



Metodologie di Sintesi e Sviluppo Farmaceutico

Synthesis and Development Pharmaceutical Methodologies

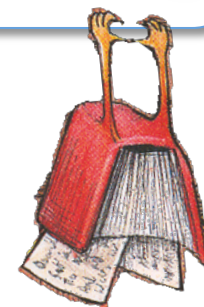
Laurea Magistrale in Chimica a.a. 2019/2019



How to acquire and product scientific knowledge

**"SCIENTIFIC KNOWLEDGE IS IN PERPETUAL
EVOLUTION; IT FINDS ITSELF CHANGED FROM
ONE DAY TO THE NEXT."**

JEAN PIAGET



The scientific knowledge



The Alchemist (N. C. Wyeth – 1937)

- Someone that pay the bill
- A knowledge transfer/discussion
- Some technology involved



Modern times

The scientific knowledge

Primary Sources

A primary source provides direct or firsthand evidence about an event, object, person, or work of art.

Primary sources include results of experiments, statistical data and empirical studies—research where an experiment was performed or a direct observation was made. The results of empirical studies are typically found in scholarly articles or papers delivered at conferences.

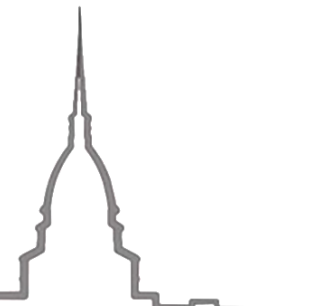
- Articles

The scientific knowledge

Secondary Sources

Secondary sources describe, discuss, interpret, comment upon, analyze, evaluate, summarize, and process primary sources.

- Patents
- Internal reports/publicatoions
- Technical or research reports;
- Research projects;
- Meeting abstracts;
- PhD / Master Thesis
- Books and educational material
- Lab guedelines
- pre-print manuscript



Scientific paper

A scientific paper is a written and published report describing **original research results**. That short definition must be qualified, however, by noting that a scientific paper **must be written in a certain way** and it **must be published in a certain way**, as defined by three centuries of developing tradition, editorial practice, scientific ethics, and the interplay of printing and publishing procedures.

A **Journal** is a periodical publication that contain articles on a specific topic.



Year, volume, page

J. Med. Chem. **2015**, 58, 4590–4609

<http://pubs.acs.org/journal/jmcmar>

Protect (or NOT) yourself!!!

You make money your research???

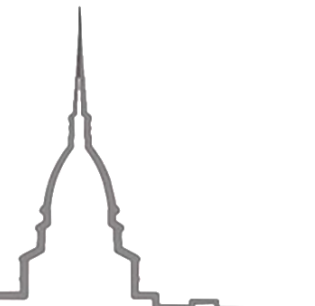
The fact that the **privately owed** journals are **highly expansive** create a limitation of knowledge diffusions.

This fact create a big controversial inside th4 scientific community that if supporting the rising on the **open access Journals**



DOAJ is an online directory that indexes and provides access to high quality, open access, peer-reviewed journals.

<https://doaj.org/>



Reading a scientific paper

“**First name**”: this author is supposed to have a primary role in the all study.

“**Affiliations**”: the single groups involved. More are, better is...



IF 5,248

Journal of
**Medicinal
Chemistry**

Article

pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

Cristina Tintori,[†] Giuseppina La Sala,[†] Galia Vignaroli,[†] Lorenzo Botta,[†] Anna Lucia Fallacara,^{†,‡} Federico Falchi,[†] Marco Radi,^{†,§} Claudio Zamperini,[†] Elena Dreassi,[†] Lucia Dello Iacono,[†] Donata Orioli,[§] Giuseppe Biamonti,[§] Mirko Garbelli,[§] Andrea Lossani,[§] Francesca Gasparrini,^{‡,||} Tiziano Tuccinardi,[‡] Ilaria Laurenzana,[‡] Adriano Angelucci,[‡] Giovanni Maga,[§] Silvia Schenone,^{*,○} Chiara Brullo,[○] Francesca Musumeci,[○] Andrea Desogus,[○] Emmanuele Crespan,^{*,§} and Maurizio Botta^{†,◆}

[†]Dipartimento Biotecnologie, Chimica e Farmacia, Università degli Studi di Siena, Via A. De Gasperi 2, I-53100 Siena, Italy

[‡]Dipartimento di Chimica e Tecnologie del Farmaco, Università La Sapienza, Piazzale Aldo Moro 5, I-00185 Roma, Italy

[§]Istituto di Genetica Molecolare, IGM-CNR, Via Abbiategrasso 207, I-27100 Pavia, Italy

^{||}Dipartimento di Medicina Molecolare, Sapienza Università di Roma, Piazzale Aldo Moro 5, 00185 Roma, Italy

[‡]Dipartimento di Farmacia, Università di Pisa, Via Bonanno 6, 56126 Pisa, Italy

[◆]Laboratory of Preclinical and Translational Research, IRCCS-Centro di Riferimento Oncologico Basilicata (CROB), Via Padre Pio 1, Rionero in Vulture 85028 Potenza Italy

[○]Dipartimento di Scienze Cliniche Applicate e Biotecnologiche, Università dell'Aquila, Via Vetoio, 67100 Coppito, L'Aquila, Italy

[○]Dipartimento di Farmacia, Università di Genova, Viale Benedetto XV 3, I-16132 Genova, Italy

[◆]Biotechnology College of Science and Technology, Temple University, Biolife Science Building, Suite 333, 1900 N 12th Street, Philadelphia, Pennsylvania 19122, United States

S Supporting Information

“**Supporting information**”: some material (NMR, recipes, figures, ...), that just support the study but that can be heavy in the manuscript is placed in a separate, free of charge, editor web site.

“**Asterisc**”: this is named “Reference author”, the one that is coordinating the all project and whose must direct any further question. In a complex study, as this, could be more then one.

Reading a scientific paper

“Title”: The title of a paper is important because it is one of the first things that an editor/ reviewer/reader sees when they look at your manuscript. Therefore, it is important to grab their attention right away and give them an idea of why your paper is a scientific breakthrough! Be specific, not too technical, and concise. Must be included inside the keywords for web search.

Journal of
**Medicinal
Chemistry**

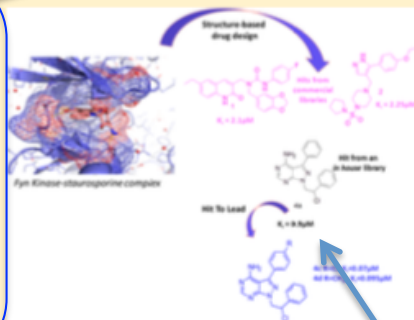
Article

pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

Cristina Tintori,[†] Giuseppina La Sala,[†] Giulia Vignaroli,[†] Lorenzo Botta,[†] Anna Lucia Fallacara,^{†,‡} Federico Falchi,^{†,‡} Marco Radi,^{†,¶} Claudio Zamperini,[†] Elena Dreassi,[†] Lucia Dello Iacono,[†] Donata Orioli,[§] Giuseppe Biamonti,[§] Mirko Garbelli,[§] Andrea Lossani,[§] Francesca Gasparrini,^{‡,||} Tiziano Tuccinardi,[⊥] Ilaria Laurenzana,[#] Adriano Angelucci,[∇] Giovanni Maga,[§] Silvia Schenone,^{*,○} Chiara Brullo,[○] Francesca Musumeci,[○] Andrea Desogus,[○] Emmanuele Crespan,^{*,§} and Maurizio Botta^{†,◆}

ABSTRACT: Fyn is a member of the Src-family of nonreceptor protein-tyrosine kinases. Its abnormal activity has been shown to be related to various human cancers as well as to severe pathologies, such as Alzheimer's and Parkinson's diseases. Herein, a structure-based drug design protocol was employed aimed at identifying novel Fyn inhibitors. Two hits from commercial sources (1, 2) were found active against Fyn with K_i of about 2 μM , while derivative 4a, derived from our internal library, showed a K_i of 0.9 μM . A hit-to-lead optimization effort was then initiated on derivative 4a to improve its potency. Slightly modifications rapidly determine an increase in the binding affinity, with the best inhibitors 4c and 4d having K_i s of 70 and 95 nM, respectively. Both compounds were found able to inhibit the phosphorylation of the protein Tau in an Alzheimer's model cell line and showed antiproliferative activities against different cancer cell lines.



“Graphical abstract”: Explain everything in just a nice attractive image!



IF 5,248

“Abstract”: Imagine you have twenty seconds to explain the project you have been working on for months or years to another scientist who is not familiar with your area of research. You would probably try and tell them the one or two main outcomes without going into excessive technical detail.

Just grab the reader's attention with the first statement and then leave them with the overall message of the manuscript in the last sentence.

Reading a scientific paper

Journal of
**Medicinal
Chemistry**

Article
pubs.acs.org/jmc

Studies on the ATP Binding Site of Fyn Kinase for the Identification of New Inhibitors and Their Evaluation as Potential Agents against Tauopathies and Tumors

■ INTRODUCTION

What was before and what this study is proposing to do. Must not be a review on the topic

■ RESULTS AND DISCUSSION

What the authors have done for support the claim. A nice readable story must be written here where any question had found a good explanation

■ CONCLUSIONS

What we have done and what we will do in future inside this research topic

■ EXPERIMENTAL SECTION

All the experimental data supporting the authors claims and the protocols used to obtain them

■ ASSOCIATED CONTENT

Some protocols or data are placed here because heavy inside the manuscript (for example the synthetic strategies inside a pharmacological journal). Because free of charge, is also a way to disseminate the group research

■ ACKNOWLEDGMENTS

Who paid the bill?
One your friend was helpful?

■ REFERENCES

Inside a manuscript there are no personal opinions but just correlations between already published fact!



IF 5,248

Each journal has a specific scope

Journal Scope

The *Journal of Medicinal Chemistry* publishes studies that contribute to an understanding of the relationship between molecular structure and biological activity or mode of action.

Some specific areas that are appropriate include the following:

- Design, synthesis, and biological evaluation of novel biologically active compounds, diagnostic agents, or labeled ligands employed as pharmacological tools.
- Molecular modifications of reported series that lead to a significantly improved understanding of their structure-activity relationships (SAR). Routine extensions of existing series that do not utilize novel chemical or biological approaches or do not add significantly to a basic understanding of the SAR of the series will normally not be accepted for publication.
- Structural biological studies (X-ray, NMR, etc.) of relevant ligands and targets with the aim of investigating molecular recognition processes in the action of biologically active compounds.
- Molecular biological studies (e.g., site-directed mutagenesis) of macromolecular targets that lead to an improved understanding of molecular recognition.
- Computational studies that provide fresh insight into the SAR of compound series that are of current general interest or analysis of other available data that subsequently advance medicinal chemistry knowledge.
- Substantially novel computational chemistry methods with demonstrated value for the identification, optimization, or target interaction analysis of bioactive molecules.
- Effect of molecular structure on the distribution, pharmacokinetics, and metabolic transformation of biologically active compounds. This may include design, synthesis, and evaluation of novel types of prodrugs.
- Novel methodology with *broad* application to medicinal chemistry, but only if the methods have been tested on relevant molecules.



IF 5,248

If you want to publish on JMC, your study MUST contain novelty in design and synthesis of new bioactive candidates. The compound must be fully characterized for the pharmacological/Biochemistry profile. X-ray crystallography and cell based study are well accepted...

Each journal has a specific scope

Journal Scope

The Journal of Organic Chemistry (JOC) welcomes original contributions of fundamental research in all branches of the theory and practice of organic chemistry.

Since mid-2011, *JOC* has been publishing Brief Communications—preliminary results of unusual novelty and urgency that justify immediate disclosure, and *JOC* Synopses—focused short reviews of current topics, in addition to Articles, Notes, and Perspectives.

The *Journal of Organic Chemistry* now publishes *JOC* Featured Articles—full papers selected by Editor-in-Chief C. Dale Poulter and the *JOC* Associate Editors for special consideration as exceptional contributions to the journal as identified during the review process. Upon acceptance, the galley proofs of these selected manuscripts are prepared and sent to the author on an expedited schedule to facilitate more rapid online and print publication. In addition to being identified as Featured Articles on the index page of each issue, they are posted on a special *JOC* Featured Articles Web page.

Authors may choose to have the accepted version of the manuscript file appear on the Web as a *Just Accepted manuscript* until the copyedited, proof-corrected version is published as an ASAP Article or in an issue. If this option is selected, the official publication date is the date the manuscript is posted on the ACS Publications Web site as *Just Accepted*.



IF 4.721

If you want to publish on JOC, your study MUST contain novelty in chemistry related topic. In this case the bio part is less important.

Other journals are more general and ready to accept everything of high profile inside the scientific research..



Impact Factor is 42.351
(2014)



Impact Factor is 33.611
(2014)

Full article, short article or communication (Letter)?

An **article**, both full or short (less pages) is a complete study where all the literature and the experimental material supporting are included.
Difficult to do, high value.



Editor-in-Chief:
Gunda I. Georg
and
Shaomeng Wang

Editors & Editorial Board
Recommend this Journal
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Total Citations
63,060

Impact Factor
5.447

Articles Published
773

2014 Journal Citation Reports® by Thomson Reuters, 2015



Editor-in-Chief:
Dennis C. Liotta

Editors & Editorial Board
Recommend this Journal
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Total Citations
2,385

Impact Factor
3.120

Articles Published
226

2014 Journal Citation Reports® by Thomson Reuters, 2015

What about writing a Review?

Review articles are an attempt to summarize the current state of understanding on a topic. As example of grey literature, a review article re-presents previously published material, rather than reporting new facts or analysis. Academic publications that specialize in review articles are known as review journals.

Recent Update on Human Lactate Dehydrogenase Enzyme 5 (hLDH5) Inhibitors: A Promising Approach for Cancer Chemotherapy
Reshma Rani and Vinit Kumar
pp 487-496
Publication Date (Web): September 4, 2015 (Perspective)
DOI: 10.1021/acs.jmedchem.5b00168

JMC “perspective” series



ACS Chemical Review
IF 48.6

Will the journal accept my manuscript? (unlucky, probably not ☺☺ !!!)

The Impact Factor

Impact factor (IF). Introduced from ISI (Institute for Scientific Information), and published each year inside Journal Citation Reports. The IF is correlated from the citation inside the bibliography parts of the specific journal. More the research inside the journal has a high impact, more the article is cited and by reflex the IF go higher.



High IF journals are
selective ...

How to choose the right journal?

Publishing a scientific paper

Will the journal accept my manuscript? (unlucky, probably not ☺☺ !!!)

The Impact Factor



IF 5.447

IF 3,944

IF 3,346

IF 3,151

IF 2,921

Marco L. Lolli

University of Torino (UniTO)

Will the journal accept my manuscript (probably not ☺)?

The Impact Factor



Impact Factor is 5.447
(2014)



Impact Factor is 42.351
(2014)

The IF are not perfectly comparable and **must** be considered inside a specific field. If a good research inside is inside a field with low impact inside the research community, it will be receive the a low IF

Will the journal accept my manuscript (probably not ☺)?

The Impact Factor



Impact Factor is 5.447
(2014)

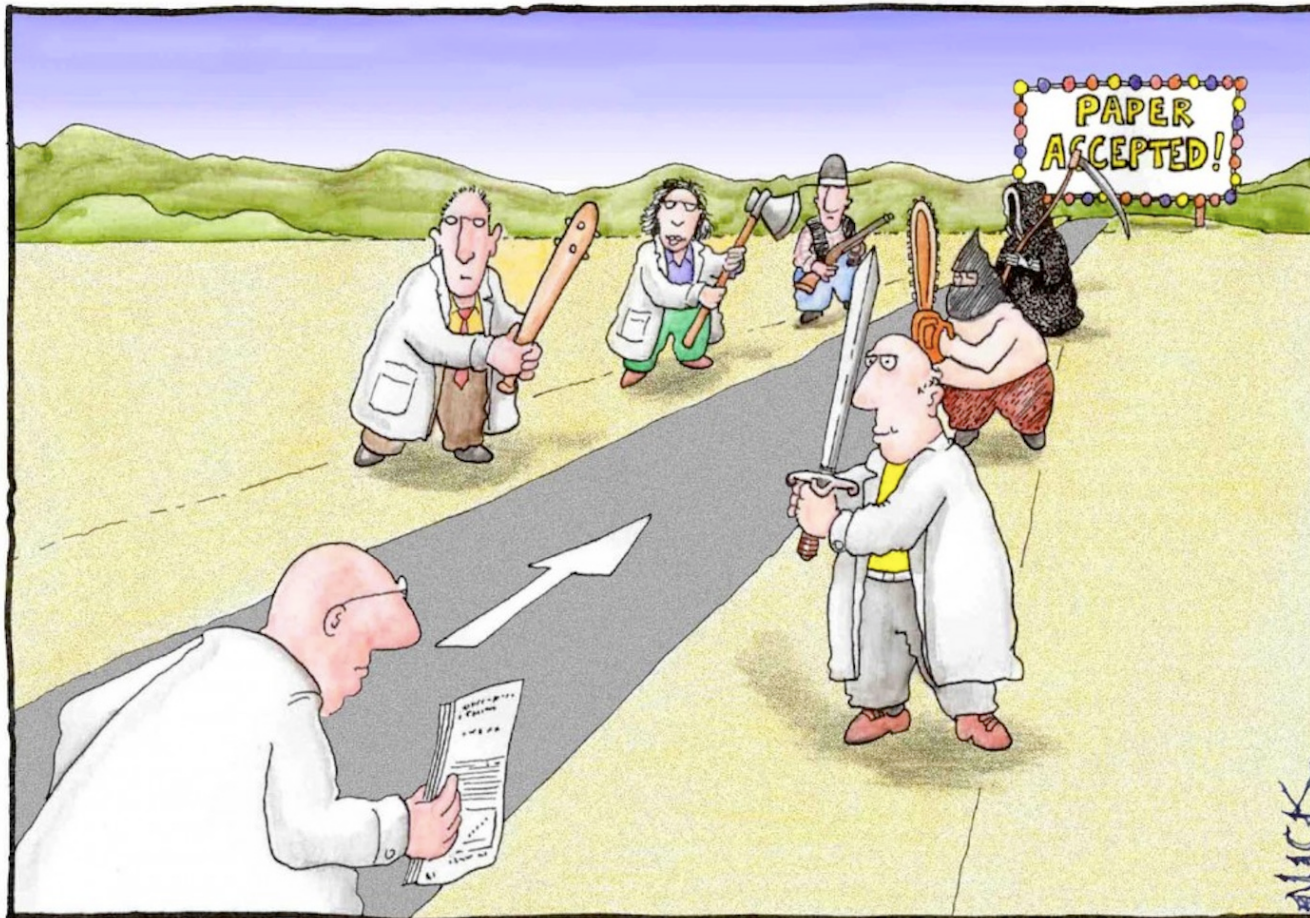


Impact Factor is 48.6
(2016)

Beside the fact that is not containing novelty, a good review has always an high impact on the field.

How be sure that real is real?

The **peer review** vs **IF** mechanism



Most scientists regarded the new streamlined peer-review process as "quite an improvement."

The **peer review** system

A blind judgment of three field expert (reviews) will judge:

- if the article fit the journal requisite
 - if the article fit the journal value (IF)
 - if the study is coherent and well done
 - the novelty of the proposal research
 - if the study is complete or some important parts are missing
 - if the experimental protocols are complete and well written
 - if the general manuscript editing is acceptable for publication (figures, mistakes, ...)
-
- Then propose to the editor to “**accept for publication** ” of “**reject**” it.

Referee (3x) Judgement





Manuscript
Submission



Rejection



OUT



Editor Judgement
STEP I

Marco L. Lolli



Editor Judgement
STEP 2

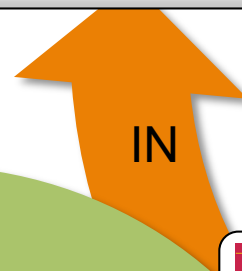
Referee (3x) Judgement



Accepted for
publication!!!



IN



University of Torino (UniTO)

The peer review system: example



The editor answer

Dear Dr. Lolli:

Below are the editor's comments and reviews for your manuscript. The reviewers have suggested major revisions before your manuscript can be accepted. Please submit a revised version of your manuscript along with a cover letter that explains point-by-point how you have responded to the comments.

Please also note that the editors are encouraging authors to submit molecular formula strings and the associated biochemical and biological data as supporting information. Providing these data is of great value to readers and can increase an article's discoverability and citability. See complete submission instructions here: http://pubs.acs.org/page/jmcmr/submission/jmcmr_mfstrings.html

We would like to receive your revision as soon as possible, 17-May-2016 at the latest.

The peer review system: example



The referee#1 answer

This manuscript is describing the design, synthesis and evaluation of 7 inhibitors of DHODH. The results presented here are worth a publication in J. Med. Chem. although along with decent science, a lot of “noise” has been slipped in the paper. For instance all the comments on the Scaffold similarity and in silico ADME/Toxicity evaluation are absolutely useless and are only lending to computer science as it does not do: proper prediction of these properties. The same goes for the content of the figure 6. This is only a fancy method to state that the series of compounds are original. Still about the computer use, several docking poses are described in the manuscript and are thus providing nice pictures. This is the only thing they do, docking calculations are still not accurate enough, despite the many useless academic papers pretending the contrary. Moreover, it would be remarkably ludicrous to try to pretend that the chemists did not designed and start to prepare the analogues (fairly obvious in view of the inhibitors reported in ref 17) in this manuscript before the docking calculations. In other words, this manuscript would be much better as a note or with much more X-ray structure which would confirm (or not) the calculations provided. This referee would also suggest to test compound 17 for its possible effect on DHODH.

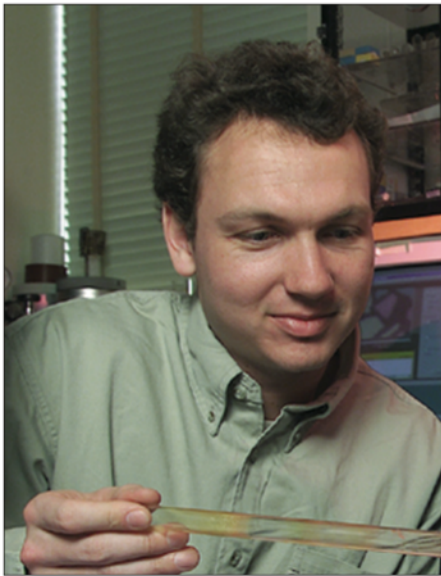
The peer review system... **limits**

Feature: Physics fraud

physicsworld.com

The rise and fall of a physics fraudster

Seven years after rumours of massive fraud began to surface, the repercussions of Jan Hendrik Schön's lies still reverberate. In her new book *Plastic Fantastic*, abridged and edited here, **Eugenie Samuel Reich** chronicles how his fraud shook the scientific world



The Schön scandal concerns German physicist Jan **Hendrik Schön** who briefly rose to prominence after a series of apparent breakthroughs with semiconductors that were later discovered to be fraudulent. The scandal provoked discussion in the scientific community about the degree of responsibility of coauthors and reviewers of scientific papers. The debate centered on whether **peer review**, traditionally designed to find errors and Determine relevance and originality of papers, should also be required to detect deliberate fraud.

Referee (3x) Judgement



What happen next?

Publishing a scientific paper

How judge the value of a single article (not only Journal Impact Factor)


Science Citation Index

The **Science Citation Index** (SCI) is a sub-set of the Science Citation Index Expanded (SCIE), containing journals that rank competitively among the most highly-cited core journals in their category or categories. The Science Citation Index Expanded is essentially the web version of what used to be a database available only on CDRom/ Diskette.



Searching the literature

Bibliopass

 UNIVERSITÀ
DEGLI STUDI
DI TORINO

Torna -> www.unito.it

Servizio di accesso alla Biblioteca Digitale Unito dalle reti esterne all'Ateneo, riservato agli utenti istituzionali (studenti in corso e personale con contratto in essere). Più informazioni sull'accesso da casa [qui](#)

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Searching the literature

Sezione area biomedica

- [Dizionari Zanichelli online](#) - Vocabolari, dizionari monolingue e bilingue, dizionari tecnici di Italiano, Inglese, Francese, Russo, Tedesco.
- [Elsevier - Ebook](#) - Accesso agli ebook dell'editore Elsevier
- [Elsevier Science Direct](#) - Accesso a periodici elettronici e ebook di uno dei fornitori di contenuti più importanti per le discipline scientifiche, tecniche e mediche. Anche le scienze umane e sociali sono rappresentate con alcuni titoli.
- [Embase](#) - Embase è una banca dati biomedica e farmacologica che indicizza letteratura biomedica internazionale dal 1947 ad oggi.
- [Harrison's Principles of Internal Medicine](#) - Principale manuale di riferimento per la medicina interna per medici, specializzandi e studenti.
- [In Pratica - Pensiero Scientifico Editore](#) - Collezione di e-books per medici e bibliotecari.
- [JAMA Network](#) - Pacchetto di riviste elettroniche pubblicate dall'American Medical Association.
- [JOVE - Journal of Visual Experiments](#) - JOVE pubblica video scientifici sottoposti a peer-review in campo biomedico, chimico e fisico. L'Ateneo sottoscrive la sezione Neuroscience e la banca dati Science Education.
- [Micromedex](#) - Informazioni evidence-based su farmaci e loro interazioni, tossicologia, analisi di laboratorio e medicina alternativa.
- [Nature](#) - Accesso ai periodici dell'editore Nature, di riferimento per le scienze biologiche, mediche e naturali.
- [New England Journal of Medicine](#) - Il NEJM è la più antica e una delle più importanti pubblicazioni di Medicina generale al mondo.
- [Oxford English Dictionary \(OED\)](#) - Dizionario della lingua inglese: fornisce definizione, storia e pronuncia di oltre 600.000 parole.
- [Oxford Scholarship Online](#) - Accesso a una selezione di ebook dell'Oxford University Press per le Neuroscienze.
- [PLOS Public Library of Science](#) - Periodici ad accesso aperto di area scientifica e biomedica.
- [ProQuest - PILOTS](#) - Fornisce indici, abstracts e full-text di periodici inerenti le discipline psicologiche.
- [Proceedings of the National Academy of Sciences \(PNAS\)](#) - Rivista ufficiale della National Academy of Sciences degli Stati Uniti.
- [PsycInfo](#) - Contiene abstracts di riviste accademiche, libri e tesi nell'ambito delle scienze comportamentali e della salute mentale.
- [PubMed](#) - Banca dati che comprende più di 25 milioni di citazioni di letteratura biomedica, tra cui Medline, curata dalla National Library of Medicine (USA). Le citazioni possono essere corredate da link al full-text in PubMed Central o sul sito dell'editore.
- [SciVal](#) - SciVal offre strumenti per l'analisi dei risultati della ricerca a partire dai dati della produzione scientifica.
- [Scopus](#) - Database di citazioni ed abstracts dell'editore Elsevier. Indicizza riviste e conference papers.
- [SpringerLink](#) - Piattaforma di accesso ai contenuti digitali (ejournals e ebook) dell'editore Springer.
- [Taylor and Francis Online](#) - Piattaforma di periodici elettronici gestita da Taylor & Francis, gruppo editoriale internazionale.
- [UpToDate](#) - Banca dati di informazioni evidence-based per il supporto alle decisioni cliniche sul point of care.
- [Web of Science](#) - Banca dati interdisciplinare a carattere citazionale. Comprende i tre indici disciplinari Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (AHCI) e il Journal Citation Reports (JCR) per la ricerca dell'Impact Factor delle riviste.
- [Wiley - Ebooks](#) - Piattaforma di ebooks dell'editore Wiley.
- [Wiley Online](#) - Piattaforma che rende disponibili online i contenuti dell'editore Wiley.

Screenshot

Search engines

Scopus

www.scopus.com

Elsevier ha introdotto nel 2004 in rete Scopus che combina le caratteristiche di PubMed e Web of Science.

Scopus - Document search - Windows Internet Explorer

http://www.scopus.com/search/form.url?zone=TopNavBar&origin=resultlist

drummond.york

Google drummond.york Effettua la ricerca Altro >> Entra

Scopus - Document search

Google Questa pagina è in inglese. Tradurre la pagina con Google Toolbar? Ulteriori informazioni Non in inglese? Traduci Disattiva traduzione inglese

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Add search field Search

Limit to: Date Range (inclusive)
☒ Published 2007 to 2007
☐ Added to Scopus in the last 7 days

Document Type
All

Subject Areas
☒ Life Sciences (> 4,300 titles) ☒ Physical Sciences (> 7,200 titles)
☒ Health Sciences (> 6,800 titles. 100% Medline coverage) ☒ Social Sciences & Humanities (> 5,300 titles)

Search

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Resource Library:
• Brochures
• User guides
• Fact sheets

Example of a SCOPUS related research

Answering:

“what happen in drug design inside the malaria topic in the last five years?”

Here is the topic where we start:

“Malaria”

Keyword TITLE-ABS-KEY (malaria)

Only article and review, no Patent

DOCTYPE (ar OR re)

SUBJAREA

(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal)

In which field are we looking?

PUBYEAR > 2009

Since the 2009

Keyword ((drug target))

We are interested in new “drug targets”, in order to include some innovation

Keyword (j med CHEM)

We are restrict the field....

Example of a SCOPUS related research

Answering:

“what happen in drug design inside the malaria topic in the last five years?”

The citation number reflex the impact of this paper on the field. Already 40 citation in only two years

Hit number#1

1 ☐ Discovery of a new family of carbonic anhydrases in the malaria pathogen *Plasmodium falciparum* - The η -carbonic anhydrases

TROVA

Click here and get the PDF

Del Prete, S., Vullo, D., Fisher, G.M., (...), Capasso, C., Supuran, C.T.

2014 Bioorganic and Medicinal Chemistry Letters

40

IF 2.42, medium level

Example of a SCOPUS related research

Answering:

“what happen in drug design inside the malaria topic in the last five years?”

Only 1 citation in the same two years ☹️

Hit number#53

53 Synthesis of gallinamide A analogues as potent falcipain inhibitors and antimalarials

TROVA

Click here and get the PDF

Conroy, T., Guo, J.T., Elias, N., (...), Hunt, N.H., Payne, R.J.

2014 Journal of Medicinal Chemistry

1

IF 5.44, high level

Protect yourself!!!

Submit a PATENT!

A **patent** is an exclusive right given by law to inventors to make use of, and exploit, their inventions for a limited period of time. By granting the inventor a temporary monopoly in exchange for a full description of how to perform the invention, patents play a key role in developing industry around the world.

- A patent is done to **protect** knowledge and not to **share**
- A patent coverage is quite expansive
- Patented literature is also **source of information**, not always reliable

Protect yourself!!!

Submit a PATENT!

Few engines allow to search the patent world:

- Esp@cenet: European Patent Office (EPO) database
(<http://www.epo.org/searching/free/espacenet.html>)
- US Patent and Trademark Office (USPTO)
(<http://www.uspto.gov/patft/>)
- The World Intellectual Property Organization (WIPO)
(http://www.wipo.int/about-wipo/en/what_is_wipo.html).



United States Patent and Trademark Office
An Agency of the Department of Commerce

Patent Full-Text Databases

Searching the literature

Sezione area Scientifica

^ AREA SCIENTIFICA

- [APS Journals](#) - Accesso ai periodici dell'American Physical Society.
- [AdisInsight](#) - Database che raccoglie dati su farmaci in via di sperimentazione a livello globale (studi clinici, casi di reazioni avverse a farmaci...).
- [American Chemical Society](#) - Accesso al full text delle riviste pubblicate dall'American Chemical Society, una fra le più importanti società scientifiche nel campo della chimica.
- [Cambridge Structural Database \(CSD\)](#) - Contiene dati cristallografici di composti organici, organometallici e di complessi metallici.
- [DigiZeitschriften](#) - Archivio retrospettivo di periodici accademici in lingua tedesca, in ambito umanistico, scientifico e nelle scienze sociali.
- [Dizionari Zanichelli online](#) - Vocabolari, dizionari monolingue e bilingue, dizionari tecnici di Italiano, Inglese, Francese, Russo, Tedesco.
- [Elsevier Science Direct](#) - Accesso a periodici elettronici e ebook di uno dei fornitori di contenuti più importanti per le discipline scientifiche, tecniche e mediche. Anche le scienze umane e sociali sono rappresentate con alcuni titoli.
- [PubMed](#) - Banca dati che comprende più di 25 milioni di citazioni di letteratura biomedica, tra cui Medline, curata dalla National Library of Medicine (USA). Le citazioni possono essere corredate da link al full-text in PubMed Central o sul sito dell'editore.
- [Reaxys](#) - Database bibliografico e fattuale per le scienze chimiche.
- [Royal Society of Chemistry](#) - Piattaforma di riviste online dell'editore Royal Society of Chemistry.
- [SciFinder](#) - Banca dati prodotta dal Chemical Abstract Service, contiene il repertorio della letteratura chimica a partire dalla fine dell'Ottocento applicata alle diverse scienze. Per la consultazione, è necessaria la creazione di un account individuale previa registrazione a questo [link](#).
- [SciVal](#) - SciVal offre strumenti per l'analisi dei risultati della ricerca a partire dai dati della produzione scientifica.
- [Science Online](#) - Accesso alle riviste della American Association for the Advancement of Science, dedicate alle discipline scientifiche, con particolare riguardo per le scienze biologiche e mediche.
- [Scopus](#) - Database di citazioni ed abstracts dell'editore Elsevier. Indicizza riviste e conference papers.
- [SpringerLink](#) - Piattaforma di accesso ai contenuti digitali (ejournals e ebook) dell'editore Springer.
- [Taylor and Francis Online](#) - Piattaforma di periodici elettronici gestita da Taylor & Francis, gruppo editoriale internazionale.
- [UlrichsWeb](#) - Repertorio di informazioni relative a periodici pubblicati a livello internazionale.
- [Walter De Gruyter Journals](#) - Pacchetto multidisciplinare di riviste pubblicate dall'editore tedesco De Gruyter.
- [Web of Science](#) - Banca dati interdisciplinare a carattere citazionale. Comprende i tre indici disciplinari Science Citation Index Expanded (SCIE), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (AHCI) e il Journal Citation Reports (JCR) per la ricerca dell'Impact Factor delle riviste.
- [Wiley Online](#) - Piattaforma che rende disponibili online i contenuti dell'editore Wiley.

Fishing the scientific knowledge

How it work?



Chemical Abstracts

- Since 1907 the Chemical Abstract Service (CAS) is published by the American Chemical Society. It fully cover the chemistry related scientific production, patent and more then 14 000 specific publication are covered.

<https://www.cas.org/>

Fishing the scientific knowledge

How it work?



- Topic

- Author

- Structures

- **Abstract:** important to understand what happened also if the access to the article is impossible.

- Keywords

ACS | Infectious Diseases

Letter

pubs.acs.org/journal/aidcbc

Onchocerca volvulus Molting Inhibitors Identified through Scaffold Hopping

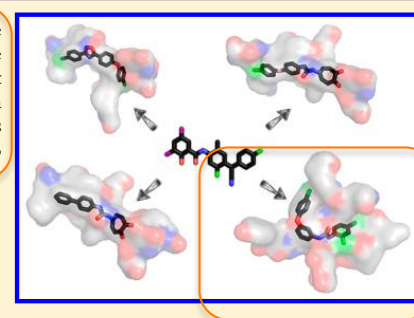
Major Gooyit,[†] Tyler L. Harris,[†] Nancy Tricoche,[‡] Sacha Javor,[†] Sara Lustigman,[‡] and Kim D. Janda^{*,†}

[†]Departments of Chemistry and Immunology and Microbial Science, The Skaggs Institute for Chemical Biology, and The Worm Institute of Research and Medicine, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, United States

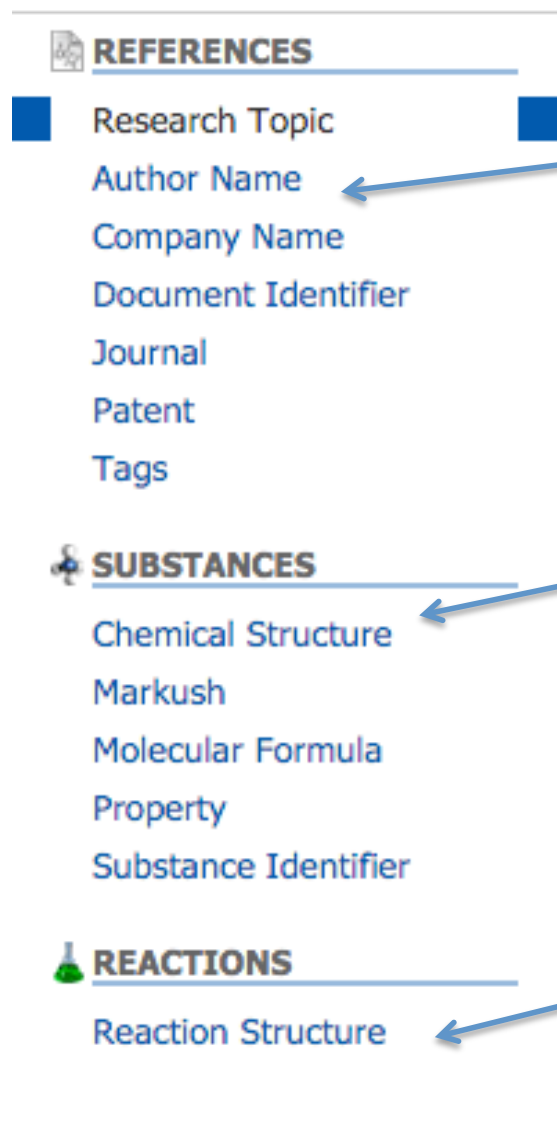
[‡]Lindsley F. Kimball Research Institute, New York Blood Center, New York, New York 10065, United States

Supporting Information

ABSTRACT: The anthelmintic closantel has shown promise in abrogating the L3 molting of *Onchocerca volvulus*, the causative agent of the infectious disease onchocerciasis. In our search for alternative scaffolds, we utilized a fragment replacement/modification approach to generate novel chemotypes with improved chitinase inhibitory properties. Further evaluation of the compounds unveiled the potential of urea-tropolones as potent inhibitors of *O. volvulus* L3 molting



KEYWORDS: onchocerciasis, tropolones, molting



Topic research.... What we want to know??

A topic, a person, a field, a molecule name....

A specific structure is needed?

A specific reaction???

Example of a SciFinder related research

Answering:

“Searching for GABA analogues in neurotransmission”



www.scifinder.com

REFERENCES: RESEARCH TOPIC ?

Examples:
The effect of antibiotic residues on dairy products
Photocyanation of aromatic compounds

Search

[Advanced Search](#) ☒ Always Show

Publication Years
Examples: 1995, 1995-1999, 1995-, -1995

Document Types

<input type="checkbox"/> Biography	<input type="checkbox"/> Historical
<input type="checkbox"/> Book	<input checked="" type="checkbox"/> Journal
<input type="checkbox"/> Clinical Trial	<input checked="" type="checkbox"/> Letter
<input type="checkbox"/> Commentary	<input type="checkbox"/> Patent
<input type="checkbox"/> Conference	<input type="checkbox"/> Preprint
<input type="checkbox"/> Dissertation	<input type="checkbox"/> Report
<input type="checkbox"/> Editorial	<input checked="" type="checkbox"/> Review

Languages

<input type="checkbox"/> Chinese	<input type="checkbox"/> Japanese
<input checked="" type="checkbox"/> English	<input type="checkbox"/> Polish
<input type="checkbox"/> French	<input type="checkbox"/> Russian
<input type="checkbox"/> German	<input type="checkbox"/> Spanish
<input type="checkbox"/> Italian	

Let's limit to the last 6 years and only to papers

Example of a SciFinder related research

Answering:

"Searching for GABA analogues in neurotransmission"



www.scifinder.com

Select All Deselect All

0 of 2 Research Topic Candidates Selected

		References
<input type="checkbox"/>	24 references were found containing " gaba analogues " as entered.	24
<input type="checkbox"/>	296 references were found containing the concept " gaba analogues ".	296

First here, then expand to
the other 296

Example of a SciFinder related research



www.scifinder.com

Answering:

“Searching for GABA analogues in neurotransmission”

Here we are....

Reactions

Cited references

Research Topic "gaba analogues" with limiters > **references (24)**

REFERENCES ?

Get Substances Get Reactions Get Related Citations Tools

Analyze Refine Categorize

Sort by: Accession Number

0 of 24 References Selected

Analyze by: Author Name

Chebib Mary 2

Gajcy K 2

Grygorenko Oleksandr O 2

Hawker Dustin D 2

Komarov Igor V 2

Librowski T 2

Lochynski S 2

Radchenko Dmytro S 2

Silverman Richard B 2

Yamamoto Izumi 2

Show More

- 1. Probing the Mode of Neurotransmitter Binding to GABA Receptors Using Selectively Fluorinated GABA Analogues**
Quick View Other Sources
By Absalom, Nathan; Yamamoto, Izumi; O'Hagan, David; Hunter, Luke; Chebib, Mary
From Australian Journal of Chemistry (2015), 68(1), 23-30. | Language: English, Database: CAPLUS
- 2. HClO₄-SiO₂-mediated improved isomerization of glycidic esters to α -hydroxy- β,γ -unsaturated esters: application in the formal synthesis of (R)-baclofen and β -phenyl GABA analogues**
Quick View Other Sources
By Basak, Ranjan; Dharuman, Suresh; Reddy, Y. Suman; Doddli, Venkata Ramana; Vankar, Yashwant D.
From Chemistry Letters (2012), 41(3), 325-327. | Language: English, Database: CAPLUS
- 3. Effectiveness of antiepileptic GABA analogues for the treatment of neuropathic pain**
Quick View Other Sources
By Yogeewari, P.; Ragavendran, J. V.; Sriram, D.; Priyanka, A.; Ganguly, S.; Reddy, A. Sunil Kumar; Semwal, Arvind
From Pharmacologyonline (2010), (1), 575-590. | Language: English, Database: CAPLUS
- 4. Esterase-mediated synthesis of optically active GABA analogues containing a stereogenic all-carbon quaternary carbon atom**
Quick View Other Sources
By Felluga, Fulvia; Ghelfi, Franco; Pitacco, Giuliana; Roccaglia, Fabrizio; Valentin, Ennio; Venneri, Cesare Daniele
From Tetrahedron: Asymmetry (2010), 21(17), 2183-2191. | Language: English, Database: CAPLUS
- 5. Stereochemistry of terpene derivatives. Part 7: Novel rigidified amino acids from (+)-3-carene designed as chiral GABA analogues**
Quick View Other Sources
By Gajcy, Kamila; Pekala, Jolanta; Frackowiak-Wojtaszek, Bozena; Librowski, Tadeusz; Lochynski, Stanislaw
From Tetrahedron: Asymmetry (2010), 21(16), 2015-2020. | Language: English, Database: CAPLUS
- 6. A role of GABA analogues in the treatment of neurological diseases**
Quick View Other Sources
By Gajcy, K.; Lochynski, S.; Librowski, T.
From Current Medicinal Chemistry (2010), 17(22), 2338-2347. | Language: English, Database: CAPLUS
- 7. Synthesis of 2-azaspiro[3.3]heptane-derived amino acids: ornithine and GABA analogues**
Quick View Other Sources
By Radchenko, Dmytro S.; Grygorenko, Oleksandr O.; Komarov, Igor V.
From Amino Acids (2010), 39(2), 515-521. | Language: English, Database: CAPLUS

Example of a SciFinder related research



www.scifinder.com

Answering:

“Searching for GABA analogues in neurotransmission”

Substance involved

Reactions

The screenshot displays the SciFinder search results page. At the top, there are tabs for 'REFERENCES', 'Get Substances', and 'Get Reactions'. Below these, there are buttons for 'Analyze', 'Refine', and 'Categorize'. The 'Refine' button is selected. On the left side, under 'Refine by:', there are radio buttons for 'Research Topic', 'Author', 'Company Name', 'Document Type', 'Publication Year', 'Language', and 'Database'. The 'Research Topic' radio button is selected. Below this, there is a text input field containing the word 'bioisosterism'. Underneath the input field, there are examples of research topics: 'The effect of antibiotic residues on dairy products' and 'Photocyanation of aromatic compounds'. A 'Refine' button is located at the bottom of this section. On the right side, there is a list of search results. The first result is '1. Probing the Mode of Neurotran' by Absalom, Nathan; Yamamoto, Izumi; From Australian Journal of Chemistry (2012). The second result is '2. HClO4·SiO2-mediated improve analogues' by Basak, Kanjan; Dharuman, Suresh; R From Chemistry Letters (2012), 41(3), 3. The third result is '3. Effectiveness of antiepileptic G' by Yogeeswari, P.; Ragavendran, J. V.; From Pharmacologyonline (2010), (1), 3. The fourth result is '4. Esterase-mediated synthesis of' by Felluga, Fulvia; Ghelfi, Franco; Pitacco From Tetrahedron: Asymmetry (2010), 20(1), 1. The fifth result is '5. Stereochemistry of terpene dei'.

Refinement with the keyword
“bioisosterism”

Example of a SciFinder related research



www.scifinder.com

Answering:

“Searching for GABA analogues in neurotransmission”

Substances involved

REFERENCES ?

Get Substances Get Reactions Get Related Citations Tools

Analyze Refine Categorize

Sort by: Accession Number

0 of 1 Reference Selected

1. Probing the orthosteric binding site of GABAA receptors with heterocyclic GABA carboxylic acid bioisosteres

Quick View Other Sources

By Petersen Jette G; Bergmann Rikke; Krogsgaard-Larsen Povl; Balle Thomas; Frolund Bente

From Neurochemical research (2014), 39(6), 1005-15. | Language: English, Database: MEDLINE

Analyze by: Author Name

Balle Thomas 1

Bergmann Rikke 1

Frolund Bente 1

Krogsgaard Larsen Povl 1

Petersen Jette G 1

reference

Authors

Example of a SciFinder related research

Answering:
Structure research



www.scifinder.com

Go on structure research

Write here your molecule

The screenshot shows the SciFinder Structure Editor interface. On the left, a sidebar contains a 'Click to Edit' button, which is highlighted by a blue arrow pointing from the text 'Go on structure research'. The main workspace displays a chemical structure of a five-membered ring containing two nitrogen atoms and one sulfur atom, with a carbonyl group and a methyl group attached. A blue arrow points from the text 'Write here your molecule' to the top of the workspace. Another blue arrow points from the text '“Lock” the position that you DO NOT want to be substituted' to a red 'X' icon in the left toolbar, which is highlighted by a blue box. A yellow banner at the top of the workspace reads 'Click an atom to block substitution.' On the right, the 'Drawing Editor' panel shows 'Structure' selected, and the 'Get substances that match y query using:' section shows 'Substructure search' selected. The bottom status bar displays the molecular formula C4H7N3OS and the molecular weight 145.19.

Example of a SciFinder related research

Answering:
Structure research



www.scifinder.com

Go for the Glu analogue

Sort by: Relevance Display Options

☐ 0 of 5 Substances Selected

☐ 1. **1257861-34-9**

~1

C₄H₇N₃O S
1,2,5-Thiadiazol-3(2H)-one, 4-(2-aminoethyl)-
[Key Physical Properties](#)

☐ 2. **313352-02-2**

~4

C₅H₇N₃O₃ S
1,2,5-Thiadiazole-3-propanoic acid, α-amino-4,5-dihydro-4-oxo-, (αR)-
[Key Physical Properties](#)

☐ 3. **313352-03-3**

~4

C₅H₇N₃O₃ S
1,2,5-Thiadiazole-3-propanoic acid, α-amino-4,5-dihydro-4-oxo-, (αS)-
[Key Physical Properties](#)

☐ 4. **472965-79-0**

~1 ~1

C₅H₇N₃O₃ S
1,2,5-Thiadiazole-3-propanoic acid, α-amino-4,5-dihydro-4-oxo-
[Key Physical Properties](#)

☐ 5. **1629999-87-6**

~1

C₁₉H₁₇Cl₂N₃O S
1,2,5-Thiadiazol-3(2H)-one, 4-[2-(2,7-dichloro-9,9-dimethyl-10(9H)-acridinyl)ethyl]-
[Key Physical Properties](#)

Rule of five.pdf Supplementary Figs_2.docx PLAA-D-16-00074.pdf PLAA-D-16-00074.pdf [Mostra tutte](#)

We did not “Lock” this position

Example of a SciFinder related research

Answering:
Structure research



www.scifinder.com

Be AWARE... predicted properties

CAS Registry Number 313352-02-2



C₅ H₇ N₃ O₃ S

1,2,5-Thiadiazole-3-propanoic acid, α -amino-4,5-dihydro-4-oxo-, (*αR*)-

Molecular Weight

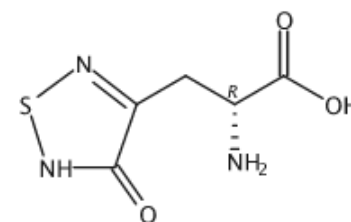
189.19

Density (Predicted)

Value: 1.94±0.1 g/cm³ | Condition: Temp: 20 °C Press: 760 Torr

pKa (Predicted)

Value: 1.97±0.10 | Condition: Most Acidic Temp: 25 °C



Rotation (-), Absolute stereochemistry.

► PREDICTED PROPERTIES

► PREDICTED SPECTRA

► TARGET INDICATORS

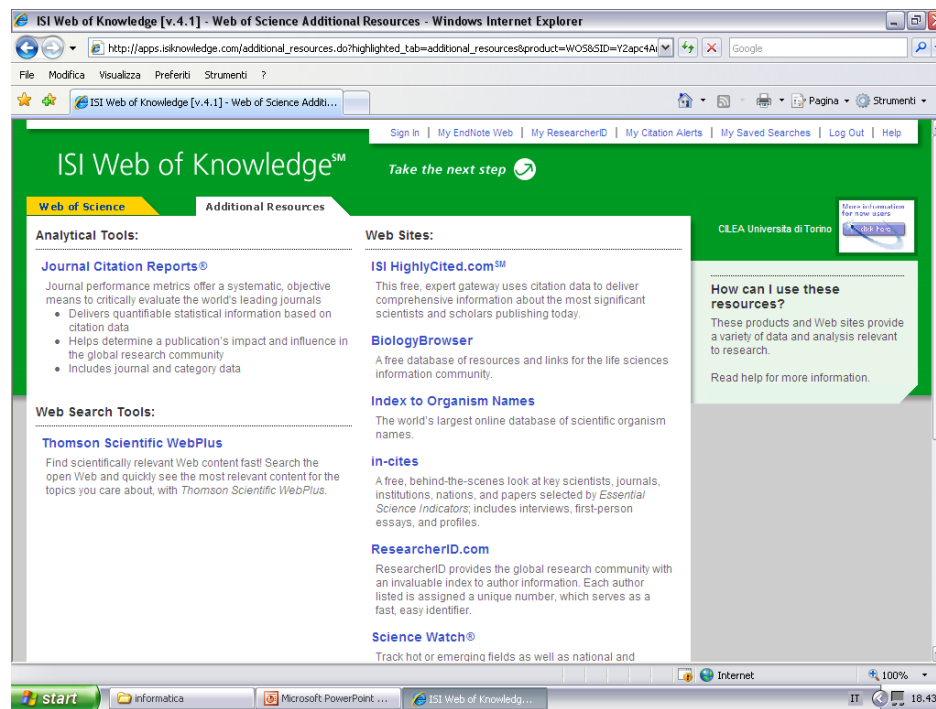
► CAS REFERENCE ROLES

► ADDITIONAL DETAILS

Search engines

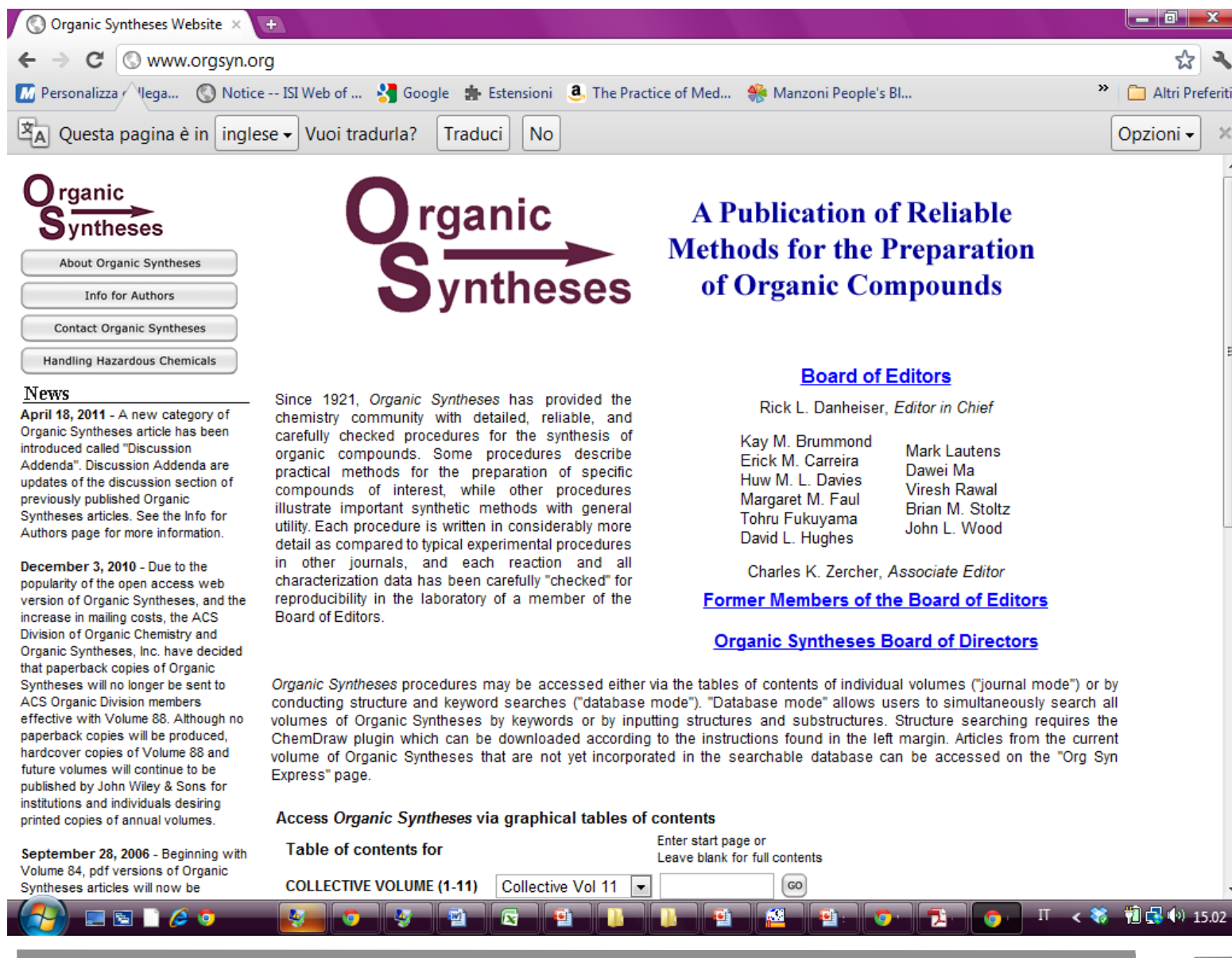
ISI Web of Science

L'Institute for Scientific Information (ISI) ha introdotto nel 2001 in rete il web ok knowledge, che è un sistema di segnalazione rapida dei documenti pubblicati in tutto il mondo dalle fonti primarie più importanti. Tale sistema è costituito da altri sottosistemi di alta utilità, tra cui: il Web of Science e il Journal Citation Reports.



<http://www.orgsyn.org/>

Property/Reactions search engines



The screenshot shows the homepage of the Organic Syntheses website. The browser window has a purple title bar and address bar showing 'www.orgsyn.org'. The website layout includes a left sidebar with navigation links, a main content area with a large logo and text, and a right sidebar with editor and board member information. At the bottom, there is a section for accessing the database via graphical tables of contents.

Organic Syntheses

About Organic Syntheses
Info for Authors
Contact Organic Syntheses
Handling Hazardous Chemicals

News

April 18, 2011 - A new category of Organic Syntheses article has been introduced called "Discussion Addenda". Discussion Addenda are updates of the discussion section of previously published Organic Syntheses articles. See the Info for Authors page for more information.

December 3, 2010 - Due to the popularity of the open access web version of Organic Syntheses, and the increase in mailing costs, the ACS Division of Organic Chemistry and Organic Syntheses, Inc. have decided that paperback copies of Organic Syntheses will no longer be sent to ACS Organic Division members effective with Volume 88. Although no paperback copies will be produced, hardcover copies of Volume 88 and future volumes will continue to be published by John Wiley & Sons for institutions and individuals desiring printed copies of annual volumes.

September 28, 2006 - Beginning with Volume 84, pdf versions of Organic Syntheses articles will now be

Organic Syntheses

A Publication of Reliable Methods for the Preparation of Organic Compounds

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Since 1921, *Organic Syntheses* has provided the chemistry community with detailed, reliable, and carefully checked procedures for the synthesis of organic compounds. Some procedures describe practical methods for the preparation of specific compounds of interest, while other procedures illustrate important synthetic methods with general utility. Each procedure is written in considerably more detail as compared to typical experimental procedures in other journals, and each reaction and all characterization data has been carefully "checked" for reproducibility in the laboratory of a member of the Board of Editors.

Organic Syntheses procedures may be accessed either via the tables of contents of individual volumes ("journal mode") or by conducting structure and keyword searches ("database mode"). "Database mode" allows users to simultaneously search all volumes of Organic Syntheses by keywords or by inputting structures and substructures. Structure searching requires the ChemDraw plugin which can be downloaded according to the instructions found in the left margin. Articles from the current volume of Organic Syntheses that are not yet incorporated in the searchable database can be accessed on the "Org Syn Express" page.

Access Organic Syntheses via graphical tables of contents

Table of contents for

Enter start page or
Leave blank for full contents

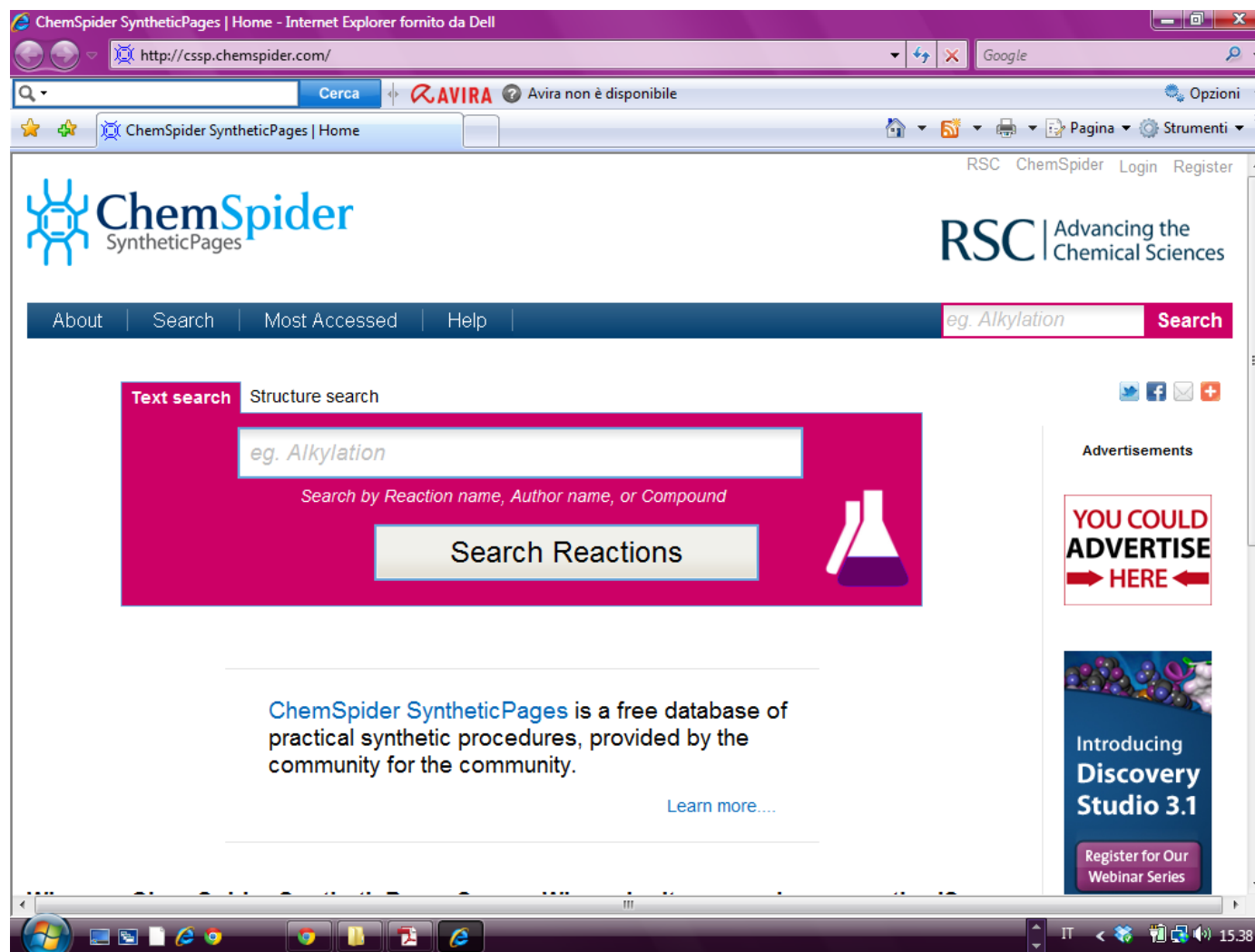
COLLECTIVE VOLUME (1-11) Collective Vol 11 GO

Marco L. Lolli

University of Torino (UniTO)

<http://cssp.chemspider.com/>

Property/Reactions search engines



Marco L. Lolli

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Fund rising campaign

Someone that pay your research bill



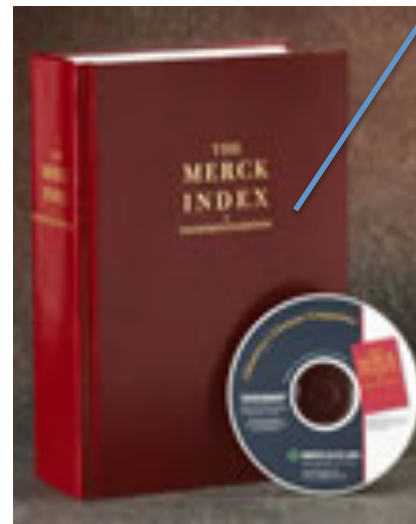
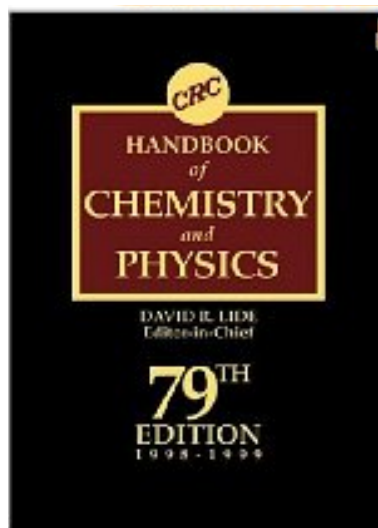
- **University** based sources
ex60%
- **Foundations** based sources
San Paolo, CRT, Bill&Melinda Gates, ...
- **European** based sources
H2020, ITN, Marie Curie, ...
- **Company** based sources
Bayer, ...
- ***Business Angels*** – seed accelerators
BioveloclTA, AutoraTT, ..

Other grey sources:

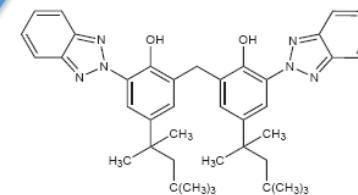
Manuals and Encyclopaedias

Manuals contain a significant amount of data scattered in diverse primary sources. Encyclopedias allow quick access to concise information. They are not updated to the latest data (eg .The Merck Index).

Good for properties....



1294. Bisotrizole. [103597-45-1] 2,2'-Methylenebis[6-(2*H*-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol]; MBBT; Tinosorb M; Tinuvin 360. $C_{41}H_{50}N_6O_2$; mol wt 658.87. C 74.74%, H 7.65%, N 12.76%, O 4.86%. UV-A filter with dual mechanism of action. Photostable organic molecule with broad UV absorption; microfine structure causes light scattering and reflection. Prep and use in light stabilizer formulations: N. Kubota, A. Nishimura, *EP 180992*; *idem*, *US 4681905* (1986, 1987 both to Adeka Argus). Light stabilization of polymers: G. Rytz *et al.*, *Angew. Makromol. Chem.* **247**, 213 (1997). Skin photoprotection study: C. Gélis *et al.*, *Photodermatol. Photobiomed. Photomed.* **19**, 242 (2003). HPLC determ in suncre formulations: C. G. Smyrniotakis, H. A. Archontaki, *J. Chromatogr. A* **1031**, 319 (2004). UV attenuating properties of microparticles: B. Herzog *et al.*, *J. Colloid Interface Sci.* **276**, 354 (2004).



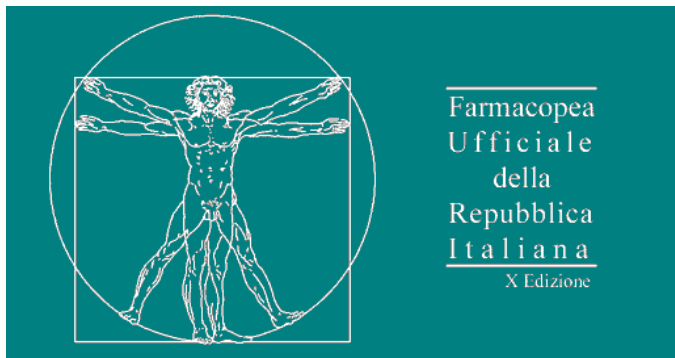
Slightly yellow powder, mp 195°. Flash pt: >200°C. d^{20}_4 1.2. Vapor pressure (25°): 6×10^{-13} Pa. Soly at 20° (%w/w): water < 0.001; acetone 0.05; chloroform 100; *n*-hexane 0.03; methylene chloride 75; toluene 34. Absorption max (chloroform): 308, 349 nm (ϵ 31895). Absorption max (*n*-heptane): 348 nm (ϵ 31600).
USE: Light stabilizer in polymers and resins.
THERAP CAT: Ultraviolet screen.

Other grey sources:

Manuals and Encyclopaedias

“La Farmacopea Ufficiale rappresenta la norma farmaceutica obbligatoria destinata ad assicurare, in una data entità politica, l'uniformità di contenuto, di composizione, di qualità e concentrazione dei principi attivi, nonché ad indicare i mezzi necessari al controllo tecnico ed analitico delle varie forme farmaceutiche”

La Farmacopea Ufficiale



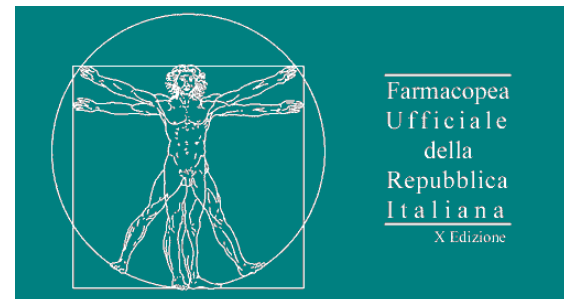
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II. INTRODUZIONE	XI
III. COMMISSIONE PERMANENTE PER LA REVISIONE E LA PUBBLICAZIONE DELLA FARMACOPEA UFFICIALE	XIII
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CAPITOLI GENERALI

Apparecchiature, metodi generali fisici e chimicofisici

Identificazione

Reattivi

MONOGRAFIE

In certe monografie o altri testi, i termini “adeguato” o “appropriato” sono usati per qualificare un reattivo, microorganismo, un metodo, ecc.; se i criteri di adeguatezza non sono descritti nella monografia, l'adeguatezza stessa deve essere riconosciuta dall'Autorità competente.

1.2. ALTRE DISPOSIZIONI RELATIVE AI CAPITOLI GENERALI E MONOGRAFIE

Quantità. Nei saggi con limiti numerici e nei dosaggi, le quantità indicate, per l'esecuzione analitica, sono approssimate. La quantità realmente usata, che può differire per non più del 10 per cento da quella indicata, deve essere esattamente pesata o misurata; il risultato è calcolato in base a questa quantità esatta. Nei saggi dove il limite non è numerico, ma dipende usualmente dal confronto con il comportamento di una sostanza di riferimento nelle stesse condizioni, viene utilizzata la quantità indicata. I reattivi vengono utilizzati nelle quantità prescritte.

Le quantità sono pesate o misurate con una accuratezza corrispondente al grado di precisione indicato. Nel caso delle pesate, la precisione corrisponde a più o meno 5 unità dopo l'ultima cifra indicata (ad esempio 0,25 g deve essere interpretata come una quantità compresa tra 0,245 g e 0,255 g). Per la misura dei volumi, se la cifra dopo il punto decimale è zero o finisce con uno zero (per esempio 10,0 ml o 0,50 ml), si utilizza a seconda del caso una pipetta, un pallone tarato o una buretta; negli altri casi può essere impiegato un cilindro o una pipetta graduata. I volumi indicati in microlitri vengono misurati mediante una micropipetta o microsirina.

E' tuttavia ammesso che, in certi casi, la precisione con la quale le quantità vengono indicate non corrisponda al numero di cifre significative indicato in uno specifico limite numerico. Le pesate e le misure vengono in questo caso effettuate con un sufficiente grado di accuratezza.

Apparecchi e procedure. La vetreria volumetrica soddisfa ai requisiti di Classe A delle appropriate Norme Internazionali stabilite dalla Organizzazione Internazionale di Normalizzazione.

Se non diversamente prescritto, le procedure analitiche vengono effettuate ad una temperatura compresa tra 15 °C e 25 °C.

Se non diversamente prescritto, i saggi comparativi vengono effettuati in tubi identici di vetro incolore, trasparente, neutro aventi un fondo piatto ed un diametro interno di 10 mm. Volumi uguali dei liquidi da comparare vengono esaminati secondo l'asse verticale dei tubi contro un fondo bianco o, se necessario, contro un fondo nero. L'esame viene effettuato con luce diffusa. Tutti i solventi impiegati in un saggio o dosaggio che prevede l'uso di un indicatore vengono preventivamente neutralizzati in presenza di quell'indicatore, a meno che non sia prescritto un saggio in bianco.

Bagno maria. Il termine “bagno-maria” significa un bagno di acqua bollente a meno che non venga indicata acqua ad un'altra temperatura. Possono essere usati altri metodi di riscaldamento a condizione che la temperatura sia vicina, ma non superiore ai 100 °C o alla temperatura prescritta.

Seccare e calcinare a massa costante. I termini “seccare a massa costante” e “calcinare a massa costante” significano che due pesate consecutive non differiscono per più di 0,5 mg; la seconda pesata viene effettuata dopo un ulteriore periodo di essiccamento o calcinazione appropriato alla natura e quantità del residuo.

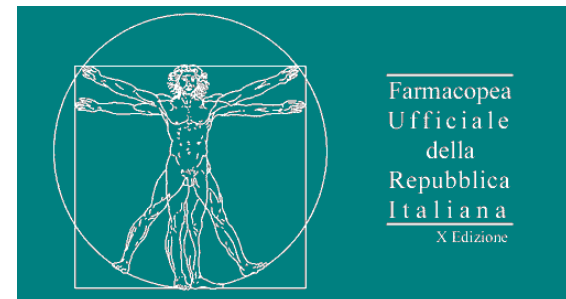
Dove è prescritto l'essiccamento utilizzando una delle espressioni “in essiccatore” o “nel vuoto” esso viene effettuato usando le condizioni descritte in 2.2.32 *Perdita all'essiccamento*.

REATTIVI

La realizzazione corretta delle procedure analitiche descritte nella Farmacopea e la attendibilità dei risultati dipende, in parte, dalla qualità dei reattivi usati. I reattivi sono descritti nel capitolo generale 4. Si assume che i reattivi utilizzati siano di qualità analitica; per alcuni reattivi sono inclusi nelle specifiche i saggi per determinare la loro adeguatezza.

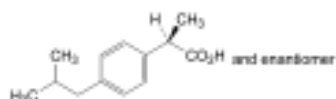
SOLVENTI

Solventi. Il termine “soluzione”, senza indicazione del solvente, indica una soluzione acquosa. Quando l'uso dell'acqua è prescritto o implicito per le procedure analitiche descritte nella Farmacopea o per la preparazione dei reattivi, l'acqua usata deve essere conforme alle specifiche della monografia *Acqua depurata* (8). Il termine “acqua distillata” indica acqua depurata preparata mediante distillazione. Il termine “etanolo” senza altra qualificazione significa alcool contenente circa il 96 per cento V/V di etanolo (C₂H₅O). Altre diluizioni di etanolo sono indicate con il termine “alcool” seguito dall'indicazione della percentuale in volume di etanolo (C₂H₅O) richiesta.



Prescrizioni generali

07/2002:0721 TESTS

IBUPROFEN**Ibuprofenum** $C_{13}H_{18}O_2$ M_r 206.3**DEFINITION**(2*S*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS**Appearance:** white, crystalline powder or colourless crystals.**Solubility:** practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.**IDENTIFICATION****First identification:** A, C.**Second identification:** A, B, D.**A.** Melting point (2.2.14): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of sodium hydroxide *R* and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (2.2.25), using a spectrophotometer with a band width of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm and 2 absorption maxima, at 264 nm and 272 nm. The ratio of the absorbance measured at the maximum at 264 nm to that measured at the shoulder at 258 nm is 1.20 to 1.30. The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (2.2.24).**Preparation:** discs.**Comparison:** ibuprofen CRS.**D.** Thin-layer chromatography (2.2.27).**Test solution.** Dissolve 50 mg of the substance to be examined in methylene chloride *R* and dilute to 10 ml with the same solvent.**Reference solution.** Dissolve 50 mg of ibuprofen CRS in methylene chloride *R* and dilute to 10 ml with the same solvent.**Plate:** TLC silica gel plate *R*.**Mobile phase:** anhydrous acetic acid *R*, ethyl acetate *R*, hexane *R* (5:24:71 V/V/V).**Application:** 5 µl.**Development:** over a path of 10 cm.**Drying:** at 120 °C for 30 min.**Detection:** lightly spray with a 10 g/l solution of potassium permanganate *R* in dilute sulphuric acid *R* and heat at 120 °C for 20 min. Examine in ultraviolet light at 365 nm.**Result:** the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.**TESTS****Solution S.** Dissolve 2.0 g in methanol *R* and dilute to 20 ml with the same solvent.**Appearance of solution.** Solution S is clear (2.2.1) and colourless (2.2.2, Method II).**Angle of optical rotation (2.2.7):** -0.05° to $+0.05^\circ$.Dissolve 0.50 g in methanol *R* and dilute to 20.0 ml with the same solvent.**Related substances.** Liquid chromatography (2.2.29).**Test solution.** Dissolve 20 mg of the substance to be examined in 2 ml of acetonitrile *R* and dilute to 10.0 ml with mobile phase A.**Reference solution (a).** Dilute 1.0 ml of the test solution to 100.0 ml with mobile phase A.**Reference solution (b).** Dissolve 20 mg of ibuprofen CRS in 2 ml of acetonitrile *R*, add 1.0 ml of a 0.05 g/l solution of ibuprofen impurity B CRS in acetonitrile *R* and dilute to 10.0 ml with mobile phase A.**Column:**

- size: $L = 0.15$ m, $\varnothing = 4.6$ mm,
- stationary phase: octadecylsilyl silica gel for chromatography *R* (5 µm).

Mobile phase:

- mobile phase A: mix 0.5 volumes of phosphoric acid *R*, 340 volumes of acetonitrile *R* and 660 volumes of water *R*; allow to equilibrate and dilute to 1000 volumes with water *R*,
- mobile phase B: acetonitrile *R*.

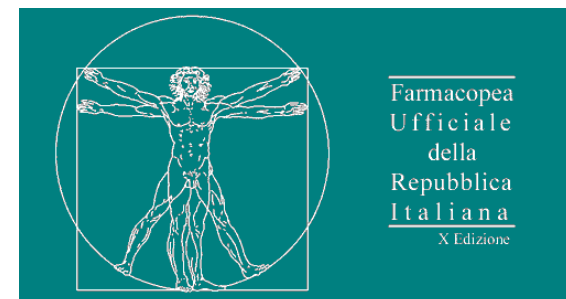
Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 – 25	100	0
25 – 35	100 → 15	0 → 85
35 – 70	15	85
70 – 12	15 → 100	85 → 0

Flow rate: 2 ml/min.**Detection:** spectrophotometer at 214 nm.**Equilibration:** for about 45 min with mobile phase A.**Injection:** 20 µl.**System suitability:** reference solution (b):

- peak-to-valley ratio: minimum of 1.5, where H' = height above the baseline of the peak due to impurity B, and H'' = height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen. If necessary, adjust the concentration of acetonitrile in mobile phase A.

Limits:

- impurity B: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- any other impurity: not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),
- total of all impurities apart from impurity B: not more than 0.7 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.7 per cent),
- disregard limit: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Impurity F. Gas chromatography (2.2.28): use the normalisation procedure.

Monografia

Ibuprofen

Monographs
D-B

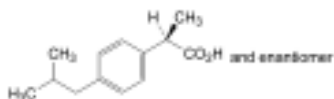
Marco L. Lolli

University of Torino (UniTO)

01/2002:0721 TESTS

IBUPROFEN

Ibuprofenum

 $C_{13}H_{18}O_2$ M_r 206.3**DEFINITION**

(2*S*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.
Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white, crystalline powder or colourless crystals.
Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: A.

Second identification: A, B, D.

A. Melting point (2.2.14): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of sodium hydroxide *R* and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (2.2.25), using a spectrophotometer with a bandwidth of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm, 2 absorption maxima, at 264 nm and 272 nm. The ratio of the absorbance measured at the maximum at 264 nm that measured at the shoulder at 258 nm is 1.20 to 1.5. The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.

Comparison: ibuprofen CRS.

D. Thin-layer chromatography (2.2.27).

Test solution. Dissolve 50 mg of the substance to be examined in methylene chloride *R* and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 50 mg of ibuprofen CRS in methylene chloride *R* and dilute to 10 ml with the same solvent.

Plate: TLC silica gel plate *R*.

Mobile phase: anhydrous acetic acid *R*, ethyl acetate *R*, hexane *R* (5:24:71 V/V/V).

Application: 5 µl.

Development: over a path of 10 cm.

Drying: at 120 °C for 30 min.

Detection: lightly spray with a 10 g/l solution of potassium permanganate *R* in dilute sulphuric acid *R* and heat at 120 °C for 20 min. Examine in ultraviolet light at 365 nm.

Result: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

TESTS

Solution S. Dissolve 2.0 g in methanol *R* and dilute to 20 ml with the same solvent.

Appearance of solution. Solution S is clear (2.2.1) and colourless (2.2.2, Method 1).

Angle of optical rotation (2.2.7): -0.05° to $+0.05^\circ$.

Dissolve 0.50 g in methanol *R* and dilute to 20.0 ml with the same solvent.

Related substances. Liquid chromatography (2.2.29).

Test solution. Dissolve 20 mg of the substance to be examined in 2 ml of acetonitrile *R* and dilute to 10.0 ml with mobile phase A.

Reference solution (a). Dilute 1.0 ml of the test solution to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve 20 mg of ibuprofen CRS in 2 ml of acetonitrile *R* and dilute to 10.0 ml with mobile phase A.

Limits:

- size: $L = 0.15$ m, $\phi = 4.6$ mm,
- stationary phase: octadecylsilyl silica gel for

- mobile phase B: acetonitrile *R*,

Time	Mobile phase A	Mobile phase B
10 min	100/0	0/100
20 min	90/10	0/100
30 min	80/20	0/100
40 min	70/30	0/100
50 min	60/40	0/100
60 min	50/50	0/100
70 min	40/60	0/100
80 min	30/70	0/100
90 min	20/80	0/100
100 min	10/90	0/100
110 min	0/100	100/0

Flow rate: 2 ml/min.

Detection: spectrophotometer at 214 nm.

Equilibration: for about 45 min with mobile phase A.

Injection: 20 µl.

System suitability: reference solution (b):

- peak-to-valley ratio: minimum of 1.5, where H_1 = height above the baseline of the peak due to impurity B, and H_2 = height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen. If necessary, adjust the concentration of acetonitrile in mobile phase A.

Limits:

- impurity B: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- any other impurity: not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),
- total of all impurities apart from impurity B: not more than 0.7 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.7 per cent),
- disregard limit: 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Impurity F. Gas chromatography (2.2.28): use the normalisation procedure.

Definizione

Caratteri

Identificazione

Monografia

Ibuprofen

Tests

Impurezze



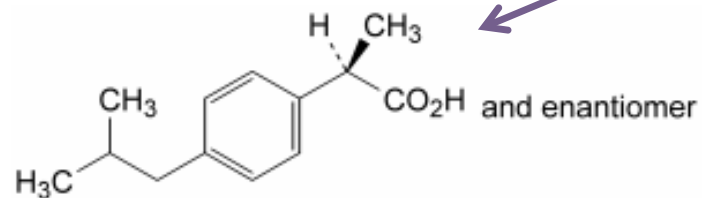
Formula bruta

07/2002:0721 TESTS

IBUPROFEN

Ibuprofenum

Formula di
Struttura



$C_{13}H_{18}O_2$

DEFINITION

(2*RS*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white, crystalline powder or colourless crystals.

Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: A, C

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Monografia

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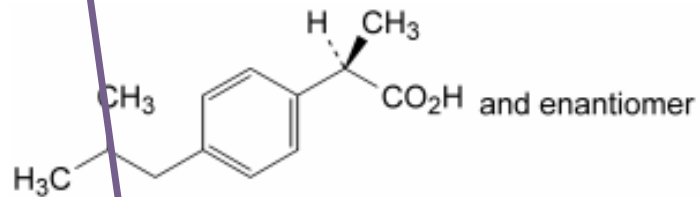
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IBUPROFEN

Ibuprofenum



$C_{13}H_{18}O_2$

M_r 206.3

DEFINITION

(2*RS*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white, crystalline powder or colourless crystals.

Solubility: practically insoluble in water, freely soluble in acetone, in methanol and in methylene chloride. It dissolves in dilute solutions of alkali hydroxides and carbonates.

IDENTIFICATION

First identification: A, C

07/2002:0721 TESTS

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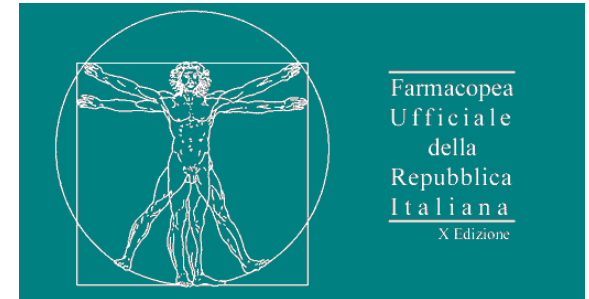
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Monografia

Ibuprofen

Profilo di Solubilità



in dilute solutions of alkali hydroxide

IDENTIFICATION

First identification: A, C.

Second identification: A, B, D.

A. Melting point (2.2.14): 75 °C to 78 °C.

B. Dissolve 50.0 mg in a 4 g/l solution of sodium hydroxide R and dilute to 100.0 ml with the same alkaline solution. Examined between 240 nm and 300 nm (2.2.25), using a spectrophotometer with a band width of 1.0 nm and a scan speed of not more than 50 nm/min, the solution shows a shoulder at 258 nm and 2 absorption maxima, at 264 nm and 272 nm. The ratio of the absorbance measured at the maximum at 264 nm to that measured at the shoulder at 258 nm is 1.20 to 1.30. The ratio of the absorbance measured at the maximum at 272 nm to that measured at the shoulder at 258 nm is 1.00 to 1.10.

C. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.

Comparison: ibuprofen CRS.

D. Thin-layer chromatography (2.2.27).

Test solution. Dissolve 50 mg of the substance to be examined in methylene chloride R and dilute to 10 ml with the same solvent.

Reference solution. Dissolve 50 mg of ibuprofen CRS in methylene chloride R and dilute to 10 ml with the same solvent.

Plate: TLC silica gel plate R.

Identificazione
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Monografia

Ibuprofen

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Hydrochloric acid. 1043500. [7647-01-0].

See *Concentrated hydrochloric acid* (0002).

Hydrochloric acid R1. 1043501.

Contains 250 g/l of HCl.

Dilute 70 g of *hydrochloric acid R* to 100 ml.

CAS number

Hydrochloric acid, brominated. 1043507.

To 1 ml of *bromine solution R* add 100 ml of *hydrochloric acid R*.

Hydrochloric acid, dilute. 1043503.

Contains 73 g/l of HCl.

Dilute 20 g of *hydrochloric acid R* to 100 ml with *water R*.

Reattivi

Hydrochloric acid, dilute, heavy metal-free. 1043509.

Complies with the requirements prescribed for *dilute hydrochloric acid R* and with the following maximum contents of heavy metals:

CAS number

Alcohol. 1002500. [64-17-5].

See *Ethanol (96 per cent) R*.

