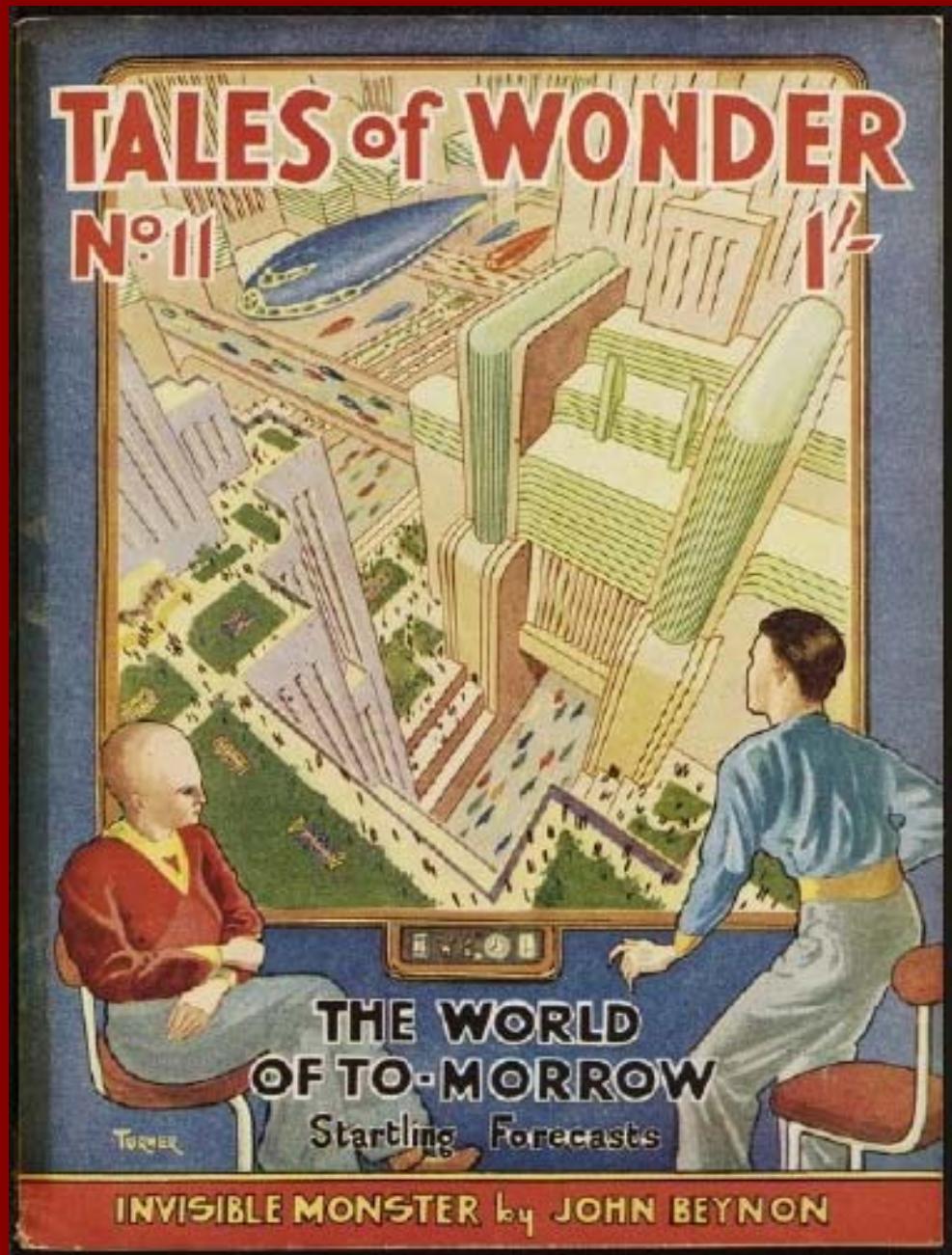
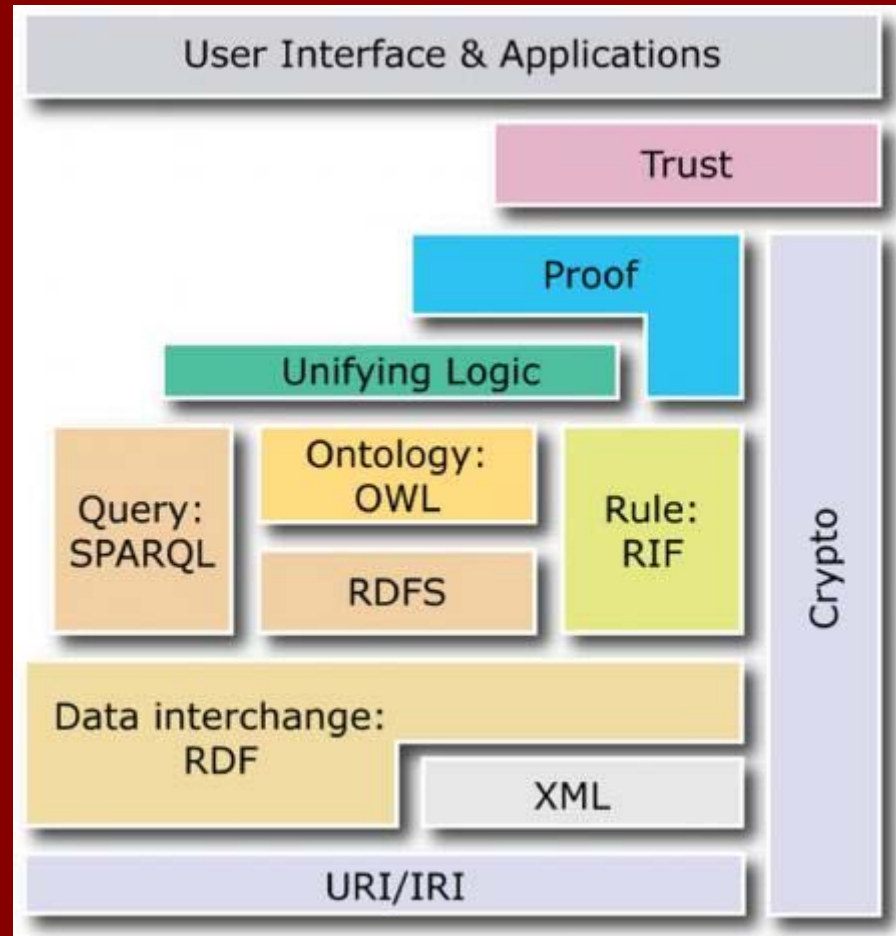


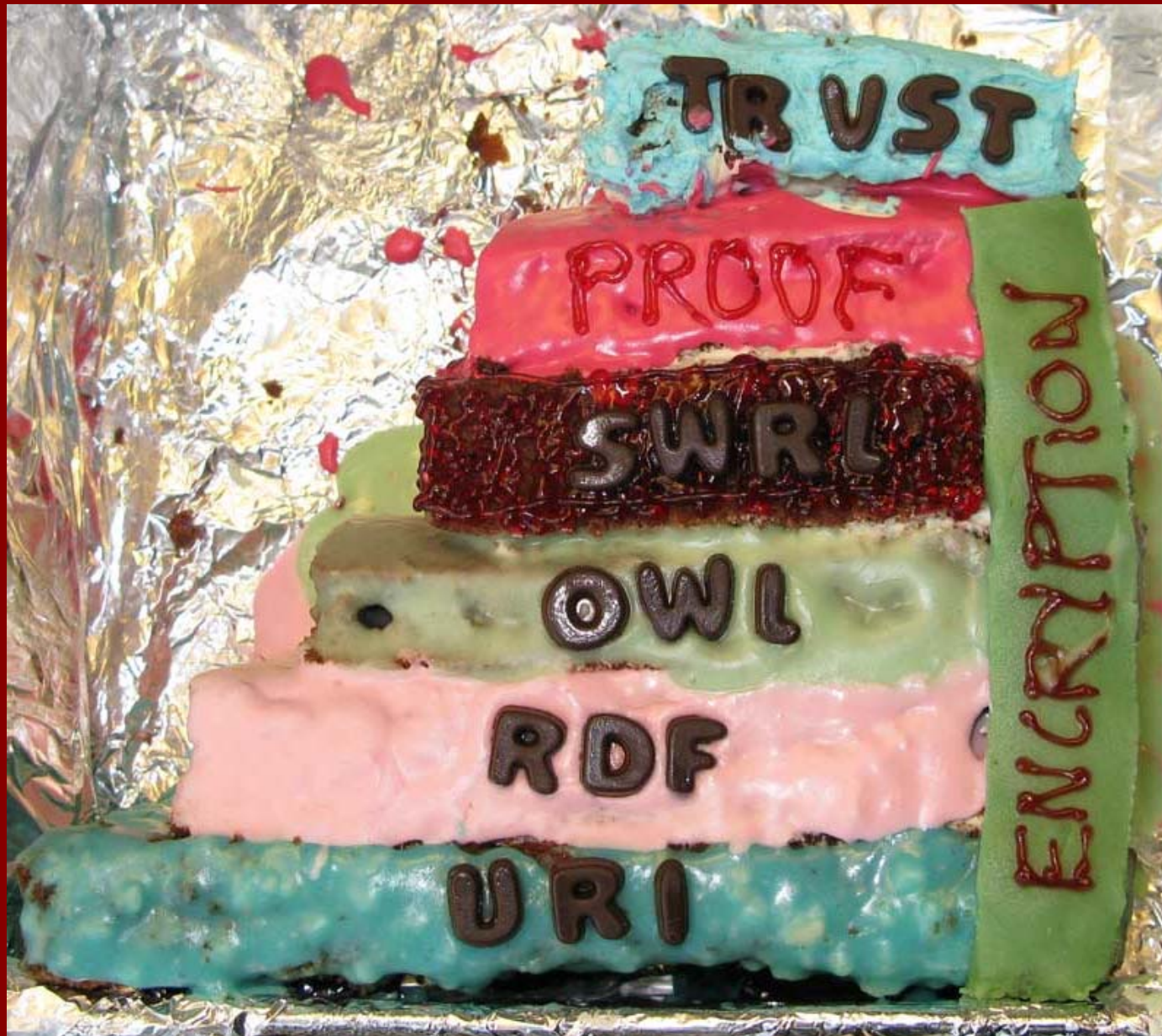
Find and Use: New Standards Link Information to Provide New Answers



RSCPublishing

Are we at a tipping point when the tools and approaches common within bioinformatics finally cross over into chemistry and provide compelling use cases?





RSC Publishing

<http://www.leirdal.net>

The logo for InChI TRUST is centered in a white rectangular box. It features the text "InChI TRUST" in a green, sans-serif font. Behind the text is a grey hexagonal emblem containing a balance scale, a flask, and a globe.

InChI TRUST

Role:

- To fund development and support of the IUPAC InChI standard
- Working groups set up by IUPAC
Subcommittee: reactions, organometallics, polymers, markush, business rules for structure input

RSC Publishing



Current members of the
Trust:

ACD/Labs

ChemAxon

Elsevier

FIZ Chemie

Informa / Taylor & Francis

NPG

OpenEye

RSC

Symyx Technologies

Thomson-Reuters

Wiley-Blackwell

RSC Publishing



- Project Director: Steve Heller
- Board Chairman: Jason Wilde, NPG
- Secretary: Alan McNaught
- Treasurer: Richard Kidd, RSC


RInChI

- Reactions

The RInChI Project

The aim of the RInChI project, in the same vein as InChI, is to create a unique data string to describe a reaction. Reaction InChIs, or RInChIs, are such data strings. They use the InChI software and from an rxn input file a RInChI can be created. The tools for doing this are below, and some helpful information is given in the [help](#) pages.

- Jonathan Goodman
- <http://www-rinchi.ch.cam.ac.uk/>


Version: 0.2

[Home](#)
[Resolver](#)
[Generator](#)
[Web Service](#)
[Configurations](#)
[News](#)

The InChI Resolver provides online access to a series of tools supporting the generation and look-up of InChIStrings and InChIKeys.

InChI Generation: Convert SMILES, load or draw chemical structures and convert to InChIStrings and InChIKeys.

InChI Resolver: Input InChIString or InChIKey and lookup the associated chemical structure.

Web Services: Integrate to our web services to perform InChI Generation and Lookup.

Configurations: Learn about the versions of InChI supported by the resolver.

Resolver Examples

By InChIKey: **RDHQFKQINGIED-IKLDFB CSAV**
VXPBDCBTMSKCKZ-UHFFFAOYAL
ADVPTQAUNPRNPO-UHFFFAOYSA-N

By partial InChIKey: **RDHQFKQINGIED**
VXPBDCBTMSKCKZ
ADVPTQAUNPRNPO

By InChI: **InChI=1/C9H17NO4/c1-7(11)14-8(5-9(12)13)6-10(2,3)4/h8H,5-6H2,1-4H3/p+1**
InChI=1/C20H32O5/c1-2-3-6-9-15(21)12-13-17-16(18(22)14-19(17)23)10-7-4-5-8-11-20(24)25/h12-13,16-17,19,23H,2-11,14H2,1H3,(H,24,25)
InChI=1S/C3H7NO4S/c4-2(3(5)6)1-9(7)8/h2H,1,4H2,(H,5,6)(H,7,8)

By SMILES: **O=C(OC(C[N+](C)(C)C)CC(=O)O)C**
O=C1CC(O)C(C=CC(=O)CCCC)C1CCCCC(=O)O
O=C(O)C(N)CS(=O)O


REST Examples

Get InChI: **RDHQFKQINGIED-IKLDFB CSAV**

Get InChIKey: **O=C(O)C(N)CS(=O)O**
InChI=1/C9H17NO4/c1-7(11)14-8(5-9(12)13)6-10(2,3)4/h8H,5-6H2,1-4H3/p+1

Get SDF: **VXPBDCBTMSKCKZ**

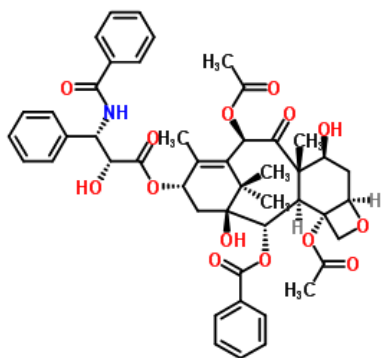
Get CSID: **RDHQFKQINGIED-IKLDFB CSAV**



Internet 100%

RSC Publishing

inchis.chemspider.com


[Download MOL](#)
[Download SDF](#)
ChemSpider ID: **10368587**

SMILES: O=C(N[C@@H](c1ccccc1)[C@@H](O)C(=O)[C@H]5C[C@@]6(O)[C@@H](OC(=O)c2ccccc2))[C@H]3[C@@](C)([C@@H](O)C[C@H]4OC[C@@]34OC(C)=O)C(=O)[C@H](OC(C)=O)N(C=C/C)[C@]6(C)C)c7ccccc7

Molecular Formula: $C_{47}H_{51}NO_{14}$

Molecular Weight: 853.9061

InChI (v1.02b): InChI=1/C47H51NO14/c1-25-31(60-43(56)36(52)35(28-16-10-7-11-17-28)48-41(54)29-18-12-8-13-19-29)23-47(57)40(61-42(55)30-20-14-9-15-21-30)38-45(6,32(51)22-33-46(38,24-58-33)62-27(3)50)39(53)37(59-26(2)49)34(25)44(47,4)5/h7-21,31-33,35-38,40,51-52,57H,22-24H2,1-6H3,(H,48,54)/t31-,32-,33+,35-,36+,37+,38-,40-,45+,46-,47+/m0/s1

InChI Key (v1.02b): RCINICONZNXQF-MZXODVADBU

InChI (v1.02b, fixedH): InChI=1/C47H51NO14/c1-25-31(60-43(56)36(52)35(28-16-10-7-11-17-28)48-41(54)29-18-12-8-13-19-29)23-47(57)40(61-42(55)30-20-14-9-15-21-30)38-45(6,32(51)22-33-46(38,24-58-33)62-27(3)50)39(53)37(59-26(2)49)34(25)44(47,4)5/h7-21,31-33,35-38,40,51-52,57H,22-24H2,1-6H3,(H,48,54)/t31-,32-,33+,35-,36+,37+,38-,40-,45+,46-,47+/m0/s1/f/h48H

InChI Key (v1.02b, fixedH): RCINICONZNXQF-GXKQXQCCDN

InChI (v1.02s): InChI=1S/C47H51NO14/c1-25-31(60-43(56)36(52)35(28-16-10-7-11-17-28)48-41(54)29-18-12-8-13-19-29)23-47(57)40(61-42(55)30-20-14-9-15-21-30)38-45(6,32(51)22-33-46(38,24-58-33)62-27(3)50)39(53)37(59-26(2)49)34(25)44(47,4)5/h7-21,31-33,35-38,40,51-52,57H,22-24H2,1-6H3,(H,48,54)/t31-,32-,33+,35-,36+,37+,38-,40-,45+,46-,47+/m0/s1

InChI Key (v1.02s): RCINICONZNXQF-MZXODVADSA-N

Linked to literature

InChI Key (v1.02b, fixedH): HVYWMOMLDIMFJA-DPAQBDFB

InChI (v1.02s): InChI=1S/C27H46O/c1-18(2)7-6-8-19(3)23-11-12-24-22-10-9-20-17-21(28)13-15-26(20,4)25(22)14-16-27(23,24)5/h9,18-19,21-25,28H,6-8,10-17H2,1-5H3/t19-,21+,22+,23-,24+,25+,26+,27-/m1/s1

InChI Key (v1.02s): HVYWMOMLDIMFJA-DPAQBDFSA-N

- References:** Mével Mathieu. **Novel neutral imidazole-lipophosphoramides for transfection assays**, Chemical Communications, 2008
[DOI: [10.1039/b805226c](https://doi.org/10.1039/b805226c)]
- Aparicio Jesús F.. **Microbial cholesterol oxidases: bioconversion enzymes or signal proteins?**, Molecular BioSystems, 2008
[DOI: [10.1039/b717500k](https://doi.org/10.1039/b717500k)]
- Numata Munenori. **Creation of polynucleotide-assisted molecular assemblies in organic solvents: general strategy toward the creation of artificial DNA-like nanoarchitectures**, Organic & Biomolecular Chemistry, 2008
[DOI: [10.1039/b713354e](https://doi.org/10.1039/b713354e)]
- Gater Deborah L.. **Formation of the liquid-ordered phase in fully hydrated mixtures of cholesterol and lysopalmitoylphosphatidylcholine**, Soft Matter, 2008
[DOI: [10.1039/b710726a](https://doi.org/10.1039/b710726a)]
- Tawakol Ahmed. **Intravascular detection of inflamed atherosclerotic plaques using a fluorescent photosensitizer targeted to the scavenger receptor**, Photochemical & Photobiological Sciences, 2008
[DOI: [10.1039/b710746c](https://doi.org/10.1039/b710746c)]
- Tadashi Yoshida, Akira Honda, Hiroshi Miyazaki and Yasushi Matsuzaki. **Determination of Key Intermediates in Cholesterol and Bile Acid Biosynthesis by Stable Isotope Dilution Mass Spectrometry**, Analytical Chemistry Insights 2008:3 45-60
[DOI:]
- Polozov et al.. **Progressive Ordering with Decreasing Temperature of the Phospholipids of Influenza Virus**, Nature Chemical Biology, doi: 10.1038/nchembio.77, published online 2 March 2008
[DOI: [10.1038/nchembio.77](https://doi.org/10.1038/nchembio.77)]
- Meloni et al.. **Metal swap between Zn7-metlothionein-3 and amyloid-beta Cu protects against amyloid-beta toxicity**, Nature Chemical Biology, doi: 10.1038/nchembio.89, published online 4 May 2008.
[DOI: [10.1038/nchembio.89](https://doi.org/10.1038/nchembio.89)]

Resolve the skeleton

InChI, InChIKey or SMILES:

Found by part of InChIKey

The image displays a search interface for chemical structures. At the top, there is a search bar containing the InChIKey RCINICONZNJXQF and a 'Search' button. Below the search bar, the text 'Found by part of InChIKey' is centered. The main area of the interface is a grid of 24 chemical structures, arranged in 4 rows and 6 columns. These structures represent different ways to resolve the complex molecule from its InChIKey. The structures are rendered in black and red, with some atoms highlighted in blue or green. The top row shows the most complete and recognizable structures, while the bottom rows show increasingly fragmented and less recognizable skeletal representations. The background of the interface is white.

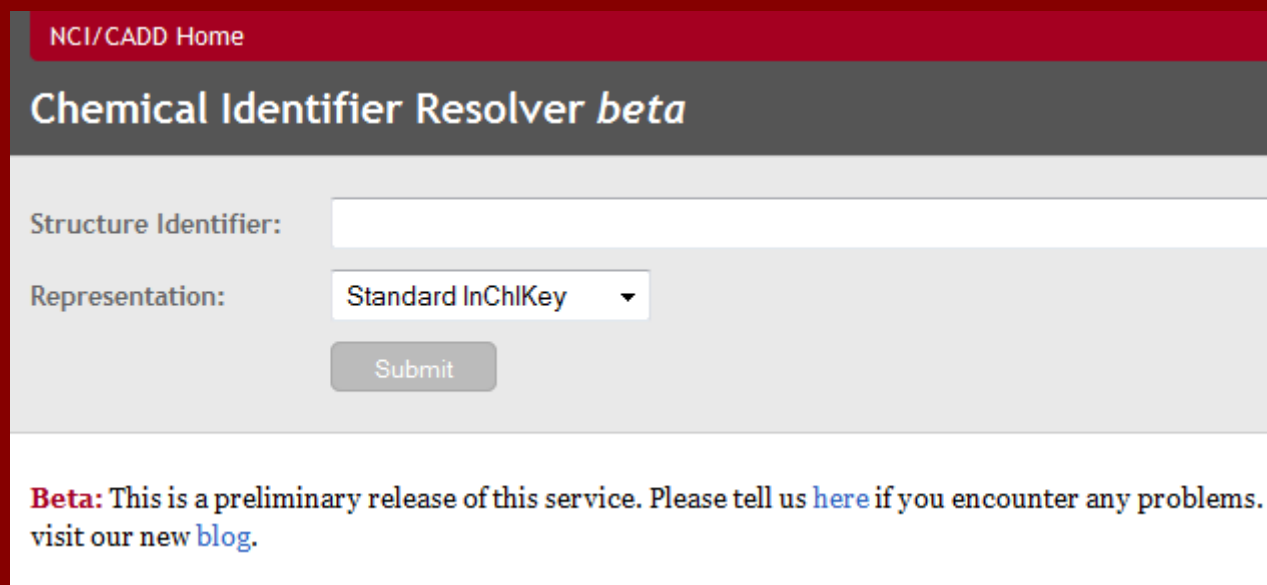
Serve Up Services

InChI

The following operations are supported. For a formal definition, please review the [Service Description](#).

- [GenerateInChI](#)
- [GenerateInChIInfo](#)
- [GenerateInChIKey](#)
- [ResolveInChIKey](#)

NCI Resolver



NCI/CADD Home

Chemical Identifier Resolver *beta*

Structure Identifier:

Representation:

Beta: This is a preliminary release of this service. Please tell us [here](#) if you encounter any problems. visit our new [blog](#).

- So we need a Resolver Protocol

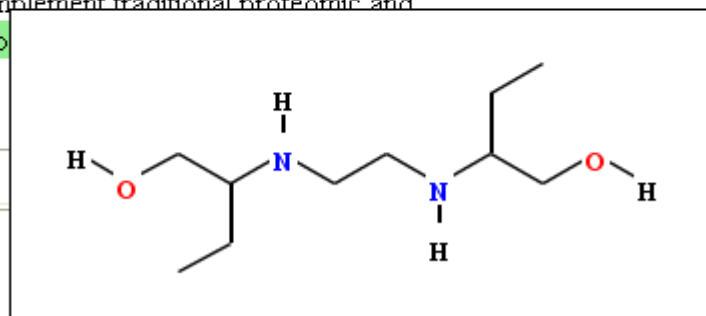
Publishers' semantic markup



RSCPublishing

RSC and mining

Bacterial surface-associated **proteins** play essential roles in mediating pathogen–host interactions and represent privileged targets for anti-adhesion therapy. We used **atomic force microscopy (AFM)** to investigate, *in vivo*, the binding strength and surface distribution of fibronectin attachment **proteins (FAPs)** in *Mycobacterium bovis bacillus* Calmette-Guérin (BCG). We measured the specific binding forces of FAPs (~50 pN) and found that they increased with the loading rate, as observed earlier for other **receptor–ligand** systems. We also mapped the distribution of FAPs, revealing that the **proteins** are widely exposed on the mycobacterial surface. To demonstrate that the **proteins** are surface-associated, we showed that treatment of the cells with **pullulanase**, an enzyme possessing **carbohydrate-degrading** activities, or with **protease**, an enzyme that conducts **proteolysis**, led to a substantial reduction of the FAP surface density. A similar trend was also noted following treatment with **ethambutol**, an **antibiotic** which inhibits the synthesis of **cell wall polysaccharides**. The nanoscale analyses presented here complement traditional proteomic and molecular biology approaches for the functional analysis of surface-associated **pro** novel anti-adhesive **drugs**.



Insight, innovation, integration

Studying the structure and function of bacterial cell adhesion **proteins**—referred to as adhesins—is essential given

Enhanced HTML

Proteolysis

Definition: The chemical reactions and pathways resulting in the breakdown of a protein by the destruction of the native, active configuration, with the hydrolysis of peptide bonds.

ID: GO:0006508

Synonyms:

- peptidolysis
- ATP-dependent proteolysis

Articles referencing this term

Microcins, gene-encoded antibacterial peptides from enterobacteria

Sophie Duquesne, Delphine Destoumieux-Garzón, Jean Peduzzi and Sylvie Rebuffat, *Nat. Prod. Rep.*, 2007 , 24 , 708

DOI: 10.1039/b516237h

The type I fatty acid and polyketide synthases: a tale of two megasynthases

Stuart Smith and Shiou-Chuan Tsai, *Nat. Prod. Rep.*, 2007 , 24 , 1041

DOI: 10.1039/b603600g

The ubiquitous carrier protein – a window to metabolite biosynthesis

Why are we doing this?

A solution looking for many problems

- Enhanced reader experience
- Current awareness
- Information retrieval (pre-indexing)

XML



Text mining (Oscar)

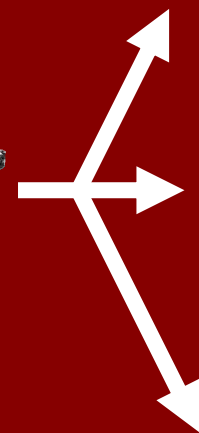
<http://www.sciborg.org.uk/>

<http://oscar3-chem.sourceforge.net/>

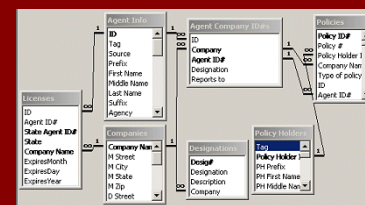
RSC Publishing



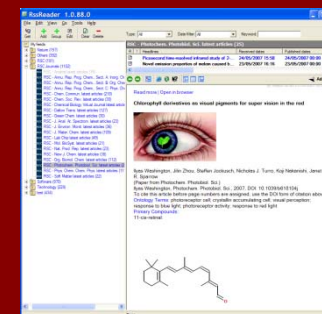
Manual QA



Enhanced HTML



Database



Enhanced RSS

Resources we use

Static

IUPAC Gold Book

Dynamic

OBO biomedical ontologies, especially ChEBI

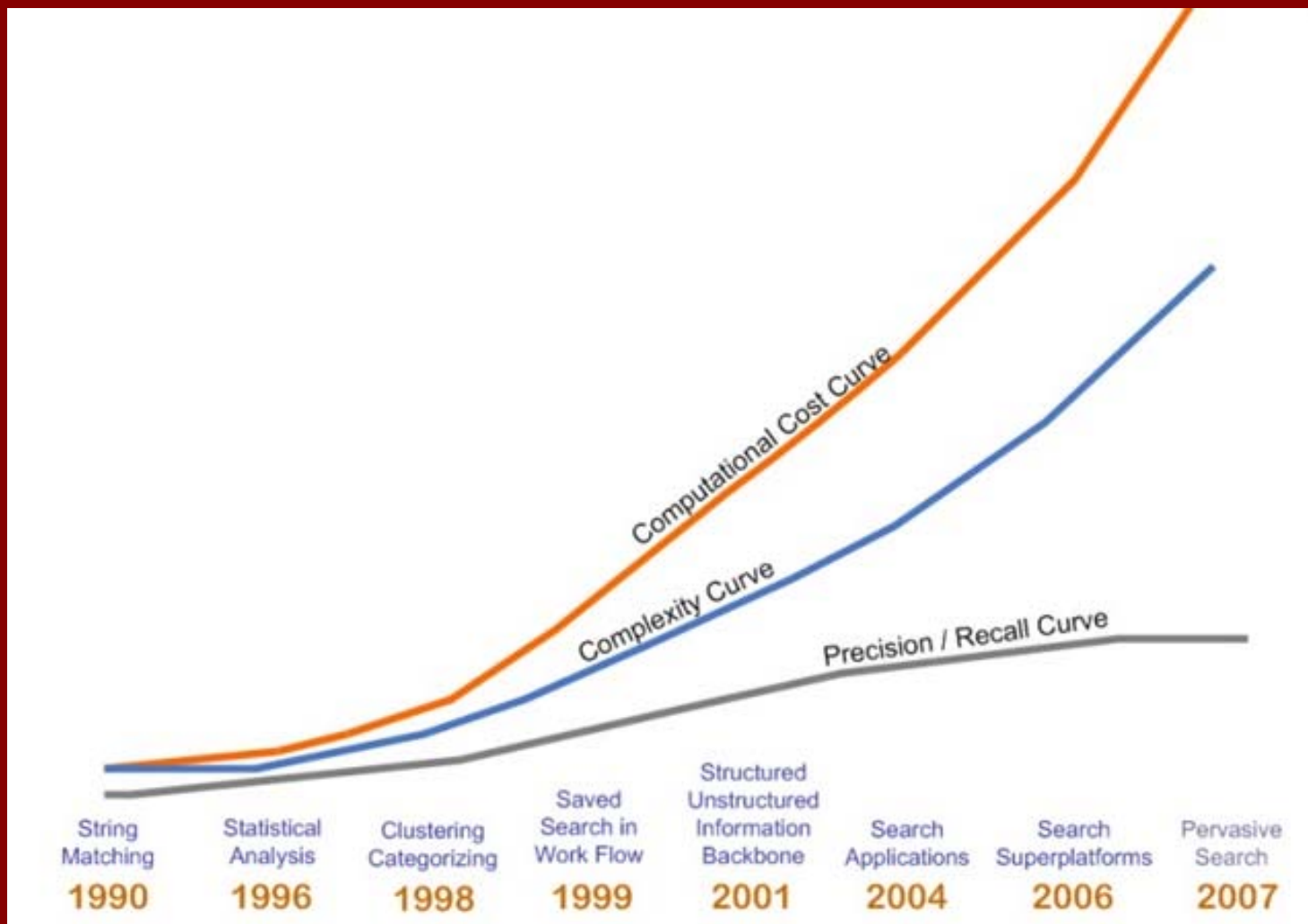
RSC ontologies (<http://www.rsc.org/ontologies>)

CMO, RXNO, MOP (and more to come)

RSC Ontology development

Annotations to a particular ontology are a moving target

And we can't guarantee completeness



Stephen Arnold
 Search: The Three Curves of Despair
 March 2008

RSC Publishing

ChemMantis

Accepted: 20 February 2004 / Published: 24 February 2004

nisidine, **o-vanillin**, Schiff bases, biological activity.

Interesting biological

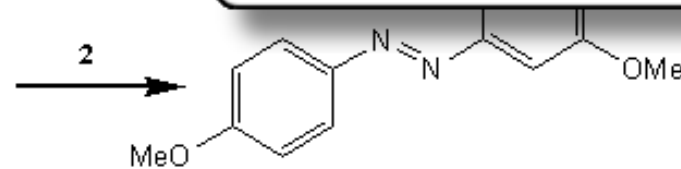
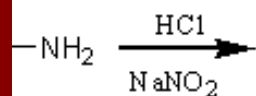
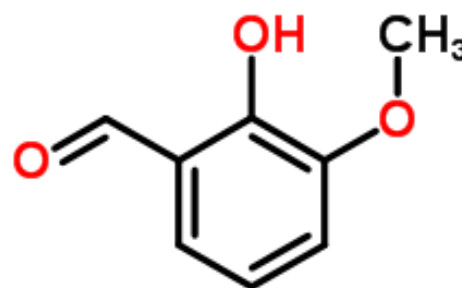
the methoxy groups

el azoaldehyde with

Chemical Name

o-vanillin

[ChemSpider](#) [Entrez](#) [MeSH](#) [Google](#) [Wiki](#)



ce of an **azo** functionality in n

activities [6]. As such, we sy

ponding Schiff bases. Their

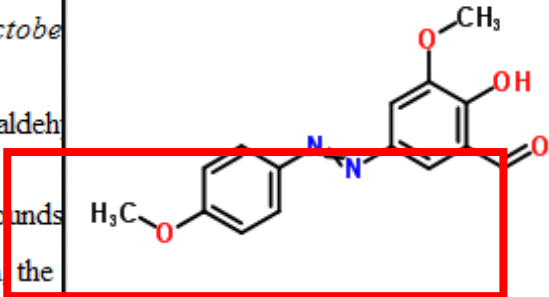
Deposit Structures

Synthesis of 2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde

A. A. Jarrahpour*,
Department of Chem
jarrah@chem.susc.a
Received: 8 Octobe
Keywords : azoaldehy
Diaz compounds
[5]. In addition the
methoxy groups. Re
presented in the near future.

Shiraz 71454, Iran Te
blished: 24 February
logical activity.
was shown that the pr
lecules enhanced the b
aromatic amines affor

Chemical Name
2-hydroxy-3-methoxy-5-(4-methoxyphenylazo) benzaldehyde
[ChemSpider](#) [Entrez](#) [MeSH](#) [Google](#) [Wiki](#)



Edit Deposit Clear Good Bad

Deposit new structure into ChemSpider

COc1ccc(N)cc1 $\xrightarrow[\text{NaNO}_2]{\text{HCl}}$ $\left[\text{COc1ccc(N}_2^+)cc1 \right] \text{Cl}^-$

Annotation: where and when?



Pre-publication?

(by authors)

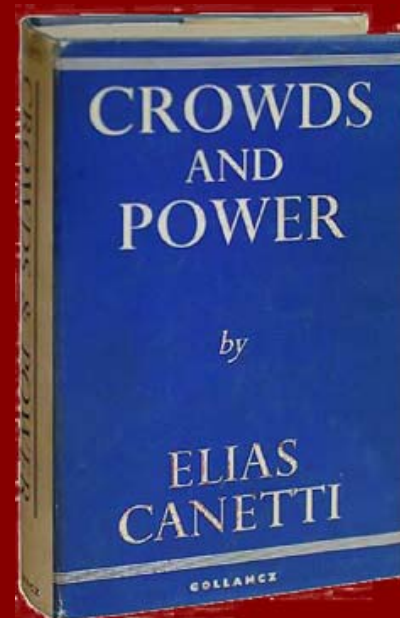
?



At publication?

(by editors)

Prospect



After publication?

(by the crowd)

ChemMantis

RSC Publishing

Challenges

Open problems

- Chemical structures from images
- Productive identifiers for productively-named entities

Putting ChemMantis and Prospect together

- Backfile (to 1841)
- Community curation

NPG

nature
chemistry

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[Journal home](#) > [Current Issue](#) > [Article](#) > [Full text](#) > [Compound 9](#)

Compound 9

From the following article

[Asymmetric total syntheses of \(+\)- and \(-\)-versicolamide B and biosynthetic implications](#)

Kenneth A. Miller, Sachiko Tsukamoto & Robert M. Williams

Nature Chemistry **1**, 63-68 (2009) Published online: 19 March 2009

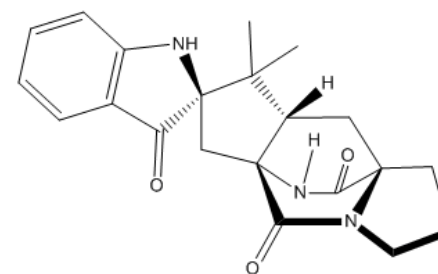
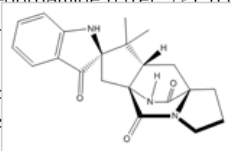
doi:10.1038/nchem.110

[Supplementary information](#)

Work from our laboratory⁴, as well as that from Sammes² and others³ revealed that these alkaloids are all derived from one or two isoprene units, tryptophan, and a cyclic amino acid such as 1-methylproline or pipercolic acid. Significant experimental evidence for the bicyclo[2.2.2]diazaoctane core common to all of these natural products arises biosynthetically via an intramolecular hetero-Diels–Alder (IMHDA) reaction of 5-hydroxypyrazin-2(1H)-one^{4,9}. Indeed, we have applied these strategies to the total synthesis of several of these prenylated alkaloids including D,L-stephacidin A (refs [11,12](#)), D,L-brevianamide B (refs [13,14](#)), D,L-marcfortine C (ref. [16](#)), D,L-notoamide B (ref. [12](#)), D,L-aminomycin A (refs [17,18](#)), and, most recently, D,L-versicolamide B (ref. [19](#)).

Within the family of prenylated alkaloids, the bicyclo[2.2.2]diazaoctane core, two distinct stereochemical configurations at the C19 stereocenter are observed. Whereas the brevianamides [9](#) and [10](#) possess an *anti* relationship between the members of the paraherquamide and notoamide family, [11](#) and [12](#) possess a *syn* relative configuration. To date, all of the stephacidins also possess a *syn* configuration (C6, stephacidin numbering). A notable exception, versicolamide B ([8](#); ref. [20](#)). Owing to this stereochemical anomaly, versicolamide B ([8](#)) attracted our interest from a biogenetic and a synthetic perspective.

As mentioned above, it has been hypothesized that the bicyclo[2.2.2]diazaoctane core common to all of these natural products arises biosynthetically via an intramolecular hetero-Diels–Alder reaction, and evidence is mounting that this key transformation is enzyme-mediated. Enzyme-catalysed Diels–Alder reactions have been reported for the synthesis of the bicyclo[2.2.2]diazaoctane core²¹.



[back to article](#)

Compound 9 (-)-Brevianamide A

[View in PubChem](#)

[View in 3D \(5 KB\)](#) | [Download CML file \(4 KB\)](#) | [Download ChemDraw file of structure \(4 KB\)](#)

Synonyms

Spiro(5H,6H-5a,9a-(iminomethano)-1H-cyclopent(f)indolizine-7(8H),2'-(2H)indole)-3',5,10(1'H)-trione, 2,3,8a,9-tetrahydro-8,8-dimethyl-, (2'S,5aR,8aS,9aR)-

Chemical Formula: C₂₁H₂₃N₃O₃

Molecular Weight: 365.43

Elemental Analysis: C, 69.02; H, 6.34; N, 11.50; O, 13.13

InChI=1/C21H23N3O3/c1-18(2)14-10-19-8-5-9-24(19)17(27)20(14,23-16(19)26)11-21(18)15(25)12-6-3-4-7-13(12)22-21/h3-4,6-7,14,22H,5,8-11H2,1-2H3,(H,23,26)/t14-,19+,20+,21-/m0/s1

InChIKey: MWOFQPILIIIPR-DJJZHVJBBC

Standard InChI=1S/C21H23N3O3/c1-18(2)14-10-19-8-5-9-24(19)17(27)20(14,23-16(19)26)11-21(18)15(25)12-6-3-4-7-13(12)22-21/h3-4,6-7,14,22H,5,8-11H2,1-2H3,(H,23,26)/t14-,19+,20+,21-/m0/s1

Standard InChIKey: MWOFQPILIIIPR-DJJZHVJBSA-N

RSC Publishing

InfoChem

- Chemisches Zentralblatt
 - Digitised
 - Structure searchable
 - 98k unique names
 - 48k unique structures
- Text searchable from FIZ Chemie



Microsoft External Research

- Organization within Microsoft Research that engages in strong **partnerships** with academia, industry and government to advance computer science, education, and research in fields that rely heavily upon advanced computing
- Initiatives that focus on the **research process** and its role in the innovation ecosystem, including support for open access, open tools, open technology, and interoperability
- Developers of **advanced technologies** and services to support every stage of the research process

Ontology Add-in for Word 2007



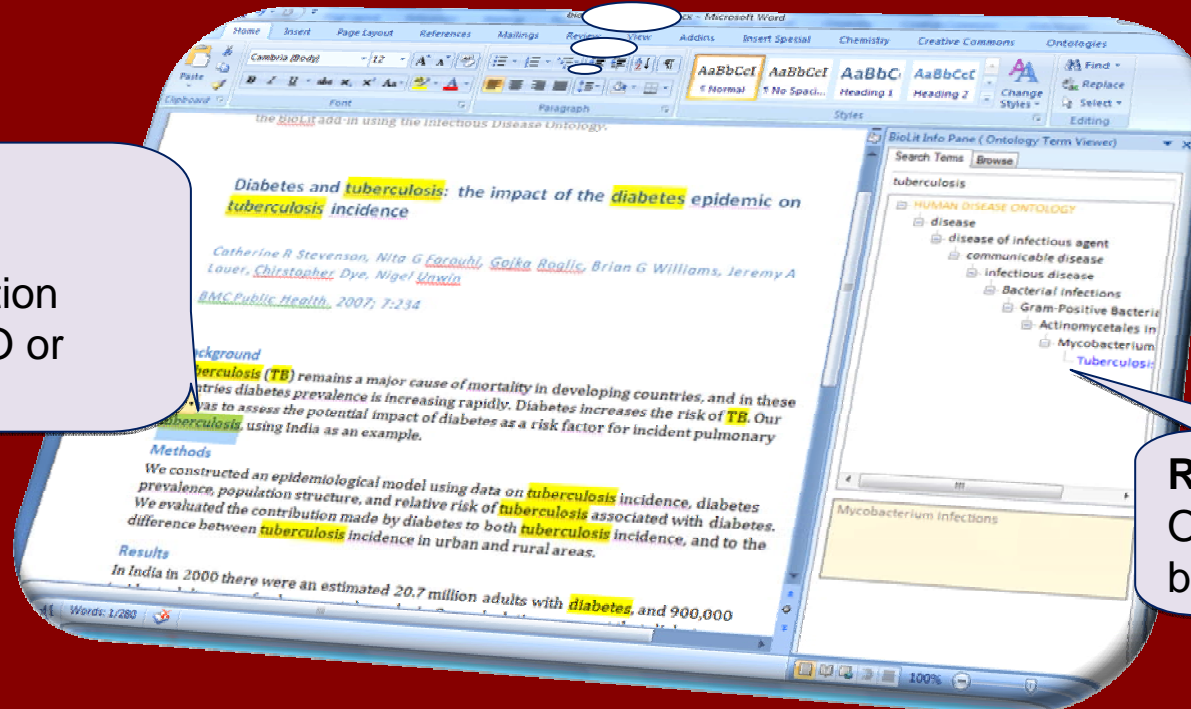
- John Wilbanks

Services: Ontology
download web service



- Phil Bourne
- Lynn Fink

Intent: Term
recognition
& disambiguation
based on OBO or
OWL formats



Relationships:
Ontology
browser

Source code and binary:

<http://research.microsoft.com/ontology/>

RSC Publishing

Chem4Word – Chemistry Drawing in Word



UNIVERSITY OF
CAMBRIDGE

- Peter Murray-Rust
- Joe Townsend
- Jim Downing

Intent: Recognizes chemical dictionary and ontology terms

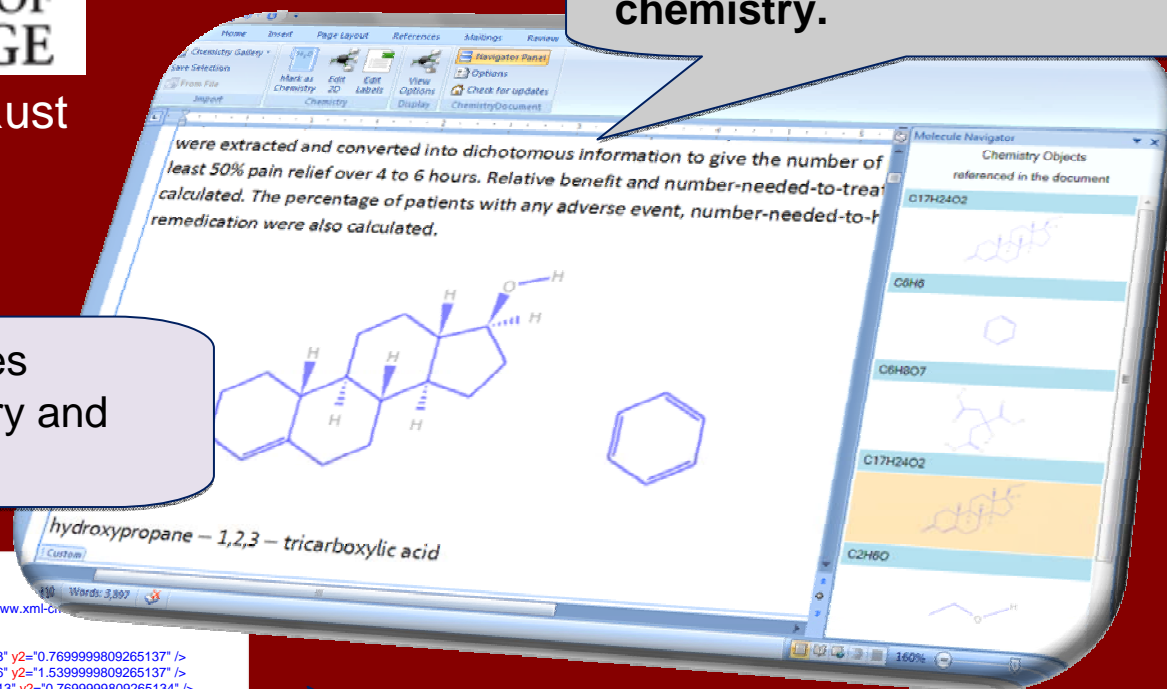
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<bond />  
</bondArray>  
</mole  
</cml>
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Data: Semantics stored in Chemistry Markup Language

Intelligence: Verifies validity of authored chemistry

Relationships: Navigate and link referenced chemistry

Author and edit 1D and 2D chemistry.



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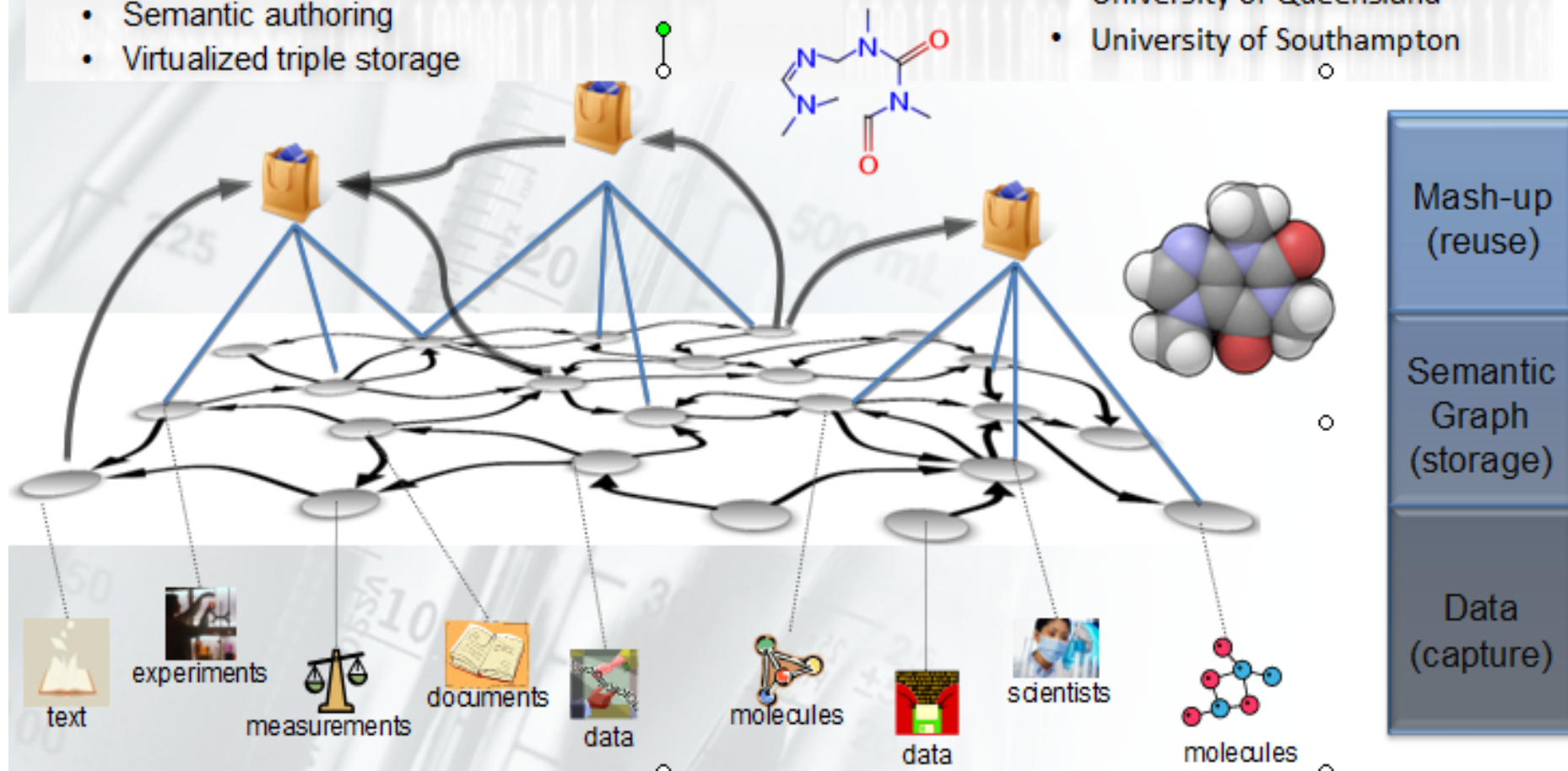
Available soon:
<http://research.microsoft.com/chem4word/>

OreChem – the Chemical Semantic Web (?)

- Large collaboration project focusing on interoperability
- At-source capture of chemistry data
- Chemical structure search
- Compound object authoring
- Retrospective harvesting of chemistry data
- Reuse through common ORE data model
- Semantic authoring
- Virtualized triple storage

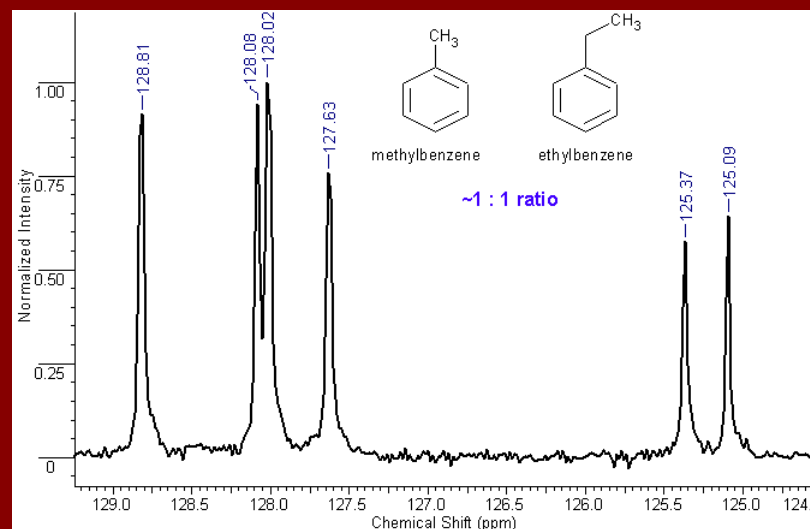
Participating Institutions:

- University of Cambridge
- Cornell University
- Indiana University
- Penn State University
- University of Queensland
- University of Southampton



Extraction of NMR data

- PDF
- Extraction of lines, polylines, text
- CML spectrum

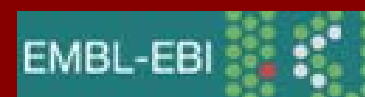


- Mark Borkum, Southampton

Semantic Enrichment of the Scientific Literature (SESL)

- Pistoia-funded
- EBI
- Elsevier, NPG, OUP, RSC

- Oct 2009 – Oct 2010



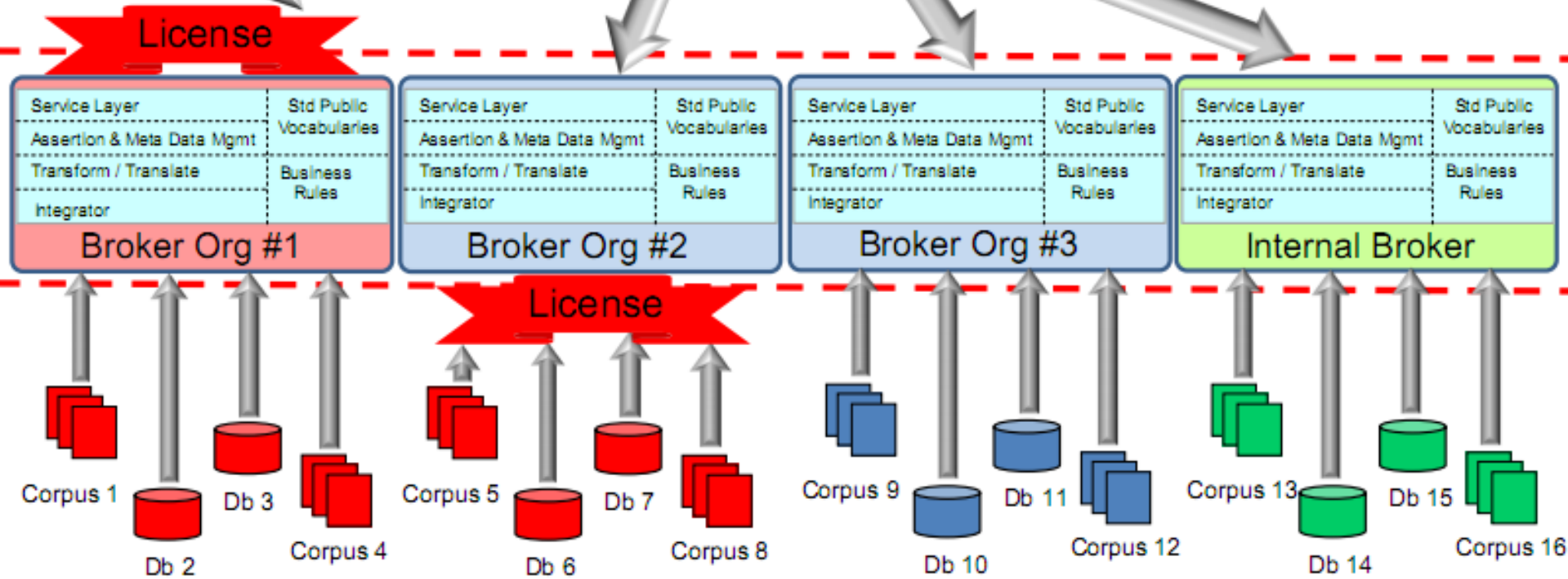
A Production Service ...



Consumer Side



Exemplar Application



Supplier Side

SESL deliverables

- Pilot to deliver target-disease assertions
- Publication of data, application and web service standards
- So: to deliver standards for semantic delivery

RSC Publishing

CITY OF THE FUTURE

What will the city of tomorrow be like? Here is the giant plastic, metal, and unbreakable glass city of the 21st century. A city of science, of atomic power, of space travel, and of high culture. See page 240 for complete story.



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Are we there yet?

- InChI Trust
 - Compound standards
 - Reaction InChIs
 - Resolver Protocol
- Pistoia/EBI
 - Semantic standards for web services
- Microsoft/Academia
 - oreChem
 - Chem4Word
- Semantic markup by publishers



Images

<http://www.pantopicon.be>

<http://www.leirdal.net>

<http://www.baekdal.com>

Microsoft Research

Pistoia Alliance

Steve Arnold

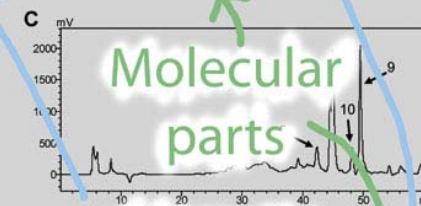
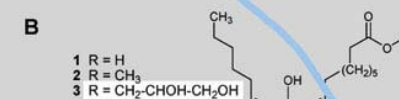
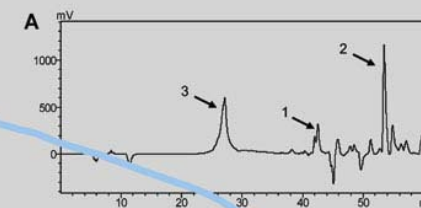
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Richard Kidd
kiddr@rsc.org

metabolite profiles indicating that epigenetic modifiers impacted fungi in a manner that was functionally distinct from that of a general cytotoxic response. Interestingly, a combination treatment, composed of a DNA methyltransferase inhibitor and histone deacetylase inhibitor, was tested and determined to be only modestly effective due to significant growth restriction and/or generation of metabolite profiles dominated by the effects of a single component in the mixture (e.g. effects of individual compound treatments were not additive as a mixture).

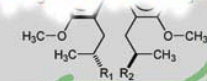
In order to probe the nature of metabolic remodeling induced by epigenetic modifier treatment, two fungi were selected for scale-up studies. The first isolate was obtained from a tidal pool along the coastline of Casco Bay, Portland, Maine, USA, and identified as *Cladosporium cladosporioides* by analysis of a 300 base pair sequence of the D2 region of the 26S large ribosomal subunit rRNA gene and morphological considerations.† This culture exhibited divergent responses to the small-molecule epigenetic modifiers 5-azacytidine and suberoylanilide hydroxamic acid which led to dramatic restructuring of its secondary metabolome with both treatments (Fig. 1A,C). Treatment of *C. cladosporioides* with 5-azacytidine elicits the *de novo* production of several oxylipins, three of which were characterized by NMR and MS analysis as 9Z,12Z)-11-hydroxyoctadeca-9,12-dienoic acid (1), its methyl ester (2), and glycerol conjugate (3) in substantial yields (Fig. 1B). The production of these compounds is of considerable interest since these types of metabolites are widely recognized for their important roles as intra- and inter-species cell signaling molecules. In contrast, suberoylanilide hydroxamic acid induced the production of a complex series of perylenequinones, two of which were characterized as new metabolites, cladochroms F (4) and G (5), along with four known cladochroms A (6), B (7), D (8), and E (9) and calphostin B (10) (Fig. 1D, and see ESI†). This is remarkable since this is the first reported co-occurrence of such an extensive range of cladochrom-calphostin metabolites from a single source. Moreover, the identification of 6 and 7 under epigenetic stimulation is significant since these compounds were first unique products of *Clad sporium* infection of seedlings, yet could not be obtained from any mono-culture fermentations.¹⁰ While it was not clear if 6 and 7 might be the products of mixed biosynthesis, their selective production in suberoylanilide hydroxamic acid treated *Cladosporium* that their biogenesis is normally tightly regulated by some yet undefined host-specific signaling event.

The second fungal isolate was obtained from the foregut of a fifth instar luna moth (*Actias luna*; Saturniidae) larva that was cultured on an exclusive diet of sweet gum (*Liquidambar styraciflua* L.; Hamamelidaceae) leaves. Initial characterization of the fungus by analysis of the 26S rRNA gene gave homology to *Diatrype disciformis*. While control cultures of this *Diatrype* sp. were relatively void of any secondary metabolites, addition of 5-azacytidine triggered a significant change in the organism's metabolic profile (Fig. 2A), resulting in the production of two new polyketides, lunalides A (11) and B (12) (Fig. 2B). It is interesting to note that one other non-epigenetic culture treatment, elicitation with *E. coli*,† resulted in the biosynthesis of 11 and 12 which were otherwise repressed under axenic culture conditions. The results suggest that their production is under specific control of a unique environmental cue.



D

Molecular parts
 Sequence information



- 4 R₁ = OH; R₂ = *p*-hydroxybenzoate
- 5 R₁ = OH; R₂ = *p*-hydroxycarboxylate
- 6 R₁ = R₂ = β-hydroxybutyrate
- 7 R₁ = β-hydroxybutyrate; R₂ = benzoate
- 8 R₁ = α-hydroxycarbonate; R₂ = *p*-hydroxybenzoate
- 9 R₁ = α-hydroxycarbonate; R₂ = benzoate
- 10 R₁ = OH; R₂ = benzoate

Fig. 1. Different chromatograms and structures of *C. cladosporioides* metabolites. The chromatograms were generated by subtracting the chromatogram of the untreated control from the treatment groups. Peaks phasing upward represent metabolites expressed only upon epigenetic treatment or production at higher concentrations. (A) Difference chromatogram of untreated control and 5-azacytidine treatment yielding oxylipins 1–3. (B) Chemical structures of oxylipins 1–3. (C) Difference chromatogram of untreated control and suberoylanilide hydroxamic acid on secondary metabolite expression leading to the production of cladochroms 4–10. (D) Chemical structures of cladochroms 4–10. The structures were characterized by HRESIMS and compared to values published in the literature.

The successful identification of new natural products from fungi using epigenetic modifiers indicates that this technique is a very promising and rational approach for the native expression of silent biosynthetic pathways.