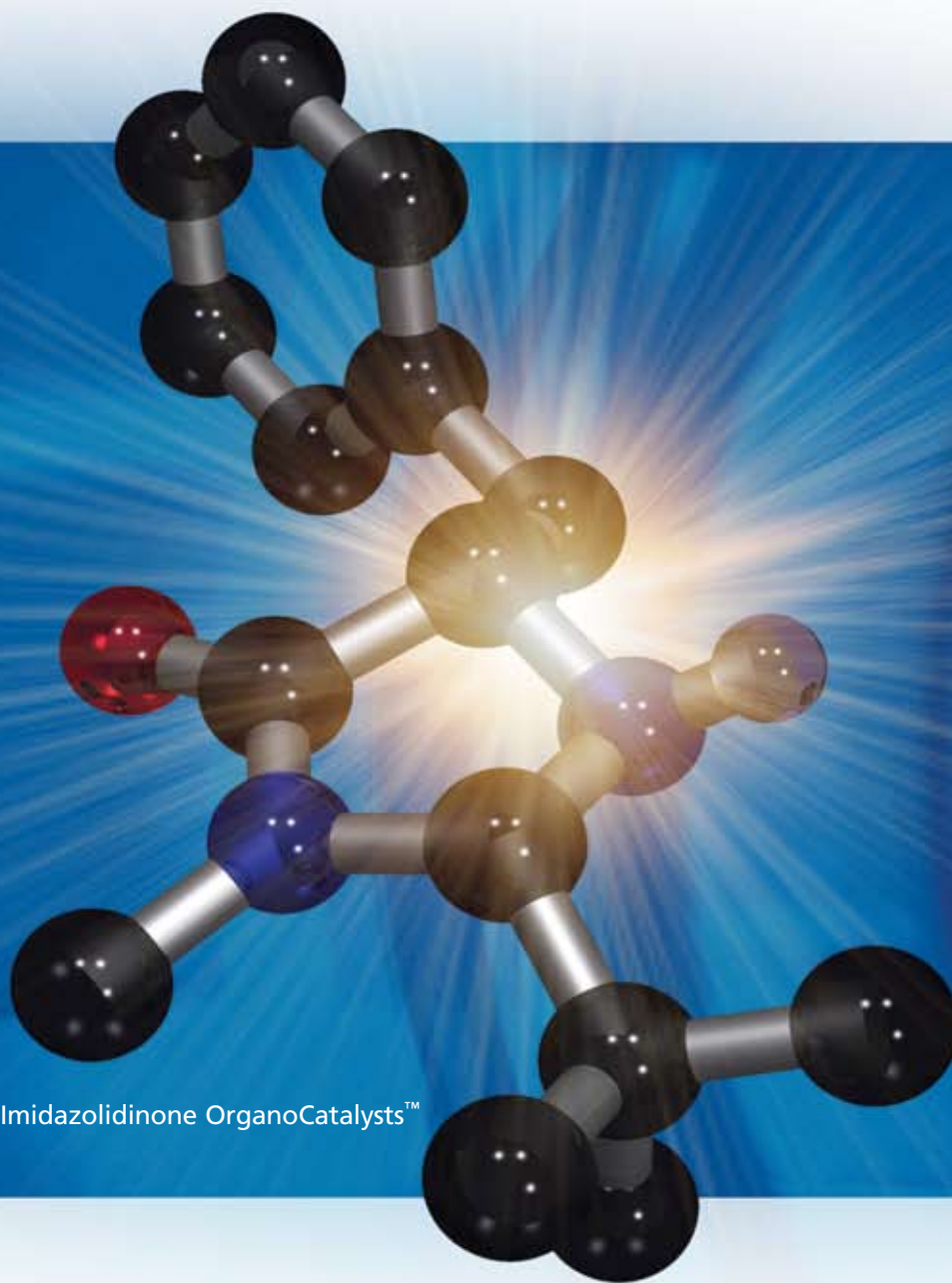


Synthetic Methods

Asymmetric Organocatalysis



MacMillan Imidazolidinone OrganoCatalysts™

Proline Analogs

MacMillan Imidazolidinone
OrganoCatalysts™

Cinchona Alkaloids

TADDOLs

Schaus MBH Catalyst

Rovis Triazolium Catalyst

Introduction

The field of organocatalysis has recently gained much attention in the chemical research community.¹ For most chemists, the term catalysis was commonly equated to transition metal-mediated reactions or to enzyme-aided biocatalysis. However, small organic molecules can also achieve remarkably selective and efficient transformations—as intense research efforts in this emerging area are proving. The commercial potential of organocatalysis in the manner described is immense. The applied catalysts are of low molecular weight, easy to synthesize, chemically robust, and affordable. Additionally, the organocatalytic reactions are often carried out under “open-flask” conditions.

This edition of *ChemFiles* describes applications of our existing products in the field of organocatalysis as well as exciting new additions to our organocatalysis portfolio. At Sigma-Aldrich, we are committed to being your preferred supplier of organocatalysts. Please visit sigma-aldrich.com/organocatalysis for a comprehensive listing of products. If you cannot find an organocatalyst, we welcome your input and will use it to broaden our product range even further. “Please Bother Us” at dweibel@europe.sial.com with your suggestions!

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About Our Cover

The cover illustration depicts one of the chiral MacMillan Imidazolidinone OrganoCatalysts™. These compounds were successfully employed in numerous organocatalytic transformations such as 1,3-dipolar cycloadditions, Friedel–Crafts alkylations, α -chlorinations, and intramolecular Michael reactions. Particularly noteworthy, the first direct organocatalytic enantioselective α -fluorination of aldehydes has been accomplished to afford a broad spectrum of highly enantioenriched α -fluoro aldehydes, which are valuable synthons for medicinal agent synthesis.

ChemFiles

Vol. 6 No. 4

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Proline Analogs

Coined by Jacobsen² as the “simplest enzyme,” L-proline is capable of effecting a variety of catalytic asymmetric transformations. The first examples were reported in the mid-70s, when L-proline was applied to Robinson annulation reactions.³ However, the big potential of proline as an organocatalyst was discovered in the beginning of the 21st century. One explanation for such a delay might be that the scope of highly selective transformations was considered to be rather narrow, and the development of metal catalysts seemed more promising.

The bifunctional structure of the sole cyclic proteinogenic amino acid is a crucial factor. L-proline contains both a nucleophilic secondary amino group and a carboxylic acid moiety functioning as a Brønsted acid. This facilitates a highly pre-organized transition state during the reaction pathway, which results in exceptionally high enantioselectivities (**Scheme 1**).⁴

Moreover, as a small organic molecule, proline is available in both enantiomeric forms, which is a definite advantage over enzymatic methods. Numerous proline-catalyzed reactions have been developed (**Scheme 2**).⁵

Stimulated by such a vast number of successful examples, many research groups have developed synthetic proline analogs with optimized properties (see: *ChemFiles* Vol. 5 No. 12, **Tools for Drug Discovery**). Some examples will be presented here in more detail.

The catalytic asymmetric α -alkylation of aldehydes was recently described by List.⁶ To date, this transformation was usually accomplished with the help of covalently attached auxiliaries. In comparison to L-proline, α -methyl-L-proline (**17249**) gives higher enantioselectivities and improved reaction rates (**Scheme 3**).

Organocatalytic cyclopropanation reactions were typically performed using catalyst-bound ylides.⁷ However, MacMillan demonstrated that activation of olefin substrates using catalytic (S)-(-)-indoline-2-carboxylic acid (**346802**) is a viable route for the formation of highly enantioenriched cyclopropanes (**Scheme 4**).⁸

Aggarwal utilized protonated (S)-(-)-2-(diphenylmethyl)pyrrolidine (**552534**) as an organocatalyst in a novel process for the enantioselective epoxidation of alkenes.⁹ Although the reaction proceeds under phase-transfer conditions (PTC), it was found that secondary amines catalyzed the reaction at remarkably higher rates, implying that **552534** does not act only as a PTC. However, best results were obtained with the chiral pyrrolidine bearing 1-naphthyl substituents (**Scheme 5**).

L-Proline, ReagentPlus™, $\geq 99\%$

C₅H₉NO₂
MW: 115.13
[α] -84.7° ± 1°, c = 4 in water
[147-85-3]



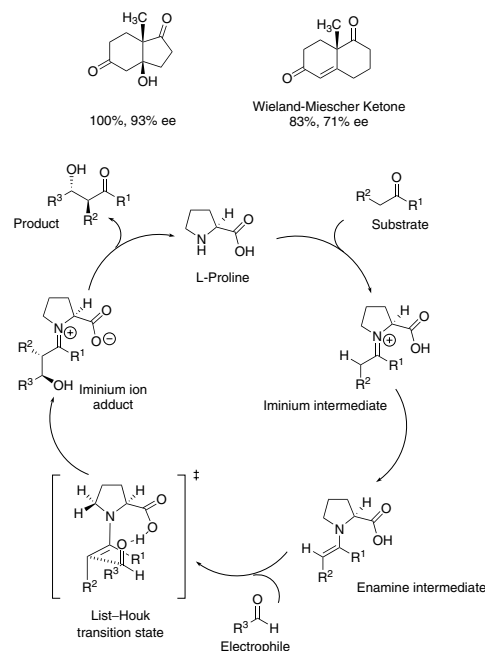
P0380-10MG	10 mg
P0380-100G	100 g
P0380-1KG	1 kg
P0380-5KG	5 kg

L-Proline, BioChemika, $\geq 99.0\%$ NT

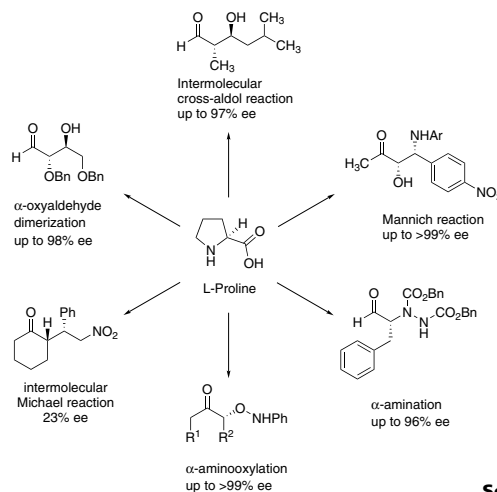
C₅H₉NO₂
MW: 115.13
[α]_D -84.5° ± 1°, c = 5% in water
[147-85-3]



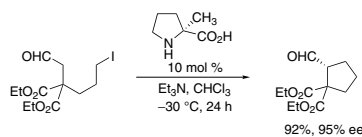
81710-10G	10 g
81710-50G	50 g
81710-250G	250 g



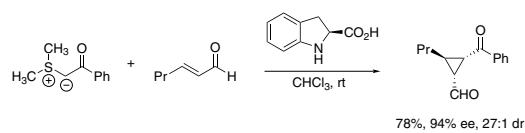
Scheme 1



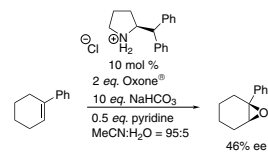
Scheme 2



Scheme 3



Scheme 4



Scheme 5

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D-Proline, $\geq 99\%$ C₅H₉NO₂

MW: 115.13

[α]_D²⁰ +85.0°, c = 4 in water

[344-25-2]

858919-500MG	500 mg
858919-5G	5 g

**D-Proline, puriss., $\geq 99.0\%$ NT**C₅H₉NO₂

MW: 115.13

[α]_D²⁰ +85° ± 2°, c = 5% in water

[344-25-2]

81705-1G	1 g
81705-5G	5 g
81705-25G	25 g

 **α -Methyl-L-proline, purum, $\geq 98.0\%$ TLC**C₆H₁₁NO₂

MW: 129.16

[α]_D²⁰ -75° ± 2°, c = 1% in methanol

[42856-71-3]

17249-250MG	250 mg
17249-1G	1 g

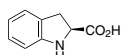
**(S)-(-)-Indoline 2-carboxylic acid, 99%**C₉H₉NO₂

MW: 163.17

[α]_D²⁰ -114° c = 1 in 1N HCl

[79815-20-6]

346802-1G	1 g
346802-5G	5 g

**(R)-(+)-Indoline 2-carboxylic acid**

NEW

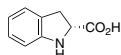
C₉H₉NO₂

MW: 163.17

[α]_D²⁰ +114° c = 1 in 1N HCl

[98167-06-7]

51266-500MG	500 mg
-------------	--------

**3,4-Dehydro-L-proline, BioChemika, $\geq 99.0\%$ TLC**C₅H₇NO₂

MW: 113.11

[α]_D²⁰ -400° ± 10° c = 0.2% in water

[4043-88-3]

30890-10MG	10 mg
30890-50MG	50 mg

**L-4-Thiazolidinecarboxylic acid, purum, $\geq 99.0\%$ T**C₄H₇NO₂S

MW: 133.17

[α]_D²⁰ -101° ± 2°, c = 1% in 1 M HCl

[34592-47-7]

88400-10G	10 g
88400-50G	50 g

**L-Azetidine-2-carboxylic acid, purum, $\geq 98.0\%$ NT**C₄H₇NO₂

MW: 101.10

[α]_D²⁰ -123° ± 2°, c = 4% in water

[2733-34-8]

11542-500MG	500 mg
11542-2.5G	2.5 g

**L-Pipecolic acid, puriss., $\geq 99.0\%$ NT**C₆H₁₁NO₂

MW: 129.16

[α]_D²⁰ -26° ± 1°, c = 4% in water

[3105-95-1]

80615-100MG	100 mg
80615-500MG	500 mg

**D-Pipecolic acid, purum, $\geq 99.0\%$ NT**C₆H₁₁NO₂

MW: 129.16

[α]_D²⁰ +27° ± 1°, c = 1% in water

[1723-00-8]

80617-100MG	100 mg
80617-500MG	500 mg

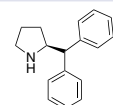
**(S)-(-)-2-(Diphenylmethyl)pyrrolidine, 97%**C₁₇H₁₉N

MW: 237.34

[α]_D²⁰ -3.0°, c = 1% in chloroform

[119237-64-8]

552534-500MG	500 mg
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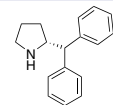
**(R)-(+)-2-(Diphenylmethyl)pyrrolidine, 97%**C₁₇H₁₉N

MW: 237.34

[α]_D²⁰ +3.0°, c = 1% in chloroform

[22348-31-8]

552542-1G	1 g
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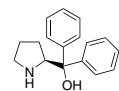
 **α,α -Diphenyl-L-prolinol, purum, $\geq 99.0\%$ HPLC sum of enantiomers**C₁₇H₁₉NO

MW: 253.34

[α]_D²⁰ -69° ± 2°, c = 3% in chloroform

[112068-01-6]

43182-1G	1 g
43182-5G	5 g

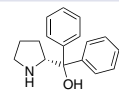
 **α,α -Diphenyl-D-prolinol, purum, $\geq 99.0\%$ HPLC sum of enantiomers**C₁₇H₁₉NO

MW: 253.34

[α]_D²⁰ +69° ± 3°, c = 3% in chloroform

[22348-32-9]

43179-100MG	100 mg
43179-500MG	500 mg

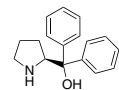
**(S)-(-)- α,α -Diphenyl-2-pyrrolidinemethanol, 99%**C₁₇H₁₉NO

MW: 253.34

[α]_D²⁰ -67°, c = 3 in chloroform

[112068-01-6]

368199-1G	1 g
368199-5G	5 g

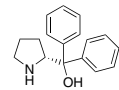
**(R)-(+)- α,α -Diphenyl-2-pyrrolidinemethanol, 98%**C₁₇H₁₉NO

MW: 253.34

[α]_D²⁰ +69°, c = 3% in chloroform

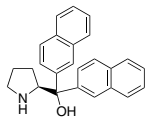
[22348-32-9]

382337-100MG	100 mg
382337-1G	1 g
382337-5G	5 g



(S)-(-)- α,α -Di(2-naphthyl)-2-pyrrolidinemethanol, 99%

C₂₅H₂₃NO
 MW: 353.46
 $[\alpha]_D^{20}$ -101°, c = 0.7 in methanol
 [127986-84-9]



445398-250MG	250 mg
445398-1G	1 g

(S)-(+)-1-(2-Pyrrolidinylmethyl)pyrrolidine, 96%

C₉H₁₈N₂
 MW: 154.25
 $[\alpha]_D^{20}$ +7.0°, c = 2.4 in ethanol
 [51207-66-0]



324450-250MG	250 mg
324450-1G	1 g

(S)-(+)-2-(Methoxymethyl)pyrrolidine, purum, $\geq 98.0\%$ GC sum of enantiomers

C₆H₁₃NO
 MW: 115.17
 $[\alpha]_D^{20}$ +2.4° ± 0.3°, c = 2% in benzene
 [63126-47-6]



65090-1ML	1 mL
65090-5ML	5 mL

(S)-(+)-2-(Methoxymethyl)pyrrolidine, 99%

C₆H₁₃NO
 MW: 115.17
 $[\alpha]_D^{20}$ +2.4°, c = 2 in benzene
 [63126-47-6]



277053-100MG	100 mg
277053-500MG	500 mg
277053-5G	5 g

(R)-(-)-2-(Methoxymethyl)pyrrolidine, purum, $\geq 98.0\%$ GC sum of enantiomers

C₆H₁₃NO
 MW: 115.17
 $[\alpha]_D^{20}$ -2.4° ± 0.3°, c = 2% in benzene
 [84025-81-0]



65089-1ML	1 mL
-----------	------

MacMillan Imidazolidinone Organocatalysts™

Developed by Professor David MacMillan at Caltech, imidazolidinone-based organocatalysts are designed to serve as general catalysts for a myriad of asymmetric transformations. The first highly enantioselective organocatalytic Diels–Alder reaction using a chiral organocatalyst (**569763**) was reported in his pioneering work in 2000 (**Scheme 6**).¹⁰ The activated iminium ion, formed through condensation of the imidazolidinone and an α,β -unsaturated aldehyde, reacted with various dienes to give [4+2] cycloadducts in excellent yields and enantioselectivities.

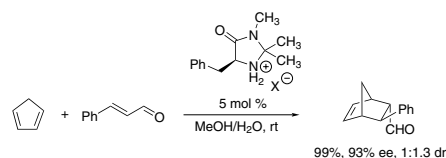
Other organocatalytic transformations such as 1,3-dipolar cycloadditions,¹¹ Friedel–Crafts alkylations,¹² α -chlorinations,¹³ α -fluorinations,¹⁴ and intramolecular Michael reactions¹⁵ using MacMillan's organocatalyst technology (**569763**) were reported, all proceeding with impressive levels of enantioselectivity (**Scheme 7**).

Having established iminium and enamine catalysis using organocatalyst **569763**, MacMillan found an optimized structure in organocatalyst **663107** for the Friedel–Crafts alkylation of indoles (**Scheme 8**),¹⁶ which are known to be privileged structures in drug discovery. See *ChemFiles* Vol. 4 No. 8, **Indoles** (US) or Vol. 4 Supplement II (Europe).

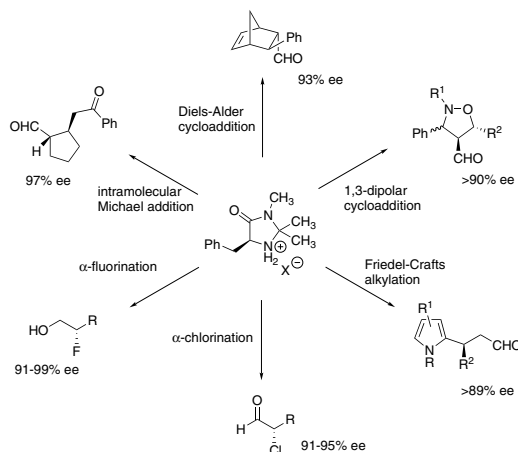
MacMillan later demonstrated the synthetic utility of this concept in the total synthesis of (-)-flustramine B, a biologically active alkaloid bearing a pyrroloindoline architecture. The fused ring system was cleanly assembled with the aid of imidazolidinone organocatalyst **663107** (**Scheme 9**).¹⁷

Imitating nature's stereoselective enzymatic transfer hydrogenation with NADH cofactor, MacMillan's variant used the combination of organocatalyst **661902** and Hantzsch ester **127220** to reduce simple α,β -unsaturated aldehydes in a highly enantioselective manner (**Table 1**).¹⁸

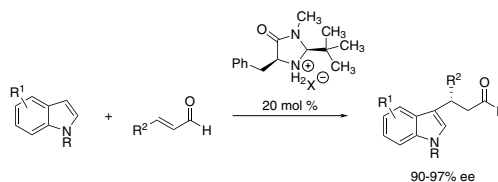
In sharp contrast to metal-mediated hydrogenations, the *E/Z* geometry of the enal substrates did not have a significant influence on the outcome of the absolute configuration of the newly created stereocenter. In an elegant organocascade reaction, MacMillan



Scheme 6



Scheme 7



Scheme 8

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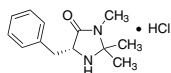
showed that both LUMO-lowering iminium- and HOMO-raising enamine catalysis could coexist without deleterious catalyst-catalyst interactions by substrate activation in an orthogonal mode, hence leading to highly enantioenriched products with increased structural complexity in just one step. Using both organocatalytic transfer hydrogenation (Hantzsch ester, **120227**) and α -halogenation methodologies (*N*-fluorobenzenesulfonimide, **392715**), the formal addition of HF to α,β -unsaturated aldehydes could be achieved with very high levels of enantio- and diastereoselectivity (**Scheme 10**). Various examples have been reported.¹⁹

(5R)-2,2,3-Trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride, 97% NEW

C₁₃H₁₈N₂O · HCl
MW: 254.76

[α]_D²⁰ +64°, c = 1 in water
[323196-43-6]

663069-500MG 500 mg
663069-2G 2 g

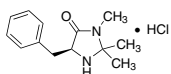


(5S)-2,2,3-Trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride, 97%

C₁₃H₁₈N₂O · HCl
MW: 254.76

[α]_D²⁰ -64°, c = 1 in water
[278173-23-2]

569763-2G 2 g

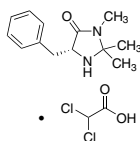


(5R)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone dichloroacetic acid, 97% NEW

C₁₅H₂₀Cl₂N₂O₃
MW: 347.24

[α]_D²⁰ +52°±4°, c = 1% in methanol

663077-500MG 500 mg
663077-2G 2 g

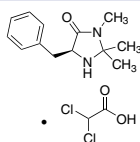


(5S)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone dichloroacetic acid, 97% NEW

C₁₅H₂₀Cl₂N₂O₃
MW: 347.24

[α]_D²⁰ -52°±4°, c = 1% in methanol

663085-500MG 500 mg
663085-2G 2 g

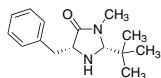


(2R,5R)-(+)-2-tert-Butyl-3-methyl-5-benzyl-4-imidazolidinone, 97% NEW

C₁₅H₂₂N₂O
MW: 246.35

[α]_D²⁰ +72°±4°, c = 1% in chloroform
[390766-89-9]

663093-500MG 500 mg
663093-1G 1 g

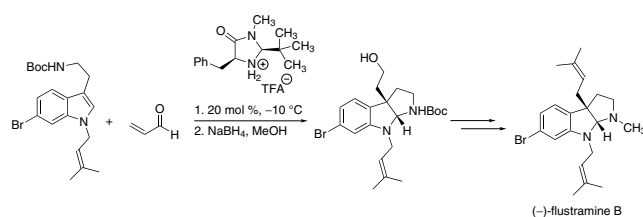
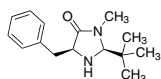


(2S,5S)-(-)-2-tert-Butyl-3-methyl-5-benzyl-4-imidazolidinone, 97% NEW

C₁₅H₂₂N₂O
MW: 246.35

[α]_D²⁰ -72°±4°, c = 1% in chloroform
[346440-54-8]

663107-500MG 500 mg
663107-1G 1 g



Scheme 9

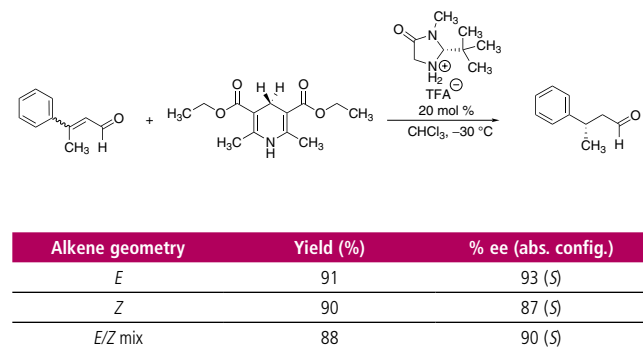
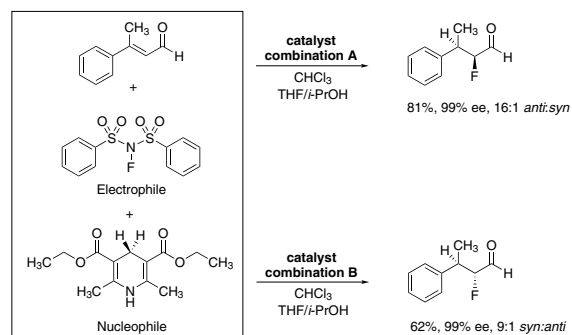
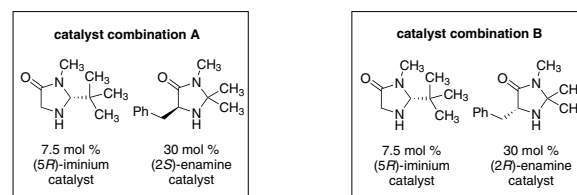


Table 1

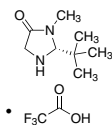


Scheme 10

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(R)-2-(tert-Butyl)-3-methyl-4-imidazolidinone trifluoroacetate

NEW

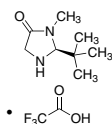
C₁₀H₁₇N₂O₃F₃
MW: 270.25

661910-500MG 500 mg

661910-2G 2 g

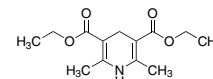
(S)-2-(tert-Butyl)-3-methyl-4-imidazolidinone trifluoroacetate

NEW

C₁₀H₁₇N₂O₃F₃
MW: 270.25

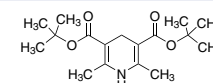
661902-500MG 500 mg

661902-2G 2 g

Diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate, 95%C₁₃H₁₉NO₄
MW: 253.29
[1149-23-1]

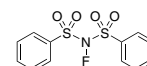
120227-1G

1 g

Di-tert-butyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, 97%C₁₇H₂₇NO₄
MW: 309.4
[55536-71-5]

659142-1G

1 g

N-Fluorobenzenesulfonimide, 97%C₁₂H₁₀FNO₄S₂
MW: 315.34
[113745-75-2]

392715-1G

1 g

392715-5G

5 g

Cinchona Alkaloids

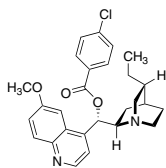
Desymmetrization

Abundant in nature, cinchona alkaloids are readily accessible chiral amine catalysts that exist in pseudoenantiomeric forms. Indeed, some of the very first examples of organocatalyzed reactions were mediated by *O*-acetylated quinine.^{3a} Deng has used modified cinchona alkaloids as ligands in Sharpless' asymmetric dihydroxylation catalyst system and in the desymmetrization of anhydrides (**Scheme 11**).

A high degree of asymmetric induction using cinchona catalysts can be achieved in desymmetrization of meso anhydrides to form the corresponding hemiesters (**Scheme 12**). Biscinchona alkaloids such as (DHQD)₂AQN (**456713**) were more efficient in this transformation.²⁰

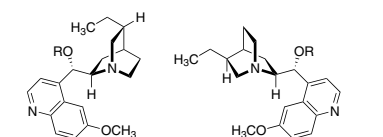
Other highly enantioselective reactions using cinchona alkaloids include cyanation of ketones,²⁰ 1,4-additions of thiols to enones,²⁰ dimerizations of methylketene,²¹ asymmetric Baylis–Hillman reactions,²² synthesis of β-lactams,²³ α-halogenations,²⁴ aza-Henry-reactions,²⁵ and intramolecular aldol reactions.²⁶

Nonracemic planar chiral (arene)Cr(CO)₃ complexes are increasingly important chiral building blocks in highly diastereoselective transformations and they can also serve as ligands in catalytic reactions.²⁷ Kündig has shown that chiral diamine **07317** performed well in the asymmetric benzylation/desymmetrization of a meso Cr complex.²⁸ Enantiomeric excess only marginally decreased (to 98%) when diamine **39867** was employed in the same reaction (**Scheme 13**).

Hydroquinidine 4-chlorobenzoate, 98%C₂₇H₂₉ClN₂O₃
MW: 464.98
[α]_D -73°, c = 1 in ethanol
[113162-02-0]

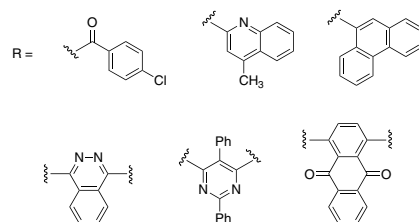
336483-1G 1 g

336483-5G 5 g

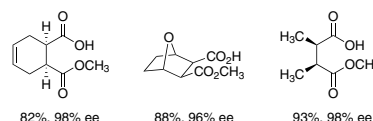
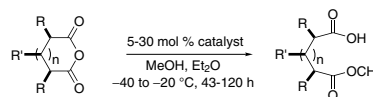


Dihydroquinidyl (DHQD)

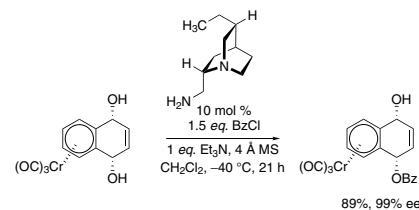
Dihydroquinyl (DHQ)



Scheme 11



Scheme 12



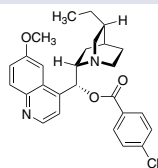
89%, 99% ee

Scheme 13

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O-(4-Chlorobenzoyl)hydroquinine, 98%

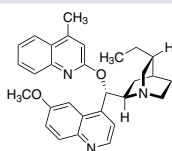
$C_{27}H_{29}ClN_2O_3$
 MW: 464.98
 $[\alpha]_D^{20} +150^\circ$, $c = 1$ in ethanol
 [113216-88-9]



336491-1G 1 g

Hydroquinidine 4-methyl-2-quinolyl ether, 97%

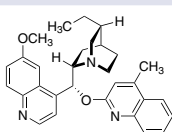
$C_{30}H_{33}N_3O_2$
 MW: 467.60
 $[\alpha]_D^{20} -168^\circ$, $c = 1$ in ethanol
 [135042-89-6]



381942-1G 1 g

Hydroquinine 4-methyl-2-quinolyl ether, 98%

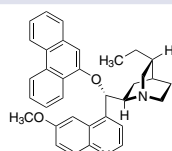
$C_{30}H_{33}N_3O_2$
 MW: 467.60
 $[\alpha]_D^{20} +260^\circ$, $c = 1$ in ethanol
 [135096-79-6]



381969-1G 1 g

Hydroquinidine 9-phenanthryl ether, 96%

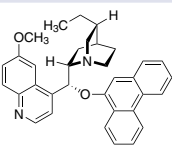
$C_{34}H_{34}N_2O_2$
 MW: 502.65
 $[\alpha]_D^{20} -348^\circ$, $c = 1$ in ethanol
 [135042-88-5]



381950-250MG 250 mg
 381950-1G 1 g

Hydroquinine 9-phenanthryl ether, 97%

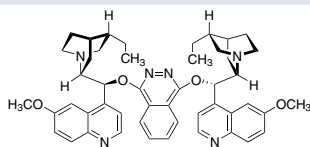
$C_{34}H_{34}N_2O_2$
 MW: 502.65
 $[\alpha]_D^{20} +420^\circ$, $c = 1$ in ethanol
 [135096-78-5]



381977-100MG 100 mg
 381977-500MG 500 mg

(DHQD)₂PHAL, ≥95%

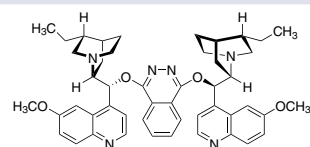
$C_{48}H_{54}N_6O_4$
 MW: 778.98
 $[\alpha]_D^{20} -262^\circ$, $c = 1.2$ in methanol
 [140853-10-7]



392731-1G 1 g

(DHQ)₂PHAL, ≥95%

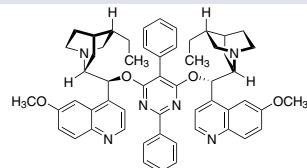
$C_{48}H_{54}N_6O_4$
 MW: 778.98
 $[\alpha]_D^{20} +336^\circ$, $c = 1.2$ in methanol
 [140924-50-1]



392723-500MG 500 mg

(DHQD)₂Pyr, 97%

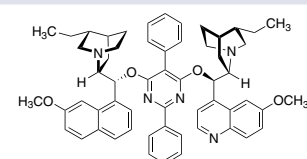
$C_{56}H_{60}N_6O_4$
 MW: 881.11
 $[\alpha]_D^{20} -390^\circ$, $c = 1.2$ in methanol
 [149725-81-5]



418951-250MG 250 mg
 418951-1G 1 g

(DHQ)₂Pyr, 97%

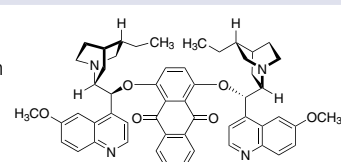
$C_{56}H_{60}N_6O_4$
 MW: 881.11
 $[\alpha]_D^{20} +455^\circ$, $c = 1.2$ in methanol
 [149820-65-5]



418978-250MG 250 mg
 418978-1G 1 g

(DHQD)₂AQN, 95%

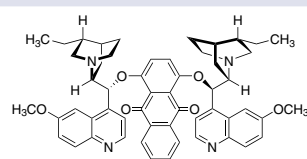
$C_{54}H_{56}N_4O_6$
 MW: 857.05
 $[\alpha]_D^{20} -468^\circ$, $c = 1$ in chloroform
 [176298-44-5]



456713-500MG 500 mg

(DHQ)₂AQN, 95%

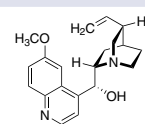
$C_{54}H_{56}N_4O_6$
 MW: 857.05
 $[\alpha]_D^{20} +495^\circ$, $c = 1$ in chloroform
 [176097-24-8]



456705-500MG 500 mg

Quinine, purum, for fluorescence, anhydrous, ≥98.0% NT dried material

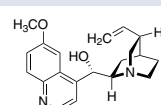
$C_{20}H_{24}N_2O_2$
 MW: 324.42
 $[\alpha]_D^{20} -126^\circ \pm 5^\circ$, $c = 1\%$ in chloroform
 [130-95-0]



22620-5G 5 g
 22620-25G 25 g
 22620-100G 100 g

Quinidine, purum, crystallized, ≥98.0% NT dried material

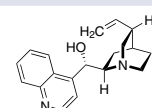
$C_{20}H_{24}N_2O_2$
 MW: 324.42
 $[\alpha]_D^{20} +265^\circ \pm 5^\circ$, $c = 0.8\%$ in ethanol dry matter
 [56-54-2]



22600-10G-F 10 g
 22600-50G-F 50 g

Cinchonine, purum, crystallized, ≥98.0% NT

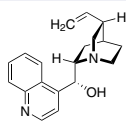
$C_{19}H_{22}N_2O$
 MW: 294.39
 $[\alpha]_D^{20} +225^\circ \pm 5^\circ$, $c = 0.5\%$ in ethanol
 [118-10-5]



27370-25G 25 g
 27370-100G 100 g

Cinchonidine, purum, $\geq 98.0\%$ NT dried material

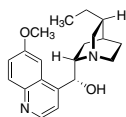
$C_{19}H_{22}N_2O$
 MW: 294.39
 $[\alpha]_D^{20} -108^\circ \pm 3^\circ$, $c = 5\%$ in ethanol
 [485-71-2]



27350-25G-F	25 g
27350-100G-F	100 g

Hydroquinine, 98%

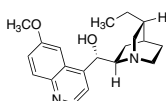
$C_{20}H_{26}N_2O_2$
 MW: 326.43
 $[\alpha]_D^{20} -148^\circ$, $c = 1$ in ethanol
 [522-66-7]



337714-1G	1 g
337714-5G	5 g

Hydroquinidine, 95%

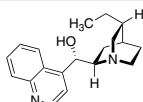
$C_{20}H_{26}N_2O_2$
 MW: 326.43
 $[\alpha]_D^{20} +226^\circ$, $c = 2$ in ethanol
 [1435-55-8]



359343-1G	1 g
359343-5G	5 g

Hydrocinchonine, purum, $\geq 97.0\%$ GC sum of enantiomers

$C_{19}H_{24}N_2O$
 MW: 296.41
 $[\alpha]_D^{20} +197^\circ \pm 4^\circ$, $c = 0.5\%$ in ethanol
 [485-65-4]



54060-500MG	500 mg
-------------	--------

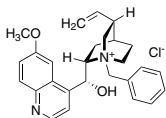
Asymmetric Phase-Transfer Reactions

Asymmetric phase-transfer catalysis (PTC) has been recognized as a "green" alternative to many homogeneous synthetic organic transformations, and has found widespread application. Synthetically modified cinchona alkaloids are typical chiral organocatalysts used in asymmetric PTC. Several generations of *O*-alkyl *N*-arylmethyl derivatives were developed, which finally led to highly enantioselective alkylation reactions of glycine imines to generate a range of α -amino acid derivatives (Table 2).²⁹

In an attempt to further improve catalyst enantioselectivities, Jew and Park linked two cinchona alkaloid moieties via spacer units.³⁰ With such a dimeric cinchona alkaloid (**06542**), enantioselectivity for the above mentioned glycine imine alkylation was optimized to 97–99% ee.

***N*-Benzylquininium chloride, 95%**

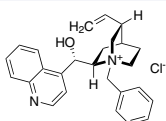
$C_{27}H_{31}ClN_2O_2$
 MW: 451.00
 $[\alpha]_D^{20} -235^\circ$, $c = 1.5$ in water
 [67174-25-8]



374482-1G	1 g
374482-5G	5 g

***N*-Benzylcinchoninium chloride, purum, $\geq 98.0\%$ AT**

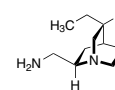
$C_{26}H_{29}ClN_2O$
 MW: 420.97
 $[\alpha]_D^{20} +169^\circ \pm 3^\circ$, $c = 0.4\%$ in water
 [69221-14-3]



13288-10G	10 g
13288-50G	50 g

(2*R*,4*S*,5*R*)-2-Aminomethyl-5-ethylquinuclidine

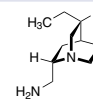
$C_{10}H_{20}N_2$
 MW: 168.28
 $[\alpha]_D^{20} +143^\circ$, $c = 1$ in ethanol
 [475160-67-3]



39867-100MG	100 mg
39867-500MG	500 mg

(2*S*,4*S*,5*R*)-2-Aminomethyl-5-ethylquinuclidine

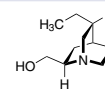
$C_{10}H_{20}N_2$
 MW: 168.28
 $[\alpha]_D^{20} -28^\circ$, $c = 1$ in ethanol
 [475160-59-9]



07317-100MG	100 mg
07317-500MG	500 mg

(2*R*,4*S*,5*R*)-2-Hydroxymethyl-5-ethylquinuclidine

$C_{10}H_{19}NO$
 MW: 169.26
 $[\alpha]_D^{20} +147^\circ$, $c = 1$ in chloroform
 [219794-87-7]



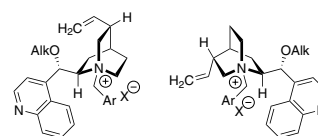
49463-100MG	100 mg
49463-500MG	500 mg

(2*S*,4*S*,5*R*)-2-Hydroxymethyl-5-ethylquinuclidine

$C_{10}H_{19}NO$
 MW: 169.26
 $[\alpha]_D^{20} -5.1^\circ$, $c = 1$ in chloroform
 [219794-79-3]

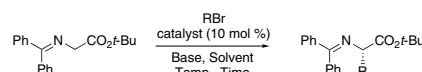


51957-100MG	100 mg
51957-500MG	500 mg



Cinchonidinium PTC

Cinchoninium PTC

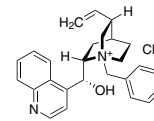


Cinchona PTC						
Cat. No.	<i>N</i> -Ar	<i>O</i> -Alk	X ⁻	Cat. Gen.	R-Br	% Y % ee
524433	Benzyl	H	Br	1st	PhCH ₂ -	85 60
359580	Benzyl	H	Cl	1st	4-Cl-C ₆ H ₄ -CH ₂ -	95 66
514276	Benzyl	Allyl	Br	2nd	4-Cl-C ₆ H ₄ -CH ₂ -	- 81
515701	9-Anthracenylmethyl	H	Cl	3rd	PhCH ₂ -	68 91
499617	9-Anthracenylmethyl	Allyl	Br	3rd	PhCH ₂ -	87 94
06542	2,7-Naphthalenediyl dimethyl	Allyl	Br	dimeric	4-NO ₂ -C ₆ H ₄ -CH ₂ -	91 99

Table 2

(8*S*,9*R*)-(-)-*N*-Benzylcinchonidinium chloride, 98%

$C_{26}H_{29}ClN_2O$
 MW: 420.97
 $[\alpha]_D^{20} -180^\circ$, $c = 1.3$ in water
 [69257-04-1]

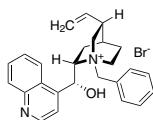


359580-2G	2 g
359580-10G	10 g

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N-Benzylcinchonidinium bromide, 97%

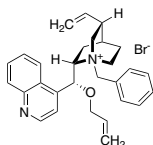
C₂₆H₂₉BrN₂O
 MW: 465.43
 [α]_D²⁰ -138°, c = 1 in chloroform
 [118089-84-2]



524433-5G 5 g

O-Allyl-N-benzylcinchonidinium bromide

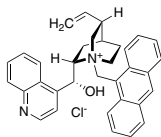
C₂₉H₃₃BrN₂O
 MW: 505.49
 [α]_D²⁰ -158°, c = 1 in chloroform
 [158195-40-5]



514276-1G 1 g

N-(9-Anthracenylmethyl)cinchonidinium chloride, 85%

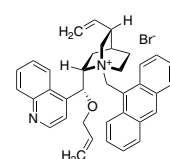
C₃₄H₃₃ClN₂O
 MW: 521.09
 [199588-80-2]



515701-5G 5 g
 515701-25G 25 g

O-Allyl-N-(9-Anthracenylmethyl)cinchonidinium bromide, 95%

C₃₇H₃₇BrN₂O
 MW: 605.61
 [α]_D²⁰ -340°, c = 0.45 in chloroform
 [200132-54-3]

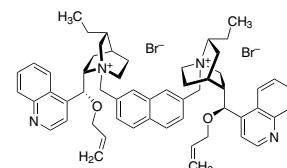


499617-1G 1 g
 499617-5G 5 g

O,O'-Diallyl-N,N'-(2,7-naphthalenediyl)dimethyl)bis(hydrocinchonidinium) dibromide

NEW

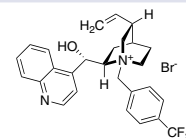
C₅₆H₆₆Br₂N₄O₂
 MW: 986.96
 [480427-57-4]



06542-100MG 100 mg

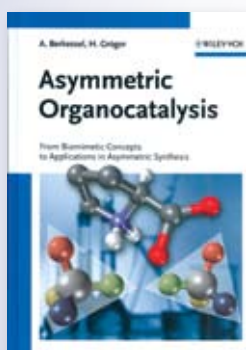
N-(4-Trifluoromethylbenzyl)cinchoninium bromide, purum, ≥98.0% AT

C₂₇H₂₈BrF₃N₂O
 MW: 533.42
 [α]_D²⁰ +140° ± 20° in ethanol
 [95088-20-3]



91851-1G 1 g
 91851-5G 5 g

Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis



A. Berkessel and H. Gröger, Wiley-VCH, 2005, 454pp. Hardcover.

Asymmetric catalysis represents one of the major challenges in modern organic chemistry. Besides the well-established asymmetric metal-complex-catalyzed syntheses and biocatalyses, the use of "pure" organic catalysts turned out to be an additional efficient tool for the synthesis of chiral building blocks. Experienced authors provide the first overview of the important use of such metal-free organic catalysts. With its comprehensive description of numerous reaction types, e.g., nucleophilic substitution and addition reactions, as well as cycloadditions and redox reactions, this book targets organic chemists working in industry and academia.

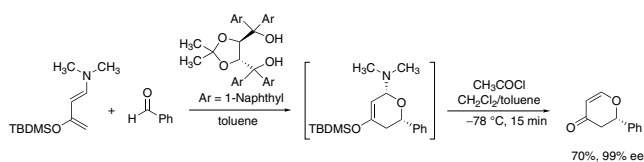
Z704113

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TADDOLs

Chiral Brønsted acid catalysts have recently become an important alternative to metal catalysts.³¹ Similar to several enzymatic processes, these reactions proceed through hydrogen-bonding activation.

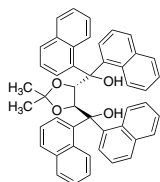
Apart from numerous examples using TADDOLs in metal-catalyzed asymmetric reactions,³² Rawal recently reported that TADDOLs could be used as Brønsted acid organocatalysts in highly stereoselective hetero-Diels–Alder reactions.³³ The reaction of an electron-rich diene with benzaldehyde using 10 mol % TADDOL **395242** provides the dihydropyrene as a single stereoisomer (Scheme 14).



Scheme 14

(4S,trans)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(1-naphthyl)-1,3-dioxolane-4,5-dimethanol, 99%

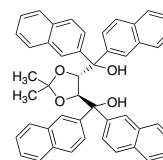
C₄₇H₃₈O₄
MW: 666.80
[α]_D²⁰ +280°, c = 1 in ethyl acetate
[171086-52-5]



395242-1G 1 g

(4S,5S)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, purum, $\geq 98.0\%$ HPLC sum of enantiomers

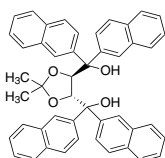
C₄₇H₃₈O₄
MW: 666.80
[α]_D²⁰ +116° ± 2°, c = 1% in ethyl acetate
[137365-16-3]



59488-5G-F 5 g

(4R,5R)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, 99%

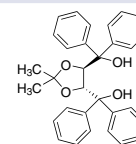
C₄₇H₃₈O₄
MW: 666.80
[α]_D²⁰ -116°, c = 1 in ethyl acetate
[137365-09-4]



393754-250MG 250 mg
393754-1G 1 g

(4R,5R)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol

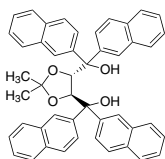
C₃₁H₃₀O₄
MW: 466.57
[α] -62.6°, c = 1 in chloroform
[93379-48-7]



265004-250MG 250 mg
265004-1G 1 g

(4S,5S)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, 98%

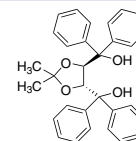
C₄₇H₃₈O₄
MW: 666.80
[α]_D²⁰ +116°, c = 1 in ethyl acetate
[137365-16-3]



393762-250MG 250 mg
393762-1G 1 g

(4R,5R)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol, purum, $\geq 97.0\%$ HPLC sum of enantiomers

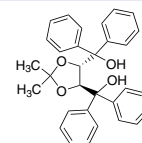
C₃₁H₃₀O₄
MW: 466.57
[α]_D²⁰ -67° ± 2°, c = 1% in chloroform
[93379-48-7]



59532-1G 1 g

(4S,5S)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol

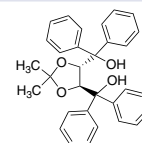
C₃₁H₃₀O₄
MW: 466.57
[α] +67°, c = 1 in chloroform
[93379-49-8]



264997-250MG 250 mg
264997-1G 1 g

(4S,5S)-2,2-Dimethyl- $\alpha,\alpha,\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol, purum, $\geq 97.0\%$ HPLC sum of enantiomers

C₃₁H₃₀O₄
MW: 466.57
[α]_D²⁰ +67° ± 2°, c = 1% in chloroform
[93379-49-8]



59534-1G-F 1 g

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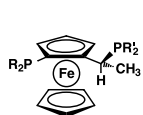


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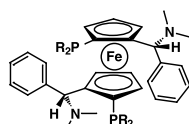
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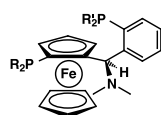
Josiphos



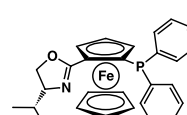
Walphos



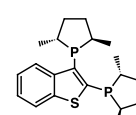
Mandyphos



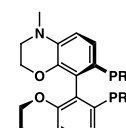
Taniaphos



Naud



Butiphane



Solphos

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1 Kit

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Schaus MBH Catalyst

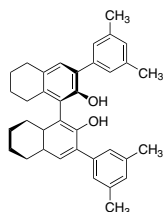
A highly enantioselective addition of cyclohexenone to different aldehydes (asymmetric Morita–Baylis–Hillman reaction) catalyzed by octahydro-BINOL-derived Brønsted acid **669172** was reported by Schaus (Scheme 15). Important for achieving high enantioselectivity were both the partial saturation and substitution at the 3,3'-positions of the BINOL derivative.³⁴

(R)-3,3'-Bis-(3,5-dimethylphenyl)-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol

NEW

(R)-3,3'-bis-(3,5-dimethylphenyl)-5,6,7,8,5',6',7',8'-octahydro-[1,1']binaphthalenyl-2,2'-diol

C₃₆H₃₈O₂
MW: 502.69



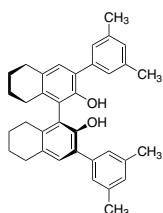
669180-100MG 100 mg

(S)-3,3'-Bis-(3,5-dimethylphenyl)-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol

NEW

(S)-3,3'-bis-(3,5-dimethylphenyl)-5,6,7,8,5',6',7',8'-octahydro-[1,1']binaphthalenyl-2,2'-diol

C₃₆H₃₈O₂
MW: 502.69

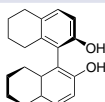


669172-100MG 100 mg

Related Products

(R)-5,5',6,6',7,7',8,8'-Octahydro-bi-2-naphthol, 98%

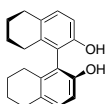
C₂₀H₂₂O₂
MW: 294.39
[α]_D²⁰ +75°, c = 1% in THF
[65355-14-8]



540560-100MG 100 mg
540560-1G 1 g

(S)-5,5',6,6',7,7',8,8'-Octahydro-bi-2-naphthol, 97%

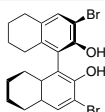
C₂₀H₂₂O₂
MW: 294.39
[α]_D²⁰ -75°, c = 1% in THF
[65355-00-2]



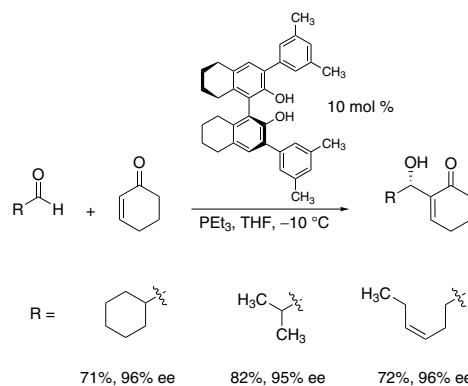
540579-100MG 100 mg
540579-1G 1 g

(R)-(+)-3,3'-Dibromo-5,5',6,6',7,7',8,8'-octahydro(1,1'-binaphthalene)-2,2'-diol, 97%

C₂₀H₂₀Br₂O₂
MW: 452.18
[α]_D²⁰ +53°, c = 1% in THF
[65355-08-0]



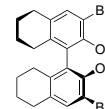
540587-100MG 100 mg
540587-1G 1 g



Scheme 15

(S)-(+)-3,3'-Dibromo-5,5',6,6',7,7',8,8'-octahydro(1,1'-binaphthalene)-2,2'-diol, 97%

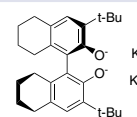
C₂₀H₂₀Br₂O₂
MW: 452.18
[α]_D²⁰ -53°, c = 1% in THF
[765278-73-7]



540595-100MG 100 mg
540595-1G 1 g

(R)-3,3'-Di-tert-butyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol dipotassium salt, purum, ≥95.0% (dry substance, CHN)

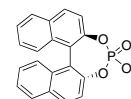
C₂₈H₃₆K₂O₂
MW: 482.78
[350683-75-9]



77939-100MG-F 100 mg

(R)-(-)-1,1'-Binaphthyl-2,2'-diyl hydrogenphosphate, ≥98.0%

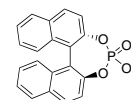
C₂₀H₁₃O₄P
MW: 348.29
[α]_D²⁰ -605°, c = 1.35% in methanol
[39648-67-4]



248932-250MG 250 mg
248932-1G 1 g
248932-5G 5 g

(S)-(+)-1,1'-Binaphthyl-2,2'-diyl hydrogenphosphate, 97%

C₂₀H₁₃O₄P
MW: 348.29
[α]_D²⁰ +595°, c = 1.35% in methanol
[35193-64-7]



248940-250MG 250 mg
248940-1G 1 g
248940-5G 5 g

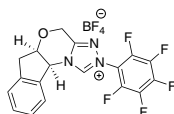
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5a(R),10b(S)-5a,10b-Dihydro-2-(pentafluorophenyl)-4H,6H-indeno[2,1-b][1,2,4]triazolo[4,3-d][1,4]oxazinium tetrafluoroborate

C₁₈H₁₁BF₄N₃O
MW: 467.10

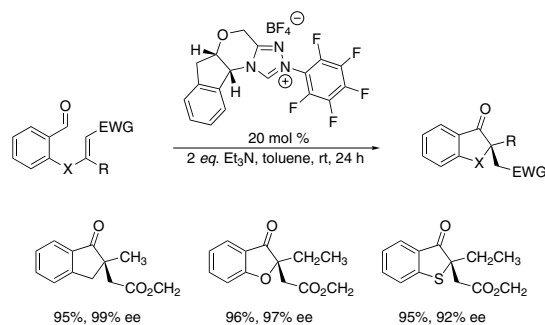


674788-250MG

250 mg

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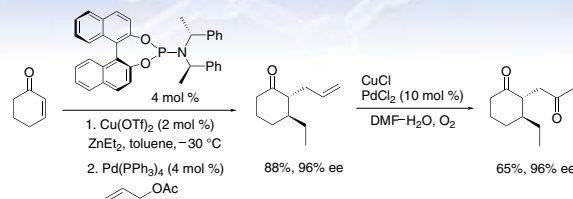
Scheme 16

DSM MonoPhos™ Family

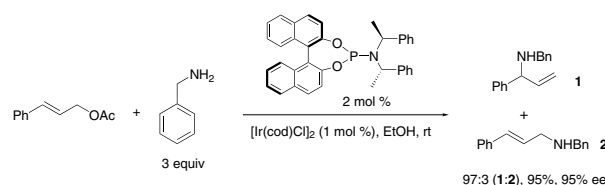
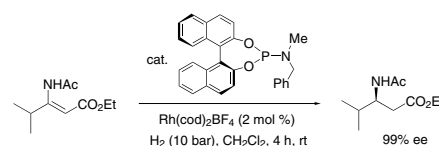
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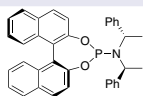
Feringa and co-workers have invented a diverse array of chiral, monodentate phosphoramidites based on the privileged BINOL platform.¹ The MonoPhos™ family has exhibited high levels of enantiocontrol in synthetic transformations ranging from metal-catalyzed asymmetric 1,4-additions of organometallic reagents to allylic alkylations to desymmetrization of *meso*-cycloalkene oxides.² Impressively, the (*S*)-*N*-benzyl-*N*-methyl-MonoPhos™ derivative has been utilized in highly selective hydrogenations of (*E*)-*N*-acylated dehydro-β-amino acid esters, affording the corresponding enantiopure β-amino acid derivatives.³ Sigma-Aldrich, in collaboration with DSM, is pleased to offer a range of MonoPhos™ ligands for the research market.[†]



(*S,S,S*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine, 97%

NEW

C₃₆H₃₀NO₂P
FW: 539.6
[380230-02-4]

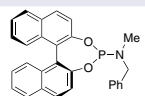


665290-100MG	100 mg
665290-500MG	500 mg
665290-2G	2 g

(*S*)-(+)-Benzyl-(3,5-dioxa-4-phosphacyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)methylamine, 97%

NEW

C₂₈H₂₂NO₂P
FW: 435.45
[490023-37-5]

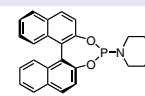


665355-100MG	100 mg
665355-500MG	500 mg
665355-2G	2 g

(*S*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)piperidine, 97%

NEW

C₂₅H₂₂NO₂P
FW: 399.42

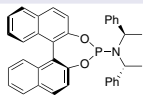


665479-100MG	100 mg
665479-500MG	500 mg
665479-2G	2 g

(*S,R,R*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine, 97%

NEW

C₃₆H₃₀NO₂P
FW: 539.6
[415918-91-1]

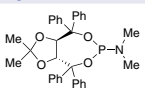


665363-100MG	100 mg
665363-500MG	500 mg
665363-2G	2 g

(3*aR*,8*aR*)-(-)-(2,2-Dimethyl-4,4,8,8-tetraphenyl-tetrahydro-[1,3]dioxolo(4,5-e)[1,3,2]dioxaphosphin-6-yl)Dimethylamine, 96%

NEW

C₃₃H₃₄NO₂P
FW: 539.6
[213843-90-4]

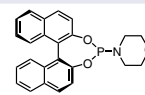


665460-100MG	100 mg
665460-500MG	500 mg

(*S*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)morpholine, 97%

NEW

C₂₄H₂₀NO₃P
FW: 401.39



665487-100MG	100 mg
665487-500MG	500 mg
665487-2G	2 g

(1) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346. (2) (a) Feringa, B. L. et al. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2620 (b) Martina, S. L. X. et al. *Tetrahedron Lett.* **2005**, *46*, 7159 (c) Malda, H. et al. *Org. Lett.* **2001**, *3*, 1169 (d) Alexakis, A. et al. *Chem. Commun.* **2005**, 2843 (e) Streiff, S. et al. *Chem. Commun.* **2005**, 2957 (f) Bertozzi, F. et al. *Org. Lett.* **2000**, *2*, 933. (g) Ohmura, T. et al. *J. Am. Chem. Soc.* **2002**, *124*, 15164. (3) (a) Pena, D. et al. *J. Am. Chem. Soc.* **2002**, *124*, 14552 (b) Van den Berg, M. et al. *Adv. Synth. Catal.* **2003**, *345*, 308.

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