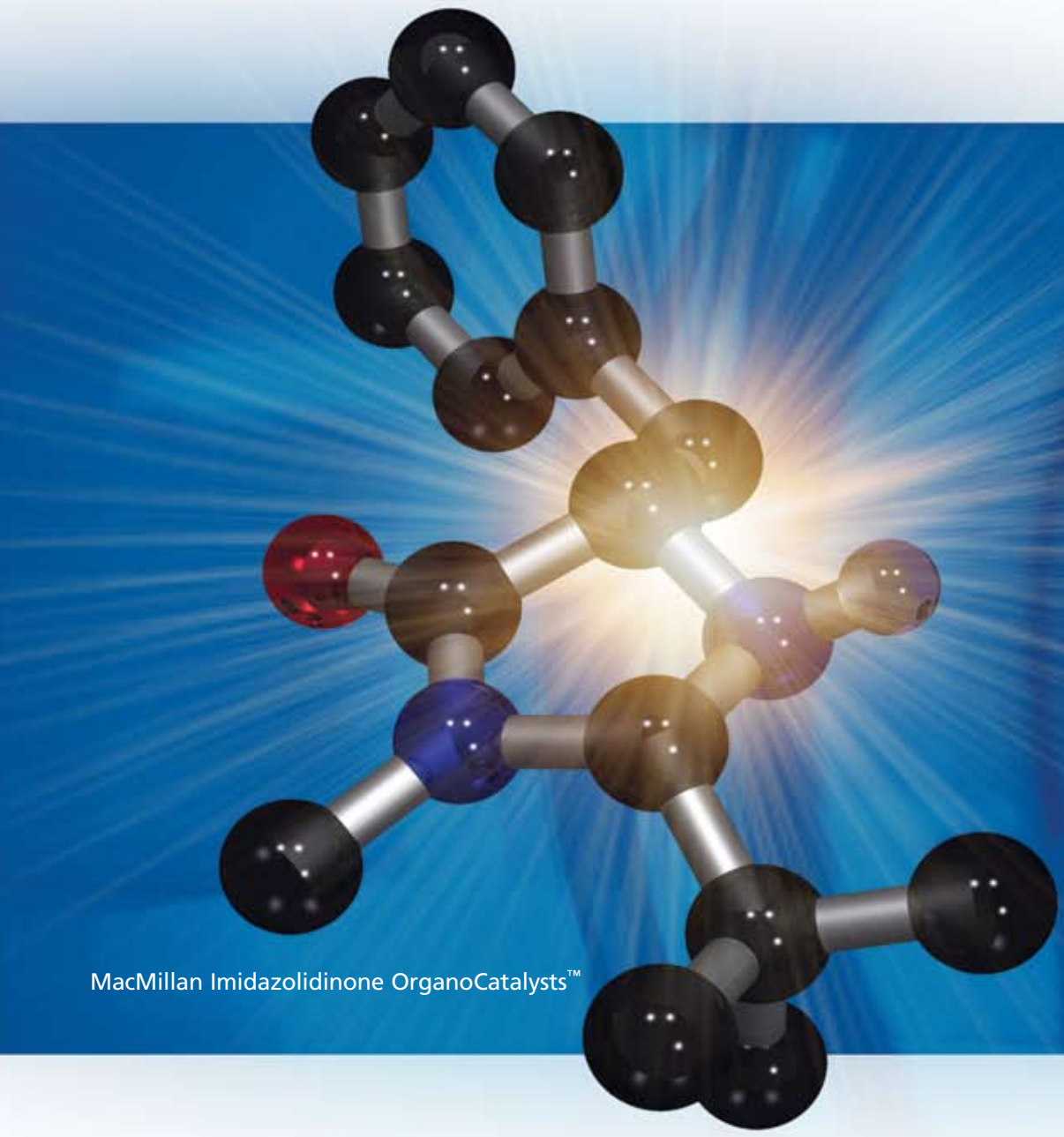
ChemFiles

Vol. 6 No. 4

Synthetic Methods

Asymmetric Organocatalysis



MacMillan Imidazolidinone OrganoCatalysts™

- Proline Analogs
- MacMillan Imidazolidinone OrganoCatalysts™
- Cinchona Alkaloids
- TADDOLs
- Schaus MBH Catalyst
- Rovis Triazolium Catalyst

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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!

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.

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Proline Analogs

Coined by Jacobsen[2] 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]

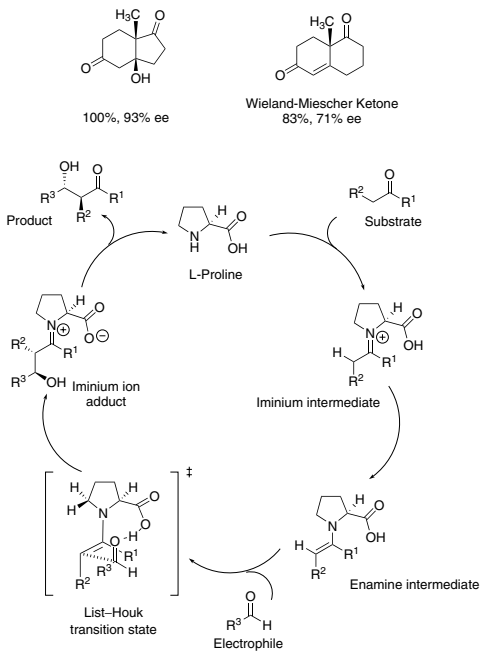
Moreover, as a small organic molecule, proline is available in both enantiomeric forms, which is a definite advantage over enzymatic methods. Numerous proline-catalyzed reactions have been developed (**Scheme 2**).[5]

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.

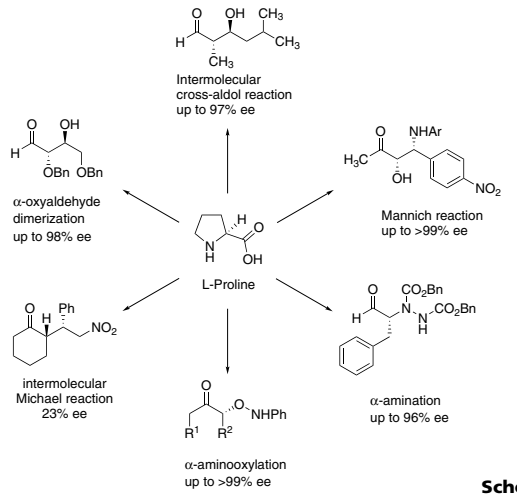
The catalytic asymmetric α-alkylation of aldehydes was recently described by List.[6] To date, this transformation was usually accomplished with the help of covalently attached auxiliaries. In comparison to L-proline, α-methyl-L-proline (**17249**) gives higher enantioselectivities and improved reaction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

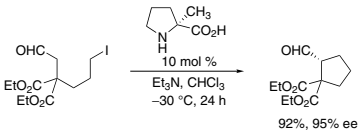
Aggarwal utilized protonated (*S*)-(–)-2-(diphenylmethyl)pyrrolidine (**552534**) as an organocatalyst in a novel process for the enantio-selective epoxidation of alkenes.[9] Although the reaction proceeds under phase-transfer conditions (PTC), it was found that secondary amines catalyzed the reaction 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**).



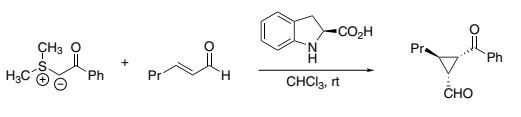
Scheme 1



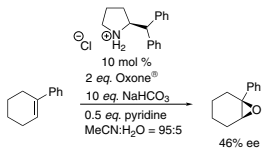
Scheme 2



Scheme 3



Scheme 4



Scheme 5

L-Proline, ReagentPlus™, ≥99%

$C_5H_9NO_2$
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, ≥99.0% NT

$C_5H_9NO_2$
MW: 115.13
$[\alpha]_D^{20}$ –84.5° ± 1°, c = 5% in water
[*147-85-3*]

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

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D-Proline, ≥99%

$C_5H_9NO_2$
MW: 115.13
[α] +85.0°, c = 4 in water
[*344-25-2*]

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

D-Proline, puriss., ≥99.0% NT

$C_5H_9NO_2$
MW: 115.13
$[\alpha]_D^{20}$ +85° ± 2°, c = 5% in water
[*344-25-2*]

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

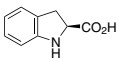
α-Methyl-L-proline, purum, ≥98.0% TLC

$C_6H_{11}NO_2$
MW: 129.16
[α] –75° ± 2°, c = 1% in methanol
[*42856-71-3*]

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

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

$C_9H_9NO_2$
MW: 163.17
$[\alpha]_D^{20}$ –114° c = 1 in 1N HCl
[*79815-20-6*]

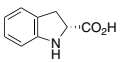


346802-1G	1 g
346802-5G	5 g

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

NEW

$C_9H_9NO_2$
MW: 163.17
$[\alpha]_D^{20}$ +114° c = 1 in 1N HCl
[*98167-06-7*]



51266-500MG	500 mg

3,4-Dehydro-L-proline, BioChemika, ≥99.0% TLC

$C_5H_7NO_2$
MW: 113.11
$[\alpha]_D^{20}$ –400° ± 10° c = 0.2% in water
[*4043-88-3*]

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

L-4-Thiazolidinecarboxylic acid, purum, ≥99.0% T

$C_4H_7NO_2S$
MW: 133.17
$[\alpha]_D^{20}$ –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, ≥98.0% NT

$C_4H_7NO_2$
MW: 101.10
$[\alpha]_D^{20}$ –123° ± 2°, c = 4% in water
[*2133-34-8*]

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

L-Pipecolic acid, puriss., ≥99.0% NT

$C_6H_{11}NO_2$
MW: 129.16
$[\alpha]_D^{20}$ –26° ± 1°, c = 4% in water
[*3105-95-1*]

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

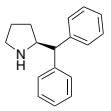
D-Pipecolic acid, purum, ≥99.0% NT

$C_6H_{11}NO_2$
MW: 129.16
$[\alpha]_D^{20}$ +27° ± 1°, c = 1% in water
[*1723-00-8*]

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

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

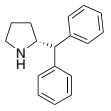
$C_{17}H_{19}N$
MW: 237.34
[α] –3.0°, c = 1% in chloroform
[*119237-64-8*]



552534-500MG	500 mg

(*R*)-(+)-2-(Diphenylmethyl)pyrrolidine, 97%

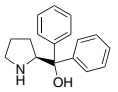
$C_{17}H_{19}N$
MW: 237.34
$[\alpha]_D^{20}$ +3.0°, c = 1% in chloroform
[*22348-31-8*]



552542-1G	1 g

α,α-Diphenyl-L-prolinol, purum, ≥99.0% HPLC sum of enantiomers

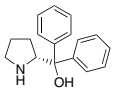
$C_{17}H_{19}NO$
MW: 253.34
$[\alpha]_D^{20}$ –69° ± 2°, c = 3% in chloroform
[*112068-01-6*]



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

α,α-Diphenyl-D-prolinol, purum, ≥99.0% HPLC sum of enantiomers

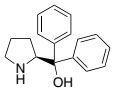
$C_{17}H_{19}NO$
MW: 253.34
$[\alpha]_D^{20}$ +69° ± 3°, c = 3% in chloroform
[*22348-32-9*]



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

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

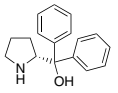
$C_{17}H_{19}NO$
MW: 253.34
$[\alpha]_D^{20}$ –67°, c = 3 in chloroform
[*112068-01-6*]



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

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

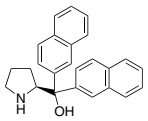
$C_{17}H_{19}NO$
MW: 253.34
$[\alpha]_D^{20}$ +69°, c = 3% in chloroform
[*22348-32-9*]



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

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

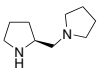
$C_{25}H_{23}NO$
MW: 353.46
$[\alpha]_D^{20}$ –101°, c = 0.7 in methanol
[*127986-84-9*]



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

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

$C_9H_{18}N_2$
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, ≥98.0% GC sum of enantiomers

$C_6H_{13}NO$
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%

$C_6H_{13}NO$
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, ≥98.0% GC sum of enantiomers

$C_6H_{13}NO$
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.

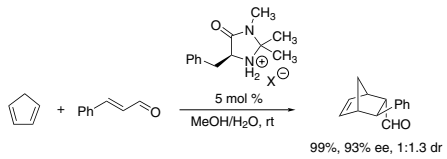
Other organocatalytic transformations such as 1,3-dipolar cycloadditions,[11] Friedel–Crafts alkylations,[12] α-chlorinations,[13] α-fluorinations,[14] and intramolecular Michael reactions[15] using MacMillan's organocatalyst technology (**569763**) were reported, all proceeding with impressive levels 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).

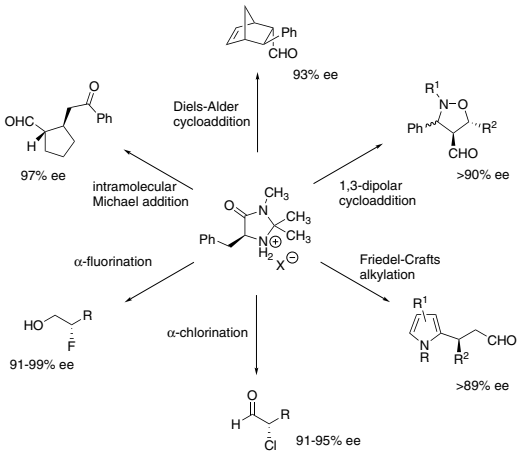
MacMillan later demonstrated the synthetic utility of this concept in the total synthesis of (–)-flustramine B, a biologically active alkaloid bearing a pyrroloindoline architecture. The fused ring system was cleanly assembled with the aid of imidazolidinone organocatalyst **663107** (**Scheme 9**).[17]

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]

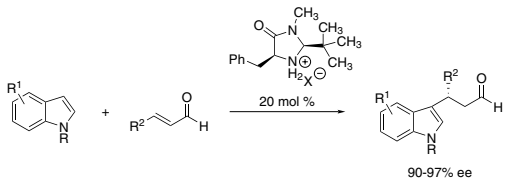
In sharp contrast to metal-mediated hydrogenations, the *E/Z* geometry of the enal substrates did not have a significant influence on the outcome of the absolute configuration of the newly created stereocenter. In an elegant organocascade reaction, MacMillan



Scheme 6



Scheme 7



Scheme 8

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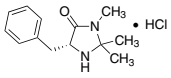
showed that both LUMO-lowering iminium- and HOMO-raising enamine catalysis could coexist without deleterious catalyst–catalyst interactions by substrate activation in an orthogonal mode, hence leading to highly enantioenriched products with increased structural complexity in just one step. Using both 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]

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

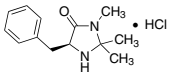
$C_{13}H_{18}N_2O \cdot HCl$
MW: 254.76
$[\alpha]_D^{20}$ +64°, c = 1 in water
[*323196-43-6*]



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

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

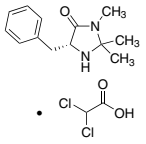
$C_{13}H_{18}N_2O \cdot HCl$
MW: 254.76
$[\alpha]_D^{20}$ –64°, c = 1 in water
[*278173-23-2*]



569763-2G	2 g

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

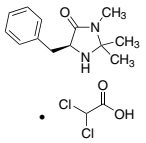
$C_{15}H_{20}Cl_2N_2O_3$
MW: 347.24
$[\alpha]_D^{20}$ +52°±4°, c = 1% in methanol



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

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

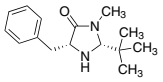
$C_{15}H_{20}Cl_2N_2O_3$
MW: 347.24
$[\alpha]_D^{20}$ –52°±4°, c = 1% in methanol



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

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

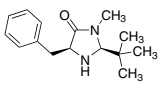
$C_{15}H_{22}N_2O$
MW: 246.35
$[\alpha]_D^{20}$ +72°±4°, c = 1% in chloroform
[*390766-89-9*]



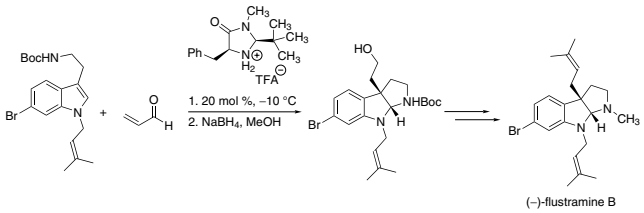
663093-500MG	500 mg
663093-1G	1 g

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

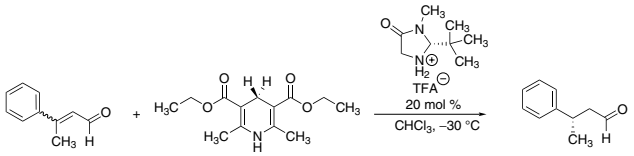
$C_{15}H_{22}N_2O$
MW: 246.35
$[\alpha]_D^{20}$ –72°±4°, c = 1% in chloroform
[*346440-54-8*]



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

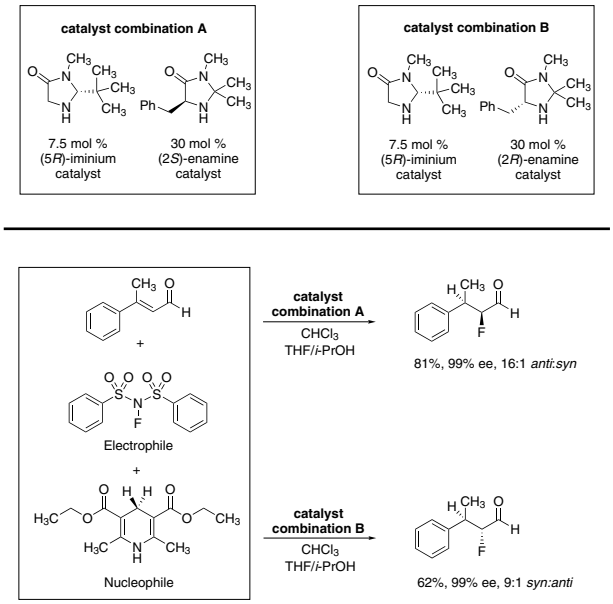


Scheme 9



Alkene geometry	Yield (%)	% ee (abs. config.)
E	91	93 (*S*)
Z	90	87 (*S*)
E/*Z* mix	88	90 (*S*)

Table 1



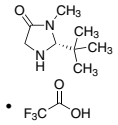
Scheme 10

TO ORDER: Contact your local Sigma-Aldrich office (see back cover), call 1-800-325-3010 (USA), or visit sigma-aldrich.com/chemicalsynthesis.

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

NEW

$C_{10}H_{17}N_2O_3F_3$
MW: 270.25

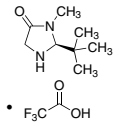


661910-500MG	500 mg
661910-2G	2 g

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

NEW

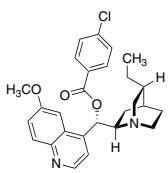
$C_{10}H_{17}N_2O_3F_3$
MW: 270.25



661902-500MG	500 mg
661902-2G	2 g

Hydroquinidine 4-chlorobenzoate, 98%

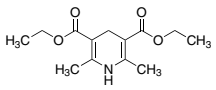
$C_{27}H_{29}ClN_2O_3$
MW: 464.98
[α] –73°, c = 1 in ethanol
[*113162-02-0*]



336483-1G	1 g
336483-5G	5 g

Diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate, 95%

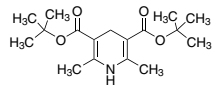
$C_{13}H_{19}NO_4$
MW: 253.29
[*1149-23-1*]



120227-1G	1 g

Di-*tert*-butyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, 97%

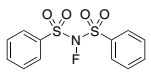
$C_{17}H_{27}NO_4$
MW: 309.4
[*55536-71-5*]



659142-1G	1 g

N-Fluorobenzenesulfonimide, 97%

$C_{12}H_{10}FNO_4S_2$
MW: 315.34
[*113745-75-2*]



392715-1G	1 g
392715-5G	5 g

Cinchona Alkaloids

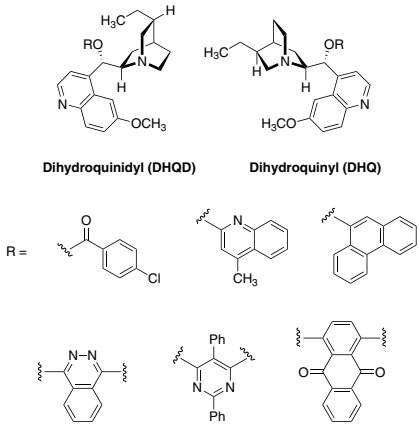
Desymmetrization

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**).

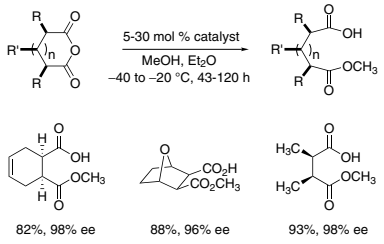
A high degree of asymmetric induction using cinchona catalysts can be achieved in desymmetrization of meso anhydrides to form the corresponding hemiesters (**Scheme 12**). Biscinchona alkaloids such as $(DHQD)_2AQN$ (**456713**) were more efficient in this transformation.[20]

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]

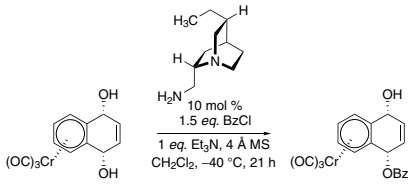
Nonracemic planar chiral (arene)$Cr(CO)_3$ complexes are increasingly important chiral building blocks in highly diastereoselective transformations and they can also serve as ligands in catalytic reactions.[27] Kündig has shown that chiral diamine **07317** performed well in the asymmetric benzoylation/desymmetrization of a meso Cr complex.[28] Enantiomeric excess only marginally decreased (to 98%) when diamine **39867** was employed in the same reaction (**Scheme 13**).



Scheme 11



Scheme 12



Scheme 13

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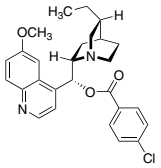
O-(4-Chlorobenzoyl)hydroquinine, 98%

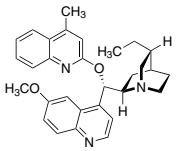
$C_{27}H_{29}ClN_2O_3$
MW: 464.98
[α] +150°, c = 1 in ethanol
[*113216-88-9*]



336491-1G	1 g

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

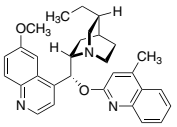
$C_{30}H_{33}N_3O_2$
MW: 467.60
[α] –168°, c = 1 in ethanol
[*135042-89-6*]



381942-1G	1 g

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

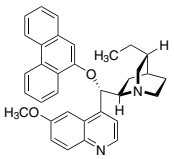
$C_{30}H_{33}N_3O_2$
MW: 467.60
$[\alpha]_D^{20}$ +260°, c = 1 in ethanol
[*135096-79-6*]



381969-1G	1 g

Hydroquinidine 9-phenanthryl ether, 96%

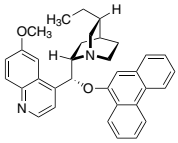
$C_{34}H_{34}N_2O_2$
MW: 502.65
$[\alpha]_D^{20}$ –348°, c = 1 in ethanol
[*135042-88-5*]



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

Hydroquinine 9-phenanthryl ether, 97%

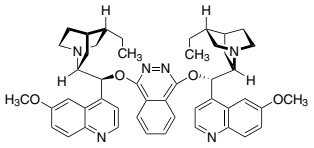
$C_{34}H_{34}N_2O_2$
MW: 502.65
$[\alpha]_D^{20}$ +420°, c = 1 in ethanol
[*135096-78-5*]



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

$(DHQD)_2PHAL$, ≥95%

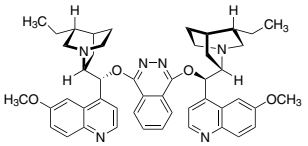
$C_{48}H_{54}N_6O_4$
MW: 778.98
[α] –262°, c = 1.2 in methanol
[*140853-10-7*]



392731-1G	1 g

$(DHQ)_2PHAL$, ≥95%

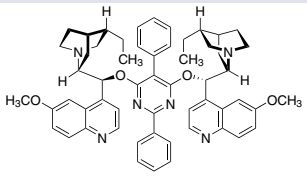
$C_{48}H_{54}N_6O_4$
MW: 778.98
[α] +336°, c = 1.2 in methanol
[*140924-50-1*]



392723-500MG	500 mg

$(DHQD)_2Pyr$, 97%

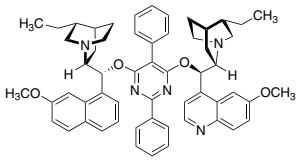
$C_{56}H_{60}N_6O_4$
MW: 881.11
$[\alpha]_D^{20}$ –390°, c = 1.2 in methanol
[*149725-81-5*]



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

$(DHQ)_2Pyr$, 97%

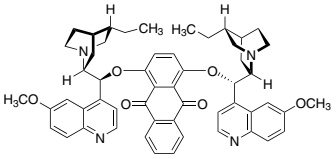
$C_{56}H_{60}N_6O_4$
MW: 881.11
$[\alpha]_D^{20}$ +455°, c = 1.2 in methanol
[*149820-65-5*]



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

$(DHQD)_2AQN$, 95%

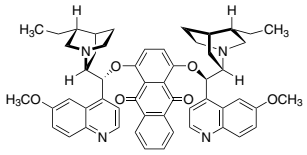
$C_{54}H_{56}N_4O_6$
MW: 857.05
$[\alpha]_D^{20}$ –468°, c = 1 in chloroform
[*176298-44-5*]



456713-500MG	500 mg

$(DHQ)_2AQN$, 95%

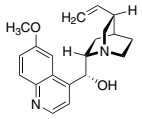
$C_{54}H_{56}N_4O_6$
MW: 857.05
$[\alpha]_D^{20}$ +495°, c = 1 in chloroform
[*176097-24-8*]



456705-500MG	500 mg

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

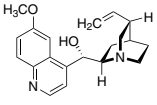
$C_{20}H_{24}N_2O_2$
MW: 324.42
$[\alpha]_D^{20}$ –126° ± 5°, c = 1% in chloroform
[*130-95-0*]



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

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

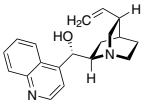
$C_{20}H_{24}N_2O_2$
MW: 324.42
$[\alpha]_D^{20}$ +265° ± 5°, c = 0.8% in ethanol dry matter
[*56-54-2*]



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° ± 5°, c = 0.5% in ethanol
[*118-10-5*]



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

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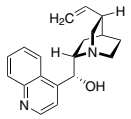
Cinchonidine, purum, ≥98.0% NT dried material

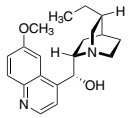
$C_{19}H_{22}N_2O$
MW: 294.39
$[\alpha]_D^{20}$ –108° ± 3°, c = 5% in ethanol
[*485-71-2*]



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

Hydroquinine, 98%

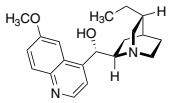
$C_{20}H_{26}N_2O_2$
MW: 326.43
$[\alpha]$ –148°, c = 1 in ethanol
[*522-66-7*]



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

Hydroquinidine, 95%

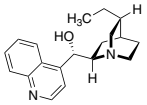
$C_{20}H_{26}N_2O_2$
MW: 326.43
$[\alpha]$ +226°, c = 2 in ethanol
[*1435-55-8*]



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

Hydrocinchonine, purum, ≥97.0% GC sum of enantiomers

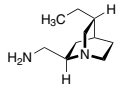
$C_{19}H_{24}N_2O$
MW: 296.41
$[\alpha]_D^{20}$ +197° ± 4°, c = 0.5% in ethanol
[*485-65-4*]



54060-500MG	500 mg

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

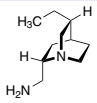
$C_{10}H_{20}N_2$
MW: 168.28
$[\alpha]_D^{20}$ +143°, c = 1 in ethanol
[*475160-61-3*]



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

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

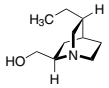
$C_{10}H_{20}N_2$
MW: 168.28
$[\alpha]_D^{20}$ –28°, c = 1 in ethanol
[*475160-59-9*]



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

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

$C_{10}H_{19}NO$
MW: 169.26
$[\alpha]_D^{20}$ +147°, c = 1 in chloroform
[*219794-81-7*]



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

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

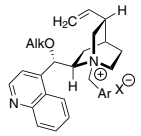
$C_{10}H_{19}NO$
MW: 169.26
$[\alpha]_D^{20}$ –5.1°, c = 1 in chloroform
[*219794-79-3*]

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

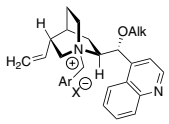
Asymmetric Phase-Transfer Reactions

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]

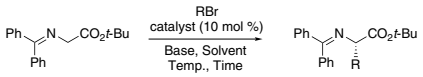
In an attempt to further improve catalyst enantioselectivities, Jew and Park linked two cinchona alkaloid moieties via spacer units.[30] With such a dimeric cinchona alkaloid (**06542**), enantioselectivity for the above mentioned glycine imine alkylation was optimized to 97–99% ee.



Cinchonidinium PTC



Cinchoninium PTC

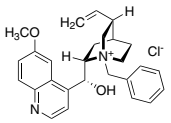


Cat. No.	Cinchona PTC *N*-Ar	*O*-Alk	X^-	Cat. Gen.	R-Br	% Y	% ee
524433	Benzyl	H	Br	1st	$PhCH_2$-	85	60
359580	Benzyl	H	Cl	1st	4-Cl-C_6H_4-CH_2-	95	66
514276	Benzyl	Allyl	Br	2nd	4-Cl-C_6H_4-CH_2-	–	81
515701	9-Anthracenylmethyl	H	Cl	3rd	$PhCH_2$-	68	91
499617	9-Anthracenylmethyl	Allyl	Br	3rd	$PhCH_2$-	87	94
06542	2,7-Naphthalenediyldimethyl	Allyl	Br	dimeric	4-NO_2-C_6H_4-CH_2-	91	99

Table 2

N-Benzylquininium chloride, 95%

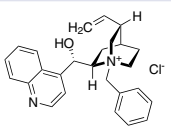
$C_{27}H_{31}ClN_2O_2$
MW: 451.00
$[\alpha]_D^{20}$ –235°, c = 1.5 in water
[*67174-25-8*]



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

N-Benzylcinchoninium chloride, purum, ≥98.0% AT

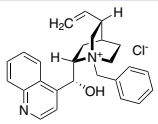
$C_{26}H_{29}ClN_2O$
MW: 420.97
$[\alpha]_D^{20}$ +169° ± 3°, c = 0.4% in water
[*69221-14-3*]



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

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

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



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

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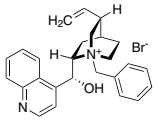
N-Benzylcinchonidinium bromide, 97%

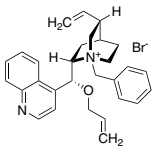
$C_{26}H_{29}BrN_2O$
MW: 465.43
$[\alpha]_D^{20}$ –138°, c = 1 in chloroform
[*118089-84-2*]



524433-5G	5 g

O-Allyl-*N*-benzylcinchonindinium bromide

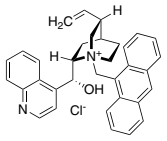
$C_{29}H_{33}BrN_2O$
MW: 505.49
$[\alpha]_D^{20}$ –158°, c = 1 in chloroform
[*158195-40-5*]



514276-1G	1 g

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

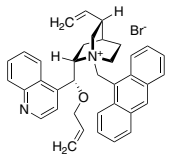
$C_{34}H_{33}ClN_2O$
MW: 521.09
[*199588-80-2*]



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

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

$C_{37}H_{37}BrN_2O$
MW: 605.61
$[\alpha]_D^{20}$ –340°, c = 0.45 in chloroform
[*200132-54-3*]

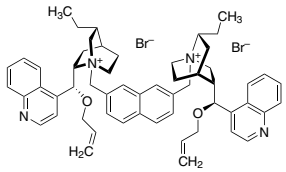


499617-1G	1 g
499617-5G	5 g

O,O'-Diallyl-*N,N'*-(2,7-naphthalenediyldimethyl) bis(hydrocinchonidinium) dibromide

NEW

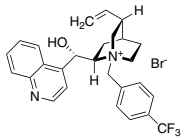
$C_{56}H_{66}Br_2N_4O_2$
MW: 986.96
[*480427-57-4*]



06542-100MG	100 mg

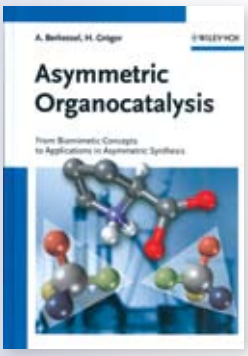
N-(4-Trifluoromethylbenzyl)cinchoninium bromide, purum, ≥98.0% AT

$C_{27}H_{28}BrF_3N_2O$
MW: 533.42
$[\alpha]_D^{20}$ +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-VHC, 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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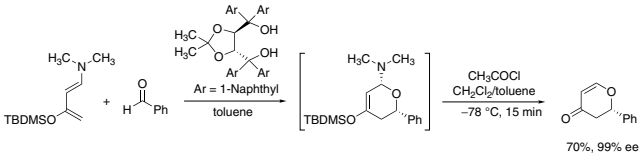
TADDOLs

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.

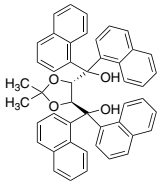
Apart from numerous examples using TADDOLs in metal-catalyzed asymmetric reactions,[32] Rawal recently reported that TADDOLs could be used as Brønsted acid organocatalysts in highly stereoselective hetero-Diels–Alder reactions.[33] The reaction of an electron-rich diene with benzaldehyde using 10 mol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



Scheme 14

(4*S*-*trans*)-2,2-Dimethyl-α,α,α′,α′-tetra(1-naphthyl)-1,3-dioxolane-4,5-dimethanol, 99%

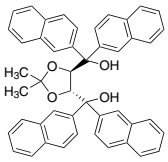
$C_{47}H_{38}O_4$
MW: 666.80
$[\alpha]_D^{20}$ +280°, c = 1 in ethyl acetate
[*171086-52-5*]



395242-1G	1 g

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, 99%

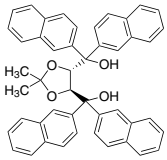
$C_{47}H_{38}O_4$
MW: 666.80
$[\alpha]_D^{20}$ –116°, c = 1 in ethyl acetate
[*137365-09-4*]



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

(4*S*,5*S*)-2,2-Dimethyl-α,α,α′,α′-tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, 98%

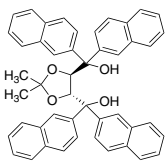
$C_{47}H_{38}O_4$
MW: 666.80
$[\alpha]_D^{20}$ +116°, c = 1 in ethyl acetate
[*137365-16-3*]



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

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, purum, ≥99.0% HPLC sum of enantiomers

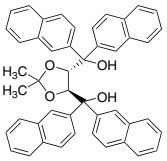
$C_{47}H_{38}O_4$
MW: 666.80
$[\alpha]_D^{20}$ –116° ± 2°, c = 1% in ethyl acetate
[*137365-09-4*]



59490-1G-F	1 g
59490-5G-F	5 g

(4*S*,5*S*)-2,2-Dimethyl-α,α,α′,α′-tetra(2-naphthyl)-1,3-dioxolane-4,5-dimethanol, purum, ≥98.0% HPLC sum of enantiomers

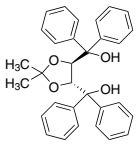
$C_{47}H_{38}O_4$
MW: 666.80
$[\alpha]_D^{20}$ +116° ± 2°, c = 1% in ethyl acetate
[*137365-16-3*]



59488-5G-F	5 g

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol

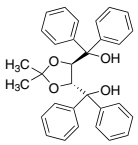
$C_{31}H_{30}O_4$
MW: 466.57
[α] –62.6°, c = 1 in chloroform
[*93379-48-7*]



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

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol, purum, ≥ 97.0% HPLC sum of enantiomers

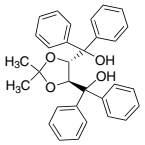
$C_{31}H_{30}O_4$
MW: 466.57
$[\alpha]_D^{20}$ –67° ± 2°, c = 1% in chloroform
[*93379-48-7*]



59532-1G	1 g

(4*S*,5*S*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol

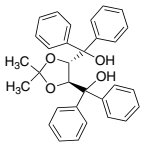
$C_{31}H_{30}O_4$
MW: 466.57
[α] +67°, c = 1 in chloroform
[*93379-49-8*]



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

(4*S*,5*S*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol, purum, ≥97.0% HPLC sum of enantiomers

$C_{31}H_{30}O_4$
MW: 466.57
$[\alpha]_D^{20}$ +67° ± 2°, c = 1% in chloroform
[*93379-49-8*]



59534-1G-F	1 g

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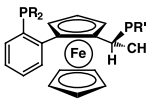
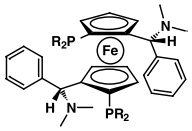
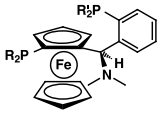
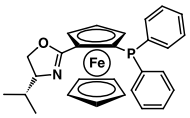

Walphos


Mandyphos


Taniaphos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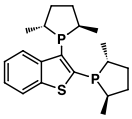
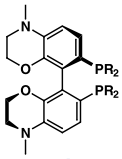

Butiphane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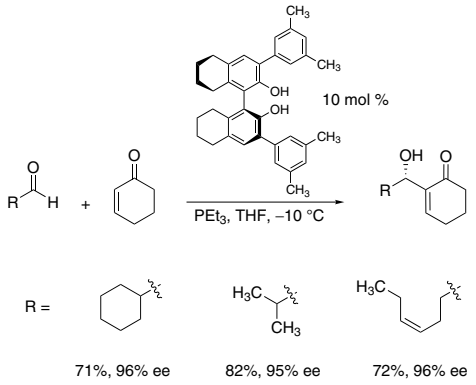
Schaus MBH Catalyst

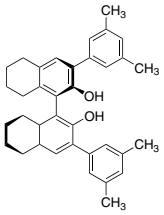
A highly enantioselective addition of cyclohexenone to different aldehydes (asymmetric Morita–Baylis–Hillman reaction) catalyzed by octahydro-BINOL-derived Brønsted acid **669172** was reported by Schaus (**Scheme 15**). Important for achieving high enantioselectivity were both the partial saturation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



Scheme 15

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

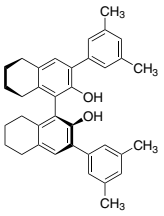
(*R*)-3,3′-bis-(3,5-dimethylphenyl)-5,6,7,8,5′,6′,7′,8′-octahydro-[1,1′]binaphthalenyl-2,2′-diol
$C_{36}H_{38}O_2$
MW: 502.69



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
$C_{36}H_{38}O_2$
MW: 502.69

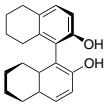


669172-100MG	100 mg

Related Products

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

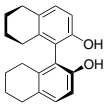
$C_{20}H_{22}O_2$
MW: 294.39
$[\alpha]_D^{20}$ +75°, c = 1% in THF
[*65355-14-8*]



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

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

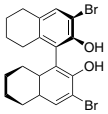
$C_{20}H_{22}O_2$
MW: 294.39
$[\alpha]_D^{20}$ –75°, c = 1% in THF
[*65355-00-2*]



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%

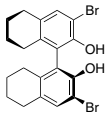
$C_{20}H_{20}Br_2O_2$
MW: 452.18
$[\alpha]_D^{20}$ +53°, c = 1% in THF
[*65355-08-0*]



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

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

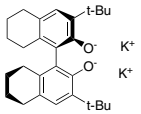
$C_{20}H_{20}Br_2O_2$
MW: 452.18
$[\alpha]_D^{20}$ –53°, c = 1% in THF
[*765278-73-7*]



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)

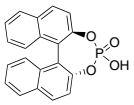
$C_{28}H_{36}K_2O_2$
MW: 482.78
[*350683-75-9*]



77939-100MG-F	100 mg

(*R*)-(–)-1,1′-Binaphthyl-2,2′-diyl hydrogenphosphate, ≥98.0%

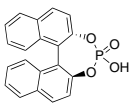
$C_{20}H_{13}O_4P$
MW: 348.29
$[\alpha]_D^{20}$ –605°, c = 1.35% in methanol
[*39648-67-4*]



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

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

$C_{20}H_{13}O_4P$
MW: 348.29
$[\alpha]_D^{20}$ +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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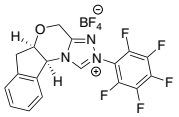
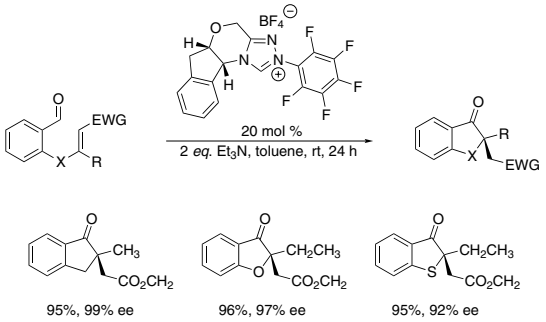
5a(*R*),10b(*S*)-5a,10b-Dihydro-2-(pentafluorophenyl)-4H,6H-indeno[2,1-*b*][1,2,4]triazolo[4,3-*d*][1,4]oxazinium tetrafluoroborate NEW

$C_{18}H_{11}BF_4N_3O$
MW: 467.10



674788-250MG	250 mg



Scheme 16

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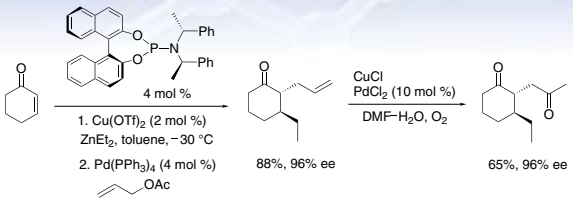

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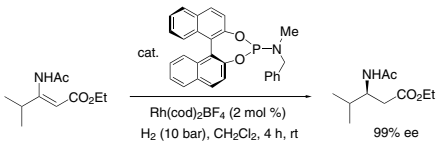
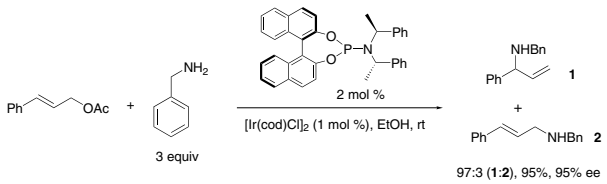
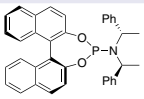




(*S,S,S*)-(+)-(3,5-Dioxa-4-phospha-cyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)bis(1-phenylethyl)amine, 97% NEW

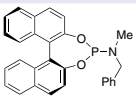
$C_{36}H_{30}NO_2P$
FW: 539.6
[*380230-02-4*]



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

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

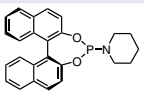
$C_{28}H_{22}NO_2P$
FW: 435.45
[*490023-37-5*]



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

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

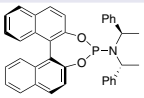
$C_{25}H_{22}NO_2P$
FW: 399.42



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

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

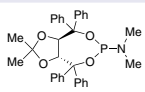
$C_{36}H_{30}NO_2P$
FW: 539.6
[*415918-91-1*]



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

(3a*R*,8a*R*)-(–)-(2,2-Dimethyl-4,4,8,8-tetraphenyl-tetrahydro-[1,3]dioxolo(4,5-e)[1,3,2]dioxaphosphepin-6-yl)Dimethylamine, 96% NEW

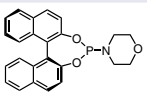
$C_{33}H_{34}NO_4P$
FW: 539.6
[*213843-90-4*]



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

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

$C_{24}H_{20}NO_3P$
FW: 401.39



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

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