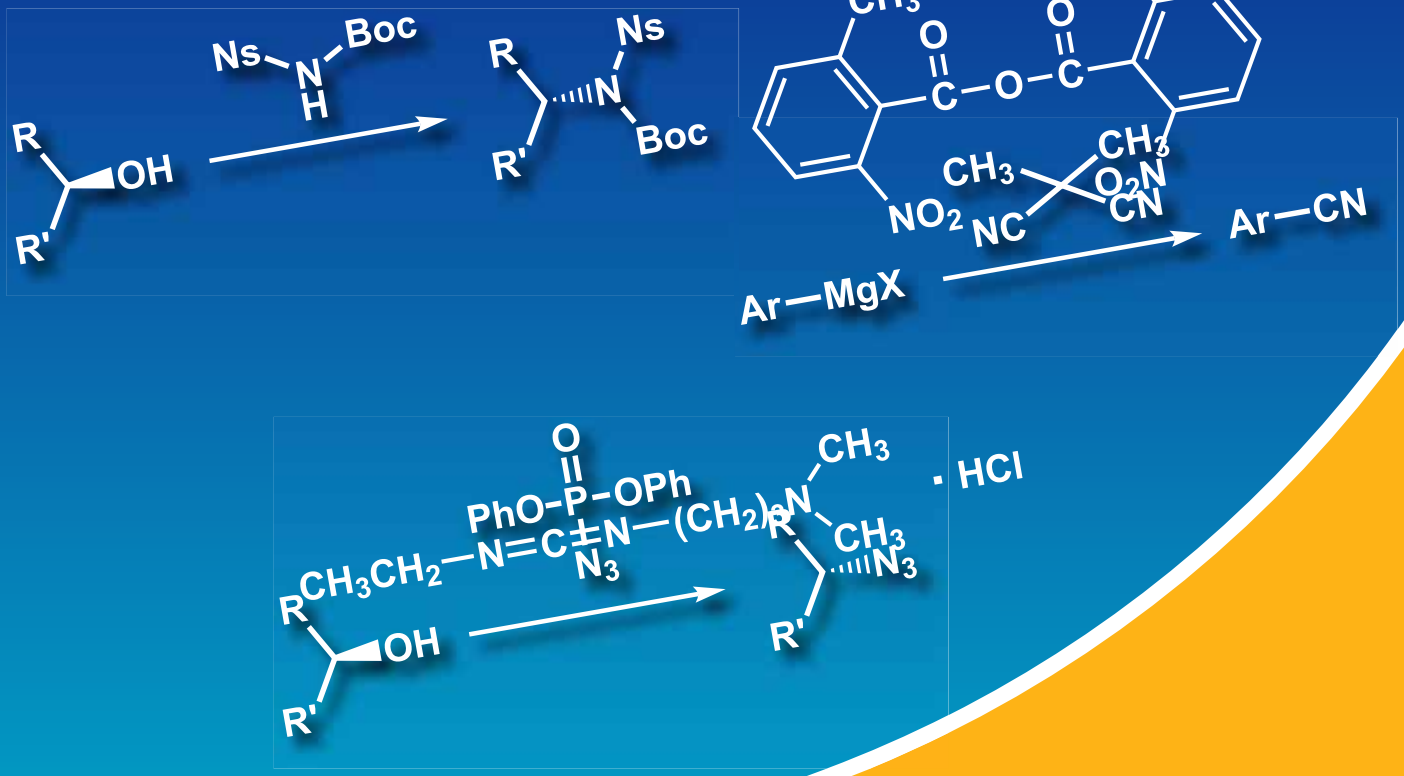
CHEMISTRY

C-N键形成反应

C-N Bond Formation Reactions



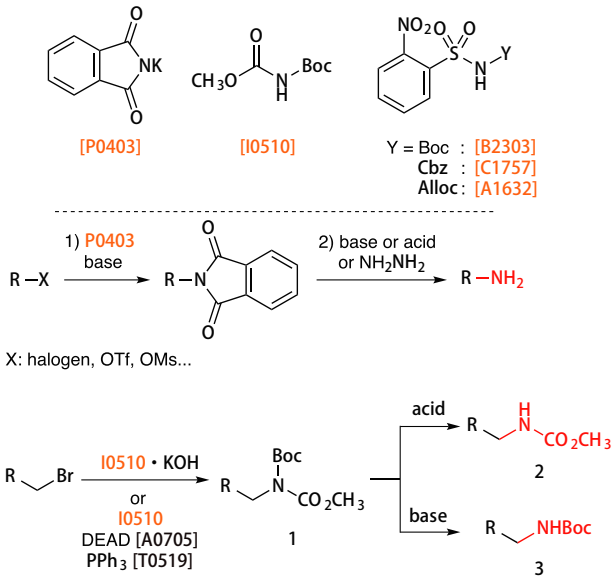
- 胺化试剂
- 硝化试剂
- 氰化试剂
- 叠氮化和重氮化试剂
- 胍基化试剂

C-N键形成反应

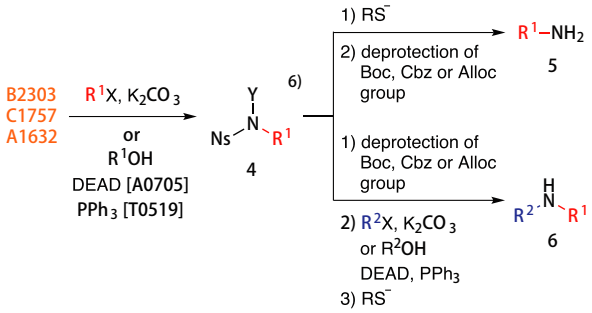
含氮化合物广泛存在于从天然产物如氨基酸、核酸和生物碱到合成化合物如电子材料和聚酰胺中。此外，不同的含氮官能团如氨基和硝基具有不同的偶联反应式和氧化态，因此C-N键因官能团不同其成键反应也不同。由于C-N键形成反应包含了从简单引入官能团到构建杂环等多种方法，我们很难完全彻底介绍C-N键成键反应，因此本手册主要介绍TCI试剂通过C-N键形成反应构建含氮官能团。此外，手册中有些氰化剂可能不适用于C-N键形成反应，但是氰基可以转化为其他含氮官能团供参考。

胺化试剂

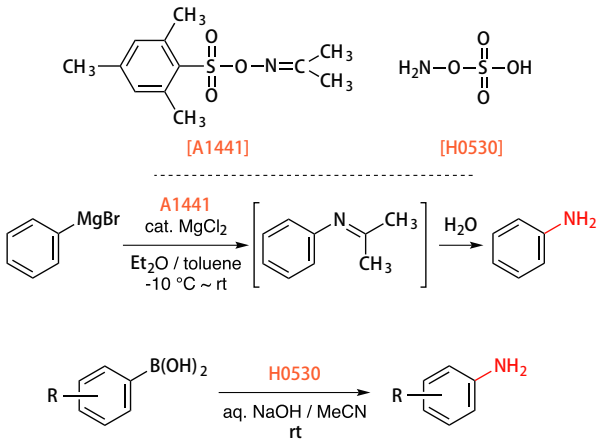
Gabriel胺合成法[1]是目前广泛使用的亲核胺化反应，邻苯二甲酰亚胺钾以及相似的胺化试剂也已有报道。亚氨基二甲酸叔丁酯钾盐[I0510]与卤代烷反应生成酰亚胺1[2]。1分别经酸或碱处理得到N-甲氧基羰基胺2和N-Boc胺3。此外，I0510可用于Mitsunobu反应，将羟基转化为氨基[3]。



与此同时，福山等人报道了用邻硝基苯磺酰基（Ns）保护的磺胺类化合物[B2303][C1757][A1632]合成胺的方法[4]。这些物质分别在碱性条件下与卤代烷或在含醇条件下通过Mitsunobu反应得到含保护基的胺**4**。通过选择性地去除两个保护基团可得到伯胺**5**。然而，当保留**4**的Ns基团时，可以在烷基化后并相继去除保护基得到仲胺**6**。

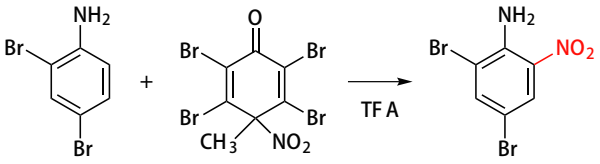


乙酰肟*O*-(2,4,6-三甲基苯磺酸盐)[A1441]可用作亲电胺化试剂[6]。A1441在催化量的氯化镁下与格氏试剂反应可高产率生成伯胺[7]。此外，羟胺-磺酸（HSA）[H0530]也可用作胺化试剂。HSA作为氨基阳离子，通过苯硼衍生物处理可生成伯苯胺。该反应优点是不需要过渡金属催化剂就能进行反应，操作方便[7]。



● 硝化试剂

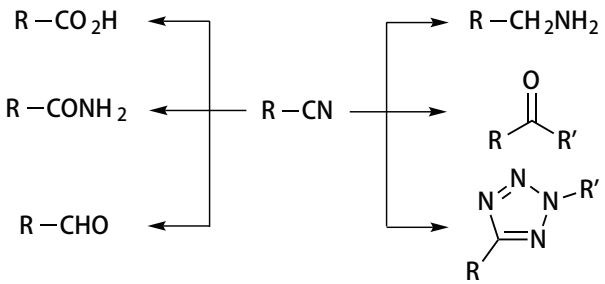
硝基是强吸电子官能团，可以降低芳香环的电子密度，增加硝基烷a-位质子的酸度。因此，含硝基的化合物可以发生独特的反应，如Henry反应和Nef反应。芳环的硝化一般是通过浓硝酸和浓硫酸进行亲电取代反应。而2,3,5,6-四溴-4-甲基-4-硝基-2,5-环己二酮[T1431]是一种温和的芳香族化合物硝化试剂[9,10]。例如，富含电子的芳香族化合物如苯胺，经T1431处理可发生邻位或对位硝化反应。



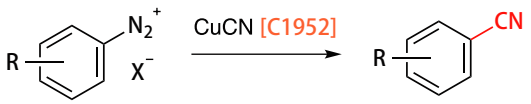
[T1431]

● 氰化试剂

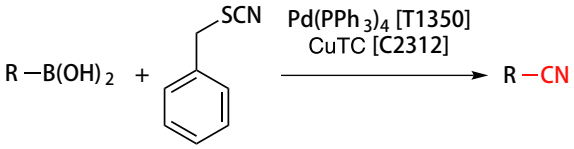
氰基是强吸电子基团，许多氰化试剂广泛用于有机合成中。氰基可以通过水解转化为其他官能团，例如羧酸或酰胺，也可通过一些还原剂还原为胺或醛。此外，还可以通过与格氏试剂或有机锂的亲核加成反应，将腈转化为相应的不对称酮。另一方面，氰基还可用于和其他多键化合物的环加成反应。例如，烷基腈与叠氮化物环合得到四唑。为了引入氰基，氰化钾[P1613]与烷基卤的反应是一种典型的合成方法，氰化铜介导的Sandmeyer反应和Rosenmund-von Braun反应也久负盛名。近年来发展了钯催化剂与一些氰化试剂的氰化反应。硫氰酸苄酯[T0198][11]，氰基乙酸乙酯[C0441][12]，丁基叔丁基[B1274][13]和丙酮氰醇[M0361][14]作为氰离子等价物。近来，一些研发小组报道了乙腈[15]和二甲基丙二腈[16][D5514]可以用作氰基源。这样，有多种氰化试剂可用于不同物质的直接氰化反应。



Sandmeyer reaction

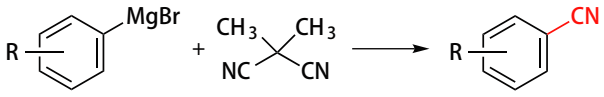


Pd-Catalyzed cross-coupling cyanation



[T0198]

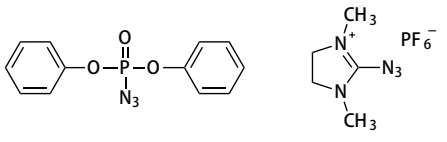
Cyanation of Grignard reagent



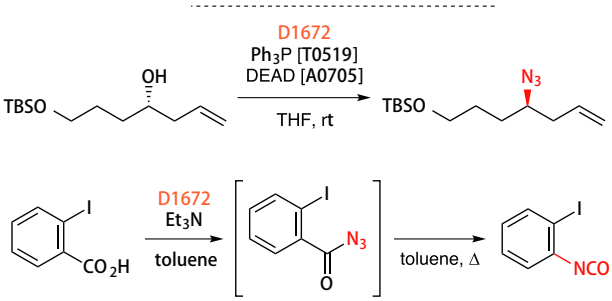
[D5514]

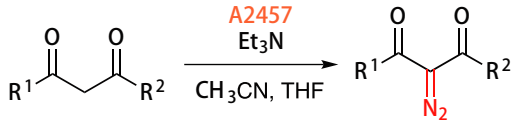
● 叠氮化和重氮化试剂

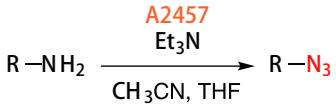
有机叠氮化物可以通过叠氮化钠[S0489]与卤代烷基化合物反应，或与三氟甲磺酰基叠氮化物和伯胺的反应来合成。然而，这些叠氮化物源因具有高度爆炸性所以很难处理。相比之下，Shioiri等人开发了一种稳定易操作的叠氮化试剂DPPA[D1672][17]。当在Mitsunobu条件下用DPPA处理乙醇时，可以高收率得到构型翻转的叠氮化合物。DPPA不仅用于Curtius重排，还可用作缩合试剂[18]。此外，Kitamura等人开发的2-叠氮基-1,3-二甲基咪唑啉六氟磷酸盐（ADMP）[A2457]是一种热稳定性高、对冲击和摩擦反应性低的结晶重氮转移试剂。ADMP可与多种伯胺反应生成叠氮化物[19]，同时可与1,3-二羰基化合物高产率生成α-重氮化合物[20]。



[D1672] [A2457]

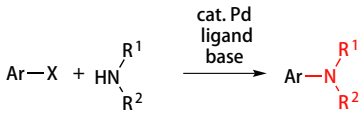




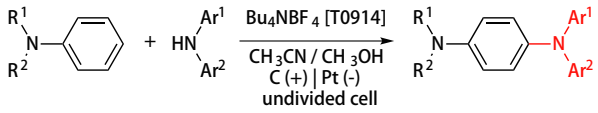


R: alkyl, aryl

Buchwald-Hartwig cross-coupling

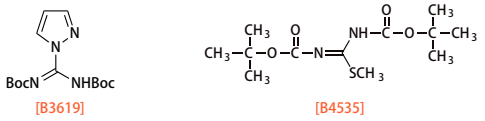


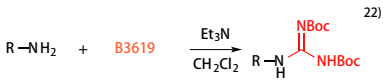
Electrooxidative C-N cross-coupling

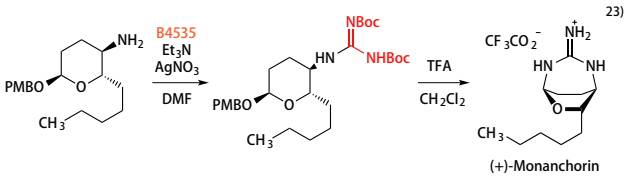


● 胍基化试剂

胍基是有机碱性中具有较强碱性的基团，存在于许多具有生物活性的化合物以及精氨酸中。例如，源于河豚毒素的石房蛤毒素和河豚毒素，以及海绵中作为HIV抑制剂的batzelladine A均为含有胍基的化合物。因此，胍基化试剂常被用于药物研发领域中胍类衍生物的合成[21]。胍基的引入主要是通过与氨基的加成反应获得。







● 通过交叉偶联反应形成C-N键

Buchwald[24]和Hartwig[25]分别独立报道了在钯催化剂和强碱存在下，胺和芳基卤化物的一种新型偶联反应。这个反应称为Buchwald-Hartwig交叉偶联反应。该反应将氨基引入芳族化合物，也可用于构建含氮杂芳环[26]。因此，该反应广泛应用于天然产物的全合成、药物化学和过程化学。最近报道了一种新的电氧化C-N交叉偶联反应[27]。该反应具有以下优点：对位选择性交叉偶联反应；无金属催化剂反应；该反应唯一的副产物是通过C-H键活化产生的氢气，因此被称为绿色反应。

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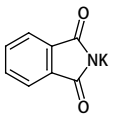
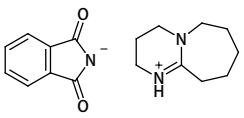
胺化试剂
Reagents for Amination

P0403 25g 500g



Phthalimide Potassium Salt
CAS RN: 1074-82-4

P1235 25g



Phthalimide DBU Salt
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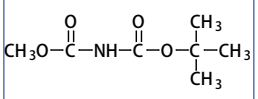
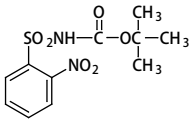
I0510 5g



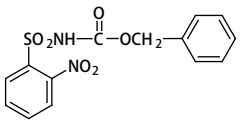
tert-Butyl Methyl Iminodicarboxylate
CAS RN: 66389-76-2

B2303 1g 5g 25g



N-Boc-2-nitrobenzenesulfonamide
CAS RN: 198572-71-3

C1757 5g 25g



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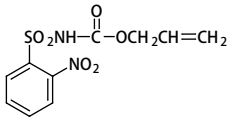
A1632 5g



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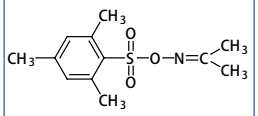
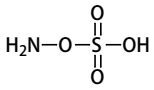
CAS RN: 90916-29-3

A1441 5g 25g



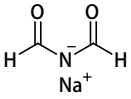
Acetoxime *O*-(2,4,6-Trimethylphenylsulfonate)
CAS RN: 81549-07-7

H0530 25g 100g 500g



Hydroxylamine-*O*-sulfonic Acid
CAS RN: 2950-43-8

D2479 25g



Sodium Diformylamide
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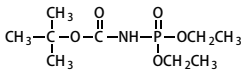
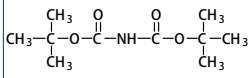
B1734 5g



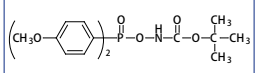
N-Boc-phosphoramidic Acid Diethyl Ester
CAS RN: 85232-02-6

I0497 5g 25g



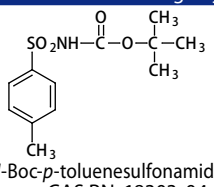
Di-*tert*-butyl Iminodicarboxylate
CAS RN: 51779-32-9

B2857 1g 5g



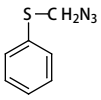
tert-Butyl [Bis(4-methoxyphenyl)-phosphinyloxy]carbamate
CAS RN: 619333-95-8

B1648 10g 25g



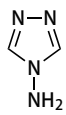
N-Boc-*p*-toluenesulfonamide
CAS RN: 18303-04-3

A1341 5g



Azidomethyl Phenyl Sulfide
CAS RN: 77422-70-9

A1137 25g 250g



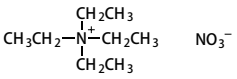
4-Amino-1,2,4-triazole
CAS RN: 584-13-4

硝化试剂
Reagents for Nitration

T1431 5g 25g

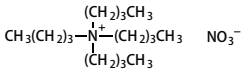
2,3,5,6-Tetrabromo-4-methyl-4-nitro-2,5-cyclohexadien-1-one
CAS RN: 95111-49-2

T3082 5g 25g



Tetraethylammonium Nitrate
CAS RN: 1941-26-0

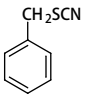
T3651 5g 25g



Tetrabutylammonium Nitrate
CAS RN: 1941-27-1

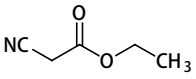
氰化试剂
Reagents for Cyanation

T0198 25g 500g



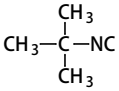
Benzyl Thiocyanate
CAS RN: 3012-37-1

C0441 25g 500g



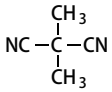
Ethyl Cyanoacetate
CAS RN: 105-56-6

B1274 5mL 25mL



tert-Butyl Isocyanide
CAS RN: 7188-38-7

D5514 5g 25g



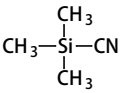
Dimethylmalononitrile
CAS RN: 7321-55-3

C1952 25g 300g

CuCN

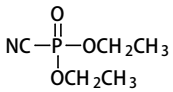
Copper(I) Cyanide
CAS RN: 544-92-3

T0990 25mL 100mL 500mL



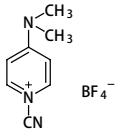
Trimethylsilyl Cyanide
CAS RN: 7677-24-9

C1242 5g 25g



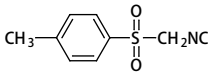
Diethyl Cyanophosphonate
CAS RN: 2942-58-7

C2348 100mg



1-Cyano-4-(dimethylamino)-pyridinium Tetrafluoroborate
CAS RN: 59016-56-7

T1046 5g 25g



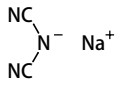
TosMIC
CAS RN: 36635-61-7

C3003 1g 5g

2-Chlorobenzyl Thiocyanate
CAS RN: 2082-66-8

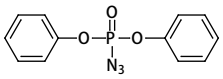
叠氮化和重氮化试剂
Reagents for Azidation and Diazotization

S0838 25g 100g



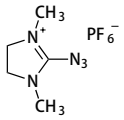
Sodium Dicyanamide
CAS RN: 1934-75-4

D1672 5g 25g 250g



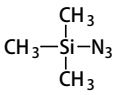
DPPA
CAS RN: 26386-88-9

A2457 5g



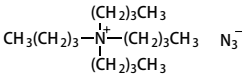
2-Azido-1,3-dimethylimidazolinium Hexafluorophosphate
CAS RN: 1266134-54-6

T0801 5g 25g 100g



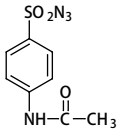
Trimethylsilyl Azide
CAS RN: 4648-54-8

T0920 5g 25g



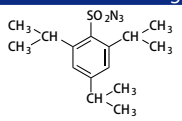
Tetrabutylammonium Azide
CAS RN: 993-22-6

A1786 5g 25g 100g



4-Acetamidobenzenesulfonyl Azide
CAS RN: 2158-14-7

T3434 1g 5g



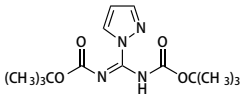
2,4,6-Triisopropylbenzenesulfonyl Azide (wetted with *ca.* 10% Water)
CAS RN: 36982-84-0

D2580 25g

Dodecylbenzenesulfonyl Azide (soft type) (mixture)
CAS RN: 79791-38-1

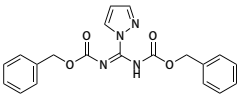
胍基化试剂
Reagents for Guanidinylation

B3619 1g 5g



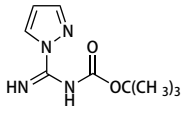
1-[*N*,*N*'-(Di-Boc)amidino]-pyrazole
CAS RN: 152120-54-2

B3605 1g 5g



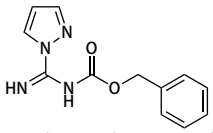
1-[*N*,*N*'-(Di-Cbz)amidino]-pyrazole
CAS RN: 152120-55-3

B4028 5g



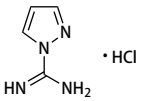
1-(*N*-Boc-amidino)pyrazole
CAS RN: 152120-61-1

C2709 1g 5g



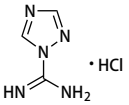
1-(*N*-Cbz-amidino)pyrazole
CAS RN: 152120-62-2

A2055 5g 25g



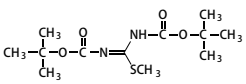
1-Amidinopyrazole Hydrochloride
CAS RN: 4023-02-3

T3124 1g 5g



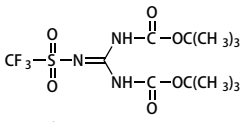
1-Carbamimidoyl-1,2,4-triazole Hydrochloride
CAS RN: 19503-26-5

B4535 5g 25g



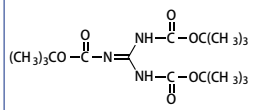
N,*N*'-Di-Boc-*S*-methylisothiourea
CAS RN: 107819-90-9

B3625 1g 5g



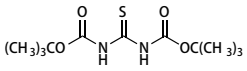
Goodman's Reagent
CAS RN: 207857-15-6

T2964 1g 5g



1,2,3-Tri-Boc-guanidine
CAS RN: 216584-22-4

B4559 1g 5g



1,3-Di-Boc-thiourea
CAS RN: 145013-05-4

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