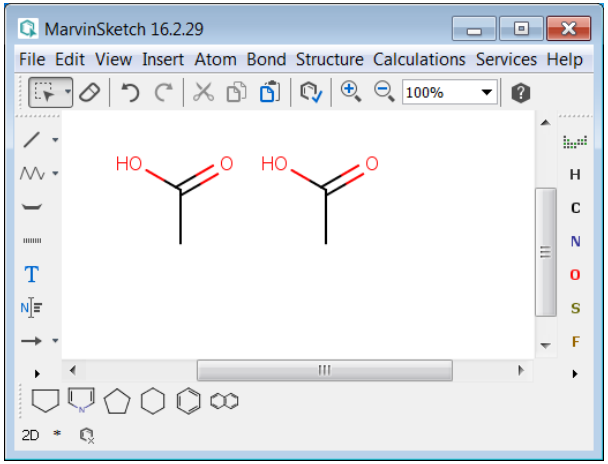
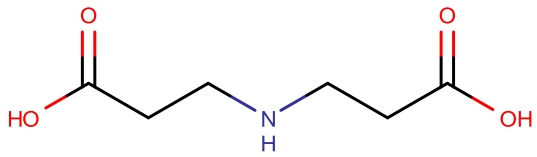


is_a: dicarboxylic acid

ontology





is_part: 2 carboxylic acid moieties

„partology“ (Bolton, Hastings)
SSS based

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Ontology…

Why in chemistry ?

- Organizing knowledge
- Conserving old knowledge
- Transporting our knowledge
  - e.g. teaching humans and computers
- Using our knowledge
  - e.g. data mining, property predictions, knowledge inference,
  - … creating new products

...need to build on common rules

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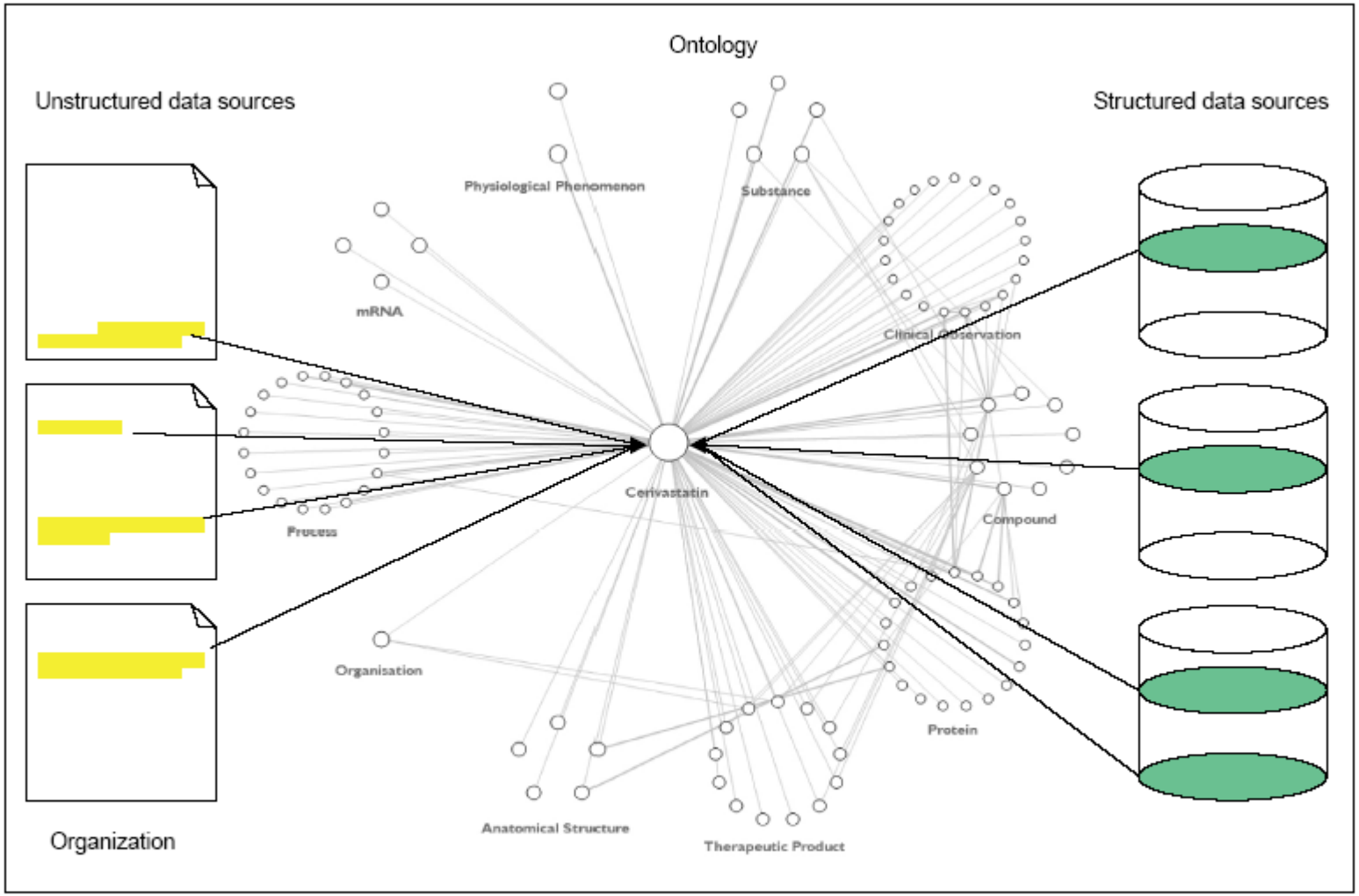

FIGURE 2

Granular semantic data integration using an ontology. An ontology can be used as a semantic middle layer to map references semantically to the same concepts among multiple data sources. In the example shown, the concept 'Cerivastatin' in the ontology is used as a consistent marker to connect data from multiple structured and unstructured data sources that refer to 'Cerivastatin', 'Baycol' or other equivalent terms.

Source: Gardner, S. (2005) Ontologies and semantic data integration. *DDT* 10(14) 1004

SODIAC: Automated Classifications

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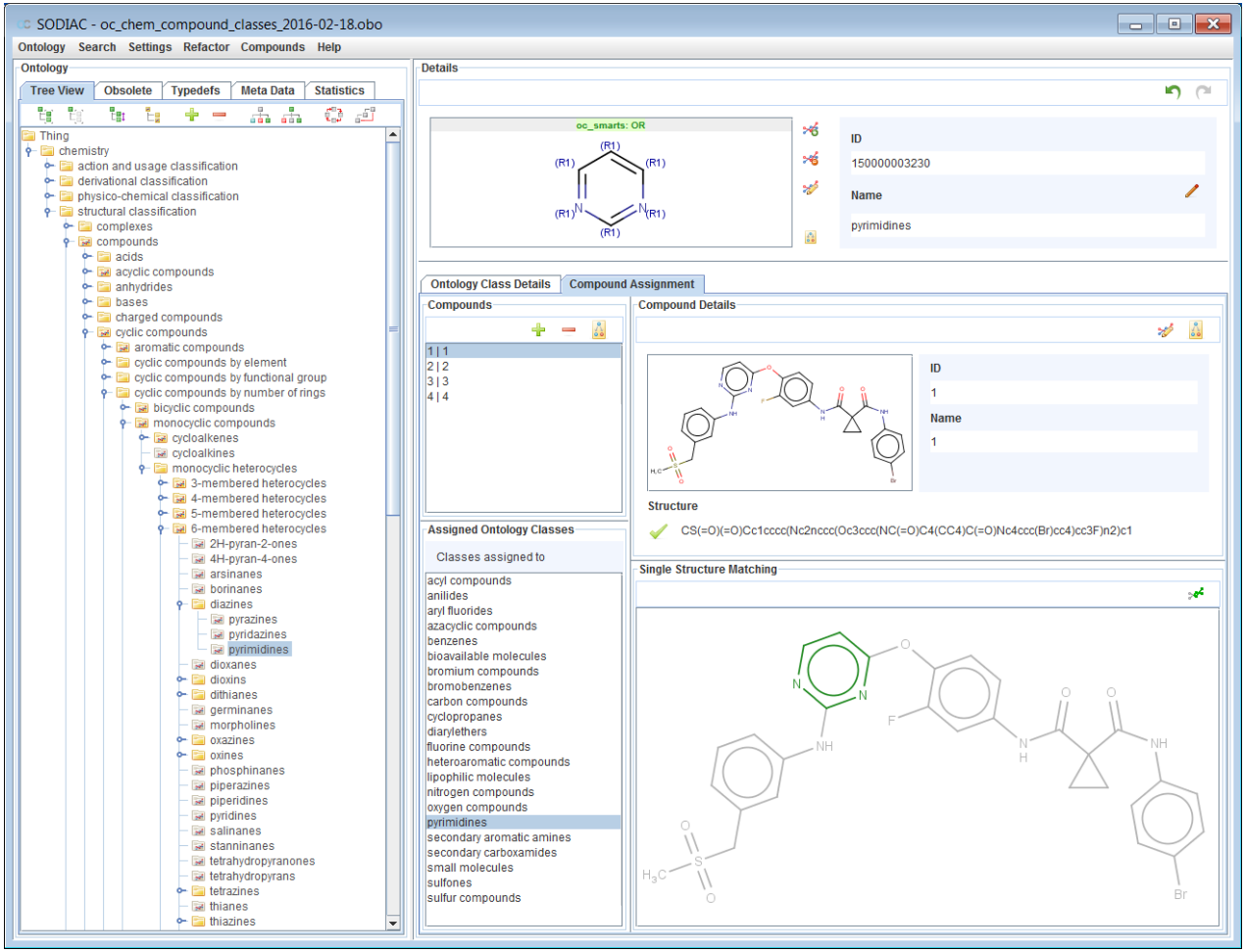
Assignment of organic compounds in structure files, databases, documents

Organic Chemistry:

7,916 class concepts

32,469 synonyms

4,698 SMARTS concepts



SODIAC: Automated Classifications

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Assignment of compounds in structure files, databases, documents

SMARTS based

e.g. alkylbromides

[C;\!$(C=[O,S,N,P])]Br

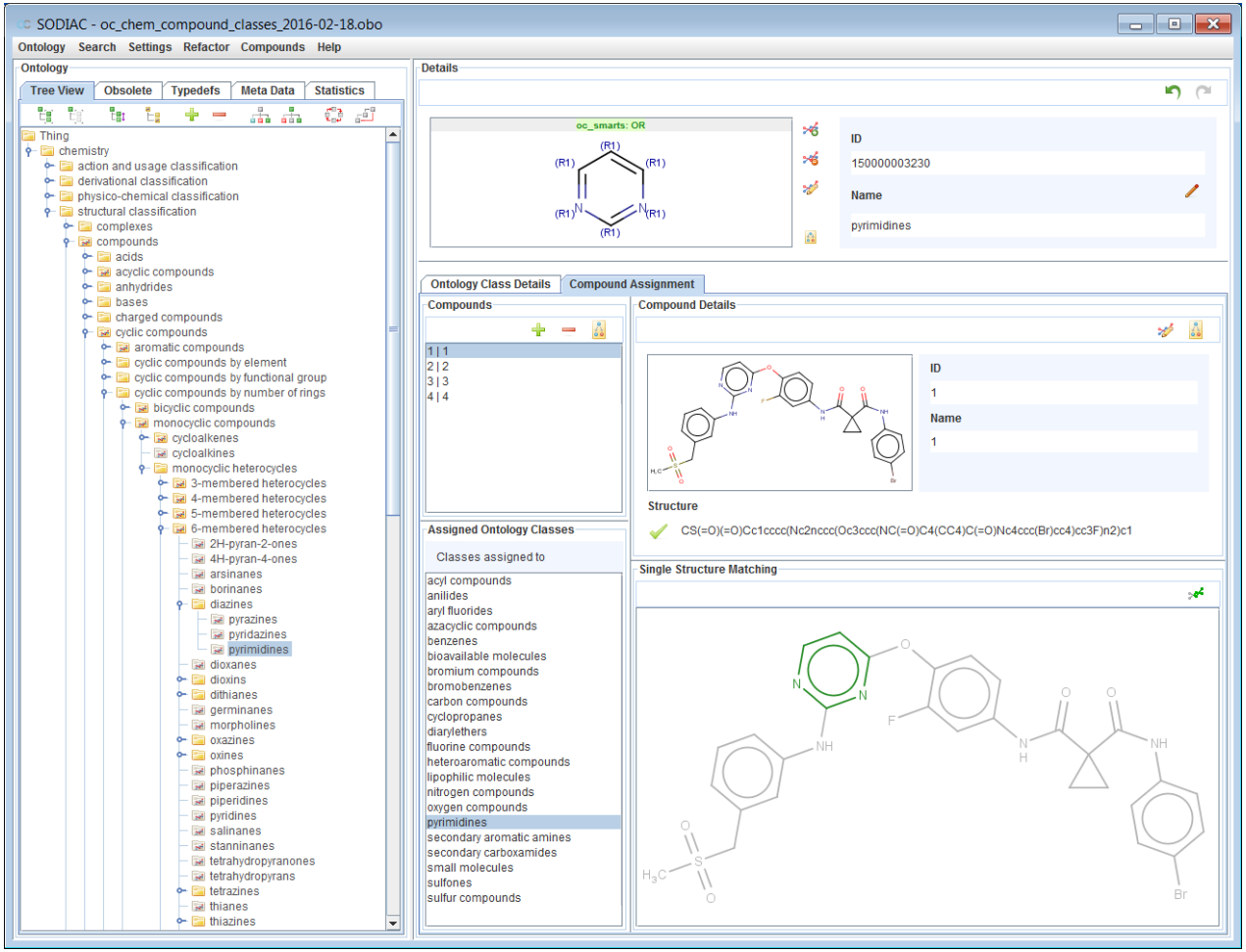
D. Weininger

AND, OR, NOT logic

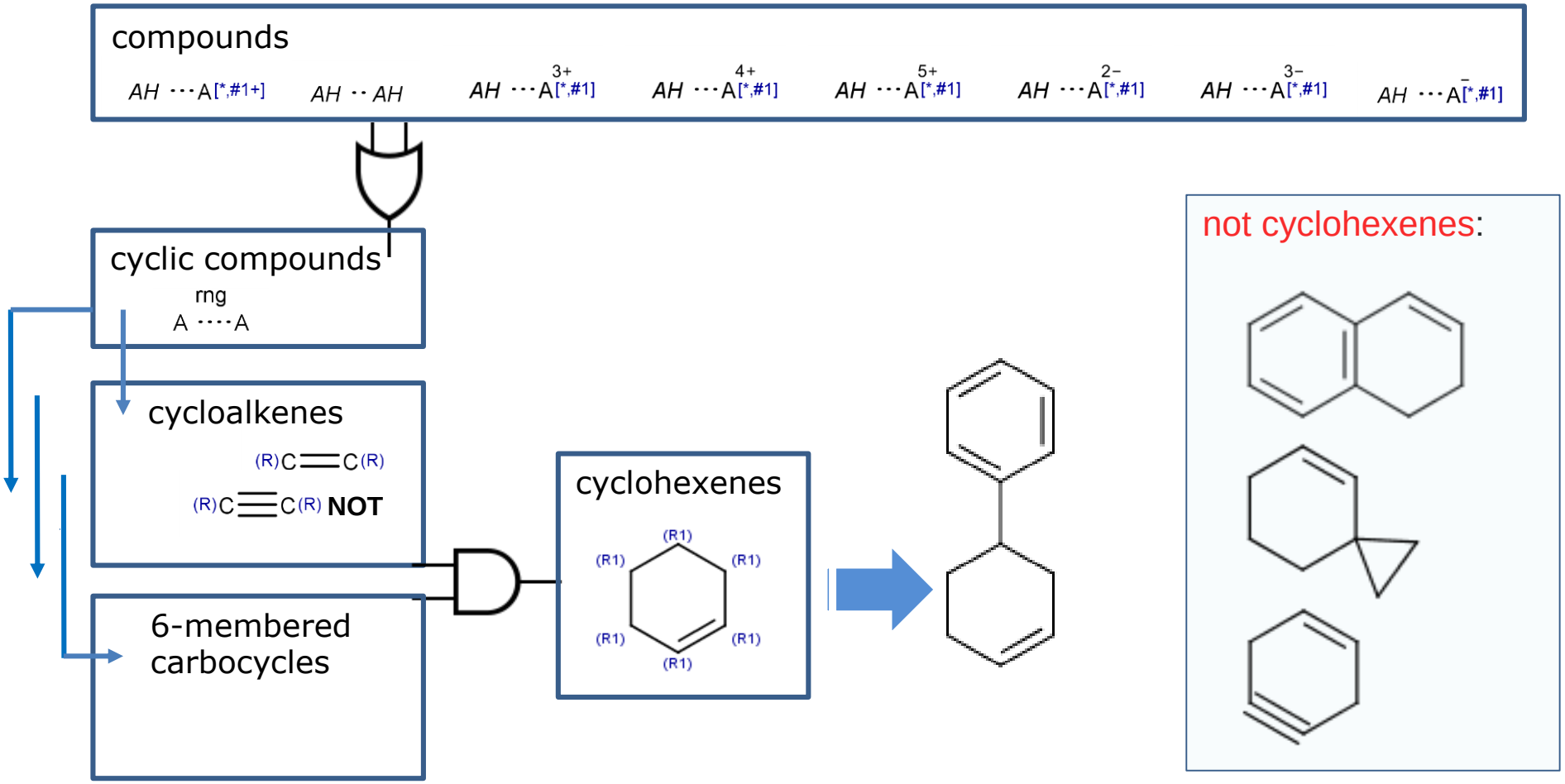
e.g. AND NOT for alkenes:

C=C
!c:c

OR



using SMARTS filters with AND, OR & NOT – a *hierarchical state machine* on DB



Quality of Classifications ?

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Testing **Sodiac** by annotating public databases:

- **ChEBI** (from E. Bolton, PubChem, March 1, 2016): 42,055 compounds
- **MeSH** (from E. Bolton, PubChem, March 1, 2016): 116,542 compounds
- **ChEMBL** (from Steve Boyer, IBM, February 2, 2016): 1,456,019 compounds
- **PubChem** (downloaded Sept. 2015, PubChem): 68,420,615 compounds

  performance: takes 6 hours to load db, takes 4h to assign classes
- **Patent** full text documents: >90 million full text documents

ChEBI Classifications

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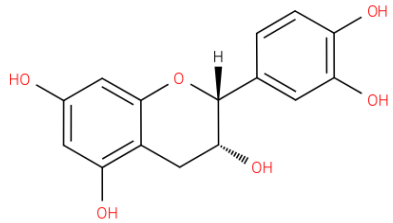
ChEBI

- Manually curated, can we do it automatically ?
- Can we recognize the correct ChEBI parent ID for a compound ?
  - 61,904 ChEBI concepts in total, 3,584 ChEBI concepts contain a * in a SMILES
  - 45,748 ChEBI concepts are compounds with SMILES, 44,355 after cleaning

Assignment

1,164 ChEBI compounds are present as scaffold concepts in SODIAC as well,
e.g. CHEBI:90 (-)-epicatechin



ChEBI Classifications

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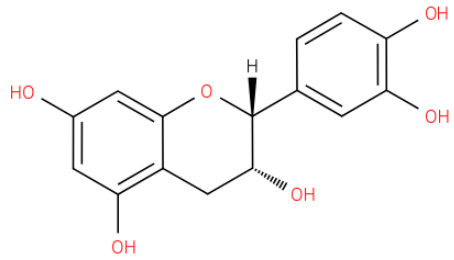
Assignment of ChEBI concepts

CHEBI:90 (-)-epicatechin



is_a catechin (CHEBI:23053)

is_a polyphenol (CHEBI:26195)

has_role antioxidant (CHEBI:22586)

is_enantiomer_of (+)-epicatechin (CHEBI:76125)

SODIAC:150000000071 (-)-epicatechin

is_a (-)-epicatechin derivatives; alkylarylethers; aromatic compounds; carbon compounds; chromanes; oxacyclic compounds; oxygen compounds; polyols; **pyrocatechols**; secondary alcohols; triols;

ChEBI Classifications

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ChEBI – SODIAC (ChEBI) matches:

ChEBI

1,888 ChEBI parent concepts have been assigned to the **Test Set** of **1,164 ChEBI** compounds (avg 1.62 parent classes / compound)

SODIAC

1,056 ChEBI parents were assigned by SODIAC from 1,888 ***is_a*** ChEBI parents = 56%

832 ChEBI concepts not found as they are not represented in SODIAC

29,833 SODIAC classes assigned to 1,164 ChEBI compounds (avg. 26 classes/compound)

14,476 ChEBI concepts found by SODIAC that were not assigned as parents

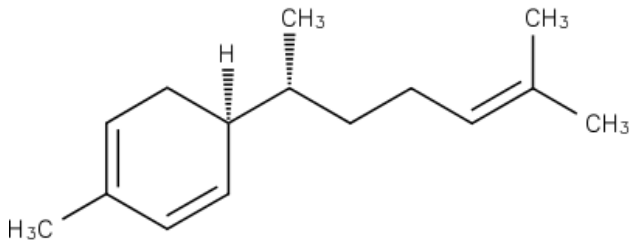
ChEBI Classifications

ChEBI – SODIAC (ChEBI) matches: CHEBI:583099 ent-zingiberene

ChEBI: ***is_a*** sesquiterpene (CHEBI:35189)

SODIAC: 16 new proposals:

CHEBI:33654 **alicyclic compound**
CHEBI:33653 **aliphatic compound**
CHEBI:32878
CHEBI:36480
CHEBI:33598
CHEBI:33595
CHEBI:33643
CHEBI:33646 **alkadiene**
CHEBI:24632
CHEBI:18059
CHEBI:33661
CHEBI:35187
CHEBI:50073 **p-menthadiene**
CHEBI:25826
CHEBI:50034
CHEBI:35186



ChEBI Classifications

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ChEBI – SODIAC (ChEBI)

cyclobutane (CHEBI:30377) ***is_a*** cycloalkane (CHEBI:23453)

cyclohexane (CHEBI:29005) ***is_a*** cycloalkane (CHEBI:23453)

cyclopentane (CHEBI:23492) ***is_a*** cycloalkane (CHEBI:23453)

cyclopentane (CHEBI:23492) ***is_a*** cyclopentanes (CHEBI:23493)

…. automation could help to eliminate human inconsistencies

Ontology Matching & Merging

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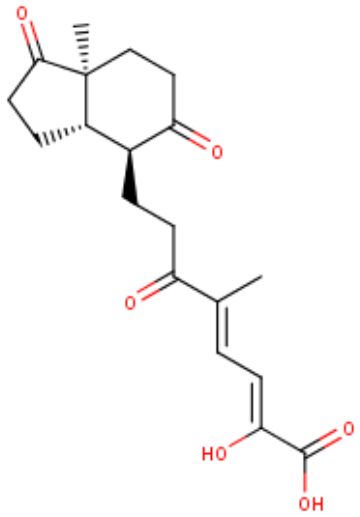
SODIAC coverage from 7,916 compound class concepts in common:

ChEBI: 3,468 (of 16,156) **MeSH**: 2,570 (of 3,943) **ClassyFire**: 483 (of 4,832)

Next steps: complete overlap with ChEBI and MeSH



pubchem_ID
25244777

SODIAC parents	SODIAC_xrefs	ClassyFire parents	ClassyFire_xref
4,5:9,10-diseco-androstenes; acyclic ketones; alkene; bicyclic compounds; carbocycles; carbon compounds; carboxylic acids; cyclic ketones; dienes; oxygen compounds;	CHEBI:32878; MeSH:D000475; CHEBI:33636; CHEBI:33575; MeSH:D002264; CHEBI:3992; CHEBI:33646; MeSH:D000466; MeSH:D017601;	Medium-chain keto acids and derivatives; Hydroxy fatty acids; Branched fatty acids; Unsaturated fatty acids; Alpha-branched alpha,beta-unsaturated ketones; Enones; Acryloyl compounds; Cyclic ketones; Monocarboxylic acids and derivatives; Enols; Carboxylic acids; Organic oxides; Hydrocarbon derivatives	CHEBI:25754; CHEBI:24654; CHEBI:35819; CHEBI:27208; CHEBI:51689; CHEBI:51689; CHEBI:78840; CHEBI:3992; CHEBI:25384; CHEBI:33823; CHEBI:33575; CHEBI:25701; CHEBI:72695

SODIAC / ClassyFire top-bottom statistics

SODIAC_ID	SODIAC_name	count	ClassyFire_ID	ClassyFire_name	count	difference
OC:150000001336	alkene	8781	CHEMONTID:0002501	Alkenes	0	8781
OC:150000001344	alkene derivatives	4910	CHEMONTID:0002501	Alkenes	0	4910
OC:150000002891	organic anions	7219	CHEMONTID:0003608	Organic anions	4481	2738
OC:150000003997	cyclic ketones	3945	CHEMONTID:0003487	Cyclic ketones	1433	2512
OC:150000003142	primary aromatic amines	2606	CHEMONTID:0002453	Primary aromatic amines	101	2505
OC:150000001993	dienes	2487	CHEMONTID:0001019	Alkadienes	0	2487
OC:150000003333	secondary alcohols	17455	CHEMONTID:0001661	Secondary alcohols	15293	2162
OC:150000002989	phenols	1714	CHEMONTID:0000134	Phenols	256	1458
OC:150000003335	secondary amines	1389	CHEMONTID:0002451	Secondary amines	99	1290
OC:150000002484	inorganic compounds	1251	CHEMONTID:0000001	Inorganic compounds	0	1251
OC:150000003568	thioethers	1132	CHEMONTID:0001202	Thioethers	0	1132
OC:150000003231	pyrocatechols	1642	CHEMONTID:0000135	Catechols	713	929
OC:159000000021	acetate salts	8	CHEMONTID:0003919	Acetate salts	1459	-1451
OC:150000001734	carboxylic acid salts	1090	CHEMONTID:0001166	Carboxylic acid salts	3141	-2051
OC:150000002341	glycosylamines	41	CHEMONTID:0002203	Glycosylamines	2402	-2361
OC:150000003527	tetrahydropyrans	4079	CHEMONTID:0002012	Oxanes	6583	-2504
OC:150000003141	primary amines	45	CHEMONTID:0002450	Primary amines	2980	-2935
OC:150000001241	acetals	1588	CHEMONTID:0001656	Acetals	4947	-3359
OC:150000001735	carboxylic acids	5969	CHEMONTID:0001205	Carboxylic acids	11204	-5235
OC:150000004030	azacyclic compounds	6174	CHEMONTID:0004139	Azacyclic compounds	11970	-5796
OC:150000001728	carbonyl compounds	1335	CHEMONTID:0001831	Carbonyl compounds	18235	-16900

PubChem Classifications

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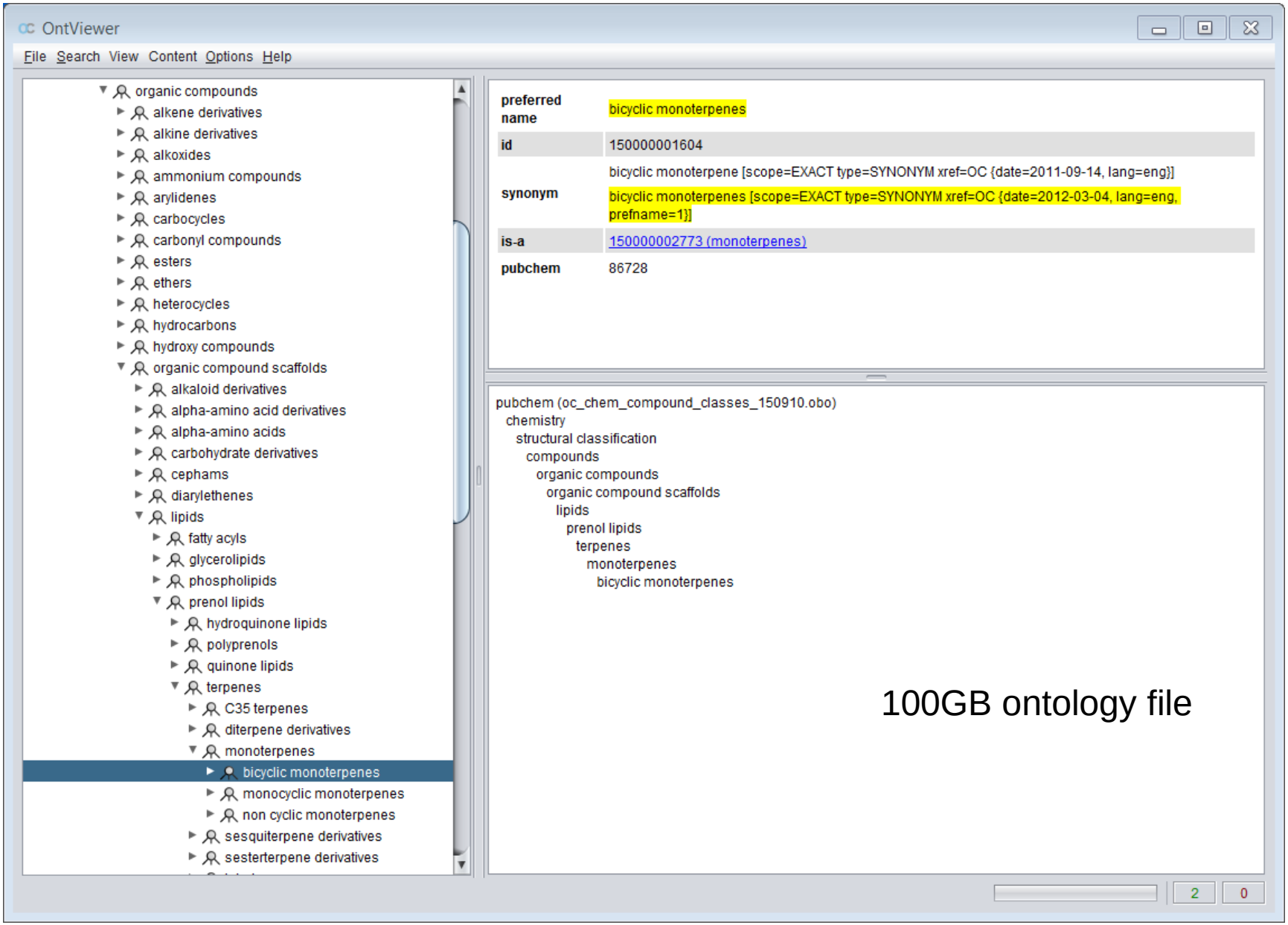

PubChem Classifications

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Statistics: find missing/wrong definitions / wrong compounds?

Concept	Aggregated Children	Direct Children	Concept
chemistry	1,242,661,248		chemistry
structural classification	1,240,832,811		structural classification
compounds	1,227,157,075		compounds
organic compounds	574,930,108	**52,160**	organic compounds
cyclic compounds	379,604,259	**221,327**	cyclic compounds
element compounds	248,665,892		element compounds
organic nitrogen compounds	175,349,613	1,083,882	organic nitrogen compounds
carbonyl compounds	169,293,274	1,342,539	carbonyl compounds
cyclic compounds by element	135,330,213		cyclic compounds by element
cyclic compounds by ring size	96,080,495		cyclic compounds by ring size
5-7-membered cyclic compounds	91,681,812		5-7-membered cyclic compounds
chalcogen compounds	84,914,021		chalcogen compounds
organic halogen compounds	83,842,178	21,610	organic halogen compounds
cyclic compounds by number of rings	83,377,605		cyclic compounds by number of rings
heterocycles	74,645,912	60,802	heterocycles

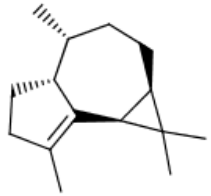
e.g. organic compound:

2-Benzofuranmethyl [CH2]c1occ2ccccc12 |^1:0

radicals?

(-)-α-gurjunene

missing scaffold



PubChem Classifications

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Statistics: Find missing / wrong definitions

Concept	Aggregated Children	Direct Children	Concept
iron cyano complex	0		iron cyano complex
iron nitroso complex	0		iron nitroso complex
2-exo-hydroxy-1,4-cineole derivatives	0		2-exo-hydroxy-1,4-cineole derivatives
Eucarvone derivatives	0		Eucarvone derivatives
pinocarvone derivatives	0		pinocarvone derivatives
ocimene derivatives	0		ocimene derivatives
β-ocimene derivatives	0		β-ocimene derivatives
(Z)-β-ocimene derivatives	0		(Z)-β-ocimene derivatives
(E)-β-ocimene derivatives	0		(E)-β-ocimene derivatives
radium salts	0		radium salts
unclassified entities	0		unclassified entities
iron cyano complex	0		iron cyano complex
iron nitroso complex	0		iron nitroso complex
2-exo-hydroxy-1,4-cineole derivatives	0		2-exo-hydroxy-1,4-cineole derivatives
Eucarvone derivatives	0		Eucarvone derivatives

Patent Classifications: ChemAnalyser

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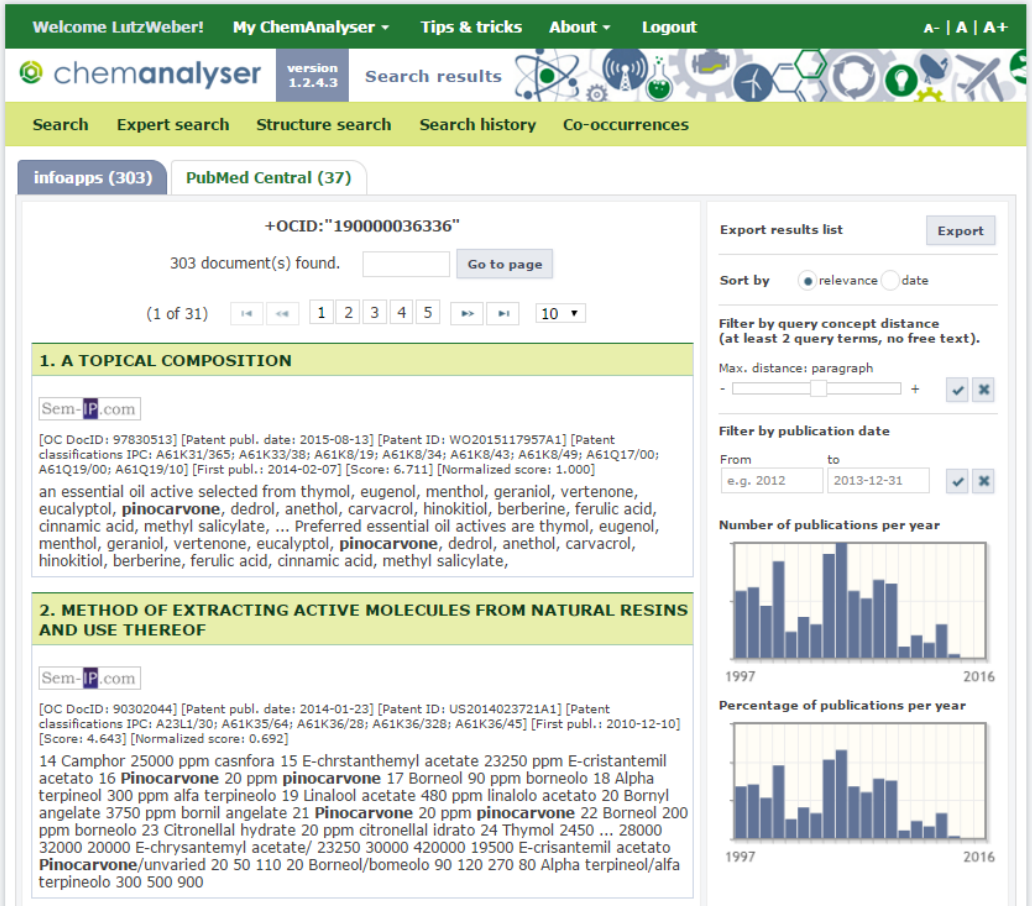
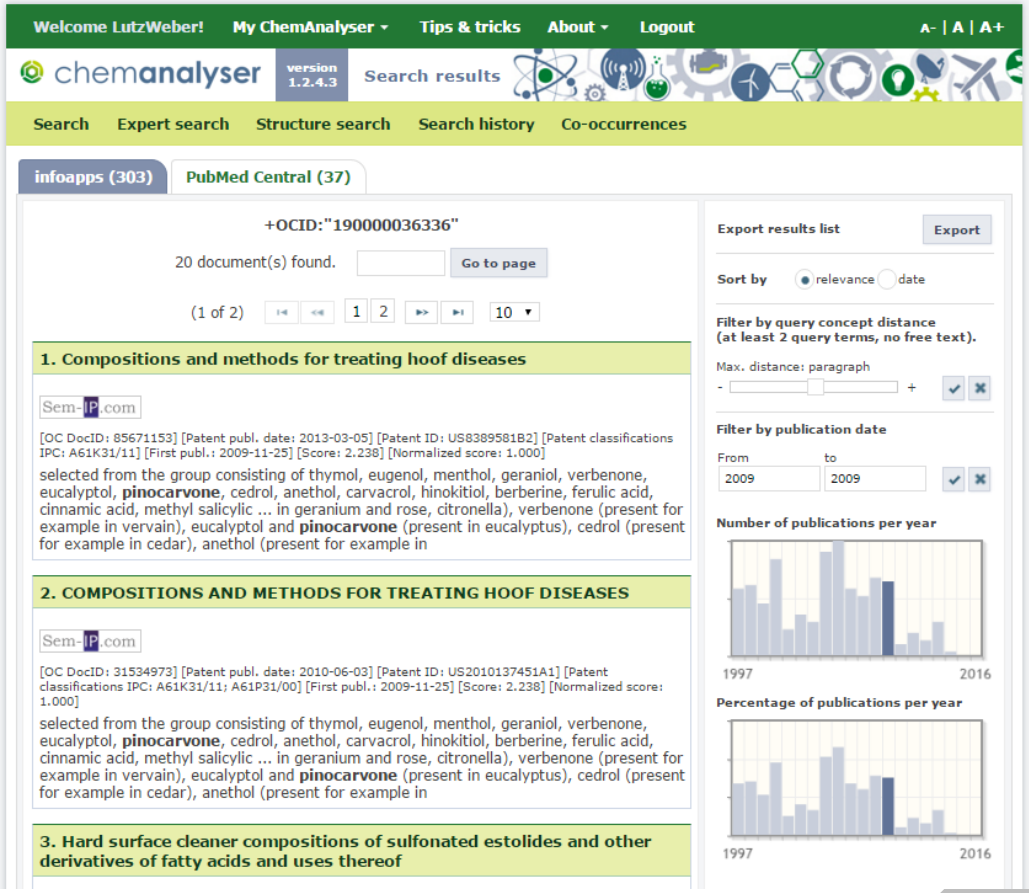
ChemAnalyser: searching "pinocarvone" in patent and non-patent literature:

303 patent hits in total
(53 in SciFinder)



20 patent hits in 2009
(1 in SciFinder)



ChemAnalyser: Cognitive Search

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Search term "tomatidine" (a class of natural products for food)**:**

ChemAnalyser	664 patent hit documents
SciFinder	57 patent hit documents

Search term "sesquiterpenes" (a class of natural products for food)**:**

ChemAnalyser	318,707 patent hit documents
SciFinder	1,837 patent hit documents

Search terms "food additives" + "natural products" + "triterpenes"

ChemAnalyser	362,406 patent hit documents
SciFinder	33 all hit documents

ChemAnalyser: Searching Materials

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Search term "neodymium iron boron magnet":

ChemAnalyser	25,616 patent hit documents
SciFinder	0 patent hit documents

Search term "NdFeB":

ChemAnalyser	25,616 patent hit documents
SciFinder	6 patent hit documents

Search term "304 stainless steel":

ChemAnalyser	14,578 patent hit documents
SciFinder	2,487 patent hit documents

Search term "cosmetic formulation" + "glyzyrrhizin":

ChemAnalyser	51,024 patent hit documents
SciFinder	No References were found containing all of the concepts "cosmetic", "formulation" and "glyzyrrhizin"

Thanks!

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Special thanks to

Stephen Boyer @IBM

Evan Bolton @NCBI

Yannick Djoumbou Feunang @ualberta.ca

Claudia Bobach & Anett Püschel @ontochem.com

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