Alcohols, ethers and phenols

C. S. HAU, ASHLEY N. JARVIS and JOSEPH B. SWEENEY‡

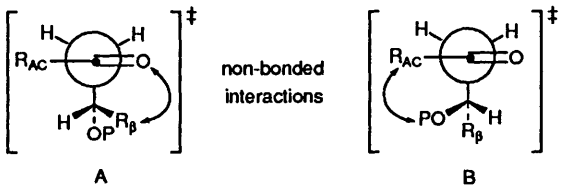
School of Chemistry, University of Bristol, Cantock's Close, Bristol BS8 1TS, UK
‡Present address: Department of Chemistry, University of Reading, PO Box 224, Whiteknights, Reading RG6 2AD, UK

Reviewing the literature published between August 1993 and February 1995
Continuing the coverage in *Contemporary Organic Synthesis* 1994, **1**, 243

1 Preparation of alcohols

1.1 From carbonyl compounds

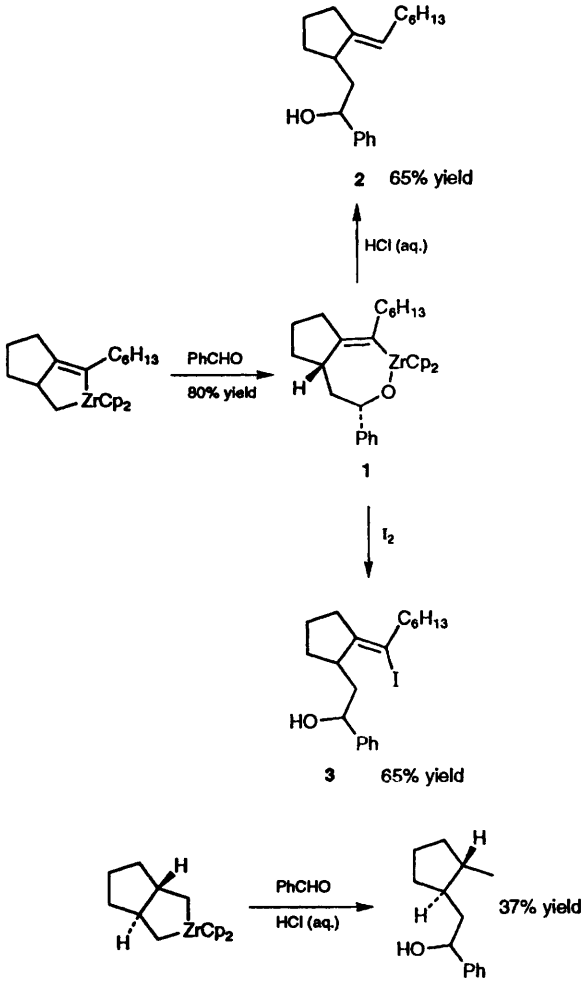
Evans, Dart and Duffy have examined the origins of 1,3-asymmetric induction in two well-known and much-utilised reactions of carbonyl compounds: hydride addition[1] and Mukaiyama-type aldol reactions.[2] As a result of these authors' experiments analysing the effects of acyl substituents (R_{AC}), β-substituents (R_β) and the steric demand of reducing agent, they have concluded that a revision of the original 'polar Cram model'[3] is necessary to account for *syn*-selectivity in non chelation-controlled reactions. Transition states (TS) A and B are proposed as those responsible for the observed stereoinductive effects, with A generally favoured in hydride reduction except when R_β is sterically demanding, in which case B may be preferred. In the case of Mukaiyama aldol reactions, TS B is generally preferred, because there is no acyl substituent (*i.e.* R_{AC} = H) and TS B minimises the non-bonded interaction shown in **Scheme 1**.



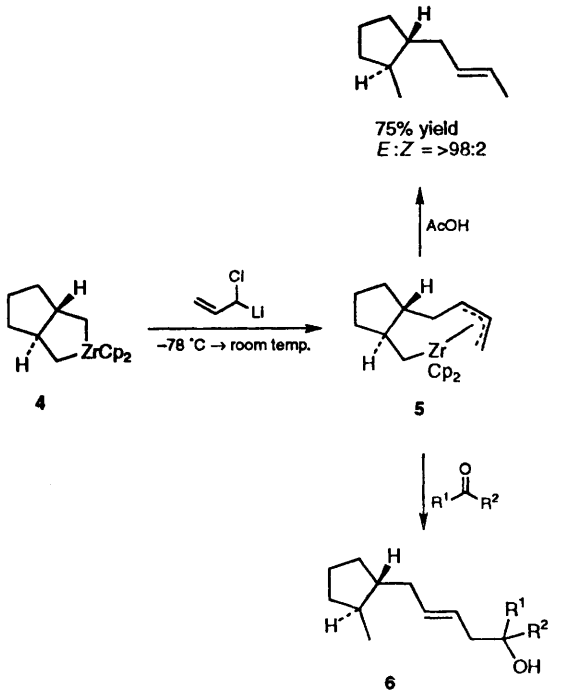
Scheme 1

1.1.1 Via carbon–carbon bond-forming reactions

3-Zircona-1-cyclopentenes and zirconacyclopentanes react with aldehydes to give oxazirconocycles **1** which may be protiolysed to (*E*)-pent-1-en-5-ols **2** or converted via reaction with elemental iodine to the corresponding 1-iodo analogues **3** (**Scheme 2**).[4] In a similar vein, Whitby and co-workers' contributions to organozirconium chemistry continue: zircona-cyclopentanes **4** undergo sequential insertion reaction with α-lithioallychloride (to give η^3-ally complex **5**) and aldehydes or ketones to give (after protonation) (*E*)-5-cyclopentylpent-3-en-1-η ols **6** in good yield (**Scheme 3**).[5] Where stereoisomers are produced, diastereoselectivities are low.

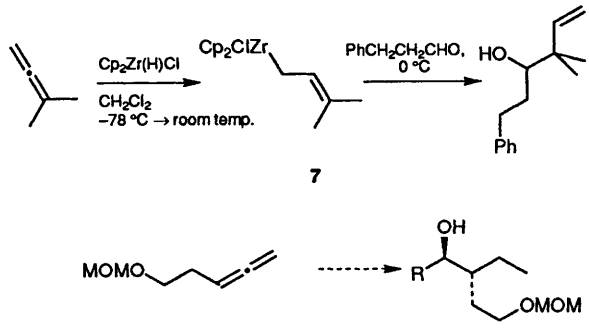


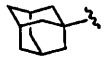
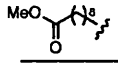
Scheme 2



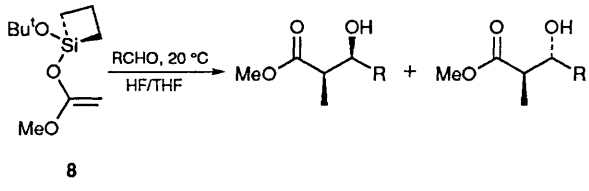
R^1	R^2	Yield of 6 (%)
H	Ph	90
H	2,4-di-MeO-Ph	60
H	Pr^i	90
H	Pr^n	95
Me	Me	54
Ph	Ph	57
—$(CH_2)_5$—		56

Scheme 3



R	Yield (%)	*anti*:*syn*
C_5H_{11}	79	96:4
C_3H_7	82	90:10
Ph	95	95:5
	77	99:1
	88	99:1
	90	95:5

Scheme 4



E:*Z* in **8**	R	Solvent	Yield (%)	*syn*:*anti*
0:100	Ph	$CDCl_3$	80	42:58
95:5	Ph	$CDCl_3$	94	95:5
89:11		$CDCl_3$	95	93:7
89:11	C_5H_{11}	$CDCl_3$	91	93:7
89:11	C_6H_{11}	$CDCl_3$	85	>99:1

Scheme 5

Hydrozirconation of 1,1-dimethylpropa-1,2-diene gives chlorodicyclopentadienylprenylzirconium **7** which allylates aldehydes and ketones in good yield with high *anti*:*syn* selectivity and with allylic rearrangement (**Scheme 4**).[6] The reaction may be applied to a range of other allenes.

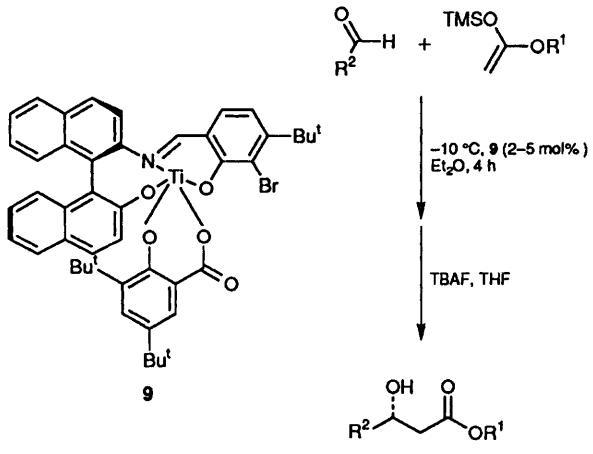
Enol(oxysilacyclobutanes) **8**, prepared from dichlorosilacyclobutanes[7] undergo highly diastereoselective and *uncatalysed* aldol addition reactions with aldehydes[8] (**Scheme 5**). However, only predominantly (*E*)-enols undergo diastereoselective aldol reaction. The reaction is proposed to proceed via the ubiquitous six-membered transition state.

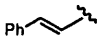
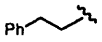
A new catalyst for asymmetric Mukaiyama aldol reactions has been reported.[9] Thus, catalyst **9**[10] effects highly enantioselective acetate aldol addition reactions (**Scheme 6**).

The aldol reactions of the lithium enolates of chiral *N*,*N*-dialkyl-α-aminomethylketones **10** are enantioselective,[11] due (it is proposed) to the boat-like chelate formed by the neighbouring amine (**Scheme 7**). This proposal is necessary because methylketone-derived lithium enolates usually react with poor enantioselectivity.

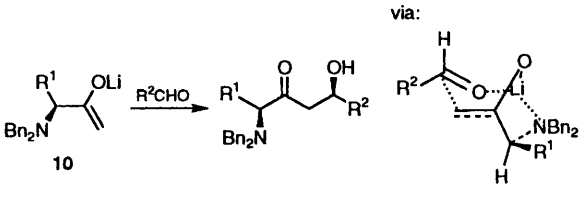
The Baylis–Hillman-like aldol condensation of α-allenic esters with aldehydes allows (*inter alia*) direct preparation of enynes (**Scheme 8**).[12] Microwave irradiation is reported to accelerate the rate of the Baylis–Hillman reaction of aldehydes and α,β-unsaturated esters and nitriles in the presence of DABCO.[13] At room temperature, these reactions can be notoriously sluggish, sometimes requiring 14 days for complete reaction. Using microwaves, the reactions are complete within 40 minutes.

Tetraallyltin is a chemoselective allylator of aldehydes; reaction of these components in aqueous HCl/THF mixtures gives an excellent yield of homoallylic alcohol (**Scheme 9**).[14] This contrasts very favourably with the less selective behaviour of many



R^2	ee (%) R^1 = Et	ee (%) R^1 = Me
	92	97
	88	95
	93	97
	81	94
C_6H_{11}	94	95
Ph	93	96

Scheme 6

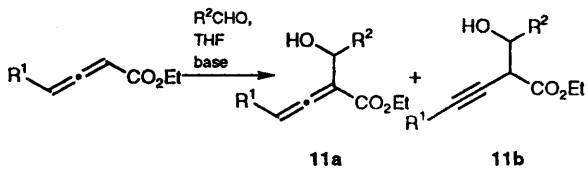


R^1	R^2	Yield (%)	de (%)
Me	Ph	84	60
Me	Pr^i	95	64
Me	Bu^t	91	76
Bu	Pr^i	81	78
Bu	Bu^t	78	80
Bu	Ph	76	85
Pr^i	Ph	90	>96
Pr^i	Pr^i	64	>96
Pr^i	Bu^t	88	>96

Scheme 7

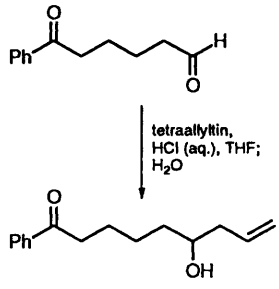
carbonyl allylators. Dials may react to give lactols (**Scheme 10**).

Titanocene monochloride facilitates a Prins-type reaction of cycloheptatriene with aldehydes (**Scheme 11**).[15] Yields are moderate and diastereoselectivities mediocre. The combination of trichlorosilane and a catalytic amount of $Pd(PPh_3)_4$ effects another high-



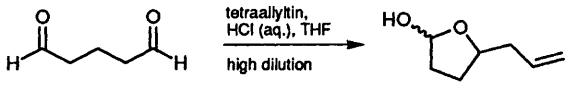
R^1	R^2	Base	Yield of **11a** (%)	Yield of **11b** (%)
H	Et	DABCO	41	0
H	Et	BuLi	58	0
H	Hex	DABCO	54	0
H	Ph	BuLi	56	0
H	C_9H_{19}–≡	BuLi	66	0
Me	Pr	BuLi	0	73
Me	Bu	BuLi	0	61
Me	Hex	BuLi	0	59
Et	Hex	BuLi	64	0

Scheme 8



98% yield

Scheme 9



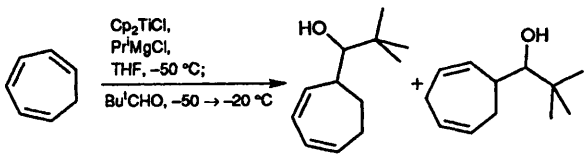
78% yield

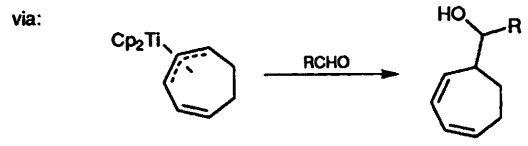
Scheme 10

yielding Prins-type reaction of 1,3-dienes with aldehydes (**Scheme 12**). Under these conditions, however, the reactions are highly diastereoselective, in favour of *syn* isomer.[16]

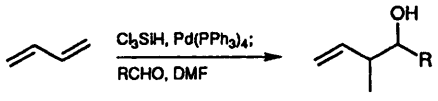
Allylic sulfones may be used as equivalents of allylic anions (**Scheme 13**) and used to prepare homoallylic alcohols.[17] Ytterbium triflate catalytically promotes allylation of aldehydes by allyltributyltin, in contrast to most other promoters which must be present in stoichiometric amounts.[18] Germanium iodide promotes allylation of aldehydes by allylic bromides[19] in the presence of diiodomethane. Zinc mediates allylation of aldehydes and ketones with cinnamyl chloride in an aqueous medium (**Scheme 14**).[20]

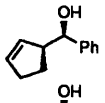
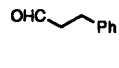
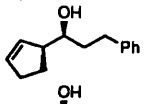
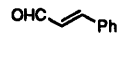
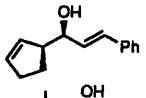
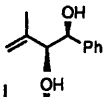
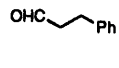
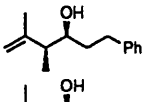
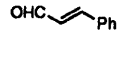
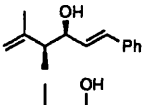
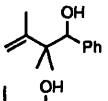
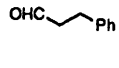
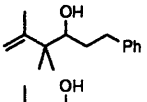
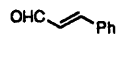
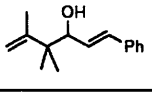
The enhanced thermal stability of fluorinated propenylzinc reagents compared to the



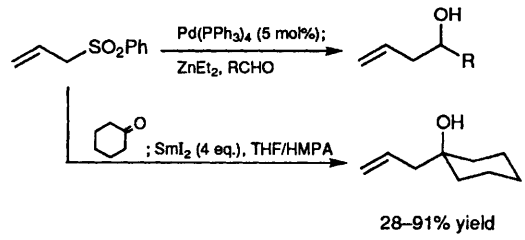


Scheme 11

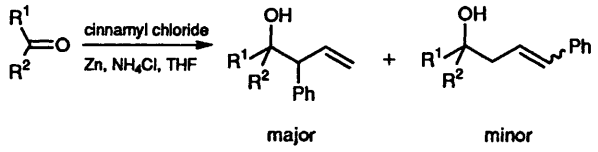


Diene	Aldehyde	Product	Yield (%)	Stereoselectivity
	PhCHO		91	>91% *syn*
			87	>99% *syn*
			86	>99% *syn*
	PhCHO		91	94% *syn*
			81	92% *syn*
			92	92% *syn*
	PhCHO		92	–
			83	–
			87	–

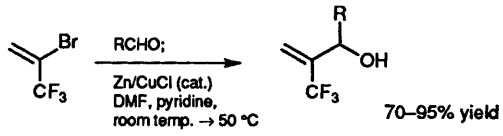
Scheme 12



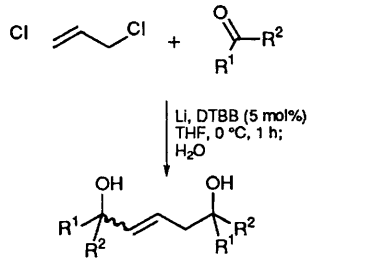
Scheme 13



Scheme 14



Scheme 15



R^1	R^2	Yield (%)	*E*:*Z*
Me	Me	72	1.3:1
Et	Et	60	1.6:1
—$(CH_2)_4$—		67	1.9:1
—$(CH_2)_5$—		50	1.3:1
Bu^t	H	64	1.1:1

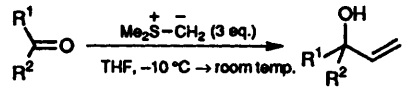
Scheme 16

corresponding lithium[21] and magnesium species[22] allows high-yielding preparation of 2 (trifluoromethyl)allylic alcohols via a Barbier-type reaction of 2-bromo-3,3,3-trifluoropropene with aldehydes (**Scheme 15**).[23]

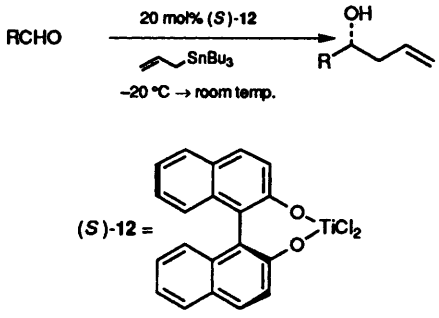
The use of 1,3-dichloropropene as a source of 1,3-dilithiopropene has been reported in full.[24] Reaction of 1,3-dichloropropene with lithium metal in the presence of a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB) and two equivalents of non-enolisable ketones and aldehydes gives substituted pent-3-ene-1,5-diols in moderate to good yield (**Scheme 16**). The reactions are believed to proceed by sequential metal–halogen exchange/carbonyl addition processes. *Z*:*E* ratios approach unity.

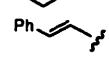
Treatment of carbonyl compounds with an excess of sulfonium ylid leads to an efficient vinylation reaction to give allylic alcohols (**Scheme 17**). The reaction involves nucleophilic addition to give a *β*-sulfonium alkoxide from which dimethyl sulfide is eliminatively removed by the excess ylid.[25]

Asymmetric carbonyl alkylation reactions involving organostannanes have continued to be of



Scheme 17

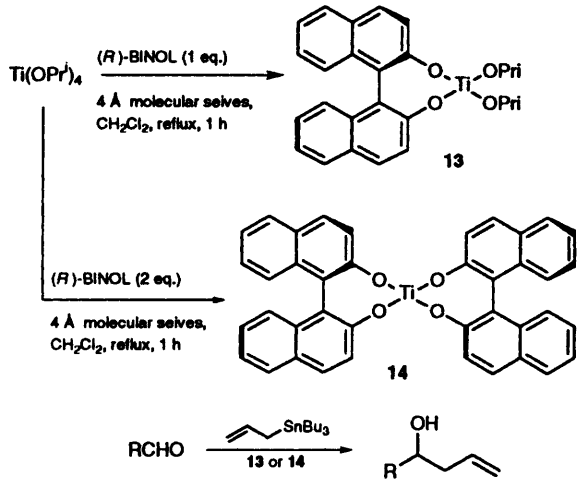


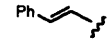
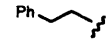
R	Yield (%)	ee (configuration) (%)
C_7H_{15}	83	97.4 (*R*)
C_5H_{11}	75	98.4 (*R*)
	75	92.6 (*S*)
	85	88.8 (*S*)
Ph	96	82.0 (*S*)
4-Py	90	80.2 (*S*)

Scheme 18

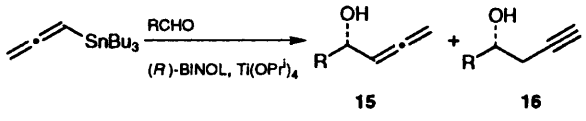
interest. Chiral binaphthyl titanates catalyse asymmetric allylation of aldehydes by allyltributyl tin, as has been described by several groups during the period covered by this review. (*S*)-Binaphthol-derived dichlorotitanate **12** asymmetrically catalyses the allylation of aromatic and aliphatic aldehydes with good to excellent enantioselectivity (**Scheme 18**).[26] The presence of molecular sieves is vital to the success of the reaction. In a similar study, Keck *et al.* report that reaction of titanium tetra-isopropoxide with either one or two equivalents of enantiomerically-pure BINOL gives catalysts **13** or **14** which exhibit good to excellent enantiocontrol in the allylation of a range of aryl, aliphatic and heteroaromatic aldehydes (**Scheme 19**).[27]

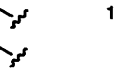
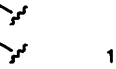
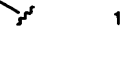
The Lewis acids derived from the reaction of (*R*)-BINOL with either a full or one half equivalent of $Ti(OPr^i)_4$ asymmetrically mediate the reaction of aryl and aliphatic aldehydes with allenyltributyl-stannane (**Scheme 20**).[28] Allenyl alcohols **15** rather than homoprop-2-ynylic alcohol **16** dominate the reaction mixtures; extensive conjugation in the carbonyl component leads to only allenic product, perhaps due to the concomitant rigidity of such systems. Although the reactions require stoichiometric amounts of catalyst and are not uniformly high-yielding, the enantioexcesses obtained are of useful levels (≥82% ee, often (≥90% ee).



R	Yield (%)	ee (%)	Catalyst
Ph	88	95	13
	95	92	14
	42 78	89 77	13 14
	98	96	14
	89	96	13
	73	96	13

Scheme 19



R	$Ti(OPr^i)_4$ (mol%)	Yield (%)	ee 15 (%)	15:16
Ph	50	48	>99	14:1
Ph	100	58	95	7:1
	50	50	94	>95:5 ("traces of B")
	100	52	94	>95:5 ("traces of B")
	50	25	82	100:0
	100	27	82	100:0
	50	76	95	23:1
	100	80	92	11:1
	50	64	89	4:1
	100	82	89	4:1

Scheme 20

Stoichiometric asymmetric allylation reactions have also been reported. The double asymmetric induction in the reaction of mannose-derived homochiral allylstannane **17** with homochiral aldehydes is pronounced; **17**, it is suggested, has a preference for *si*-face attack, but this preference is inherently weak, as shown in its reaction with achiral aldehydes. A mechanistic rationale, based on a Felkin–Ahn transition state, is proposed, to explain the underlying motives for matched and mismatched bond formation (**Scheme 21**).[29]

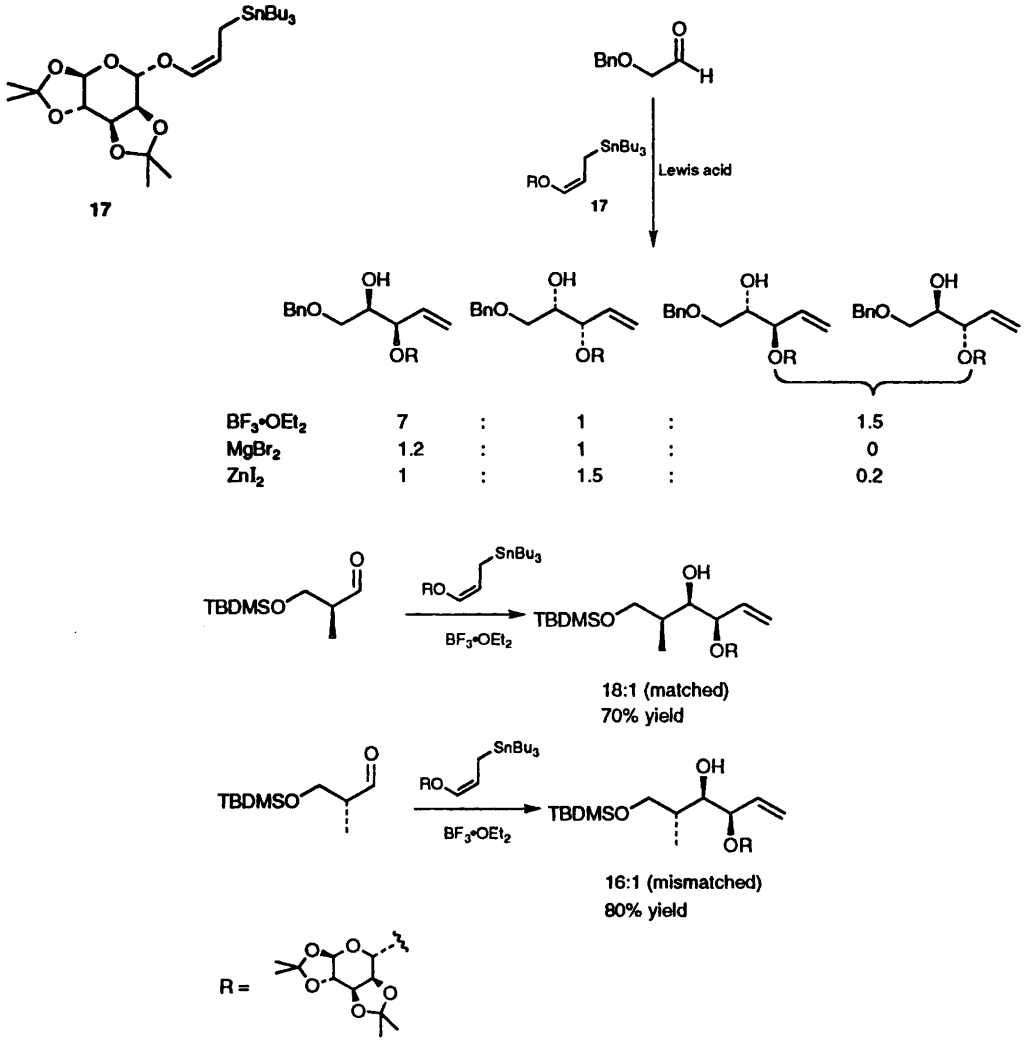
The demonstrated utility of remote asymmetric induction in reaction of δ-amino and δ-hydroxy-allylstannanes[30] with aldehydes has been extrapolated to allow an efficient 1,7-asymmetric induction. Thus, homochiral 6-hydroxyallylstannanes **18** react with aryl and aliphatic aldehydes in the presence of tin(IV) bromide to give predominantly *syn*-(*Z*)-hept-4-ene-1,7-diols in moderate to good yield (**Scheme 22**).[31] A review has appeared concerning the utility of such homochiral δ-oxygenated allylstannanes in the asymmetric allylation of aldehydes.[32]

L-Quebrachitol has been employed as a chiral auxiliary in the asymmetric [3+2]-cycloaddition reaction of allylsilanes with α-ketoesters. Diastereocontrol and enantiocontrol in the reaction is impressive (**Scheme 23**).[33]

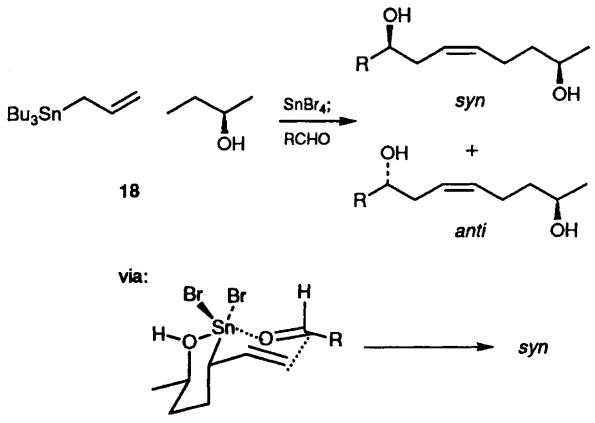
Acylsilanes may be enantioselectively allylated using *B*-allyl diisopinocampheylborane. Enantioexcesses are moderate to low (**Scheme 24**).[34]

Soai has described the asymmetric alkenylation of prochiral enals using diastereoface-selective delivery of vinylzinc reagents (**Scheme 25**).[35] Using proline-derived chiral chaperones, the yields and enantioexcesses of the reaction were moderate. The chemo- and enantioselective alkylative addition reactions of ketoaldehydes with diethylzinc in the presence of (−)-*N,N*-dibutyl norephedrine [(−)-DBNE] has been described in full by the same group (**Scheme 26**).[36] Enantioexcesses were moderate (≈80%) while chemoselectivity was excellent.

The reaction of esters with a double equivalent of Grignard reagent in the presence of tetrapropyl titanate or tributyl vanadate is known to give α-alkylcyclopropanols.[37] Corey has found that use of

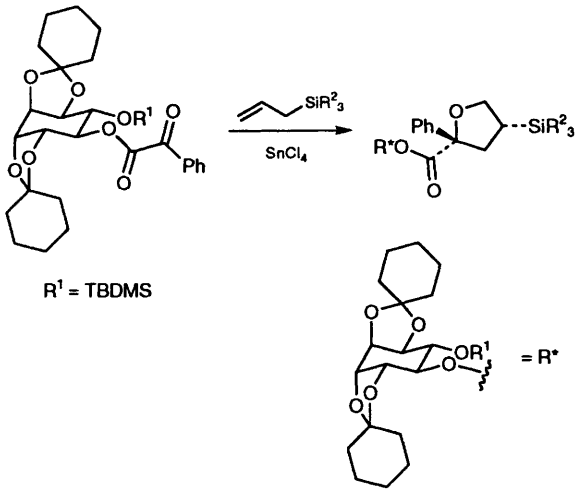


Scheme 21



R	Yield (%)	*syn* : *anti*
Ph	72	92:8
4-Cl-C_6H_4	71	92:8
4-Me-C_6H_4	47	89:11
2-Naphthyl	65	93:7
Pr^i	63	89:11
Me	36	90:10
Et	61	91:9
Bu^i	58	85:15
Bu^t	38	95:5

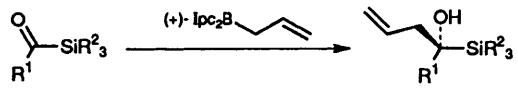
Scheme 22



SiR^2_3	Yield (%)	de (%)	ee (%)
Me_3Si	72	>98	95
$PhMe_2Si$	78	>98	>98
Bu^tMe_2Si	83	>98	96
Bu^tPh_2Si	85	>98	98

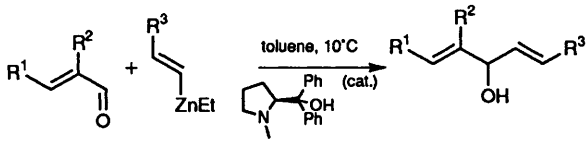
Scheme 23

catalytic amounts of chloro(triisopropyloxy)-titanium(IV) in place of the full alkoxide and use of an excess of magnesium allows a diastereoselective synthesis of *cis*-1,2-disubstituted cyclopropanols from esters (**Scheme 27**).[38] The reaction is not



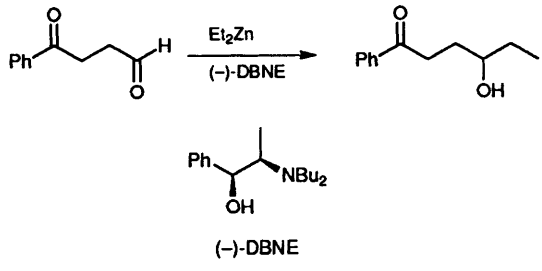
R^1	SiR^2_3	Yield (%)	ee (%)
2-thienyl	$SiMe_2Ph$	81	17
4-CF_3-C_6H_4	$SiMe_2Ph$	81	36
4-CH_3-C_6H_4	$SiMe_2Ph$	65	26
c-C_5H_9	$SiMe_2Ph$	70	42
prenyl	TMS	72	89

Scheme 24



R^1	R^2	R^3	Yield (%)	ee (%)
Ph	H	Bu	59	77
Ph	Me	Bu	56	75
Ph	Me	$(CH_2)_{12}CH_3$	39	73

Scheme 25

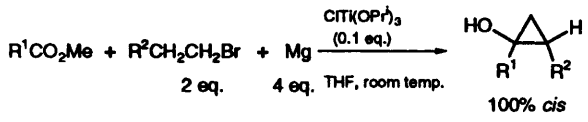


Scheme 26

applicable to benzoates and α-branched esters. When TADDOL catalysis was applied, moderate enantioselectivity was obtained (~70% ee).

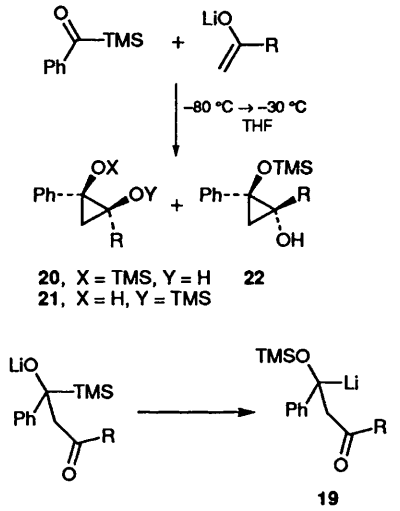
Takeda *et al.* have found that a 3-*exo*-trig reaction of a Brook rearrangement derived α-silyloxy anion **19** allows preparation of 1,2-dihydroxycyclopropanes **20–22** in good yields (**Scheme 28**).[39] Anion **19** is generated by reaction of an acyl silane with a lithium enolate of a methyl ketone. *cis*-Isomers predominate, but in these isomers the silyl group is scrambled between both hydroxy groups. When silylvinyl ketones are employed in the reaction, yields are lower because of competing Michael addition, but no migration of silicon is observed and only *trans*-diastereoisomers are obtained (**Scheme 29**).

The same authors also reported a similar Brook rearrangement at the heart of a novel



R^1	R^2	Yield of alcohol (%)
Pr	Et	79
Hex	Et	81
Hex	Hex	88
$PhCH_2CH_2$	Et	79
$PhCH_2CH_2$	Me	83
H	Hex	72
H	Ph	80
Me	Me	80
Me	Ph	83

Scheme 27



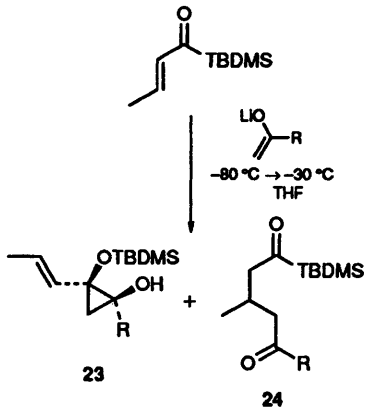
R	Yield (%) 20	21	22
Et	64	21	0
Pr^n	59	21	0
Pr^i	90	7	0
Bu^t	75	0	9

Scheme 28

[3+2]-cyclopentene annulation reaction between 3-heterosubstituted α,β-unsaturated acyl silanes and ketone enolates (**Scheme 30**).[40] The reaction was utilised in a synthesis of clavulone II (**Scheme 31**).

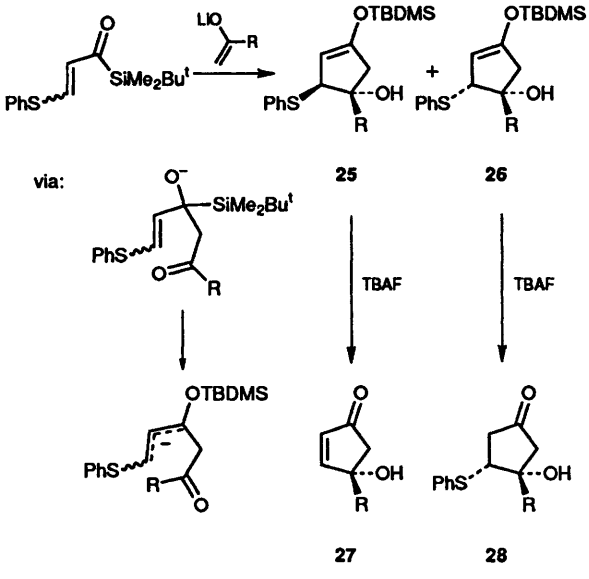
Benzocyclobuten-1-ol derivatives may be prepared by 4-*exo*-trig cyclisation of *O*-acyl benzylic anions (**Schemes 32 and 33**).[41]

The recent popularity for oxazaborolidine-mediated asymmetric reactions has led to a concomitant demand for homochiral 2,2-dialkylated amino alcohols. Luche *et al.* have reported a simple racemisation-free method for preparation of such dialkylated aminols from L-valine (**Scheme 34**).[42]



R	Yield (%) 23	24
Et	35	53
Pr^n	30	51
Pr^i	40	50
Bu^t	36	21

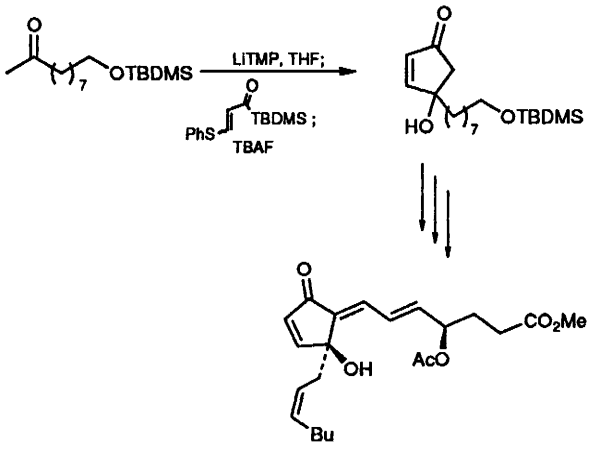
Scheme 29



R	Yield (%) 25	26	27	28
Pr^i	55	19	17	19
Et	70	5	70	83
Pr^n	74	7	77	87
Oct	71	8	66	73

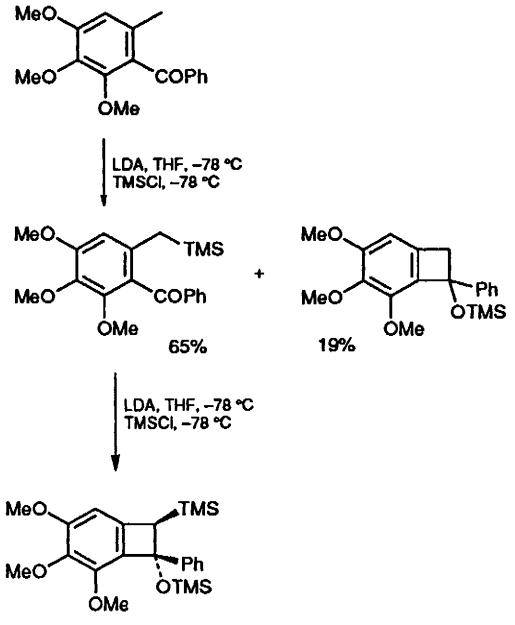
Scheme 30

1,1-Dichloro-2-hydroxynitroalkanes may be prepared efficiently via a Reformatsky-like version of the Nef reaction. Thus trichloronitromethane reacts with aryl and aliphatic aldehydes in the presence of tin(II) chloride to give the coupled products.[43]

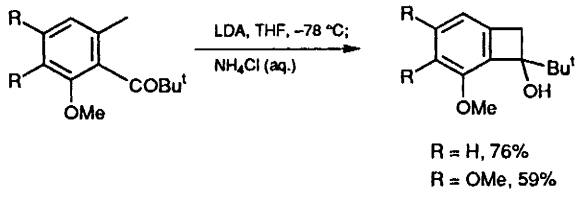


clavulone II

Scheme 31



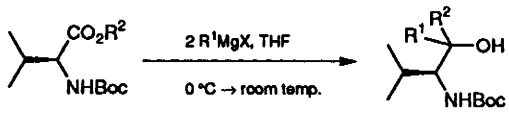
Scheme 32



Scheme 33

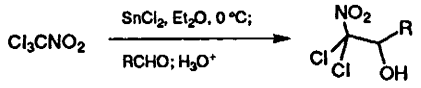
1.1.2 Alcohol synthesis by reductive addition to carbonyl compounds

Homochiral α-amino aldehydes may be pinacol-coupled using the well-documented low-valent metal reagents of Pedersen (**Scheme 36**). Thus, a slight excess of an aliphatic aldehyde reacts with such



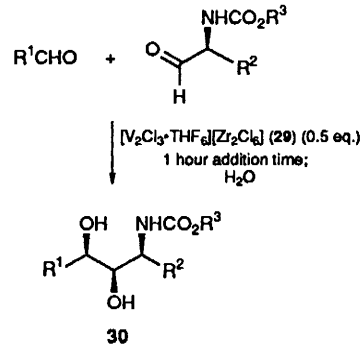
R^1	Yield (%)
Me	84
Bu^n	71
$C_{10}H_{21}$	48
Bu^i	87
neo-C_5H_{11}	10
Ph	78

Scheme 34



52–92% yield

Scheme 35



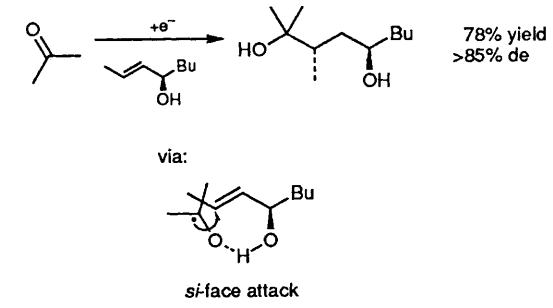
30

R^1	R^2	R^4	R^5	Yield (%)	de
Pr^i	Pr^i	H	Bu^t	70	>20:1
Bu^i	$PhCH_2$	H	Bu^t	67	>20:1
$PhCH_2CH_2$	$PhCH_2$	H	Bu^t	67	>20:1
c-C_6H_{11}	$ZNH(CH_2)_4$	H	Bn	75	>20:1
$C_{12}H_{25}$	$BnOCH_2$	H	Bn	54	>20:1

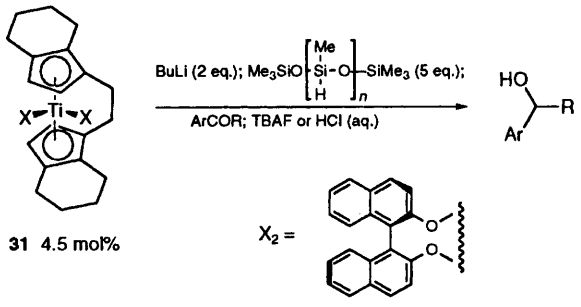
Scheme 36

aldehydes in the presence of low-valent vanadium reagent **29** to give 1,2-*syn*-2,3-*syn*-2-amino-1,2-diols of general formula **30**, in good yield.[44] Allylic alcohols may be electrochemically-coupled with ketones to give 1,4-diols (**Scheme 37**).[45]

Full details of what is claimed to be the first efficient asymmetric hydrosilylation protocol for reduction of aryl ketones has been unveiled by S. L. Buchwald *et al.* (**Scheme 38**).[46] Thus chiral catalyst **31** mediates hydrosilylation of aryl alkyl ketones by polymethylsiloxane according to the previously proposed mechanistic pathway (**Scheme 39**).[47] Enantioselectivities are generally high (⩾90% ee). Polymethylsiloxane (PHMS) also reduces carboxylic

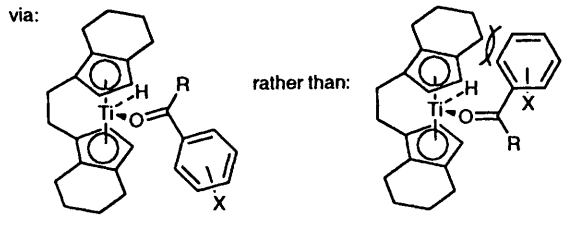


Scheme 37

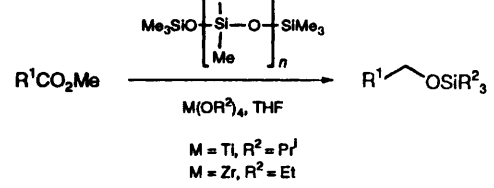


Ar	R	Configuration of product	Yield (%)	ee (%)
Ph	Me	*S*	73	97
2-Naphthyl	Me	*S*	84	95
2-Cl-C_6H_4	Me	*S*	78	90
4-Me-C_6H_4	Me	*S*	84	96
4-F_3C-C_6H_4	Me	*S*	66	65

Scheme 38

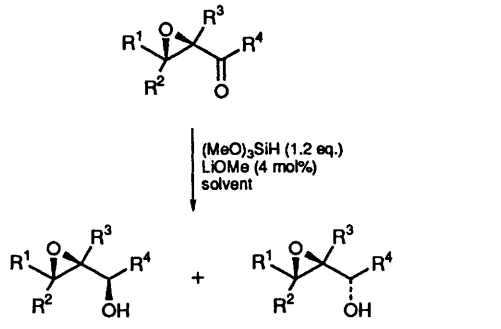


Scheme 39



R	Equivalents of PHMS	Equivalents of $M(OR^2)_4$	Yield of silyl ether (%)
Ph	0.1	1	86
Bn	0.1	1	76
	0.1	1	65
	0.1	1	82
4-NO_2-C_6H_4	0.1	1	84
	0.1	1	89

Scheme 40



R^1	R^2	R^3	R^4	Solvent	Yield (%)	*syn*:*anti*
H	H	H	Ph	Et_2O	100	8:92
H	H	Me	Ph	Et_2O	91	34:66
Me	H	H	Ph	Et_2O	99	9:91
Me	Me	H	Ph	Et_2O	88	0:100
H	H	H	Bu	Et_2O	78	11:89
H	H	Me	Bu	Et_2O	84	11:89
H	H	H	Ph	HMPA	98	90:10
H	H	Me	Ph	HMPA	91	72:28
Me	H	H	Ph	HMPA	99	93:7
Me	Me	H	Ph	HMPA	100	60:40
H	H	H	Bu	HMPA	88	81:19
H	H	Me	Bu	HMPA	90	44:56

Scheme 41

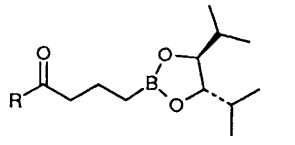
esters to give silylated primary alcohols in the presence of titanates and zirconates (**Scheme 40**).[48] Alcohols are liberated from the silyl ethers by alkaline hydrolysis. Carboxylic acids are also reduced to primary alcohols (63–80% yield).

α,β-Epoxyketones may be reduced to the appropriate alcohol by trimethoxysilane in the presence of lithium methoxide catalyst (**Scheme 41**). The diastereoselectivity of the process is solvent-dependent, allowing for choice of chelation-controlled or Felkin–Ahn-type transition states. At best, exclusive *anti* or very predominantly *syn* products may be obtained. Yields are generally good.[49]

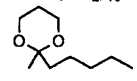
A pronounced 1,7-asymmetric induction is seen when boronate-containing β-γ-unsaturated ketones

(prepared by 1,4-addition of boronomethylzinc reagents to enones) are reduced using borane complexes (**Scheme 42**).[50] Thus, ketoborinates are reduced with high enantioselectivity by achiral borane–dimethylsulfide. The authors propose a pseudo-axial attack of hydride on a half-chair chelated conformer to rationalise the results (**Scheme 43**).

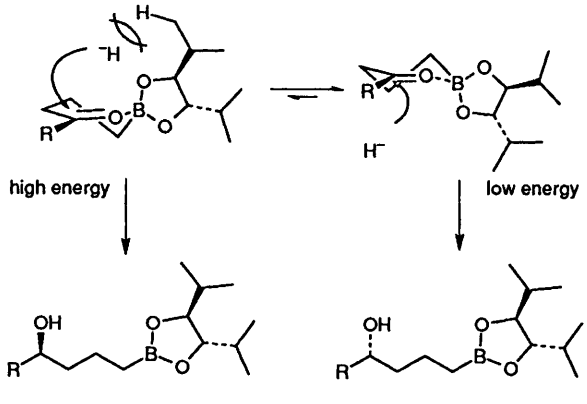
Evans and co-workers have described the results of their studies into asymmetric catalysis of the Meerwein–Ponndorf–Verley reduction of prochiral ketones.[51] The authors replaced the aluminium isopropoxide of the classical reaction by samarium(IV) species **32**, readily prepared from benzylamine and commercially available (*R*)-styrene oxide. This complex catalyses a highly enantioselective reduction of aryl alkyl ketones (**Scheme 44**).



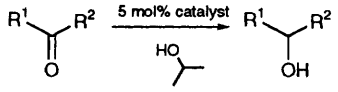
major minor

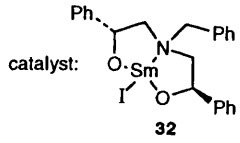
R	ee (%)	Yield (%)
Me	85	83
Pent	42	87
Hex	>98	85
Ph	97	95
$Cl(CH_2)_3$	93	97
$NC(CH_2)_{10}$	97	81
	98	89
$MeO_2C(CH_2)_4$	>96	95

Scheme 42

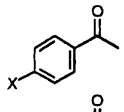
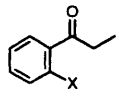
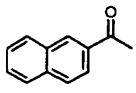
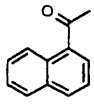


Scheme 43





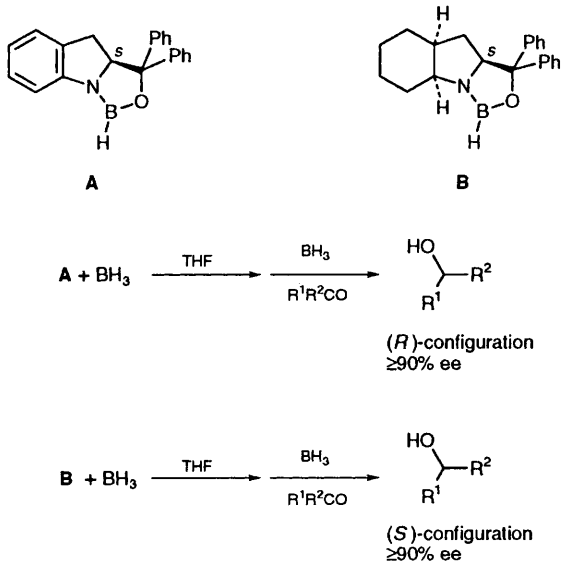
32

Substrate		Yield of alcohol (%)	ee (%)
	X		
	Cl	96	97
	H	74	96
	OMe	95	96
	X		
	OMe	31	92
	NO_2	77	94
	X		
	Cl	78	68
	H	63	73
		82	96
		95	97

Scheme 44

Oxazaborolidines derived from (*S*)-indoline-2-carboxylic acid asymmetrically catalyse the reduction of prochiral ketones. Whilst in itself not entirely without precedent, the ability to prepare from a common precursor chiral controllers which provide either enantiomer of an alcohol is of interest (**Scheme 45**).[52]

Noroyi *et al.* have reported the reduction of carbonyl compounds using a simple metal hydride



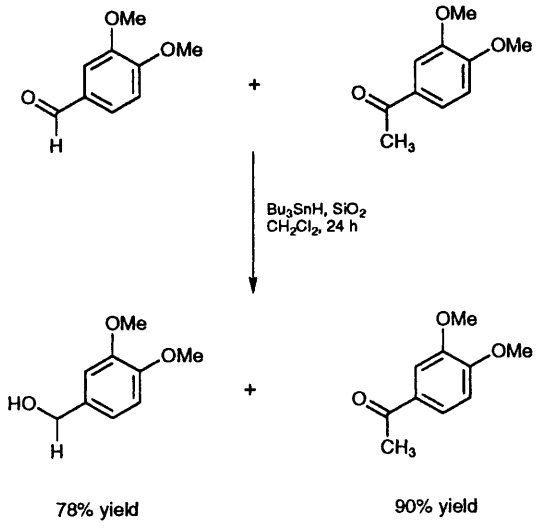
Scheme 45

(**Scheme 46**).[53] The authors found that the combination of commercial LiH and TMSCl in the presence of a catalytic amount of metallic zinc or a zinc(II) salt would reduce aldehydes and ketones to the corresponding TMS ethers in good yield.

Silica gel enhances remarkably the carbonyl-reducing activity of Bu_3SnH.[54] Aryl and aliphatic ketones and aldehydes undergo reduction, but the reduction is chemoselective, with the carbonyl of greater electrophilicity reacting preferentially (**Scheme 47**).

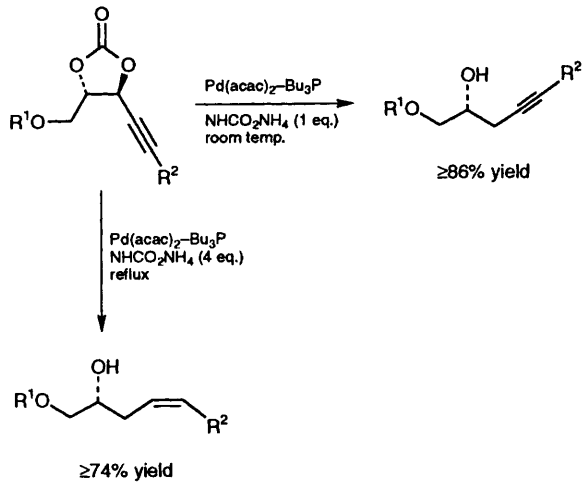
R^1	R^2	Catalyst	Yield of silyl ether (%)
Ph	Me	Zn	90
Ph	Me	$Zn(OSO_2Me)_2$	92
C_6H_{13}	CH_3	$ZnCl_2$	92
Bu^t	CH_3	$Zn(OSO_2Me)_2$	85
$-(CH_2)_5-$		Zn	89
Ph	H	$Zn(OSO_2Me)_2$	88
Bu^t	H	$Zn(OSO_2Me)_2$	96

Scheme 46

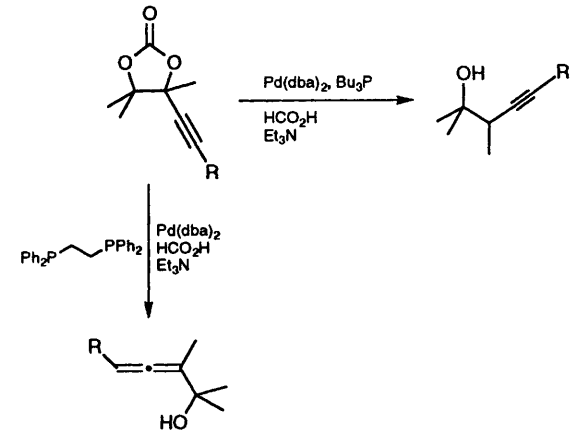


Scheme 47

Prop-2-ynylic cyclic carbonates may be reduced to either (*Z*)-homoallylic alcohols or homoprop-2-ynylic alcohols by catalytic hydrogenolysis using $Pd(acac)_2$ (**Scheme 48**).[55] The former are obtained by carrying the reaction out at the boiling point of toluene, whilst the latter result from reduction at ambient temperature. In a related reaction, alkynyl cyclic carbonates are reduced to *either* homoprop-2-ynylic alcohols or α-allenyl alcohols by a ligand-tuneable catalytic hydrogenolysis using $Pd(dba)_2$ (**Scheme 49**).[56] Simple monodentate phosphine ligands favour formation of alkynes, while biphosphines favour allenes.



Scheme 48



Scheme 49

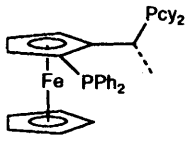
1.2 Oxidative methods for alcohol synthesis

Full details have appeared concerning the utility of (*R*)-1-[(*S*)-2-(diphenylphosphino)ferrocenyl]-ethyldicyclohexylphosphine **33**, better and more comfortably christened (*R*)-(*S*)-josiphos (after the technician involved in its preparation). This catalyst allows highly enantioselective hydroboration of alkenes to give, after usual peroxidative work-up, enantiomerically enriched alcohols. Yields of the process are good and enantioselectivities are moderate to high (**Scheme 50**).[57] The catalyst also mediates asymmetric reduction of β-ketoesters, but the ee's of the β-hydroxyesters produced are not as high as Noroyi's Ru–BINAP system (84–97% versus >99% ee).

Samarium(III) iodide catalyses the hydroboration of alkenes by catechol borane (**Scheme 51**).[58] The samarium species is present in one-tenth stoichiometry and was selected as the best catalyst from a range of lanthanide complexes. The reactions do not proceed to completion in several cases and high selectivity is not ubiquitous.

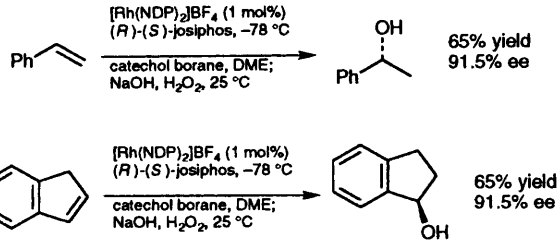
The usually less reactive conjugated double bond of cyclohexenones may be selectively hydroxylated

to either *cis*- or *anti*-1,3-diols by a two-step reduction–oxidation process (**Scheme 52**).[59] Thus, reaction of pulegone with a higher-order phenyldimethylsilyl cuprate gives the chromatographically-separable 1,4-addition products which may be selectively reduced: dissolving metal reduction of the addition products followed by peroxidative

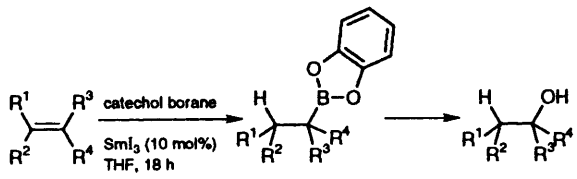


(*R*)-(*S*)-josiphos

33

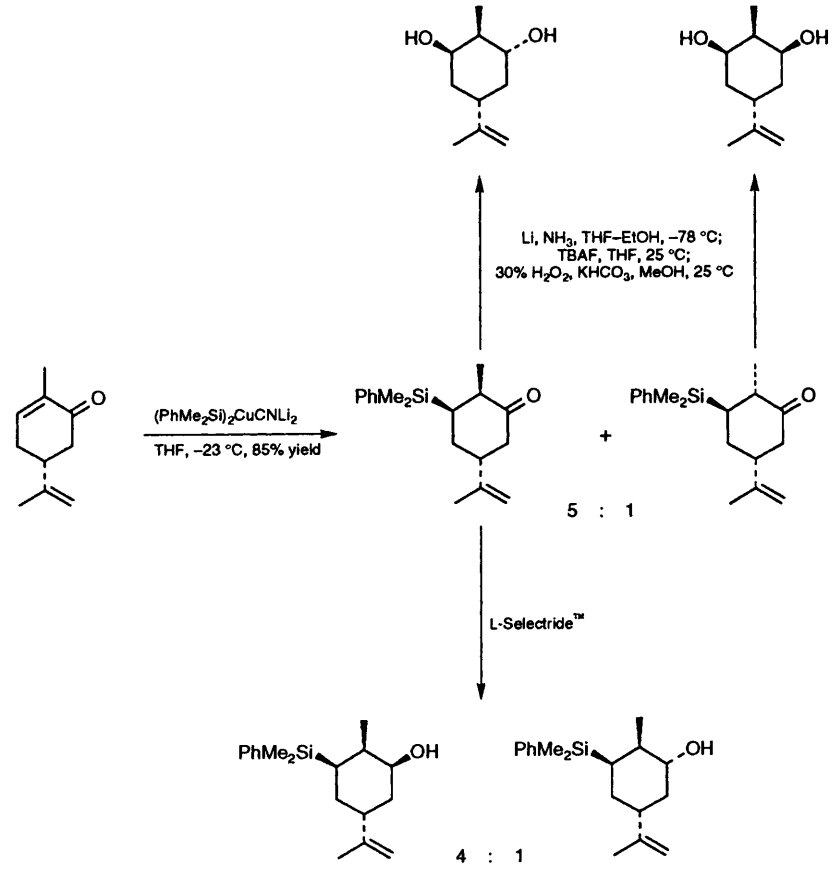


Scheme 50



Alkene	Yield (conversion) (%)	Selectivity
C_8H_{17}	79(98)	50:1 (primary:secondary)
Ph	47(59)	5:1 (primary:secondary)
Ph	81(91)	>99:1 (primary:tertiary)
	78(97)	27:1 (*exo*:*endo*)
Ph Ph	67(86)	–
Ph	64(85)	>99:1 (*trans*:*cis*)
	61(79)	
OH Ph	85(99)	2:1 (*syn*:*anti*)

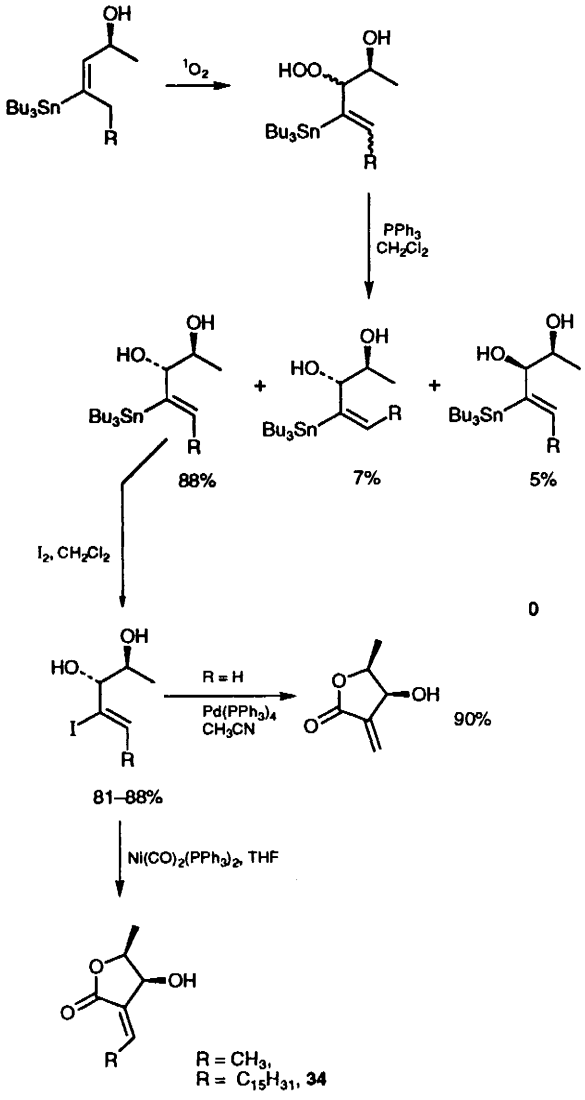
Scheme 51



Scheme 52

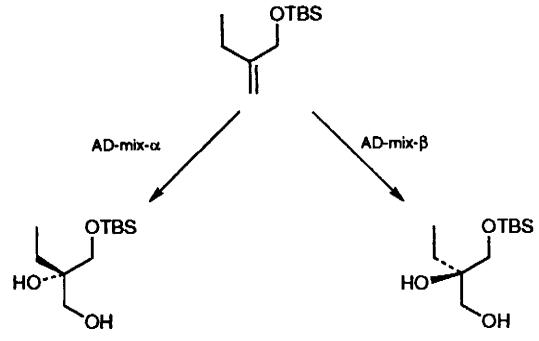
desilylative hydroxylation gives *anti*-diols exclusively, whereas use of L-Selectride™ as reducing agent gives the *syn*-isomer.

The Schenk reaction has been employed to good effect in a concise synthesis of homochiral α-methylene lactones. Thus, homochiral 3-tributylstannyl allyl alcohols react with singlet oxygen in a highly diastereoselective fashion to give (after reductive work-up) mainly *trans*-diols (**Scheme 53**). The major product of the reaction was converted in a two-step process to α-methylene lactones, including dihydromanubanolide B **34**.[60]



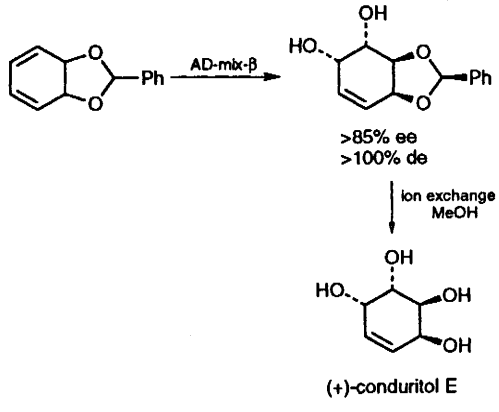
Scheme 53

Interest in asymmetric dihdroxylation (AD) of alkenes has continued unabated, as expected. A review of the area has appeared,[61] along with a review of the general ligand-accelerated catalysis,[62] the cornerstone of the AD reaction. What *is* surprising is an example of AD which apparently violates the predictive mnemonic of Sharpless. Hale and co-workers have reported that 1,1-disubstituted alkenes in which one of the substituents is a silyloxymethyl moiety undergo AD with *opposite* enantioinduction to that expected (**Scheme 54**).[63] In most cases, enantioexcesses are low, perhaps indicating that these inverted preferences are to do with steric inhibition.

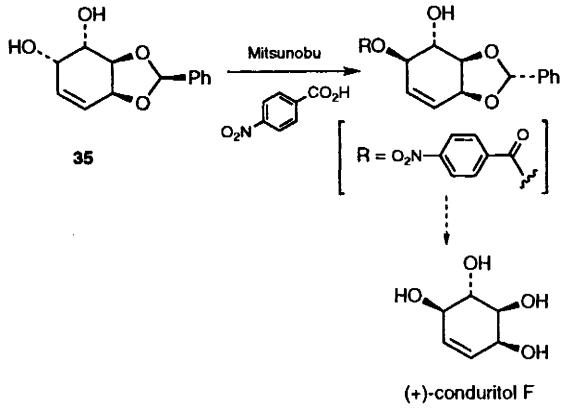


Scheme 54

Methanesulfonamide-accelerated AD was also used in the synthesis of a conditurol. Thus, the benzylidine acetal of *cis*-1,2-dihydroxycyclohexa-3,5-diene underwent diastereo- and enantioselective dihydroxylation, and deprotection of the resulting diol gave (+)-conduritol E (**Scheme 55**).[64] The same group further reports that acetonide diol **35** may be subjected to a Mitsunobu reaction to give (after deprotection) (+)-conditurol-F (**Scheme 56**).[65]

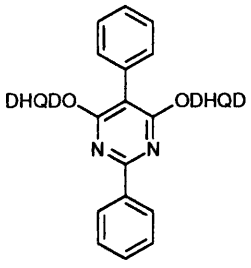


Scheme 55



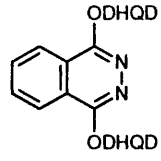
Scheme 56

Several other interesting reports have emerged from the Scripps Institute: firstly, an improved method for the asymmetric dihydroxylation of tetrasubstituted alkenes.[66] The use of the 'methanesulfonamide addition effect'[67] leads to good yields of *cis*-diols: enantioselectivities are, however, variable (20–97% ee). Terminal alkenes undergo dihydroxylation with improved enantioexcess using cinchona alkaloids bonded to pyrimidines and phthalizines (**36** and **37** respectively) (**Scheme 57**).[68]



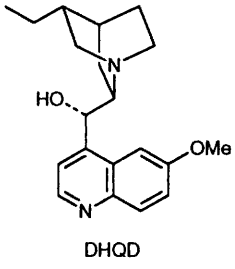
$(DHQD)_2$-PYR

36



$(DHQD)_2$-PHAL

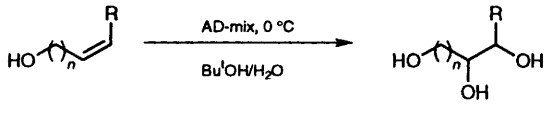
37

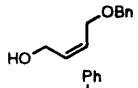
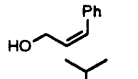
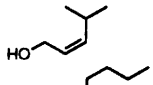
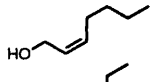
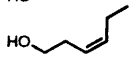


DHQD

Scheme 57

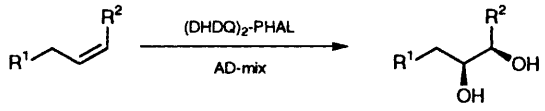
An improvement to the reaction of *cis*-allylic and homoallylic alcohols has been reported.[69] This paper reports the results of the study into the suitability of the various AD-mixes with such substrates: these data are summarised diagrammatically in **Scheme 58**. The enantioselectivity of the reaction is



Substrate	ee (%) (absolute configuration) $(DHDQ)_2$-PHAL	$(DHQ)_2$-PHAL	DHQD-IND
	64 (2*S*, 3*R*)	57 (2*R*, 3*S*)	31 (2*S*, 3*R*)
	71 (2*S*, 3*R*)	73 (2*R*, 3*S*)	72 (2*S*, 3*R*)
	74 (2*S*, 3*R*)	64 (2*R*, 3*S*)	51 (2*S*, 3*R*)
	64 (2*S*, 3*R*)	–	–
	54 (3*S*, 4*R*)	45 (3*R*, 4*S*)	–

Scheme 58

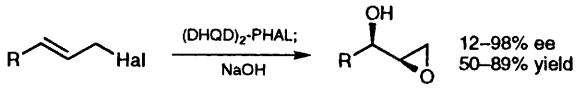
moderate, but the authors point out that, in the homoallylic example, the near symmetry of the alkene makes *any* selectivity surprising. The authors suggestion of an hydrogen-bonding rôle for the OH group is reinforced by the poor ee shown in dihydroxylation of the corresponding methyl ethers (**Scheme 59**).



R^1	R^2	ee (%)
MeO	CH_2OBu	23
MeO	Ph	13
$MeOCH_2$	Et	0
H	Ph	35

Scheme 59

Homochiral 2,3-epoxyalcohols may be prepared from allylic halides in a two-step sequence involving asymmetric dihydroxylation followed by ring-closure (**Scheme 60**).[70] Yields and enantioexcesses are moderate to excellent.

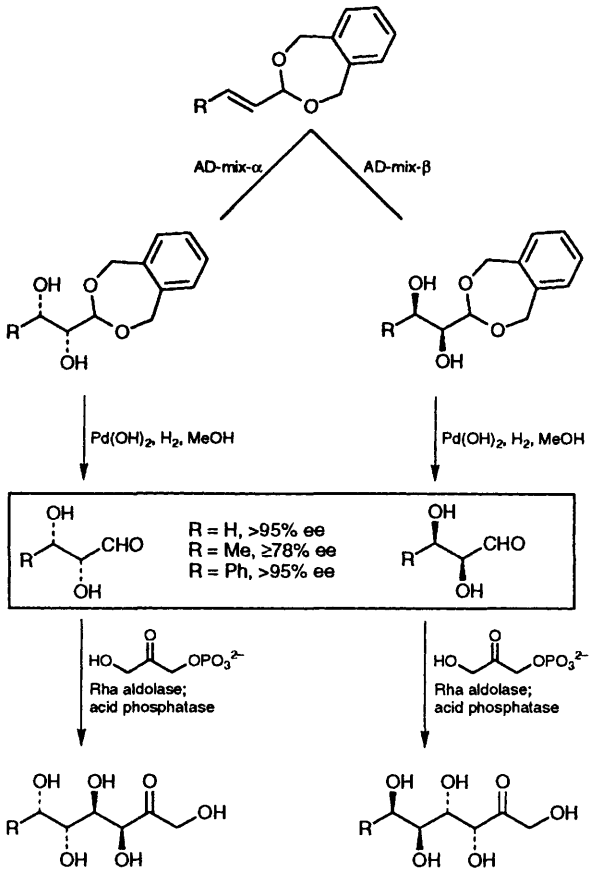


Scheme 60

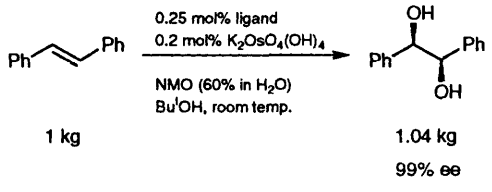
Sharpless and Wong have joined forces to devise a chemoenzymatic synthesis of carbohydrates.[71] When the products of the AD reactions of α,β-unsaturated aldehydes (or equivalents) are subjected to reaction with hydroxy acetone monophosphate in the presence of aldolase enzymes, ketotetrols are obtained in high enantioexcess (**Scheme 61**).

The AD of olefins containing sulfur has been reported: the reaction is chemoselective in the presence of sulfides, dithianes and disulfides.[72] Sharpless has reported at length on the mechanistic studies underway to elucidate the exact species involved in the AD reaction.[73] Full details have appeared concerning the highly diastereo- and enantio-selective asymmetric dihydroxylation reaction of polyenes using phthalazine-modified AD protocols.[74]

An impressive example of the ease of use of the Sharpless AD reaction has been reported to allow a 'solid-to-solid' asymmetric synthesis of hydrobenzoin on a kilogram scale (**Scheme 62**).[75] Bu'OH lowers the solubility of stilbene, thereby approximating the optimal 'slow addition' protocol required for high enantioexcess. Furthermore, hydrobenzoin is also poorly soluble in the solvent. Thus, the reaction is marked by the slow disappearance of solid substrate



Scheme 61

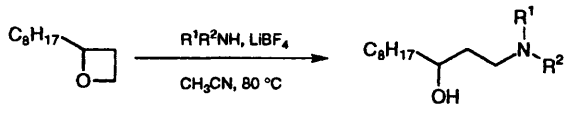


Scheme 62

and the concomitant appearance of solid enantiomerically pure product. This is probably as close as research chemists will get to Cornforth's idea of a process chemist's ideal reaction (a one-armed man pouring reagents into a bath and collecting pure product from the drain pipe)!

1.3 Alcohol synthesis

Crotti's work on selectivity and efficacy of epoxide heterolysis continues unabated. Lanthanide(III) trifluoromethanesulfonates have been unveiled as the latest catalyst for such reactions, in particular for aminolysis of monosubstituted epoxides and cycloalkene oxides.[76] A similar reaction using cuprate reagents has been reported.[77] Crotti has also published details of the $LiBF_4$-promoted aminolysis of oxetanes.[78] Ring-opening nucleophilic attack

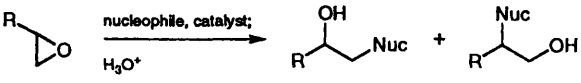


R^1	R^2	Yield (%)
Bu^t	H	95
Et	Et	88
Pr^i	Pr^i	92
Ph	H	98
		86

Scheme 63

occurs at the carbon atom of lesser substitution (**Scheme 63**).

Organoimido complexes of transition metals have been demonstrated to be effective in the regioselective ring opening of epoxides (**Scheme 64**). These complexes (previously used in ROMP processes[79]) are highly soluble in organic solvents, have ligand-tuneable Lewis acidity and a high tolerance of spectator functionality. Metal ions examined were Cr(V), Cr(VI), Mo(VI) and W(VI) and this order reflects the order of electrophilicity.[80]

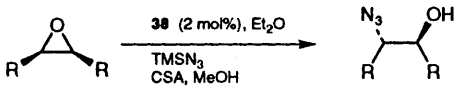


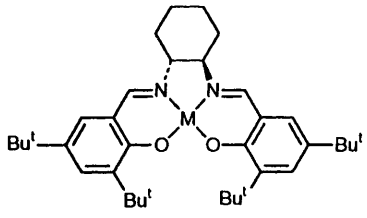
R	Nucleophile	Nu	Catalyst	Yield of A (%)	Yield of B (%)	Reaction time (h)
Ph	$TMSN_3$	N_3	1	31	64	3
Ph	$TMSN_3$	N_3	2	0	95	12
Ph	$TMSN_3$	N_3	3	0	45	48
Ph	$TMSN_3$	N_3	4	0	95	120
Bu^n	$TMSN_3$	N_3	1	26	39	72
Bu^n	$TMSN_3$	N_3	4	0	80	120
Ph	Bu^{t}NHTMS	Bu^{t}NH	1	27	33	120
Ph	Bu^{t}NHTMS	Bu^{t}NH	2	7	68	240
Ph	Et_2NHTMS	Et_2NH	1	15	25	120
Ph	Et_2NHTMS	Et_2NH	2	8	23	240

Catalysts:
1. $Cr(NBu^t)Cl_3(dme)$
2. $Cr(NBu^t)_2Cl_2$
3. $Mo(NBu^t)_2Cl_2(dme)$
4. $W(NBu^t)_2(NHBu^t)_2$

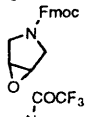
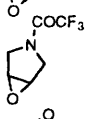
Scheme 64

The impressive work of the Jacobsen group concerning asymmetric processes involving epoxides continues. The most recent report of their studies concerns asymmetric ring cleavage of *meso*-epoxides by $TMSN_3$ (**Scheme 65**).[81] Furthermore, the process may also be used to allow a kinetic resolution of racemic mixtures of monosubstituted epoxides (**Scheme 66**). The reaction may be performed with the utmost 'atom economy': for instance, no solvent



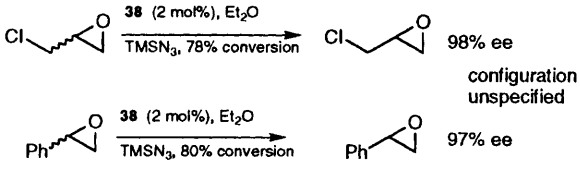


(*R*,*R*)-**38**
M = CrCl

Epoxide	Yield (%)	ee (%)
	80	88
	94	94
	98	98
	95	95
	95	95
	72	81
	65*	82

* isolated as the TMS ether

Scheme 65

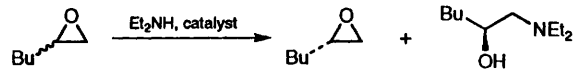


Scheme 66

is necessary and, when the product of the reaction is distilled from the neat mixture, the catalyst may be recycled four times, performing sequential asymmetrical ring-openings of different epoxides without any loss of enantioselectivity.

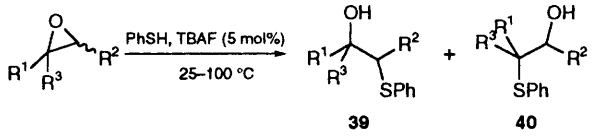
BINOL-derived Lewis acids effect a kinetic resolution of racemic chiral epoxides via nucleophilic ring cleavage by secondary amines (**Scheme 67**).[82] Thus, mixtures of aluminium and titanium Lewis acids and (*R*)-(+)-binaphthol mediate the ring opening of simple monosubstituted epoxides by diethylamine. The (*R*)-enantiomer reacts more slowly than the (*S*)-antipode, so that the ring-opened product has primarily the (*S*)-configuration, but ee's of the products (both epoxide and amino alcohol) are mediocre.

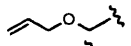
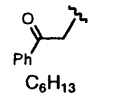
Regioselective ring opening of epoxides by thiols is strongly catalysed by tetrabutylammonium fluoride. The isomer **39** formed via nucleophilic attack at the carbon atom of lesser substitution, is usually observed (**Schemes 68** and **69**).[83]



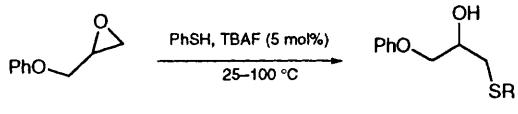
Catalyst	Conversion (%)	ee epoxide (%)	ee amino alcohol (%)
Ti(OPr^i)$_4$/BINOL	45	22	27
EtAlCl$_2$/BINOL	47	52	58
Et$_2$AlCl/BINOL	48	48	24
Et$_3$Al/BINOL	59	75	91

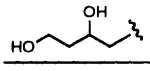
Scheme 67



R^1	R^2	R^3	Yield (%) **39**:**40**
$PhOCH_2$	H	H	100:0
$MeOCH_2$	H	H	100:0
	H	H	100:0
	H	H	94:6
C_6H_{13}	H	H	99:1
Ph	H	H	64:34
$-(CH_2)_4-$		H	100:0
cis-Ph	Ph	H	100:0
trans-Ph	Ph	H	100:0
$-(CH_2)_4-$		Ph	64:23

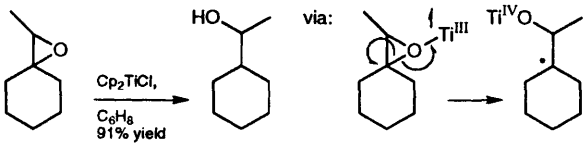
Scheme 68

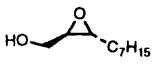
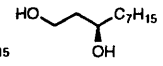
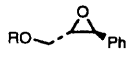
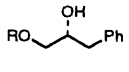
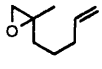
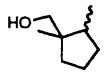


R	Yield (%)
$PhCH_2$	96
	98
	88

Scheme 69

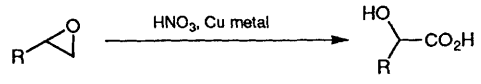
Low-valent titanium radicals promote reductive ring cleavage of epoxides to give alcohols arising from (overall) proteolysis at the *most* hindered carbon atom (**Scheme 70**).[84] When the epoxide contains a remote alkenic functionality, intramolecular cyclisations are observed.



Epoxide	Product	Yield (%)
		69
		62 (R = H), 25 (R = Ts)
		41 (R = Ts)
		94 (*cis* :*trans* = 1:1)

Scheme 70

The direct conversion of epoxides to α-hydroxy-acids is accomplished by a copper-mediated hydrolytic oxidative ring opening (**Scheme 71**).[85] The reaction is only synthetically useful when the substrates are perfluorinated.

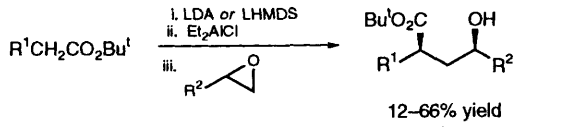


R	Reaction conditions	Yield (%)
F_3C	60% HNO_3 (5 eq.), Cu (3%), 80 °C	84
Me	12% HNO_3 (5 eq.), Cu (3%), 80 °C	15
F_5C_6	35% HNO_3 (5 eq.), Cu (3%), 80 °C	93
C_6H_5	37% HNO_3 (5 eq.), Cu (3%), room temp.	2

Scheme 71

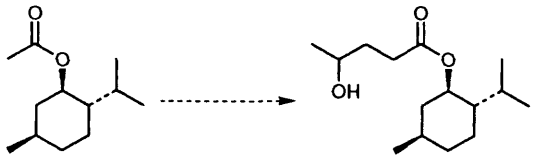
Lithium enolates react with epoxides in the presence of Lewis acid to give δ-hydroxy esters in moderate yield (**Scheme 72 and 73**).[86] The reaction exhibits only moderate stereoselectivity (and, in the cases of the menthyl esters, virtually no diastereoselectivity), but these data represent the first stereoselective epoxide opening by ester enolates.

(*S*)-Trifluoromethyloxirane may be prepared in 96% ee via (−)-DIP chloride mediated reduction of trifluoromethyl bromomethyl ketone. The ring opening reactions of trifluoromethyloxirane have been studied in detail by the same workers (**Scheme 74**).[87]



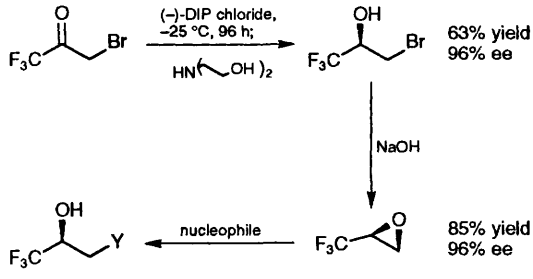
12–66% yield
syn:*anti* = 95:5 to 56:44

Scheme 72



14% ee

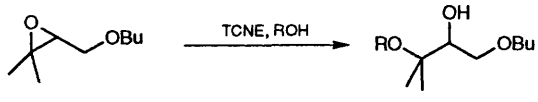
Scheme 73



Nucleophile	Y	Yield (%)	ee (%)
NaN_3	N_3	65	96
NaCN	CN	65	96
$LiAlH_4$	H	70	96
$C_5H_{11}MgBr$	C_5H_{11}	75	96
PhH, $AlCl_3$	Ph	72	96

Scheme 74

Tetracyanoethylene (TCNE) catalyses the alcoholysis of trisubstituted epoxides (**Scheme 75**).[88] The reaction is highly regioselective, with nucleophilic attack occurring at the more substituted carbon atom, and yields of ring-opened products are high for attack by primary alcohols. Disubstituted

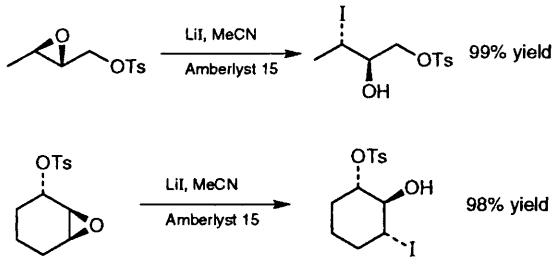


R	TCNE eq.	Yield (%)
Me	0.1	97
allyl	0.1	95
prop-2-ynyl	0.1	91
Pr^i	0.2	61
Bn	0.2	71

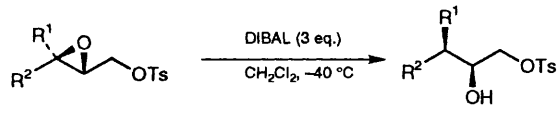
Scheme 75

and terminal epoxides do not undergo selective alcoholysis under the conditions. The mechanism of the process is unproven, but is postulated to involve SET.

The reactions of 2,3-epoxytosylates have caused some controversy during the period covered by this review. The ring opening of 2,3-epoxytosylates by halide ions in acetonitrile in the presence of Amberlyst 15 resin is highly regio- and diastereoselective (**Scheme 76**).[89] No epoxide was obtained despite what might be expected. These authors reported that it is not possible to reduce 2,3-epoxytosylates to alcohols as the former are easily over-reduced; but Chong and Johannsen have clearly shown that this is not the case by exposing such epoxytosylates to up to eight equivalents of DIBAL to give (after work-up) 2-hydroxytosylates in excellent yield (**Scheme 77**).[90] The nature of the solvent employed in the reaction was important: only in dichloromethane and ether was the reaction feasible. Use of THF gave only starting materials (returned in greater than 95% yield) and hexane solvents induced over-reduction to 2-alkanols.



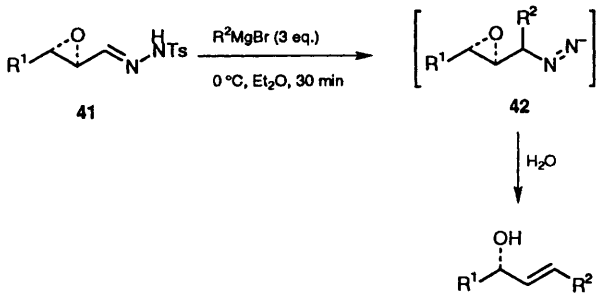
Scheme 76

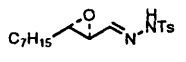
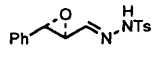
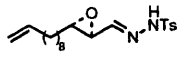
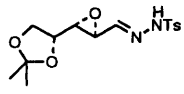


R^1	R^2	Yield (%)
$C_{10}H_{21}$	H	96
H	$C_{10}H_{21}$	96
C_6H_{13}	H	94
H	C_6H_{13}	96
H	Ph	98
H	c-C_6H_{11}	96
Me	Me	83
Me		91

Scheme 77

A variant of the Wharton rearrangement allows for a highly stereoselective alkylative elimination of tosylhydrazones derived from homochiral α,β-epoxy aldehydes (**Scheme 78**). Thus, hydrazones **41** react with Grignard reagents to give diazo anions **42** as intermediates. These species lose diatomic nitrogen

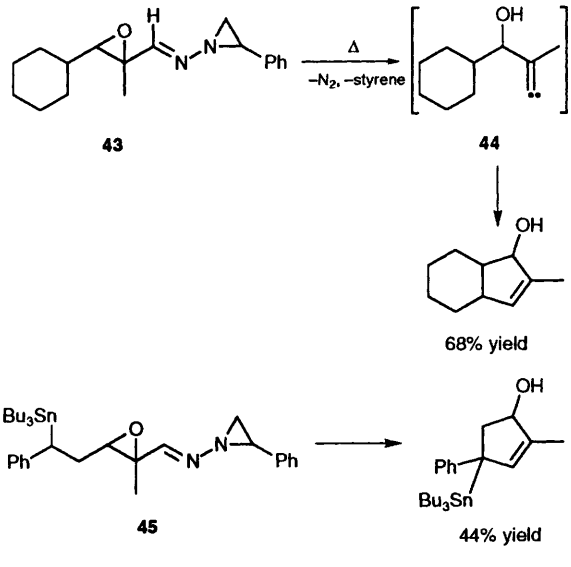


Epoxyhydrazone	R^2	Yield of allylic alcohol (%)
	Bu	68
	Et	66
	Ph	58
	Bu	65
	Et	67
	Ph	70
	Bu	65
	Et	62
	Bu	71
	Bu	62
	Ph	60

Scheme 78

with concomitant epoxide ring cleavage to give (*E*)-allylic alcohols in acceptable yields.[91]

Imines **43** derived from α,β-epoxyaldehydes and *N*-amino-1-phenylaziridine undergo thermal fragmentation to give α-hydroxy methylene carbenes **44**, which insert into a C–H bond five atoms distant to give cyclopent-s-enols in moderate to good yield (**Scheme 79**).[92] The authors demonstrated that the

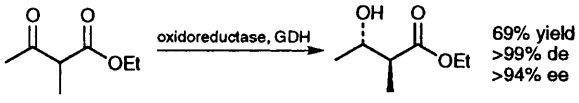


Scheme 79

C–H insertion process is *not* homolytic by examining the reaction of stannylepoxide **45**. Had the insertion been homolytic, one would (the authors suggest) have expected to see a preferential C–Sn insertion: this reaction was not observed.

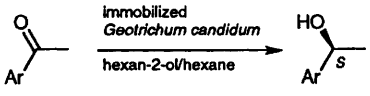
1.4 Alcohol synthesis via biotransformations

An oxidoreductase from *Geotrichum candidum* effects highly diastereo- and enantio-selective reduction of ethyl 2-methyl ketobutyrate (**Scheme 80**).[93] Thus, the isolated enzyme (as a 10% glycerol solution) was incubated with substrate in the presence of glucose, using GDH to regenerate NADPH. *anti*-Ethyl-(2*S*,3*S*)-2-methyl-3-hydroxybutanoate was isolated in 69% yield with >99% de and 94% ee after 48 h.



Scheme 80

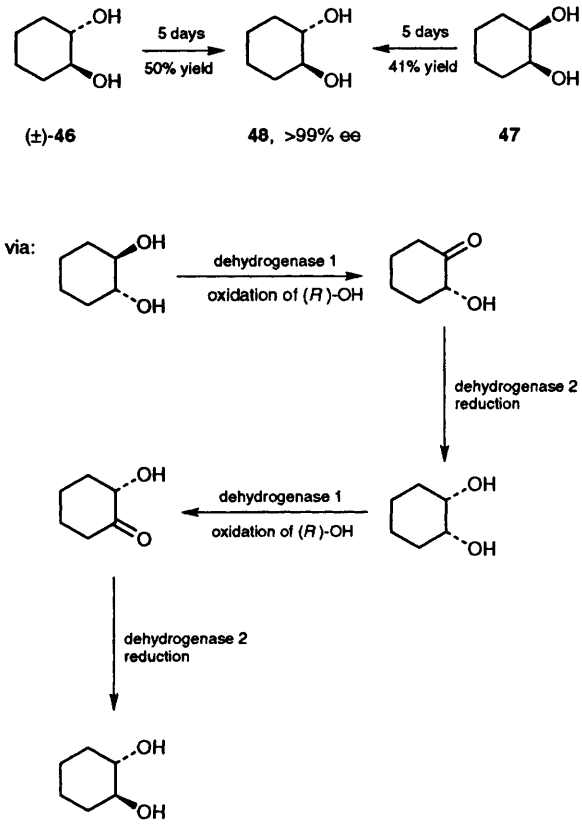
Two features of *Geotrichum candidum*-mediated reductions of carbonyl compounds have been exploited to allow for improvement to the enantioselectivity of such biotransformations (**Scheme 81**).[94] Thus, immobilisation of the microorganism upon a water-absorbent polymeric support and addition of alcohols to the reaction mixture leads to high levels of enantioselection in reductions of arylmethyl ketones. The rôle of the alcoholic component is to improve recycling of NAD^+ by inducing activity of the glycerol dehydrogenase present in the cell.



Ar	Additive	Yield (%)	ee (%)	Absolute configuration
Ph	none	52	28	*R*
Ph	propan-2-ol	29	>99	*S*
Ph	cyclopentanol	58	>99	*S*
Ph	hexan-2-ol	73	>99	*S*
Ph	hexan-2-ol	38	98	*S*
2-furyl	hexan-2-ol	81	>99	*S*
2-Cl-C_6H_4	hexan-2-ol	99	89	*S*
m-Cl-C_6H_4	hexan-2-ol	81	>99	*S*
p-Cl-C_6H_4	hexan-2-ol	41	92	*S*
o-Tol	hexan-2-ol	59	>99	*S*
m-Tol	hexan-2-ol	60	>99	*S*
p-Tol	hexan-2-ol	40	99	*S*

Scheme 81

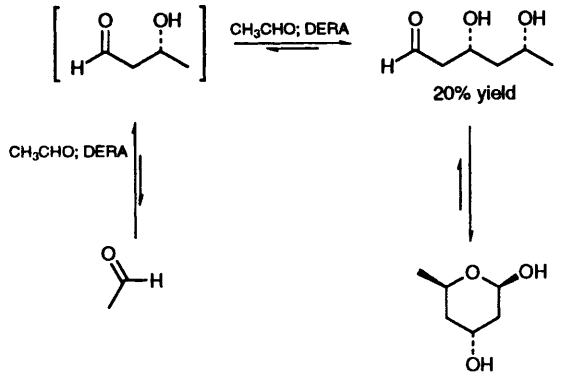
The previously known[95] enantioselective hydrolysis of cyclohexene oxide by *Corynosporium cassiicola* has been re-investigated in depth.[96] The authors found that racemic diol **46** and *meso*-diol **47** could be converted into the same single enantiomer **48** of *trans*-cyclohexane-1,2-diol with very high enantiomeric purity. This, along with similar findings using other diols, suggests that *C. cassiicola* contains two or more dehydrogenase enzymes which operate a tandem oxidation–reduction transformation (**Scheme 82**).



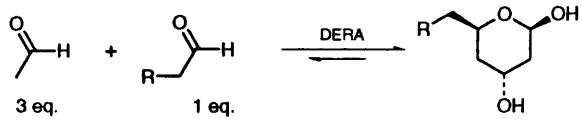
Scheme 82

A one-pot sequence of three sequential asymmetric aldol reactions involving three equivalents of a chiral aldehyde component is carried out by the enzyme 2-deoxyribose-5-phosphate aldolase (DERA). The general reaction is shown in **Scheme 83**.[97] When three equivalents of acetaldehyde and one equivalent of a substituted acetaldehyde are employed in the reaction, substitute pyranosides may be obtained from the reaction (**Scheme 84**). The products of these reactions are useful synthons for analogues of HMG-CoA reductase inhibitors. Since DERA has been overexpressed in *E. coli*, large quantities of this enzyme are available, thereby making the transformation of considerable synthetic utility.

The interest in bacterial hydroxylation reactions has continued unabated. The reaction of 1,4-disubstituted aromatics in the presence of strains



Scheme 83

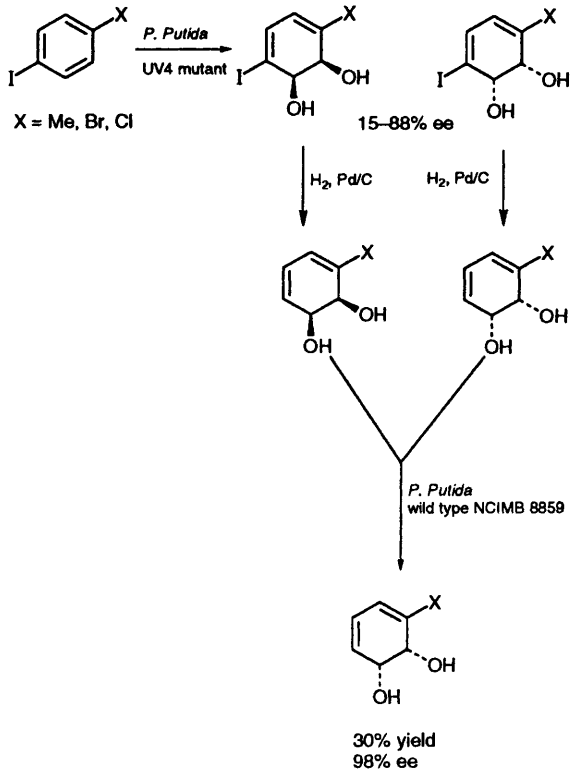


R	Yield (%)
H	20
OH	<3
OMe	65
Cl	70
Br	–
N_3	23

Scheme 84

of *P. Putida* is tuneable, with different strains having different substrate preferences, thus allowing preparation of *both* enantiomers of benzenoid *cis*-1,2-diols (**Scheme 85**). *para*-Dihalobenzenes and *para*-iodotoluene react in the presence of mutant UV4 to give *cis*-diols of *opposite* configuration to those usually obtained from the wild-type oxidation, although the enantioexcesses of these diols is inferior to that normally observed in the 'natural' oxidation. Hydrogenolysis of the C–I bond furnishes diols which may then be exposed to wild-type NCIMB8859: this organism selectively oxidises the 'natural' *cis*-diols, thereby leading to an enantiomeric enrichment of the 'unnatural' antipode. Other wild-type and mutant strains of *P. Putida* were examined by the authors and found to *cis*-hydroxylate naphthoquinones, indenes and homologues with variable enantiocontrol (35 to >98% ee).[98]

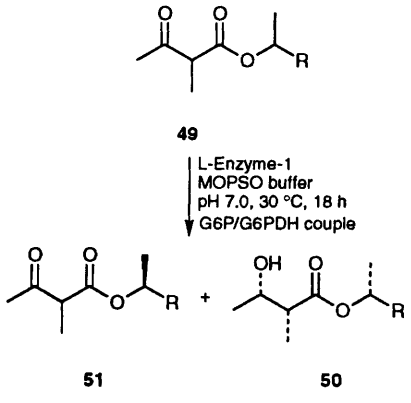
An isolated β-ketoester reductase from Baker's yeast allows introduction of multiple asymmetry, via an enantioselective reduction and a dynamic kinetic resolution.[99] Thus, when racemic ketoesters **49**, in which the ester component contains an α-asymmetric centre, are reacted with reductase L-enzyme-1[100] in the presence of NADPH (regenerated using the G6P couple) one diastereoisomer of **49** is reduced to give enantiomerically pure (>99% ee) stereotriad **50**. The



Scheme 85

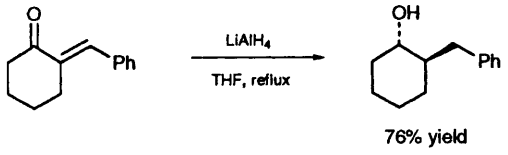
unreacted diastereoisomers undergo epimerisation at the acidic C–H position under the reaction conditions, but the configuration of the stereocentre of the pendant ester moiety remains intact (**Scheme 86**).

Double reduction of 2-benzylidenecyclohexanone has recently been shown to be highly selective



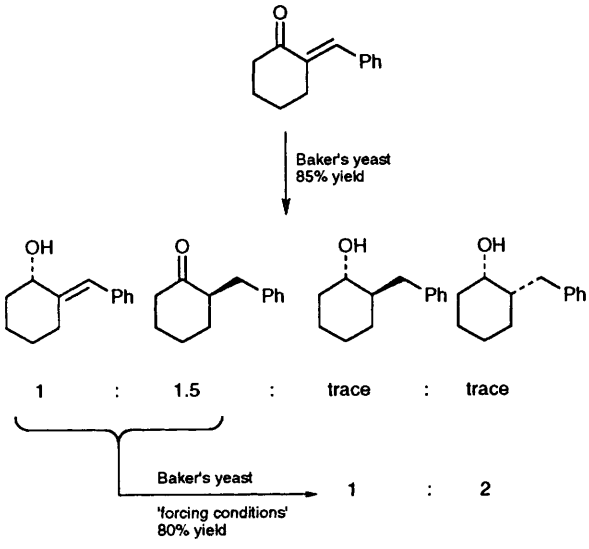
R	Yield of **51** (%) (ee) (%)	Yield of **50** (%) (ee) (%)	de of **50** (%)
C_6H_{11}	64 (32)	34 (>99)	66
Ph	52 (68)	48 (>99)	74
2-Cl-C_6H_4	64 (39)	36 (>99)	70
4-Cl-C_6H_4	69 (36)	31 (>99)	77
4-Me-C_6H_4	56 (58)	44 (>99)	75
4-NO_2-C_6H_4	59 (35)	41 (>99)	80

Scheme 86



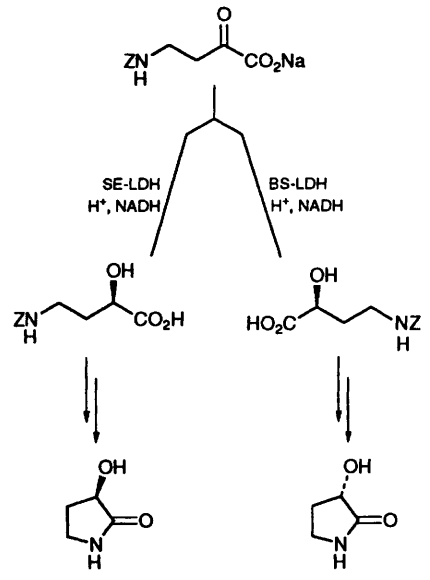
Scheme 87

(**Scheme 87**).[101] When the same enone is subjected to reductive biotransformation (on a 50 g scale), the reaction exhibits variable levels of stereocontrol (**Scheme 88**).[102] Thus, under typical conditions, 1,2- and 1,4-reduced products are obtained in roughly equal amounts. When forcing conditions (twice the amount of yeast) are employed, double reduction is observed but the reaction is poorly diastereoselective.



Scheme 88

Both enantiomers of 3-hydroxypyrrolidin-2-one are accessible via lactate dehydrogenase (LDH) reduction of *N*-protected 4-amino-2-keto-carboxylates (**Scheme 89**).[103]

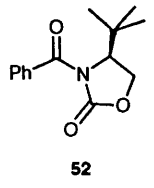


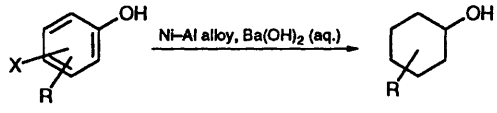
Scheme 89

1.5 Miscellaneous methods for alcohol synthesis

Capitalising upon the fact that oxazolidinones are good leaving groups, the *N*-benzoyloxazolidinone **52** derived from *tert*-leucinol acts as an asymmetric benzoyl transfer reagent upon reaction with secondary alcohols.[104] Racemic aryl alkyl carbinols react, in large excess (10 equivalents), with **52** in the presence of methyl magnesium bromide to give (*R*)-benzoates. Lack of an aryl group in the alcohol leads to poor enantioexcess.

Halophenols are easily exhaustively hydrogenated to the corresponding dehalogenated cyclohexanols upon reaction with Raney nickel–aluminium alloy in saturated barium hydroxide solution. The reduction is independent of the number of halogen atoms



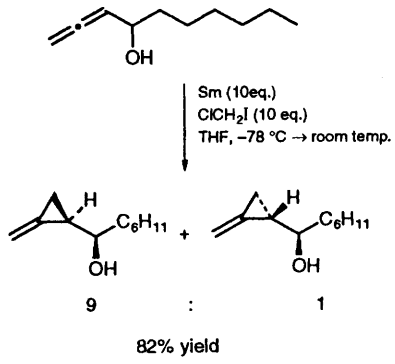


Halophenol				Product
X	R	$Ba(OH)_2$ (ml)	Ni–Al alloy (g)	Yield (%)
3-Br	H	60	8	54
4-Br	H	60	9	74
2,4-Br	H	60	10	65
$2,4,6\text{-}Br_3$	H	55	12	42
$3\text{-}Cl\text{-}2,4,6\text{-}Br_3$	H	130	16.5	62
$2,3,4,6\text{-}Br_4$	H	130	16.5	52
$2,4,6\text{-}Cl_3$	H	50	8.3	65
$2,3,4,6\text{-}Cl_4$	H	50	8.3	62
$2,3,4,5,6\text{-}Cl_5$	H	100	12.0	91
$2,4,6\text{-}Cl_3$	3-Me	20	8.0	30 *cis*, 45 *trans*
$2,6\text{-}Cl_2$	4-Me	50	20.0	45 *cis*, 49 *trans*

Scheme 90

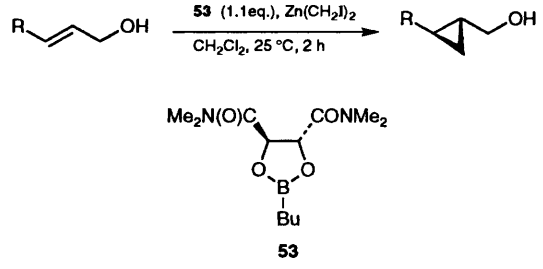
present, but chlorophenols are reduced more easily than bromophenols (**Scheme 90**).[105]

Lautens and Delanghe have reported in detail their studies on the cyclopropanation of α-allenic alcohols.[106] Following a thorough screening of a wide range of cyclopropanation protocols, the samarium metal–chloroiodomethane combination was shown to deliver the best diastereoselectivity (**Scheme 91**).



Scheme 91

A highly stereoefficient asymmetric Simmons–Smith cyclopropanation of allylic alcohols using the boronate **53** derived from (+)-*N,N,N′,N′*-tetramethyl tartaric acid diamide has been reported. Thus, at room temperature, allylic alcohols are cyclopropanated in 91–94% ee by $Zn(CH_2I)_2$ in the presence of stoichiometric amounts of **53** (**Scheme 92**).[107]



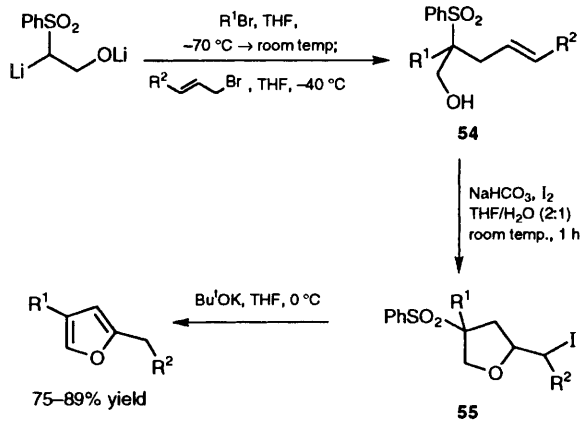
R	Yield (%)	ee (%)
Ph	>98	93
Pr	80	93
(*Z*)-Et	90	93
(*Z*)-TBDMSOCH$_2$	80	91

Scheme 92

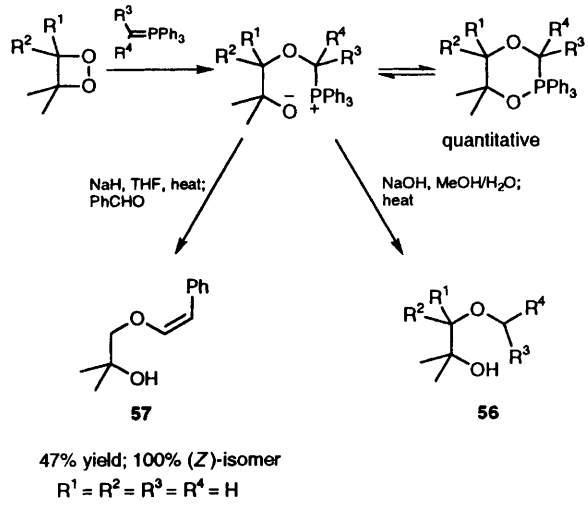
Dianions derived from (2-hydroxy)ethylphenyl sulfone may be dialkylated efficiently to give α-disubstituted hydroxy sulfones **54**. These products may be cyclised via iodetherification to give substituted iodomethyl tetrahydrofuranyl sulfones **55** which may in turn be converted by double elimination to 2,4-disubstituted furans (**Scheme 93**).[108] Yields of the overall process are good.

Alkylidenephosphoranes undergo an insertion reaction with 1,2-dioxetanes to give phosphorinanes in quantitative yield.[109] These species may be converted to the monoethers of 1,2-diols **56** or to 2-oxyvinylalcohols (**Scheme 94**).

An asymmetric Meisenheimer rearrangement allows the asymmetric preparation of allylic alcohols of high ee (**Scheme 95**).[110] Thus, C-2 symmetric pyrrolidine **58** is converted into a range of allylic tertiary amines and oxidised to the *N*-oxide, which undergoes asymmetric [2,3]-rearrangement to give



Scheme 93



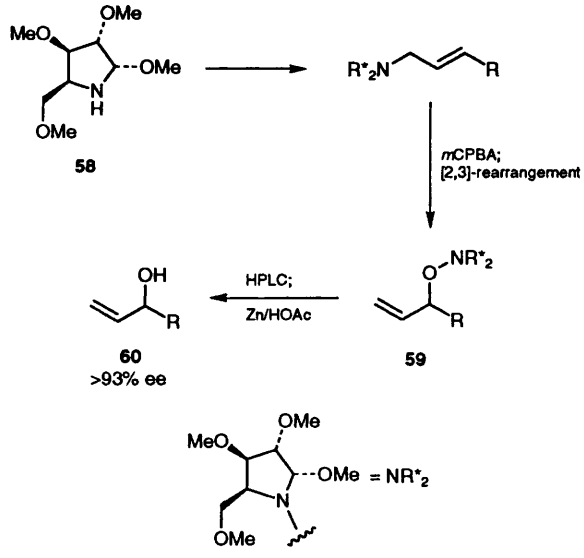
Scheme 94

hydroxylamines **59** in good yield and mediocre de (62–73%). These compounds were purified by HPLC and converted to allylic alcohols **60** of >93% ee.

2 Preparation of ethers and phenols

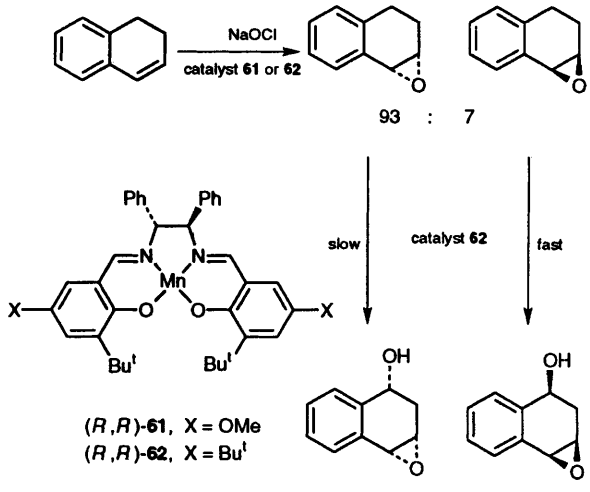
A review has appeared delineating the use of α-haloethers in preparation of ethers.[111]

Jacobsen and Larrow have observed a kinetic resolution in effect during the authors' previously well-documented Mn–salen catalysed asymmetric epoxidation process (**Scheme 96**).[112] The authors observed that the ee of the product of asymmetric epoxidation of 1,2-dihydronaphthalene increased with reaction time, at the expense of yield. Surmising that there was a secondary kinetic resolution process in effect, they exposed racemic 1-2-dihydronaphthalene oxide to the system utilised in asymmetric epoxidation, whereupon they observed a benzylic oxidation reaction; the enantiomer which reacted slower was that corresponding to the major product from the



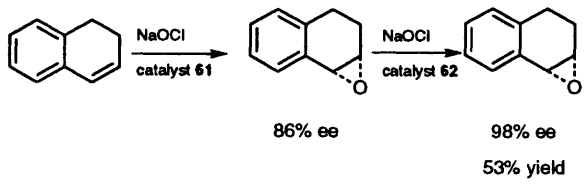
R	ee of 60 (%)	Configuration
Me	95.2	*R*
Et	91.5	*R*
Pr^n	96.3	*R*
Pr^i	96.0	*R*
Bu^t	93.1	*S*

Scheme 95



Scheme 96

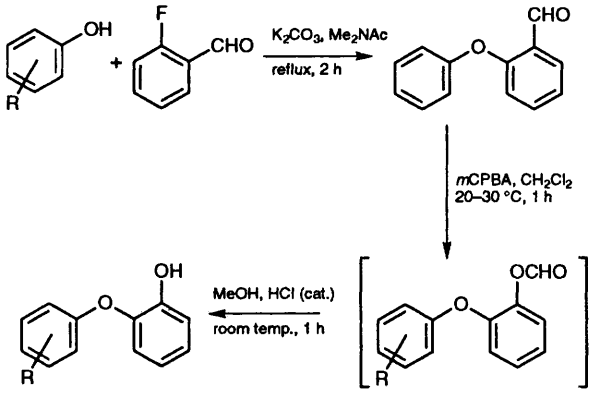
epoxidation of 1,2-dihydronaphthalene, while the enantiomer which is the minor product of epoxidation was rapidly oxidised to *syn*-epoxy alcohol. Thus the authors devised a one-pot, two-catalyst system to allow rapid epoxidation and subsequent rapid C–H oxidation to take place (**Scheme 97**). The mechanism does not involve an epoxide-directed C–H insertion reaction, as might naïvely be expected, but rather a stepwise radical process in which preferential abstraction of a



Scheme 97

pseudo-axial hydrogen atom leads to a pseudo-axial hydroxy group. This was confirmed when epoxides having little energetic difference between pseudo-axial and pseudo-equatorial C–Hs were shown to react with poor diastereoselectivity.

An *umpolung* may be exploited to allow the efficient preparation of 2-aryloxyphenols by means of a two-step analogue of the Ullman condensation.[113] Thus, 2-fluorobenzaldehyde is alkylated in high yield by phenols to give the corresponding 2′-formylbiphenylethers which undergo Bæyer–Villiger reaction to give the aforementioned aryloxyphenols (**Scheme 98**).



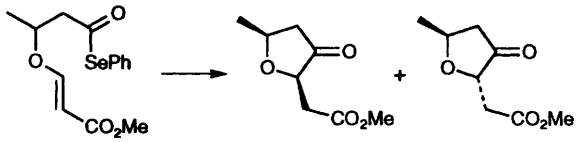
R	Yield (%)
H	96
Cl	89
Br	90
Bu^t	87
OMe	79
OPh	85

Scheme 98

Radical cyclisation of the 3-hydroxybutyrate-derived oxygen-tethered α,β-unsaturated ester **63** gives *cis*-2,5-disubstituted tetrahydrofuran-3-ones with high *syn*-selectivity (**Scheme 99**). Slow addition (syringe pump) is vital, and so the reaction may be less feasible on a large scale.[114]

O-Alkylthiophenols may be prepared by aromatisation of 2-alkylthiocyclohexanones in the presence of molecular bromine (**Scheme 100**).[115]

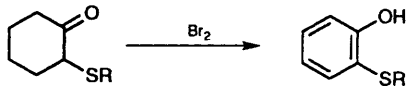
α,α-Difluoroethers and acetals formally derived from carbonyl difluoride may be prepared by fluorinative desulfonylation of thioesters and



63

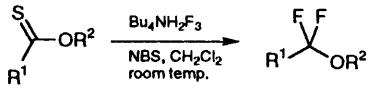
Reaction conditions	*syn*:*anti*	Yield (%)
Ph_3SnH, AIBN, Δ, 3 h	88:12	82
Bu_3SnH, AIBN, Δ, 2.5 h	85:15	94
Ph_3SnH, Et_3B, air, rt, 96 h	≥95:5	63
Ph_3SnH, Et_3B, air, Δ, 4 h	94:6	97

Scheme 99



R	Yield (%)
Bu	81
c-C_6H_{11}	81
Ph	92
2-NO_2-C_6H_4	70

Scheme 100



R^1	R^2	Yield (%)
Me	Bu	37
Me	4-biphenyl	74
Et	4-biphenyl	77
Ph	Et	43
Ph	Bn	76
Ph	Ph	76

Scheme 101

thiocarbonates respectively (**Scheme 101**).[116] Tetrabutylammonium perfluoride is the reagent which allows these transformations to be realised. Rozen's method[117] allows preparation of α,α-difluoroethers from thioesters, but uses the more exotic BrF_3.

3 References

1 D. A. Evans, M. J. Dart and J. L. Duffy, *Tetrahedron Lett.*, 1994, **35**, 8537.
2 D. A. Evans, M. J. Dart and J. L. Duffy, *Tetrahedron Lett.*, 1994, **35**, 8537.
3 T. J. Leitereg and D. J. Cram, *J. Am Chem. Soc.*, 1968, **90**, 4011.
4 C. Copérat, E. Negishi, Z. Xi and T. Takahashi, *Tetrahedron Lett.*, 1994, **35**, 695.
5 T. Luker and R. J. Whitby, *Tetrahedron Lett.*, 1994, **35**, 785.
6 M. Chiro, T. Matsumoto and K. Suzuki, *Synlett*, 1994, 359.
7 N. Auner, J. Grobe and R. Damrauer, *J. Organomet. Chem.*, 1980, **188**, 25; N. S. Namekin, N. V. Ushakov and M. V. Vdovin, *Zh. Obshch. Khim.*, 1974, **44**, 1970; P. Jutzi and P. Langer, *J. Organomet. Chem.*, 1977, **132**, 45.
8 S. E. Denmark, B. D. Griedel, D. M. Coe and M. E. Schnuti, *J. Am. Chem. Soc.*, 1994, **116**, 7026.
9 E. M. Carriera, R. A. Singer and W. Lee, *J. Am. Chem. Soc.*, 1994, **116**, 8837.
10 H. Nitta, D. Yu, M. Kudo and A. Mori, *J. Am. Chem. Soc.*, 1992, **114**, 7969. M. Hayashi, Y. Miyamoto, T. Inoue and N. Ogumi, *J. Org. Chem.*, 1993, **58**, 1515.
11 B. R. Lago, H. M. Crane and D. C. Liotta, *J. Org. Chem.*, 1993, **58**, 4191.
12 S. Tsuboi, H. Kuroda, S. Takatsuka, T. Fukawa, T. Sakai and M. Utaka, *J. Org. Chem.*, 1993, **58**, 5952.
13 M. K. Kundu, S. B. Mukherjee, N. Balu, R. Padmakumar and S. V. Bhat, *Synlett*, 1994, 444.
14 A. Yanagisawa, H. Inone, M. Morodome and H. Yamamoto, *J. Am. Chem. Soc.*, 1993, **115**, 10 356.
15 J. Synoniak, D. Felix and C. Moïse, *Tetrahedron Lett.*, 1994, **35**, 8617.
16 S. Kobayashi and K. Nishio, *Synthesis*, 1994, 457.
17 J. M. Clayden and M. Julia, *J. Chem. Soc., Chem. Commun.*, 1994, 2261.
18 H. C. Aspinall, A. F. Browning, N. Greeves and P. Ravenscroft, *Tetrahedron Lett.*, 1994, **35**, 4639.
19 Y. Hashimoto, H. Kagoshima and K. Saigo, *Tetrahedron Lett.*, 1994, **35**, 4805.
20 R. Sjoholm, R. Rairama and M. Ahonen, *J. Chem. Soc., Chem. Commun.*, 1994, 1217.
21 J.-F. Normant, *J. Organomet. Chem.*, 1990, **400**, 19.
22 R. N. Haszeldine, *J. Chem. Soc.*, 1954, 1273.
23 F. Hong, X. Tang and C. Hu, *J. Chem. Soc., Chem. Commun.*, 1994, 289.
24 A. Guijario and M. Yús, *Tetrahedron*, 1994, **51**, 13 269.
25 J. J. Harnett, L. Alcarez, C. Miokowski, J. P. Martel, T. Le Gall, D.-S. Shin and J. R. Falck, *Tetrahedron Lett.*, 1994, **35**, 2009.
26 A. L. Costa, M. G. Piazza, E. Tagliavini, C. Trombini and A. Umani-Ronchi, *J. Am. Chem. Soc.*, 1993, **115**, 7001.
27 G. E. Keck, T. H. Tarbet and L. S. Cieraci, *J. Am. Chem. Soc.*, 1993, **115**, 8467.
28 G. E. Keck, D. Krishnamurthy and X. Chen, *Tetrahedron Lett.*, 1994, **35**, 8323.
29 W. R. Roush and M. S. van Nieuwenhze, *J. Am. Chem. Soc.*, 1994, **116**, 8536.
30 S. J. Stanway and E. J. Thomas, *J. Chem. Soc., Chem Commun.*, 1994, 285.
31 J. S. Carey and E. J. Thomas, *J. Chem. Soc., Chem. Commun.*, 1994, 283.
32 A. H. McNeill and E. J. Thomas, *Synthesis*, 1994, 322.
33 T. Akiyama, T. Yasusa, K. Ishikawa and S. Ozaki, *Tetrahedron Lett.*, 1994, **35**, 8401.
34 J. D. Buynak, B. Geng, S. Uang and J. B. Strickland, *Tetrahedron Lett.*, 1994, **35**, 985.
35 K. Soai and K. Takahashi, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1257.
36 M. Watanabe and K. Soai, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3125.

37 O. G. Kulinkovich, V. L. Sorokin and A. V. Kelin, *Zh. Org. Khim.*, 1993, **29**, 66.
38 K. Takeda, S. A. Rao and M. C. Noe, *J. Am. Chem. Soc.*, 1994, **116**, 9345.
39 K. Takeda, J. Nakatani, H. Nakamura, K. Sako, E. Yoshi and K. Yamaguchi, *Synlett,* 1993, 841.
40 K. Takeda, M. Fujisawa, T. Makino and E. Yoshii, *J. Am. Chem. Soc.*, 1993, **115**, 9351.
41 K. Kobayashi, M. Kawakita, T. Mannami and H. Konishi, *Tetrahedron Lett.*, 1995, **36**, 733.
42 P. Delair, C. Einhorn, J. Einhorn and J. L. Luche, *J. Org. Chem.*, 1994, **59**, 4680.
43 A. S. Demir, C. Tanyeli, A. S. Mahawneh and H. Aksoy, *Synthesis,* 1994, 155.
44 A. W. Konradi, S. J. Kemp and S. F. Pedersen, *J. Am. Chem. Soc.*, 1994, **116**, 1317.
45 T. Shono, Y. Morishima, N. Moriyoshi and M. Ishifume, *J. Org. Chem.*, 1994, **59**, 273.
46 M. B. Carter, B. Schiøtt, A. Gutiérrez and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 11 667.
47 J. W. Lauher and R. Hoffman, *J. Am. Chem. Soc.*, 1976, **98**, 1729.
48 S. W. Breedon and N. J. Lawrence, *Synlett,* 1994, 833.
49 M. Hojo, A. Fujii, C. Murakami, H. Aihara and A. Hosomi, *Tetrahedron Lett.*, 1995, **36**, 571.
50 G. A. Molander and K. L. Bobbitt, *J. Am. Chem. Soc.*, 1993, **115**, 7517.
51 D. A. Evans, S. G. Nelson, M. R. Gagné and A. R. Muci, *J. Am. Chem. Soc.*, 1993, **115**, 9800.
52 Y. H. Kim, D. H. Park and I. S. Bynn, *J. Org. Chem.*, 1993, **58**, 511.
53 T. Ohkuma, S. Hashiguchi and R. Noroyi, *J. Org. Chem.*, 1994, **59**, 217.
54 B. Figadère, C. Chaboche, X. Franck, J.-F. Peyrat and A. Cavé, *J. Org. Chem.*, 1994, **59**, 7138.
55 S. K. Kang, D. C. Park, D. G. Cho, J. U. Chung and K. Y. Jung, *J. Chem. Soc., Perkin Trans. 1*, 1994, 237.
56 C. Dariel, S. Bartoch, C. Bruneau and P. H. Dixneuf, *Synlett,* 1994, 457.
57 A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert and A. Tijani, *J. Am. Chem. Soc.*, 1994, **116**, 4062.
58 D. A. Evans, A. R. Muci and R. Sturmer, *J. Org. Chem.*, 1993, **58**, 5307.
59 D. F. Taber, L. Yet and R. S. Bhamidipati, *Tetrahedron Lett.*, 1995, **36**, 351.
60 W. Adam and P. Klug, *Synlett,* 1994, 567.
61 H. C. Kolb, M. S. van Nieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483.
62 D. J. Berrisford, C. Bolm and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1059.
63 K. J. Hale, S. Manaviazar and S. A. Peak, *Tetrahedron Lett.*, 1994, **35**, 425.
64 S. Takano, T. Yoshimitsu and K. Ogasawara, *J. Org. Chem.*, 1994, **59**, 54; 1995, **60**, 1478.
65 T. Yoshimitou and K. Ogasawara, *Synlett,* 1995, 257.
66 K. Morikawa, J. Park. P. G. Anderson, T. Hashiyana and K. B. Sharpless, *J. Am. Chem. Soc.*, 1993, **115**, 8463.
67 K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. S. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z.-M. Wang, D. Xu and X.-L. Zhang, *J. Org. Chem.*, 1992, **57**, 2768.
68 G. A. Crispino, K. S. Jeong, H. C. Kolb, Z. M. Wang, D. Xu and K. B. Sharpless, *J. Org. Chem.*, 1993, **58**, 3785.
69 M. S. van Nieuwenhze and K. B. Sharpless, *Tetrahedron Lett.*, 1994, **35**, 843.
70 K. P. M. Vanhessche, Z. M. Wang and K. B. Sharpless, *Tetrahedron Lett.*, 1994, **35**, 3469.
71 I. Henderson, K. B. Sharpless and C. H. Wong, *J. Am. Chem. Soc.*, 1994, **116**, 559.
72 P. J. Walsh, P. T. King, S. B. King and K. B. Sharpless, *Tetrahedron Lett.*, 1994, **35**, 5129.
73 H. C. Kolb, P. G. Andersson, Y. L. Bennani, G. A. Crispino, K. S. Jeong, H. L. Kwong and K. B. Sharpless, *J. Am. Chem. Soc.*, 1993, **115**, 12 226; T. Gobel and K. B. Sharpless, *Angew. Chem., Int. Ed. Engl.*, 1993, **43**, 1329; D. V. McGrath, G. D. Brabson, K. B. Sharpless and L. Andrews, *Inorg. Chem.*, 1993, **32**, 4164; H. C. Kolb, P. G. Andersson and K. B. Sharpless, *J. Am. Chem. Soc.*, 1994, **116**, 1278; P. O. Norrby, H. C. Kolb and K. B. Sharpless, *Organometallics*, 1994, **13**, 344.
74 H. Becker, M. A. Soler and K. B. Sharpless, *Tetrahedron,* 1995, **51**, 1345.
75 Z.-M. Wang and K. B. Sharpless, *J. Org. Chem.*, 1994, **59**, 8302.
76 M. Chini, P. Crotti, L. Favero, F. Macchia and M. Pineschi, *Tetrahedron Lett.*, 1994, **35**, 433.
77 Y. Yamamoto, N. Asao, M. Meguro, M. Tsukada, H. Nemoto, N. Sayadori, J. G. Wilson and H. Nakamura, *J. Chem. Soc., Chem. Commun.*, 1993, 1201.
78 M. Chini, P. Crotti, L. Favero and F. Macchia, *Tetrahedron Lett.*, 1994, **35**, 761.
79 R. R. Schrock, *Acc. Chem. Res.*, 1991, **23**, 1580.
80 W. H. Leung, E. K. F. Chow, M. C. Wu, P. W. K. Kum and L. L. Yeung, *Tetrahedron Lett.*, 1995, **36**, 107.
81 L. E. Martinez, J. L. Leighton, D. H. Carsten and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1995, **117**, 5897.
82 M. Brunner, L. Mussmann and D. Vogt, *Synlett,* 1994, 69.
83 D. Albanese, D. Landini and M. Penso, *Synthesis,* 1994, 34.
84 T. V. Rajan Babu and W. A. Nugent, *J. Am. Chem. Soc.*, 1994, **116**, 987.
85 T. Katagiri, F. Obara, S. Toda and K. Furahashi, *Synlett,* 1994, 507.
86 S. K. Taylor, J. A. Fried, Y. N. Grassl, A. E. Marelewski, E. A. Pelton, T.-J. Poel, D. S. Rezanka and M. R. Whittaker, *J. Org. Chem.*, 1994, **59**, 7304.
87 P. V. Ramachandran, B. Gong and H. C. Brown, *J. Org. Chem.*, 1995, **60**, 41.
88 Y. Masaki, T. Miura and M. O. Chiai, *Synlett,* 1993, 847.
89 C. Bonini, L. Chiammiento and M. Funicello, *Tetrahedron Lett.*, 1994, **35**, 797.
90 J. M. Chong and J. Johannsen, *Tetrahedron Lett.*, 1994, **35**, 7197.
91 S. Chandrasekhar, M. Takhi and J. S. Yadav, *Tetrahedron Lett.*, 1995, **36**, 307.
92 S. Kim and C. M. Cho, *Tetrahedron Lett.*, 1994, **35**, 8405.
93 Y. Kawai, K. Tananobe, M. Tsujimoto and A. Ohno, *Tetrahedron Lett.*, 1994, **35**, 147.
94 K. Nakamura, Y. Inoue and A. Ohno, *Tetrahedron Lett.*, 1995, **36**, 265.
96 A. J. Carnell, G. Iacazio, S. M. Roberts and A. J. Willetts, *Tetrahedron Lett.*, 1994, **35**, 331.
97 H. J. M. Gijsen and C.-H. Wong, *J. Am. Chem. Soc.*, 1994, **116**, 8422.
98 C. C. R. Allen, D. R. Boyd, H. Dalton, N. D. Sharma, I. Brannigan, N. A. Kerly, G. N. Sheldrake and S. C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1995, 117.
99 Y. Kawai, K. Hida, K. Nakamura and A. Ohno, *Tetrahedron Lett.*, 1995, **36**, 591.
100 K. Nakamura, Y. Kawai, N. Nakajima and A. Ohno, *J. Org. Chem.*, 1991, **56**, 4778; K. Nakamura, Y. Kawai, T. Miyai, S. Honda, N. Nakajima and A. Ohno, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 1467.

101 K. Koch and J. H. Smitrovich, *Tetrahedron Lett.*, 1994, **35**, 1137.
102 G. Fronza, G. Fogliato, C. Fuganti, S. Lanati, R. Rallo and S. Servi, *Tetrahedron Lett.*, 1995, **36**, 123.
103 J. M. Bentley, H. J. Wadsworth and C. L. Willis, *J. Chem. Soc., Chem. Commun.*, 1995, 231.
104 D. A. Evans, J. C. Anderson and M. K. Taylor, *Tetrahedron Lett.*, 1993, **34**, 5563.
105 T. Tsukinoki, T. Kakinami, Y. Iida, M. Ueno, T. Mashimo, H. Tsuzuki and M. Tashiro, *J. Chem. Soc., Chem. Commun.*, 1995, 209.
106 M. Lautens and P. H. M. Delanghe, *J. Am. Chem. Soc.*, 1994, **116**, 8526. *J. Org. Chem.*, 1993, **58**, 5037
107 A. B. Charette and H. Juteau, *J. Am. Chem. Soc.*, 1994, **116**, 2651.
108 J. H. Jung, J. W. Lee and D. Y. Oh, *Tetrahedron Lett.*, 1995, **36**, 923.
109 W. Adam, H. M. Harrer and A. Treiber, *J. Am. Chem. Soc.*, 1994, **116**, 7581.
110 D. Enders and H. Kempen, *Synlett,* 1994, 969.
111 T. Benneche, *Synthesis*, 1995, 1.
112 J. F. Larrow and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1994, **16**, 12 129.
113 G. W. Yeager and D. N. Schissel, *Synthesis*, 1995, 28.
114 P. A. Evans and J. D. Roseman, *Tetrahedron Lett.*, 1995, **36**, 31.
115 V. V. Samashin and K. V. Kudrayavtser, *Tetrahedron Lett.*, 1994, **35**, 7413.
116 M. Kuorboshi and T. Hiyama, *Synlett,* 1994, 251.
117 S. Rozen and E. Mishani, *J. Chem. Soc., Chem. Commun.*, 1993, 1761.