Reaxys中化学和药学相关信息的获取和应用

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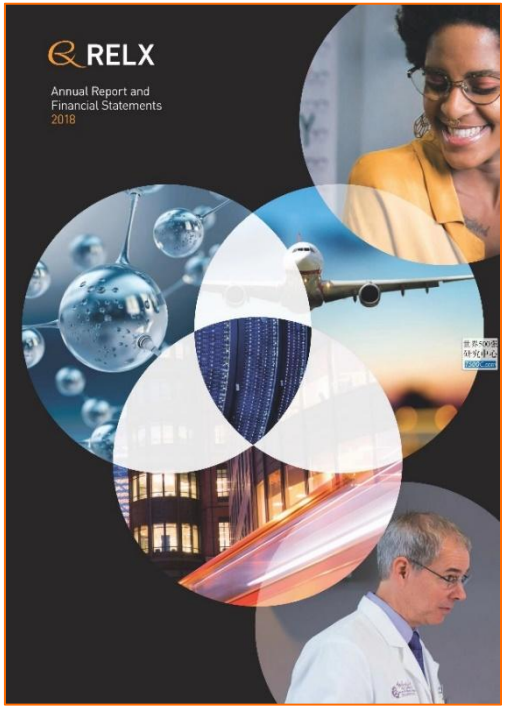
Agenda

- Reaxys的底层逻辑和发展方向
  - Reaxys及其对于科技文献的提炼
- Reaxys中科研数据的获取和应用场景
  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- Q&A

Elsevier Life Science是RELX集团Elsevier旗下的生命科学产品线



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RELX Group 全球排名第1的科技和医学信息和分析服务提供商

Elsevier Life Science一直致力于为全球用户提供科研数据支持

- 过去二十年， Elsevier Life Science长期以数据服务的形式为国内外的药物研究机构提供药物研发所需要的科研数据。

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Reaxys是Elsevier Life Science产品线中的化学及相关学科的科研信息平台

Reaxys是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

16,300 期刊
(journals, books and patents)

6,300万文献

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

105专利机构专利

WPO, USPO, EPO [≈ mid 70´s >]

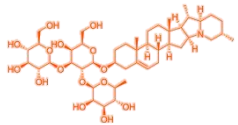
PO: JP, KR, CN, TW [2015 >]

38万书的章节

Beilstein, Gmelin,….

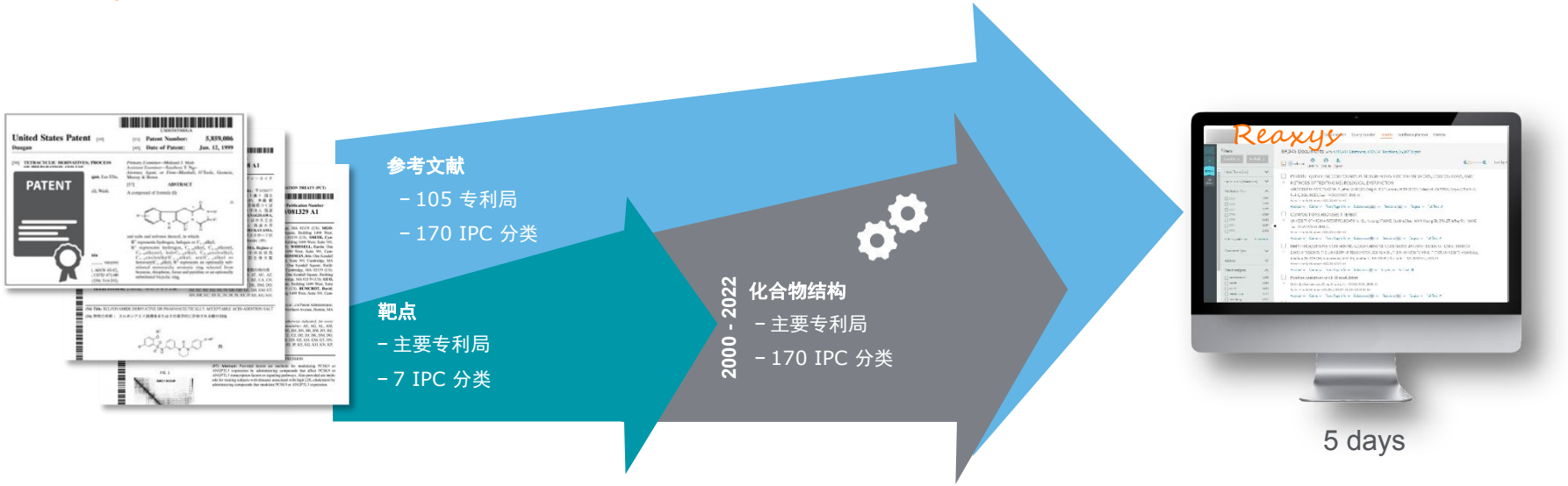
[自动抽提]

≈ 450 journals + PO
[人工抽提]



ELSEVIER

Reaxys数据库全面强化----药学相关专利内容



内容+功能扩容：

1. 7个专利局—扩容105个专利局 （同类型覆盖面最广）
2. 专利内容扩容到170种技术领域：全面覆盖小分子，蛋白药，抗体药物，疫苗，医药材料，医疗器械等
3. 改进化合物提取技术(NER+I2S)，尽可能全面抓取小分子化合物, 降低漏检风险
4. 从专利‘发明描述及claim’内容索引专利，可以便捷进行: 靶点，蛋白名，制剂，工艺等专利检索（独有）
5. 从技术领域分类检索专利，专利公开5-7天，自动推送给用户，如: 适应症，结构式描述等技术领域推送（独有）
6. 强化专利分类功能，快速分类专利局，权益人，溯源专利权益变更，溯源家族专利等（独有）

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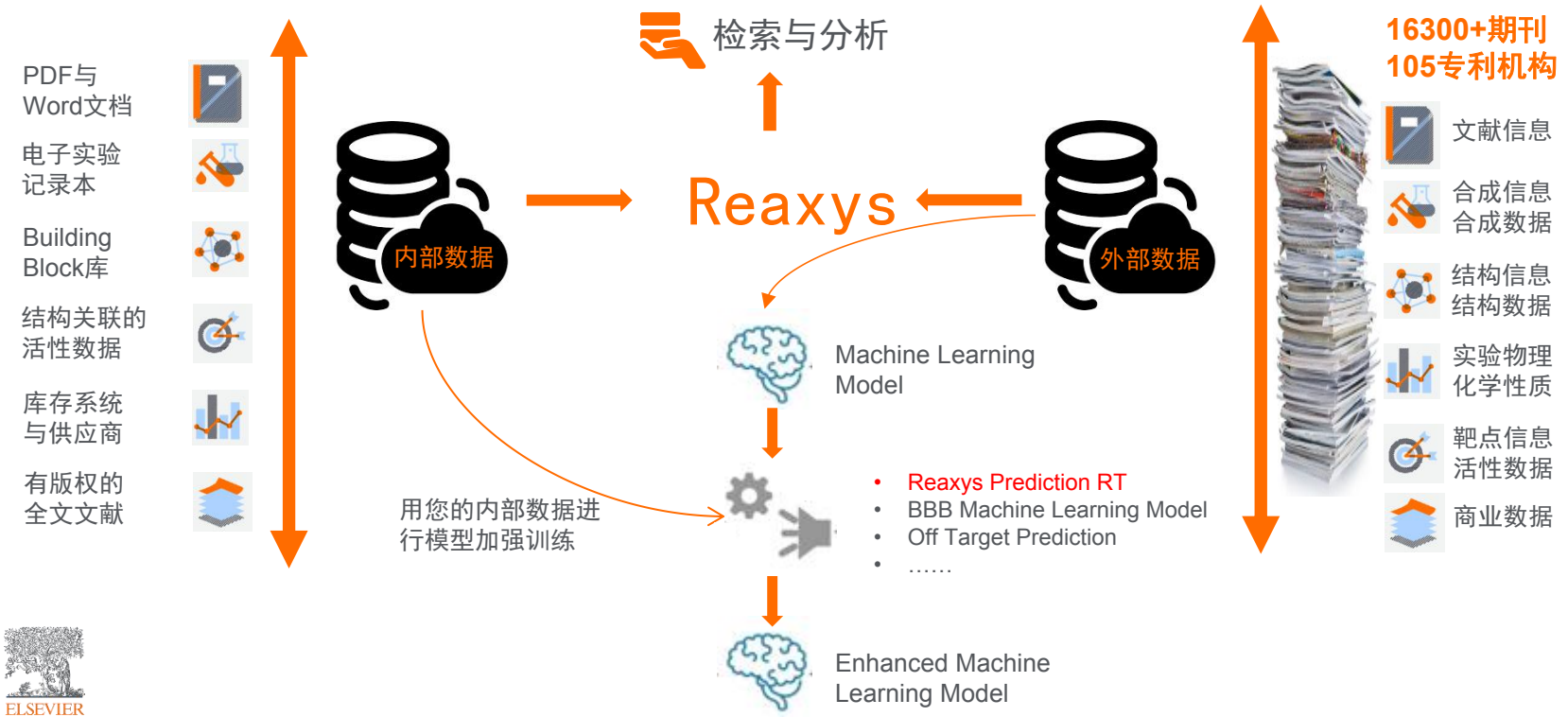
Reaxys—从科学数据到数据科学的跨越

Reaxys是Elsevier旗下Life Science产品线中基于数据深度提炼与挖掘，且可以整合内部与外部化学相关学科科学数据的信息检索，分析，数据科学应用平台。



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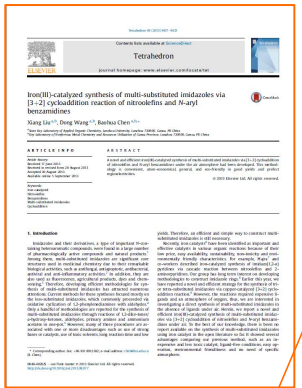
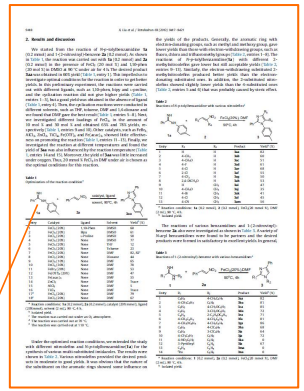
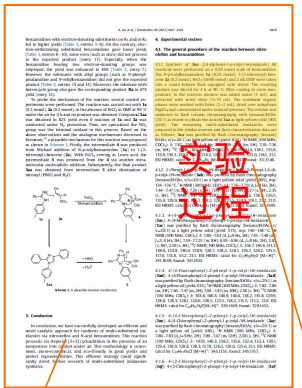
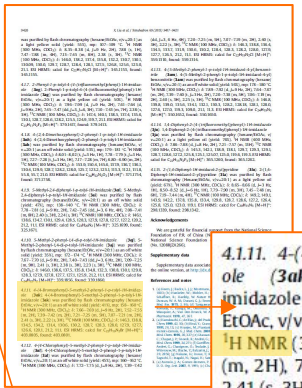
从一篇常见的药物化学文献看科研工作者的信息数据关注点





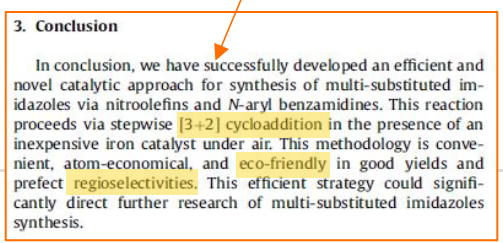




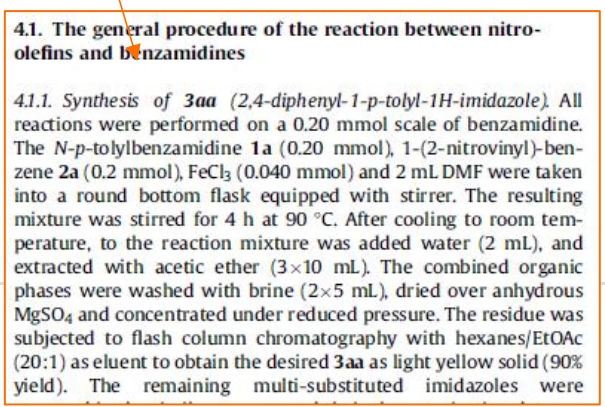
一篇全文以及Support Information中有大量的数据，科研人员如果要获取，需要花费多的时间去阅读全文。

实验过程

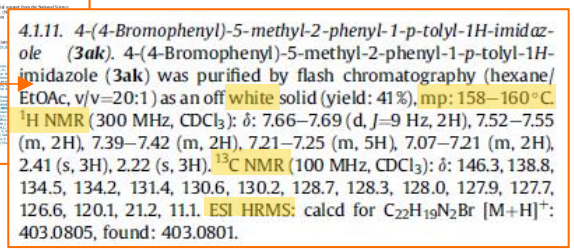
结论



- 新的催化剂
- 3+2环化加成
- 区域选择性
- 环保



化合物性质数据



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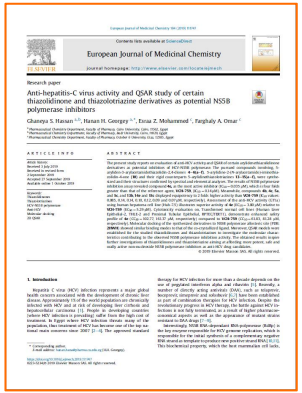
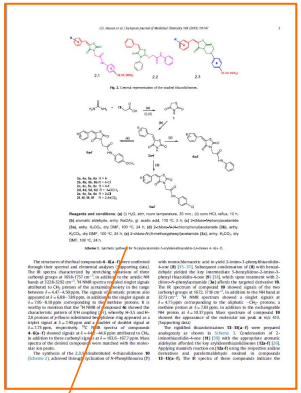
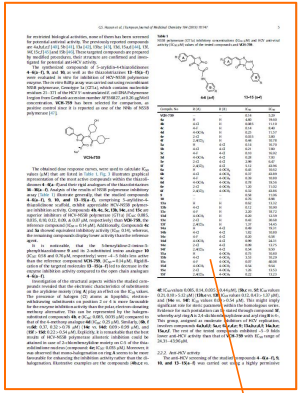
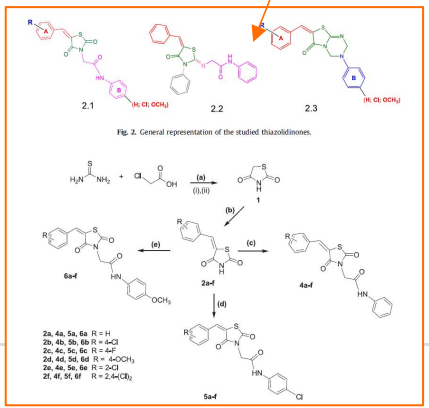
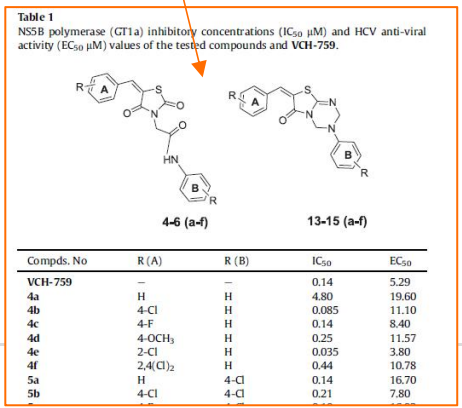
Reaxys中的所有数据源自期刊与专利报导





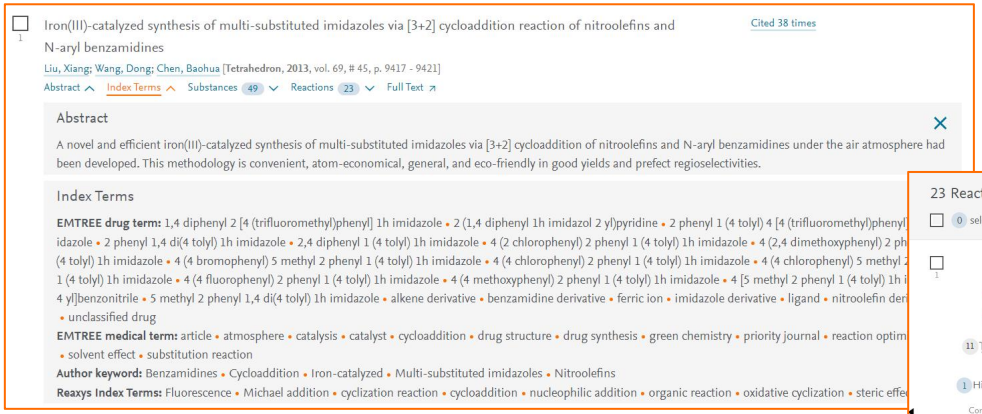


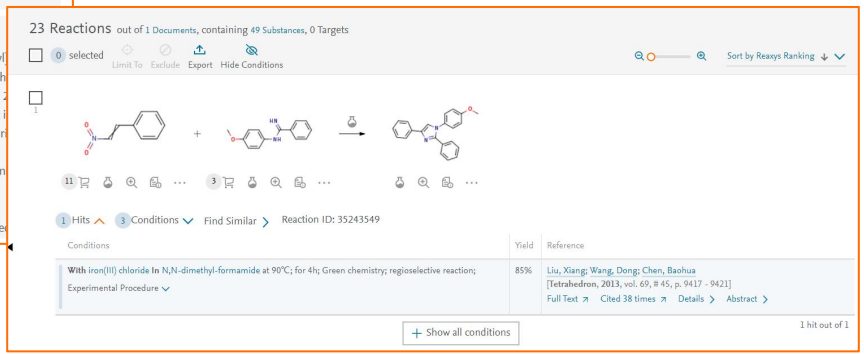


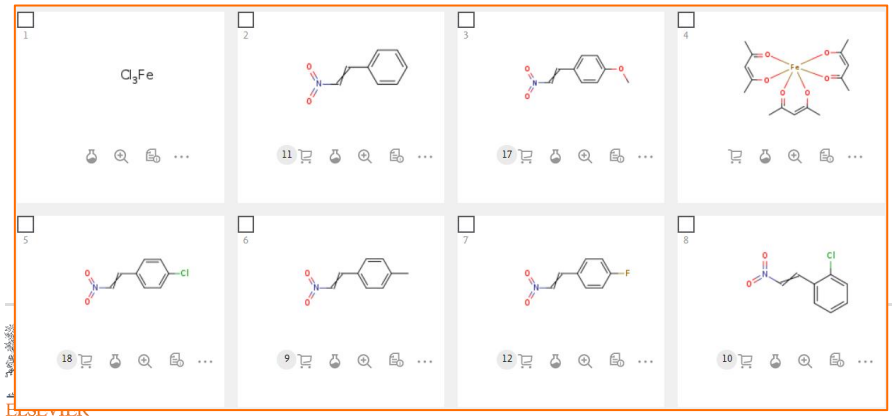


一篇全文以及Support Information中有大量的数据，科研人员如果要获取，需要花费多的时间去阅读全文。

Reaxys对这篇全文的提炼—概览





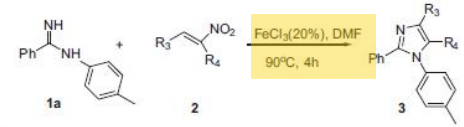


Reaxys提炼全文中的：

- 题录，摘要，关键词
- 物质结构，
- 反应Scheme

Reaxys对全文中的合成线路的相关数据提炼

Table 2
Reactions of *N*-*p*-tolylbenzamidine with various nitroolefins[a]



1a 2 3

Entry	R_3	R_4	Product	Yield[b] (%)
1	H	H	**3aa**	82
2	4-CH_3	H	**3ab**	60
3	4-CH_3O	H	**3ac**	51
4	4-F	H	**3ad**	61
5	4-Cl	H	**3ae**	68
6	2-Cl	H	**3af**	55
7	4-CF_3	H	**3ag**	50
8	2,4-$DiCH_3O$	H	**3ah**	53
9	H	CH_3	**3ai**	47
10	4-CH_3O	CH_3	**3aj**	35
11	4-Br	CH_3	**3ak**	41
12	4-Cl	CH_3	**3al**	45
13	4-CN	CH_3	**3am**	56

3. Conclusion

In conclusion, we have successfully developed an efficient and novel catalytic approach for synthesis of multi-substituted imidazoles via nitroolefins and *N*-aryl benzamidines. This reaction proceeds via stepwise [3+2] cycloaddition in the presence of an inexpensive iron catalyst under air. This methodology is convenient, atom-economical, and eco-friendly in good yields and prefect regioselectivities. This efficient strategy could significantly direct further research of multi-substituted imidazoles synthesis.

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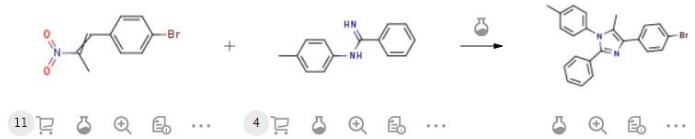

11 4

1 Hits/Conditions Find Similar Reaction ID: 36429699

Conditions	Yield	Reference
With iron(III) chloride In N,N-dimethyl-formamide at 90°C; for 4h; Green chemistry; regioselective reaction; Experimental Procedure	41%	Liu, Xiang; Wang, Dong; Chen, Baohua [Tetrahedron, 2013, vol. 69, # 45, p. 9417 - 9421] Full Text Cited 38 times Details Abstract

11 The general procedure of the reaction between nitroolefins and benzamidines

General procedure: 4.1.1 Synthesis of 3aa (2,4-diphenyl-1-p-tolyl-1H-imidazole) All reactions were performed on a 0.20mmol scale of benzamidine. The N-p-tolylbenzamidine 1a (0.20mmol), 1-(2-nitrovinyl)-benzene 2a (0.2mmol), $FeCl_3$ (0.040mmol) and 2mL DMF were taken into a round bottom flask equipped with stirrer. The resulting mixture was stirred for 4h at 90°C. After cooling to room temperature, to the reaction mixture was added water (2mL), and extracted with acetic ether (3×10mL). The combined organic phases were washed with brine (2×5mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash column chromatography with hexanes/EtOAc (20:1) as eluent to obtain the desired 3aa as light yellow solid (90% yield). The remaining multi-substituted imidazoles were preparedin the similar manner and their characterization data are as follows: 3aa was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as light yellow oil (yield: 82%). 4.1.11 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-p-tolyl-1H-imidazole (3ak) 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-p-tolyl-1H-imidazole (3ak) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 41%), mp: 158-160 °C. ^1H NMR (300 MHz, $CDCl_3$): δ: 7.66-7.69 (d, J=9 Hz, 2H), 7.52-7.55 (m, 2H), 7.39-7.42 (m, 2H), 7.21-7.25 (m, 5H), 7.07-7.21 (m, 2H), 2.41 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.3, 138.8, 134.5, 134.2, 131.4, 130.6, 130.2, 128.7, 128.3, 128.0, 127.9, 127.7, 126.6, 120.1, 21.2, 11.1. ESI HRMS: calcd for $C_{22}H_{19}N_2Br$ $[M+H]^+$: 403.0805, found: 403.0801.

实验过程与条件

Reaxys对全文中的化合物（产物）的相关数据提炼

*4.1.11. 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-p-tolyl-1H-imidazole (**3ak**).* 4-(4-Bromophenyl)-5-methyl-2-phenyl-1-*p*-tolyl-1*H*-imidazole (**3ak**) was purified by flash chromatography (hexane/EtOAc, v/v=20:1) as an off white solid (yield: 41%), mp: 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.66–7.69 (d, *J*=9 Hz, 2H), 7.52–7.55 (m, 2H), 7.39–7.42 (m, 2H), 7.21–7.25 (m, 5H), 7.07–7.21 (m, 2H), 2.41 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.3, 138.8, 134.5, 134.2, 131.4, 130.6, 130.2, 128.7, 128.3, 128.0, 127.9, 127.7, 126.6, 120.1, 21.2, 11.1. ESI HRMS: calcd for $C_{22}H_{19}N_2Br$ $[M+H]^+$: 403.0805, found: 403.0801.

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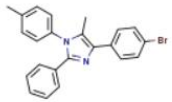

4-(4-bromophenyl)-5-methyl-2-phenyl-1-(p-tolyl)-1H-imidazole

$C_{23}H_{19}BrN_2$ 403.321 24040362 1462876-22-7

Hit Data - 6 | Druglikeness | Spectra - 3

Identification | Physical Data - 2

NMR Spectroscopy - 2 hits out of 2

Description (NMR Spectroscopy)	Nucleus (NMR Spectroscopy)	Solvents (NMR Spectroscopy)	Frequency (NMR Spectroscopy), MHz	Original Text (NMR Spectroscopy)
Chemical shifts, Spectrum	1H	chloroform-d1	300	^{1}H NMR (300 MHz, $CDCl_3$): δ: 7.66-7.69 (d, J=9 Hz, 2H), 7.52-7.55 (m, 2H), 7.39-7.42 (m, 2H), 7.21-7.25 (m, 5H), 7.07-7.21 (m, 2H), 2.41 (s, 3H), 2.22 (s, 3H)
Chemical shifts, Spectrum	13C	chloroform-d1	100	^{13}C NMR (100 MHz, $CDCl_3$): δ: 146.3, 138.8, 134.5, 134.2, 131.4, 130.6, 130.2, 128.7, 128.3, 128.0, 127.9, 127.7, 126.6, 120.1, 21.2, 11.1

Hit Data - 6

- Substance Label - 1 hits out of 1
- Melting Point - 1 hits out of 1
- Crystal Property Description - 1 hits out of 1
- NMR Spectroscopy - 2 hits out of 2
- Mass Spectrometry - 1 hits out of 1

Label: 3ak

Melting Point, °C: 158 - 160

Colour & Other Properties: white

Description (Mass Spectrometry)

high resolution mass spectrometry (HRMS), electrospray ionisation (ESI), spectrum

Peak

403.0801 m/z

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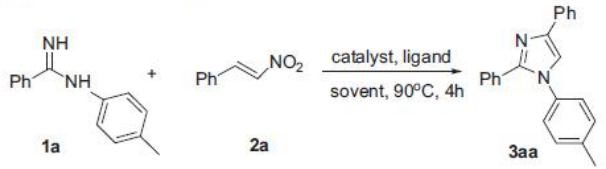
Reaxys对全文中的化合物（催化剂）的相关数据提炼

Table 1
Optimization of the reaction condition[a]



Entry	Catalyst	Ligand	Solvent	Yield[b] (%)
1	$FeCl_3$ (20%)	1,10-Phen	DMSO	60
2	$FeCl_3$ (20%)	Bipy	DMSO	61
3	$FeCl_3$ (20%)	L-Proline	DMSO	58
4	$FeCl_3$ (20%)	None	DMSO	77
5	$FeCl_3$ (20%)	None	THF	12
6	$FeCl_3$ (20%)	None	Toluene	23
7	$FeCl_3$ (20%)	None	DMF	82, 82[c]
8	$FeCl_3$ (20%)	None	Dioxane	44
9	$FeCl_3$ (10%)	None	DMF	65
10	$FeCl_3$ (30%)	None	DMF	78
11	$FeBr_3$ (20%)	None	DMF	53
12	$Fe(OTf)_3$ (20%)	None	DMF	47
13	$Fe(acac)_3$	None	DMF	55
14	$ZnCl_2$	None	DMF	Trace
15	$AlCl_3$	None	DMF	5
16	$TiCl_4$	None	DMF	Trace
17[d]	$FeCl_3$ (20%)	None	DMF	79
18[e]	$FeCl_3$ (20%)	None	DMF	67

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), catalyst (20% mmol), ligand (20%mmol), solvent (2 mL), 90 °C, 4 h.
[b] Isolated yield.
[c] The reaction was carried out under an O_2 atmosphere.
[d] The reaction was carried out at 70 °C.
[e] The reaction was carried out at 110 °C.

Cl_3Fe

iron(III) chloride

Cl_3Fe 162.206 11323458 Retrieve CAS RN

Hit Data - 4 | Physical Data - 26
Identification | Spectra - 58
Druglikeness | Other Data - 128
Bioactivity (All)

Hit Data - 4

Catalyst Investigation - 4 hits out of 303

Show/Hide columns

Investigated characteristic(s)	Specification of catalysis	Type of reaction (Catalyst Investigation)	Co-catalyst/co-substrate name	Reference
Catalytic activity	Regioselective catalysis	Cycloaddition		Liu, Xiang; Wang, Dong; Chen, Baohua[Tetrahedron, 2013, vol. 69, # 45, p. 9417 - 9421] Full Text Cited 38 times Details Abstract
Catalytic activity	Regioselective catalysis	Cycloaddition	[2,2]bipyridinyl	Liu, Xiang; Wang, Dong; Chen, Baohua[Tetrahedron, 2013, vol. 69, # 45, p. 9417 - 9421] Full Text Cited 38 times Details Abstract
Catalytic activity	Regioselective catalysis	Cycloaddition	1,10-Phenanthroline	Liu, Xiang; Wang, Dong; Chen, Baohua[Tetrahedron, 2013, vol. 69, # 45, p. 9417 - 9421] Full Text Cited 38 times Details Abstract
Catalytic activity	Regioselective catalysis	Cycloaddition	L-proline	Liu, Xiang; Wang, Dong; Chen, Baohua[Tetrahedron, 2013, vol. 69, # 45, p. 9417 - 9421] Full Text Cited 38 times Details Abstract

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Reaxys对全文中的化合物生物活性的提炼(所有活性数据在RMC模块中）

Compds. No	R (A)	R (B)	IC_{50}	EC_{50}
VCH-759	–	–	0.14	5.29
4a	H	H	4.80	19.60
4b	4-Cl	H	0.085	11.10
4c	4-F	H	0.14	8.40
4d	4-OCH_3	H	0.25	11.57
4e	2-Cl	H	0.035	3.80
4f	2,4$(Cl)_2$	H	0.44	10.78

In vitro: Efficacy - 2

Quantitative Results

Show/Hide columns

pX	Parameter	Value (quant)	Unit	Biological Species	Action on target	Target	Cell	Effect	Reference
7.46	IC50	0.035	μM	Hepatitis C virus subtype 1a	Inhibitor	NS5B RNA dependent RNA polymerase, hepatitis C virus [Hepatitis C virus]:Wild		anti-HCV	Hassan, Ghaneya S.; Georgey, Hanan H.; Mohammed, Esraa Z.; Omar, Farghaly A.[**European Journal of Medicinal Chemistry, 2019**, vol. 184, art. no. 111747] Full Text Cited 1 times Details Abstract
5.42	EC50	3.8	μM		Inhibitor	NS5B RNA dependent RNA polymerase, hepatitis C virus [Hepatitis C virus]:Wild	Huh-7.5 cell line	anti-HCV	Hassan, Ghaneya S.; Georgey, Hanan H.; Mohammed, Esraa Z.; Omar, Farghaly A.[**European Journal of Medicinal Chemistry, 2019**, vol. 184, art. no. 111747] Full Text Cited 1 times Details Abstract

Table 2
Cytotoxicity (CC_{50}, μM)[a] and Selectivity index (SI)[b] values of the tested compound and **VCH-759**.

Code	THLE-2 cell line		RPTEC/TERT1 cell line	
	CC_{50}	SI	CC_{50}	SI
VCH-759	61.83	11.69	81.28	15.36
4e	102.77	27.04	161.37	42.47

[a] **CC_{50}** is the concentration of compounds that reduce the cell viability by 50%.
[b] **SI:** is the ratio of CC_{50} values on normal cells to EC_{50} on hepatoma infected cell lines (Huh7.5).

Toxicity/Safety Pharmacology - 2

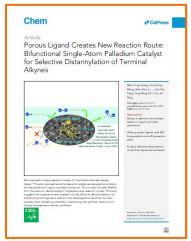
Quantitative Results

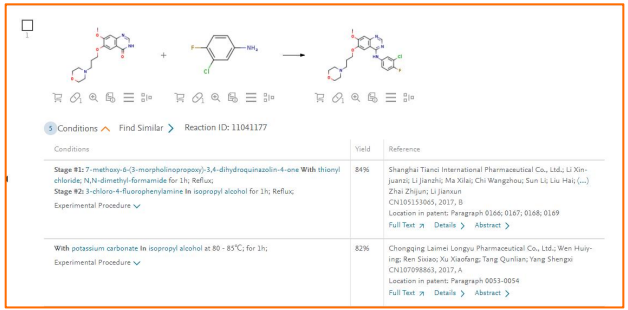
Show/Hide columns

pX	Parameter	Value (quant)	Unit	Cell	Effect	Reference
3.99	CC50 (cytotoxic concentration)	102.77	μM	THLE-2 cell line	Cytotoxic	Hassan, Ghaneya S.; Georgey, Hanan H.; Mohammed, Esraa Z.; Omar, Farghaly A.[**European Journal of Medicinal Chemistry, 2019**, vol. 184, art. no. 111747] Full Text Cited 1 times Details Abstract
3.79	CC50 (cytotoxic concentration)	161.37	μM	RPTEC/TERT1 cell line	Cytotoxic	Hassan, Ghaneya S.; Georgey, Hanan H.; Mohammed, Esraa Z.; Omar, Farghaly A.[**European Journal of Medicinal Chemistry, 2019**, vol. 184, art. no. 111747] Full Text Cited 1 times Details Abstract

ELSEVIER

Reaxys将文献中报道的科学数据进行了抽提，归纳，标准化





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Reaxys从文献中提炼出来的内容

文献记录：
>111 million
17000+期刊
105专利机构的专利
38万书的章节

化合物记录：
>177 million
期刊，专利，商品
2022年开始回溯98家专利机构2000年以来专利中的物质及反应

化学反应记录：
>65.0 million
单步多步反应，同时提炼文献与专利中的实验过程

实验性质记录：
> 1.0 Billion
化合物实验数据，并提炼实验数据检测条件

生物活性记录：
> 45.6 million数据
> 40,700靶点
> 8.6 million化合物
化合物在不同生物体内活性数据

数据更新时间：2024/2/27

Agenda

- Reaxys的底层逻辑和发展方向
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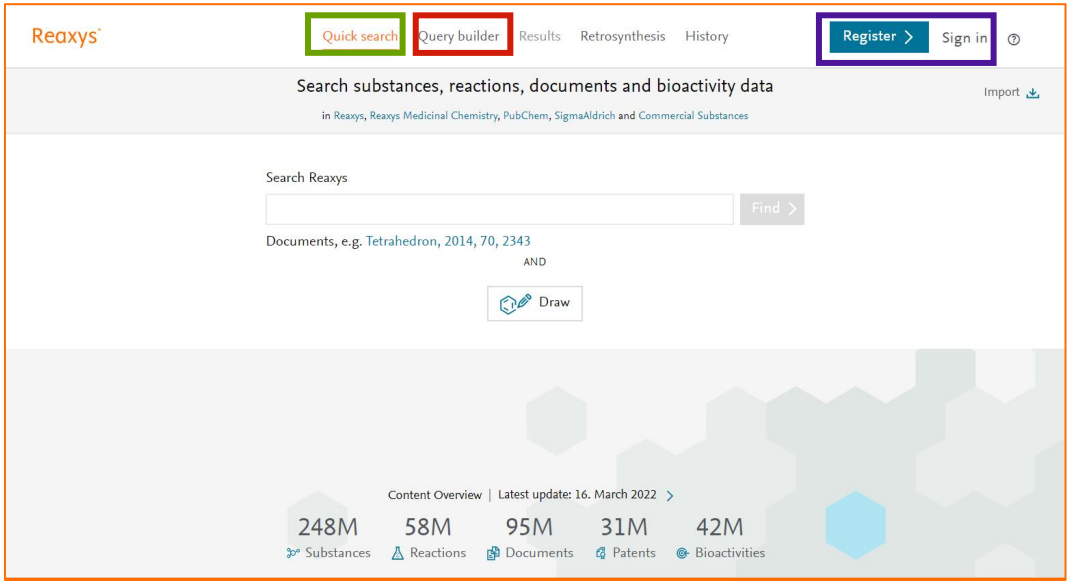
  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- Q&A

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:

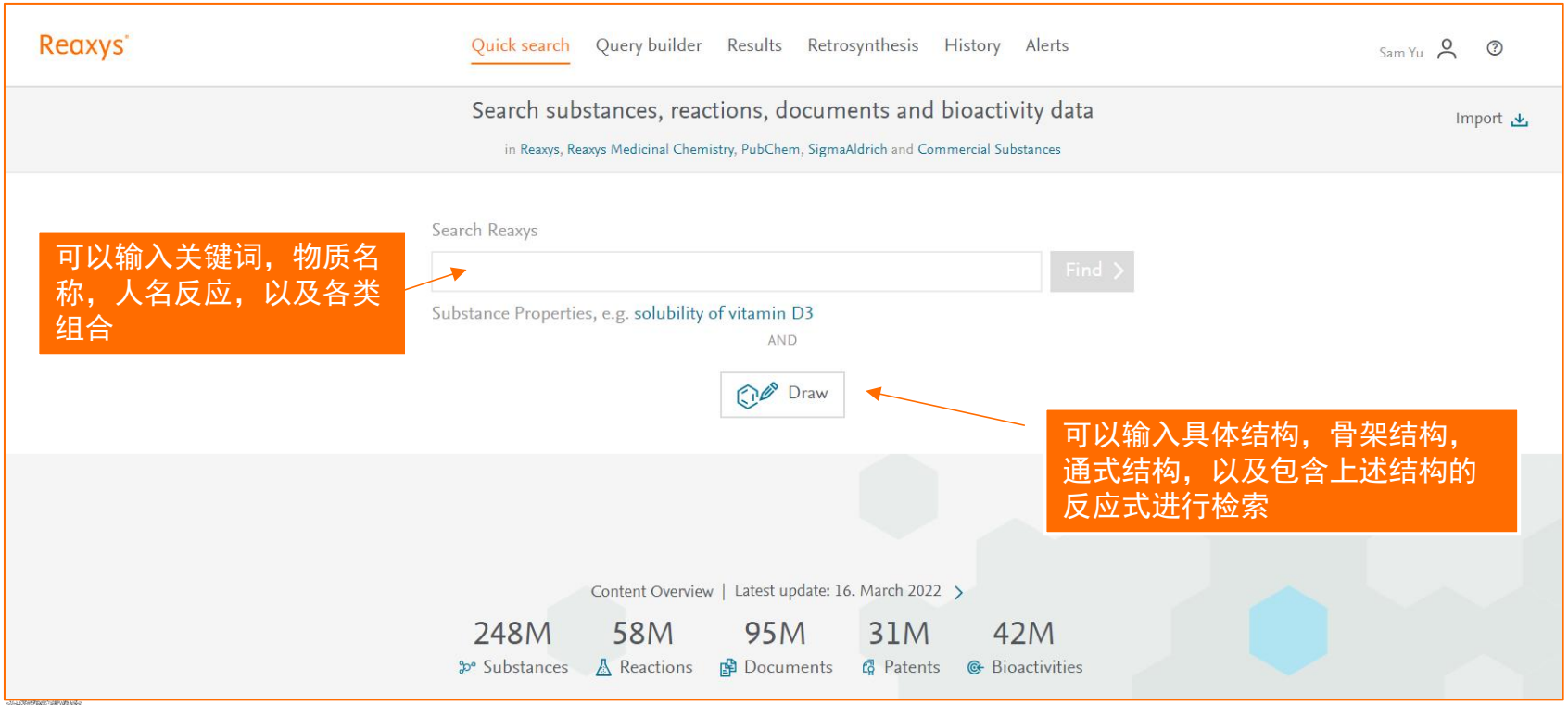
1. 账号注册（可选），注册帐号后，可以使用提醒，结果集保存，结果导出功能（2020.8以后）
2. Quick Search，快速检索，结构反应检索，或者输入自然语言，Reaxys智能分析语义进行检索。
3. Query Builder，组合检索，利用Reaxys中的各种字段进行组合，实现不同检索需求。

视频介绍：

1. Reaxys主界面：https://www.bilibili.com/video/BV1T5411L7Ec
2. Quick Search：https://www.bilibili.com/video/BV1az4y1C7ZL
3. Query Builder：https://www.bilibili.com/video/BV1UK4y1774Q
4. Reaxys账号注册与应用 https://www.bilibili.com/video/BV1NA41147if

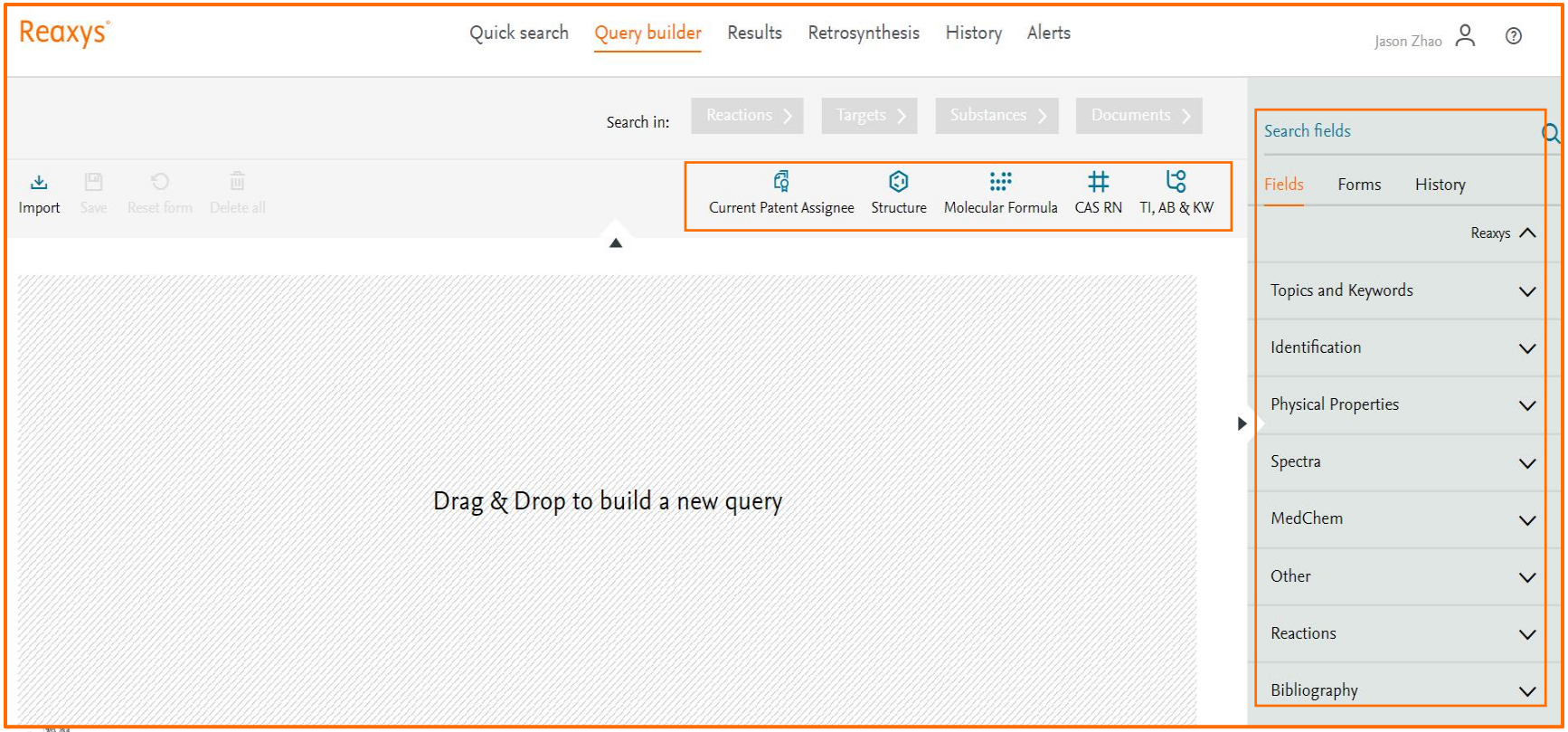
ELSEVIER

Quick Search界面

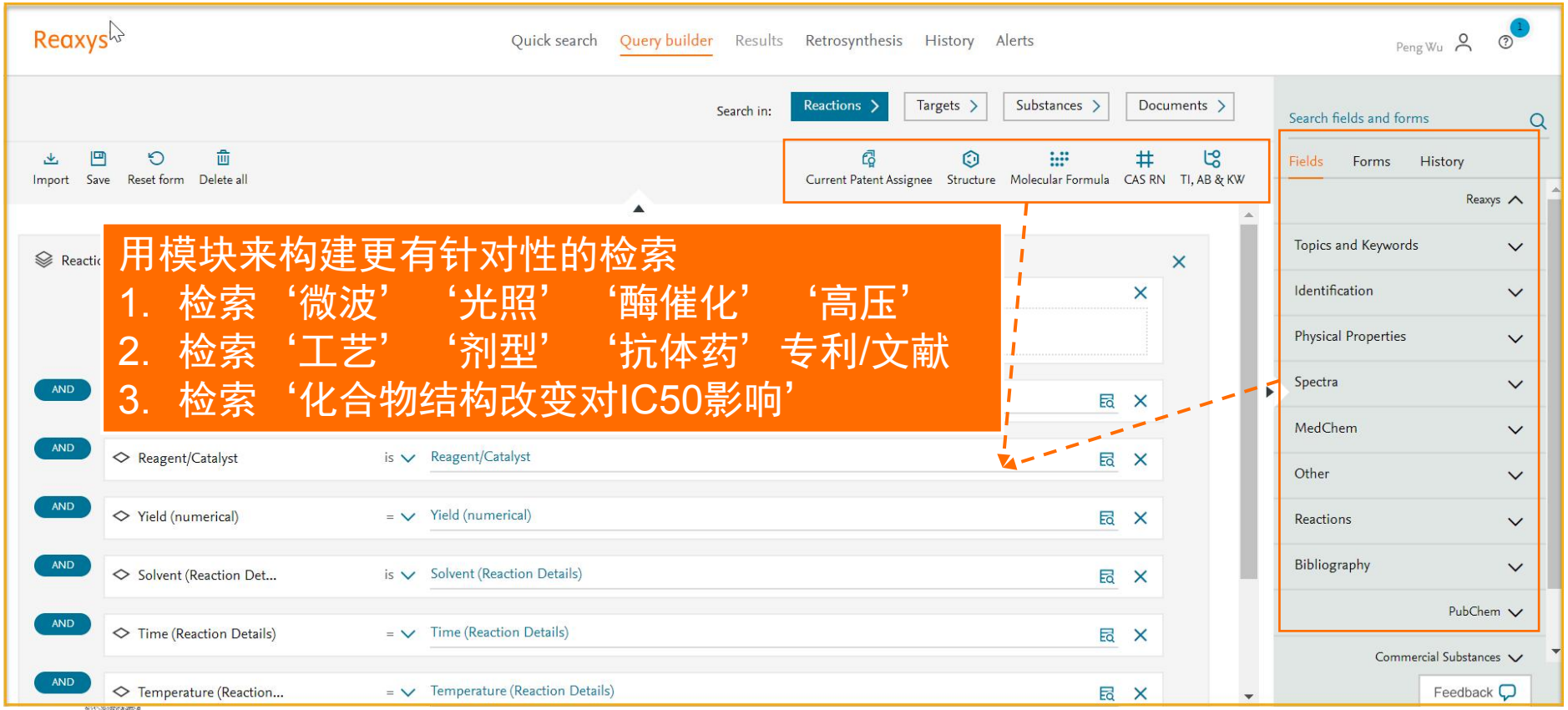


ELSEVIER

Reaxys的登录界面-模块检索界面



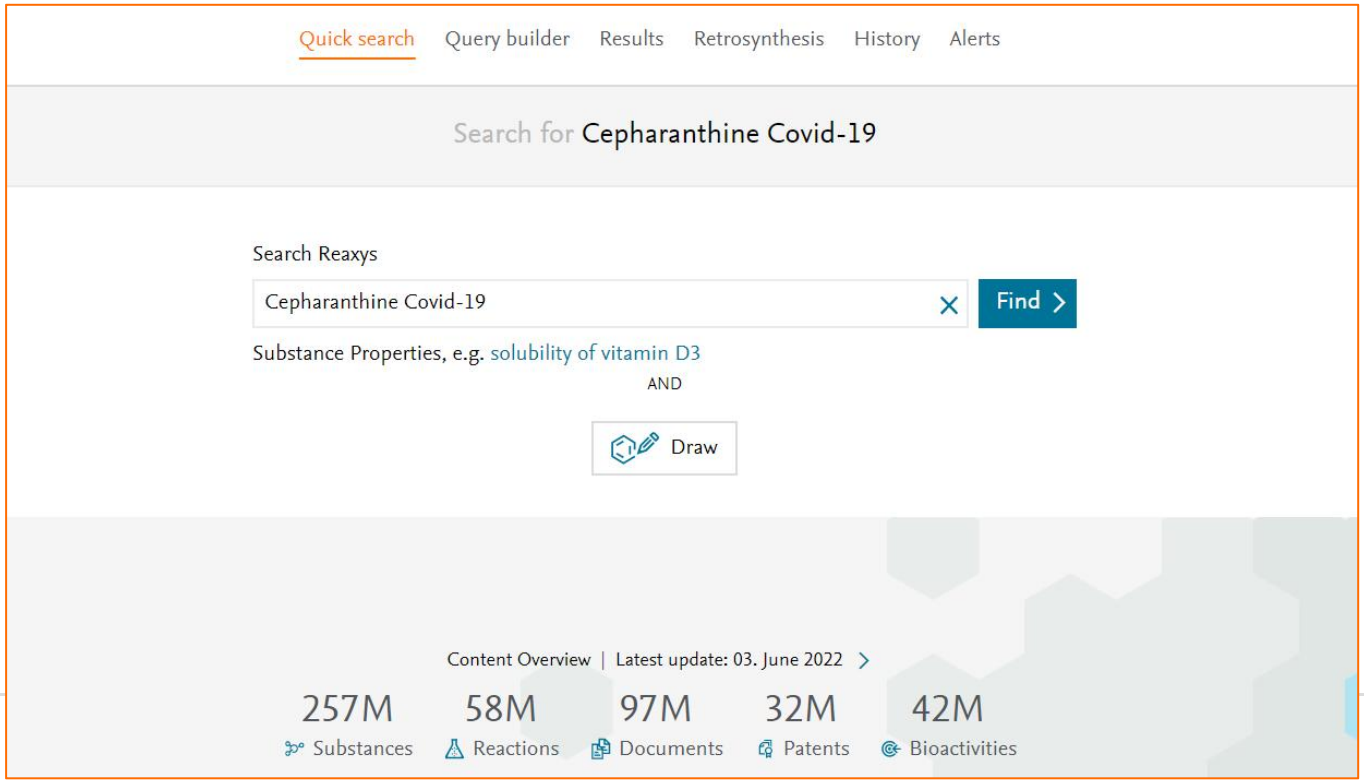
Reaxys的登录界面-模块检索界面



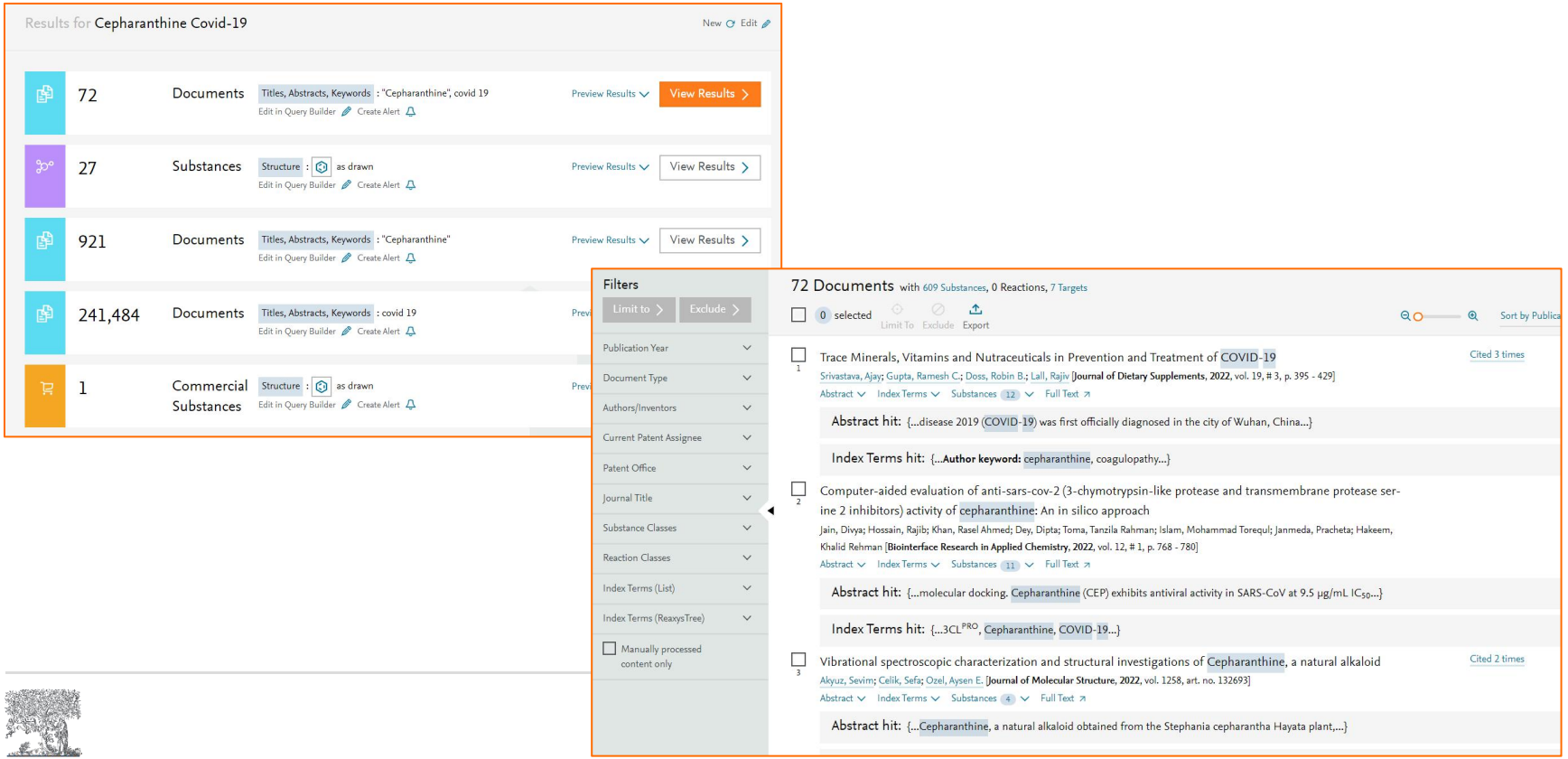
ELSEVIER

Case 1：关键词检索—千金藤素 Covid-19

- Cepharanthine Covid-19

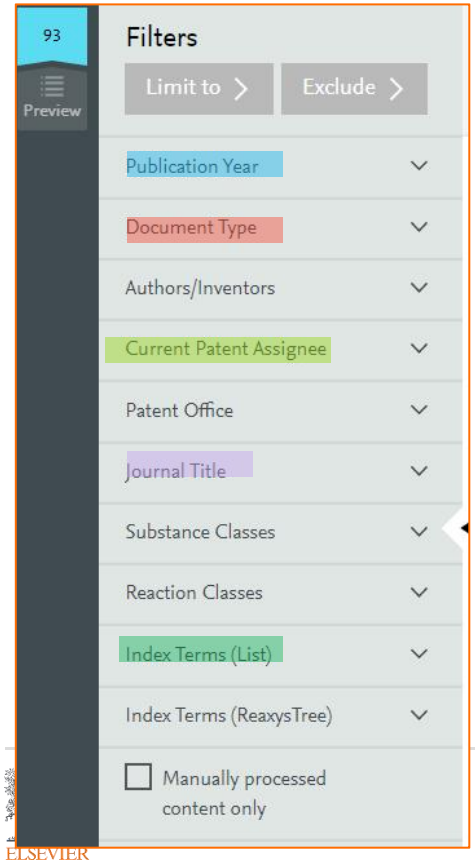


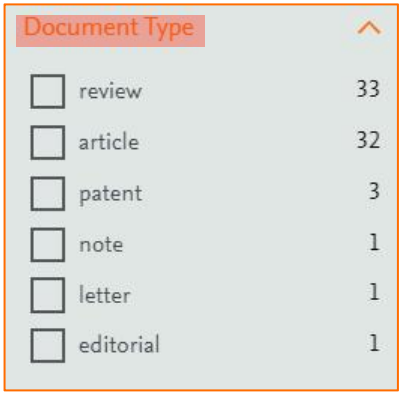
Reaxys中的检索结果

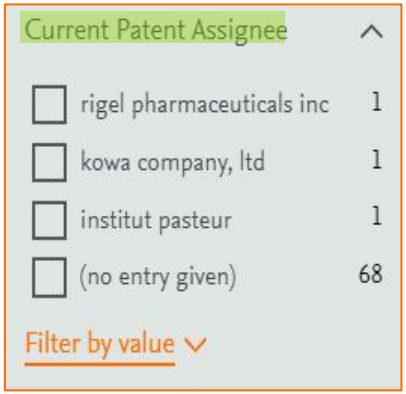


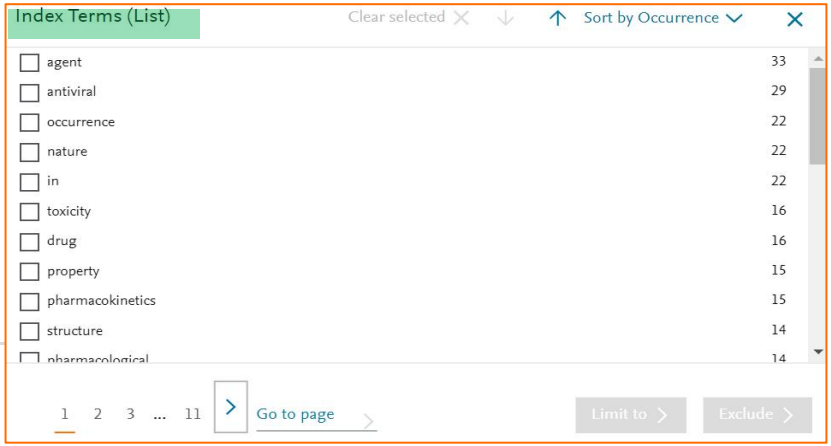
ELSEVIER

Reaxys中对于文献检索结果的分析

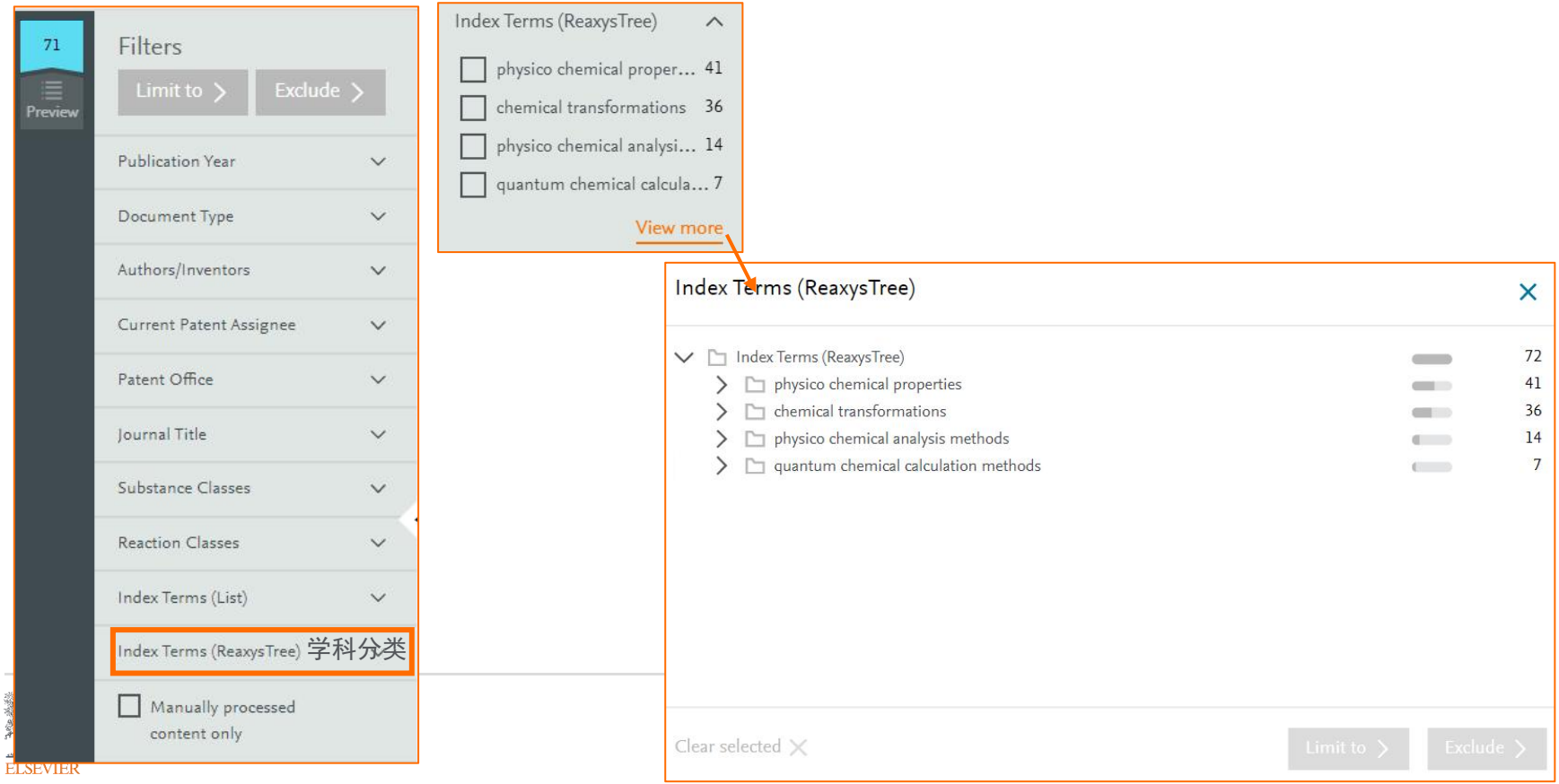




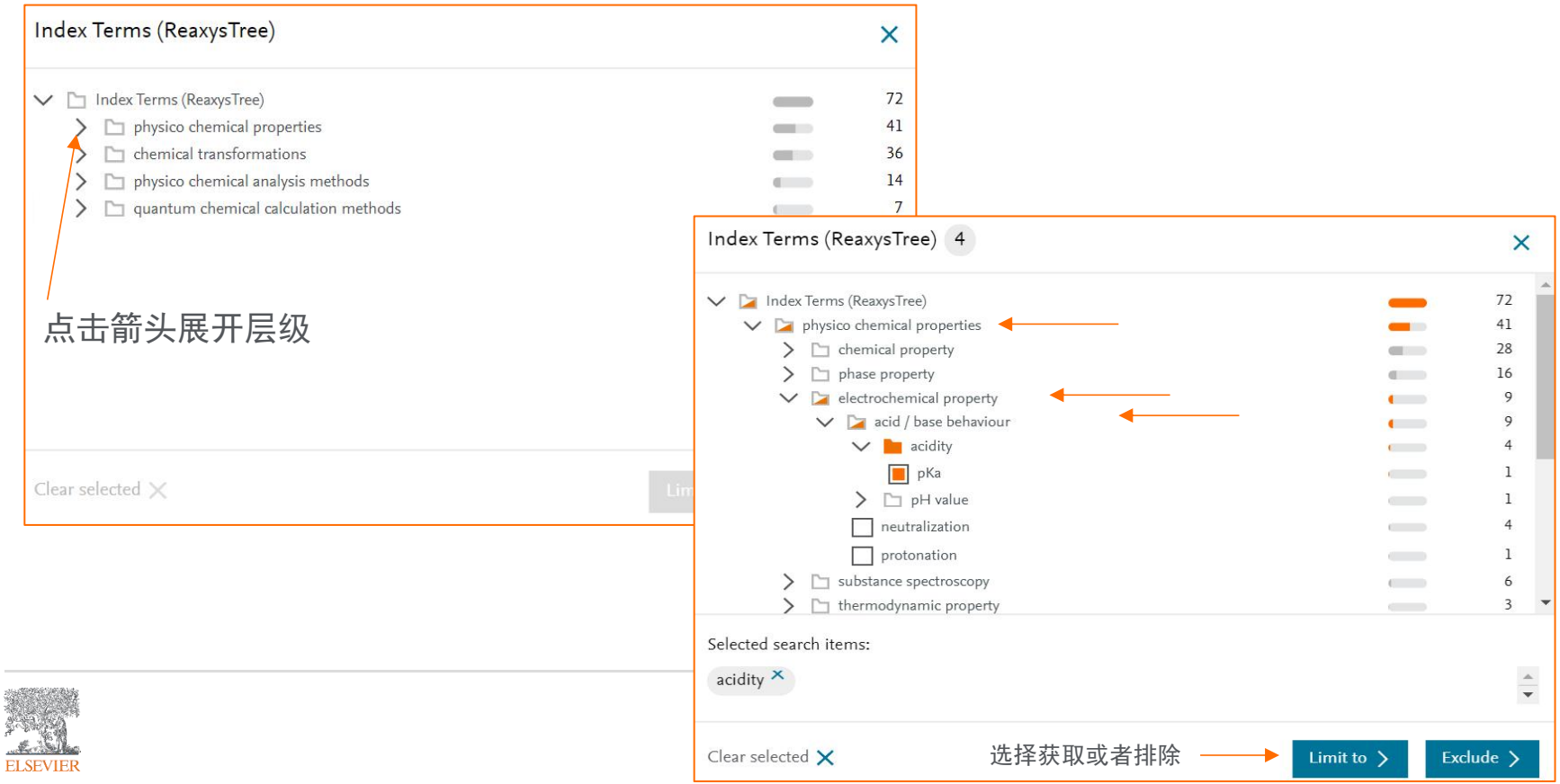




Reaxys中的Index Terms（Reaxys Tree）学科分类



利用树状图进行学科分类



ELSEVIER

最后的检索结果

2 Computer-aided evaluation of anti-sars-cov-2 (3-chymotrypsin-like protease and transmembrane protease serine 2 inhibitors) activity of cepharanthine: An in silico approach

Jain, Divya; Hossain, Rajib; Khan, Rasel Ahmed; Dey, Dipta; Toma, Tanzila Rahman; Islam, Mohammad Torequl; Janmeda, Pracheta; Hakeem, Khalid Rehman [**Biointerface Research in Applied Chemistry, 2022**, vol. 12, # 1, p. 768 - 780]

Abstract ^ Index Terms ^ Substances 11 v Full Text ↗

全文链接，如果是OA或者学校已经订购可以直接打开

Abstract

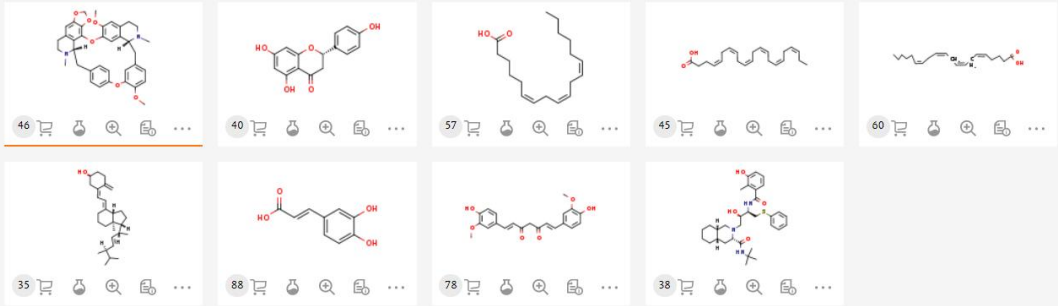
3-chymotrypsin-like protease ($3CL^{PRO}$) is found in severe acute respiratory syndrome coronavirus (SARS CoV)-2, and transmembrane protease serine 2 (TMPRSS-2) in humans, both of them have a role in viral attachment and proliferation. $3CL^{PRO}$ and TMPRSS-2 are the most vital target for the discovery of an anti-corona virus. One efficient approach used to screen potential active compounds against specific target proteins, such as $3CL^{PRO}$ and TMPRSS-2, is molecular docking. Cepharanthine (CEP) exhibits antiviral activity in SARS-CoV at 9.5 μg/mL IC_{50} level. This study aims to perform an in silico study on CEP aga
ing studies were carried out using compounds against $3CL^{PRO}$ and TMPRS
software. CEP displayed strong binding interactions-8.5 and-7.4 Kcal/mol
proved anti-corona virus drug (Camostat mesylate, CAM) is currently underused in COVID-19. CEP may be one of the potentials leads to fighting against SARS-CoV-2. Further in vivo studies should be required to support the findings of this study.

Cepharanthine (CEP) exhibits antiviral activity in SARS-CoV at 9.5 μg/mL IC50 level.

Index Terms

Author keyword: $3CL^{PRO}$ • Cepharanthine • COVID-19 • Molecular dockin
Reaxys Index Terms: Hydrogen bond • IC50 • LD50 • Permeability • Pi-pi
rence in nature • pharmacokinetics • reactivity • toxicity

Substances



ELSEVIER

Agenda

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  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
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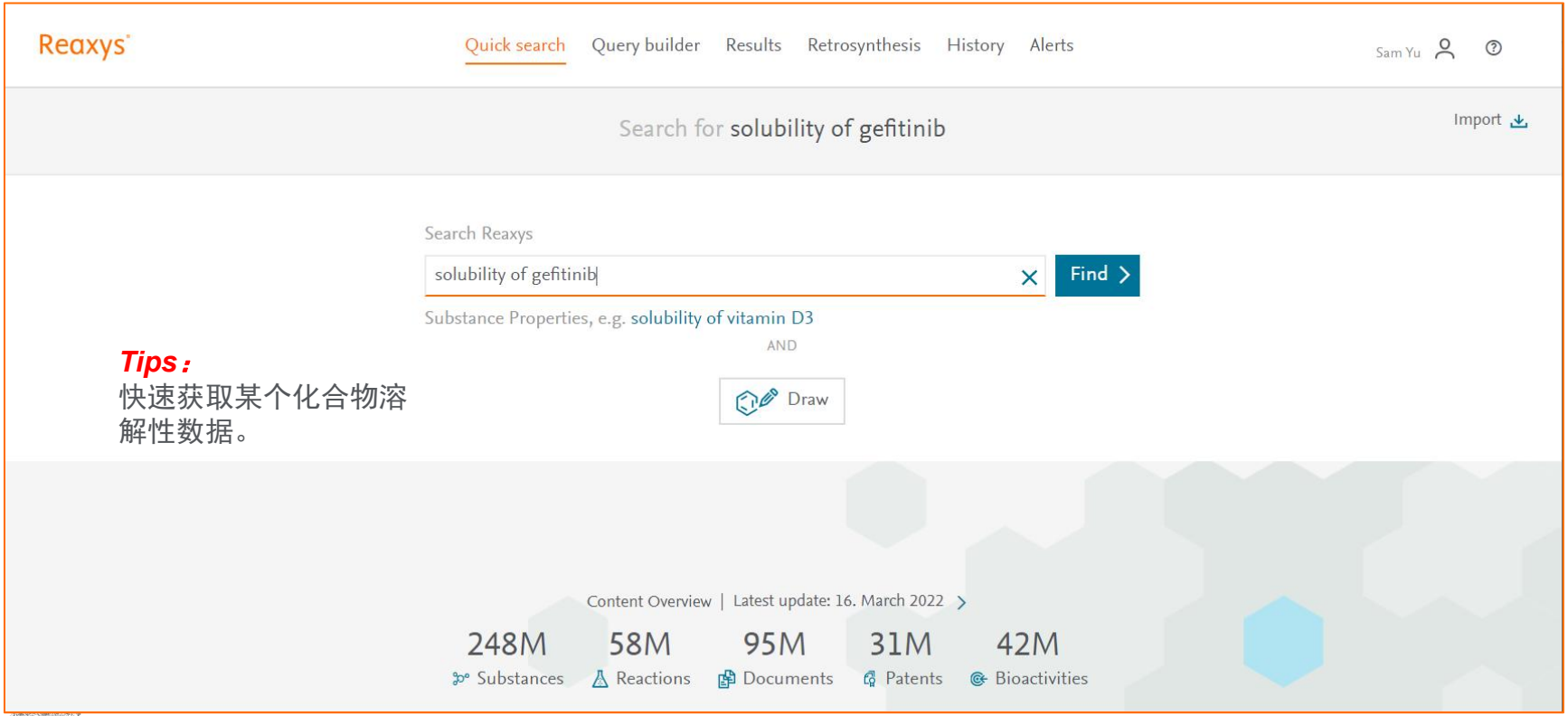
  - Reaxys中的AI逆合成模块介绍
- Q&A

Case 2：Reaxys中化合物理化性质的快速获取

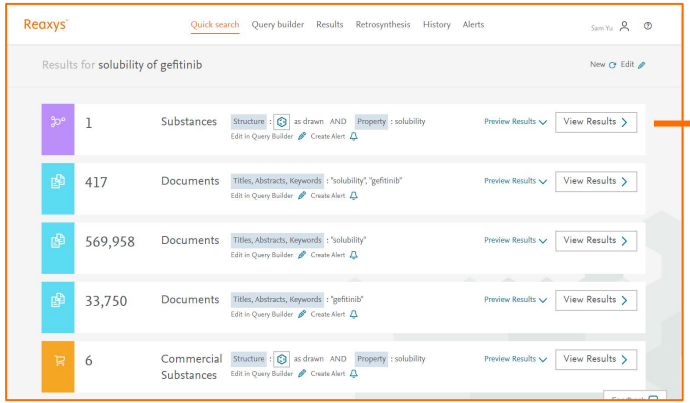


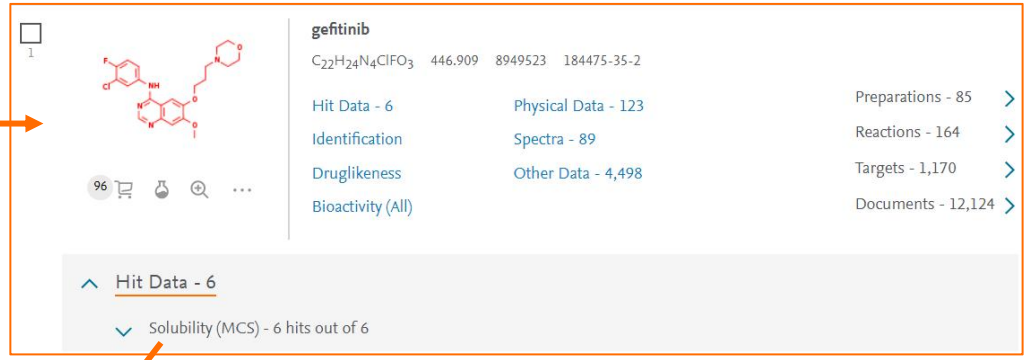
Tips：

快速获取某个化合物溶解性数据。

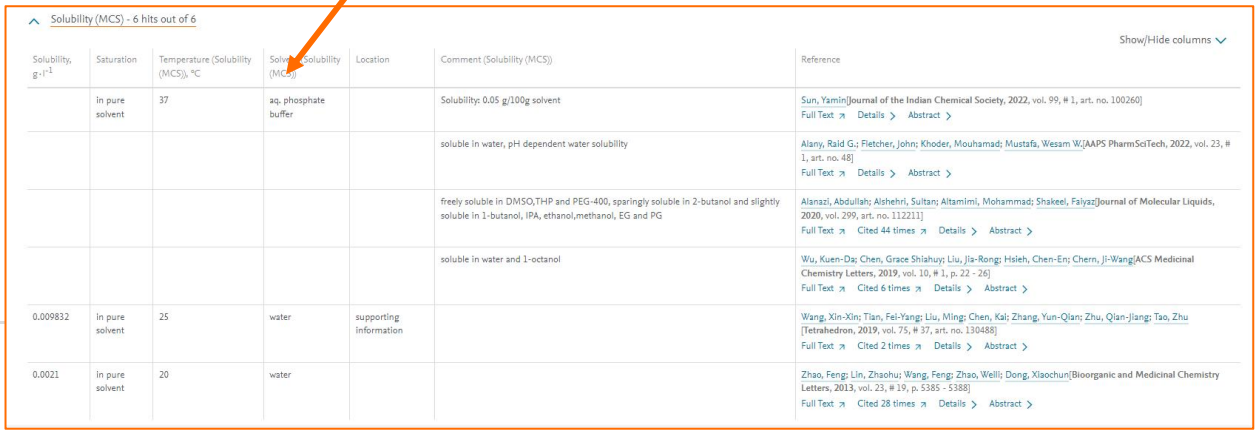
ELSEVIER

Reaxys中的结果

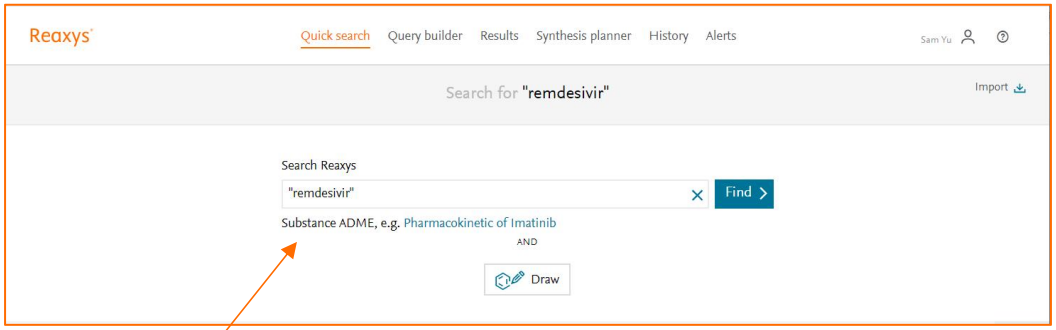




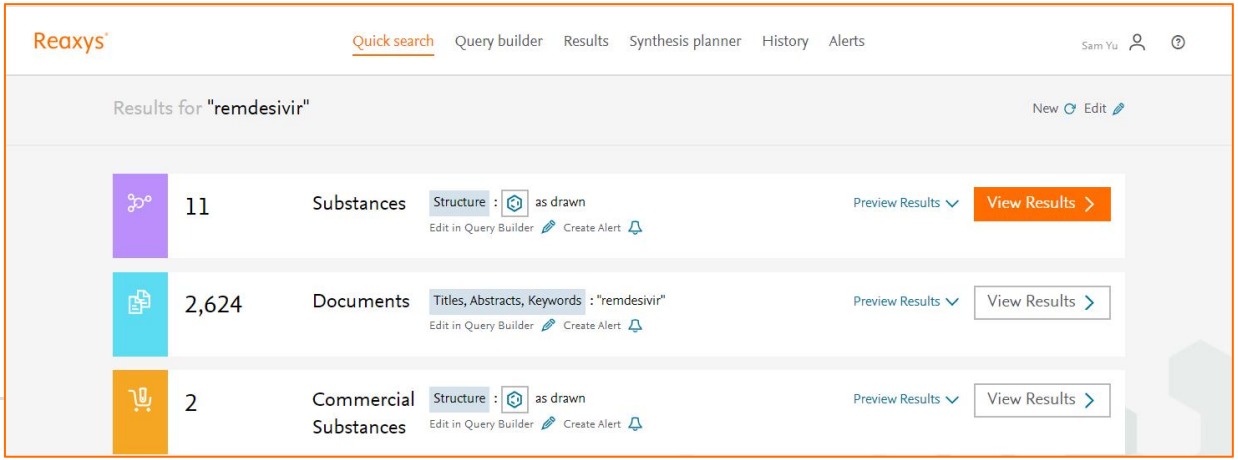
抽提的数据包括具体的数值，
或者相关的文字性描述



Case 3：快速获取化合物的活性数据—Remdesivir

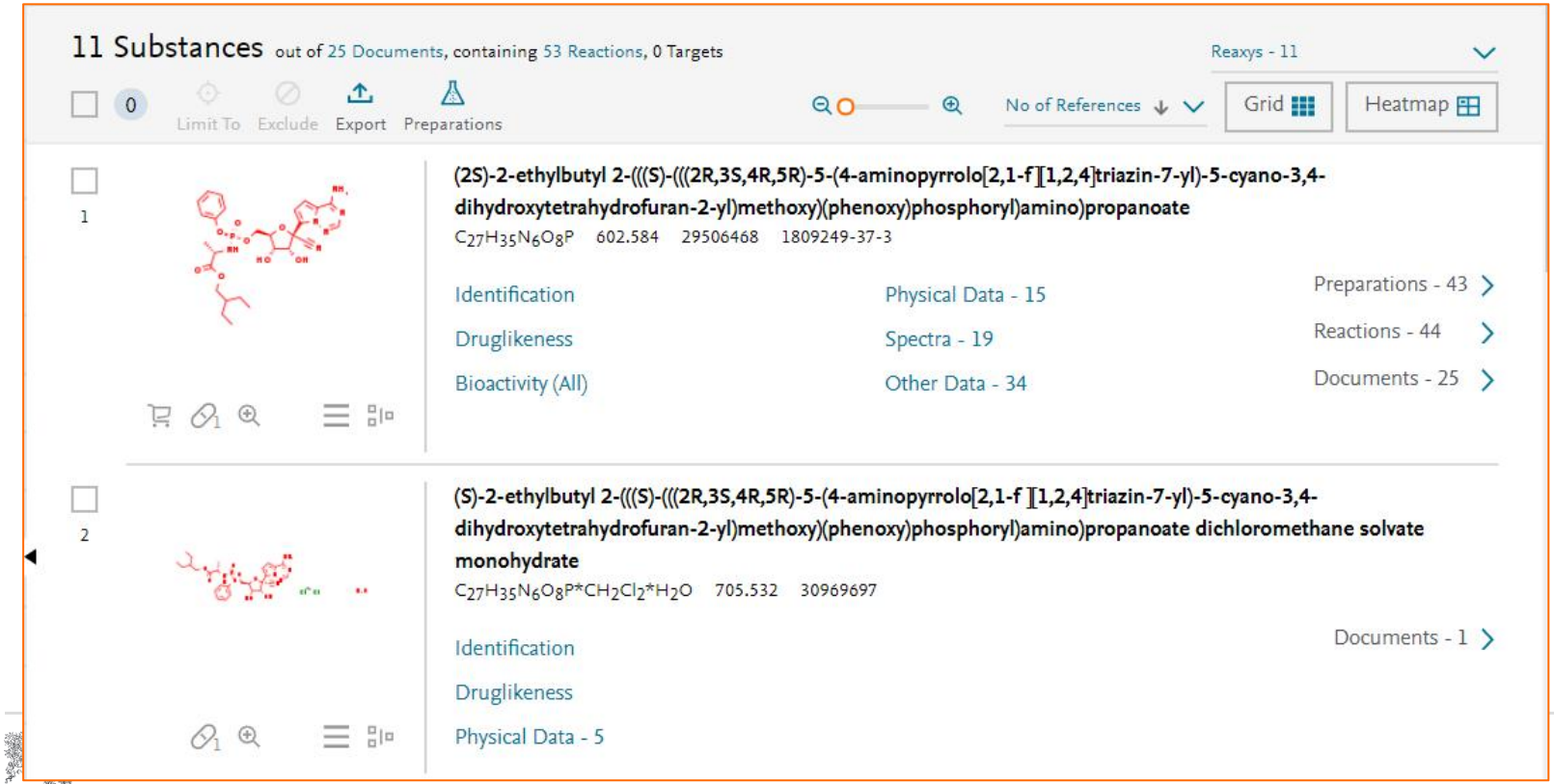


直接输入Remdesivir
进行检索



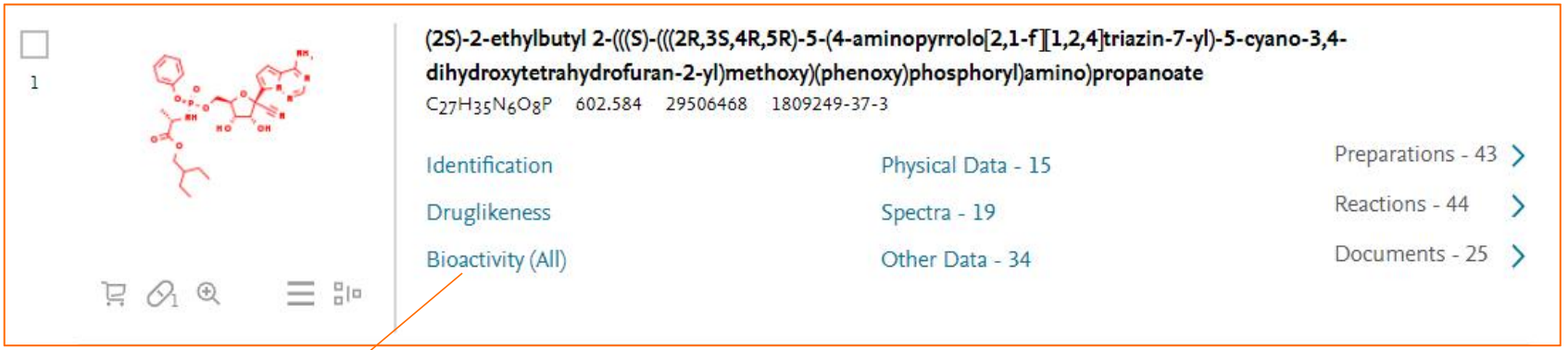
ELSEVIER

Reaxys中的结果（含结构分身，盐，混合物等）



ELSEVIER

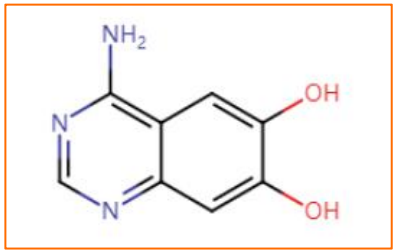
Reaxys中生物活性数据

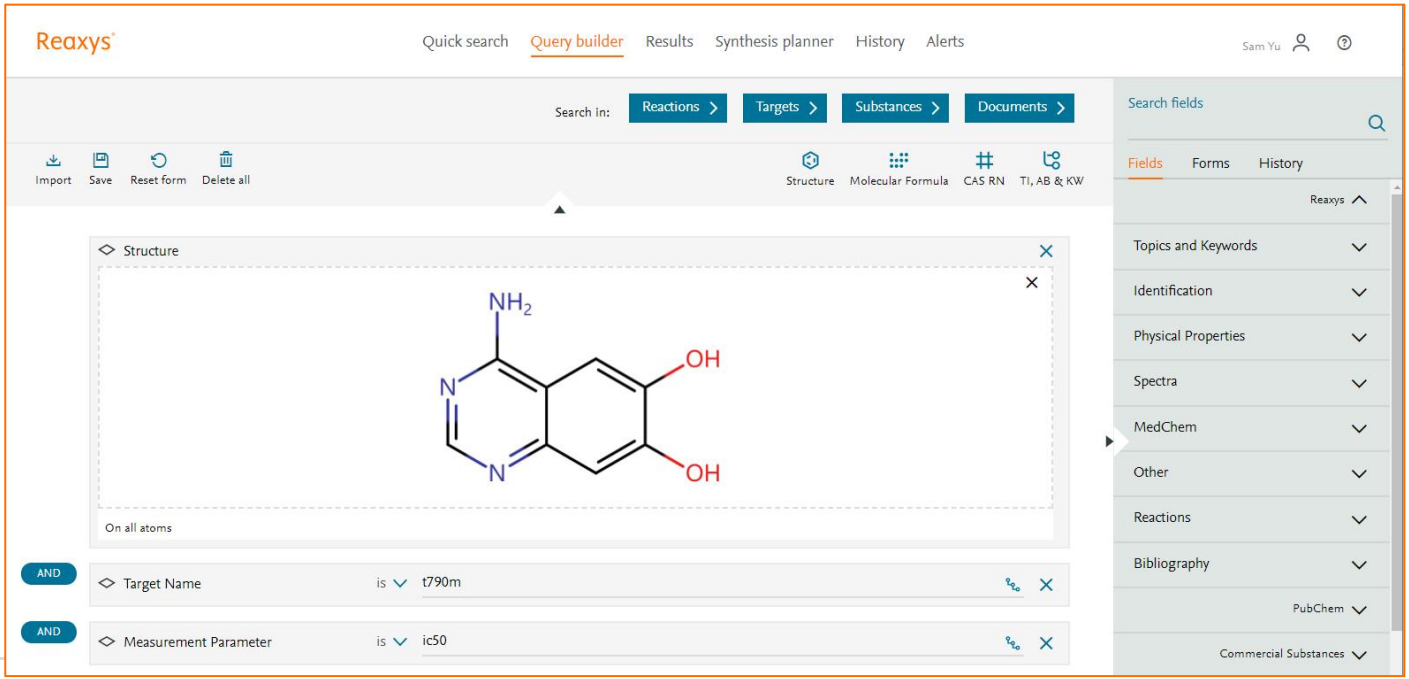


ELSEVIER

Case 4：骨架化合物活性获取

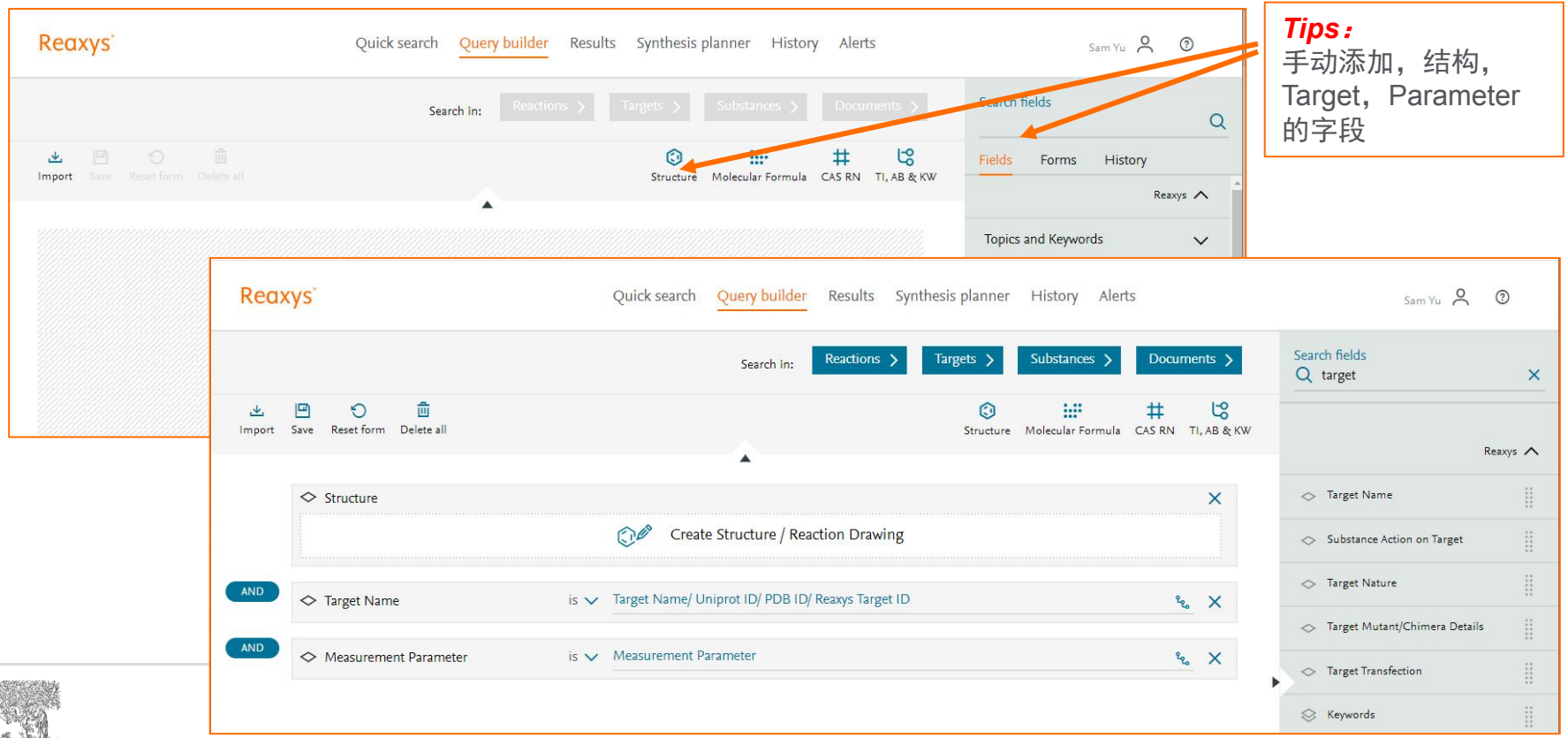
- 获取包含下面骨架，且在EGFR-T790M上有活性，且有ic50报道的化合物





ELSEVIER

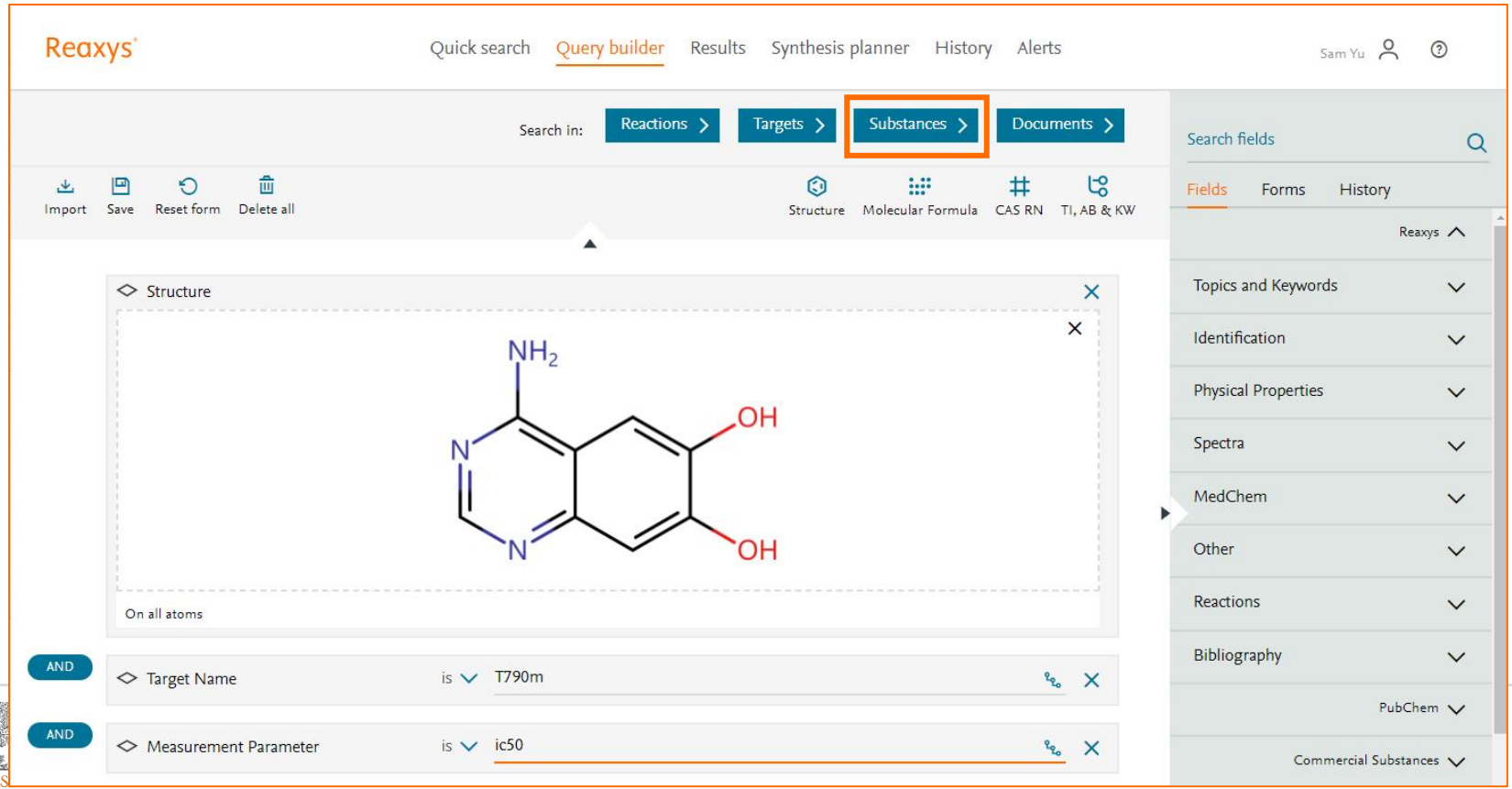
检索策略的构建



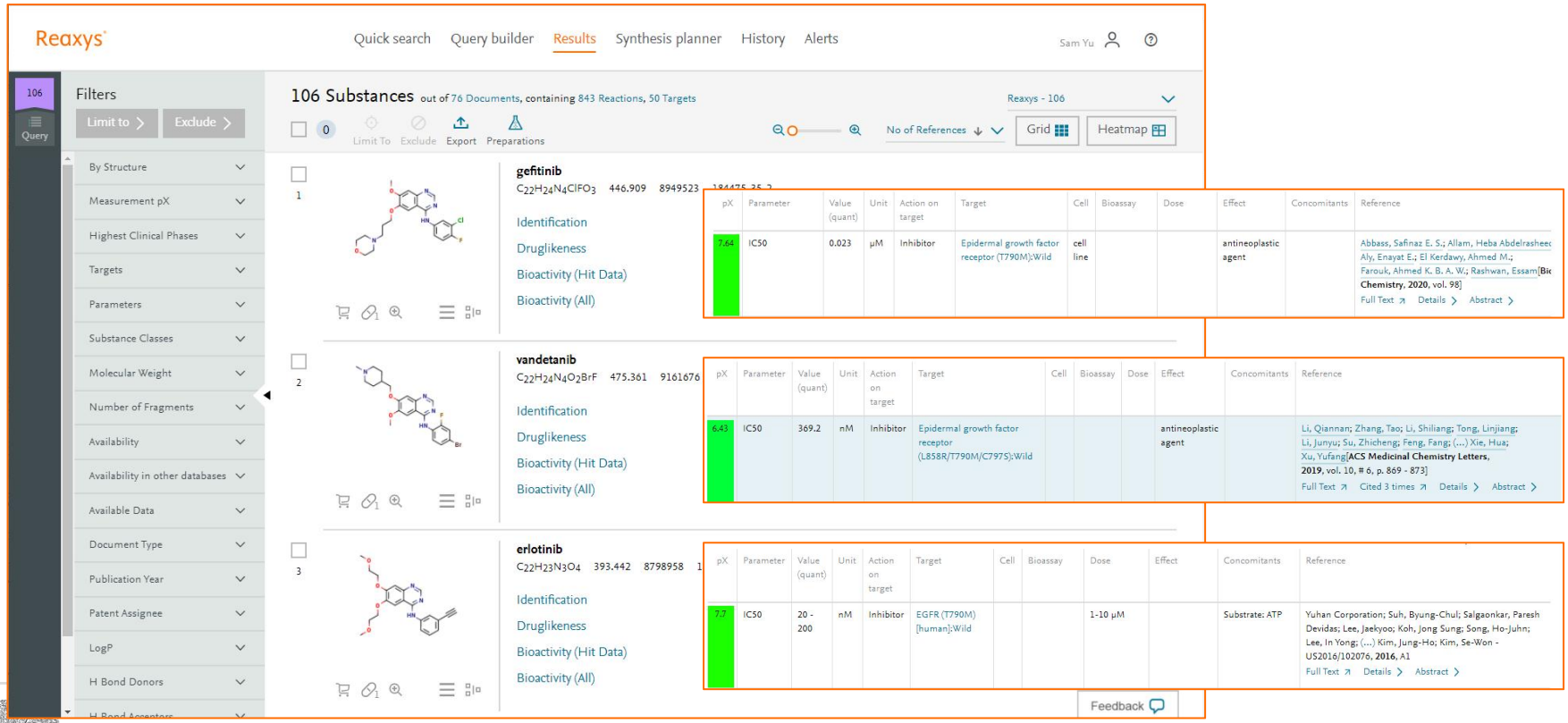
Tips：
手动添加，结构，Target，Parameter的字段

ELSEVIER

条件的输入

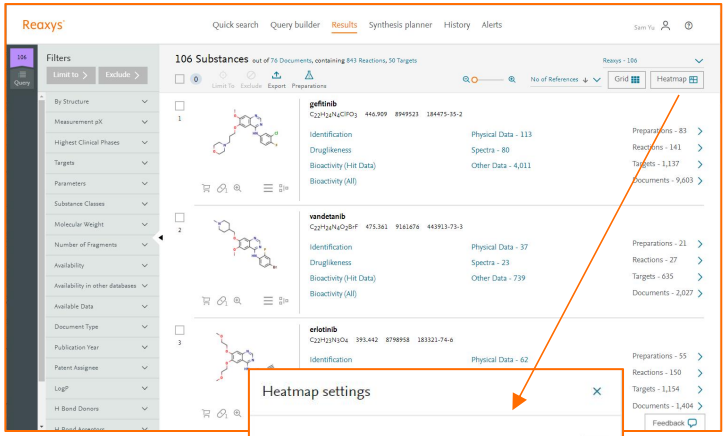

Reaxys
Quick search
Query builder
Results
Synthesis planner
History
Alerts
Sam Yu
Search in:
Reactions
Targets
Substances
Documents
Import
Save
Reset form
Delete all
Structure
Molecular Formula
CAS RN
TI, AB & KW
Structure
NH2
OH
N
N
OH
On all atoms
AND
Target Name
is
T790m
AND
Measurement Parameter
is
ic50
Search fields
Fields
Forms
History
Reaxys
Topics and Keywords
Identification
Physical Properties
Spectra
MedChem
Other
Reactions
Bibliography
PubChem
Commercial Substances

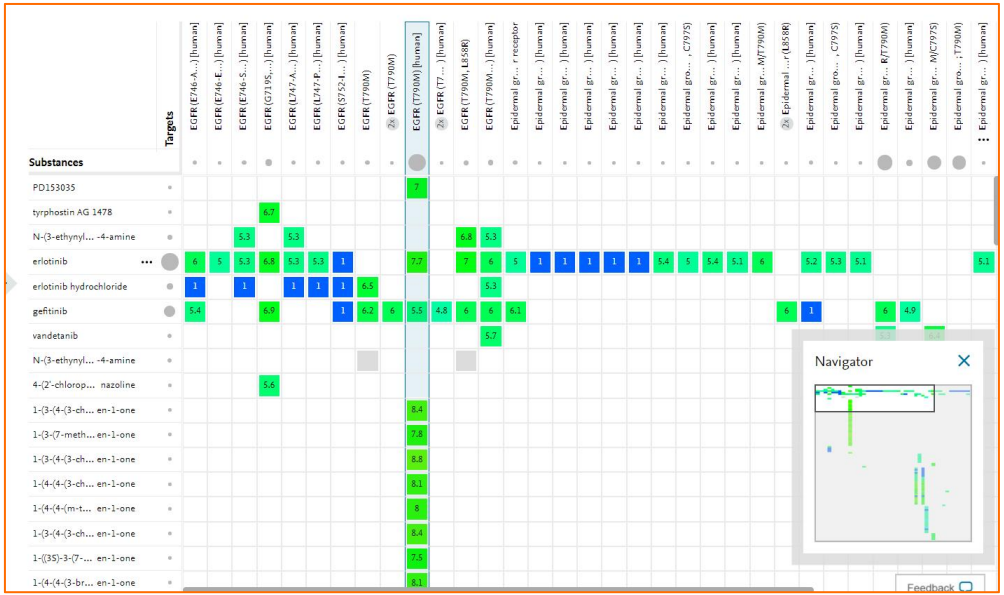
最后的结果



ELSEVIER

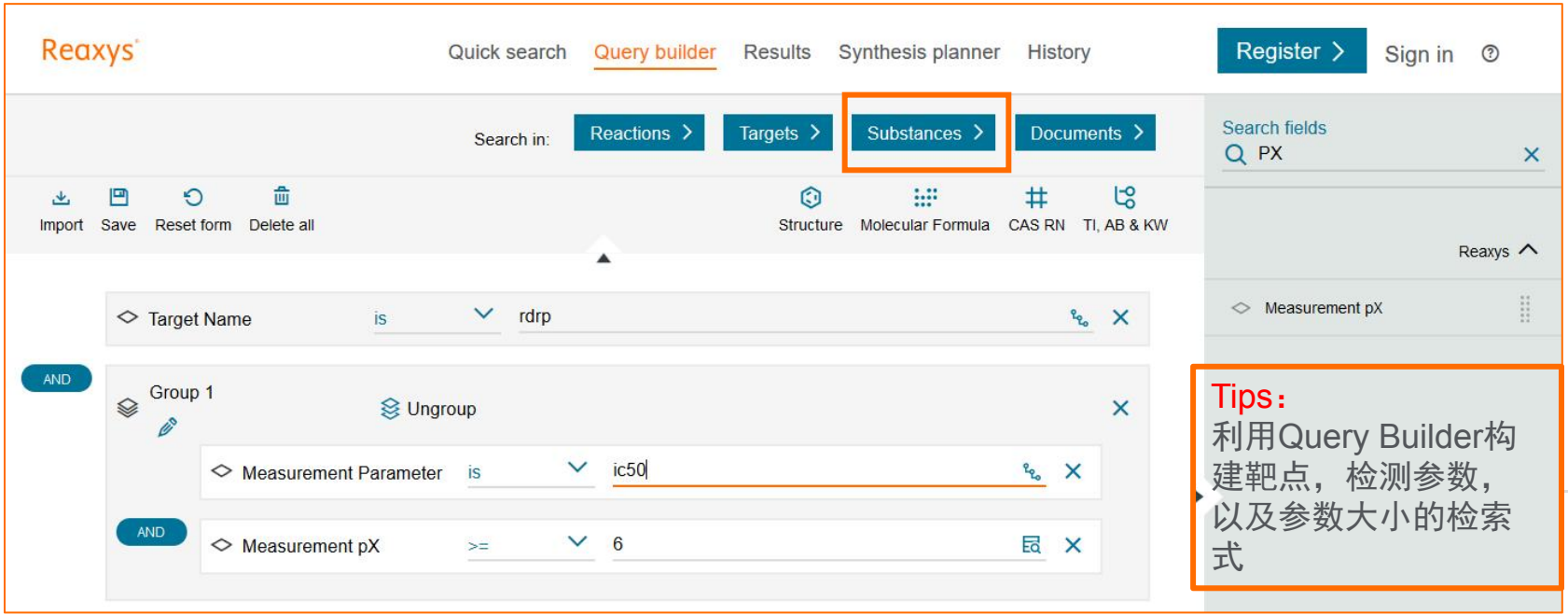
查看活性热图关系



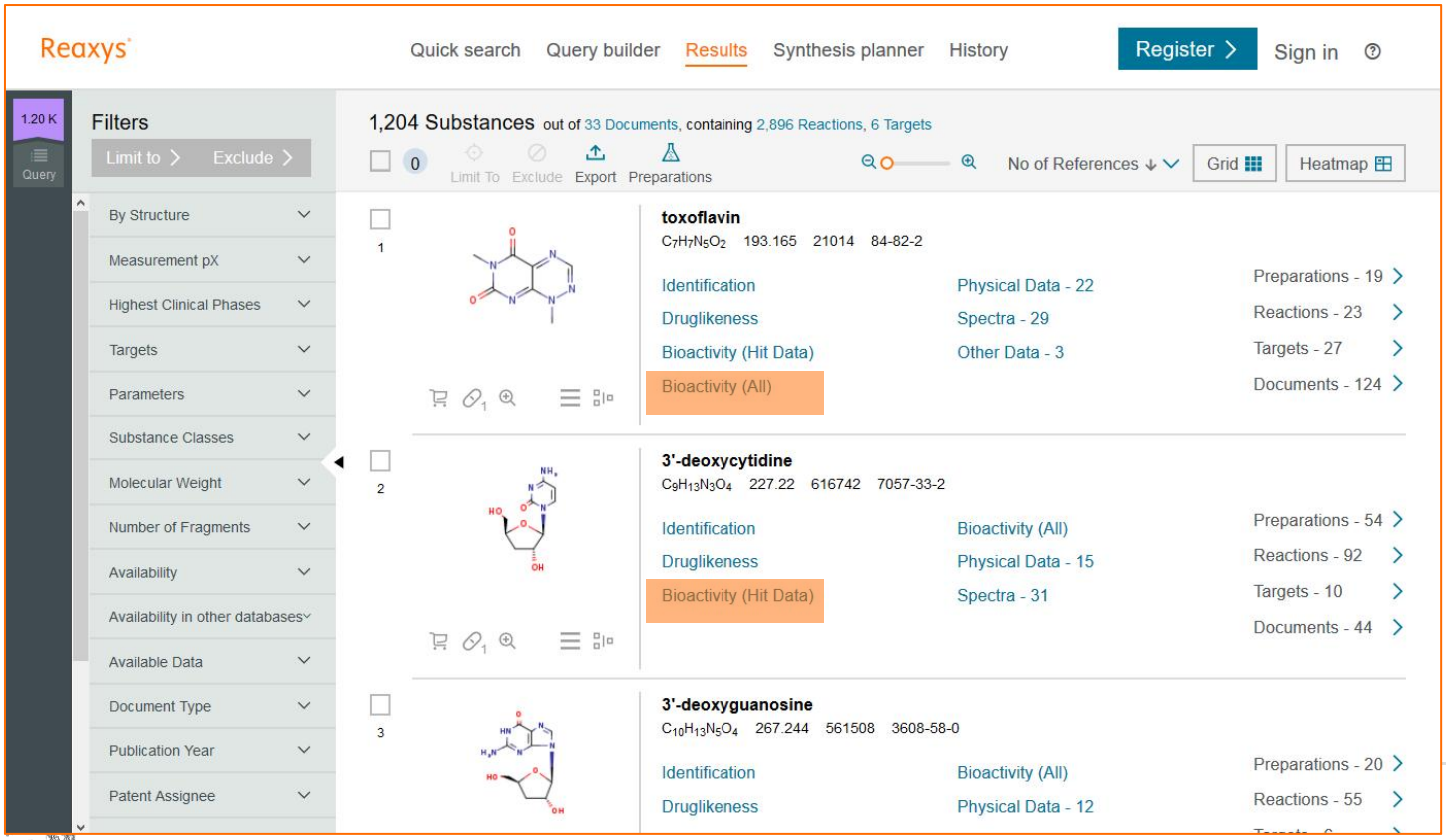


Case 5：如何用Reaxys快速筛选对“冠状病毒”有活性的化合物

- 获取文献中报道的对“RNA依赖的RNA聚合酶（RdRp）”有活性报道的化合物
- 希望这些化合物的IC50在um级别
- 视频操作：https://www.bilibili.com/video/bv1pK411G7rX



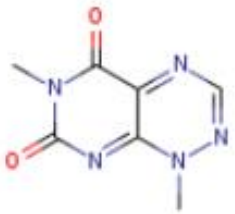
Reaxys中的结果



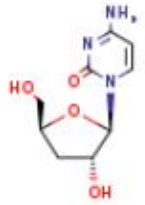
Reaxys直接给出符合条件的化合物，大量节省了科研人员阅读文献，并查找数据的时间，可以通过各自的Hit Data查看具体数据

ELSEVIER

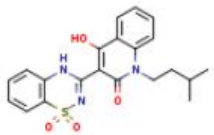
Reaxys中的结果



pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
6.22	IC50	=	0.6	μM	Hepatitis C virus	Inhibitor	RNA-dependent RNA polymerase [Hepatitis C virus]:Wild	Other compound: ATP; Radioligand: [3H]UTP;	Middleton; Lim; Montgomery; Rockway; Liu; Klein; Qin; Harlan; Kati; Molla[**Letters in drug design and discovery**, **2007**, vol. 4, # 1, p. 1 - 8] Full Text ↗ Cited 3 times ↗ Details › Abstract ›



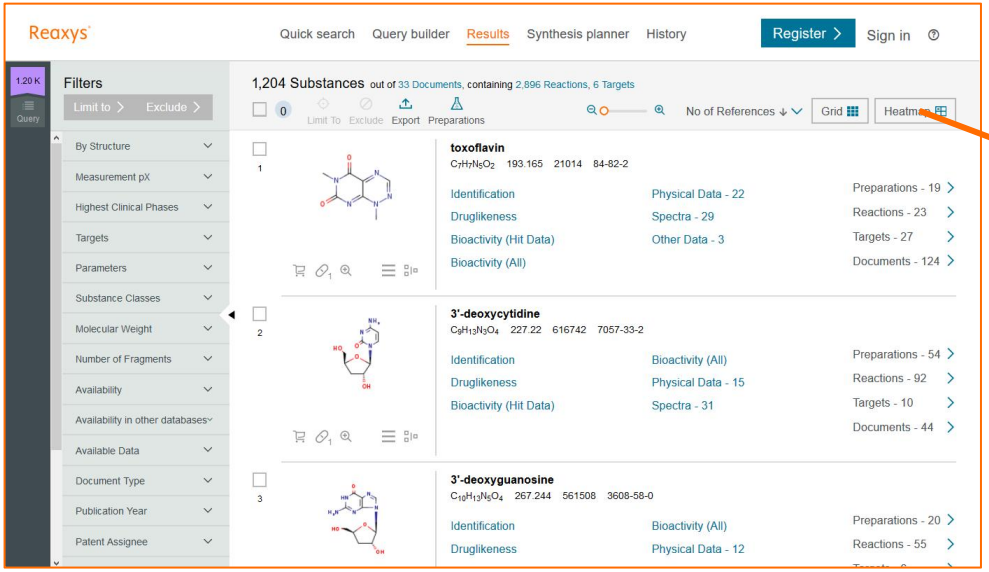
pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
7.1	IC50		0.08 - 1.2	μM	Hepatitis C virus		RNA-dependent RNA polymerase [Hepatitis C virus]:Wild		Mayhoub, Abdelrahman S.[**Bioorganic and Medicinal Chemistry**, **2012**, vol. 20, # 10, p. 3150 - 3161] Full Text ↗ Cited 35 times ↗ Details › Abstract ›

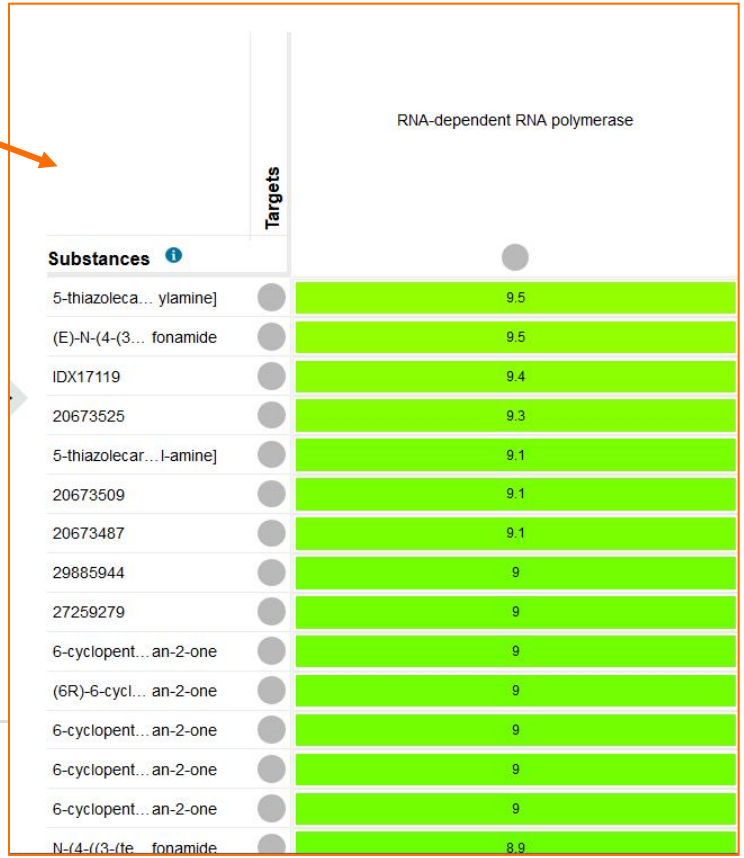


pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Concomitants	Reference
7.1	IC50	=	0.08	μM	Hepatitis C virus (strain DELTA 21)	Inhibitor	RNA-dependent RNA polymerase [Hepatitis C virus]:Wild		Dhanak, Dashyant; Duffy, Kevin J.; Johnston, Victor K.; Lin-Goerke, Juili; Darcy, Michael; Shaw, Antony N.; Gu, Baohua; (…) Keenan, Richard M.; Sarisky, Robert T. [**Journal of Biological Chemistry**, **2002**, vol. 277, # 41 p. 38322 - 38327] Full Text ↗ Cited 172 times ↗ Details › Abstract

ELSEVIER

利用HeatMap看结构与靶点关系





利用Reaxys中的Heat Map，直接进行查看，靶点，结构，活性数据之间的关系，并可将活性从高到低进行排序。

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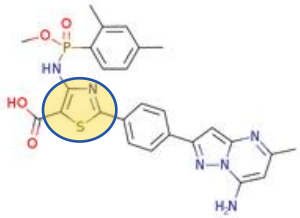
一些非常有意思的结构

Substances	Targets	RNA-dependent RNA polymerase
5-thiazolec… ylamine]		9.5
(E)-N-(4-(… fonamide		9.5
IDX17119		9.4
20673525		9.3
5-thiazolec… l-amine]		9.1
20673509		9.1
20673487		9.1
29885944		9
27259279		9
6-cyclope… an-2-one		9
(6R)-6-cy… an-2-one		9
6-cyclope… an-2-one		9
6-cyclope… an-2-one		9
6-cyclope… an-2-one		9
N-(4-((3-(t… fonamide		8.9
5-[2-(4-flu…boxamide		8.7
(1aR,12b… boxamide		8.7
20673500		8.7
N-[4-(2-[2-…cetamide		8.7
6-cyclope… an-2-one		8.7
6-cyclope… an-2-one		8.7
N-[2-[4-(2-…cetamide		8.7
6-cyclope… an-2-one		8.7



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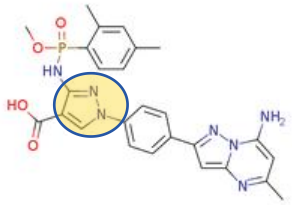

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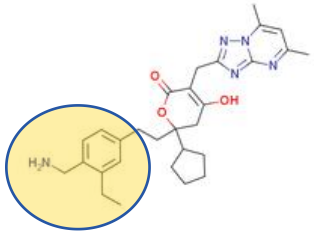

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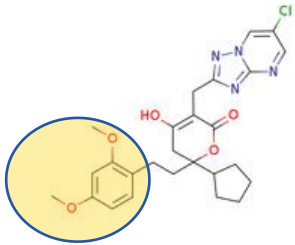

PX=7.7

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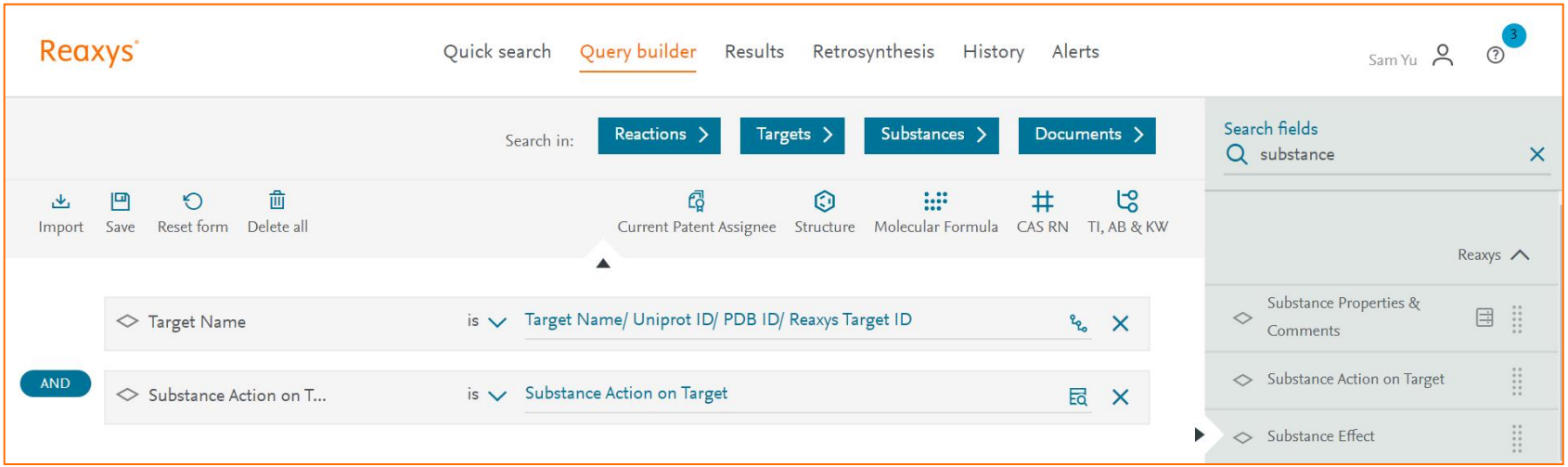
Agenda

- Reaxys的底层逻辑和发展方向
  - Reaxys及其对于科技文献的提炼
- Reaxys中科研数据的获取和应用场景
  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- Q&A

CASE 6：SAR分析与全新化合物设计

- 案例背景：
  - 我们知道SCD1缺陷型小鼠可以明显抵抗肥胖及其相关胰岛素抵抗的发生
  - SCD有两种亚型，SCD1在脂肪组织中表达，SCD5在大脑中表达
  - 因此开发一种有效的SCD1抑制剂以最小限度地抑制SCD5对项目的成功至关重要
- 检索困难点：
  - Selectivity Profile需要进行数值的输入，但是在这个案例中没有要求
  - 如何获悉哪些片段是有积极或者负面的活性影响的

获取SCD1[Human]上有活性的化合物

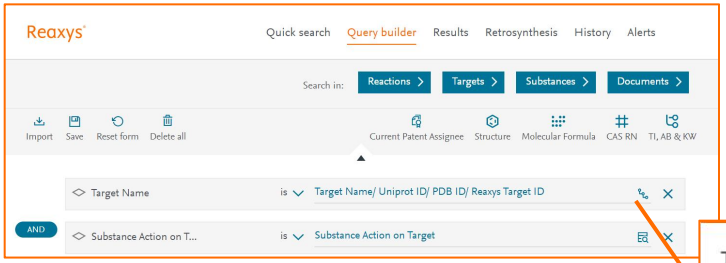


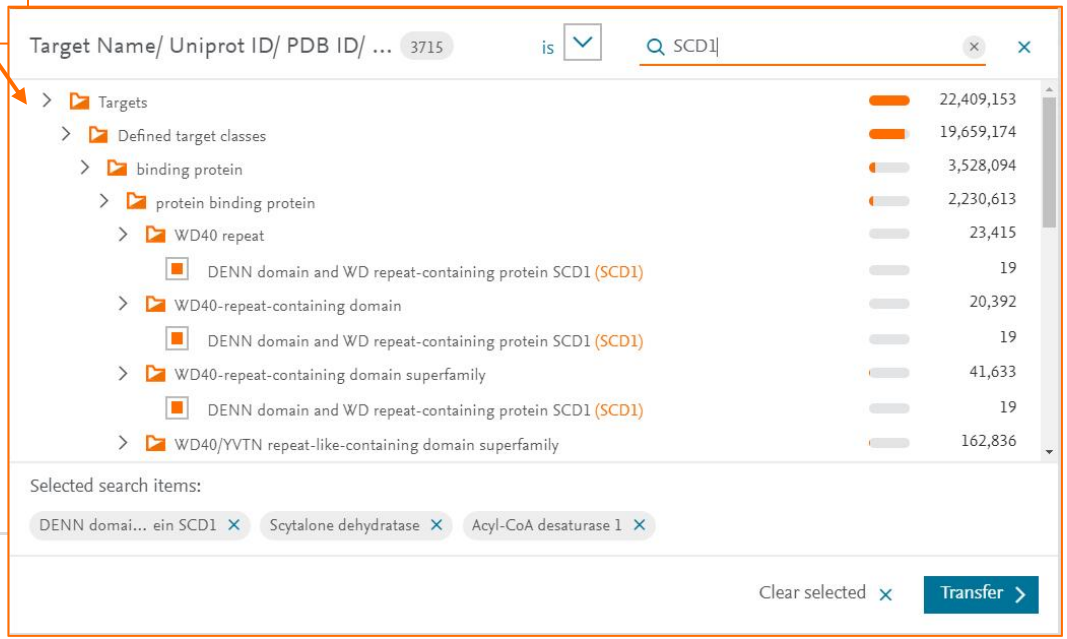
检索策略的构建：

1：Target Name

2：Substance Action on Target

检索条件的输入1





输入SCD1进行靶点的扩展

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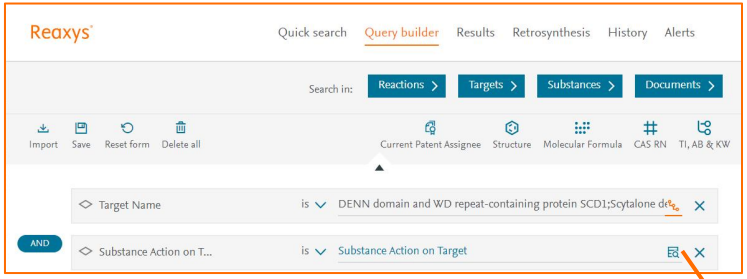
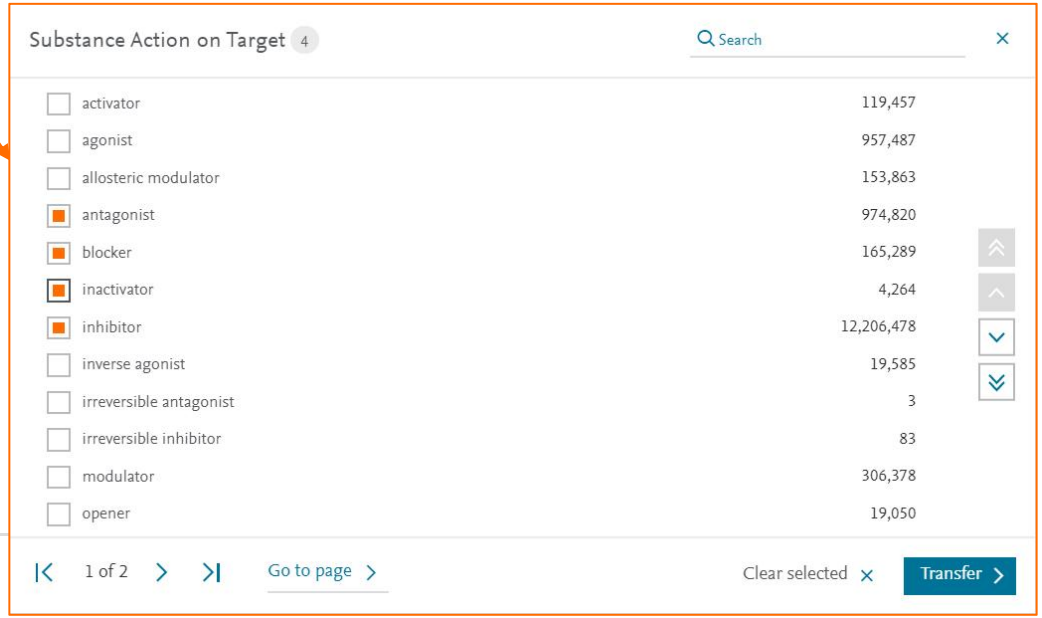
检索条件的输入2





获取在SCD1上有，inhibitor, Inactivator, blocker, antagonist作用的化合物

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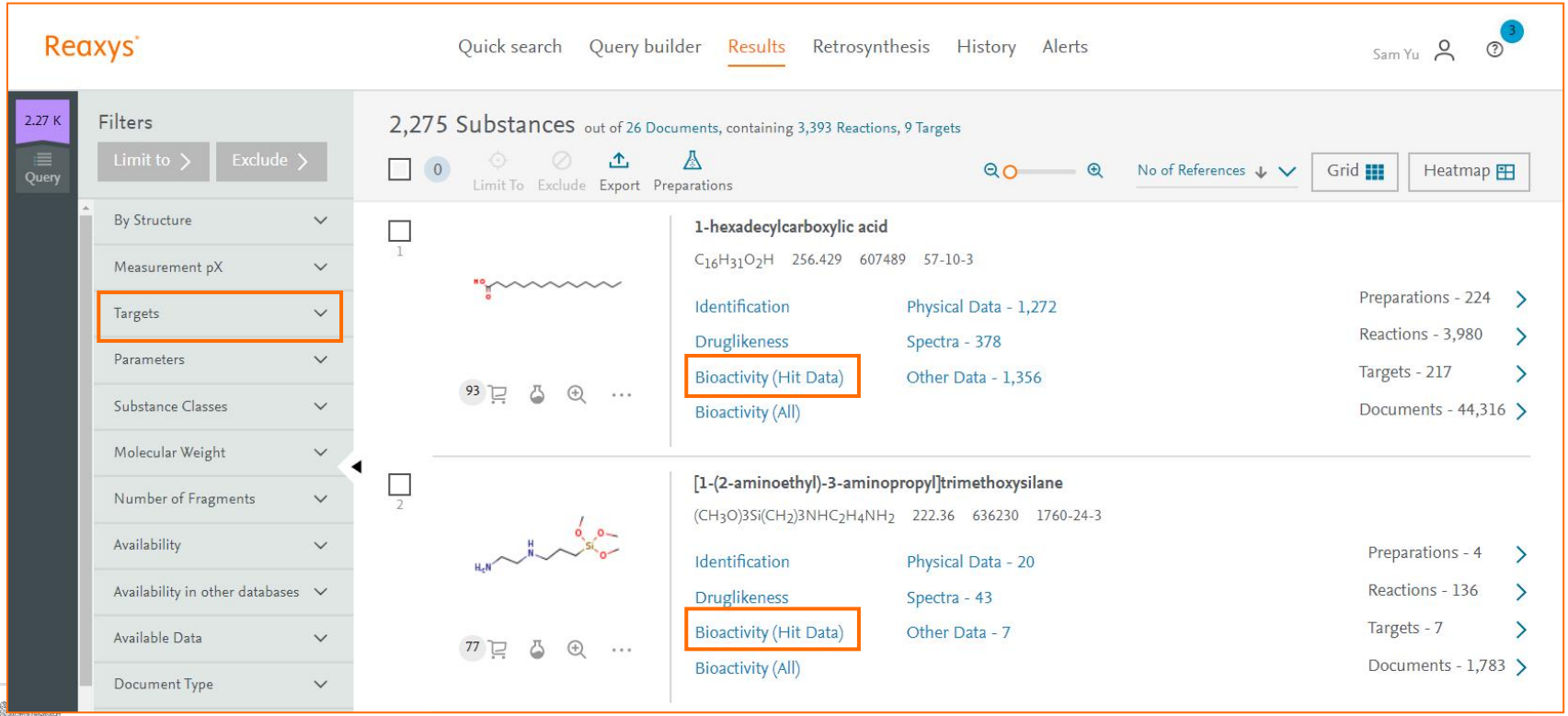
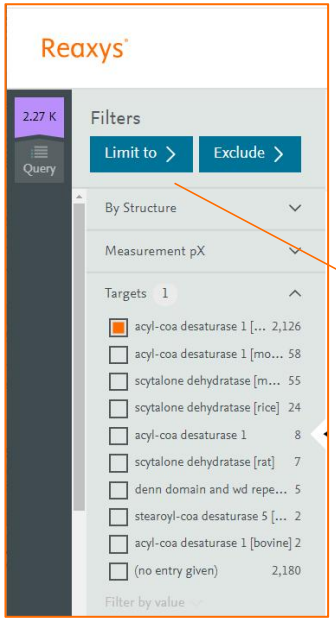
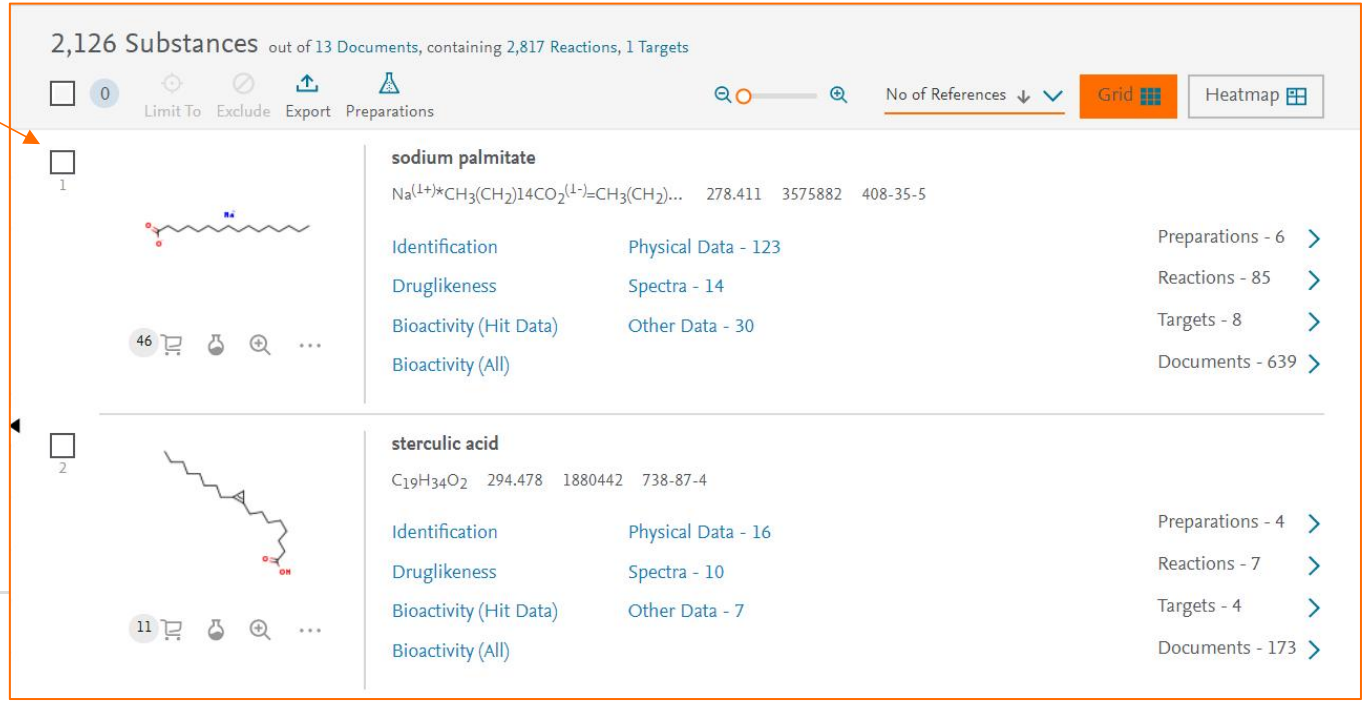
物质检索的结果



靶点分析，获取涉及“人”的靶点

选择Acyl-CoA desaturase 1 [human]:Wild，确保与人相关。





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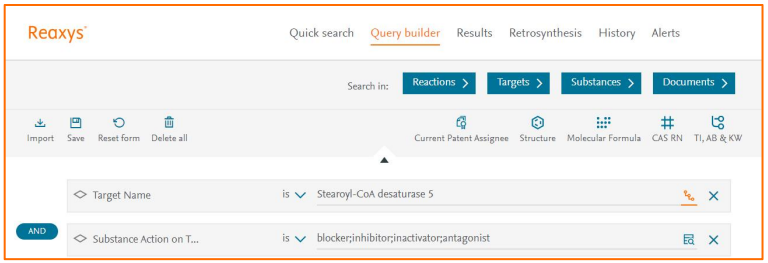
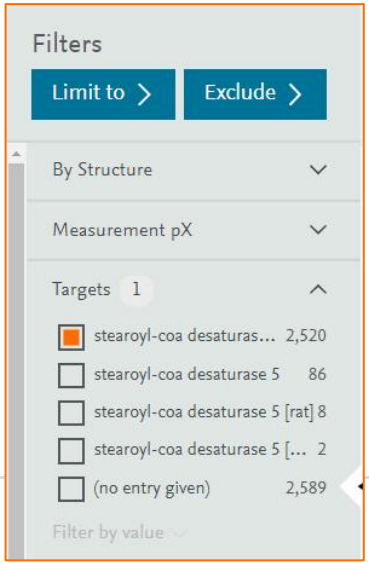
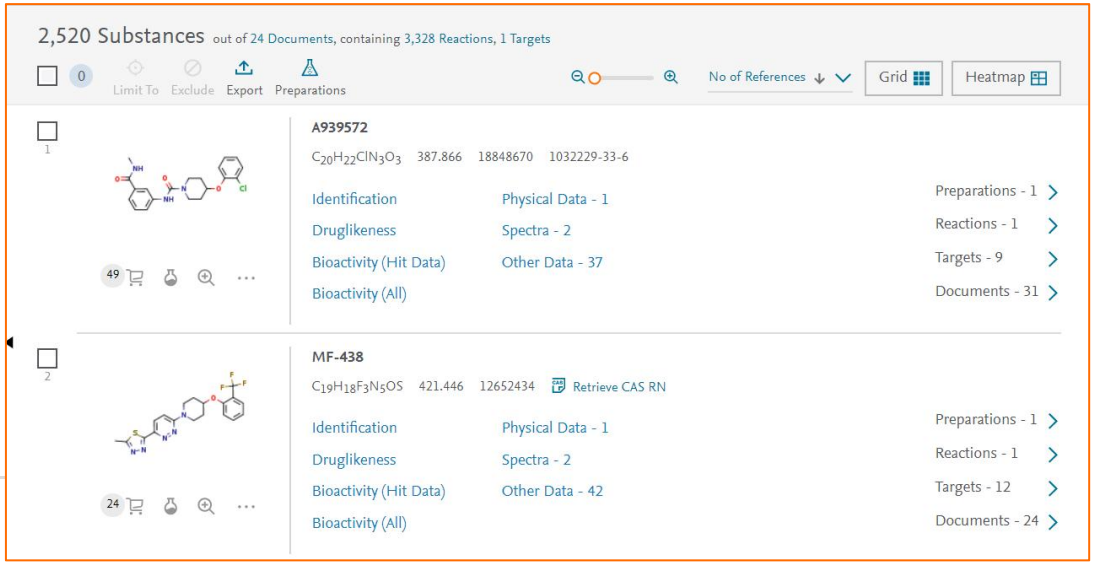
相同的步骤获取SCD5[Human]上有活性的化合物







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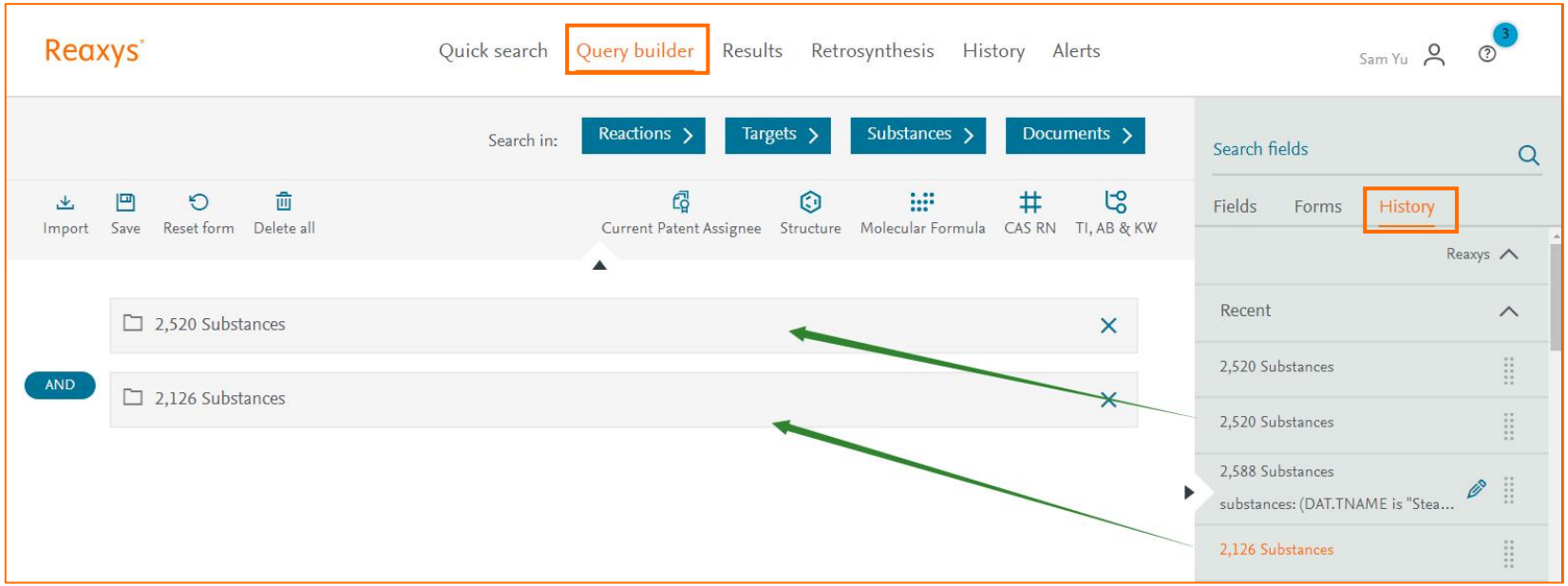
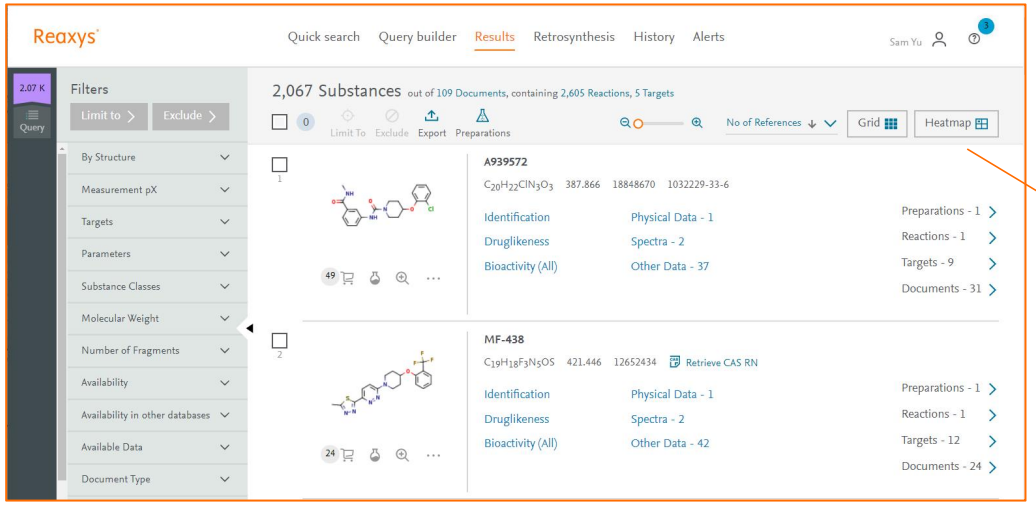
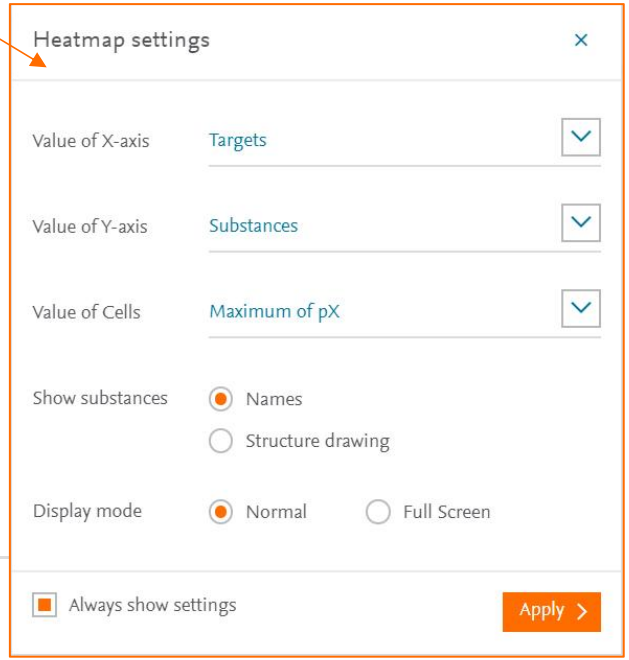
利用Query Builder获取两个结果集的交集



最后的检索结果





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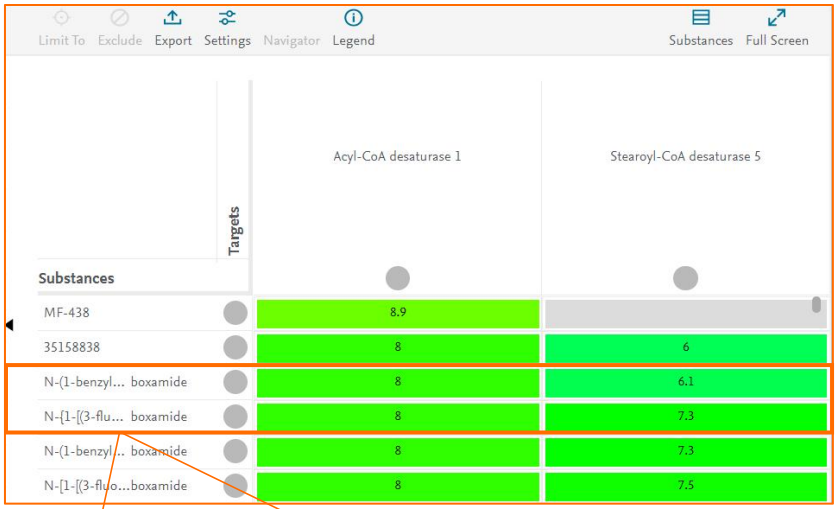
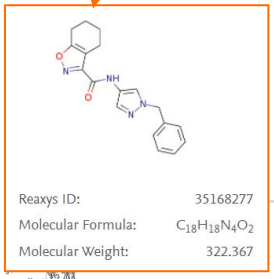
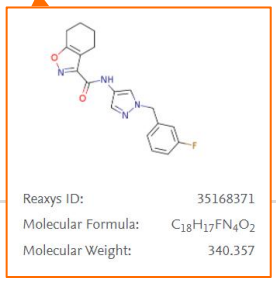
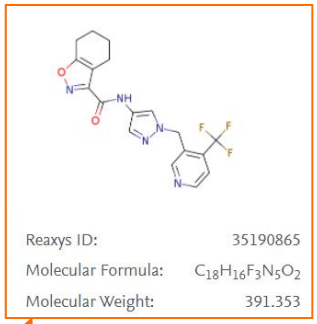
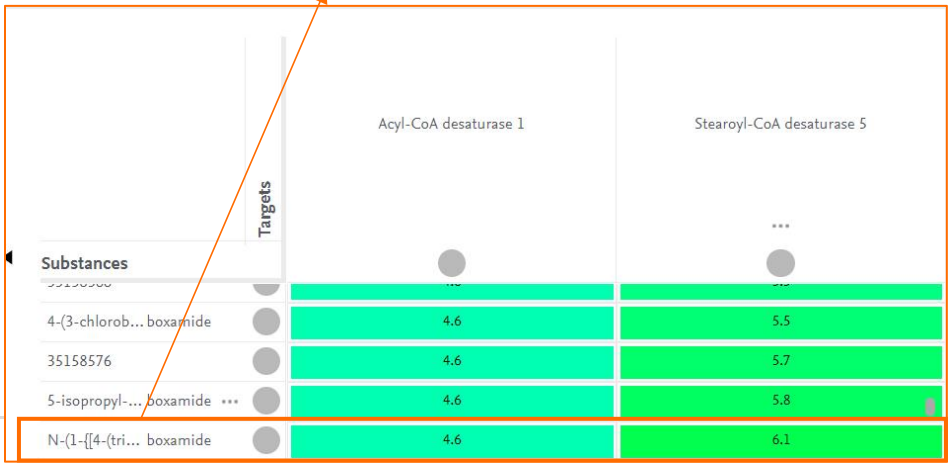
Heat Map结果



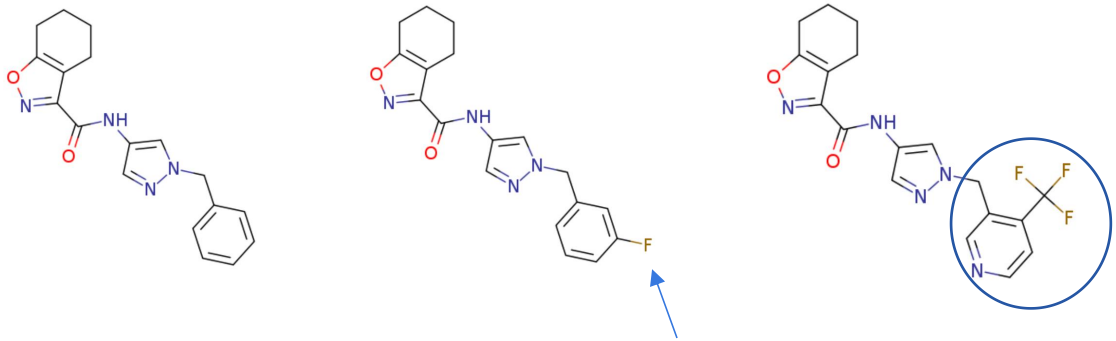






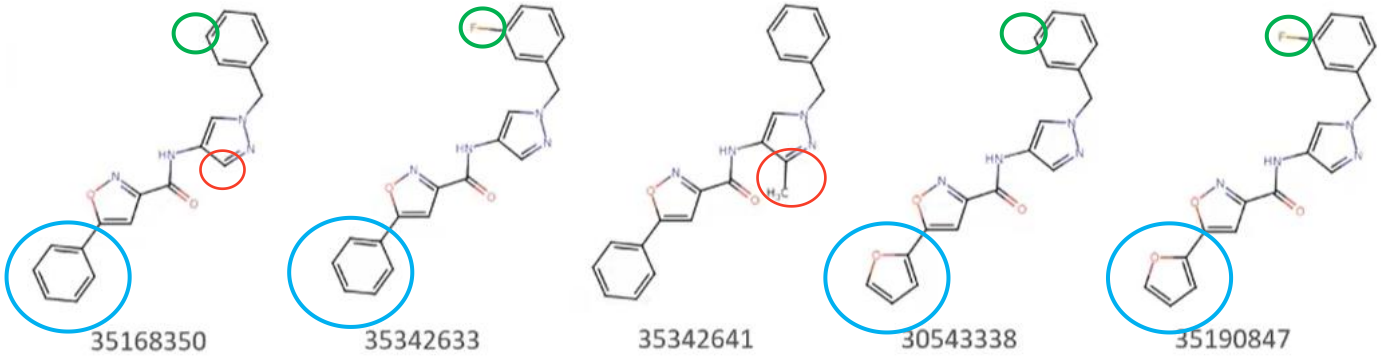


SAR分析数据



	PX		
SCD1	8.0	8.0	4.6
SCD5	6.15	7.3	6.3

SAR深度分析



	PX				
SCD1	6.3	7.1	5.7	7	8
SCD5	7	1	1	7.1	7.5

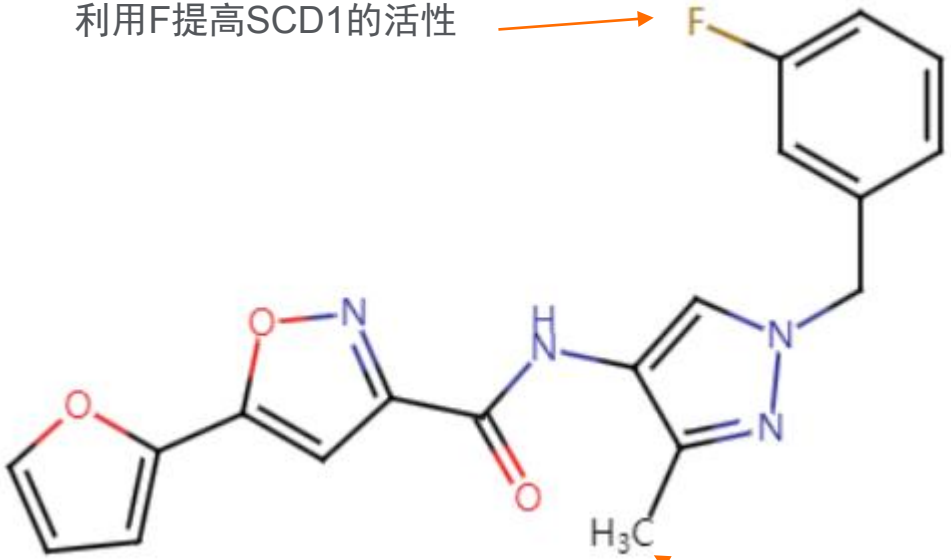
1：F的对SCD1的影响可能是积极的

2：苯环换成呋喃环对SCD1的影响也是积极的

3：结构中甲基对于靶点的选择性存在积极作用

设计新的结构并合成（该结构Reaxys中不存在）

利用F提高SCD1的活性

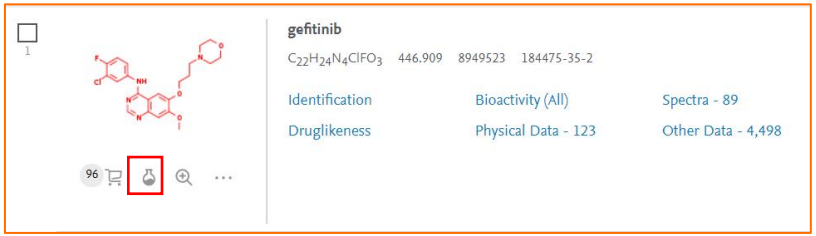


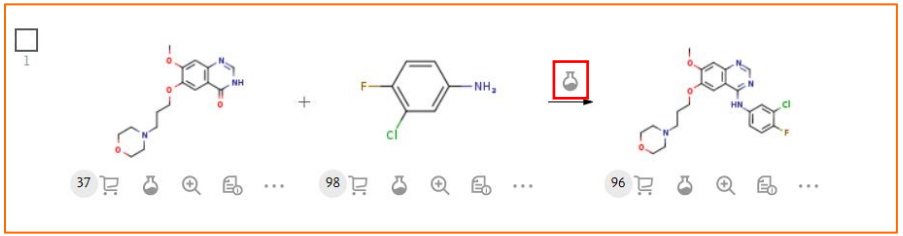
利用呋喃环提高SCD1活性

利用CH3提高选择性

Case 7：Reaxys中合成计划的制作

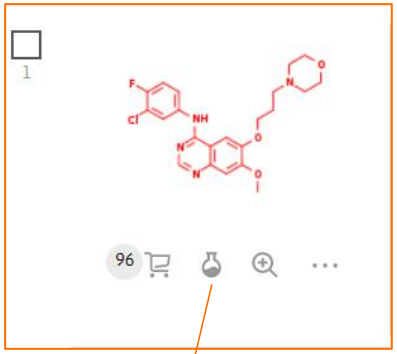
- 针对具体的化合物进行合成计划制作
  - 需要自行注册账号才可以用这个功能
  - 可以直接从物质界面，或者反应界面直接进入，也可以通过Retrosynthesis功能进入

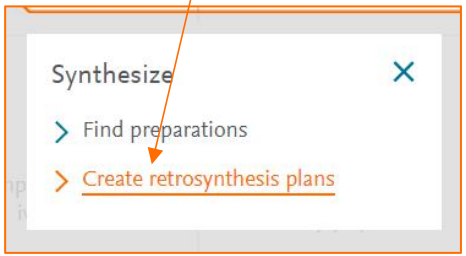


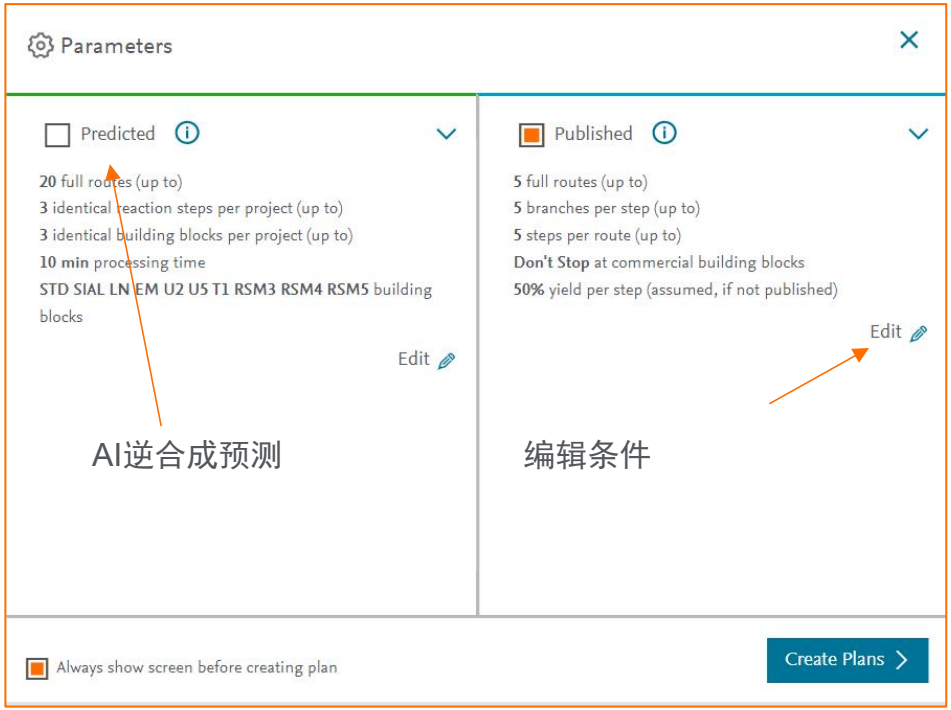


视频操作过程：
https://www.bilibili.com/video/BV1oL411u7yP

从具体物质出发的合成计划制作



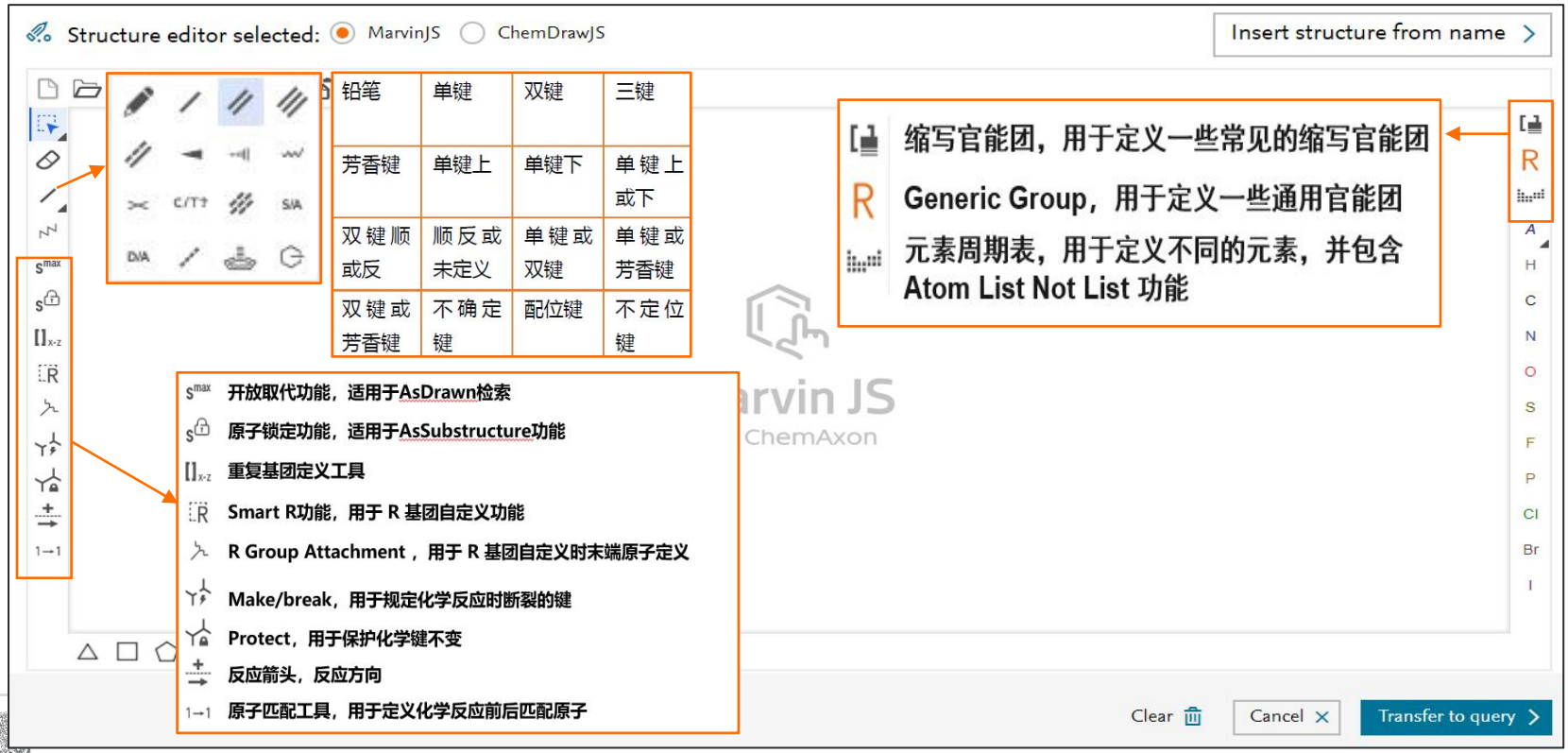




Agenda

- Reaxys的底层逻辑和发展方向
  - Reaxys及其对于科技文献的提炼
- Reaxys中科研数据的获取和应用场景
  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- Q&A

Reaxys中的结构面板

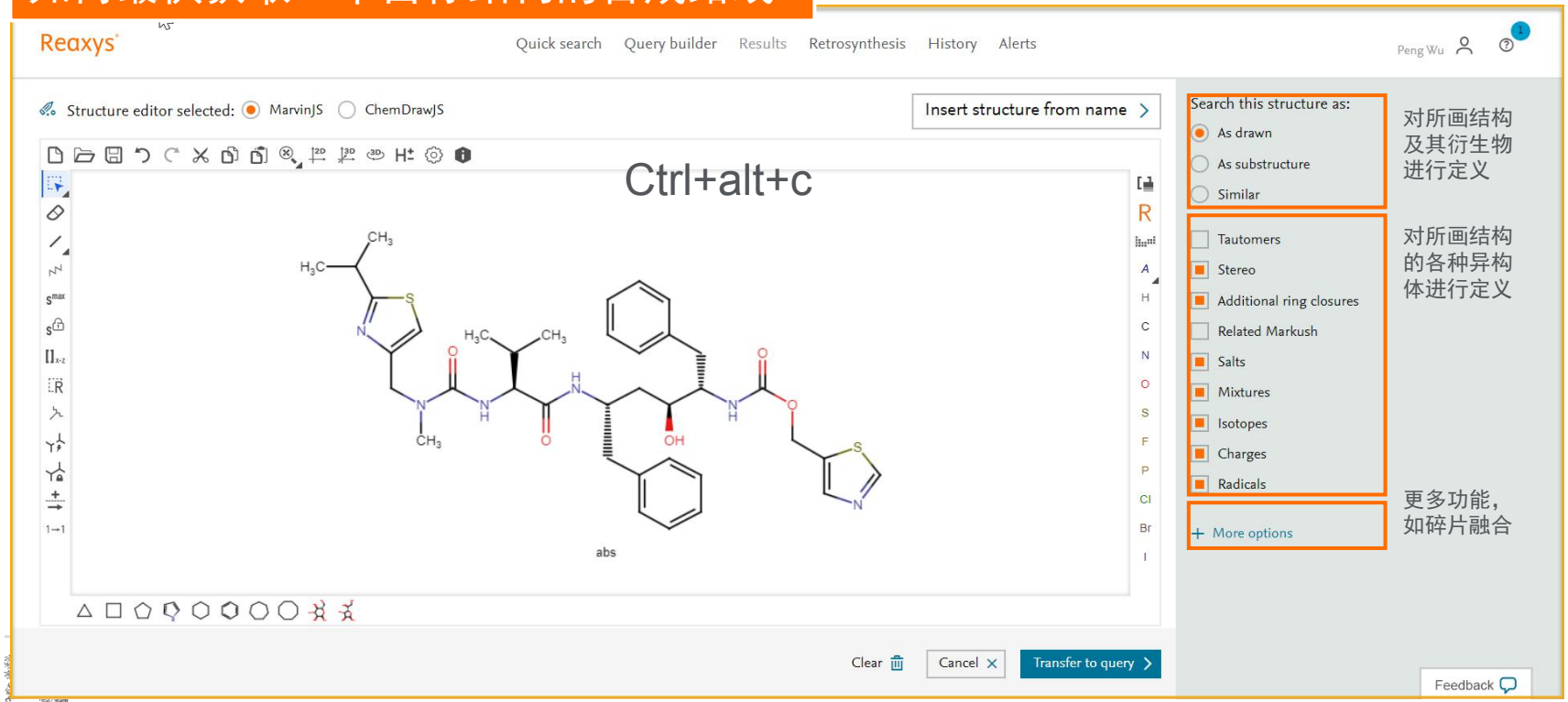


一些常见的功能使用视频

常用功能	视频链接	
最基本功能	https://www.bilibili.com/video/BV13i4y177wV	基础结构面板使用
不定位键	https://www.bilibili.com/video/BV1LK411P7nW	
通用/缩写官能团	https://www.bilibili.com/video/BV1PV41117J6	
原子列表与列表非	https://www.bilibili.com/video/BV1Ay4y1z7a5	
R基团定义	https://www.bilibili.com/video/BV1654y1r7be	
原子锁定与环锁定	https://www.bilibili.com/video/BV175411V77h	
G Group与通用原子	https://www.bilibili.com/video/BV1fy4y1B7LU	
原子属性列表	https://www.bilibili.com/video/BV1uD4y1R7K2	
盐，自由基，同位素	https://www.bilibili.com/video/BV1Rr4y1c7AL	
反应定义基本操作	https://www.bilibili.com/video/BV19r4y1w7Z5	基础反应功能使用
反应条件的定义	https://www.bilibili.com/video/BV1Af4y1q7xk	
合成计划的制作	https://www.bilibili.com/video/BV1oL411u7yP	
机理性文献查询	https://www.bilibili.com/video/BV1pK4y1E7Qx	

Case 5：Reaxys中快速获取化学合成路线

如何最快获取一个目标结构的合成路线



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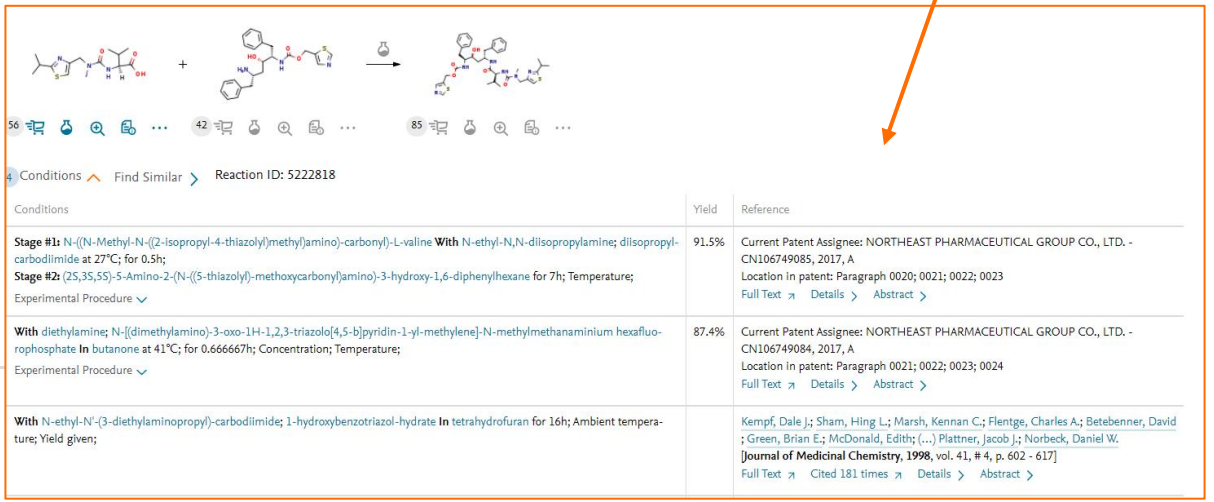
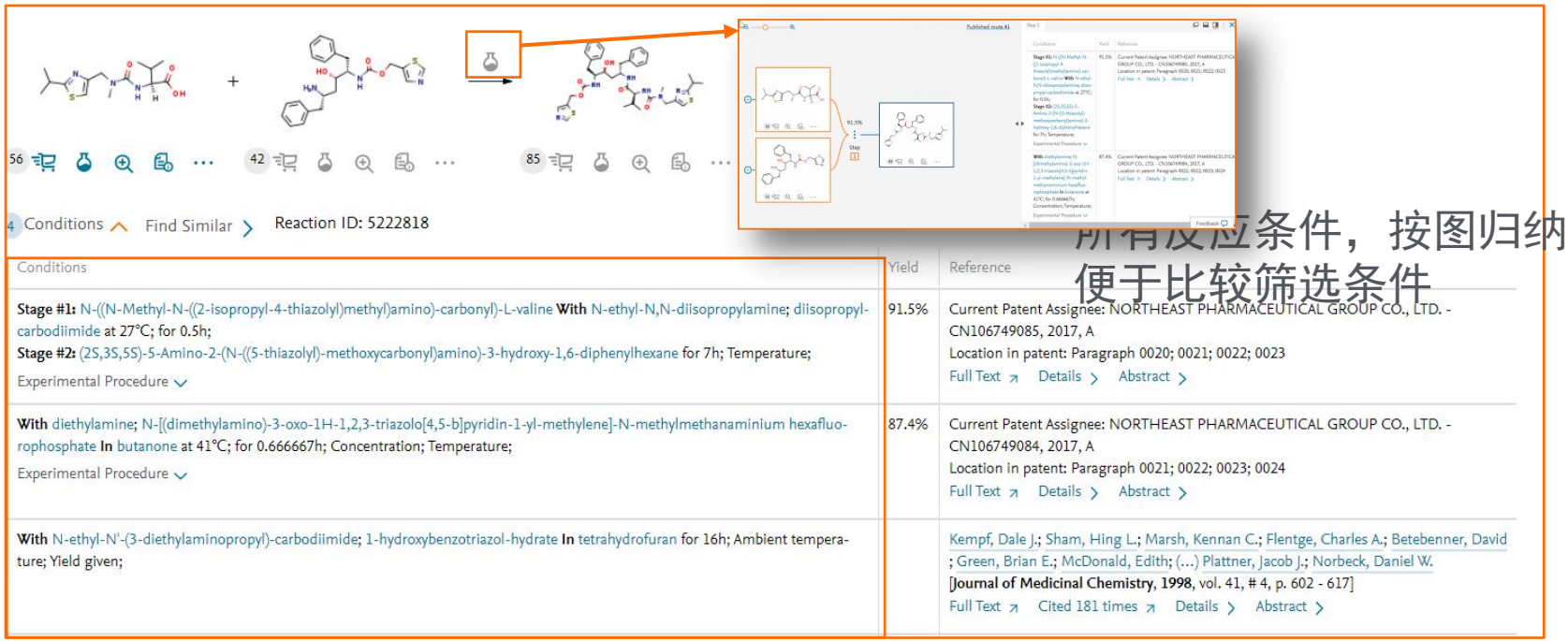
Reaxys中一次性获取所有信息



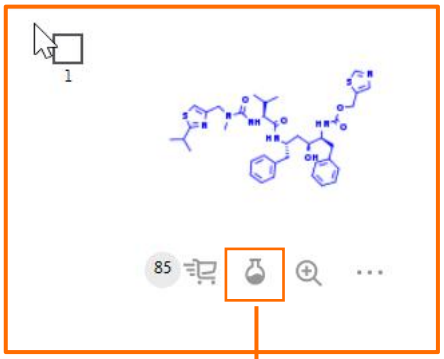
ELSEVIER

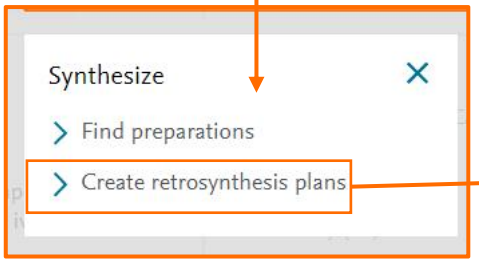
所有关键信息都会进行归纳整理

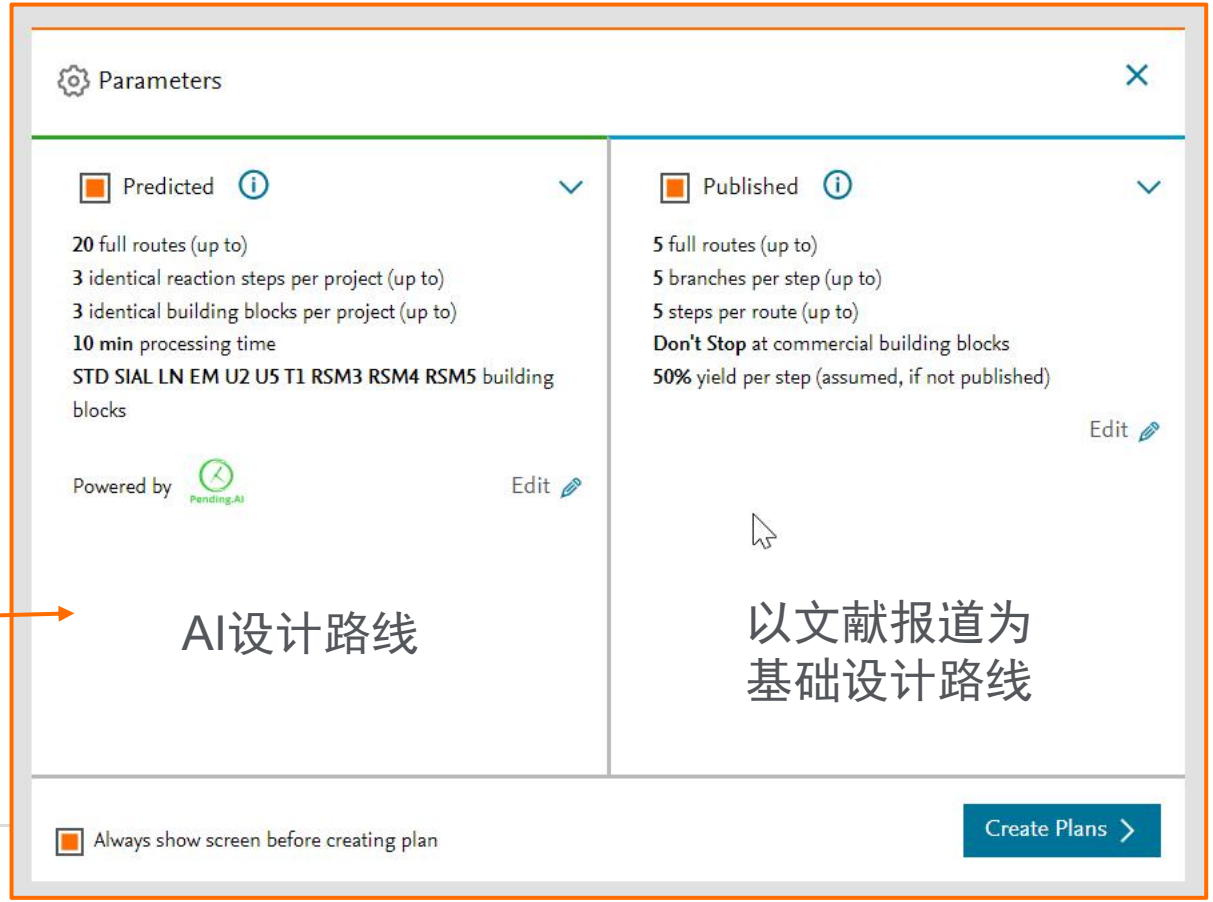


所有反应条件，按图归纳
便于比较筛选条件

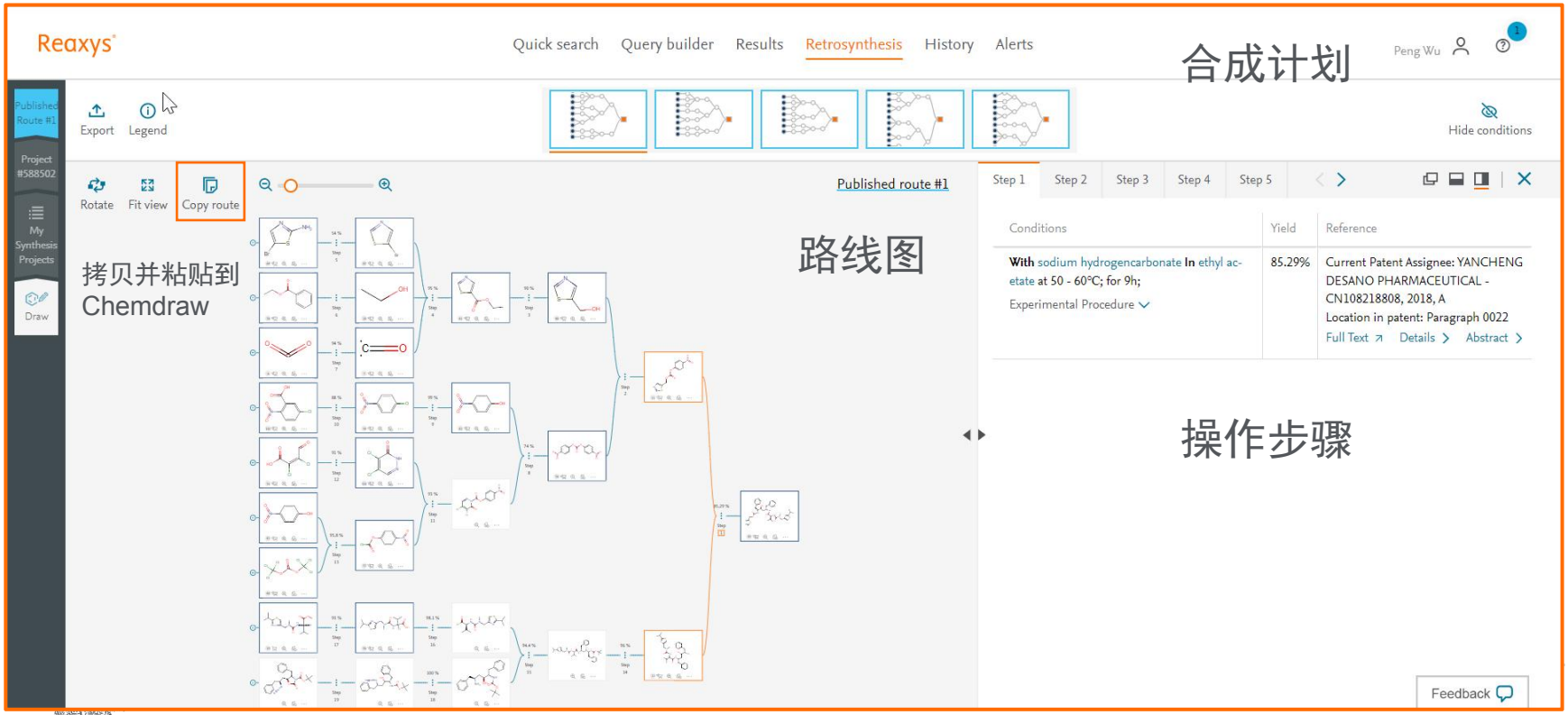
Conditions	Yield	Reference
Stage #1: N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)-carbonyl)-L-valine **With** N-ethyl-N,N-diisopropylamine; diisopropyl-carbodiimide at 27°C; for 0.5h; **Stage #2:** (2S,3S,5S)-5-Amino-2-(N-((5-thiazolyl)-methoxycarbonyl)amino)-3-hydroxy-1,6-diphenylhexane for 7h; Temperature; Experimental Procedure	91.5%	Current Patent Assignee: NORTHEAST PHARMACEUTICAL GROUP CO., LTD. - CN106749085, 2017, A Location in patent: Paragraph 0020; 0021; 0022; 0023 Full Text Details Abstract
With diethylamine; N-[(dimethylamino)-3-oxo-1H-1,2,3-triazolo[4,5-b]pyridin-1-yl-methylene]-N-methylmethanaminium hexafluo-rophosphate **In** butanone at 41°C; for 0.666667h; Concentration; Temperature; Experimental Procedure	87.4%	Current Patent Assignee: NORTHEAST PHARMACEUTICAL GROUP CO., LTD. - CN106749084, 2017, A Location in patent: Paragraph 0021; 0022; 0023; 0024 Full Text Details Abstract
With N-ethyl-N'-(3-diethylaminopropyl)-carbodiimide; 1-hydroxybenzotriazol-hydrate **In** tetrahydrofuran for 16h; Ambient tempera-ture; Yield given;		Kempf, Dale J.; Sham, Hing L.; Marsh, Kennan C.; Flentge, Charles A.; Betebenner, David ; Green, Brian E.; McDonald, Edith; (...) Plattner, Jacob J.; Norbeck, Daniel W. [**Journal of Medicinal Chemistry**, **1998**, vol. 41, # 4, p. 602 - 617] Full Text Cited 181 times Details Abstract


1
85


Synthesize
Find preparations
Create retrosynthesis plans


Parameters
Predicted
20 full routes (up to)
3 identical reaction steps per project (up to)
3 identical building blocks per project (up to)
10 min processing time
STD SIAL LN EM U2 U5 T1 RSM3 RSM4 RSM5 building blocks
Powered by
Edit
Published
5 full routes (up to)
5 branches per step (up to)
5 steps per route (up to)
Don't Stop at commercial building blocks
50% yield per step (assumed, if not published)
Edit
AI设计路线
以文献报道为基础设计路线
Always show screen before creating plan
Create Plans

强大的运算功能，快捷给出不同的合成方案



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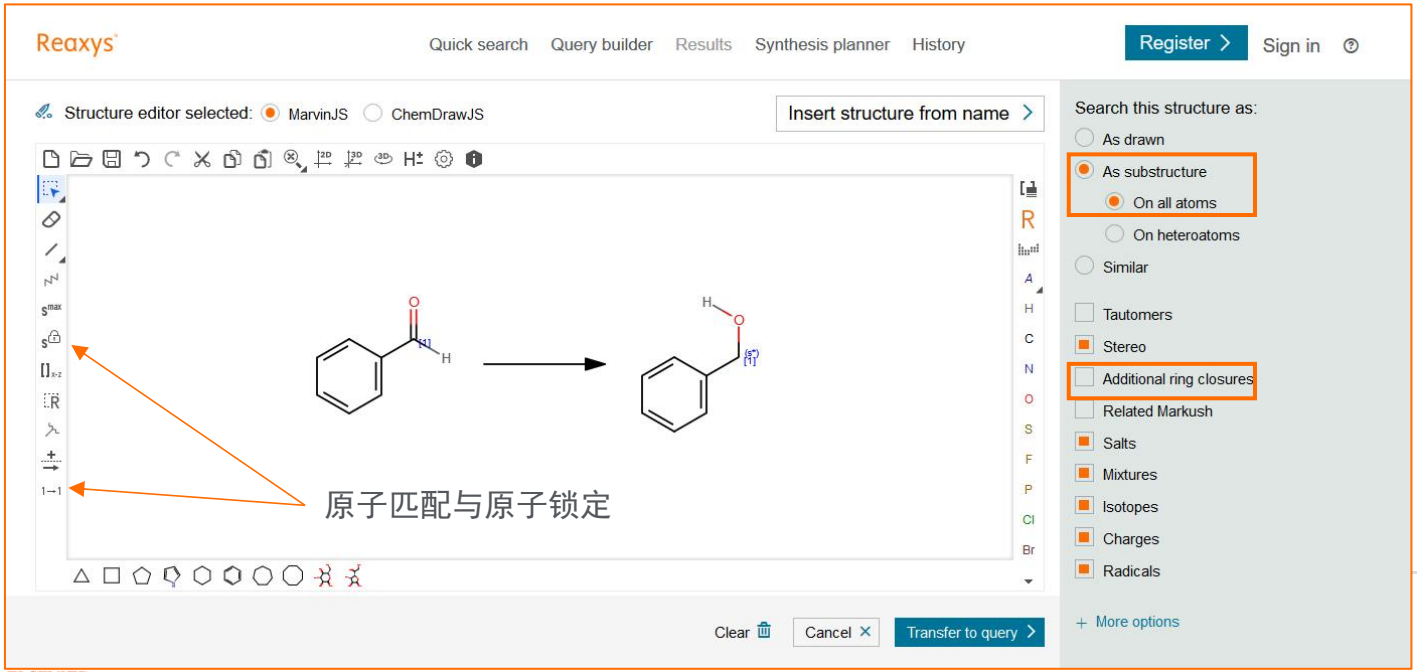
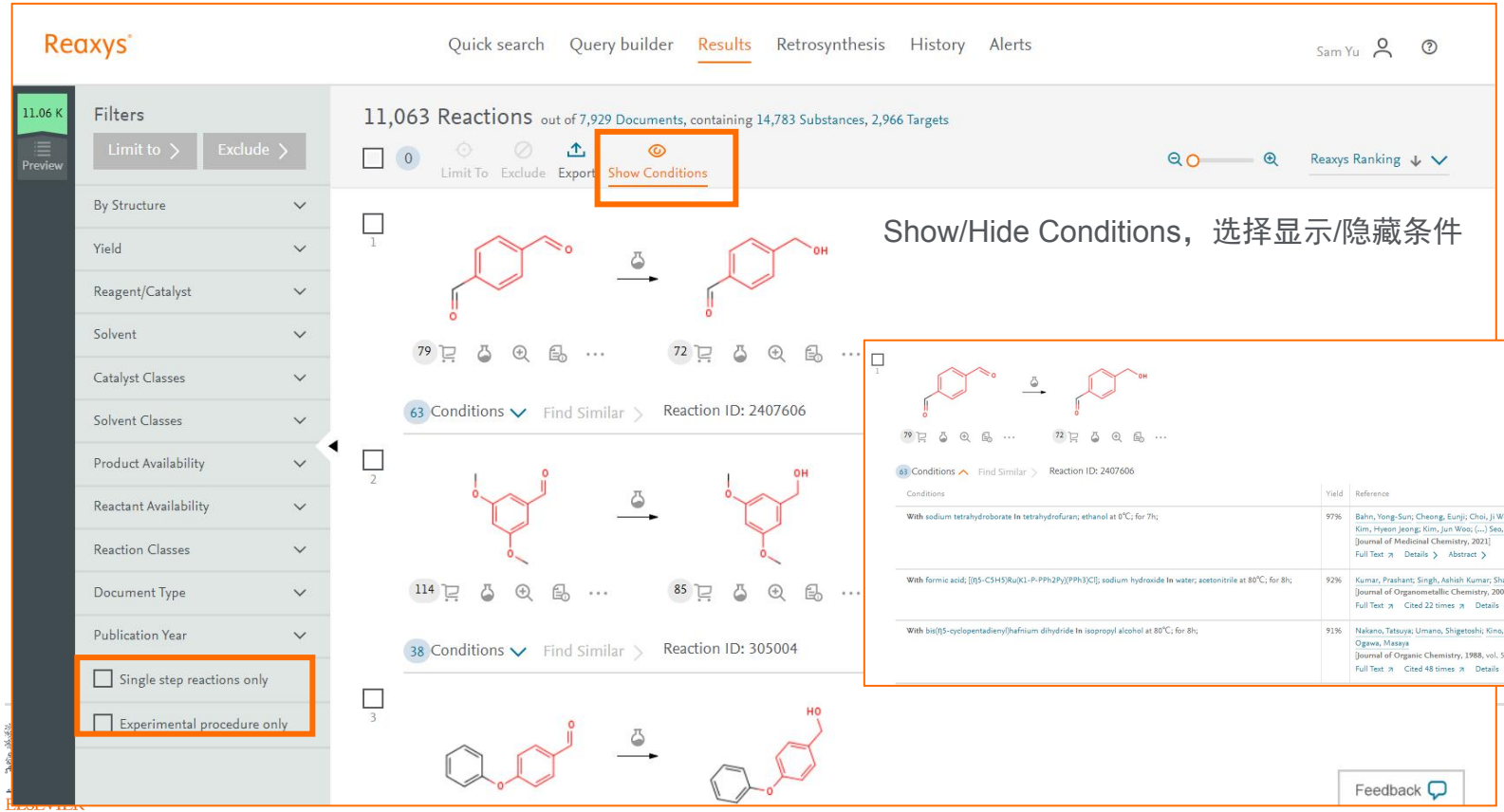
Case 6：Reaxys中最简单的反应定义与筛选

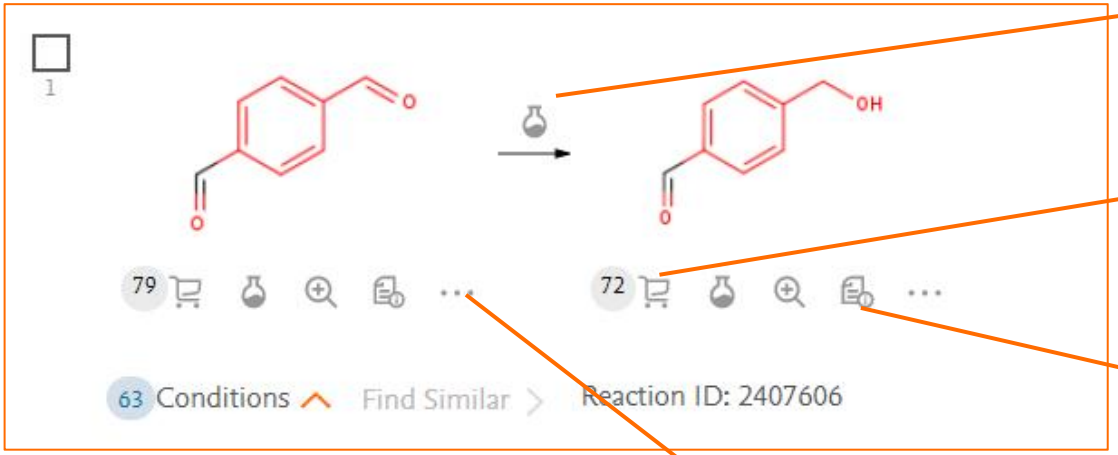
- 检索以下核心结构反应并进行反应筛选操作
- 视频操作过程
  - https://www.bilibili.com/video/BV1BT4y1F7vT



Reaxys中的结果

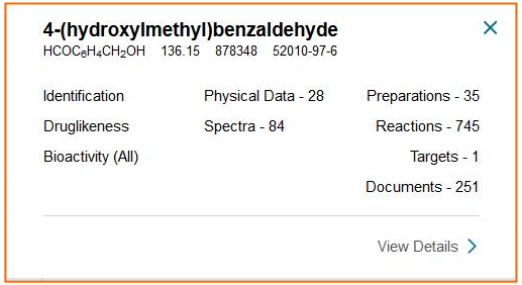

Reaxys
Quick search
Query builder
Results
Retrosynthesis
History
Alerts
Sam Yu
11.06 K
Preview
Filters
Limit to
Exclude
By Structure
Yield
Reagent/Catalyst
Solvent
Catalyst Classes
Solvent Classes
Product Availability
Reactant Availability
Reaction Classes
Document Type
Publication Year
Single step reactions only
Experimental procedure only
11,063 Reactions out of 7,929 Documents, containing 14,783 Substances, 2,966 Targets
Limit To
Exclude
Export
Show Conditions
Reaxys Ranking
63 Conditions
Find Similar
Reaction ID: 2407606
114 Conditions
Find Similar
Reaction ID: 305004
38 Conditions
Find Similar
Reaction ID: 305004
Feedback
Show/Hide Conditions，选择显示/隐藏条件

Reaxys的一条反应的界面



进行合成计划

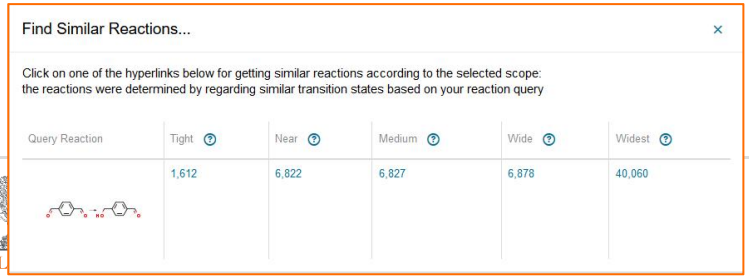
查看商业来源

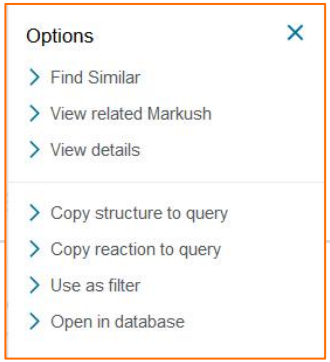


查看物质详情

查看条件

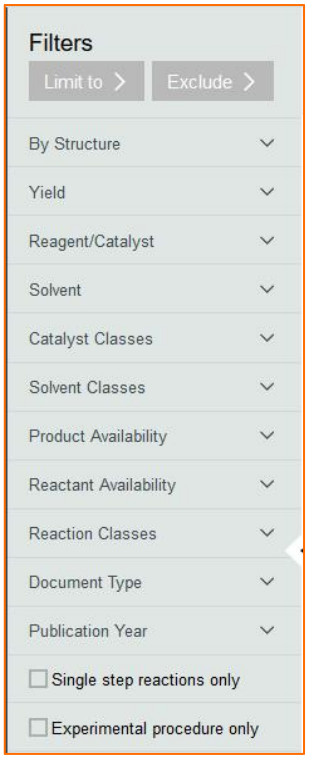
寻找相似反应

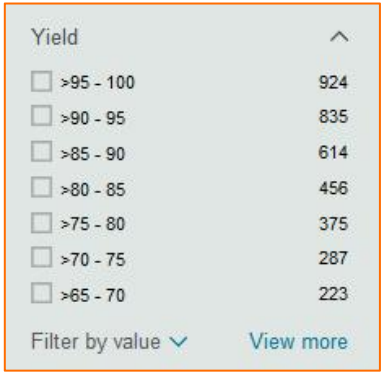


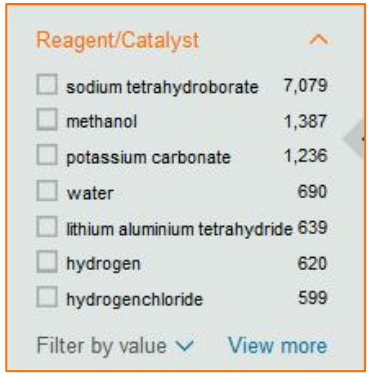


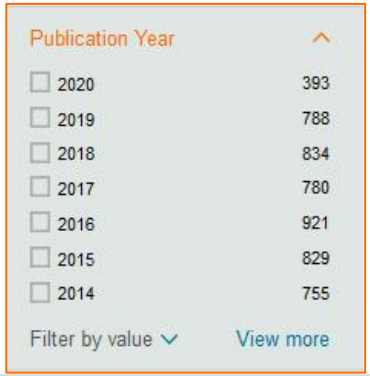
更多与物质相关操作

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

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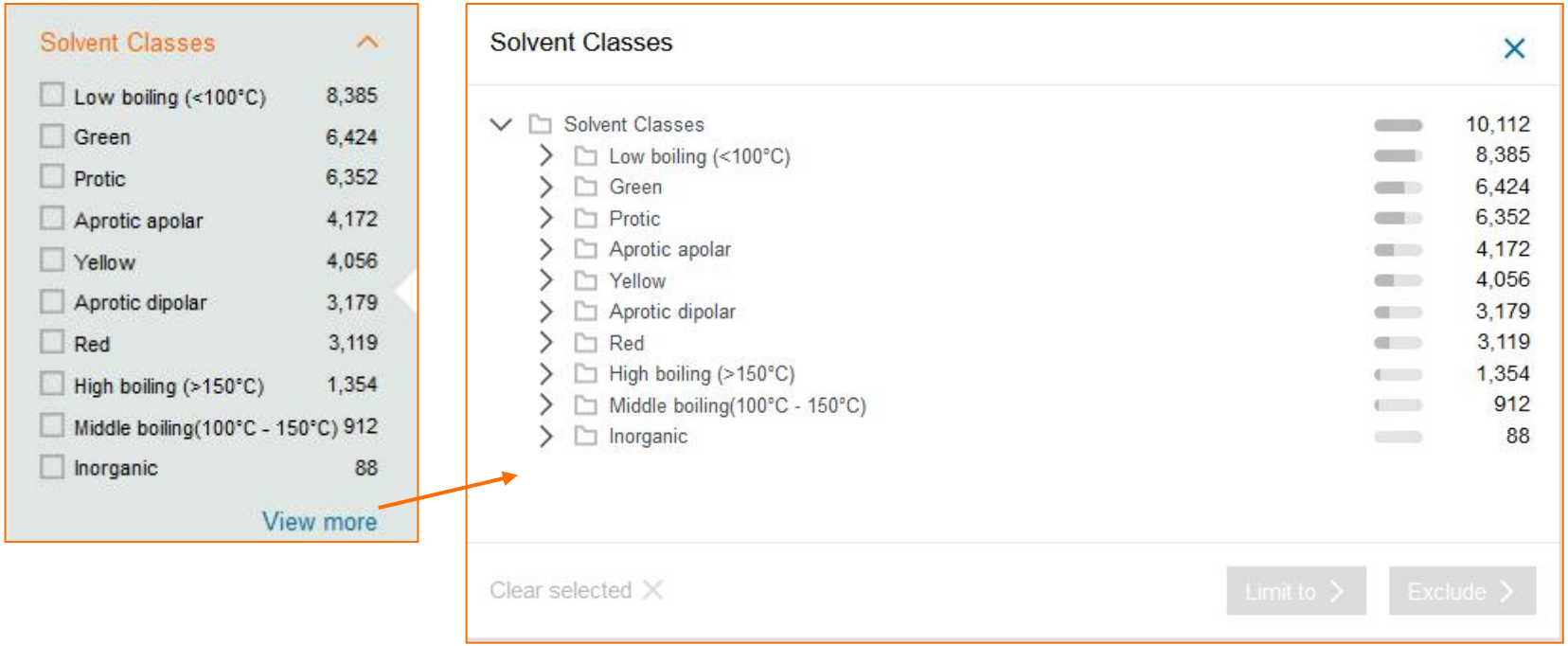
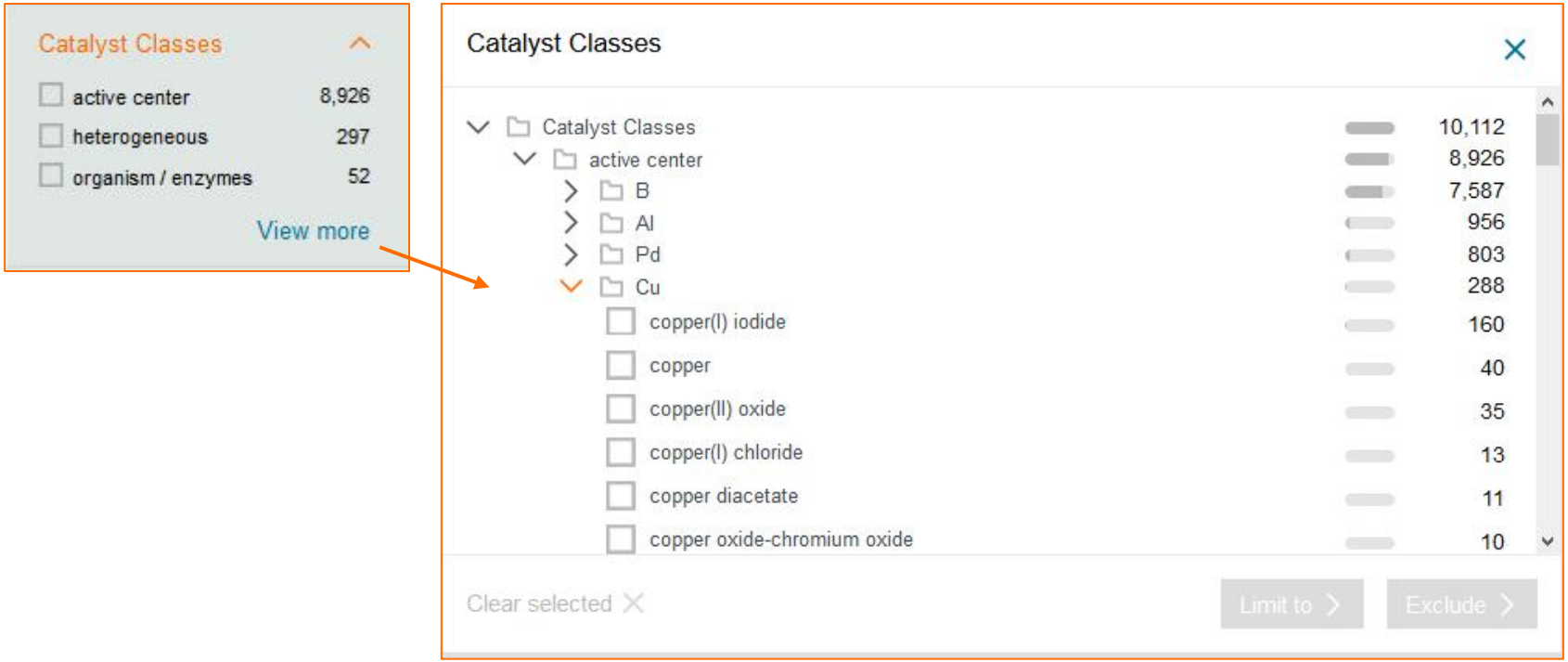
Reaxys中的一些特殊筛选工具—溶剂分类

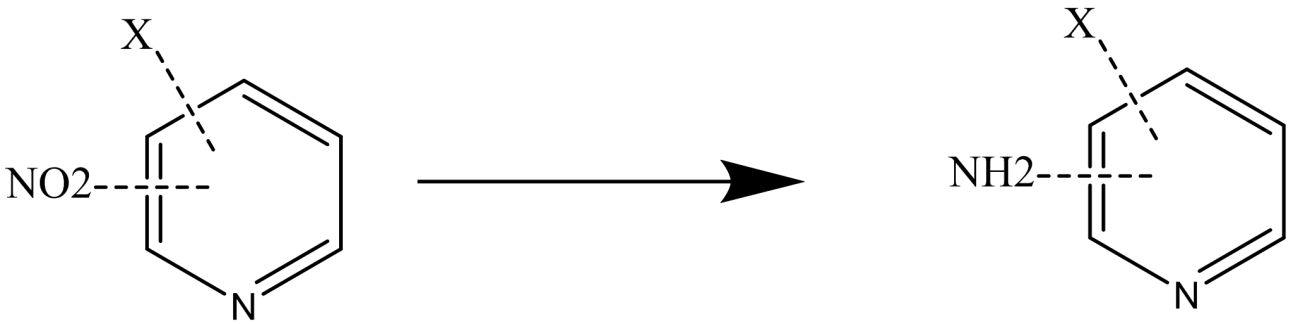


Reaxys中的一些特殊筛选工具—催化剂分类



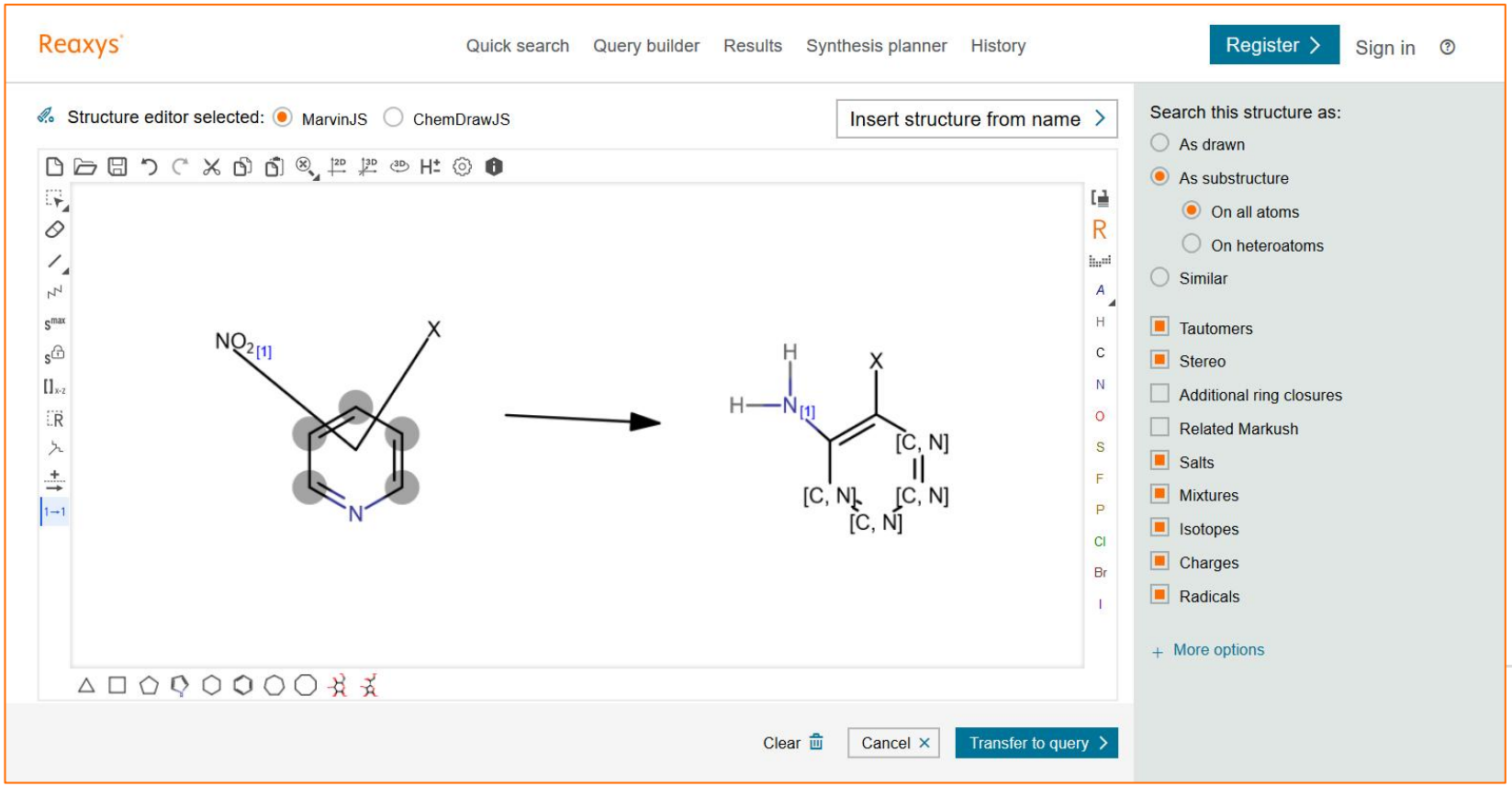
Case 7：结构中有特殊需求的反应定义

- 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

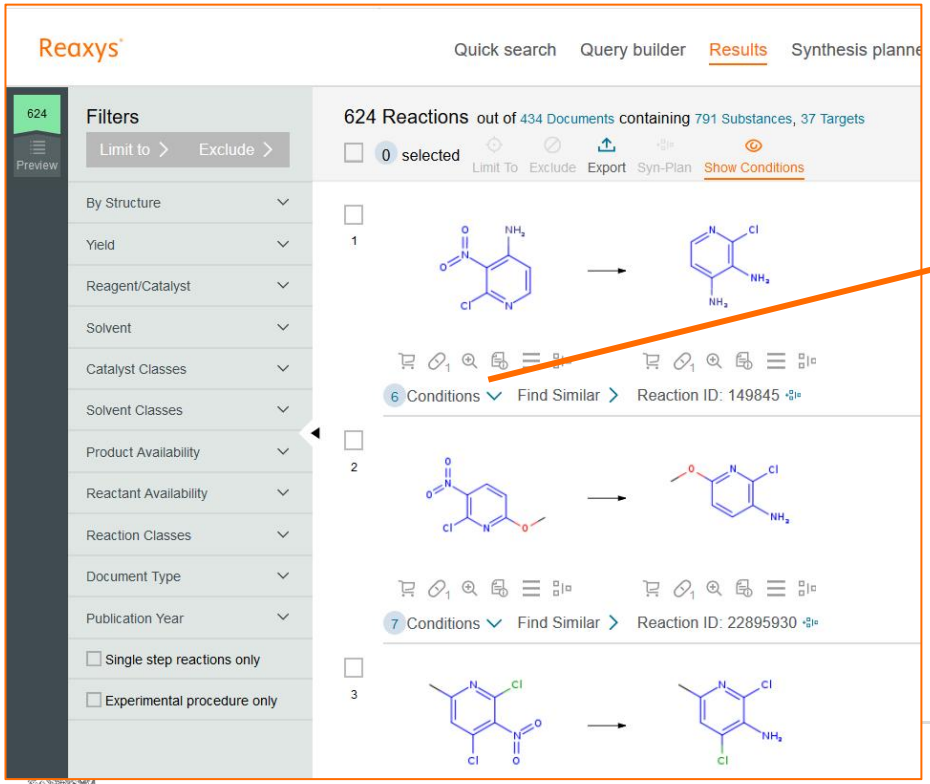


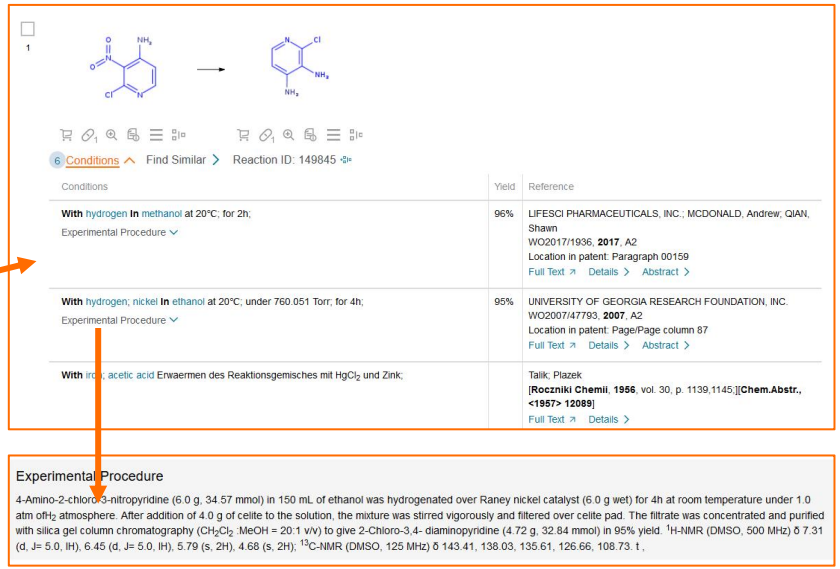
视频操作过程：
https://www.bilibili.com/video/BV1si4y177as

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 ofH_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, lH), 6.45 (d, J= 5.0, lH), 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。

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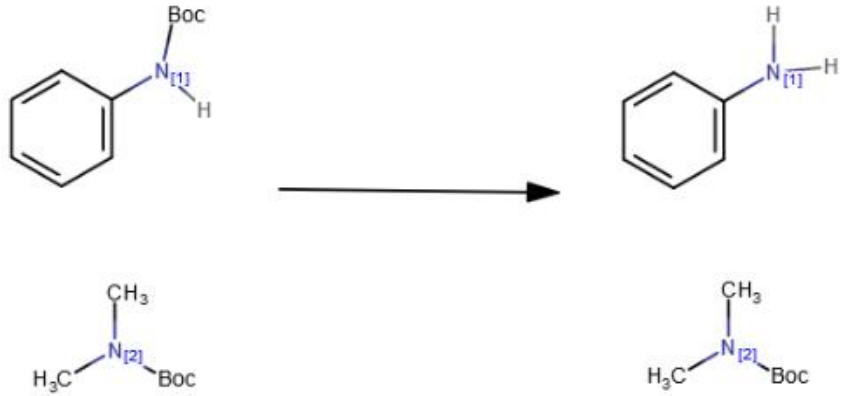
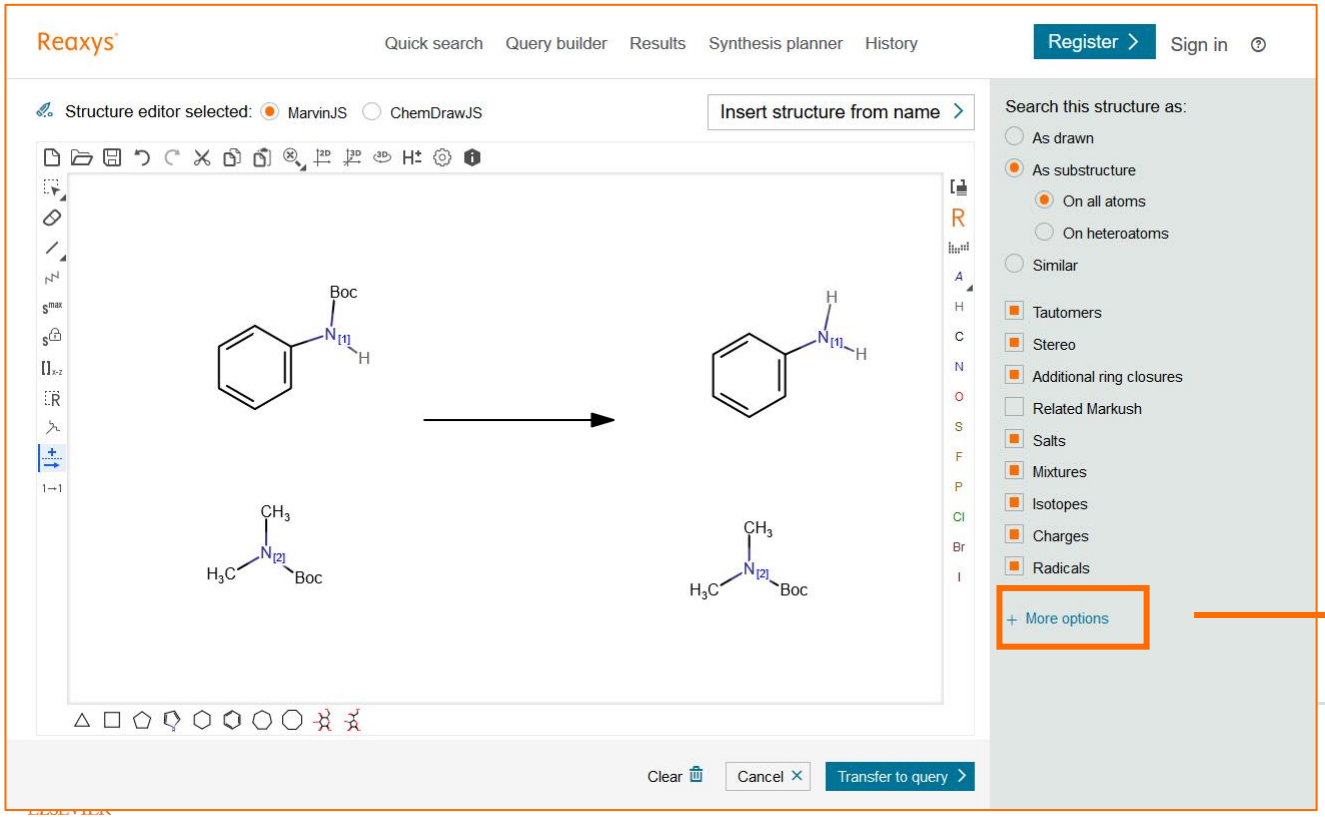
Case 8：选择性氧化还原脱保护反应的定义

- 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



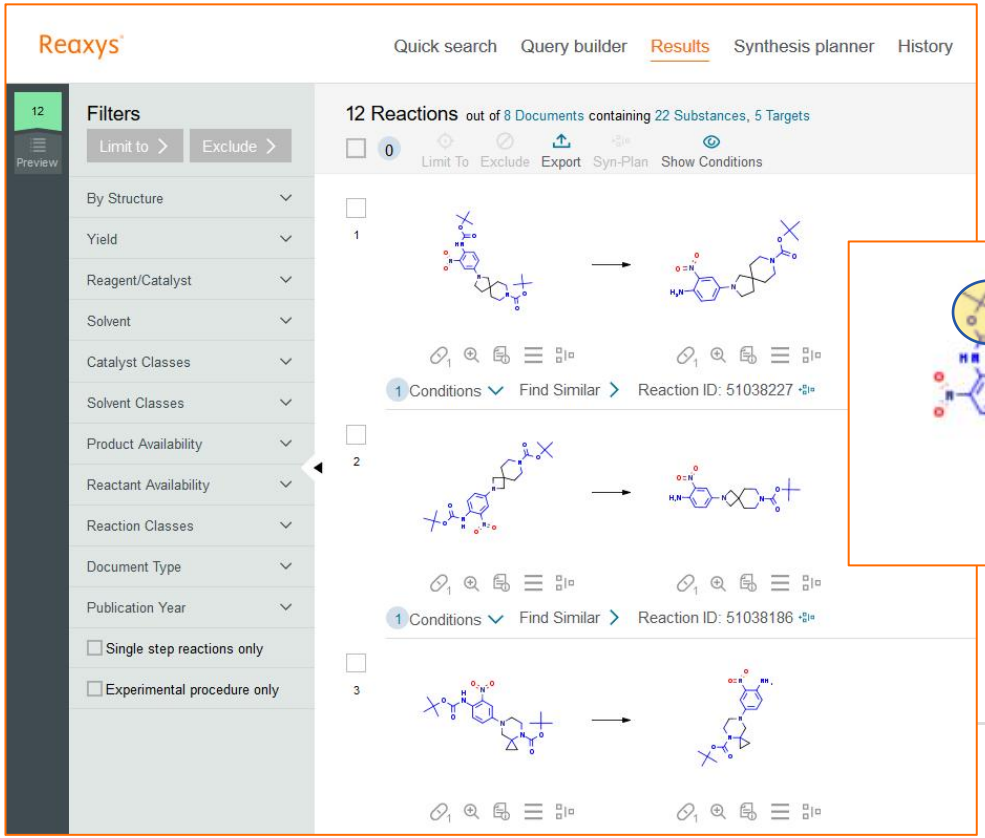
视频操作过程：
https://www.bilibili.com/video/BV1Vv411r7Bc

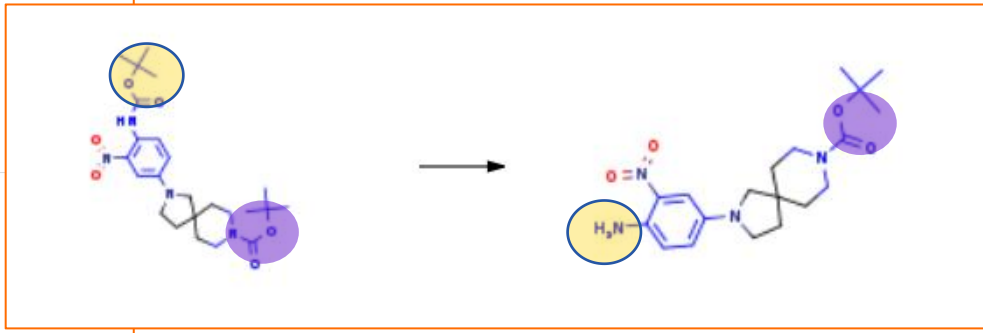
Reaxys中的结构定义



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

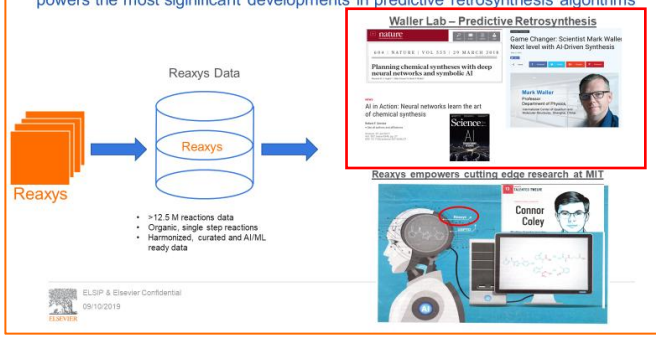


Agenda

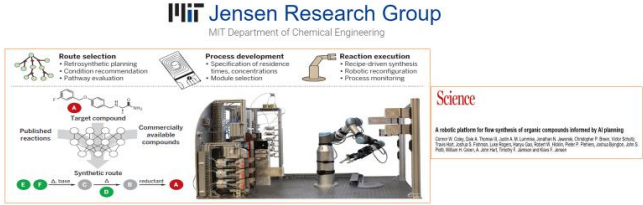
- Reaxys的底层逻辑和发展方向
  - Reaxys及其对于科技文献的提炼
- Reaxys中科研数据的获取和应用场景
  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- Q&A

Reaxys AI逆合成—基于深度神经网络算法的逆合成模型

Elsevier collaboration with leading academics and and the use of Reaxys data powers the most siginificant developments in predictive retrosynthesis algorithms



Reaxys data is helping Jensen group transform the design of industrial processes for chemical and drug manufacturing



From 12.5 million published single-step reactions tabulated in the **Reaxys** database, they prepared a library of **163,723 rules**. Transformations with **stereochemistry** were included in the rules.

Reaxys data is powering Lapkin Group's reasearch into planning supply chains in the chemical industry that can help to improve sustainability

Algorithm finds the 569 molecules that might drive a waste-free economy

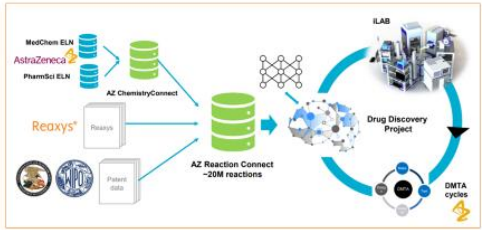
Interview with Professor Alexei Lapkin, University of Cambridge

Introduction

The task of reaction engineers is to develop optimized and clean chemical processes. Professor Alexei Lapkin met with Elsevier to discuss the importance of easy access to high-quality data in successful reaction engineering, explaining how data science is emerging as an important field in process chemistry.

Lapkin group gratefully acknowledges collaboration with RELX Intellectual Properties SA and their technical support, which enabled us to mine Reaxys. Reaxys data were made accessible to our research project via the Elsevier R&D Collaboration Network. Read more in ChemRxiv.

Reaxys data is key component of reaction knowledge base that is helping AstraZeneca to embed predictive algorithms in their drug development projects



European Laboratory Research & Innovation Group: https://elrig.org/downloads/ri19/Ola_Engkvist.pdf

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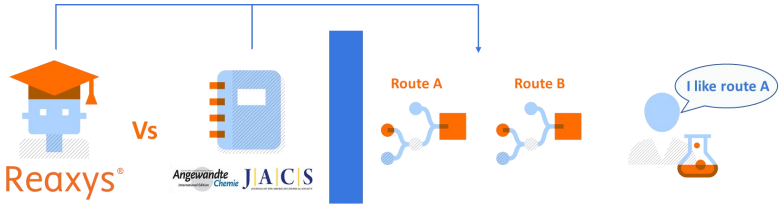
Elsevier Life Science逆合成模型的定量评估

Quantitative evaluation against other predictive models and tools for 100 chEMBL molecules.

Retrosynthesis method	% of molecules for which a route was predicted	# of molecules for which a route was predicted using only the indicated method
Reaxys Predictive Retrosynthesis	**95%**	**24**
AiZynthFinder	54%	2
ASKCOS	64%	0

Qualitative double-blind test carried out with 45 organic chemists

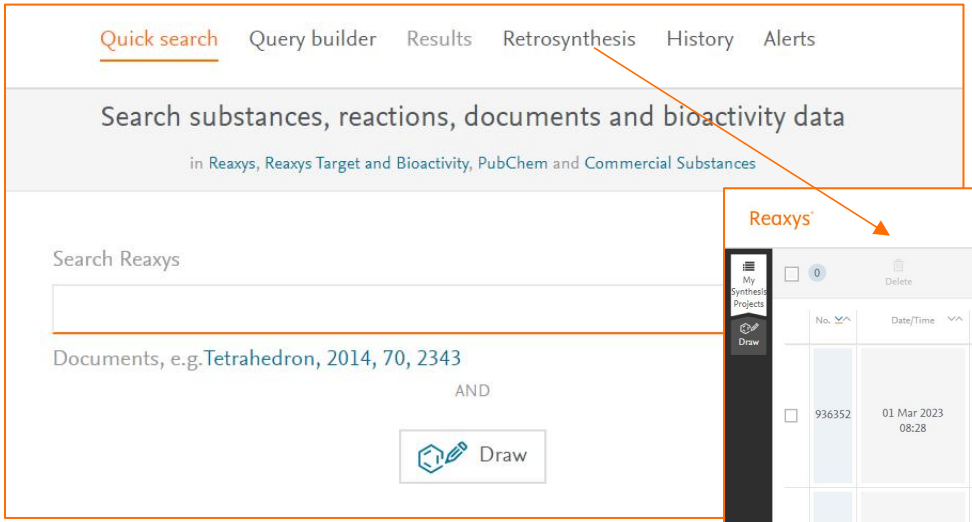


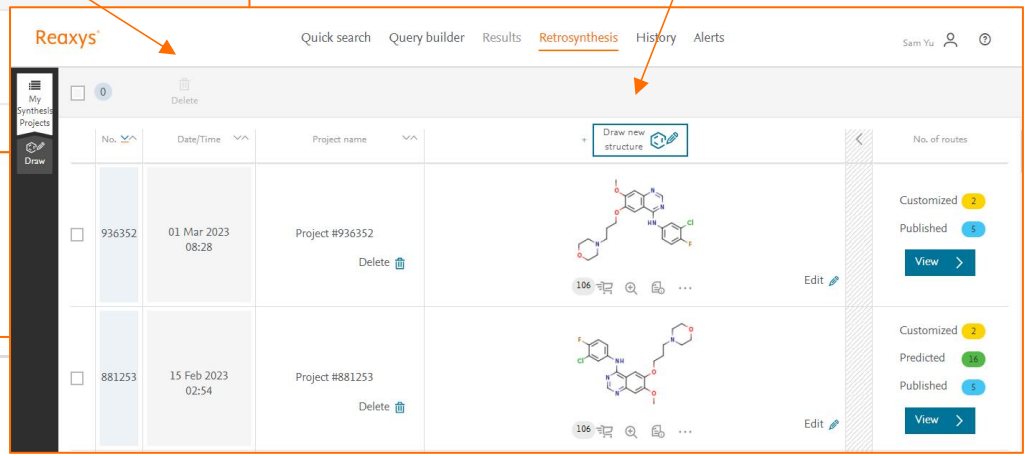
Experts chose Reaxys predictive retrosynthesis routes 57% of the time versus 43% choosing the literature routes

Reaxys AI使用方法(需要有开通权限)

- 针对具体的化合物进行合成计划制作（可以是已知的，也可以是未知的）
  - 需要自行注册账号才可以用这个功能
  - 全新化合物需要通过Retrosynthesis功能进入

通过结构面板添加结构





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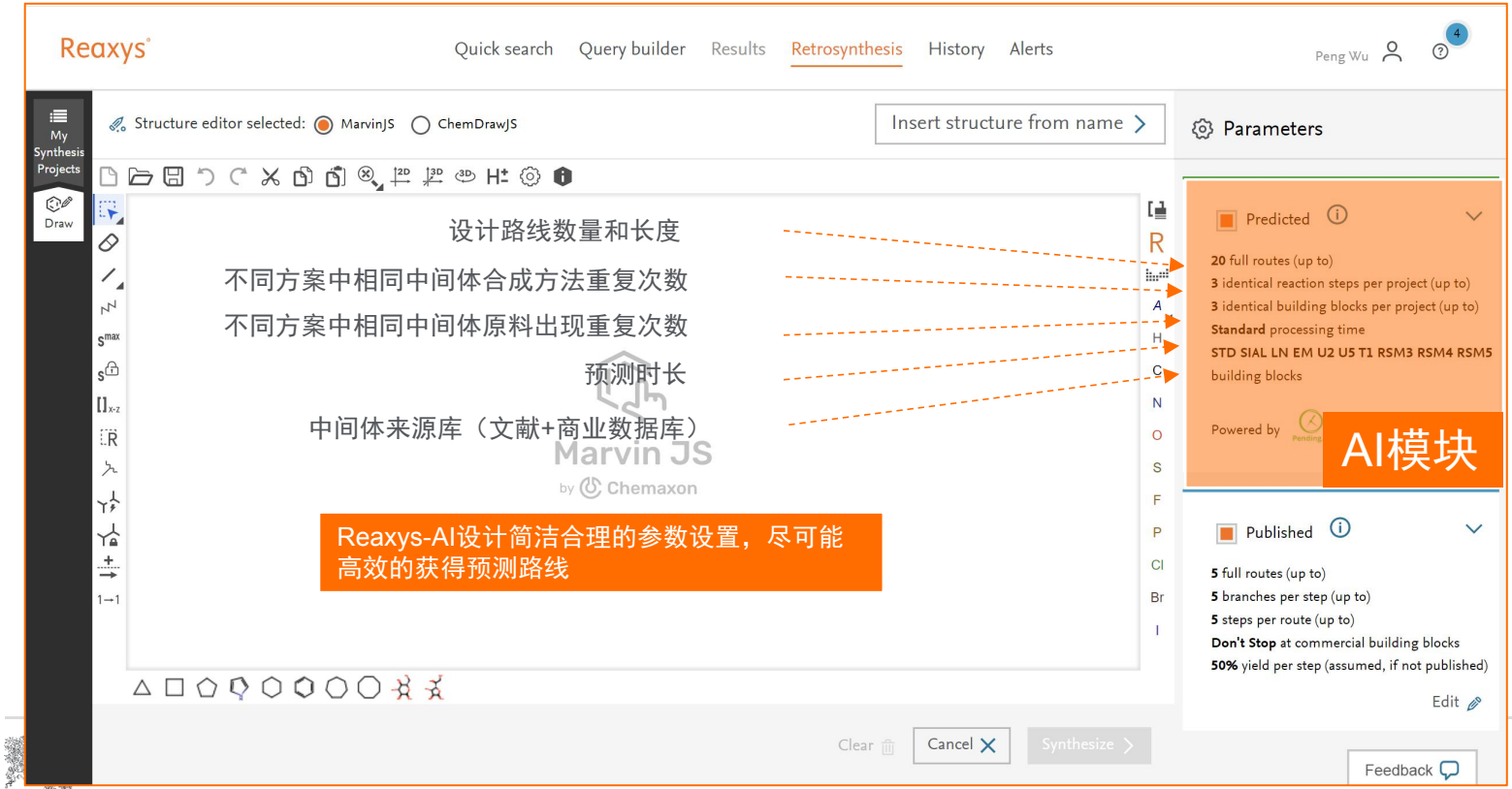
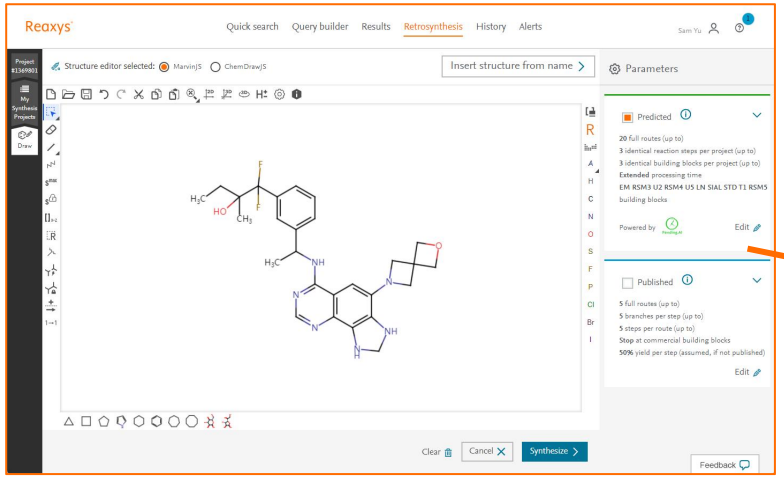
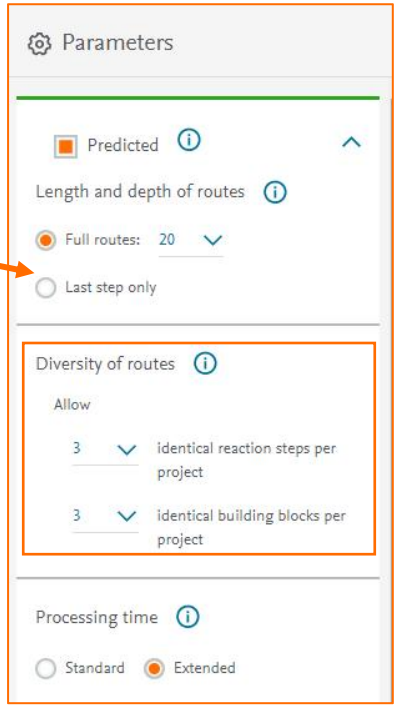
参数设置：概览


Reaxys
Quick search
Query builder
Results
Retrosynthesis
History
Alerts
Peng Wu
My Synthesis Projects
Draw
Structure editor selected:
MarvinJS
ChemDrawJS
Insert structure from name
Parameters
设计路线数量和长度
不同方案中相同中间体合成方法重复次数
不同方案中相同中间体原料出现重复次数
预测时长
中间体来源库（文献+商业数据库）
Marvin JS
by Chemaxon
Reaxys-AI设计简洁合理的参数设置，尽可能高效的获得预测路线
Predicted
20 full routes (up to)
3 identical reaction steps per project (up to)
3 identical building blocks per project (up to)
Standard processing time
STD SIAL LN EM U2 U5 T1 RSM3 RSM4 RSM5 building blocks
Powered by
AI模块
Published
5 full routes (up to)
5 branches per step (up to)
5 steps per route (up to)
Don't Stop at commercial building blocks
50% yield per step (assumed, if not published)
Edit
Clear
Cancel
Synthesize
Feedback

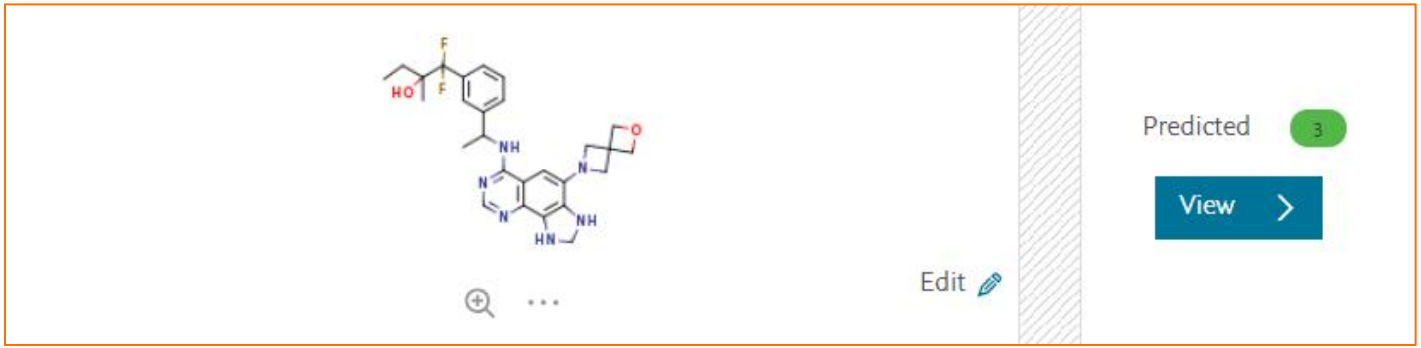
参数设置：详细功能设定



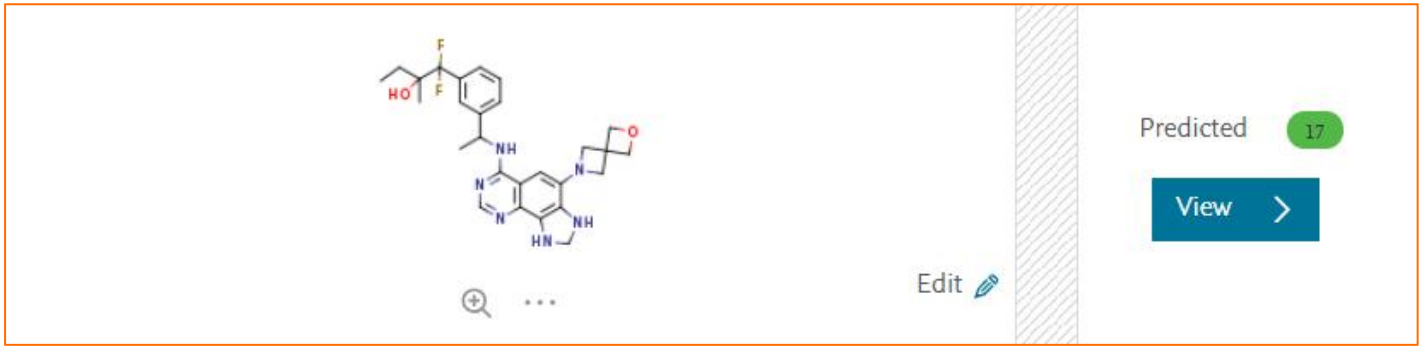


1. 预测20条全路线，还是最后一步
2. 多样性设置，相同的步骤最多出现在几条线路中，相同BB最多出现在几条线路中
3. 时长，15min、30min
4. BB源头的设置

Reaxys AI逆合成后的结果（不同参数设置，结果不一样）

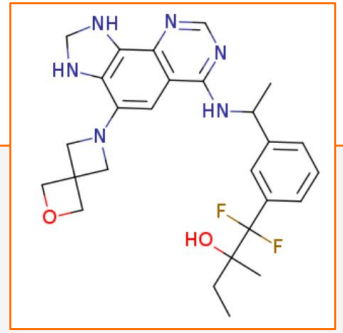


全线路3条

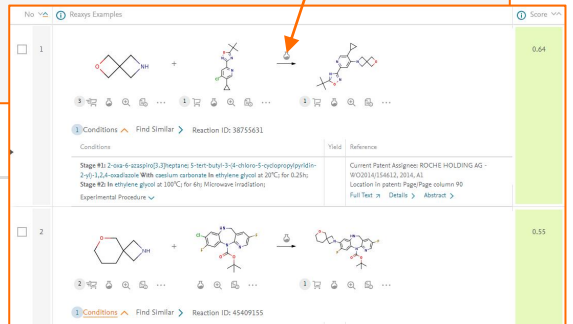


最后一步17条

一条完整的线路



倒推到原料可购买(或容易获取）且全部提供参考路线条件



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Agenda

- Reaxys的底层逻辑和发展方向
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  - Reaxys中的文献与专利的获取
  - Reaxys中物质理化性质的获取，反向应用，可视化分析
  - Reaxys中化合物活性数据在先导化合物优化方面的应用
  - Reaxys中结构面板与反应数据的获取
  - Reaxys中的AI逆合成模块介绍
- 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
- 多种途径的Elsevier Life Science网络社区服务：
  - B站：ELS生命科学，提供Elsevier Life Science数据库的使用视频
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