



ELSEVIER

# Elsevier Life Science Solution 获取药物研发信息系列主题培训

Jul 2020



# Agenda

- 7月8日
  - 15: 00-15: 10: Elsevier Life Science整体解决方案介绍
  - 15: 10-16: 30: 物质结构/合成信息的获取与精炼
- 7月15日
  - 15: 00-16: 00: 生物活性数据与文献的获取与提炼
- 7月22日
  - 15: 00-16: 00: 化合物毒理药理学文献的获取
- 7月29日
  - 15: 00-16: 00: Elsevier Life Science整体解决方案数据库使用答疑
- 8月5日
  - 15: 00-16: 00: 如何将Elsevier Life Science整体解决方案贯穿药物研发的全流程

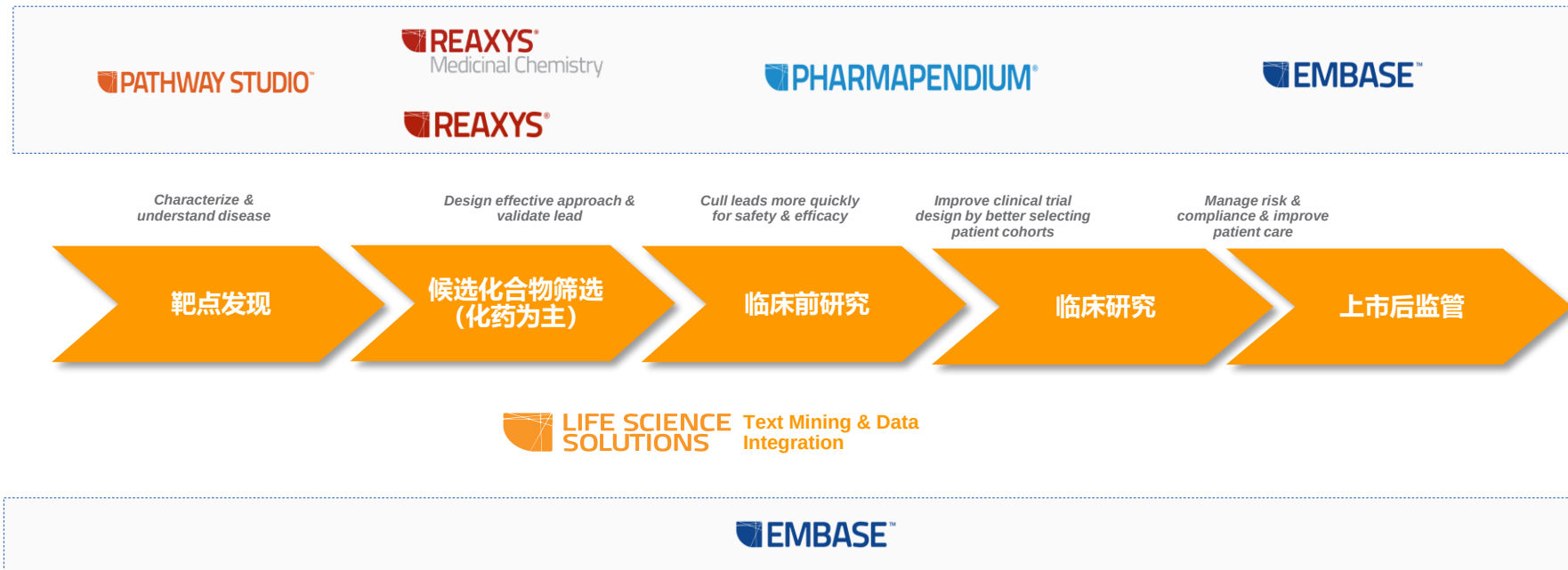


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## Elsevier Life Science整体解决方案



# Elsevier 生命科学解决方案



药物研发的全生命周期的每一个阶段都有专业化的解决方案

# 什么是Reaxys

Reaxys是Elsevier Life Science Solution中基于数据深度提炼的科研信息平台

## 6000万文献

(Elsevier, ACS, Nature-Springer, Blackwell, Taylor and Francis, etc)

## 150万专利

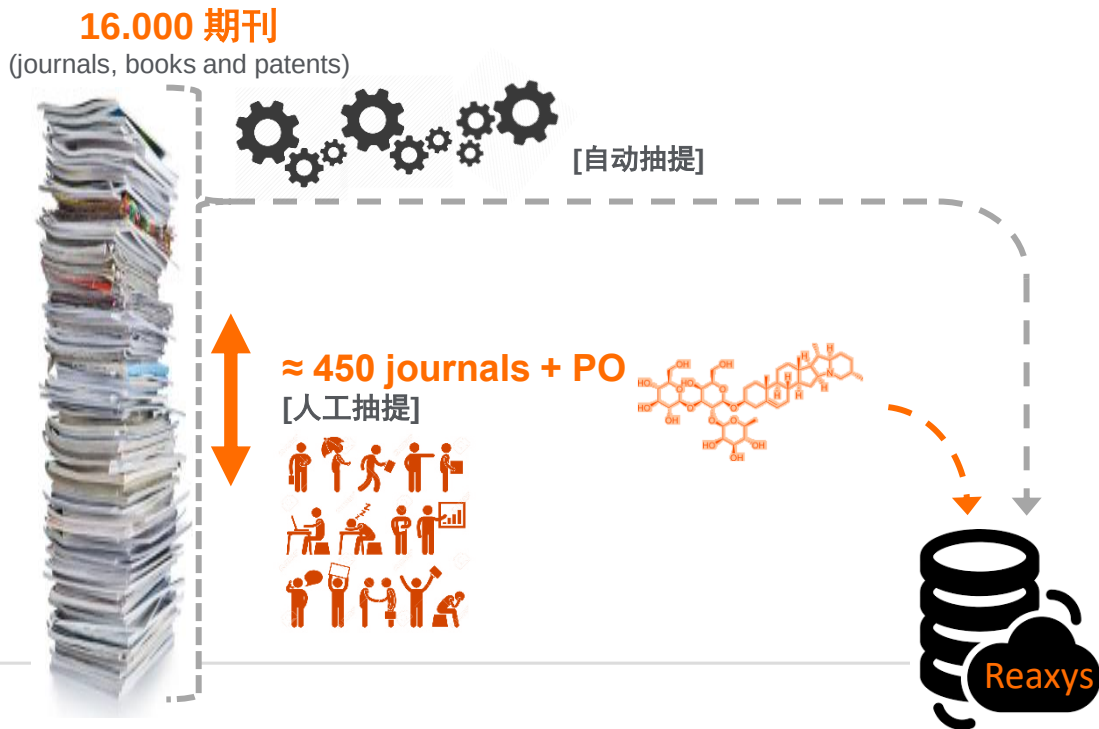
WPO, USPO, EPO [≈ mid 70's >]

PO: JP, KR, CN, TW [2015 >]

2020年将扩展到100家专利机构

## 38万书的章节

Beilstein, Gmelin, ....



# 什么是RMC (Reaxys Medicinal Chemistry)

- RMC是建立在Reaxys平台上的，和药物化学相关数据有关的数据库。
  - 包含真实的，实验确证的，小分子化合物在不同生物体系中的相关实验数据
  - 是市场上最全的，最广泛的小分子生物活性数据库
  - 实验数据源自对学术全文，专利中的相关数据的摘取，以及来自GOSTAR数据库的相关数据，并将二者在底层数据上进行整合。
  - RMC中所提供的文献，包含所有摘录的相关信息和数据，可靠，可信

## Patents Origin and starting date

- **>126 600 Patents**
- US : 1971-present
- EP : 1979-present
- WO : 1978-present (English only)
- Patents are coming from the A61K class mainly but not only.

## Articles and Journals

- **>5000 Journals Covered**
- **>353 400 Articles**
- From 1980 to Present

## Drugable Targets

- **>12 700 Drugable Targets**

# 什么是Embase

## Embase

收录超过8,200期刊 / 3,500万条文献记录！

其中超过 2,900  
种期刊在  
Medline未收录

包含100%的MEDLINE内容\*



对药物、疾病和医疗器械进行深度索引，主题性检索词是MEDLINE的两倍之多



强大的检索功能和过滤器，帮助精确查找最相关的结果



独特的信息管理功能帮助研究人员储存和修改复杂的检索策略，并可以和其他研究人员分享检索策略



独有的超过300万条会议摘要，自2009年开始已经收录超过9000个会议期刊的文摘



涵盖更多非英语类文献

Embase被众多国际性标准制定机构、研究机构推荐

# 什么是PharmaPendium

- PharmaPendium是唯一提供上市药物，临床前与临床，药效，药物安全与药代动力学、药物代谢与转运酶，药物不良反应报告等数据的一站式平台；同时还收录此领域的权威期刊书籍内容，如Meyler副反应大全和Mosby用药参考等，助力药物筛选和研发进程。

FDA & EMA所有的approval package (FDA: 1938年- 今，EMA: 1995年— 今)

2.29M+

FDA 审评文件

200K+

EMA 审评文件

9.45M+

FDA 药物不良反  
应报告

673K+

FDA 咨询委员会  
会议档案

Extracted Data:

PK Module

MET Module

FDA AERS

Efficacy Module

DDI Risk

4450

种药物的可  
检索信息

1.6M+

药代动力学信息

305K+

药物代谢与转运  
酶信息

1.66M+

药物安全信息

2.45M+

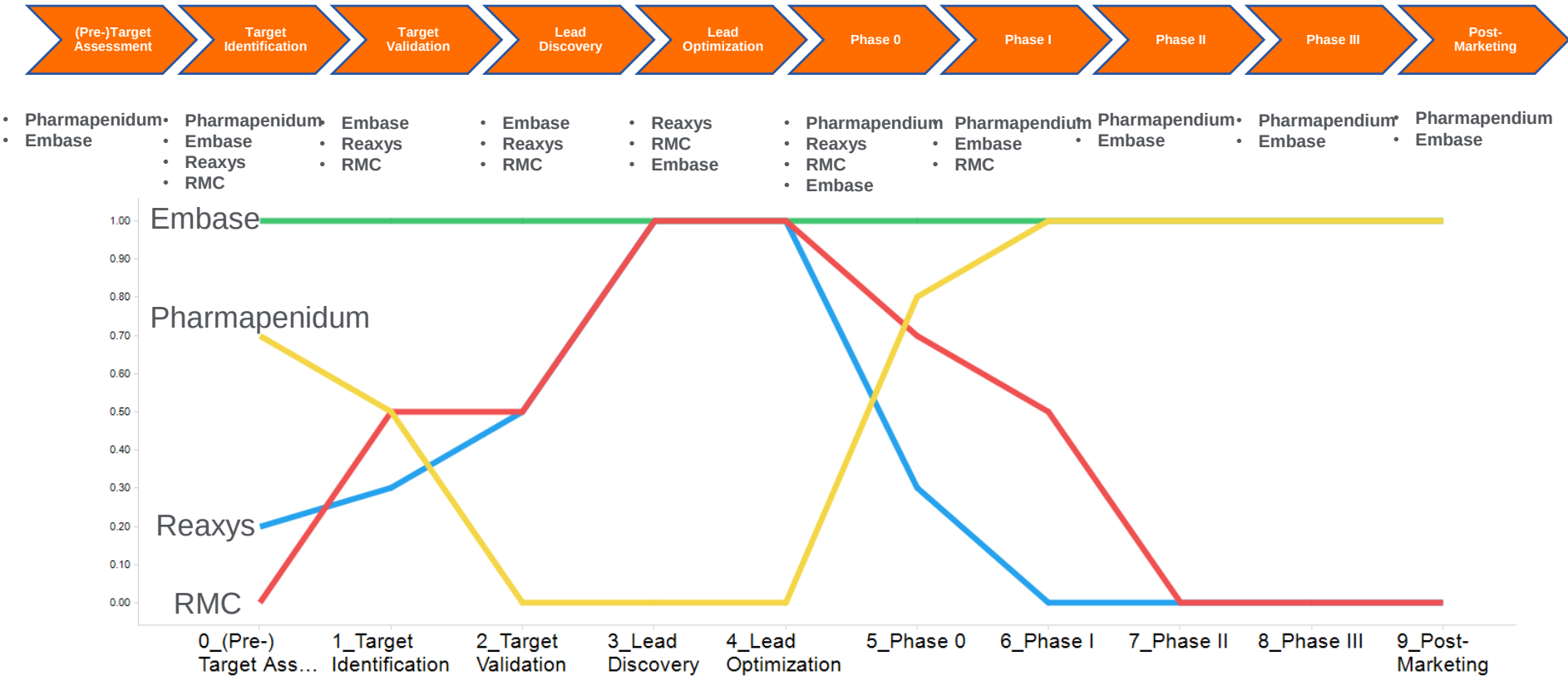
药效信息

115K+

生物活性信息



# Elsevier 生命科学解决方案在不同药物研发阶段的推荐程度





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## 物质结构/合成信息的获取与精炼

涉及：Reaxys



# Agenda

- Reaxys中的物质理化性质获取与反向物质查询
- Reaxys中结构面板使用技巧与复杂结构设计
- Reaxys中的反应设计与筛选
- Reaxys中的逆合成模块在全新化合物合成中的应用

## Case 1: 快速获取化合物的理化性质

Reaxys<sup>®</sup>

[Quick search](#) [Query builder](#) [Results](#) [Synthesis planner](#) [History](#)

Register > Sign in ⓘ

Search for solubility of gefitinib Import ⬇

Search Reaxys

solubility of gefitinib × Find >

Substance Properties, e.g. [ferroelectric materials](#)

AND

 Draw

**Tips :**  
快速获取某个化合物  
溶解性数据。

Content Overview | Latest update: 30. March 2020 >

118M

49M

59M

37M

 Substances

 Reactions

 Documents

 Bioactivities

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Cookies are used by this site. To decline or learn more, visit our [Cookies page](#)

 RELX Group™

# Reaxys中的结果

Quick search Query builder Results Synthesis planner History

Results for **solubility of gefitinib** New Edit

| Substances | Structure | as drawn AND Property       | solubility                | Preview Results | View Results |
|------------|-----------|-----------------------------|---------------------------|-----------------|--------------|
| 1          |           |                             |                           |                 |              |
| 178        | Documents | Titles, Abstracts, Keywords | "solubility", "gefinitib" | Preview Results | View Results |
| 341,792    | Documents | Titles, Abstracts, Keywords | "solubility"              | Preview Results | View Results |
| 23,178     | Documents | Titles, Abstracts, Keywords | "gefinitib"               | Preview Results | View Results |

1 Substances out of 7,831 Documents, containing 130 Reactions, 1,103 Targets

0 selected Limit To Exclude Export Preparations

gefinitib C22H24N4ClFO3 446.909 8949523 184475-35-2

Hit Data - 4  
Identification  
Druglikeness

Bioactivity (All)  
Physical Data - 98  
Spectra - 75

Other Data - 3,436

Preparations - 83  
Reactions - 130  
Targets - 1,103  
Documents - 7,831

Hit Data - 4  
Solubility (MCS) - 4 hits out of 4

抽提的数据包括  
具体的数值，或  
者相关的文字性  
描述

Solubility (MCS) - 4 hits out of 4

Show/Hide columns

| Solubility, g l <sup>-1</sup> | Saturation      | Temperature (Solubility (MCS)), °C | Solvent (Solubility (MCS)) | Location               | Comment (Solubility (MCS))                                                                                                                   | Reference                                                                                                                                                                                      |
|-------------------------------|-----------------|------------------------------------|----------------------------|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                               |                 |                                    |                            |                        | freely soluble in DMSO, THP and PEG-400, sparingly soluble in 2-butanol and slightly soluble in 1-butanol, IPA, ethanol, methanol, EG and PG | Alanazi, Abdullah; Alshehri, Sultan; Altamimi, Mohammad; Shakeel, Faiyaz [Journal of Molecular Liquids, 2020, vol. 299, art. no. 112211]<br>Full Text Details Abstract                         |
|                               |                 |                                    |                            |                        | soluble in water and 1-octanol                                                                                                               | Wu, Kuen-Da; Chen, Grace Shiahuy; Liu, Jia-Rong; Hsieh, Chen-En; Chern, Ji-Wang [ACS Medicinal Chemistry Letters, 2019, vol. 10, # 1, p. 22 - 26]<br>Full Text Cited 1 times Details Abstract  |
| 0.009832                      | in pure solvent | 25                                 | water                      | supporting information |                                                                                                                                              | Wang, Xin-Xin; Tian, Fei-Yang; Liu, Ming; Chen, Kai; Zhang, Yun-Qian; Zhu, Qian-Jiang; Tao, Zhu [Tetrahedron, 2019, vol. 75, # 37, art. no. 130488]<br>Full Text Details Abstract              |
| 0.0021                        | in pure solvent | 20                                 | water                      |                        |                                                                                                                                              | Zhao, Feng; Lin, Zhaochu; Wang, Feng; Zhao, Wei; Dong, Xiaochun [Bioorganic and Medicinal Chemistry Letters, 2013, vol. 23, # 19, p. 5385 - 5388]<br>Full Text Cited 22 times Details Abstract |

# Reaxys中化合物更多的理化性质

1 Substances out of 7,831 Documents, containing 130 Reactions, 1,103 Targets

0 selected Limit To Exclude Export Preparations

Sort by No of References ↓

Grid Heatmap

**gefitinib**  
C22H24N4ClFO3 446.909 8949523 184475-35-2

Hit Data - 4  
Identification  
Druglikeness

Bioactivity (All)  
Physical Data - 96  
Spectra - 75

Other Data - 8,436  
Preparations - 83  
Reactions - 130  
Targets - 1,103  
Documents - 7,831

Hit Data - 4  
Solubility (MCS) - 4 hits out of 4

直接获取化合物的理化性质或者谱图数据

## Physical Data - 104

- ✓ Melting Point - 25
- ✓ Association (MCS) - 12
- ✓ Chromatographic Data - 5
- ✓ **Conformation - 1**
- ✓ Crystal Phase - 7
- ✓ Crystal Property Description - 24
- ✓ Crystal System - 1
- ✓ Dissociation Exponent - 3
- ✓ Further Information - 1
- ✓ Interatomic Distances and Angles - 2

## Spectra - 77

- ✓ NMR Spectroscopy - 46
- ✓ IR Spectroscopy - 9
- ✓ Mass Spectrometry - 14
- ✓ UVVIS Spectroscopy - 6
- ✓ Raman Spectroscopy - 1

## Case 2: 理化性质的高级应用

- 获取KCl在乙醇中的溶解度

Reaxys

Quick search **Query builder** Results Synthesis planner History

Register > Sign in

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

Drag & Drop to build a new query

Search fields

Fields Forms History

Reaxys ^

Topics and Keywords v

Identification v

Physical Properties v

Spectra v

MedChem v

Other v

Reactions v

Bibliography v

PubChem v

eMolecules v

LabNetwork v

Reaxys中的Query Builder可以按照一定的规则构建检索式，Reaxys一共提供180+字段和字段组，科研人员可以自由的对这些字段和字段组进行组合，同时Reaxys也根据一些常见的需求，内置了多种检索策略模板，如“天然产物”，“hERG”等

# 检索策略的构建

Reaxys® Quick search Query builder Results Synthesis planner History Register > Sign in ⓘ

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

◇ Molecular Formula is Molecular Formula

AND ◇ Solubility

Find any Hide fields ^

= Solubility, g·l<sup>-1</sup>

is Saturation

= Temperature (Solubility (MCS)), °C

is Solvent (Solubility (MCS))

is Ratio of Solvents

Search fields  
Q solubility

Reaxys ^

◇ Solubility

◇ Solubility Product

**Tips:**  
手动添加MF 与 Solubility的字段



# 条件的输入

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

Search in: Reactions > Targets > **Substances >** **Advanced >**

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

◇ Molecular Formula is KCl

AND ◇ Solubility

- ☐ Find any Hide fields ^
- = Solubility, g l<sup>-1</sup>
- is Saturation
- = Temperature (Solubility (MCS)), °C
- is ethanol
- is Ratio of Solvents

Step3: 进行物质检索

Step1: 输入分子式KCl

Step2: 在溶剂一块选择乙醇

Solvent (Solubility (MCS)) 1

eth

|                                     |                       |       |
|-------------------------------------|-----------------------|-------|
| <input type="checkbox"/>            | ethane-1,2-diamine    | 23    |
| <input type="checkbox"/>            | ethane-1,2-diol       | 100   |
| <input type="checkbox"/>            | ethanesulfonic acid   | 1     |
| <input checked="" type="checkbox"/> | ethanol               | 5,024 |
| <input type="checkbox"/>            | ethanol (99.4percent) | 1     |
| <input type="checkbox"/>            | ethanol (99.8percent) | 1     |
| <input type="checkbox"/>            | ethanol (99.9percent) | 2     |
| <input type="checkbox"/>            | ethanol (99percent)   | 3     |
| <input type="checkbox"/>            | ethanolamine          | 3     |
| <input type="checkbox"/>            | ethyl acetate         | 1,062 |
| <input type="checkbox"/>            | ethyl benzoate        | 7     |
| <input type="checkbox"/>            | ethyl carbamate       | 6     |
| <input type="checkbox"/>            | ethyl nitrate         | 2     |

38 of 67

Go to page >

Clear selected ×

Transfer >

# 最后的结果

1 Substances out of 7,363 Documents, containing 4,322 Reactions, 68 Targets

Reaxys - 1

0 selected Limit To Exclude Export Preparations

Sort by No of References

Grid Heatmap

potassium chloride  
CIK 74.5513 3534978

Hit Data - 20  
Identification  
Druglikeness

Bioactivity (All)  
Physical Data - 2,976  
Spectra - 184

Other Data - 791

Preparations - 415  
Reactions - 4,322  
Targets - 68  
Documents - 7,363

Hit Data - 20

Solubility (MCS) - 20 hits out of 429

Solubility (MCS) - 20 hits out of 429

Show/Hide columns

| Solubility, g l <sup>-1</sup> | Temperature (Solubility (MCS)), °C | Solvent (Solubility (MCS)) | Comment (Solubility (MCS))              | Reference                                                                                                                                                                                                                                                                                                                                    |
|-------------------------------|------------------------------------|----------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                               | 20                                 | ethanol                    | Solubility: 0.012 mol/kg solvent        | <a href="#">El-Dossoki</a> [ <a href="#">Indian Journal of Chemistry, Section A: Inorganic, Physical, Theoretical and Analytical, 2005, vol. 44, # 8, p. 1594 - 1596</a> ]<br><a href="#">Full Text</a> <a href="#">Cited 6 times</a> <a href="#">Details</a> <a href="#">Abstract</a>                                                       |
|                               | 25                                 | ethanol                    | Solubility: 0.025 mol/kg solvent        | <a href="#">El-Dossoki</a> [ <a href="#">Indian Journal of Chemistry, Section A: Inorganic, Physical, Theoretical and Analytical, 2005, vol. 44, # 8, p. 1594 - 1596</a> ]<br><a href="#">Full Text</a> <a href="#">Cited 6 times</a> <a href="#">Details</a> <a href="#">Abstract</a>                                                       |
|                               | 30                                 | ethanol                    | Solubility: 0.037 mol/kg solvent        | <a href="#">El-Dossoki</a> [ <a href="#">Indian Journal of Chemistry, Section A: Inorganic, Physical, Theoretical and Analytical, 2005, vol. 44, # 8, p. 1594 - 1596</a> ]<br><a href="#">Full Text</a> <a href="#">Cited 6 times</a> <a href="#">Details</a> <a href="#">Abstract</a>                                                       |
|                               | 35                                 | ethanol                    | Solubility: 0.043 mol/kg solvent        | <a href="#">El-Dossoki</a> [ <a href="#">Indian Journal of Chemistry, Section A: Inorganic, Physical, Theoretical and Analytical, 2005, vol. 44, # 8, p. 1594 - 1596</a> ]<br><a href="#">Full Text</a> <a href="#">Cited 6 times</a> <a href="#">Details</a> <a href="#">Abstract</a>                                                       |
| 0.320571                      |                                    | ethanol                    |                                         | <a href="#">Abakshin, V. A.; Eliseeva, O. V.; Krasnoperova, A. P.; Lebedeva, L. T.; Krestov, G. A.</a> [ <a href="#">Doklady Physical Chemistry, 1991, vol. 317, p. 303 - 306</a> ][ <a href="#">Dokl. Phys. Chem. (Transl. of Dokl. Akad. Nauk.), 1991, vol. 317, p. 1140 - 1143</a> ]<br><a href="#">Full Text</a> <a href="#">Details</a> |
|                               | 20                                 | ethanol                    | Solubility: 1.270E0 mol/1000mol solvent | <a href="#">Kirm; Dunlap</a> [ <a href="#">Journal of the American Chemical Society, 1931, vol. 53, p. 393</a> ]<br><a href="#">Full Text</a> <a href="#">Details</a>                                                                                                                                                                        |
|                               | 45                                 | ethanol                    | Solubility: 1.277E0 mol/1000mol solvent | <a href="#">Kirm; Dunlap</a> [ <a href="#">Journal of the American Chemical Society, 1931, vol. 53, p. 393</a> ]<br><a href="#">Full Text</a> <a href="#">Details</a>                                                                                                                                                                        |

Reaxys直接给出具体的数据和数据的文献出处，其实也可以设定更多的条件，如温度.....

## Case 3: 反向物质查询

- 检索可用于立体选择性催化的含Fe的催化剂

Reaxys® Quick search Query builder Results Synthesis planner History Register > Sign in ?

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

Search fields  
Q catalyst X

Reaxys ^

◇ Molecular Formula is Molecular Formula

AND

◇ Catalyst Investigation

☐ Find any Hide fields ^

is Investigated characteristic(s)

is Specification of catalysis

is Classification of catalysis

is Type of reaction

is Co-catalyst/co-substrate name

# 条件的输入

Search in: Reactions > Targets > **Substances >** Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

◇ Molecular Formula contains ▼ Fe

AND

◇ Catalyst Investigation

☐ Find any Hide fields ^

is ▼ Investigated characteristic(s)

is ▼ stereoselective catalysis

is ▼ Classification of catalysis

is ▼ Type of reaction

is ▼ Co-catalyst/co-substrate name

Step3: 进行物质检索

Step1: 输入分子式Fe, 并将逻辑关系改成“Contains”, 即只要分子式中包含Fe, 就检索出来

Step2: Specification of Catalysis部分选择  
立体选择性催化

## Specification of catalysis 1

|                                     |                           |       |
|-------------------------------------|---------------------------|-------|
| <input type="checkbox"/>            | chemoselective catalysis  | 2,481 |
| <input type="checkbox"/>            | immobilised catalyst      | 452   |
| <input type="checkbox"/>            | phase-transfer catalysis  | 419   |
| <input type="checkbox"/>            | regioselective catalysis  | 2,516 |
| <input checked="" type="checkbox"/> | stereoselective catalysis | 9,365 |

# 最后的结果

0 selected Limit To Exclude Export Preparations

**iron(II) chloride**  
FeCl<sub>2</sub> 126.753 8135986

Hit Data - 11  
Identification  
Druglikeness

Bioactivity (All)  
Physical Data - 406  
Spectra - 43

Other Data - 56

Preparations - 225  
Reactions - 5,649  
Targets - 27  
Documents - 4,796

Hit Data - 11

Catalyst Investigation - 11 hits out of 102

| Investigated characteristic(s)            | Specification of catalysis                          | Type of reaction (Catalyst Investigation) | Location               | Co-catalyst/co-substrate name | Reference                                                                                                                                                                                                   |
|-------------------------------------------|-----------------------------------------------------|-------------------------------------------|------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Catalytic activity                        | Stereoselective catalysis, Regioselective catalysis | Oxidative coupling                        | supporting information |                               | Liu, Rui-Hua; Shen, Zhen-Yao; Wang, Cong; Loh, Teck-Peng; Hu, Xu-Hong[ <i>Organic Letters</i> , 2020, vol. 22, # 3, p. 944 - 949]<br>Full Text > Details > Abstract >                                       |
| Catalytic activity, Diastereomeric excess | Stereoselective catalysis                           |                                           | supporting information |                               | Wu, Chuan-Shuo; Li, Rong; Wang, Qi-Qiang; Yang, Luo[ <i>Green Chemistry</i> , 2019, vol. 21, # 2, p. 269 - 274]<br>Full Text > Cited 12 times > Details > Abstract >                                        |
| Catalytic activity, Diastereomeric excess | Regioselective catalysis, Stereoselective catalysis | Methylation                               | supporting information |                               | Sugano, Goshi; Kawada, Kojiro; Shigeta, Masayuki; Hata, Takeshi; Urabe, Hirokazu[ <i>Tetrahedron Letters</i> , 2019, vol. 60, # 13, p. 885 - 890]<br>Full Text > Cited 2 times > Details > Abstract >       |
| Catalytic activity, Diastereomeric excess | Stereoselective catalysis                           | Cross-coupling reaction                   |                        |                               | Hofmayer, Maximilian S.; Hammann, Jeffrey M.; Cahiez, Gérard; Knöchel, Paul[ <i>Synlett</i> , 2018, vol. 29, # 1, art. no. 57-2017-80542-L, p. 65 - 70]<br>Full Text > Cited 1 times > Details > Abstract > |
| Catalytic activity                        | Stereoselective catalysis                           | Silylation                                |                        |                               | Xu, Rui; Cai, Chun[ <i>Catalysis Communications</i> , 2018, vol. 107, p. 5 - 8]<br>Full Text > Cited 4 times > Details > Abstract >                                                                         |

Reaxys给出的结果与证据

Download PDF Share Export

**Tetrahedron Letters**  
Volume 60, Issue 13, 28 March 2019, Pages 885-89028 March 2019, Pages 885-890

Iron-catalyzed  $\delta$ -selective conjugate addition of methyl and cyclopropyl Grignard reagents to  $\alpha,\beta,\gamma,\delta$ -unsaturated esters and amides

Goshi Sugano, Kojiro Kawada, Masayuki Shigeta, Takeshi Hata, Hirokazu Urabe

Show more

<https://doi.org/10.1016/j.tetlet.2018.12.043> Get rights and content

Highlights

- A strictly ordered combination of three different units is attained in one flask.
- Iron and copper play complementary roles to determine the structure of olefins.
- Iron leads environmentally friendly and economical synthesis of valuable compounds.
- Superior production of a single isomer among possible five is artificially realized.

# Agenda

- Reaxys中的物质理化性质获取与反向物质查询
- Reaxys中结构面板使用技巧与复杂结构设计
- Reaxys中的反应设计与筛选
- Reaxys中的逆合成模块在全新化合物合成中的应用

# Reaxys中的结构面板



R基团定义工具

Reaxys

Quick search Query builder Results Synthesis planner History

Structure editor selected: ☒ MarvinJS ☐ ChemDrawJS

Insert structure from name >

Left sidebar: A vertical toolbar with icons for drawing, editing, and viewing. The 'R' icon for defining R groups is highlighted with a red box.

Right sidebar: A vertical list of chemical symbols and groups. The 'R' icon is highlighted with a red box.

缩写官能团，通用官能团，原子列表/列表非原子属性列表

## 一些常见的功能使用视频

| 常用功能         | 视频链接                                                                                                  |
|--------------|-------------------------------------------------------------------------------------------------------|
| 最基本功能        | <a href="https://www.bilibili.com/video/av92474230">https://www.bilibili.com/video/av92474230</a>     |
| 不定位键         | <a href="https://www.bilibili.com/video/av92568326">https://www.bilibili.com/video/av92568326</a>     |
| 通用/缩写官能团     | <a href="https://www.bilibili.com/video/av92474816">https://www.bilibili.com/video/av92474816</a>     |
| 原子列表与列表非     | <a href="https://www.bilibili.com/video/av92571129">https://www.bilibili.com/video/av92571129</a>     |
| R基团定义        | <a href="https://www.bilibili.com/video/av92569854">https://www.bilibili.com/video/av92569854</a>     |
| 原子锁定与环锁定     | <a href="https://www.bilibili.com/video/av92833557">https://www.bilibili.com/video/av92833557</a>     |
| G Group与通用原子 | <a href="https://www.bilibili.com/video/BV1Tp4y1y7SS">https://www.bilibili.com/video/BV1Tp4y1y7SS</a> |
| 原子属性列表       | <a href="https://www.bilibili.com/video/BV1B54y197G6">https://www.bilibili.com/video/BV1B54y197G6</a> |
| 盐，自由基，同位素    | <a href="https://www.bilibili.com/video/BV1pg4y1z7AB">https://www.bilibili.com/video/BV1pg4y1z7AB</a> |

可以扫二维码进群，PPT会分享到群里面



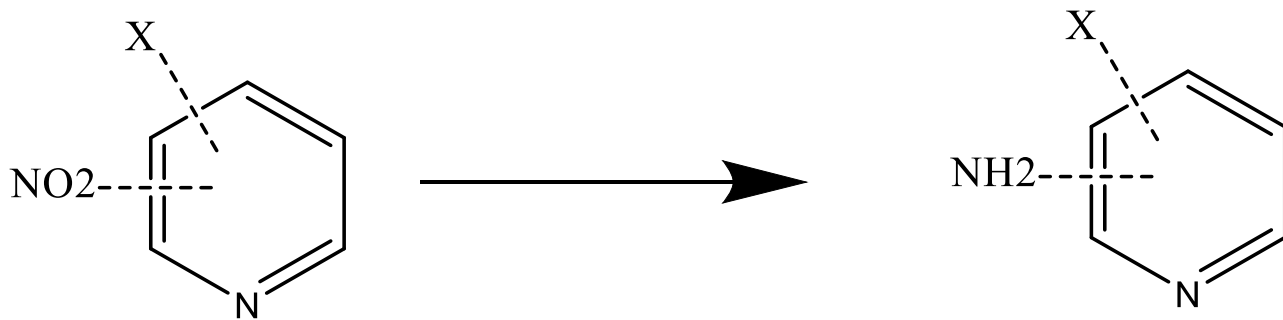


# Agenda

- Reaxys中的物质理化性质获取与反向物质查询
- Reaxys中结构面板使用技巧与复杂结构设计
- Reaxys中的反应设计与筛选
- Reaxys中的逆合成模块在全新化合物合成中的应用

## Case 4: 结构中有特殊需求的反应定义

- 检索以下反应
  - 吡啶环上存在一个硝基，一个卤素，且这两个官能团处于邻位
  - 反应过后硝基还原成氨基
  - 定义难点：如果确保NO<sub>2</sub>和卤素处于邻位



视频操作过程:

<https://www.bilibili.com/video/BV1ua4y147q2>

# Reaxys中的结构定义

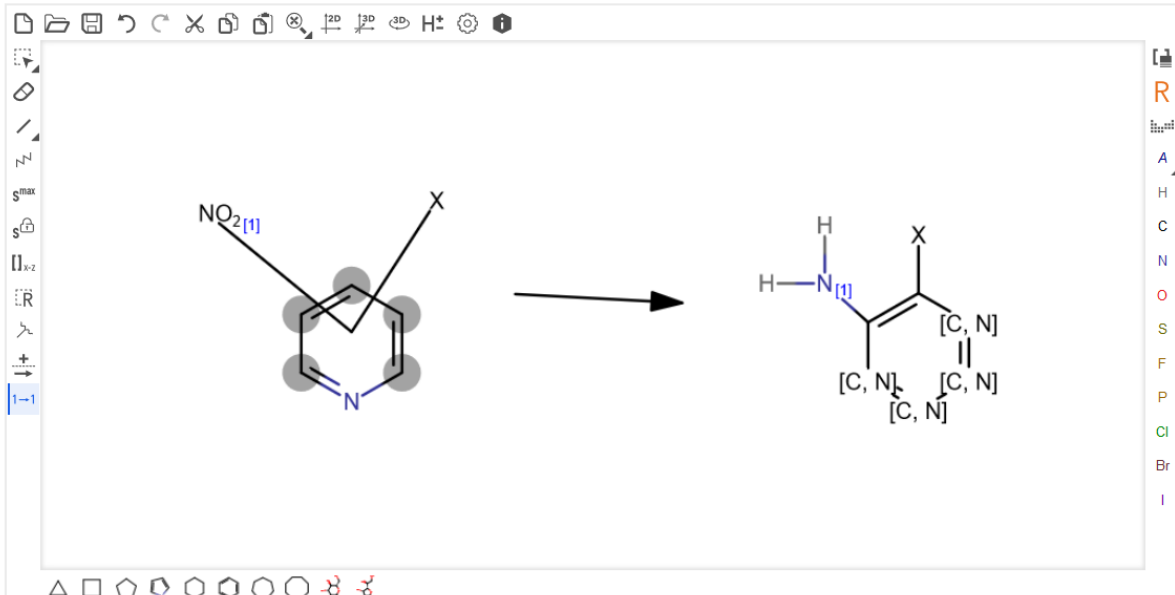
Reaxys

Quick search Query builder Results Synthesis planner History

Register > Sign in ?

Structure editor selected: ☒ MarvinJS ☐ ChemDrawJS

Insert structure from name >



Search this structure as:

- ☐ As drawn
- ☒ As substructure
  - ☒ On all atoms
  - ☐ On heteroatoms
- ☐ Similar

- ☒ Tautomers
- ☒ Stereo
- ☐ Additional ring closures
- ☐ Related Markush
- ☒ Salts
- ☒ Mixtures
- ☒ Isotopes
- ☒ Charges
- ☒ Radicals

+ More options

Clear Cancel X Transfer to query >

# 最后的结果

Reaxys® Quick search Query builder **Results** Synthesis planner

624 Filters

Limit to > Exclude >

By Structure > Yield > Reagent/Catalyst > Solvent > Catalyst Classes > Solvent Classes > Product Availability > Reactant Availability > Reaction Classes > Document Type > Publication Year >

624 Reactions out of 434 Documents containing 791 Substances, 37 Targets

0 selected Limit To Exclude Export Syn-Plan Show Conditions

1

2

3

6 Conditions Find Similar > Reaction ID: 149845

7 Conditions Find Similar > Reaction ID: 22895930

1

Conditions Find Similar > Reaction ID: 149845

| Conditions                                                                                        | Yield | Reference                                                                                                                                                        |
|---------------------------------------------------------------------------------------------------|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| With hydrogen in methanol at 20°C, for 2h;<br>Experimental Procedure >                            | 96%   | LIFESCI PHARMACEUTICALS, INC., MCDONALD, Andrew, QIAN, Shawn<br>WO2017/1936, 2017, A2<br>Location in patent: Paragraph 00159<br>Full Text > Details > Abstract > |
| With hydrogen, nickel in ethanol at 20°C, under 760.051 Torr, for 4h;<br>Experimental Procedure > | 95%   | UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.<br>WO2007/47793, 2007, A2<br>Location in patent: Page/Page column 87<br>Full Text > Details > Abstract >         |
| With iron, acetic acid Erwärmen des Reaktionsgemisches mit HgCl <sub>2</sub> und Zink.            |       | Talik, Plazek<br>[Roczniki Chemii, 1956, vol. 30, p. 1139,1145.]Chem.Abstr., <1957> 12089<br>Full Text > Details >                                               |

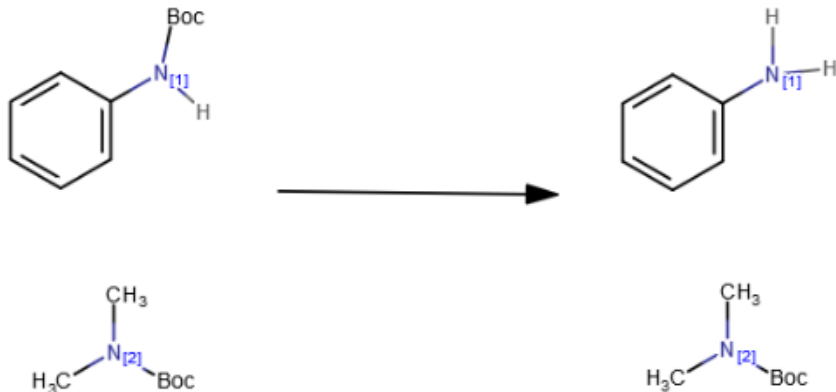
## Experimental Procedure

4-Amino-2-chloro-3-nitropyridine (6.0 g, 34.57 mmol) in 150 mL of ethanol was hydrogenated over Raney nickel catalyst (6.0 g wet) for 4h at room temperature under 1.0 atm of H<sub>2</sub> atmosphere. After addition of 4.0 g of celite to the solution, the mixture was stirred vigorously and filtered over celite pad. The filtrate was concentrated and purified with silica gel column chromatography (CH<sub>2</sub>Cl<sub>2</sub>:MeOH = 20:1 v/v) to give 2-Chloro-3,4-diaminopyridine (4.72 g, 32.84 mmol) in 95% yield. <sup>1</sup>H-NMR (DMSO, 500 MHz) δ 7.31 (d, J = 5.0, 1H), 6.45 (d, J = 5.0, 1H), 5.79 (s, 2H), 4.68 (s, 2H); <sup>13</sup>C-NMR (DMSO, 125 MHz) δ 143.41, 138.03, 135.61, 126.66, 108.73, 1.

Reaxys将相同scheme的反应全部整合成1条反应，在同样的反应下列举不同的反应条件。

## Case 5: 选择性氧化还原脱保护反应的定义

- 结构中两个带Boc的片段，两个片段以任意的形式相接在一个分子中
- 反应过后把其中一个片段的Boc脱掉，但是另外一个Boc不变



视频操作过程:

<https://www.bilibili.com/video/av92577868>

# Reaxys中的结构定义

Reaxys

Quick search Query builder Results Synthesis planner History Register > Sign in ?

Structure editor selected: ☒ MarvinJS ☐ ChemDrawJS

Insert structure from name >

Search this structure as:

- ☐ As drawn
- ☒ As substructure
  - ☒ On all atoms
  - ☐ On heteroatoms
- ☐ Similar

- ☒ Tautomers
- ☒ Stereo
- ☒ Additional ring closures
- ☐ Related Markush
- ☒ Salts
- ☒ Mixtures
- ☒ Isotopes
- ☒ Charges
- ☒ Radicals

+ More options

Clear Cancel Transfer to query >

Reaxys可以直接设定这些片段在一个结构中

☐ Ignore Atom Mappings

☒ Keep fragments

☐ Separate ☒ Together

# Reaxys中结果

Reaxys<sup>®</sup> Quick search Query builder **Results** Synthesis planner History

12 Filters

Limit to > Exclude >

12 Reactions out of 8 Documents containing 22 Substances, 5 Targets

0 Limit To Exclude Export Syn-Plan Show Conditions

By Structure ▾

Yield ▾

Reagent/Catalyst ▾

Solvent ▾

Catalyst Classes ▾

Solvent Classes ▾

Product Availability ▾

Reactant Availability ▾

Reaction Classes ▾

Document Type ▾

Publication Year ▾

☐ Single step reactions only

☐ Experimental procedure only

1

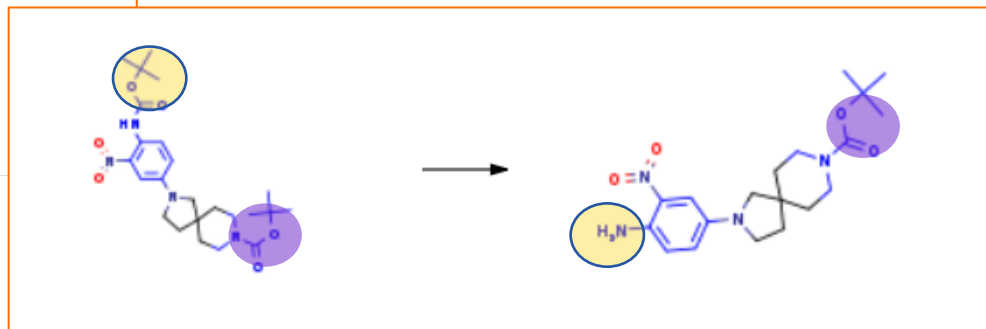
2

3

1 Conditions Find Similar > Reaction ID: 51038227

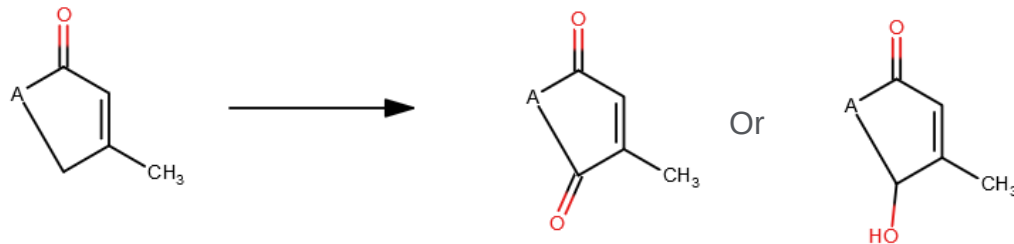
1 Conditions Find Similar > Reaction ID: 51038186

1 Conditions Find Similar > Reaction ID: 51038186



## Case 6: 涉及环上定义的反应

- 检索以下反应



### **Requirement:**

- $\geq 5$ 元环系
- 甲基不能有取代

视频操作过程:

<https://www.bilibili.com/video/BV1Y5411Y7AV>



# Reaxys中的结构定义

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History Register > Sign in ⓘ

Structure editor selected: ☒ MarvinJS ☐ ChemDrawJS Insert structure from name >

Search this structure as:

- ☐ As drawn
- ☒ As substructure
  - ☒ On all atoms
  - ☐ On heteroatoms
- ☐ Similar

☐ Tautomers

☒ Stereo

☒ Additional ring closures

☐ Related Markush

☒ Salts

☒ Mixtures

☒ Isotopes

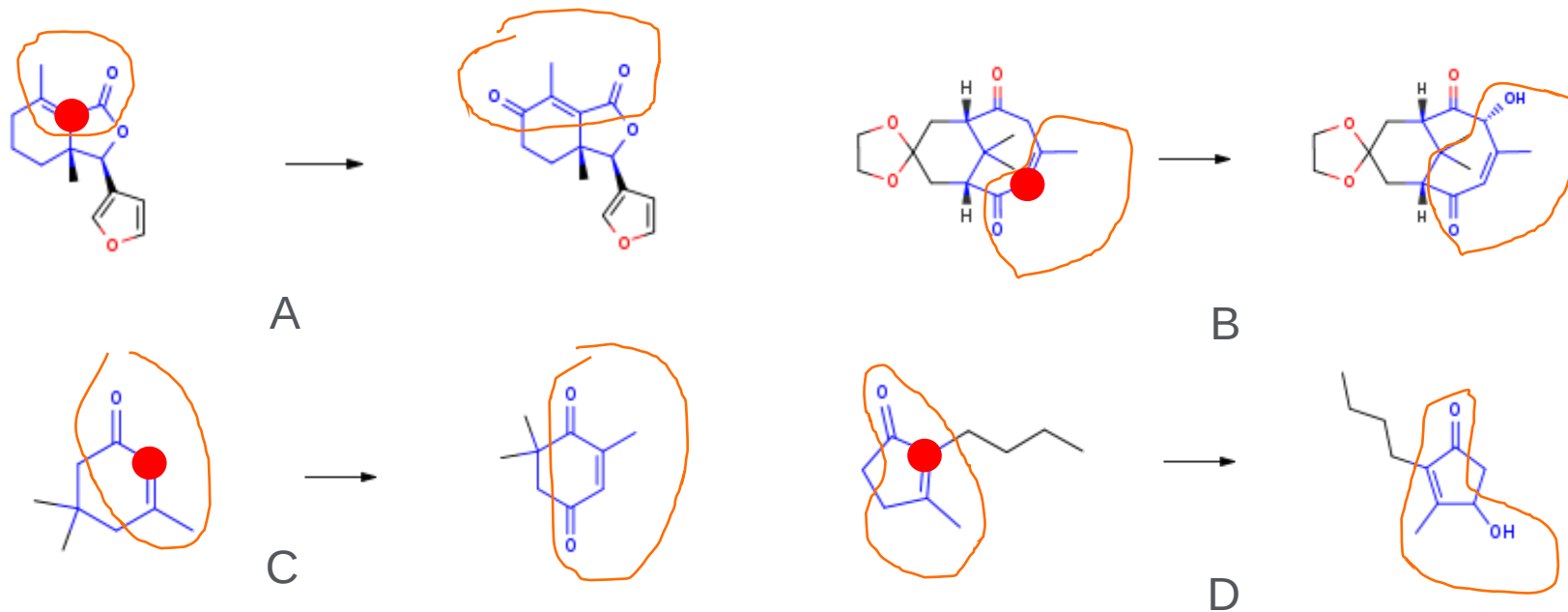
☒ Charges

☒ Radicals

+ More options

Clear

## Reaxys中结果



能否获得红色标记C原子只出现在一个环系中的结构，即可以获得BCD，但是A检索不出来

# Reaxys中的结构定义

Reaxys

Quick search Query builder Results Synthesis planner History

Register > Sign in

Structure editor selected: ☒ MarvinJS ☐ ChemDrawJS

Insert structure from name >

Search this structure as:

- ☐ As drawn
- ☒ As substructure
  - ☒ On all atoms
  - ☐ On heteroatoms

query prop.

A Q M X

AH QH MH XH

? query prop.

Salts

Mixtures

Atom query properties

|     |      |      |     |
|-----|------|------|-----|
| .H+ | .h+  | .v+  | .X+ |
| .H- | .h-  | .v-  | .X- |
| .R+ | .r+  | .rb+ | .s+ |
| .R- | .r-  | .rb- | .s- |
| .u  | .a/A | .rb* | .s* |

The screenshot displays the Reaxys software interface. The main workspace shows a chemical reaction scheme. On the left, a reactant is a five-membered ring with a carbonyl group (C=O) and a double bond. The ring atoms are labeled with atom queries: [A] for the carbonyl carbon, [1-10] for the ring carbons, and [rb2] for the ring nitrogens. A methyl group (CH3) is attached to one of the ring nitrogens. An arrow points to the right, leading to the product. The product is a similar five-membered ring with a carbonyl group and a double bond. The ring atoms are labeled with atom queries: [A] for the carbonyl carbon, [1-10] for the ring carbons, and [rb2] for the ring nitrogens. A methyl group (CH3) is attached to one of the ring nitrogens. Below the reaction scheme, the R1 group is defined as a fragment with a carbonyl group and a hydroxyl group, labeled with atom queries [1] and [2].

# Reaxys中最后的结果

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History

34 Filters

Limit to > Exclude >

By Structure >

Yield >

Reagent/Catalyst >

Solvent >

Catalyst Classes >

Solvent Classes >

Product Availability >

Reactant Availability >

Reaction Classes >

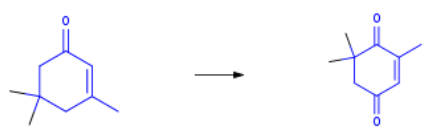
Document Type >

Publication Year >

34 Reactions out of 41 Documents containing 43 Substances, 3 Targets

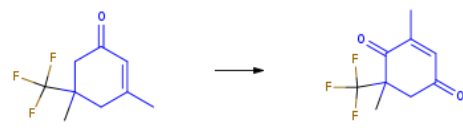
☐ 0 selected Limit To Exclude Export Syn-Plan Show Conditions

1



18 Conditions Find Similar > Reaction ID: 1732207

2



3 Conditions Find Similar > Reaction ID: 37390289

# 可以利用Reaxys的结果集处理来判断都去除了哪些反应

Reaxys<sup>®</sup> Quick search Query builder Results Synthesis planner History Register > Sign in ?

Search in: Reactions > Targets > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

46 Reactions (substructure search), isotopes, stereo\_absolute, salts, charges, radicals, mixtures, align

NOT 34 Reactions (substructure search), isotopes, stereo\_absolute, salts, charges, radicals, mixtures, align

Search fields

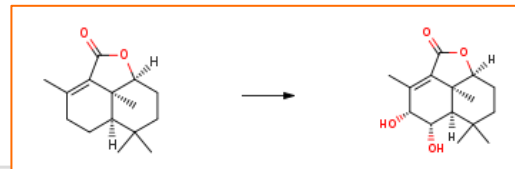
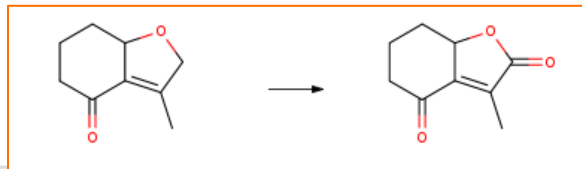
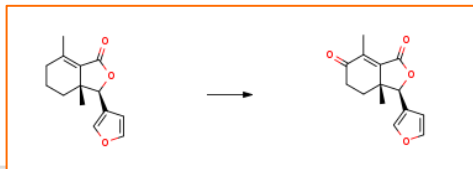
Fields Forms History

Reaxys ^

Recent ^

34 Reactions (substructure search), isotop...

46 Reactions (substructure search), isotop...



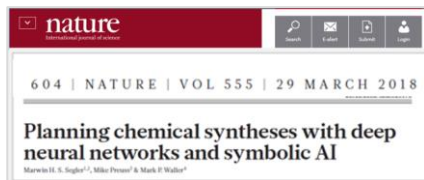
# Agenda

- Reaxys中的物质理化性质获取与反向物质查询
- Reaxys中结构面板使用技巧与复杂结构设计
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- Reaxys中的逆合成模块在全新化合物合成中的应用

# Reaxys-AI逆合成工具--新颖的算法+高质量数据

在化学AI逆合成领域，最被引用的著作之一是由爱思唯尔、马文·塞格勒博士和马克·沃勒教授合作完成的

## Reaxys预测性逆合成工具文献之一



**AI in Action: Neural networks learn the art of chemical synthesis**

Robert F. Service  
See all authors and affiliations

Science 07 Jul 2017  
Vol. 357, Issue 6346, pp. 27  
DOI: 10.1126/science.357.6346.27



NEWS • 28 MARCH 2018

## Need to make a molecule? AI gives instructions

Artificial-intelligence tool that has digested nearly every chemical reaction in the literature could transform chemistry.



ELSIP & Elsevier Confidential

08/07/2020

**Game Changer: Scientist Mark Waller**  
Next level with AI-Driven Synthesis

May 15, 2018

Share Facebook Twitter LinkedIn Google+ YouTube Print

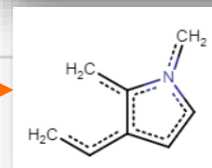
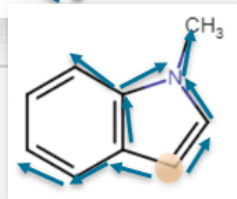
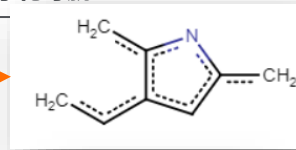
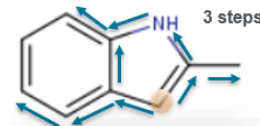


## Reaxys-RT相对于其他RTs的优势

- 不依赖于手动提取和编码规则（手动）
- 集成高自由度的中间体库和专有的反应数据
- 为更多的无文献报道的分子或新颖分子提供逆合成解决方案
- 比传统的计算机辅助方法快30倍

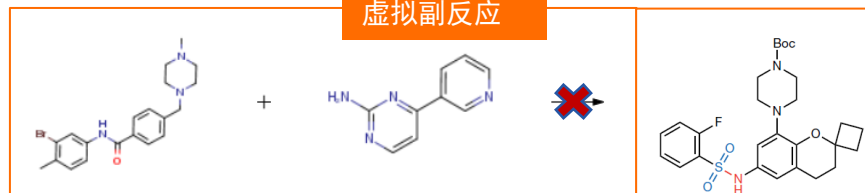
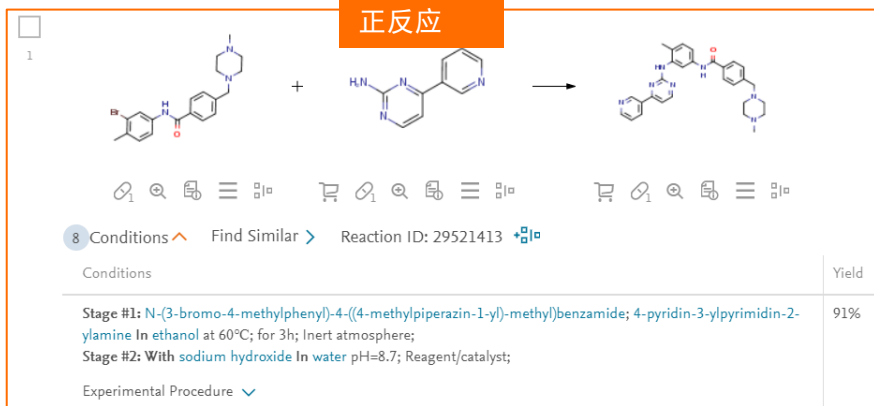
## 预测性逆合成的价值

- 新观念的产生：寻找新化合物的合成途径
- 省时：减少开发合成路线的时间和精力
- 降低研发成本：提高合成成功率
- 知识扩充：为化学家提供路线设计的数字化导航

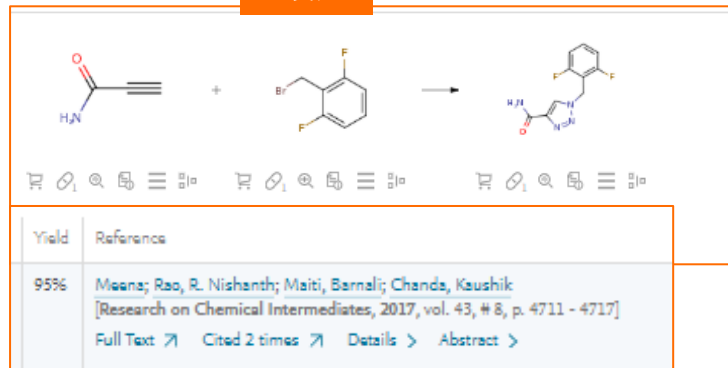


# 深层神经网络利用虚拟副反应对Reaxys预测逆合成训练

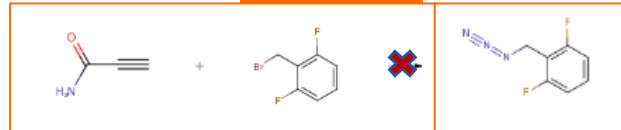
## 自动创建虚拟副反应训练AI举例



## 正反应



## 虚拟副反应



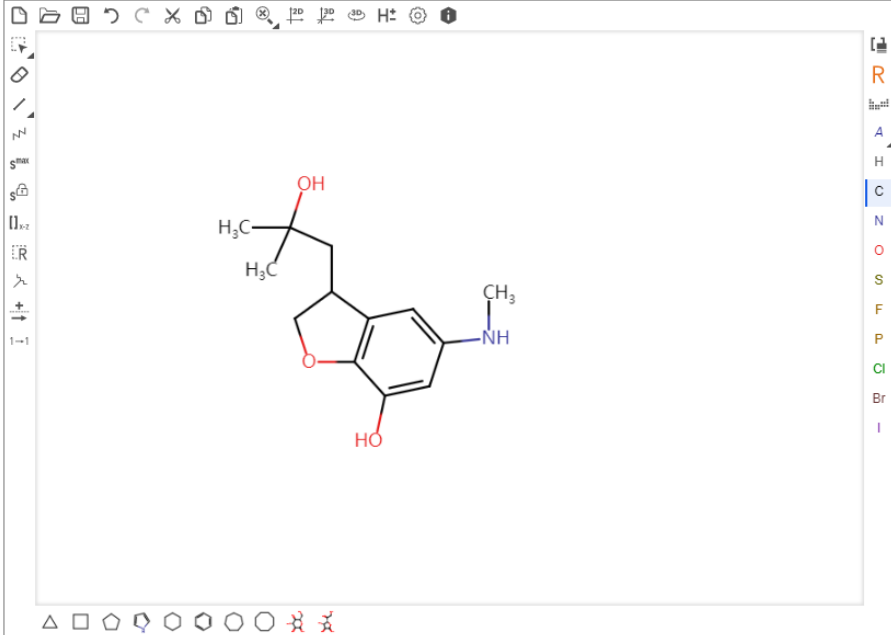
1. 根据这一原理，通过对相关的产物和对和相应的反应进行洗牌，产生了否定的例子
2. 利用这些数据增强策略，我们从2015年之前发布的培训反应中产生了1亿个负面反应



# Reaxys逆合成模块

Retrosynthetic Route Designer Powered by Reaxys and Pending.AI My Synthesis Projects Draw a Target Logout

Draw a target substance



Retrosynthesis Parameters

Length and depth of synthesis plans ①

☒ Full synthesis plan 20 ☐ Last step only

Diversity of synthesis plans ①

Reaction Step to occur: 3 times

Building block to occur: 3 times

Processing time ①

2 30

Select Building Block Libraries ①

☒ Standard Lab Chemicals

☒ Reaxys common substrates

☒ Sigma Aldrich

☒ LabNetworks

☒ emolecules

Clear Cancel Synthesize >

Feedback

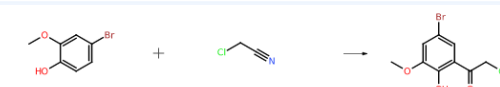
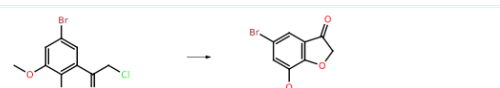
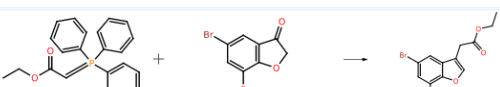
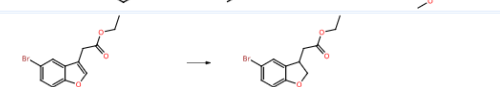
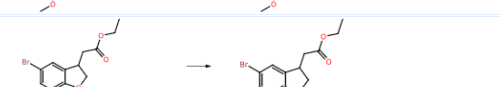
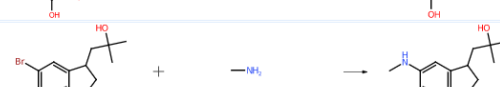
线路长短设置

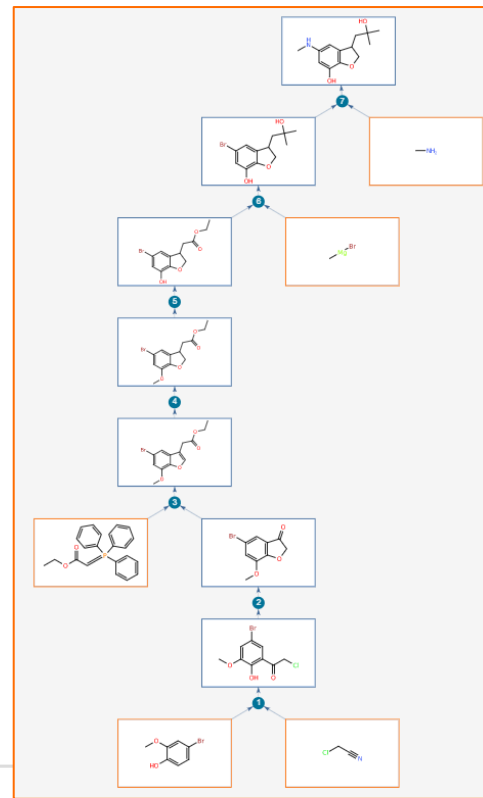
多样性设置

时间设置

起始原料设置

## 最后的结果—其中一条反应

| Step no. | Reaction                                                                          | Step confidence score                          |
|----------|-----------------------------------------------------------------------------------|------------------------------------------------|
| 1        |  | 0.92 <a href="#">Show Reaxys Examples &gt;</a> |
| 2        |  | 1 <a href="#">Show Reaxys Examples &gt;</a>    |
| 3        |  | 1 <a href="#">Show Reaxys Examples &gt;</a>    |
| 4        |  | 0.97 <a href="#">Show Reaxys Examples &gt;</a> |
| 5        |  | 0.99 <a href="#">Show Reaxys Examples &gt;</a> |
| 6        |  | 1 <a href="#">Show Reaxys Examples &gt;</a>    |
| 7        |  | 0.96 <a href="#">Show Reaxys Examples &gt;</a> |



## 物质结构/合成信息的获取与精炼小结

- Reaxys从大量文献中摘取和物质性质相关的所有数据，帮助科研人员获得标准化，规范化，格式化的物性数据列表及参考文献
- Reaxys中的Query Builder检索帮助科研人员通过简便的方式，获得精准，跨学科精确答案
- Reaxys中的结构面板，能实现科研人员绝大部分的结构绘制要求，帮助科研人员用最直接的方式获得相应的物质和反应
- Reaxys培训中心
  - <https://www.elsevier.com/zh-cn/rd-solutions/pharma-and-life-sciences-solutions/life-sciences-online-training-center>



# 生物活性数据与文献的获取与提炼内容预告

- RMC, PharmaPendium
- 构效关系的获取
- 先导化合物优化
- FDA/EMA审评文档中活性数据的获取。



Thank you

