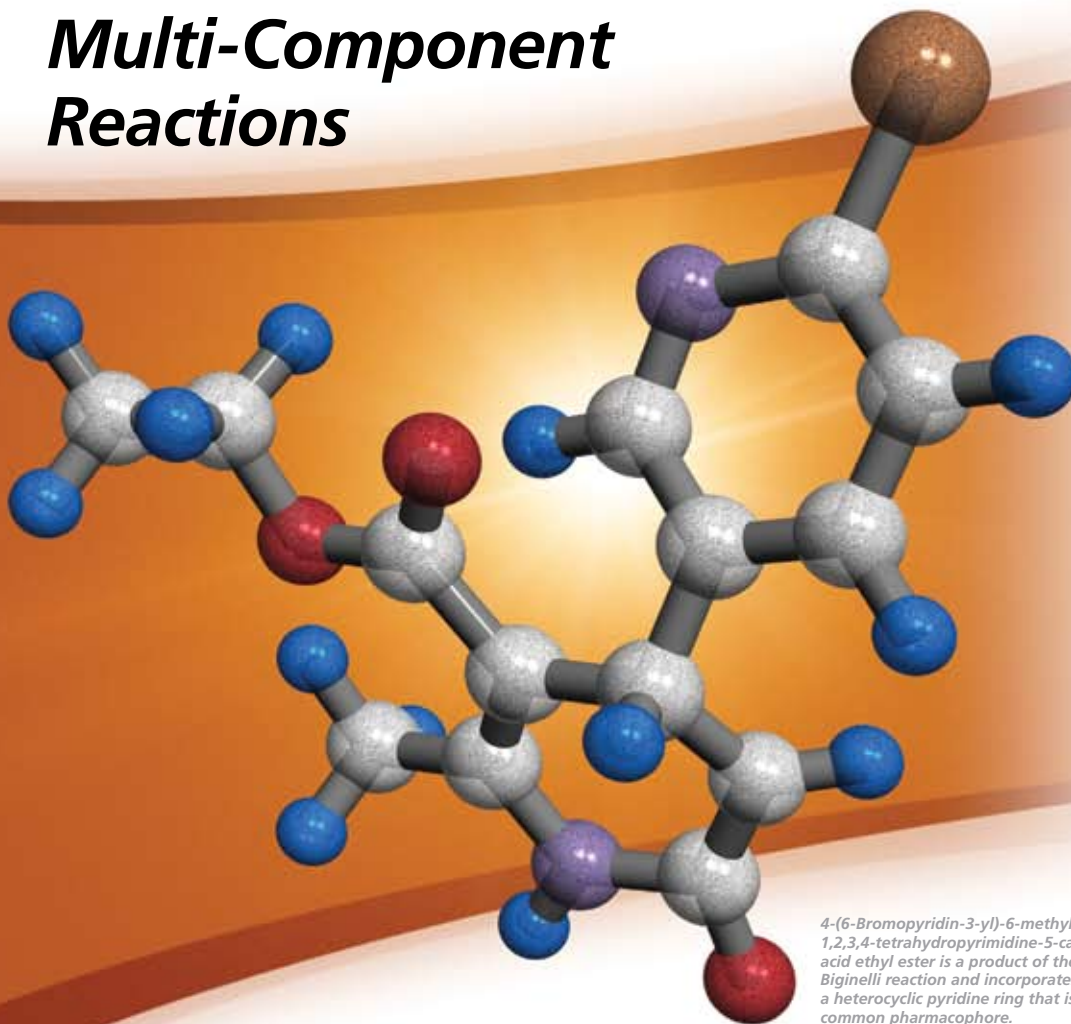




## Multi-Component Reactions



UGI REACTION

PASSERINI REACTION

BIGINELLI REACTION

*4-(6-Bromopyridin-3-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester is a product of the Biginelli reaction and incorporates a heterocyclic pyridine ring that is a common pharmacophore.*



## Introduction

Multi-component reactions (MCRs) play an important role in combinatorial chemistry because of its ability to synthesize small drug-like molecules with several degrees of structural diversity. A MCR is defined as three or more different starting materials that react to form a product, where most, if not all of the atoms are incorporated in the final product. This reaction tool allows compounds to be synthesized in a few steps and usually in a one-pot operation.<sup>1</sup> Another typical benefit from these reactions is simplified purification, because all of the reagents are incorporated into the final product.

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### About Our Cover

The cover illustration depicts the structure of a Biginelli compound developed by the Sigma-Aldrich R&D group. The Biginelli reaction has had a recent resurgence due to the pharmacological properties affiliated with the dihydropyrimidine scaffold. These compounds have shown biological activity as antiviral, antitumor, and antibacterial agents.



# ChemFiles

Vol. 6 No. 7

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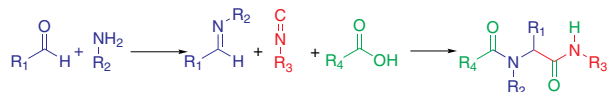
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## Ugi Reaction

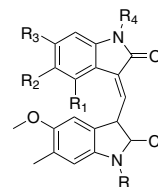
The Ugi reaction (**Scheme 1**) is an isonitrile-based MCR that provides a rapid route for the preparation of  $\alpha$ -aminoacyl amide derivatives. The Ugi 4 component condensation of an amine, oxo compound, carboxylic acid and an isocyanide is the most documented and versatile MCR.

Combined with combinatorial chemistry, Musonda et al. describe using the Ugi MCR to develop a library of novel compounds to screen against known antimalarial pharmacophores. The library consisted of aminoquinoline containing  $\alpha$ -aminoacyl amides that were used in structure-activity relationship (SAR) studies. This approach allowed them to synthesize a number of compounds in very few reaction steps and screen them rapidly.<sup>2</sup>

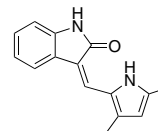
The Ugi reaction can be coupled with a post condensation reaction to increase the number of possible pharmacologically important scaffolds. An example is the Heck reaction. Umkehrer et al. recently demonstrated that the Ugi/Heck combination works well for high-throughput combinatorial library production of indol-2-ones having four points of diversity. This scaffold is of interest because it has shown biological effect as antitumor(**1**) and tyrosine kinase(**2**) inhibitor activity.<sup>3</sup>



**Scheme 1**



**1**



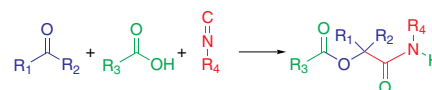
**2**

## Passerini Reaction

The Passerini Reaction is another isonitrile-based MCR that yields  $\alpha$ -acyloxy carboxamides in a one-pot synthesis from an aldehyde, isonitrile, and carboxylic acid. Of the three components, the carbonyl group is one of the most critical reactants because of the pronounced reactivity of the divalent isonitrile carbon atom towards the C(sp<sup>2</sup>) electrophilic center.

This reaction can be sluggish with low yields if a strong carboxylic acid or an unusually electrophilic carbonyl compound is not used.<sup>4</sup>

The traditional Passerini reaction involves an aldehyde in the one pot reaction. In some cases, the aldehydes are not stable or are difficult to handle. Nguansavanh et al. recently describes substituting the aldehyde with the corresponding alcohol and using 2-iodoxybenzoic acid (IBX) (**3**) (**661384**). This increases the versatility and the number of compounds available using this reaction scheme.<sup>5</sup>



**Scheme 2**

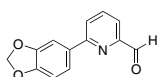


**3**

## Aldehydes

### 6-(1,3-Benzodioxol-5-yl)-2-pyridinecarboxaldehyde, 97%

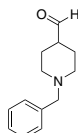
C<sub>13</sub>H<sub>9</sub>NO<sub>3</sub>  
FW: 227.22  
[834884-78-5]



655813-1G 1 g  
655813-5G 5 g

### N-Benzylpiperidine-4-carboxaldehyde, 96%

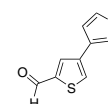
C<sub>13</sub>H<sub>17</sub>NO  
FW: 203.28  
[22065-85-6]



664081-1G 1 g  
664081-5G 5 g

### [3,3'-Bithiophene]-5-carboxaldehyde, 97%

C<sub>9</sub>H<sub>6</sub>OS<sub>2</sub>  
FW: 194.27  
[137320-59-3]



657824-1G 1 g  
657824-5G 5 g

### 2,5-Dibromo benzaldehyde

C<sub>7</sub>H<sub>4</sub>Br<sub>2</sub>O  
FW: 263.91  
[74553-29-0]



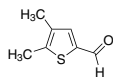
661899-1G 1 g  
661899-5G 5 g

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**4,5-Dimethylthiophene-2-carboxaldehyde, 97%**

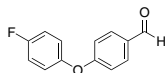
C<sub>7</sub>H<sub>8</sub>OS  
FW: 140.2  
[5928-48-3]



668354-1G 1 g

**4-(4-Fluorophenoxy)benzaldehyde, 97%**

C<sub>13</sub>H<sub>9</sub>FO<sub>2</sub>  
FW: 216.21  
[137736-06-2]



661287-1G 1 g  
661287-5G 5 g

**2-Fluoro-3-pyridinecarboxaldehyde, 97%**

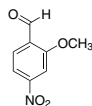
C<sub>6</sub>H<sub>4</sub>FNO  
FW: 125.1  
[36404-90-7]



664111-5G 5 g

**2-Methoxy-4-nitrobenzaldehyde, 97%**

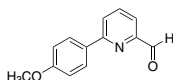
C<sub>8</sub>H<sub>7</sub>NO<sub>4</sub>  
FW: 181.15  
[136507-15-8]



658324-1G 1 g  
658324-5G 5 g

**6-(4-Methoxyphenyl)-2-pyridinecarboxaldehyde, 97%**

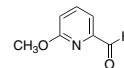
C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub>  
FW: 213.23  
[502925-47-5]



655783-1G 1 g  
655783-5G 5 g

**6-Methoxy-2-pyridinecarboxaldehyde, 97%**

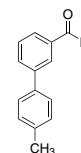
C<sub>7</sub>H<sub>7</sub>NO<sub>2</sub>  
FW: 137.14  
[54221-96-4]



662933-1G 1 g  
662933-5G 5 g

**3-(4-Methylphenyl)benzaldehyde, 97%**

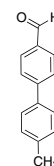
C<sub>14</sub>H<sub>12</sub>O  
FW: 196.24  
[116470-54-3]



664790-250MG 250 mg  
664790-1G 1 g

**4-(4-Methylphenyl)benzaldehyde, 97%**

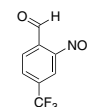
C<sub>14</sub>H<sub>12</sub>O  
FW: 196.24  
[36393-42-7]



664782-250MG 250 mg  
664782-1G 1 g

**2-Nitro-4-(trifluoromethyl)benzaldehyde, 97%**

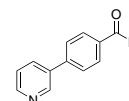
C<sub>8</sub>H<sub>4</sub>F<sub>3</sub>NO<sub>3</sub>  
FW: 219.12  
[109466-87-7]



664952-1G 1 g

**4-(Pyridin-3-yl)benzaldehyde, 98%**

C<sub>12</sub>H<sub>9</sub>NO  
FW: 183.21  
[127406-55-7]



668303-1G 1 g  
668303-5G 5 g

**Amines****3-Amino-2-bromopyridine, 97%**

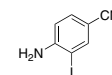
C<sub>5</sub>H<sub>5</sub>BrN<sub>2</sub>  
FW: 173.01  
[39856-58-1]



661228-1G 1 g

**4-Amino-3-iodobenzonitrile**

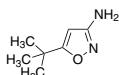
C<sub>7</sub>H<sub>5</sub>IN<sub>2</sub>  
FW: 244.03  
[33348-34-4]



657123-1G 1 g  
657123-5G 5 g

**3-Amino-5-tert-butylisoxazole, 97%**

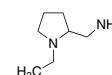
C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>O  
FW: 140.18  
[55809-36-4]



666580-5G 5 g  
666580-25G 25 g

**2-(Aminomethyl)-1-ethylpyrrolidine, 97%**

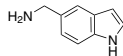
C<sub>7</sub>H<sub>16</sub>N<sub>2</sub>  
FW: 128.22  
[26116-12-1]



655600-5G 5 g  
655600-25G 25 g

**5-(Aminomethyl)indole, 95%**

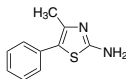
C<sub>9</sub>H<sub>10</sub>N<sub>2</sub>  
FW: 146.19



655864-1G	1 g
655864-5G	5 g

**2-Amino-5-methyl-4-phenylthiazole, 97%**

C<sub>10</sub>H<sub>10</sub>N<sub>2</sub>S  
FW: 190.26  
[30709-67-2]



658480-1G	1 g
658480-10G	10 g

**3-Amino-2-methylpyridine, 97%**

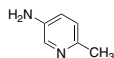
C<sub>6</sub>H<sub>8</sub>N<sub>2</sub>  
FW: 108.14  
[3430-10-2]



662690-250MG	250 mg
662690-1G	1 g

**5-Amino-2-methylpyridine, 97%**

C<sub>6</sub>H<sub>8</sub>N<sub>2</sub>  
FW: 108.14  
[3430-14-6]



662704-250MG	250 mg
662704-1G	1 g

**4-Amino-3-(trifluoromethyl)pyridine, 97%**

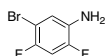
C<sub>6</sub>H<sub>5</sub>F<sub>3</sub>N<sub>2</sub>  
FW: 162.11  
[387824-61-5]



661090-100MG	100 mg
661090-500MG	500 mg

**5-Bromo-2,4-difluoroaniline, 97%**

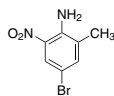
C<sub>6</sub>H<sub>4</sub>BrF<sub>2</sub>N  
FW: 208  
[452-92-6]



656372-5G	5 g
656372-25G	25 g

**4-Bromo-2-methyl-6-nitroaniline, 97%**

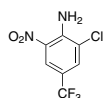
C<sub>9</sub>H<sub>7</sub>BrN<sub>2</sub>O<sub>2</sub>  
FW: 231.05  
[77811-44-0]



655988-1G	1 g
655988-5G	5 g

**2-Chloro-6-nitro-4-(trifluoromethyl)aniline, 97%**

C<sub>7</sub>H<sub>4</sub>ClF<sub>3</sub>N<sub>2</sub>O<sub>2</sub>  
FW: 240.57  
[57729-79-0]



656038-1G	1 g
656038-5G	5 g

**2-Chloro-4-(trifluoromethoxy)aniline, 97%**

C<sub>7</sub>H<sub>5</sub>ClF<sub>3</sub>NO  
FW: 211.57  
[69695-61-0]



655929-1G	1 g
655929-5G	5 g

**3,5-Dibromo-4-methylaniline, 97%**

C<sub>7</sub>H<sub>7</sub>Br<sub>2</sub>N  
FW: 264.95  
[13194-73-5]



658367-1G	1 g
658367-5G	5 g

**2,4-Dichloro-6-(trifluoromethyl)aniline, 97%**

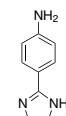
C<sub>7</sub>H<sub>4</sub>Cl<sub>2</sub>F<sub>3</sub>N  
FW: 230.01  
[62593-17-3]



656011-1G	1 g
656011-5G	5 g

**4-(4,5-Dihydro-1H-imidazol-2-yl)phenylamine, 97%**

C<sub>9</sub>H<sub>11</sub>N<sub>3</sub>  
FW: 161.2



666084-1G	1 g
-----------	-----

**4-Iodo-2-nitroaniline, 97%**

C<sub>6</sub>H<sub>5</sub>IN<sub>2</sub>O<sub>2</sub>  
FW: 264.02  
[20691-72-9]



654108-1G	1 g
654108-10G	10 g

**2-Morpholinoaniline, 97%**

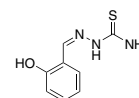
C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>O  
FW: 178.23  
[5585-33-1]



663204-5G	5 g
663204-25G	25 g

**Salicylaldehyde thiosemicarbazone, 95%**

C<sub>8</sub>H<sub>9</sub>N<sub>3</sub>OS  
FW: 195.24  
[5351-90-6]

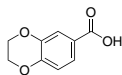


658774-1G	1 g
658774-10G	10 g

## Carboxylic Acids

**1,4-Benzodioxane-6-carboxylic acid, 97%**

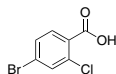
$C_8H_8O_4$   
FW: 180.16  
[4442-54-0]



658375-5G	5 g
658375-25G	25 g

**4-Bromo-2-chlorobenzoic acid, 97%**

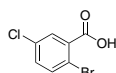
$C_7H_4BrClO_2$   
FW: 235.46  
[59748-90-2]



664014-5G	5 g
664014-25G	25 g

**2-Bromo-5-chlorobenzoic acid, 96%**

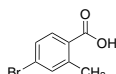
$C_7H_4BrClO_2$   
FW: 235.46  
[21739-93-5]



664022-5G	5 g
664022-25G	25 g

**4-Bromo-2-methylbenzoic acid, 97%**

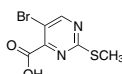
$C_8H_7BrO_2$   
FW: 215.04  
[68837-59-2]



665126-5G	5 g
665126-25G	25 g

**5-Bromo-2-(methylthio)pyrimidine-4-carboxylic acid, 97%**

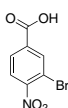
$C_6H_5BrN_2O_2S$   
FW: 249.09  
[50593-92-5]



656739-1G	1 g
-----------	-----

**3-Bromo-4-nitrobenzoic acid, 97%**

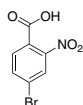
$C_7H_4BrNO_4$   
FW: 246.01  
[101420-81-9]



659304-1G	1 g
659304-5G	5 g

**4-Bromo-2-nitrobenzoic acid, 97%**

$C_7H_4BrNO_4$   
FW: 246.01  
[99277-71-1]



664855-1G	1 g
664855-5G	5 g

**2-Chloro-3-methoxybenzoic acid, 97%**

$C_8H_7ClO_3$   
FW: 186.59  
[33234-36-5]



657905-1G	1 g
657905-10G	10 g

**4-Chloronicotinic acid, 96%**

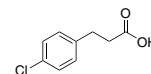
$C_6H_4ClNO_2$   
FW: 157.55  
[10177-29-4]



660396-1G	1 g
-----------	-----

**3-(4-Chlorophenyl)propionic acid, 97%**

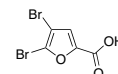
$C_9H_9ClO_2$   
FW: 184.62  
[2019-34-3]



656151-1G	1 g
656151-5G	5 g

**4,5-Dibromo-2-furoic acid, 97%**

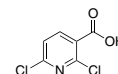
$C_5H_2Br_2O_3$   
FW: 269.88  
[2434-03-9]



656291-5G	5 g
656291-25G	25 g

**2,6-Dichloronicotinic acid, 97%**

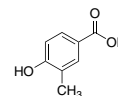
$C_6H_3Cl_2NO_2$   
FW: 192.00  
[38496-18-3]



658219-1G	1 g
658219-5G	5 g
658219-25G	25 g

**4-Hydroxy-3-methylbenzoic acid, 97%**

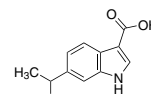
$C_8H_8O_3$   
FW: 152.15  
[499-76-3]



659282-1G	1 g
659282-10G	10 g

**6-Isopropylindole-3-carboxaldehyde, 97%**

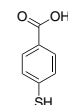
$C_{12}H_{12}NO$   
FW: 187.24  
[870703-65-4]



659800-1G	1 g
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**4-Mercaptobenzoic acid**

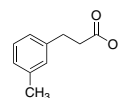
$C_7H_6O_2S$   
FW: 154.19  
[1074-36-8]



662534-5G	5 g
662534-25G	25 g

**3-(3-Methylphenyl)propionic acid, 97%**

$C_{10}H_{12}O_2$   
FW: 164.2  
[3751-48-2]



656178-1G	1 g
656178-5G	5 g

**4-Methylpyridine-3-carboxylic acid, 97%**

C<sub>7</sub>H<sub>7</sub>NO<sub>2</sub>  
FW: 137.14  
[3222-50-2]



656410-1G 1 g

**1,2,4-Triazole-3-carboxylic acid, 97%**

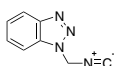
C<sub>3</sub>H<sub>3</sub>N<sub>3</sub>O<sub>2</sub>  
FW: 113.07  
[4928-87-4]



658472-1G 1 g  
658472-10G 10 g

**Isocyanides****1H-Benzotriazol-1-ylmethyl isocyanide, 94%**

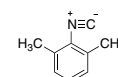
C<sub>8</sub>H<sub>6</sub>N<sub>4</sub>  
FW: 158.16  
[87022-42-2]



367990-1G 1 g  
367990-5G 5 g

**2,6-Dimethylphenyl isocyanide, 96%**

C<sub>9</sub>H<sub>9</sub>N  
FW: 131.17  
[2769-71-3]



594881-1G 1 g  
594881-5G 5 g

**Benzyl isocyanide, 98%**

C<sub>8</sub>H<sub>7</sub>N  
FW: 117.15  
[10340-91-7]



133299-250MG 250 mg  
133299-1G 1 g  
133299-5G 5 g

**Isopropyl isocyanide, 97%**

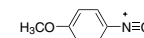
C<sub>4</sub>H<sub>7</sub>N  
FW: 69.11  
[598-45-8]



553344-500MG 500 mg

**4-Methoxyphenyl isocyanide, 97%**

C<sub>8</sub>H<sub>7</sub>NO  
FW: 133.15  
[10349-38-9]



594458-1G 1 g

**tert-Butyl isocyanide, 98%**

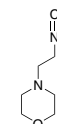
C<sub>5</sub>H<sub>9</sub>N  
FW: 83.13  
[7188-38-7]



260630-250MG 250 mg  
260630-1G 1 g  
260630-5G 5 g

**2-Morpholinoethyl isocyanide, 98%**

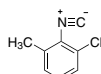
C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>O  
FW: 140.18  
[78375-48-1]



69893-10ML 10 ml  
69893-50ML 50 ml

**2-Chloro-6-methylphenyl isocyanide, 97%**

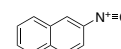
C<sub>8</sub>H<sub>6</sub>ClN  
FW: 151.59  
[118923-96-9]



594342-1G 1 g

**2-Naphthyl isocyanide, 97%**

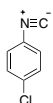
C<sub>11</sub>H<sub>7</sub>N  
FW: 153.18  
[10124-78-4]



594784-1G 1 g

**4-Chlorophenyl isocyanide, 97%**

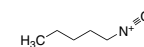
C<sub>7</sub>H<sub>4</sub>ClN  
FW: 137.57  
[1885-81-0]



594229-1G 1 g

**1-Pentyl isocyanide, 97%**

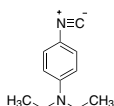
C<sub>6</sub>H<sub>11</sub>N  
FW: 97.16  
[18971-59-0]



536202-1G 1 g  
536202-5G 5 g

**4-Diethylaminophenyl isocyanide, 97%**

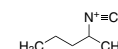
C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>  
FW: 174.24  
[42549-09-7]



594555-1G 1 g

**2-Pentyl isocyanide, 97%**

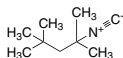
C<sub>6</sub>H<sub>11</sub>N  
FW: 97.16  
[355377-26-3]



536199-1G 1 g  
536199-5G 5 g

**1,1,3,3-Tetramethylbutyl isocyanide**

C<sub>9</sub>H<sub>17</sub>N  
FW: 139.24  
[14542-93-9]



226491-1G	1 g
226491-5G	5 g

**2-Tolylisocyanide, 95%**

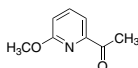
C<sub>8</sub>H<sub>7</sub>N  
FW: 117.15  
[10468-64-1]



593907-1G	1 g
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**Ketones****2-Acetyl-6-methoxypyridine, 97%**

C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub>  
FW: 151.16  
[21190-93-2]



662542-1G	1 g
662542-5G	5 g

**6-Chloro-1-indanone, 96%**

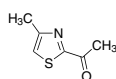
C<sub>9</sub>H<sub>7</sub>ClO  
FW: 166.6  
[14548-38-0]



656828-1G	1 g
656828-5G	5 g

**2-Acetyl-4-methylthiazole, 97%**

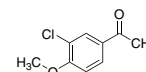
C<sub>6</sub>H<sub>7</sub>NOS  
FW: 141.19  
[7533-07-5]



656313-1G	1 g
656313-5G	5 g

**3'-Chloro-4'-methoxyacetophenone, 99%**

C<sub>9</sub>H<sub>9</sub>ClO<sub>2</sub>  
FW: 184.62  
[37612-52-5]



648809-1G	1 g
648809-5G	5 g

**3-Bromo-2-butanone, 97%**

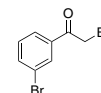
C<sub>4</sub>H<sub>7</sub>BrO  
FW: 151.00  
[814-75-5]



662747-1G	1 g
662747-5G	5 g

**2,3'-Dibromoacetophenone, 97%**

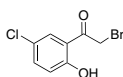
C<sub>8</sub>H<sub>6</sub>Br<sub>2</sub>O  
FW: 277.94  
[18523-22-3]



654787-1G	1 g
654787-5G	5 g

**2-Bromo-5'-chloro-2'-hydroxyacetophenone, 97%**

C<sub>8</sub>H<sub>6</sub>BrClO<sub>2</sub>  
FW: 249.49  
[52727-99-8]



663689-1G	1 g
663689-5G	5 g

**4,4-Dimethylcyclohexanone, 97%**

C<sub>8</sub>H<sub>14</sub>O  
FW: 126.2  
[4255-62-3]



663654-250MG	250 mg
663654-1G	1 g

**4-Bromo-1-indanone, 97%**

C<sub>9</sub>H<sub>7</sub>BrO  
FW: 211.06  
[15115-60-3]



644366-1G	1 g
644366-5G	5 g

**6-Fluoro-1-indanone, 96%**

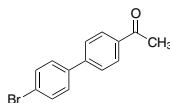
C<sub>9</sub>H<sub>7</sub>FO  
FW: 150.15  
[1481-32-9]



663123-1G	1 g
663123-5G	5 g

**4'-(4-Bromophenyl)acetophenone, 97%**

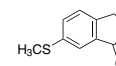
C<sub>14</sub>H<sub>11</sub>BrO  
FW: 275.14  
[5731-01-1]



640468-25G	25 g
640468-100G	100 g

**6-(Methylthio)-1-indanone, 96%**

C<sub>10</sub>H<sub>10</sub>OS  
FW: 178.25  
[138485-82-2]



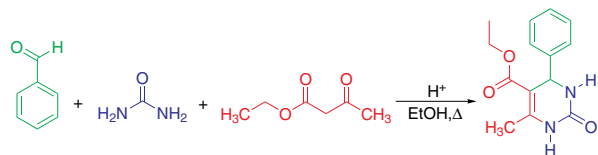
656143-1G	1 g
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## Biginelli Reaction

The Biginelli Reaction (**Scheme 3**) is an acid catalyzed, three-component reaction between an aldehyde,  $\beta$ -ketoester, and urea that produces tetrahydropyrimidones, which have potential pharmaceutical applications.

This reaction was first reported in 1893 and has increased interest because of the final products close structural relationship to the clinically important dihydropyrimidines.<sup>6</sup> These compounds are known to show biological activities such as antiviral, antitumor, antibacterial, anti-inflammatory, and more recently, antihypertensive agents.<sup>7</sup>

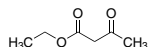
The mechanism for this reaction is believed to first be the condensation between the aldehyde and the urea. This produces an iminium intermediate that is the electrophile for the nucleophilic addition of the ketoester enol. The ketone carbonyl that is formed then goes under a condensation reaction with the  $\text{NH}_2$  of the urea. This gives the cyclized final product.



**Scheme 3**

### Ethyl acetoacetate, 99%

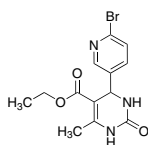
$\text{C}_6\text{H}_{10}\text{O}_3$   
FW: 130.14  
[141-97-9]



537349-1KG	1 kg
537349-3KG	3 kg

### 4-(6-Bromopyridin-3-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester, 98%

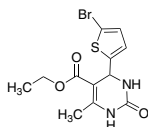
$\text{C}_{13}\text{H}_{14}\text{BrN}_3\text{O}_3$   
FW: 340.17



668087-1G	1 g
668087-5G	5 g

### 4-(5-Bromothiophen-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester, 98%

$\text{C}_{12}\text{H}_{13}\text{BrN}_2\text{O}_3\text{S}$   
FW: 345.21



668133-1G	1 g
668133-5G	5 g

### Urea, 98%

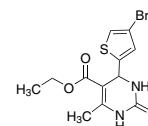
$\text{CH}_4\text{N}_2\text{O}$   
FW: 60.06  
[57-13-6]



208884-1KG	1 kg
208884-5KG	5 kg
208884-10KG	10 kg

### 4-(4-Bromothiophen-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester, 98%

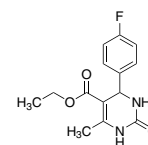
$\text{C}_{12}\text{H}_{13}\text{BrN}_2\text{O}_3\text{S}$   
FW: 345.21



668095-1G	1 g
-----------	-----

### Ethyl 4-(4-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-5-pyrimidinecarboxylate, 97%

$\text{C}_{14}\text{H}_{15}\text{FN}_2\text{O}_3$   
FW: 278.28  
[5937-24-6]



631183-5G	5 g
-----------	-----

## References

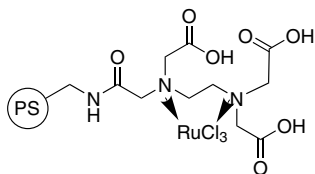
- (1) Xu, L. et al. *J. Org. Chem.* **2004**, 69, 8482–8484.
- (2) Musonda, C. et al. *Bioorg. Med. Chem. Lett.* **2004**, 14, 3901–3905.
- (3) Umkehrer et al. *Tetrahedron Lett.* **2006**, 47, 2391–2393.
- (4) Xia, Q.; Ganem, B. *Org. Lett.* **2002**, 4, 1631–1634.
- (5) Nguouansavanh, T. et al. *Angew. Chem. Int. Ed.* **2006**, 45, 3495–3497.
- (6) Kappe, C.O. *J. Org. Chem.* **1997**, 62, 7201–7204.
- (7) Rafiee, E.; Jafari, Hadi. *Bioorg. Med. Chem. Lett.* **2006**, 16, 2463–2466.

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# The Strecker Reaction Catalyzed by Polymer-Supported Ruthenium Complex

The one-pot synthesis of  $\alpha$ -amino nitriles by reaction of an aldehyde, ammonia, and hydrogen cyanide is commonly known as the Strecker reaction.<sup>1</sup> Recent modifications to the traditional Strecker reaction have seen the replacement of the cyanide source from toxic hydrogen cyanide to the comparatively mild trimethylsilyl cyanide.<sup>2,3</sup> Ruthenium has also been demonstrated to catalyze the Strecker reaction.<sup>4</sup>

Sigma-Aldrich now offers a polymer-supported ruthenium complex to be used as a mild catalyst for the Strecker reaction.

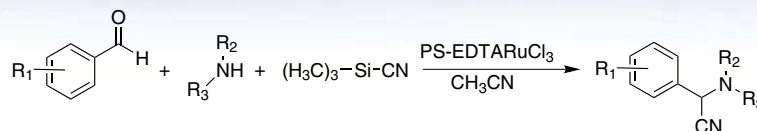


## Ethylenediaminetriacetic acid-ruthenium(III) chloride complex, polymer-bound

668079-1G	1 g
668079-5G	5 g

(1) Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27. (2) Yadav, J. S. et al. *Tetrahedron* **2004**, *60*, 1767. (3) Mai, K.; Patil, G. *Tetrahedron Lett.* **1984**, *25*, 4583. (4) De, S. K. *Synth. Commun.* **2005**, *35*, 653.

## Scheme 1



## Typical Experimental Procedure

Ethylenediaminetriacetic acid-ruthenium(III) chloride complex, polymer-bound (15 mg, 0.005 mmol) was charged into a reaction vessel followed by the addition of acetonitrile (2.0 mL), the aldehyde (1.0 mmol), the amine (1.15 mmol), and trimethylsilyl cyanide (1.5 mmol). The resulting mixture was stirred at room temperature overnight, filtered, and the filtrate collected. The resin was washed with several portions of acetonitrile, and the filtrates combined and evaporated to dryness. The residue was purified by flash column chromatography (20 g of silica gel; 1.5 × 20 cm column; ethyl acetate:hexane 1:9 as eluent) to yield the desired product. The structures of the isolated products were confirmed by <sup>1</sup>H NMR and mass spectrometry.

## Isolated Percent Yields of Substituted $\alpha$ -Amino Nitriles

	<i>N</i> -Boc-amino-piperidine	Morpholine	Phen-ethylamine
4-Bromobenzaldehyde	83	95	95
4-Cyanobenzaldehyde	70	62	53
3,5-Dimethoxybenzaldehyde	86	92	51

For more information, please visit us at [sigma-aldrich.com](http://sigma-aldrich.com).

# MacMillan Imidazolidinone OrganoCatalysts™

## Metal-Free Asymmetric Catalysis

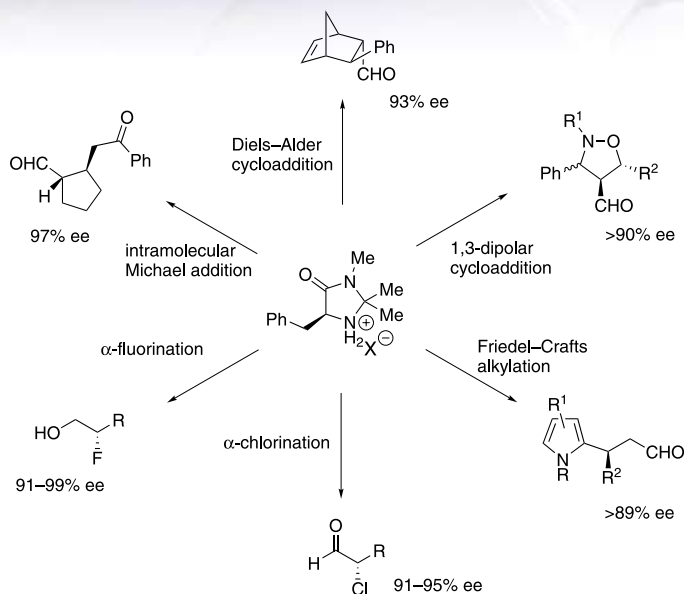
### Product Highlights

- Superior enantiocontrol in numerous transformations
- High activities at low catalyst loadings
- Extraordinary functional group tolerance

MacMillan and co-workers have created chiral imidazolidinone organocatalysts that function as the linchpin in a variety of directed enantioselective organic reactions including Diels–Alder and 1,3-dipolar cycloadditions, conjugate additions such as  $\alpha$ -fluorinations,  $\alpha$ -chlorinations and Friedel–Crafts alkylations, epoxidations, transfer hydrogenations, and organo-cascade reactions. Sigma-Aldrich, in collaboration with Materia, Inc., is pleased to offer ten imidazolidinone organocatalysts that mediate rapid and enantiocontrolled C–C and C–X (X = H, O, halogen) bond formation.

### References

(1) For a review on organocatalysis, see Lelais, G.; MacMillan, D. W. C. *Aldrichimica Acta* **2006**, 39, 79. (2) Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, 122, 4243. (3) Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, 124, 2458. (4) Huang, Y.; Walji, A. M.; Larsen, C. H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, 127, 15051. (5) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, 123, 4370.



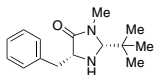
#### (2*R*,5*R*)-(+)-2-*tert*-Butyl-3-methyl-5-benzyl-4-imidazolidinone, 97%

NEW

[390766-89-9]

C<sub>15</sub>H<sub>22</sub>N<sub>2</sub>O

FW: 246.35



663093-500MG

500 mg

663093-1G

1 g

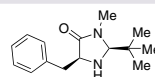
#### (2*S*,5*S*)-(–)-2-*tert*-Butyl-3-methyl-5-benzyl-4-imidazolidinone, 97%

NEW

[346440-54-8]

C<sub>15</sub>H<sub>22</sub>N<sub>2</sub>O

FW: 246.35



663107-500MG

500 mg

663107-1G

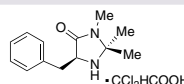
1 g

#### (5*S*)-(–)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone dichloroacetic acid, 97%

NEW

C<sub>15</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>

FW: 347.24



663085-500MG

500 mg

663085-2G

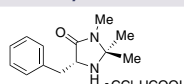
2 g

#### (5*R*)-(+)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone dichloroacetic acid, 97%

NEW

C<sub>15</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub>

FW: 347.24



663077-500MG

500 mg

663077-2G

2 g

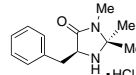
#### (5*S*)-2,2,3-Trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride, 97%

NEW

[278173-23-2]

C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>O·HCl

FW: 254.76



569763-500MG

500 mg

569763-2G

2 g

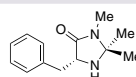
#### (5*R*)-(+)-2,2,3-Trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride, 97%

NEW

[323196-43-6]

C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>O·HCl

FW: 254.76



663069-500MG

500 mg

663069-2G

2 g

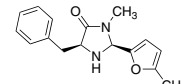
#### (2*S*,5*S*)-5-Benzyl-3-methyl-2-(5-methyl-2-furyl)-4-imidazolidinone

NEW

[415678-40-9]

C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>

FW: 270.33



668540-250MG

250 mg

668540-1g

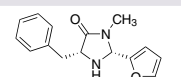
1 g

#### (2*R*,5*R*)-5-Benzyl-3-methyl-2-(5-methyl-2-furyl)-4-imidazolidinone

NEW

C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>

FW: 270.33



668842-250MG

250 mg

668842-1g

1 g

#### MacMillan Organocatalyst Kit I

NEW

Kit contains: 569763-500mg, 661902-500mg, 663085-500mg, 663107-500mg, 668540-250mg

674575-1KT

1 KT

For more information,  
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