钱欣博士
Application Specialist

cqian@acs-i.org

# 如何使用SciFinder检索反应信息

SCIFINDER®
A CAS SOLUTION

# 反应检索

- 反应检索绘制工具及反应信息详情
- 如何通过Analyze、Refine来精选反应
- 巧用原子标记工具和位置标记工具提高检索精度
- 通过PatentPak节省反应信息检索时间
- 高级反应案例分享
  - 片段反应
  - 按照化合物类型查找反应
- 手性反应专题
  - 手性分子合成反应
  - 手性构型翻转反应
  - 手性分子拆分反应

# 反应检索：精确结构反应检索

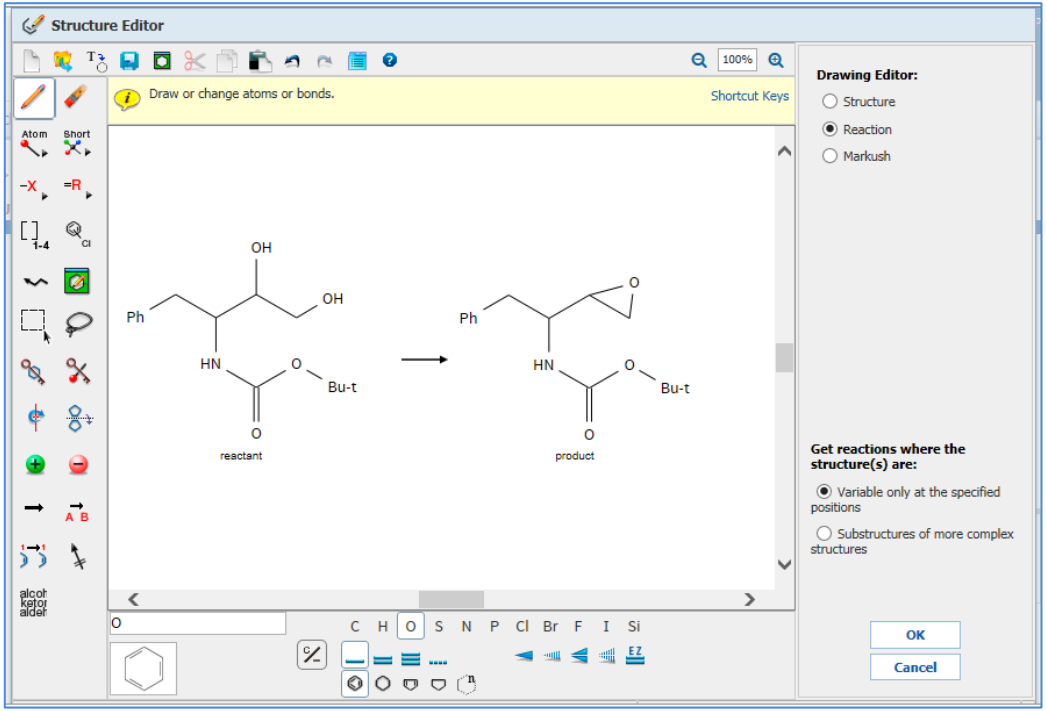
反应箭头

反应角色定义工具

反应原子标记工具

反应位置标记工具

官能团列表



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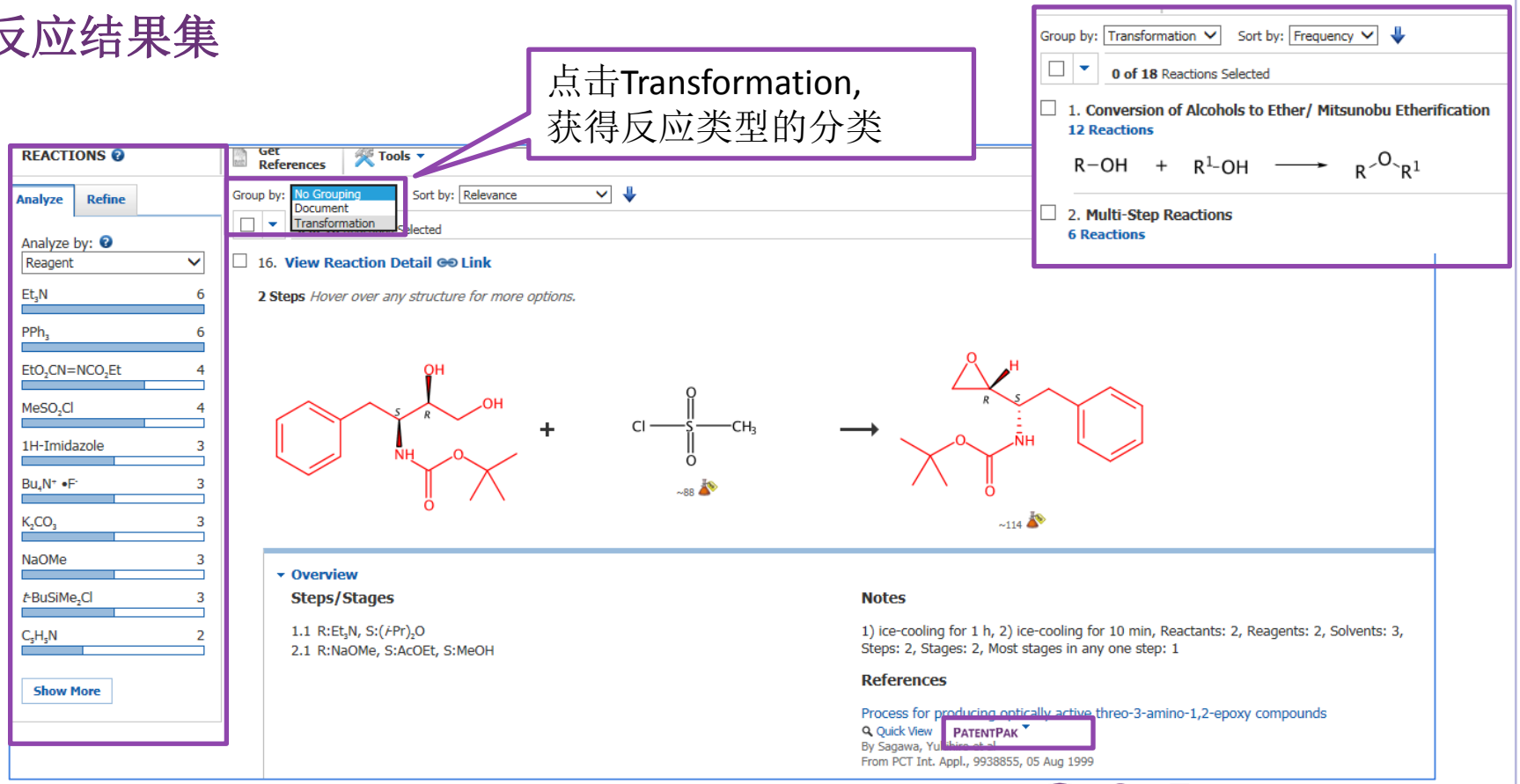
# 反应结果集

点击Transformation,
获得反应类型的分类



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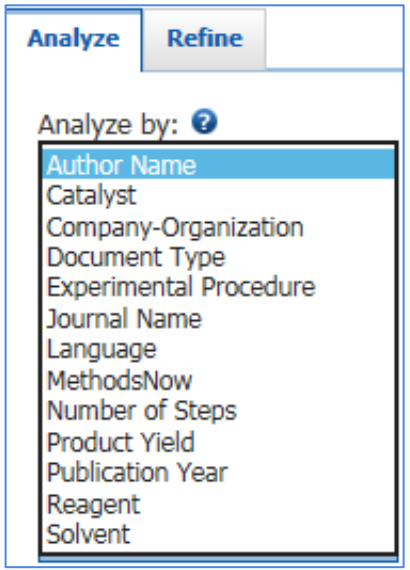
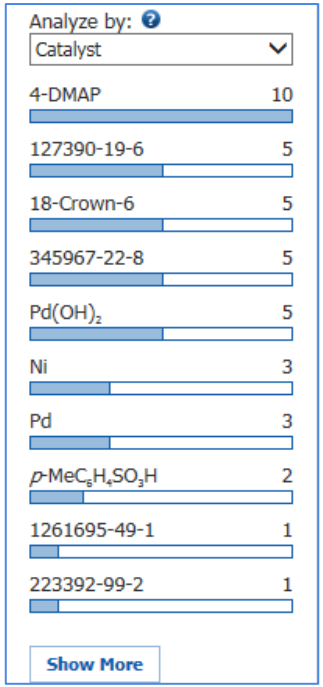
# 反应结果处理：分析

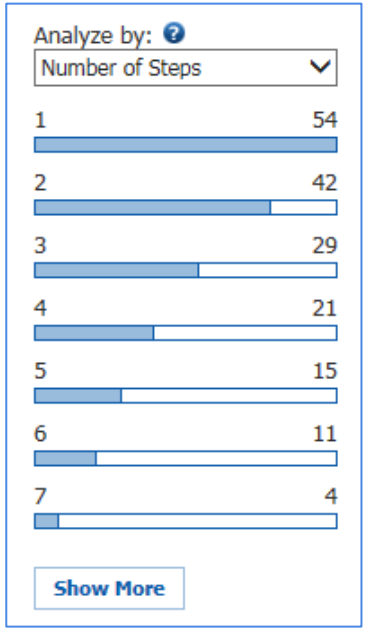
13种分析选项



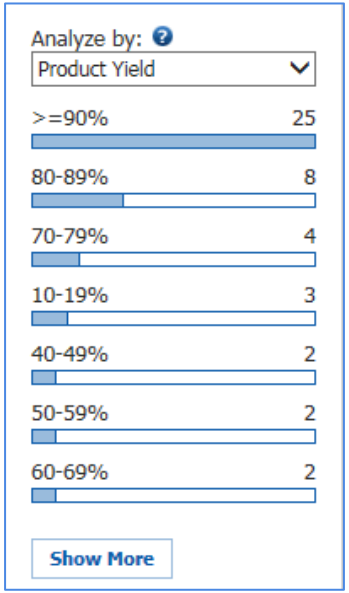

催化剂




反应步数




产率



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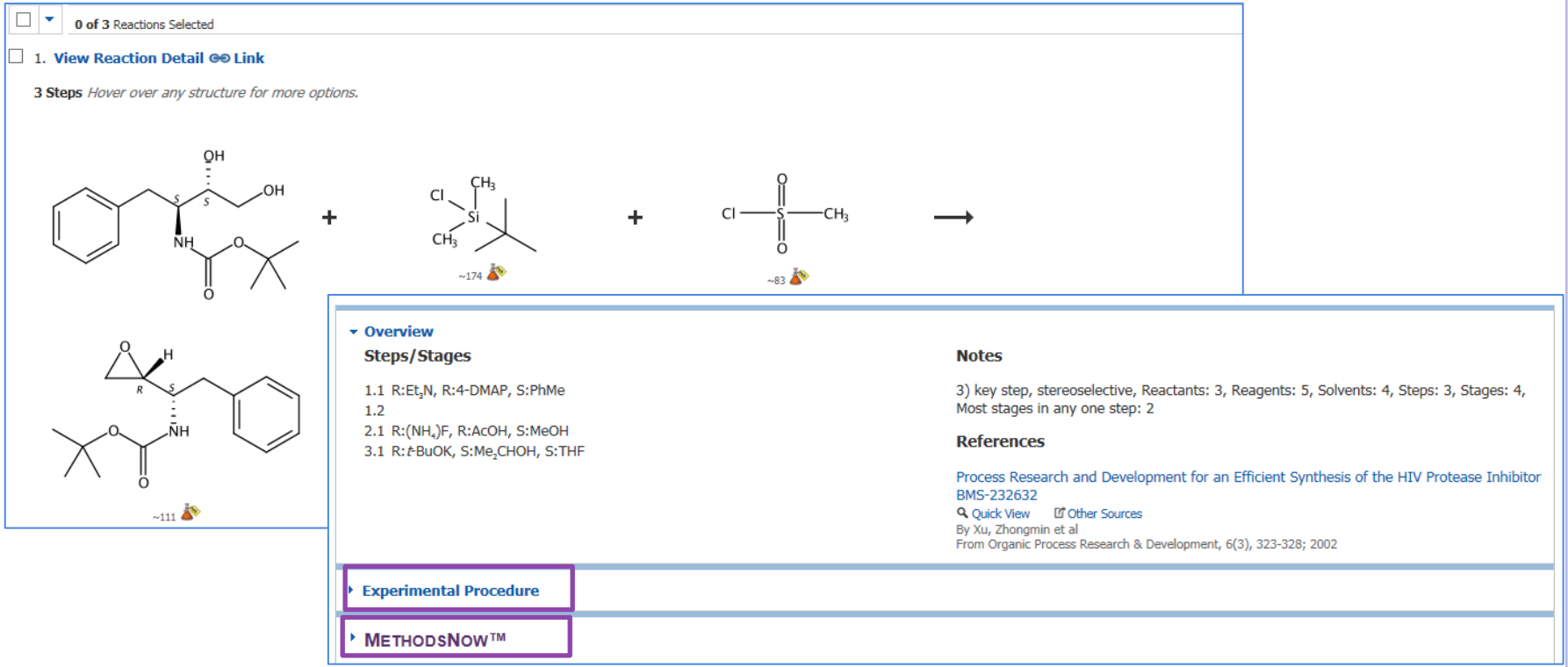
# 针对感兴趣的反应查看实验详情



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# Experimental Procedure

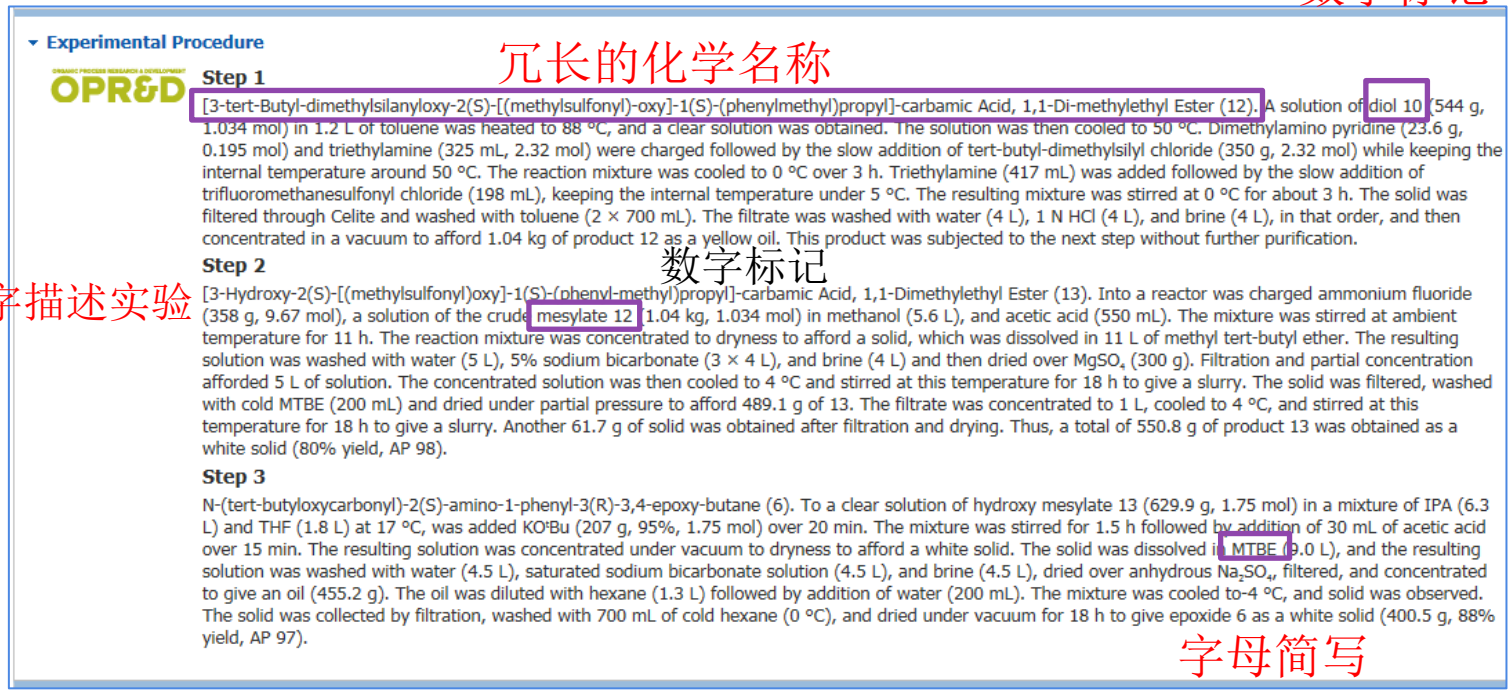
数字标记

冗长的化学名称

整段文字描述实验步骤

数字标记

字母简写



Experimental Procedure

OPR&D

**Step 1**

[3-tert-Butyl-dimethylsilanyloxy-2(S)-[(methylsulfonyl)-oxy]-1(S)-(phenylmethyl)propyl]-carbamic Acid, 1,1-Di-methylethyl Ester (12). A solution of diol 10 (544 g, 1.034 mol) in 1.2 L of toluene was heated to 88 °C, and a clear solution was obtained. The solution was then cooled to 50 °C. Dimethylamino pyridine (23.6 g, 0.195 mol) and triethylamine (325 mL, 2.32 mol) were charged followed by the slow addition of tert-butyl-dimethylsilyl chloride (350 g, 2.32 mol) while keeping the internal temperature around 50 °C. The reaction mixture was cooled to 0 °C over 3 h. Triethylamine (417 mL) was added followed by the slow addition of trifluoromethanesulfonyl chloride (198 mL), keeping the internal temperature under 5 °C. The resulting mixture was stirred at 0 °C for about 3 h. The solid was filtered through Celite and washed with toluene (2 × 700 mL). The filtrate was washed with water (4 L), 1 N HCl (4 L), and brine (4 L), in that order, and then concentrated in a vacuum to afford 1.04 kg of product 12 as a yellow oil. This product was subjected to the next step without further purification.

**Step 2**

[3-Hydroxy-2(S)-[(methylsulfonyl)oxy]-1(S)-(phenyl-methyl)propyl]-carbamic Acid, 1,1-Dimethylethyl Ester (13). Into a reactor was charged ammonium fluoride (358 g, 9.67 mol), a solution of the crude mesylate 12 (1.04 kg, 1.034 mol) in methanol (5.6 L), and acetic acid (550 mL). The mixture was stirred at ambient temperature for 11 h. The reaction mixture was concentrated to dryness to afford a solid, which was dissolved in 11 L of methyl tert-butyl ether. The resulting solution was washed with water (5 L), 5% sodium bicarbonate (3 × 4 L), and brine (4 L) and then dried over $MgSO_4$ (300 g). Filtration and partial concentration afforded 5 L of solution. The concentrated solution was then cooled to 4 °C and stirred at this temperature for 18 h to give a slurry. The solid was filtered, washed with cold MTBE (200 mL) and dried under partial pressure to afford 489.1 g of 13. The filtrate was concentrated to 1 L, cooled to 4 °C, and stirred at this temperature for 18 h to give a slurry. Another 61.7 g of solid was obtained after filtration and drying. Thus, a total of 550.8 g of product 13 was obtained as a white solid (80% yield, AP 98).

**Step 3**

N-(tert-butyloxycarbonyl)-2(S)-amino-1-phenyl-3(R)-3,4-epoxy-butane (6). To a clear solution of hydroxy mesylate 13 (629.9 g, 1.75 mol) in a mixture of IPA (6.3 L) and THF (1.8 L) at 17 °C, was added KO$^t$Bu (207 g, 95%, 1.75 mol) over 20 min. The mixture was stirred for 1.5 h followed by addition of 30 mL of acetic acid over 15 min. The resulting solution was concentrated under vacuum to dryness to afford a white solid. The solid was dissolved in MTBE (9.0 L), and the resulting solution was washed with water (4.5 L), saturated sodium bicarbonate solution (4.5 L), and brine (4.5 L), dried over anhydrous $Na_2SO_4$, filtered, and concentrated to give an oil (455.2 g). The oil was diluted with hexane (1.3 L) followed by addition of water (200 mL). The mixture was cooled to-4 °C, and solid was observed. The solid was collected by filtration, washed with 700 mL of cold hexane (0 °C), and dried under vacuum for 18 h to give epoxide 6 as a white solid (400.5 g, 88% yield, AP 97).

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# MethodsNow Synthesis——人工标引的反应信息，节省您宝贵的时间

- 详细、明确的物质信息
- 全面、有条理的实验过程信息
- 更好的阅读体验——表格形式
- 无需查看原文直接获取实验详情——反应物，反应条件，步骤，产物性质，谱图等

SciFinder® A CAS SOLUTION

# MethodsNow窗口

CAS RN即时查看物质

MethodsNow

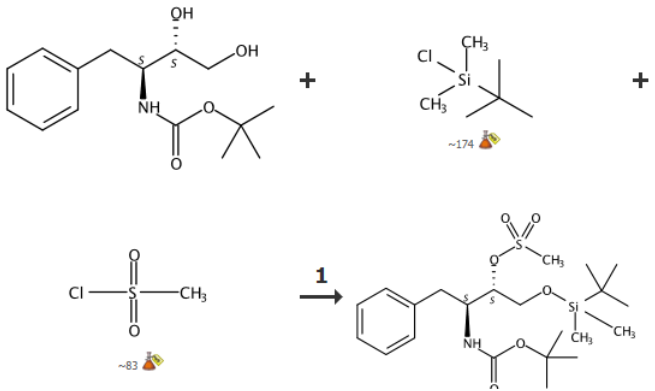
**Process Research and Development for an Efficient Synthesis of the HIV Protease Inhibitor BMS-232632**

By Xu, Zhongmin; Singh, Janak; Schwinden, Mark D.; Zheng, Bin; Kissick, Thomas P.; Patel, Bharat; Humora, Michael J.; Quiroz, Fernando; Dong, Lin; Hsieh, Dau-Ming et al

From Organic Process Research & Development, 6(3), 323-328; 2002

Published by American Chemical Society

Reaction Steps 1 2 3




产物，反应物，试剂，溶剂，步骤，反应类型，规模，CAS方法号

MethodsNow

| | |
|---|---|
| **Products** | Carbamic acid, [(1*S*,2*S*)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-[(methylsulfonyl)oxy]-1-(phenylmethyl) propyl]-, 1,1-dimethylethyl ester, CAS RN: 437713-03-6 |
| **Reactants** | Carbamic acid, *N*-[(1*S*,2*S*)-2,3-dihydroxy-1-(phenylmethyl)propyl]-, 1,1-dimethylethyl ester, CAS RN: 149451-80-9<br>*tert*-Butyldimethylsilyl chloride, CAS RN: 18162-48-6<br>Methanesulfonyl chloride, CAS RN: 124-63-0 |
| **Reagents** | Triethylamine, CAS RN: 121-44-8<br>4-(Dimethylamino)pyridine, CAS RN: 1122-58-3 |
| **Solvents** | Toluene, CAS RN: 108-88-3 |
| **Procedure** | 1. Heat the solution of chiral diol (544 g) in 1.2 L of toluene to 88 °C.<br>2. Col the solution to 50 °C.<br>3. Charge the dimethylamino pyridine (23.6 g, 0.195 mol) and triethylamine (325 mL, 2.32 mol) followed by the slow addition of tert-butyl-dimethylsilyl chloride (350 g, 2.32 mol) while keeping the internal temperature around 50 °C.<br>4. Cool the reaction mixture to 0 °C over 3 hours.<br>5. Add triethylamine (417 mL) followed by the slow addition of trifluoromethanesulfonyl chloride (198 mL) while keeping the internal temperature under 5 °C.<br>6. Stir the resulting mixture at 0 °C for about 3 hours.<br>7. Filter the solid through Celite.<br>8. Wash the solid with toluene (2 x 700 mL).<br>9. Wash the filtrate with water (4 L), 1 N HCl (4 L) and brine (4 L).<br>10. Concentrate the filtrate in a vacuum. |
| **Scale** | gram |
| **CAS Method Number** | 3-008-CAS-1545731 |

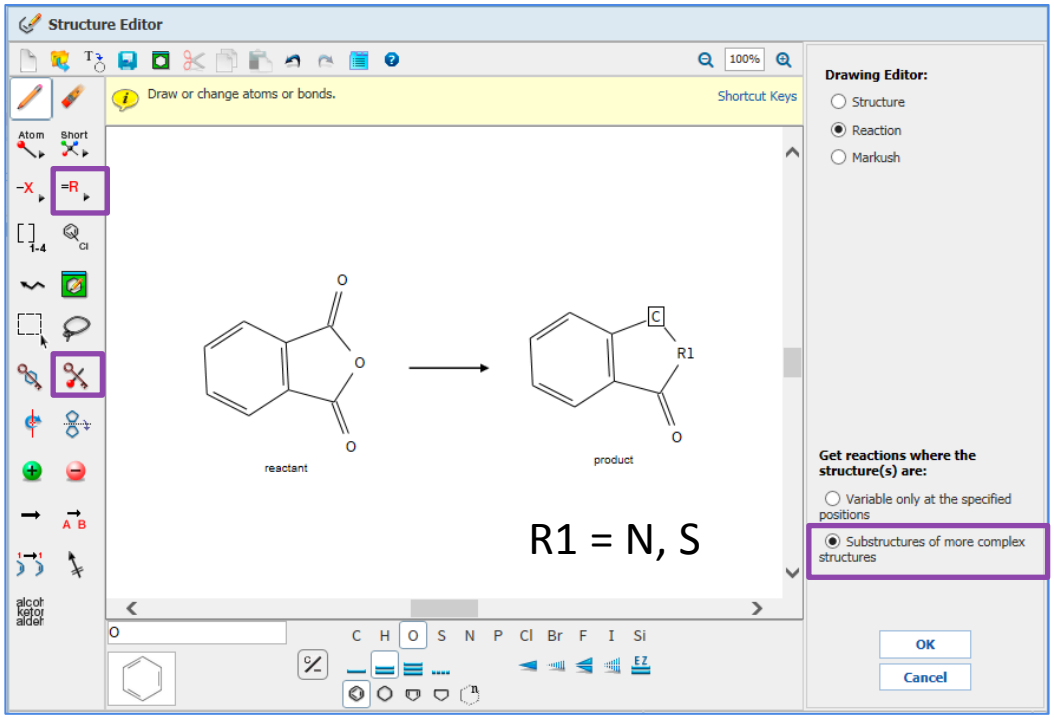
PDF或XLS格式

Print/Export Close



A CAS SOLUTION

# 反应检索：亚结构反应检索

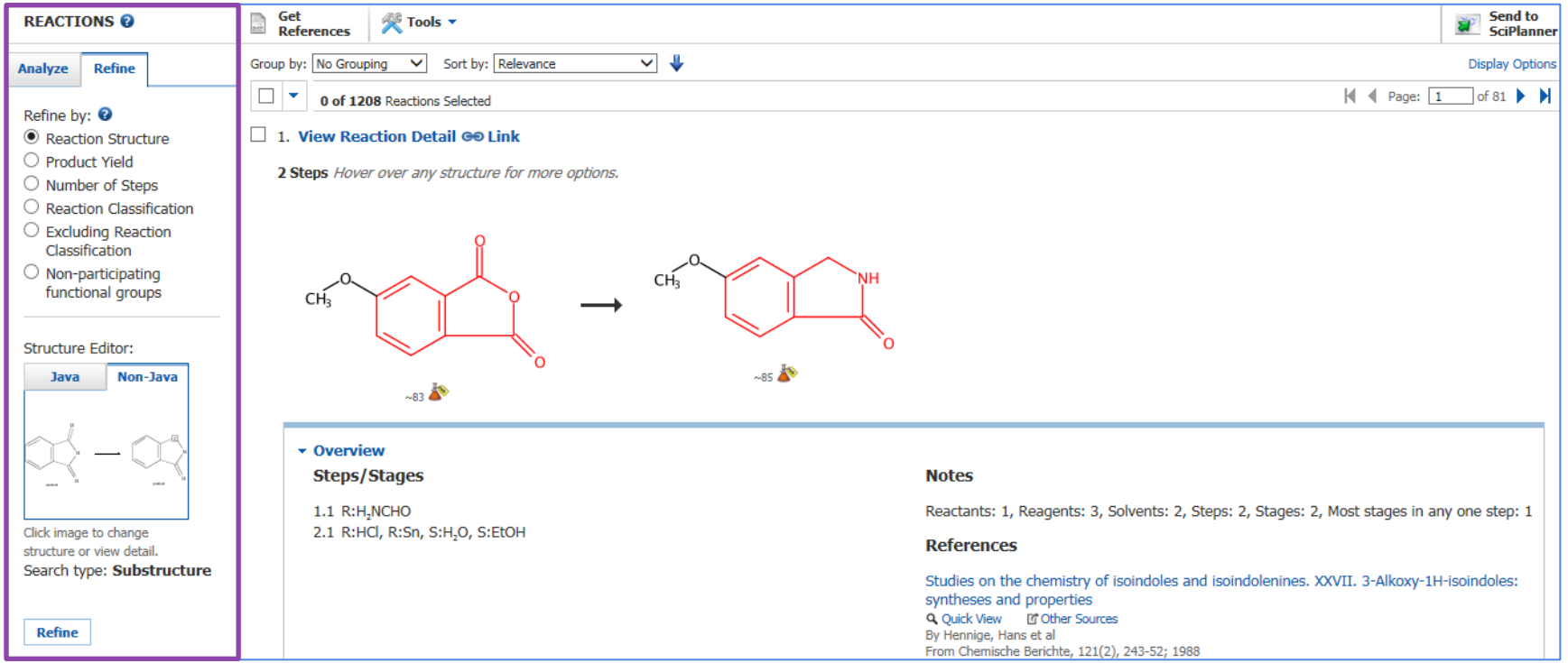



输入的反应物和产物的结构会被修饰，但母体结构不变



SciFinder® A CAS SOLUTION

# 反应结果集



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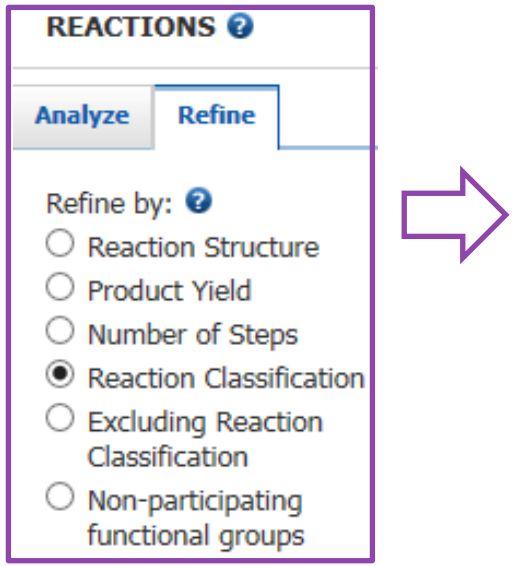
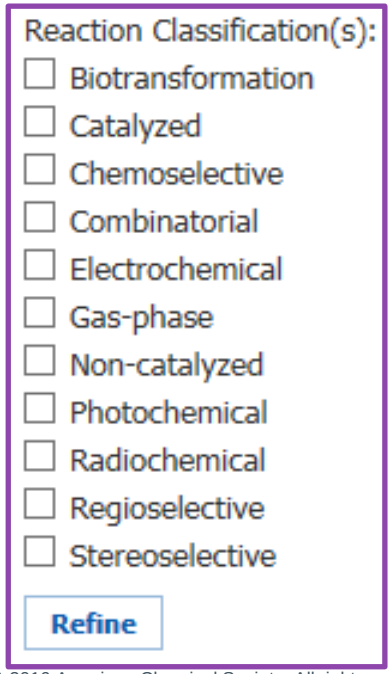
# 反应结果处理：筛选

6种筛选选项：反应结构、产率、反应步数、包含/排除的反应类型(11种)、反应官能团(217种)




- 生物转化
- 催化反应
- 化学选择性
- 组合化学
- 电子化学
- 气相反应
- 非催化反应
- 光化学
- 放射化学
- 区域选择反应
- 立体选择反应

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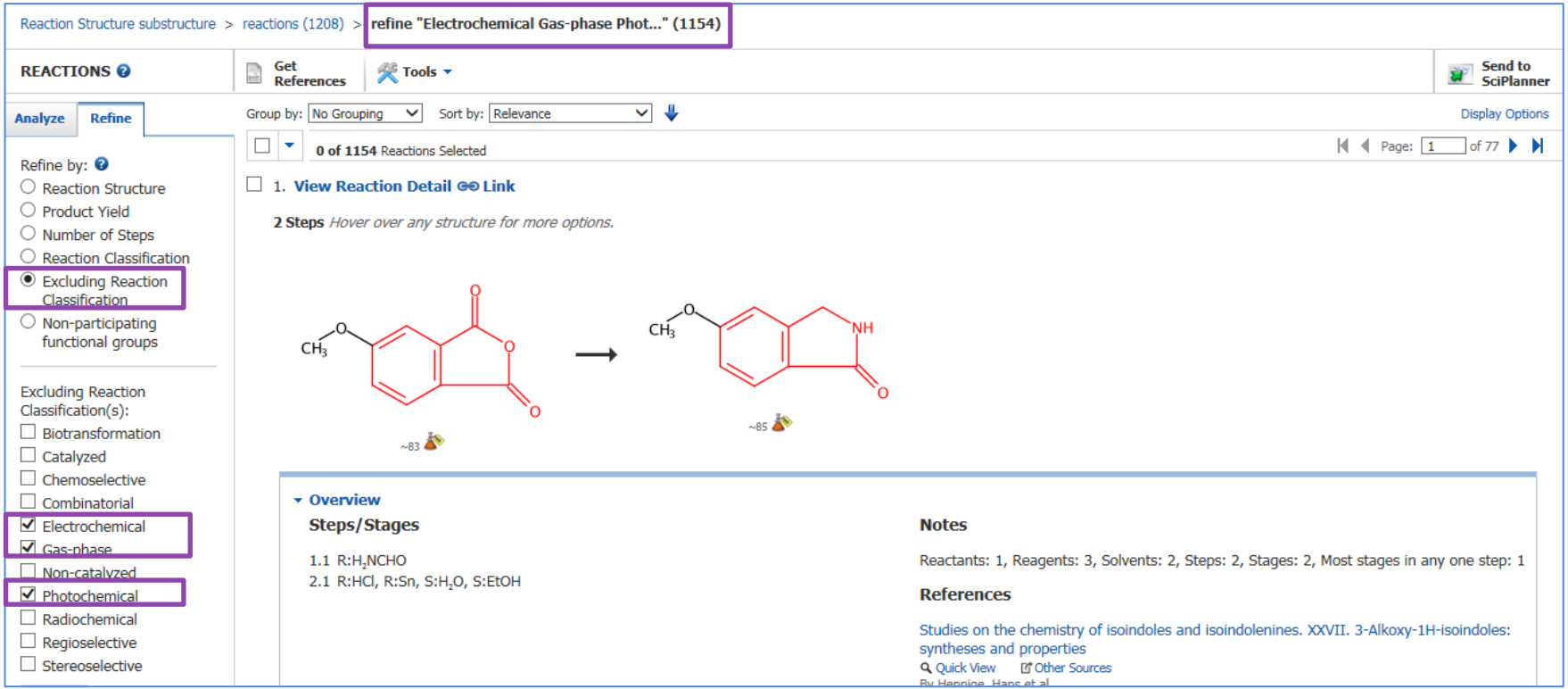
# 反应类型筛选



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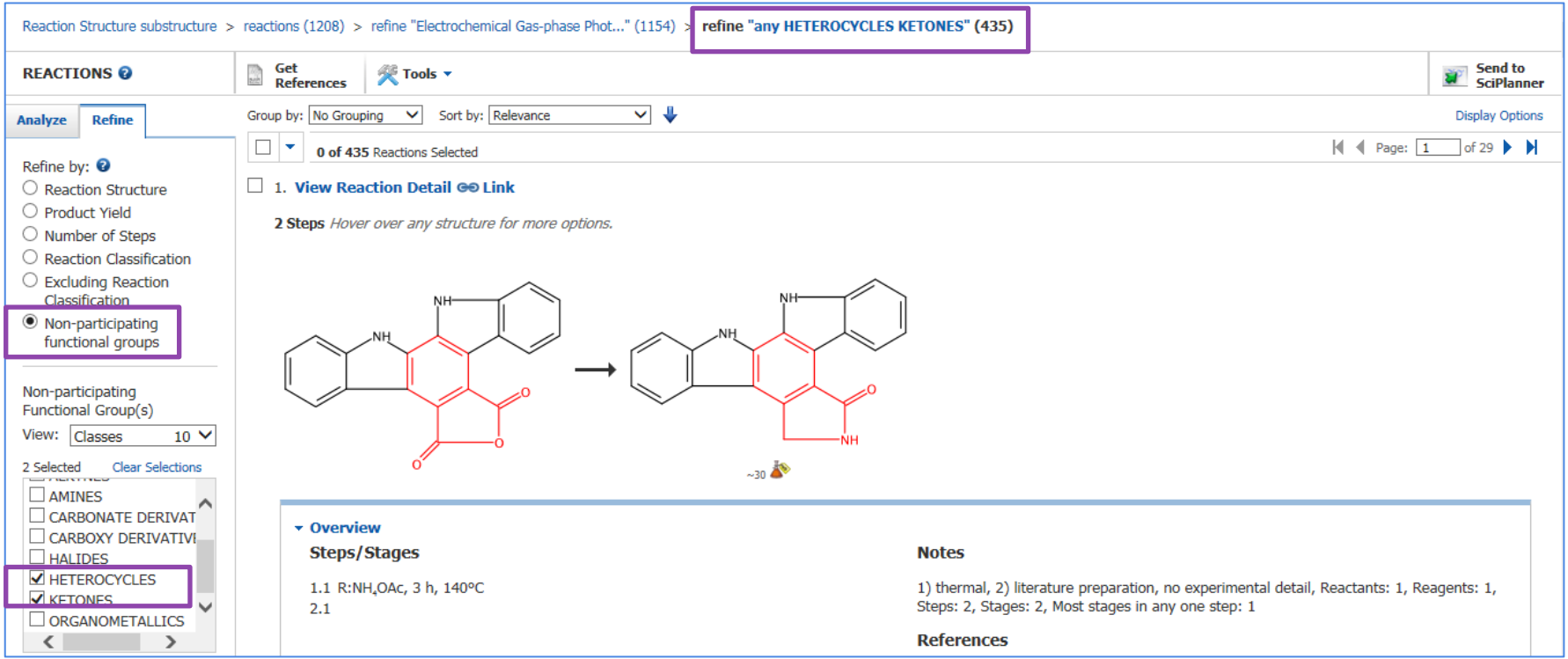
# 限定某官能团参与反应



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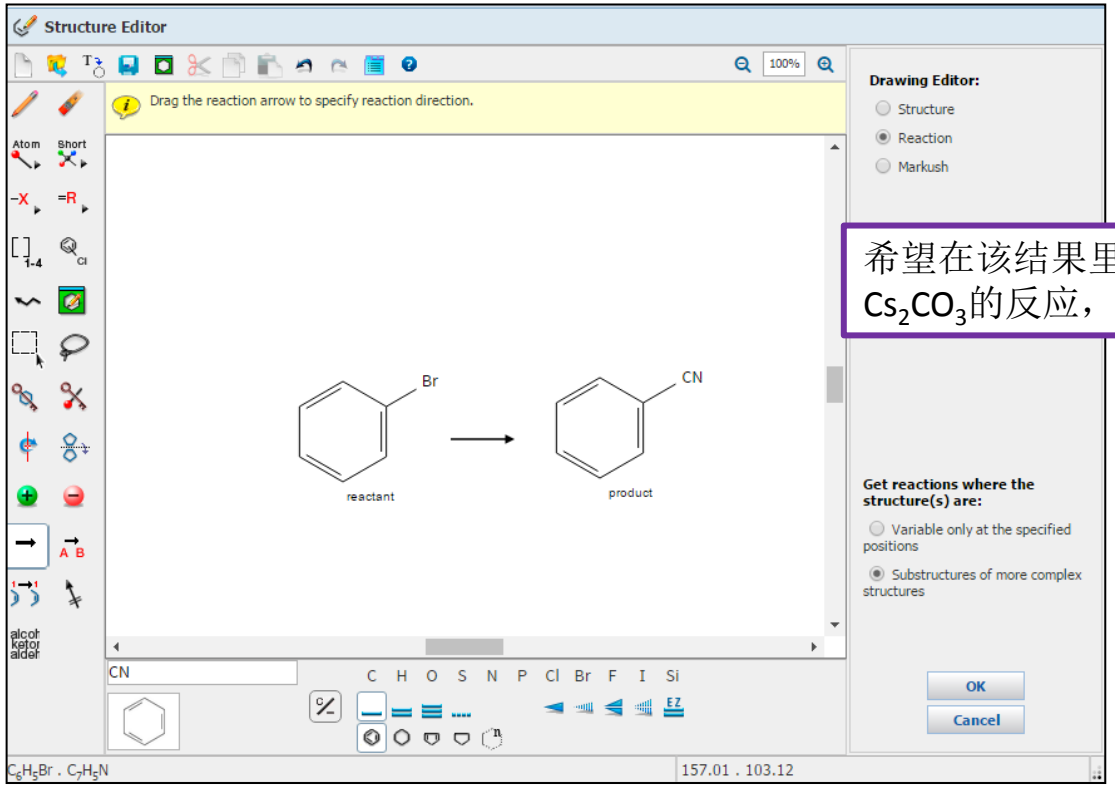
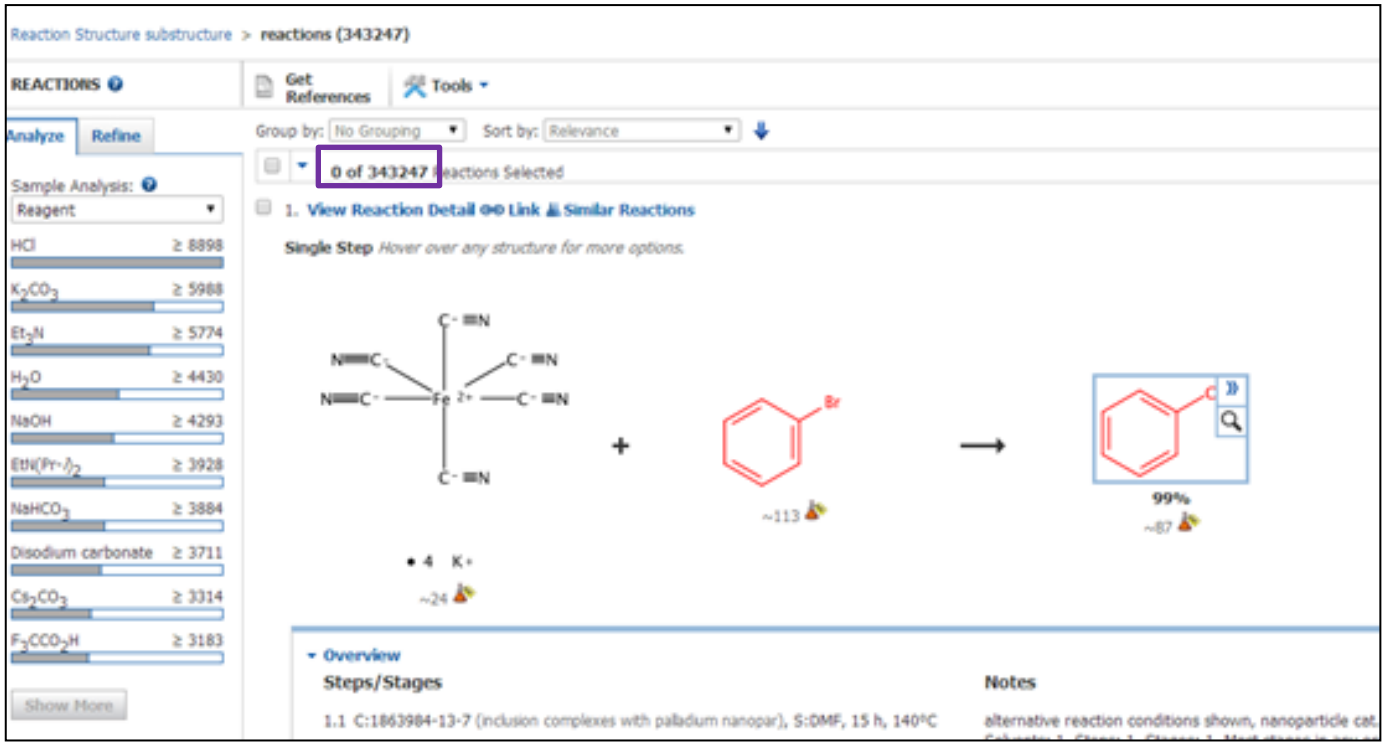
  - 手性分子拆分反应

# 案例一：检索由溴苯转化为苯腈的反应

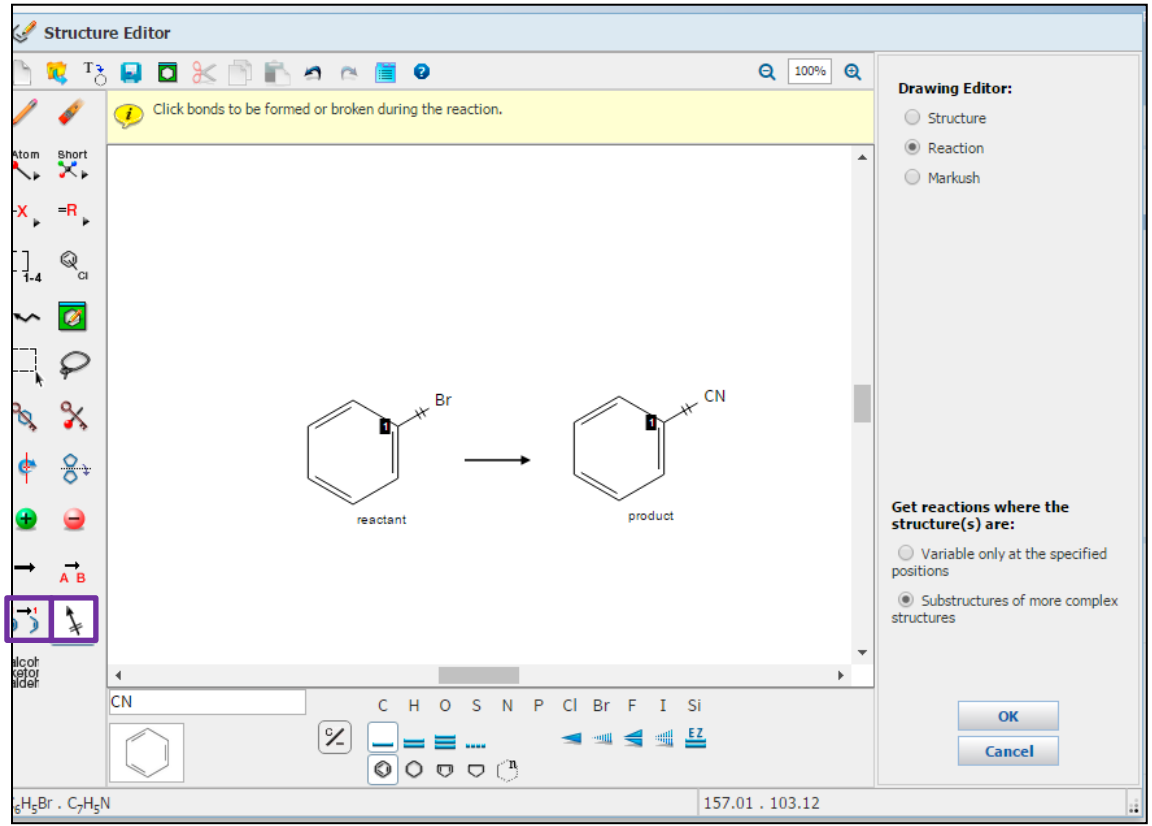



希望在该结果里进一步限定:溶剂为DMF，试剂为$Cs_2CO_3$的反应，应如何操作？

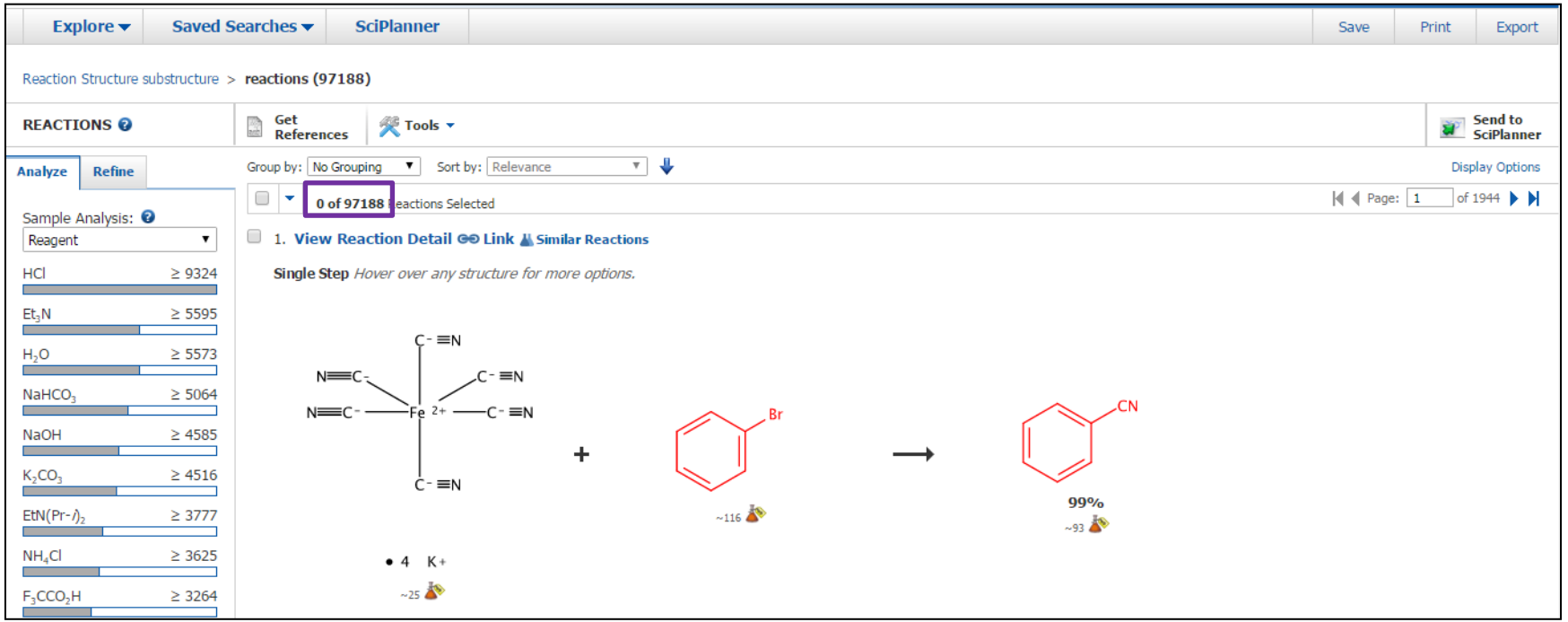
# 获得34万多条反应，噪音较大



# 可以通过反应原子标记工具和反应位置标记工具提高反应检索精度

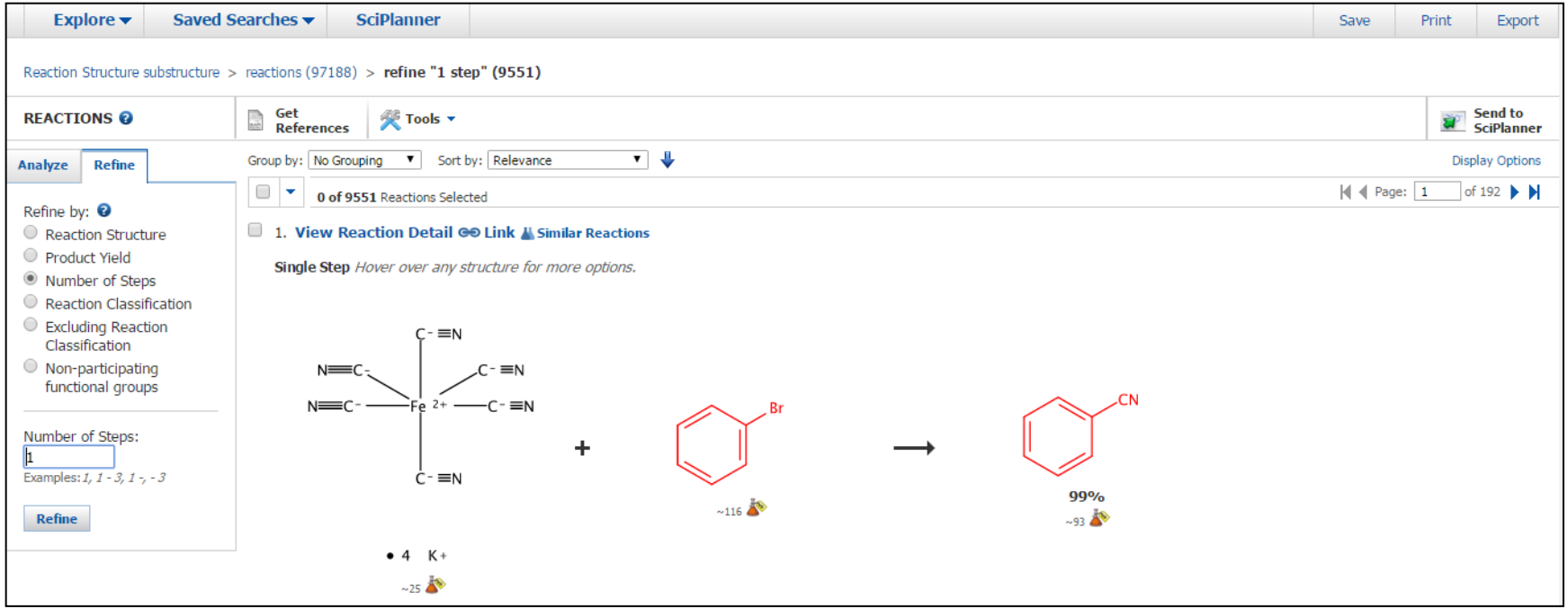


# 获得反应97188条

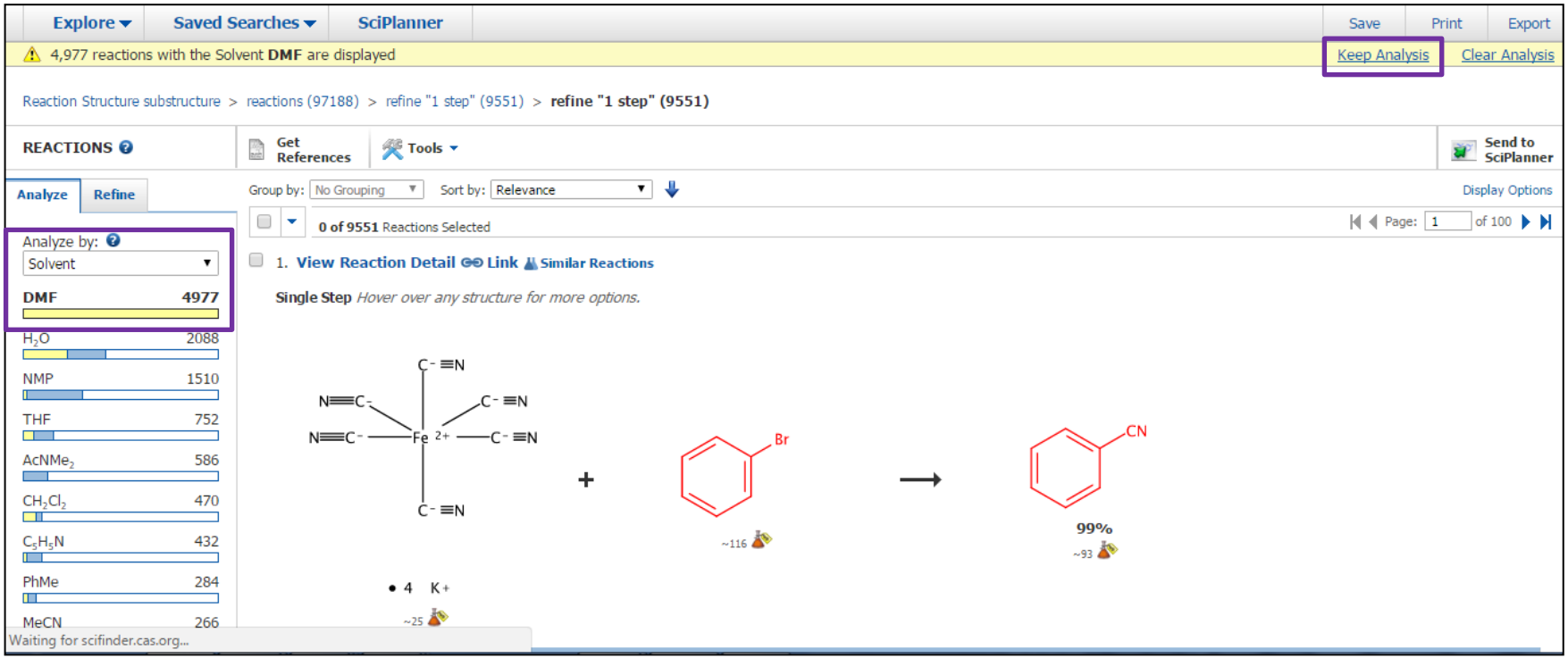



使用反应结果集中的Analyze功能，需要将结果集压缩到20000以下

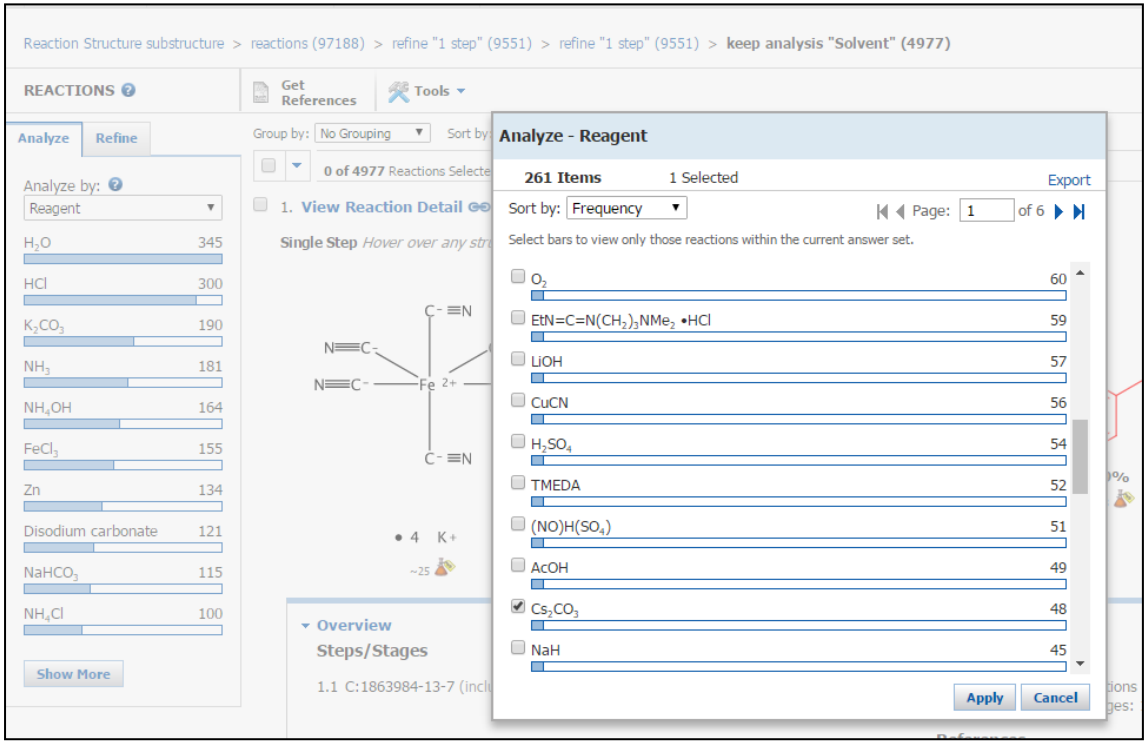
# 将反应限定为1步反应


Explore
Saved Searches
SciPlanner
Save
Print
Export
Reaction Structure substructure > reactions (97188) > refine "1 step" (9551)
REACTIONS
Get References
Tools
Send to SciPlanner
Analyze
Refine
Group by: No Grouping
Sort by: Relevance
Display Options
0 of 9551 Reactions Selected
Page: 1 of 192
Refine by:
Reaction Structure
Product Yield
Number of Steps
Reaction Classification
Excluding Reaction Classification
Non-participating functional groups
Number of Steps:
1
Examples: 1, 1 - 3, 1 -, - 3
Refine
1. View Reaction Detail Link Similar Reactions
Single Step Hover over any structure for more options.
Br
CN
99%
~116
~93
~25

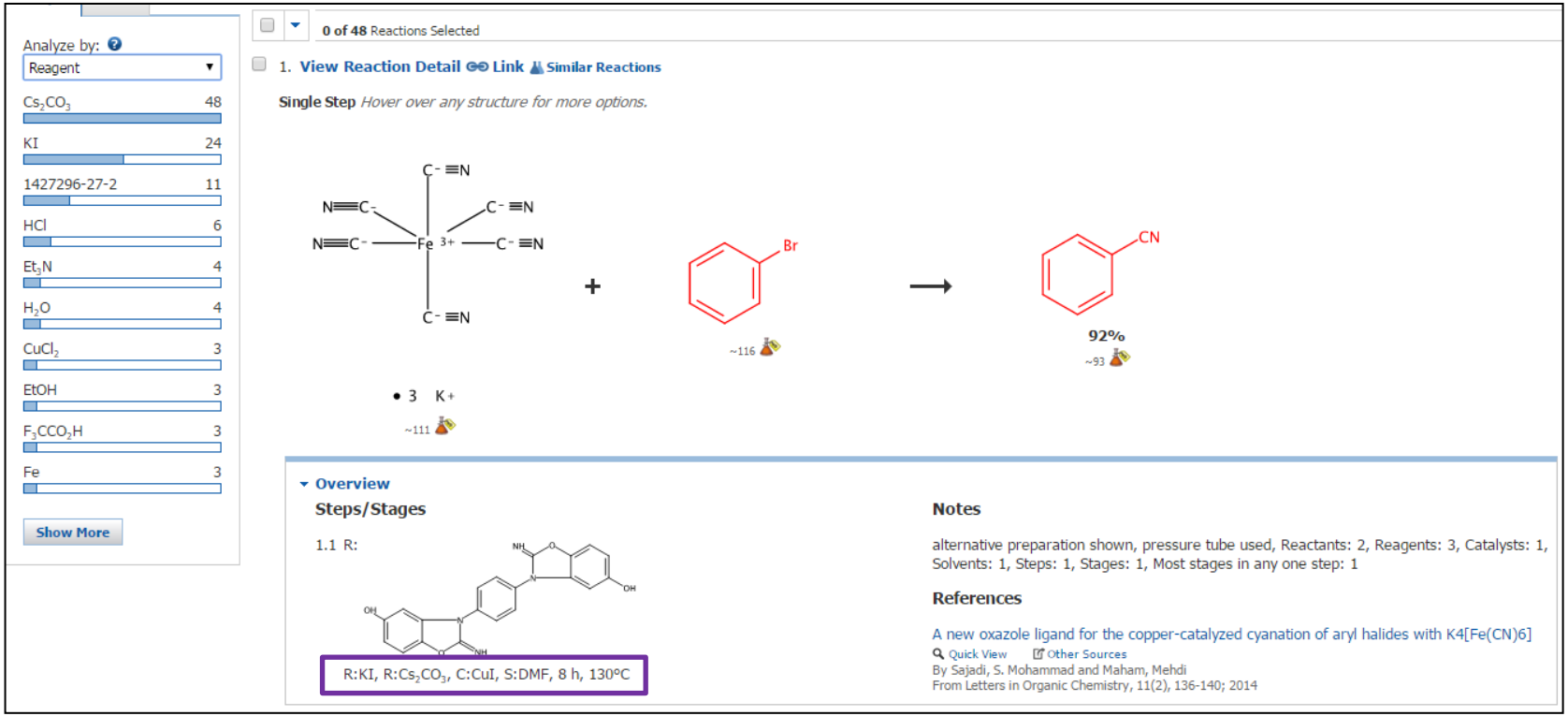
# 通过Analyze by Solvent选择在DMF溶剂中进行的反应



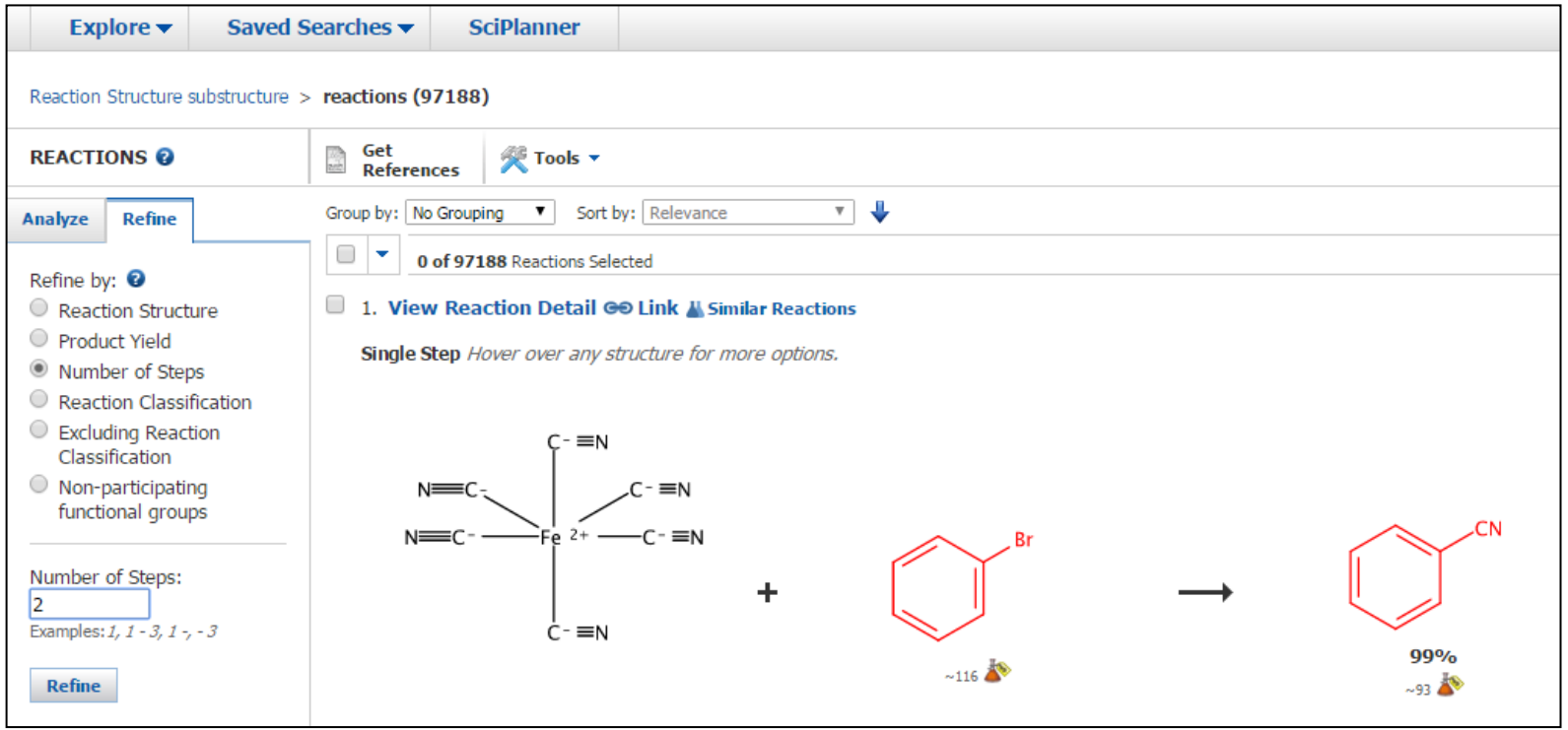
# 在反应结果集中继续通过Analyze by Reagent选择$Cs_2CO_3$作为试剂的反应



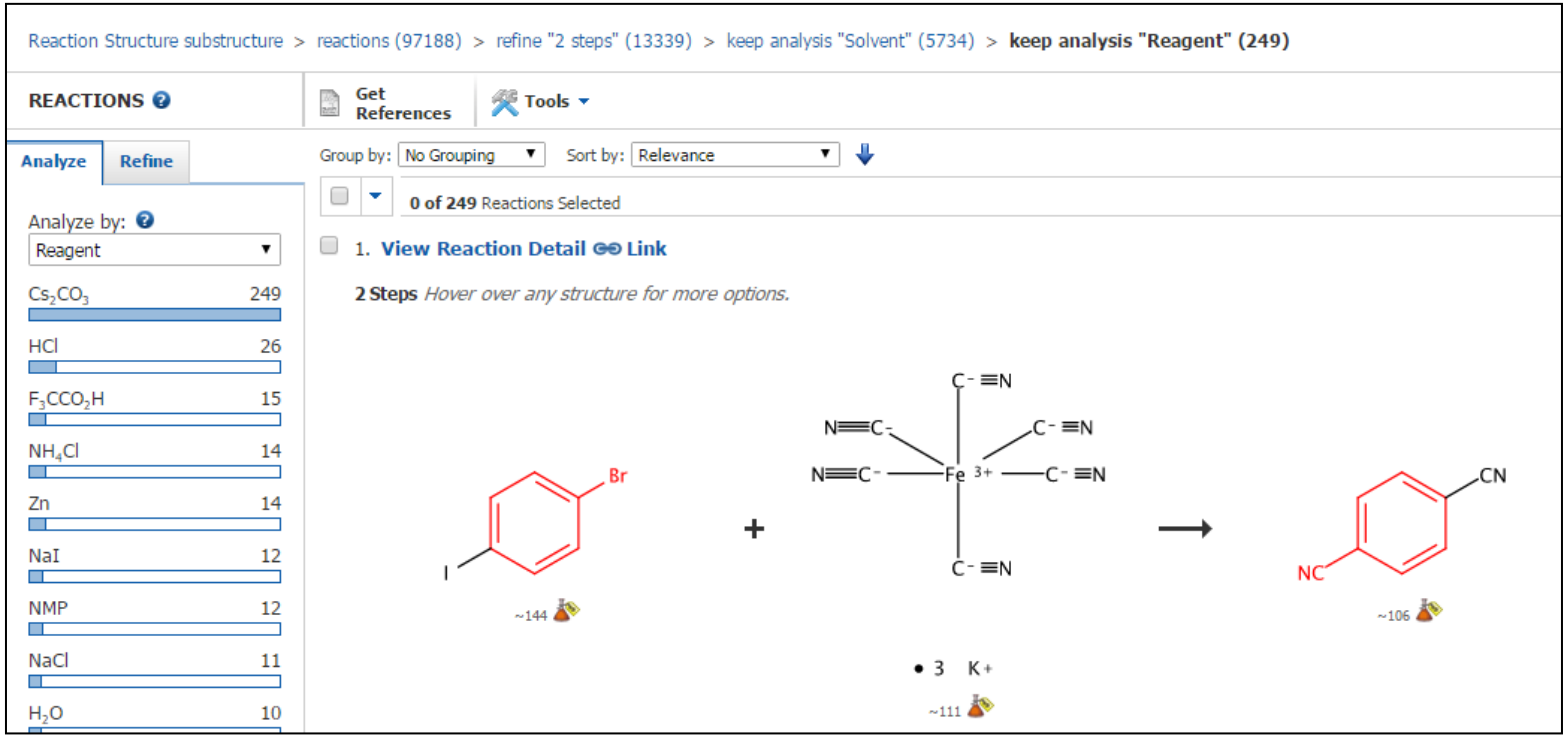
# 获得以 DMF为溶剂， $Cs_2CO_3$为试剂的一步反应，保存结果集



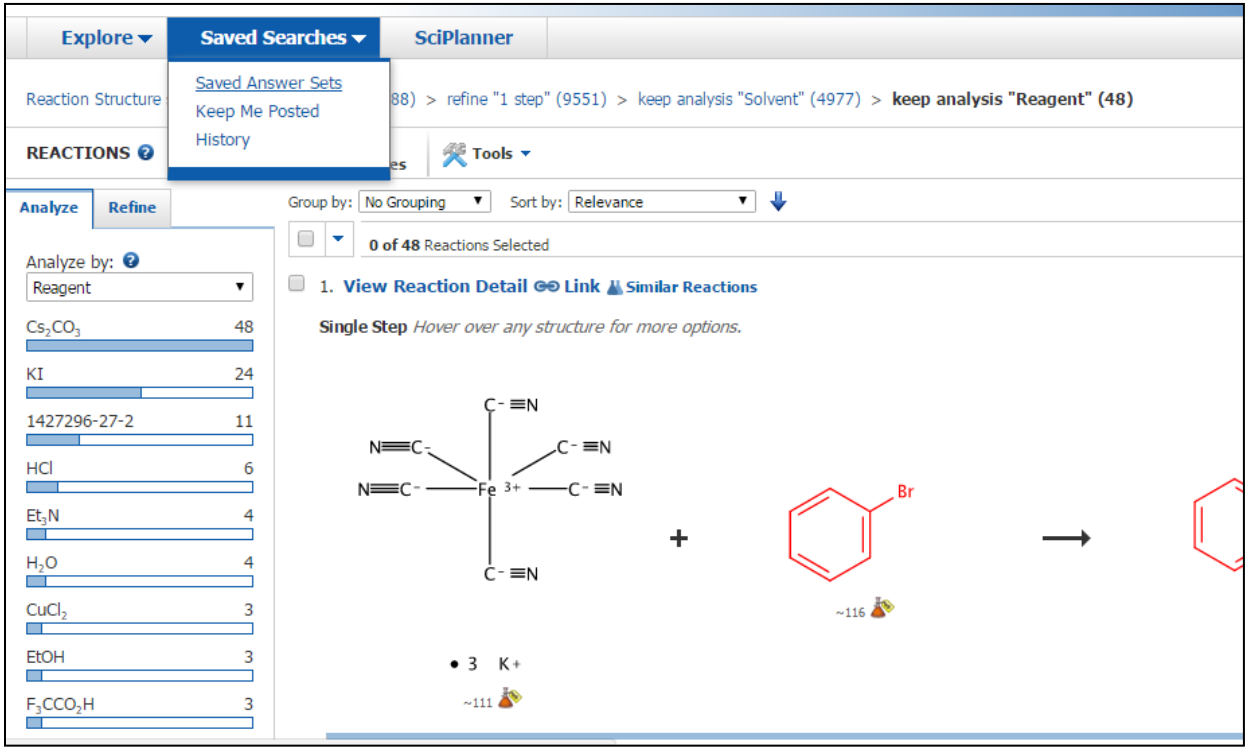
# 在初始反应结果集中限定2步反应，重复刚才的步骤



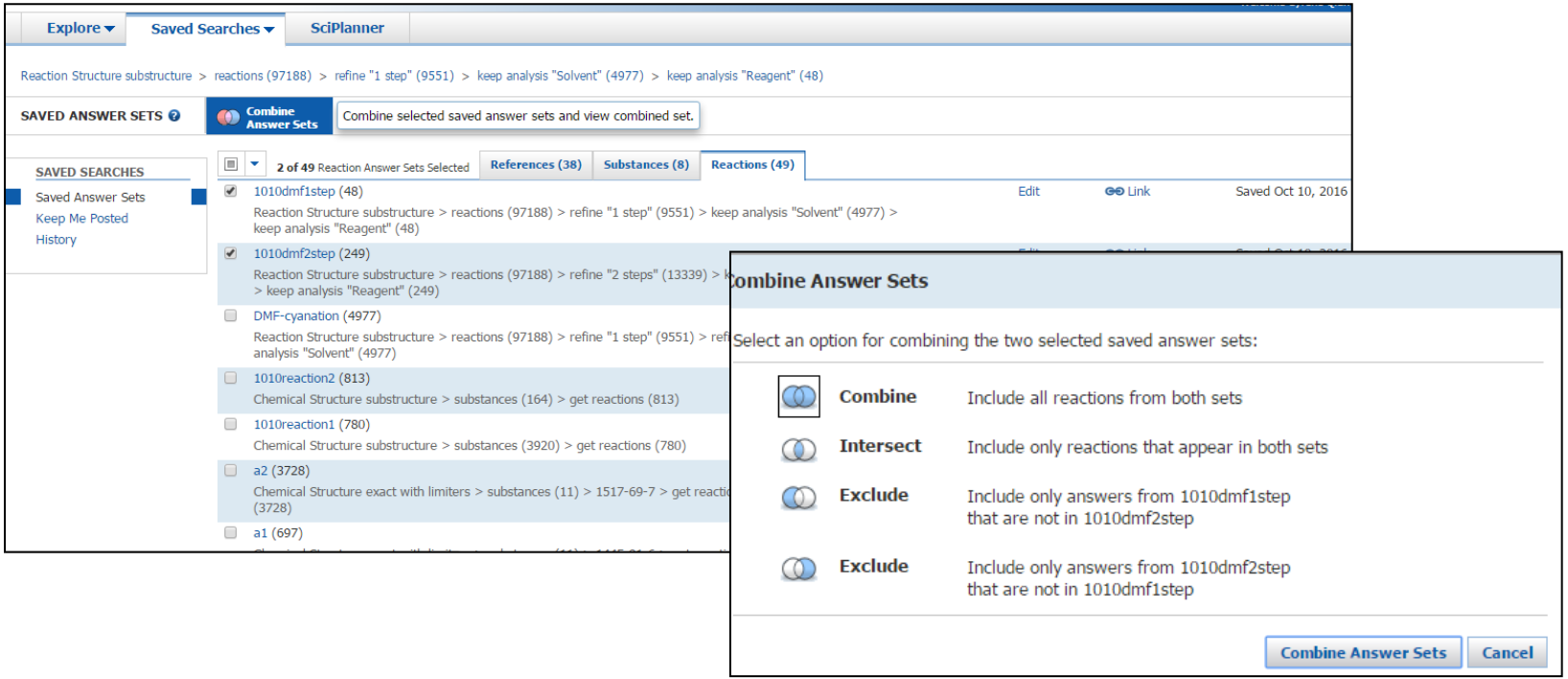
# 获得以 DMF为溶剂， $Cs_2CO_3$为试剂的2步反应，保存结果集



# 在Saved Searches中的反应结果集中找到刚保存过的结果集



# 合并结果集


Explore
Saved Searches
SciPlanner
Reaction Structure substructure > reactions (97188) > refine "1 step" (9551) > keep analysis "Solvent" (4977) > keep analysis "Reagent" (48)
SAVED ANSWER SETS
Combine Answer Sets
Combine selected saved answer sets and view combined set.
SAVED SEARCHES
Saved Answer Sets
Keep Me Posted
History
2 of 49 Reaction Answer Sets Selected
References (38)
Substances (8)
Reactions (49)
1010dmf1step (48)
Edit
Link
Saved Oct 10, 2016
Reaction Structure substructure > reactions (97188) > refine "1 step" (9551) > keep analysis "Solvent" (4977) > keep analysis "Reagent" (48)
1010dmf2step (249)
Reaction Structure substructure > reactions (97188) > refine "2 steps" (13339) > keep analysis "Reagent" (249)
DMF-cyanation (4977)
Reaction Structure substructure > reactions (97188) > refine "1 step" (9551) > analysis "Solvent" (4977)
1010reaction2 (813)
Chemical Structure substructure > substances (164) > get reactions (813)
1010reaction1 (780)
Chemical Structure substructure > substances (3920) > get reactions (780)
a2 (3728)
Chemical Structure exact with limiters > substances (11) > 1517-69-7 > get reactio (3728)
a1 (697)
Combine Answer Sets
Select an option for combining the two selected saved answer sets:
Combine
Include all reactions from both sets
Intersect
Include only reactions that appear in both sets
Exclude
Include only answers from 1010dmf1step that are not in 1010dmf2step
Exclude
Include only answers from 1010dmf2step that are not in 1010dmf1step
Combine Answer Sets
Cancel

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  - 手性分子合成反应
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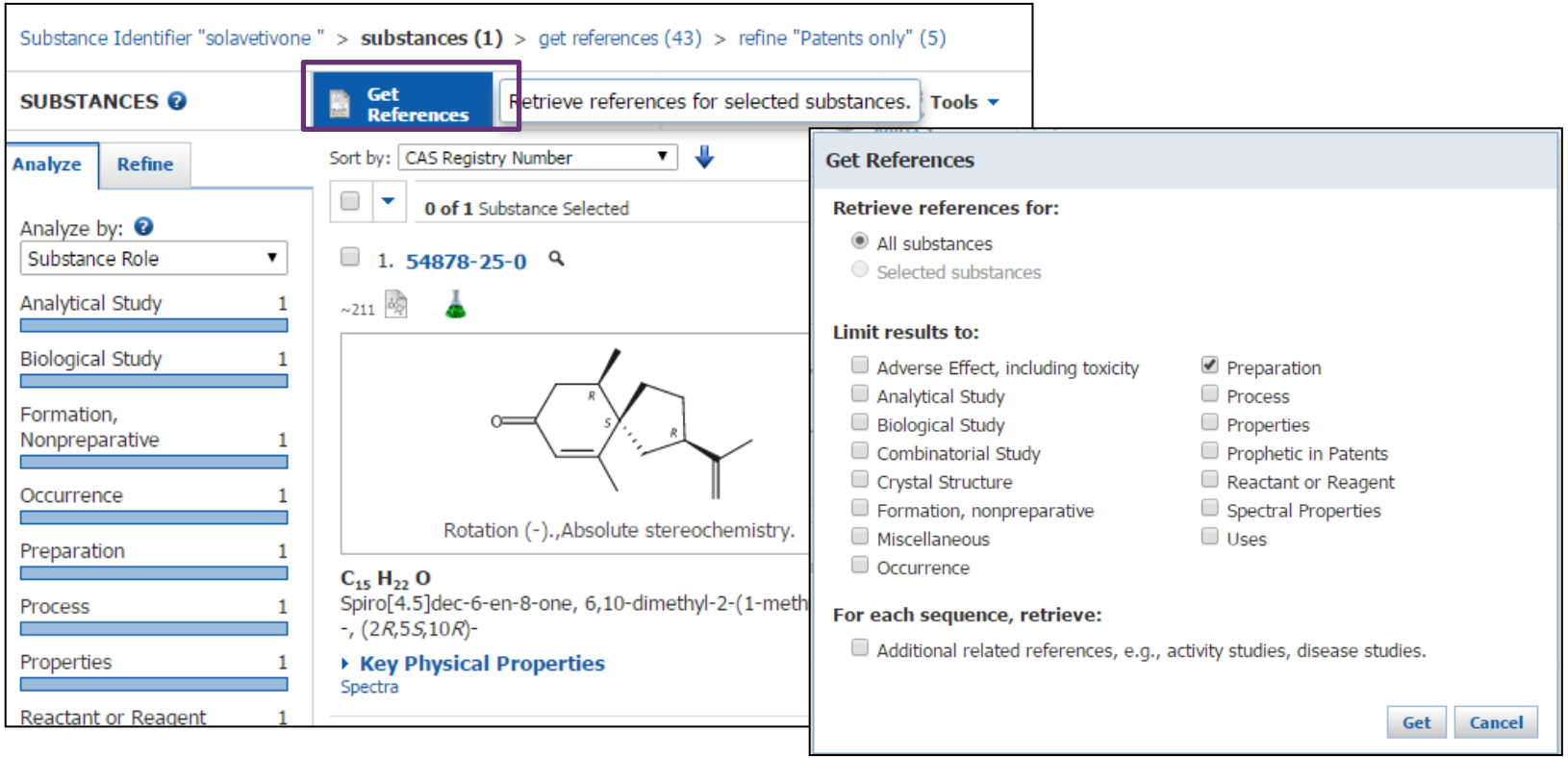
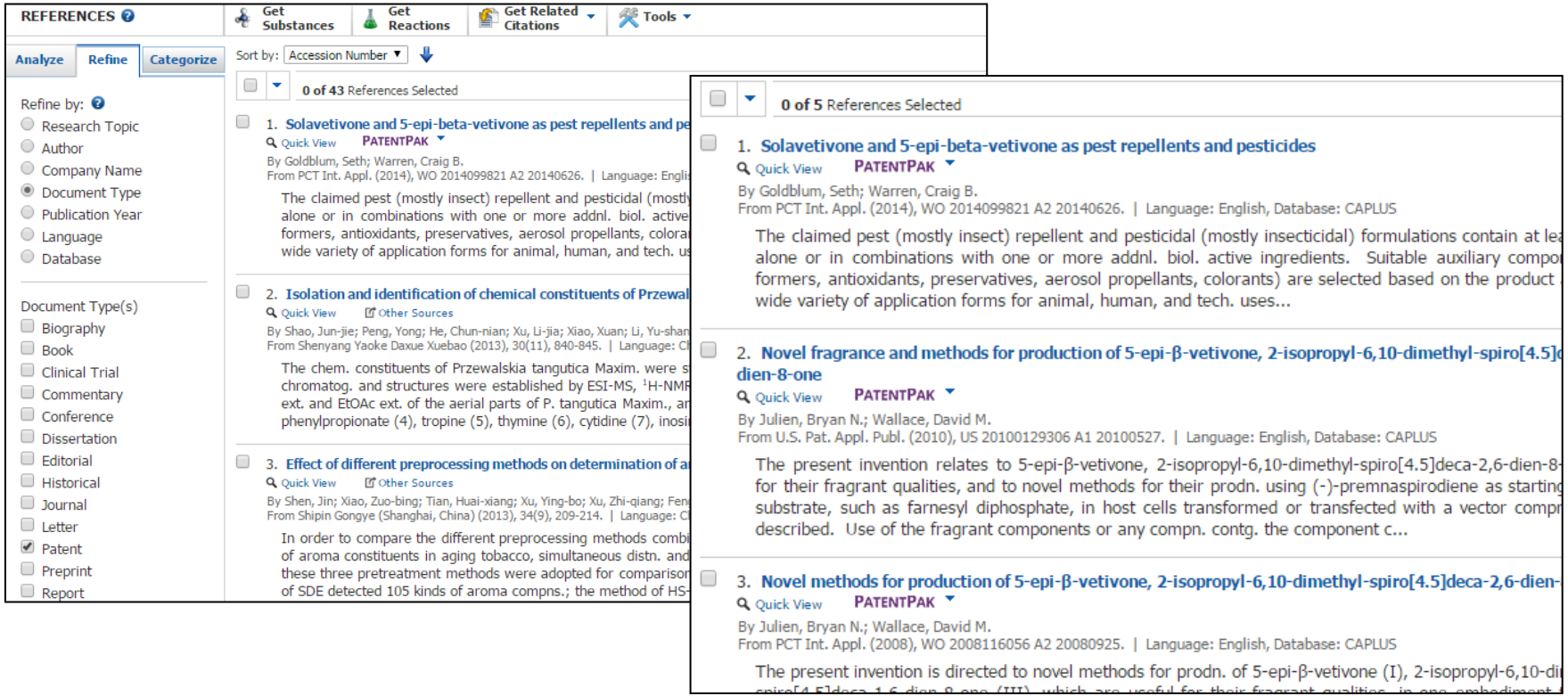
  - 手性分子拆分反应

# 通过物质检索获得香根酮的制备的专利文献



# 将文献结果集限定为专利，获得所有专利文献

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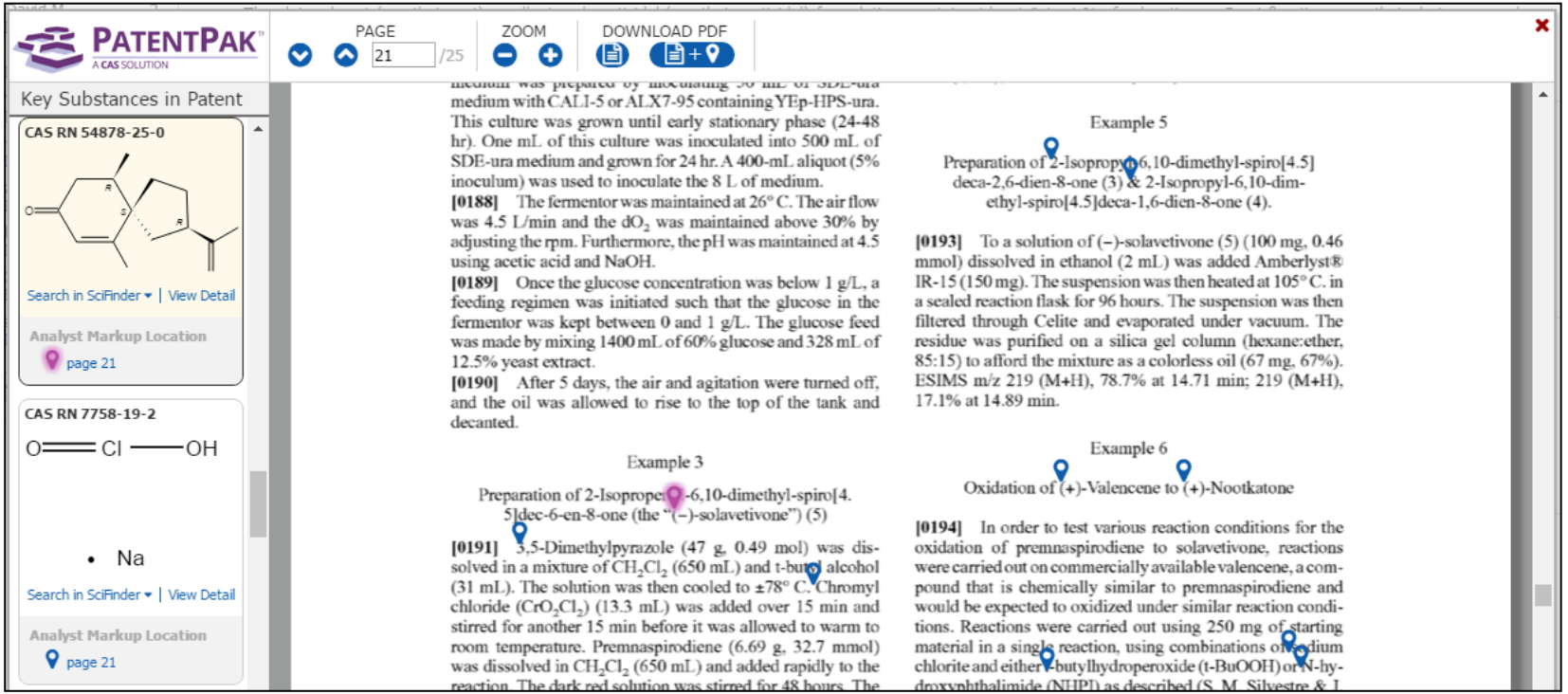
# 通过PatentPak快速获取到香根酮的制备信息



# 节省你最宝贵的资源——时间


- 即时获得来自世界上主要专利授权机构的专利PDF文件
- 专利族涵盖了多种语言
- 定位标引的重要化学物质所在专利页码
- 专利研究安全保密
- 每日更新
- SciFinder检索功能中内置交互式浏览器

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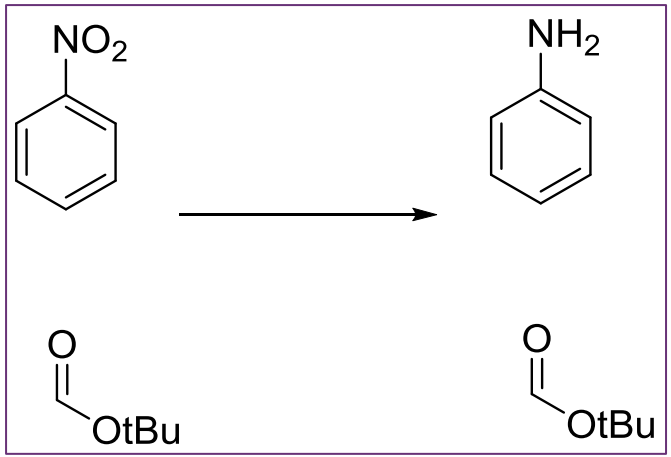
A CAS SOLUTION

# 反应检索

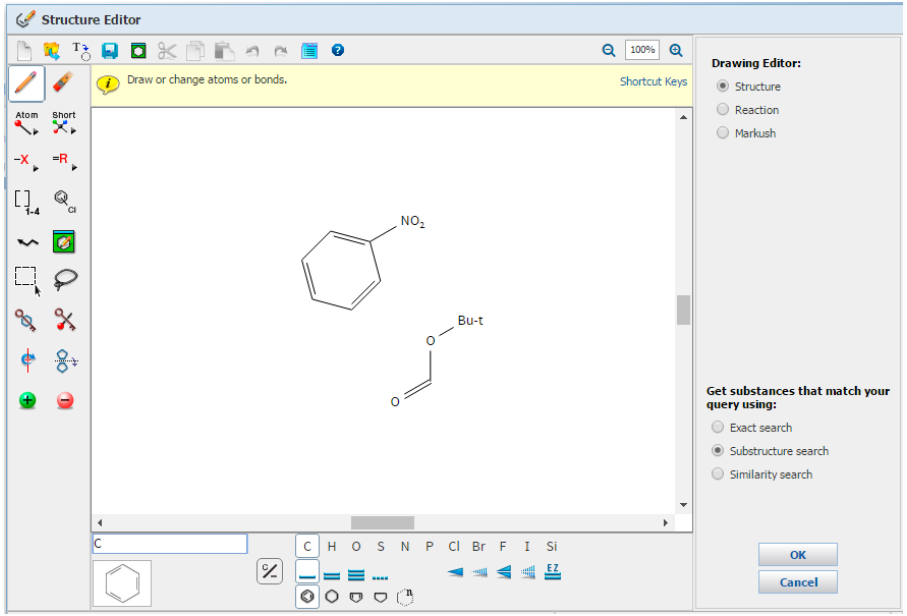
- 反应检索绘制工具及反应信息详情
- 如何通过Analyze、Refine来精选反应
- 巧用原子标记工具和位置标记工具提高检索精度
- 通过PatentPak节省反应信息检索时间
- 高级反应案例分享
  - 片段反应
  - 按照化合物类型查找反应
- 手性反应专题
  - 手性分子合成反应
  - 手性构型翻转反应
  - 手性分子拆分反应

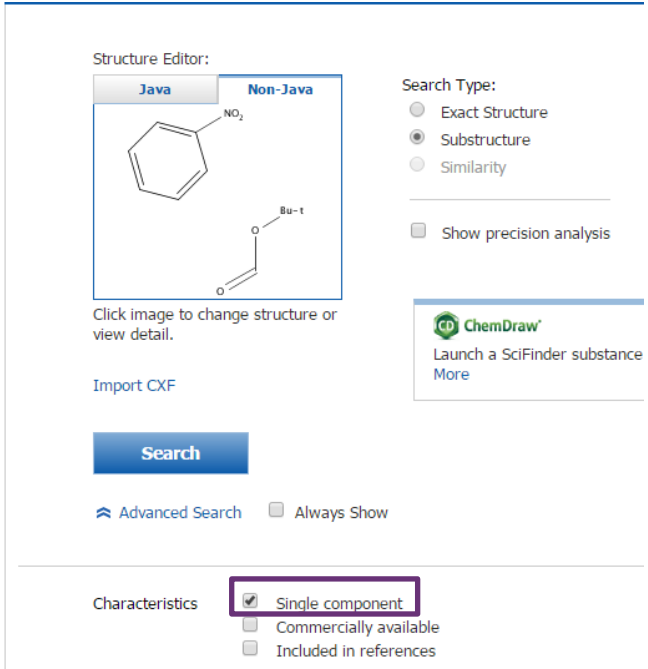
# 片段反应检索

- 检索要求：
  - 起始物上带有BOC基团
  - 苯环上的硝基还原为氨基
  - BOC基团不变
- 检索思路：
  - 要保证苯环和BOC基团在同一个结构上，需要从物质结构检索开始，通过物质获得反应，再对反应进行限定。

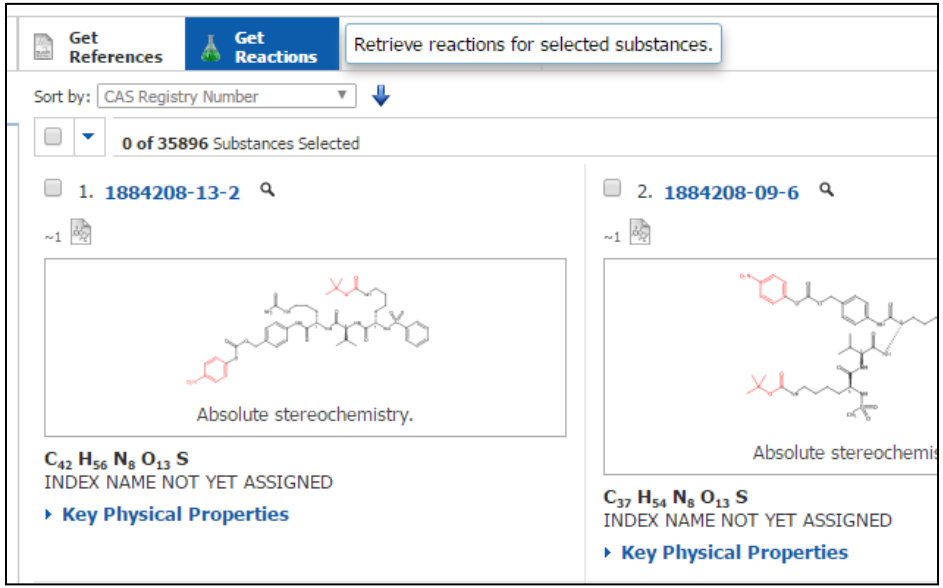


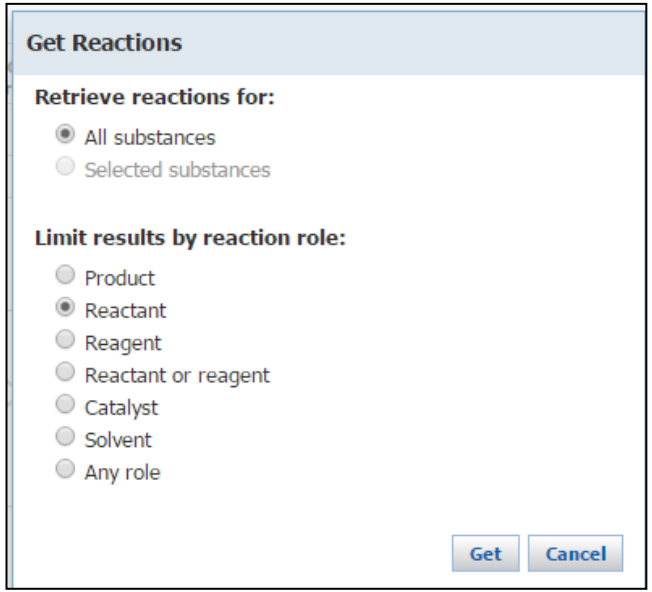
# 绘制片段结构，选择亚结构反应检索，并定义为单一组分



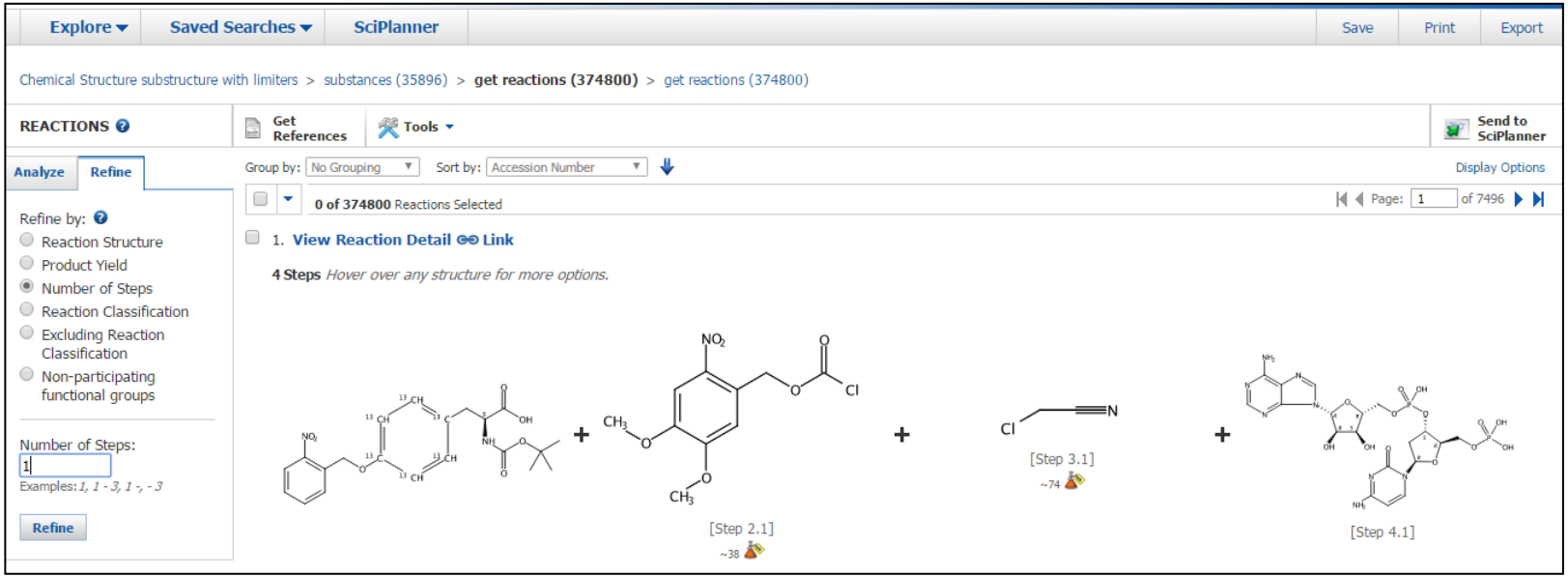



# 获得亚结构检索结果，并获得这些物质作为反应物的反应

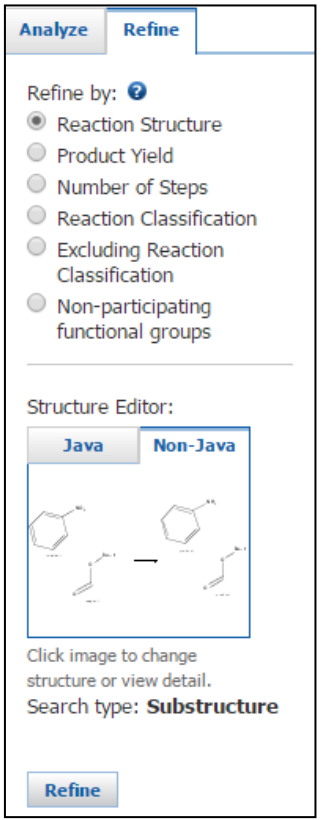


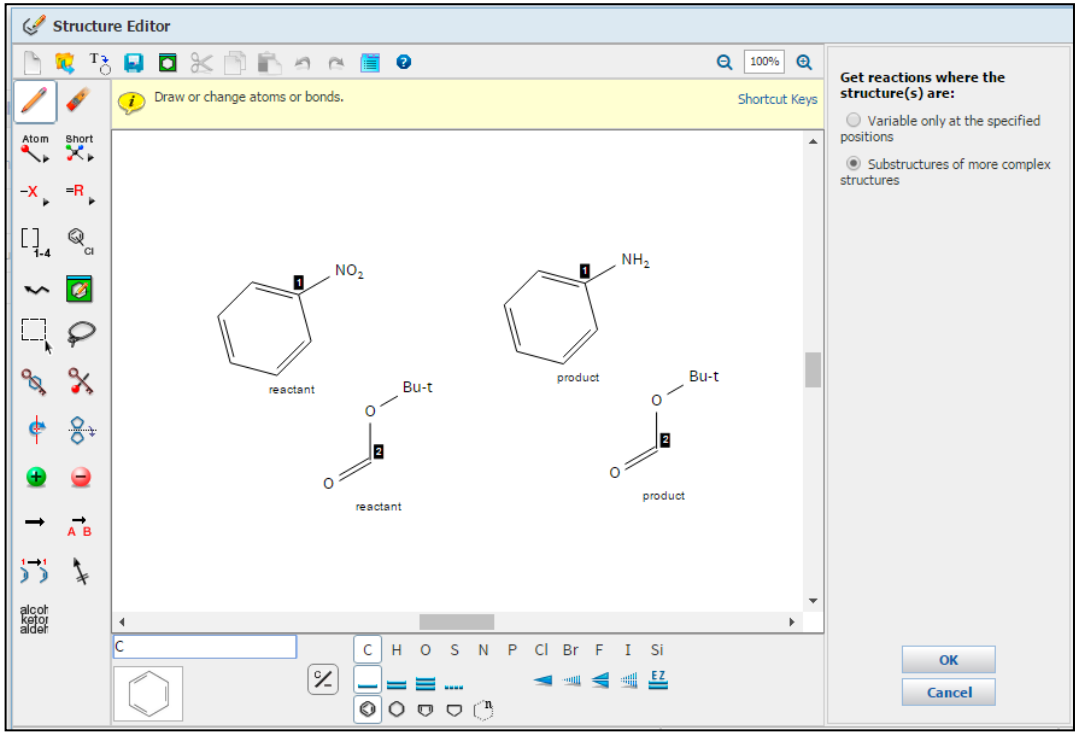



# 限定反应步数为一步反应

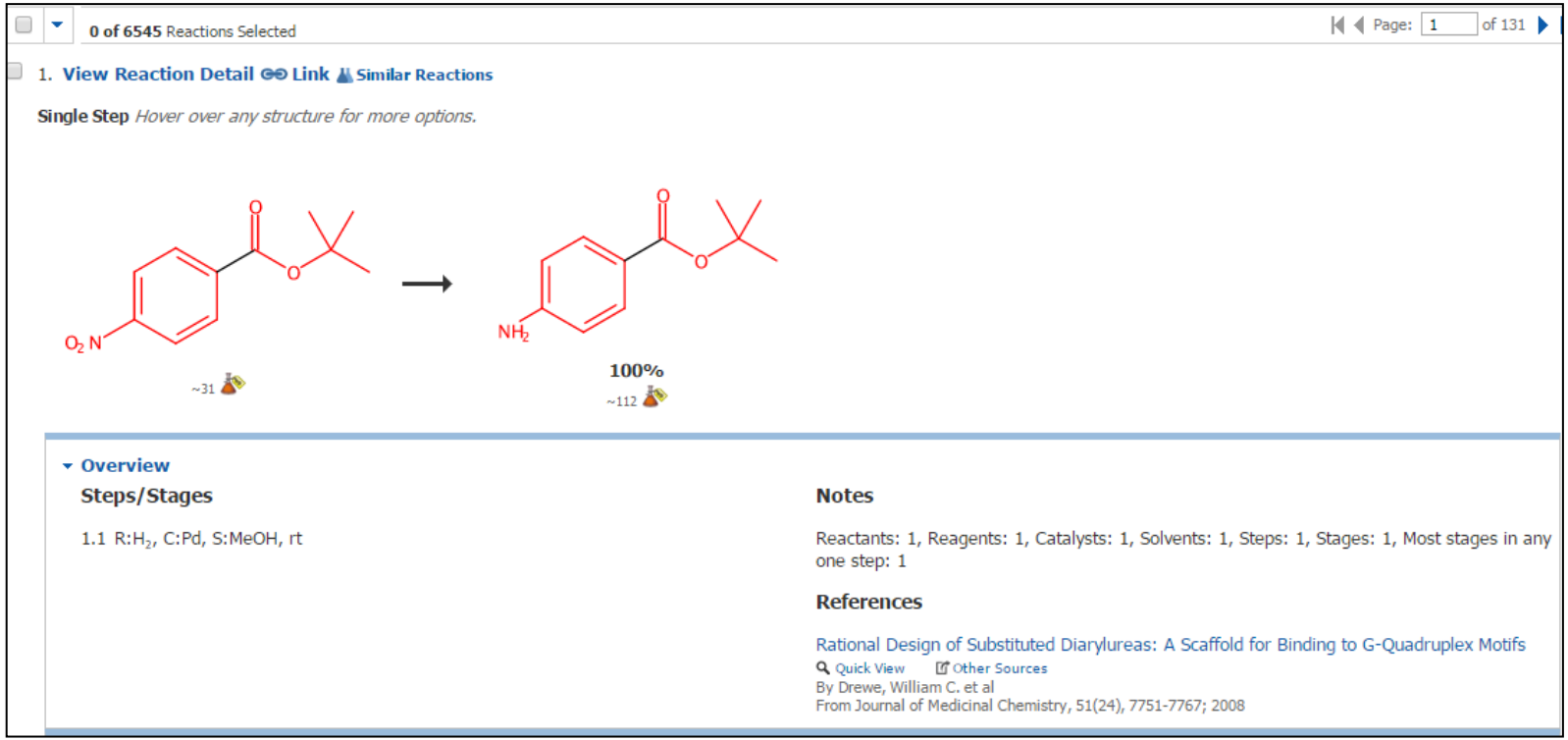


# 反应结构限定

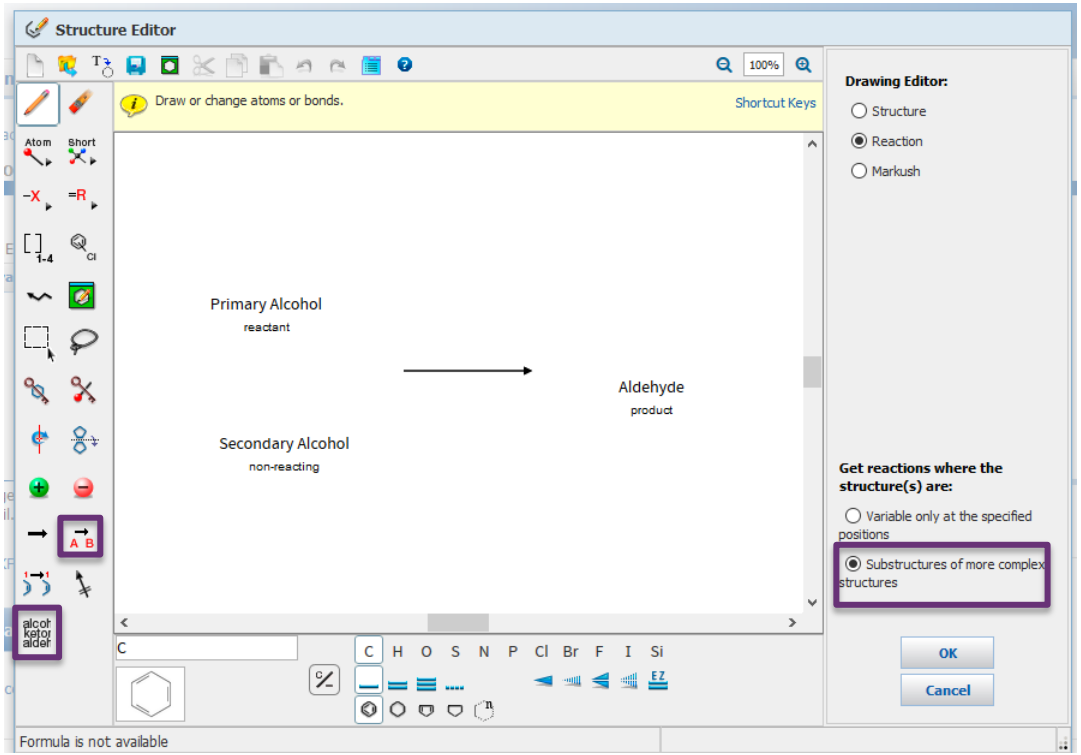

Analyze
Refine
Refine by:
Reaction Structure
Product Yield
Number of Steps
Reaction Classification
Excluding Reaction Classification
Non-participating functional groups
Structure Editor:
Java
Non-Java
Click image to change structure or view detail.
Search type: Substructure
Refine


Structure Editor
Draw or change atoms or bonds.
Shortcut Keys
Get reactions where the structure(s) are:
Variable only at the specified positions
Substructures of more complex structures
reactant
product
reactant
product
OK
Cancel

# 符合检索要求的反应

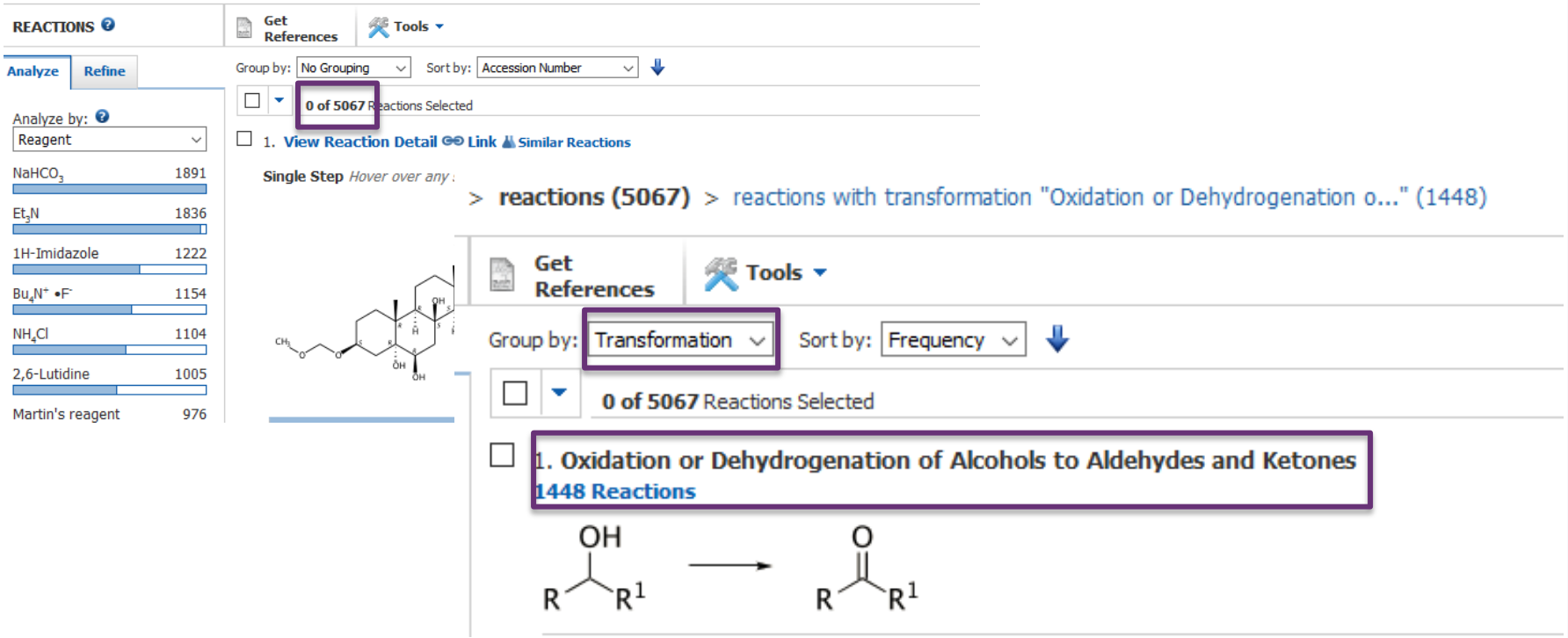

0 of 6545 Reactions Selected
Page: 1 of 131
1. View Reaction Detail Link Similar Reactions
Single Step Hover over any structure for more options.
O
O
O2N
~31
100%
O
O
NH2
~112
Overview
Steps/Stages
1.1 R:H2, C:Pd, S:MeOH, rt
Notes
Reactants: 1, Reagents: 1, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1
References
Rational Design of Substituted Diarylureas: A Scaffold for Binding to G-Quadruplex Motifs
Quick View
Other Sources
By Drewe, William C. et al
From Journal of Medicinal Chemistry, 51(24), 7751-7767; 2008

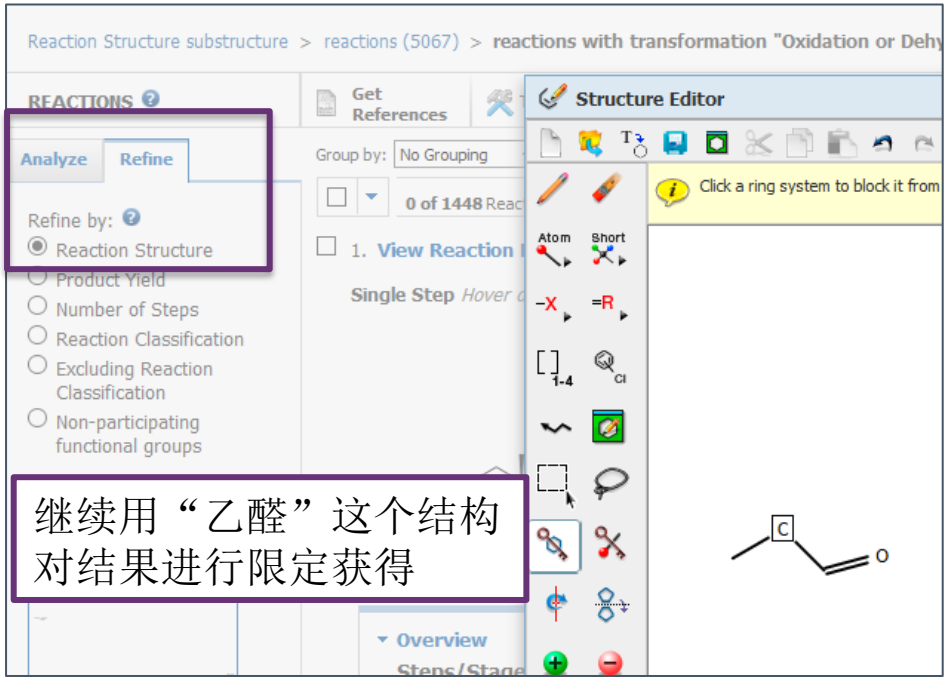
# 案例：在非反应仲醇存在的条件下，将伯醇转换为乙醛



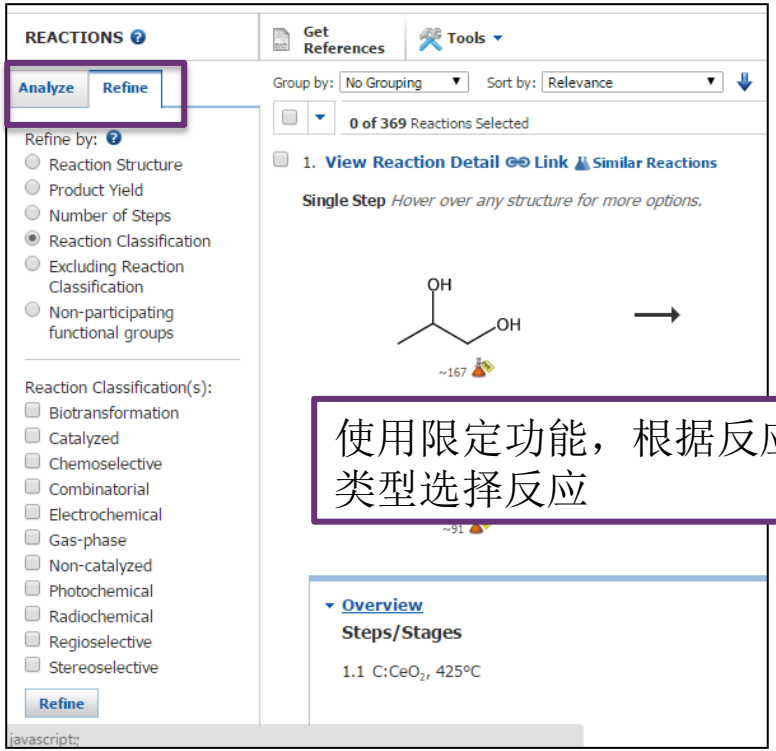

使用反应角色定义工具和官能团列表

# 案例：在非反应仲醇存在的条件下，将伯醇转换为乙醛






继续用“乙醛”这个结构对结果进行限定获得




使用限定功能，根据反应类型选择反应

# 反应检索

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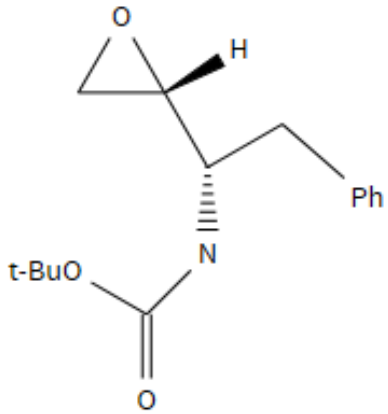
- 手性反应专题
  - 手性分子合成反应
  - 手性构型翻转反应
  - 手性分子拆分反应

# 不对称合成反应

如何合成如下绝对立体构型的手性分子？ 或检索此分子参与的所有反应？




思路：从物质检索出发，然后从具有绝对构型的物质获取反应



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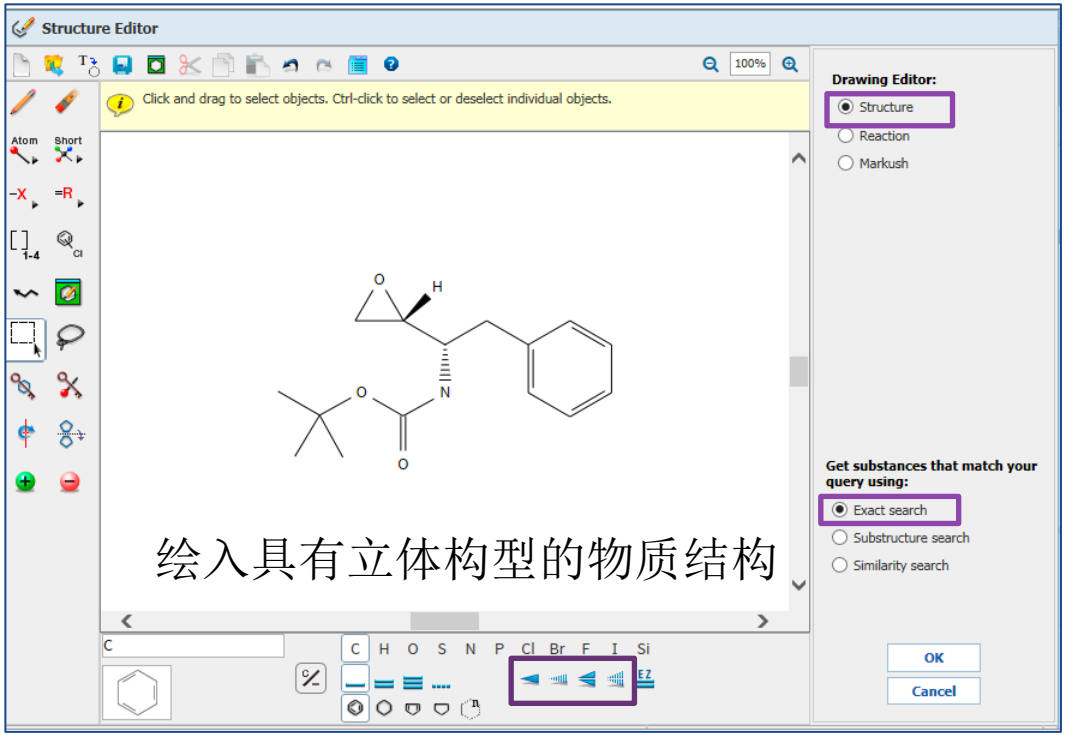
# 不对称合成反应：从物质检索出发




物质检索

精确结构检索



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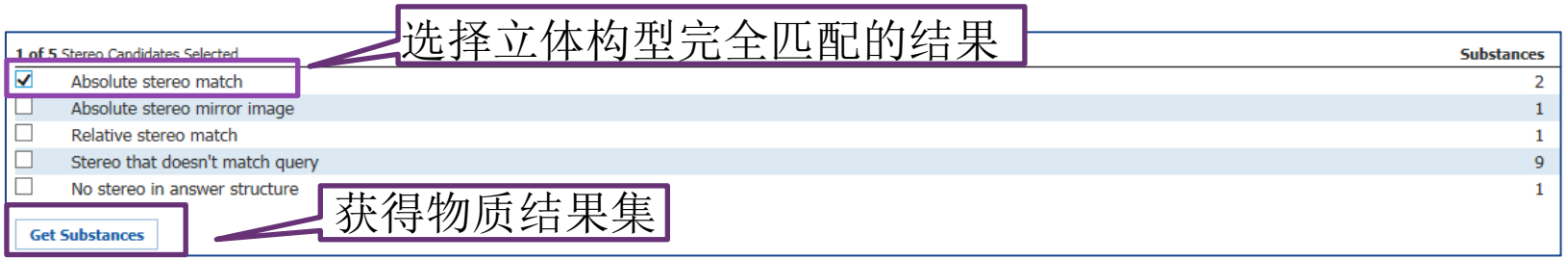
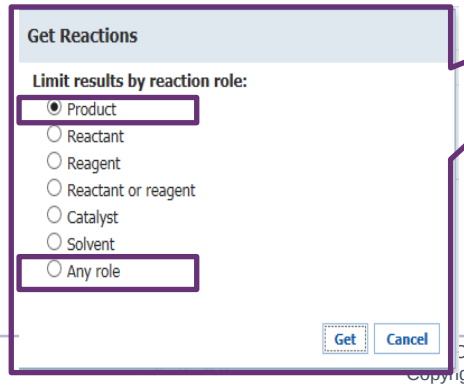
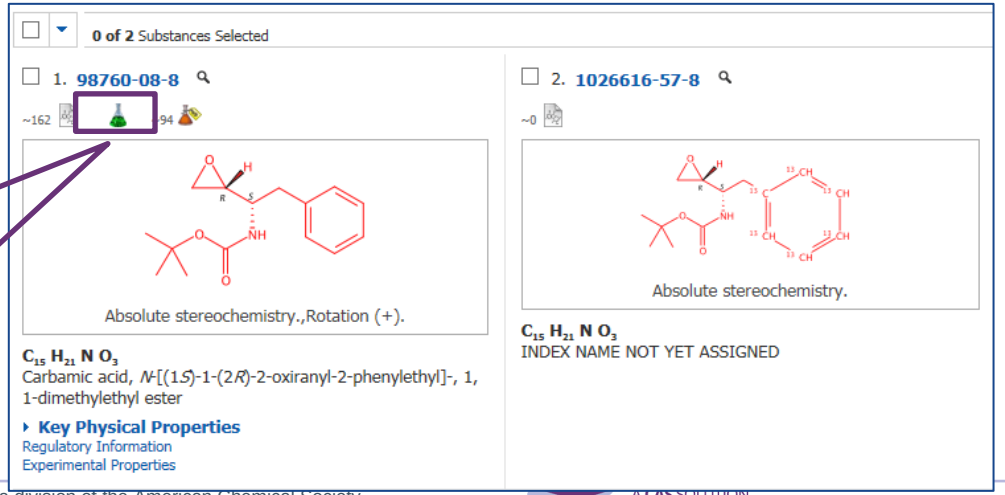
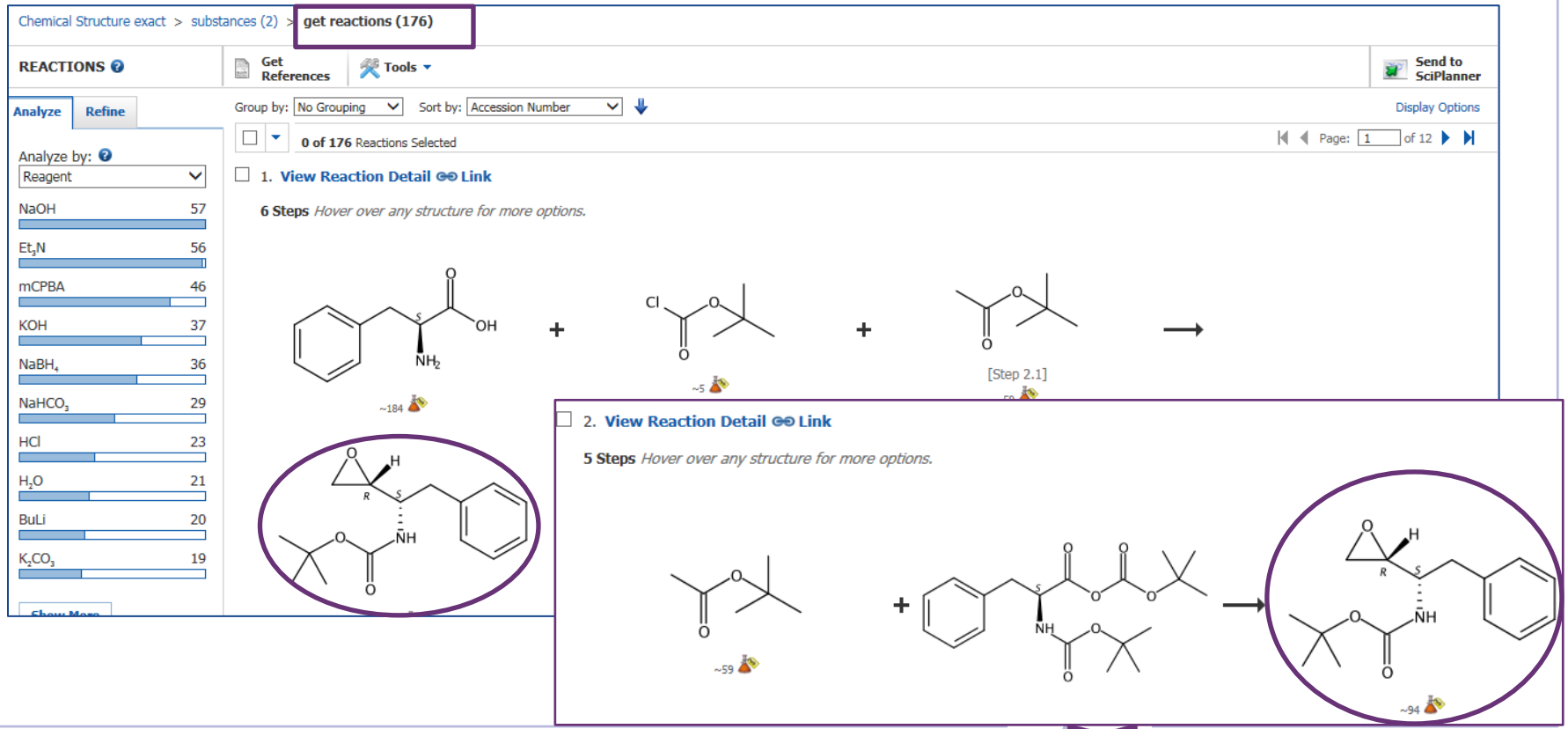
# 不对称合成反应：获得物质结果集，再从物质获取反应



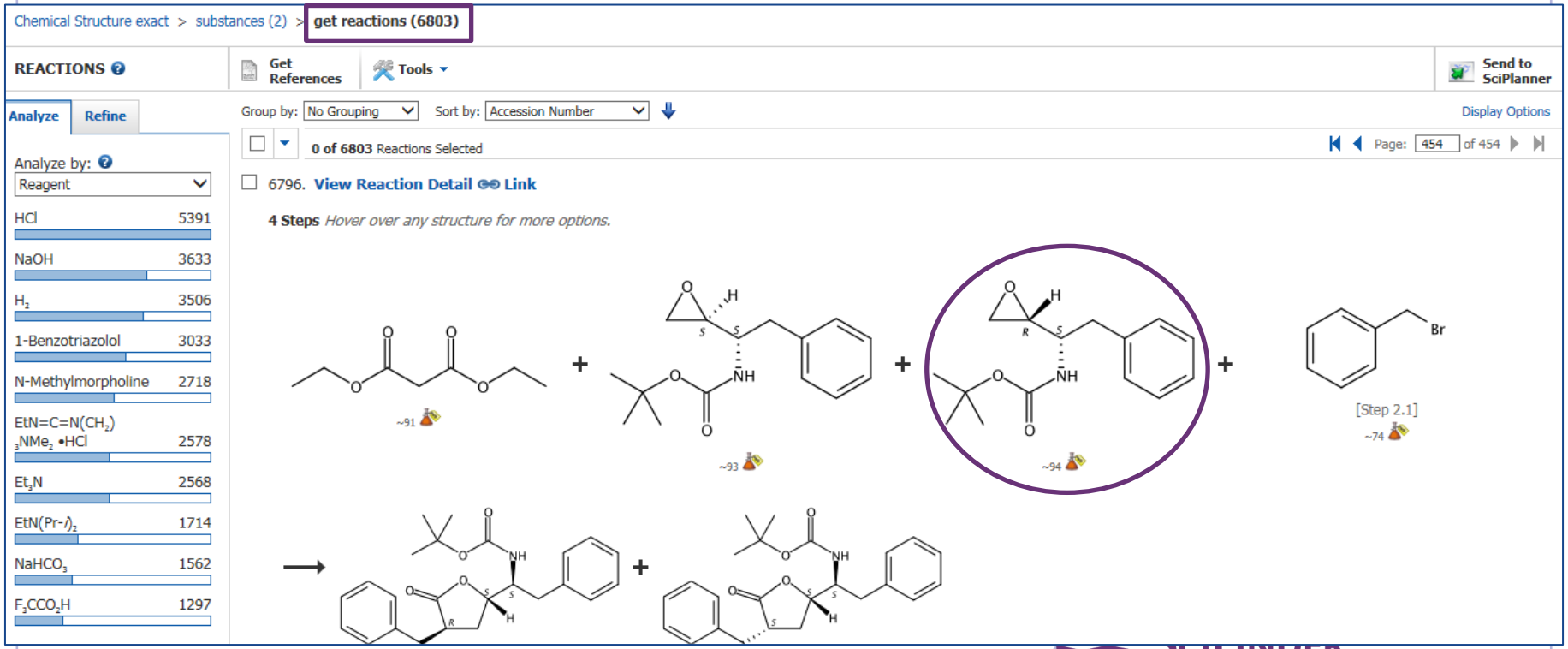
# 不对称合成反应：获得作为产物的反应结果






A CAS SOLUTION

# 不对称合成反应：获得作为任意角色的反应结果



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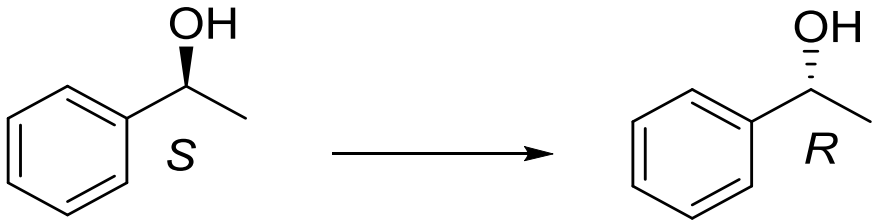
# 提纲

- 手性反应专题
  - 手性分子合成反应
  - **手性构型翻转反应**
  - 手性分子拆分反应
  - 手性分子分离的分析方法

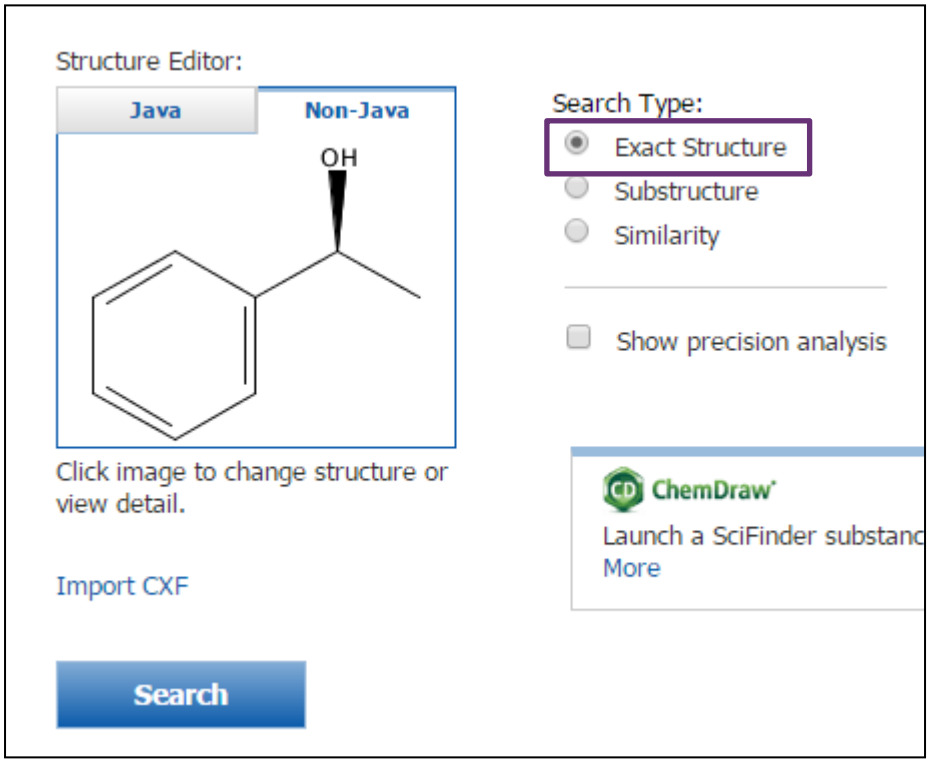
# 手性翻转反应

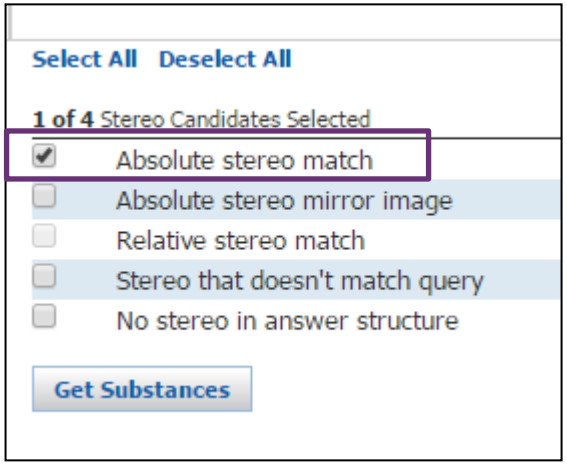
如何通过精确反应检索如下的一步手性翻转反应？



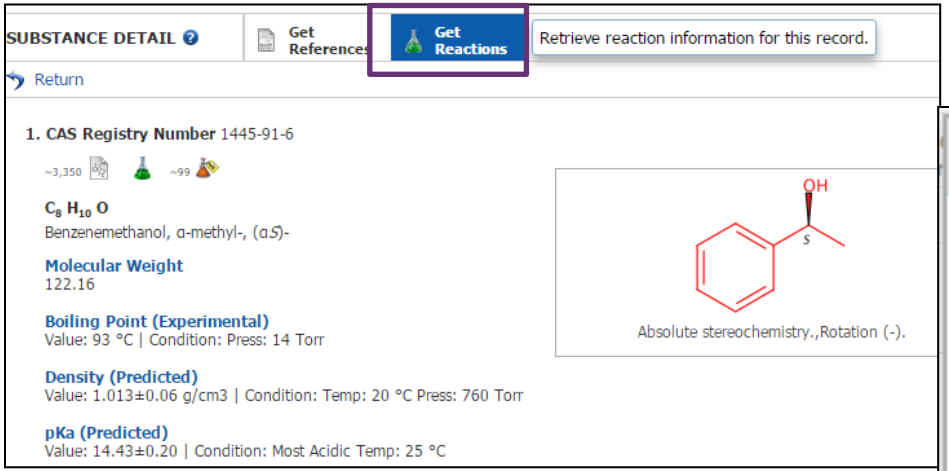

思路：通过物质检索，分别获得起始物和产物的一步反应，再对结果集进行交集。

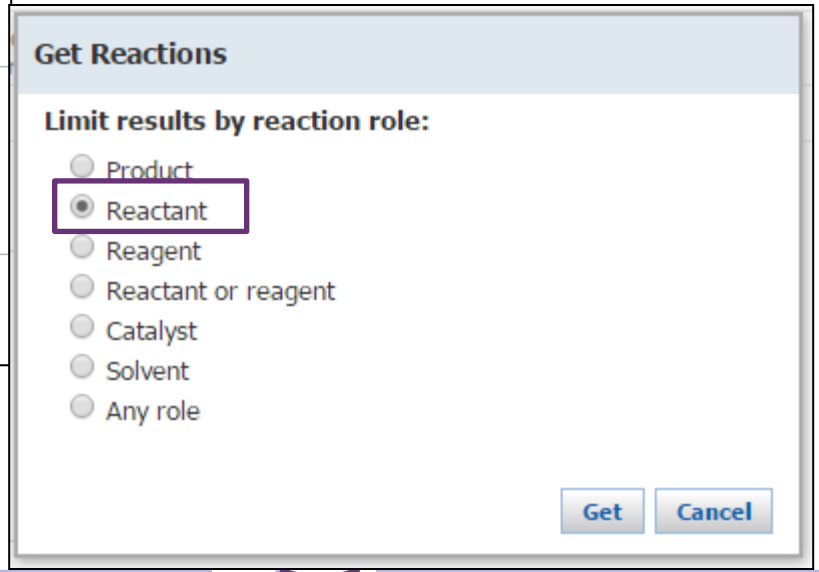
# 手性翻转反应：通过精确结构检索S构型起始物



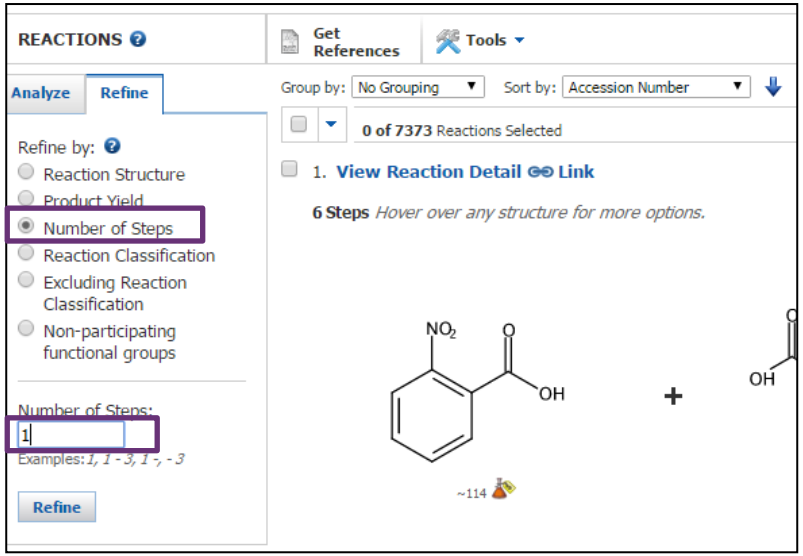



# 手性翻转反应：得到S构型物质，并通过Get Reaction获取其为“反应物”的反应

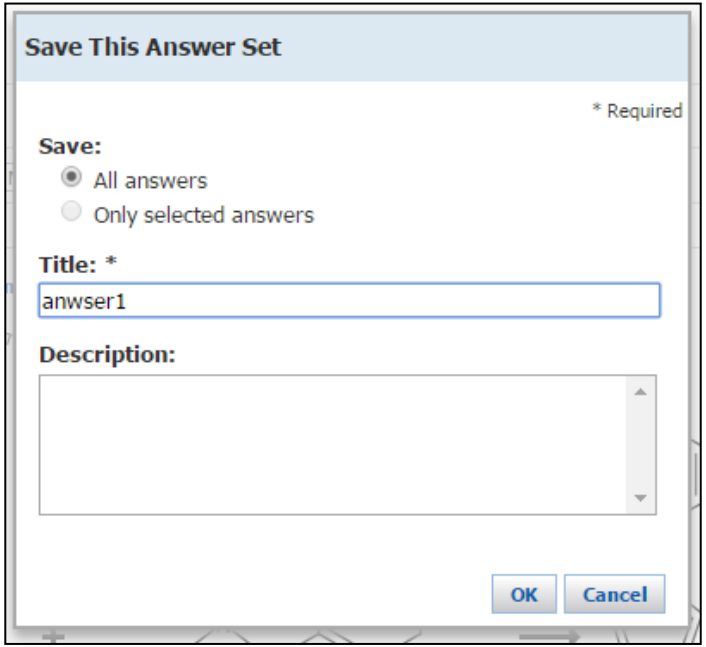


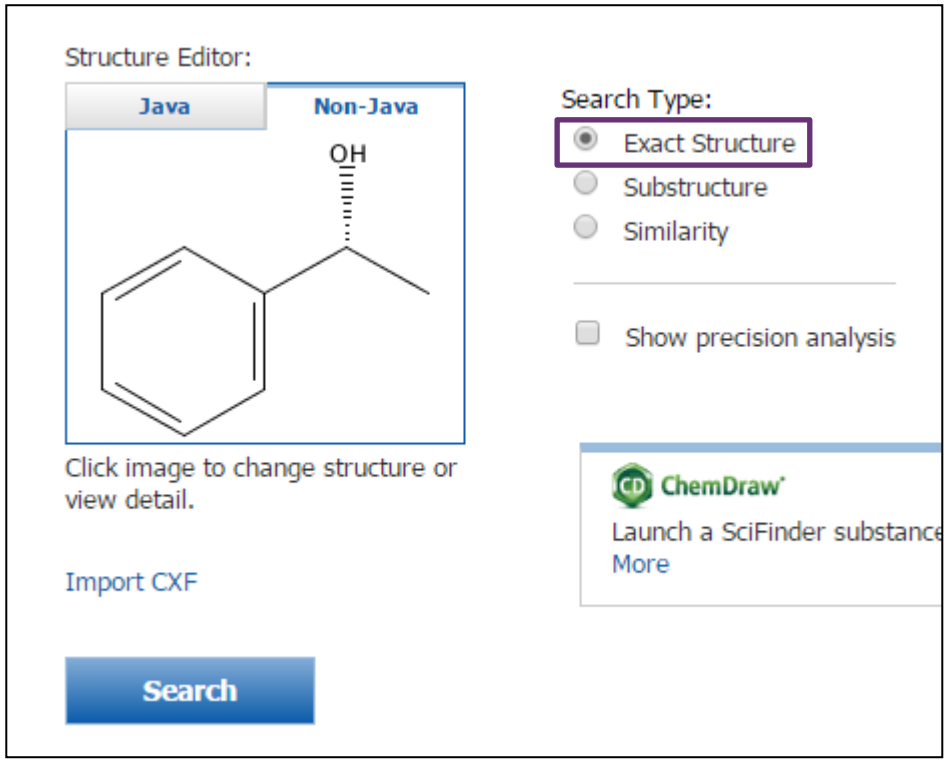
# 手性翻转反应：将反应结果集限定为一步反应，并存为answer1

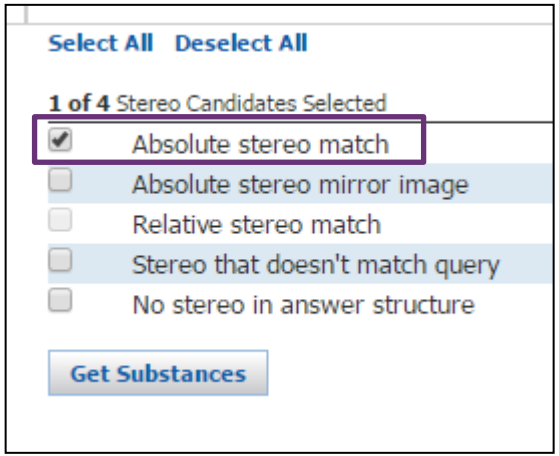



将所得结果集保存为”answer1”



# 手性翻转反应：通过精确结构检索R构型产物



# 手性翻转反应：得到R构型物质，并通过Get Reaction获得其为“产物”的反应

**1. CAS Registry Number** 1517-69-7

~3,242 ~104

$C_8 H_{10} O$

Benzenemethanol, α-methyl-, (α*R*)-

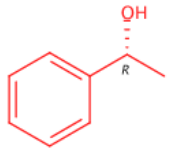
**Molecular Weight**
122.16

**Melting Point (Experimental)**
Value: 9-11 °C

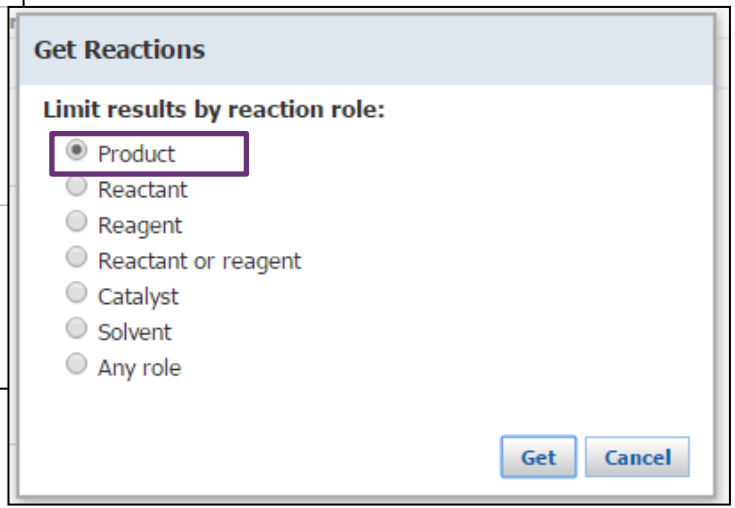
**Boiling Point (Experimental)**
Value: 98 °C

**Density (Predicted)**
Value: 1.013±0.06 g/cm3 | Condition: Temp: 20 °C Press: 760 Torr

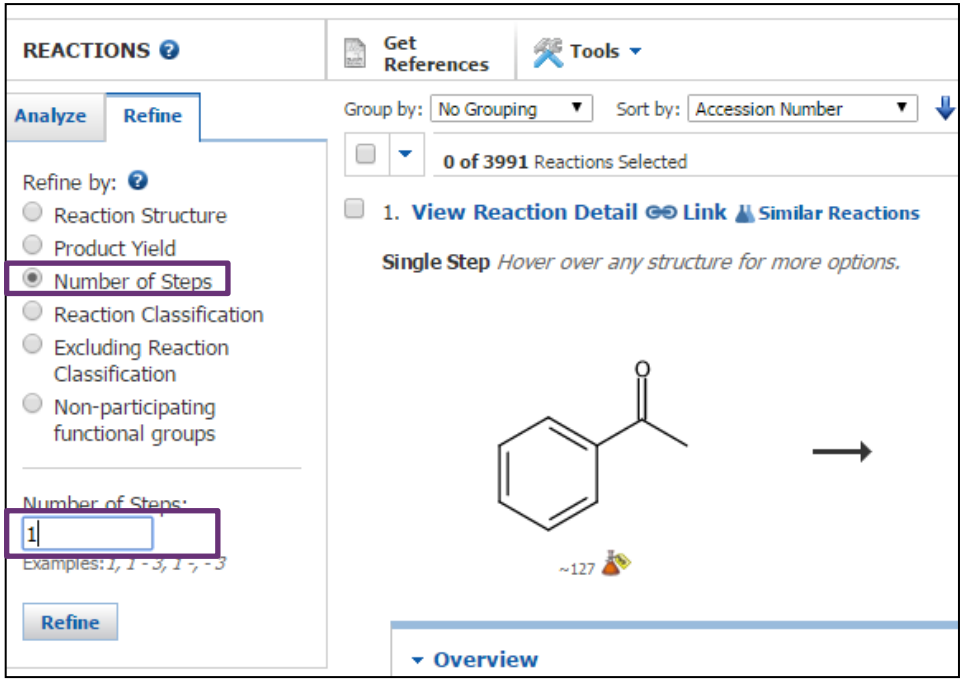
**pKa (Predicted)**
Value: 14.43±0.20 | Condition: Most Acidic Temp: 25 °C



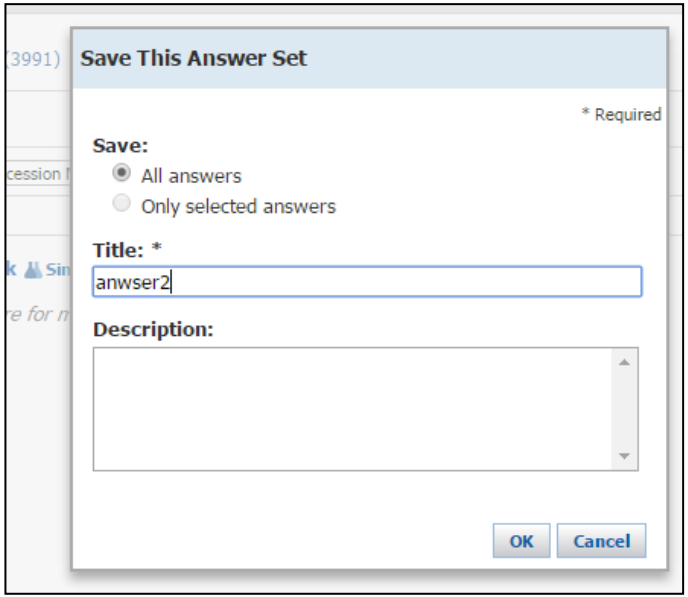

Absolute stereochemistry.,Rotation (+).



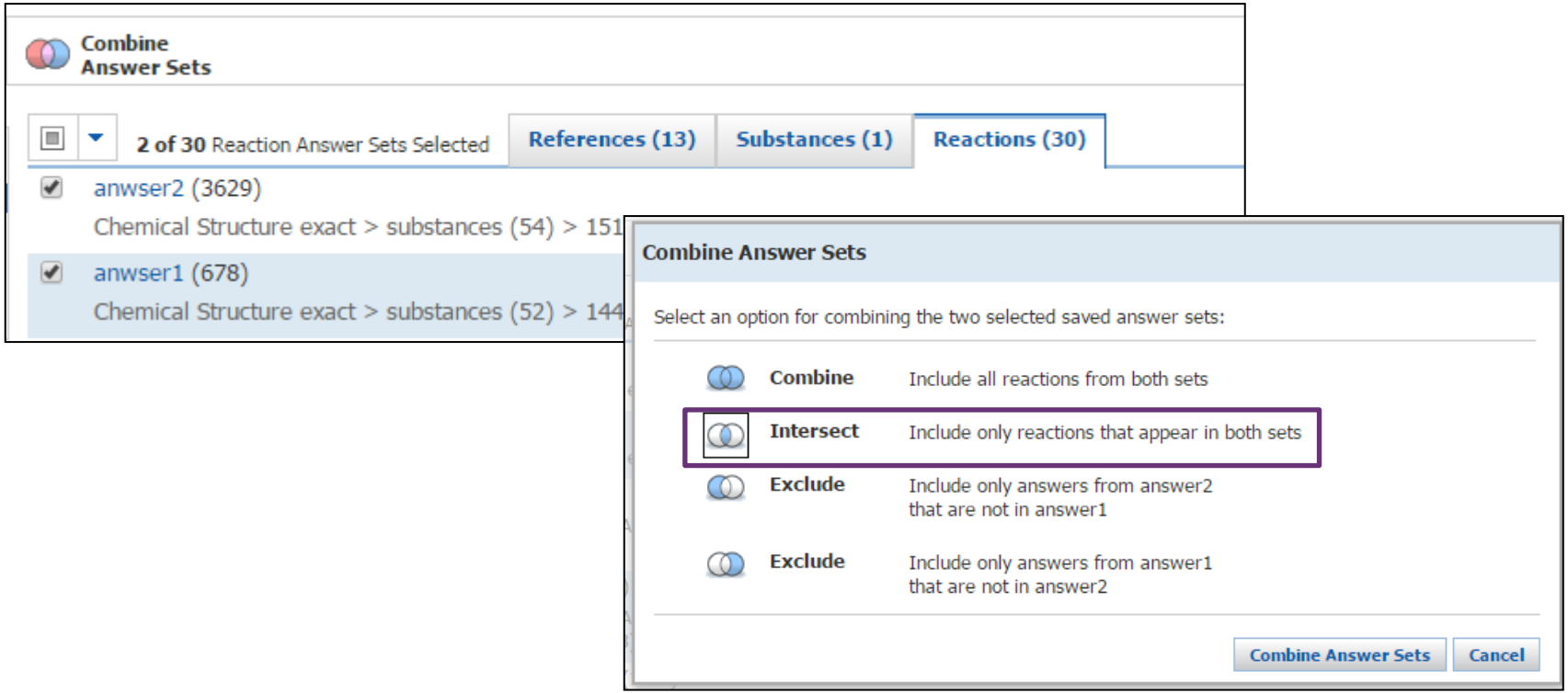
# 手性翻转反应：将反应结果集限定为一步反应，并存为answer2



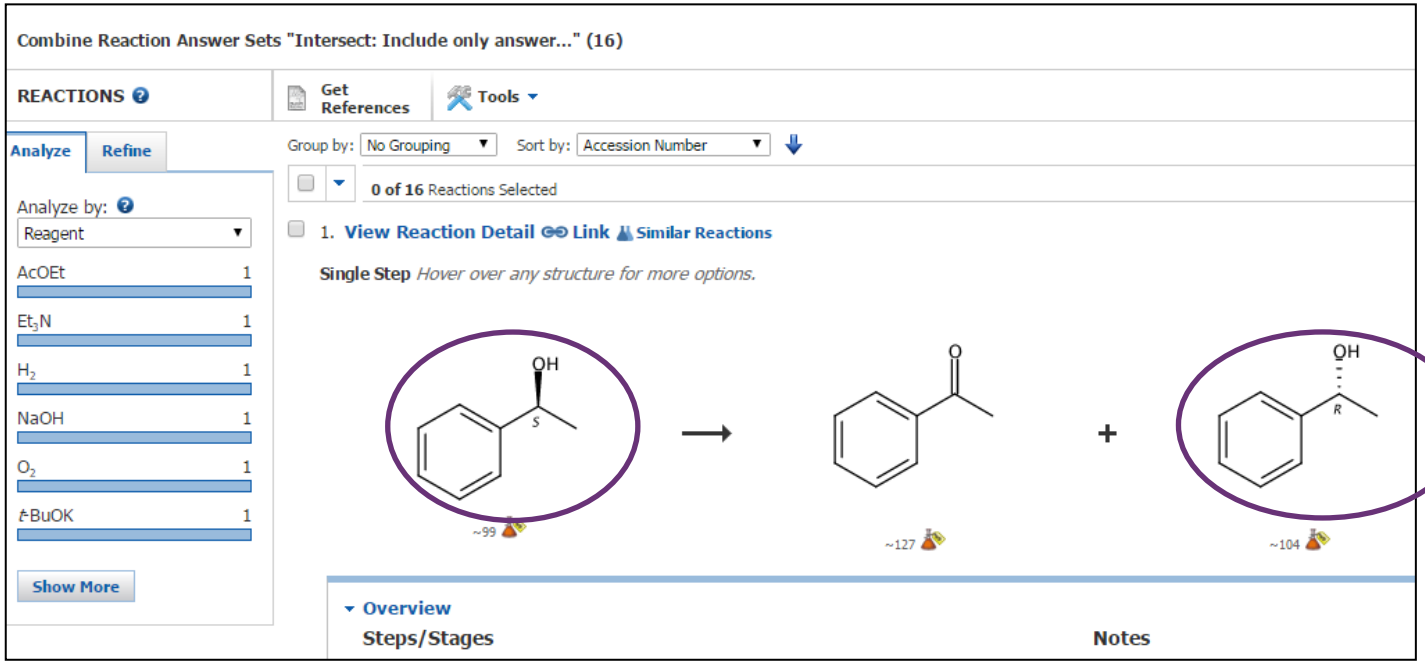

将所得结果集保存为”answer2”



# 手性翻转反应：点击Tools，将answer1和answer2合并取交集



# 手性翻转反应：获得准确的反应结果



# 提纲

- 手性反应专题
  - 手性分子合成反应
  - 手性构型翻转反应
  - **手性分子拆分反应**



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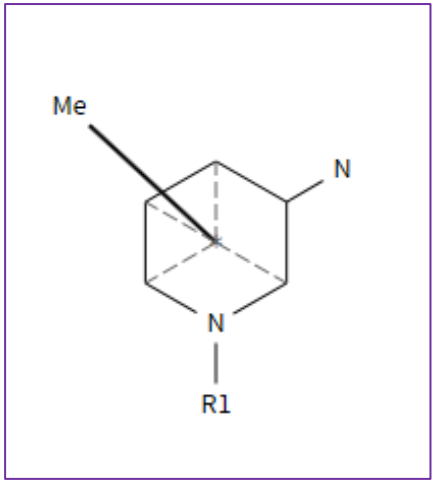
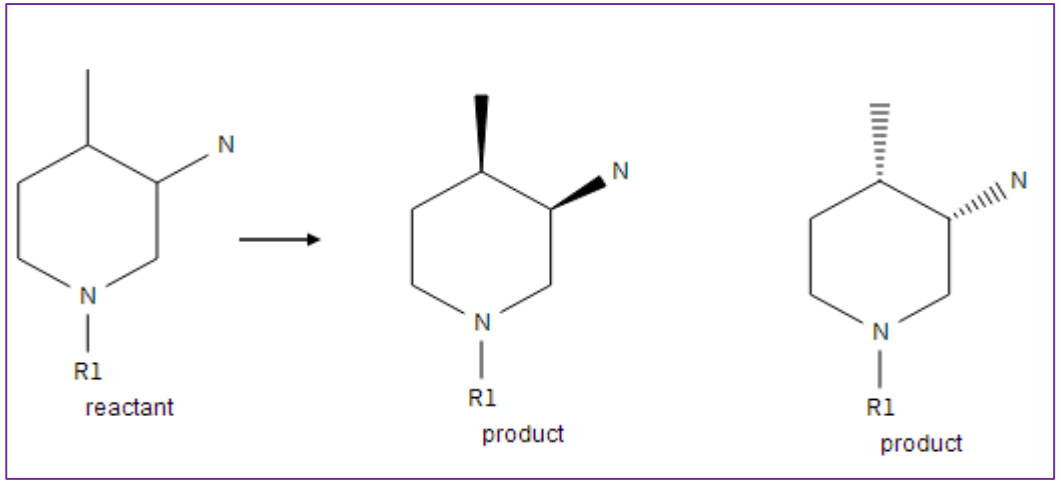
# 手性拆分反应

如何检索如下消旋体拆分获得绝对构型的反应？




N-保护的3-氨基-甲基哌啶

举例：R1可以是一些保护基，比如Boc、Cbz等，
甲基可以在吡啶环的2,4,5或6位的任意位置。

# 手性拆分反应：检索思路1

- **从产物检索出发**

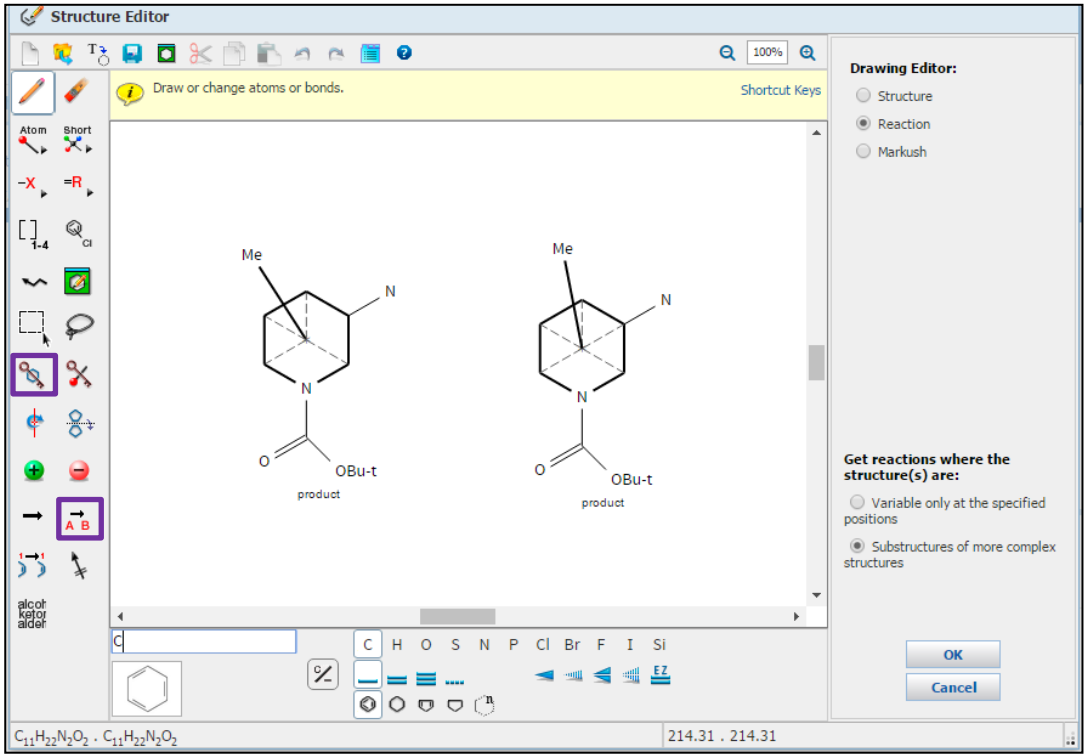
  在反应结构编辑器中，同时绘制两个产物结构（无需画立体构型），选择亚结构反应检索

- **限定反应物**

  在反应结果集中，通过Refine: Reaction structure对反应进行限定，所画结构为没有立体构型的反应物

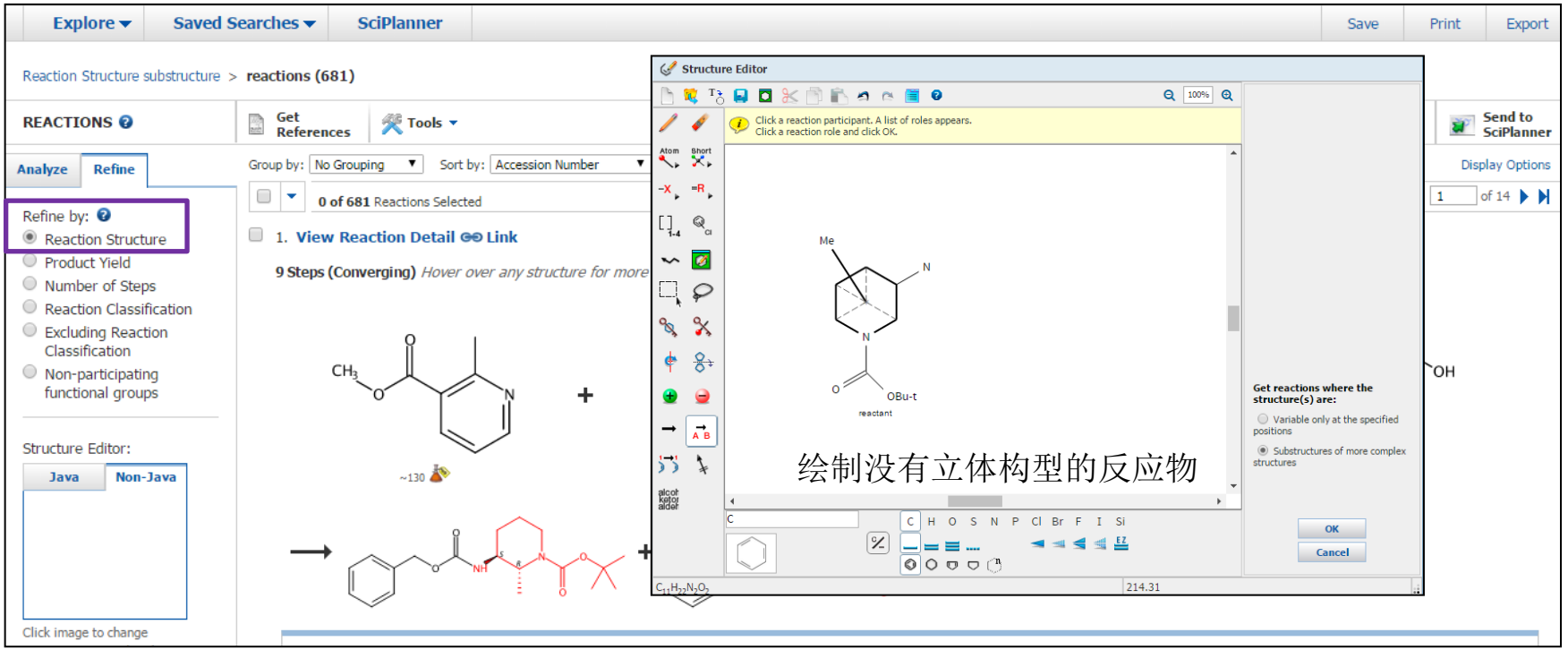
- **获得结果集**

# 手性拆分反应：从产物检索出发




在反应结构编辑器中绘制产物结构，无需绘制立体键，选择亚结构反应检索

# 手性拆分反应：限定反应物




在反应结果集中通过Reaction Structure限定反应物

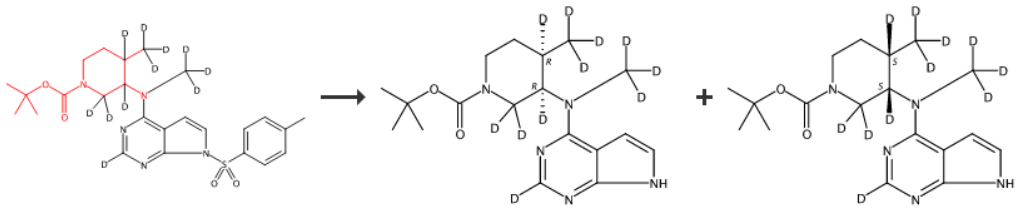
# 手性拆分反应：获得反应结果集

2. Deuterated tasocitinib derivatives as Janus kinase 3 inhibitors and their preparation and use for the treatment and prevention of Janus kinase 3-mediated diseases

Quick View PATENTPAK

8 Reactions

**2 Steps** *Hover over any structure for more options.*



**Overview**

**Steps/Stages**

1.1 S:NaOD, 2 h, 100°C
2.1

消旋体的拆分

**Notes**

2) sepn. by column chromatog. on Chiralpak IC, Reactants: 1, Solvents: 1, Steps: 2, Stages: 2, Most stages in any one step: 1

**References**

Deuterated tasocitinib derivatives as Janus kinase 3 inhibitors and their preparation and use for the treatment and prevention of Janus kinase 3-mediated diseases

Quick View PATENTPAK

By Rao, Tadimeti S. and Zhang, Chengzhi

From PCT Int. Appl., 2010123919, 28 Oct 2010

**Experimental Procedure**

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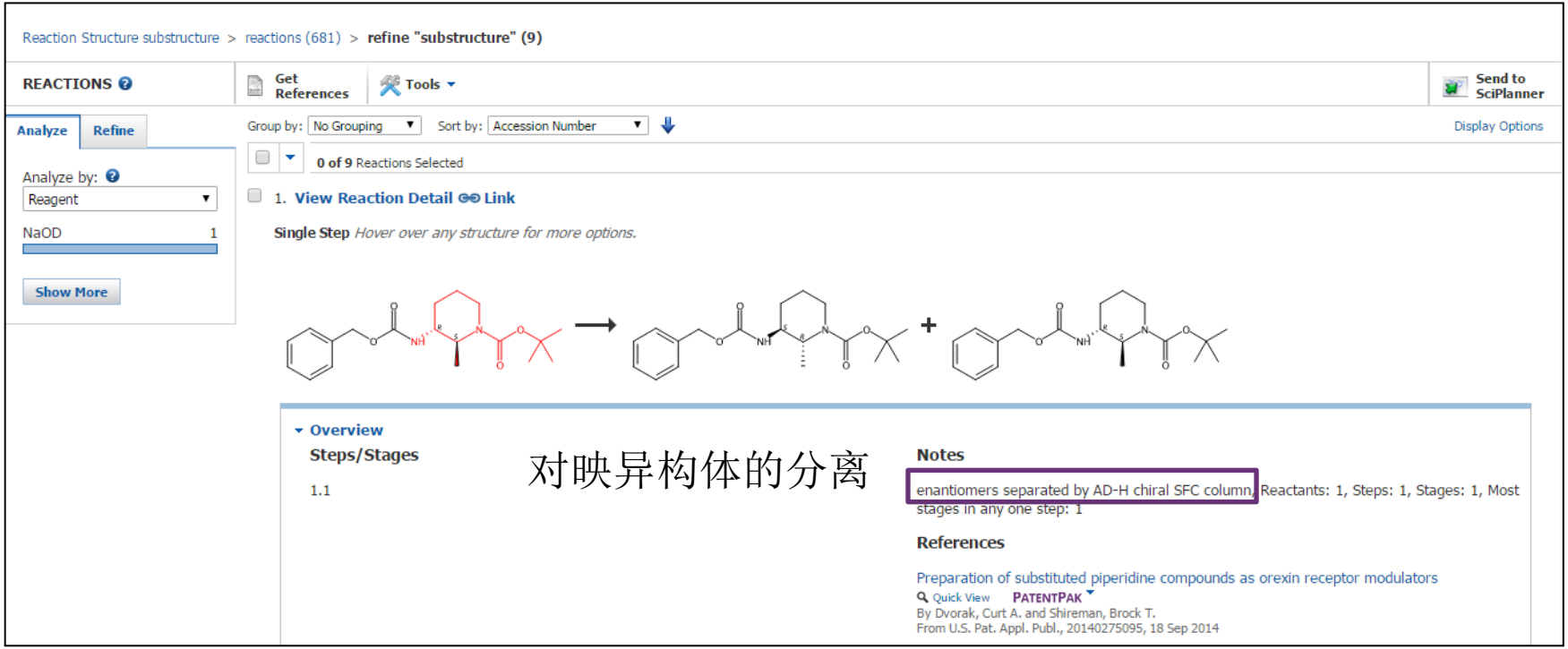
# 手性拆分反应：获得反应结果集



# 谢谢关注！

美国化学文摘社北京代表处
电话：010-62508026/7
电子邮箱：china@acs-i.org
中文网站：http://www.cas-china.org/
英文网站：http://www.cas.org/

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