CHAPTER 1

# Reactions of Aldehydes and Ketones and their Derivatives

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## Formation and Reactions of Acetals and Related Species

A water-soluble self-assembled host molecule $[Ga_4L_6]^{12-}$ has been found to catalyse the hydrolysis of orthoformates $HC(OR)_3$ in basic solution with marked rate accelerations of up to 3900 (R = Pr) relative to the uncatalysed reaction.[1] Enzyme-like Michaelis–Menten kinetics apply and $^{13}C$ labeling experiments have helped to establish that the neutral substrate is encapsulated in the host in the resting state; this is consistent with the more negative entropy of activation found for the catalytic process. The solvent isotope effects $k(H_2O)/k(D_2O) = 1.6$ is indicative of an A-$S_E2$ mechanism with rate-limiting proton transfer, in contrast with the $A1$ mechanism for the catalysed reaction which involves rate-limiting decomposition of the protonated substrate.

Pyridinium salt derivatives have been found to catalyse (at 0.1% loading) acetalization reactions of both aldehydes and ketones in methanol at room temperature more efficiently than Brønsted acids of $pK_a = 2.2$.[2]

A study of the effects of the strength of the nucleophile (Nu-$SiMe_3$) on the stereochemical outcome of substitution reactions of cyclic acetals (in $CH_2Cl_2$ in the presence of $Me_3SiOTf$ or $BF_3OEt_2$) has revealed a continuum of mechanisms. Stereoselective $S_N1$ mechanisms (via the oxocarbenium ion intermediate) occur with weak and moderate nucleophiles and poor leaving groups, whereas strong nucleophiles adopt unselective diffusion-limited $S_N1$ and $S_N2$ pathways.[3]

A highly enantioselective (up to 99% *ee*) and diastereoselective aldol-type reaction of $\beta$-keto esters with acetals has been achieved under the catalytic influence of chiral cationic Pd(II)–and Pt(II)–binap complexes which can act as acid/base catalysts, with simultaneous activation of both the nucleophile (as chiral metal enolate) and acetal;[4] the enantioselectivity is apparently dependent on conversion of the acetal into the oxonium ion, by protonation under the acidic conditions used.

A Lewis base-catalysed diastereoselective and enantioselective glycolate aldol reaction has been developed whereby a range of aldehydes can be converted to both *syn*- and *anti*-1,2-diols under the same catalytic system by adjusting the size of the silyl ketene acetal $[R^3OCH{=}C(OR^2)OSiR^1{}_3]$ used as the nucleophilic component; these Mukaiyama-type aldol reactions are conducted in $CH_2Cl_2$ at $-78^\circ C$ in the presence of $SiCl_4$, $i$-$Pr_2NEt$ and a bisphosphoramide catalyst.[5]

The Brønsted acid catalysed aza-Ferrier reaction of *N*-Boc-2-(1,3-dienyloxy) pyrrolidines has been found to proceed via heterolytic C–O cleavage to give the iminium alkoxide, from which the corresponding $\alpha$-(*N*-Boc-2-pyrrolidinyl)aldehyde is formed in excellent yield and high $\alpha$-regioselectivity by C–C bond formation.[6]

## Reactions of Glucosides and Nucleosides

Nucleophilic substitution reactions of 2-phenylthio-substituted carbohydrate acetals and related systems have been reviewed, with particular reference to episulfonium ions vs oxocarbenium ions as reactive intermediates in stereocontrolled glycosylation reactions.[7]

Mechanistic study (using kinetic experiments, Hammet plots, DFT calculations and $^{11}B$ NMR) of regioselective borane reductive openings of cyclic acetals has established

that the outcome depends on the electrophile with which the more electron-rich oxygen associates, and this can be altered by Lewis acid activation of the borane.[8]

A plausible mechanism has been suggested to account for $\alpha$-selective glucosylation which allowed the synthesis of the tetrasaccharide [Glc$\alpha$1 $\rightarrow$ 2Glc$\alpha$1 $\rightarrow$ 3Glc$\alpha$1 $\rightarrow$ 3Man], enabled by the synergistic effect of combined etheral and halogenic solvents.[9]

Hydrolysis of toxic 7-hydroxycoumarin glucosides and other aryl and alkyl glucosides catalysed by modified $\alpha$- and $\beta$-cyclodextrin dicyanohydrins has been found to follow Michaelis–Menten kinetics and to display rate increases of up to $k_{cat}/k_{uncat} = 7569$ (for the hydroxycoumarin glucoside).[10]

Results of a DFT study of suitable analogues have explained the relative O(3)/O(4) reactivities previously reported for reaction of glycosyl donors with both $\alpha$- and $\beta$-methyl glycosides of *N*-dimethylmaleoyl (DMM) glucosamine acceptors protected at O(6).[11] The preferential or exclusive substitution at O(3) for the $\alpha$-anomers and at O(4) for the $\beta$-anomers has been attributed to the different alignments for the DMM ring: for the $\beta$-anomers the ring is parallel to the C(2)–H(2) bond for steric reasons, whereas for the $\alpha$-anomers it is tilted such that a strong hydrogen bond between one of its carbonyl groups and HO(3) makes O(3) more reactive.

A study of potential neighbouring group participation by non-vicinal esters in glycosylation reactions has found that glycopyranosylation is aided by intermediate formation of a 1,3-*O*-cyclic carbonate ester, with loss of a *t*-butyl cation from a *t*-butoxycarbonyl ester group axially substituted at C(3), but that the corresponding 3-*O*-equatorial, 4-*O*-axial and -equatorial, and 6-*O* carbonates do not undergo intramolecular reaction under typical glycosylation conditions.[12] Galactopyranosylation reactions of a 4-*O*-(2-carboxy)benzoate ester and a 4-*O*-(4-methoxybenzoate) ester also failed to exhibit neighbouring group participation; this was particularly clear for the latter, for which $^{18}O$ quenching failed to detect bridging intermediates. The unesterified hydroxyl groups were protected as benzyl ethers.

## Formation and Reactions of Nitrogen Derivatives

### *Imines: Synthesis, Tautomerism, Catalysis*

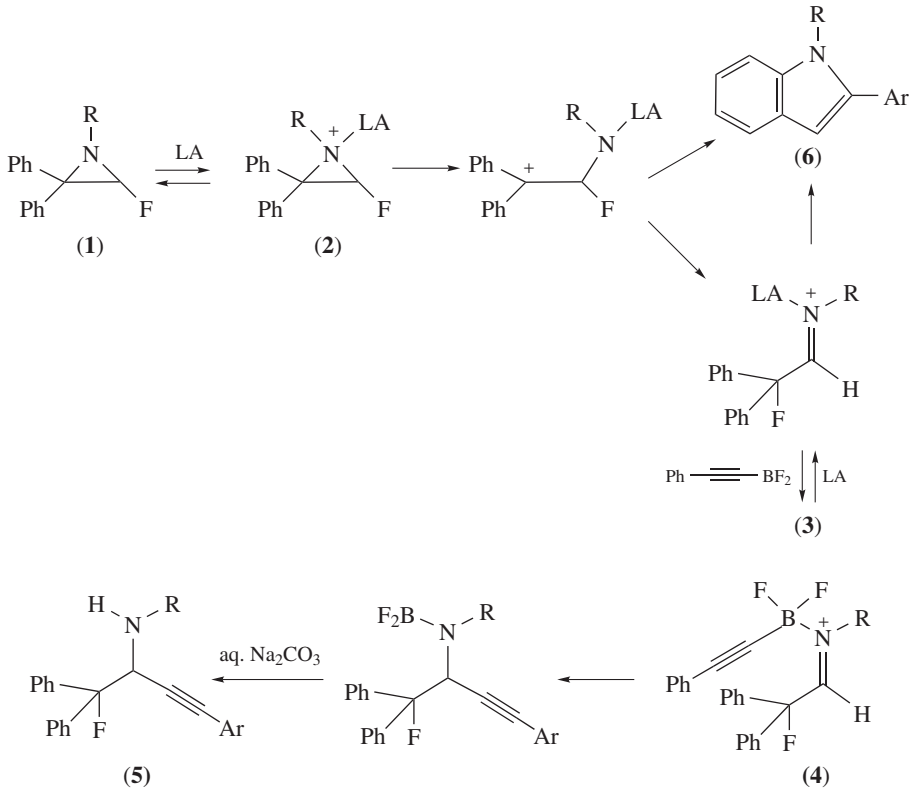
Isomerization of the imine derived from benzylamine and trifluoroacetophenone to the corresponding *N*-benzylidene-2,2,2-trifluoro-1-(phenyl)ethylamine has been found to proceed by a concerted mechanism via a virtually unionized transition state when catalysed by triethylamine in acetonitrile.[13]

Triarylmethyl chlorides have been used as efficient organic catalysts for synthesis of *N*-sulfonylimines, via condensation of sulfonamides with aldehydes or ketones, under mild metal-free conditions at 40 °C in neutral media; the carbonyl compounds are believed to be activated by complexation with triarylmethyl cation.[14]

Individual equilibrium constants have been determined for the three steps whereby *o*-phthalaldehyde [*o*-$C_6H_4(CHO)_2$] reacts with ammonia to give an isoindole derivative; cyclization of the initially formed carbinolamine intermediate to the 1,3-dihydroxyindole and subsequent imine formation by dehydration are both acid catalysed; the concentrations of the intermediates are negligible at equilibrium and the same applies for the corresponding reaction with 2-aminoethanol, for which

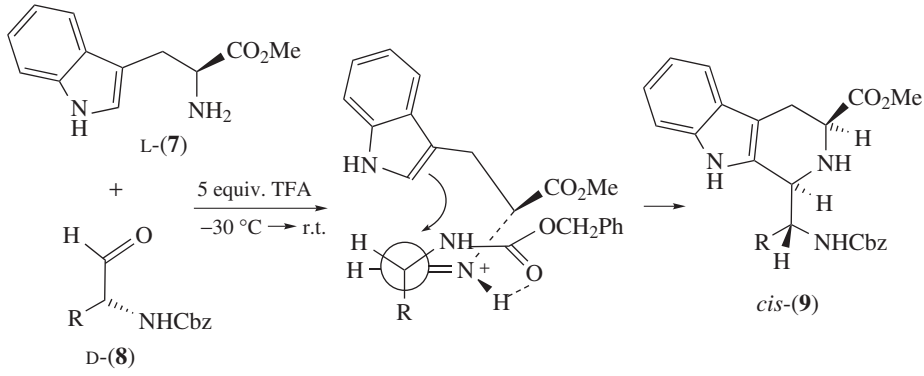
initial formation of carbinolamine was too fast to measure by the combination of spectrophotometric and polarographic techniques used.[15]

2-Fluoro-1,1-diphenylaziridines (**1**) have been found to react with arylethynylborates in the presence of $BF_3{\cdot}OEt_2$ to form monofluorinated propargylamines (**5**) in 30–66% yield, along with indoles (**6**) (Scheme 1).[16] This modified Petasis reaction proceeds by isomerization to $\alpha$-fluorinated imines (**3**), which react with alkynyldifluoroborane generated *in situ* from the potassium alkynyltrufluoroborates and $BF_3{\cdot}OEt_2$.




SCHEME 1

A study of the diastereoselectivity of the Pictet–Spengler condensation of tryptophan methyl ester (**7**) and $\alpha$-aminoaldehydes (**8**) derived from L- or D-amino acids as chiral carbonyl components has established that there is chirality transfer from C(2) of the $\alpha$-aminoaldehyde to the newly created stereogenic centre in the tetrahydro-$\beta$-carboline derivative (**9**).[17] The diastereomeric products (*cis/trans*) obtained from various combinations of enantiomers of the chiral reactants were such that *cis* and *trans* (65–100%) 1,3-disubstituted 1,2,3,4-tetrahydro-$\beta$-carbolines are formed ('mismatched' situation) from L,L or D,D combinations, whereas only the *cis* diastereomer ('matched situation') is obtained from combinations of opposite configuration (L,D or




SCHEME 2

D,L), (e.g. Scheme 2). This has been interpreted in terms of the Felkin–Ahn model and hydrogen bonding interactions of an intermediate iminium cation.

*The Mannich and Nitro-Mannich Reactions*

An overview of the recent history of the asymmetric organocatalysed Mannich reaction has addressed its scope and limitations, and application of different catalyst systems.[18] Organocatalytic reactions of acetaldehyde have been highlighted with particular mention of the Mannich reaction as a powerful method of forming C–C bonds.[19] A review of enantioselective organocatalysis by primary amino acids has illustrated their unique reactivity and stereoselectivity in aldol and Mannich reactions and greater versatility than proline and its analogues.[20]

Quantum mechanical calculations have provided good agreement between calculated and observed diastereoisomeric and enantiomeric excess values for the direct *anti*- and *syn*-Mannich reactions between $\alpha$-hydroxyacetone, *p*-anisidine, and *p*-nitrobenzaldehyde catalysed by two kinds of amino acid catalysts, L-proline (secondary) and L-tryptophan (primary).[21] The *syn* selectivity promoted by secondary cyclic amino acids contrasts with the *anti* selectivity obtained with the acyclic primary amino acids as a consequence of stereochemical features of the transition states for the C–C bond forming reactions between the corresponding intermediate enamine and imine (activated forms of the ketone and aldehyde, respectively).

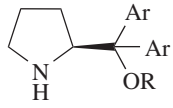
Previously proposed transition state models have been used to explain the *syn* and *anti* selectivities and enantioselectivities found for amino acid-catalysed Mannich reactions of *N*-Tos-protected $\alpha$-imino ethylglyoxylate with unmodified carbonyl donors in DMSO.[22]

Results of a kinetic and mechanistic study of aldol condensation of acetaldehyde catalysed by amino acids (glycine, alanine, serine, arginine, and proline) in aqueous salt solutions at room temperature have established that at low amino acid concentrations (<0.1 M) formation of the enamine intermediate is rate determining (first order in $CH_3CHO$ and in amino acid), whereas at higher amino acid concentration (>0.3 M) the results suggest the involvement of two amino acid molecules and are consistent

with rate-determining C–C bond formation through Mannich reaction of enamine with an intermediate imine (second-order dependence on both substrate and amino acid), although the contribution of an aldol process could not be excluded.[23]

A theoretical investigation of the stereoselectivity of the proline-catalysed Mannich reaction has been modelled on the previously proposed mechanism whereby cyclohexanone reacts with (*S*)-proline to form an enamine, formaldehyde reacts with aniline to form an imine, and the subsequent enantioselective C–C bond formation is controlled by the conformation around the C–N bond of the enamine.[24] The results of calculations at the MP2 level, with polarizable continuum modelling of the effects of DMSO as solvent, attribute the favoured formation of product of *S*-configuration to a lower energy barrier (8.5 vs 12.4 kcal $mol^{-1}$) for formation of its C–C bond, rather than to differences in activation barriers for proton transfer from *syn* and *anti* conformers of the enamine (which require only 4.2 kcal $mol^{-1}$ to interconvert).

A chiral diaryl prolinol silyl ether (**10**) has been used as an organocatalyst, with *p*-nitrobenzoic acid, to promote the direct asymmetric Mannich reaction of acetaldehyde with a range of imines, bearing *N*-benzoyl, *N*-*t*-butylcarbonyl, and *N*-(*p*-toluenesulfonyl) groups, to give $\beta$-aminoaldehydes in good yields with excellent enantioselectivity.[25] The role of the acid has been explored by a quantum mechanical study of reaction between *N*-benzoyl-*N*-benzylidenamine and acetaldehyde catalysed by 2-methylpyrrolidine, as a model for the catalyst (**10**); this involved restricted B3LYP calculations with the 6–31G(d) basis set. The calculations focused on a reaction path involving C–C bond formation between the *si*-face of the *N*-protonated imine and the face of the enamine opposite the 2-methyl substituent and leading to *N*-protonated Mannich product. It was concluded that C–C bond formation takes place with almost no activation barrier and that the rate-limiting step is enamine formation.




(**10**)

**a**; R = TMS, Ar = 3,5-$(CF_3)_2C_6H_3$

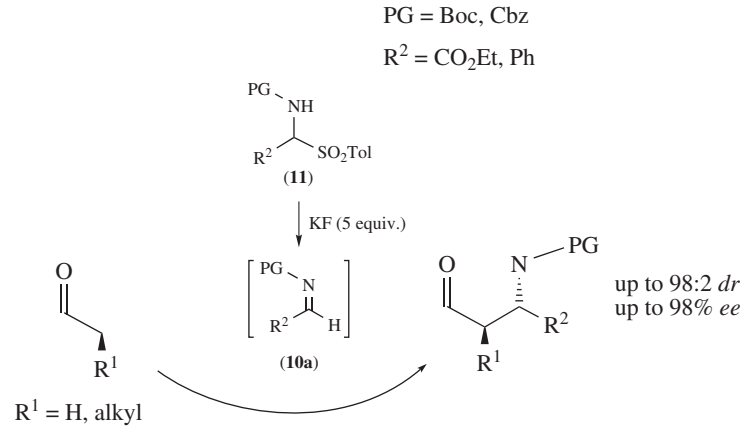
**b**; R = H, Ar = 3,5-$(CF_3)_2C_6H_3$

**c**; R = TMS, Ar = Ph

**d**; R = H, Ar = Ph

Secondary amine (**10a**) has also been used to promote *anti*-selective Mannich reaction of aldehydes with *N*-Cbz- and *N*-Boc-protected imines generated *in situ* from stable $\alpha$-amido sulfones (**11**), (Scheme 3);[26] the products were obtained in high yield with high diastereo- and enantio-selectivity.

Direct asymmetric *syn*-selective Mannich reaction catalysed by L-proline is believed to occur as shown in Scheme 4, whereby the $\alpha$-carboxyl group controls the orientation of the enamine *si*-face by steric repulsion and the coordination pattern of the *re*-face of $\alpha$-imino ester (**15**) by acid–base interaction, respectively.[27] Consequently, as anticipated, pyrrolidine-based aminosulfonamides (*R*,*R*)-(**12**), (*S*)-(**13**), and (*S*)-(**14**) have proved to be effective promoters of the *anti*-selective C–C bond formation, since they can direct the opposite facial orientation of (**15**).



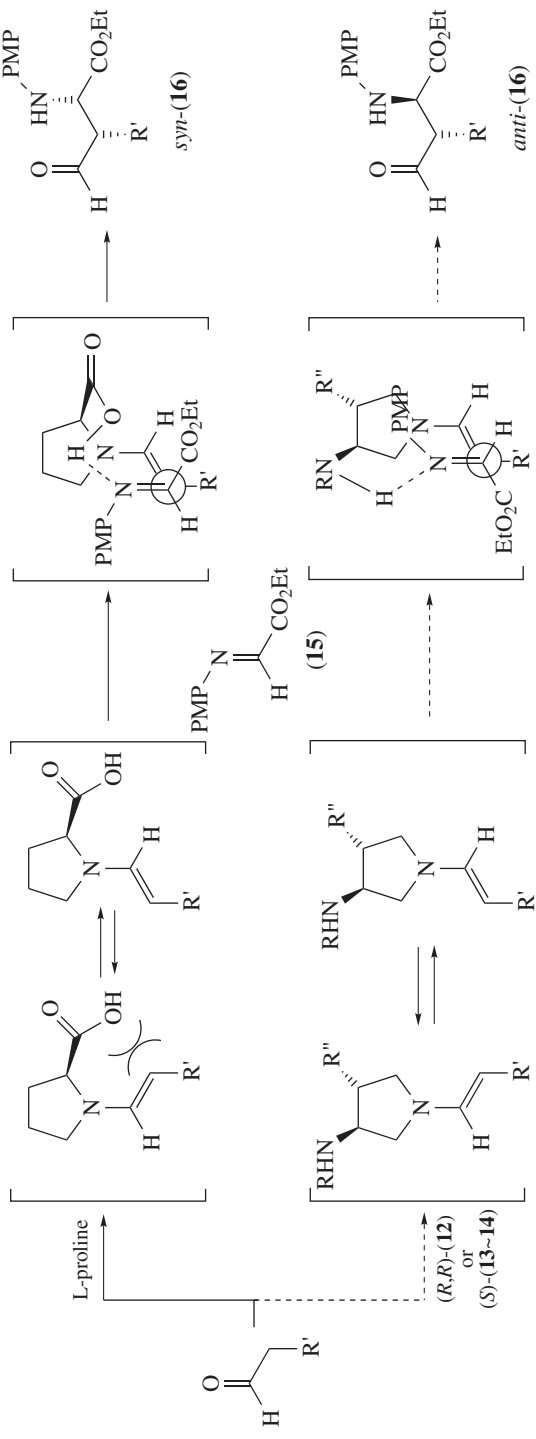

SCHEME 3

Only limited enantioselectivities have been achieved for addition of diethylmalonate (up to 71% *ee*) and 1,3-diketones (up to 61% *ee*) to *N*-CBz-imines under the influence of chiral bifunctional thiourea organocatalysts obtained by combining (*S*)-*t*-leucine derivatives with (1*R*,2*R*)-*trans*-1,2-diaminocyclohexane.[28] A chiral primary amine–thiourea organocatalyst (also derived from (1*R*,2*R*)-*trans*-1,2-diaminocyclohexane) has been reported to promote a Mannich-type reaction of unmodified ketones with $\alpha$-hydrazono esters in high yield (up to 89%), high enantioselectivity (up to 99% *ee*), and without the need to preform enolate equivalents.[29] Calculations suggest that the nucleophile is an organocatalyst–enol complex, rather than an enamine intermediate.

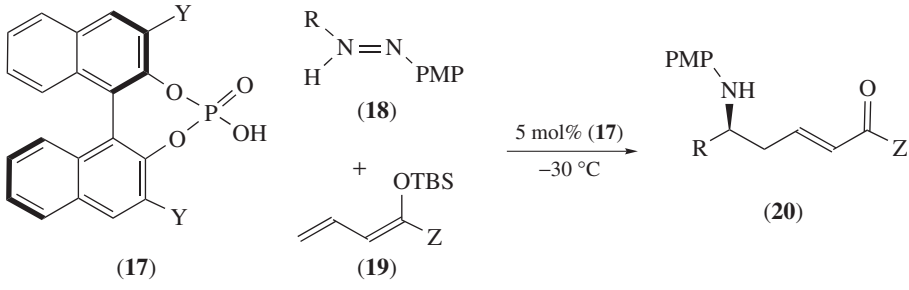
A BINOL-derived chiral 1,1′-binaphthyl-2,2′-disulfonic acid has been used in 1:2 combination with 2,6-diarylpyridines to form disulfonate salts which act as Brønsted acid–base organocatalysts to promote Mannich-type reactions of diketones and keto ester equivalents with aldimines in 91–99% yield and with up to 84–98% *ee*.[30]

Chiral phosphoric acids (**17a**)[31] and (**17b**)[32] have been used as Brønsted acid catalysts to promote enantioselective vinylogous Mukaiyama–Mannich reactions of *N*-(*p*-methoxyphenyl)imines (**18**) with vinylketene silyl *O*,*O*-acetals (**19a**)[31] and *N*,*O*-acetals (**19b**).[32] These high yield reactions proceed with complete $\gamma$-regioselectivity to give the corresponding $\delta$-amino $\alpha,\beta$-unsaturated esters (**20a**) and amides (**20b**), respectively, in one step (Scheme 5); a catalytic cycle involving attack of the nucleophile on the chiral salt formed between (**17**) and (**18**) is proposed and up to 92% *ee* has been achieved. This is consistent with a more general interpretation of the enantiomeric transformations effected by such catalysts.[33]

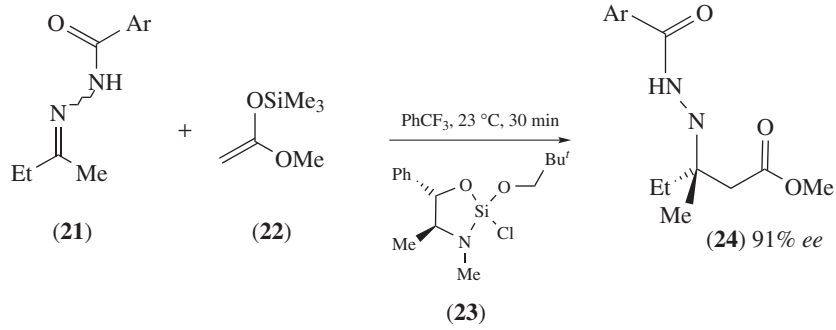
A general method for highly enantioselective Mannich reaction of aliphatic ketimines has been developed using a chiral silane Lewis acid to promote reaction between ketone-derived hydrazones and silyl ketene acetals; 91% *ee* was reported even for the hydrazone from butan-2-one (Scheme 6).[34]




SCHEME 4



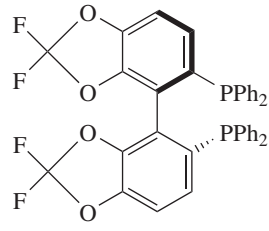

SCHEME 5




SCHEME 6

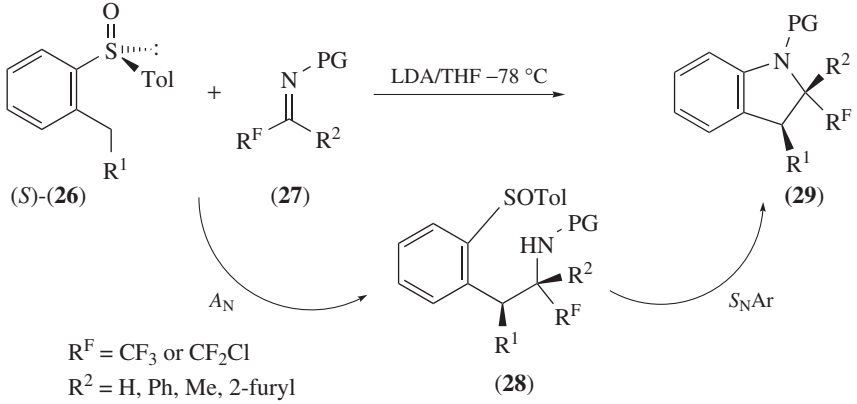
A mechanistic study of the formation of *o*-aminomethyl derivatives of phenols by their Mannich reaction with 1,3,5-trialkylhexahydro-1,3,5-triazines, as a source of *N*-methylenealkylamines, has been reported.[35] A Mannich-type reaction of $\alpha$-bromo ketones with simple *N*-alkylaldimines has been promoted by germanium(II), which acts as a reducing agent [with $Yb(OTf)_3$ or $Bi(OTf)_3$ catalysts] to form a nucleophile for C–C bond formation.[36] A highly diastereoselective ($dr = 2{:}1$–$99{:}1$) reductive Mannich reaction between ketimines and $\alpha,\beta$-unsaturated esters, using pinacolborane as the reducing agent in the presence of a catalytic complex of CuOAc with $PPh_3$ or $MePPh_2$, has been reported.[37] Further development of the methodology, by use of $(EtO)_3SiH$ as reducing agent and CuOAc–(*R*)-DIFLUORPHOS (**25**) as the catalyst, achieved high enantioselectivity (82-93% *ee*) and enabled products ($\beta$-amino acid precursors) containing contiguous tri- and tetra-substituted carbons to be formed with high stereoselectivity.

A mechanistic study of an asymmetric Mannich-type addition of malonates to dihydroisiquinolines, catalysed by chiral Pd(II)–SEGPHOS complexes, has assisted the development of oxidative Mannich-type reactions starting from tetrahydroisoquinolines.[38]



(**25**)

Diastereoselective Mannich reaction of chiral sulfinyl carbanions with fluorinated imines (**27**), followed by intramolecular nucleophilic aromatic displacement of the sulfinyl group by nitrogen of the intermediate adduct (**28**), has enabled one-pot synthesis of optically pure fluorinated indolines (**29**) from 2-*p*-tolylsulfinylalkylbenzenes (**26**) to be achieved.[39]




*Addition of Organometallics*

The catalytic enantioselective addition of organozinc reagents to imines has been reviewed[40–42] and the important role of copper catalysis has been emphasized[41] with particular reference to the formation of tertiary alcohols and $\alpha$-tertiary amines by C–C bond formation to ketones nd ketimines.[42]

The diastereoselective addition of enantiopure $\alpha$-lithio-vinyl and -dienyl sulfoxides to enantiomerically pure *N*-sulfinimines is primarily directed by *N*-sulfinimine sulfur, to give allylic amines from which highly functionalized enantiopure 3-sulfinyl-2,5-*cis*-dihydropyrroles have been formed.[43] An addition–$S_N$i mechanism has been proposed to account for the formation of (2*R*,1′*S*)-2-(1′-aminoalkyl)aziridine with very high diastereoselectivity, in enantiopure form, on reaction of the chiral *N*-tosylaldimine formed from phenylalaninal with *in situ*-generated iodomethyllithium; the procedure is applicable to the synthesis of aziridines in general.[44]

Optically active (up to 99% *ee*) *N*-formyl-protected amines (RR′CHNHCHO) have been synthesized in high yields by copper/phosphoramidite-catalysed addition of organozinc and organoaluminium reagents (RM) to *N*-acylimines (R′CH=NCHO), generated *in situ* from aliphatic and aromatic $\alpha$-amidosulfones [R′CH(Ts)NHCHO].[45] Asymmetric 1,2-additions of allylmagnesium bromide to aldimines bearing a chiral $C_2$-symmetric *N*-phosphinyl group form the corresponding chiral *N*-phosphinyl homoallylic amines in excellent yields and good diastereoselectivities.[46]

The reactivity and selectivity shown by triorganozincates towards (*R*)-*N*-(*t*-butanesulfinyl)imines have been found to differ from those of the Grignard reagents from which they were derived, in some cases permitting the same imine to be converted to either enantiomer of the product; the $\alpha$-branched sulfinamides obtained, with diastereomeric ratios of up to 98:2, can be desulfinated under acidic conditions to give chiral primary amines with up to 96% *ee*. Additions to aromatic and aliphatic aldimines, and also activated ketimines, have been studied and advantage has been taken of the relatively slow transfer of the methyl group from mixed triorganozincates.[47,48]

The importance of furans and pyrroles as synthons in organic synthesis has been highlighted in a report of their formation by addition/oxidative rearrangement of 3-furfurals and 3-furylimines;[49] the *N*-tosylimines react with organometallic reagents (RM) to form furylsulfonamides, which rearrange to 2-R-substituted 3-formylpyrroles on treatment with NBS.

A novel direct addition of cycloalkanes to imines, mediated by peroxide and tolerant of a wide range of functional groups, has provided a metal-free route to Grignard-type addition products.[50]

### *Oxidation and Reduction of Imines*

Oxidation reactions of Schiff bases have been reviewed.[51]

Excellent enantioselectivities (up to 99.6% *ee*) have been reported for reduction of aromatic *N*-alkylketimines by trichlorosilane promoted by a Lewis base organocatalyst having both *C*- and *S*-chirality (an *N*-*t*-butylsulfinylprolinamide).[52]

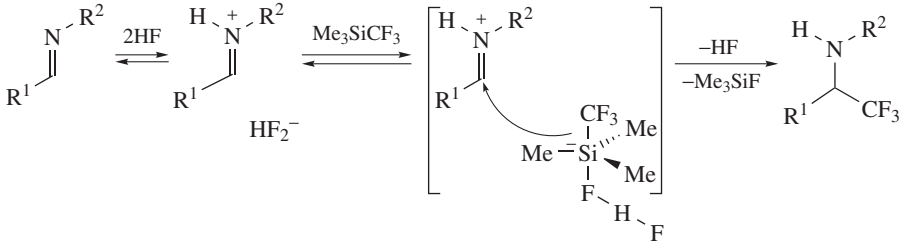
The mechanism of the Hantzsch ester hydrogenation of imines $R^1R^2C{=}NAr$ catalysed by chiral BINOL-phosphoric acid (**17**, $Y = R^3$) has been studied by DFT methods which suggest that the catalyst not only acts as a Brønsted acid to activate the imine group but also interacts with the Hantzsch ester in a manner which accounts for the enantioselectivity.[53] A chiral diamine-ligated Ir(III) catalyst in combination with a chiral phosphate counterion from (**17**, Y = R) promotes asymmetric hydrogenation of a wide range of acyclic imines to afford chiral amines in up to 99% *ee*.[54]

### *Iminium Species*

No-barrier theory has been applied successfully to those examples of the Strecker reaction for which rate and equilibrium data in aqueous solution are available; it has been possible to calculate rate constants for cyanide ion addition to the iminium ion and to make comparison between experimental and calculated values.[25]

Hydroxyalkylsulfonates $RCH(OH)SO_3^-$ on reaction in water with aniline derivatives $R'C_6H_4NH_2$ equilibrate with anilinoalkanesulfonates $R'C_6H_4NHCH(R)SO_3^-$.[56] The kinetics are consistent with a mechanism involving dissociation to RCHO followed by formation of a carbinolamine intermediate which undergoes acid-catalysed dehydrative formation of an iminium ion to which sulfite ion adds rapidly. Rate and equilibrium studies have revealed a change in rate-determining step from carbinolamine formation to dehydration as the pH is increased, and the electronic effects of R and R′.

Nucleophilic trifluoromethylation of imines by using $Me_3SiCF_3$ under acidic conditions (HF generated *in situ*) has been reported for the first time and is believed to involve concerted transfer of the $CF_3$ group from silicon to the iminium electrophile (Scheme 7); the C=N bond was found to be more reactive than C=O.[57]



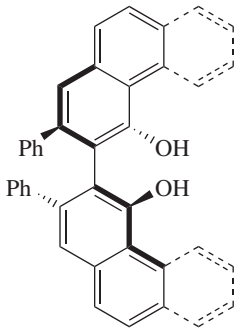

SCHEME 7

A Brønsted acid-catalysed imino–ene reaction has been reported whereby the ene component is a simple unactivated alkene $PhMeC{=}CH_2$ and the imine ($TsN{=}CHCO_2Et$) has been activated by phosphonic acid.[58]

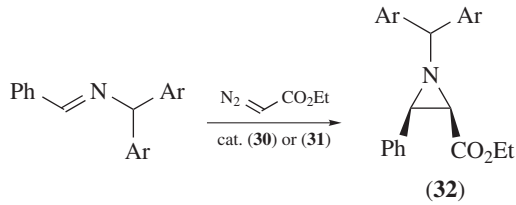
*Imine Cycloadditions*

Asymmetric aziridination of imines continues to attract attention.[59–62] Structures and applications of the catalysts for aziridination of imines with ethyl diazoacetate formed from either the VANOL (**30**) or VAPOL (**31**) ligand and triphenylborate have been discussed in detail.[60] Although these chemzymes have different surface areas, they have been found to give nearly the same degree of asymmetric induction for a range of imines $PhCH{=}NCHAr_2$; it has been concluded that the active site is larger than expected since both rate and enantioselection increase with alkyl (but not perfluoroalkyl) substitution of the aryl group (Scheme 8).[59]

Sulfur ylide-promoted asymmetric aziridinations of imines have also been reported.[61,62] Thus, ($S_S$)-*t*-butylphenylsulfinimine has been converted to chiral non-racemic vinylaziridines on reaction with a range of allyltetrahydrothiophenium salts with varying substitutions on the alkenyl group,[61] and a DFT investigation of factors influencing the stereochemistry found for addition of bicyclic sulfur ylides (stabilized and semistabilized) to substituted benzaldimines (*N*-$SO_2Me$,




(*S*)-VANOL (**30**) unextended
(*S*)-VAPOL (**31**) extended



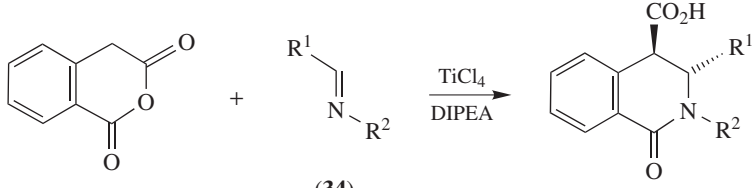

(**32**)

| Aryl substitution | Realtive rate | *% ee* |
|---|---|---|
| 3,6-$(CF_3)_2$ | 1 | 37 |
| H | 50 | 89 |
| 3,6-$(CH_3)_2$ | 500 | 92 |
| 3,6-$(Bu^t)_2$-4-MeO | 800 | 99 |

SCHEME 8

and *N*-$CO_2$Me substituted) has concluded that correct prediction of the extent of enantioselection requires knowledge of the activation barriers for elementary steps beyond the initial addition step;[62] in the case of stabilized ylides, the ring closure (or elimination of sulfur compound) is crucial in controlling enantio- and diastereo-selection.

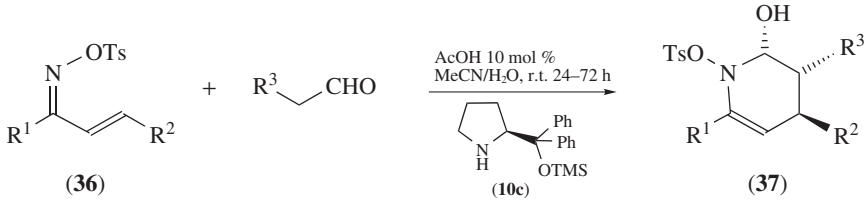
Reaction between homophthalic anhydride (**33**) and imines (**34**) in the presence of $TiCl_4$ and diisopropylethylamine (Scheme 9) has been found to be *trans*-selective (66–96% *de*), in contrast with the relatively unselective direct reaction.[63] DFT calculations on the 'Perkin–Mannich' process indicate that the intermediate titanium complex is closed shell in nature and that a transition state with a boat conformation features in the C–C bond-forming step; cyclization of the anionic intermediate is *trans*-stereocontrolled by repulsion between the imine aryl group and a chlorine atom of the octahedral titanium. Enantiocontrol of the diastereoselective reaction can be achieved using homochiral imines.




(**33**) (**34**) *trans*-(**35**) (66–96% *de*)

SCHEME 9

A versatile asymmetric inverse-electron-demand aza-Diels–Alder reaction of *N*-sulfonyl-1-azabuta-1,3-dienes (**36**) with aldehydes to form (**37**) has been catalysed by the $\alpha,\alpha$-diphenylprolinol derivative (**10c**); transformation efficiency is aided by the presence of water.[64]




*Other Reactions of Imines*

Enantioselective addition of alcohols $R^1OH$ to imines $R^2CH{=}NCOPh$ has been promoted catalytically by BINOL-phosphoric acid (**17**, R = 9-anthryl) in EtOAc to give the respective chiral *N*,*O*-aminals in high yield and excellent *ee*.[65]

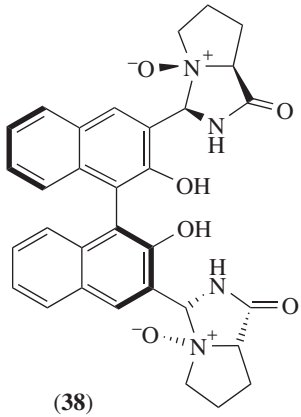
*N*-*t*-Butylsulfinylimines undergo highly selective addition of the $\alpha$-acylvinyl anion equivalent lithium allenolates ($LiOR^1C{=}C{=}CHR^2$) formed on reaction of *n*-BuLi with $\alpha$-hydroxypropargylsilanes; the $\beta$-substituted aza-MBH-type products so formed are obtained in high yields from a diverse selection of imines with good to excellent diastereoselectivity and regioselectivity, favouring the *Z*-isomer of the alkene.[66]

*N*-Diphenylphosphinoyl derivatives of aromatic, heteroaromatic, and aliphatic ketoimines have been found to undergo asymmetric addition of allylic cyanides ($RCH{=}CHCH_2CN$) catalysed by a bimetallic system comprising (*R*,*R*)-Ph-BPE/$[Cu(CH_3CN)_4]ClO_4$/LiOAr.[67] The intermediate $\alpha$-adducts isomerize to synthetically useful $\alpha,\beta$-unsaturated nitriles (*E*:*Z* up to 2:98, *ee* up to 94%) bearing an optically active tetrasubstituted carbon.

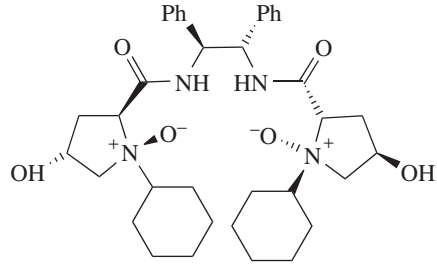
Highly enantioselective Strecker reactions of imines with TMSCN have been catalysed by chiral organocatalysts derived from L-proline to give the corresponding $\alpha$-aminonitriles.[68,69] Direct reactions of ketoimines[68] were promoted by (*S*)-BINOL derivative (**38**), with up to 99% *ee*, and three-component reactions of both aromatic and aliphatic aldehydes with (1,1-diphenyl)methylamine and TMSCN were promoted by novel *trans*-4-hydroxy-L-proline-derived *N*,*N*-dioxides (**39**) with up to 95% *ee*.[69]

*Oximes, Hydrazones, and Related Species*

The pH–rate profile for oxime formation from benzoylformic acid ($pK_a = 1.39$) is consistent with a rate-determining combination of acid-catalysed dehydration reactions of the equilibrating carbinolamines derived from the acid and its anion. The overall second-order rate constants observed are linearly related to the hydronium ion concentration from pH 5.5 to ~2.2 and deviate only slightly from the slope of −1 as the pH is reduced further to 0.25 (as a consequence of the very similar values of the limiting rate constants of the two forms of the substrate.[70]



(**38**)



(**39**)

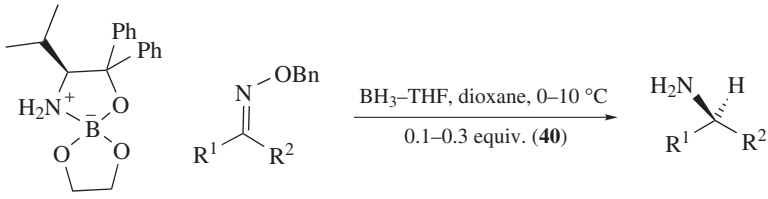
A theoretical study of the [1,3]-prototropic rearrangements of oximes and their ethers has highlighted the highly endothermic nature of the $CH_3$–CH=NOH to $CH_2$=CH–NHOH rearrangement (16.4 kcal $mol^{-1}$), attributed to destabilization of the N–O bond by the increased charge on nitrogen.[71]

Results of DFT calculations which model $H^+$ transfer in the Beckmann rearrangement of acetaldoxime have revealed three stages: formation of acetaldoxime cation by $H^+$ transfer from the C atom to the N atom of the imine; formation of an enolic imine by an intermolecular mechanism;[72] and formation of acetamide (also by an intermolecular mechanism). A molecular orbital study of the Beckmann rearrangement of oximes (using acetone oxime as a model) has determined that the rearrangement step is concerted.[73]

*Ab initio* and DFT calculations have of molecular elimination kinetics of benzaldoxime in the gas phase suggest that the transition state is a near-planar semi-polar four-membered cyclic structure in which the benzylic C–H bond is slightly more polarized than is N–OH;[74] the best agreement between calculated and experimental thermodynamic and kinetic parameters was obtained at the B3LYP/6–31G level. The elimination kinetics observed for formation of ArCN from (*E*)-2,4-dinitrobenzaldehyde *O*-benzoyloximes [ArCH=NOC(O)Ar] promoted by $R_2NH/R_2NH_2^+$ in 70 mol% MeCN are consistent with the $(E1cB)_{irr}$ mechanism; thus, the second-order kinetics exhibit Brønsted $\beta = 0.27$–$0.32$, $|\beta_{lg}| = 0.28$–$0.32$, and a negligible coefficient for interaction between the base catalyst and the leaving group.[75]

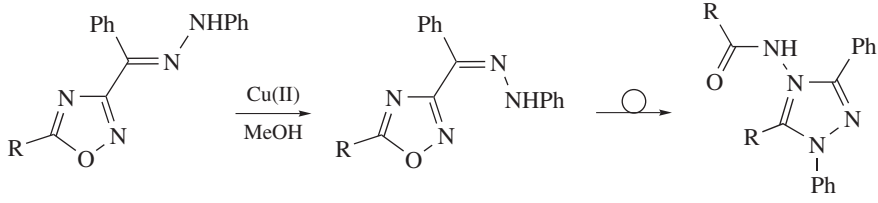
Non-racemic amines bearing heterocyclic and heteroaromatic rings have been synthesized by highly enantioselective boron reduction of the corresponding *O*-benzyl ketoximes catalysed by a novel spiroborate ester (**40**) derived from (*S*)-diphenylvalinol and ethylene glycol.[76]

Studies of regioselective additions of pyrroles to optically active nitrones under acidic conditions have been extended to include functionalized nitrones, with control of the stereochemical outcome.[77] Nitrones featuring a chiral auxiliary on the nitrogen atom or a chiral lateral chain have been explored and glyoxylate-based chiral nitrones have been found to react at the C(2) or C(3) position of the pyrrole nucleus to afford *N*-hydroxyamino esters in high yields as single diastereoisomers.




(**40**)

Investigation of the isomerization and rearrangenent of (*E*)- and (*Z*)-phenylhydrazones (**41**, R = Ph) of 3-benzoyl-5-phenyl-1,2,4-oxadiazole catalysed by copper salts in methanol has revealed that the choice of counterion is important since $E \rightarrow Z$ isomerization promoted by the Lewis acid catalyst may be followed by rearrangement of the *Z*-isomer to the corresponding 4-benzoylamino-2,5-diphenyl-1,2,3-triazole (**42**, R = Ph).[78] This mononuclear rearrangement of the heterocycle is a consequence of bifunctional catalysis by Lewis salts and occurs with the hydrated Cu(II) acetate, chloride, and bromide but not the sulfate or perchlorate; it has been attributed to coordination of the hydrazone with Lewis acid, thereby increasing the acidity of the hydrazone NH, which is then able to interact with the basic anions in the rearrangement transition state. The kinetics of rearrangement of oxadiazoles (*Z*)-(**41**) to triazoles (**42**), in solution at different proton concentrations and in the gas phase, have been studied for alkyl chains R of length $C_4$–$C_{12}$.[79] The rates are relatively insensitive to R but there is some evidence of substrate self-assembly with increasing chain length in both the gas phase and in dioxane–water solutions, for which there is spectroscopic support.



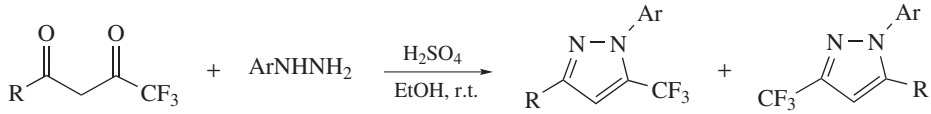

(*E*)-(**41**) (*E*)-(**41**) (**42**)

Implications of acid-catalysed isomerization and decomposition of ketone 2,4-dinitrophenylhydrazones in quantitative analysis of ketones using DNPH have been addressed.[80]

The kinetics of the uncatalysed Strecker-type reaction of aldehyde and ketone *N*,*N*-dialkyl hydrazones with TMSCN in pure water suggest that HCN is generated *in situ* and that its rate-determining direct reaction with the hydrazone is activated by an intramolecular association with the dialkylamino lone pair.[81]

A protonated cinchonine derivative has been used under environmentally benign conditions to promote (through hydrogen bonding) highly enantioselective formation of chiral amines by addition of radicals (from RI) to *N*-benzoyl hydrazones.[82]

A study, by $^{19}F$ NMR spectroscopy, of the kinetics and mechanism of pyrazole formation on condensation of 1,3-diketones (**43**) in ethanol with selected arylhydrazines has revealed that the regiochemistry is influenced by reactant ratio, substituents, and acidity;[83] bulky substituents on the diketone increase the proportion of pyrazole (**45**), whereas excesses of either reactant increase the proportion of (**44**), which is also favoured by high acidity. The reactions are first order in both diketone and arylhydrazine but the rate-determining step shifts with pH. At pH 1.9–2.1, rate-determining ring closure of the intermediate arylhydrazone is supported by direct observation and determination of the Hammett $\rho = -2.3$.




(**43**) (**44**) (**45**)

## C–C Bond Formation and Fission: Aldol and Related Reactions

*Regio-, Enantio-, and Diastereo-selective Aldol Reactions*

The use of amino acid residues, proline in particular, continues to dominate approaches to enantiocontrol of aldol-type reactions.[84–104] New development of aldol reactions using proline derivatives has been reviewed[84] and the stereoselectivity of (*S*)-proline-catalysed direct aldol reaction of acetone with isobutyraldehyde has been explored by B8LYP calculation.[85]

A novel chiral ionic liquid, based on D-camphor-10-sulfonic acid, has been found to promote L-proline-catalysed aldol reactions with good chemoselectivity in water and in organic solvents, by stabilizing the transition state through hydrogen bonding.[86]

DFT methods used to explore the effects of different amino acid catalysts on the direct aldol reactions between $\alpha$-hydroxy ketones and isobutyraldehyde or 4-nitrobenzaldehyde have provided good explanations for the opposite *syn* and *anti* diastereoselectivities for the C–C bond-forming step found, respectively, when the catalyst is acyclic and primary (such as threonine) or cyclic and secondary cyclic (such as proline).[87] Good agreement between observed and calculated diastereomeric and enantiomeric ratios was also found for *syn*- and *anti*-aldol reactions between $\alpha$-substituted ketones and 4-nitrobenzaldehyde, catalysed by L-leucine amino alcohol amides and L-proline amino alcohol amides, respectively.[88] DFT and AIM calculations have rationalized the reversal of chirality (from *S* to *R*) observed for the L-proline-catalysed cross-aldol addition of acetone to isatin and 4,6-dibromoisatin, respectively; the stereoelectronically favoured transition state for the former reaction becomes inhibited sterically by the bromo substituents.[89]

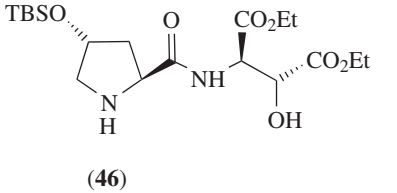
HF/6–31G(d) calculations have elucidated the origins of double asymmetric induction found for L- and D-proline-catalysed aldol reactions between 2-azido-3-*O*-benzyl-2-deoxy-D-glyceraldehyde and an achiral dioxanone.[90]

By providing an optimum environment for aldol reactions to proceed in water, an enzyme-like polymer catalyst consisting of a hyperbranched polyethylenimine derivative with proline is able to prevent enolizable aldehydes from undergoing unwanted irreversible self-condensation reactions, rather than the cross-aldol reactions intended.[91]

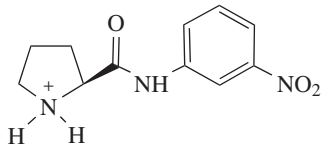
A temperature study of reaction between nicotinaldehyde (3-pyridinecarbaldehyde) and cyclohexanone in water, catalysed by morpholine and by *trans*-4-*t*-butyldimethylsilyloxy-L-proline, has established that the *anti*:*syn* diastereomeric ratio for the former remains constant but that for the latter the non-linear behaviour of the Eyring plot, with the presence of an inversion temperature, is indicative of dynamic solvation effects.[92]

A cysteine-derived prolinamide structure has been optimized to promote asymmetric aldol reactions of propanone with a broad range of aldehydes with up to 94% *ee*.[93] Oxazoline-substituted prolinamides have been used to catalyse the direct asymmetric aldol reaction between cyclohexanone and a range of aldehydes; electron-deficient aldehydes gave the highest yields, with up to 84% *ee*.[94]

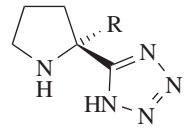
Two inherently chiral calix[4]arene-based bifunctional organocatalysts, each featuring an L-prolinamido group and a *m*-dimethylamino group on one of the aryl rings, have been created to promote enantioselective aldol reactions between ketones and aromatic aldehydes in the presence of acetic acid;[95] high enantio- and diastereoselectivities have been reported. As little as 1% of prolinamide (**46**) has been found to organocatalyse direct aldol reactions of acyclic and cyclic ketones with a wide range of aromatic aldehydes in water with up to >99:1 diastereoselectivity and 98% *ee*.[96] Protonated prolinamide (**47**) promotes reaction of unmodified ketones with aromatic aldehydes in water with similar stereoselectivities.[97]



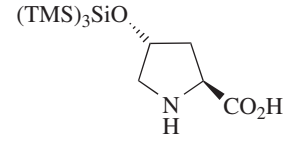

(**46**)




(**47**)




(**48**) **a**; R = H, **b**; R = Me




(**49**)

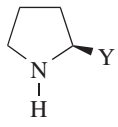
The novel organocatalyst (**48b**) has been found to catalyse the aldol reaction between acetone and various aldehydes with greater *ee* than obtained using (*S*)-proline or (**48a**); studies of the effect of $\alpha$-substitution of other proline-based organocatalysts and application of (**48b**) to other reactions are ongoing.[98] An unexpected 1,2-aldol reaction, rather than Michael reaction, of $\alpha,\beta$-unsaturated trifluoromethylketones ($F_3CCOCH{=}CHC_6H_4.X$-*p*) with acetone in $CH_2Cl_2$ catalysed

by L-proline derivatives has been investigated; (**49**) proved to be particularly effective.[99]

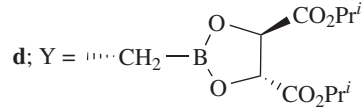
Side-chain protonated amino acids (arginine and lysine) have been used to promote asymmetric aldol reactions of cyclic ketones (via intermediate enamine) with aromatic aldehydes in ionic liquids and DMSO.[100] A recyclable non-immobilized siloxyserine organocatalyst for asymmetric direct aldol reaction has also been used in ionic liquids.[101]

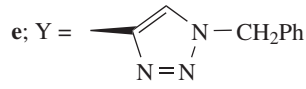
Small peptides have also been used to promote asymmetric direct aldol reactions.[102–104] DFT calculations have revealed the origin of the poor enantioselectivity found for reaction between acetone and 4-nitrobenzaldehyde catalysed by (*S*,*S*)-proline dipeptide,[102] and have established that the main source of stereoselectivity of reaction of cyclohexanone as donor with benzaldehyde as acceptor, catalysed by (*S*)-Ala-(*S*)-Ala, is interaction of the N-terminal amino acid side-chain with the cyclohexene ring of the enamine.[103] Structures of a series of new proline-based dipeptide catalysts, featuring two amide units which stabilize the aldol transition state in chloroform by hydrogen bonding to the aldehyde and favour one of its faces for the attack by the enamine derived from cyclohexanone, have been fine tuned to achieve yields and *anti* diastereoselectivities of up to 99% and up to 98% *ee*.[104]

A range of (*S*)-pyrrolidine derivatives (**50**) have been used with varying degrees of success to catalyse asymmetric direct aldol reactions, as follows: sulfonamide (**50a**) for aryl methyl ketones with aromatic aldehydes;[105] diarylprolinol (**50b**) for self-reaction of acetaldehyde;[106] phosphinyl oxides (**50c**, with and without *N*-glucosylation) with a range of cyclic ketones and aromatic aldehydes;[107] the homoboroproline (**50d**) with acetone and *p*-nitrobenzaldehyde;[108] and the pyrrolidine–triazole conjugate catalyst (**50e**) for Michael and aldol reactions.[109] Chiral (*S*)- and (*R*)-BINOL-derived zincate complexes bearing two prolinol residues (**10d**) N-attached, respectively, to *o*- and *o*′-methyl groups have been used to achieve up to 97% yield and up to 80% enantioselectivity for aldol addition of aryl ketones to aryl aldehydes.[110]



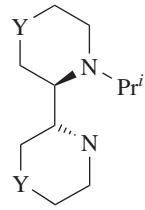
**a**; Y = $CH_2NHTf$
**b**; Y = $C(OH)[3,6\text{-}(CF_3)_2C_6H_3]_2$
**c**; Y = $Ar_3P{=}O$





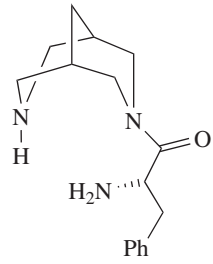
Biomorpholine-based catalysts (**51a**) have been found to be more efficient and reactive than the corresponding bipiperidine derivatives (**51b**) in asymmetric intra- and inter-molecular aldol reactions, as a consequence of the greater nucleophilicity of the amine and corresponding enamine intermediate.[111]

The primary–secondary amine organocatalyst (**52**) based on bispidine catalyses reactions of propanone and butanone with functionalized ketones RCOX [X = $PO(OR)_2$, $CO_2Me$, $CH(OR)_2$, H] to give chiral *t*-alcohols in 97% yield and up to 98% *ee*.[112]

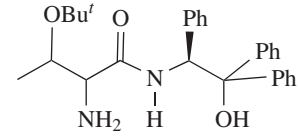


(**51**)

**a**; Y = O, **b**; Y = $CH_3$



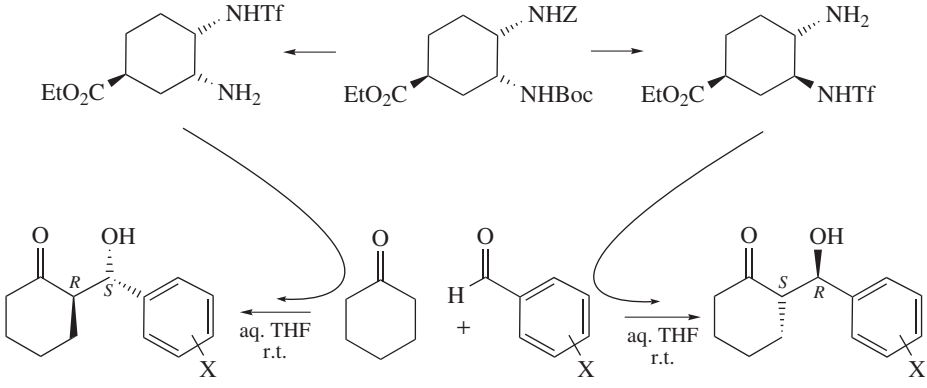
(**52**)



(**53**)

*Syn*-aldol products have been formed with up to 99% *ee* and *dr* up to 8:1 and 11:1, respectively, by reaction of unprotected or protected dihydroxyacetone with a variety of aldehydes catalysed by (**53**).[113] Organocatalysed aldol additions of dihydroxyacetone have featured in methodologies for total synthesis of carbohydrates.[114]

It has been possible to effect a complete switch in product selectivity, and thereby obtain both enantiomeric aldol products, using two different chiral organocatalysts from a common chiral source, as illustrated in Scheme 10.[115]



SCHEME 10

High *anti* selectivity and high *ee* have been reported for direct aldol reactions of ketones with aromatic aldehydes promoted by chiral bis(oxazolinyl)phenylrhodium complexes in combination with AgOTf;[116] synergetic involvement of Lewis acid and Brønsted base sites is proposed.

Diastereo- and enantio-selective reductive aldol addition reactions of vinyl ketones via catalytic hydrogenation have been reviewed.[117] Ytterbium complexes with amino acid-armed chiral ligands have been used to effect tandem aldol reduction reactions giving rise to 1,3-*anti*-diols with three stereogenic centres on condensation of aliphatic ketones with aromatic aldehydes with up to 64% *ee*.[118]

$TiCl_3(i\text{-PrO})$-mediated aldol reactions of $\alpha$-benzyloxy methyl ketones with aliphatic, aromatic, and $\alpha,\beta$-unsaturated aldehydes exhibit high yields and remarkable 1,4-*anti* induction.[119]

A tutorial review describes the high levels of substrate-controlled 1,5-*anti* stereoinduction featured in the boron-mediated aldol reactions of $\beta$-oxygenated methyl ketones with achiral and chiral aldehydes.[120] Based on DFT investigation of the effects of the alkoxy protecting group (OMe, OPMB, PMP, acetate, tetrahydropyran, and OTBS) present on the intermediate boron enolate, it has been concluded that formation of a 1,5-*anti* adduct is a consequence of a stabilizing formyl hydrogen bond between the alkoxy oxygen and aldehyde proton, within a boat-shaped transition state, and minimization of steric interaction between the $\beta$-alkyl group and one of the ligands on boron;[121] this conformation is not adopted by silyl ethers.

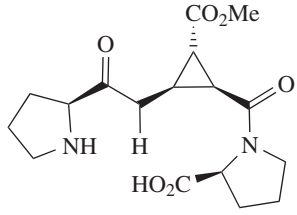
Asymmetric aldol reactions of enolizable carbon pronucleophiles with formaldehyde and ethyl glyoxylate have been catalysed by Pd(II)–BINAP complexes.[122]

Exclusive regioselective formation of carbinol allenoates on $(t\text{-Bu})_4NF$-mediated aldol reaction of propargyl or allenyl esters with aldehydes has been attributed to thermodynamic control.[123]

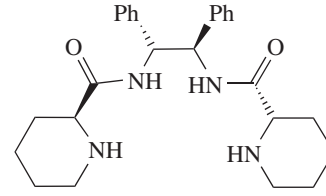
An aldol process could not be ruled out for amino acid-catalysed condensation of acetaldehyde in aqueous solution.[124]

### *Intramolecular Aldols*

Proline asymmetry has featured in control of several intramolecular aldol reactions.[125–127] The transition state for intramolecular aldol reaction of 1,7-dialdehydes catalysed by (*S*)-proline has been analysed by DFT methods, which validated the enamine-based mechanism, revealed the associated steric and electrostatic influences, and suggested that a water molecule may control the stereoselectivity.[125] Short $\alpha/\beta$-peptides, such as (**54**), featuring turn-inducing elements have been used to catalyse intra- and inter-molecular aldol reactions in homogeneous and heterogeneous aqueous solutions and in organic solvents.[126] A *trans*-4-fluoroproline has been used to promote enantioselective transannular aldolization of cyclooctane-1,4-diones to the corresponding cyclic $\beta$-hydroxy ketones [en route to (+)-hirsutene].[127]

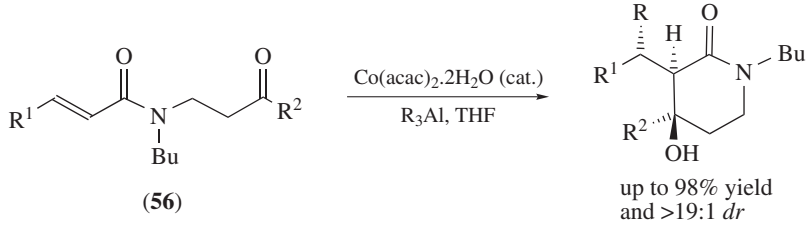



(**54**)



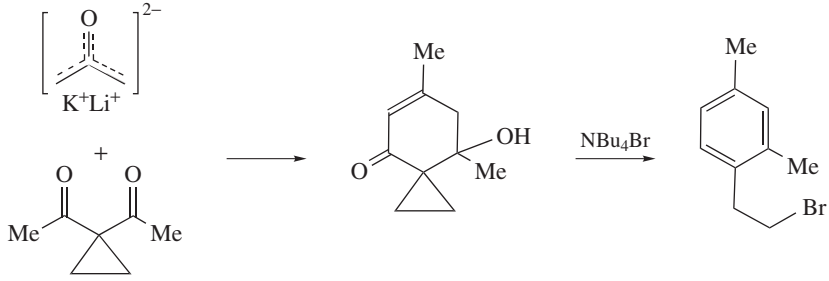

(**55**)

$\alpha,\beta$-Unsaturated amides (**56**) with neighbouring ketone groups undergo diastereoselective alkylative aldol cyclizations, to give $\beta$-hydroxylactams containing three contiguous stereocentres (Scheme 11), on reaction with trialkylaluminium reagents and $Co(acac)_2{\cdot}2H_2O$ as precatalyst.[128] Similar compounds, in which the tether to the carbonyl group is through an amide or ester linkage with one or two methylene groups, have been reported to undergo reductive aldol cyclizations using diethylzinc [and $Ni(acac)_2$ precatalyst] to deliver hydride to the $\beta$-position; deuterium labelling studies have revealed the complex nature of the reactions.[129]




SCHEME 11

The dianions of acetone and of diethyl 2-oxopropylphosphonate react with 1,1-diacylcyclopropanes to form hydroxyspiro[5.2]cyclooctenones (Scheme 12), from which functionalized phenols can be formed.[130]

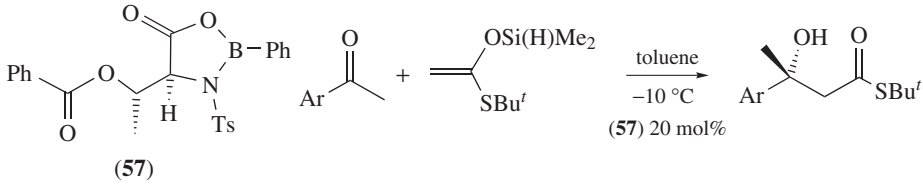



SCHEME 12

*Mukaiyama and Vinylogous Aldols*

Asymmetric Mukaiyama aldol reaction of non-activated ketones has been achieved for the first time by using an oxazaborolidinone catalyst (**57**) derived from *O*-benzoyl-*N*-tosyl-*allo*-threonine; a means of obtaining *t*-$\beta$-hydroxy carbonyl compounds is illustrated in Scheme 13.[131]

*Ab initio* calculations have established that the mechanism of the halogen-catalysed Mukaiyama aldol reaction is substituent dependent; thus trihydrosilyl enol ether and methanal react by a concerted pathway, whereas combination of 1-phenyl-1-(trimethylsilyloxy)ethene with benzaldehyde proceeds stepwise.[132]




SCHEME 13

*Nitrile/Nitro/Nitroso Aldols*

The application of chiral Brønsted acids to the nitroso aldol reaction has been reviewed.[133]

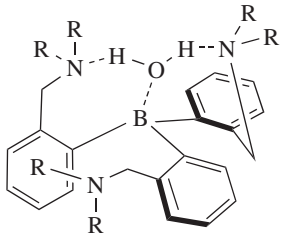
The corresponding nitro[$^{11}$C]aldol products have been obtained in 3–25% radiochemical yields with 39–51% *ee* by reaction of nitro[$^{11}$C]methane with aldehydes in the presence of a chiral metal catalyst based on (*R*)-binaphtol[134] and Henry reaction of nitromethane with *p*-nitrobenzaldehyde has been achieved with up to 82% *ee* under the catalytic influence of a range of chiral Schiff bases in $CH_2Cl_2$.[135]

A DFT study of the cinchona thiourea-catalysed Henry reaction of aromatic aldehydes with nitromethane has revealed two competing C–C bond-forming pathways[136] and a $C_2$-symmetric bisoxazolidine ligand catalyses the reaction with aliphatic and aliphatic aldehydes to give the $\beta$-hydroxynitroalkanes in up to 99% yield and 95% *ee*.[137]

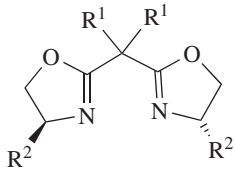
Excellent enantioselectivities (up to 99% *ee*) have been reported for Henry reaction of aromatic heteroaromatic and aliphatic $\alpha$-ketophosphonates promoted by secondary amine–amide organocatalyst (**55**); hydrogen bonding in the transition state was revealed by theoretical study.[138]

Study of a series of aqua-aminoorganoboron catalysts (**58**) in the formation and reaction of nitronate species has established the pivotal role played by a single-coordinated water molecule.[139] Thus, kinetic studies with $D_2O$ derivative (**58b**) using $CD_3NO_2$ and hexanal in THF at 27 °C revealed that the initial rate was 35 times faster than with $Et_3N$ alone (no water) and about 1.5 times greater than for (**58a**) with $CH_3NO_2$ ($k_H/k_D = 0.68$), suggesting that $\alpha$-C–H bond cleavage is not rate determining (in contrast with $Et_3N$, for which $k_H/k_D = 1.19$). It is suggested that one of the three amino residues (identical on the NMR time-scale) deprotonates the nitroalkane and that there is an attractive interaction between the nitronate ion and the boron-coordinated water molecule; (**58d**) and also (**58a**) in which one aryl group is replaced by a 2,6-dimethylphenyl group are unreactive.

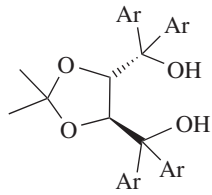
Asymmetric Henry reactions catalysed by chiral copper(II) complexes have featured: boron-bridged bisoxazolines (borabox) ligands (**59**) and reaction of nitroethane and nitropropane with cyclohexanecarboxaldehyde;[140] sulfonyldiamine ligands and reaction of nitroethane with methanal;[141] chiral $C_2$-symmetric secondary bisamines (based on 1,2-diaminocyclohexane) and reaction of nitromethane with aromatic and aliphatic aldehydes;[142] and binuclear Schiff base complexes.[143]



(**58**)

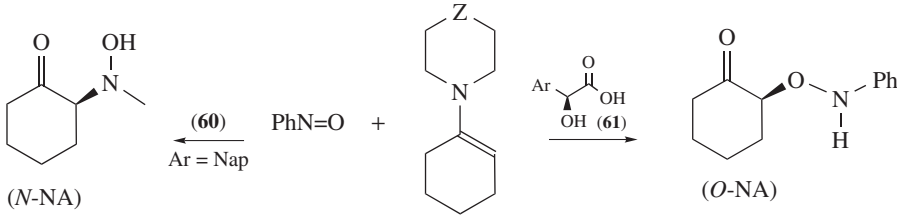


(**59**)



(**60**)

**a**; R = Me, **b**; R = Me, $H_2O = D_2O$
**c**; R,R = $(CH_2)_4$, **d**; R = $Pr^i$



Scheme 14

Regio- and diastereo-selectivity of nitroso aldol reactions (Scheme 14) between achiral enamines and PhNO, catalysed by chiral Brønsted acid catalysts [(*S*,*S*)-TADDOL (**60**) or (*S*)-1-naphthylglycolic acid (**61**)], have been explored by experimental and theoretical study.[144] Calculations suggest that an earlier observation that organic acids with an alcohol group promote C–N bond-forming reactions (*N*-NA reactions), whereas organic acids with a carboxylic acid group promote C–O bond-forming reactions (*O*-NA reactions) are a consequence of a seven-membered ring coordination of the alcohol to the oxygen of N=O (and *o*-H) in contrast to eight-membered ring coordination of the carboxylic acid with the nitrogen, thereby activating the N and O atoms, respectively. This permitted interpretation of the enantioselectivity observed for the chiral catalysts (**60**) and (**61**) for which energy gaps of 0.9 and 1.6 kcal $mol^{-1}$ are calculated to favour the product enantiomer indicated, respectively.

*Other Aldol-type Reactions*

Addition of the chiral magnesium enolate of readily available (*R*)- and (*S*)-*t*-butyl *p*-tolyl sulfinyl acetates to various aldehydes (some $\alpha$-substituted) favours *syn* stereochemistry of the two stereocentres created.[145] DFT calculations for reactivity of the lithium sulfinyl carbanion derived from 2,3-dihydro-1-benzothiophene-1-oxide towards aldehydes and imines have rationalized the formation of products with high

stereoselectivity at the sulfinyl $C_\alpha$ but low diastereoselectivity at the hydroxyl or amino centre.[146] Reactions of $\alpha$-sulfonyl carbanions (from $RSO_2CH_2Ar$ and *n*-BuLi)) with various aldehydes, promoted in toluene by chiral bis(oxazoline)s (**5**, B = C), have been found to proceed with excellent *syn* diastereoselectivities and high enantioselectivities when R = $CF_3$, $R^1$ = Bn, and $R^2$ = Ph.[147]

Aldol addition and condensation between hydroxyacetone or acetone and different aldehydes in water have been promoted through *in situ* formation of a boron complex enolate with the aminoboronate catalyst *N*-Butyl-1-benzimidazole-2-phenylboronic acid hydroxide.[148] The catalytic reactivity has been attributed to cooperation between the boronate and imidazole functions.

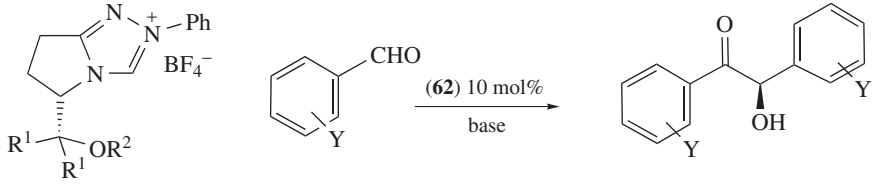
Enantioselective aldol additions of $\alpha$-isothiocyanato imides to aldehydes, organocatalysed by a thiourea derivative, have provided a route to protected $\beta$-hydroxy-$\alpha$-amino acids.[149]

### *Pinacol- and Benzoin-type Coupling*

Recent advances in the metal-catalysed one-electron reductive coupling of carbonyl compounds have been reviewed.[150]

Benzoin reactions in aqueous media have been catalysed effectively by the dicarbene obtained on treatment of a methylene-bridged bis(benzimidazolium) salt with base;[151] the benzoin yield increased with the length of the methylene bridge $(CH_2)_n$ from $n = 3$ to 6 to 12.

The *N*-heterocyclic carbenes obtained by base treatment of enantiopure 1,2,4-triazolium salts (**62**) [synthesized from (*S*)-pyroglutamic acid] have been found to catalyse asymmetric benzoin condensation of ArCHO with up to 95% *ee*.[152]




(**62**) **a**; $R^1$ = TBS, $R^2$ = Ph, **b**; $R^1$ = TMS, $R^2$ = Me, **c**; $R^1$ = TMS, $R^2$ = Ph

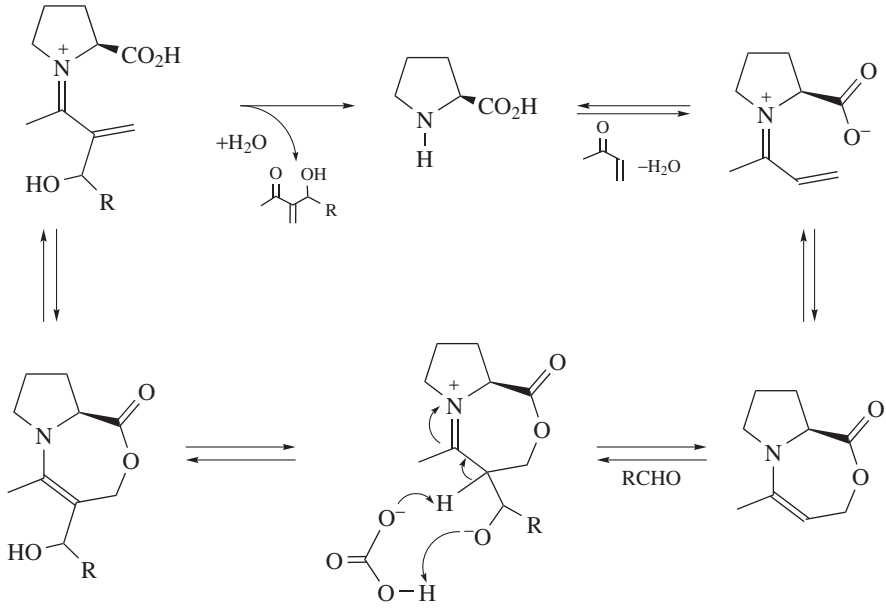
### *The Baylis–Hillman and its Aza and Morita Variants*

Reviews of Baylis–Hillman (B–H) reactions have featured recent advances in their application to synthesis of cyclic frameworks,[153] reactions in non-traditional media,[154] and asymmetric reactions using cinchona alkaloids.[155]

Potential energy profiles for *syn* and *anti* reaction channels for B–H reaction of acraldehyde and formaldehyde, promoted by $Me_3N$, have been obtained by DFT calculations.[156] Electronic structure calculations applied to the transition state for B–H reaction of *p*-fluorobenzaldehyde with cyclohex-2-enone, promoted by DMAP, have assisted the design of bis(thiourea) cocatalysts capable of hydrogen bonding with

the electrophile and nucleophile in the activated complex, thereby accelerating the reaction.[157] Chiral bisthiourea organocatalysts (from 1,2-diaminocyclohexane[158] and 1,1-binaphthyl-2,2-diamine[159]) have also been used in conjunction with a Lewis base to promote enantioselective Morita B–H (M-B–H) reactions, by forming a chiral double hydrogen-bonding network.

The first evidence of proline acting as a bifunctional catalyst in the B–H reaction of alkyl vinyl ketones with arylaldehydes and a Lewis base has been published.[160] Screening of several amine catalysts showed that an ionizable carboxylic function directly linked to the secondary amine catalyst plays an important role and proline, sarcosine, pipecolinic acid, and homoproline are believed to act as bifunctional catalysts via a bicyclic enaminolactone intermediate. Scheme 15 outlines the mechanism for the proline/$NaHCO_3$-catalysed reaction, for which more detail was obtained by computational methods; no enantioselectivity was found.

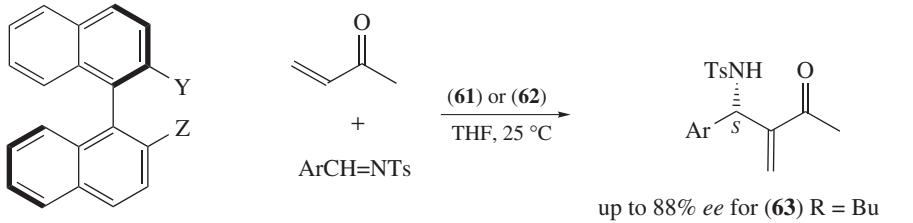



SCHEME 15

In contrast, the enantioselectivities (up to 83% *ee* for the predominant (*R*)-hydroxy compound)) reported for M-B–H reaction of methyl vinyl ketone and aromatic aldehydes cocatalysed by L-proline in combination with chiral amines are determined by the proline stereochemistry; a transition state based on the traditional M-B–H reaction with intermediate enamine has been proposed.[161]

Aza-MBH reaction of *N*-tosylsalicylaldehyde imines with $\alpha,\beta$-unsaturated ketones, directed by $\beta$-isocupreidine (10%), has been found to proceed with up to 99% *ee* but with opposite absolute configuration to that obtained for *N*-tosylaldimines as a consequence of the *o*-OH substituent; the scope and mechanism are under investigation.[162]

Fast catalytic aza-MBH reactions of methyl vinyl ketone with *N*-sulfonylated imines have been promoted by chiral bifunctional phosphane Lewis bases (**63**)[163] (with up to 88% *ee)* and (**64**)[164] (with up to 95% *ee*) under mild conditions.



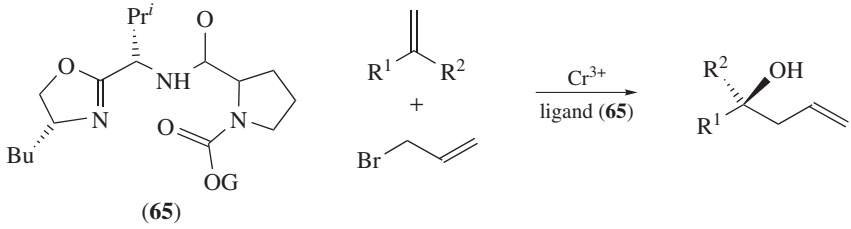

up to 88% *ee* for (**63**) R = Bu
up to 95% *ee* for (**64**) R = COMe

(**63**) Y = OH, Z = PPhR, R = Et, *i*-Pr, *n*-Bu, Cy
(**64**) Y = NHR, Z = $PPh_2$, R = $SO_2Me$, $SO_2CF_3$, $SO_2Tol$, COPh, COMe, $POPh_2$

*Allylation and Related Reactions*

A review of development of the chromium mediated asymmetric Nozaki–Hiyama–Kishi reaction has revealed its importance for allylation, methallylation, allenylation, propargylation, and vinylation of a range of aldehydes, with only limited application to ketone substrates.[165]

For carbonyl allylation reactions [of $BrCH_2CH{=}CH_2$ catalysed by Cr(III), for three different carbonyl substrates] (Scheme 16) the product enantiomeric ratio has been found[166] to correlate with the size of substituent G on the chiral co-catalyst (**65**), using steric parameters developed by Charton.




SCHEME 16

Barbier allylation of a series of *para*-substituted benzaldehydes with allyl bromide in the presence of metals and has been studied by competition experiments which indicated (through Hammett correlation) a build-up of negative charge and, for Zn, In, Sn, Sb, and Bi, an inverse secondary isotope effect ($k_H/k_D = 0.75–0.95$).[167] These results are consistent with the formation of an organometallic intermediate prior to allylation via a closed six-membered transition state and supported by DFT calculations. However, for Mg the larger negative charge build-up and small positive isotope effect (1.06) are consistent with reaction via a radical anion.

A chiral nitrogen functional group on an allyl tin reagent has been used to achieve 1,4-asymmetric induction on allylation of various aldehydes in the presence of a Lewis

acid; 1,4-amino alcohols have been obtained diastereoselectively using $Yb(OTf)_3$ (85–93% *syn*) and $SnCl_4$ (87–100% *anti*), respectively.[168]

Good agreement between theoretically predicted enantioselectivities and experimental data has been reported for highly diastereoselective allylation of aldehydes with allyltrichlorosilanes catalysed by QUINOX (a chiral isoquinoline *N*-oxide).[169] An associative pathway involving a neutral octahedral silicon complex (with one molecule of catalyst) and the aldehyde in a chair-like transition state has been proposed.

Excellent diastereo- and enantio-selectivities (up to >99:1 and 99%, respectively) have been reported for carbonyl–ene reactions [$R^3CH{=}CR^2CH_2R^1 + O{=}CHCO_2R^4 \rightarrow R^1CH{=}CR^2CHR^3CH(OH)CO_2R^4$] catalysed by In(III)–pybox complex.[170]

A TMSOTf-promoted electrophilic addition of aldehydes to alkynes, via a hydroxy enol, has provided a route to chalcones and chroman-4-ones.[171]

### *Alkynations*

Enantioselective alkynations of aldehydes ArCHO by PhCCZn have been catalysed by a new chiral oxazolidine–titanium complex (in THF with up to 95% *ee*)[172] and by chiral Tf-based sulfamide-amine alcohols (in toluene with up to 92% *ee*)[173] to give chiral propargylic alcohols. Ethoxyacetylide addition followed by Sc(III) triflate-catalysed Meyere–Schuster rearrangement of the resulting ethoxyalkynyl carbinols have been combined as a strategy for olefination of aldehydes and ketones $R^1R^2CO$ to give $R^1R^2C{=}CHCO_2Et$; the procedure works well even with hindered ketones and is stereoselective in the case of aldehydes.[174] A chelation-controlled model has been proposed to account for the highly stereoselective addition of lithioacetylides (2.1 equiv.) to $\alpha$-hydroxy ketones in THF at $-78\,^{\circ}C$.[175]

### *Michael Additions*

A review of organocatalysis of asymmetric cascade reactions catalysed by secondary amines includes examples of Michael–aldol–dehydration sequences.[176]

Michael addition of various cyclic ketones to vinyl sulfone $CH_2{=}C(SO_2Ph)_2$ catalysed by a cinchona alkaloid-derived primary amine in $CHCl_3$ has been achieved with 88–97% *ee*[177] and addition of aldehydes to $\gamma$-keto-$\alpha,\beta$-unsaturated esters catalysed by the TMS-ether of prolinol (**10d**)–HOAc provides a highly regio- and enantioselective route to synthetically useful cyclohexenones, cyclohexanones, piperidines, and $\gamma$-lactones.[178]

DFT calculations on the mechanism and intermediates for a model asymmetric Stetter reaction have revealed that, in contrast to Breslow's mechanism for benzoin condensation, rate-determining C–C coupling of the enolamine intermediate (formed by coupling of an aldehyde with the carbene catalyst) and the Michael acceptor ($\alpha,\beta$-unsaturated ketone) precedes proton transfer and that the stereoselectivity depends on the relative stability of Breslow intermediate isomers.[179]

Highly enantioselective (up to 97% *ee*) conjugate addition of diethylzinc to substituted chalcones has been catalysed by Cu(II) complexes of chiral 2-(2-diphenylphosphino)benzylideneamino alcohols (tridentate P,N,O ligands).[180]

## Other Addition Reactions

### *General and Theoretical*

Quantum mechanical calculations have been used to design enzyme active sites by predicting the rate-determining transition state of a particular reaction in presence of the optimal arrangement of catalytic functional groups (theozyme).[181] For each of the reactions (including the aldol and Diels–Alder reactions) the rate-determining transition state for the uncatalysed reaction in water was calculated, whereupon naturalistic catalytic units were introduced and their positions optimized for rate acceleration.

### *Addition of Organozincs*

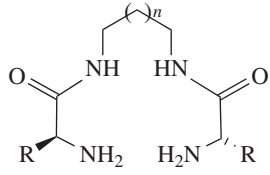
Theoretical models and rate equations relating to amplification of enantiometric excess and chiral symmetry breaking, as featured in the autocatalytic Soai reaction, have been reviewed.[182,183]

A reversal of enantioselectivity [from pro-(*R*) to pro-(*S*)] induced by an achiral catalyst (*N*,*N*-dimethylaminoethanol) in association with a chiral catalyst [(1*R*,2*S*)-*N*,*N*-dimethylnorephedrine] has been reported for addition of diisopropyl zinc to a pyrimidine-5-carbaldehyde; the behaviour has been attributed to the creation of a new dimeric catalyst by aggregation of the achiral and chiral components (each coordinated to zinc).[184]

For dimethylaminoisoborneol-catalysed addition of $R_2Zn$ to benzaldehyde, kinetic modelling of the behaviour of 19 species involved in 36 coupled processes has confirmed that the non-linear correlation between enantiomeric excess of the chiral auxiliary and of the product is a consequence of accumulation of heterochiral alkylzinc amino alkoxide dimer (reservoir effect).[185]

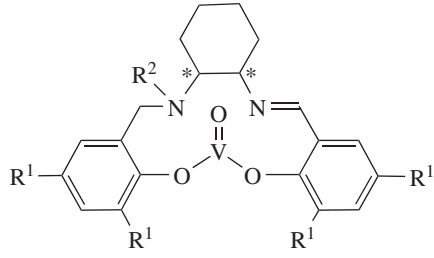
Enantioselective addition of diethylzinc to benzaldehydes catalysed by chiral amino alcohols continues to be an active research area.[186–192] This has included: determination of structural factors which influence the enantioselectivity of diethylzinc to aldehydes catalysed by $\beta$-amino alcohols derived from [(1*R*,2*S*)-pseudonorephedrine] and [(1*R*,2*S*)-norephedrine];[186] synthesis and use of a new class of chiral non-racemic $\gamma$- and $\delta$-amino alcohol catalysts based on bicyclo[2.2.1]heptane and bicyclo[2.2.2]octane;[187] catalysis by 14-hydroxy-substituted morphine alkaloids (with up to 95% *ee*);[188] application of 1,1′-binaphthylazepine-based ligands to reactions of $R_2Zn$ with arylaldehydes (with up to 90, 97 and 96% *ee* for R = Me. Et and Bu, respectively);[189] and comparison of the catalytic efficasy of a range of isoborneols.[190–192] A new N/N/O-tridentate chiral diamino ligand [10-(4-methylpiperaxin-1-yl)isoborneol] has been compared with N/N/O, N/O/O, and N/O isoborneol ligands previously studied,[190] and the catalytic properties of two series (10-amino and 10-amino-10-oxo) of related enantiopure isoborneols have been found to respond very differently to identical structural modifications, apparently as a consequence of respective zinc coordination abilities;[191] three camphor-based *t*-amidoisoborneols have also proved to be effective catalysts in the absence of $Ti(O\text{-}i\text{-}Pr)_4$, with up to 98% yield and 90% *ee*.[192] (*S*)-2-Piperidinyl-1,1,2-triphenylethanol has been used to promote the formation of the (*R*)-alcohol on reaction of alkyl and aryl zinc reagents with an isoxazole aldehyde.[193]

Enantioselective addition of $Et_2Zn$ to aldehydes has also been promoted by new enantiopure imidazolinium carbene ligands incorporating two hydroxy functions in combination with metal salts,[194] tridentate $\beta$-hydroxysalicylhydrazone ligands prepared from ephedrine and norephedrine,[195] and by (*R*,*R*)-hydrobenzoin with and without Ti(O-*i*-Pr)$_4$ present (giving predominant *R*- and *S*-enantioselection, respectively).[196] Effective asymmetric ligand catalysts able to coordinate through two or more amino nitrogens have included 2-(2′-piperidinyl)pyridine (up to 100% *ee*),[197] a series of mono- and di-alkylated derivatives of $C_2$-symmetric *N*-tosyl-1,2-diphenylethylenediamines,[198] and new chiral tetraaza ligands (**66**) for which DFT calculations explained the enantioselection (up to 99% *ee*) obtained with benzaldehydes.[199]




(**66**)

**a**–**f**; *n* = 0, 1, 2, 3, 4, 6 and R = *i*-Pr
**g**–**i**; R = Me, $CH_2Ph$, $CH(CH_3)CH_2CH_3$ and *n* = 1




(**67**) $R^1$ = *t*-Hex, $R^2$ = Et

Seventeen enantiopure ferrocenes bearing a sulfide or sulfoxide group along with a side-chain having a nitrogen substituent have been screened as catalysts for addition of diethylzinc to benzaldehyde.[200]

Ready boron to zinc transmetallation from arylboronic acids and triarylboroxines to diethylzinc has been exploited to effect enantioselective arylation of aryl′-aldehydes (by ArZnEt) with a $\beta$-amino alcohol as the chiral ligand.[201]

In the presence of $Me_2Zn$, enantioselective Reformatsky reactions of ethyl iodoacetate with aldehydes have been catalysed by a chiral Schiff base[202] (up to 72% *ee*) and (*S*)-*o*,*o*-ditrimethylsilyl-BINOL[203] (up to 84% *ee*, in $Et_2O$) with $O_2$ necessarily present; high enantioselectivity (up to 91% *ee*) was also achieved with dialkyl and challenging diaryl ketones when the BINOL was used.[204,205]

### *Addition of Other Organometallics*

By low-temperature rapid-injection NMR studies of reaction with MeI and with benzaldehydes in THF–$Me_2O$ solutions, it has been found for tris(trimethylsilyl)methyllithium (RLi) that the contact ion R–Li dissociates to the separated ion $R^-//Li^+$ before reacting and that the latter reacts faster than can be measured at $-130\,^\circ C$; the triple ion $R–Li^–R$ reacts faster with electron-rich than with

electron-deficient benzaldehydes.[206] HMPA catalyses dissociation of the triple ion and greatly deactivates the separated ion.

Asymmetric ethylation of aldehydes with $Et_3B$ achieved using a 3-(3,5-diphenylphenyl)-$H_8$-BINOL-derived titanium(IV) catalysts is the subject of further study.[207]

DFT studies of the diboration of aldehydes [to form a RCH(O-boryl)boryl structures] catalysed by copper(I) boryl complexes (NHC)Cu(boryl) featuring *N*-heterocyclic carbene (NHC) show that the reaction proceeds through aldehyde insertion into Cu–B to give a Cu–O–C(boryl) species followed by $\sigma$-bond metathesis with a diboron reagent.[208]

Formation of methyl ketones from aldehydes on reaction with dimethylaluminium reagents is believed to involve an intramolecular rearrangement–Oppenauer oxidation sequence.[209]

A study of facial stereoselectivity in methylation of 4-chloroadamantan-2-ones by MeLi and by $CH_3MgCl$–$CeCl_3$ in THF has established that the stereochemistry of the substituent directs attack of the nucleophile; thus, when the chlorine atom is in the axial position exclusive *anti* addition occurs, whereas preferential *syn* addition is found when the chlorine is equatorial.[210]

### *Grignard-type Reactions*

Aryl and alkyl Grignard reagents have been used in the asymmetric alkylation and arylation (up to 97% *ee*) of aromatic and unsaturated aldehydes in the presence of a 3-(3,5-diphenylphenyl)-$H_8$-BINOL-derived titanium(IV) catalyst and excess Ti(O-*i*-Pr)$_4$.[211,212]

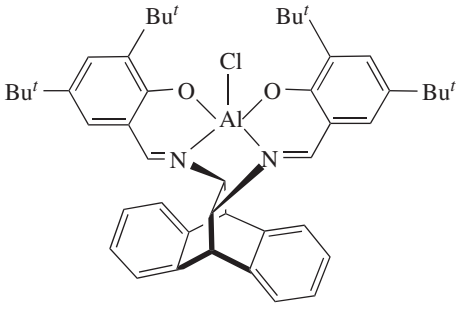
### *Hydrocyanation and Cyanosilylation*

Lewis acid-catalysed asymmetric cyanohydrin synthesis has been reviewed[213] and a theoretical study, at the B3LYP/6–311 + G** level, of the effect of solvent on the mechanism of reaction of pentafulvenone with HCN has established that the reaction is consistent with that in the gas phase but of lower activation energy.[214]

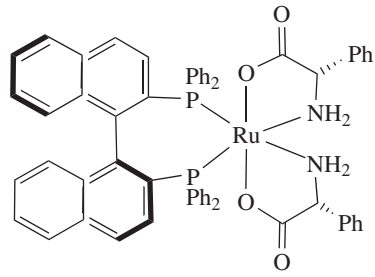
A computational study, by B3LYP//ONIUM methods, of enantioselective cyanation of benzaldehyde by HCN catalysed by titanium–salicylaldehyde catalysts has revealed that attack of cyanide is rate determining and that the stereochemistry, which is dependent on the mode of coordination of benzaldehyde to the chiral catalyst, can be qualitatively predicted for five chiral ligands.[215]

Asymmetric transcyanation (with 91–95% *ee*) of aliphatic aldehydes with acetone cyanohydrin in $CH_2Cl_2$ has been catalysed by oxovanadium(IV)(salalen) complex *R*,*R*-(**67**).[216]

Asymmetric trimethylcyanation of aldehydes has been achieved with excellent enantioselectivitiy by reaction of a range of aldehydes with $Me_3SiCN$ in the presence of catalyst systems comprising: tributylphosphane oxide with chiral Al(III)(salen) complex (**68**) (1 mol%) in $CH_2Cl_2$, to afford predominantly *R*- or *S*-products;[217] and $Li_2CO_3$ with chiral [Ru{(*S*)-PhGly}$_2${(*S*)-binap)}] complex (*S*,*S*,*S*)-(**69**) in $Et_2O$ with a substrate-to-catalyst ratio of 10 000:1 to afford *R*-products.[218] The corresponding cyanohydrins are obtained on hydrolysis.




(**68**)



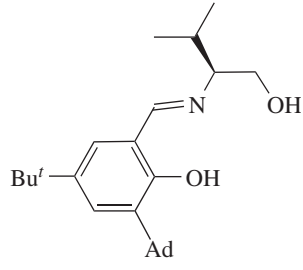

(**69**)

*Hydrosilylation and Hydrophosphonylation*

A DFT study of the mechanism of $MoO_2Cl_2$-catalysed hydrosilylation of benzaldehyde concluded that the reaction features initial silane activation and proceeds via thermoneutral intermediates.[219] This is in contrast to the behaviour of $MO_4$-type compounds (M = Ru, Os, Mn), for which catalysis is precluded by formation of highly exergonic intermediates.

B3LYP DFT calculations four alternative reaction mechanisms for hydrosilylation of unsaturated compounds by a neutral hydrido(hydrosilylene)tungsten complex $Cp'(CO)_2(H)W{=}Si(H)[C(SiMe_3)_3]$ ($Cp' = Cp^*$, $C_5Me_4Et$) indicate that the reaction of acetone proceeds by a metal hydride migration mechanism but that addition to a nitrile involves a silyl migration.[220] Kinetic and thermodynamic considerations suggest that it may be difficult to achieve catalytic conditions for such reactions.

Chiral $\alpha$-hydroxyphosphonates have been formed in good yields with excellent enantioselectivities (up to 97% *ee*) by hydrophosphonylation of aldehydes with $O{=}PH(OEt)_2$ in $CH_2Cl_2$–THF catalysed by a dimeric Al(III) complex of tridentate Schiff base of (**70**) with $Et_2AlCl$.[221]



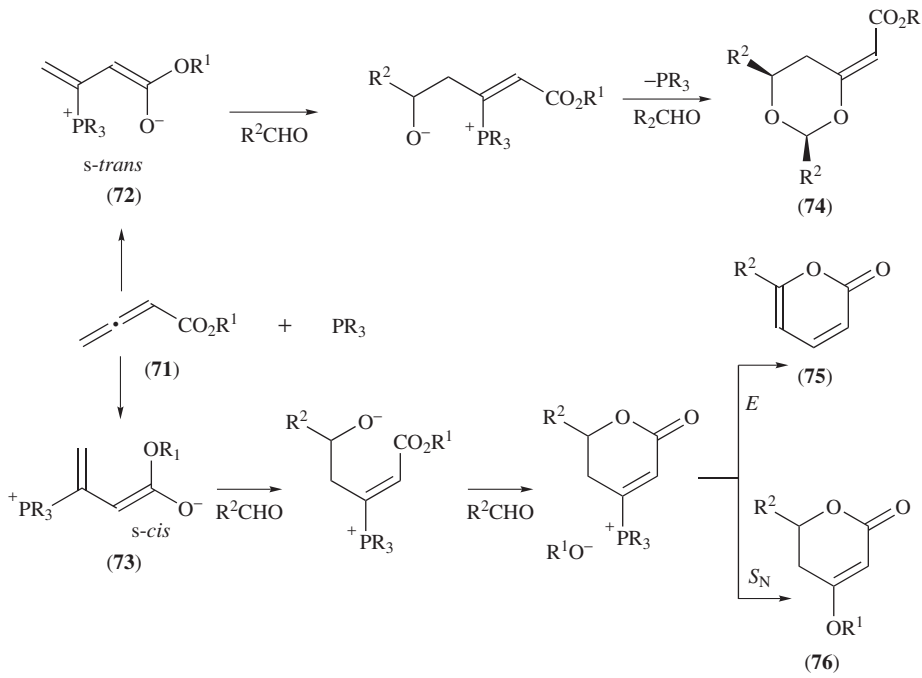

(**70**)

*Miscellaneous Additions*

The Prins reaction, whereby aldehydes and ketones undergo electrophilic addition to alkenes, has been reviewed[222] and density functional computations of Rh(I)-catalysed hydroacylation and hydrogenation of ethene using formic acid have been reported.[223]

A catalytic system based on [Rh(cod)(DPEphos)][$ClO_4$], where DPEphos is a hemilable bis(2-diphenylphosphinophenyl)ether P–O–P ligand, has been designed and used to promote hydroacylation reactions of *β*-*S*-substituted aldehydes with unactivated alkenes and alkynes.[224]

The phosphine-catalysed addition of buta-2,3-dienoates (**71**) to aldehydes has been extended to achieve formation of disubstituted dihydro-2-pyrones (**76**), via s-*cis* intermediate zwitterionic *β*-phosphonium dienolates (**73**), by using a Brønsted acid to disrupt the Coulombic interaction that would otherwise favour the s-*trans* form (**72**) and lead to formation of dioxane (**74**) (Scheme 17).[225] The approach has been supported by DFT calculations.




SCHEME 17

The surprisingly high efficiency of 2-hydroxypyridine as a catalyst for hydration of the carbonyl group has been reproduced theoretically and attributed to the exceptional thermodynamic stability of the principal reactant complex, which contains a dihydrate of 2-pyridone, rather than to bifunctional catalysis.[226]

DFT study of the mechanism of addition of $H_2S$ to 1,3-dihalopropan-2-ones in the presence of HCl indicates that it occurs by direct nucleophilic attack on the carbonyl group, rather than preliminary enolization.[227]

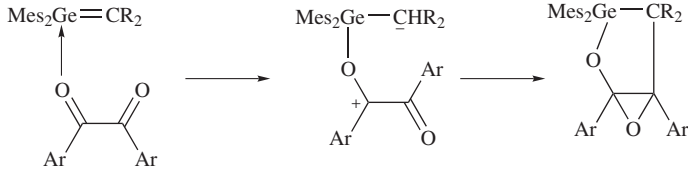
The third-order rate constants and V-shaped pH-dependent rate profile for formation of carbinolamide $ArCONHCH_2OH$ on reaction of *para*-substituted benzamides

with formaldehyde in water has been attributed to rate-determining proton transfer from general acids (as evidenced by buffer catalysis) at pH < 4 and a specific-base mechanism in the hydroxide-dependent region at pH > 6.[228] Corresponding equilibrium constants for the favoured carbinolamide formation were estimated by coupling the rates observed with those previously reported for the reverse reaction.

Diastereoisomer ratios of cyclopropanols obtained by reductive cyclization of $\beta$-iodoketones by treatment with zinc or *c*-$C_6H_{11}MgBr$ [with or without Ti(O-*i*-Pr)$_4$] match those observed for cyclopropanation reactions of carboxylic acid esters with substituted alkoxytitanacyclopropane reagents–which are therefore believed to proceed by an ate complex mechanism via the $\beta$-titanoketone intermediates with the metal atom bound to a secondary carbon.[229] It has been suggested that metal ligands influence the preferential formation of *cis*-1,2-disubstituted cyclopropanols through release of repulsive strain.

*N*,*N*′-Diarylureas have been shown for the first time to catalyse sulfonium ylide-mediated aldehyde epoxidation reactions.[230] The catalytic behaviour, which has been ascribed to bidentate hydrogen bonding between the urea and the carbonyl oxygen, is superior to that found for the thiourea analogues. Reactions of a range of aromatic and aliphatic aldehydes and ureas were explored.

A mechanism has been proposed to account for the unexpected epoxidation of benzil derivatives in their reaction with germene $Mes_2Ge{=}CR_2$ ($R_2$ = fluorenylidene) (Scheme 18); the C–O and C–C bond formations may be consecutive or concerted.[231]

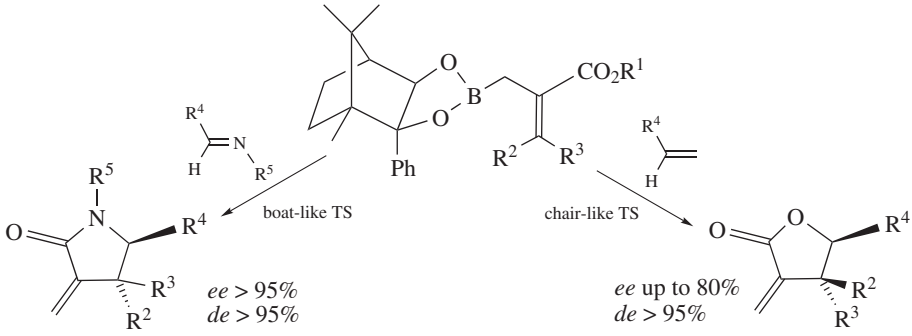



SCHEME 18

The regioselectivity of the condensation of electronically unsymmetrical 1,3-diaryl-1,3-diketones with 2-hydrazinopyridine and 2,6-bis-hydrazinopyridine to form *N*-(2-pyridyl)-3,5-diarylpyrazoles has been studied.[232] For both nucleophiles the regiochemistry is consistent with initial reaction of the hydrazine $NH_2$ group at the carbonyl (or enol) carbon closer to the more electron-withdrawing aryl group; the electronic effects correlate well with the difference between Hammett $\sigma^+$ values for *para*-substituents on the aryl rings. Contrasting regiochemistry reported for reactions with perfluoroalkyl 1,3-diketones has been discussed.

Acceleration of acid-catalysed dehydrative cyclization of 1,3,5-triketones to $\gamma$-pyrones by neighbouring acyl groups in the $\beta$-position has been attributed to intramolecular general base participation.[233] A bulky silyloxy group in the $\beta$-position retards cyclization.

The nature of the electrophile, aldehyde vs aldimine, has a dramatic influence on the stereochemistry (Scheme 19) of enantioselective additions of $\beta$-functionalized




SCHEME 19

allylboronates (**74**) to form $\alpha$-methylene-$\gamma$-lactones and lactams, respectively.[234] A classical chair-like transition state is proposed to account for the formation of *cis*- and *trans*-lactones from (*E*)- and (*Z*)-crotylboronate, respectively, on reaction with aldehydes; the contrasting formation of *trans*- and *cis*-lactams, respectively, on their reaction with aldimines has been attributed to adoption of a boat-like transition state as a consequence of the substituent on the nitrogen.

## Enolization and Related Reactions

The haloform reaction has been reviewed[235] and direct asymmetric iodination of aldehydes with NIS has been promoted by an axially chiral bifunctional amino alcohol catalyst.[236] Highly selective rapid catalyst-free $\alpha$-halogenation of ketones using *N*-halosuccinimides in DMSO has also been reported.[237]

Studies of tautomerism have included solvent effects on the rate of keto–enol interconversion of 2-nitrocyclohexanone,[238] NMR investigation of cinnolin-4-ol, cinnoline-4-thiol, and cinnolin-4-amine,[239] and theoretical investigation of 4(3*H*)-pyrimidinone and its analogues.[240]

Kinetic discrimination between carbon and oxygen reactivity of enols has been studied.[241]

$^6$Li NMR spectroscopy has been used to characterize forms of aggregation of lithium enolates of relatively simple ketones in solution.[242] The influence of $Et_3N$ on the high *E*/*Z* selectivities of enolates generated by reaction of acyclic ketones and esters with lithium hexamethyldisilazide has been explored and the $Et_3N$-solvated enolates have been found to display higher and often complementary diastereoselectivities for aldol and Ireland–Claisen reactions (with 20-fold acceleration and evidence of autocatalysis for the latter) compared with those in THF.[243] An efficient synthesis of ketones $\alpha$-aminated on quaternary carbon has involved electrophilic amination of a samarium enolate intermediate formed by reaction of $SmI_2$ with the $\alpha$-heterosubstituted ketone.[244]

Enantioselective protonation of silyl enol ethers by a chiral *N*-triflylthiophosphoramide Brønsted acid [the enantiomer of (**17**), Y = Ar, S = O, OH = NHTf] has been demonstrated.[245]

## Oxidation and Reduction of Carbonyl Compounds

*Regio-, Enantio-, and Diastereo-selective Reduction Reactions*

Reviews have featured: Leuche reduction of $\alpha,\beta$-unsaturated aldehydes with $NaBH_4$ and $CeCl_3$ to give allylic alcohols;[246] Midland reduction of ketones with Alpineborane;[247] Noyori catalytic asymmetric hydrogenation of ketones and alkenes;[248] Meerwein–Ponndorf–Verley reduction of carbonyl compounds to alcohols;[249] reductive aldol, Michael, and Mannich reactions;[250] and reductive amination of carbonyl compounds in the presence of $HCO_2H$ (Leuckart–Wallach reaction).[251]

DFT calculations suggest that steric effects of solvent may influence the diastereoselection found for $LiAlH_4$ reduction of acyclic ketones having an oxygen-containing functional group $\alpha$- to the carbonyl.[252]

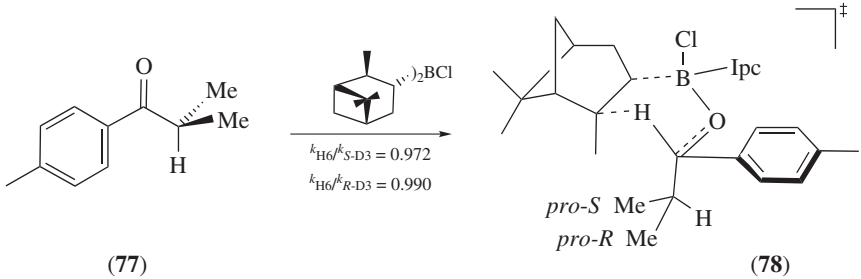
Enantioselective reduction of ketones by hydrogen transfer from ruthenium, rhodium, or iridium catalysts has been the topic of several investigations, with varying degrees of success.[253–257]

High Felkin–Anh selectivity ($\beta,\gamma$-*syn*) up to 98% accompanied by $\alpha,\beta$-*anti* diastereoselectivity and high *ee* (up to 99%) has been found for Rh(bisoxazolinylphenyl)-catalysed reductive aldol coupling reactions of 2-phenylpropionaldehyde and acrylate derivatives.[258]

A range of dihydroxy chiral ligands (2,5- and 2,6-BODOLs) derived from bicyclo[2.2.2]octane have been synthesized and tested [together with $Ti(O\text{-}i\text{-}Pr)_4$] in the asymmetric reduction (up to 98% *ee*) of acetophenone by catecholborane.[259]

Asymmetric reduction of prochiral ketones by borane has been effected by a recoverable proline derived $C_3$-symmetric sulfonamide (up to 97% *ee* in refluxing THF)[260] and by a chiral diamide [(2*S*)-5-oxo-2-(arylamino)carbonylpyrrolidine];[261] a four-step mechanism for the latter was deduced by DFT calculations.

Isotope effects resulting from deuteration of the enantiotopic methyl groups of 4′-methylisobutyrophenone (**77**) have been used to probe their respective environments in the transition state (**78**) for asymmetric reduction by (−)-*B*-chlorodiisocampheylborane.[262] The study involved determination of $^2H$ KIEs for the respective $d_3$-methyl isotopomers and also the $d_6$-dimethyl KIE with respect to the perprotiated substrate. The results were interpreted in terms of the effects of steric crowding on the anharmonicity of C–H bonds in the transition structure relative to the reactant state.




(**77**) (**78**)

*Oxidation Reactions*

One-pot oxidative esterification and amidation of aldehydes has been reviewed[263] and an oxidative cycle has been proposed for amidation of aldehydes and alcohols with primary amines catalysed by KI–TBHP.[264]

Baeyer–Villiger oxidation has been reviewed[265] and a linear relationship between electrophilicity and Hammett $\sigma_p$ constants has been reported for such oxidations of aromatic aldehydes and ketones.[266] A mechanism has been proposed for metalloporphyrin-catalysed selective Baeyer–Villiger oxidation of ketones by molecular oxygen.[267]

*N*-Heterocyclic carbenes (NHCs) have been used as organocatalysts for oxidations of aldehydes to esters promoted by the TEMPO radical[268] and by alcohols (primary, secondary and tertiary).[269,270] Lanthanide formamidinates have been found to be an improved class of catalysts for conversion of aldehydes to esters by the Tishchenko reaction.[271]

Kinetic studies have explored: effects of transition ion catalysts on oxidation of benzaldehyde by bromine[272] and by Ce(IV);[273] the mechanism of oxidation of aromatic aldehydes by morpholinium chlorochromate(VI);[274] C–C bond cleavage in the oxidation of diketones by quinolinium dichromate;[275] formation of hydrates from asymmetric and cyclic ketones in their oxidation by alkaline hexacyanoferrate(III);[276] and oxidation of mannitol by Cr(IV) in acid perchlorate medium.[277]

Theoretical investigation of the HO•-initiated oxidation of benzaldehyde in the troposphere[278] and a shock-tube and modelling study of acetaldehyde pyrolysis and oxidation[279] have been undertaken.

## Other Reactions

Aldehyde decarbonylations have been catalysed by rhodium[280] and iridium;[281] the mechanism of the former was deduced using Hammett studies and KIEs combined with DFT calculations (B3LYP), which support a cycle of oxidative addition into the C(O)–H bond followed by a rate-limiting extrusion of CO and reductive elimination.

Rate coefficients for reaction of HO• with glyoxal [HC(O)C(O)H] at 210–390 K in the gas phase have been determined for atmospheric modelling purposes,[282] and quantum mechanical studies of the reaction of chlorine atoms with formaldehyde[283] and of the Horner–Wadsworth–Emmons reaction of benzyl pyridyl ketone[284] have been conducted.

A chiral binaphthyl-based aminosulfonamide organocatalyst has been used to direct asymmetric $\alpha$-aminoxylation of aldehydes by PhNO[285] and $\alpha$-trifluoromethylation of ketone silyl enol ethers has been accelerated by late transition metal catalysts (with $R_2Zn$).[286]

Aryl diazoacetates $ArC(=N_2)CO_2R$ have been inserted (with loss of $N_2$) into the $sp^2$-C–CHO bond of aromatic and $\alpha,\beta$-unsaturated aldehydes, thereby permitting the formation of a chiral (up to> 95% *de*) all-carbon quaternary centre by using a phenylmenthyl moiety as a chiral auxiliary R.[287]

Results of a deuterium labelling study suggest that the *N*-heterocyclic carbene-catalysed intramolecular addition of carbonyl anion equivalents to enol ethers

(whereby salicylaldehyde-based enol ethers give benzofuranones in excellent yield) proceeds through a nucleophilic addition mechanism.[288]

Asymmetric ring expansion of 4-*t*-butylcyclohexanone to seven-membered iminium ions (with a five- or six-membered oxacycle fused to C=N) has been promoted by 1,2- and 1,3-hydroxyalkylazides and investigated computationally.[289]

Studies of heterocycle formation by combination of three components have included: intermolecular silacarbonyl ylide 1,3-dipolar cycloadditions with carbonyl compounds and alkynes to give oxasilacyclopentenes;[290] enantioselective Biginelli reactions of aldehyde, urea, and $\beta$-keto ester (catalysed by a proline derived secondary amine) to give dihydropyrimidines (with up to 98% *ee*);[291] and support for the Cremer–Subbaratnam mechanism for the Latif reaction for thiopyran formation from benzaldehyde and sodium sulfide in aqueous EtOH.[292]

## References


1 Pluth, M. D., Bergman, R. G., and Raymond, K. N., *J. Am. Chem. Soc*., **130**, 11423 (2008).
2 Procuranti, B. and Connon, S. J., *Org. Lett*., **10**, 4935 (2008).
3 Krumper, J. R., Salamant, W. A., and Woerpel, K. A., *Org. Lett*., **10**, 4907 (2008).
4 Umebayashi, N., Hamashima, Y., Hashizume, D., and Sodeoka, M., *Angew. Chem. Int. Ed*., **47**, 4196 (2008).
5 Denmark, S. E. and Chung, W.-j., *Angew. Chem. Int. Ed*., **47**, 1890 (2008).
6 Tayama, E., Otoyama, S., and Isaka, W., *Chem. Commun. (Cambridge)*, **2008**, 4216.
7 Beaver, M. G., Billings, S. B., and Woerpel, K. A., *Eur. J. Org. Chem*., **2008**, 771.
8 Johnsson, R., Olsson, D., and Ellervik, U., *J. Org. Chem*., **73**, 5226 (2008).
9 Ishiwata, A., Munemura, Y., and Ito, Y., *Tetrahedron*, **64**, 92 (2008).
10 Bjerre, J., Nielsen, E. H., and Bols, M., *Eur. J. Org. Chem*., **2008**, 745.
11 Bohn, M. L., Colombo, M. I., Rúveda, E. A., and Stortz, C. A., *Org. Biomol. Chem*., **6**, 554 (2008).
12 Crich, D., Hu, T., and Cai, F., *J. Org. Chem*., **73**, 8942 (2008).
13 Nagy, P., Hisanori, U., Berbucx, D. O., and Soloshonok, V. A., *Chem. Abs*., **149**, 307231 (2008).
14 Khalafi-Nezhad, A., Parhami, A., Zare, A., Shirazi, A. N., Zare, A. R. M., and Hassaninejad, A., *Can. J. Chem*., **86**, 456 (2008).
15 Kulla, E. and Zuman, P., *Org. Biomol. Chem*., **6**, 3771 (2008).
16 Konev, A. S., Stas, S., Novikov, M. S., Khlebnikov, A. F., and Tehrani, A., *Tetrahedron*, **64**, 117 (2008).
17 Pulka, K., Kulis, P., Tymecka, D., Frankiewicz, L., Wilczek, M., Kozminski, W., and Misicka, A., *Tetrahedron*, **64**, 1506 (2008).
18 Verkade, J. M. M., van Hemert, L. J. C., Quaedflieg, P. J. L. M., and Rutjes, F. P. J. T., *Chem. Soc. Rev*., **37**, 29 (2008).
19 Alcaide, B. and Almendros, P., *Angew. Chem. Int. Ed*., **47**, 4632 (2008).
20 Xu, L.-W. and Lu, Y., *Org. Biomol. Chem*., **6**, 2047 (2008).
21 Fu, A., Li, H., Si, H., Yuan, S., and Duan, Y., *Tetrahedron: Asymmetry*, **19**, 2285 (2008).
22 Das, S. and Singh, R. K., *Chem. Abs*., **149**, 556037 (2008).
23 Nozière, B. and Córdova, A., *J. Phys. Chem. A*, **112**, 2827 (2008).
24 Parasuk, W. and Parasuk, V., *J. Org. Chem*. **73**, 9388 (2008).
25 Hayashi, Y., Okano, T., Itoh, T., Urushima, T., Ishikawa, H., and Uchimaru, T., *Angew. Chem. Int. Ed*., **47**, 9053 (2008).
26 Gianelli, C., Sambri, L., Carlone, A., Bartoli, G., and Melchiorre, P., *Angew. Chem. Int. Ed*., **47**, 8700 (2008).
27 Kano, T., Hato, Y., Yamamoto, A., and Maruoka, K., *Tetrahedron*, **64**, 1197 (2008).
28 Puglisi, A., Benaglia, M., Annunziata, R., and Rossi, D., *Tetrahedron: Asymmetry*, **19**, 2258 (2008).
29 Yalalov, D. A., Tsogoeva, S. B., Shubina, T. E., Martynova, I. M., and Clark, T., *Angew. Chem. Int. Ed*., **47**, 6624 (2008).
30 Hatano, M., Maki, T., Moriyama, K., Arinobe, M., and Ishihara, K., *J. Am. Chem. Soc*., **130**, 16858 (2008).
31 Sickert, M. and Schneider, C., *Angew. Chem. Int. Ed*., **47**, 3631 (2008).

[32] Giera, D. S., Sickert, M., and Schneider, C., *Org. Lett*., **10**, 4259 (2008).
[33] Terada, M., *Chem. Commun. (Cambridge)*, **2008**, 4097.
[34] Notte, G. T. and Leighton, J. L. *J. Am. Chem. Soc*., **130**, 6676 (2008).
[35] Bujnowski, K., Adamczyk-Wozniak, A., and Synoradzki, L., *Chem. Abs*., **149**, 401791 (2008).
[36] Tanaka, S., Tagashira, N., Chiba, K., Yasuda, M., and Baba, A., *Angew. Chem. Int. Ed*., **47**, 6620 (2008).
[37] Du, Y., Xu, L.-W., Shimizu, Y., Oisaki, K., Kanai, M., and Shibasaki, M., *J. Am. Chem. Soc*., **130**, 16146 (2008).
[38] Dubs, C., Hamashima, Y., Sasamoto, N., Seidel, T., Suzuki, S., Hashizume, D., and Sodeoka, M., *J. Org. Chem*., **73**, 5859 (2008).
[39] Ruano, J. L. G., Alemán, J., Catalán, S., Marcos, V., Monteagudo, S., Parra, A., del Pozo, C., and Fustero, S., *Angew. Chem. Int. Ed*., **47**, 7941 (2008).
[40] Xu, C.-l., Ma, J.-s., Wang, M.-c., Wang, Q., Hou, X.-h., and Zhang, Q.-j., *Chem. Abs*., **149**, 104160 (2008).
[41] Yamada, K.-i. and Tomioka, K., *Chem. Rev*., **108**, 2874 (2008).
[42] Shibasaki, M. and Kanai, M., *Chem. Rev*., **108**, 2853 (2008).
[43] Viso, A., de la Pradilla, R. F., Ureña, M., and Colomer, I., *Org. Lett*., **10**, 4775 (2008).
[44] Concellón, J. M., Rodríguez-Solla, H., and Simal, C., *Org. Lett*., **10**, 4457 (2008).
[45] Pizzuti, M. G., Minnaard, A. J., and Feringa, B. L., *J. Org. Chem*., **73**, 940 (2008).
[46] Kattuboina, A., Kaur, P., Nguyen, T., and Li, G., *Tetrahedron Lett*., **49**, 3722 (2008).
[47] Almansa, R., Guijarro, D., and Yus, M., *Tetrahedron: Asymmetry*, **19**, 603 (2008).
[48] Almansa, R., Guijarro, D., and Yus, M., *Tetrahedron: Asymmetry*, **19**, 2484 (2008).
[49] Kelly, A. M., Kerrigan, M. H., and Walsh, P. J., *J. Am. Chem. Soc*., **130**, 4097 (2008).
[50] Deng, G. and Li, C.-J., *Tetrahedron Lett*., **49**, 5601 (2008).
[51] Minbaev, B. O., *Chem. Abs*., **149**, 331726 (2008).
[52] Wang, C., Wu, X., Zhou, L., and Sun, J., *Chem. Eur. J*., **14**, 8789 (2008).
[53] Sinón, L. and Goodman, J. M., *J. Am. Chem. Soc*., **130**, 8741 (2008).
[54] Li, C., Wang, C., Villa-Marcos, B., and Xiao, J., *J. Am. Chem. Soc*., **130**, 14450 (2008).
[55] Guthrie, J. P. and Bhaskar, G., *Can. J. Chem*., **86**, 285 (2008).
[56] Crampton, M. R., Lowry, P. M., and Smith, I. J., *Org. Biomol. Chem*., **6**, 2405 (2008).
[57] Levin, V. V., Dilman, A. D., Belyakov, P. A., Struchkova, M. I., and Tartakovsky, V. A., *Eur. J. Org. Chem*., **2008**, 5226.
[58] Oliver, L. H., Puls, L. A., and Tobey, S. L., *Tetrahedron Lett*., **49**, 4636 (2008).
[59] Zhang, Y., Lu, Z., Desai, A., and Wulff, W. D., *Org. Lett*., **10**, 5429 (2008).
[60] Zhang, Y., Desai, A., Lu, Z., Hu, G., Ding, Z., and Wulff, W. D., *Chem. Eur. J*., **14**, 3785 (2008).
[61] Chigboh, K., Morton, D., Nadin, A., and Stockman, R. A., *Tetrahedron Lett*., **49**, 4768 (2008).
[62] Janardanan, D. and Sunoj, R. B., *J. Org. Chem*., **73**, 8163 (2008).
[63] Vara, Y., Bello, T., Aldaba, E., Arietta, A., Pizarro, J. L., Arriortua, M. I., Lopez, X., and Cossío, F. P., *Org. Lett*., **10**, 4759 (2008).
[64] Han, B., Li, J.-L., Ma, C., Zhang, S.-J., and Chen, Y.-C., *Angew. Chem. Int. Ed*., **47**, 9971 (2008).
[65] Li, G., Fronczek, F. R., and Antilla, J. C., *J. Am. Chem. Soc*., **130**, 12216 (2008).
[66] Reynolds, T. E., Binkley, M. S., and Scheidt, K. A., *Org. Lett*., **10**, 5227 (2008).
[67] Yazaki, R., Nitabaru, T., Kumagai, N., and Shibasaki, M., *J. Am. Chem. Soc*., **130**, 14477 (2008).
[68] Hou, Z., Wang, J., Liu, X., and Feng, X., *Chem. Eur. J*., **14**, 4484 (2008).
[69] Wen, Y., Gao, B., Fu, Y., Dong, S., Liu, X., and Feng, X., *Chem. Eur. J*., **14**, 6789 (2008).
[70] Malpica, A., Calzadilla, M., and Mejias, I., *Int. J. Chem. Kinet*., **40**, 554 (2008).
[71] Kobychev, V. B., Vitkovskaya, N. M., and Trofimov, B. A., *Chem. Abs*., **149**, 576097 (2008).
[72] Kereselidze, J. A. and Pachuliya, Z. V., *Chem. Abs*., **149**, 576048 (2008).
[73] Nakamura, S., Kanda, K., Turcotte, P., Itagaki, H., Mikami, M., Hara, Y., Saito, Y., Sasaki, K., Matsuoka, T., Teduka, M., Suzuki, T., Mori, Y., Tanabe, K., Takahara, J., and Setoyama, T., *Chem. Abs*., **148**, 517093 (2008).
[74] Mora, J. R., Cordova, T., and Chuchani, G., *Chem. Abs*., **149**, 447737 (2008).
[75] Pyun, S. Y. and Cho, B. R., *J. Org. Chem*., **73**, 9451 (2008).
[76] Huang, K., Merced, F. G., Oritz-Marciales, M., Meléndez, H. J., Correa, W., and De Jesús, M., *J. Org. Chem*., **73**, 4017 (2008).
[77] Berini, C., Minassian, F., Pelloux-Léon, N., Denis, J.-N., Vallée, Y., and Philouze, C., *Org. Biomol. Chem*., **6**, 2574 (2008).
[78] D'Anna, F., Frenna, V., Guernelli, S., Macaluso, G., Marullo, S., and Spinelli, D., *J. Phys. Org. Chem*., **21**, 306 (2008).

[79] Fontana, A., Guernelli, S., Meo, P. L., Mezzina, E., Morganti, S., Noto, R., Rizzato, E., Spinelli, D., and Zappacosta, R., *Tetrahedron*, **64**, 733 (2008).
[80] Uchiyama, S., Kaneko, T., Tokunaga, H., Ando, M., and Otsubo, Y., *Chem. Abs*., **148**, 168260
[81] Marqués-López, Herrera, R. P., Fernández, R., and Lassaletta, J. M., *Eur. J. Org. Chem*., **2008**, 3457.
[82] Jang, D. O. and Kim, S. Y., *J. Am. Chem. Soc*., **130**, 16152 (2008).
[83] Sloop, J. C., Lechner, B., Washington, G., Bumgardner, C. L., Loehle, W. D., and Creasy, W., *Int. J. Chem. Kinet*., **40**, 370 (2008).
[84] Hayashi, Y., *Chem. Abs*., **149**, 78961 (2008).
[85] Sun, Y., Fan, J., and Xu, J., *Chem. Abs*., **149**, 31846 (2008).
[86] Zhou, W., Xu, L.-W., Qui, H.-Y., Lai, G.-Q., Xia, C.-G., and Jiang, J.-X., *Helv. Chim. Acta*, **91**, 53 (2008).
[87] Fu, A., Li, H., Yuan, S., Si, H., and Duan, Y., *J. Org. Chem*., **73**, 5264 (2008).
[88] Fu, A., Li, H., Tian, F., Yuan, S., Si, H., and Duan, Y., *Tetrahedron: Asymmetry*, **19**, 1288 (2008).
[89] Corrêa, R. J., Garden, S. J., Angelici, G., and Tomasini, C., *Eur. J. Org. Chem*., **2008**, 736.
[90] Calderón, F., Doyagüez, E. G., Cheong, P. H.-Y., Fernández-Mayoralas, A., and Houk, K. N., *J. Org. Chem*., **73**, 7916 (2008).
[91] Chi, Y., Scroggins, S. T., Boz, E., and Fréchet, J. M. J., *J. Am. Chem. Soc*., **130**, 17287 (2008).
[92] Emer, E., Galletti, P., and Giacomini, D., *Tetrahedron*, **64**, 11205 (2008).
[93] Schwab, R. S., Galetto, F. Z., Azeredo, J. B., Braga, A. L., Lüdtke, D. S., and Paixão, M. W., *Tetrahedron Lett*., **49**, 5094 (2008).
[94] Doherty, S., Knight, J. G., McRae, A., Harrington, R. W., and Clegg, W., *Eur. J. Org. Chem*., **2008**, 1759.
[95] Xu, Z.-X., Li, G.-K., Chen, C.-F., and Huang, Z.-T., *Tetrahedron*, **64**, 8668 (2008).
[96] Zhao, J.-F., He, L., Jiang, J., Tang, Z., Cun, L.-F., and Gong, L.-Z., *Tetrahedron Lett*., **49**, 3372 (2008).
[97] Chimni, S. S., Singh, S., and Mahajan, D., *Tetrahedron: Asymmetry*, **19**, 2276 (2008).
[98] Tong, S.-T., Harris, P. W. R., Barker, D., and Brimble, M. A., *Eur. J. Org. Chem*., **2008**, 164.
[99] Zhang, D. and Yuan, C., *Tetrahedron*, **64**, 2480 (2008).
[100] Lombardo, M., Easwar, S., Pasi, F., Trombini, C., and Dhavale, D. D., *Tetrahedron*, **64**, 9203 (2008).
[101] Teo, Y.-C. and Chua, G.-L., *Tetrahedron Lett*., **49**, 4235 (2008).
[102] Fan, J.-F., Wu, L.-F., and Tao, F.-M., *Chem. Abs*., **148**, 307754 (2008).
[103] Hammar, P., Córdova, A., and Himo, F., *Tetrahedron: Asymmetry*, **19**, 1617 (2008).
[104] Chen, F., Huang, S., Zhang, H., Liu, F., and Peng, Y., *Tetrahedron*, **64**, 9585 (2008).
[105] Mei, K., Zhang, S., He, S., Li, P., Jin, M., Xue, F., Luo, G., Zhang, H., Song, L., Duan, W., and Wang, W., *Tetrahedron Lett*., **49**, 2681 (2008).
[106] Hayashi, Y., Samanta, S., Itoh, T., and Ishikawa, H., *Org. Lett*., **10**, 5581 (2008).
[107] Liu, X.-W., Le, T. N., Lu, Y., Xiao, Y., Ma, J., and Li, X., *Org. Biomol. Chem*., **6**, 3997 (2008).
[108] Arnold, K., Batsanov, A. S., Davies, B., Grosjean, C., Schütz, T., Whiting, A., and Zawatsky, K., *Chem. Commun. (Cambridge)*, **2008**, 3879.
[109] Chandrasekhar, S., Tiwari, B., Parida, B. B., and Reddy, C. R., *Tetrahedron: Asymmetry*, **19**, 495 (2008).
[110] Li, H., Da, C.-S., Xiao, Y.-H., Li, X., and Su, Y.-N., *J. Org. Chem*., **73**, 7398 (2008).
[111] Laars, M., Kriis, K., Kailas, T., Müürisepp, A.-M., Pehk, T., Kanger, T., and Lopp, M., *Tetrahedron: Asymmetry*, **19**, 641 (2008).
[112] Liu, J., Yang, Z., Wang, Z., Wang, F., Chen, X., Liu, X., Feng, X., Su, Z., and Hu, C., *J. Am. Chem. Soc*., **130**, 5654 (2008).
[113] Ramasastry, S. S. V., Albertshofer, K., Utsumi, N., and Barbas, C. F., *Org. Lett*., **10**, 1621 (2008).
[114] Markert, M. and Mahrwald, R., *Chem. Eur. J*., **14**, 40 (2008).
[115] Nakayama, K. and Maruoka, K., *J. Am. Chem. Soc*., **130**, 17666 (2008).
[116] Inoue, H., Kikuchi, M., Ito, J.-i., and Nishiyama, H., *Tetrahedron*, **64**, 493 (2008).
[117] Han, S. B., Hassan, A., and Krische, M. J., *Chem. Abs*., **149**, 532697 (2008).
[118] Stodulski, M., Jaźwiński, J., and Mlynarski, J., *Eur. J. Org. Chem*., **2008**, 5553.
[119] Pellicena, M., Solsona, J. G., Romea, P., and Urpí, F., *Tetrahedron Lett*., **49**, 5265 (2008).
[120] Dias, L. C. and Aguilar, A. M., *Chem. Soc. Rev*., **37**, 451 (2008).
[121] Paton, R. S. and Goodman, J. M., *J. Org. Chem*., **73**, 1253 (2008).
[122] Fukuchi, I., Hamashima, Y., and Sodeoka, M., *Chem. Abs*., **148**, 379052 (2008).
[123] Xu, B. and Hammond, G. B., *Angew. Chem. Int. Ed*., **47**, 689 (2008).
[124] See earlier comments on ref. 23
[125] Duarte, F. J. S., Cabrita, E. J., Frenking, G., and Santos, A. G., *Eur. J. Org. Chem*., **2008**, 3397.
[126] D'Elia, V., Zwicknagl, H., and Reiser, O, *J. Org. Chem*., **73**, 3262 (2008).

[127] Chandler, C. L. and List, B., *J. Am. Chem. Soc*., **130**, 6737 (2008).
[128] Rudkin, M. E., Joensuu, P. M., MacLachlan, W. S., and Lam, H. W., *Org. Lett*., **10**, 2939 (2008).
[129] Joensuu, P. M., Murray, G. J., Fordyce, E. A. F., Luebbers, T., and Lam, H. W., *J. Am. Chem. Soc*., **130**, 7328 (2008).
[130] Rasool, N., Rashid, M. A., Adeel, M., Görls, H., and Langer, P., *Tetrahedron Lett*., **49**, 2254 (2008).
[131] Adachi, S. and Harada, T., *Org. Lett*., **10**, 4999 (2008).
[132] Wang, L. and Wong, M. W., *Tetrahedron Lett*., **49**, 3916 (2008).
[133] Momiyama, N. and Yamamoto, H., *Chem. Abs*., **149**, 53336 (2008).
[134] Kato, K., Gustavsson, S. A., and Långström, B., *Tetrahedron Lett*., **49**, 5837 (2008).
[135] Çolak, M. and Demirel, N., *Tetrahedron: Asymmetry*, **19**, 635 (2008).
[136] Hammar, P., Marcelli, T., Hiemstra, H., and Himo, F., *Chem. Abs*., **148**, 517081 (2008).
[137] Liu, S. and Wolf, C., *Org. Lett*., **10**, 1831 (2008).
[138] Chen, X., Wang, J., Zhu, Y., Shang, D., Gao, B., Liu, X., Feng, X., Su, Z., and Hu, C., *Chem. Eur. J*., **14**, 10896 (2008).
[139] Yoshimoto, J., Sandoval, C. A., and Saito, S., *Chem. Lett*., **37**, 1294 (2008).
[140] Toussaint, A. and Pfaltz, A., *Eur. J. Org. Chem*., **2008**, 4591.
[141] Arai, T., Takashita, R., Endo, Y., Watanabe, M., and Yanagisawa, A., *J. Org. Chem*., **73**, 4903 (2008).
[142] Kowalczyk, R., Sidorowicz, L., and Skarzewski, J., *Tetrahedron: Asymmetry*, **19**, 2310 (2008).
[143] Jammi, S., Saha, P., Sanyashi, S., Sakthivel, S., and Punniyamurthy, T., *Tetrahedron*, **64**, 11724 (2008).
[144] Akakura, M., Kawasaki, M., and Yamamoto, H., *Eur. J. Org. Chem*., **2008**, 4245.
[145] Bauder, C., *Tetrahedron Lett*., **49**, 2243 (2008).
[146] Cadoni, E., Arca, M., Usai, M., Fattuoni, C., Perra, E., Cabiddu, M. G., De Montis, S., and Cabiddu, S., *Tetrahedron*, **64**, 6349 (2008).
[147] Nakamura, S., Hirata, N., Yamada, R., Kita, T., Shibata, N., and Toru, T., *Chem. Eur. J*., **14**, 5519 (2008).
[148] Aelvoet, K., Batsanov, A. S., Blatch, A. J., Grosjean, C., Patrick, L. G. F., Smethurst, C. A., and Whiting, A., *Angew. Chem. Int. Ed*., **47**, 768 (2008).
[149] Li, L., Klauber, E. G., and Seidel, D., *J. Am. Chem. Soc*., **130**, 12248 (2008).
[150] Hirao, T., *Chem. Abs*., **149**, 355182 (2008).
[151] Iwamoto, K.-i., Kimura, H., Oike, M., and Sato, M., *Org. Biomol. Chem*., **6**, 912 (2008).
[152] Enders, D. and Han, J., *Tetrahedron: Asymmetry*, **19**, 1367 (2008).
[153] Singh, V. and Batra, S., *Tetrahedron*, **64**, 4511 (2008).
[154] Zhao, S.-H., Zhao, M.-G., Zhang, H.-R., and Chen, Z.-B., *Chem. Abs*., **148**, 168175 (2008).
[155] Hatakeyama, S., *Chem. Abs*., **149**, 53335 (2008).
[156] Yang, C.-h. and Fan, J.-f., *Chem. Abs*., **148**, 238614 (2008).
[157] Jones, C. E. S., Turega, S. M., Clarke, M. L., and Philp, D., *Tetrahedron Lett*., **49**, 4666 (2008).
[158] Sohtome, Y., Takemura, N., Takagi, R., Hashimoto, Y., and Nagasawa, K., *Tetrahedron*, **64**, 9423 (2008).
[159] Shi, M. and Liu, X.-G., *Org. Lett*., **10**, 1043 (2008).
[160] Gruttadauria, M., Giacalone, F., Meo, P. L., Marculescu, A. M., Riela, S., and Noto, R., *Eur. J. Org. Chem*., **2008**, 1589.
[161] Tang, H., Zhao, G., Zhou, Z., Gao, P., He, L., and Tang, C., *Eur. J. Org. Chem*., **2008**, 126.
[162] Shi, M., Qi, M.-J., and Liu, X.-G., *Chem. Commun. (Cambridge)*, **2008**, 6025.
[163] Lei, Z.-Y., Ma, G.-N., and Shi, M., *Eur. J. Org. Chem*., **2008**, 3817.
[164] Qi, M.-J., Ai, T., Shi, M., and Li, G., *Tetrahedron*, **64**, 1181 (2008).
[165] Hargaden, G. C. and Guiry, P. J., *Chem. Abs*., **148**, 355180 (2008).
[166] Miller, J. J. and Sigman, M. S., *Angew. Chem. Int. Ed*., **47**, 771 (2008).
[167] Dam, J. H., Fristrup, P., and Madsen, R., *J. Org. Chem*., **73**, 3228 (2008).
[168] Nishigaichi, Y., Tamura, K.-i., Ueda, N., Iwamoto, H., and Takuwa, A., *Tetrahedron Lett*., **49**, 2124 (2008).
[169] Malkov, A. V., Ramírez-López, P., Biedermannová, L., Rulíšek, L., Dufková, L., Kotora, M., Zhu, F., and Kočovský, P., *J. Am. Chem. Soc*., **130**, 5341 (2008).
[170] Zhao, J.-F., Tsui, H.-Y., Wu, P.-J., Lu, J., and Loh, T.-P., *J. Am. Chem. Soc*., **130**, 16492 (2008).
[171] Park, J. Y., Ullapu, P. R., Choo, H., Lee, J. K., Min, S.-J., Pae, A. N., Kim, Y., Baek, D.-J., and Cho, Y. S., *Eur. J. Org. Chem*., **2008**, 5461.
[172] Xu, Z., Mao, J., and Zhang, Y., *Org. Biomol. Chem*., **6**, 1288 (2008).
[173] Li, H., Huang, Y., Jin, W., Xue, F., and Wan, B, *Tetrahedron Lett*., **49**, 1686 (2008).
[174] Engel, D. A., Lopez, S. S., and Dudley, G. B., *Tetrahedron*, **64**, 6988 (2008).

[175] Dunford, D., Guyader, M., Jones, S., Knight, D. W., Hursthouse, M. B., and Coles, S. J., *Tetrahedron Lett*., **49**, 2240 (2008).
[176] Yu, X. and Wang, W., *Org. Biomol. Chem*., **6**, 2037 (2008).
[177] Zhu, Q., Cheng, L., and Lu, Y., *Chem. Commun. (Cambridge)*, **2008**, 6315.
[178] Wang, J., Ma, A., and Ma, D., *Org. Lett*., **10**, 5425 (2008).
[179] Hawkes, K. J. and Yates, B. F., *Eur. J. Org. Chem*., **2008**, 5563.
[180] Biradar, D. B. and Gau, H.-M., *Tetrahedron: Asymmetry*, **19**, 733 (2008).
[181] Zhang, X., DeChancie, J., Gunaydin, H., Chowdry, A. B., Clemente, F. R., Smith, A. J. T., Handel, T. M., and Houk, K. N., *J. Org. Chem*., **73**, 889 (2008).
[182] Saito, Y. and Hyuga, H., *Chem. Abs*., **149**, 425341 (2008).
[183] Lavabre, D., Micheau, J.-C., Islas, J. R., and Buhse, T., *Chem. Abs*., **149**, 425340 (2008).
[184] Lutz, F., Igarashi, T., Kinoshita, T., Asahina, M., Tsukiyama, K., Kawasaki, T., and Soai, K., *J. Am. Chem. Soc*., **130**, 2956 (2008).
[185] Micheau, J.-C., Buhse, T., Lavabre, D., and Islas, J. R., *Tetrahedron: Asymmetry*, **19**, 416 (2008).
[186] Parrott, R. W. and Hitchcock, S. R., *Tetrahedron: Asymmetry*, **19**, 19 (2008).
[187] Olsson, C., Helgesson, S., and Frejd, T., *Tetrahedron: Asymmetry*, **19**, 1484 (2008).
[188] Dabiri, M., Salehi, P., Kozehgary, G., Heydari, S., Heydari, A., and Esfandyari, M., *Tetrahedron: Asymmetry*, **19**, 1970 (2008).
[189] Pisani, L. and Superchi, S., *Tetrahedron: Asymmetry*, **19**, 1784 (2008).
[190] Engel, T. de la C., Maroto, B. L., Martínez, A. G., and Cerero, S. de la M., *Tetrahedron: Asymmetry*, **19**, 269 (2008).
[191] Engel, T. de la C., Maroto, B. L., Martínez, A. G., and Cerero, S. de la M., *Tetrahedron: Asymmetry*, **19**, 2003 (2008).
[192] Engel, T. de la C., Maroto, B. L., Martínez, A. G., and Cerero, S. de la M., *Tetrahedron: Asymmetry*, **19**, 646 (2008).
[193] Nelson, J. K., Twamley, B., Villalobos, T. J., and Natale, N. R., *Tetrahedron Lett*., **49**, 5957 (2008).
[194] Gilani, M. and Wilhelm, R., *Tetrahedron: Asymmetry*, **19**, 2346 (2008).
[195] Parrott, R. W., Dore, D. D., Chandrashekar, S. P., Bentley, J. T., Morgan, B. S., and Hitchcock, S. R., *Tetrahedron: Asymmetry*, **19**, 607 (2008).
[196] Dean, M. A. and Hitchcock, S. R., *Tetrahedron: Asymmetry*, **19**, 2563 (2008).
[197] Cheng, Y.-Q., Bian, Z., Kang, C.-Q., Guo, H.-Q., and Gao, L.-X., *Tetrahedron: Asymmetry*, **19**, 1572 (2008).
[198] Martins, J. E. D. and Wills, M., *Tetrahedron: Asymmetry*, **19**, 1250 (2008).
[199] Burguete, M. I., Escorihuela, J., Luis, S. V., Lledós, A., and Ujaque, G., *Tetrahedron*, **64**, 9717 (2008).
[200] Grach, G., Reboul, V., and Metzner, P., *Tetrahedron: Asymmetry*, **19**, 1744 (2008).
[201] Jimeno, C., Sayalero, S., Fjermestad, T., Colet, G., Maseras, F., and Pericàs, M. A., *Angew. Chem. Int. Ed*., **47**, 1098 (2008).
[202] Tanaka, T. and Hayashi, M., *Chem. Lett*., **37**, 1298 (2008).
[203] Fernández-Ibáñez, M. A., Maciá, B., Minnaard, A. J., and Ferina, B. L., *Angew. Chem. Int. Ed*., **47**, 1317 (2008).
[204] Fernández-Ibáñez, M. A., Maciá, B., Minnaard, A. J., and Ferina, B. L., *Org. Lett*., **10**, 4041 (2008).
[205] Fernández-Ibáñez, M. A., Maciá, B., Minnaard, A. J., and Ferina, B. L., *Chem. Commun. (Cambridge)*, **2008**, 2571.
[206] Jones, A. C., Sanders, A. W., Sikorski, W. H., Jansen, K. L., and Reich, H. J., *J. Am. Chem. Soc*., **130**, 6060 (2008).
[207] Ukon, T. and Harada, T., *Eur. J. Org. Chem*., **2008**, 4405.
[208] Zhao, H., Dang, L., Marder, T. B., and Lin, Z., *J. Am. Chem. Soc*., **130**, 5586 (2008).
[209] Shigeru, N., Takatoshi, S., and Koohtaro, T., *Chem. Abs*., **148**, 144196 (2008).
[210] Barboni, L., Filippi, A., Fraschetti, C., Giuli, S., Marcolini, M., and Marcantoni, E., *Tetrahedron Lett*., **49**, 6065 (2008).
[211] Muramatsu, Y. and Harada, T., *Angew. Chem. Int. Ed*., **47**, 1088 (2008).
[212] Muramatsu, Y. and Harada, T., *Chem. Eur. J*., **14**, 10560 (2008).
[213] North, M., Usanov, D. L., and Young, C., *Chem. Rev*., **108**, 5146 (2008).
[214] Jia, X.-J., Pan, X.-M., Wang, L.-W., Liu, Y., Sun, H., Su, Z.-M., and Wang, R.-S., *Chem. Abs*., **149**, 447773 (2008).
[215] Qin, S., Hu, C., Yang, H., Su, Z., and Tang, D., *J. Org. Chem*., **73**, 4840 (2008).
[216] Takaki, J., Egami, H., Matsumoto, K., Saito, B., and Katsuki, T., *Chem. Lett*., **37**, 502 (2008).
[217] Zeng, Z., Zhao, G., Zhou, Z., and Tang, C., *Eur. J. Org. Chem*., **2008**, 1615.
[218] Kurono, N., Arai, K., Uemura, M., and Ohkuma, T., *Angew. Chem. Int. Ed*., **47**, 6643 (2008).
[219] Drees, M. and Strassner, T., *Chem. Abs*., **148**, 54533 (2008).

[220] Zhang, X.-H., Chung, L. W., Lin, Z., and Wu, Y.-D., *J. Org. Chem*., **73**, 820 (2008).
[221] Zhou, X., Liu, X., Yang, X., Shang, D., Xin, J., and Feng, X., *Angew. Chem. Int. Ed*., **47**, 392 (2008).
[222] Mergott, D. J., *Chem. Abs*., **148**, 537510 (2008).
[223] Wang, F., Meng, Q., and Li, M., *Chem. Abs*., **149**, 401789 (2008).
[224] Moxham, G. L., Randell-Sly, H., Brayshaw, S. K., Weller, A. S., and Willis, M. C., *Chem. Eur. J*., **14**, 8383 (2008).
[225] Creech, G. S., Zhu, X.-F., Fonovic, B., Dudding, T., and Kwon, O., *Tetrahedron*, **64**, 6935 (2008).
[226] Hsieh, Y.-H., Weinberg, N., and Wolfe, S., *Can. J. Chem*., **86**, 81 (2008).
[227] Shagun, V. A., Shagun, L, G., Dorofeev, I. A., Mikhailova, I. A., and Voronkov, M. G. *Chem. Abs*., **148**, 537572 (2008).
[228] Ankem, R. V., Murphy, J. L., and Nagorski, R. W., *Tetrahedron Lett*., **49**, 6547 (2008).
[229] Kananovich, D. G. and Kulinkovich, O. G., *Tetrahedron*, **64**, 1536 (2008).
[230] Kavanagh, S. A., Piccinini, A., Fleming, E. M., and Connon, S. J., *Org. Biomol. Chem*., **6**, 1339 (2008).
[231] El Kettani, S. E.-C., Lazraq, M., Ouhsaine, F., Gornitzka, H, Ranaivonjatovo, H., and Escudié, J., *Org. Biomol. Chem*., **6**, 4064 (2008).
[232] Duncan, N. C., Garner, C. M., Nguyen, T., Hung, F., and Klausmeyer, K., *Tetrahedron Lett*., **49**, 5766 (2008).
[233] Sakakura, A., Watanabe, H., and Ishihara, K., *Org. Lett*., **10**, 2569 (2008).
[234] Chataigner, I., Zammattio, Z., Lebreton, J., and Villiéras., *Tetrahedron*, **64**, 2441 (2008).
[235] Gribble, G. W., *Chem. Abs*., **148**, 537505 (2008).
[236] Kano, T., Ueda, M., and Maruoka, K., *J. Am. Chem. Soc*., **130**, 3728 (2008).
[237] Sreedhar, B., Reddy, P. S., and Madhavi, M., *Chem. Abs*., **148**, 238534 (2008).
[238] Siani, G., Angelini, G., De Maria, P., Fontana, A., and Pierini, M., *Org. Biomol. Chem*., **6**, 4236 (2008).
[239] Holzer, W., Eller, G. A., and Schoenberger, S., *Chem. Abs*., **148**, 262090 (2008).
[240] Li, B. Z., *Chem. Abs*., **148**, 238635 (2008).
[241] García-Río, L., Mejuto, J. C., Parajó, M., and Pérez-Lorenzo, M., *J. Org. Chem*., **73**, 8198 (2008).
[242] Liou, L. R., McNeil, A. J., Ramirez, A., Toombes, G. E. S., Gruver, J. M., and Collum, D. B., *J. Am. Chem. Soc*., **130**, 4859 (2008).
[243] Godenschwager, P. F. and Collum, D. B., *J. Am. Chem. Soc*., **130**, 8726 (2008).
[244] Sun, X.-W., Wang, W., Xu, M.-H., and Lin, G.-Q., *Tetrahedron Lett*., **49**, 5807 (2008).
[245] Cheon, C. H. and Yamamoto, H., *J. Am. Chem. Soc*., **130**, 9246 (2008).
[246] Mullins, R. J., Gregg, J. J., and Hamilton, G. A., *Chem. Abs*., **148**, 537478 (2008).
[247] Clay, J. M., *Chem. Abs*., **148**, 537474 (2008).
[248] Lall, M. S., *Chem. Abs*., **148**, 537475 (2008).
[249] Clay, J. M., *Chem. Abs*., **149**, 331724 (2008).
[250] Nishiyama, H. and Shiomi, T., *Chem. Abs*., **149**, 355184 (2008).
[251] Brewer, A. R. E., *Chem. Abs*., **148**, 537499 (2008).
[252] Suzuki, Y., Kaneno, D., Miura, M., and Tomoda, S., *Tetrahedron Lett*., **49**, 4223 (2008).
[253] Hut'ka, M. and Toma, Š., *Monatsh. Chem*., **139**, 793 (2008).
[254] Paptchikhine, A. K. K. and Andersson, P. G., *Chem. Abs*., **148**, 379051 (2008).
[255] Cortez, N. A., Aguirre, G., Parra-Hake, M., and Somanathan, R., *Tetrahedron: Asymmetry*, **19**, 1304 (2008).
[256] Liu, J., Zhou, Y., Wu, Y., Li, X., and Chan, A. S. C., *Tetrahedron: Asymmetry*, **19**, 832 (2008).
[257] Bi, S., Xie, Q., Zhao, X., Zhao, Y., and Kong, X., *Chem. Abs*., **148**, 307821 (2008).
[258] Hashimoto, T., Ito, J.-i., and Nishiyama, H., *Tetrahedron*, **64**, 9408 (2008).
[259] Friberg, A., Sarvary, I., Wendt, O. F., and Frejd, T., *Tetrahedron: Asymmetry*, **19**, 1765 (2008).
[260] Li, G.-Q., Yan, Z.-Y., Niu, Y.-N., Wu, L.-Y., Wei, H.-L., and Liang, Y.-M., *Tetrahedron: Asymmetry*, **19**, 816 (2008).
[261] Sun, L., Tang, M., Wang, H., Wei, D., and Liu, L., *Tetrahedron: Asymmetry*, **19**, 779 (2008).
[262] West, J. D., Stafford, S. E., and Meyer, M. P., *J. Am. Chem. Soc*., **130**, 7816 (2008).
[263] Ekoue-Kovi, K. and Wolf, C., *Chem. Eur. J*., **14**, 6302 (2008).
[264] Reddy, K. R., Maheswari, C. U., Venkateshwar, M., and Kantam, M. L., *Eur. J. Org. Chem*., **2008**, 3619.
[265] Curran, T. T., *Chem. Abs*., **148**, 537481 (2008).
[266] Meneses, L., Araya, A., Pilaquinga, F., and Fuentealba, P., *Chem. Abs*., **149**, 246128 (2008).
[267] Zhou, X.-T., Ji, H.-B., and Yuan, Q.-L., *Chem. Abs*., **149**, 493214 (2008).
[268] Guin, J., De Sarkar, S., Grimme, S., and Studer, A., *Angew. Chem. Int. Ed*., **47**, 8727 (2008).

[269] Maki, B. E. and Scheidt, K. A., *Org. Lett*., **10**, 4331 (2008).
[270] Noonan, C., Baragwanath, L., and Connon, S. J., *Tetrahedron Lett*., **49**, 4003 (2008).
[271] Zuyls, A., Roesky, P. W., Deacon, G. B., Konstas, K., and Junk, P. C., *Eur. J. Org. Chem*., **2008**, 693.
[272] Dayalan, A. and Martin, S., *Chem. Abs*., **148**, 471450 (2008).
[273] Tandon, P. K., Purwar, M., Dwivedi, P. B., and Srivastava, M., *Chem. Abs*., **149**, 493213 (2008).
[274] Sharma, M., Sheikh, H. N. and Kalsotra, B. L., *Chem. Abs*., **148**, 214635 (2008).
[275] Das, S. and Mahanti, M. K., *Chem. Abs*., **148**, 214636 (2008).
[276] Tandon,, P. K., Kumar, S., Srivastava, M., and Singh, S. B., *Chem. Abs*., **148**, 537648 (2008).
[277] Soni, N. K., Sharma, G., Khandelwal, C. L., and Sharma, P. D., *Chem. Abs*., **148**, 121303 (2008).
[278] Iuga, C., Galano, A., and Vivier-Bunge, A., *Chem. Phys. Chem*., 9, 1453 (2008).
[279] Yasunaga, K., Kubo, S., Hoshikawa, H., Kamesawa, T., and Hidaka, Y., *Int. J. Chem. Kinet*., **40**, 73 (2008).
[280] Fristrup, P., Kreis, M., Palmelund, A., Norrby, P.-O., and Madsen, R., *J. Am. Chem. Soc*., **130**, 5206 (2008).
[281] Iwai, T., Fujihara, T., and Tsuji, Y., *Chem. Commun. (Cambridge)*, **2008**, 6215.
[282] Feierabend, K. J., Zhu, L., Talukdar, R. K., and Burkholder, J. B., *J. Phys. Chem. A*, **112**, 73 (2008).
[283] Gruber-Stadler, M., Mühlhäuser, M., Sellevåg, S. R., and Nielsen, C. J., *J. Phys. Chem. A*, **112**, 9 (2008).
[284] Kim, J., Park, K.-S., Yeo, W.-S., and Chong, Y., *Chem. Abs*., **149**, 533675 (2008).
[285] Kano, T., Yamamoto, A., and Maruoka, K., *Tetrahedron Lett*., **49**, 5369 (2008).
[286] Tomita, Y., Itoh, Y., and Kochi, M., *Chem. Lett*., **37**, 1080 (2008).
[287] Hashimoto, T., Naganawa, Y., and Maruoka, K., *J. Am. Chem. Soc*., **130**, 2434 (2008).
[288] He, J., Tang, S., Liu, J., Su, Y., Pan, X., and She, X., *Tetrahedron*, **64**, 8797 (2008).
[289] Katz, C. E., Ribelin, T., Withrow, D., Basseri, Y., Manukyan, A. K., Bermudez, A., Nuera, C. G., Day, V. W., Powell, D. R., Poutsma, J. L., and Aubé, J., *J. Org. Chem*., **73**, 3318 (2008).
[290] Bourque, L. E. and Woerpel, K. A., *Org. Lett*., **10**, 5257 (2008).
[291] Xin, J., Chang, L., Hou, Z., Shang, D., Liu, X., and Feng, X., *Chem. Eur. J*., **14**, 3177 (2008).
[292] Das, G. C., Halder, D. C., Rahman, M. T., Bahar, M. H., and Olsson, T., *Chem. Abs*., **148**, 214616 (2008).