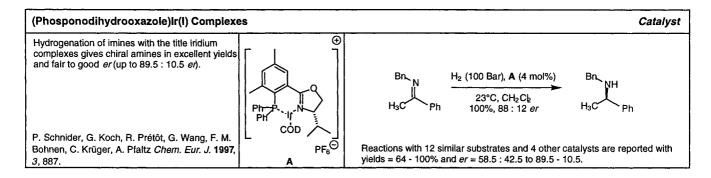
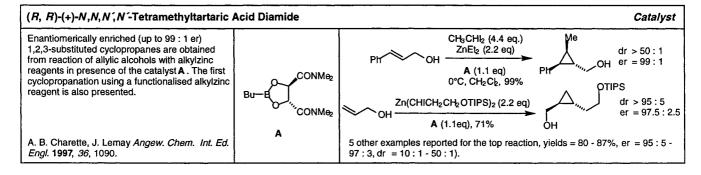
SYNTHESIS ALERTS

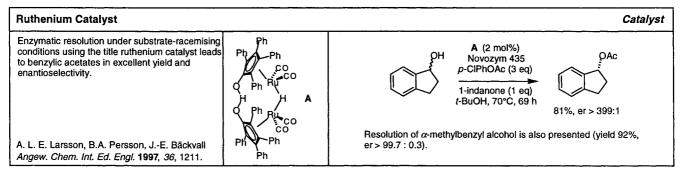
Synthesis Alerts is a monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered if they are used in novel and useful reactions. In each abstract, a specific example of a transformation is given in a concise format designed to aid visual retrieval of information.

Synthesis Alerts is a personal selection by Paul Blakemore, Brian Dymock, Philip Hall, Philip Kocienski, J.-Y. Le Brazidec and Alessandro Pontiroli of the University of Glasgow. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin de la Societe Chimie de France, Bulletin of the Chemical Society of Japan, Chemische Berichte, Chemistry Letters, Helvetica Chimica Acta, Journal of Organic Chemistry, Journal of Organometallic Chemistry, Journal of the American Chemical Society, Liebigs Annalen, Tetrahedron Letters.

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1209

 $Zr_{0.8}Ni_{0.2}O_2$

A (10 m/m) KOH (1 eq) IPrOH, Δ , 3 h 19 examples; yields 72-96%.

T. T. Upadhya, S. P. Katdare, D. P. Sabde, V.

Ramaswamy, A. Sudalai Chem. Commun. 1997,

Cobalt(II) Complex Catalysts

NaBH (1 eq)

Enantioselective borohydride reductions of N-diphenylphosphinyl imines using optically active cobalt(II) complex catalysts progress in high vield and ee.

K. D. Sugi, T. Nagata, T. Yamada, T. Mukaiyama Chem. Lett. 1997, 493.

EtOH (1 eq) CHCl_e, 0°C, 3 h A (1 mol%) B (1.5 eq) 97% yield; er = 200:1

10 examples using 3 different catalysts. Yields >80%. er >9:1. The products may be hydrolysed to amines in 85% yield with HCI/MeOH.

Catalyst

Catalyst

Polymer-Enlarged Oxazaborolidine

A polymer-enlarged homogeneously soluble oxazaborolidine catalyst for the asymmetric reduction of ketones by borane.

A (0.1 eq) BH₃•SMe₂ (1 eq) THF, rt, 0.5 h 86%, er = 98.5:1.5 (4 examples)

M. Felder, G. Giffels, C. Wandrey *Tetrahedron:* Asymmetry **1997**, *8*, 1975.

Catalyst Copper(I) lodide Using cuprous iodide in NMP, vinyl stannanes may be coupled with iodides. No palladium catalyst is necssary A (0.1 eq) NaCl (1 eq) Cul NMP, 90°C, 10 h 90% Α 15 different examples. Manganese bromide may be used instead of copper iodide, but in most cases the yields are slightly depressed.

S.-K. Kang, J.-S. Kim, S.-C.Choi, J. Org. Chem. 1997, 62, 4208.

Copper(I) Chloride

Catalyst

Reaction of alkynylsilanes with the title reagent A in 1,3-dimethyl-2-imidazolidinone (DMI) results in the first direct alkynyl group transfer from silicon to copper. The resultant alkynylcopper(I) species are quenched in situ with acyl halides to form alkynyl ketones in good yield.

H. Ito, K. Arimoto, H. Sensui, A. Hosomi *Tetrahedron Lett.* **1997**, *38*, 3977.

CuCl

11 examples (yields 10, 69-98%).

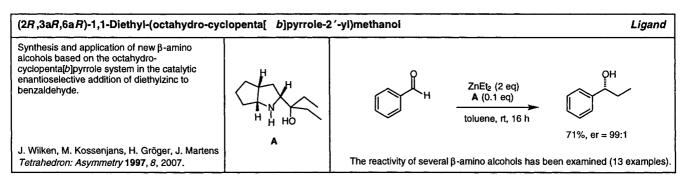
4 examples (yields 60-96%, %ee 88-97%).

(*R*)-2-(Diphenylphosphino)-1,1 '-binaphthalen-2 '-yl (*S*)-1,1'-binaphthalene-2,2 '-diyl Phosphite (BINAPHOS) Asymmetric hydroformylation of conjugated dienes using BINAPHOS-Rh(I) complex as a catalyst yields β_T unsaturated aldehydes with high regio- and enantioselectivity. $H_2 / \text{CO (1: 1, 50 atm)} \\ Rh(\text{acac)}(\text{CO}_{\mathbb{R}} \text{ (7 mol\%)} \\ PPH_2 \\ Rh(\text{aco}) \\ (R,S)-A \text{ (27 mol\%)} \\ PhH, 40^{\circ}\text{C, 96 h} \\ 85\% \text{ conversion} \\ er = 98:2$

T. Horiuchi, T. Ohta, E. Shirakawa, K. Nozaki, H. Takaya *Tetrahedron* **1997**, *53*, 7795.

The optically active title complexes catalyse allylic oxidation of cycloalkenes with poor to very good enantioselectivity. PhCO₃Bu-t, A (7.5 mol%) CuOTf (5 mmol%), acetone MS-4A, 0°C,150 h PhCO₃Bu-t, A (7.5 mol%) Reactions under a variety of conditions led to lower yields (8 - 70%) and er between 41:59 and 96.5:3.5.

Diazaphospholidines Ligand Allylic substitutions using diazaphospholidine ligands may be achieved in up to 89% ee. QAc A (20 mol%) 63% = 79:21 [Pd(n-C3H5)CI] NaOAc CH₂Cl₂ 21 examples using 9 different ligands. Yields 45-97%; er = 16 h H. Tye, D. Smyth, C. Eldred, M. Wills Chem. 94.5:5.5 to 63:37. Commun. 1997, 1053.



(S)-2-Amino-1,1-diphenyl-4-(methylthio)butan-1-ol

Sulfur-containing β-amino alcohols as ligand in enantioselective synthesis.

MeS—H, NH₂
Ph OH

THF, 30°C, 2 h

W. Trentmann, T. Mehler, J. Martens
Tetrahedron: Asymmetry 1997, 8, 2033.

Ligand

Protecting Group

Protecting Group

Reagent

Reagent

Bis-oxazolines

The cyclopropyl derived oxazoline ligand / magnesium iodide system effectively catalyses the asymmetric Michael addition of radicals to α.β-unsaturated imides.

M.P. Sibi, J. Ji J. Org. Chem. 1997, 62, 3800.

A (0.3 eq) Mgk (0.3 eq) i-Prl, BusnH, Е₿В CH₂Cl₂, -78°C 91% R configuration

er = 66:1The ligand shown was the best out of several examined. Notably, the conjugate addition may also be performed at room temeprature with no significant loss of asymmetric induction.

p-Nitrobenzyloxycarbonyl

The p-nitrobenzyloxycarbonyl group serves as an N-protecting group which can be easily removed either by hydrogenolysis or by reaction with sodium dithionite under neutral conditions.

HC HQ H₂, Pd/C OMe MeQH PNZ 76% ŇНь OB_n 'nН

X. Qian, O. Hindsgaul Chem. Commun. 1997,

This paper also contains an example of the PNZ group participating in the stereoselective formation of a 2-amino-β-glycoside.

9 H-Xanthen-9-yi (Xan) and 2-Methoxy- 9 H-xanthen-9-yi (2-Moxan) Groups

Reaction of the xanthydrois A or B with cysteine results in sulfur protection. The resulting protected sulfhydryl group is stable to conditions for Fmoc protection of the amino group.



A: R = H, Xan B: R = OMe, 2-Moxan

Fmoc NH OH (a)L-cysteine, TFA/DME, rt, 30 min. A or B (b)Fmoc -OSu, EtaN

Cleaved with TFA/Et₃SiH, or via oxidation using I₂ or TI(CF₃CO₂)₃.

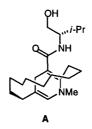
Y. Han, G. Barany J. Org. Chem. 1997, 62, 3841

Asymmetric reduction of methyl benzoylformate with the title NADH model A and Mg(ClQ₄)₂

2,5-Pyridinophane NADH Model

yields the corresponding alcohol with excellent enantioselectivity.

N. Kanomata, T. Nakata Angew. Chem. Int. Ed. Engl. 1997, 36, 1207.



Mg(ClO₄)₂ (1 eq)

3 other diastereomers of the cyclophane were also tested with similar results. Preparation of A is described.

1-Halo-1-(dimethylamino)-2-methylprop-1-ene

α-Halo enamines may be conveniently prepared using oxalyl halides. These enamines may then be applied in the halogenation of β -hydroxy cyclic ethers and lactones.

J. G. Bendali, A. N. Payne, T. E. O. Screen, A. B. Holmes *Chem. Commun.* 1997, 1067.

В

(a) A or B (10 eq), 4Å MS propylene oxide -78°C → rt, 12 h (b) MeOH

8 examples; yields 42-97% (Br) and 56-86% (Cl).

OTBDPS OAc

X = Cl 71% X = Br 45%

Reagent

N-Glyoxyloyl-(2 R)-bornane-10,2-sultam

The asymmetric ene reaction of N-glyoxyloyl-(2R)-bornane-10,2-sultam with alk-1-ene promoted by different Lewis acids has been examined.

1-Pentene (excess) ZnBr₂ (1.1 eq) CH₂Cl₂, 5°C, 48 h

50.5%, dr = 90:10

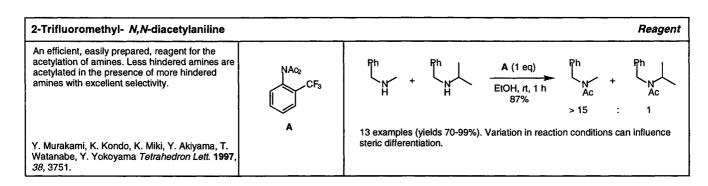
A. Jezewski, K. Chajewska, Z. Wielogórski, J.

Jurczak Tetrahedron: Asymmetry 1997, 8, 1741.

The reactivity of A and its methoxy hemiacetal has been checked with pent-1-ene and hex-1-ene using different Lewis acid (20 examples).

Samarium Diiodide Reagent Highly regio- and stereoselective synthesis of allylsilanes via palladium(0)-catalyzed reductive metallation of allylic phosphates with OPO(OEt)₂ SiMe₃ Sml2-HMPA system. Pd(0) (0.05 eq), Sml₂ (2.5 eq) Sml₂ HMPA (10 eq) TMSCI (10 eq) (17 examples) 69%, E:Z = 3:97 T. Hanamoto, A. Sugino, T. Kikukawa, J. Inanaga Bull. Soc. Chim. Fr. 1997, 134, 391.

Chiral Allyl Bornonate Reagent The bornane derived functionalised boronate A effects the asymmetric allylation of aldehydes. The resultant γ -hydroxy esters are precursors to chiral α -methylene- γ -lactones. 99%, er = 89:11 5 examples (yields 67-99%, %ee 30, 78-96%). Use of chiral aldehydes results in double stereodifferentiation. I. Chataigner, J. Lebreton, F. Zammattio, J. Villiéras Tetrahedron Lett. 1997, 38, 3719.



| Chromium Dioxide (Magtrieve™) | | Reagent |
|---|------------------|---|
| A mild selective oxidant for a variety of alcohols being superior to activated MnO ₂ in most cases. The reagent is magnetically retrievable and may be regenerated simply by heating in air. | CrO ₂ | OH CrO ₂ (10 eq w/w) PhMe, Δ, 5.5 h 95% 5 examples (yields 61-95%). In each case identical transformations are attempted with MnO ₂ (for the illustrated example yield <10% with MnO ₂). |
| R. A. Lee, D. S. Donald <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3857. | | |

Zinc Azide Pyridine Complex Reagent Activation of alcohols by triphenylphosphine and dienone **B** in the presence of the zinc azide complex **A** results in azidination. Zn(N₃)₂•2Py A (6 eq), B (3 eq) PPh₃ (3 eq) CH₀CN:PhMe:HMPA rt, 3h, 75% 16 examples (yields 60-100%). Clean inversion is observed for all 2° alcohols. A. Saito, K. Saito, A. Tanaka, T. Oritani Tetrahedron Lett. 1997, 38, 3955.

| Triphenyl Phosphine / Diethyl Azodicarboxylate (DEAD) | | Reagent |
|--|--------|--|
| Treatment of equatorial cyclohexanols with methanesulfonic acid (MsOH) under standard Mitsunobu conditions (title reagents) results in clean conversion to axial mesylates. Reaction of the latter with sodium azide yields the corresponding equatorial azides. | PPhs A | CO ₂ Me A (3 eq), B (3 eq) MsOH (2 eq) THF, 40°C, 1 d >75% MsO |
| A. P. Davis, S. Dresen, L. J. Lawless <i>Tetrahedron</i> Lett. 1997, 38, 4305. | В | 4 steroidal examples (yields 74-87%). |

| Methylenecyclopropane | | | | Reagent |
|---|----------|---|----------------------------|--------------------------|
| The title reagent undergoes Prins-type reactions with aldehydes in the presence of titanium tetrachloride. | <u> </u> | Me H A (3 eq) TiCl ₄ (1.5 eq) CH ₂ Cl ₂ , -78°C, 2 h | OH CI + OBn 62%, dr > 98:2 | Me OBn 14%, dr > 98:2 |
| K. Miura, M. Takasumi, T. Hondo, H. Saito, A. Hosomi <i>Tetrahedron Lett</i> . 1997 , <i>38</i> , 4587. | | 15 examples of mostly achira Conjugated aldehydes are po | | |

| Nitrogen Dioxide / Lithium Hydroperoxide | • | | Reagent |
|---|-------------------------|---------------------------|---|
| Secondary amides of polyfunctional molecules may be hydrolysed via a mild 2-step sequence comprised of <i>N</i> -nitrosation with A followed by treatment with lithium hydroperoxide (B). D. A. Evans, P. H. Carter, C. J. Dinsmore, J. C. Barrow, J. L. Katz, D. W. Kung <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 4535. | N₂O₄ A LiOOH B | hydrolysed selectively in | OAllyl TBSO OSO ₂ Me HO HCF ₃ e also featured. In the latter in the presence of a 1° amide d). |

| 1-Trimethylsilylpropan-2-one | | Reagent |
|---|-----|--|
| 2,4-Substituted butyrolactones are obtained in high stereopurity via a sequence of cross aldol-type coupling of 4-substituted butyrolactones with the title ketone, Peterson elimination and hydrogenation. | TMS | BnQ (a) LiHMDS, THF BnQ -78°C, 1 h then A , 20 min, 89% (b) HF-Pyr, MeCN, rt 30 min, 94% |
| S. Hanessian, T. Abad-Grillo, G. McNaughton-Smith <i>Tetrahedron</i> 1997 , <i>53</i> , 6281. | A | dr = 11 : 1 Routes to all four diastereoisomers of 4-hydroxymethyl-2-(2-propyl)-butyrolactone are also presented. |