



Reaxys中的化学信息检索

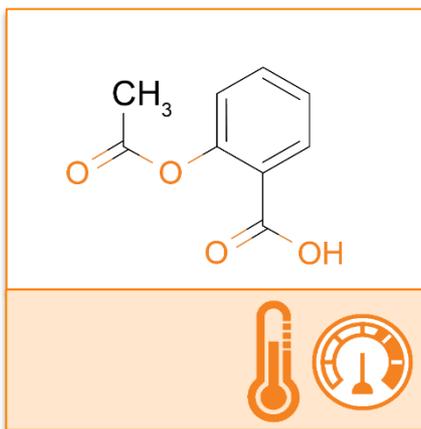
俞靓

Elsevier生命科学产品客户顾问

提纲

- Reaxys数据库的介绍与更新
- Reaxys数据库与同类数据库的比较
 - 索引内容比较
 - 可检索性比较
- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

什么是Reaxys?



>110 M 物质记录
>500 M 实验数据
物理的, 化学的, 光谱
数据, 生态学, 生物活
性数据

Chemistry fundamentals



>47M 反应记录
以及这些反应的条件,
溶剂, 催化剂, 收率,
反应中心, 反应类型


Linked
to



>57 M 文献记录
>16,000 期刊, 专利
涉及有机化学, 材料化学,
生物医药, 地球科学, 工
程等多种领域

**Uses across
disciplines**

Reaxys更新—Auto Suggest自动弹出建议词条

- Quick Search中输入Key Word检索，会自动弹出建议的词语。
- 使用建议词语检索，可以自动添加一些相关概念，用于获得全面结果

The image illustrates the Reaxys search interface. On the left, a search box contains the text "suzuki". Below it, a dropdown menu lists suggested search terms under the heading "Concepts". The terms are: "suzuki", "suzuki (kyodai) nitration", "suzuki coupling", "suzuki cross coupling", "suzuki reaction" (highlighted with a red underline), "suzuki synthesis", "suzuki-miyaura", "suzuki-miyaura coupling", "suzuki-miyaura reaction", and "suzuki-miyaura synthesis". An orange arrow points from the highlighted "suzuki reaction" term to a second search box on the right. This second search box shows the search term updated to "\"suzuki reaction\"". Below the search box, the word "AND" is displayed. At the bottom of the search box, there is a button with a chemical structure icon and the text "Create Structure or Reaction Drawing".

Reaxys更新—优化检索结果集界面

- 预览结果界面优化
- 当前界面可直接返回Quick Search界面，进行检索式修改

直接当前页面返回Quick Search页面进行检索式修改

The screenshot shows the Reaxys search results page for 'suzuki reaction'. The top navigation bar includes 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. A 'Register' button and 'Sign in' link are on the right. Below the navigation, there are 'New' and 'Edit' icons. The main content area displays two result types: 'Reactions' (3,500 results) and 'Documents' (22,448 results). Each result type has a 'View Results' button and a 'Create Alert' button. An orange arrow points to the 'Edit' icon in the top left, and another orange arrow points to the 'Documents' result type icon.

Result Type	Count	Condition	Actions
Reactions	3,500	Condition : suzuki reaction	Preview Results, View Results, Edit in Query Builder, Create Alert
Documents	22,448	Titles, Abstracts, Keywords : suzuki reaction	Preview Results, View Results, Edit in Query Builder, Create Alert

新增结果类型图标，对结果类型的呈现更为直观

反应结果集检索结果

Reaxys® Quick search Query builder ^{new} Results Synthesis planner History Register > Sign in ?

3,500 Filters and Analysis 3,500 Reactions out of 4,438 Documents containing 5,369 Substances, 853 Targets

By Structure 0 Limit To Exclude Export Syn-Plan No of References ↓

Yield Reaction ID: 4033276

Reagent/Catalyst

Solvent

Catalyst Classes

Solvent Classes

Product Availability 50 Hits 1,299 Conditions Find Similar >

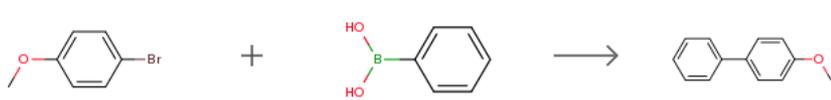
Reactant Availability

Reaction Classes

Document Type

Publication Year

Single step reactions only



Yield	Conditions	References
100%	With [PdCl ₂ (2-ethyl-2-oxazoline) ₂]; potassium carbonate In toluene at 110°C; for 3h; Suzuki reaction;	Gossage, Robert A.; Jenkins, Hilary A.; Yadav, Paras N. - Tetrahedron Letters, 2004, vol. 45, # 41, p. 7689 - 7691 Full Text ↗ Cited 78 times ↗ Details > Abstract >
99%	With 1,8-diazabicyclo[5.4.0]undec-7-ene; palladium diacetate In ethanol; water at 20 - 150°C; Suzuki reaction; microwave irradiation;	Chanthavong, Florine; Leadbeater, Nicholas E. - Tetrahedron Letters, 2006, vol. 47, # 12, p. 1909 - 1912 Full Text ↗ Cited 45 times ↗ Details > Abstract >
99%	With sodium carbonate; polystyrene-supported N-heterocyclic carbene-Pd catalyst In N,N-dimethyl-formamide at 20°C; for 24h; Suzuki reaction;	Kang, Tairan; Feng, Qiang; Luo, Meiming - Synlett, 2005, # 15, p. 2305 - 2308 Full Text ↗ Cited 66 times ↗ Details > Abstract >

Reaxys更新—新增Chemdraw JS结构面板

- 结构面板进入后，可以选择Chemdraw JS结构面板

The screenshot displays the Reaxys web interface. At the top, there are navigation links: "Quick search", "Query builder ^{new}", "Results", "Synthesis planner", and "History". On the right side, there are buttons for "Register >" and "Sign in ?". The main area is the "Structure editor", which has a title bar "ChemAxon's MarvinJS" and a "Create structure template from name >" button. A dropdown menu is open, showing two options: "ChemAxon's MarvinJS" (selected) and "PerkinElmer's ChemDraw JS". An orange arrow points to the "PerkinElmer's ChemDraw JS" option. Below the dropdown, the text "下拉菜单选择ChemDraw JS" is written. The central workspace shows the "Marvin JS by ChemAxon" logo. On the right, there is a "Search this structure as:" panel with various search options like "As drawn", "As substructure", "Similar", "Tautomers", "Stereo", "Additional ring closures", "Related Markush", "Salts", "Mixtures", "Isotopes", "Charges", "Radicals", and "More options". At the bottom, there are buttons for "Clear", "Cancel", and "Transfer to query".

提纲

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工具类数据库的核心—数据库索引体系的建立



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Bioorganic &
Medicinal
Chemistry

New homocamptothecins: Synthesis, antitumor activity, and molecular modeling

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Abstract—Homocamptothecins (hCPTs) represent a class of new emerging antitumor agents, which contains a seven-membered β -hydroxylactone in place of the conventional six-membered α -hydroxylactone ring (E ring) of camptothecins. Some novel 7-substituted hCPTs were designed and synthesized based on a newly developed synthetic route which couples ring A with ring C, E and D. Most of the synthesized compounds exhibit very high cytotoxic activity on tumor cell line A549. Some compounds, such as **9b**, **9l**, and **9y**, show broad in vitro antitumor spectrum and are more potent than topotecan. Three-dimensional quantitative structure-activity relationship (3D-QSAR) methods, CoMFA and CoMSIA, were applied to explain the structure-activity relationship (SAR) of the synthesized compounds. Furthermore, molecular docking was used to clarify the binding mode of the synthesized compounds to human DNA topoisomerase I. The important hydrophobic, base-pair stacking, and hydrogen-bonding interactions were observed between the hCPT derivatives and their receptor. The results from molecular modeling will guide the design of novel hCPTs with higher antitumor activity.
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1. Introduction

Camptothecin (CPT) was first isolated from the Chinese tree *Camptotheca acuminata* by Wall et al. in 1966.¹ The compound exhibits potent antitumor activity and has been evaluated in clinic.² However, the therapeutic application of unmodified CPT is hindered due to its poor aqueous solubility and high in vivo hepatotoxicity. Subsequently, the structural modification of natural CPT has generated many new CPT derivatives with improved pharmacological or pharmacokinetic profile.^{3–5} Among those, topotecan⁶ and irinotecan⁷ (Chart 1) have entered clinical use and several drug candidates, such as rubitecan,⁸ lurtotecan,⁹ and exatecan,¹⁰ are currently in different stages of the clinical trials.

Human DNA topoisomerase I (Topo I) is the molecular target of CPT derivatives.¹¹ These compounds act by binding to a transient Topo I-DNA covalent complex, leading to an accumulation of DNA strand breaks upon replication, ultimately causing cell death during the S phase of the cell cycle.^{12–14} Although CPT analogues remain a promising class of antitumor agents, the intrinsic instability of the highly electrophilic α -hydroxylactone of the E ring undergoes rapid hydrolysis to the biologically inactive carboxylate form under physiological conditions.¹⁵ This chemical feature diminishes efficacy of various CPT derivatives in vivo compared to the spectacular results often obtained from in vitro studies and xenograft models.¹⁶ Thus, extensive efforts have been put to synthesize new CPT analogues with a prolonged biological life maintaining its active lactonic form. In 1997, Lavergne et al. reported the insertion of a methylene spacer between alcohol and carboxyl functions of CPT to obtain homocamptothecin (hCPT).¹⁷ The replacement of the six-membered α -hydroxylactone with a seven-membered β -hydroxylactone reduces considerably the electrophilicity of the lactone and hence decreases the rate of lactone hydrolysis to the

Keywords: Homocamptothecins; Antitumor activity; 3D-QSAR; Molecular docking.

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† These two authors contributed equally to this work.

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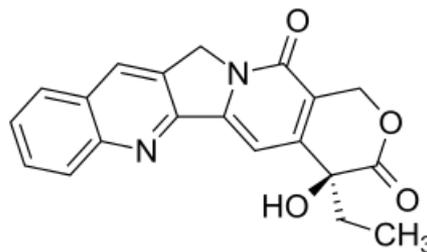
Tips:

这是一篇讲述喜树碱衍生物及其合成，分子模型的文献，我们从全文中的关键内容和检索性便捷性的角度去比较 Reaxys 和其他数据库的区别

文献中的包含的:

题录，摘要，作者，发表时间，期刊名称……

Camptothecin

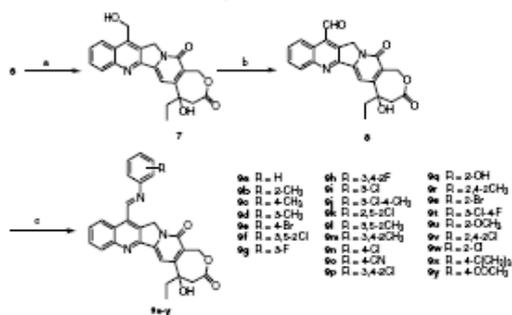


一篇全文期刊中的中的内容—与结构有关的内容

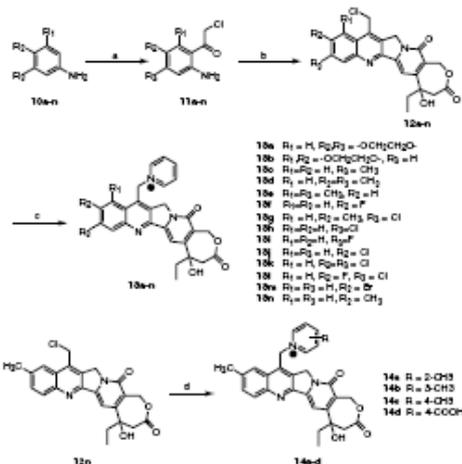
文献中包含的内容:

反应, 结构, 反应条件(溶剂, 催化剂, 产率, 实验过程, 时间, 温度, 压力, 反应类型文字描述, 机理研究等)

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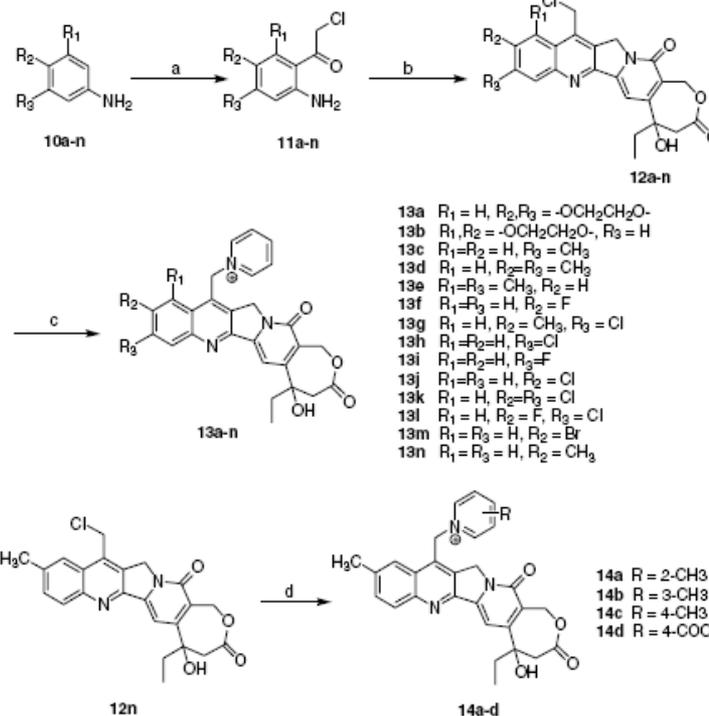
Scheme 2. Reagents and conditions: (a) H₂O₂, CH₃OH, Pd/Cq (7H₂O), rt, 14 h, 64.7%; (b) CH₂COOH, 130 °C, 5h, 52.7%; (c) substituted aniline, rt, 10–24 h, 14.5–30.7%.



Scheme 3. Reagents: (a) BCl₃; (b) *p*-TSA; (c) pyridine, DMSO; (d) substituted pyridine, DMSO.

7-iminomethyl hCPTs (Table 2). Most compounds are more sensitive against A549 cell line than LOVO and MCF-7 with their IC₅₀ values in the range of 19.6 μM to 7 nM. Only 13a is more potent than topotecan with the IC₅₀ value against A549 lower than 0.2 nM. For

A549 cell line, the antitumor activity was increased when A-ring was substituted with a methyl group. However, the pyridyl group of C-7 is suitable to be unsubstituted because the incorporation of the methyl or carboxyl group could lead to a decrease



一篇全文期刊中的中的内容—实验数据（物理化学数据）

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¹H, *J* = 8.5 Hz), 9.00 (d, 1H, *J* = 8.5 Hz), 9.71 (s, 1H). MS (ESI): 522 (M+H)⁺. Anal. Calcd for C₂₃H₂₁N₃O₄: C, 73.68; H, 5.99; N, 8.06. Found C, 73.81; H, 5.98; N, 8.03.

5.1.32. 7-(4-Acetyloxyphenyl)homocamptothecin (9b). The titled compound was prepared from 8 and 1-(4-amino-phenyl)-ethanone according to the method of compound 9a. yield: 15.4%. ¹H NMR (DMSO-*d*₆): 0.89 (t, 3H, *J* = 7.3 Hz), 1.88 (q, 2H, *J* = 8.2 Hz), 2.65 (s, 9H), 3.08–3.48 (q, 2H, *J* = 12.4 Hz), 5.42–5.55 (q, 2H, *J* = 15.2 Hz), 5.61 (s, 2H), 6.06 (s, 1H), 7.46 (s, 1H), 7.65 (d, 2H, *J* = 8.0 Hz), 7.86 (t, 1H, *J* = 7.4 Hz), 7.91 (t, 1H, *J* = 7.4 Hz), 8.13 (d, 2H, *J* = 8.0 Hz), 8.30 (d, 1H, *J* = 8.5 Hz), 9.02 (d, 1H, *J* = 8.5 Hz), 9.74 (s, 1H). MS (ESI): 508 (M+H)⁺. Anal. Calcd for C₂₀H₁₇N₃O₆: C, 68.82; H, 4.81; N, 8.03. Found C, 68.99; H, 4.81; N, 8.00.

5.1.33. 10,11-(Methylenedioxy)-7-(pyridiniummethyl)homocamptothecin chloride (13a). A 1 L flask was charged with dry methylene chloride (50 mL) and 1,4-benzodioxan-6-amine (1.5 g, 10 mmol) and was cooled to 0 °C followed by slow addition of a 1 M solution of boron trichloride in methylene chloride solution (40 mL) while maintaining an internal temperature at or below 10 °C under N₂. Aluminum chloride (1.3 g, 10 mmol) was added quickly in three portions followed by addition of chloroacetonitrile (0.7 mL, 11 mmol). The reaction mixture was stirred for 30 min at 0 °C and then heated to reflux for 16 h. The reaction mixture was allowed to cool to room temperature and then was quenched into a mixture of ice (100 g)/2 N HCl (50 mL). The aqueous layer was extracted by methylene chloride (100 mL). The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure, and the residue was purified by chromatography over silica gel (2% MeOH/CH₂Cl₂) to give 2-amino-2-chloro-4-*N*-(methylenedioxy)acetophenone (11a) as a yellow solid. 0.45 g (35.2%). ¹H NMR (DMSO-*d*₆): 4.22–4.24 (m, 2H), 4.34–4.36 (m, 2H), 4.75 (s, 2H), 6.22 (s, 1H), 6.87 (s, 1H). MS (ESI): 228 (M+H)⁺.

A solution of 11a (0.25 g, 1.1 mmol) and tricyclic ketone 5 (0.28 g, 1.0 mmol) in toluene (85 mL) was refluxed using a Dean–Stark trap for 30 mins. *p*-Toluenesulfonic acid (0.03 g) was then added and refluxing was continued for an additional 1 h. The solution was allowed to cool to room temperature and the solid was filtered off and washed by acetone (20 mL) and methanol (20 mL) to give 10,11-(methylenedioxy)-7-(chloromethyl)-homocamptothecin (12a) as yellow solid; yield 0.38 g (80.6%). ¹H NMR (DMSO-*d*₆): 0.88 (t, 3H, *J* = 7.0 Hz), 1.90 (q, 2H, *J* = 8.1 Hz), 3.06–3.46 (q, 2H, *J* = 14.0 Hz), 4.45–4.47 (m, 4H), 5.28–5.37 (m, 4H), 5.40–5.54 (q, 2H, *J* = 15.4 Hz), 6.04 (s, 1H), 7.33 (s, 1H), 7.57 (s, 1H), 7.75 (s, 1H). MS (ESI): 470 (M+H)⁺.

10,11-(Methylenedioxy)-7-(chloromethyl)-homocamptothecin 12a (47 mg, 0.1 mmol) was added to anhydrous pyridine (1 mL) and DMSO (2 mL) at 50 °C. This was stirred for 12 h before the addition of diethyl

ether (1 mL) which precipitated the desired product. The yellow solid was filtered off and washed once with ethanol (2 mL) and twice with diethyl ether (5 mL) to afford 13a as a yellow solid; yield 19 mg (34.7%). ¹H NMR (DMSO-*d*₆): 0.86 (t, 3H, *J* = 7.1 Hz), 1.86 (q, 2H, *J* = 8.1 Hz), 3.05–3.51 (q, 2H, *J* = 13.8 Hz), 4.25–4.41 (m, 4H), 5.36 (s, 2H), 5.38–5.52 (q, 2H, *J* = 14.8 Hz), 6.04 (s, 1H), 6.45 (q, 2H, *J* = 14.9 Hz), 7.39 (s, 1H), 7.57 (s, 1H), 7.65 (s, 1H), 8.13 (q, 2H, *J* = 7.1 Hz), 8.62 (t, 1H, *J* = 7.5 Hz), 9.06 (d, 2H, *J* = 5.9 Hz). MS (ESI): 512 (M⁺). Anal. Calcd for C₂₀H₁₆ClN₃O₄: C, 63.56; H, 4.78; N, 7.67. Found C, 63.79; H, 4.77; N, 7.65.

5.1.34. 9,10-(Methylenedioxy)-7-(pyridiniummethyl)homocamptothecin chloride (13b). The titled compound was prepared according to the method of compound 13a. yield: 39.0%. ¹H NMR (DMSO-*d*₆): 0.88 (t, 3H, *J* = 7.3 Hz), 1.87 (q, 2H, *J* = 8.1 Hz), 3.06–3.52 (q, 2H, *J* = 13.8 Hz), 4.34–4.26 (m, 4H), 5.41–5.51 (q, 2H, *J* = 15.1 Hz), 5.51 (s, 2H), 6.07 (s, 1H), 6.41 (q, 2H, *J* = 14.7 Hz), 7.41 (s, 1H), 7.50 (d, 1H, *J* = 7.5 Hz), 7.78 (d, 1H, *J* = 7.5 Hz), 8.07 (t, 2H, *J* = 7.2 Hz), 8.59 (t, 1H, *J* = 7.5 Hz), 9.03 (d, 2H, *J* = 6.0 Hz). MS (ESI): 512 (M⁺). Anal. Calcd for C₂₀H₁₆ClN₃O₄: C, 63.56; H, 4.78; N, 7.67. Found C, 63.75; H, 4.78; N, 7.66.

5.1.35. 11-Methyl-7-(pyridiniummethyl)-homocamptothecin chloride (13c). The titled compound was prepared according to the method of compound 13a. yield: 40.4%. ¹H NMR (DMSO-*d*₆): 0.88 (t, 3H, *J* = 7.2 Hz), 1.87 (q, 2H, *J* = 8.1 Hz), 2.56 (s, 3H), 3.07–3.51 (q, 2H, *J* = 13.9 Hz), 5.38–5.53 (q, 2H, *J* = 15.3 Hz), 5.41 (s, 2H), 6.08 (s, 1H), 6.55 (q, 2H, *J* = 14.6 Hz), 7.45 (s, 1H), 7.59 (d, 1H, *J* = 7.3 Hz), 8.03 (d, 1H, *J* = 7.5 Hz), 8.05 (s, 2H), 8.12 (t, 2H, *J* = 7.4 Hz), 8.62 (t, 1H, *J* = 7.4 Hz), 9.09 (d, 2H, *J* = 6.0 Hz). MS (ESI): 468 (M⁺). Anal. Calcd for C₂₀H₁₈ClN₃O₄: C, 66.73; H, 5.20; N, 8.34. Found C, 66.55; H, 5.21; N, 8.36.

5.1.36. 9,11-Dimethyl-7-(pyridiniummethyl)-homocamptothecin chloride (13d). The titled compound was prepared according to the method of compound 13a. yield: 45.6%. ¹H NMR (DMSO-*d*₆): 0.87 (t, 3H, *J* = 7.4 Hz), 1.87 (q, 2H, *J* = 8.1 Hz), 2.48 (s, 3H), 2.47 (s, 3H), 3.06–3.51 (q, 2H, *J* = 13.7 Hz), 5.38 (s, 2H), 5.40–5.52 (q, 2H, *J* = 15.1 Hz), 6.07 (s, 1H), 6.52 (q, 2H, *J* = 14.7 Hz), 7.43 (s, 1H), 7.94 (s, 1H), 8.04 (s, 1H), 8.13 (t, 2H, *J* = 7.3 Hz), 8.62 (t, 1H, *J* = 7.4 Hz), 9.10 (d, 2H, *J* = 6.1 Hz). MS (ESI): 482 (M⁺). Anal. Calcd for C₂₂H₂₀ClN₃O₄: C, 67.34; H, 5.45; N, 8.11. Found C, 67.43; H, 5.44; N, 8.13.

5.1.37. 9,11-Dimethyl-7-(pyridiniummethyl)-homocamptothecin chloride (13e). The titled compound was prepared according to the method of compound 13a. yield: 41.5%. ¹H NMR (DMSO-*d*₆): 0.87 (t, 3H, *J* = 7.4 Hz), 1.87 (q, 2H, *J* = 8.3 Hz), 2.51 (s, 3H), 2.58 (s, 3H), 3.05–3.51 (q, 2H, *J* = 13.7 Hz), 5.27 (s, 2H), 5.40–5.52 (q, 2H, *J* = 15.1 Hz), 6.07 (s, 1H), 6.59 (q, 2H, *J* = 14.8 Hz), 7.43 (s, 1H), 7.96 (s, 1H), 8.14 (t, 2H, *J* = 7.5 Hz), 8.64 (t, 1H, *J* = 7.4 Hz), 8.93 (d, 2H, *J* = 6.2 Hz). MS (ESI): 482 (M⁺). Anal. Calcd for

文献中包含的内容:

文献中提到了很多化合物以及这些化合物的谱图数据，还有这个化合物的晶型描述，化合物在文献中的标识符

A solution of 11a (0.25 g, 1.1 mmol) and tricyclic ketone 5 (0.28 g, 1.0 mmol) in toluene (85 mL) was refluxed using a Dean–Stark trap for 30 mins. *p*-Toluenesulfonic acid (0.03 g) was then added and refluxing was continued for an additional 1 h. The solution was allowed to cool to room temperature and the solid was filtered off and washed by acetone (20 mL) and methanol (20 mL) to give 10,11-(methylenedioxy)-7-(chloromethyl)-homocamptothecin (12a) as yellow solid; yield 0.38 g (80.6%). ¹H NMR (DMSO-*d*₆): 0.88 (t, 3H, *J* = 7.0 Hz), 1.90 (q, 2H, *J* = 8.1 Hz), 3.06–3.46 (q, 2H, *J* = 14.0 Hz), 4.45–4.47 (m, 4H), 5.28–5.37 (m, 4H), 5.40–5.54 (q, 2H, *J* = 15.4 Hz), 6.04 (s, 1H), 7.33 (s, 1H), 7.57 (s, 1H), 7.75 (s, 1H). MS (ESI): 470 (M+H)⁺.

一篇全文期刊中的中的内容—实验数据（生物活性数据）

文献中包含的内容:

大量的不同结构对应的实验数据（生物活性数据）

Z. Miao et al. / *Bioorg. Med. Chem.* 16 (2008) 1493–1510 1497

Table 1. In vitro antitumor activity of 7-aryliminomethyl hCPT derivatives

Compound	IC ₅₀ (μM)		
	A-549	LOVO	MCF-7
7	0.017	0.050	4.33
8	0.026	0.024	3.55
9a	0.002	0.014	0.488
9b	<0.0002	0.0008	0.517
9c	0.038	0.035	5.882
9d	0.093	0.125	20.855
9e	0.002	0.011	2.324
9f	0.828	0.533	9.291
9g	0.0008	0.014	9.245
9h	0.003	0.023	0.441
9i	5.822	5.192	>20
9j	0.013	0.020	1.344
9k	0.226	0.381	6.621
9l	<0.0002	<0.0002	0.003
9m	0.0006	0.007	0.559
9n	<0.0002	0.0004	2.000
9o	0.538	0.368	25.994
9p	0.0009	0.032	6.847
9q	<0.0002	0.002	20.768
9r	13.926	10.729	20.259
9s	<0.0002	0.018	0.035
9t	<0.0002	0.040	0.492
9u	<0.0002	0.015	2.765
9v	0.0009	0.060	3.943
9w	<0.0002	0.003	1.154
9x	0.002	0.021	0.853
9y	<0.0002	<0.0002	0.852
Topotecan	0.005	0.036	0.488
Irinotecan	6.528	9.015	17.403

Table 2. In vitro antitumor activity of 7-substituted pyridine quaternary-salt hCPT derivatives

Compound	IC ₅₀ (μM)		
	A-549	LOVO	MCF-7
13a	1.122	>19.51	>19.51
13b	2.017	>19.51	>19.51
13c	2.391	>21.34	>21.34
13d	0.313	>20.72	>20.72
13e	0.290	>20.72	>20.72
13f	0.381	>21.16	>21.16
13g	0.007	7.08	>19.88
13h	18.282	>20.45	>20.45
13i	2.850	>21.16	>21.16
13j	3.49	9.039	>20.45
13k	19.608	>19.11	>19.11
13l	>19.73	>19.73	>19.73
13m	0.729	7.912	>18.75
13n	<0.0002	3.543	6.937
14a	5.015	9.318	>20.72
14b	2.072	>20.72	>20.72
14c	2.114	>20.72	>20.72
14d	7.316	>19.51	>19.51
Topotecan	0.005	0.036	0.488
Irinotecan			

of antitumor activity. Although the in vitro cytotoxicities of these water soluble hCPTs are not very satisfying, we expect that the in vivo studies of these compounds can provide some hints for the future inhibitor design.

3.3. In vivo antitumor activity

For most antitumor agents, their in vivo activity usually does not correlate well with their in vitro data. Thus, a preliminary in vivo screening of the synthesized compounds against C26 colon cancer model was performed (data not shown). Compounds 9j and 13j were found to be good candidates, which were selected for further detail in vivo studies. Dose-effect relationship studies revealed that the tumor growth inhibition rate of compounds 9j and 13j was increased with the addition of their dose. At the dose of 4 mg/kg, compounds 9j and 13j achieved tumor growth inhibition rate of 30.99% and 36.21%, respectively, which was almost equivalent to that of TPT at a dose of 1 mg/kg (Table 3). It is worth noting that when the dose of TPT was added to 1.5 mg/kg, all the mice in the group died after the treatment, while all the mice in the group of compounds 9j and 13j at the dose of 4 mg/kg remained alive. According to this, compounds 9j and 13j may be safer than TPT, although they were less effective than TPT at the same dosage. Further pharmacological and toxicological evaluation of these two compounds is in progress.

3.4. 3D-QSAR

A data set to perform the FA¹⁶ and t analysis (Co bust 3D-QSAR such as grid erred during t suits were o values. It ha fields are not dependenc tistical signi SAMPLS w SIA fields w by the com (Fig. 2). The field, indicat and the hydr other two t hydrogen at gen-bond as model (g_{max} ² of 0.90541 of q² of 0.701 FA and Co viewpoint o predictiveab uated which the compos values (Tabl set of six pre (compounds ability of th that the bio also predicte

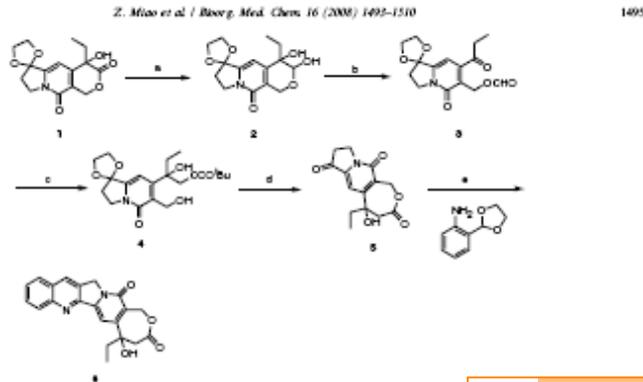
Table 1. In vitro antitumor activity of 7-aryliminomethyl hCPT derivatives

Compound	IC ₅₀ (μM)		
	A-549	LOVO	MCF-7
7	0.017	0.050	4.33
8	0.026	0.024	3.55
9a	0.002	0.014	0.488
9b	<0.0002	0.0008	0.517
9c	0.038	0.035	5.882
9d	0.093	0.125	20.855
9e	0.002	0.011	2.324
9f	0.828	0.533	9.291
9g	0.0008	0.014	9.245
9h	0.003	0.023	0.441
9i	5.822	5.192	>20
9j	0.013	0.020	1.344
9k	0.226	0.381	6.621
9l	<0.0002	<0.0002	0.003
9m	0.0006	0.007	0.559
9n	<0.0002	0.0004	2.000
9o	0.538	0.368	25.994
9p	0.0009	0.032	6.847
9q	<0.0002	0.002	20.768
9r	13.926	10.729	20.259
9s	<0.0002	0.018	0.035

Table 2. In vitro antitumor activity of 7-substituted pyridine quaternary-salt hCPT derivatives

Compound	IC ₅₀ (μM)		
	A-549	LOVO	MCF-7
13a	1.122	>19.51	>19.51
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13g	0.007	7.08	>19.88
13h	18.282	>20.45	>20.45
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13j	3.49	9.039	>20.45
13k	19.608	>19.11	>19.11
13l	>19.73	>19.73	>19.73
13m	0.729	7.912	>18.75
13n	<0.0002	3.543	6.937
14a	5.015	9.318	>20.72
14b	2.072	>20.72	>20.72
14c	2.114	>20.72	>20.72
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Topotecan	0.005	0.036	0.488
Irinotecan	6.528	9.015	17.403

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Scheme 1. Reagents and conditions: (a) KH_2 , CH_2OH , π , 20 min, 80%; (b) CH_2COOH , $NaIO_4$, rt, 30 min, 75°C, 5h, 97%; (c) CF_3COOH , π , 10 h, 94%; (d) toluene, *p*-TSA, 130°C, 1.5h, 80%.

7-Hydroxymethylhomocamtptotecin **7** could be obtained by the reaction of **6** with hydrogen peroxide and methanol. The hydroxymethyl group was oxidized to form 7-formylhomocamtptotecin **8**, which was allowed to react with different substituted anilines to generate the corresponding derivatives **9a–y** (Scheme 2).

Various 1-(2-amino substituted phenyl)-2-chloro-ethanones **10a–n** were obtained by reacting substituted anilines **10a–n** with chloroacetonitrile under the catalysis of BCl_3 , which were treated with the intermediate **5** to give the 7-chloromethylhomocamtptotecin A ring substituted derivatives **13a–n** (Scheme 3). Compounds **13a–n** reacted with the substituted pyridines to afford quaternary-salt derivatives **13a–n** and **14a–d**.

3. Results and discussion

3.1. 7-Aryliminomethyl hCPT derivatives

Numerous reports indicated that the CPT derivatives with substitutions at quinoline (A/B) ring,³ especially at C-7, C-9, and C-10, are of great interest and several good drug candidates (such as exatecan, hirtotecan, and silatocan) are under clinical trials. The importance of the lipophilic groups linked to position 7 of camptotecin has been demonstrated to increase inhibitor intracellular uptake and cytotoxic activities.³² The crystal structures of Topo I-DNA in complex with topotecan and CPT^{33,34} also revealed that the substituents on C-7 were located into the major groove of DNA and they could reinforce the stability of the inhibitor-Topo I-DNA covalent complex. Moreover, some 7-aryliminomethyl CPT analogues have shown good in vitro antitumor activity.³⁵ Therefore, we designed and synthesized a series of 7-aryliminomethyl hCPT derivatives. The so-

lid tumor cell lines, A-549 (for non-small cell lung cancer), LOVO (for colon cancer), and MCF-7 (for breast cancer), were chosen for testing the in vitro antitumor activities of the 7-aryliminomethyl hCPT derivatives. Topotecan and irinotecan were used as the reference compounds. The inhibitory activities suggested that the arylimino-methyl group in the 7-position can promote antitumor activity. These results revealed that the compounds were more sensitive against A-549 and LOVO cell lines than against MCF-7 cell line (Table 1), which is consistent with the clinical behavior of CPT derivatives.³⁵ For A-549 cell line, most compounds showed high inhibitory activities with the IC_{50} values lower than 0.2 nM, which were lower than 0.2 nM. In the most promising compounds, the inhibitory activities were lower than 0.2 nM. In the most promising compounds, the inhibitory activities were lower than 0.2 nM. In the most promising compounds, the inhibitory activities were lower than 0.2 nM.

3.2. Water soluble hCPT derivatives

The clinical success of the topotecan and irinotecan has demonstrated the importance of new water soluble CPT derivatives, which has become a major research field. We designed and synthesized a series of 7-aryliminomethyl hCPT derivatives in this study. The toxicity evaluations indicated that the hCPTs were less active than

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lid tumor cell lines, A-549 (for non-small cell lung cancer), LOVO (for colon cancer), and MCF-7 (for breast cancer), were chosen for testing the in vitro antitumor activities of the 7-aryliminomethyl hCPT derivatives. Topotecan and irinotecan were used as the reference compounds. The inhibitory activities suggested that the arylimino-methyl group in the 7-position can promote antitumor activity. These results revealed that the compounds were more sensitive against A-549 and LOVO cell lines than against MCF-7 cell line (Table 1), which is consistent with the clinical behavior of CPT derivatives.³⁵ For A-549 cell line, most compounds showed high inhibitory activities with the IC_{50} values

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EMTREE drug term: 10 methyl 11 chloro 7 (pyridiniummethyl)homocamptothecin chloride, 7 (2 bromophenyl)iminomethylhomocamptothecin, 7 (2 hydroxyphenyl)iminomethylhomocamptothecin, 7 (2 methoxyphenyl)iminomethylhomocamptothecin, 7 (2 methylphenyl)iminomethylhomocamptothecin, 7 (2,4 dichlorophenyl)iminomethylhomocamptothecin, 7 (2,4 dimethylphenyl)iminomethylhomocamptothecin, 7 (2,5 dichlorophenyl)iminomethylhomocamptothecin, 7 (3 chloro 4 fluorophenyl)iminomethylhomocamptothecin, 7 (3 chloro 4 methylphenyl)iminomethylhomocamptothecin, 7 (3 chlorophenyl)iminomethylhomocamptothecin, 7 (3 fluorophenyl)iminomethylhomocamptothecin, 7 (3 methylphenyl)iminomethylhomocamptothecin, 7 (3,4 dichlorophenyl)iminomethylhomocamptothecin, 7 (3,4 difluorophenyl)iminomethylhomocamptothecin, 7 (3,4 dimethylphenyl)iminomethylhomocamptothecin, 7 (3,5 dichlorophenyl)iminomethylhomocamptothecin, 7 (3,5 dimethylphenyl)iminomethylhomocamptothecin, 7 (4 bromophenyl)iminomethylhomocamptothecin, 7 (4 chlorophenyl)iminomethylhomocamptothecin, 7 (4 cyanophenyl)iminomethylhomocamptothecin, 7 (4 methylphenyl)iminomethylhomocamptothecin, 7 formylhomocamptothecin, 7 hydroxymethylhomocamptothecin, 7 phenyliminomethylhomocamptothecin, antineoplastic agent, camptothecin derivative, irinotecan, topotecan, unclassified drug

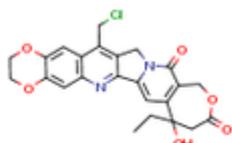
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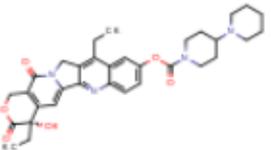
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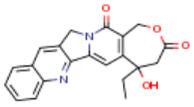
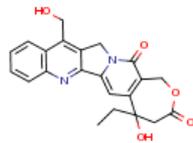
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5.04	IC50	=	9.015	μM	LoVo	Miao, Zhenyuan; Sheng, Chunquan; Zhang, Wannian; Ji, Haitao; Zhang, Jing; Shao, Luecheng; You, Liang; Zhang, Min; Yao, Jianzhong; Che, Xiaoyin - Bioorganic and Medicinal Chemistry, 2008, vol. 16, # 3, p. 1493 - 1510 Full Text ↗ Cited 24 times ↗ Details > Abstract >
4.76	IC50	=	17.403	μM	MCF7	Miao, Zhenyuan; Sheng, Chunquan; Zhang, Wannian; Ji, Haitao; Zhang, Jing; Shao, Luecheng; You, Liang; Zhang, Min; Yao, Jianzhong; Che, Xiaoyin - Bioorganic and Medicinal Chemistry, 2008, vol. 16, # 3, p. 1493 - 1510 Full Text ↗ Cited 24 times ↗ Details > Abstract >

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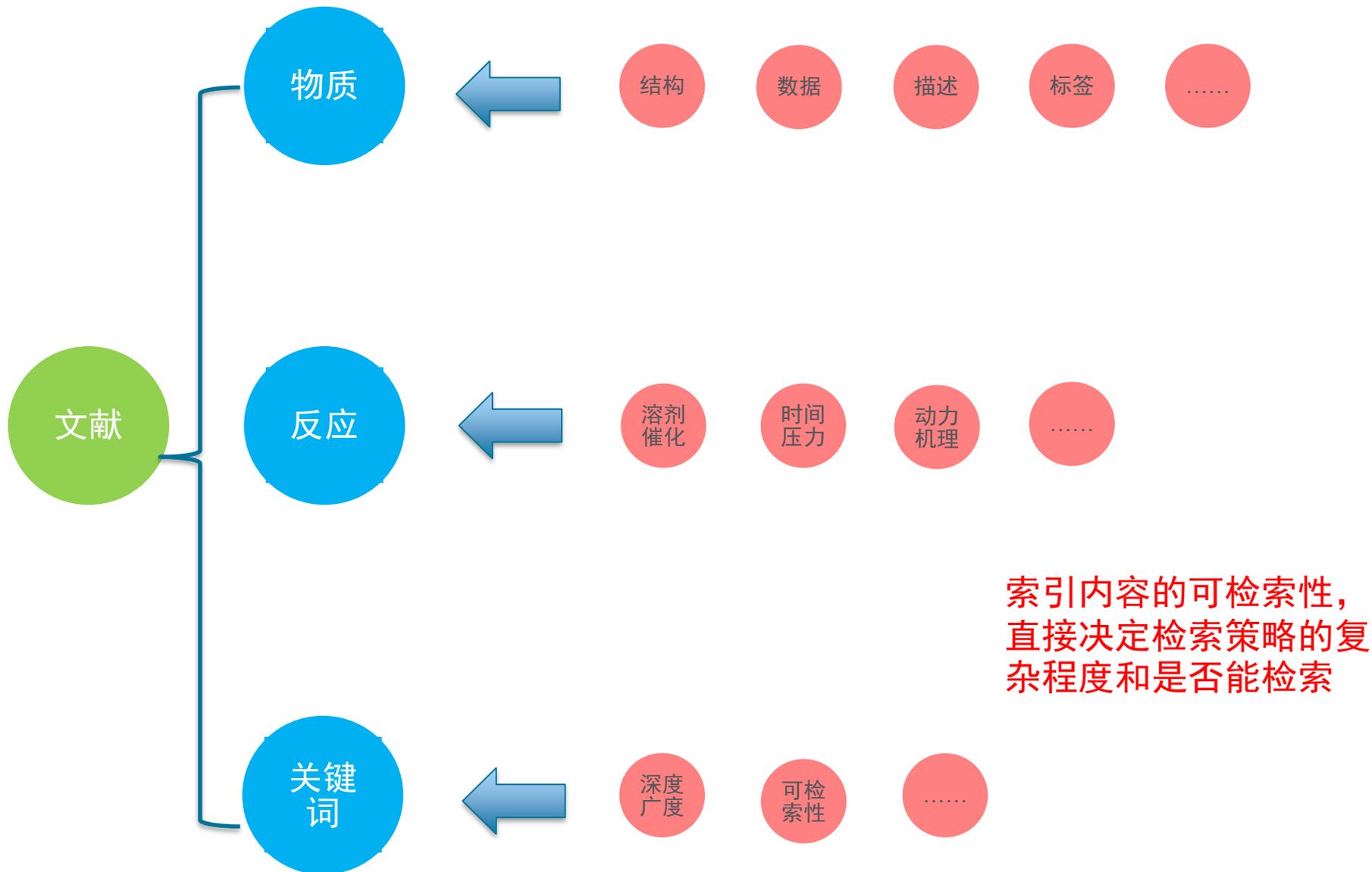
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64.7%	With sulfuric acid; dihydrogen peroxide; iron(II) sulfate In water at 20°C; for 14h;	Miao, Zhenyuan; Sheng, Chunquan; Zhang, Wannian; Ji, Haitao; Zhang, Jing; Shao, Luecheng; You, Liang; Zhang, Min; Yao, Jianzhong; Che, Xiaoyin - Bioorganic and Medicinal Chemistry, 2008, vol. 16, # 3, p. 1493 - 1510 Full Text ↗ Cited 24 times ↗ Details > Abstract >

本篇文献中的条件，以及其他文献中报道的条件，用于快速比较，

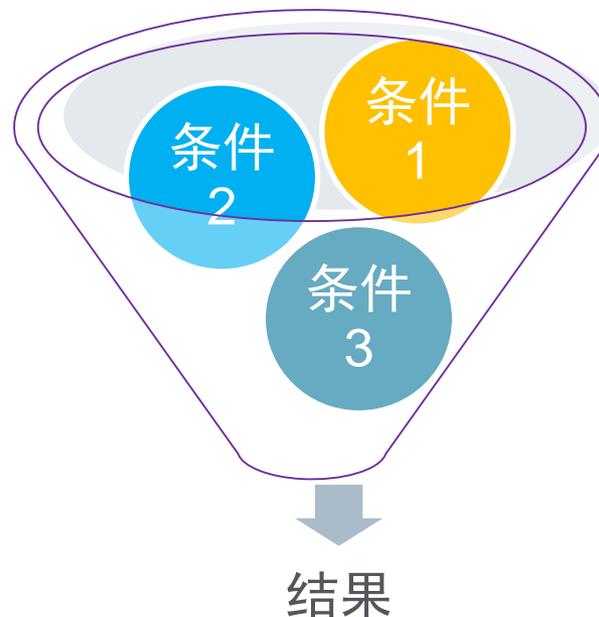
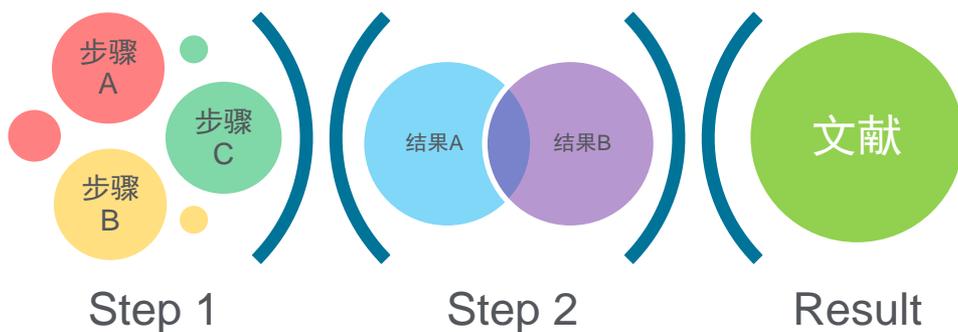
提纲

- Reaxys数据库的介绍与更新
- Reaxys数据库与同类数据库的比较
 - 索引内容比较
 - 可检索性比较
- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

可检索性是一个复杂的问题（一个简单的诠释图）



可检索性导致的检索策略和检索复杂程度



不同的数据库由于数据结构不同，在完成同样的检索需求时，检索策略有很大的区别

Case 1: 检索氯化钾在乙醇中的溶解度

- Reaxys中的检索策略

The screenshot displays the Reaxys query builder interface. At the top, navigation tabs include 'Quick search', 'Query builder' (selected), 'Results', 'Synthesis planner', and 'History'. On the right, there are buttons for 'Register' and 'Sign in'. Below the navigation, a 'Search in:' section has tabs for 'Reactions', 'Targets', 'Substances' (highlighted with a red box), and 'Documents'. A toolbar contains icons for 'Import', 'Save', 'Reset form', and 'Delete all'. On the right side, a sidebar titled 'Find search fields and forms' lists various search categories like 'Basic Indexes', 'Identification', 'Physical Properties', etc.

The main query builder area shows two search criteria:

- Solubility** (Find any):
 - = Solubility, g·l⁻¹
 - is Saturation
 - = Temperature (Solubility (MCS)), °C
 - is Solvent (Solubility (MCS)) ethanol (indicated by a red arrow)
 - is Ratio of Solvents
- AND**
- Chemical Name**:
 - is Chemical Name potassium chloride (indicated by a red arrow)

Case 1: 检索氯化钾在乙醇中的溶解度 (耗时2分钟)

1 Substances out of 7,118 Documents, containing 4,141 Reactions, 60 Targets Reaxys - 1

0 selected Limit To Exclude Export Sort by No of References ↓ Grid Heatmap

1 CIK potassium chloride
CIK 74.5513 3534978

Hit Data - 20 Bioactivity (All) Other Data - 784 Preparations - 414 >
Identification Physical Data - 2,972 Reactions - 4,141 >
Druglikeness Spectra - 182 Targets - 60 >
Documents - 7,118 >

Hit Data - 20

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 Chemistry, 2005, vol. 44, # 8, p. 1594 - 1596] Full Text Cited 4 times Details Abstract
	25	ethanol	Solubility: 0.025 mol/kg solvent	El-Dossoki - [Indian Journal of Chemistry - Section A Inorganic, Physical, Theoretical and Analytical Chemistry, 2005, vol. 44, # 8, p. 1594 - 1596] Full Text Cited 4 times Details Abstract
	30	ethanol	Solubility: 0.037 mol/kg solvent	El-Dossoki - [Indian Journal of Chemistry - Section A Inorganic, Physical, Theoretical and Analytical Chemistry, 2005, vol. 44, # 8, p. 1594 - 1596] Full Text Cited 4 times Details Abstract
	35	ethanol	Solubility: 0.043 mol/kg solvent	El-Dossoki - [Indian Journal of Chemistry - Section A Inorganic, Physical, Theoretical and Analytical Chemistry, 2005, vol. 44, # 8, p. 1594 - 1596] Full Text Cited 4 times Details Abstract

Case 2: 检索下面反应的机理性文献

- Reaxys中的检索策略

The screenshot displays the Reaxys web interface. At the top, there are navigation tabs: "Quick search", "Query builder" (which is underlined), "Results", "Synthesis planner", and "History". The user's name "Sam Yu" and notification icons are visible in the top right corner.

The main search area includes a "Search in:" dropdown menu with options for "Reactions", "Targets", "Substances", and "Documents". Below this are icons for "Import", "Save", "Reset form", and "Delete all". Further down are icons for "Structure", "Molecular Formula", "CAS RN", and "Doc. Index".

The central workspace is divided into two main sections. The top section, titled "Structure", contains a chemical reaction diagram showing the reduction of benzaldehyde to benzyl alcohol. The reaction is: c1ccccc1C=O >> c1ccccc1CO. Below the diagram is a button labeled "As drawn".

The bottom section, titled "Subject Studied", contains a search term "is" followed by a dropdown arrow and the text "Subject Studied mechanism". A red arrow points to a blue "AND" button located between the "Structure" and "Subject Studied" sections.

On the right side of the interface, there is a sidebar titled "Find search fields and forms" with a search icon. It lists various search fields and forms: "Fields", "Forms", and "History". The "Fields" section is expanded, showing a list of search fields: "Reaxys", "Basic Indexes", "Identification", "Physical Properties", "Spectra", "MedChem", "Other", "Reactions", "Yield", "Yield (numerical)", and "Solvent".

Case 2: 检索下面反应的机理性文献（耗时2分钟）

Reaction ID: 601797  

1      



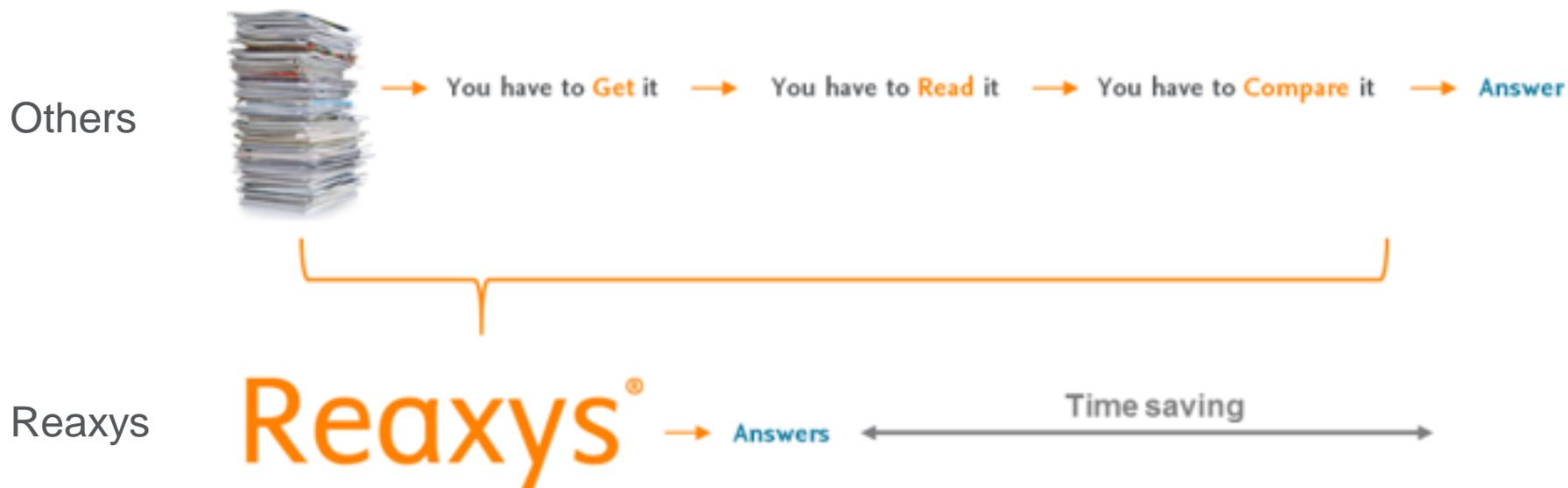
     

7 Hits  745 Conditions  Find Similar 

Yield	Conditions	References
95%	With cobalt(II) chloride; zinc In water; N,N-dimethyl-formamide for 0.5h; Mechanism; Ambient temperature; var. aldehydes and ketones;	Baruah, Robindra N. - Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry, 1994, vol. 33, # 2, p. 182 - 183 Full Text  Details  Abstract 
88%	With dodecane; Triethoxysilane; hydridoiron(II) (trimethylphosphane)3(benzophenone imine) In tetrahydrofuran at 55°C; for 1h; Mechanism; Solvent; Temperature; Time; Reagent/catalyst; Concentration; Schlenk technique; Inert atmosphere;	Zuo, Zhenyu; Sun, Hongjian; Wang, Lin; Li, Xiaoyan - Dalton Transactions, 2014, vol. 43, # 30, p. 11716 - 11722 Full Text  Cited 22 times  Details  Abstract 
73%	Stage #1: benzaldehyde With [Ru ^{VI} (N)(N,N'-bis(salicylidene)-o-cyclohexyldiamine dianion)(CH ₃ OH)](ClO ₄); phenylsilane In toluene for 0.666667h; Reflux; Stage #2: With hydrogenchloride In diethyl ether; water; toluene Mechanism;	Abbina, Srinivas; Bian, Shi; Oian, Casey; Du, Guodong - ACS Catalysis, 2013, vol. 3, # 4, p. 678 - 684 Full Text  Cited 31 times  Details  Abstract 

Reaxys与其他数据库在可检索性上的比较

- Reaxys的多角度可检索性，在帮助科研人员节省大量的文献检索时间的同时，还能快速获得最相关结果



提纲

- Reaxys数据库的介绍与更新
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 - 索引内容比较
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- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

Case Study 1: 通过理化性质检索物质

- 检索要求
 - 乙烯衍生物，不能成环
 - 具备“机械性能”报道的化合物
 - 按照以下的标签顺序进行“理化性质”反推的检索

The screenshot displays the Reaxys Query Builder interface. The top navigation bar includes 'Quick search', 'Query builder' (highlighted with an orange box and labeled '1'), 'Results', 'Synthesis planner', and 'History'. On the right, there are 'Register >' and 'Sign in ?' buttons. Below the navigation bar, there are search filters for 'Reactions', 'Targets', 'Substances', and 'Documents'. A search input field is labeled 'Search in:'. Below this, there are icons for 'Structure', 'Molecular Formula', 'CAS RN', and 'Doc. Index'. On the right side, there is a 'Find search fields and forms' dropdown menu with a search icon. The dropdown menu is open, showing a list of search fields: 'Fields' (highlighted with an orange box and labeled '2'), 'Forms', and 'History'. Under 'Fields', there is a list of categories: 'Basic Indexes', 'Identification', 'Physical Properties' (highlighted with an orange box and labeled '3'), 'Spectra', 'MedChem', 'Other', 'Reactions', and 'Bibliography'. The main area of the interface is a large grey box with the text 'Drag & Drop to build a new query'. At the bottom left, there are icons for 'Import', 'Save', 'Reset form', and 'Delete all'.

Reaxys的理化性质列表

The image displays a screenshot of the Reaxys software interface, showing a list of physical properties. The 'Physical Properties' section is expanded, and the 'Mechanical Properties' item is highlighted with an orange box.

Physical Properties

- Melting Point
- Boiling Point
- Sublimation
- Refractive Index
- Density
- Adsorption
- Association
- Autoignition
- Critical Temperature
- Critical Volume
- Crystal Phase
- Crystal Property Description
- Crystal System
- Decomposition
- Dielectric Constant
- Dissociation Energy
- Dissociation Exponent
- Electrical Moment
- Electrical Polarizability
- Electrochemical Behaviour
- Electrochemical Characteristics
- Electrochemistry Data
- Electrolytic Conductivity
- Electron Binding
- Energy Barriers
- Energy Data
- Liquid/Vapour Systems
- Magnetic Data
- Magnetic Susceptibility
- Mechanical & Physical Properties
- Mechanical Properties**
- Molecular Deformation
- Mutarotation
- Optical Data
- Optical Rotatory Dispersion

添加“机械属性”列表与结构属性

The screenshot displays the Reaxys Query Builder interface. At the top, there are navigation tabs: 'Quick search', 'Query builder' (selected), 'Results', 'Synthesis planner', and 'History'. Below these are search filters for 'Reactions', 'Targets', 'Substances', and 'Documents'. A toolbar includes 'Import', 'Save', 'Reset form', and 'Delete all' buttons, along with icons for 'Structure', 'Molecular Formula', 'CAS RN', and 'Doc. Index'. The main query area shows two conditions: 'Mechanical Properties' and 'Structure', connected by an 'AND' operator. The 'Mechanical Properties' condition has a 'Find any' button highlighted with an orange box. An orange arrow points from this button to the 'Structure' condition. The 'Structure' condition has a 'Create Structure / Reaction Drawing' button. On the right side, there is a panel titled 'Find search fields and forms' with tabs for 'Fields', 'Forms', and 'History'. The 'Fields' tab is active, showing a list of search fields: 'Ionization Potential', 'Isoelectric Point pH', 'Kinematic Viscosity', 'Liquid Phase', 'Liquid/Liquid Systems', 'Liquid/Solid Systems', and 'Liquid/Vapour Systems'.

Tips:

通过Query Builder将结构和“机械属性”联合起来，点击结构添加“乙烯”

结构的绘制

The screenshot displays the Reaxys software interface for structure editing. At the top, navigation links include 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. The main workspace shows the chemical structure of ethylene, $\text{H}_2\text{C}=\text{CH}_2$. A search panel on the right is titled 'Search this structure as:' and contains several options:

- As drawn
- As substructure
 - On all atoms
 - On heteroatoms
- Similar
- Tautomers
- Stereo
- Additional ring closure
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

Tips:

亚结构检索确保是乙烯衍生物，Additional Ring Closure去掉确保不成环。

最后的检索式

The screenshot displays the Reaxys Query Builder interface. At the top, the navigation bar includes "Quick search", "Query builder" (which is underlined), "Results", "Synthesis planner", and "History". On the right side of the navigation bar are icons for a user profile, a notification bell, and a help icon.

Below the navigation bar, there is a "Search in:" section with four dropdown menus: "Reactions", "Targets", "Substances" (which is highlighted with an orange box), and "Documents". Below these are icons for "Import", "Save", "Reset form", and "Delete all".

The main workspace contains a search query builder. It starts with a search field containing "Mechanical Properties" and a "Find any" checkbox. Below this is a blue "AND" button. The next search field is titled "Structure" and contains a chemical structure of ethylene, $\text{H}_2\text{C}=\text{CH}_2$. Below the structure is a button labeled "As drawn".

On the right side of the interface, there is a sidebar titled "Find search fields and forms" with a search icon. Below this are three tabs: "Fields", "Forms", and "History". The "Fields" tab is active, showing a list of search fields: "Reaxys", "Basic Indexes", "Identification", "Physical Properties", "Melting Point", "Boiling Point", "Sublimation", "Refractive Index", and "Density".

最后的结果—乙烯的数据

ethene
 H_2CCH_2 28.0538 1730731 74-85-1

Hit Data - 12 Bioactivity (All) Other Data - 121 Preparations - 4,591 >

Identification Physical Data - 2,344 Reactions - 20,397 >

Druglikeness Spectra - 266 Documents - 30,028 >

Hit Data - 12

Mechanical Properties - 12 hits out of 12

不同文献中报道的关于“乙烯”的“机械属性”

Description (Mechanical Properties)	Comment (Mechanical Properties)	Reference
Elastic properties	弹性属性	Maksimkin, Aleksey; Kaloshkin, Sergey; Zadorozhnyy, Mikhail; Tcherdyntsev, Victor - [Journal of Alloys and Compounds, 2014, vol. 586, # SUPPL 1, p. S214-S217] Full Text ↗ Cited 15 times ↗ Details > Abstract >
Virial coefficients of the equation of state	状态方程 维里系数	Sweet; Steele - [Journal of Chemical Physics, 1967, vol. 47, p. 3029,3033] Full Text ↗ Details > Gainar et al. - [Berichte der Bunsen-Gesellschaft, 1973, vol. 77, p. 372,373, 375] Full Text ↗ Details > Orcutt - [Journal of Chemical Physics, 1963, vol. 39, p. 605] Full Text ↗ Cited 33 times ↗ Details > Das Gupta et al. - [Journal of Chemical Physics, 1973, vol. 59, p. 1999] Full Text ↗ Cited 14 times ↗ Details >

最后的结果—衍生物的数据



styrene
CH₂CH(C₆H₅) 104.152 1071236 292638-84-7

Hit Data - 5
Identification
Druglikeness

Bioactivity (All)
Physical Data - 876
Spectra - 253

Other Data - 289

Preparations - 1,662 >
Reactions - 30,403 >
Targets - 8 >
Documents - 25,350 >

Hit Data - 5

✓ Mechanical Properties - 5 hits out of 5

涉及到“苯乙烯”的摩尔体积，可压缩性，维里系数，粘性方面的报道

Description (Mechanical Properties)	Reference
Molar volume	<p>Berberi; Decroocq - [Journal de Chimie Physique et de Physico-Chimie Biologique, 1974, vol. 71, p. 673,678] Full Text ↗ Details ></p> <p>Miller et al. - [Journal of Chemical and Engineering Data, 1975, vol. 20, p. 417,418, 419] Full Text ↗ Details ></p> <p>Ghosal, Saswati; Samoc, Marek; Prasad, Paras N.; Tufariello, Joseph J. - [Journal of Physical Chemistry, 1990, vol. 94, # 7, p. 2847 - 2851] Full Text ↗ Cited 101 times ↗ Details > Abstract ></p> <p>Hayduk, Walter; Minhas, Bhupender S. - [Journal of Chemical & Engineering Data, 1987, vol. 32, # 3, p. 285 - 290] Full Text ↗ Details > Abstract ></p>
Virial coefficients of the equation of state	<p>Balashova, I. M.; Mokrushina, L. V.; Morachevskii, A. G. - [J. Appl. Chem. USSR (Engl. Transl.), 1989, vol. 62, # 12, p. 2744 - 2750,2546 - 2551] Full Text ↗ Details > Abstract ></p>
PVT Relationship	<p>Sasuga et al. - [Journal of Physical Chemistry, 1979, vol. 83, p. 3290] Full Text ↗ Cited 6 times ↗ Details ></p>
Compressibility	<p>Yakusheva et al. - [Russian Journal of Physical Chemistry, 1977, vol. 51, p. 973] [p. 1657] Full Text ↗ Details ></p>
Viscosity	<p>Olaj - [Monatshefte fuer Chemie, 1971, vol. 102, p. 648] Full Text ↗ Cited 3 times ↗ Details ></p>

案例衍生—如果特指与“弹性”有关性能报道

- 对于以下的检索，该如何修改

The screenshot displays the Reaxys Query Builder interface. At the top, there are navigation tabs: Quick search, Query builder (selected), Results, Synthesis planner, and History. Below these are search filters for Reactions, Targets, Substances, and Documents. A search bar contains the text "Search in:". Below the search bar are icons for Import, Save, Reset form, and Delete all. To the right of these icons are icons for Structure, Molecular Formula, CAS RN, and Doc. Index. The main search area shows two criteria: "Mechanical Properties" with a "Find any" checkbox and a "Show fields" dropdown menu (highlighted with an orange box), and "Structure" with a chemical structure of ethylene ($\text{H}_2\text{C}=\text{CH}_2$) and an "As drawn" label. On the right side, there is a sidebar titled "Find search fields and forms" with a search icon and tabs for Fields, Forms, and History. The sidebar lists various search fields: Basic Indexes, Identification, Physical Properties, Melting Point, Boiling Point, Sublimation, Refractive Index, and Density.

修改检索条件

The screenshot displays the Reaxys Query Builder interface. At the top, there are navigation tabs: 'Quick search', 'Query builder' (selected), 'Results', 'Synthesis planner', and 'History'. Below these are search filters for 'Reactions', 'Targets', 'Substances', and 'Documents'. A toolbar includes 'Import', 'Save', 'Reset form', and 'Delete all' buttons, along with icons for 'Structure', 'Molecular Formula', 'CAS RN', and 'Doc. Index'. The main search area shows two conditions:

- Mechanical Properties**: A dropdown menu is set to 'contains', and the search term is 'elastic'. The field is labeled 'Description (Mechanical Properties)'. A 'Find any' checkbox and 'Hide fields' option are also visible.
- Structure**: A chemical structure is shown in a dashed box: $\text{H}_2\text{C}=\text{CH}_2$. Below the structure is the text 'As drawn'.

An orange arrow points from the 'contains' dropdown in the 'Mechanical Properties' condition to the Chinese text below the image.

On the right side, there is a sidebar titled 'Find search fields and forms' with a search icon. It lists various search fields under the 'Fields' tab, including 'Basic Indexes', 'Identification', 'Physical Properties', 'Melting Point', 'Boiling Point', 'Sublimation', 'Refractive Index', 'Density', and 'Adsorption'.

注意修改成Contains, 并添加为“弹性”词条。

最后的结果

111 Substances out of 53,348 Documents, containing 25,663 Reactions, 275 Targets Reaxys - 111

0 selected Limit To Exclude Export Sort by No of References ↓ Grid Heatmap

1

ethene
H₂CCH₂ 28.0538 1730731 74-85-1

Hit Data - 1

Identification

Druglikeness

Bioactivity (All)

Physical Data - 2,344

Spectra - 266

Other Data - 121

Preparations - 4,591 >

Reactions - 20,397 >

Documents - 30,028 >

Hit Data - 1

▼ Mechanical Properties - 1 hits out of 12

Description (Mechanical Properties)	Reference
Elastic properties	Maksimkin, Aleksey; Kaloshkin, Sergey; Zadorozhnyy, Mikhail; Tcherdy S214-S217]
	Full Text ↗ Cited 15 times ↗ Details > Abstract >

2

cis-Octadecenoic acid
C₈H₁₇CHCH(CH₂)₇COOH 282.467 17265

Hit Data - 1

Identification

Druglikeness

Bioactivity (All)

Other Data - 1,028

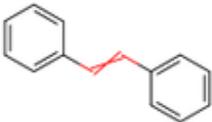
Preparations - 134 >

Hit Data - 1

▼ Mechanical Properties - 1 hits out of 6

Description (Mechanical Properties)	Reference
Elasticity constants	Bazaron et al. - [Sov. Phys. Dokl. (Engl. Transl.), 1973, vol. 17, p. 1324,769]
	Full Text ↗ Details >
	Bazaron et al. - [Sov. Phys. Dokl. (Engl. Transl.), 1973, vol. 17, p. 1325,997]
	Full Text ↗ Details >
	Bazaron et al. - [Sov. Phys. Dokl. (Engl. Transl.), 1965, vol. 10, p. 799,134]
	Full Text ↗ Details >

其中一个化合物—理化性质



stilbene
 $C_6H_5CH=CHC_6H_5$ 180.249 1904445 588-59-0

Hit Data - 1 Bioactivity (All) Other Data - 56 Preparations - 638 >

Identification Physical Data - 157 Reactions - 1,022 >

Druglikeness Spectra - 139 Documents - 1,588 >

^ Physical Data - 157

- ✓ Melting Point - 38
- ✓ Boiling Point - 8
- ✓ Density - 1
- ✓ Adsorption (MCS) - 1
- ✓ Association (MCS) - 15
- ✓ Chromatographic Data - 3
- ✓ Conformation - 1
- ✓ Crystal Phase - 1
- ✓ Crystal Property Description - 7**
- ✓ Decomposition - 1

Colour & Other Properties	Location	Reference
colourless		Potier, Jonathan; Manuel, Stephane; Rousseau, Jolanta; Tumkevicius, Sigitas; Hapiot, Frederic; Monflier, Eric - [Applied Catalysis A: General, 2014, vol. 479, p. 1 - 8] Full Text ↗ Cited 11 times ↗ Details > Abstract >
yellow		Kireenko, Marina M.; Zaitsev, Kirill V.; Oprunenko, Yuri F.; Churakov, Andrei V.; Tafeenko, Viktor A.; Karlov, Sergey S.; Zaitseva, Galina S. - [Dalton Transactions, 2013, vol. 42, # 22, p. 7901 - 7912] Full Text ↗ Cited 18 times ↗ Details > Abstract >
white	supporting information	Yang, Fu-Lai; Ma, Xian-Tao; Tian, Shi-Kai - [Chemistry - A European Journal, 2012, vol. 18, # 6, p. 1582 - 1585] Full Text ↗ Cited 92 times ↗ Details > Abstract >
white		Ren, Gerui; Cui, Xiuling; Yang, Erbing; Yang, Fan; Wu, Yangjie - [Tetrahedron, 2010, vol. 66, # 23, p. 4022 - 4028] Full Text ↗ Cited 48 times ↗ Details > Abstract >
		Lu, Jian-Mei; Ma, Hui; Li, Sha-Sha; Ma, Dan; Shao, Li-Xiong - [Tetrahedron, 2010, vol. 66, # 27-28, p. 5185 - 5189] Full Text ↗ Cited 32 times ↗ Details > Abstract >
		Tang, Yi-Qiang; Chu, Chun-Yan; Zhu, Lei; Qian, Bin; Shao, Li-Xiong - [Tetrahedron, 2011, vol. 67, # 49, p. 9479 - 9483] Full Text ↗ Cited 28 times ↗ Details > Abstract >

其中一个化合物—理化性质

stilbene
 $C_6H_5CH=CHC_6H_5$ 180.249 1904445 588-59-0

Hit Data - 1 Bioactivity (All) Other Data -
 Identification Physical Data - 157
 Druglikeness Spectra - 139

Spectra - 139

- ✓ [NMR Spectroscopy - 67](#)
- ✓ [IR Spectroscopy - 8](#)
- ✓ [Mass Spectrometry - 17](#)
- ✓ [UV/VIS Spectroscopy - 17](#)
- ✓ [ESR Spectroscopy - 2](#)

Description (NMR Spectroscopy)	Nucleus (NMR Spectroscopy)	Coupling Nuclei	Solvents (NMR Spectroscopy)	Temperature (NMR Spectroscopy), °C	Frequency (NMR Spectroscopy), MHz	Original Text (NMR Spectroscopy)	Location	Comment (NMR Spectroscopy)	Signals, ppm	Kind of signal	Reference
shifts, Spectrum						MHz, $CDCl_3$) δ : 7.12 (s, 2H), 7.27 (t, J = 7.4 Hz, 2H), 7.37 (t, J = 7.4 Hz, 4H), 7.53 (dd, J = 1.4 and 8.4 Hz, 3H)	information				- [Tetrahedron, 2017, vol. 73, # 27-28, p. Full Text ↗ Details > Abstract :
Chemical shifts, Spectrum	^{13}C		chloroform- d_1		125	^{13}C NMR (125 MHz, $CDCl_3$) δ : 127.4, 128.5, 129.5, 138.22	supporting information		127.4, 128.5, 129.5, 138.22		Tanaka, Chihiro; Nakamura, Kimiaki; Ni; - [Tetrahedron, 2017, vol. 73, # 27-28, p. Full Text ↗ Details > Abstract :

其中一个化合物—分析文献获取

stilbene
 $C_6H_5CH=CHC_6H_5$ 180.249 1904445 588-59-0

Hit Data - 1 Bioactivity (All) Other Data - 56 Preparations - 638 >

Identification Physical Data - 157 Reactions - 1,022 >

Druglikeness Spectra - 139 Documents - 1,588 >

Index Term (Reaxys Tree) 分析获取分析方面的分类

Reaxys[®] Quick search Query builder Results Synthesis planner History

1,588 Documents 24,840 Substances, 27,927 Reactions, 2 Targets Reaxys - 1,588

0 Limit To Exclude Export Publication Year Heatmap

1,588

111

Filters and Analysis

Index Terms (List)

Index Terms (Reaxys Tree)

Publication Year

Document Type

Authors

Patent Assignee

Journal Title

Substance Classes

Reaction Classes

1

2

3

Polymer-supported palladium: A hybrid system for multifunctional catalytic application
1
Taher, Abu; Choudhary, Meenakshi; Nandi, Deb Kumar; Siwal, Samarjeet; Mallick, Kaushik - [Applied Organometallic Chemistry, 2018, vol. 32, # 1]
Abstract Index Terms Substances 22 Reactions 17 Full Text [Hit Substances 1](#)

Silver sequestration of halides for the activation of Pd(OAc)₂ catalyzed Mizoroki-Heck reaction of 1,1 and 1,2 - Disubstituted alkenes
2
Bangar, Pronoy G.; Jawalkar, Priyanka R.; Dumbre, Swapnil R.; Patil, Dharmaraj J.; Iyer, Suresh - [Applied Organometallic Chemistry, 2018, vol. 32, # 3]
Abstract Index Terms Substances 57 Reactions 37 Full Text [Hit Substances 1](#) Cited 1 times

Oxidoperoxidomolybdenum(VI) complexes with acylpyrazolonate ligands: Synthesis, structure and catalytic properties
3
Begines, Emilio; Carrasco, Carlos J.; Montilla, Francisco; Álvarez, Eleuterio; Marchetti, Fabio; Pettinari, Riccardo; Pettinari, Claudio; Galindo, Agustín - [Dalton Transactions, 2018, vol. 47, # ...] Cited 2 times

Index Term Reaxys Tree的应用

Index Terms (ReaxysTree) ^

- chemical transformations 679
- physico chemical properties 408
- physico chemical analysis methods 248
- quantum chemical calculation methods

[+ More](#)

Index Term Reaxys Tree帮助快速获得文献方面的分类

Index Terms (ReaxysTree) ×

- ∨ Index Terms (ReaxysTree) 1,588
- > chemical transformations 679
- > physico chemical properties 408
- > physico chemical analysis methods 248
- > quantum chemical calculation methods 34

Clear selected × Limit To > Exclude >

Index Term Reaxys Tree中的分析文献获取

The screenshot displays the 'Index Terms (ReaxysTree)' interface. It features a tree view of index terms with associated counts and a 'Limit To' button. Three orange callout boxes highlight specific terms: '物理化学分析方法' (Physical and Chemical Analysis Methods), '晶型结构鉴定' (Crystal Structure Identification), and '热力学分析' (Thermodynamic Analysis).

Index Term	Count
Index Terms (ReaxysTree)	1,588
> chemical transformations	679
> physico chemical properties	408
< physico chemical analysis methods	248
> spectroscopical analysis	156
> crystal structure determination	94
> microscopy	79
> separation method	72
> elemental analysis	55
> thermal analysis	41
> electro analytical method	22
> quantitative analysis	4

Clear selected × Limit To > Exclude >

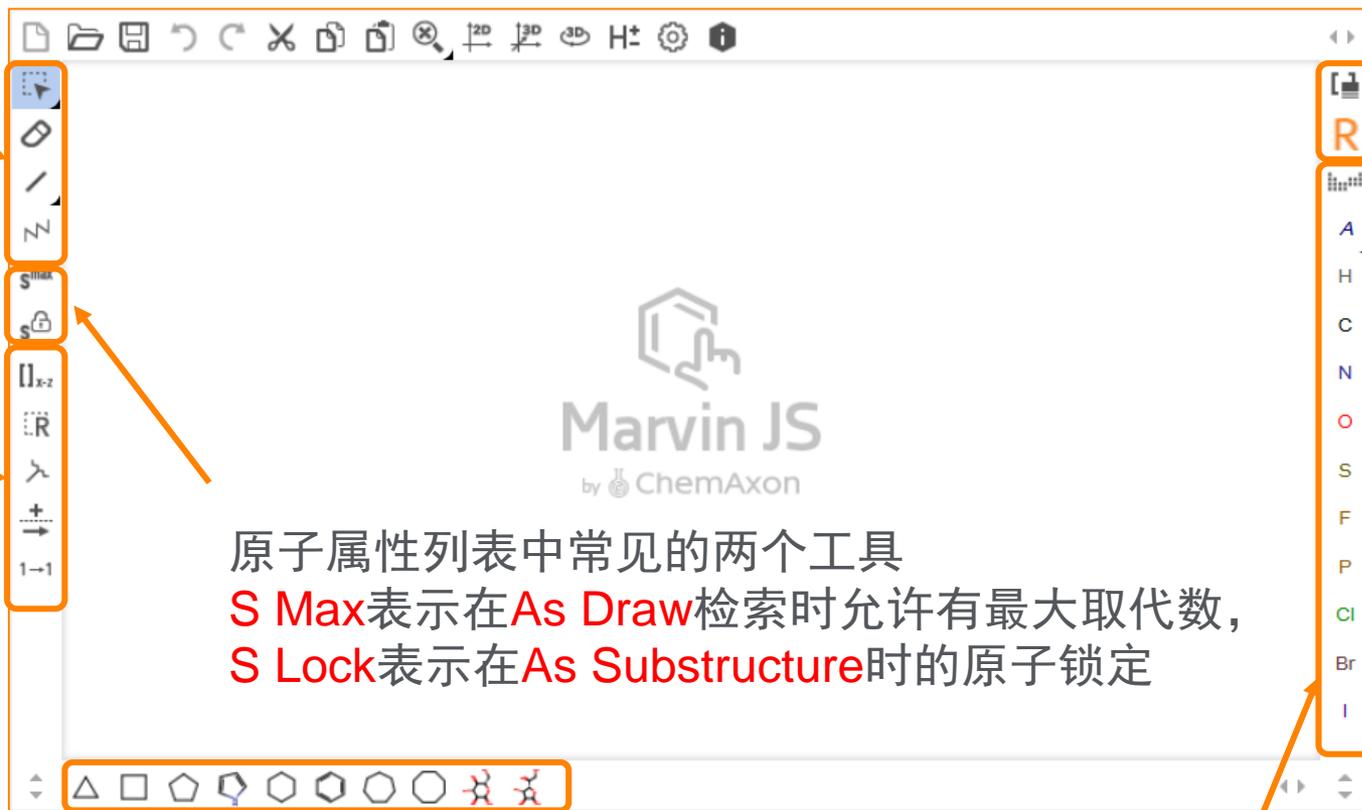
提纲

- Reaxys数据库的介绍与更新
- Reaxys数据库与同类数据库的比较
 - 索引内容比较
 - 可检索性比较
- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

Reaxys中Marvin JS结构编辑器使用

选择工具，
橡皮，键
定义，链，

重复基团，
R基团，
R基团链
接端，反
应定义工
具，原子
匹配工具



原子属性列表中常见的两个工具

S Max表示在**As Draw**检索时允许有最大取代数，
S Lock表示在**As Substructure**时的原子锁定

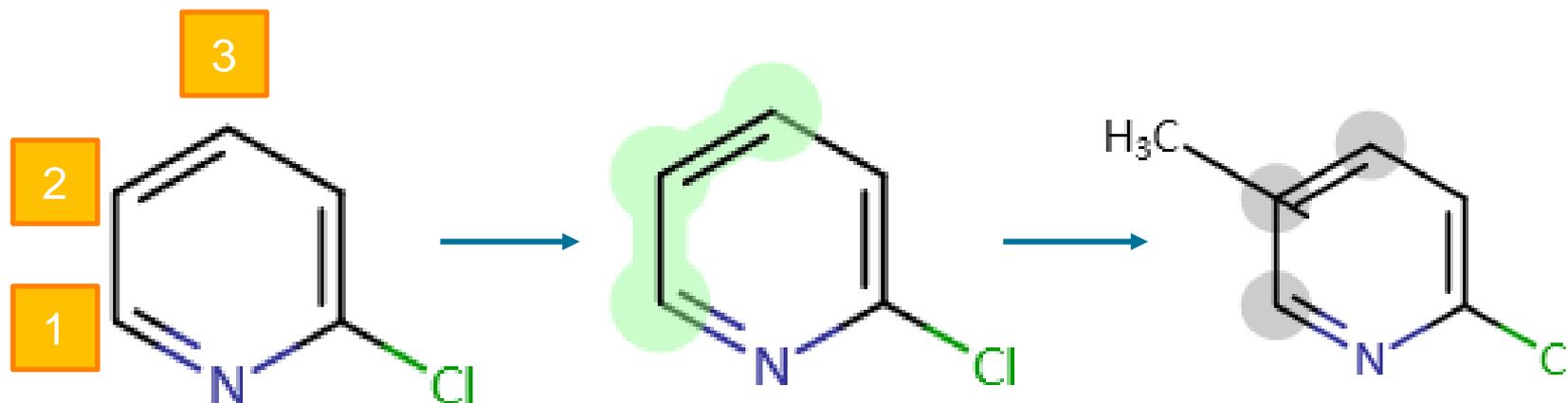
缩写官
能团，
通用官
能团定
义，

常见的环，常见的糖分子模板

元素周期表以及常用原子，
A:原子属性定义工具

不定位取代键的使用

- 不定位取代键：
 - 在选定的原子上进行基团的链接
 - 可以使用在链上，也可以使用在环上



绘制要求:

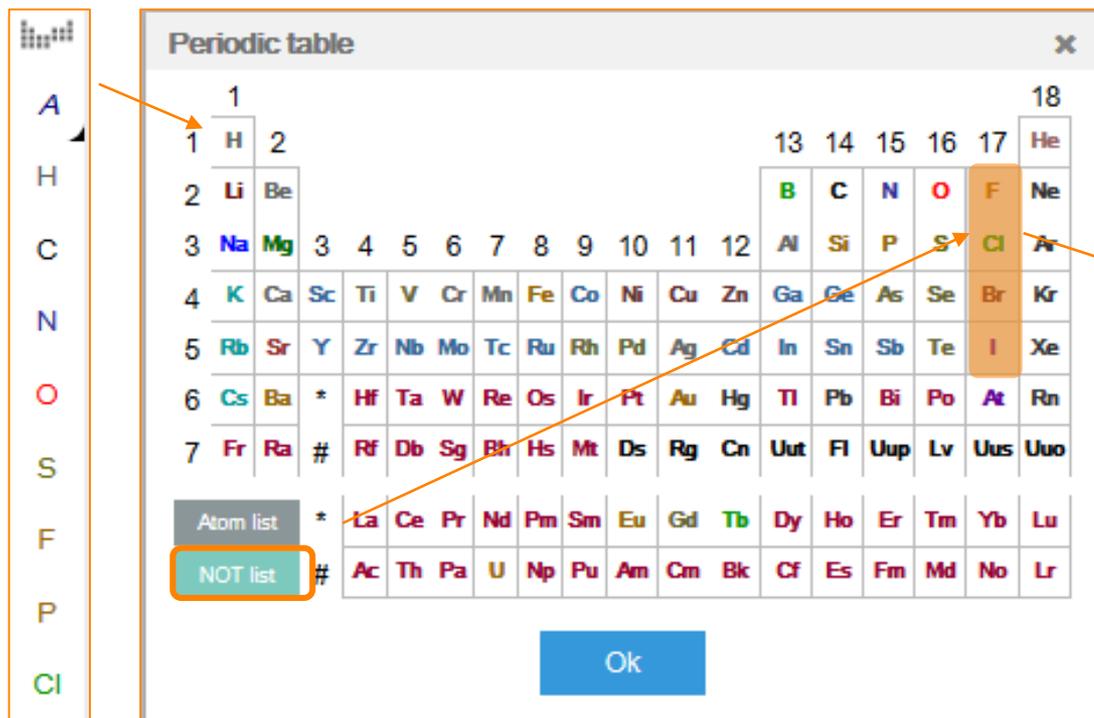
希望1, 2, 3C上存在
一个NH₂

绘制步骤:

- 用选择工具选择1, 2, 3号C原子,
- 添加不定位取代, 系统默认添加CH₃
- 将CH₃换成NH₂

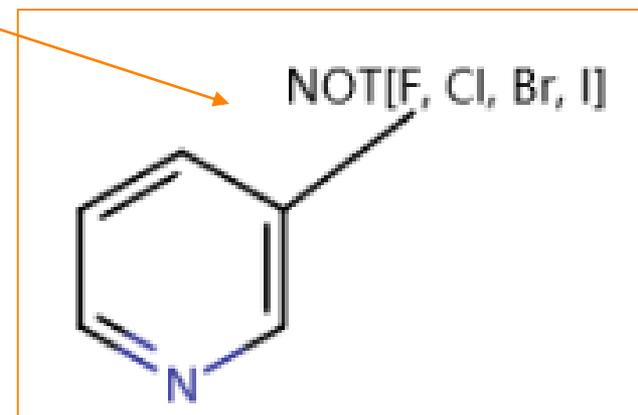
Not List的应用

- 案例:
 - 定义某位点上不能发生F, Cl, Br, I取代



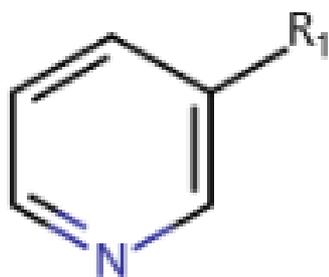
The screenshot shows a 'Periodic table' window with a vertical list of elements on the left (A, H, C, N, O, S, F, P, Cl). A 'NOT list' box is highlighted in the bottom left of the periodic table. Arrows point from this box to the elements Fluorine (F), Chlorine (Cl), Bromine (Br), and Iodine (I) in the periodic table.

1												13		14	15	16	17	18
1	H																	He
2	Li	Be											B	C	N	O	F	Ne
3	Na	Mg	3	4	5	6	7	8	9	10	11	12	Al	Si	P	S	Cl	Ar
4	K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
5	Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
6	Cs	Ba	*	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
7	Fr	Ra	#	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Uut	Ff	Uup	Lv	Uus	Uuo
Atom list			*	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
NOT list			#	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

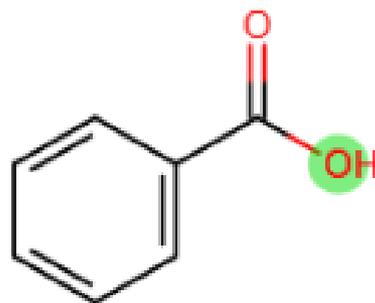


自定义R基团

- 案例
 - 定义一个结构A
 - R1分别是下面的这些结构，结构中绿色原子与A结构相连接

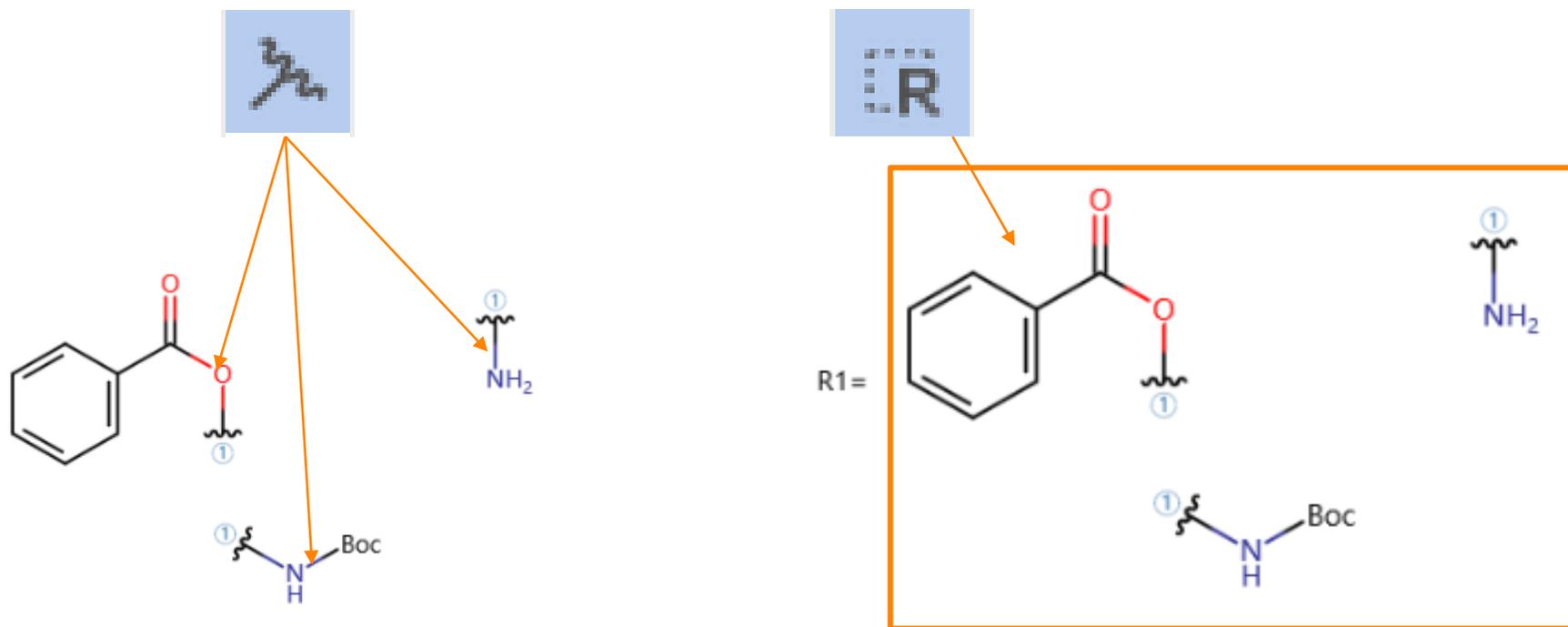


A

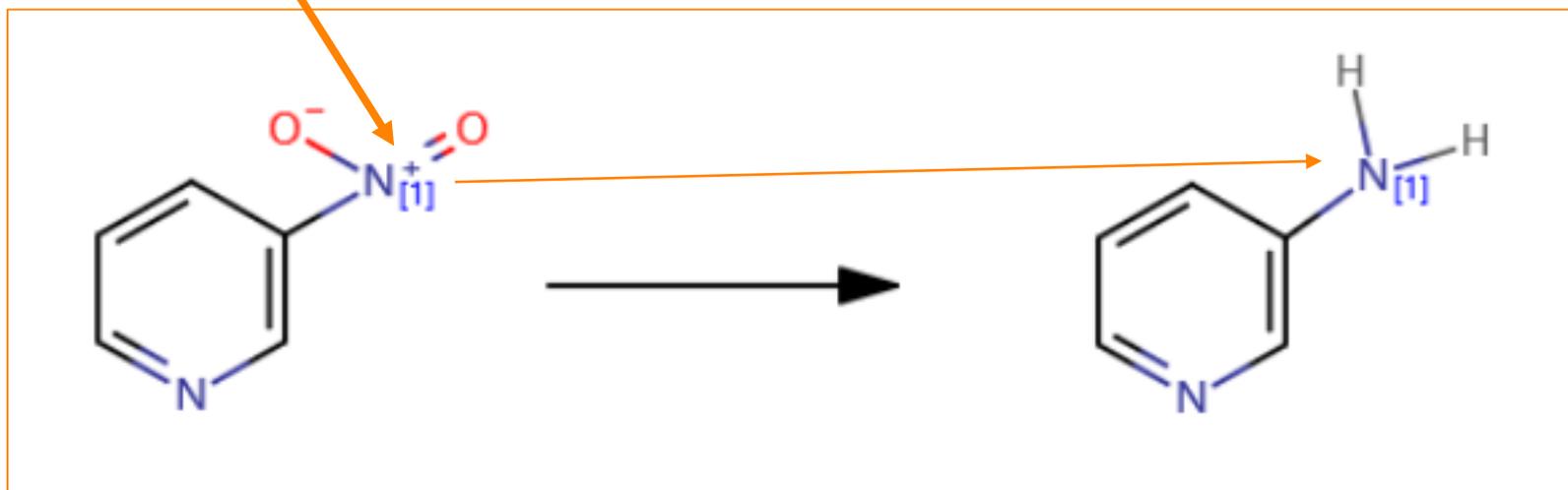
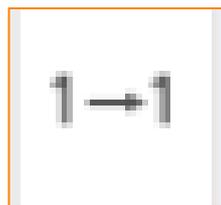


绘制方法

- 定义步骤：
 - 使用R基团末端定义工具定义绿色原子
 - 使用R基团定义工具，选择全部片段，即可完成R1的定义



反应原子标记工具



Tips:

1. 定义反应前后必须匹配的原子
2. 建议将官能团展开后进行匹配
3. 在定义原子匹配时，两工具等效。

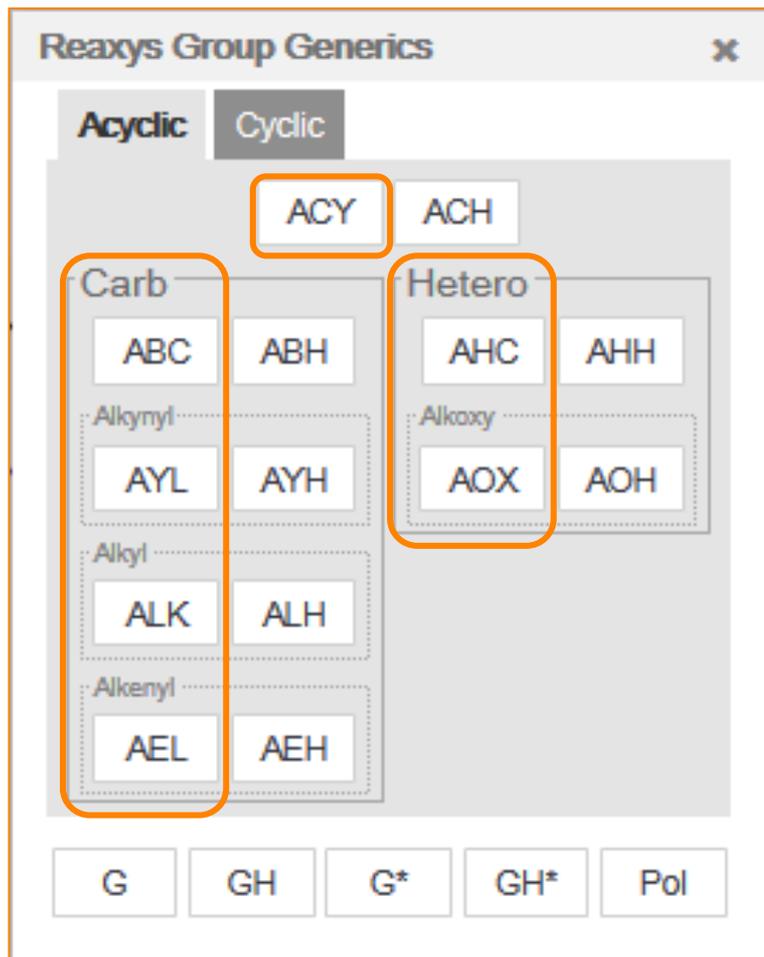
缩写官能团， Reaxys的Generic Group定义

The image displays two overlapping dialog boxes from the Reaxys software interface. The top dialog, titled 'Abbreviated groups', features a text input field containing 'BOC', an 'Expand' checkbox, a 'Boc' button, and an 'Ok' button. The bottom dialog, titled 'Reaxys Group Generics', has tabs for 'Acyclic' and 'Cyclic'. Under 'Acyclic', there are buttons for 'ACY' and 'ACH'. Below these are sections for 'Carb' (containing 'ABC' and 'ABH'), 'Alkynyl' (containing 'AYL' and 'AYH'), 'Alkyl' (containing 'ALK' and 'ALH'), and 'Alkenyl' (containing 'AEL' and 'AEH'). Under 'Hetero', there are buttons for 'AHC' and 'AHH', and a section for 'Alkoxy' (containing 'AOX' and 'AOH'). At the bottom of the dialog are buttons for 'G', 'GH', 'G*', 'GH*', and 'Pol'. An orange box on the left contains a 'R' icon and a 'Boc' icon, with arrows pointing to the 'BOC' input field and the 'Boc' button in the 'Abbreviated groups' dialog, respectively.

Tips:

1. Abbreviated Group:提供一些缩写的基团，直接键盘输入即可
2. Reaxys Generic Group: 提供一些通用官能团

Generic Group定义—链的定义



Tips:

ACY: 任意的链

ABC: 任意C链（只含C原子）

AYL: 含有炔基取代的链

ALK: 含有烷基取代的链（饱和链）

AEL: 含有烯基取代的链

AHC: 含有杂原子的链

AOX: 烷氧基

其他带H的分别是，前面对应基团或H

Generic Group定义—环的定义

Reaxys Group Generics

Acyclic Cyclic

CYC CYH

Carb

CBC CBH

Aryl

ARY ARH

Cycloalkyl

CAL CAH

Cycloalkenyl

CEL CEH

Hetero

CHC CHH

Heteroaryl

HAR HAH

No carbon

CXX CXH

G GH G* GH* Pol

Tips:

CYC: 任意的环

CBC: 任意C环（只含C原子）

ARY: 芳香基（只含C原子）

CAL: 环烷基（饱和C环）

CEL: 环烯基（不饱和C环）

CHC: 任意杂环

HAR: 含杂原子的芳香环

CXX: 不含C原子的环

其他带H的分别是，前面对应基团或H

Generic Group定义—G Group定义

G

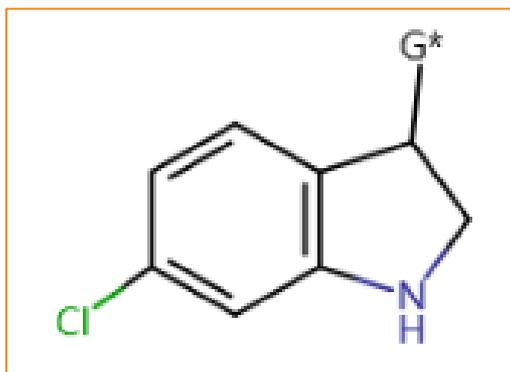
GH

G*

GH*

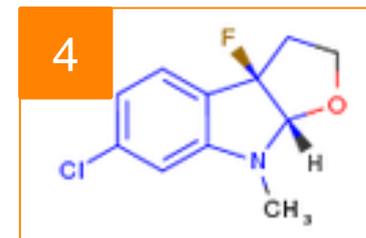
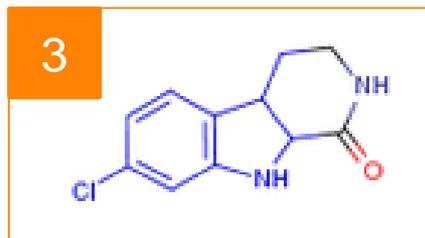
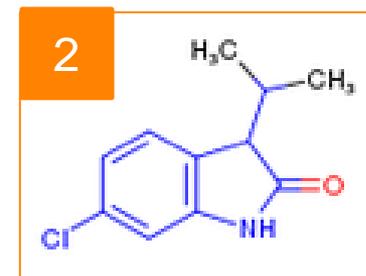
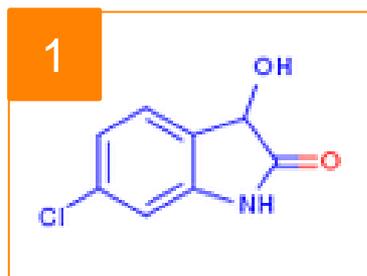
Tips:

1. G代表的是任意基团，GH表示的是任意基团或H
2. G*和G的区别是，G*所连接的基团允许和母体成环，G不允许成环



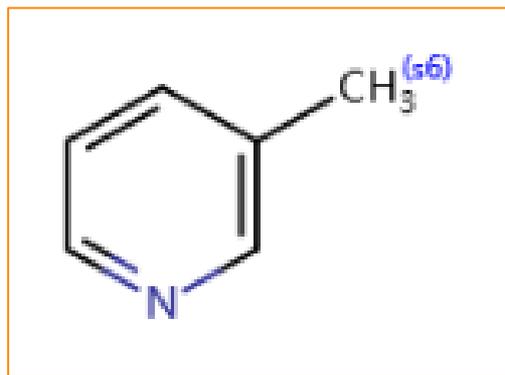
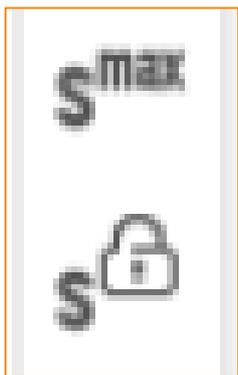
思考:

As Substructure检索这个结构，哪些结构可以被检索出来，如果不是G*，而是G呢？

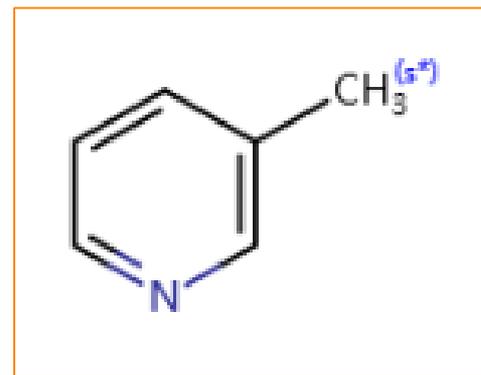


S Max和S Lock

- **S Max: As Draw**检索时有效
 - As Draw时, 所有的原子不允许有取代
 - 标记上, S Max, 等同于在As Draw时将这个位点全部开放
- **S Lock: As Substructure**检索时有效
 - As Substructure时, 所有没有画出来的H, 以及没有延展出来的H都可以随意取代
 - 标记上, S Lock, 等同于该位点上只能是H, 起到锁定作用



As Draw



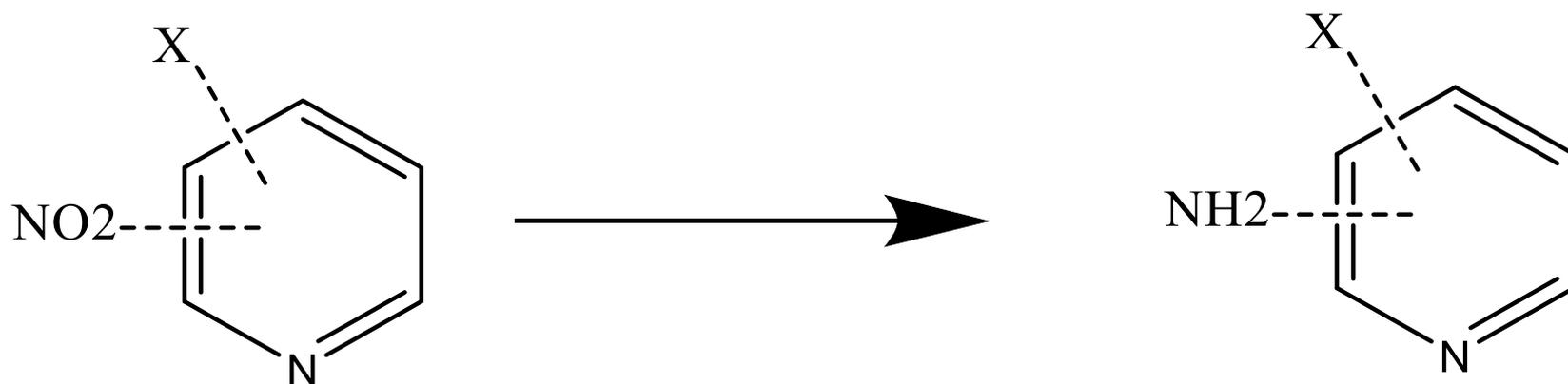
As Substructure

提纲

- Reaxys数据库的介绍与更新
- Reaxys数据库与同类数据库的比较
 - 索引内容比较
 - 可检索性比较
- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

Case Study 1

- 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



Reaxys中的结构定义

The screenshot shows the Reaxys Structure editor interface. The main workspace displays a chemical structure of a pyridine ring with two substituents: a nitro group (NO₂) and a generic substituent (X). The nitro group is labeled with an atom mapping [1] (NO₂[1]), and the nitrogen atom in the ring is labeled with an atom mapping [2] (N[2]). The generic substituent X is also labeled with an atom mapping [1] (X[1]). The interface includes a top navigation bar with options like 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. On the right side, there is a search configuration panel titled 'Search this structure as:' with various options like 'As drawn', 'As substructure', 'Similar', 'Tautomers', 'Stereo', etc. The 'As drawn' option is selected. At the bottom, there are buttons for 'Clear', 'Cancel', and 'Transfer to query'.

结构定义:

1: 使用两次不定位取代, 将NO₂和X定义在吡啶环上

2: 使用原子映射功能, 将反应前后的原子标记出来

3: As Draw检索

不定位取代的定义

1: 选择需要链接基团的原子, 用不定位取代键和不同的基团相连

2: 吡啶环上的5个C原子需要使用两次不定位取代, 一次链接X, 一次链接NO₂

检索到的结果

29 Filters and Analysis

By Structure 0 Limit To Exclude Export Syn-Plan Reaxys Ranking \downarrow

Yield

Reagent/Catalyst

Solvent

Catalyst Classes

Solvent Classes

Product Availability

Reactant Availability

Reaction Classes

Document Type

Publication Year

Single step reactions only

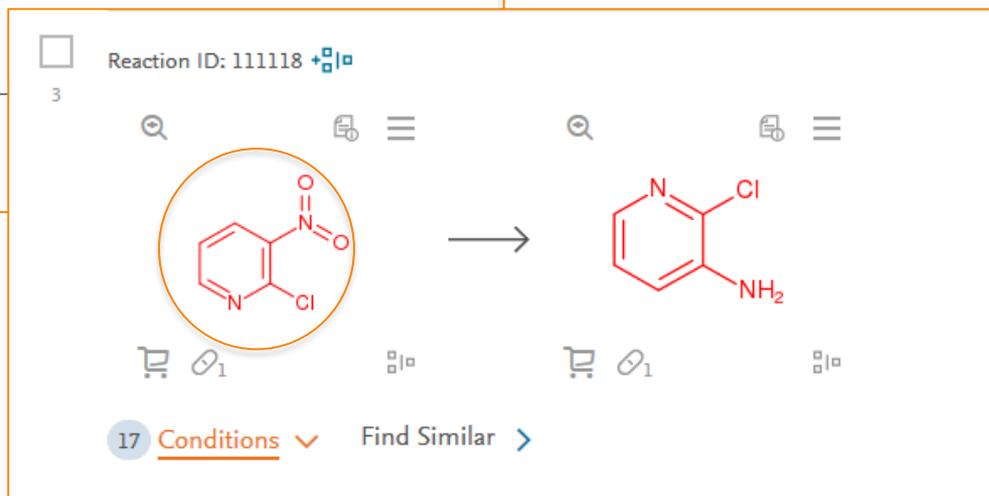
29 Reactions 96 Documents 43 Substances, 18 Targets

1 Reaction ID: 91265 $+$ \square

36 Conditions \downarrow Find Similar $>$

2 Reaction ID: 92348 $+$ \square

检索到的反应，存在
NO₂和X在邻位的，也
存在对位的反应



如何对反应进行筛选

- 想要的一定属于这个结果集的子集，可以直接使用过滤工具

The screenshot displays the Reaxys web interface. On the left, the 'Filters and Analysis' sidebar is visible, with the 'By Structure' filter category highlighted in orange. Below it, a 'Create Structure Drawing' button is also highlighted with an orange box. The main area shows search results for two reactions. The first reaction (ID: 92348) shows the reduction of 5-bromo-2-nitropyridine to 5-bromo-2-aminopyridine. The second reaction (ID: 111118) shows the reduction of 2-chloro-5-nitropyridine to 2-chloro-5-aminopyridine. Each reaction entry includes a search icon, a list icon, a zoom icon, and a 'Find Similar' link. The top navigation bar includes 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. The user's name 'Sam Yu' and notification icons are also present.

输入限定的结构

Reaxys Quick search Query builder Results Synthesis planner History Sam Yu

Structure editor Paste from Query Create structure template from name

Search this structure as:

- As drawn
- As substructure
- Similar
- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges

Periodic table

1																	18	
1	H	2											13	14	15	16	17	He
2	Li	Be											B	C	N	O	F	Ne
3	Na	Mg	3	4	5	6	7	8	9	10	11	12	Al	Si	P	S	Cl	Ar
4	K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
5	Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
6	Cs	Ba	*	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
7	Fr	Ra	#	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Uut	Fl	Uup	Lv	Uus	Uuo
Atom list *			La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	
NOT list #			Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr	

1, 打开元素周期表, 选择Atom List定义C, N
2: 在6元环上, 将其余4个C全部换成List

Clear Cancel Transfer to filter

Ok

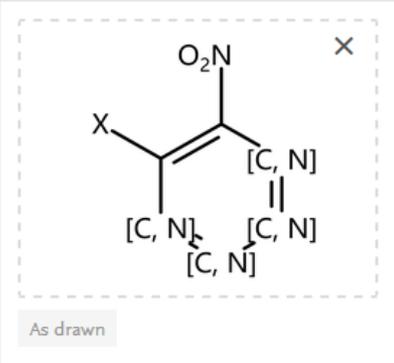
添加结构后的界面

Reaxys[®] Quick search Query builder Results Synthesis planner History Sam Yu   

29 Filters and Analysis

Limit to > Exclude >

By Structure 



As drawn

Yield 

Reagent/Catalyst 

Solvent 

Catalyst Classes 

Solvent Classes 

Product Availability 

29 Reactions out of 96 Documents containing 43 Substances, 18 Targets

0       Reaxys Ranking 

Reaction ID: 91265  

1      



36 Conditions  Find Similar >

Reaction ID: 92348  

2      



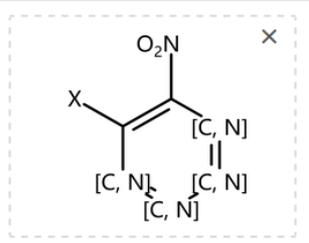
Feedback 

最后的结果

Reaxys® Quick search Query builder Results Synthesis planner History Sam Yu

12 Filters and Analysis

By Structure



As drawn

Yield Reagent/Catalyst Solvent Catalyst Classes Solvent Classes Product Availability Reactant Availability

12 Reactions out of 29 Documents containing 18 Substances, 14 Targets

0 Limit To Exclude Export Syn-Plan Reaxys Ranking ↓

Reaction ID: 111118



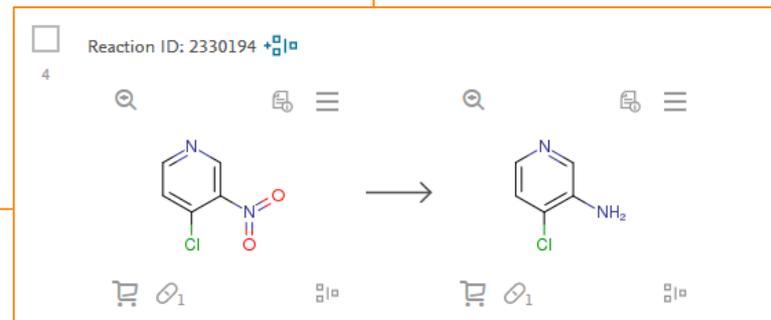
17 Conditions Find Similar

Reaction ID: 111161



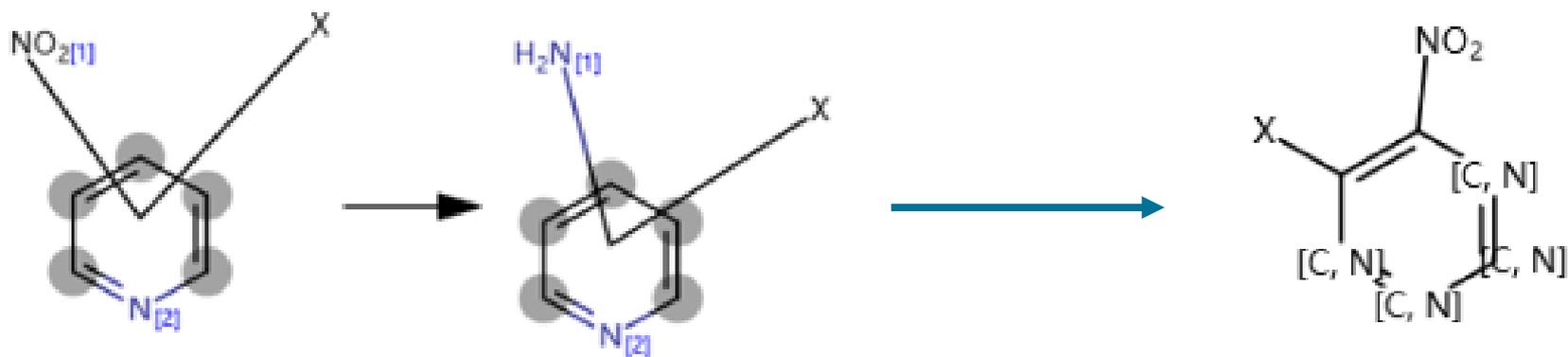
5 Conditions Find Similar

这种检索，出来的NO₂和X都处于邻位



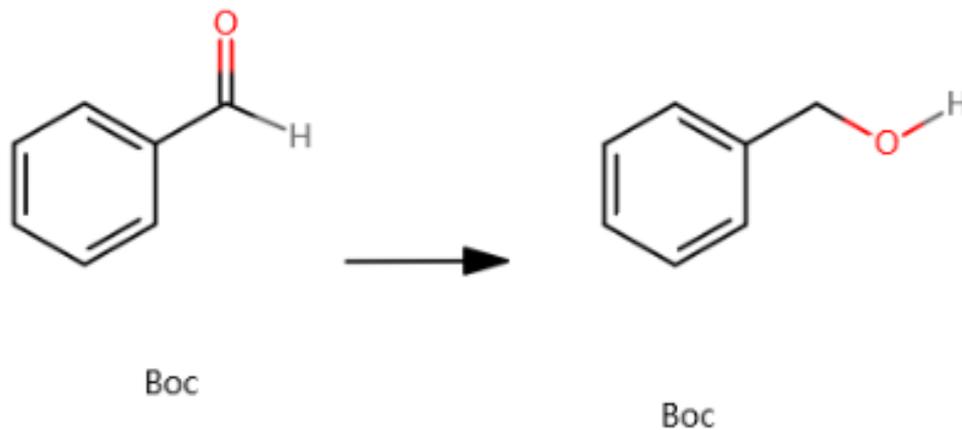
案例小结

- 当结构中存在一些特定要求，无法一次定义完全的时候，可以采用分次定义的方式
- 两次定义的结构，并不存在包容关系，这和通常意义上的限定不太一样
- 采用这种限定拿到的结果，是单独检索这两个结构的交集
- 采用这种限定策略，限定结构时必须将原有结构删除



Case Study 2

- 复杂结构中的常见问题
 - 反应中心，只是一个简单的化学变化
 - 反应物/产物，结构复杂或者新颖
 - 需要选择性的氧化，还原，脱保护等
- 检索符合以下条件的反应
 - 结构中存在Boc和苯甲醛
 - 反应后苯甲醛变成苯甲醇



Reaxys中的定义

The screenshot displays the Reaxys Structure editor interface. At the top, navigation links include "Quick search", "Query builder", "Results", "Synthesis planner", and "History". The main workspace shows a chemical reaction: benzaldehyde (left) reacts to form benzyl alcohol (right), with an arrow indicating the transformation. The left sidebar contains a "Structure editor" toolbar with various drawing tools. The right sidebar, titled "Search this structure as:", lists search criteria with checkboxes and radio buttons. The "Additional ring closures" option is highlighted with an orange box. At the bottom, there are buttons for "Clear", "Cancel", and "Transfer to query".

Structure editor

Create structure template from name >

Search this structure as:

- As drawn
- As substructure
 - On all atoms
 - On heteroatoms
- Similar
- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

+ More options

Feedback

- 1: 亚结构检索
- 2: 添加环的保护, Additional Ring closures.
- 3: S*, Atom Mapping

Reaxys中的结果

Reaxys[®] Quick search Query builder Results Synthesis planner History Sam Yu

196 Filters and Analysis

196 Reactions out of 160 Documents containing 368 Substances, 46 Targets

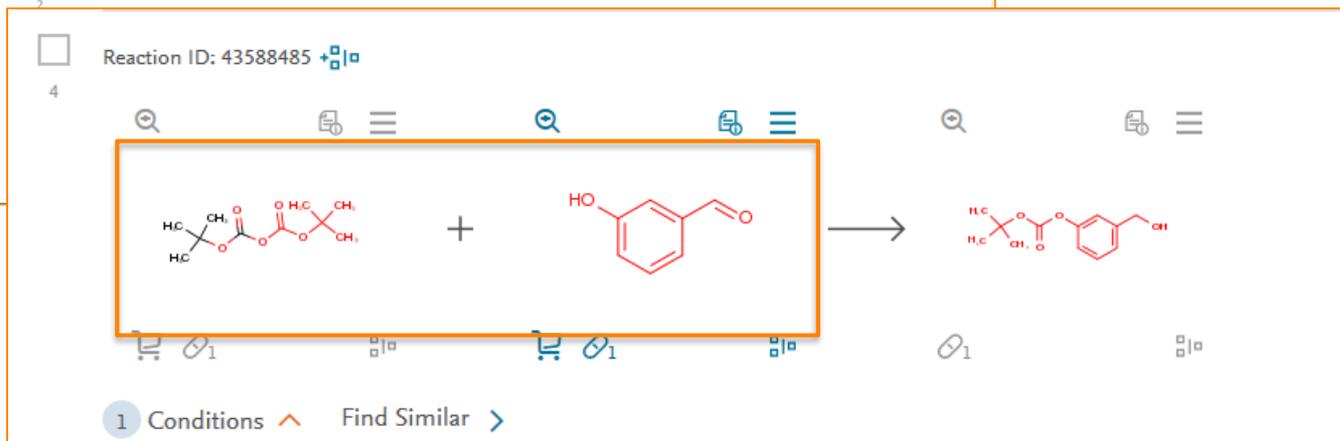
By Structure Yield Reagent/Catalyst Solvent Catalyst Classes Solvent Classes Product Availability Reactant Availability Reaction Classes Document Type Publication Year

Single step reactions only

Reaction ID: 4655509

1

Conditions Find Similar



在不做任何设置的情况下，会获得两个片段在不同结构中的反应

Reaxys在结构定义时直接定义碎片为一个整体

The screenshot displays the Reaxys Structure editor interface. The main workspace shows a chemical structure of benzaldehyde (left) and benzyl alcohol (right), with an arrow indicating the transformation. The interface includes a top navigation bar with 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. A search sidebar on the right offers options for searching the structure: 'As drawn', 'As substructure' (selected), and 'Similar'. Under 'As substructure', there are radio buttons for 'On all atoms' (selected) and 'On heteroatoms'. Other options include 'Tautomers', 'Stereo', 'Additional ring closures', 'Related Markush', 'Salts', 'Mixtures', 'Isotopes', 'Charged', and 'Radicals'. A pop-up menu is overlaid on the search options, showing 'Ignore Atom Mappings' (unchecked), 'Keep fragments' (checked), and radio buttons for 'Separate' and 'Together' (selected). The bottom of the interface has buttons for 'Clear', 'Cancel', 'Transfer to query', and '+ More options'.

New Reaxys定义的时候，可以直接选择Fragments是否在一个片段中

最后的结果

Reaxys® Quick search Query builder Results Synthesis planner History

188 Filters and Analysis 188 Reactions 156 Documents 350 Substances, 2 Targets

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

Single step reactions only

Reaction ID: 46555509

Reaction ID: 9213594

Reaction ID: 29688187

1 Conditions Find Similar

2 Conditions Find Similar

5 Conditions Find Similar

Feedback

从结构上看，所有的结构中都包含2个片段

Case Study 4

- 检索以下反应，将Br变成羰基

The screenshot displays the Reaxys Structure editor interface. At the top, there are navigation links: "Quick search", "Query builder new", "Results", "Synthesis planner", and "History". On the right side, there are buttons for "Register >" and "Sign in ?".

The main workspace is titled "Structure editor" and contains a chemical reaction diagram. On the left, the reactant is 2-amino-5-bromopyridine, with a bromine atom (Br) at the 5-position and an amino group (NH₂[1]) at the 2-position. An arrow points to the right, where the product is 2-amino-5-formylpyridine, with a formyl group (CHO) at the 5-position and the amino group at the 2-position. The formyl group is highlighted with a red circle.

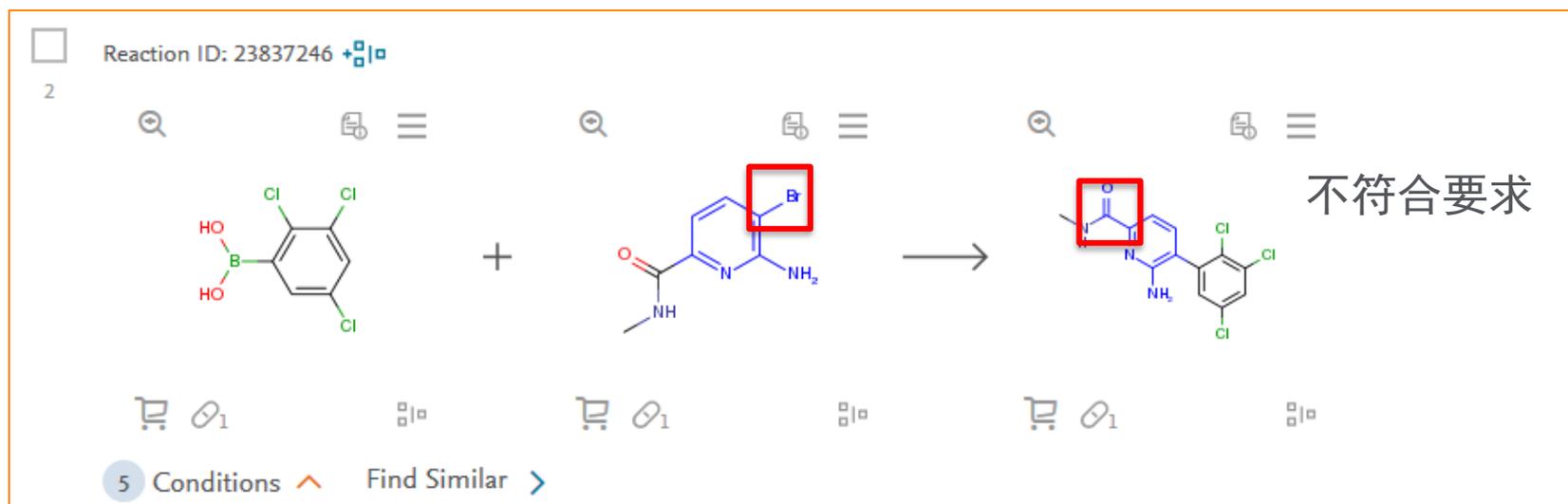
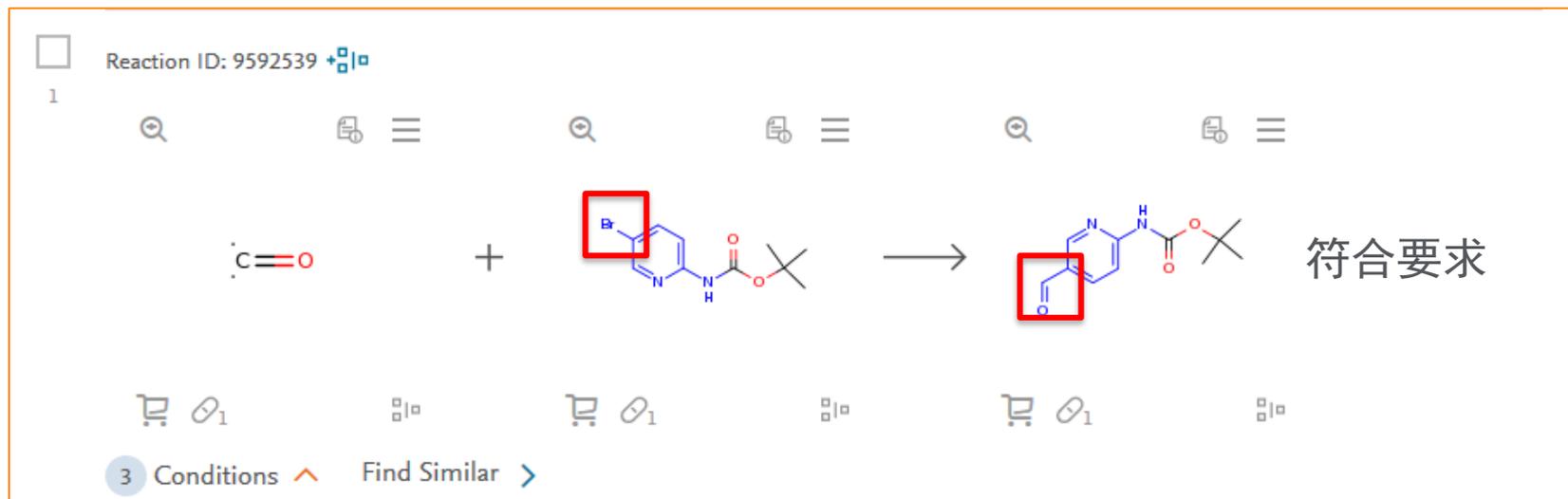
Below the reaction diagram is a toolbar with various chemical editing tools. At the bottom of the editor, there are buttons for "Clear", "Cancel", and "Transfer to query".

On the right side of the interface, there is a search panel titled "Search this structure as:". It contains several search options, each with a radio button or checkbox:

- As drawn
- As substructure
- On all atoms
- On heteroatoms
- Similar
- Tautomers
- Stereo
- Additional ring closures
- Related Markush
- Salts
- Mixtures
- Isotopes
- Charges
- Radicals

At the bottom of the search panel, there is a "+ More options" link. At the very bottom right, there is a "Feedback" button.

检索到的结果



如何解决

- 不符合要求的反应
 - C=O在原来反应物中带过来
 - 不是在Br的地方换成C=O
- 原因分析
 - 不定位取代的时候没有办法做原子映射
- 如何解决
 - Solution 1:
 - Solution 2:

Solution 1: 换一个检索模式

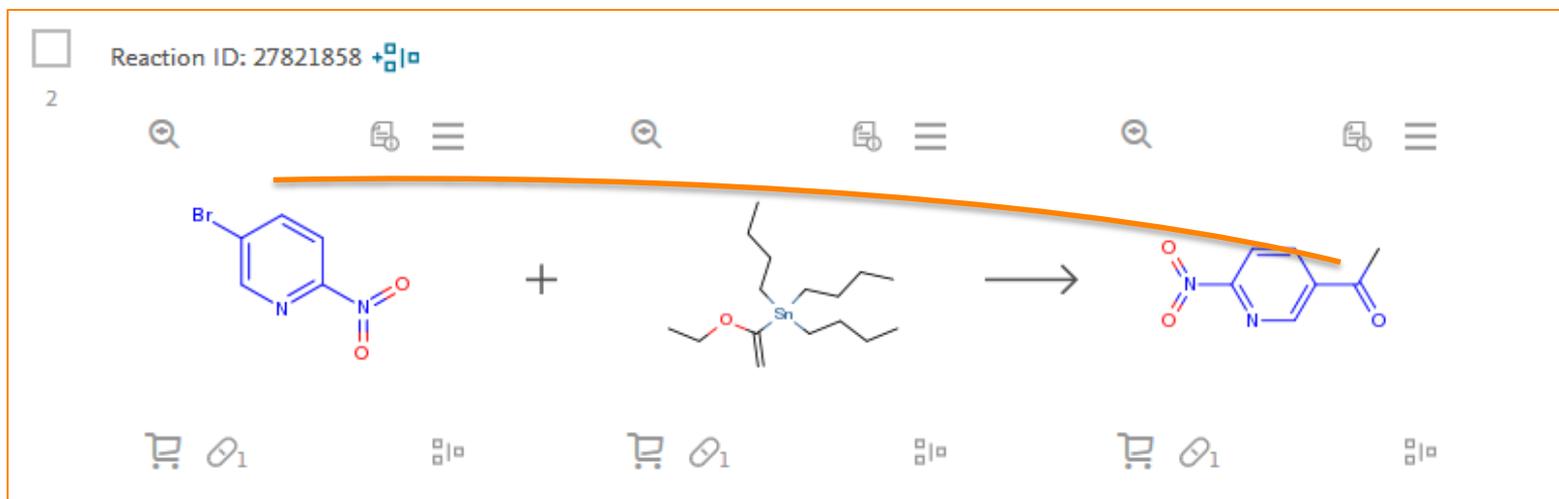
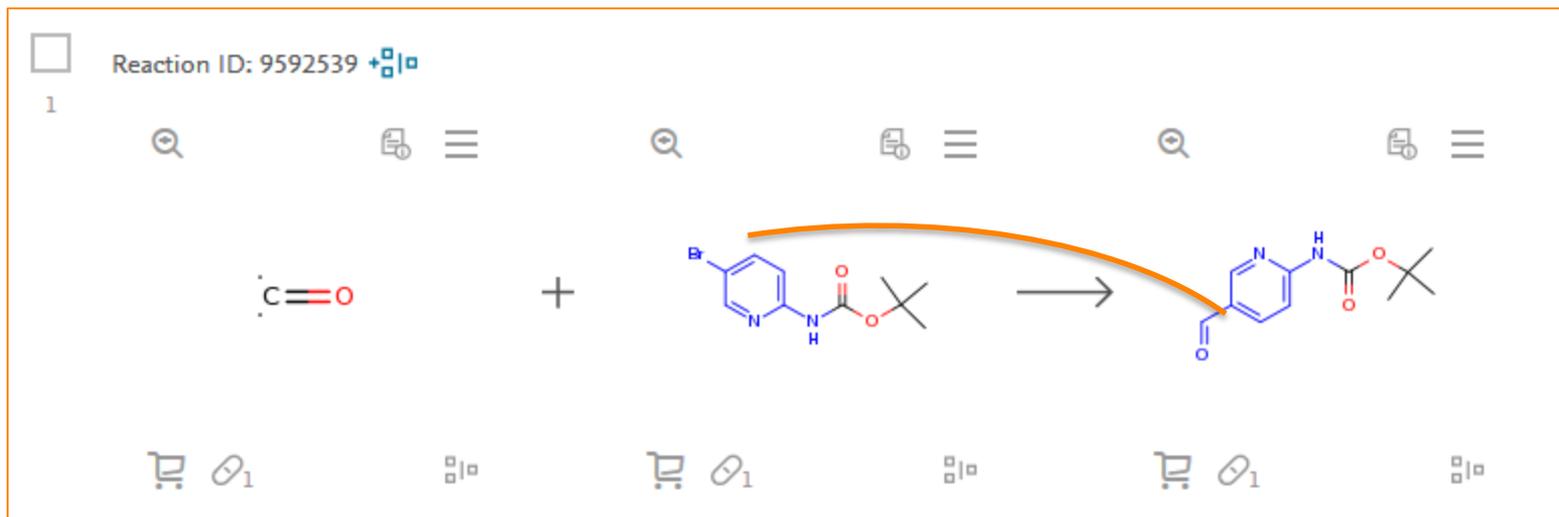
- As Draw检索同样结构

The screenshot displays the Reaxys Structure editor. The main workspace shows a chemical structure transformation. On the left, a pyridine ring has a bromine atom at the 5-position and an amino group at the 2-position. The bromine atom is labeled with 'Smax'. An arrow points to the right, where the bromine atom has been replaced by a carbonyl group (C=O), also labeled with 'Smax'. The interface includes a top navigation bar with 'Quick search', 'Query builder', 'Results', 'Synthesis planner', and 'History'. A right-hand sidebar shows search options like 'As drawn', 'As substructure', and 'Similar', with 'As drawn' selected. A bottom toolbar contains 'Clear', 'Cancel', and 'Transfer to query' buttons.

Tips:

- 使用As Draw, 可以使得Br变成C=O, 但也封闭了C=O, NH₂上的取代可能性
- 可以使用S Max标记C=O, NH₂, 在进行As Draw检索时, 实现原子的开放
- 该检索结果, 吡啶上只能有一个取代基

检索结果



Solution 2: 对于As Substructure结果的筛选

- 利用结构进行筛选

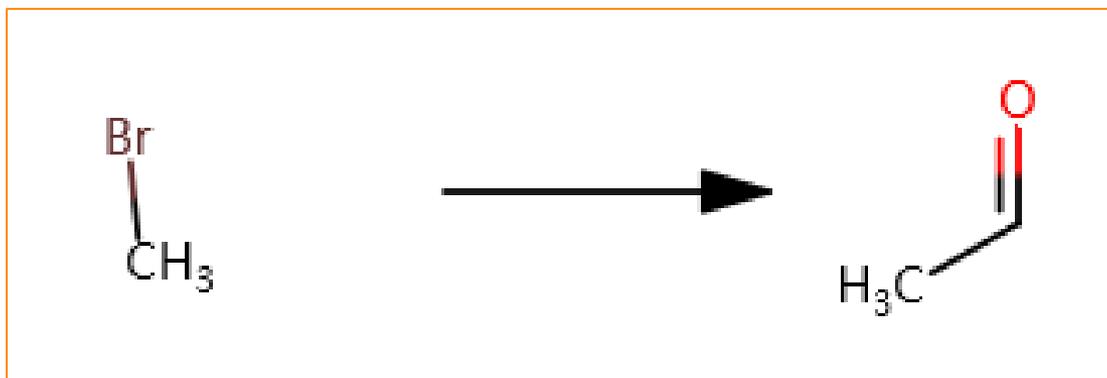
The screenshot displays the Reaxys web interface. On the left, a sidebar titled "Filters and Analysis" is visible, with a green box highlighting the "558" count and the "By Structure" filter. Below it, a "Create Structure Drawing" button is shown. The main content area shows "558 Reactions" with a search bar and various filters. Two reaction examples are shown:

Reaction 1 (ID: 9592539):
C=O + CC(C)(C)OC(=O)Nc1ccc(Br)cn1 → CC(C)(C)OC(=O)Nc1ccc(C=O)cn1

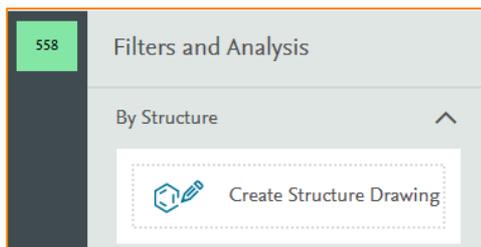
Reaction 2 (ID: 23837246):
Oc1cc(Cl)c(Cl)cc1Br + CNC(=O)c1c(N)nc2c(Br)ccc2n1 → CNC(=O)c1c(N)nc2c(Cl)c(Cl)cc2n1

筛选的出发点

- 问题的结症
 - Br和C=O接在吡啶上的位置不确定，无法保证对应
- 反应的共性
 - 但是Br，C=O都是接在C上，且该C原子一定在一个芳环，或者一定要有一个不饱和键
- 筛选的结构
 - 基本上反应中心如下

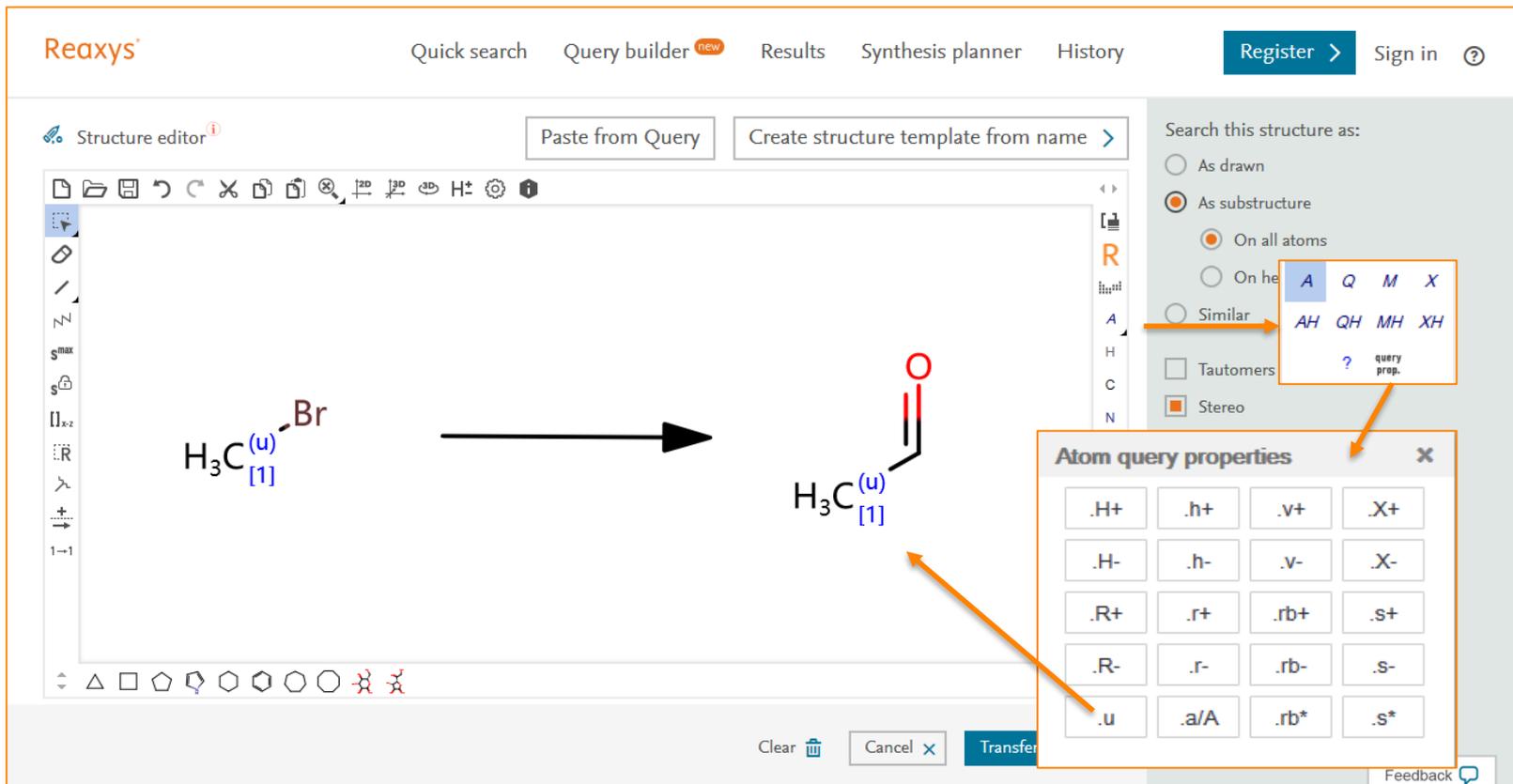


如何绘制



Tips:

1. 如果对于C原子有要求，可以带上U的定义，
2. 如果没要求，也可以不画



Reaxys

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

Structure editor

Paste from Query Create structure template from name >

Search this structure as:

- As drawn
- As substructure
- On all atoms
- On he
- Similar
- Tautomers
- Stereo

Atom query properties

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

Clear Cancel X Transfer Feedback

添加筛选后的界面

Reaxys[®] Quick search Query builder ^{new} Results Synthesis planner History Register > Sign in ?

558 Filters and Analysis

Limit to > Exclude >

By Structure

On all atoms

Yield

Reagent/Catalyst

Solvent

Catalyst Classes

558 Reactions out of 220 Documents containing 888 Substances, 103 Targets

0 Limit To Exclude Export Syn-Plan

Reaxys Ranking ↓

Reaction ID: 9592539

1

Chemical reaction scheme showing the synthesis of a substituted benzamide derivative.

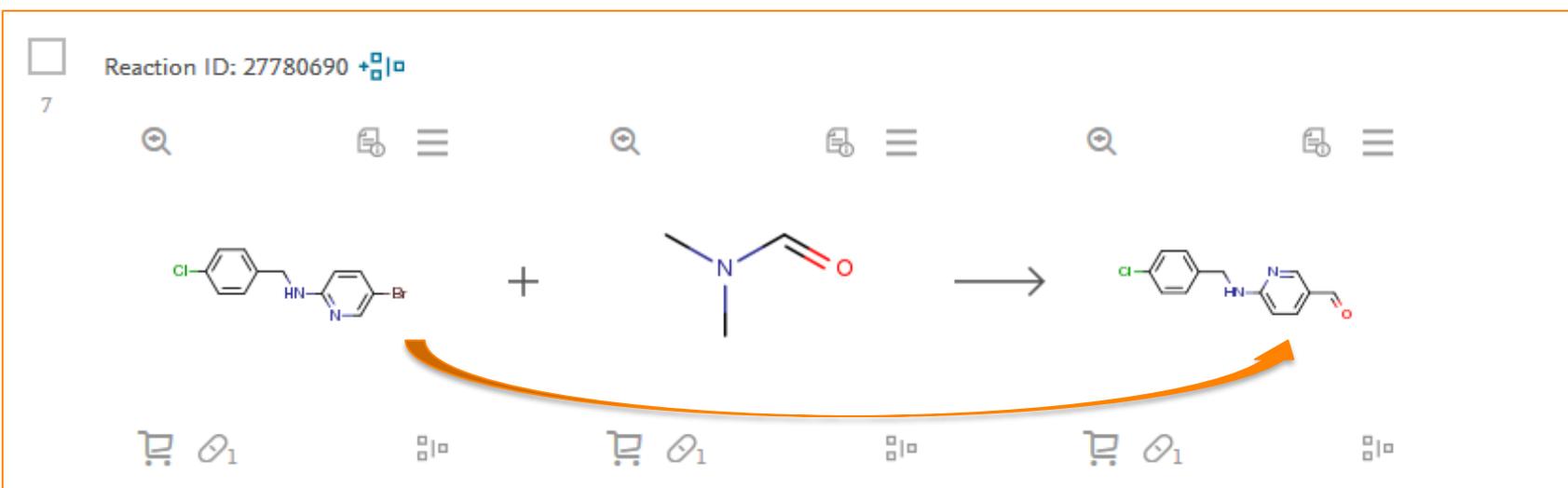
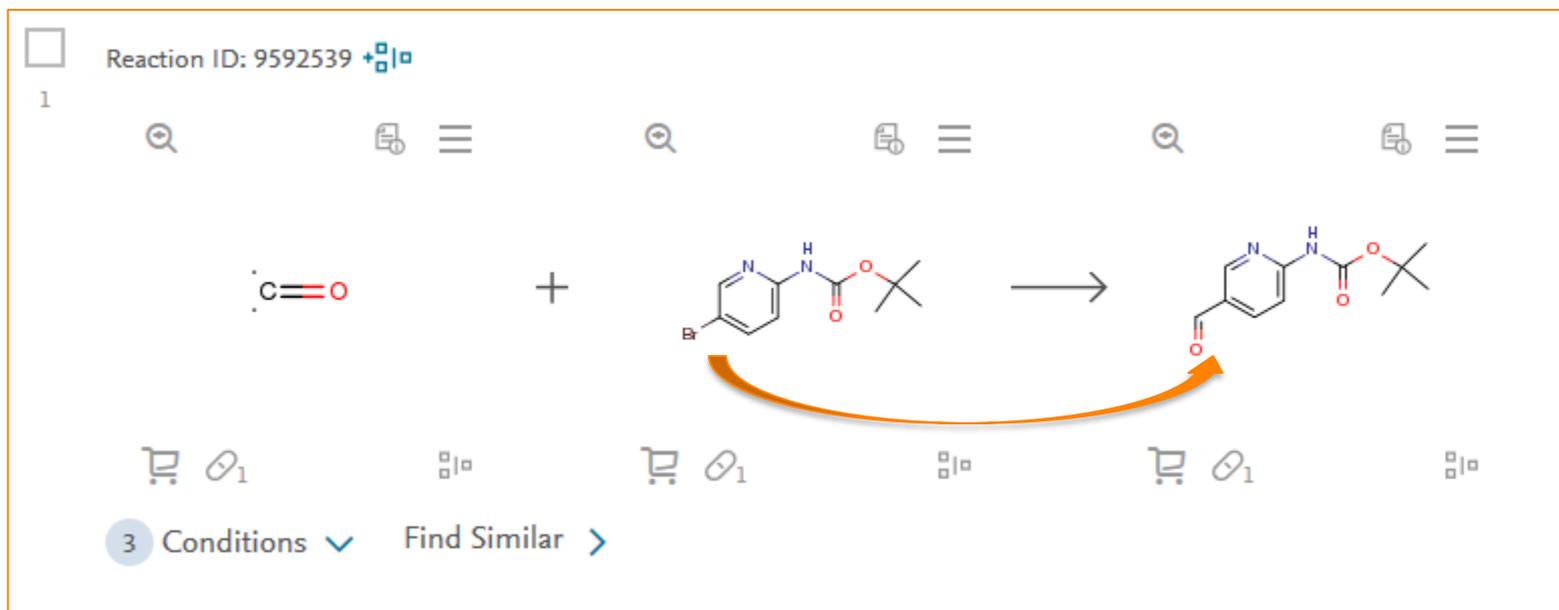
3 Conditions Find Similar >

Yield	Conditions	References
100%	With N,N,N,N-tetramethylethylenediamine; hydrogen; cat- acium A; palladium diacetate In tetrahydrofuran at 100°C; under 3750.38 Torr; for 16h;	SANOI; BOEHM, Claudius; KLEIN, Susanne; NAPIERSKI, Bernd; SOMMER, Christian - WO2012/62730, 2012, A1 Location in patent: Page/Page column 22 Full Text ↗ Details > Abstract >
100%	With N,N,N,N-tetramethylethylenediamine; hy- ladium diacetate; catacium A In tetrahydrofuran at 100°C,	NOFI; BOEHM, Claudius; KLEIN, Susanne; NAPIERSKI, Bernard; SOMMER, Christian - US2013/245274, 2013

Show Less ^

Feedback

最后的结果

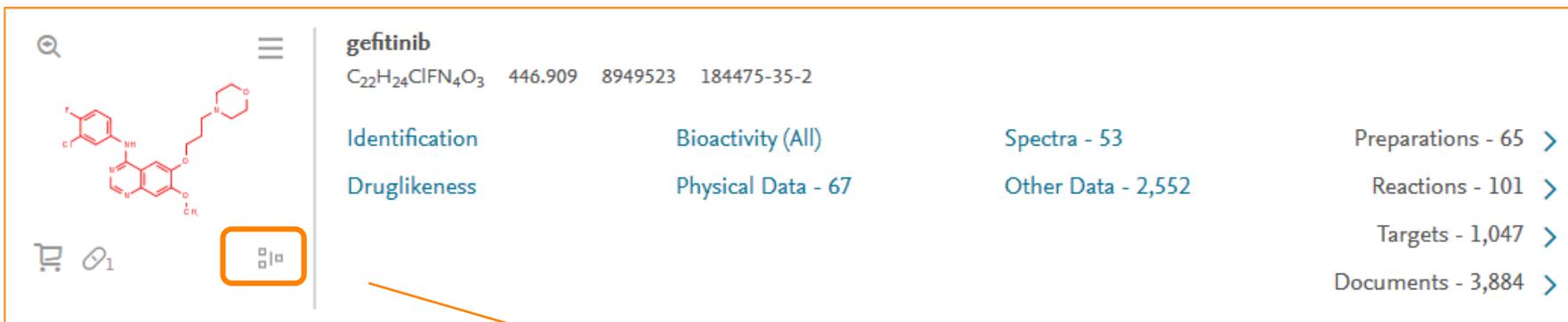


提纲

- Reaxys数据库的介绍与更新
- Reaxys数据库与同类数据库的比较
 - 索引内容比较
 - 可检索性比较
- Reaxys数据库中的检索
 - Reaxys数据库中物性数据有关的检索
 - Reaxys数据库中的结构面板与复杂结构设计
 - Reaxys数据库中的反应设计与筛选
 - Reaxys数据库中的合成路线设计
- Reaxys数据库检索小结

Reaxys中的合成计划

- 给吉非替尼制定合成计划
 - Step1: 检索到吉非替尼
 - Step2: 导入合成计划

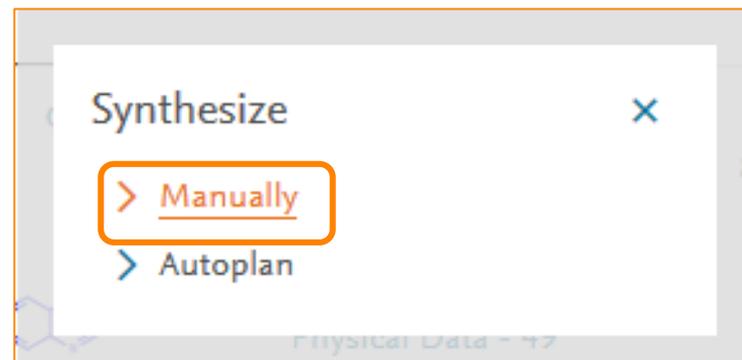


gefitinib
C₂₂H₂₄ClFN₄O₃ 446.909 8949523 184475-35-2

Identification Bioactivity (All) Spectra - 53 Preparations - 65 >
Druglikeness Physical Data - 67 Other Data - 2,552 Reactions - 101 >
Targets - 1,047 >
Documents - 3,884 >

Tips:

- 1: 通过前述的操作找到物质
- 2: 点击Synthesize图标
- 3: 打开Synthesis Plan, 这里选择手动



Synthesize X

> Manually

> Autoplan

Synthesis Plan—添加感兴趣的反应

- 可以添加多条反应在一个Plan中，用于比较

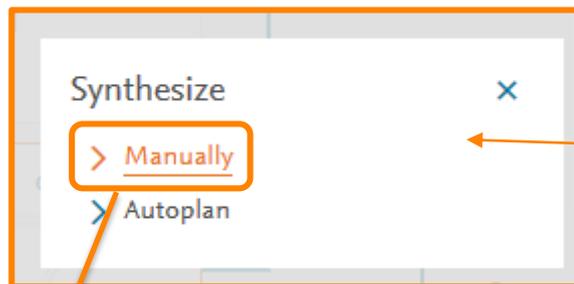
The screenshot displays the Reaxys web interface. At the top, there are navigation tabs: "Quick search", "Query builder", "Results", "Synthesis planner", and "History". The user "Sam Yu" is logged in. The main area shows "64 Reactions out of 36 Documents containing 61 Substances, 1,047 Targets". A sidebar on the left contains "Filters and Analysis" with various categories like "By Structure", "Yield", "Reagent/Catalyst", etc. In the top right of the reaction list, there are buttons for "Limit To", "Exclude", "Export", and "Syn-Plan". Two reactions are selected, indicated by orange squares and numbered 1 and 2. Reaction 1 (ID: 11041177) shows a complex heterocyclic reactant reacting with 4-chloroaniline to form a product. Reaction 2 (ID: 36604056) shows 4-chloroaniline reacting with a complex heterocyclic reactant to form the same product. Orange arrows point from the "Syn-Plan" button to the "Syn-Plan" icons on the reaction cards.

添加好的结果界面

Preparation - 1b

Yield	Conditions	Reference
78%	With acetic acid at 130°C; for 3h; Temperature; Experimental Procedure ▼	Guangzhou Baiyunshan Pharmaceutical Group Co., Ltd. Baiyunshan Pharmaceutical Zong Factory; Chen Mao; Zhu Shaoxuan; Huang Xiaoguang - CN104072426, 2017, B Location in patent: Paragraph 0050; 0051; 0052; 0053; 0054; 0055 Full Text ↗ Details > Abstract >
71.19%	With acetic acid In 5,5-dimethyl-1,3-cyclohexadiene at 135°C; Experimental Procedure ▼	Shaanxi Normal University; Li, Baolin; Ren, Yufei; Wang, Liuchang; Jia, Yucui; Ding, Siyi; Wang, Wei - CN103539702, 2016, B Location in patent: Paragraph 0094-0096 Full Text ↗ Details > Abstract >
70%	With acetic acid at 125 - 130°C; for 3h;	- Organic Process Research and Development, 2007, vol. 11, # 5, p. 813 - 816 Full Text ↗ Cited 51 times ↗ Details > Abstract >

继续的扩充反应路线



Reaxys® Quick search Query builder Results Synthesis planner History Sam Yu

33 Reactions out of 18 Documents containing 37 Substances, 0 Targets

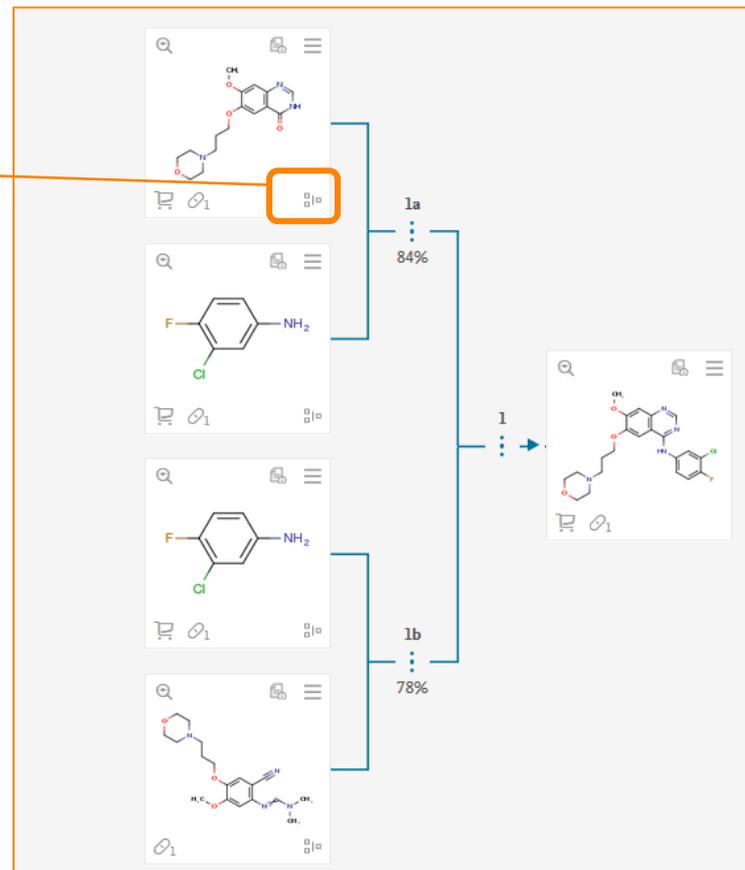
Limit To Exclude Export Syn-Plan Reaxys Ranking

Reaction ID: 29122977

Reaction ID: 43264370

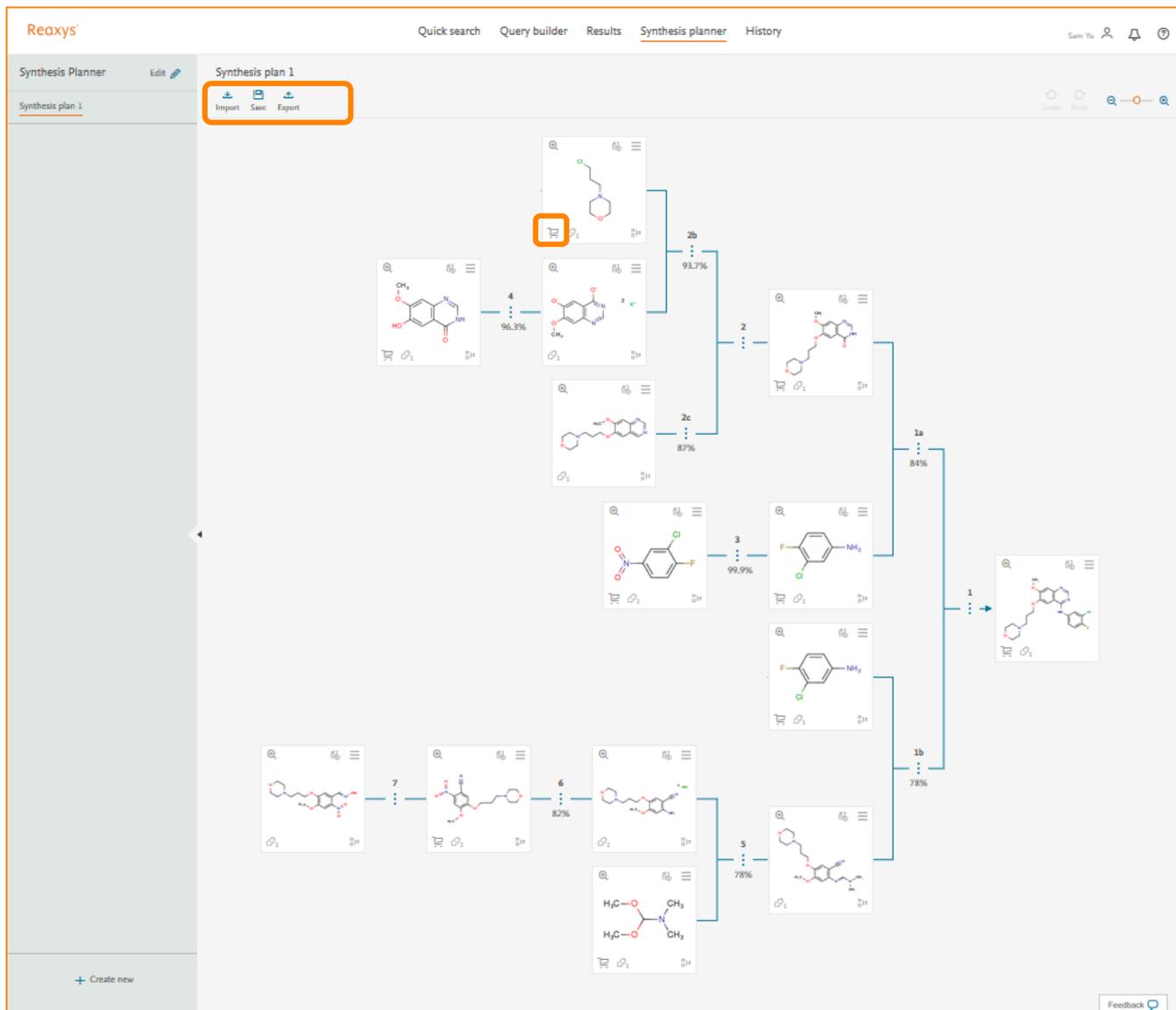
Reaction ID: 43264371

Feedback



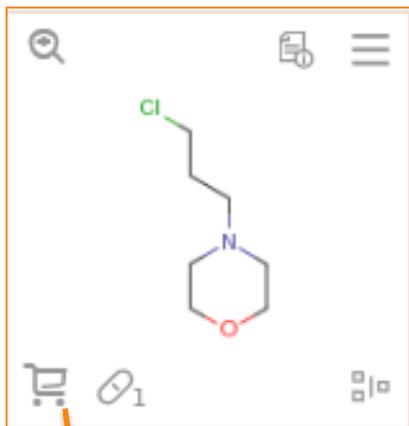
Tips:
 在Synthesis Plan上可以对任意一个物质进行同样的Synthesis的操作，可以将更多的反应添加进来

最后的结果



可以对Synthesis Plan进行导入，导出或者保存等操作。

获得物质的商业信息



Substance Availability

- Accelrys' ACD
- CambridgeSoft ACX
- Labnetwork
- Sigma Aldrich

LabNetwork 药明康德 WuXi AppTec

化学产品 | 请输入任意关键词 (CAS号、分子式) | 关键词搜索

4-(3-chloropropyl)morpholine

宽博网化合物ID: LN00004308
 CAS: 7367-67-7
 MDL: MFCD00039714
 分子式: C7H14ClNO
 分子量: 163.6454
 Log P: 暂无
 重原子个数: 10
 同位素原子数: 暂无

SMILES: C[CC]CN1CCOCC1
 InChI 编码: PIAZYBLGBSMNLX-UHFFFAO YSA-N
 InChI: InChI=1S/C7H14ClNO/c8-2-1-3-9-4-6-10-7-5-9/h1-7H2
 氢键受体数: 2
 氢键给体数: 0
 旋转键数: 3

查看大图

共显示 51 个结果

产品名称	供应商	排名	基价	纯度 (大于等于)	库存	默认
4-(3-Chloropropyl)morpholine(WX630132) 供应商ID: W0000002022	上海药明康德新药开发有限公司	★★★★★	¥375.00 (100g)	95%	询盘	- 展开
N-(3-Chloropropyl)morpholine 供应商ID: Rundang922	衢州润东化工有限公司	★★★★★	¥85.00 (10g)	暂无	50g - CN	- 展开
4-(3-Chloropropyl)morpholine 供应商ID: M402903	Atlantic Research Chemicals	★★★★★	¥89.25 (1g)	97%	494.75g - UK	- 展开
4-(3-Chloro-propyl)morpholine 供应商ID: W5-030-003	Advanced Chemical Intermediates (ACINTS)	★★★★★	¥361.00 (1g)	95%	9g - UK	- 展开
4-(3-chloropropyl)morpholine 供应商ID: 48-61-0328201	Specs	★★★★★	¥208.00 (100mg)	暂无	询盘	- 展开
N-(3-Chloropropyl)morpholine 供应商ID: A210000003	萨奥化学技术(上海)有限公司	★★★★★	¥85.00 (5g)	96%	3225g - CN	- 展开
4-(3-Chloropropyl)morpholine 供应商ID: C3403	绿希顿上海化工成工业发展有限公司	★★★★★	¥290.00 (5g)	96%	5g - CN-SH 10g - CN-TJ	- 展开
4-(3-Chloropropyl)morpholine 供应商ID: 01000003	北京飞达瑞商贸有限公司	★★★★★	¥2118 (5g)	96%	95g - CN	- 展开
4-(3-Chloropropyl)morpholine 供应商ID: 1000000	上海皓鸿生物医药科技有限公司(乐研品牌)	★★★★★	¥77.00 (25g)	95%	1000g - CN-SH	- 展开
4-(3-Chloropropyl)morpholine 供应商ID: C379750	Toronto Research Chemicals	★★★★★	¥425.00 (100mg)	暂无	询盘	- 展开

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Reaxys检索小结

- 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，跨学科的精确定案
- 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

**If you have questions feel
free to reach out**

Sam Yu
S.yu.2@Elsevier.com