Elsevier
Reaxys使用介绍

俞靓（Sam Yu）
Elsevier Life Science Customer Consultant
Mail:S.yu.2@Elsevier.com
Phone: 18930408012

Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

什么是Reaxys

Reaxys是Elsevier旗下Life Science产品线中基于数据深度提炼与挖掘的化学及相关学科的科研信息平台

6,000万文献

(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,….

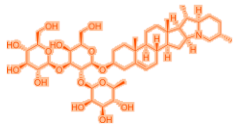
16,000 期刊

(journals, books and patents)

[自动抽提]

≈ 450 journals + PO

[人工抽提]

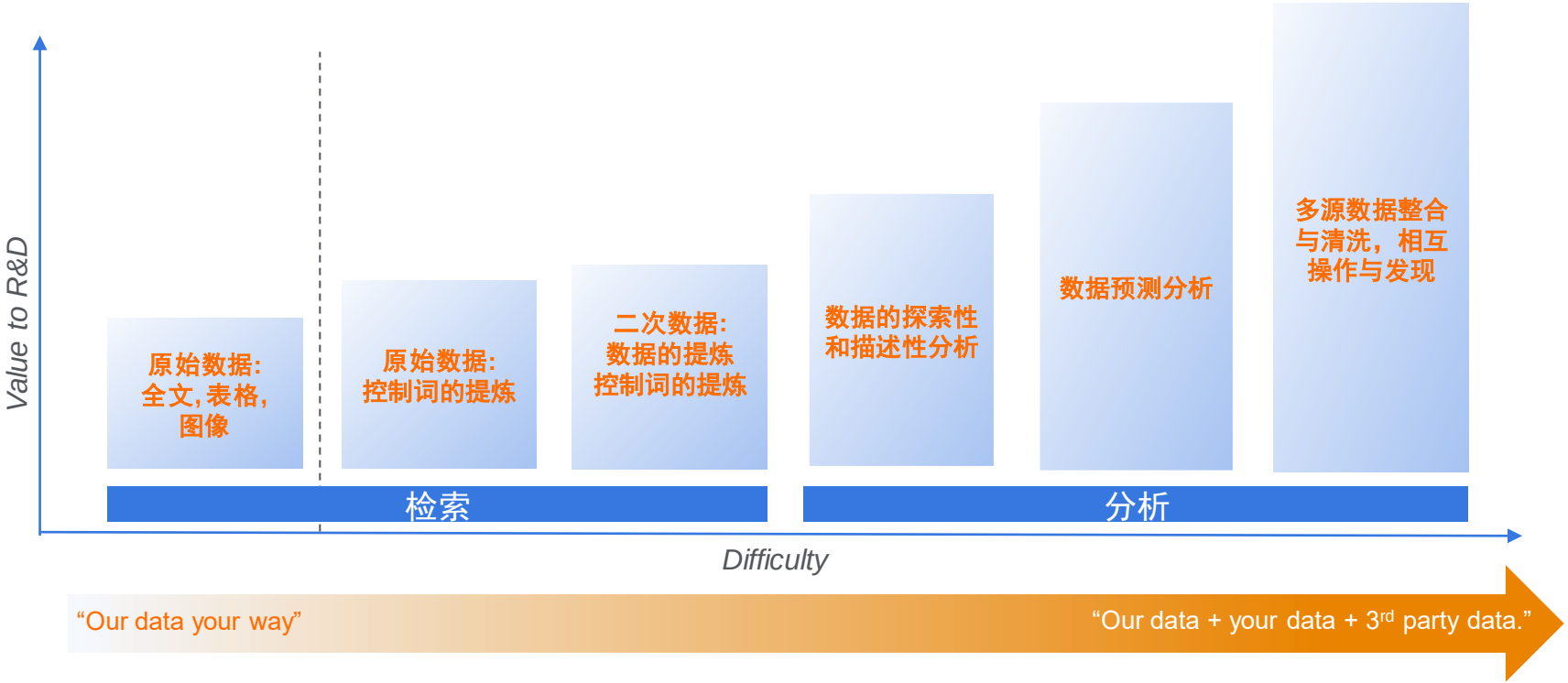


ELSEVIER

Reaxys的战略是为化学研究的全生命周期，提供完整的化学生态系统

不断利用AI/ML技术， 引领数据库到解决方案的行业升级

Reaxys等Elsevier Life Science
全线产品都在朝解决方案方向发展

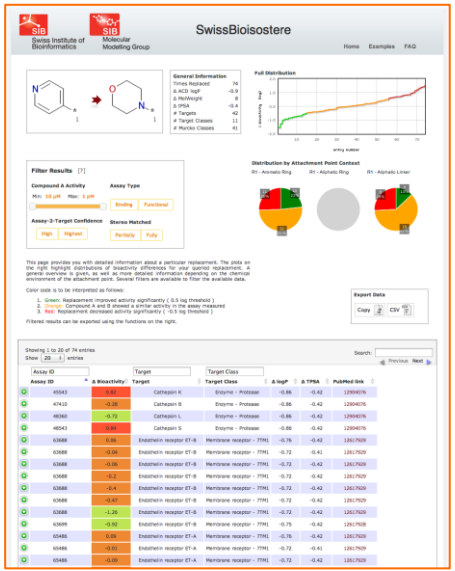


越来越多的AI/ML技术融入到数据库中

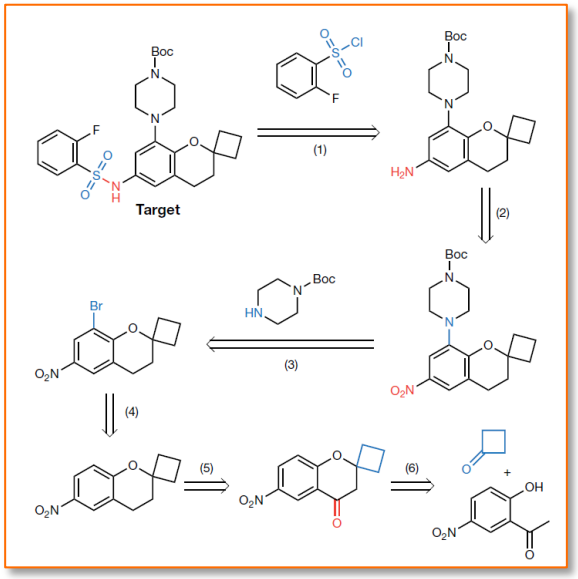
靶点预测

利用动物临床前数据预测药物临床安全性

MMP分析



合成预测



Elsevier Life Science Solution中已经开始融入不同领域的AI技术

ELSEVIER

Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

一篇常见的化学相关文献的构成


Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

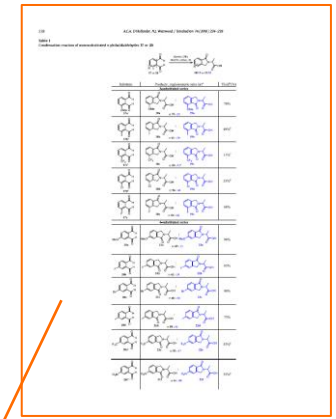
Assessment of the regioselectivity in the condensation reaction of unsymmetrical o-phthaldialdehydes with alanine

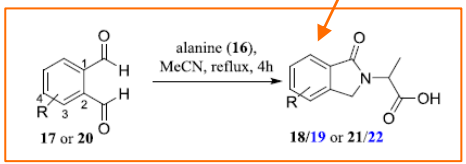
Agathe C.A. D'Hellencourt, Nicholas J. Westwood*

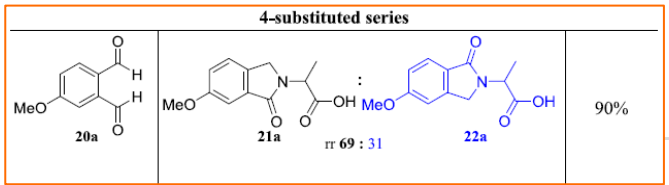
ARTICLE INFO

ABSTRACT

1. Introduction



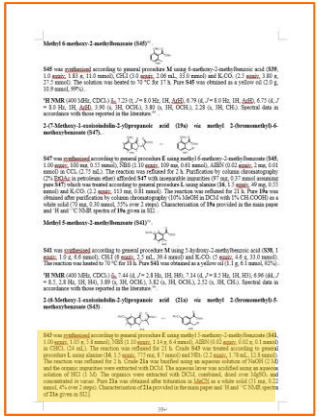




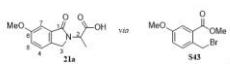
ELSEVIER

21a: Mp: 194–196 °C; IR ν_{max} cm^{-1} (thin film) 3370 (O–H stretch), 1730 (C=O stretch), 1636 (C=O stretch), 1493 (C=C stretch), 1456 (C–H bend), 1447 (C–H bend), 1196 (C–O stretch), 1022, 770; ^{1}H NMR (500 MHz, CD_3OD) δ_H 7.48 (d, J = 8.5 Hz, 1H, H4), 7.29 (d, J = 2.5 Hz, 1H, H7), 7.19 (dd, J = 8.5, 2.5 Hz, 1H, H5), 5.00 (q, J = 7.5 Hz, 1H, CH), 4.54 (d, J = 17.0 Hz, 1H, H3), 4.48 (d, J = 17.0 Hz, 1H, H3), 3.86 (s, 3H, OCH_3), 1.61 (d, J = 7.5 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, CD_3OD) δ_C 174.8 (COOH), 171.0 (C1), 161.6 (C6), 135.8 (C3a), 134.3 (C7a), 125.2 (C4), 121.0 (C5), 107.4 (C7), 56.1 (OCH_3), 51.2 (CH), 48.1 (C3), 15.9 (CH_3); **HRMS** (ES^+) m/z calculated for $C_{12}H_{14}NO_4$ $[M+H]^+$: 236.0917; found: 236.0921. See SI1 part IX for experimental procedure and SI2 for ^{1}H and ^{13}C NMR spectra.

22a: Mp: 191–193 °C; IR ν_{max} cm^{-1} (thin film) 3229 (O–H stretch), 1717 (C=O stretch), 1628 (C=O stretch), 1611 (C=C stretch), 1558 (C=C stretch), 1506 (C=C stretch), 1447 (C–H bend), 1435 (C–H bend), 1298 (C–N stretch), 1206 (C–O stretch), 1086, 1026, 845, 775; ^{1}H NMR (500 MHz, CD_3OD) δ_H 7.68 (d, J = 8.5 Hz, 1H, H7), 7.13 (d, J = 2.0 Hz, 1H, H4), 7.04 (dd, J = 8.5, 2.2 Hz, 1H, H6), 4.98 (q, J = 7.5 Hz, 1H, CH), 4.57 (d, J = 17.0 Hz, 1H, H3), 4.50 (d, J = 17.0 Hz, 1H, H3), 3.88 (s, 3H, OCH_3), 1.60 (d, J = 7.5 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, CD_3OD) δ_C 174.8 (COOH), 171.0 (C1),164.9 (C5), 146.2 (C3a), 125.6 (C7), 125.4 (C7a), 116.3 (C6), 108.8 (C4), 56.2 (OCH_3), 50.9 (CH), 48.4 (C3), 15.9 (CH_3); **HRMS** (ES^+) m/z calculated for $C_{12}H_{14}NO_4$ $[M+H]^+$: 236.0917; found: 236.0921. See SI1 part IX for experimental procedure and SI2 for ^{1}H and ^{13}C NMR spectra.



2-(6-Methoxy-1-oxoisoindolin-2-yl)propanoic acid (21a) *via* methyl 2-(bromomethyl)-5-methoxybenzoate (S43)



S43 was synthesised according to general procedure **E** using methyl 5-methoxy-2-methylbenzoate (**S41**, 1.00 equiv, 1.05 g, 5.8 mmol), NBS (1.10 equiv, 1.14 g, 6.4 mmol), AIBN (0.02 equiv, 0.02 g, 0.1 mmol) in $CHCl_3$ (24 mL). The reaction was refluxed for 21 h. Crude **S43** was treated according to general procedure **L** using alanine (**16**, 1.5 equiv, 775 mg, 8.7 mmol) and NEt_3 (2.2 equiv, 1.78 mL, 12.8 mmol). The reaction was refluxed for 2 h. Crude **21a** was basified using an aqueous solution of NaOH (2 M) and the organic impurities were extracted with DCM. The aqueous layer was acidified using an aqueous solution of HCl (1 M). The organics were extracted with DCM, combined, dried over $MgSO_4$ and concentrated *in vacuo*. Pure **21a** was obtained after trituration in MeCN as a white solid (51 mg, 0.22 mmol, 4% over 2 steps). Characterisation of **21a** provided in the main paper and ^{1}H and ^{13}C NMR spectra of **21a** given in SI2.

一篇全文以及Support Information中有大量的数据，科研人员如果要获取，需要花费多的时间去阅读全文。

Reaxys对这篇全文的提炼

1 Assessment of the regioselectivity in the condensation reaction of unsymmetrical o-phthaldialdehydes with alanine

D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239]

Abstract ^ Index Terms ^ Substances 103 v Reactions 236 v Full Text ↗

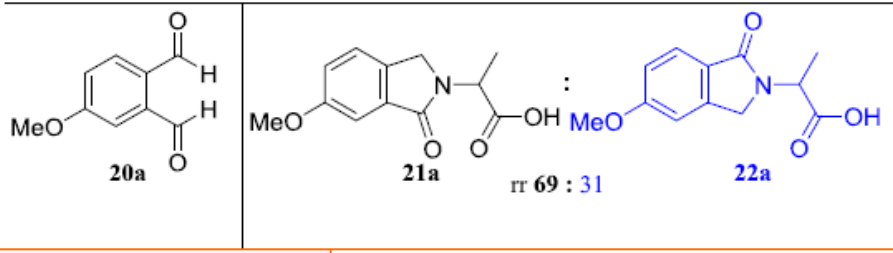
Abstract

One approach for the synthesis of isoindolinones, a privileged bioactive heterocyclic core structure, involves a conden-
sation reaction of o-phthaldialdehydes with a suitable nitrogen-containing nucleophile. This fascinating re
visited here in the context of the use of o-phthaldialdehydes that contain additional substituents in the arc
leading to a detailed analysis of the regioselectivity of the reaction. Eleven monosubstituted o-phthaldialde
synthesised and reacted with alanine. The regioselectivity observed across the eleven substrates led to the
disubstituted substrate that reacted with very high control. A gram-scale reaction followed by esterification
major regioisomer in high yield. In addition, the regioselectivity observed on reaction of two novel monod
substrates led to an increased mechanistic understanding.

Index terms

Author keyword: Condensation reaction, Mechanistic understanding, o-phthaldialdehyde, Regioselectivity
EMTREE drug term: alanine, phthalaldehyde
EMTREE medical term: Article, esterification, polymerization, priority journal, regioselectivity, synthesis
Reaxys Index Terms: Swern oxidation, condensation reaction, esterification, pure, reactivity, regioselectivity, separation method, tautomerization

4-substituted series



1 Assessment of the regioselectivity in the condensation reaction of unsymmetrical o-phthaldialdehydes with alanine

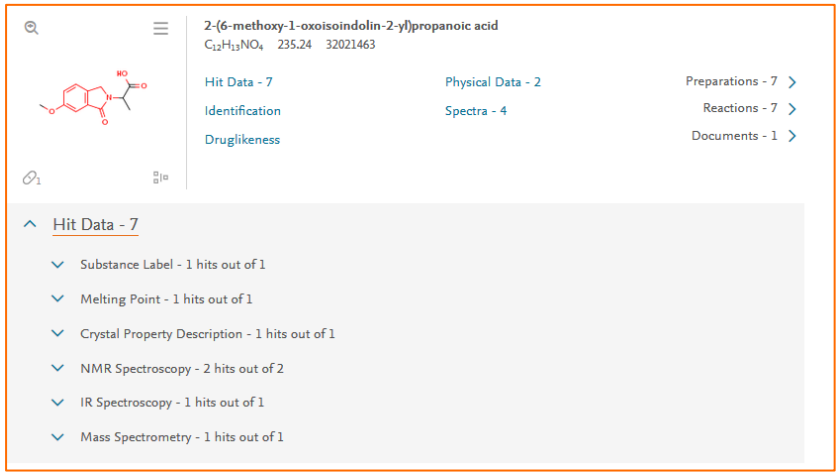
D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239]

Abstract v Index Terms v Substances 103 v Reactions 236 v Full Text ↗

Reaxys对于文献中的结构与反应都做了提炼

ELSEVIER

Reaxys对文献中的化合物的结构化数据提炼



文献中出现的化合物性质，全部直接抽提，或者给出文献中出现的位置，方便科研人员直接获取，或节省查找阅读全文的时间。

Label	Reference
21a	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239] Full Text Details Abstract

Melting Point, °C	Reference
194 - 196	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239] Full Text Details Abstract

Colour & Other Properties	Location	Reference
white	supporting information	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239] Full Text Details Abstract

Description (NMR Spectroscopy)	Nucleus (NMR Spectroscopy)	Solvents (NMR Spectroscopy)	Frequency (NMR Spectroscopy), MHz	Location	Reference
Chemical shifts, Spectrum	1H	d(4)-methanol	500	supporting information	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239] Full Text Details Abstract
Chemical shifts, Spectrum	13C	d(4)-methanol	125.8	supporting information	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, **2018**, vol. 74, # 2, p. 224 - 239] Full Text Details Abstract

ELSEVIER

Reaxys对原文反应的提炼（21a)

Reaction ID: 47133770

1 Conditions Find Similar

Yield	Conditions	Reference
	In acetonitrile for 4h; Reflux; Inert atmosphere; Overall yield = 90 per-cent; Overall yield = 38 mg; regioselective reaction;	D'Hollander, Agathe C.A.; Westwood, Nicholas J. - [Tetrahedron, 2018, vol. 74, # 2, p. 224 - 239]

Experimental Procedure

Full Text Details Abstract

General procedure: Alanine (16, 1.2 equiv.) was added to a solution of unsymmetrical o-phthaldialdehyde (1.0 equiv.) in anhydrous MeCN (3.8 mL per mmol of o-phthaldialdehyde). The reaction mixture was heated at reflux for 4 h under a nitrogen atmosphere. The solution was then cooled to rt before being concentrated in vacuo to afford the crude mixture of regioisomers.

*4.3.9. 2-(6-Methoxy-1-oxoisoindolin-2-yl)propanoic acid (**21a**) with 2-(5-methoxy-1-oxoisoindolin-2-yl)propanoic acid (**22a**)*

A mixture of **21a** and **22a** was synthesised according to general procedure **B** using 4-methoxyphthalaldehyde (**20a**, 1.0 equiv., 30 mg, 0.18 mmol) and alanine (**16**, 1.2 equiv., 19 mg, 0.22 mmol). A

ELSEVIER

Reaxys从文献中提炼出来的内容

数据更新时间：2020/8/9

Reaxys 2020年专利计划

2020年专利奖扩大到100家专利机构的专利

Existing pipeline

New pipeline

automated process:

Quality:

Time:

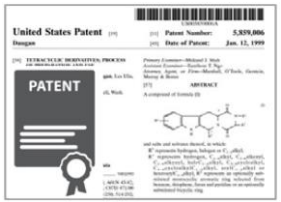
manual process:

Quality:

Time:

Limited PO & IPC classes

Patent publication



≈100 PO & all IPCs

1st focus: Target search (taxonomy assisted) and affiliation [competitive intelligence]

2nd focus: Structure search [novelty search]

1-2 days

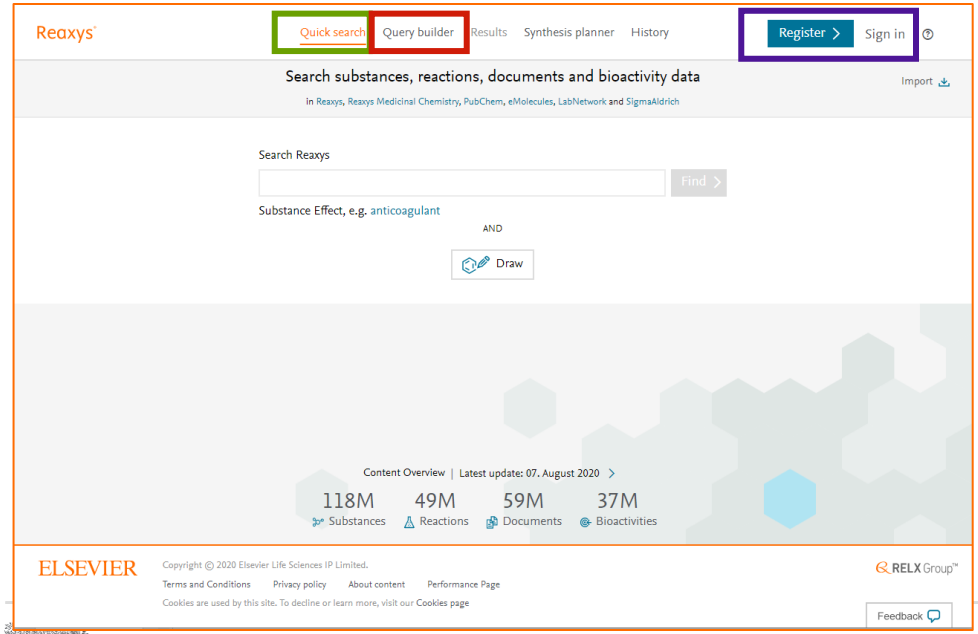
20-30 days

Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

Reaxys的登录界面

- IP范围内，浏览器输入www.Reaxys.com，可以直接进行检索，推荐Chrome，Firefox浏览器，
- 收藏夹收藏的链接建议只收藏www.Reaxys.com



Tips:

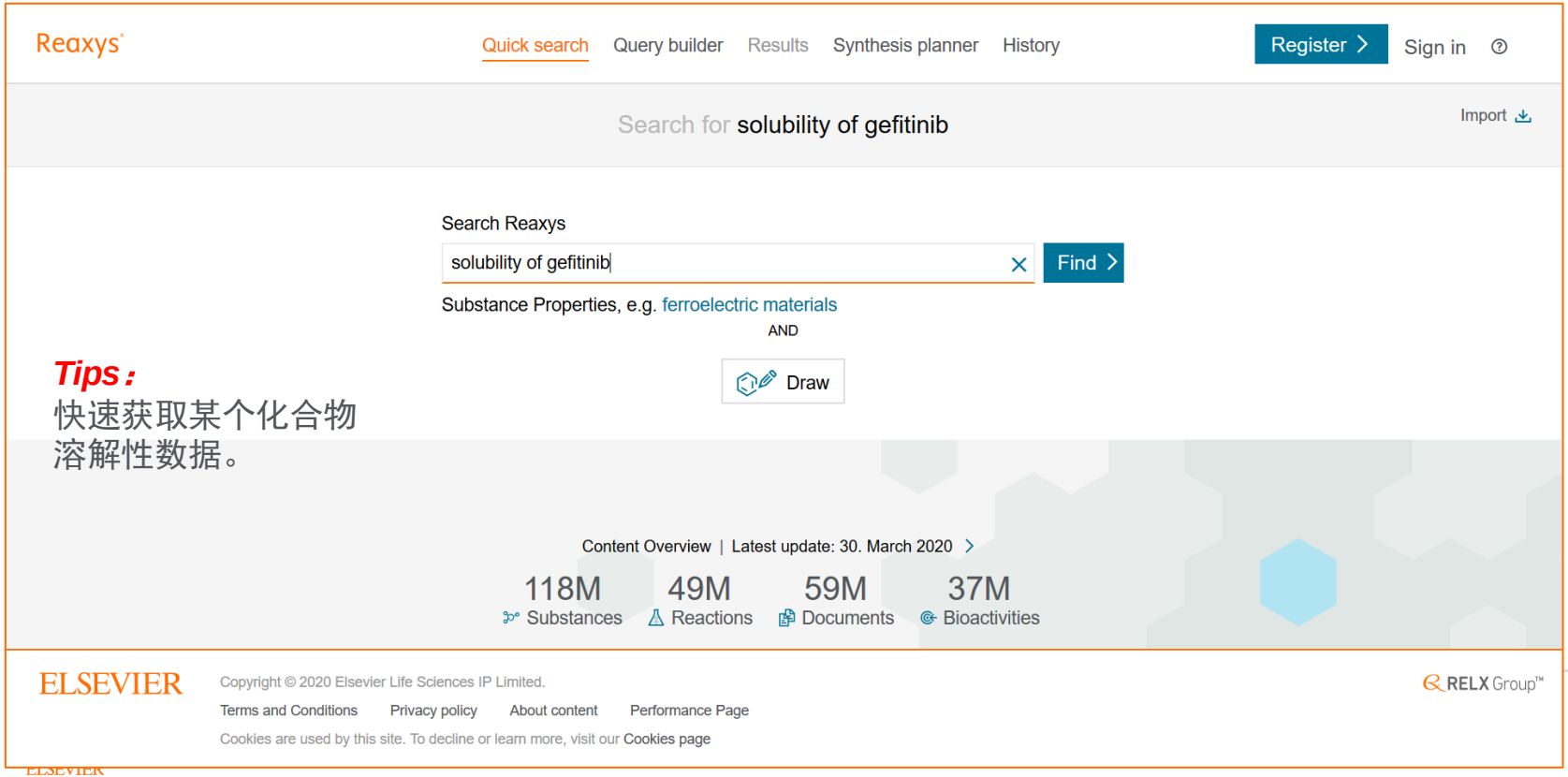
1. 账号注册（可选），注册帐号后，可以使用提醒，结果集保存，结果导出功能（2020.8以后）
2. Quick Search，快速检索，结构反应检索，或者输入自然语言，Reaxys智能分析语义进行检索。
3. Query Builder，组合检索，利用Reaxys中的各种字段进行组合，实现不同检索需求。

视频介绍：

1. Reaxys主界面：https://b23.tv/av92441795
2. Quick Search：https://b23.tv/av92445805
3. Query Builder：https://b23.tv/av92565153

ELSEVIER

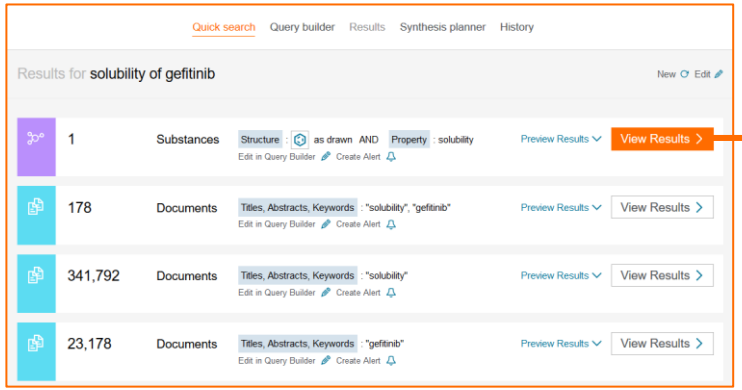
Case 1：快速获取化合物的理化性质

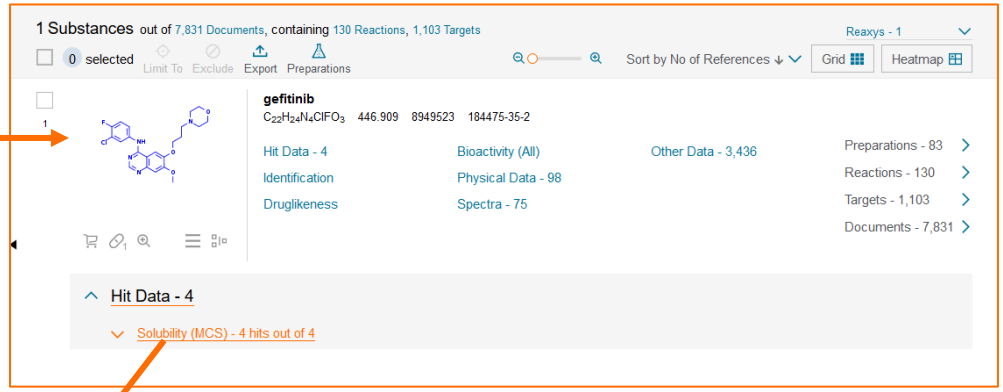


Tips：

快速获取某个化合物溶解性数据。

Reaxys中的结果





抽提的数据包括具体的数值，或者相关的文字性描述

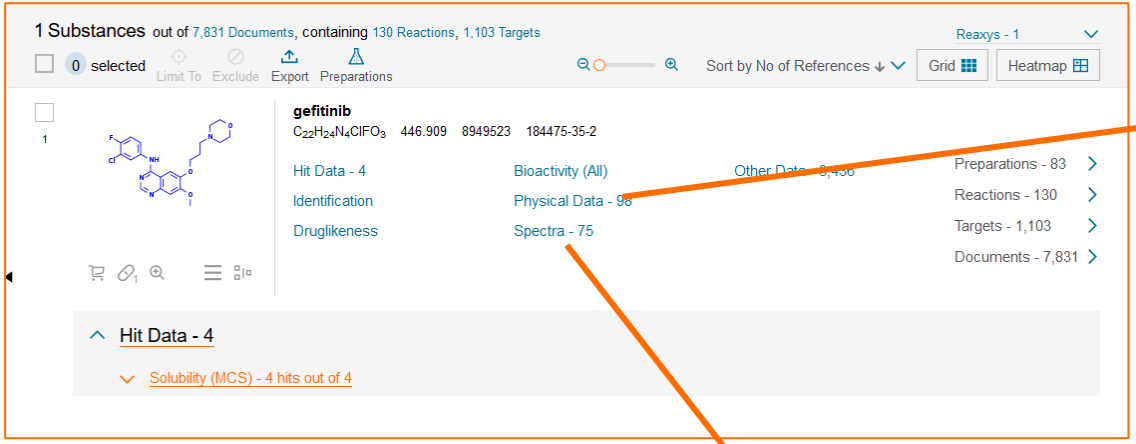
Solubility (MCS) - 4 hits out of 4

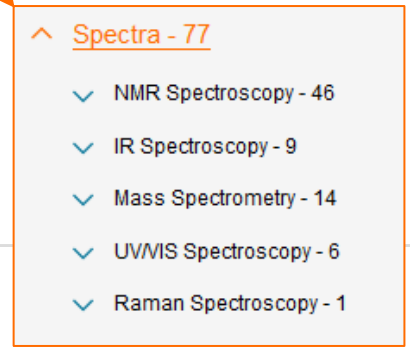
Show/Hide columns

Solubility, g·l-1	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] 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] 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] Full Text ↗ Details › Abstract ›
0.0021	in pure solvent	20	water			Zhao, Feng; Lin, Zhaohu; Wang, Feng; Zhao, Weili; Dong, Xiaochun[**Bioorganic and Medicinal Chemistry Letters**, **2013**, vol. 23, # 19, p. 5385 - 5388] Full Text ↗ Cited 22 times ↗ Details › Abstract ›

ELSEVIER

Reaxys中化合物更多的理化性质



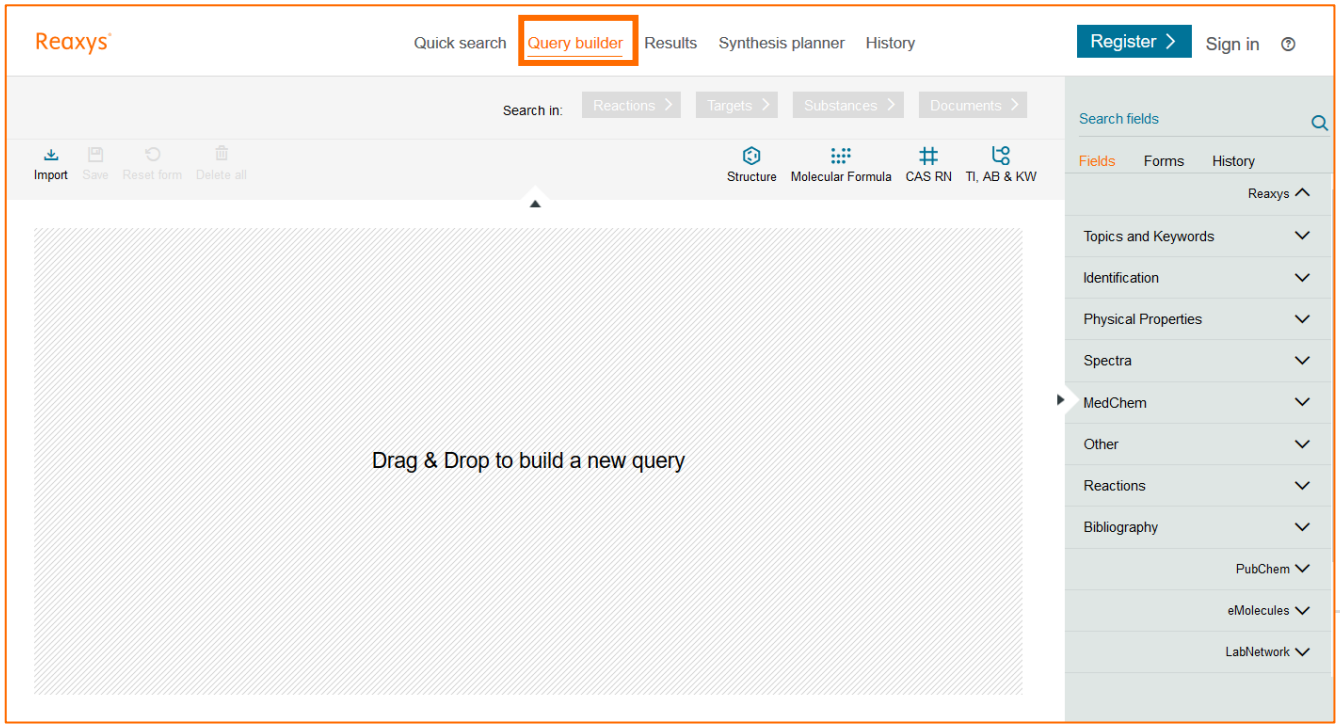


直接获取化合物的理化性质或者谱图数据

ELSEVIER

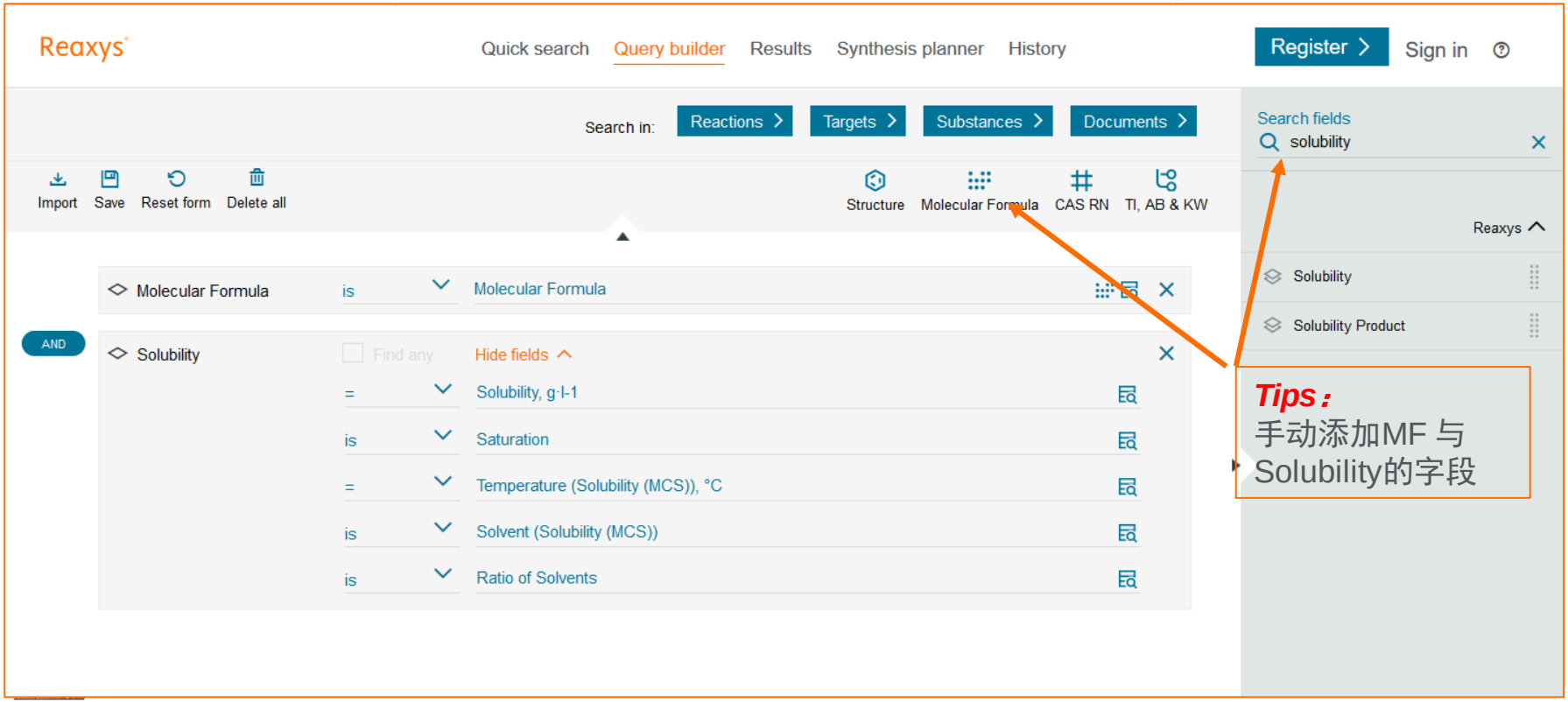
Case 2：理化性质的高级应用

- 获取KCl在乙醇中的溶解度

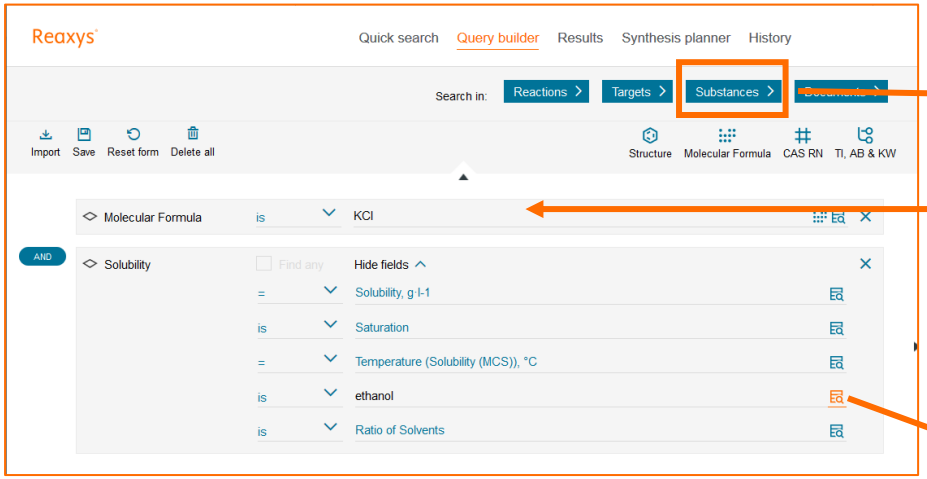


Reaxys中的Query Builder可以按照一定的规则构建检索式，Reaxys一共提供180+字段和字段组，科研人员可以自由的对这些字段和字段组进行组合，同时Reaxys也根据一些常见的需求，内置了多种检索策略模板，如“天然产物”，“hERG”等

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-1
is
Saturation
=
Temperature (Solubility (MCS)), °C
is
Solvent (Solubility (MCS))
is
Ratio of Solvents
Search fields
solubility
Reaxys
Solubility
Solubility Product
Tips：
手动添加MF 与
Solubility的字段

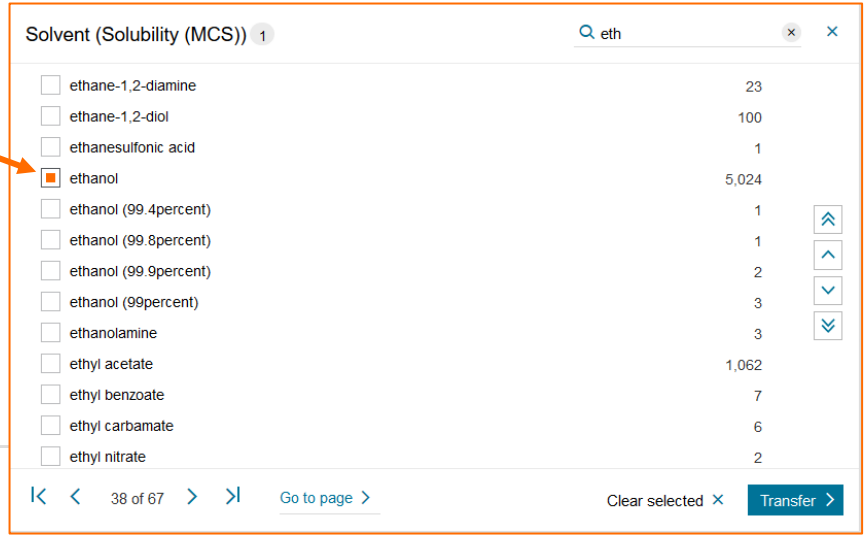
条件的输入



Step3：进行物质检索

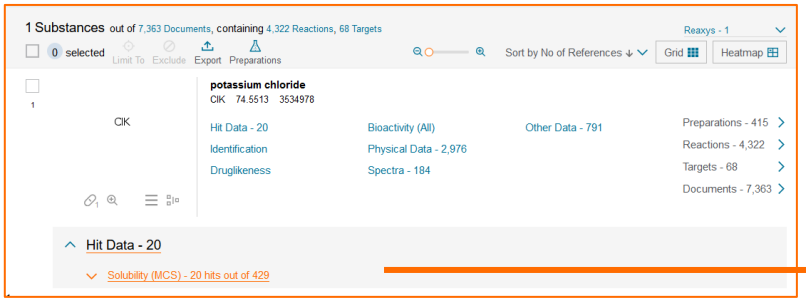
Step1：输入分子式KCl

Step2：在溶剂一块选择乙醇



ELSEVIER

最后的结果



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.....

Solubility (MCS) - 20 hits out of 429

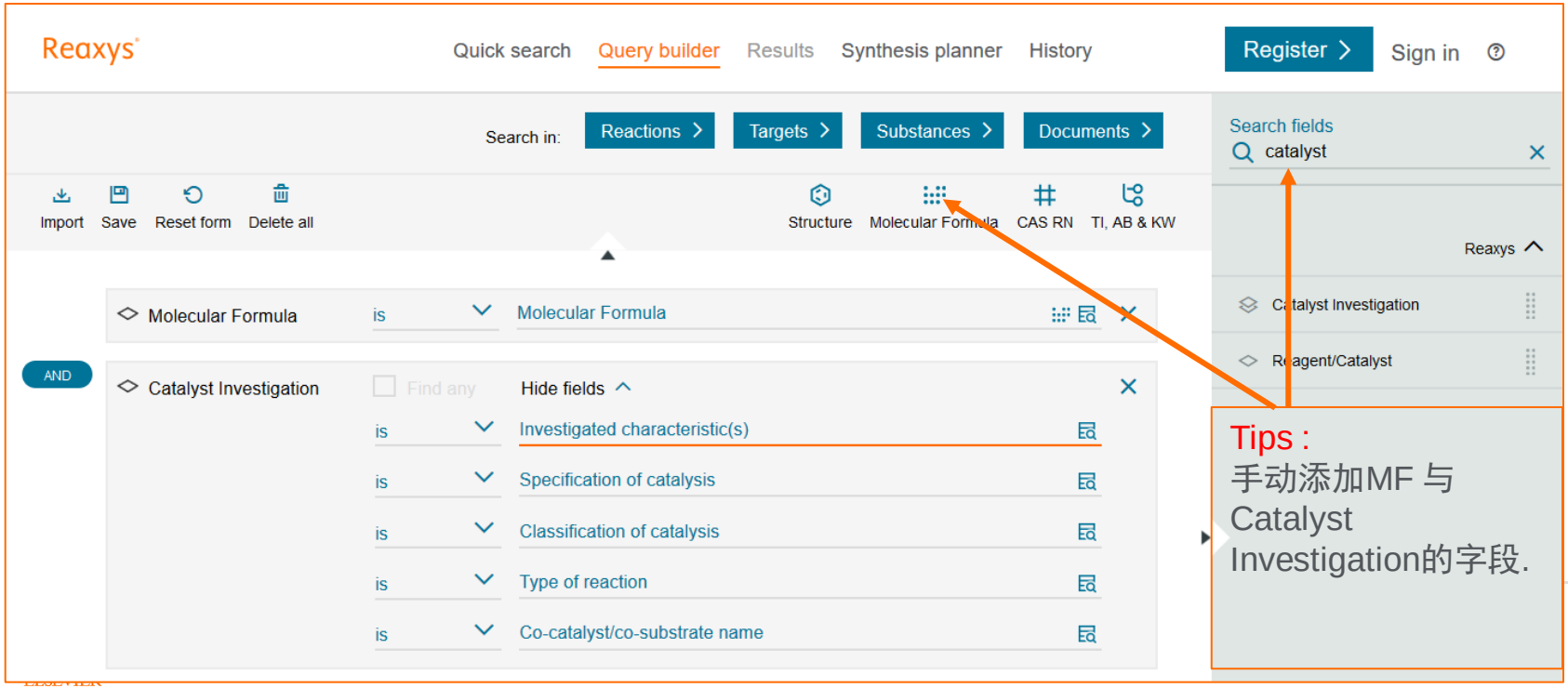
Show/Hide columns

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

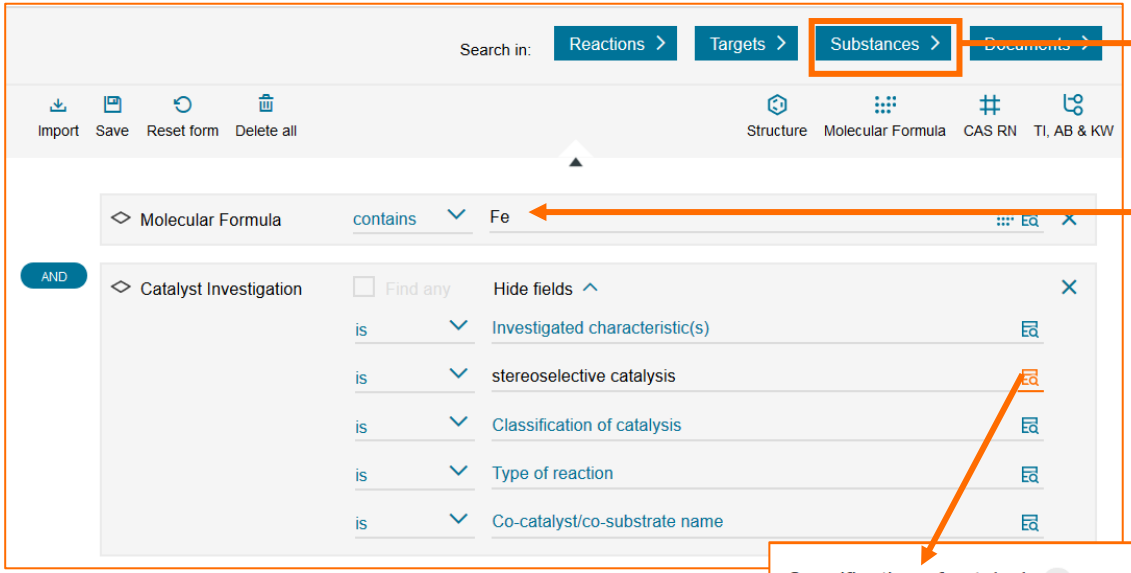
ELSEVIER

Case 3：“特定研究领域”的催化剂选择

- 检索可用于立体选择性催化的含Fe的催化剂

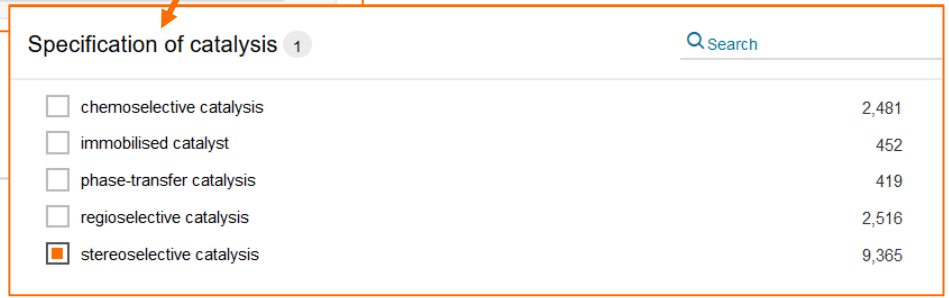


条件的输入



Step3：进行物质检索

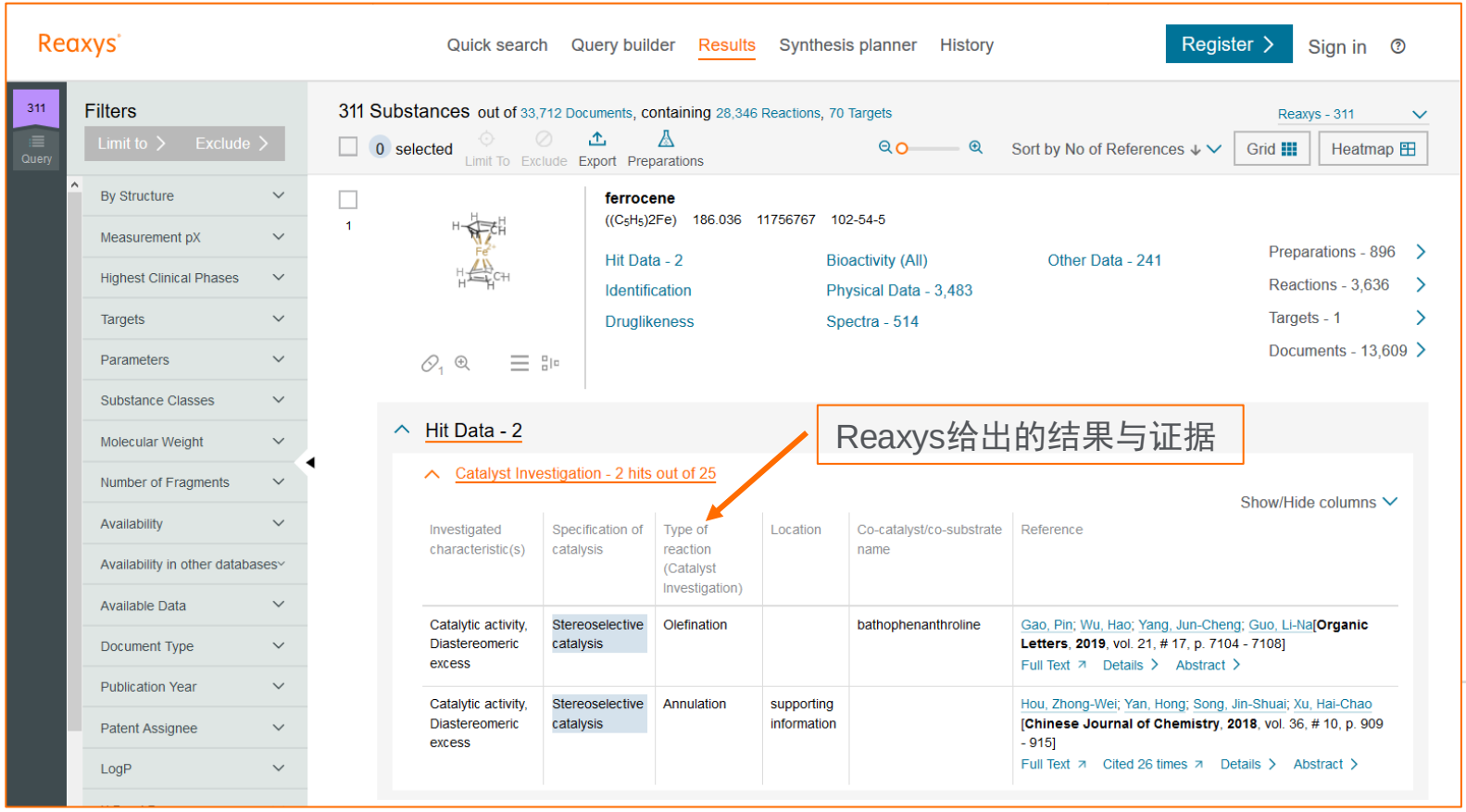
Step1：输入分子式Fe，并将逻辑关系改成“Contains”，即只要分子式中包含Fe，就检索出来



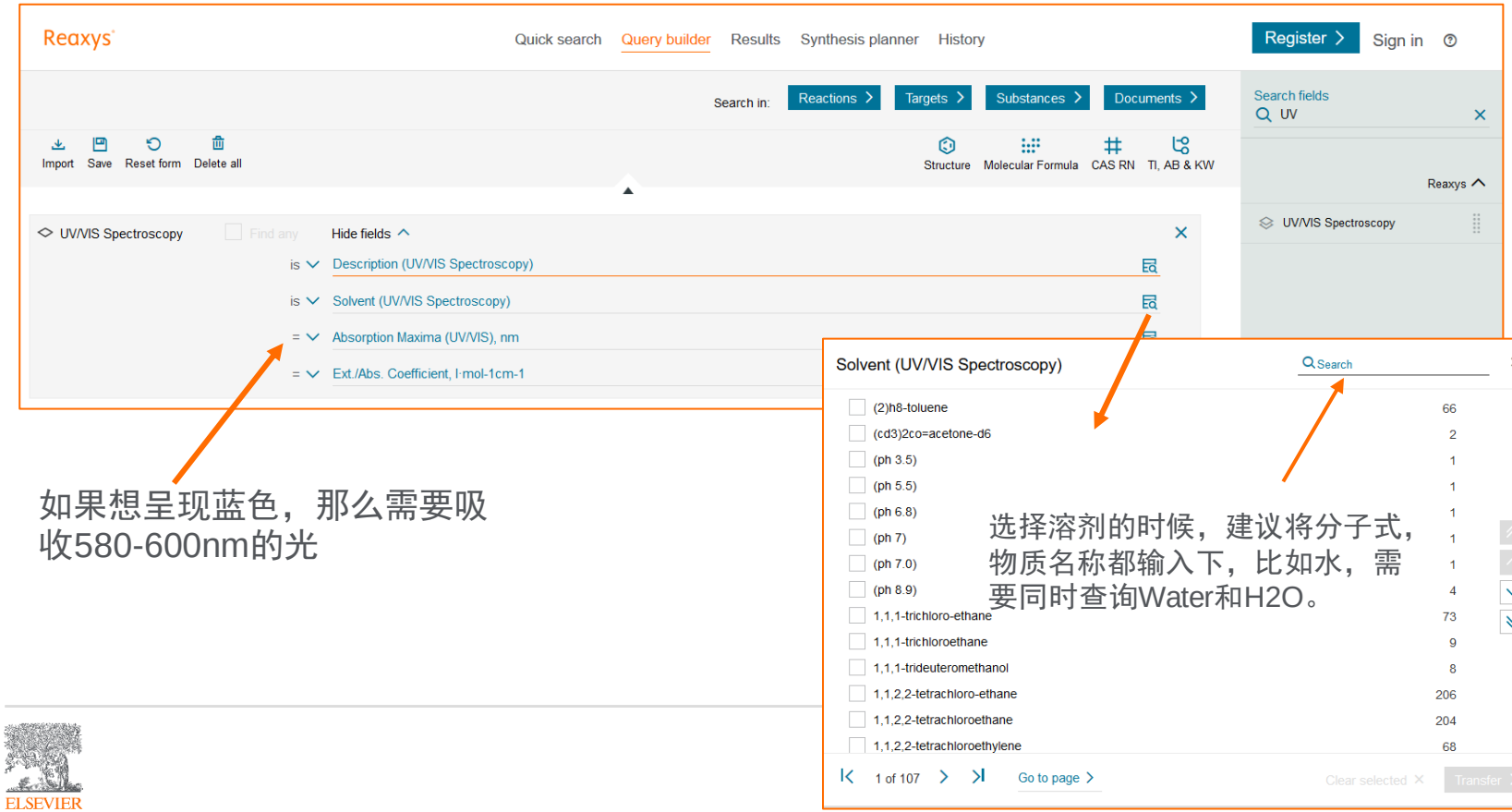
Step2：Specification of Catalysis部分选择
立体选择性催化

ELSEVIER

最后的结果


Reaxys
Quick search
Query builder
Results
Synthesis planner
History
Register
Sign in
311
Query
Filters
Limit to
Exclude
By Structure
Measurement pX
Highest Clinical Phases
Targets
Parameters
Substance Classes
Molecular Weight
Number of Fragments
Availability
Availability in other databases
Available Data
Document Type
Publication Year
Patent Assignee
LogP
311 Substances out of 33,712 Documents, containing 28,346 Reactions, 70 Targets
Reaxys - 311
0 selected
Limit To
Exclude
Export
Preparations
Sort by No of References
Grid
Heatmap
1
ferrocene
((C5H5)2Fe) 186.036 11756767 102-54-5
Hit Data - 2
Bioactivity (All)
Other Data - 241
Identification
Physical Data - 3,483
Druglikeness
Spectra - 514
Preparations - 896
Reactions - 3,636
Targets - 1
Documents - 13,609
Hit Data - 2
Reaxys给出的结果与证据
Catalyst Investigation - 2 hits out of 25
Show/Hide columns
Investigated characteristic(s)
Specification of catalysis
Type of reaction (Catalyst Investigation)
Location
Co-catalyst/co-substrate name
Reference
Catalytic activity, Diastereomeric excess
Stereoselective catalysis
Olefination
bathophenanthroline
Gao, Pin; Wu, Hao; Yang, Jun-Cheng; Guo, Li-Na[Organic Letters, 2019, vol. 21, # 17, p. 7104 - 7108]
Full Text
Details
Abstract
Catalytic activity, Diastereomeric excess
Stereoselective catalysis
Annulation
supporting information
Hou, Zhong-Wei; Yan, Hong; Song, Jin-Shuai; Xu, Hai-Chao [Chinese Journal of Chemistry, 2018, vol. 36, # 10, p. 909 - 915]
Full Text
Cited 26 times
Details
Abstract

Case 4：获取在可见光下，水溶液中呈现蓝色的化合物

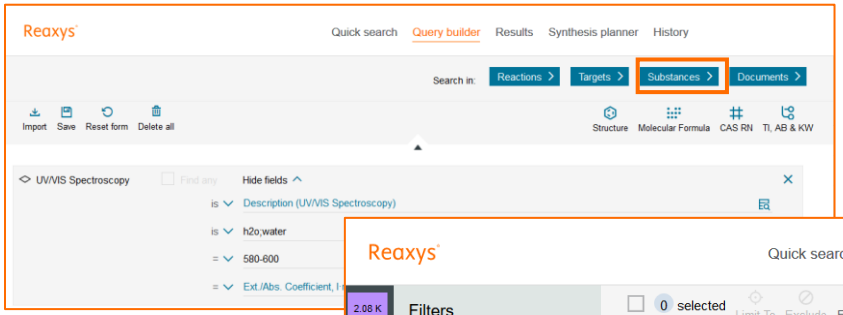


如果想呈现蓝色，那么需要吸收580-600nm的光

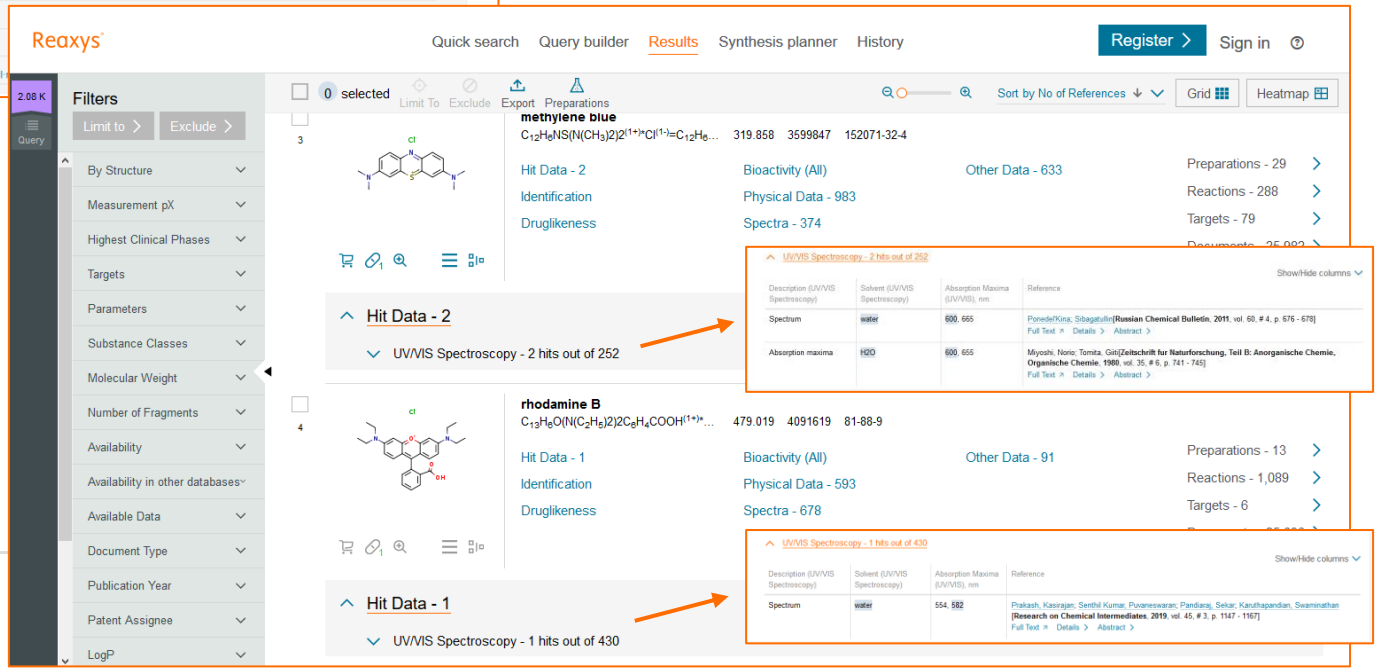
选择溶剂的时候，建议将分子式，物质名称都输入下，比如水，需要同时查询Water和H2O。

ELSEVIER

最后的检索策略与结果



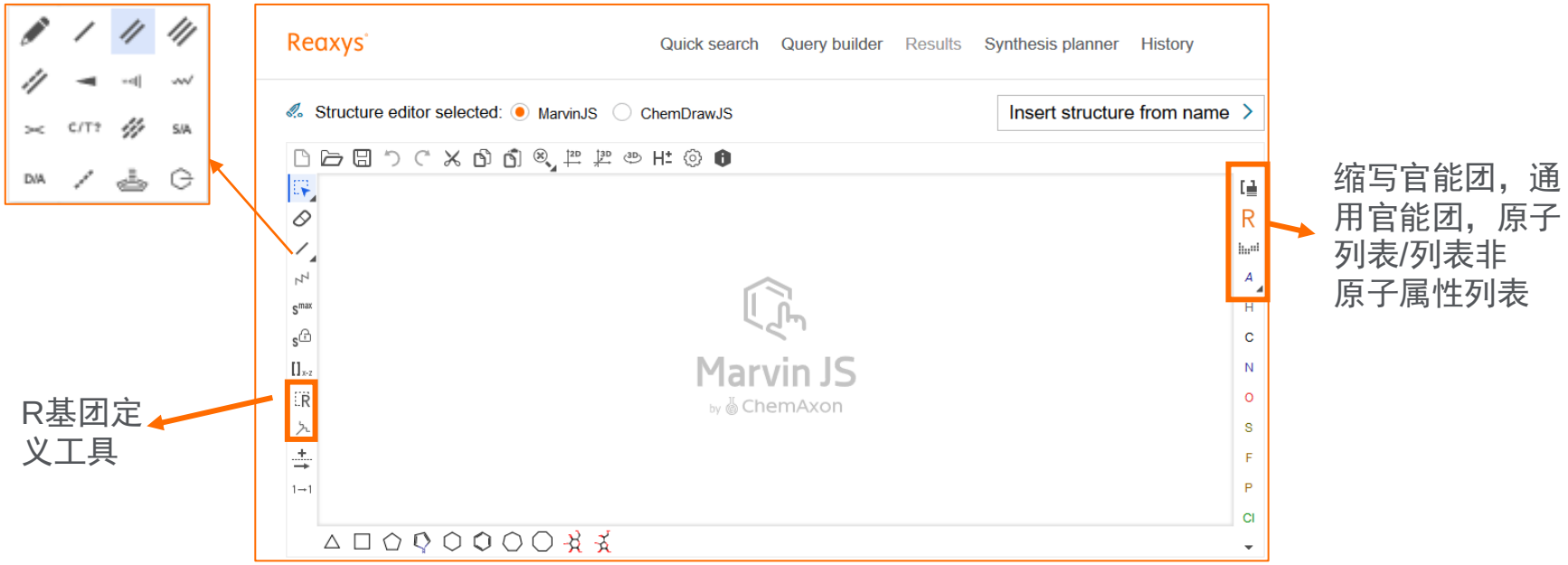
物质检索。



Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

Reaxys中的结构面板



一些常见的功能使用视频

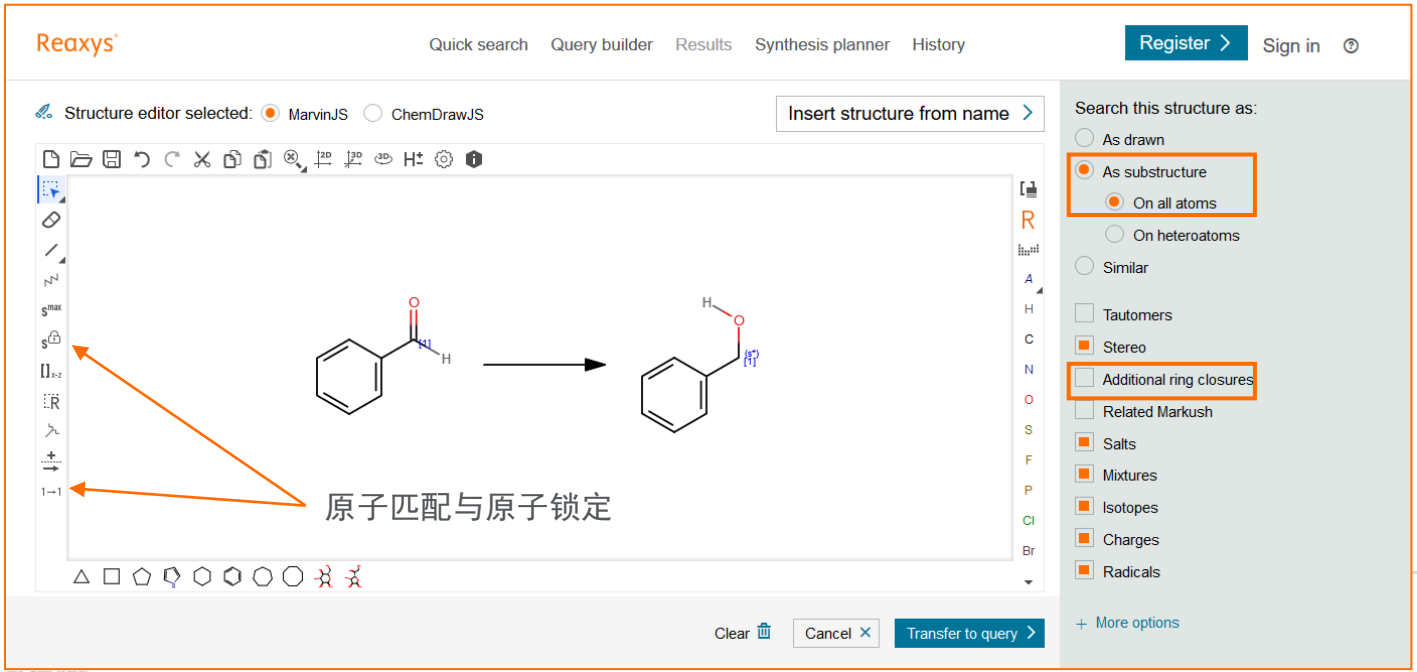
常用功能	视频链接
最基本功能	https://www.bilibili.com/video/av92474230
不定位键	https://www.bilibili.com/video/av92568326
通用/缩写官能团	https://www.bilibili.com/video/av92474816
原子列表与列表非	https://www.bilibili.com/video/av92571129
R基团定义	https://www.bilibili.com/video/av92569854
原子锁定与环锁定	https://www.bilibili.com/video/av92833557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

一些简单案例视频

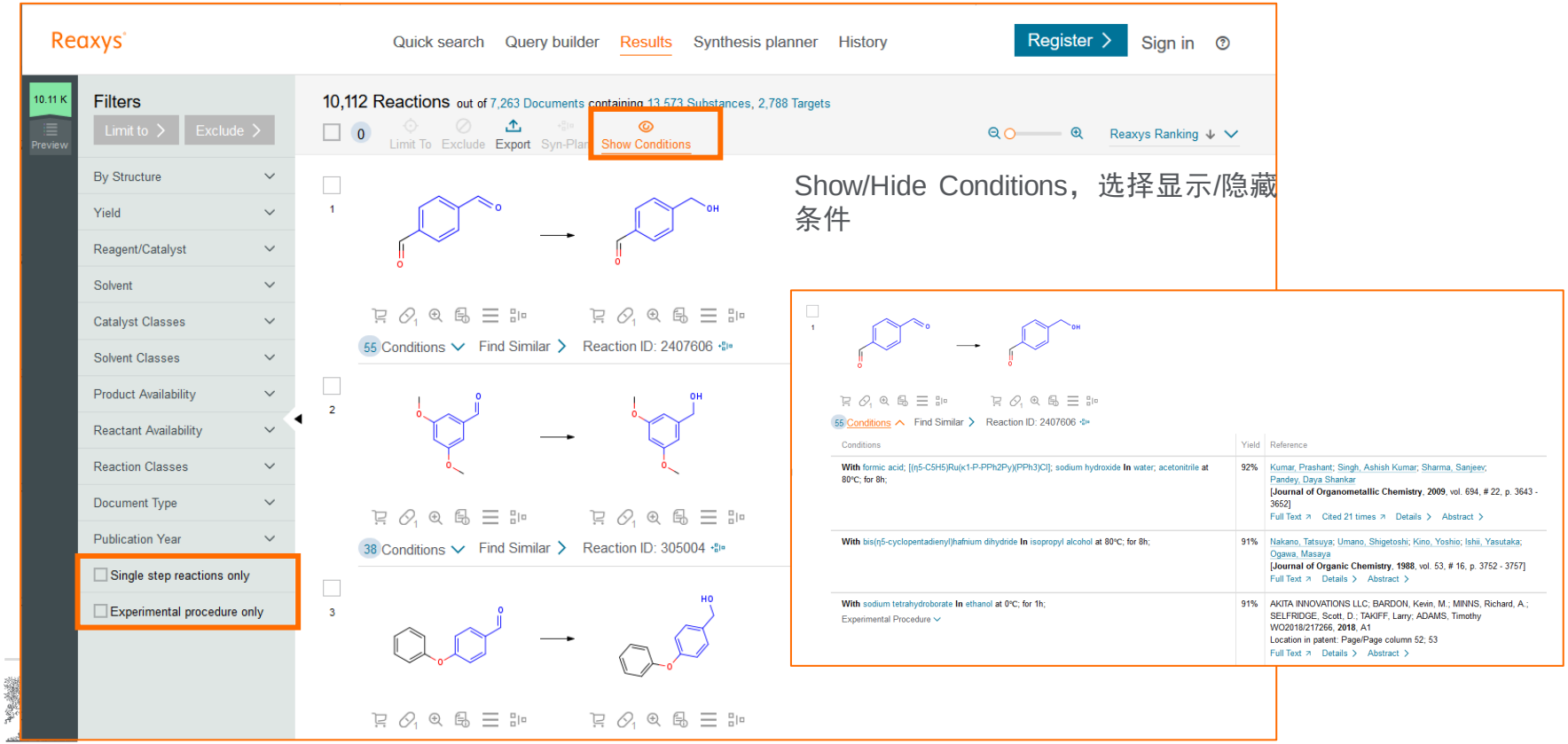
常用功能	视频链接
合成计划的制作	https://www.bilibili.com/video/av92577710
机理性文献查询	https://www.bilibili.com/video/av92580572
反应定义基本操作	https://www.bilibili.com/video/av92574819
反应条件的定义	https://www.bilibili.com/video/av92581106

Case 5：Reaxys中最简单的反应定义与筛选

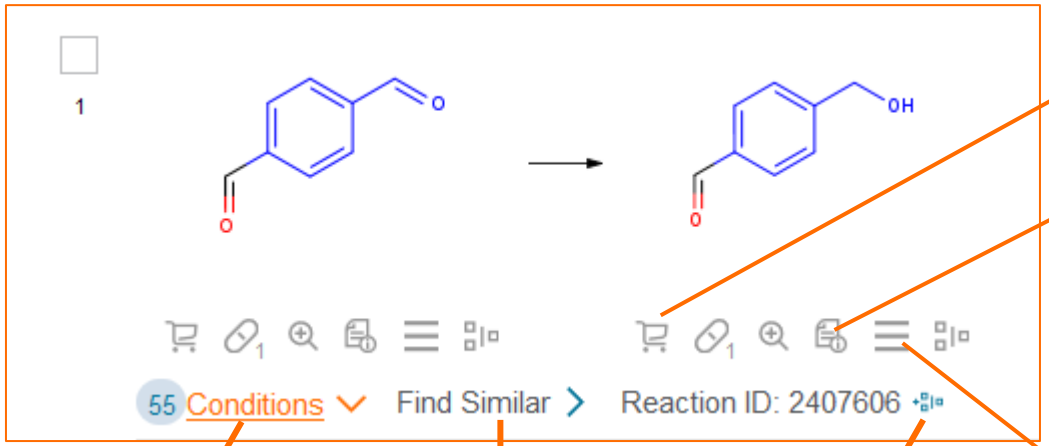
- 检索以下核心结构反应并进行反应筛选操作
- 视频操作过程
  - https://b23.tv/BV1KZ4y147PQ



Reaxys中的结果

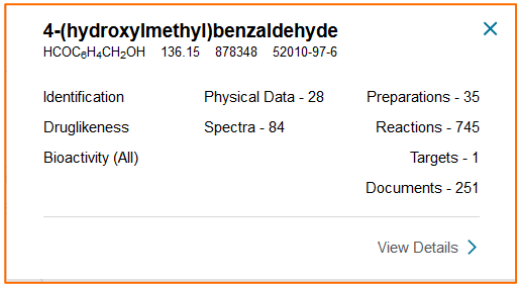

Reaxys
Quick search
Query builder
Results
Synthesis planner
History
Register
Sign in
10.11 K
Preview
Filters
Limit to
Exclude
10,112 Reactions out of 7,263 Documents containing 13,573 Substances, 2,788 Targets
Limit To
Exclude
Export
Syn-Plan
Show Conditions
Reaxys Ranking
By Structure
Yield
Reagent/Catalyst
Solvent
Catalyst Classes
Solvent Classes
Product Availability
Reactant Availability
Reaction Classes
Document Type
Publication Year
Single step reactions only
Experimental procedure only
55 Conditions
Find Similar
Reaction ID: 2407606
38 Conditions
Find Similar
Reaction ID: 305004
Show/Hide Conditions，选择显示/隐藏条件
Conditions
Yield
Reference
With formic acid; [(η5-C5H5)Ru(κ1-P-PPh2Py)(PPh3)Cl]; sodium hydroxide In water; acetonitrile at 80°C; for 8h;
92%
Kumar, Prashant; Singh, Ashish Kumar; Sharma, Sanjeev; Pandey, Daya Shankar
[Journal of Organometallic Chemistry, 2009, vol. 694, # 22, p. 3643 - 3652]
Full Text
Cited 21 times
Details
Abstract
With bis(η5-cyclopentadienyl)hafnium dihydride In isopropyl alcohol at 80°C; for 8h;
91%
Nakano, Tatsuya; Umano, Shigetoshi; Kino, Yoshio; Ishii, Yasutaka; Ogawa, Masaya
[Journal of Organic Chemistry, 1988, vol. 53, # 16, p. 3752 - 3757]
Full Text
Details
Abstract
With sodium tetrahydroborate In ethanol at 0°C; for 1h;
Experimental Procedure
91%
AKITA INNOVATIONS LLC; BARDON, Kevin, M.; MINNS, Richard, A.; SELFRIDGE, Scott, D.; TAKIFF, Larry; ADAMS, Timothy
WO2018/217266, 2018, A1
Location in patent: Page/Page column 52; 53
Full Text
Details
Abstract

Reaxys的一条反应的界面



查看商业来源

查看物质详情

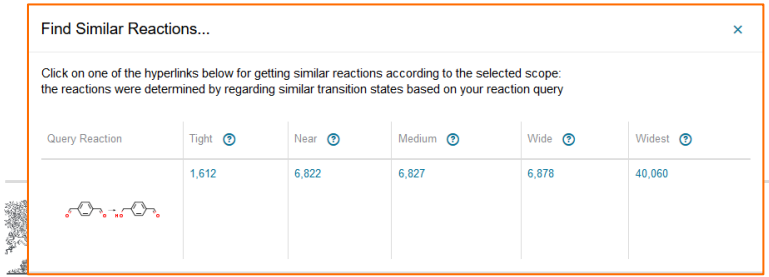


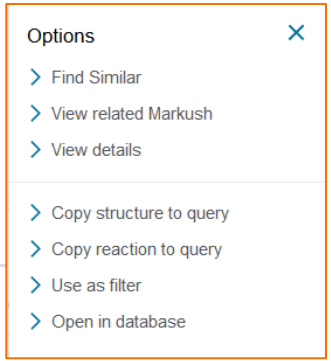
查看条件

寻找相似反应

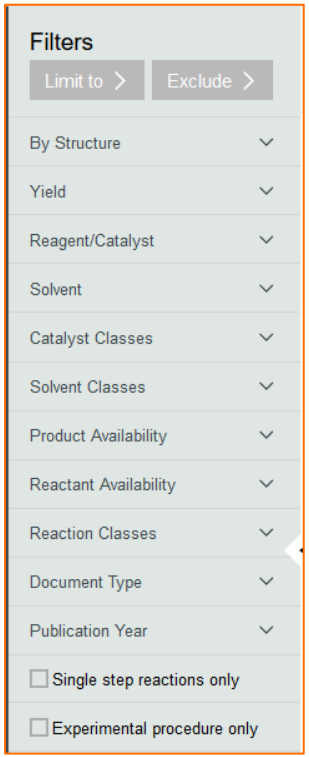
合成计划按钮

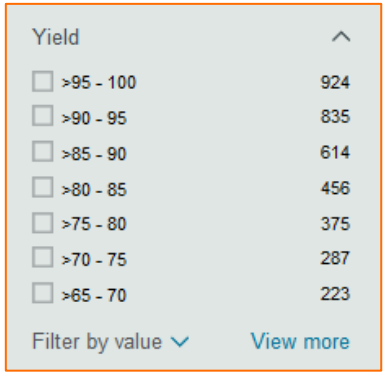
更多与物质相关操作

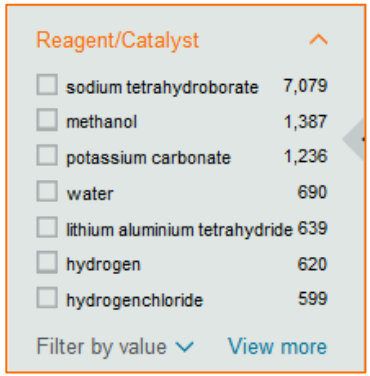


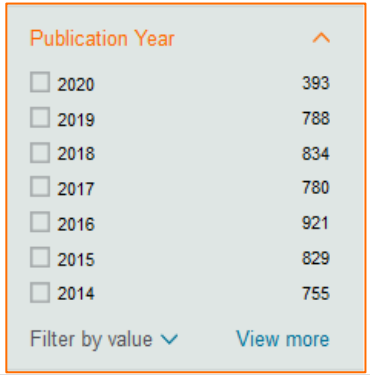


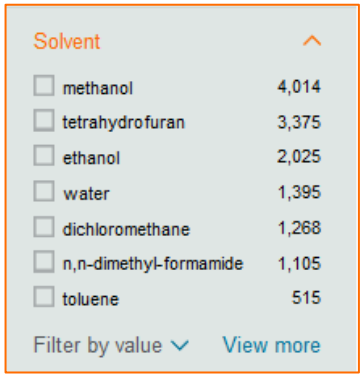
Reaxys的筛选操作









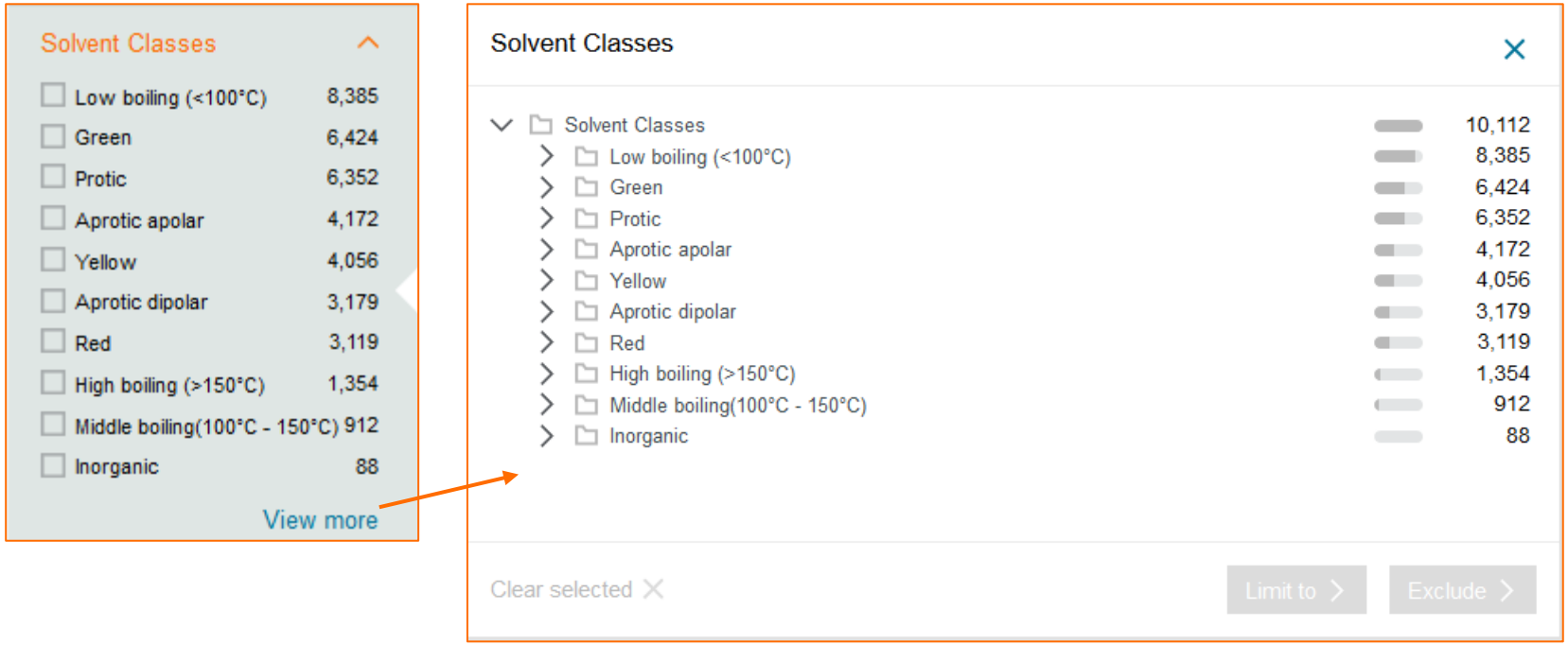


Tips:

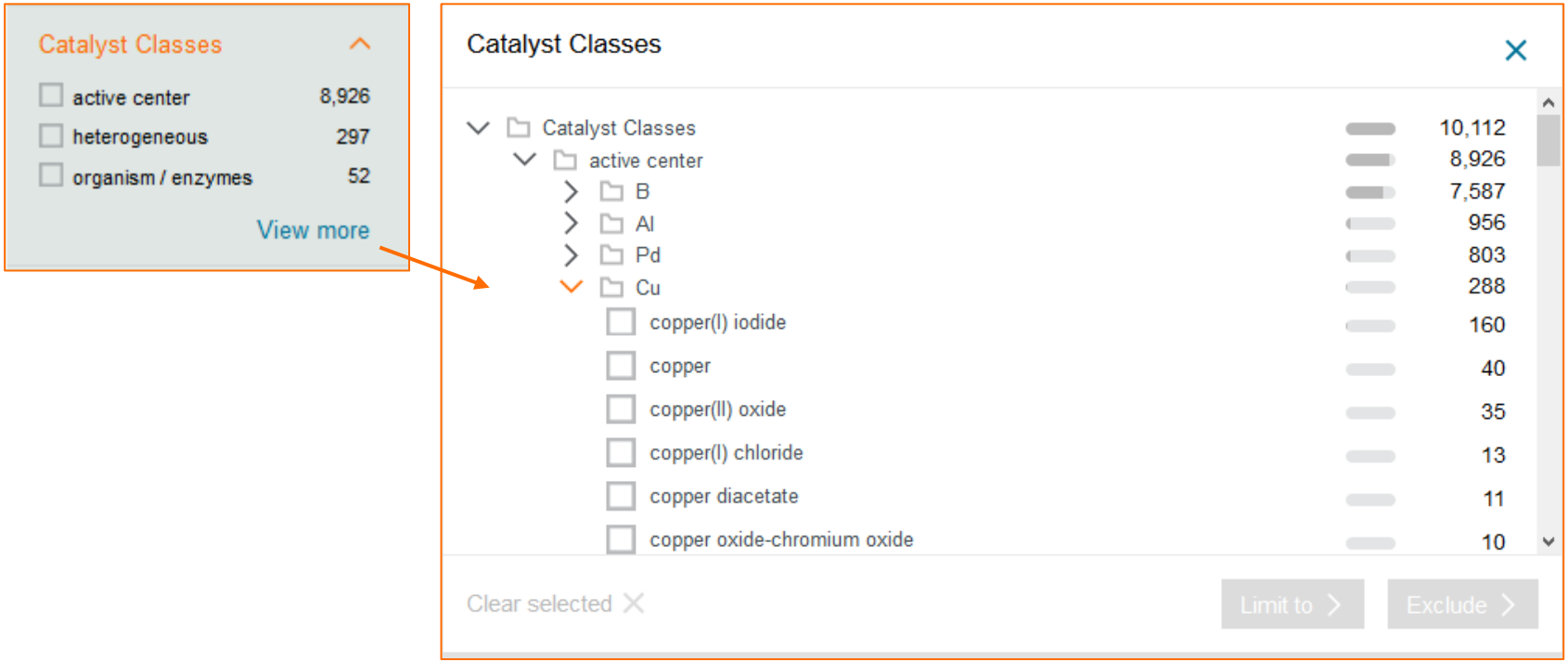
常见的一些反应筛选工具，如:收率，催化剂/试剂，溶剂，文献类型，出版年限等

ELSEVIER

Reaxys中的一些特殊筛选工具—溶剂分类

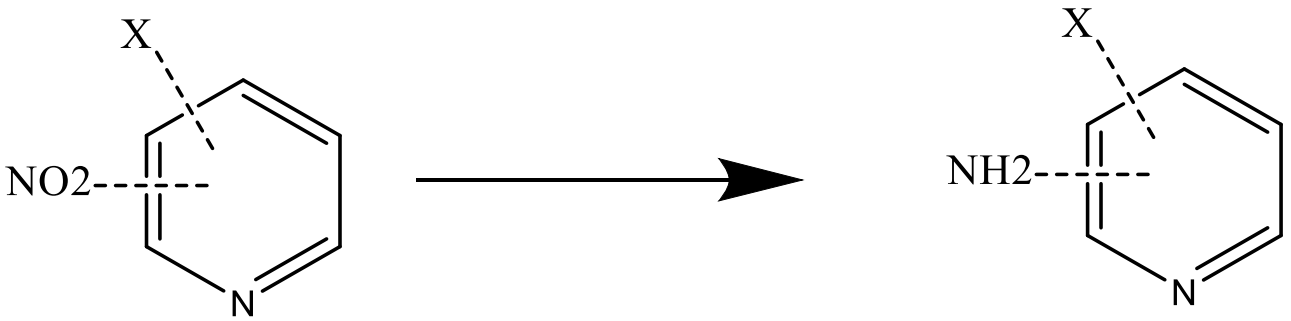


Reaxys中的一些特殊筛选工具—催化剂分类



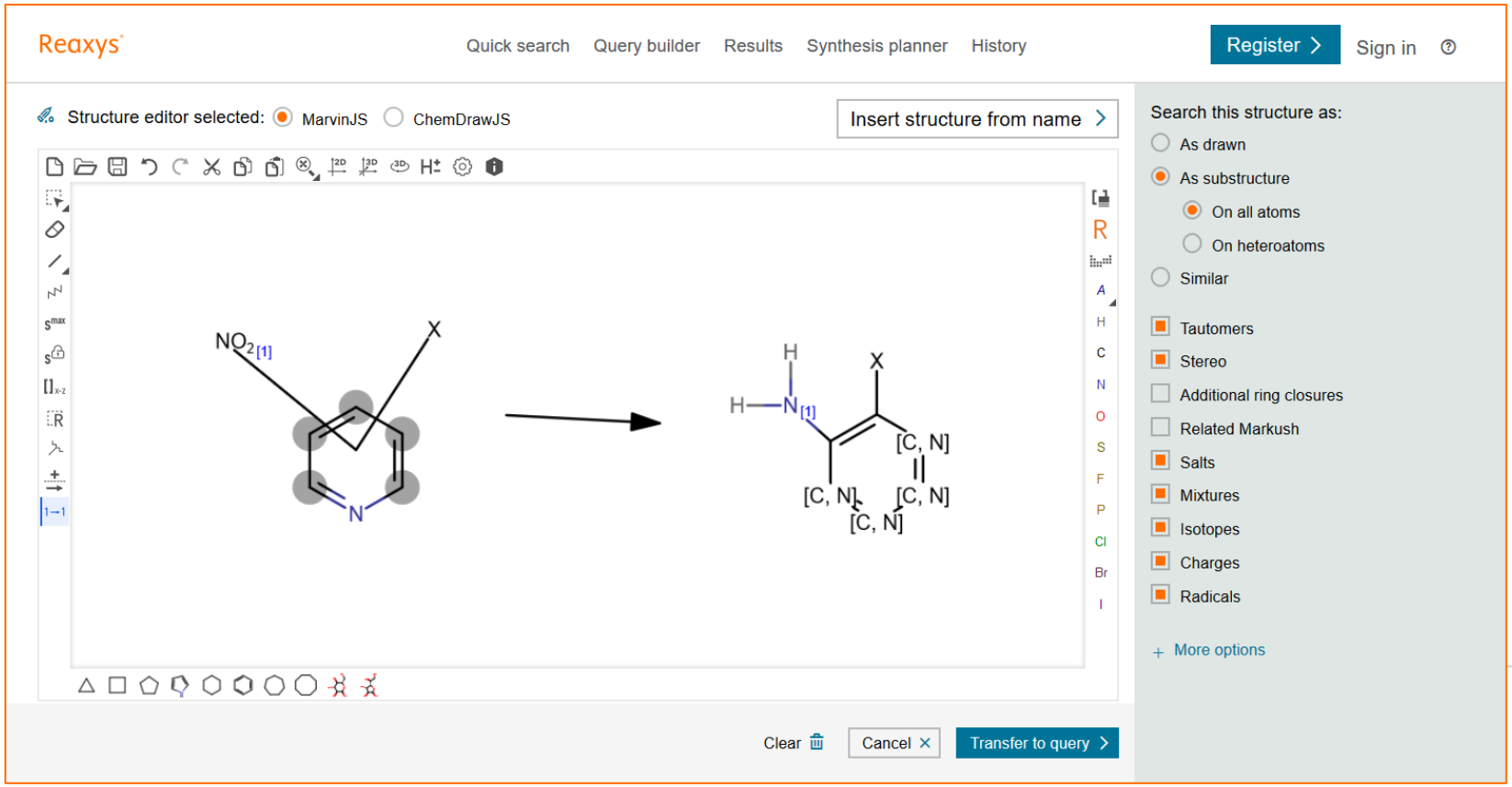
Case 6：结构中有特殊需求的反应定义

- 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NO2和卤素处于邻位

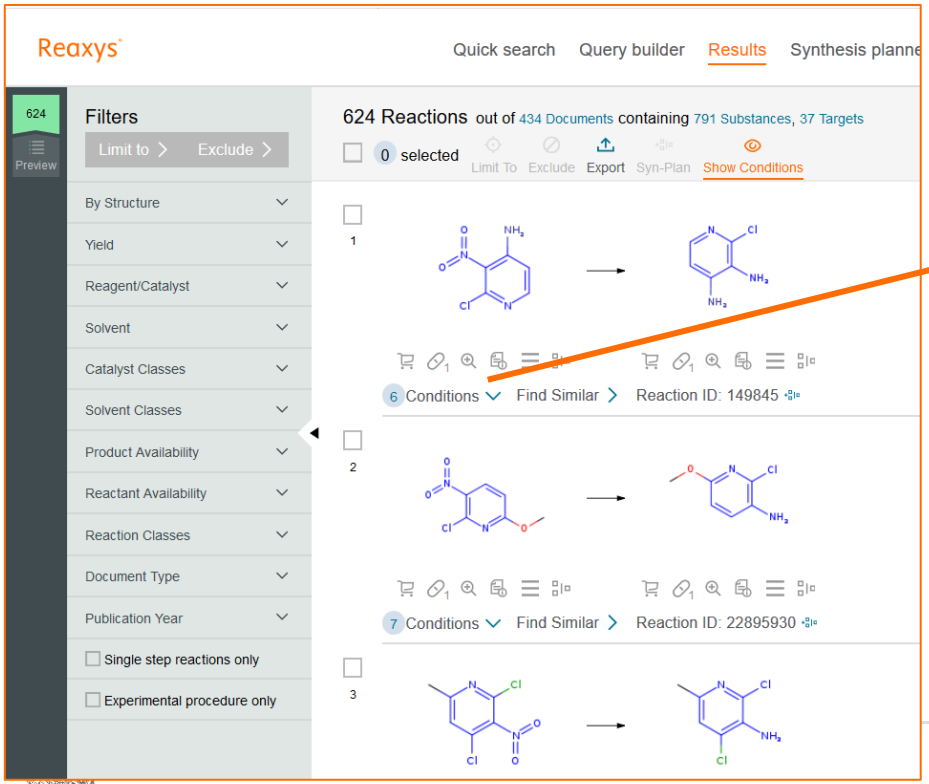


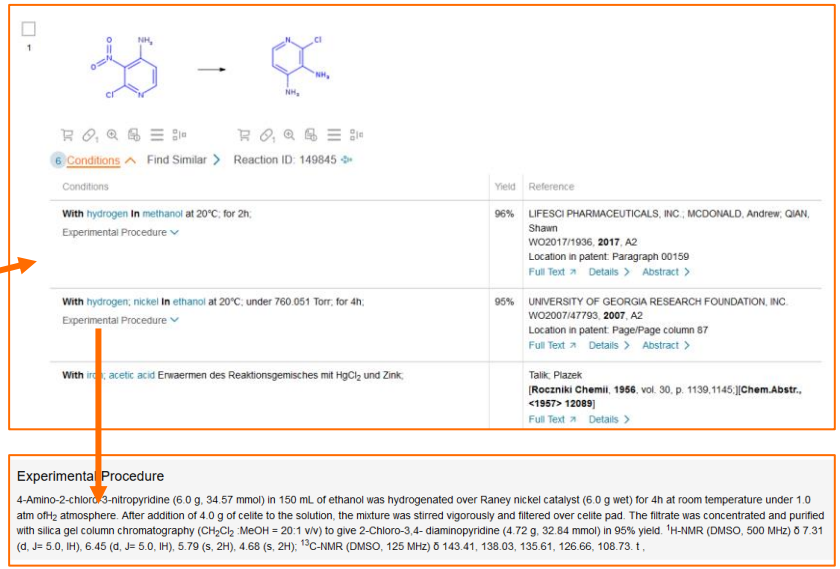
视频操作过程：
https://www.bilibili.com/video/BV1ua4y147q2

Reaxys中的结构定义



最后的结果





Experimental Procedure

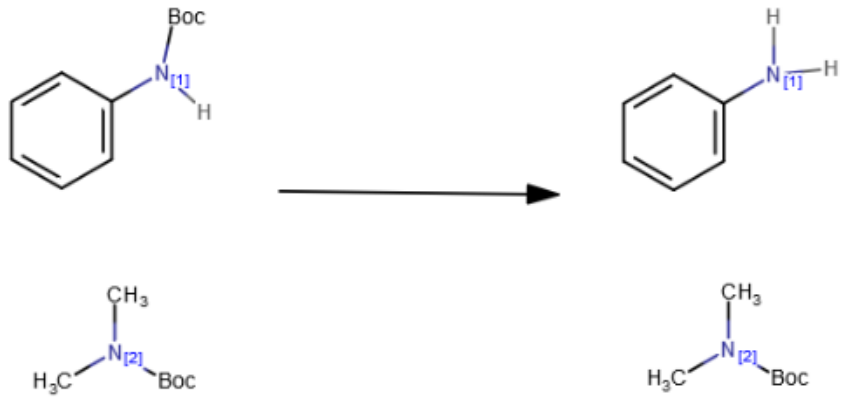
4-Amino-2-chloro-3-nitropyridine (6.0 g, 34.57 mmol) in 150 mL of ethanol was hydrogenated over Raney nickel catalyst (6.0 g wet) for 4h at room temperature under 1.0 atm of H_2 atmosphere. After addition of 4.0 g of celite to the solution, the mixture was stirred vigorously and filtered over celite pad. The filtrate was concentrated and purified with silica gel column chromatography (CH_2Cl_2 :MeOH = 20:1 v/v) to give 2-Chloro-3,4- diaminopyridine (4.72 g, 32.84 mmol) in 95% yield. ^{1}H-NMR (DMSO, 500 MHz) δ 7.31 (d, J= 5.0, IH), 6.45 (d, J= 5.0, IH), 5.79 (s, 2H), 4.68 (s, 2H); ^{13}C-NMR (DMSO, 125 MHz) δ 143.41, 138.03, 135.61, 126.66, 108.73. t ,

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。

ELSEVIER

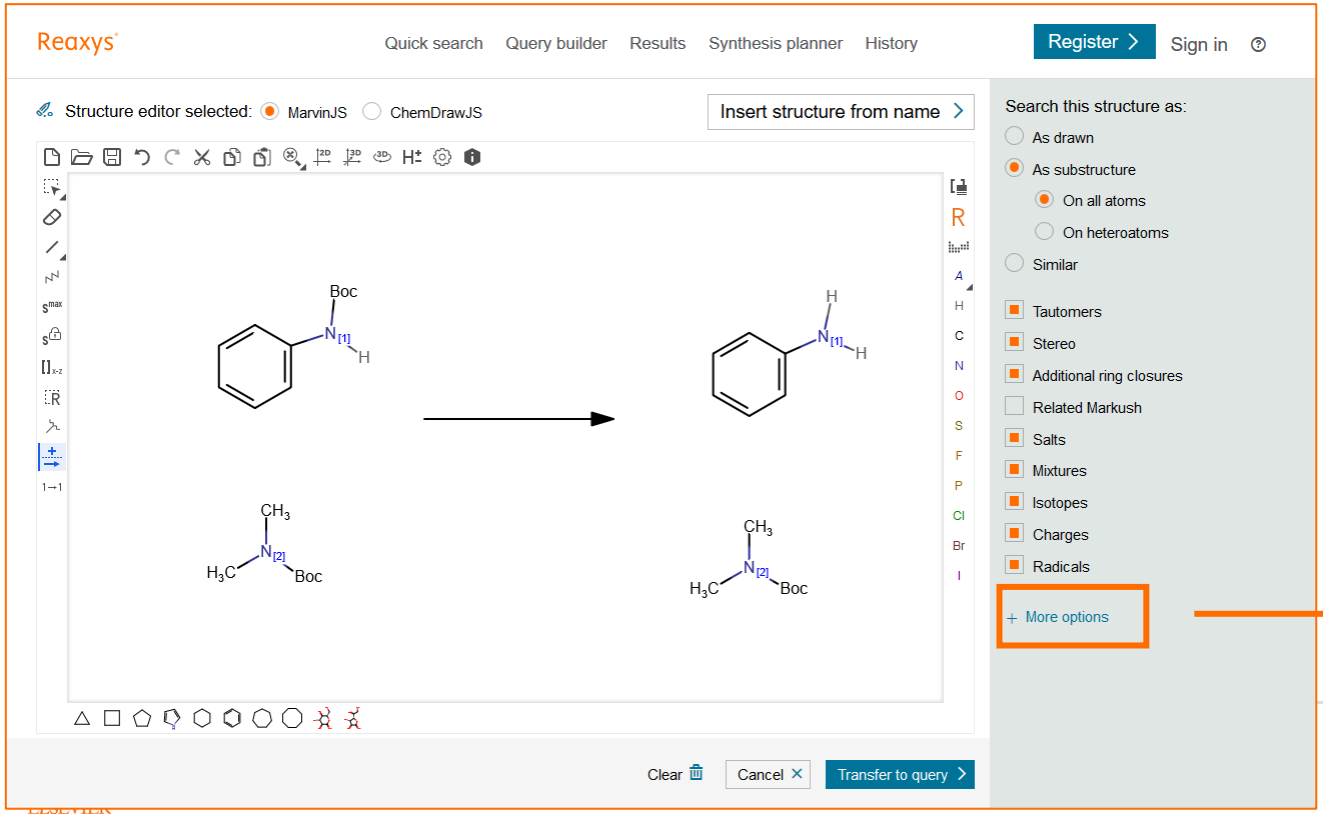
Case 7：选择性氧化还原脱保护反应的定义

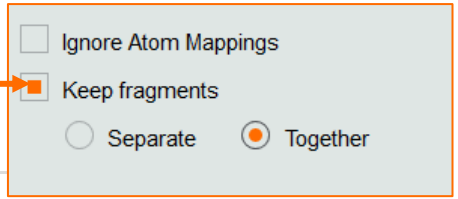
- 结构中两个带Boc的片段，两个片段以任意的形式相接在一个分子中
- 反应过后把其中一个片段的Boc脱掉，但是另外一个Boc不变



视频操作过程：
https://www.bilibili.com/video/av92577868

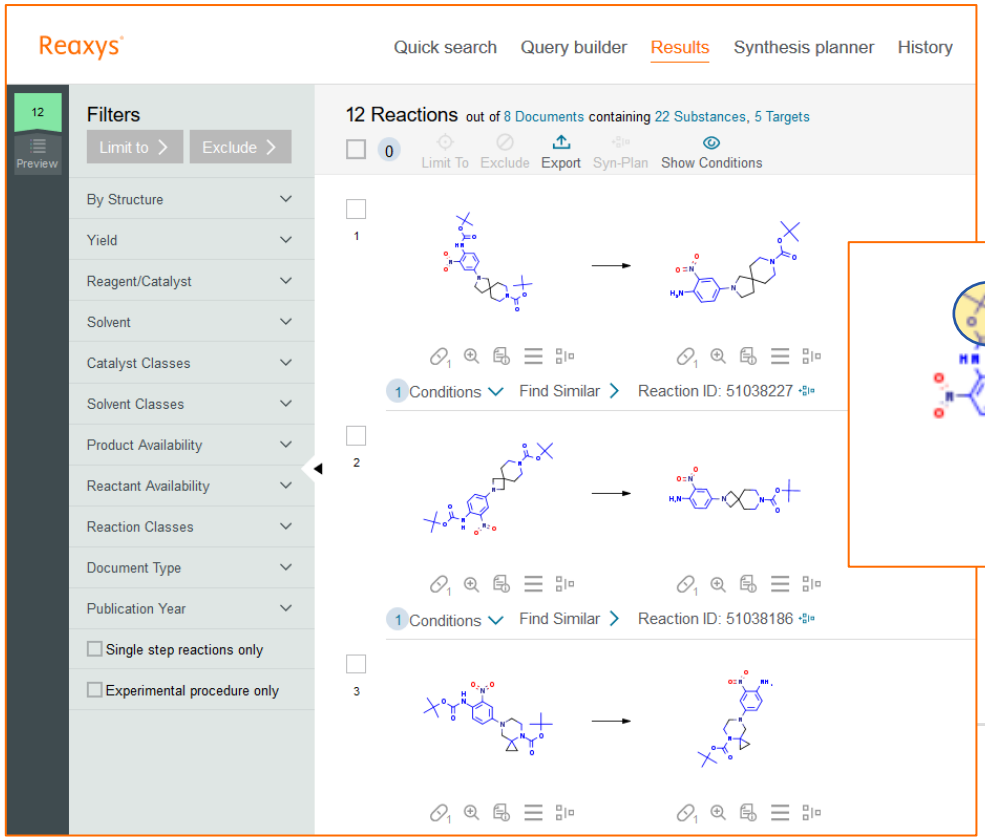
Reaxys中的结构定义

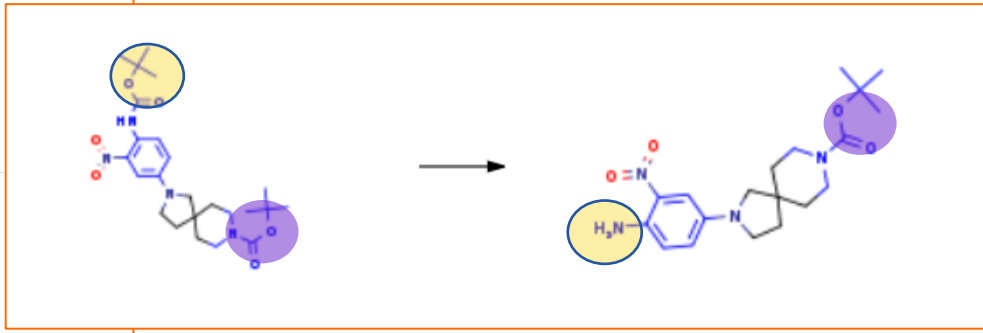




Reaxys可以直接设定这些片段在一个结构中

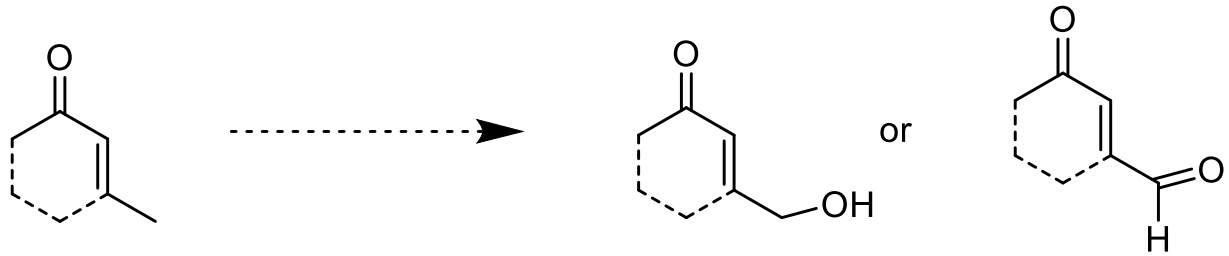
Reaxys中结果


Reaxys
Quick search
Query builder
Results
Synthesis planner
History
12
Preview
Filters
Limit to
Exclude
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
12 Reactions out of 8 Documents containing 22 Substances, 5 Targets
0
Limit To
Exclude
Export
Syn-Plan
Show Conditions
1
1 Conditions
Find Similar
Reaction ID: 51038227
2
1 Conditions
Find Similar
Reaction ID: 51038186
3



Case 8：涉及环系变化的反应定义

- 获取以下反应

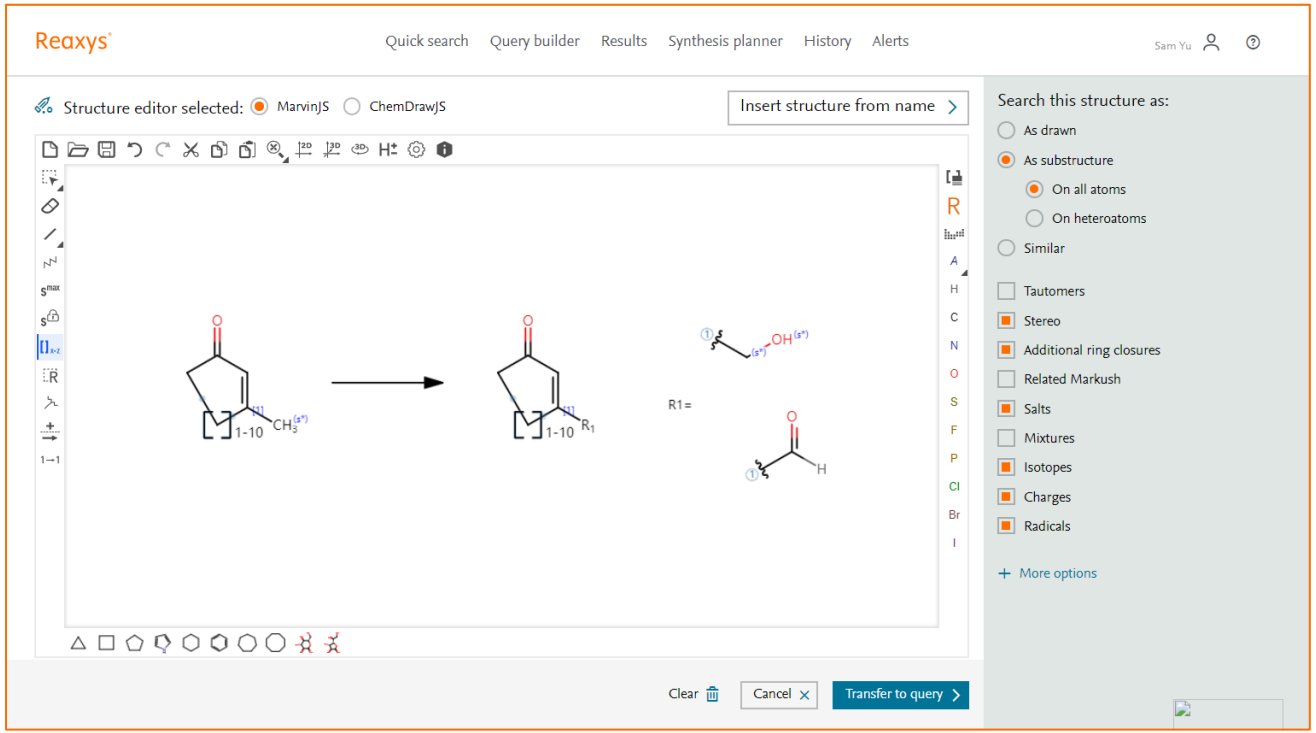


Requirement:

- 虚线部分是大于5个C原子的环
- 结构中不能发生互变异构
- 产物的CH2OH，CHO是有底物的CH3变化过来
- 视频操作（结构类似）：

https://b23.tv/S08u6p

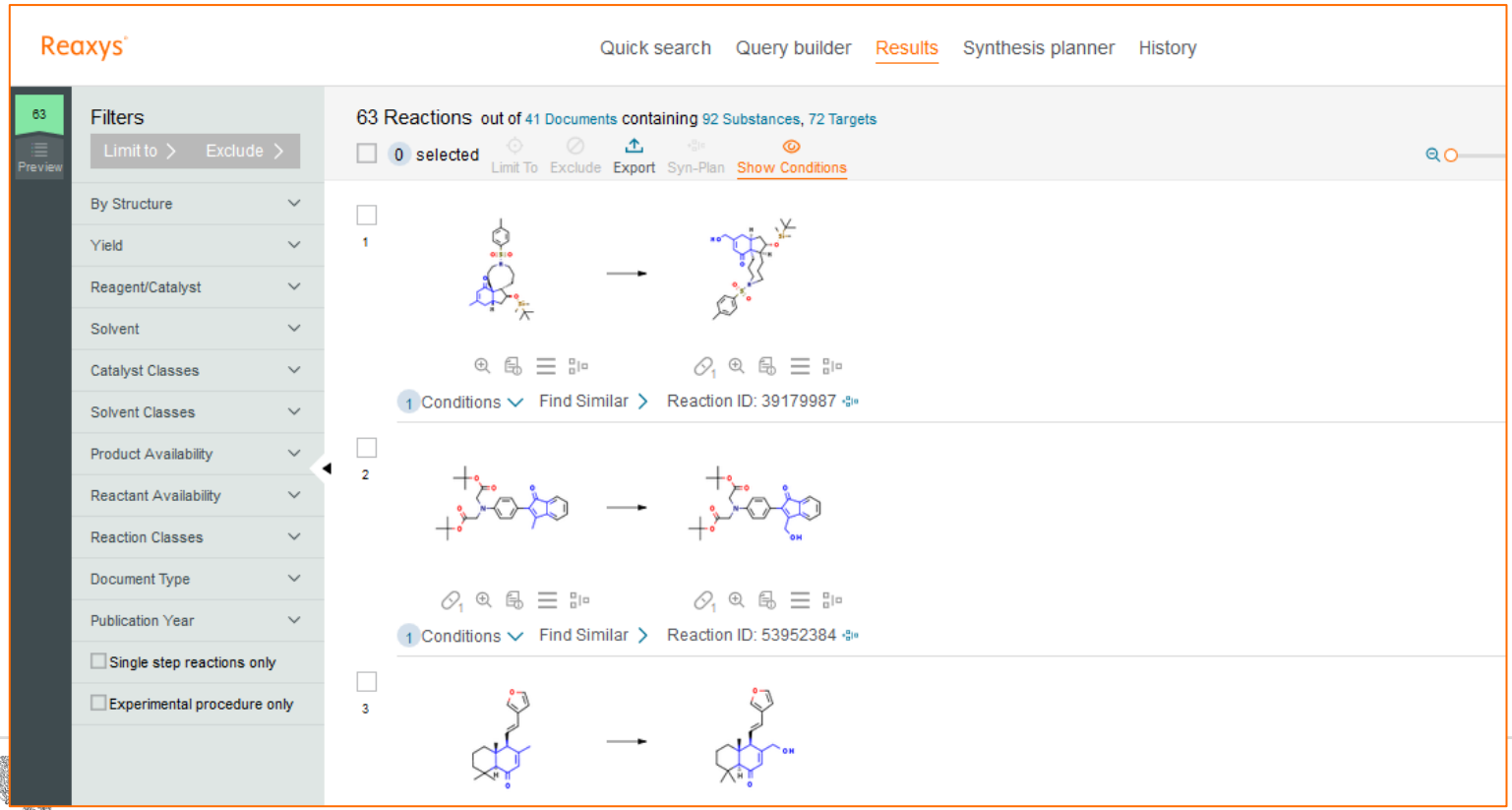
Reaxys中的定义



定义方法：

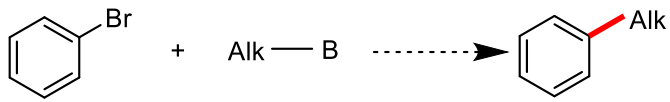
- R基团定义工具，定义侧链
- S*定义侧链CH2OH，以及底物CH3无取代
- 重复基团定义工具，定义环的大小
- 无互变异构

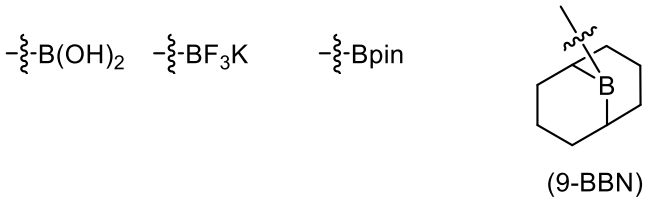
最后的结果



Case Study 9：

- 获取以下反应性对比的文献（收率）



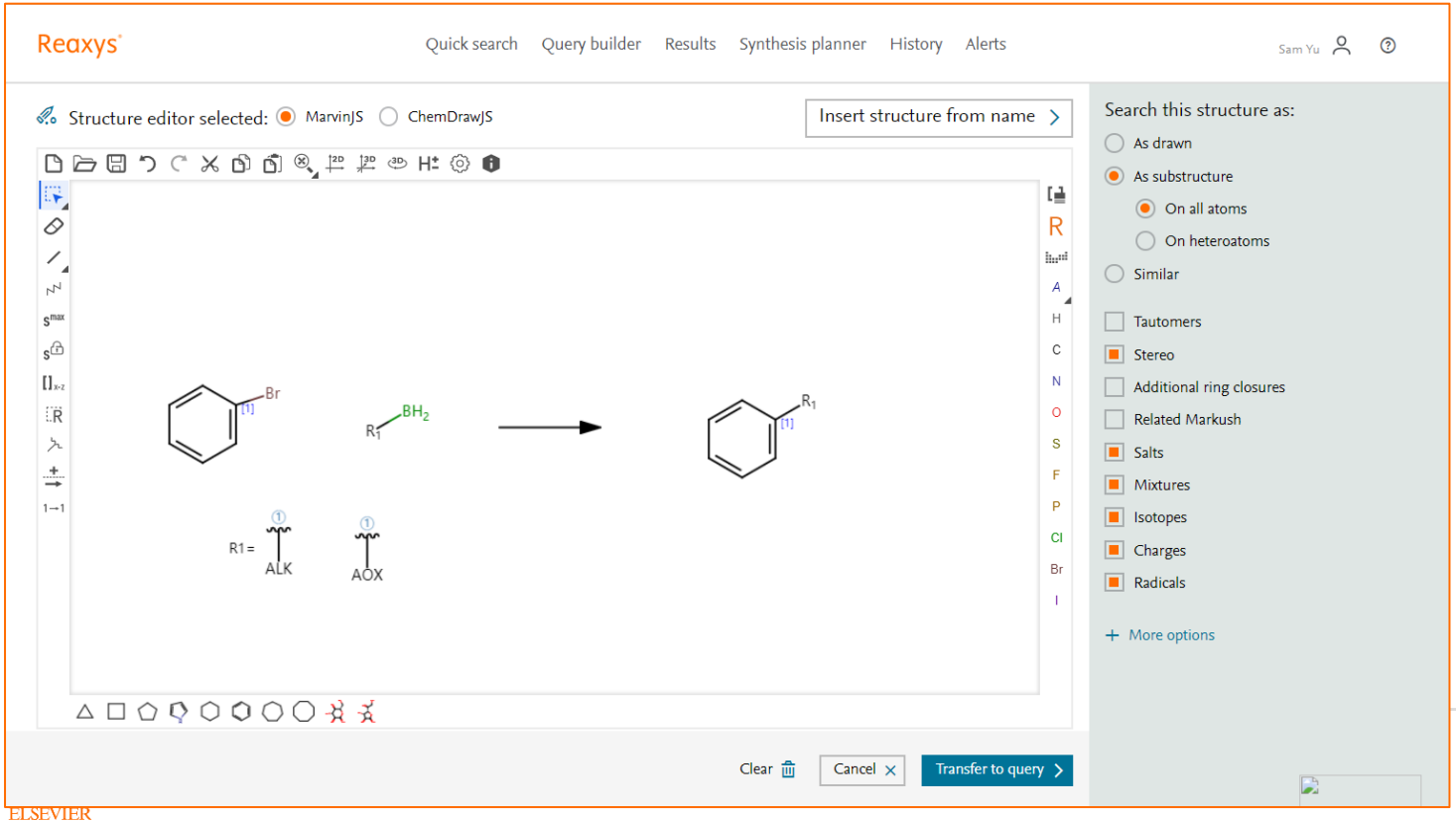


(9-BBN)

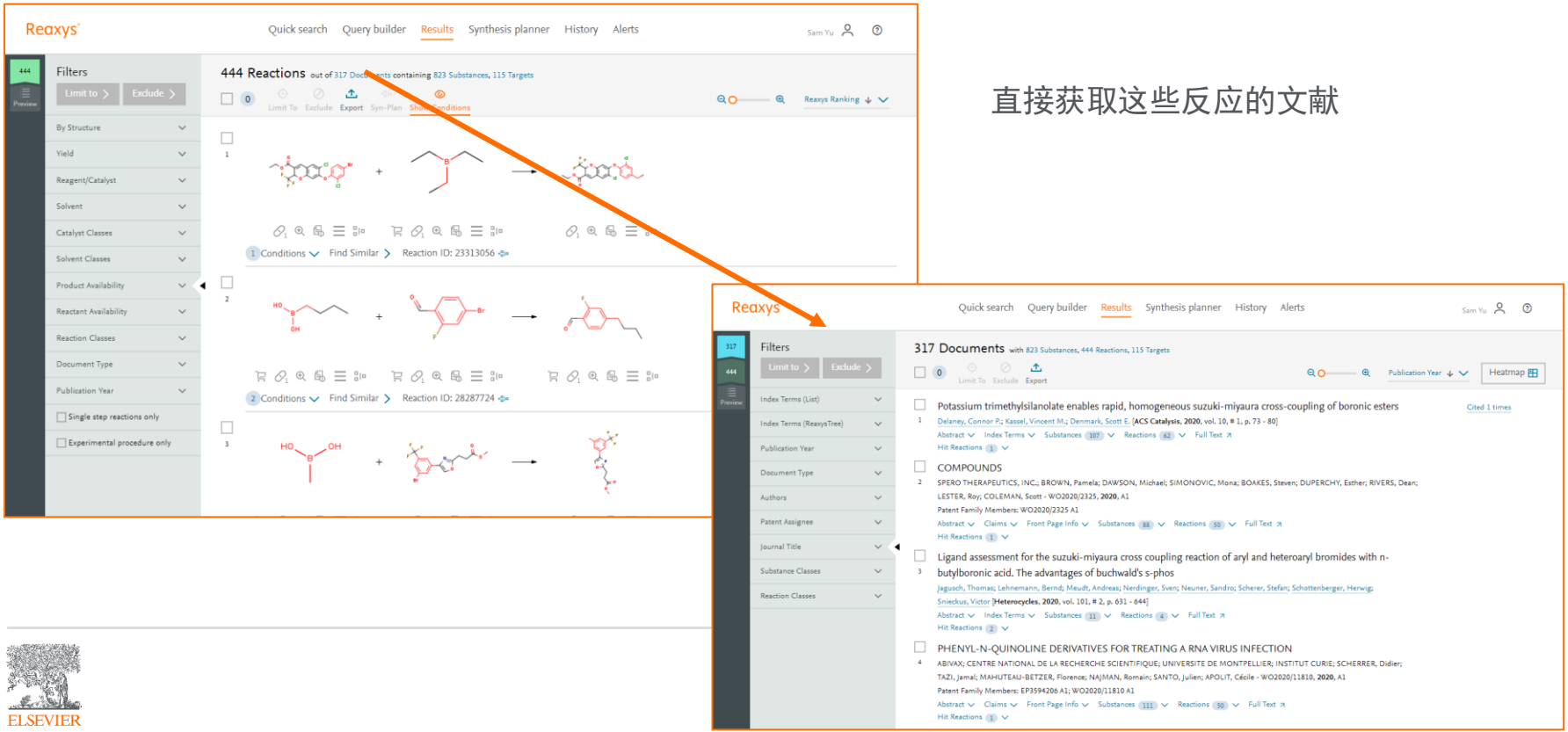
Requirement:

- 希望获得在一篇文献中讨论过同一个B试剂和不同底物反应的对比
- ALK也可以是醚

Reaxys中的解决方案



Reaxys中的结果



直接获取这些反应的文献

ELSEVIER

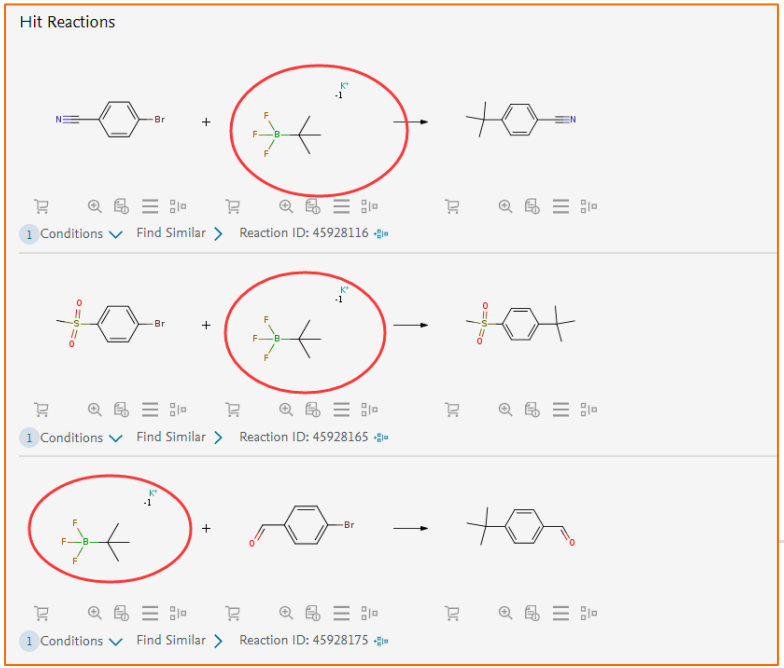
Reaxys中的结果

Enabling the Cross-Coupling of Tertiary Organoboron Nucleophiles through Radical-Mediated Alkyl Transfer

Primer, David N.; Molander, Gary A. [**Journal of the American Chemical Society, 2017**, vol. 139, # 29, p. 9847 - 9850]

Abstract Index Terms Substances 88 Reactions 58 Full Text

Hit Reactions 8



专门找Hit Reaction >1的文献，先进行预览，看是否存在相同硼试剂，不同底物的。

Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

Case 10：化合物的文献定位

Tetrahedron 74 (2018) 224–239

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Assessment of the regioselectivity in the condensation reaction of unsymmetrical *o*-phthaldialdehydes with alanine

Agathe C.A. D'Hollander, Nicholas J. Westwood*

School of Chemistry and Biomedical Sciences Research Complex, University of St Andrews and EaStCHEM, North Haugh, St Andrews, Fife, KY16 9ST, UK

ARTICLE INFO

Article history:
Received 27 July 2017
Received in revised form
5 November 2017
Accepted 13 November 2017
Available online 16 November 2017

Keywords:
o-phthaldialdehyde
Condensation reaction
Regioselectivity
Mechanistic understanding

ABSTRACT

One approach for the synthesis of isoindolinones, a privileged bioactive heterocyclic core structure, involves a condensation reaction of *o*-phthaldialdehydes with a suitable nitrogen-containing nucleophile. This fascinating reaction is revisited here in the context of the use of *o*-phthaldialdehydes that contain additional substituents in the aromatic ring leading to a detailed analysis of the regioselectivity of the reaction. Eleven monosubstituted *o*-phthaldialdehydes were synthesised and reacted with alanine. The regioselectivity observed across the eleven substrates led to the design of a disubstituted substrate that reacted with very high control. A gram-scale reaction followed by esterification gave one major regioisomer in high yield. In addition, the regioselectivity observed on reaction of two novel monodeuterated substrates led to an increased mechanistic understanding.

1. Introduction

The isoindolinones make up an important class of bioactive molecules that includes the known drugs Pazinaclone (**1**),[1a] Indoprofen (**2**)[1b] and Chlorthalidone (**3**)[1c] (Fig. 1a).

Common methods of obtaining isoindolinones that are unsubstituted in the aromatic ring, for example compound **4** (Fig. 1b), include selective reduction of **5**,[2] reductive amination-cyclisation of **6**[3] or **7**[4] with a primary amine (RNH_2) and, of interest here, the condensation reaction of *o*-phthaldialdehyde (**8**) with a primary amine (RNH_2).[5,6a]

To date, the majority of studies performed on this condensation reaction have focused on evaluating the scope of the amine nucleophile that can be tolerated in the reaction[5a,5b,5d,6a,6b] and/or proposing potential reaction mechanisms.[5a,5b,6] In contrast, examples of the use of this condensation reaction with monosubstituted *o*-phthaldialdehydes are rare (SI1 part I). One report describes a regioselectivity of 1:1 for the products **11**:**12** resulting from the condensation of **9** with **10** (Scheme 1a).[7] However, the observed regioselectivity was measured only after filtration or purification by column chromatography. Isolated yields for the formation of a single isomer, **14** in most cases, resulting from the condensation of **13** with various amines have also been reported (Scheme 1b).[8]

Other studies have provided only isolated yield(s) after purification (for one or for each isomer), incomplete regioisomeric ratio (rr) data within a series or have claimed to form a single regioisomer (no yield provided) without discussing the other possible isomer (SI1 part I).[7–9]

The work reported here revisits this issue by presenting a detailed study of the regiochemical outcome of the condensation of alanine (**16**) with 3-monosubstituted *o*-phthaldialdehydes **17** (to give **18** and **19**, Scheme 1c) and with 4-monosubstituted *o*-phthaldialdehydes **20** (to give **21** and **22**, Scheme 1d). Based on the initial results, the design of a highly regioselective substrate was achieved consistent with an improved understanding of the reaction. Further mechanistic insights were provided by the use of novel mono-deuterated substrates.

2. Results and discussions

2.1. Synthesis of monosubstituted *o*-phthaldialdehydes

Five 3-substituted *o*-phthaldialdehydes **17a-e** were synthesised using 2–5 step routes involving either a Swern oxidation of the corresponding diol **23** or an acetal deprotection of the corresponding monoacetal **24** or diacetal **25** (Scheme 2 and SI1 part II.1 for more details). It should be noted that the synthesis of pure samples of **17a-e** was particularly challenging (in line with literature reports[10]) with significant decomposition occurring during purification attempts and on storage. In several cases freshly

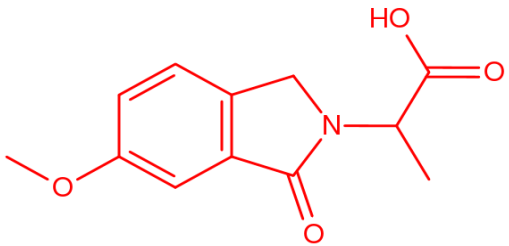
* Corresponding author.
E-mail address: njw1@st-andrews.ac.uk (N.J. Westwood).

https://doi.org/10.1016/j.tet.2017.11.035
0040-4020/

这是一篇常见的化学文献，包含：

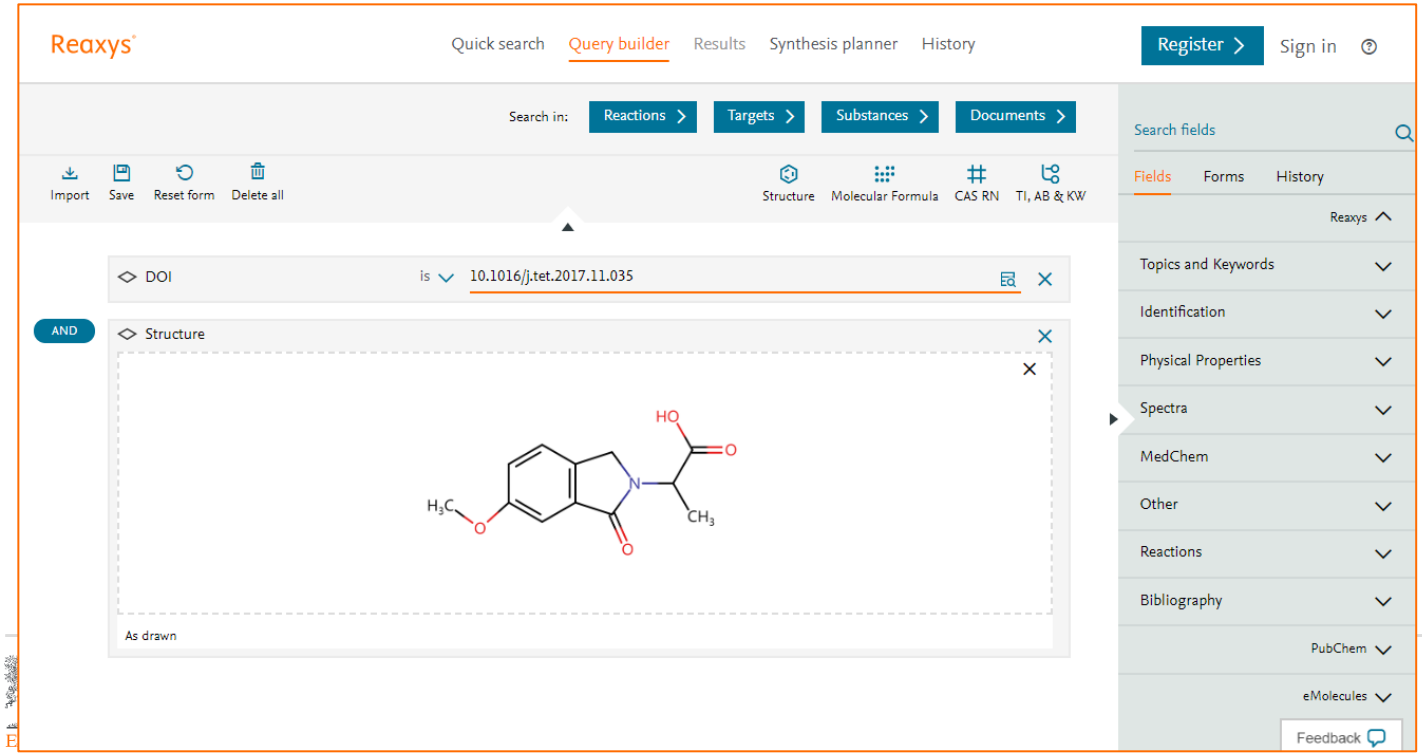
1. 16页PDF全文
2. 2个Supporting Information的Word文档，一个是44页，一个37页

已知文献中报道了这个化合物，如何在上述的97页文档中找到有关这个化合物的描述？

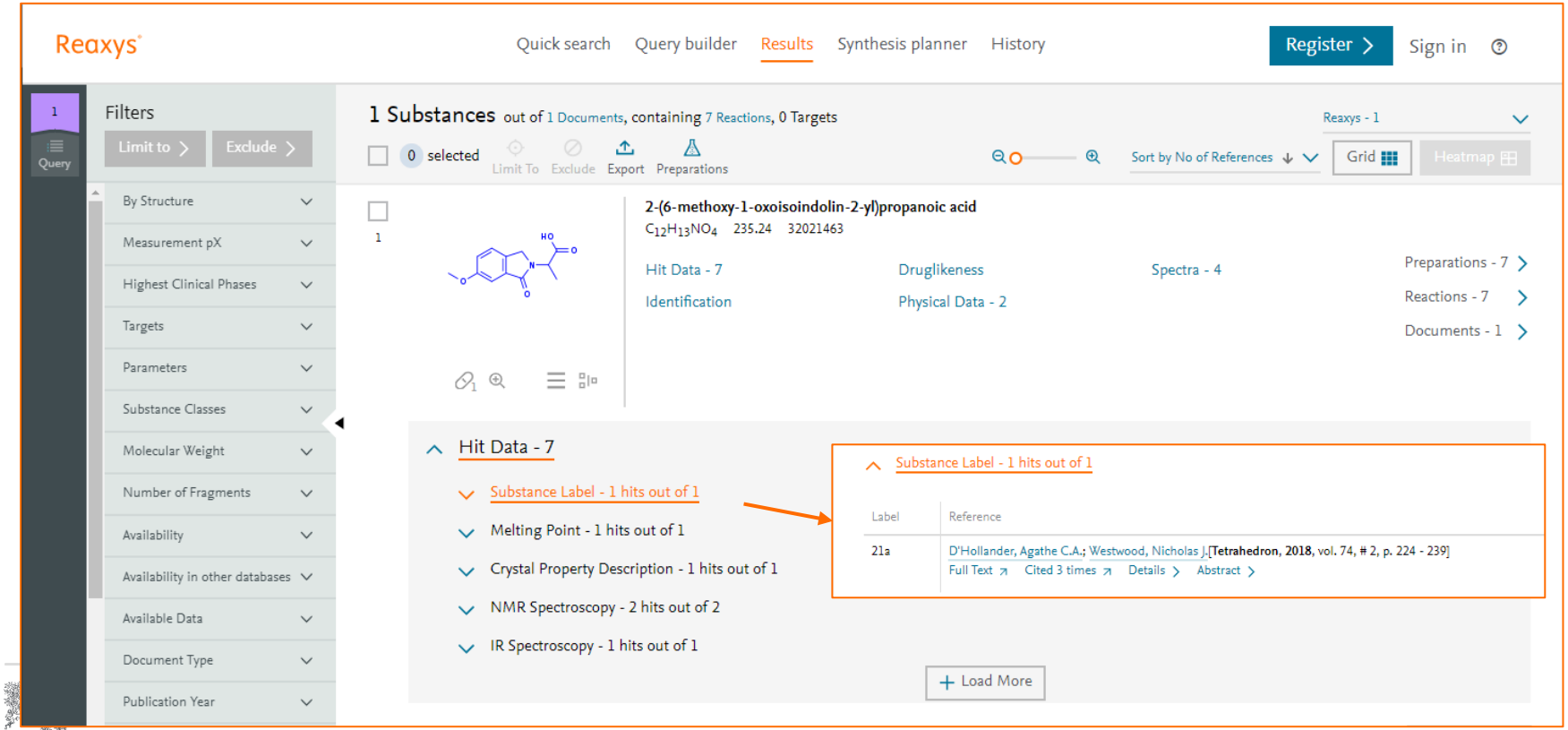


Reaxys中的检索

- Query Builder联合化合物结构与文献DOI号



Reaxys中的结果



ELSEVIER

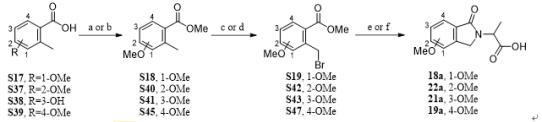
全文检索21a定位化合物

2.2. Regioselectivity of the condensation reaction of mono-substituted o-phthaldialdehydes

The mono-substituted *o*-phthaldialdehydes **17a-e** and **20a-f** were refluxed for 4 h with alanine (**16**, 1.2 equivalents) in anhydrous acetonitrile before the reaction was concentrated *in vacuo*. The crude reaction mixtures (except when specified, Table 1) were then analysed using a quantitative ^{1}H NMR experiment. A baseline correction was applied using MestReNova-9 software and integrations were calculated relative to one proton on deconvoluted peaks (see Fig. 2 for an example of the analysis applied to the formation of **18a**/**19a** and SI1 part III.1 for the rest of the NMR analysis; also see the experimental section below for a detailed explanation of the analytical protocol used).

In two of the condensation reactions the structure of the major regioisomer was identified by comparison with the ^{1}H NMR spectrum of a pure sample of one of the regioisomers (for **18a**/**19a**, **21a**/**22a**, for the synthesis of authentic isomers see SI1 part III.2). In the rest of the cases, advanced NMR techniques (HSQC, HMBC, COSY) applied to the crude reaction mixture were used to assign the structure of the major regioisomer. Considering the analysis of the regioisomeric mixture of **18b**/**19b** as an example (Fig. 3), the proximity of a carbonyl was observed to shift the signal corresponding to the aromatic H7 proton in **18b** and the methyl H1′ protons in **19b** downfield (Fig. 3a and b). Identification of H7 in **18b** was further validated by its correlation with C1 in the HMBC analysis of the regioisomeric mixture (Fig. 3a). In contrast, H4 in **19b** showed a correlation with C3 in this HMBC analysis (Fig. 3c). Using the correlations observed in the COSY spectrum (Fig. 3d), the signals corresponding to H5 and H6 for **18b** and **19b** were finally assigned. The value of the integrals in the 1D quantitative ^{1}H NMR

▪ **III.2. Synthesis of pure isoindolinones 18a, 19a, 21a and 22a.**



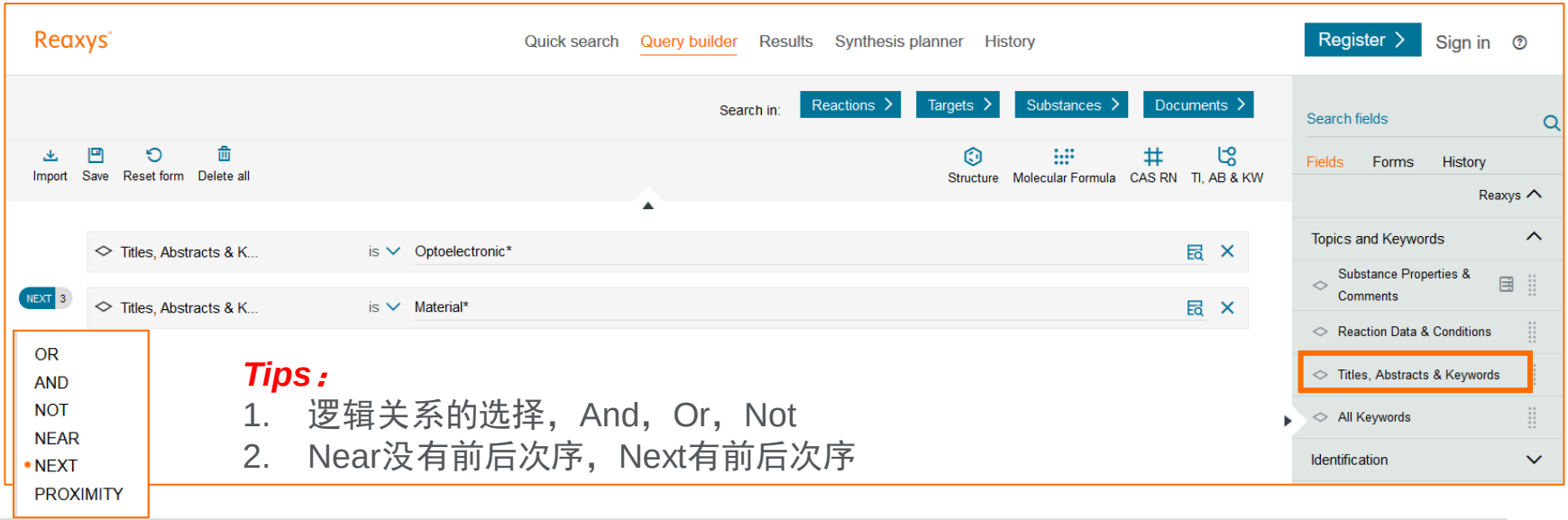
Scheme S 10: Synthesis of **18a**, **19a**, **21a** and **22a**. Reagents and conditions: (a) MeOH, H_2SO_4, reflux, 7-24 h, quant. for **S18**, 84% for **S40**; (b) MeI, K_2CO_3, DMF, 70 °C 17-18 h, 92% for **S41**, 99% for **S45**; (c) NBS, AIBN, $CHCl_3$, reflux, 2.5-21.0 h, 97% for **S19**, crude **S42** and **S43** were directly used in the next step; (d) NBS, AIBN, CCl_4, reflux, 2 h, crude **S47** was directly used in the next step; (e) alanine (**16**), MeOH, K_2CO_3, reflux 19-21 h, 61% for **18a**, 55% (2 steps) for **19a**; (f) alanine (**16**), MeOH, NEt_3, reflux 2-23 h, 4% (2 steps) for **21a**, 4% (2 steps) for **22a**.

Esterification of **S17**, **S37**, **S38** and **S39** was achieved in excellent yield using iodomethane or methanol with sulfuric acid (Scheme S 10).[8] Radical monobromination[9] of **S18**, **S40**, **S41** formed **S19**, **S42**, **S43** which were directly reacted[9] with alanine (**16**) to obtain **18a**, **22a** and **21a** respectively. To investigate the poor yield over two steps (2% for **18a**, 4% for **21a** and 4% for **22a**), radical monobromination of **S18** was repeated and the succinimide side product from *N*-bromosuccinimide was removed by a basic wash using NaOH (1 M) leading to pure **S19** in 97% yield. Reaction of **S19** with **16** and NEt_3 afforded **18a** in only 8% yield. However, concentration of the aqueous phase showed **S44** as the major product (identified by NMR spectroscopy (Figure S 5) and supported by mass spectrometric analysis (**HRMS** (ES^+) *m/z* calculated for $C_{16}H_{26}NO_3$ $[M]^+$: 280.1907; found: 280.1910) along with the remaining NEt_3 and alanine (**16**). Formation of **S44** was prevented by reacting **S19** with K_2CO_3 instead of NEt_3 to provide **18a** in good yield. This optimisation could be applied for the synthesis of **21a** and **22a** but was not performed since sufficient material was available.

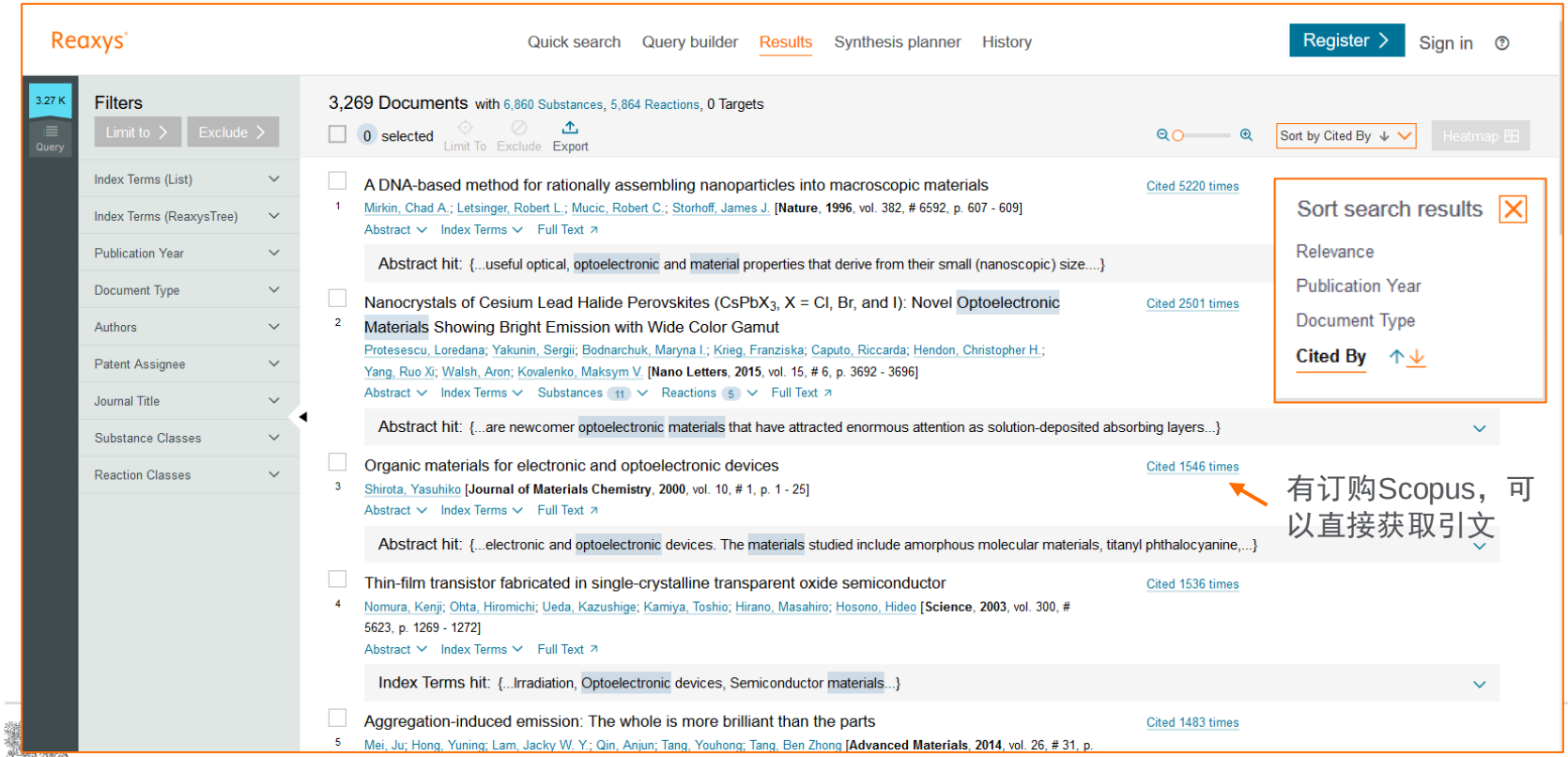
用于文献中化合物信息的快速定位。

Case 11：关键词检索时词语之间距离的设定

- 希望在主题，摘要，关键词中进行检索Optoelectronics Materials
- Optoelectronics与Materials两单词之间距离小于3，且Optoelectronics在Materials之前



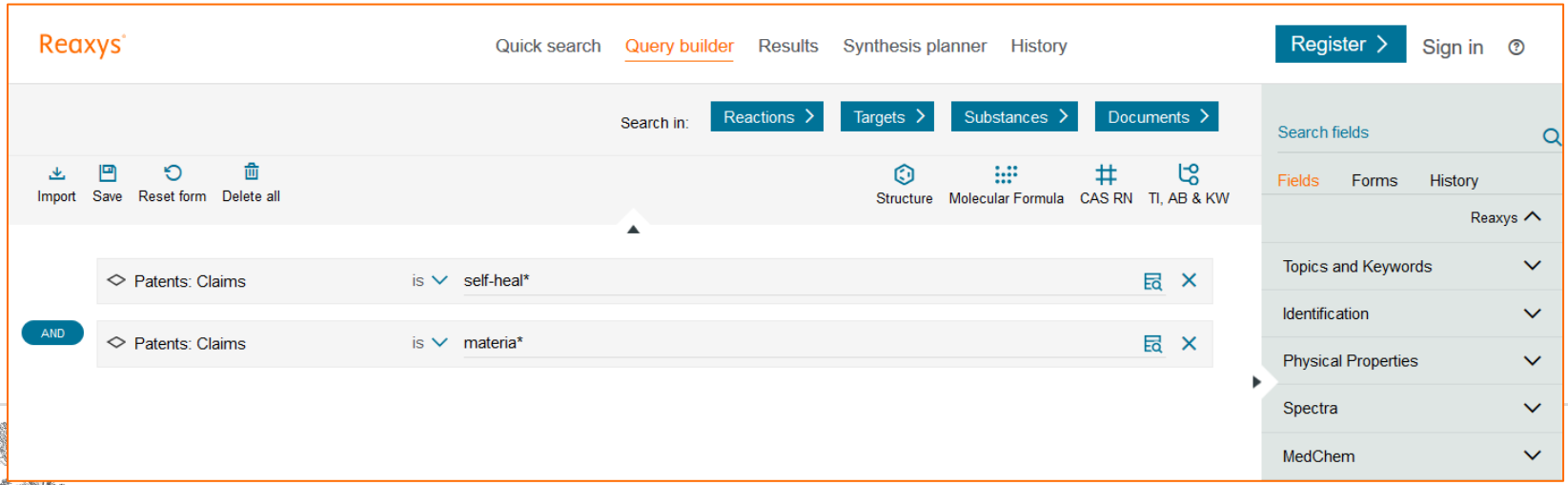
Reaxys中的结果



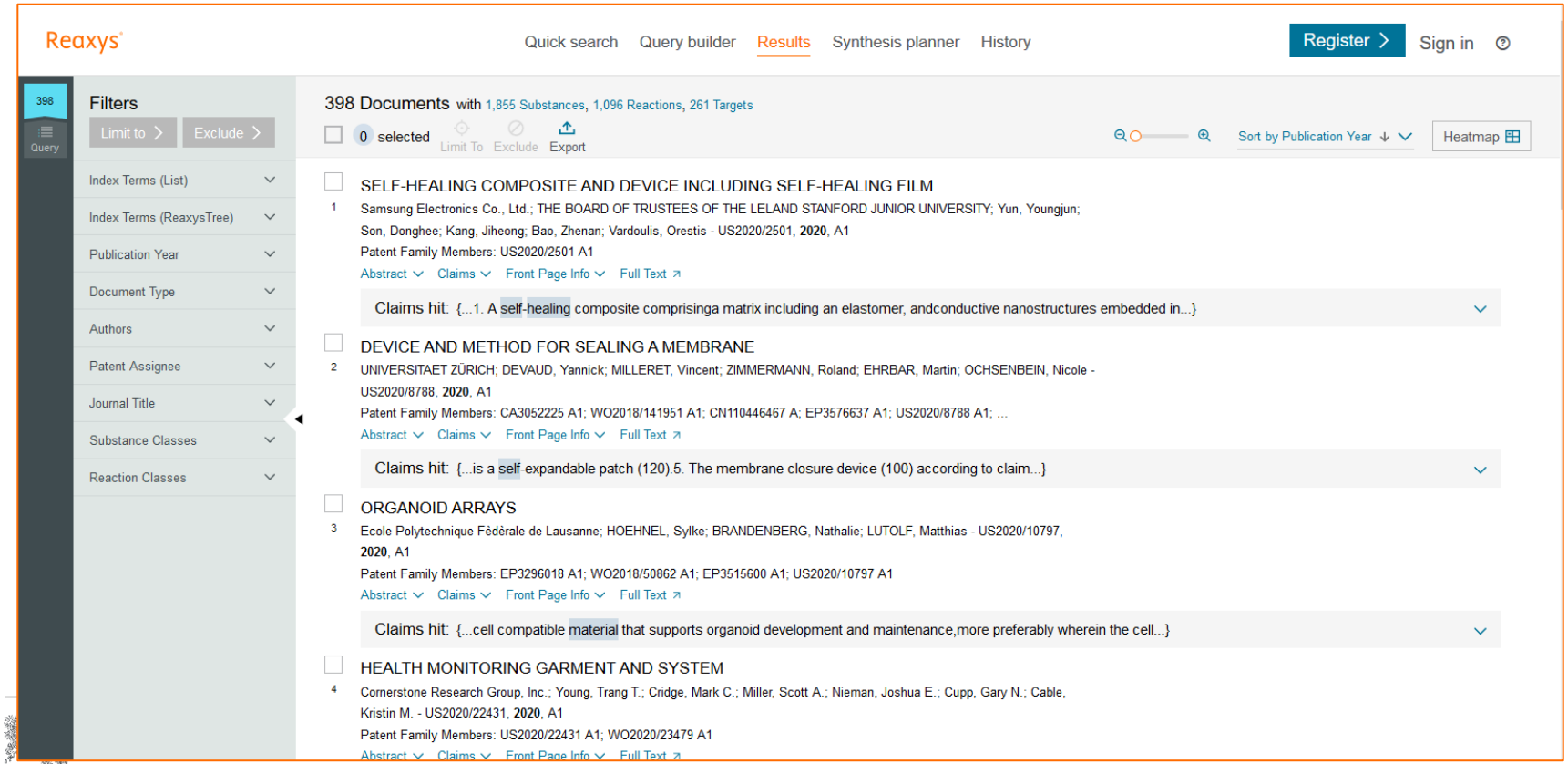
ELSEVIER

Case 12：专利Claim中的关键词检索

- Query Builder中Patent：Claim字段
- 如检索自愈材料
  - Self-heal*
  - Material*

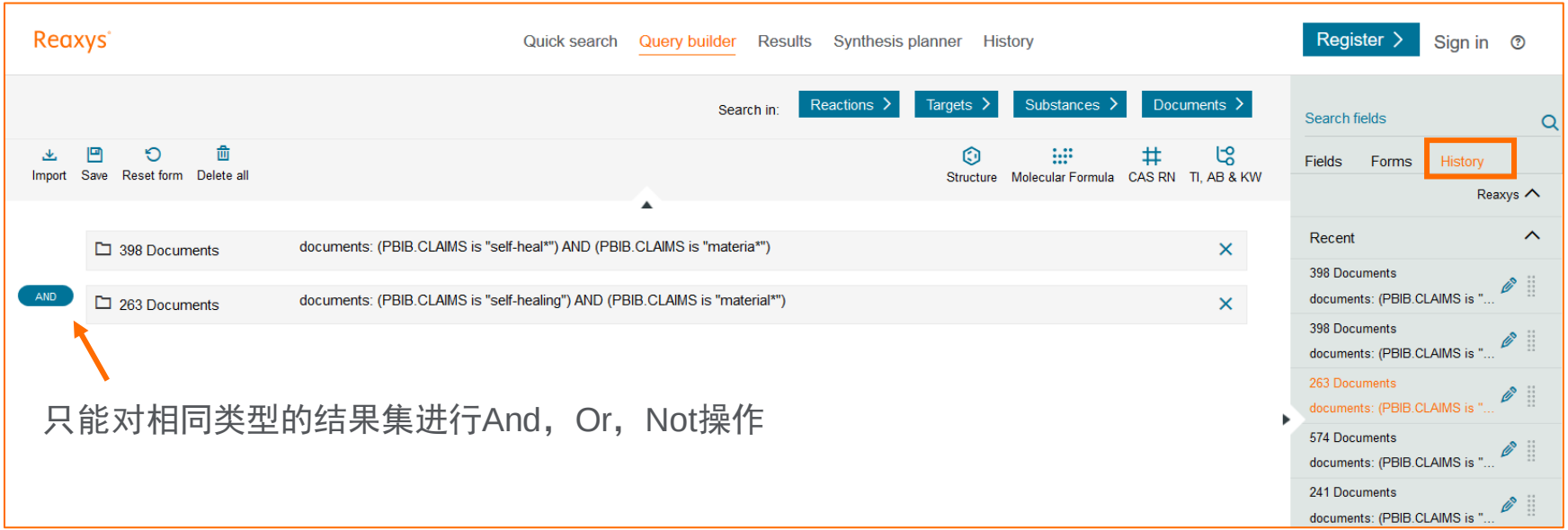


Reaxys中的结果



Case 13：结果集的逻辑处理

- Query Builder中History选择多个结果集，进行逻辑处理



ELSEVIER

Agenda

- Reaxys内容与发展规划
- Reaxys中的检索
  - Reaxys对文献的提炼
  - Reaxys中物性数据的查询与反向检索
  - Reaxys中的结构面板与复杂反应定义
  - Reaxys中的实用小案例
- Q&A

Reaxys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，跨学科的精确答案
- 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
- Elsevier Life Science线上服务：
  - 关注B站Up主：ELS生命科学，获取所有Elsevier Life Science数据库的使用视频
  - 添加Elsevier Life Science小助手微信号：ELS-LSS，邀请进Elsevier Life Science用户群，获取最新资料分享以及使用Q&A

ELSEVIER

ELSEVIER

Thank you