CHAPTER 1

Reactions of Aldehydes and Ketones and their Derivatives

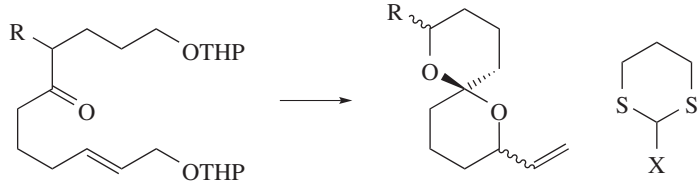
B. A. Murray

Department of Science, Institute of Technology Tallaght (ITT Dublin), Dublin, Ireland

Organic Reaction Mechanisms 2014, First Edition. Edited by A. C. Knipe.

Formation and Reactions of Acetals and Related Species

1,11-Dihydroxy-undec-9-en-5-one derivatives (**1**; R = H, Me) undergo a novel and highly stereoselective palladium(II)-catalysed intramolecular cyclization via unstable hemiacetal intermediates, to give spiroketals (**2**).[1] (*de*)



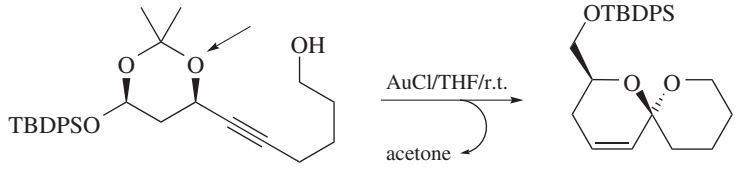
(**1**) (**2**) (**3**)

Conversion of aldehydes (RCHO) to their cyclic dithioacetals (**3**; X = R) has been simplified by the use of 2-chloro-1,3-dithiane (**3**; X = Cl) in dichloroethane at 50 °C, employing a simple iron catalyst, $FeCl_3$. A single-electron transfer (SET) mechanism is proposed.[2]

Unsaturated spiroacetal (**5**) has been prepared as a single regioisomer with *de* > 96% from a cyclic acetonide (**4**) with an appropriate alkyne–alcohol tether; the arrowed oxygen is lost with the extrusion of acetone. Catalysed by gold(I), the reaction also works for non-cyclic alkyne–triol chains, but much less cleanly. The acetone → acetonide preparative step can be considered to be a regioselectivity regulator, masking the 1,3-diol's alcohol groups.[3] (*de*)

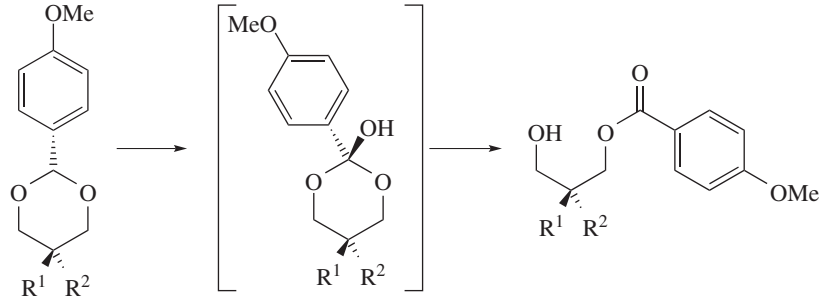
N-Boc-protected amino acid esters derived from serine and threonine forms (natural and unnatural) combine with tetramethoxyalkanes [1,2-diacetals: $R^1–\{C(OMe)_2\}_2–R^2$] to give chiral bi- and tri-cyclic *N*,*O*-acetals in high diasteriomeric excess (*de*), via an intramolecular *trans*-carbamoylation cascade.[4] (*de*)

2-Substituted and 2,2-disubstituted 1,3-diols, $HO–CH_2–CR^1R^2–CH_2OH$, have been desymmetrized through their *para*-methoxy benzylidene acetals (**6**), using



(**4**) (**5**)

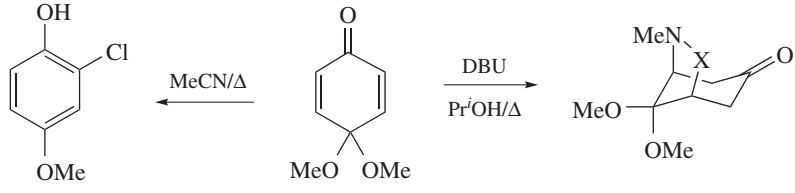
dimethyldioxirane (DMDO) to form an intermediate orthoester (**7**), followed by proton transfer using a chiral phosphoric acid to deliver the monoester product (**8**). Density functional theory (DFT) calculations indicate that the DMDO oxidation step is rate-determining, and a suitable auxiliary – a buttressed BINOL-phosphoric acid – gives yields/*ee* up to 99/95%.[5]



(**6**) (**7**) (**8**)

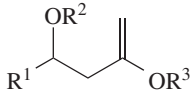
DFT has been used to study the thermal racemization of spiropyrans.[6]

Based on the reaction of a quinone monoacetal (**9**) with methylhydroxylamine hydrochloride (MeNHOH·HCl) to give a bridged isoxazolidine (**10a**) via a double hetero-Michael addition, the analogous diaza process was attempted, using the appropriate hydrazine MeNHNHMe(·2HCl) in refluxing acetonitrile. Surprisingly, this gave a new nucleophilic chlorination to yield a substituted chlorophenol (**11**) regio-selectively, presumably via acid-catalysed methoxide loss and chloride attack, or *vice versa*. The intended bridged pyrazolidines (**10b**) could be accessed via base catalysis in a protic solvent.[7]

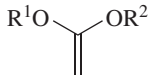


(**11**) (**9**) (**10a**; X = O,
10b; X = NMe)

Trimethylsilyl triflate is an efficient Lewis acid catalyst for oxygen-to-carbon rearrangement of vinyl and ketene acetals (**12** and **13**) to give chain-extended ketones or esters, respectively, giving fair yields in 30 min in dichloromethane (DCM) at −78 °C, with 0.01 mol% trimethylsilyl trifluoromethanesulfonate (TMSOTf). The method has been applied to stereoselective synthesis of *C*-glycosides from the corresponding anomeric vinyl ethers. Starter (**12**) can be prepared by methenylation of the corresponding acetal-ester with Tebbe's reagent, and (**13**) via elimination of an appropriate *β*-iodo-acetal.[8]



(**12**)



(**13**)

Selective Heck arylation of acrolein diethyl acetal in water has been achieved by appropriate choice of base: sodium acetate favours reaction with cinnamaldehydes, while diisopropylamine works with 3-propionic esters. In the presence of such a base, the ligands in the $[Pd(NH_3)_4]Cl_2$ catalyst are exchanged.[9]

Alkynyldimethylaluminium reagents, derived from terminal alkynes and trimethylaluminium, doubly add to *N*,*N*-disubstituted formamides, or to the corresponding *O*,*O*-acetals, while similar *N*,*O*-acetals undergo mono-addition.[10]

Alkynylation of *N*,*O*-acetals and related pro-electrophiles has been carried out using Au(I) carbophilic catalysts, LAuX, with specific counteranions, $X^- = {}^-OTf$ or ${}^-NTf_2$.[11]

A study of nucleophilic substitutions of five-membered ring acetals bearing fused rings indicates that subtle changes in the structure of the latter can dramatically affect *de*. An unconstraining ring allowed selectivity comparable to a non-fused analogue, with 'inside' attack on the oxocarbenium ion, but if the second ring included at least one oxygen, the *de* fell considerably. DFT-calculated transition states (TSs) for the addition of allyltrimethylsilane correlated with the results, which are also compared with the better known six-membered series.[12] (*de*)

An experimental and theoretical study examines why silylated nucleobase additions to acyclic *α*-alkoxythiacarbenium intermediates proceed with high 1,2-*syn* stereocontrol, opposite to that expected for the corresponding activated aldehydes. The acyclic thioaminals formed undergo intramolecular cyclizations to provide nucleoside analogues.[13] (*de*)

A new oxidant, *N*-chloroisonipecotamide, has been characterized and tested with benzaldehyde di-*n*-alkyl acetals in acetonitrile: kinetic orders are first and zero, respectively.[14]

An easily prepared and handled palladium(II) complex has been used for the deprotection of acetals and dioxolanes while leaving acid-sensitive groups unaffected.[15]

For reports on acetals termed 'aziridine aldehyde dimers', see the Ugi reaction under 'Imines: Synthesis and General and Iminium Ion Chemistry' section. For preparation of bicyclic acetals via an acetalization/oxa-Michael process, see 'Michael Additions and Related Reactions' section.

Reactions of Glucosides

The 'formose reaction', in which formaldehyde is dimerized to glycolaldehyde ($HOCH_2CHO$) and onward to sugar-like substances, is a candidate for prebiotic simple sugars. Though a mechanism was proposed by Breslow in 1959,[16a] it has remained controversial. New deuterium studies have clarified the route, retaining the original intermediates but changing some connecting steps. Glycolaldehyde formation is autocatalytic, and deuterium is not readily incorporated[16b]: this is inconsistent with enolization pathways, and the original author now puts the relevant isomerizations down to hydride shifts.[16c]

6-Deoxy-L-hexoses are rare but biologically important. All eight have now been prepared as their thioglycoside glycosyl donors, starting from L-rhamnose or L-fucose, using protecting-group manipulations and highly selective epimerizations. The following trends are observed: (i) *cis*-diols can be prepared using stereoselective reduction of a ketone with a chelating α-substituent, and (ii) *trans*-diols can be prepared via Mitsonobu reaction or stereoselective reduction without a chelating α-substituent.[17]

In an organocatalytic approach, which mimics dihydroxyacetone phosphate aldolases, *de novo* syntheses of 1-deoxy-D-ketohexoses and D-ketohexoses have been carried out using chiral diamide catalysts, and hydroxy- or dihydroxy-acetone, respectively, with the (*R*)-isomer of glyceraldehyde acetonide. This enamine-based $C_3 + C_3$ methodology also works for the L-series, using the (*S*)-acetonide. The authors also note that the enamine process faces competition: simple achiral 1°, 2°, and 3° amines also catalyse the reactions, giving *syn*-aldols.[18] (de) (ee)

A short review (63 references) examines a number of unusual enzymatic glycoside cleavage mechanisms that differ significantly from the classical Koshland retaining and inverting glycosidases. Typically, they cleave glycosides by mechanisms involving either elimination or hydration, and – in contrast to the exclusively cationic TSs of Koshland – they can involve development of either positive or negative charge in the TS. Some can cleave otherwise resistant thioglycosides. As some of these enzymes are sourced from pathogens, their selective inhibition may facilitate effective treatments of the related diseases with minimal side effects.[19] (de)

N-Benzylgalactonoamidine exhibits characteristics of a TS analogue for enzymatic hydrolysis of aryl-β-D-galactopyranosides; its inhibition constants for a range of substrates range from 12 to 56 nM.[20]

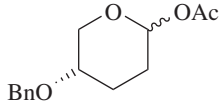
A DFT investigation of anomeric equilibration in sugars via oxocarbenium ions has examined the reaction series from an α-covalent triflate intermediate to the corresponding α-contact ion pair, the solvent-separated ion pair, and on to the β-analogues. Attempting geometry optimization of ion pairs without solvent resulted in re-formation of the covalent α- and β-triflates, but as few as four DCM molecules provided sufficient stabilization. Gibbs activation energies for the formation of the contact ion pairs were calculated as 10.4 and 13.5 kcal mol^{-1} for α- and β-, respectively.[21] (de)

Ab initio molecular dynamics has been employed to model the ring-opening and isomerization of glucose to fructose, catalysed by chromium(III) chloride. The hydride shift is the overall rate-limiting step.[22]

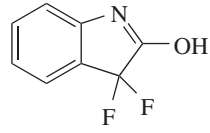
Mechanisms of glycosylation have been reviewed, with a focus on computation, covering neighbouring group and solvent effects, the influence of the conformational flexibility of the glycosyl donor on reactivity/selectivity, and *endo*- versus *exo*-cyclic cleavage of pyranosides.[23]

Linear and branched α-glucans have been synthesized using hydrogen-bond-mediated aglycone delivery (HAD), where pyridylmethyl or pyridylcarbonyl substituents are employed remotely. Linear cases from di- to penta-saccharides were achieved with complete stereoselectivity in all glycosylations, but the method may be affected by the increased bulk of the glycosyl acceptor. Branched structures proved more problematic.[24]

Nucleophilic substitution reactions of tetrahydropyran acetals (**14**) with $H_2C{=}C(OPh)OTMS$ are promoted by TMS-triflate, with significant solvent effects: polar solvents favour S_N1 products, and non-polar favour S_N2. Trichloroethylene was identified as the solvent most likely to give S_N2 products in both C- and O-glycosylations.[25] *de*



(**14**)



(**15**)

An attempt to promote highly α-selective glycosylation by six-ring neighbouring group participation has studied glycosyl donors with novel 2-iodo- and 2-(phenylseleno)-ethyl ether protecting groups. While participation was not seen for the iodo-ethyl ether case, the seleno-substituent did show participation (as shown by the observation of cyclic intermediates by low-T NMR), but even here it was not enough to prevent a significant flux to β-product.[26] *de*

The use of aryl and alkyl sulfenyl triflates as promoters of glycosylation has been reviewed.[27]

Difficulties in using triflic anhydride to mediate direct dehydrative glycosylation have been overcome by using a strained olefin such as β-pinene as an acid scavenger.[28] *de*

Phenyl(trifluoroethyl)iodonium triflimide, $Ph{-}I^{+}{-}CH_2CH_2CF_3\ {}^{-}NTf_2$, is an air- and water-soluble activator of thioglycosides, allowing glycosylation at ambient temperature in good to very high yields, and high *de* in some cases, over a wide range of donors, including sensitive 2- and 6-deoxy sugars.[29] *de*

3,3-Difluoroxindole (**15**, 'HOFox') has been used to mediate glycosylation. Both the *in situ* synthesis of OFox glycosyl donors and activation thereof can be performed regeneratively, so only catalytic amounts of the OFox imidate donor and Lewis acid activator are required.[30] *de*

The combination of $AuCl_3$ and phenylacetylene promotes both Ferrier rearrangement of glycols with nucleophiles, and also O-glycosylation of 1-*O*-acetyl sugars.[31] *de*

The kinetics of the hydrolytic cleavage of non-terminal α-glycosidic bonds in cyclodextrins have been measured in DMSO–water mixtures and compared to those of D-maltose. In particular, the yield of 5-hydroxymethyl-2-furaldehyde was monitored with a view to optimizing green routes to its generation from biomass.[32]

Following the screening of 26 representative metal salts, strontium dichloride emerged as the most efficient co-catalyst for acidic hydrolysis of methyl glycosides, with short reaction times, high yields, and fewer by-products.[33]

Cellobiose can be hydrolysed to glucose in ionic liquids (ILs). An *ab initio* quantum study suggests an S_N1-type mechanism, and the energetics are compared with those of gas phase and aqueous solution.[34]

A review attempts to develop a comprehensive kinetic and mechanistic picture of the conversion of pentoses to furfural in aqueous acidic media, although the variations in the specific conditions of each study examined make concise comparison difficult.[35]

D-Glucose has been converted to 5-hydroxymethylfurfural in DMSO at 150 °C, using an acidic IL, namely 1-(1-propylsulfonic)-3-methylimidazolium chloride, as catalyst. The mechanism has been studied by visible spectroscopy and ^{1}H and ^{13}C NMR, including the use of glucose labelled at C(1) or C(2). Glucose is isomerized to fructose via the complexation of the open-chain form with the imidazolium cation. Yields are low, being limited by the formation of humin.[36]

The condensation and dehydration reactions of glucose in DMSO have been studied computationally and compared with experiment: the reactions are initiated by protonation of C(1)–OH and C(2)–OH, respectively. While the mechanisms are similar to those in aqueous solution, the magnitudes of the barriers are quite solvent-dependent.[37]

Direct umpolung of glycals with ketones has been carried out using samarium diiodide: for the hexose series, the allyl samarium reagent produced is highly stereoselective, reacting with ketones at the C(3) position *anti* to a C(4) substituent.[38] (de)

3,4,6-Tri-*O*-acetyl-D-galactal is selectively converted to 1-*O*-aryl-2-deoxy derivatives or chiral bridged benzopyrans depending on reaction conditions, using $Al(OTf)_3$ catalysis, with easy onward access to chiral chromenes and chromans.[39]

Tosylation of L-rhamnose, followed by reduction and acetylation, yields 2,3,4-triacetyl-1,6-dideoxy-L-mannose and tetraacetyl-3,6-dideoxy-L-mannitol; the mechanism has been probed via DFT.[40]

A titrimetric method has been used to study the kinetics of palladium(II)-catalysed oxidation of D-(+)-galactose by cerium(IV) in aqueous acid from 308 to 333 K. Arabinose and formic acid are the main products.[41]

The kinetics of the ruthenium(III)-catalysed oxidation of D-arabinose by *N*-bromophthalimide were measured in acid from 303 to 323 K: the main products are erythronic and formic acids.[42]

The kinetics of oxidation of D-(+)-trehalose by *N*-bromoacetamide has been studied in acid solution over a range of temperatures. Using a rhodium(III) pentachloride catalyst, the order is one with respect to substrate, catalyst, oxidant, and hydronium ion, with arabinonic and formic acids as the main products.[43]

The kinetics of the oxidation of glucose and fructose by *N*-chloronicotinamide has been studied in alkaline solution from 308 to 328 K, giving gluconate and formate, respectively; 1,2-enediol intermediates are discussed.[44] A similar study using *N*-bromonicotinamide in alkaline solution has found the rates for glucose to be first order in alkali concentration, but the fructose exhibits inverse first order.[45]

Ruthenium(III)-catalysed oxidation of xylose by potassium bromate has been studied from 30 to 45 °C in both acidic and alkaline media. In acid, the order in bromate is one at

low concentration, but then saturates, and pH has negligible effect, which is also found in base. D_2O also has little effect on the rate.[46]

The kinetics of iodate oxidation of lactose have been studied in aqueous alkaline medium, using an iridium(III) catalyst.[47]

The kinetics of the oxidation of galactose by cerium(IV) has been studied in acid from 308 to 328 K.[48]

The kinetics of oxidation of several simple saccharides by alkaline permanganate have been studied spectrophotometrically. An enediol intermediate complex is proposed, and the reactivity order is glucose ~ galactose > maltose > fructose > sucrose[49]; a similar study of lactose has been performed.[50]

The kinetics of ruthenium(III)-catalysed oxidation of maltose by potassium permanganate in acid show orders 1, 0, 1, and 1, respectively. A spectrophotometric study suggests $[Ru(H_2O)_4O]^{2+}$ as the active Ru(III) species.[51]

Several reports under 'Formation and Reactions of Acetals and Related Species' section are relevant to glucosides, and synthesis of a new carbohydrated-related skeleton is reported under 'Other Asymmetric Aldols' section.

Reactions of Ketenes and Keteniminium Species

A synthetic exploration of the possibilities provided by ynimines, $R^1–C{\equiv}C–N{=}CR^2R^3$, under anionic conditions highlights their use as precursors of metalated ketenimines via *in situ* reaction with organolithium or other strong bases. Onward reaction with various electrophiles provides nitriles, α,β-unsaturated nitriles, and α,β-unsaturated amides.[52]

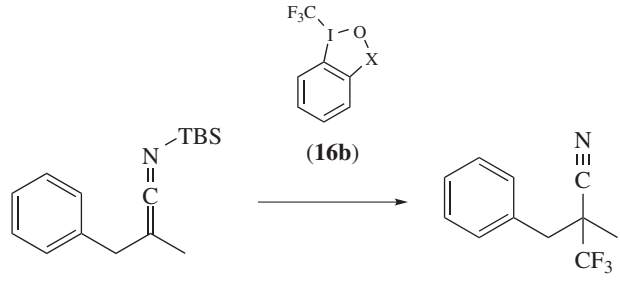
Given the role of 3° amines in generating ketenes and in catalysing their reactions, and their degradation in some reactions, an experimental and computational study of reaction of such aliphatic amines with aryl ketenes, 4-X-C_6H_4–CH=C=O, has been carried out. Using typical photogeneration of a ketene with triethylamine in acetonitrile at 25 °C, triethylamine attack on the carbonyl gives a zwitterion, $Ar–CH{=}C(O^-)–{}^+NEt_3$, which loses an ethyl cation (quaternizing external triethylamine), giving an enolate-type intermediate which protonates to give amide $ArCH_2CONEt_2$. For the parent compound (X = H), ketene decay is ~8 times faster than formation of amide, while a nitro group accelerates the decay (×400) and even more dramatically slows the amide formation (÷5000). Among other amines examined, *N*-methyldialkyls strongly prefer methyl loss by displacement, isopropyl loss involves elimination, while DABCO forms a long-lived zwitterion, helping to explain how cinchona alkaloids can add to ketenes with zwitterion formation and promote subsequent stereoselective additions even in the presence of triethylamine. The dealkylation process is also found for reaction of tertiary amines with the much more stable diphenyl ketene.[53]

A phase space approach has been used to explore mechanisms of ketene isomerization.[54]

Quantum chemical methods have been used to study the dimerization of alkyl ketenes.[55]

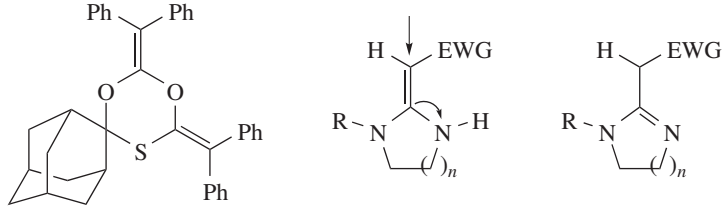
Silyl ketene imines (e.g. **16a**) have been electrophilically trifluoromethylated using hypervalent iodine reagents (**16b**; X = C=O or CMe_2) to give quaternary α-trifluoromethyl nitriles (**17**); the latter are easily transformable into a range of useful

organofluorine building blocks. The reaction gives yields up to 89% in a day at ambient temperature, using a vanadium(IV)-salen catalyst, without solvent.[56] (de)



(**16a**) (**16b**) (**17**)

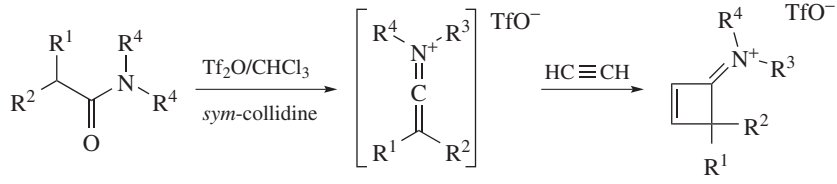
The first report of the formation of a 1,3,5-dioxathiane in a ketene reaction describes the reaction of two moles of diphenylketene with adamantanethione to give 2,4-bis (diphenylmethylidene)-1,3,5-dioxathiane (**18**) via ketene-thione zwitterions.[57]



(**18**) (**19a**) (**19b**)

A range of heterocyclic ketene aminals (**19a**; $n = 0–3$), which have two nucleophilic centres (arrowed), form adducts with ninhydrin, with further isomerization under kinetic or thermodynamic control, and a significant dependence on the solvent. The possible role of the amidine tautomer (**19b**) is discussed.[58]

Tertiary amides bearing at least one α-hydrogen (**20**), when treated with hindered base and triflic anhydride in refluxing chloroform, give keteniminium salts (**21**). When $R^1 = H$ (i.e. an 'aldo'-keteniminium), these react with acetylene to give cyclobuteniminium salts (**22**): these in turn are dienophiles in Diels–Alder reactions, and better than cyclobutenones.[59]



(**20**) (**21**) (**22**)

Formation and Reactions of Nitrogen Derivatives

Imines: Synthesis, and General and Iminium Chemistry

A new general organocatalytic method for the preparation of aldimines from aldehydes and amines uses pyrrolidine without acids or metals. Yields are close to quantitative, covering virtually all types of imines: *N*-alkyl, -aryl, -sulfinyl, -sulfonyl, and -phosphinoyl. Aldehydes employed were typically aromatic (or cinnamyl), though aliphatic aldehydes *did* work for the *N*-sulfinyl cases, with *t*-butyl-sulfinamide proving more successful than *para*-tolyl.[60]

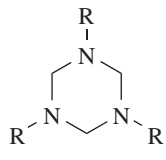
N-Sulfonyl imines, Ar–CH=N–Ts, have been prepared from aldehydes and chloramine-T (Na^+ ^-NClTs), using proline as organocatalyst, in aqueous medium at ambient temperature; enals are particularly reactive, including aliphatic cases.[61]

A systematic NMR study of the effect of ILs on reactivity examined imine formation from 1-aminohexane and either benzaldehyde or *para*-methoxy benzaldehyde in d_3-acetonitrile, with controlled amounts of 1-butyl-3-methylimidazolium salts or other ILs. ILs increased the reaction rate constant in proportion to their mole fraction, and temperature variation allowed separation of enthalpic and entropic contributions, which varied with the salt used. The approach should enhance the predictability of the effects of varying the IL cation, anion, and concentration.[62]

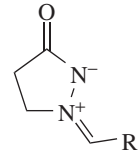
A ruthenium(II) *NNN*-pincer complex catalyses direct coupling of 1° alcohols and 1° amines in air, to give imines. For example, benzyl alcohol and benzylamine gives 97% yield of $PhCH{=}NCH_2Ph$ in 12 h in toluene at 70 °C, using 0.01 mol% catalyst. The first step is considered to be dehydrogenation of the alcohol to the aldehyde (which requires oxygen), with the aldehyde remaining bound to the metal: this can be observed in the absence of amine. Stereoselective versions are being explored.[63]

N-Alkylation can be achieved by the oxidation of primary alcohols to aldehydes, condensation of the latter with the amine, and subsequent reduction of the imine product. The copper(II)-catalyst variant has been studied by DFT: the first two steps are significantly uphill, but the imine reduction acts as the driving force. The calculated turnover frequency agrees well with the experimental value.[64]

With a view to better understand poly(hexahydrotriazine) polymers from reactions of diamines with formaldehyde, an experimental and computational study of the monoamine version of formation of cyclic hemiaminals (**23**) – via the imine, $R{-}N{=}CH_2$ – has been undertaken. Mechanisms involving water-promoted sequential condensations are preferred to amine catalyses, and results explain the higher reactivity of electron-rich amines. In contrast, trifluoromethylamine is markedly less reactive.[65]



(**23**)



(**24**)

AM1 and DFT methods have been applied to the mechanism of reaction of phenylpropan-2-one with ethylamine.[66]

Triflic acid catalyses the reaction of aldehydes with 2-vinylaniline to give substituted quinolines; a similar reaction with biphenyl-2-amine gives substituted phenanthridines. Both proceed via imine formation, protonation, and then cyclization.[67]

Addition of 1° amines to α,β-unsaturated aldehydes and ketones to produce imines can proceed with either 1,2- or 1,4-addition. An *in situ* IR and NMR study, combined with DFT, has been used to identify what governs the selectivity. 1,2-Addition predominates, typically under kinetic control, and exceptions such as methyl vinyl ketone have been explained in terms of conformational effects. The *in situ* methodologies are particularly useful, given the instability of the imines towards hydrolysis, polymerization, and so on.[68]

Kinetics of the formation of 2-HO–C_6H_4–CH=N–C_6H_4-4-Me, from salicylaldehyde and 4-toluidine,[69] of the 5-chloro-derivative *N*-(5-chloro-salicylidene)-4-methylaniline,[70] and of the Schiff bases from salicylaldehyde with *meta*-chloro-[71] and *para*-chloro-aniline[72] have all been studied in ethanol from 303 to 318 K.

A kinetic and mechanistic study of Schiff base formation from the reaction of L-α-glutamic acid with pyridoxal shows that subsequent hydrolysis completes the transamination; that is, yields pyridoxamine and α-ketoglutaric acid. Reaction of L-glutamine with pyridoxal has also been studied.[73]

The mechanisms of reaction of benzaldehyde with 4-amino-4*H*-1,2,4-triazole to give Schiff base, via a hemaminal, have been probed computationally.[74]

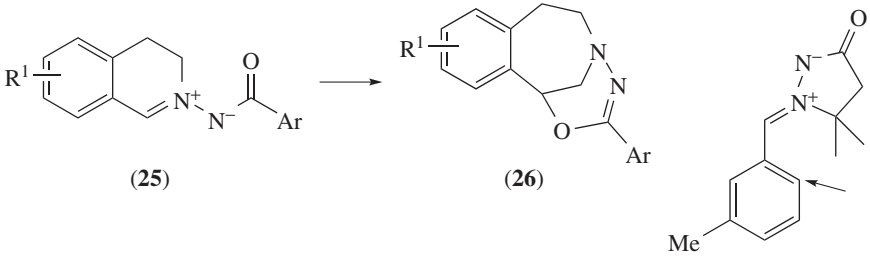
Enantioselective methodologies using *N*-carbamoyl-imines have been reviewed (153 references): key advantages include their increased reactivity towards nucleophiles, and the relative ease of later removal of the carbamoyl moiety.[75]

Imine metathesis is catalysed by 1° aliphatic amines, and a kinetic NMR study of transiminations of both aromatic–aromatic and aromatic–aliphatic imines in organic solvents at ambient temperature indicates that these exchange reactions are fast enough to allow them to catalyse the metathesis in the absence of acid or metal catalysis. Hammett plots generated by varying the *ortho*-substituent of benzaldimines are non-linear, with both donating (OMe) and withdrawing (NO_2) substituents retarding the process. This somewhat unusual 'concave-down' plot is attributed to a change in the rate-determining step. The results hold promise for the generation of dynamic combinatorial libraries under the conditions employed.[76]

The use of imine and iminium precursors as versatile intermediates in enantioselective catalysis has been reviewed (127 references).[77] (*de*) (*ee*)

A range of *N*,*N*′-cyclic azomethine imines (**24**) undergo phosphination and hydrophosphonylation with diarylphosphinoxides or dialkylphosphites, using chiral squaramide catalysts derived from dihydroquinine, in yields/*ee* up to 99/99%.[78] Aromatic cases (e.g. **24**; R = Ph) allow easy access to dinitrogen-fused heterocycles via a phosphine-catalysed 3 + 2-cycloaddition to bis(phenylsulfonyl)alkenes.[79] (*ee*)

C,*N*-Cyclic-*N*′-acyl azomethine imines (**25**) undergo ring expansion to 3-benzazepines (**26**) using sulfonium ylide generated *in situ* from a suitable salt, for example, $PhSMe_2^+$ BF_4^-.[80]



(**25**) (**26**) (**27**)

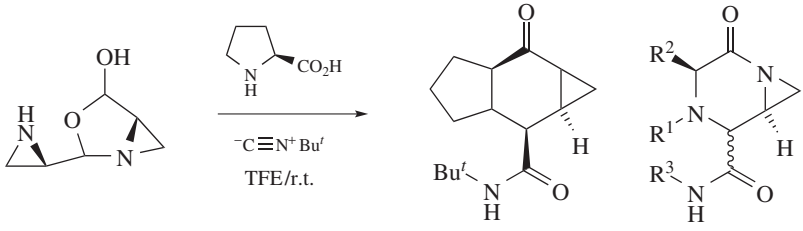
An azomethine imine (**27**) undergoes rhodium(III)-catalysed C–H alkynylation at the *ortho*-position, using an alkynylated hypervalent iodine reagent. The azomethine imine acts as a masked aldehyde directing group, easily converted back to aldehyde by hydrolysis. Without the methyl group 'blocker' on the aromatic ring, both *ortho* positions react. The method also overcomes the poor directing effect of the aldehyde.[81]

An N-heterocycle (NHC)-catalysed 3 + 4-cycloaddition of azomethine imines and enals generates dinitrogen-fused seven-membered heterocycles in high *de*/*ee*. The method also kinetically resolves the imines.[82] (*de*) (*ee*)

Bromodifluoromethylation of iminium ions with TMS–CF_2Br has been described. The iminium ions are generated *in situ* from aldehydes, 2° amines, proton sponge, and silyl triflate. TMS–CF_2Br can be activated with HMPA at ambient temperature to generate difluorocarbene, which converts to bromodifluoromethyl carbanion in the presence of excess bromide. Similar chloro- and iodo-difluoromethylations are also reported.[83]

Electrospray ionization tandem mass spectrometry (ESI-MS/MS) has been used to characterize intermediates in the Ugi and Ugi–Smiles reactions and the related Mumm rearrangement.[84a] A key nitrilium ion intermediate is described, and the Ugi–Smiles mechanism is characterized as ionic, with an earlier theoretical investigation of a hemiaminal intermediate[84b] being discussed. No evidence for such a hemiaminal was found, supporting the Ugi–Smiles reaction as being essentially mechanistically identical to the Ugi.

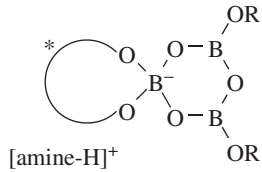
The 'aziridine aldehyde dimer' [(*R*)-**28**] reacts with L-proline and *t*-butyl isocyanide to give a chiral piperazinone (**29**). The kinetics of this Ugi-type multi-component reaction are first order in dimer (**28**) and zero order in other species. DFT calculations indicate selective formation of a *Z*-iminium ion.[85] (*de*)



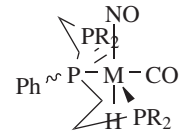
(*R*)-(**28**) (**29**) (*S*)-(**30**)

Another aziridine aldehyde dimer [(*S*)-**30**] undergoes a 'disrupted' Ugi reaction with an amino acid [$R^1HN–C(R^2)–CO_2H$, R = H, Ar, alkyl] and an isocyanide ($R^3N{\equiv}C$) to give piperazinones: *trans*- if R^1 = H, and *cis*- for aryl/alkyl.[86] (*de*)

The three-component Ugi reaction of an aldehyde, an amine, and an isocyanide has been catalysed by a range of BOROX catalysts (**31**) in fair to good *ee*. The BOROX methodology was conveniently screened using a catalyst 'library' prepared by combination of borane (as its dimethyl sulfide complex), water, an alcohol (ROH), an amine, and a chiral biaryl diol. An ion pair between a chiral boroxinate anion and an achiral iminium ion is proposed as the catalytically active species.[87] (*ee*)



(**31**)



(**32**; M = Mo, W, R = Pr^i, ~3:1 *syn*:*anti*)

Aryl aldehydes react with TMS-azide in the presence of a Lewis acid catalyst to generate azidocarbenium ion intermediates [Ar–CH=N–N_2^+]; these can be trapped in one pot with nucleophiles to give azides Ar–CH(Nu)–N_3. The nucleophile could be the azide itself (from TMS-azide), giving a *gem*-diazido-product, $ArCH(N_3)_2$, easily reducible to mono-azide (i.e. $ArCH_2N_3$) with triethylsilane. An enantioselective variant is also reported, as is the preparation of *β*-azido-dicarbonyl compounds. Schmidt rearrangement does *not* intervene.[88] (*ee*)

Reduction and Oxidation of Imines

A short review examines a metal-organo cooperative approach to asymmetric hydrogenation of imines, using a chiral phosphoric acid and an iridium complex.[89] (*ee*)

Unprotected NH imines of substituted acetophenones – prepared as their hydrochloride salts, Ar–C(Me)=$NH_2^+Cl^-$ – have been asymmetrically hydrogenated to give the corresponding amine salts in yields/*ee* up to 97/95%. A standard rhodium catalyst $[Rh(cod)Cl]_2$ and a bisphosphinyl-ferrocene with a pendant chiral thiourea effect the transformation, with hydrogen-bonding dual activation from the auxiliary, including anion binding of the chloride. Further mechanistic investigation by counterion variation, ^1H NMR, and deuterium labelling is also reported.[90]

A range of Mo(0) and W(0) trisphosphine-substituted nitrosyl hydride complexes (**32**) have been prepared and tested as catalysts of hydrogenation of imines, using an acidic co-catalyst $[H(Et_2O)_2][B(C_6F_5)_4]$. An 'ionic hydrogenation mechanism' is proposed, with heterocyclic splitting of molecular hydrogen followed by 'proton before hydride' transfers. This is supported by linear Hammett plots for a series of *para*,*para′*-disubstituted benzylideneaniline substrates, Ar^1–CH=N–Ar^2, where *ρ* values of −10.5 and +0.86 were found for the *C*- and *N*-sides, respectively. Iminium intermediates were observed, there was a linear dependence on $p(H_2)$, and a dynamic kinetic isotope effect of 1.38 was measured. H_2 addition is proposed to be rate-limiting.[91]

NHC complexes of zincocenes and dizincocenes catalyse hydrogenation of imines and ketones, respectively.[92]

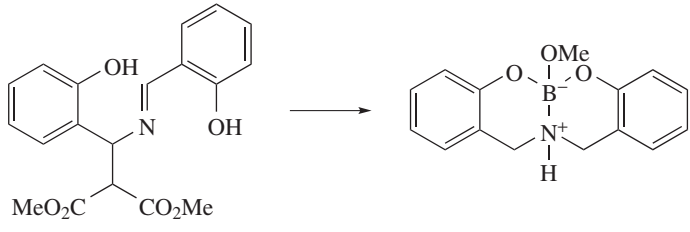
An experimental and computational study has examined the effect of arene variation in the use of Noyori's [RuCl(TsDPEN)(η^6-arene)] catalysts for transfer hydrogenation of 3,4-dihydroisoquinolines.[93] ee

An unusual chiral cationic Lewis base, a quaternized picolinamide-cinchona organocatalyst, efficiently adds trichlorosilane to ketone imines, reducing them to the amines in good yield and up to 91% *ee*, sometimes in 15 min with 0.5 mol% loading.[94] ee

Other uses involving trichlorosilane include 2-pyridoyl esters of D-glucosamine derivatives catalysing the reduction of *N*-Boc aryl aldimines with good yields and fair *ee*s,[95] a new organocatalyst combining a carbohydrate and *N*-formyl-L-valine giving yields/*ee* up to 98/94% in the reduction of arylidene anilines,[96] and a new chiral axial amide *N*,*N*′-dioxide derived from L-tryptophan, reducing ketimines in good *ee*.[97] ee ee ee

α-Silylimines undergo Meerwein–Ponndorf–Verley (MPV)-type reduction to α-silylamines in high *ee* using a chiral lithium amide; the authors have modified their previously proposed chair-like six-membered TS[98a] in the light of the current results,[98b] and used DFT to further clarify the mechanism. ee ee

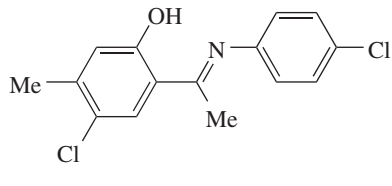
Malonate-imine (**33**), derived from dimethyl malonate and two moles of salicylaldehyde, was expected to reductively ring-close to the corresponding benzoxazine on treatment with borohydride in methanol. Instead, a boramide (**34**) is formed, with loss of the malonate moiety. X-ray crystallography indicates *cis*-fusion of the rings, with B and N atoms approximately tetrahedral. The B–O(Me) bond is very short (1.42 Å), yet the methoxy is easily lost in positive-electrospray MS. In solution, (**34**) exhibits a solvent-dependent *cis*–*trans* equilibrium. Loss of the malonate probably occurs early on, as direct reaction of salicylaldehyde and its unsubstituted imine with $NaBH_4$ also yields (**34**).[99]



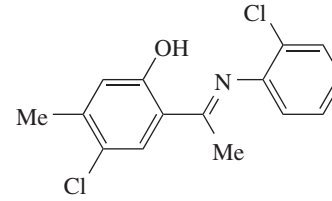
(**33**) (**34**)

A ruthenium-catalysed reductive methylation of nitrogen employs carbon dioxide and molecular hydrogen as C and H sources: starting from aldimine R^1–N=CHR^2, a ruthenium(triphos) catalyst delivers an *N*-methylamine, R^1–N(Me)–CH_2R^2, in up to 99% yield, using the two gases at 20 and 60 atm, respectively. The reaction can also be performed *in situ*, starting from the amine R^1NH_2 and aldehyde R^2CHO, demonstrating excellent atom and step economy.[100]

The kinetics of the oxidation of diaryl ketimine (**35**) by cerium(IV) in aqueous sulfuric acid indicate a first-order dependence on substrate and oxidant. Ionic strength and solvent effects are reported, as well as activation parameters.[101]



(**35**)



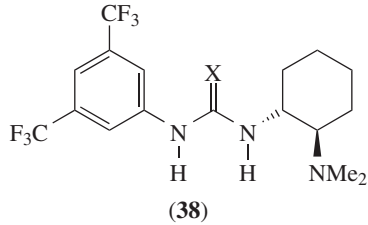
(**36**)

An isomer (**36**) has been similarly studied kinetically over a range of temperatures.[102]

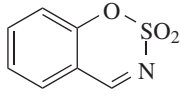
Mannich, Mannich-type, and Nitro-Mannich Reactions

Single and double A^3-coupling Mannich reactions of terminal alkynes, pyrrolidine, and formaldehyde are catalysed by copper(I)-biphenylphosphine complexes. The catalysis has been compared with that by the less effective gold(I) complexes.[103]

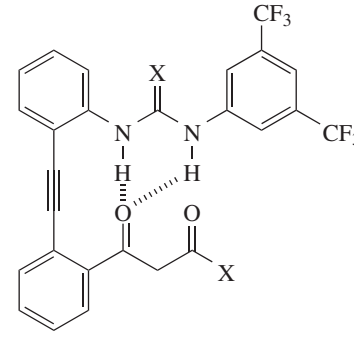
A cyclic imine (**37**) undergoes direct Mannich reaction with methyl alkyl ketones in up to 97% *ee*, using an alkaloid-derived 1°–3° diamine organocatalyst. The regioselectivity is under steric control, with the reaction occurring at the methyl side of the ketone.[104] (*de*) (*ee*)



(**38**)



(**37**)



(**39**)

The mechanism of the enantioselective Mannich reaction catalysed by hydrogen-bond-donor bifunctional organocatalysts – chiral amino-(thio)ureas (**38**; X = O, S) – has been investigated by tethering on a β-dicarbonyl moiety to generate a binary complex to act as a model of a catalyst and nucleophile, the so-called 'snap-shot structural analysis'. While the urea might be expected to form individual hydrogen bonds to the two carbonyls, X-ray crystallography of two models [diketone (X = Ph) and keto-ester (X = OMe)] clearly showed a double-hydrogen-bond interaction to one carbonyl (**39**). In another case with an amino substituent on the urea, an ammonium-enolate intermediate could be directly observed by X-ray crystallography and in solution by NMR. Nucleophilic reactions of imines with the binary-complex models have also been carried out.[105] (*de*) (*ee*)

Aliphatic, aromatic, and heteroaromatic *N*-Boc aldimines undergo enantioselective Mannich reaction with β-keto esters, using a chiral bifunctional urea-thiourea catalyst; the products can be decarboxylated to β-amino ketones without loss of *ee*.[106] (*ee*)

An air-stable organometallic and a simple Brønsted acid/base have been combined for cooperative catalysis: titanocene dichloride and *para*-aminophenol allow direct Mannich three-component reactions to be carried out efficiently under mild conditions.[107]

Benzothiazolyl imines undergo Mannich reactions with *t*-butyl acetoacetate with yields/*ee* up to 99/98%, using a chiral squaramide catalyst.[108] (de) (ee)

Asymmetric Mannich reaction of α-thio acetaldehyde has been exploited in a remote chirality control strategy leading to 1,4-amino alcohols and 1,4-diamines.[109] (de) (ee)

2,3-Diaryl-β-amino acid derivatives have been prepared from arylimines and aryl(thio) acetic esters, in a Mannich-like reaction promoted by $TiCl_4/Et_3N$. *Syn*/*anti*-diastereoselection shows significant dependence on the nature of an *ortho*-substituent in the arylacetate because of specific heteroatom–titanium coordination.[110]

Imines derived from ketones undergo direct asymmetric Mannich-type reaction with α-isocyanoacetates, using a cinchona alkaloid/$Cu(OTf)_2$/base combination, to give β-tetrasubstituted α,β-diamino acids $R^1R^2C(NH_2)–CH(NH_2)–CO_2H$ with good yields and *de*/*ee* up to 84/99%.[111] (de) (ee)

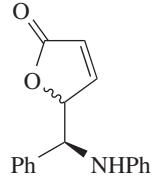
Ureidopeptide Brønsted-base organocatalysts convert aldimines (R^1–CH=NBoc) and (arylsulfonyl)acetonitriles ($N\equiv C–CH_2–SO_2R^2$, acting as acetonitrile anion equivalents) to give β-amino nitriles $R–CH^*(NHBoc)CH_2C\equiv N$ with *ee* up to 98%.[112] (ee)

Quaternary stereogenic β-amino indanones and indanoles have been prepared in yields/*ee* up to 98/98% via Mannich-type additions of 1-indanones and *N*-*t*-butanesulfinyl ketimines.[113] (ee)

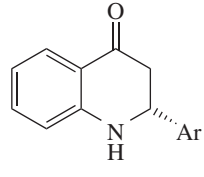
An *S*-chiral sulfinyl aldimine, $F_3C–CH=N–{}^*S(=O)–t\text{-}Bu$, undergoes a Mannich-type reaction with C(5)-lithiated thiazola[3,2-*b*]-[1,2,4]triazoles with near-quantitative diastereoselectivity.[114] (de)

N-*t*-Butanesulfinimines derived from isatin undergo diastereoselective vinylogous Mannich reaction with silyloxyfurans, promoted by trimethylsilyl triflate.[115] (de)

Mixing furan-2-OTMS with an imine (Ph–CH=N–Ph) and water (without other solvent) yields δ-amino-γ-butenolide (**40**) as an *anti*/*syn*-mixture. This vinylogous Mannich-type reaction has been investigated by the artificial force induced reaction (AFIR) method, and surprisingly yielded five plausible working pathways. All have comparable barriers and compete with each other, and have a common rate-determining step: concerted Si–O bond formation through nucleophilic attack of water, followed by proton transfer from water to the imine. The complexity of the manifold – including formation of regioisomers which then undergo retro-Mannich processes to eventually yield (**40**) – militates against accurate calculation of the *anti*/*syn*-ratio, or viable suggestions on how to control or modify it.[116] (de)



(**40**)



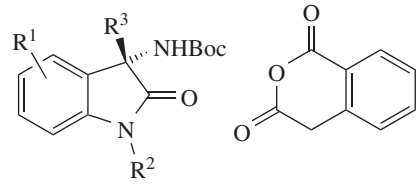
(**41**)

Primary amino acid derivatives such as O-Bu^t-L-threonine catalyse direct intramolecular Mannich reaction between 2-amino acetophenone and aldehydes (ArCHO), to give 2-aryl-2,3-dihydro-4-quinolines (**41**) in good yield and *ee*, without the need for *N*-protection.[117] (*ee*)

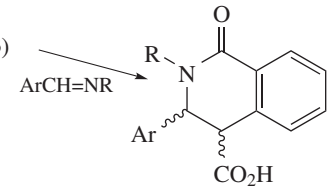
The boronic acid Mannich reaction has been reviewed from the points of view of its mechanism, stereochemistry, scope, and limitations, covering product types including amino acids, 1,2-amino alcohols, benzylamines, and heterocycles.[118]

3-Amino-2-oxindoles (**42**) have been prepared from isatin imines and 4-bromo ethylacetoacetate via a domino Mannich-cyclization reaction catalysed by a chiral squaramide, in high yield and *ee*.[119] (*ee*)

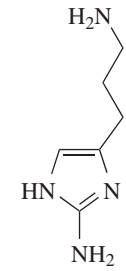
Aromatic cyclic sulfinyl aldimines undergo copper(I)-catalysed decarboxylative Mannich reactions with β-keto-acids; a chiral bisoxazoline (BOX) ligand renders the reaction highly enantioselective.[120] (*ee*)



(**42**) (**43**)



(**44**)



(**45**)

Aldimines react with homophthalic anhydride (**43**) to give a tetrahydroisoquinolonic carboxylate (**44**) as formal cycloadduct. Addition of *N*-methylimidazole raises the yield and reduces the amount of elimination by-product. It also promotes isomerization of the *cis*/*trans*-(**44**) mixture to the all-*trans* form. The *N*-methylimidazole catalyst appears to act as an acyl transfer agent.[121] (*de*)

Pictet–Spengler reaction of aminopropyl-2-aminoimidazole (**45**) with enantiopure aldehydes derived from amino acids exhibits 92% *anti*-selectivity, with the *de* dependent on the steric bulk of the amino acid sidechain. While the Pictet–Spengler reaction is typically acid-catalysed, for imidazoles it is accelerated by bases such as triethylamine. Addition of Lewis acids *did* increase the rate (even in the presence of excess base), but had no marked effect on the *de*.[122] (*de*)

Nitro-Mannich reactions of two *trans*-alkanes, R–CH=CH–NO_2 (R = CO_2Et, Ph), with non-zinc nucleophiles have been investigated, with mixed success.[123] (*de*)

Addition of Organometallics to Imines

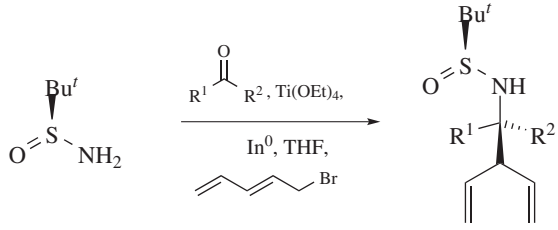
Steric and electronic factors have been investigated in the carbolithiation of imines by a variety of organolithiums; cases of polar versus SET mechanisms have been teased out.[124]

Cyclic α,β-unsaturated *N*-tosyl ketimines add organoaluminium reagents in a rhodium(I)-catalysed reaction: 1,2- or 1,4-addition may occur (depending on substituents) to give α-tertiary allylic amines or 3-substituted cycloalkyl amines (after reduction). BINAP facilitates up to 99% *ee* for both routes.[125] (*ee*)

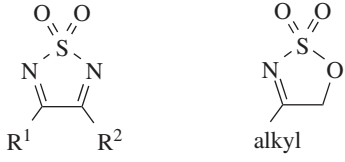
Nucleophilic 1,2-addition of MeMgBr or MeLi to (*S*)-*N*-benzylidene-2-methylpropane-2-sulfinamide is stereoselective, and DFT has been used to explain why. The *E*/*Z*-isomerization of the imine is fast, with the *E*-isomer preferred. The organometallic reagents are bifunctional, serving as nucleophiles but also as Lewis acids, with the latter role being stereo-determining.[126] (*de*)

A new generation of NHCs – imidazolium salts derived from amino acids and containing a pyridine ring – catalyse asymmetric alkylation of *N*-sulfonimines by dialkylzincs in the presence of copper(II) chloride in toluene: an excess of HMPA is critical to both yield and *ee*.[127] (*ee*)

Chiral *t*-butylsulfinimines, generated *in situ* from sulfonamide (**46**) and a carbonyl compound, react with an *in situ* generated pentadienyl-indium to form α-substituted (1,4-pentadien-3-yl)amines (**47**) in up to 90% yield and >96% *de*. The γ-regioselectivity is found for a wide range of carbonyl compounds (R^1 = alkyl, aryl; R^2 = H, Me), and products are usefully modifiable: hydrogenation gives α-substituted (3-pentyl)amines, and a hydroboration–oxidation/Mitsonobu cyclization sequence gives a pyrrolidine-ethanol derivative. The simple one-pot aminopentadienylation protocol is non-toxic and tolerates moisture and/or air.[128] (*de*)



(**46**) (**47**)



(**48**) (**49**)

Arylations, Alkenylations, Allylations, and Alkynylations of Imines

Cyclic diketimines (**48**) undergo rhodium-catalysed arylation with arylboronic acids, using a chiral olefin-sulfinamide ligand to give 1,2,5-thiadiazoline 1,1-dioxides in up to 99% *ee*, the latter being readily convertible to tertiary α-amino ketones.[129] (*ee*)

Cyclic *N*-sulfamidate alkylketimines (**49**) undergo enantioselective arylation; reduction of the product provides chiral β-alkyl-β-aryl-β-amino alcohols. Using an

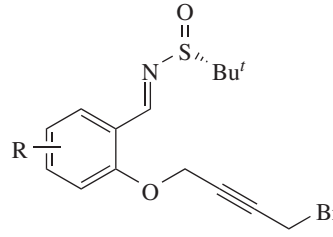
arylboronate and a rhodium–chiral diene complex as catalyst, up to 99% *ee* was obtained.[130] (ee)

Cyclic *N*-sulfonyl ketimines undergo asymmetric arylation (using arylboronic acids) to give the corresponding chiral cyclic sulfamidates in high yields and *ee* up to 99.9%, using a cationic palladium complex with a chiral phosphine-oxazoline ligand.[131] (ee)

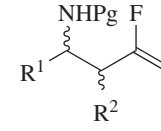
A new series of tunable *P*-chiral *P*,π-hybrid ligands has been prepared that catalyse addition of aryl boronic acids to arylaldimines in up to 98% *ee*.[132] (ee)

N-Nosylaldimines undergo highly enantioselective alkenylation with potassium alkenyltrifluoroborates, using a rhodium–diene complex.[133] (ee)

Indium promotes intramolecular cyclization of *ortho*-propargyloxy aryl *N*-*t*-butanesulfinyl imines (**50**) to give 3-allenyl-4-aminochromanes in up to 99% *de*. An allyloxy variant of (**50**) yields the corresponding 3-vinyl-4-aminochromane.[134] (de)



(**50**)



(**51**)

$ReBr(CO)_5$-catalysed addition of 1-octyne to *N*-(diphenylmethyl)aldimines, RCH=N–$CHPh_2$ [toluene/110 °C/$P(C_6F_5)_3$], yields isomerized *N*-allyl ketimines, H_2C=C(Hex)–CHR–N=CPh_2. Deuterium labelling experiments indicate that additions of both hydrogen and of the *N*-alkylidene-aminoalkyl group to the terminal alkyne are stereoselective.[135]

Protected aldimines, R^1–CH=N–Pg [Pg = Ts, *S(=O)–*t*-Bu], react with suitable halofluoroalkenes (X–CH_2–CF=CHR^2; X = Cl, Br) under Barbier conditions to give fluorinated homoallylic amines (**51**) with yields/*de* up to 99/100%. The γ-selective process is promoted by indium metal. X-ray analysis of the configuration of the product suggests a six-membered cyclic intermediate.[136] (de)

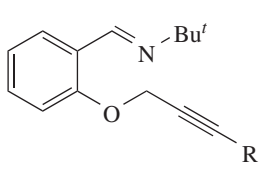
Indium promotes allylation of enantiomerically pure *N*-*t*-butylsulfinyl imines in high *de*; acid treatment easily deprotects the products to give free amines.[137] *N*-*t*-Butanesulfinyl imines undergo diastereoselective palladium-catalysed allylation and crotylation with allylic alcohols in the presence of indium(I) iodide as reducing agent.[138] (de) (de)

Cyclic sulfonylimines have been allylated in high *ee* and *de* using allylrhodium species generated from γ,γ- or α,α-disubstituted potassium allyltrifluoroborates. The initially formed allylrhodium species undergo isomerization via a 1,4-rhodium(I) migration.[139] (de) (ee)

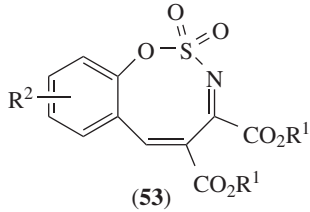
Enantioselective allylation of *N*-sulfonylimines with allyltin has been achieved using an *in situ* generated Cu(II)-Schiff base derived from a chiral amino alcohol.[140] (ee)

(2-Propargyl ether) arylimines (**52**; R = Ar) deliver 3-amino-2-styryl-benzofurans via *t*-butoxide-mediated intramolecular cyclization in THF at ambient temperature in an hour, typically with *Z*-alkene stereochemistry. The base promotes the formation of an

allenyl anion, the attack of which on the imino carbon is regioselective: formation of the alternative seven-membered ring is not observed. The reaction also works for the terminal alkyne (i.e. R = H), but not for alkyl.[141]



(**52**)



(**53**)

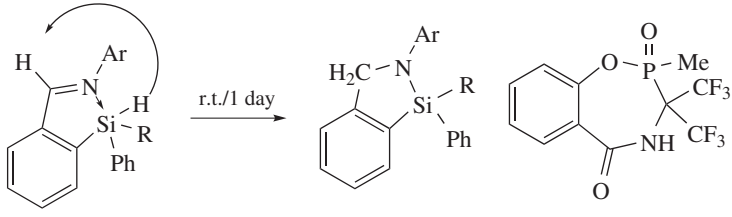
Alkoxyethynyl aluminium reagents generated *in situ* have been added to *N-t*-butylsulfinyl aldimines in >96% *de*, with quantitative conversion, to give oxygenated propargylamines in one step from simple dichloroenol ethers.[142]

N-Arylbenzaldimines react with alkynes bearing at least one electron-withdrawing group to give 2-arylquinolines under $FeCl_3$ catalysis; a one-pot *in situ* version from aldehyde, amine, and alkyne also works.[143]

Sulfamate-derived (hexa)cyclic imines undergo ring expansion with acetylenedicarboxylates to give benzo[*g*][1,2,3]oxathiazocine-4,5-dicarboxylate 2,2-dioxide derivatives (**53**) in high yields. The reactions are catalysed by triphenylphosphine, which reacts with the alkyne to give a zwitterion, which then attacks the imine carbon. The reaction typically works in minutes in benzene.[144]

Other Additions to Imines

Organosilanes with an appropriately placed nitrogen (**54**) spontaneously convert into 1-aza-silole-type structures (**55**) in the absence of catalysis. This can be considered an intramolecular hydrosilylation of an aldimine induced by N → Si intramolecular coordination. X-ray and NMR analysis, together with MO calculations, suggest a very short N–Si bond in (**55**), with significant N^-–Si^+ character.[145]



(**54**) (**55**) (**56**)

Cationic iridium(III) metallacycles efficiently catalyse hydrosilylation of ald- and ket-imines, particularly with a non-coordinating counterion such as $^-B[C_6H_3\text{-}3,5\text{-}(CF_3)_2]_4$.[146]

N-Sulfonyl aldimines undergo asymmetric silylation at carbon; stereospecific carboxylation (catalysed by fluoride) gives α-amino acids (in *N*-sulfonyl protected form). A chiral copper/2°-diamine complex gives *ee*s up to >99% for the silylation. The overall process generates optically active α-amino acids from gaseous CO_2 (1 atm) and imines.[147] (*ee*)

A dynamic kinetic resolution strategy (DKR) has been used on a series of cyclic ketimines via an asymmetric organocatalysed hydrosilylation, but the methodology is hampered by imine tautomerization.[148] (*ee*)

Catalytic asymmetric access to α-silylated amines has been achieved by enantioselective addition of silicon nucleophiles to aldimines, using a preformed NHC–copper(I) complex as catalyst.[149] (*ee*)

DFT has been used to study the reaction of hexafluoroacetonimine with 2-methylbenzo[*d*][1,3,2]dioxaphosphin-4(4*H*)-one to give the '*P–C–N*' product (**56**) and the *P–N–C* isomer [where NH and $C(CF_3)_2$ moieties are reversed].[150]

An extensive review surveys the development of a one-step synthesis of 3-phosphonylated aminophosphonates from 1-azadienes (i.e. α,β-unsaturated imines) via tandem 1,4-/1,2-phosphite addition. The method has been extended to unsaturated imine functions inherent in aromatic sextets, such as quinolines, phenanthrolines, and naphthyridines. Reactions of other nitrogen functions such as oximes and hydrazones are also described.[151]

A bifunctional quinine-squaramide catalyses the addition of diphenylphosphite to *N*-Boc ketimines derived from isatins in yield/*ee* up to 98/98%.[152] (*ee*)

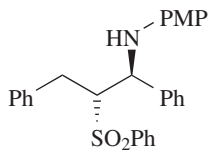
A cinchona-based squaramide catalyst delivers yields/*ee* up to 99/98% in a Strecker reaction of *N*-thiazolyl imines and trimethylsilyl cyanide.[153] (*ee*)

Silver(I) catalyses the reaction of 2-alkynylaryl aldimines with trimethylsilyl trifluoromethane to give 1-(trifluoromethyl)-1,2-dihydroquinolines.[154]

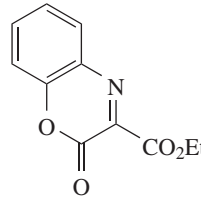
A complex of copper(I) iodide with TMEDA (tetramethylethylenediamine) catalyses the synthesis of 2*H*-indazoles from aryl azide and phenylimine. DFT calculations suggest that the azide is activated by a $Cu(\mu\text{-}H_2)Cu$(TMEDA) dimer.[155]

2-(Phenylsulfonyl)ethylbenzene, $PhCH_2CH_2SO_2Ph$, undergoes BuLi-promoted 1,2-addition to *N*-(*para*-methoxyphenyl)imines (e.g. Ph–CH=N–PMP) to give *anti*-β-aminosulfone (**57**) as the only diastereomer.[156] (*de*)

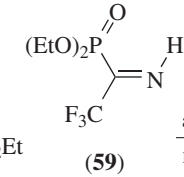
In a rare example of enantioselective addition to a non-aromatic ketimine, indole adds to a cyclic imine (**58**) in up to 99/99% yield/*ee* with catalysis by a buttressed BINOL-phosphoric acid.[157] (*ee*)



(**57**)

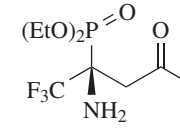


(**58**)



(**59**)

acetone/
L-proline



(**60**)

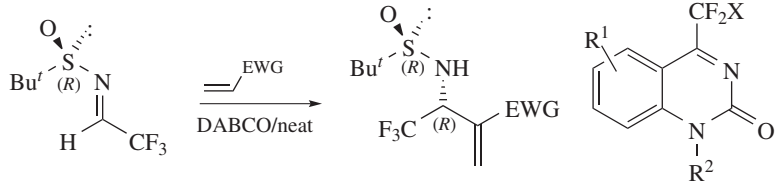
Sources of aminomethyl radicals such as *N*-(iodomethyl)succinimide have been used to effect radical aminomethylation of *N*-Boc aldimines. Xanthates can be used instead of iodides, but with a trade-off: the higher the stability of the precursor, the lower the nucleophilicity of the radical generated.[158]

O,*O*-Diethyl α-iminotrifluoroethyl-phosphonate (**59**) reacts with acetone at ambient temperature using L-proline as catalyst to give (*R*)-diethyl α-amino-α-trifluoromethyl-γ-oxobutyl-phosphonate (**60**) in 81/90% yield/*ee*; such α-amino-γ-keto-phosphonates allow easy access to a range of enantiopure heterocyclics via cyclocondensation.[159] (*ee*)

α-Oxygenated sulfinylimines undergo Honda–Reformatsky reaction with ethyl bromodifluoroacetate to give β,β-difluorosulfinylamines in up to 90% *de*.[160] (*de*)

Aza-Baylis–Hillman Reactions of Imines, and their Morita Variants

(*R*)-*N*-*t*-Butanesulfinyl-3,3,3-trifluoroacetaldimine (**61**) undergoes a very fast and highly diastereoselective aza-Baylis–Hillman reaction with various Michael acceptors. The product (**62**) is readily desulfinated, giving access to previously unknown enantiomerically pure α-methylene β-trifluoromethyl β-amino esters or acids (for EWG = CO_2R or CO_2H). The DABCO-catalysed aza-Baylis–Hillman process is much faster and more selective than the non-fluorinated counterpart.[161] (*ee*)



(**61**) (**62**) (**63**)

Allenoates, $H_2C{=}C{=}CH{-}CO_2R$, react with a range of cyclic ketimines (**63**) to give substituted allenoates via an aza-MBH (Morita–Baylis–Hillman) reaction when pyridine is used as catalyst, but with DABCO, [2 + 2] annulation gives azetidine derivatives, while triphenylphosphine catalyses [3 + 2] annulations to give dihydropyrroles. These diverse synthetic outcomes from the same reactants upon simple variation of the Lewis base are quite striking, but reflect the fact that Lewis base attack on the central carbon of the allenoate can generate a zwitterion in which the anion is α-localized, γ-localized, or a 1,3-dipole.[162]

DFT has been used to probe the origin of the enantioselectivity in the aza-MBH reaction of a nitroalkene and an *N*-tosylimine, using a thiourea/tertiary amine catalyst. The amine acts as a Lewis base to activate the alkene, while the imine is activated by an aryl stacking interaction, and the thiourea sets up a hydrogen-bonded network.[163] (*ee*)

An enantioselective aza-MBH reaction of acrylates with *N*-Boc ketimines derived from isatins has been reported: a chiral bifunctional phosphine-squaramide catalyses high yields and up to 91% *ee*, at 25 °C.[164] (*ee*)

A DFT investigation of an NHC-catalysed aza-MBH reaction – that of *N*-mesylbenzaldimine with cyclopentenone – reveals a substrate-catalysed process: two molecules of the benzaldimine can assist proton transfer.[165]

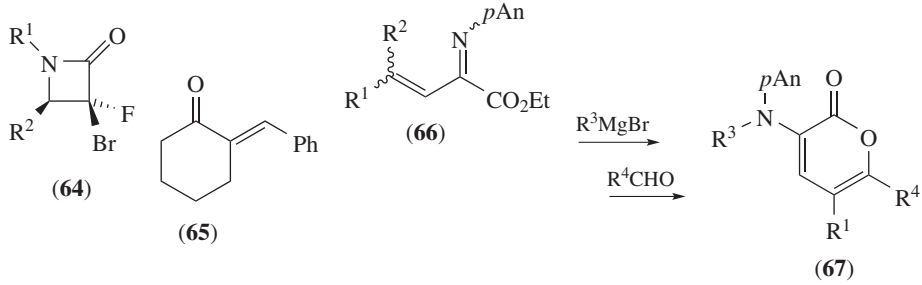
Staudinger and Aza-Henry Reactions, and Additions Involving Nitriles

2-Azetidinones have been prepared directly from an appropriate aldimine and substituted acetic acid, using DMSO 'solvent' with acetic anhydride present. The key intermediate is actually the 1:1 adduct formed by these reagents, that is, $[Me_2S^+–OCOMe]\ ^-OAc$, a reagent already known to dehydrate aldoximes and oxidize alcohols. In the present case, it dehydrates the substituted acetic acid to the corresponding ketene, which – under Et_3N catalysis – cyclizes with the imine as per the Staudinger mechanism. The optimum protocol was found to be DCM at ambient temperature with 1.5 equiv each of DMSO and Ac_2O, giving 2-azetidinone in yields of ~80–90% for a wide variety of aldimine types, and phenoxy-, methoxy-, or phthalimido-acetic acids. Aqueous workup then removes all by-products.[166] (*de*)

A rhodium(I)-catalysed oxygenative 2 + 2-cycloaddition of terminal alkynes and *N*-alkyl aldimines employs 4-methylpyridine-*N*-oxide and yields *β*-lactams with high *trans de*. While a ketene-like intermediate appears to be involved, a metalloketene is proposed rather than a free species.[167] (*de*)

Diastereo- and enantio-selective preparation of *gem*-bromofluoro-*β*-lactams (**64**) has been achieved using ethyl dibromofluoroacetate ($Br_2CF–CO_2Et$) and protected aldimines, $R^2CH{=}NR^1$ (R^1 = Bn, PMB). This imino-Reformatsky reaction requires diethylzinc and a chiral 1,2-amino alcohol organocatalyst.[168] (*de*) (*ee*)

Enones (e.g. **65**) have been prepared from benzaldehyde and *N*-Boc cyclohexanone imine in an aldol-like reaction. Performed at ambient temperature in DCM, a simple Brønsted acid $(EtO)_2PO_2H$ catalyses the process via imine-to-enamine tautomerization. The method is widely applicable, including aliphatic aldehdyes.[169]



β,*γ*-Alkenyl *α*-amino esters, in protected form (**66**), undergo a tandem N-alkylation/vinylogous aldol reaction to give 3-amino-2-pyrones (**67**, after an oxidative final step), with improved regioselectivity if R^2 = SMe.[170]

Isatin *N*-Boc ketimines undergo the aza-Henry reaction to give nitroamines in high yield and up to 99.99% *ee*, using a copper(II)–BOX complex.[171] (*de*) (*ee*)

Sodium bicarbonate promotes diastereoselective addition of nitromethane and nitroethane to *N*-*t*-butylsulfinyl imines.[172] (*de*)

Enals and ketimines derived from isatins undergo a chemo- and enantio-selective cross-aza-benzoin reaction using an NHC organocatalyst. The acyl anion reaction dominates, with the homoenolate route being minimized, and the enolate process is not observed.[173] (*ee*)

N-*t*-Butanesulfinimines react with activated isocyanides, EWG-CH_2–N≡C, with a striking chemoselectivity: *aryl* aldimines undergo C–C cross-coupling to give *β*-sulfinylamino isocyanides, whereas the *alkyl* substrates form *α*-sulfene-imino acetamides, R–CH(=N–S–*t*-Bu)CONH–CH_2-EWG.[174]

Imines have been reductively cross-coupled with nitriles to generate *α*-amino ketones or – depending on the quenching protocol – 1,2-diketones. The method employs low-valent titanium species generated *in situ* from Ti(O-^{i}Pr)$_4$ and cyclopentyl magnesium chloride, leading to a titanium-imine complex.[175]

Insertion Reactions of Imines

A rhodium(III) complex catalyses a three-component reaction of imines, alkynes, and aldehydes via sp^2 C–H activation.[176]

Rhodium(I) activates the 2′-hydrogen of 2-phenylpyridine for addition to cyclic sulfinylimines. The metal is proposed to pre-coordinate pyridine, and then insert into the *ortho* C–H bond, with this step being rate-determining, as evidenced by $k_H/k_D = 1.58$.[177]

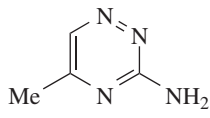
Methyl arenes (Ar–Me) undergo C–H activation in a manganese dioxide-mediated aroylation of *N*-chlorosulfoximines, $R^1R^2S(=O)=N–Cl$, to give N-aroylated sulfoximines, $R^1R^2S(=O)=N–CO–Ar$. Requiring 4 equiv of *t*-butyl hydroperoxide in refluxing acetonitrile for 1–2 days, yields are good; a wide range of *meta*- and *para*-substituents are tolerated in the aryl ring.[178]

Cycloadditions of Imines

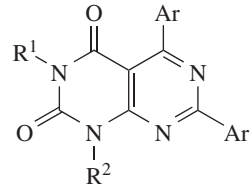
Cycloadditions of alkenes to azomethine ylides, to give pyrrolidine derivatives, have been reviewed: a wide range of organocatalysts work for these transformations.[179]

Methylglyoxal (MeCOCHO) reacts with aminoguanidine [$H_2N–C(=NH)–NH–NH_2$, also known as pimagedine] to give 5-methyl-3-amino-1,2,4-triazine (**68**). The first step, which is rate-determining, forms a guanylhydrazone-acetylcarbinol intermediate, which dehydrates, ring-closes, and further dehydrates.[180]

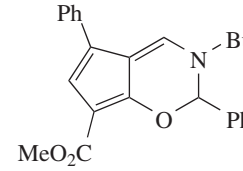
Pyrimido[4,5-*d*]pyrimidine-2,4-diones (**69**; R^1, R^2 = H/Me; Ar = Ph, 4-Me–C_6H_4, 4-$MeOC_6H_4$, thien-2-yl) have been prepared from 6-aminouracils and *N*,*N*′-bis(arylmethylidene)aryl methanes, ArCH=N–CH(Ar)–N=CHAr, using 10 mol% iodine as catalyst: the reactions take a few hours in DMSO at 100 °C. I_2 is proposed to coordinate a nitrogen of the bisimine, activating it for attack by the uracil. The second imine is extruded as arylaldehyde and ammonia as cyclization occurs, with I_2 a likely oxidant for aromatization of the new ring. Yields range from 50% to 75% (11 examples).[181]



(**68**)



(**69**)

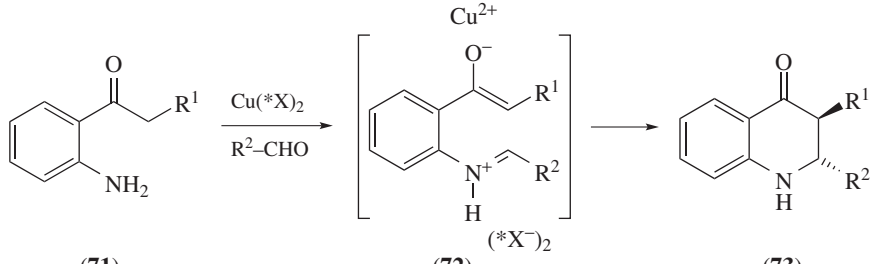


(**70**)

'Active' oxo compounds such as trifluoropyruvate or hexafluoroacetone undergo three-component domino cyclizations affording fluoralkylated (pyrrolo)quinazolines, via reaction with both amines of, for example, 2-(aminomethyl)aniline, via hemiaminal, Schiff base, and enamine intermediates.[182]

Azetine complexes, formed by the reaction of aldimines (e.g. PhCH=NBn) with non-heteroatom-stabilized chromium carbenes [$(OC)_5Cr{=}C(Ph)\text{-}C{\equiv}C\text{–}Ph$] react with alkynyl esters (e.g. $HC{\equiv}C\text{–}CO_2Me$) to give cyclopenta[*e*]-[1,3]oxazine (**70**). A DFT study of the mechanism indicates that the behaviour is borderline between Fischer- and Schrock-type carbenes, and thus difficult to predict when the substituents are varied.[183]

trans-2,3-Disubstituted dihydroquinolones (**73**) have been prepared in high yield/*de*/*ee* from *ortho*-amino carbonyl compounds (**71**) and aldehydes, via a [1,6]-aza-electrocyclization concept (**72**) with a chiral copper(II) catalyst, where the counterion ($*X^-$) is a buttressed BINOL-*N*-triflylphosphoramide (anion). The Lewis acidic method with *in situ* generation of an imine (as its iminium ion) followed immediately by cyclization overcomes problems associated with the synthesis and isolation of sensitive imines. Simple ketones are insufficiently reactive, but 1,3-dicarbonyls work with, for example, $R^1 = CONMe_2$. The aldehyde can be aliphatic.[184] (*de*) (*ee*)



(**71**) (**72**) (**73**)

The Povarov reaction has been studied in acetonitrile, where the domino process involves Lewis acid-catalysed aza-Diels–Alder reaction of an *N*-aryl imine with a nucleophilic ethylene (to give a formal 4 + 2 cycloadduct), followed by a stepwise 1,3-hydrogen shift to give a tetrahydroquinoline. DFT has been used to probe the *N*- and *E*-substituent effects in the imine.[185]

N-*t*-Butanesulfinyl imines undergo stereoselective 3 + 2-cycloaddition to arynes, giving cyclic sulfoximines with *de*/*ee* typically >98/98%.[186] (*de*) (*ee*)

A [3 + 2] annulation of ketimines with alkynes gives aminoindene derivatives via C–H activation by the iridium(I) dimer $[IrCl(cod)]_2$; NMR evidence indicates an Ir(III)–H species as an intermediate.[187]

N-Unsaturated imines undergo [4 + 2] annulation with vinyl azides to give highly functionalized pyridines and quinolines.[188]

Sulfamate-derived cyclic imines undergo a mild [3 + 2] annulation with isocyanacetate, giving sulfamate-fused 2-imidazolines in good yield and *de*.[189] (*de*)

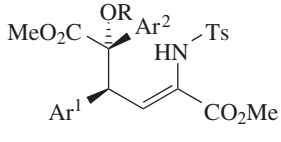
A cinchona alkaloid-catalysed 4 + 2-cyclocondensation of α,β-unsaturated acyl chlorides with imines gives dihydropyridinones in good yield and *ee*.[190] (*ee*)

A new variant on the inverse-electron-demand imino-Diels–Alder reaction fuses electron-poor chromone dienes with cyclic imines, producing aza-heterocycles in good *ee*, using a zinc/BINOL catalytic system.[191] (*ee*)

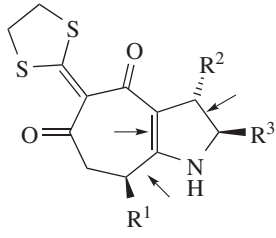
α-Heteroarylpyrrolidines have been prepared in very high *de*/*ee* via 1,3-dipolar cycloaddition between α-silylimines (e.g. 2-Py–CH=N–CH_2–TMS) and activated olefins, using copper(I) liganded with Walphos, a chiral ferrocenyl diphosphine.[192] (*de*) (*ee*)

Miscellaneous Reactions of Imines

The 1,4-conjugate addition of β,γ-unsaturated aromatic *N*-sulfonylimine methyl esters [Ar^1–CH=CH–C(=NTs)–CO_2Me] to aromatic diazoesters [Ar^2–C(=N_2)–CO_2Me] gives regioselective formation of α-hydroxy-δ-amino esters (**74**) in the presence of an alcohol (ROH). This multi-component reaction is catalysed by rhodium, effected at ambient temperature, shows high *de*, and provides highly functionalized products (**74**) suitable for further elaboration. It exploits the oxonium ylides trapping process.[193] (*de*)



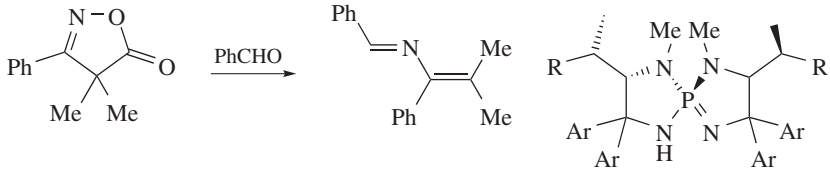
(**74**)



(**75**)

Highly functionalized cyclohepta[*b*]pyrroles (e.g. **75**) have been prepared from a dialkenyl ketene dithioacetal and an imine-nitrile (R^3–CH=N–CH_2–C≡N) via a tandem Michael addition/imine isomerization/intramolecular 3 + 2-cycloaddition. The mild, transition-metal-free transformation generates two rings and three C–C bonds (arrowed), exploiting the potential of the imine for polarity reversal.[194] (*ee*)

Palladium catalyses an aza-Wittig-type decarboxylative condensation of isoxazolone (**76**) with benzaldehyde to give 2-azabuta-1,3-dienes (**77**) – or pyrroles. Catalysed by triphenylphosphine, the reaction is proposed to proceed via a palladium–nitrene complex and an iminophosphorane.[195]



(**76**) (**77**) (**78**)

cis-Alkynyl aziridines can be prepared by the reaction of alkynyl imines with diazo compounds, using a chiral boroxinate catalyst. Surprisingly, different enantiomers are obtained depending on whether a diazo-ester or a diazo-acetamide is used, *without* changing the enantiomer of the catalyst. Calculations have identified the origin of this difference: the diazo-ester reacts with the (*E*)-imine, while the diazo-acetamide reacts with the (*Z*).[196a] (*de*) (*ee*)

N-Galactosyl aziridines have been prepared from tetrakis(*O*-pivaloyl)-β-D-galactosyl-imines with diazocarbonyls such as N_2CHCO_2Et or N_2CHCOR. Catalysed by boron trifluoride (to generate the carbene), yields/*de*/*ee* up to 88/>98/>99% were achieved. The sugar derivatives are remarkably stable, but *para*-toluene thiol and BF_3 cleave the galactose moiety off, giving enantiomerically pure β-*S*-tolylphenylalanine derivatives.[196b] (*de*) (*ee*)

A family of chiral *P*-spiro triaminoiminophosphoranes (**78**) base-catalyse Payne oxidation of *N*-sulfonyl aldimines to give *N*-sulfonyl oxaziridines, giving yields/*ee* up to 99/99% in toluene at 0 °C, using hydrogen peroxide and trichloracetonitrile for *in situ* generation of the Payne peroxyimidate oxidant $Cl_3C(=NH)–OO^-$. α-Chiral imines can also be kinetically resolved. Mechanistic studies by ^1H NMR identified that two molecules of *N*-sulfonylimine could form a dimeric peroxide under the reaction conditions. The substrate scope of the reaction includes imines derived from aromatic aldehydes (including *ortho*-substituted), cinnamaldehyde, and aliphatic aldehydes, including *t*-BuCHO.[197] (*de*) (*ee*)

An imino ene-type reaction of *N*-sulfonylaldimines proceeds smoothly at −78 °C under acetic acid catalysis, with high *de*; the sulfonyl amino-enamine product can be hydrolysed to give useful β-amino ketones. Subsequent reduction with sodium cyanoborohydride yields *N*-sulfonyl-1,3-diamines, again diastereoselectively.[198] (*de*)

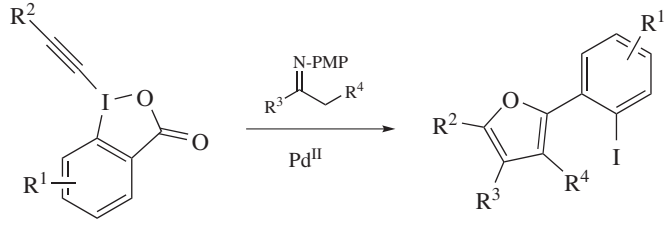
Bisoxindoles with two vicinal quaternary centres have been prepared with yields/*de*/*ee* up to 99/>98/99% from oxindoles and isatin-derived *N*-Boc imines, using a chiral Lewis base catalyst.[199] (*de*) (*ee*)

Enolates of *N*-alkyl indolin-2-ones react with (*R*)- or (*S*)-*N*-*t*-butylsulfinyl-3,3,3-trifluoroacetaldimine, *t*-Bu–*S(=O)–N=$CHCF_3$, to give oxindole derivatives which can afford access to the $F_3C–CH(NH_2)$-pharmacophore. Good yields and *de*s are reported using lithium diisopropylamide (LDA) at −78 °C.[200] (*de*)

Imine–imine cross-coupling has been used to prepare 1,2-diamines, and – with a chiral guanidine catalyst – high *ee*s are obtained. An umpolung strategy is employed: one imine bears a 9-fluorenyl moiety on its nitrogen, which acts as a nucleophile. The fluorenyl may be subsequently removed.[201] (*ee*)

In an unusual use of a hypervalent iodine species, alkynylbenziodoxolones (**79**) condense with *para*-methoxyphenyl-protected imines to give a multi-substituted furan (**80**)

plus a PMP-formamide by-product. The retention of the iodine (admittedly now monovalent) provides a versatile handle for further elaboration. Isotope-labelling studies have been used to probe the bond reorganization occurring: both the alkyne and carboxylate functions are cleaved in the process. ^{13}C- and ^{18}O-labelling of the reactants established that the alkyne carbon attached to iodine in (**79**) ends up as the formyl carbon of the formamide by-product.[202]



(**79**) (**80**)

Recyclable copper(II)–Schiff base complexes of chiral amino alcohols catalyse Friedel–Crafts alkylation of indole with aryl aldimines in yields/*ee* up to 98/97%. Ligand structure, solvent, and metal source have been varied, and a kinetic study indicated that the process was first order in catalyst and nucleophile, but not dependent on the initial concentration of the aldimine substrate.[203] (*ee*)

(*Z*)-Selective synthesis of α-alkylidene β-oxo amides has been achieved by palladium-catalysed carbonylation of α-chloro ketones in the presence of aromatic imines. For example, chloroacetone and benzylidene aniline react with CO (400 psi/Et_3N/THF/110 °C) to give (*Z*)-Ph–CH=C(Ac)–CONHPh in 81% yield in 6 h, using $Pd(PPh_3)_4$ as catalyst. *N*-Alkyl imines are well tolerated. An acyl-β-lactam route is proposed.[204]

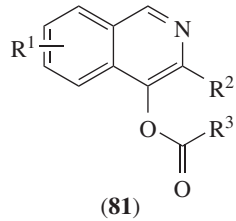
Pyrolysis of *N*-phenylimine derivatives in the gas phase has been studied by a range of theoretical methods, and compared with experimental rate data.[205]

Oximes, Oxime Ethers, and Oxime Esters

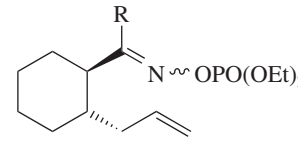
Isomeric bicyclo[2.2.1]heptane-7- and -8-oximes and their corresponding *C*-nitroso derivatives have been prepared in high yields, diastereospecifically. Their interconversion has been followed kinetically. The compounds are key intermediates for synthesis of carbanucleosides.[206] (*ee*)

While the formation of hydrazones or oximes can be slow at neutral pH, a kinetic screen has identified fast α-nucleophiles that react rapidly with appropriate aldehydes. Reagents such as alkyl hydrazines ($RNHNH_2$) or alkyl aminooxy compounds ($RONH_2$) can serve, reacting rapidly with, for example, 2-formylpyridine. For the hydrazone formation, $EtNHNH_2$ exhibits a half-life with this aldehyde of ~1 h, while its β-ammonium analogue, $Me_2NH^+–CH_2CH_2NHNH_2$, reacts in a few minutes.[207]

2-Alkynylbenzaldoximes react with aldehydes (or 1° alcohols) to give 4-carboxylated isoquinolines (**81**), using Ag(I)/Cu(I) co-catalysis in one pot.[208]



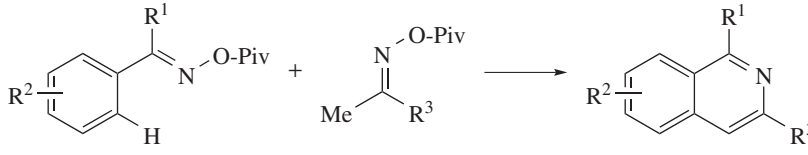
(**81**)



(**82**)

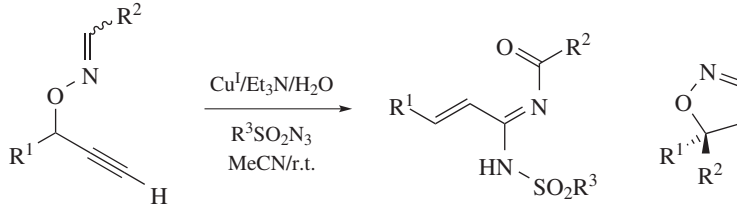
An attempt to prepare an aza-heterocycle via the amino-Heck reaction of *trans*-2-allylcyclohexylphosphinoyloxime (**82**) resulted in the isolation of functionalized bicyclo[4.3.0]nonenes.[209]

In an unusual Pd-catalysed aromatic C–H activation, two types of ketone-derived oxime ethers (**83** and **84**; $R^3 = Me$) undergo C(sp^2)–C(sp^3) coupling to regioselectively produce isoquinolines (**85**).[210]



(**83**) (**84**) (**85**)

Copper(I) catalyses a cascade reaction of *O*-propargylic aldoximes (**1**) with sulfonyl azides to give α,β-unsaturated *N*-acylamidines (**2**). Based on labelling experiments with D_2O and $H_2{}^{18}O$ and other considerations, the mechanism is proposed to involve formation of a copper acetylide, leading, via cycloaddition, to the azide on to *in situ* formation of a ketenimine, intramolecular attack of the oxime, and subsequent N–O cleavage.[211]



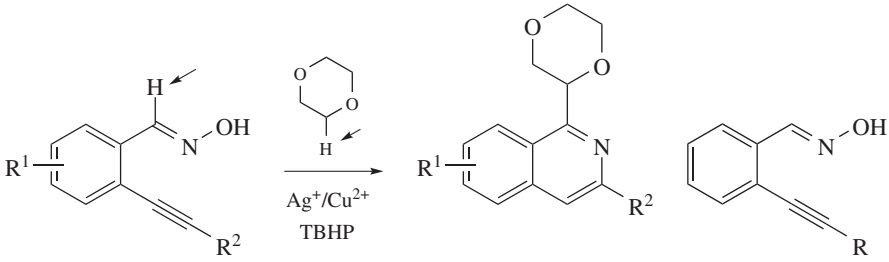
(**86**) (**87**) (**88**)

Ketoximes are known to react with enals, via organocatalytic iminium catalysis, to give oxime ether-aldehydes, $R^3R^4C{=}N{-}O{-}C(R^1R^2){-}CH_2{-}CHO$, which can undergo intramolecular oxime transfer to give isoxazolines (**88**), with expulsion of the original ketone (R^1COR^2), under general acid catalysis. The latter reaction has now been studied by DFT (using a polarizable continuum model), which indicates that the water-addition and water-expulsion steps have the highest barriers. The calculations considered all relevant diastereomers of the intermediates.[212]

2-Arylpyrroles have been accessed by copper-catalysed 5-*endo*-trig cyclization of ketoxime carboxylates.[213]

A short review (72 references) describes rearrangement of oximes and hydroxylamines with aluminium reductants, especially diisobutylaluminium hydride (DIBALH), lithium aluminium hydride (LAH), and $AlHCl_2$.[214]

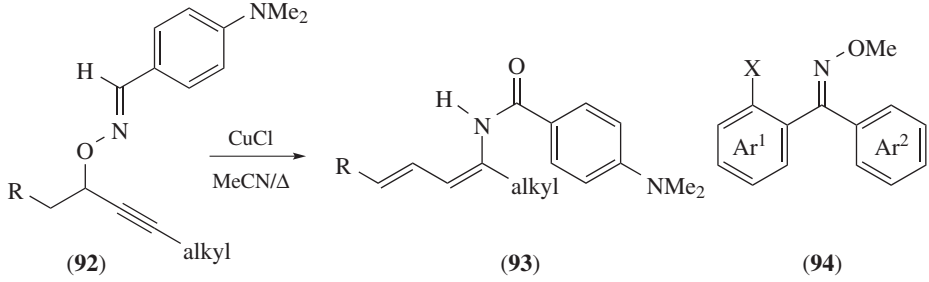
ortho-Alkynylbenzaldoximes (**89**) undergo a cross-dehydrogenative coupling with cyclic ethers such as dioxane (doubling as solvent) to give isoquinolines (**90**) using *t*-butyl hydroperoxide as oxidant at 100 °C, potassium phosphate as base, and co-catalysis by $AgOTf/Cu(OAc)_2$, each at 10 mol%. The reaction involves dual C–H activation (sp^2 and sp^3, arrowed). The silver cation should activate the alkyne for intramolecular attack to give the isoquinoline-*N*-oxide, followed by cupration, attack of dioxan-2-yl radical (generated by *t*-butoxy radical), and copper extrusion. The radical character of the mechanism was confirmed by suppression with TEMPO, (2,2,2,6-tetramethylpiperidin-1-yl)oxyl.[215]



(**89**) (**90**) (**91**)

ortho-Alkynyloximes (e.g. **91**; R = aryl or alkyl) undergo $AuCl_3$-catalysed intramolecular cyclization to give 3-(R-substituted)isoquinolines; the method has been generalized to a number of other heterocyclic syntheses.[216]

C-Electron-rich *O*-propargylic aldoximes bearing an alkyl group at the alkyne (**92**) are rearranged to amidodienes (**93**) in the presence of copper(I): 2,3-rearrangement is proposed to give *N*-allenylnitrone, with isomerization following to give amide, via an oxaziridine.[217]



(**92**) (**93**) (**94**)

Single-isomer diaryl ketoxime ethers, $Ar^1C(Ar^2)$=NOMe, have been prepared from the aldoxime ether, Ar^1CH=NOMe, via Suzuki coupling with Ar^2Y [$Y = B(OH_2)$ or

BF_3K]. With such single isomers in hand, palladium-catalysed *ortho*-monohalogenation was then carried out to see (i) whether Pd-coordination weakens the double bond sufficiently to isomerize it, and (ii) whether the oxygen directs halogenations to the aromatic ring *trans* to it. Using an *N*-halosuccinimide (Br or I) and $Pd(OAc)_2$ as catalyst in refluxing dichloroethane, the answers are unambiguously in the negative for (i) and in the affirmative for (ii): the *trans*-monohalo product (**94**) is typically the major product, with modest di-*ortho*-halogenation. (The over-product is probably disfavoured by the first halogen preventing ring-oxime coplanarity.) Electron-withdrawing groups in either ring slow the reaction and also suppress the dihalogenation. A proposed palladacycle intermediate has been prepared and characterized by X-ray crystallography. Under the reaction conditions, it gave the same product.[218]

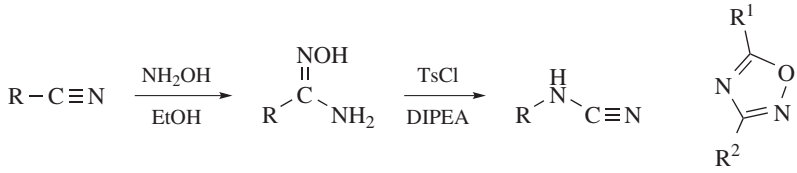
Beckmann rearrangement of acetophenone oxime and its 4-hydroxy derivative to the corresponding amides has been studied using trifluoroacetic acid as catalyst, with and without a solvent. While acid catalysis is undoubtedly involved, a more specific route has been identified: the highly reactive trifluoroacetylated amide is the effective catalyst.[219]

A Keggin-type dodecatungstophosphoric acid (DTPA, $H_3PW_{12}O_{40}$) has been employed as a cheap, moisture-tolerant, recoverable, and reusable Brønsted acid catalyst for eco-friendly Beckmann rearrangement of ketoximes; conditions are acetonitrile reflux with 0.05 mol% loading.[220]

A regioselective synthesis of *N*-aryl amides from the reaction of aryl halides with aryl aldoximes employs a simple catalyst system: *N*,*N*′-dimethylethylenediamine/$CuSO_4$/K_2CO_3. An inert atmosphere is not required, and regioselectivity problems often found with the Beckmann rearrangement are avoided.[221]

Copper catalyses an aza-Heck-like cyclization of oxime esters to give cycloalkenes, apparently via the generation and cyclization of a species with iminyl radical character. The copper protocol is more sustainable than Pd-based methods.[222]

N-Substituted cyanamides (**95**) have been prepared from nitriles (**96**) via conversion to amidoximes (**97**) and subsequent Tiemann rearrangement using tosyl (or *ortho*-nosyl) chloride and diisopropylethylamine (DIPEA). Where the amidoxime is *N*-substituted, alternative products such as ureas or carbodiimides can be prepared.[223]



(**96**) (**97**) (**95**) (**98**)

Nitriles or cyanamides, R^1–C≡N, couple with amidoximes R^2–C(=NOH)–NH_2 to give 1,2,4-oxadiazoles (**98**), using sequential Zn^{2+}/H^+-catalysis, via a zinc imidate ester.[224]

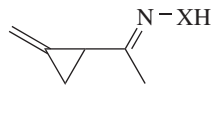
A series of *S*-arylthiooximes, *para*-R^3–C_6H_4–C(=O)–S–N=CHR^1R^2 (R^1 = H, Me; R^2 = Ph, *t*-Bu, and others), have been prepared from *S*-aroylthiohydroxylamines and aldehydes or ketones (R^1COR^2). Cysteine or water can degrade them, with release

of hydrogen sulfide. Kinetics of the cysteine-triggered process have been followed electrochemically (for fast reactions) or by UV–visible spectroscopy (for R^1, $R^2 = H$, Ph) for a wide range of R^3 substituents, giving a Hammett ρ value of 1.05. Half-lives at ambient temperature at pH 7.4 varied between 8 min ($R^3 = C{\equiv}N$) and 82 min ($R^3 = OMe$). This new functional group class holds out promise for H_2S-releasing therapeutics.[225]

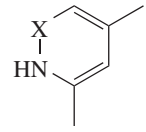
Stoichiometric copper(II) activates the 2′-hydrogen of 2-phenylpyridine to set up N-arylation of sulfoximines, $R^1R^2S(=O)=NH$, via oxidative C–N cross-coupling.[226] A similar effect with rhodium(I) is described under the section titled 'Insertion Reactions of Imines'.

Hydrazones and Related Species

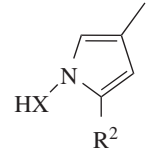
Rearrangement of methylenecyclopropyl hydrazones (e.g. **99a**) and oximes (**99b**) have been studied by ^{13}C NMR and DFT. Reports of diazadiene and oxazadiene products (**100**) have now been reassigned as pyrroles (**101**).[227]



(**99a**; X = NTs, **99b**; X = O)



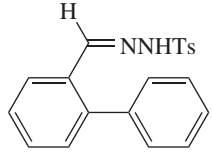
(**100**)



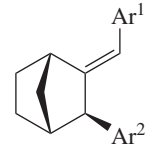
(**101**)

A computational study has investigated the copper(I)-catalysed olefination of phenylhydrazone, $Ph–CH=NNH_2$, in carbon tetrachloride, to give 1,1-dichloro-2-phenylethene, nitrogen, and HCl.[228]

Biphenyls with an *ortho*-tosylhydrazone group (**102**) have been cross-coupled with aromatic terminal alkynes to give phenanthrenes. Catalysed by $CuBr_2$, the reaction proceeds via an allene intermediate. On reversing functional groups, *ortho*-alkynylbiphenyls react with ArCH=NNHTs, catalysed by CuI, to give the same phenanthrenes, and this version can also be done from aldehyde and tosyl hydrazine in one pot.[229]



(**102**)



(**103**)

Norbornene has been conveniently doubly functionalized (**103**) via a palladium-catalysed three-component reaction of an *N*-tosylhydrazone, $Ar^1CH=NNHTs$, and an

aryl iodide, Ar^2I, proceeding via a Heck-type reaction followed by an alkyl palladium migratory insertion. Good yields and *de*s are reported using toluene/80 °C/K_2CO_3.[230] (de)

Tosylhydrazones of cyclic ketones undergo a Pd-catalysed autotandem process with 2,2′-dibromobiphenyls to give a range of spirocycles, with both nitrogens extruded.[231]

DFT has been used to probe the mechanism of palladium(0)-catalysed coupling of propargylic carbonates, $R^1O_2CO–CH(R^2)–C{\equiv}C–R^3$, with *N*-tosylhydrazones [e.g. PhC(Me)=NNTs]. Allenylpalladium forms through C–O bond cleavage of propargyl carbonate, setting up both decarboxylation and ligand exchange processes. Several further steps are then explored, and their likelihood under different conditions considered, covering products with and without nitrogen, such as $R^3–C{\equiv}C–CH(R^2)–N(Ts)–N{=}C(Me)–Ph$ and $R^2CH{=}C{=}C(R^3)–C(Ph){=}CH_2$.[232]

Sparteine has been employed as a chiral ligand to set up intermolecular chirality transfer, allowing asymmetric alkylation of dimethylhydrazones, $R^2CH_2–C(R^1){=}N–NMe_2$, to yield ketones, $R^1–CO–{}^*CHR^2R^3$, after hydrazone cleavage (R^3 derived from $R^3–X$). While the *ee*s are modest (up to 66%), the method has not yet been optimized for the chiral diamine.[233] (ee)

The mechanism of the triflimide-catalysed [3,3]-sigmatropic rearrangement of *N*-allylhydrazones has been studied by DFT. The insights gained helped the design of electron-deficient substrates that are more reactive.[234]

Activated alkenes such as $H_2C{=}CH–CO_2Et$ can be cross-coupled with *N*-tosylhydrazones [e.g. Ph–C(=NNHTs)–Me] to give chain-extended alkene derivatives [e.g. $H_2C–C(Ph)–CH_2–CH_2–CO_2Et$] with extrusion of nitrogen, using palladium(II) acetate in water. A DFT study has examined the roles of water and acetate.[235]

Both aromatic and aliphatic acyl hydrazones, $R^1CH{=}N–NHCOR^2$, react directly with allylboronic acids to give homoallylic amines *syn*-selectively, the opposite stereochemistry to that found for allylboration of imines. Chelation of the boron by the nitrogen and oxygen of the acyl hydrazone is proposed to explain the *syn*-selection. Acyl hydrazones are put forward as having more synthetic utility than imines, as they are more stable towards hydrolysis.[236] (ee)

Hydrazines catalyse carbonyl-olefin metathesis reactions, and DFT has been used to identify the ease of distortion of cyclopropene as the accelerative factor in cycloadditions, whereas strain release controls cycloreversions.[237] A similar DFT study has investigated catalysis of such reactions by (*E*/*Z*)-hydrazonium ions.[238]

Molecular iodine catalyses the sulfenylation of pyrazolones with aryl sulfonyl hydrazides, $Ar–S(=O)_2–NHNH_2$, in the presence of *para*-toluenesulfonic acid.[239]

Nitrones and Related Species

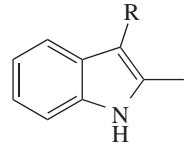
A series of α-phenyl-*N*-*t*-butyl nitrones bearing substituents on the *t*-butyl group (both α′- and β′-) have been synthesized. Cyclic voltammetry indicates that the substituent effect is more pronounced for oxidation than reduction. The rates of reaction with radicals such as $O_2^{\cdot-}$ and $HO_2\cdot$ have been measured by EPR spectroscopy, and the reactivities also were analysed by DFT. The reaction rates show reasonable correlation with the charge density on the nitronyl carbon, indicating that superoxide addition is nucleophilic in nature.[240]

A DFT investigation of the *E*/*Z*-isomerization of nitrones has ruled out several mechanisms – unimolecular torsional, isomerization through oxaziridines, concerted bimolecular, zwitterionic routes, and so on – as the energy barriers are too high. This leaves a bimolecular diradical mechanism involving C–O or C–C coupling, and the calculations favour the latter, via dimerization/de-dimerization, with a barrier of 29.9 kcal mol^{-1} for the rate-limiting step in the case of *C*-methyl nitrones.[241]

Nitrones have been used to access monofluorinated olefins: α-fluoroalkenoates such as $BrFCH–CO_2Et$ react with alkyl-aryl nitrones such as $RCH=N^+(–O^–)Ph$ to give (*E*)-α-fluoroalkenoates $RCH=CF–CO_2Et$. DFT studies help highlight the origins of the high chemo- and stereo-selectivity.[242]

Nitrones add carbamoyl anions derived from *N,N*-disubstituted formamides (using LDA) to give α-(*N*-hydroxy)amino amides, $(R^1)_2N–CO–CHR^2–N(OH)–R^3$. A diastereo-selective version has also been developed, using nitrones derived from *t*-leucine.[243]

2,3-Disubstituted indoles (**104**) have been prepared from *N*-hydroxyaniline and allenes, $H_2C=C=CHR$, using Au(I) catalysis, but benzaldehyde is also required. It appears that *N*-hydroxyaniline is not sufficiently nucleophilic on its own, but reaction with benzaldehyde gives nitrone, $PhCH=N^+(–O^–)–Ph$, which attacks the gold–π-allene complex. A control experiment with authentic nitrone works. Water is also essential, presumably to hydrolyse key iminium intermediates.[244]



(**104**)

Zinc acetylides – generated from terminal alkynes, Hunig's base, and 20 mol% zinc bromide – attack phenyl nitrones [e.g. $PhCH=N^+(–O^–)–Ph$] in a process activated by trimethylsilyl triflate. The products, R–C≡C–CH(Ph)–N(Ph)–OTMS, are easily deprotected with aqueous acid to give the *N*-hydroxyl propargylamine. The role of trimethylsilyl triflate – as well as providing the silyl group in the product – is also catalytic: it converts the nitrone into a cationic electrophile, $PhCH=N^+(Ph)–OTMS$. Evidence for this route is provided by control experiments: while no reaction is found without TMS triflate, *zinc* triflate does allow the reaction to occur, but not to the same extent as the $ZnBr_2$/TMSOTf combination.[245]

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

Reviews of Aldols, and General Reviews of Asymmetric Catalysis

The use of scanning probe microscopic methods to reveal catalytic reaction processes on surfaces during heterogenous catalysis has been reviewed (63 references). Examples using STM (scanning tunnelling microscopy), NC-AFM (non-contact atomic force microscopy), and IETS (inelastic electron tunnelling spectroscopy) are described.[246]

Applications of hydrogen-bonding aminocatalysis in asymmetric synthesis have been reviewed for cases of proline-derived systems: they have been categorized by the nature of the hydrogen-bonding scaffold and by the mode of recognition.[247] (de) (ee)

Reactivity and stereoselectivity effects in aminocatalysis have been reviewed, covering aldol, Mannich, Michael, α-amination, and aminoxylation reactions.[248] (de) (ee)

Asymmetric BINOL-phosphate-derived Brønsted acid and metal catalysis has been comprehensively reviewed (521 references), covering its history and classification by activation mode, and topics such as Brønsted acidity, hydrogen bonding, ion pairing, and metal phosphates.[249]

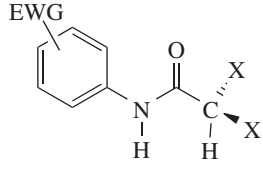
Efforts to achieve synergies between enamine and transition-metal catalysis have been reviewed (83 references), covering the first decade of this new field.[250] (de) (ee)

The spontaneous mirror symmetry-breaking seen in aldol reaction of 4-nitrobenzaldehyde in acetone (solution), in which a detectable initial *ee* is seen in ~50% of reactions with the nominal absence of any enantioselective catalyst, has been studied in more detail. The reaction was found to be not autocatalytic in the aldol product, but isolation and characterization of a double-aldol adduct suggests a network that involves both indirect autocatalysis and indirect mutual inhibition between enantiomers.[251] (ee)

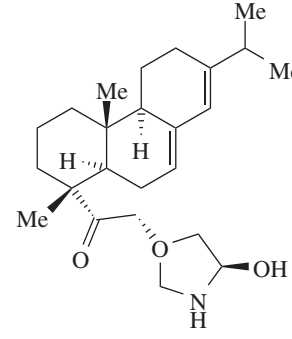
Catalytic asymmetric aldol reactions in aqueous media has been the subject of a short review (51 references),[252a] updating a previous survey by the same authors.[252b] (de) (ee)

Developments in organocatalytic additions of nitroalkyls and sulfones to C=X bonds have been reviewed.[253] (de) (ee)

α,α-Dihaloacetanilides have been developed as potential hydrogen-bonding organocatalysts, which could activate C=O bonds through NH and CH donor groups, via an appropriate conformation (**105**). X-ray structure analysis and molecular modelling have been used to characterize them, and they have been tested in the ring-opening polymerization of lactide.[254]



(**105**; X = Cl, Br)



(**106**)

Asymmetric Aldols Catalysed by Proline and its Derivatives

The role of enamine intermediates – both neutral and anionic – in the proline-catalysed aldol reaction has been studied by a range of calculation types and a comparison

of the aldehyde as electrophile with benzhydrylium cation. Solvation effects are incorporated.[255] (de) (ee)

The L-proline-catalysed model aldol reaction of cyclohexanone with *para*-nitrobenzaldehyde is efficiently co-catalysed by a simple isothiouronium salt $Bu–S^+=C(NH_2)_2\ I^-$: placing the chemicals in a fridge without stirring or solvent gives yield/*de*/*ee* of 93/86/97% in 96 h. It is proposed that the normal L-proline mechanism operates, enhanced by the co-catalyst, forming two N–H hydrogen bonds to the proline's oxygens.[256] (de) (ee)

Equilibration between a carbonyl compound and its analogues is a topic of crucial importance in organocatalysis, dynamic covalent chemistry, and other areas. Using 'best anhydrous' conditions, such interconversion has been probed for in the case of bicyclic oxazolidinones derived from proline and a typical representative aldehyde (pivaldehyde) or ketone (cyclohexanone), using NMR in d_6-DMSO and d_6-benzene, and ^{18}O-labelled cyclohexanone. Exchange with iminium ions has also been considered, or metathesis through 1,3-oxazetidinium ions. The possible roles of adventitious or added water or other likely impurities are also considered.[257]

The problem of the formation of stable but unwanted imidazolidinones in organic solvents from prolinamides and araldehydes, when the former are catalysing aldols of the latter, is suppressed in aqueous media. Novel prolinamides have been used in this way in brine solution, giving yields/*de*/*ee* up to 99/95/95%.[258] (de) (ee)

A bifunctional prolinamide catalyst including a *trans*-1,2-cyclohexanediamine gives high yields and *de*/*ee* up to 98/99% in aldol reactions, including those with O/N/S-containing heterocyclic ketones. The catalyst is recyclable and scales well.[259] (de) (ee)

Phthalimido-prolinamide catalyses direct aldols in up to 95% yield and 96% *ee* without solvent or additives, although trace addition of water does accelerate the process.[260] (ee)

Calix[4]arenes with prolinamides tethered to the 1- and 3-subunits give mixed performance in standard cyclohexanone aldols with aromatic aldehydes in water: yields of up to 95% and *ee* up to 90% were obtained, but diastereoselectivities only reached 30%.[261] (de) (ee)

New hybrid ferrocene-prolinamides catalyse asymmetric aldols in water, giving yields/*de*/*ee* up to 98/86/94%.[262] (de) (ee)

A diarylprolinol catalyses aldol reaction of formaldehyde with various aldehydes in up to 98% *ee*.[263] (ee)

Esterifying the alcohol of L-*trans*-4-hydroxy-proline with abietic acid produces a catalyst (**106**) which – in the presence of a suitable acid additive – produces superior performance in direct aldols: the reactions can be carried out in water and are very fast, and isolated yields/*anti*-*de*/*ee* results are up to 99/94/>99.9%, with only 1 mol% loading. In comparison with previous derivatives of this proline, the abietic acid residue appears to provide a near-ideal combination of hydrophobic shielding and steric environment.[264] (de) (ee)

Asymmetric Aldols Catalysed by Other Amino Acids and their Derivatives

Enantiopure β-hydroxy quaternary amino acids $Ar^*CH(OH)–C(NH_2)(Me)–CO_2H$ have been prepared starting from L-alanine using an aldol reaction with aromatic aldehydes, which exploits memory of chirality.[265] (de) (ee)

DFT has been used to probe the origin of the chemo- and stereo-selectivities in cross-aldol reactions of two enolizable aldehydes of different electronic character,

using isoleucine as organocatalyst. Examining enamine formation, the results suggest that a primary amino acid such as isoleucine can effectively discriminate between an electron-rich aldehyde as enamine component, and an electron-poor one as carbonyl component, *and* that it can do this better than proline. The authors also address the interesting behaviour of α-branched aldehydes.[266] (*de*) (*ee*)

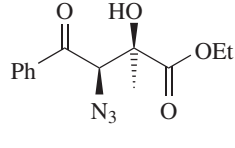
Three series of cinchonidine-amino acids have been prepared and tested in a benchmark aldol, where they performed well, but they were less successful as catalysts of Biginelli, Michael, or hydrosilylation reactions.[267] (*ee*)

Mono- and dipeptides based on the (3*S*)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid skeleton (THIQA) have been tested as catalysts of aldols: they give higher *ee* than proline analogues, albeit with lower yields.[268] (*de*)

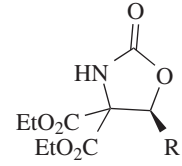
A series of tripeptides, Pro-Phe-AA-O-*t*-Bu, have been prepared and tested in a standard aldol: excellent results have been obtained for some in toluene at −20 °C, and others in H_2O/NaBr at −10 °C, with yields/*de*/*ee* up to 99/96/99%. The proline residue is presumed to perform its usual catalysis, with the amide N–H's providing further activation and selectivity via hydrogen bonding. The nature of the *C*-terminal amino acid determines the applicability to organic or aqueous medium.[269] (*de*) (*ee*)

Asymmetric Aldols Catalysed by Other Organocatalysts

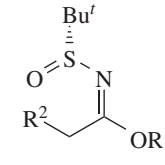
Ethyl 4-aryl-3-azido-2-hydroxy-2-methyl-4-oxobutanoates have been prepared, mainly as their *syn*-diastereomers (e.g. **107**) by aldol addition of α-azido ketones to ethyl pyruvate, using a bifunctional cinchona alkaloid-thiourea chiral catalyst: best *de*/*ee* obtained was 90/82%.[270] (*de*) (*ee*)



(**107**)



(**108**)



(**109**)

A quinidine-urea bifunctional catalyst enolizes 3-(acetyl)-2*H*-chromen-2-ones while simultaneously activating isatins by hydrogen bonding, promoting the asymmetric aldol between them.[271] (*ee*)

Chiral 4-carboxyl oxazolidinones (**108**) – structurally related to β-hydroxy α-amino acids and convertible to them – have been prepared via aldol reaction of an isocyanatomalonate diester $(EtO_2C)_2$–CH–N=C=O and an aldehyde (RCHO). Using a chiral β-amino thiourea catalyst, *ee* in the range 65–95% was achieved in toluene at −60 °C, with yields from 66% to 100%.[272] (*ee*)

N-Sulfinylimidates (**109**) have been employed as chiral amide equivalents in an asymmetric aldolization. Using triethylamine as base, the inherent reversibility of the reaction is problematic, but supplementation with 2 equiv of $TiCl_2(O\text{-}^iPr)_2$ suppresses this, setting up yields/*de* up to 98/96%.[273] (*de*)

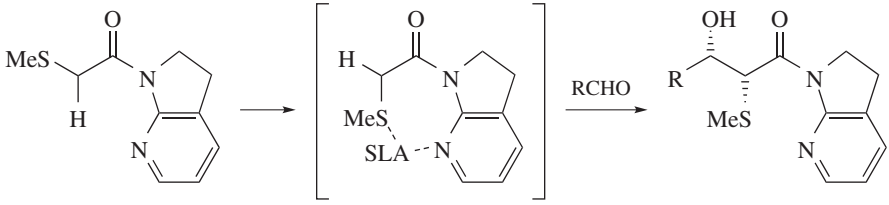
A chiral BINAP-3°/1°-diamine catalyses aldols of enones with trifluoroacetophenone with yields/*ee* up to 93/99%.[274] (*ee*)

A range of phase-transfer reactions, which usually require basic additives, have been carried out under neutral conditions using quaternary ammonium salts in water/toluene media. Examples include direct aldols of α-substituted nitroacetates with formaldehyde, as well as conjugate additions to oxindoles, and of α-substituted nitroacetates to maleimides, and amination of nitroalkenes. Enantioselective versions using chiral ammoniums salts have also been reported, and the method has been extended to quaternary phosphoniums.[275] (*ee*)

Quantum mechanics/molecular mechanics (QM/MM) Monte Carlo methods and free-energy perturbation theory have been used to identify the origin of enhanced rates and *ee*s for two catalyst systems: enamine-based catalytic antibody 33F12, and a chiral diphenyl amino alcohol organocatalyst. Using the benzaldehyde–acetone model aldol, the antibody achieved its effect mainly through pre-organization, whereas the organocatalyst worked via a combination of steric effects and electronic stabilization. In the latter case, gas-phase *ee* was modest (73%), while calculation for 'neat' acetone gave 87%, and 'on water' (aqueous organic emulsion) was enhanced at 94% (93% experimental), due to hydrogen-bonding effects.[276] (*ee*)

Other Asymmetric Aldols

An α-sulfinyl 7-azaindolinylamide (**110**) has been designed as an aldol donor for a direct catalytic asymmetric aldol reaction. Coordination of a soft Lewis acid (SLA in **111**) diminishes amide conjugation, favouring enolate formation. Reaction with an aldehyde (RCHO e.g. R = ^{i}Pr) gives the aldol product (**112**). Using the combination of SLA = $AgBF_4$, a hard Brønsted base (*para*-MeO–C_6H_4–OLi), and a chiral bis-phosphine auxiliary gives yields/*de*/*ee* of up to 87/82/99%. The amide design strategy was confirmed by the finding that the more flexible 2-Py–N(Me)–CO–CH_2–SMe gave no reaction.[277] (*de*) (*ee*)



(**110**) (**111**) (**112**)

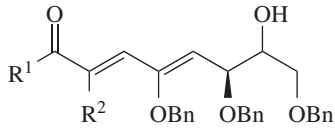
Experimental and theoretical investigations aimed at controlling stereochemistry in the synthesis of polyketides have examined the aldol addition of methyl ketones to β-super siloxy aldehydes; cases with 1,2- and 1,3-asymmetric induction were identified.[278] (*de*)

As an approach to avoiding some of the problems associated with acetaldehyde, it has been generated *in situ* from vinyl acetate. β-Carbonyls generated via cross-aldols have been used to prepare α,β-unsaturated δ-lactones.[279] (*ee*)

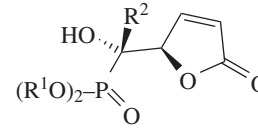
A major systematic study of diastereoselective aldols has examined reaction of 2-methylpropanol with a chiral ethyl ketone derivative. Forty examples were studied, covering the four diastereomers of the ketone, two protecting groups, and five enolate types [*E*- and *Z*-borinates and lithium enolates, and *Z*-Ti(IV) enolates]. All three factors strongly influence the observed *de*.[280] (de)

Heterofunctionalized aldehydes, Pg-X–CH_2–CHO (X = NH, O, S), undergo amine-catalysed asymmetric cross-aldols to give synthetically useful α,β-difunctionalized aldehydes. The adjacent functional groups in the products can be selected to be *syn*- or *anti*- by the choice of the amine catalyst.[281] (de)

A useful series of aldol reactions have been carried out in water, using lithium carbonate: this mild base allows many base-labile groups to survive. The reactivity is put down to the effect of a neighbouring heteroatom. The reactions can be carried out with or without phase-transfer catalysis, and the aqueous medium often gives higher yields and simpler purifications. Indeed, some of the reactions do not work in organic solvents. The method has been applied to a tetra-benzyl-protected L-glucose, reacting via the open-chain aldehyde form with a range of ketones ($R^1COCH_2R^2$), giving a new carbohydrate-derived skeleton (**113**) in up to 99% yield.[282] (de)



(**113**)



(**114**)

Alkenyl trihaloacetates undergo asymmetric aldol reactions with aldehdes catalysed by a chiral phosphine–silver complex: *ee*s up to 95% were achieved by a chiral silver enolate complex formed *in situ*.[283] (de) (ee)

The Mukaiyama Aldol

Chelation-controlled Mukaiyama aldols of chiral α- and β-alkoxy aldehydes have been reviewed (49 references),[284] as have advances in such reactions in aqueous media.[285] (de) (de)

Chiral α-hydroxy phosphonates and γ-(hydroxyalkyl)butenolides – two motifs with wide biological and medicinal relevance – have been combined in one structure (**114**) bearing two contiguous quaternary centres via a catalytic asymmetric vinylogous Mukaiyama aldol, using an *S*-chiral amino sulfoximine liganded to copper(II). Starting from an α-keto phosphonate and furan-2-OTMS, the product is formed with near-perfect efficiency, with yield/*de*/*ee* up to 99/>99/>99%, without need for a separate desilylation step.[286] (ee) (de) (ee)

DFT has been used to study the mechanism of chemoselective silyl transfer in the Mukaiyama aldol promoted by super silyl Lewis acids such as $(TMS)_3SiOTf$.[287]

A kinetic study of a Mukaiyama aldol reaction catalysed by a chiral disulfonimide has been carried out.[288a] (de) (ee)

Ab initio calculations of asymmetric catalytic Mukaiyama aldol reactions mediated by BINOL-Ti(IV), bisoxazoline-Cu(II), and BINAP-Pd(II) systems suggest the intervention of proto- and sila-tropic ene-type mechanisms.[288b] (de) (ee)

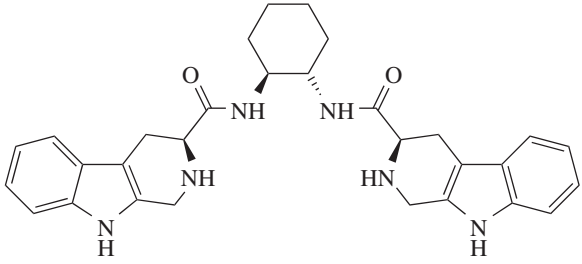
New ruthenium phosphino-oxazoline complexes are efficient catalysts.[289] (de)

Mukaiyama-aldol type reactions of dimethylacetals of enolizable aldehydes give *β*-methoxycarbonyl compounds in high yields using $FeCl_3 \cdot 6H_2O$ as catalyst, in air and without additives. The acetals can be considered as activating rather than protecting groups, as the use of the parent aldehydes – though successful – is lower yielding and much slower.[290]

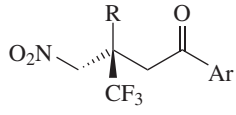
Chiral imidazolidinones catalyse organo-SOMO (singly occupied molecular orbital) reactions of aldehydes and ketones with cyclic and acyclic enol silanes in up to 90% *ee*. It did not work for silyl ketene acetals, but silyl ketene *thio*acetals were successful.[291] (ee)

The Henry (Nitroaldol) Reaction

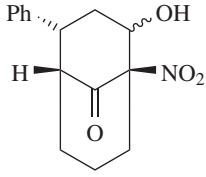
A C_2-symmetric tetradentate diamine-diamide derived from *trans*-1,2-diaminocyclohexane and L-tryptophan (**115**), complexed to copper(II), gives yields/*ee* up to 99/98% in Henry reactions of nitromethane with aromatic and aliphatic aldehydes, using DIPEA as base in isopropyl alcohol (IPA) at −30 °C; neither air nor moisture need be excluded.[292] (ee)



(**115**)



(**116**)



(**117**)

Henry reaction of benzaldehyde and nitromethane catalysed by a cyclophane–bisthiourea has been studied by DFT: the calculations show that a thiourea–nitronate complex reacts with the uncoordinated aldehyde. Enantioselectivity is found to arise from differences in hydrogen bonding in diastereomeric transition states.[293] (ee)

A series of mono- and di-alkylated chiral 1,2-diamino phosphinamido ligands that catalyse the enantioselective Henry reaction of benzaldehyde and nitromethene have been studied in terms of their *N*-substituent sizes, using physical steric parameters.[294] (ee)

New chiral *N*,*N*′-dialkyl-1,2-cyclohexanediamines give good yields/*ee* in copper(II)-catalysed Henry reactions of various aldehydes with nitromethane.[295] (*ee*)

Copper(II) complexed with a polyethylene glycol–polyglutamate copolymer and imidazolidine-4-one ligands gives 98/92% yield/*ee* in model Henry reactions of aldehydes and nitromethane. The reactions give rise to a colloid with self-organized catalyst aggregates of ~190 nm diameter, and the catalysts are recyclable.[296] (*ee*)

A series of chiral copper(II) salalen, salan, and salanan complexes catalyse nitroaldol reactions; careful control of *N*,*N*-substituents in the ligand optimizes *ee*.[297] (*ee*)

2-Acylpyridine *N*-oxides undergo direct Henry reaction with nitromethane to give tertiary nitroaldols in up to 96% *ee*, using a BOX–Cu(II) chiral complex.[298] (*ee*)

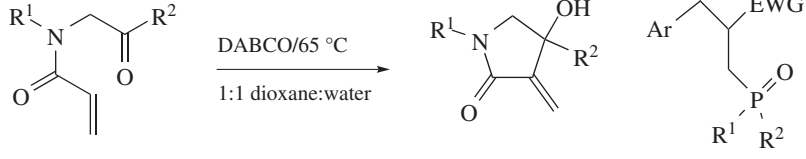
Simple new thiourea organocatalysts bearing a chiral 1° amine on one nitrogen and a basic and/or bulky group on the other give high yields and good *ee*s in conjugate addition of ketone to nitroalkene.[299] (*ee*)

Nitromethane conjugate addition to β,β-disubstituted enones (one group being $-CF_3$) efficiently delivers γ-nitroketones (**116**) with an all-carbon quaternary β-centre (R = alkyl). Accelerated by a combination of a chiral tertiary amine-thiourea and 10^4 atm pressure, yields/*ee* of up to 97/98% are reported.[300] (*ee*)

An organocatalytic cascade reaction of 2-nitrocyclohexanone with cinnamaldehyde (*trans*-Ph-CH=CH–CHO) unexpectedly yielded the product (**117**), the result of initial reaction on the non-nitro α-position of the cyclohexanone, rather than the product with nitro adjacent to phenyl. Using prolinol TMS ether as catalyst, good *de*/*ee* was obtained (with DABCO as base). The preference for reaction at the ostensibly much less basic position has been explained in terms of a dienolate–iminium mechanism, with this position of the dienolate being more reactive.[301] (*de*) (*ee*)

The Baylis–Hillman Reaction and its Morita Variant

Less reactive ketone and acrylamide moieties have been successfully employed as electrophile and activated alkene in intramolecular Baylis–Hillman reactions; for example, keto-acrylamide (**118**) converts easily to α-methylene-γ-lactam (**119**) in high yield in a few hours (R^1 = Ar; R^2 = Ar or Me). The reactant can be prepared from the appropriate α-keto amine and acryloyl chloride.[302]



(**118**) (**119**) (**120**)

Acrylamides with *N*-pendant alkyl aldehydes of appropriate lengths have been cyclized to construct a range of five- and six-membered α-methylene lactam and spirolactam derivatives, via intramolecular Baylis–Hillman reaction.[303]

The MBH reaction has been probed by ESI-MS(/MS), using an acrylate derivative charge-tagged with an imidazolium, supported by DFT calculations for three media (MeOH, MeCN, and gas phase). The nature of the IL effect is also discussed.[304]

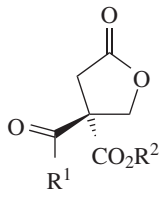
Combination of a trivalent phosphorus reagent ($R^1R^2PNEt_2$), an araldehyde (Ar-CHO), and a Michael olefin (H_2C=CH-EWG) in the presence of water leads to highly functionalized phosphine oxides (**120**), with the oxygen on phosphorus being derived from water. Essentially, a Lewis base organocatalysed MBH reaction has been developed into a multi-component synthesis of polyfunctionalized molecules.[305]

3-Arylprop-2-ynyl esters, Ar-C≡C–CH_2–O_2C–R, undergo metathesis reactions with aldehydes to give MBH-type products inaccessible by direct MBH methods. The reactions are catalysed by boron trifluoride, and the mechanism has been explored using ^{18}O-labelling and DFT.[306]

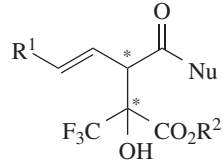
Other Aldol and Aldol-type Reactions

Butanal self-condenses to 2-ethyl-2-hexenal, an important precursor to 2-ethylhexanol. A range of synthetic sulfonic acid-functionalized ILs catalyse the reaction: rates correlate with acid strength, as determined by the Hammett UV–visible method.[307]

γ-Butyrolactones with an all-carbon quaternary centre at the β-position (**121**) are synthetically challenging, but have now been accessed in yields/*ee* up to 98/88% from acylated succinic esters, R^1–CO–$CH(CO_2R^2)$–CH_2–CO_2Me, and formaldehyde using a chiral squaramide catalyst in a one-pot aldol/lactonization sequence.[308] (*ee*)



(**121**)



(**122**)

β-Bromodicyclohexylborane has been identified as an enolization reagent and triethylamine as a base, which, together effect *anti*-selective enolization–aldolization of propanoic acid to give *anti*-β-hydroxy-α-methyl carboxylic acids. A problem of contamination inherent in the use of triflic acid has been bypassed in the protocol.[309] (*de*)

Asymmetric α-aldols of a vinylogous NHC-enolate, R^1–CH=CH–CH=$C(O^-)^+$NHC*, with trifluoropyruvate esters (F_3C–CO–CO_2R^2) as carbon electrophiles and a displacing nucleophile afford highly functionalized products (**122**) bearing adjacent tertiary and quaternary stereocentres with good *de* and excellent *ee*.[310] (*de*) (*ee*)

A thermodynamically controlled Pummerer/aldol, involving selective addition of ketones to aldehydes, uses thiol promotion to generate *syn*-β-thioketones: 3 equiv of thiol was employed, with $Cu(OTf)_2$ catalysis. A mechanistic study ruled out an aldol/Michael route, as in the absence of thiol no reaction occurred. Cross-coupling is imposed over dimerization, as the conversion of the aldehyde to an electrophilic

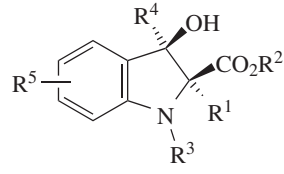
thionium ion (via the dithioacetal) is concurrent with the generation of a nucleophilic vinyl sulfide from the ketone (also via its dithioacetal). This 'vinyl sulfide as surrogate enolate' strategy obviates the need to activate the ketone in advance. In addition, protic groups are tolerated (dispensing with protection), as well as air and water.[311] (de)

DFT has been used to probe the origin of the chemoselectivity of the thiolate-catalysed cross-Tishchenko coupling for the case of two benzaldehydes, 4-chloro- and 2-methoxy-. The reaction produces esters, $Ar^1–CO_2–CH_2–Ar^2$, via the steps (i) 1,2-addition, (ii) hydride transfer, and (iii) acyl transfer. The calculations agree with experiment in identifying the 4-chloro- as a hydrogen donor (Ar^1), while the 2-methoxy- acts as a hydrogen acceptor (Ar^2). Step (ii) is typically rate-determining, but step (iii) can take over this role when steric hindrance is significant, for example, for *ortho*-methoxy groups on both sides.[312]

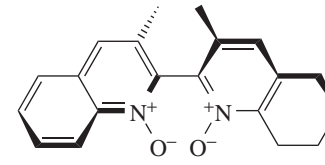
A DFT study of the intramolecular aldol condensation of 2,5-hexadione suggests that it proceeds via an asynchronous concerted mechanism[313]; another report describes the use of several levels of DFT for this reaction.[314]

2-Methylazaarenes undergo Lewis-acid-catalysed benzylic reactions with aldehydes. For example, 2-methylpyridine gives ethanol derivatives via $LiNTf_2$-promoted aldol reaction, while 2-alkenylpyridines (exclusively *E*-) were formed using $H_2NTf/LiNTf_2$ cooperative catalysis. The corresponding alkenylquinolines required lanthanum(III) tris(pentafluorobenzoate) as Lewis acid.[315]

3-Hydroxy-2,2,3-trisubstituted indolines (**123**) have been prepared from 2-aminophenyl ketones and a diazo ester [$R^1–C(=N_2)–CO_2R^2$]. Dirhodium tetraacetate is used to catalyse the decomposition of the diazo ester, leading to an intramolecular aldol-type trapping of ammonium ylides by the ketone unit; *de*s >90% are reported.[316a] (de) (ee)



(**123**)



(**124**)

Chiral *β*-hydroxy esters have been prepared via zinc-mediated Reformatsky reaction between prochiral aldehydes and *α*-bromo ethyl acetate, using a chiral amide derived from (1*S*,2*R*)-(+)norephedrine and 2-furoic acid; air is essential for the reaction.[316b] (de)

Allylation and Related Reactions

A comparative study of Lewis, Lewis acid, and Brønsted acid catalysis of enantioselective allylation of *ortho*-substituted benzaldehydes gives complicated results without a clear trend associated with the bulk of the substituent, and a general system has not yet emerged, with variable results from different catalysts and catalyst loadings.[317] (ee)

Oxazolines tagged with tosylated amino acids act as recyclable organocatalysts for enantioselective allylation of aldehydes.[318] (ee)

A DFT study of the origins of the stereoselectivity observed in allylation and propargylation reactions catalysed by Nakajima's chiral bipyridine-derived *N*,*N*′-dioxide (**124**) has thrown up a range of interesting results. The *ee*s have been identified as arising from electrostatic interactions within a hexacoordinate silicon intermediate, in conflict with a previously published TS model. The DFT studies also ranged over several popular methods, but many were found to be deficient for these reactions: even where predictions matched the experimental *ee*s, the identified TS was sometimes qualitatively incorrect. Allylation results sometimes differed significantly from those for propargylations. These findings caution against assuming that correct *ee* implies correct TS or that apparently closely related reactions necessarily have similar mechanisms.[319] (*ee*)

A DFT study of cooperative multicatalytic methods has studied the example of palladium-catalysed asymmetric Tsuji–Trost allylation of aldehydes using a BINOL-phosphoric acid. While conventional models show the chiral ligand directly bound to the transition metal, the calculations show that the chiral phosphate counterion induces the enantioselectivity.[320] (*ee*)

A tandem allylation of aldehydes (or aldimines) uses allylzincs derived from diethylzinc and cyclopropenes, via carbozincation of the cyclopropene.[321]

Barium enolates of cyclic ketones undergo asymmetric allylic alkylation using a metallacyclic iridium complex bearing a chiral phosphoramidite ligand, with *de*/*ee* up to >90/>99%. The barium counterion is critical: the use of other alkaline earth cations or lithium cation gave lower yields, generally low *de*, and often no *ee*.[322] (*de*) (*ee*)

Homoallylic propargylic alcohols useful in natural product synthesis have been prepared in yields/*ee* up to 90/91% by allylboration of propargylic aldehydes in the presence of a chiral 1,2-diol.[323] (*ee*)

Boron tris(trifluoroacetate) catalyses homoallyl- and homocrotyl-boration of aldehydes by cyclopropylcarbinylboronates. NMR results and DFT studies suggest that the active homoallylating species is $(TFAO)_2B–CH_2–$cyclopropyl.[324]

A new C–H borylation–allylboration combines exocyclic alkenes and aldehydes to give regio- and stereo-defined homoallylic alcohols, using $Pd(TFA)_2$ catalysis.[325] (*de*)

A diisopinocampheyl auxiliary has been used in the trifluorocrotylboration of aldehydes to give *syn*-*β*-trifluoromethyl homoallyl alcohols with *de*/*ee* up to 92/97%.[326] (*de*) (*ee*)

Fulvene-derived allylaluminiums – prepared by titanium-catalysed hydroalumination of conjugated dienes – react regio- and stereo-selectively with aldehydes and ketones to form homoallylic alcohols with *de* typically >95%.[327] (*de*)

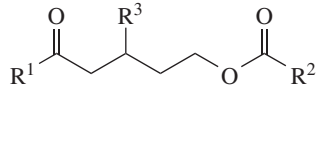
Enantioselective *α*-allylation of aldehydes with terminal alkenes has been achieved by combining asymmetric counterion catalysis and palladium-catalysed allylic C–H activation. This direct oxidative coupling of two different C–H bonds (both sp^3), also known as cross-dehydrogenative coupling (CDC), avoids the need for pre-functionalized substrates.[328] (*ee*)

(*E*)- or (*Z*)-*β*-fluoroallylic alcohols have been prepared from aldehydes by nucleophilic addition of (*Z*)- or (*E*)-*α*-fluoroalkenylchromium species, respectively.[329]

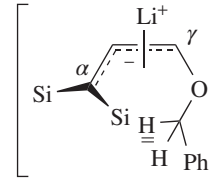
The mechanism of the bismuth chloride-mediated, aluminium-promoted aqueous Barbier-type coupling of allyl bromide with aldehydes – to give the corresponding homoallyl alcohol – has been investigated by ^1H NMR spectroscopy and gas chromatography–mass spectrometry (GC–MS). The transient allyl bismuth(III)

bromide formed *in situ* has been characterized, and the most reactive intermediate was identified as $H_2C{=}CH{-}CH_2BiBr_2$.[330]

Formal insertion of allylic alcohols, $R^3{-}CH{=}CH{-}CH_2OH$, into the C(O)–C bond of 1,3-diketones, $R^1COCH_2COR^2$, generates 5-oxopentyl esters (**125**). An iron tricarbonyl and a diarylprolinol TMS ether catalyse a cascade involving an iron-catalysed hydrogen transfer, generating an α,β-unsaturated aldehyde *in situ*, subsequent iminium activation/Michael addition, and then a retro-Claisen acyl transfer.[331] (*ee*)



(**125**)



(**126**)

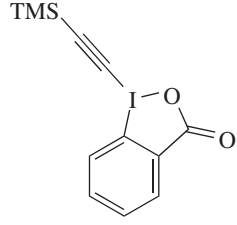
A [1,5]-anion relay has been achieved in a 3,3-bis(silyl)benzyl enol ether: deprotonation at the accessible benzyl position triggers an intramolecular proton transfer from the α-position to generate the more stable allyloxy lithium (**126**, H underlined), an *endo*-oriented allyl anion. Stable at −78 °C, it adds *syn*-selectively to the γ-position of aldehydes or ketones.[332] (*de*)

Alkynylations

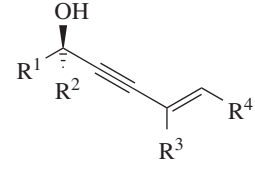
Hypervalent iodine species (**127**) serves as a source of TMS-acetylene cation to effect electrophilic α-alkynylation of ketones and aldehydes in the presence of *t*-BuOK and tetrabutylammonium fluoride in THF. Transition-metal species are not required.[333]

Novel chiral 4-phenylquinazolinols catalyse titanium(IV)-promoted addition of phenylacetylene to a variety of aldehyde types with yields/*ee* up to 98/97%.[334] (*ee*)

(*R*)-3,3′-Diformyl-BINOL has been condensed with chiral benzylamines to give new Schiff base catalysts for the addition of phenylacetylene to benzaldehyde, promoted by diethylzinc; yields/*ee* up to 83/85% are reported.[335] (*ee*)



(**127**)



(**128**)

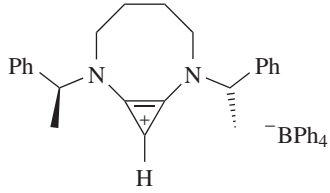
Intramolecular addition of aldehydes to non-activated alkenes yields cyclopentanes, merging iron and amine catalysis, with evidence for an enamine/π-activation mechanism.[336]

1,1-Difluoro-1-(phenylsulfonyl)-3-en-2-ones, R–CH=CH–CO–CF_2–$S(=O)_2$–Ph, undergo conjugate alkynylation with *ee* up to 99%, using a copper(I) catalyst ligated with a chiral biphenyldiphosphane. The resulting *β*-alkynylated difluoro(phenylsulfonyl) ketones are readily convertible to esters and amides using an alcohol or amine, respectively.[337] (*ee*)

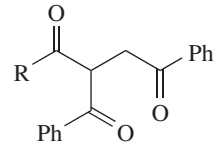
Using *n*-butyllithium in THF at −78 °C, the dilithium salt of a chiral diaryl-buttressed BINOL catalyses enyne addition to ketones in yields/*ee* up to 96/94%, giving useful 3° alcohols (**128**).[338] (*ee*)

The Stetter Reaction and the Benzoin Condensation

A short review highlights the finding that chiral diaminocyclopropenylidene cations such as (**129**) show modest *ee* when used to catalyse intermolecular Stetter reactions. Further development of such carbene-type reactivity promises a new generation of catalysts for C–C bond-forming reactions, building on the successes of NHCs.[339] (*ee*)



(**129**)



(**130**)

γ-Ketophosphonates, $ArCOCH_2CH_2P(=O)(OR)_2$, have been prepared from aryl aldehydes by Stetter reaction onto vinyl phosphates, using a simple NHC catalyst.[340]

Aromatic 1,2-diketones such as benzil (PhCOCOPh) undergo thiazolium carbene-catalysed reaction with enones ($RCOCH=CH_2$) to give the double arylation product (**130**) in good yield, with no Stetter hydroacylation product being detected. The result suggests that an aroyloxyenamine is generated from the dione, rather than a hydroxyenamine (Breslow) intermediate. Aliphatic diones work too, albeit with lower yields. This extension of the classical Stetter reaction allows the insertion of activated C–C multiple bonds into acyl compounds other than aldehydes.[341]

NHC catalysts designed with computational guidance give good *ee* in a formal [3 + 2] annulation of enals with *α*-ketophosphonates, to give *γ*-butyrolactone phosphate esters. These in turn have been converted in one simple step with retention of chirality to Stetter products, which in this case would be difficult to access by direct Stetter reaction.[342] (*ee*)

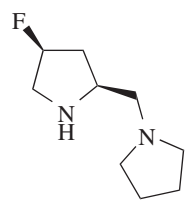
The NHC-catalysed homoenolate reaction of enals with nitroalkenes has been investigated theoretically, including the *syn*-selectivity. An alternative Stetter route has been ruled out.[343]

β-Halo *α*-keto esters undergo DKR via asymmetric cross-benzoin catalysed by potassium carbonate and a chiral NHC, giving high *de* and *ee*.[344] (*de*) (*ee*)

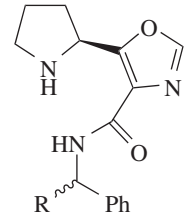
2-(Aroylvinyl)benzaldehydes undergo dimerization to give highly functionalized benzo[*a*]fluoren-11-ones using an NHC/Brønsted base co-catalysis, via a benzoin-Michael–Michael cascade.[345] (*de*)

Michael Additions and Related Reactions

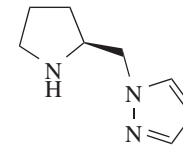
A catalyst derived from *cis*-4-fluoro-proline (**131**) has been designed to exploit the fluorine *gauche* effect: it gives yields/*de*/*ee* approaching 'all-99s' in a mild Michael addition of cyclohexanone and *trans*-nitrostyrenes.[346] (*de*) (*ee*)



(**131**)



(**132**)



(**133**)

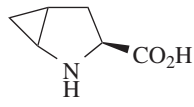
New pyrrolidinyl-oxazole-carboxamides (**132**; R = H, (*R*)-Me, (*S*)-Me) with two convergent hydrogen-bond donors catalyse solvent-free Michael addition of ketones to nitroalkenes with yields/*de*/*ee* up to 99/>98/99%.[347] (*de*) (*ee*)

Co-catalysis by a pyrrolidine–pyrazole (**133**) and benzoic acid gives good yields and *ee* for Michael additions of aldehydes generally[348] but especially *α*,*α*-disubstituted aldehydes[349] with nitroalkenes. (*ee*) (*ee*)

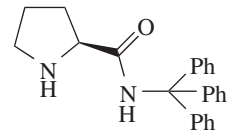
New bifunctional tertiary amine-thioureas derived from L-proline give excellent stereo-selectivities in Michael additions of *β*-diketones and *β*-ketoesters to nitroalkenes.[350] (*de*) (*ee*)

cis- and *trans*-Isomers of 4,5-methano-L-proline (**134**) are good organocatalysts of Michael addition of aliphatic aldehydes to aromatic nitroalkenes, giving *de*/*ee* up to 94/98%, with generally high yields of *syn*-products.[351] (*de*) (*ee*)

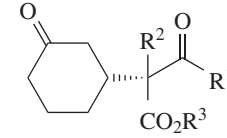
A new prolinamide, (*S*)-*N*-tritylpyrrolidine-2-carboxamide (**135**), catalyses Michael reactions of aldehydes with nitroalkenes in yields/*de*/*ee* up to 94/99/98%.[352] (*de*) (*ee*)



(**134**)



(**135**)



(**136**)

New furano-sugar amide pyrrolidines catalyse Michael addition of ketones to nitroalkenes in good yield/*de*/*ee*, at ambient temperature, without additives or solvents.[353] (*de*) (*ee*)

β-Keto esters have been added to enones in a Michael addition that is catalysed by a salt of a primary *β*-amino acid. Good *ee* but poor *de* is reported in the products (**136**; R^1 = aryl; R^2 = H, Me, F; R^3 = alkyl).[354] (*de*) (*ee*)

The effect of a very simple organocatalyst of a Michael addition can be enantioswitched just by the solvent: mono-*N*-Boc-*trans*-1,2-cyclohexanediamine gives up to

86% *ee* in conjugate addition of α,α-disubstituted aldehydes to maleimides in chloroform, whereas aqueous DMF gives *ee* down to −84%.[355] (ee)

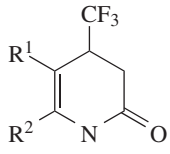
Direct Michael reaction of cyclohexanone with aromatic nitroolefins has been carried out in water with yields/*de*/*ee* up to 99/98/94%, using a new series of axially unfixed biaryl-based bifunctional organocatalysts.[356] (de) (ee)

Quantum chemical calculations have been employed to probe the mechanism of the Michael addition of *trans*-β-nitrostyrene (*trans*-O_2N–CH=CH–Ph) to isobutyraldehyde, as catalysed by a primary amine derived from a cinchona alkaloid. The iminium mechanism delineated in the study includes a proton transfer to the β-carbon of the alkene: this step determines the rate and *ee*.[357] (ee)

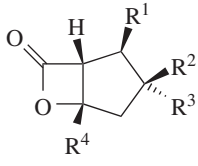
Chiral primary amine-guanidines catalyse Michael addition of isobutyraldehyde to nitroalkenes in up to 98% *ee*, using imidazole co-catalysis in aqueous DMF at 0 °C. Calculations suggest that the guanidine can block one face of the enamine intermediate, and the water can activate the nitro group by hydrogen bonding.[358] (ee)

A synthetic, X-ray crystallographic, and NMR spectroscopic study of intermediates in organocatalytic Michael additions to and Diels–Alder reactions of cinnamaldehydes has compared phenylalanine-derived *cis*- and *trans*-imidazolidinones and the corresponding ammonium and cinnamyl iminium salts in the solid state and in solution.[359] (ee)

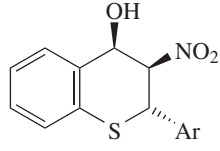
Regio- and enantio-selectivity in asymmetric organocatalytic addition of acetone to 4-(trifluoromethyl)pyrimidin-2(1*H*)-ones (**137**) in the presence of proline or other chiral secondary amine organocatalysts is dependent on the type of catalyst used and whether thermodynamic or kinetic control operates: the latter factor gives either Michael-like or Mannich-like products, respectively.[360] (ee)



(**137**)



(**138**)



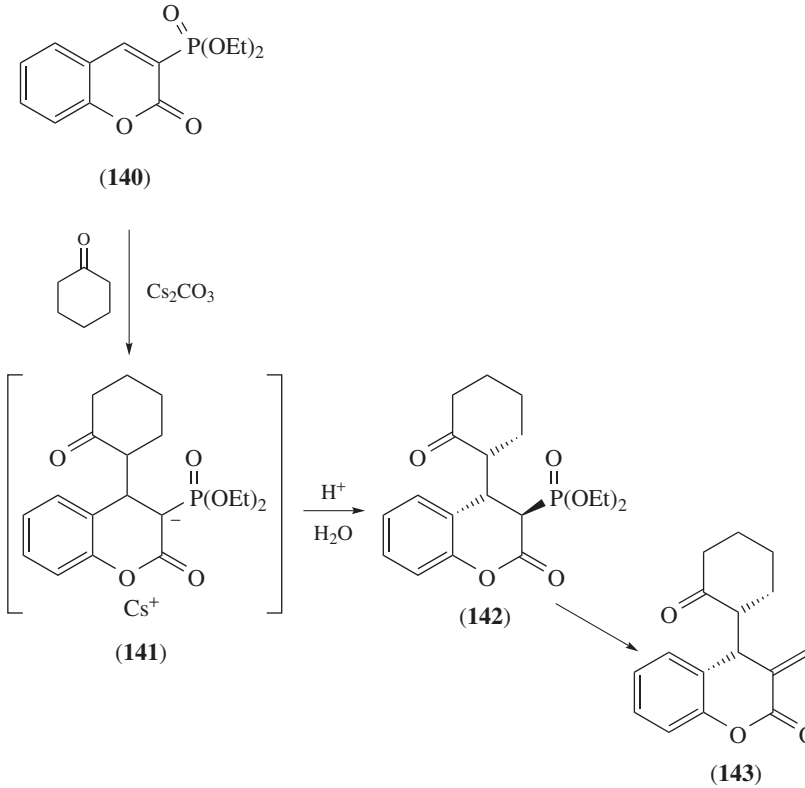
(**139**)

Highly substituted β-lactones have been accessed by the reaction of enals with β-diketones, β-ketoesters, and malonates by oxidative NHC catalysis. For example, bicyclic β-lactones (**138**) can be formed from the enal R^1–CH=CH–CHO and ketones R^4–CO–CH_2–CHR^2R^3 (where R^2, R^3 = COR or CO_2R). The reactions proceed via α,β-unsaturated acylazolium ions using simple chiral azolium-NHCs, giving high *de* and *ee*. Lithium chloride acts as a cooperative Lewis acid catalyst, but its precise roles in the cascade process of Michael addition, followed by formal [2 + 2] aldol lactonization, are unclear.[361] (de) (ee)

Diversity-oriented asymmetric catalysis (DOAC) has been used in the development of a thiochromane synthesis. Starting from a range of 2-mercaptobenzaldehydes and β-nitrostyrenes, Michael/Henry reaction gives (2*S*,3*R*,4*R*)-2-aryl-3-nitrothiochroman-4-ols (**139**), using a nickel(II)/imidazole/aminophenol catalyst system. Yields/*de*/*ee* up to >99/>99/95% were obtained in a day in toluene at −40 °C.[362] (de) (ee)

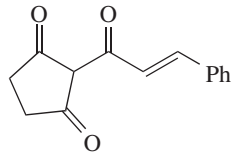
A chiral bisoxazolidine–Ni(acac)$_2$ complex catalyses a domino Michael–Henry reaction of 1,2-cyclohexanedione with nitroalkenes, generating highly functionalized bicyclo[3.2.1]octanes in yields/*de*/*ee* up to 99/99/80%; four new stereocentres are formed.[363] (*de*) (*ee*)

A highly *syn*-diastereoselective Michael addition of enolizable ketones to 3-(diethoxyphosphoryl)-coumarin (**140**) proceeds via the phosphorus-stabilized enolate (**141**), which – upon acid workup – yields an α-phosphono-δ-lactone ketone (**142**) in 62% *de*. A mild Horner–Wadsworth–Emmons reaction with formaldehyde yields potentially biologically active α-methylene-δ-lactone as a single diastereomer (**143**). The method is applicable to many cyclic and acyclic ketones.[364] (*de*)

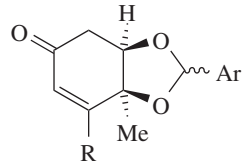


Enantioselective synthesis of enol lactones has been achieved via a tandem Michael addition of 1,3-dicarbonyls with α,β-unsaturated N-acylated succinimides (e.g. **144**), followed by lactonization and removal of the succinimide auxiliary. Chiral squaramide catalysts give yields/*ee*s up to 97/88%.[365] (*ee*)

ortho-Hydroxy β-nitrostyrenes undergo a range of triple domino reactions with acetaldehyde (Michael/aldol/oxa-Michael), which are catalysed by diphenylprolinol TMS ether; subsequent one-pot Wittig and other transformations yield chromanes or chromenes. Significant neighbouring participation by the hydroxyl group has been identified.[366] (*ee*)



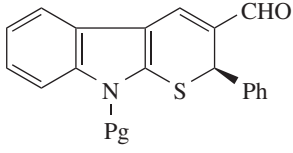
(**144**)



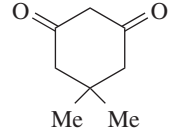
(**145**)

A range of bicyclic acetals (**145**) have been prepared from a *para*-quinol and an aromatic aldehyde via a one-pot domino sequence catalysed by DMAP (4-dimethylaminopyridine) or DABCO. This acetalization/oxa-Michael process can be extended to heteroaromatic aldehydes, and an *N*-tosyl aldimine reactant gives the corresponding hemiaminal.[367] (*de*)

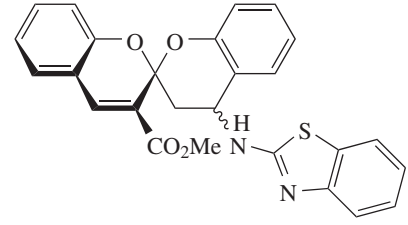
Pharmaceutically valuable dihydrothiopyrano[2,3-*b*] indoles (**146**) have been prepared in up to 96% *ee* from 2-mercaptoindole-3-carbaldehydes and enals (in this case, cinnamaldehyde), using diphenylprolinol TMS ether, via a cascade sulfa-Michael-aldol.[368] (*ee*)



(**146**)



(**147**)



(**148**)

Tetrahydrobenzo[*b*]pyrans have been prepared from dimedone (**147**), *para*-nitrobenzaldehyde, and malononitrile ($NC–CH_2–CN$) in a one-pot reaction catalysed by sodium acetate. A full mechanistic investigation is reported, including the measurement of kinetic and activation parameters and solvent effects.[369]

Miscellaneous Condensations

Recent advances and controversies in the Biginelli reaction have been reviewed (121 references, plus some experimental testing of previous literature reports). In particular, the authors question some 'catalyst-free' and 'solvent-free' manuscripts, and seek to demystify the field, where they consider that even good work is sometimes adversely affected by catchy titles and unsubstantiated claims. They finish with 11 very specific recommendations that they believe will facilitate real improvements in this important multi-component reaction.[370]

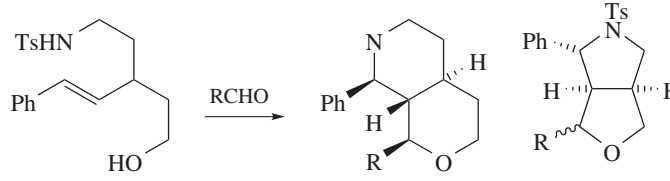
Biginelli reactions of salicylaldehyde and 2-hydroxy-1-naphthaldehyde have been reinvestigated, with the products of reaction with ethyl (or methyl) acetoacetate, ethyl benzoylacetate, and urea being unambiguously confirmed by X-ray crystallography.[371]

Biginelli-type condensation of salicylaldehyde, methyl acetoacetate, and 2-aminobenzothiazole gave unusual spiroketal isomeric products (**148**), involving 2:1:1

molar ratio of reactants (and loss of three water molecules). The reaction is reasonably generalizable, tolerating ring substituents in salicylaldehyde and benzothiazole, and also works for 2-amino-5-methylthiazole: in one of the latter cases, *de* of 98% was achieved. Hindered acetoacetates also gave high *de*.[372]

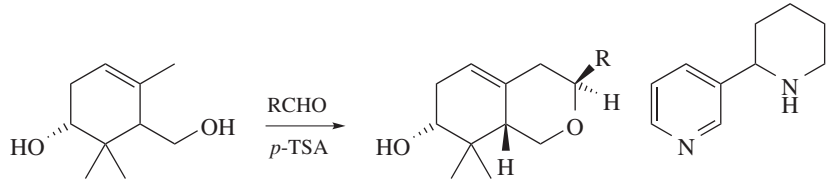
Double axially chiral bisphosphorylimides have been used as catalysts in Biginelli syntheses of dihydropyrimidinethiones from an aromatic aldehyde, thiourea, and ethyl acetoacetate, giving yields/*ee* up to 97/96% in 12 h at 20–50 °C.[373] (*ee*)

In an aminol-initiated Prins cyclization, a branched homoallylic alcohol appended with an *N*-tosyl amine (**149**) reacts with various types of aldehydes to give *trans*-fused THP (tetrahydropyran) bicycles (**150**), that is, octahydro-1*H*-pyrano[3,4-*c*]pyridines. Catalysed by $BF_3{\cdot}OEt_2$, a simple modification – shortening the *N*- and *O*-chains by one carbon each – provides access to the corresponding THF bicycles (i.e. hexahydrofuro[3,4-*c*]pyrroles) as a mixture of *cis*-fused isomers (**151**).[374] (*de*)



(**149**) (**150**) (**151**)

A novel but related Prins reaction couples a wide range of aldehyde types with a cyclic enol (**152**) in the presence of *para*-toluenesulfonic acid to deliver hexahydro-8,8-dimethyl-1*H*-isochromen-7-ols (**153**). A mechanism involving alkene isomerization (*endo*- to *exo*-) followed by Prins cyclization is discussed.[375] (*de*)



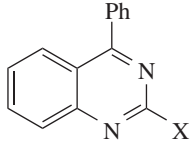
(**152**) (**153**) (**154**)

Pyridinic aldehydes such as 3-(pyridine-2-yl)propanal undergo Prins cyclization with 3-buten-1-ol, to give pyridine–tetrahydropyran conjugates; an aza-Prins version with the corresponding amine gives the alkaloid anabasine (**154**) over two steps (including a hydrogenation).[376]

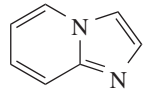
vic-Diketo amides, R^1–CO–CO–$CONR_2$, undergo Passerini reaction with isocyanides and carboxylic acids to give α-acyloxy-β-keto-carboxamides with high α-regioselectivity. In appropriate cases, a one-pot Passerini–Knoevenagel reaction is possible, either spontaneously, or on addition of base.[377]

A range of fused *N*-substituted 2-pyridone derivatives have been prepared from *β*-diketones, 1° amines, and dialkylacetylenedicarboxylates, using L-proline as catalyst in sodium dodecyl sulfate micelles in water.[378]

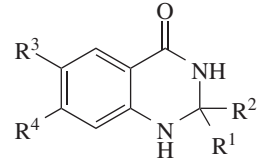
4-Phenylquinazoline (**155**; X = H) is cleanly formed by the reaction of 2-aminobenzophenone with thiourea in DMSO at 150 °C. This unexpected result, specific to DMSO solvent, is hard to explain, as related reactions would predict an amine or thiol (**155**; X = NH_2 or SH), or the thione tautomer of the latter. None of these species converts to product under the reaction conditions. Focussing both experiment and computation on the thermal decomposition of thiourea, the possibilities of ammonia and isothiocyanic acid (HN=C=S) versus hydrogen sulfide and carbodiimide (HN=C=NH) are considered, with evidence favouring the latter as the route to 4-phenylquinazoline (**155**, X = H). The use of ketones such as 1-amino-anthracene-9,10-dione and -9*H*-fluoren-9-one gives perimidines.[379]



(**155**)



(**156**)



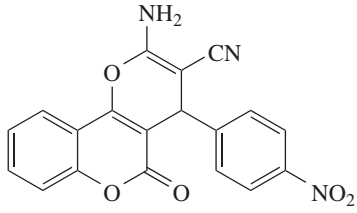
(**157**)

2,3-Disubstituted derivatives of imidazo[1,2-*a*]pyridine (**156**) have been prepared in a direct acid-catalysed reaction of 2-aminopyridines and acetophenones, via a ketimine intermediate.[380]

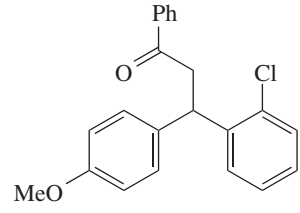
2,3-Dihydroquinazolin-4(1*H*)-ones (**157**) have been prepared via NHC catalysis from *ortho*-aminobenzonitriles and carbonyl compounds, R^1COR^2, in high yield, without solvent, at ambient temperature.[381]

A 3,4-dihydropyrano[*c*]chromene (**158**) is formed from 4-nitrobenzaldehyde, malononitrile, and 4-hydroxycoumarin in a one-pot condensation catalysed by acetate. Kinetics of its formation have been studied spectrophotometrically, including solvent effects.[382]

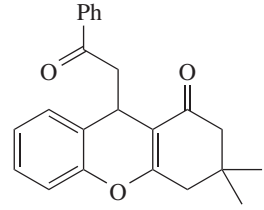
While 1,3-dicarbonyls are easily alkylated with electrophilic alcohols, simpler aryl methyl ketones are typically insufficiently nucleophilic, and precious metal catalysts and 1° alcohols are required. A new method uses the cheaper and more benign $Fe(OTf)_3$ catalyst, chlorobenzene as solvent, and benzhydrols as electrophiles (including moderately hindered cases). For example, 2-chloro-4′-methoxybenzhydrol reacts with a threefold excess of acetophenone in 4 h at 130 °C, to give the functionally dense ketone (**159**) in 60% yield, using 5 mol% catalyst. A related three-component reaction has also been developed: salicylaldehyde and dimedone (**147**) react with acetophenone under the same conditions to give a highly substituted 4*H*-chromene derivative (**160**). Acetophenone can also be replaced with phenylacetylene.[383]



(**158**)



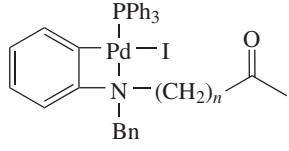
(**159**)



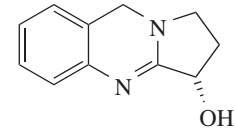
(**160**)

Other Addition Reactions

A short review describes the use of ambiphilic α-arylpalladium intermediates in intramolecular cyclization reactions (33 references). Using four-membered azapalladacycles such as (**161**) – derived from amino-tethered aryl halides and carbonyl compounds – electrophilic behaviour can be observed in α-arylation reactions, while nucleophilic reaction can occur involving direct attack of the C–Pd bond at various types of carbonyl group. Further, the arylpalladium moiety can be stabilized by the addition of phenol, which exchanges the iodide ligand.[384]



(**161**)



(**162**)

Recent progress in catalytic asymmetric protonation is the subject of a short review (66 references).[385]

The rates of two simple reactions of aldehydes – oxidation by $KMnO_4$ and reduction by $NaBH_4$ – are easily measured by UV-visible spectroscopy and have been used to measure their nucleophilicity and electrophilicity parameters (*N* and *E* values). The results have been validated using theoretical studies, and the concept can be applied to other functional group types, such as ketones and alkenes.[386]

Chirality can be achieved in an otherwise planar, prochiral carbonyl group via an $n \rightarrow \pi^*$ interaction: specifically, the delocalization of an electron pair (n) of a donor group into the anti-bonding orbital (π^*) of a carbonyl. Five pairs of diastereomers have been prepared and studied by X-ray crystallography. Such carbonyl pyramidalization may also increase the electron density on the oxygen, making it more basic and a better hydrogen-bond acceptor. A thioamide donor effects greater pyramidalization than an isosteric amide.[387] (ee)

The formation of furan from propadienylidene ($H_2C{=}C{=}C{:}$) and formaldehyde has been probed using second-order Moller–Plesset theory (MP2).[388]

Several new germanium-silicon unsaturated species, $X_2Ge{=}Si$ (X = H, Me, F, Cl, Br, and Ph), react with formaldehyde, eventually giving spiro-*Si*-heterocyclic products. An *ab initio* method has been used to probe the mechanisms.[389]

DFT has been used to study the kinetics and mechanism of the reaction of methylene and acetone in the gas phase. An asynchronous concerted mechanism is reported, and the effect of fluorine substitution in the reactants has also been calculated.[390]

Addition of Organozincs

A kinetic system to correlate *ee* with the conformational equilibria of a catalyst has been developed for an enantioselective addition of diethylzinc to benzaldehyde, leading to a quantitative relationship between conformations and *ee*: the complexity of the system is illustrated by the observed enantioselectivity *not* being the weighted average of the *ee*s of the individual conformers.[391] (de)

Naturally occurring L-vasicine (**162**) catalyses the addition of diethylzinc to *para*-chlorobenzaldehyde with yield/*ee* of 98/98% in toluene at ambient temperature. The excellent enantioselectivity is assigned to the likely rigidity of the zinc–ligand complex, given vasicine's rigid quinazoline ring and chelating *N*,*N*,*O*-tripod.[392] (ee)

New chiral diols give *ee*s up to 99% in addition of diethylzinc to aryl aldehydes.[393] (ee)

Chiral tridentate amino diol ligands give *ee* up to 96% in addition of diethylzinc to aromatic and aliphatic aldehydes. ^{1}H NMR studies of the titanium tetraisopropoxide-promoted process have helped to identify steric effects on the configuration of ligands and related enantio-control.[394] (ee)

New C_2-symmetric chiral tetradentate biPy-diols have been prepared via Mukaiyama–Michael reaction. They catalyse the addition of diethylzinc to aldehydes in up to 97% *ee*, without the need for additional Lewis acid such as titanium tetraisopropanoxide.[395] (ee)

New chiral thiophosphorimidate ligands give excellent yields/*ee* in the addition of diethylzinc to aldehydes.[396] (ee)

New aziridinyl alcohols derived from limonene oxide give yields/*ee* up to 96/95% for the addition of di- and phenyl-ethylzinc to aryl and alkyl aldehydes.[397] (ee)

Chiral 3-aminoquinazolinones catalyse additions of both diethylzinc and phenylacetylene to aldehydes, giving *ee*s up to 86% and 94%, respectively.[398] (ee)

A quantitative structure–activity relationship (QSAR) model has been constructed for the asymmetric addition of diethylzinc to acetophenone catalysed by 1,2-aminophosphoramides, with sterimol steric parameters being used for the *N*-substituents.

Molar refraction – closely related to bulkiness and polarizability – also correlated fairly well with *ee*, but Charton values were unsuitable.[399] (ee)

An autocatalytic asymmetric enhancement has been investigated in a diamine-catalysed addition of diethylzinc to α,α,α-trifluoroacetophenone, easily followed by ^{19}F NMR.[400] (ee)

New *tropos* biphenylazepine-based amino alcohols catalyse aryl transfer reactions to aromatic aldehydes in high yields and up to 96% *ee*; the arylzinc agents used are generated *in situ* from arylboronic acids and diethylzinc.[401] (ee)

Arylations

A highly hindered phosphine, $(t\text{-Bu})_2P–CH_2–t\text{-Bu}$, acts as an efficient ligand for palladium(II)-catalysed α-arylation of ketones by aryl bromides or chlorides. Use of 2-bromophenol efficiently delivers benzofurans. For sterically congested ketones, the somewhat less crowded tris(neopentyl) system $P(CH_2–t\text{-Bu})_3$ serves.[402]

Palladium-catalysed addition of an arylboronic acid, $Ar^1B(OH)_2$, to arylaldehydes, Ar^2CHO, can produce a carbinol, $Ar^1CH(Ar^2)OH$, or an ether, $O–[CH(Ar^2)Ar^1]_2$. Performed in aqueous media, the product balance can be controlled by the water content: using $Pd(OAc)_2$ and TfOH in pure water gives ether, 1:1 water:dioxane sees the production of carbinol as a minor byproduct, while 1:5 gave carbinol exclusively in high yield. Interestingly, the ether – a condensation product of the carbinol – is favoured by water solvent. A useful modification of the method allows the synthesis of 9-arylflourenes: Suzuki–Miyaura coupling of *ortho*-bromobenzaldehyde with phenylboronic acid gives 2-formylbiphenyl *in situ*; then $ArB(OH)_2/TfOH/H_2O$ forms the fluorene, with the same palladium catalyst acting.[403]

Aryl aldehydes undergo a cross-coupling reaction with arylboronic acids in water to give ketones via a cascade process involving a dirhodium tetraacetate-phosphine catalyst, giving an initial (observable) alcohol product, which is then aerobically oxidized in a process that requires the presence of the water solvent.[404]

N-Trityl-prolinal undergoes a highly diastereoselective arylation by an arylboronic acid, using diethylzinc to effect a boron/zinc exchange reaction.[405] (de)

An enantioselective arylation of aldehydes has been used to develop syntheses of both enantiomers of 3-aryl phthalides.[406] (ee)

Addition of Other Organometallics, Including Grignards

Tridentate chiral amino diols catalyse the asymmetric alkylation of aryl aldehydes by methyllithium, with yields/*ee* up to 94/96%.[407] (ee)

A chiral dilithium bisphenoxide, (*R*)-Li_2–Ph_2–BINOL, catalyses the addition of lithium acetylides to aldehydes and ketones with yields/*ee* up to 99/97% in THF at −78 °C.[408] (ee)

A green approach to carrying out chemoselective additions of organometallics to ketones in air at room temperature employs deep eutectic solvents (DESs). A typical method mixes a quaternary ammonium salt with a hydrogen-bond donor that can form a complex with the halide anion of the salt: for example, choline chloride can form a

eutectic mixture in combination with benign substances such as glycerol, lactic acid, urea, or water. Both Grignard and organolithium examples are reported.[409]

Enantioselective addition of ethylmagnesium bromide to aldehydes has been effected using optically active helical poly[3-(9-alkylfluoren-9-yl)propylene oxide.[410]

Diastereoselective addition of organometallics to β,γ-unsaturated ketones has been achieved by chelation of the alkene to zinc(II): a modest *de* of 10% using ethylmagnesium bromide is raised to 98% using Et_2Zn/EtZnCl.[411] (*de*)

Chiral BINMOLs (binaphthol-methanols) are good catalysts for a challenging Grignard reaction, that is, the enantioselective addition of aryl magnesium bromides to aryl alkyl ketones to give chiral diaryl tertiary alcohols.[412] (*ee*)

Aryl Grignards add asymmetrically to β-sulfinyl enones, *p*-tol–*S(=O)–CH=CR^1–COR^2, essentially using the chiral sulfur centre as a remote auxiliary; desulfurization is then easily effected to give optically active *t*-allylic alcohols. A seven-membered magnesium chelate ring is proposed, with an aryl-stacking interaction between the *para*-tolyl of the enone and the aryl of the Grignard also likely to be playing a role.[413] (*de*) (*ee*)

A Grignard reaction of some carbohydrate aldehydes with benzylmagnesium chloride (or bromide) displays an unusual rearrangement of the benzyl carbinol products to *ortho*-tolylcarbinols.[414]

Reaction of adamantanethione with several Grignards (Me-, Bu-, and *t*-Bu-MgCl) shows no evidence of addition to the double bond, in contrast to the corresponding ketone. Instead, the thiol is formed, with traces of thioether and episulfide.[415]

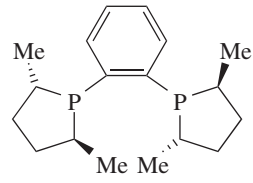
The mechanisms and green credentials of a range of direct addition of C–H bonds to aldehydes and imines have been reviewed. Although transition-metal catalysts are required, the methods espoused are more atom-efficient than organometallic processes such as Grignard.[416]

The Wittig and Related Reactions

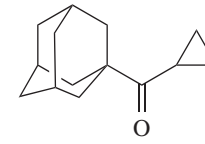
An experimental and computational study has shown up some of the limits of mechanistic investigations where the alternatives are very close in energy. Wittig reaction of *para*-methoxybenzaldehyde with a stabilized ylide, Ph_3P^+–CH=C(Me)–O^-, in refluxing THF has been studied via ^{13}C kinetic isotope effects and conventional calculations, and by molecular dynamics using a 53-molecule THF cluster. While the oxaphosphetane intermediate is well established, its formation via a betaine [Ph_3P^+–CH(Me)–CH(Ar)–O^- in this case] is largely discredited, with a concerted 2 + 2-cycloaddition (synchronous or asynchronous) being preferred. The isotope effects support cycloaddition involving the sequential transition states associated with separate C–C and P–O bond formations. The betaine structure, which lies between these two states, is essentially 'bypassed': its lifetime is too short for it to be a true intermediate, and it does not have enough time to equilibrate either the atomic motions or the solvation.[417]

Catalytic Wittig reactions of semi- and non-stabilized ylides have been reported, using a masked base: sodium *t*-butyl carbonate allows the slow release of NaO-^{t}Bu *in situ* in solution. The acidity of the ylide-forming proton was also tuned, and *E*-selectivity of up to >95:5 was achieved.[418]

The first enantioselective catalytic Wittig reaction has been reported, using as catalyst (*S*,*S*)-Me-DuPhos (**163**) at 5 mol% in one step.[419] (*ee*)



(**163**)



(**164**)

Multi-functional alkenes have been prepared from substituted acrylates and aldehydes, using a tributylphosphine-catalysed one-pot Wittig reaction, set up in such a way that the zwitterionic intermediate formed by the addition of PBu_3 to the acrylate undergoes proton transfer to give an ylide, which then reacts with aldehyde with complete *E*-selectivity.[420]

The reactivity of the Corey–Chaykovsky methylenation reagent dimethylsulfoxonium methylide [$Me_2S(=O)=CH_2$, DMSM] with bulky methyl ketones such as 1-adamantyl methyl ketone is significantly lowered as one would expect: the carbonyl carbon is less accessible. The base conditions employed facilitate enolate formation, and the more accessible α-carbon can now react to give a cyclopropyl alkoxide anion. A second DMSM can then intervene to give a cyclopropyl ketone (**164**).[421]

In a new approach to the Julia–Kocienski reaction, *gem*-difluoro-olefination of diaryl ketones and enolizable aldehydes has been achieved using difluoromethyl 2-pyridyl sulfone [2-Py–$S(=O)_2$–CHF_2], together with an amide base generated *in situ* from CsF and $(TMS)_3N$. Retro-aldol-type decomposition of the key intermediate can hamper this reaction, but the base chosen diminished undesired enolization of aliphatic aldehydes. The method can be chemoselective for multi-carbonyl substrates.[422]

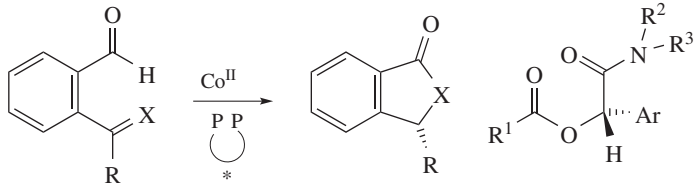
The salt potassium 2-pyridinyl sulfonyldifluoroacetate (2-Py–SO_2–CF_2–CO_2^- K^+) easily decarboxylates in polar solvents and can then react with aldehydes under Julia–Kociewski conditions. It is thus expected to become a useful *gem*-difluoro-olefination reagent.[423]

Hydroacylations

Appropriately *ortho*-substituted benzaldehydes (**165**; X = O or CH_2) undergo intramolecular hydroacylations to give phthalides or indanones (**166**), respectively, in fair to good yields and high *ee*s, using a chiral diphosphine, $CoCl_2$, and a reductant (In or Zn) in acetonitrile at 80 °C or 25 °C. The lack of a significant kinetic isotope effect for the *d*-aldehyde substrate suggests that C–H activation is not involved in the rate-limiting step.[424] (*ee*)

Aliphatic aldehydes (R^1CHO) have been cross-coupled with α-ketoamides, $ArCOCONR^2R^3$, to give α-acyloxyamides (**167**) in up to 96% *ee*. This highly atom-efficient intermolecular hydroacylation is catalysed by rhodium(I) liganded with a chiral ferrocenyl bisphosphine. Results of reaction rates and kinetic isotope effect

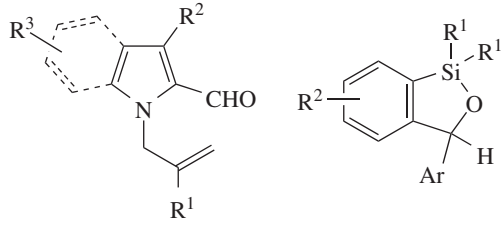
suggest a turnover-limiting oxidative addition step in which two rhodium centres – a rhodium–aldehyde complex and a rhodium–ketoamide complex – intercoordinate.[425] (ee)



(**165**) (**166**) (**167**)

DFT has been used to study the mechanisms of hydroacylation as catalysed by neutral and cationic rhodium complexes, including Wilkinson's catalyst.[426]

N-Allylindole- and *N*-allylpyrrole-2-carboxyaldehydes (**168**) undergo rhodium-catalysed intramolecular hydroacylation in up to 98/99% yield/*ee*. The formation of the six-membered ring unusually does not require chelation assistance.[427] (ee)



(**168**) (**169**)

Hydrosilylations

Outer-sphere ionic hydrosilylation catalysis has been reviewed.[428]

The commercially available complex $[Ru(p\text{-cymene})Cl_2]_2$ catalyses chemoselective hydrosilylation of aldehydes; potential intermediate hydride and bridged hydride species have been synthesized, and characterized by X-ray crystallography.[429]

Aldehydes undergo hydrosilylation by phenyldimethylsilane, $PhMe_2SiH$, in the presence of a triruthenium cluster complex. Addition of 1–2 equiv of dimethyl sulfide accelerates the process while completely suppressing reaction of ketones.[430]

An air-stable iridium–NHC complex catalyses enantioselective hydrosilylation so effectively that it works at ambient temperature.[431] (ee)

An NHC–copper(I) hydride catalyses hydrosilylation of ketones, with the kinetics being followed by *in situ* Fourier transform infrared (FT-IR) measurements. DFT studies support the monomeric catalyst as the active form, and explain the high activity of silanes of the form $(R^1O)_xR^2{}_{3-x}Si–H$.[432] (ee)

A bisphosphine-pincer ligand, which complexes iridium(III) hydride and iron(II) hydride systems, catalyses hydrosilylation of carbonyl compounds. A theoretical study has highlighted the important mechanistic differences between the two metals.[433]

Base-catalysed hydrosilylations of aldehydes, ketones, and esters by polymethylhydrosiloxane proceed via silicate species, and simple silanes (e.g. H_2SiMe_2, H_3SiMe) can be accessed by such routes. With careful control of silane equivalents, chemoselectivity between C=O types can be achieved.[434]

Benzaldehydes with arylsilyl groups at the *ortho*-position react to give 3-arylbenzoxasiloles (**169**), using an η^2-aldehyde nickel complex as an effective activator for the organosilane moiety. This generates a hypervalent silicate reactant. The reaction can also be carried out with vinyl or alkynyl groups on the silicon, instead of aryl. The formation of the η^2-aldehyde complex was directly confirmed by NMR, and the aryl transfer appears to be an *inter*molecular process.[435]

Addition of Nitrile-containing Species

Cyanoacetic acid has been used as a cyanomethylation reagent for the ketone carbonyl group of isatins: a bifunctional thiourea derived from L-proline catalyses decarboxylative cyanomethlation in good yield and *ee* in THF at ambient temperature.[436] (*ee*)

Alkylnitriles have been added directly to aldehydes to give β-hydroxy-nitriles. A transition-metal–NHC complex is an effective catalyst, overcoming the low acidity of alkylnitriles.[437] (*de*)

A facile synthesis of β-ketonitriles from aromatic aldehydes and diazoacetonitrile employs BF_3 as a catalyst, with the initial adduct undergoing a 1,2-hydride shift (and loss of N_2) to give product in up to 81% yield. Extension of the reaction to cinnamaldehydes gives access to useful γ,δ-unsaturated β-ketonitriles.[438]

The mechanism of the reaction of aldehydes with ethyl cyanoformate (EtOCOC≡N) to give cyanohydrin carbonates [R–CH(C≡N)–O–CO_2Et] has been studied kinetically for a range of tertiary amine catalysts. The rate shows a second-order dependence on amine, though this drops to first-order for hindered amines; the rate constants also correlate with the pK_a (of the conjugate acid). Order in ethyl cyanoformate and aldehyde are 1 and 0, respectively. The results are consistent with slow water attack on ethyl cyanoformate to generate cyanide, which attacks aldehyde (remaining steps being fast). The tertiary amine acts as a Brønsted base, hydrogen-bonding to water and activating it for attack. Presumably, two amine molecules can participate in the non-hindered cases.[439]

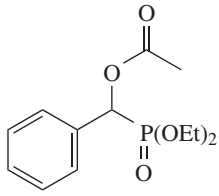
New chiral tridentate Schiff bases derived from camphor have been characterized by X-ray crystallography, and their complexes with titanium(IV) have been studied by NMR. In the latter form, they are good catalysts for cyanosilylation of a wide range of aldehyde types: one case gives >99% *ee* in the addition of TMSCN (trimethylsilyl cyanide) to cinnamaldehyde at 1% loading at −20 °C.[440] (*ee*)

Phosphonylation and Related Reactions

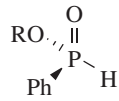
Acetoxyphosphonates (**170**) have been prepared in high yield and modest *ee* from aldehydes and diethyl acetylphosphonate using a chiral Lewis acid/achiral Lewis base/Brønsted base cooperative catalysis.[441] (*ee*)

A chiral squaramide catalyses the addition of diphenylphosphite to *para*-nitrobenzaldehyde with yield/*ee* up to 97/87%. Previously, this chiral Pudovik

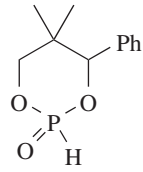
hydrophosphonylation was only effective for di*alkyl*phosphites. The reaction also works for aliphatic aldehydes.[442] (ee)



(**170**)



(**171**)



(**172**)

An optically pure *H*-phosphinate [**171**, R = (*L*)-menthyl] hydrophosphorylates ketones, giving *P*,*C*-stereogenic tertiary α-hydroxyphosphinates in up to 98% *de*. The diastereoselectivity was induced by a reversible conversion of a less stable product stereoisomer to a more stable one, a process confirmed by an aldehyde/ketone exchange reaction.[443] (de)

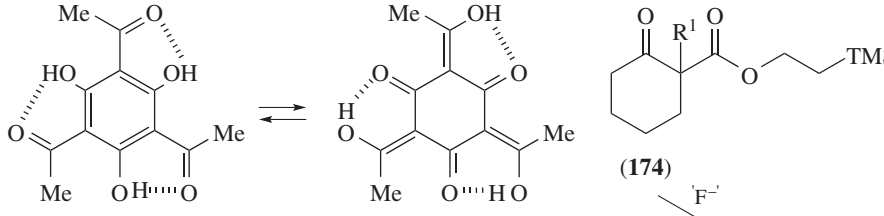
Chiral catalysts have previously been used to add P–H species to aldehydes or ketones, to give diastereopure P–C*–OH products. Now *P,C*-stereogenic phosphine oxides have been prepared by the addition of an (R_P)-phosphine oxide to aldehydes, using simple non-chiral bases, with up to >98% *de* (de_P/de_C) and 99% yields. Similarly, *P,C*-stereogenic α-hydroxyl phosphinates were prepared by the addition of an (R_P)-phosphinate to ketones. The reactions require only a mild base such as potassium carbonate in DMSO at ambient temperature, but do need extended reaction times: clear evidence is presented for thermodynamic control, with less stable diastereomers of the adduct converting to more stable ones over time, with associated increase in *de*.[444] (de)

A ^{13}C kinetic isotope effect has been measured for the Pudovik reaction of 2-nitrobenzaldehyde with 2*H*-2-oxo-5,5-dimethyl-4-phenyl-1,3,2-dioxaphosphorinane (**172**) in acetonitrile: P–C bond formation is less advanced than the π-bond cleavage of the aldehyde carbonyl.[445]

Enolization, Reactions of Enolates, and Related Reactions

A recent suggestion that 1,1′,1″-(2,4,6-trihydroxybenzene-1,3,5-triyl)triethanone (**173a**) might be tautomeric,[446a] forming asymmetric tautomers but in particular the symmetrical (**173b**), has been refuted.[446b] ^{13}C NMR shifts and deuterium isotope effects on them indicate that it is a strongly hydrogen-bonded benzene structure in both non-polar solvents such as chloroform and in donors like methanol, and these are confirmed by quantum mechanical calculations in such solvents and in the gas phase. Conventional UV–visible spectroscopic data also run counter to tautomerism but do suggest aggregation in methanol and acetonitrile. Structure (**173b**) would also be most surprising, given that exocyclic double bonds are typically not favoured in six-membered rings.

Tautomerism of pyridazin-3(2*H*)-one to pyridazin-3-ol has been studied by DFT: protic solvents are required to reduce the otherwise high activation energy.[447]



(**173a**) (**173b**)

(**174**) (**175**)

(TMS)ethyl ester 'protected enolates' (**174**) have been reported, where the problem of α-substitution has been overcome. A fluoride source generates an enolate (**175**), which alkylates easily using an allylic carbonate with palladium catalysis, in up to 96% *ee*.[448] (*de*) (*ee*)

Copper(I) iodide catalyses regio- and stereo-selective O-arylation of enolates by diaryliodonium salts such as $Ar_2I^+ {}^-OTf$.[449]

α-Substitutions

The role of hypervalent iodine reagents in the α-functionalization of carbonyl compounds has been reviewed (45 references), highlighting recent progress including chiral versions, but also identifying lacunae: high *ee*s are rare, and chiral versions of a wider range of such reagents need to be developed.[450] (*ee*)

Pyrrolidine acts as a simple, cheap, and efficient catalyst of α-deuteration of carbonyl compounds, with a wide range of carbonyl types tolerated, and up to 99% incorporation achieved, using D_2O as source.[451]

α-Branched cyclohexanones have been fluorinated in toluene at ambient temperature by Selectfluor [*N*-fluoro-*N*′-chloromethyl-DABCO $(BF_4)_2$]; yields are only fair, but *ee*s are up to 94%. Two chiral catalytic strategies are combined: a chiral anion phase-transfer cycle to active Selectfluor, and an enamine cycle to activate the ketone, using a protected amino acid organocatalyst. The latter system rarely activates α-branched ketones.[452] (*ee*)

DFT has been employed to develop a stereoselectivity model for the enamine-activated cinchona amine-catalysed α-fluorination of cyclic ketones: a seven-membered fluorine transfer cyclic TS has been identified, and its conformation determines enantioselection.[453] (*ee*)

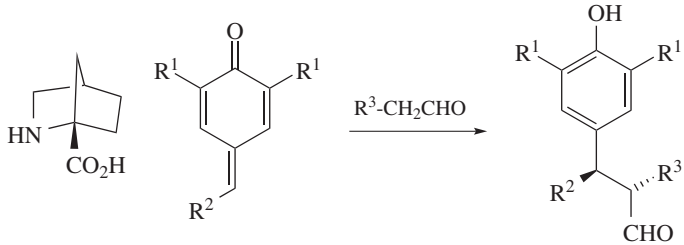
Chiral iron(III)–salan complexes catalyse α-fluorination and α-hydroxylation of β-keto esters and *N*-Boc oxindoles in high yield and *ee*.[454] (*ee*)

Diterpenoids give fair *ee* in the chlorination of β-ketoesters.[455] (*ee*)

Synthesis of α-bromocarbonyl compounds has been reviewed (130 references), covering 9 organic and 6 inorganic brominating agents.[456]

A new constrained proline (**176**) catalyses α-alkylation of α-branched aldehydes by benzyl bromides. Using the DYKAT (dynamic kinetic asymmetric transformation)

methodology, the α-alkylated aldehyde products bearing a quaternary stereocentre are formed in fair to good yield in up to 97% *ee*, using co-catalysis by a guanidine base and *para*-anisic acid in chloroform at 50 °C.[457] (ee)



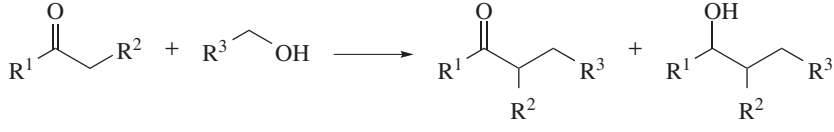
(**176**) (**177**) (**178**)

para-Quinone methides (**177**) participate in organocatalytic asymmetric alkylation of aldehydes via 1,6-conjugated addition of enamines, giving aromatic products (**178**) with two contiguous chiral centres. Using a diphenyl prolinol TMS ether with a 4-TIPSO substituent as catalyst, conversion/*de*/*ee* up to >95/81/99% were obtained. The reaction is favoured by $R^1 = t$-Bu, and its scope is enhanced by the ease of de-*tert*-butylation with aluminium trichloride.[458] (de) (ee)

Tryptophans have been prepared with yields/*de*/*ee* up to 99/76/96% by direct α-alkylation of *N*-protected α-amino aldehydes by 3-indolylmethanols via enamine catalysis using a thiourea with an *N*-(β-amine)-*N*′-(β′-alcohol) auxiliary. The aldehyde products can be reduced to 2-amino-3-(3′-indolyl)propan-2-ols by borohydride, without loss of *ee*.[459] (de) (ee)

Simple NHCs catalyse α-alkylations of ketones with primary alcohols in refluxing toluene, in the presence of KOH. Yields are highest for aryl methyl ketones reacting with aromatic primary alcohols.[460]

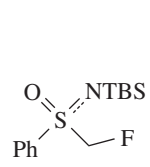
A catalyst-free dehydrative α-alkylation of ketones (**179**) has been achieved using alcohols (**180**): the green, selective, autocatalytic process yields a ketone (**181a**) or the corresponding alcohol (**181b**). If the 'wrong' product is obtained, it can be converted using a metal-free Meerwein–Ponndorf–Verley–Oppenauer-type redox process: for example, MPV reduction of (**181a**) with isopropanol yields (**181b**), plus acetone. The method requires 3 equiv of alcohol (**180**) and 1 equiv of NaOH, heated (neat) at 130 °C for 24 h under nitrogen; yields are up to 98%. The mechanism involves *in situ* generation of the aldehyde R^1–CHO, which undergoes aldol condensation. Controlled admission of air into the reaction boosts the (**181a**)/(**181b**) ratio.[461]



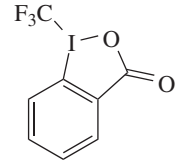
(**179**) (**180**) (**181a**) (**181b**)

Enamines of acyclic ketones undergo highly diastereo- and enantio-selective propargylic alkylation, catalysed by copper bearing a chiral *P*,*N*,*N*-tridentate ligand, effectively achieving α-propargylation of the ketone.[462] (de) (ee)

(*R*)-*N*-*t*-Butyldimethylsilyl-*S*-fluoromethyl-*S*-phenylsulfoximine (**182**) is readily prepared from the corresponding tosylate, via acidic detosylation, followed by reaction with *tert*-butyldimethylsilyl (TBS)-chloride in the presence of pyridine. It acts as a fluoromethylating agent of ketones in the presence of KHMDS (potassium hexamethyldisilazane), with yields/*de* up to 92/98%. The high *de* is ascribed to a DKR of the carbanion of (**182**), a mechanism that appears distinct from the corresponding *di*fluoromethylation, which has much lower *de*. The *de* of the latter is also further lowered by the presence of hexamethylphosphoramide (HMPA), not seen here.[463] (ee)



(**182**)



(**183**)

Togni's reagent [hypervalent iodine species (**183**)] has been used to effect copper(I)-catalysed trifluoromethylation of silyl enol ethers to give α-trifluoromethylketones. It acts as a source of [CF_3^+], and copper(I) reduces it to $CF_3\cdot$, which reacts with the silyl enol ether.[464] Compound (**183**) also facilitates C–H α-trifluoromethylation of a variety of α,β-unsaturated carbonyl compounds, *trans*-R^1–CH=CH–CO–G (G = aryl, alkyl, OR^2, SR^2, or NR^2R^3), again using copper(I) catalysis (under nitrogen); the R^1 group is *cis*- to the carbonyl in the product. Evidence for a similar radical route is described.[465]

While the Ruppert–Prakash reagent F_3C–TMS is frequently deployed as a CF_3^- equivalent, it can also serve to deliver TMS–CF_2^+: such a mode is activated by a strong Li$\cdots$F interaction. Lithium enolates have been directly α-siladifluoromethylated using this strategy. This umpolung methodology has been applied to lithium enolates of a variety of carbonyl types (ketone, ester, amide), and a diastereoselective version is also reported.[466] (ee)

Air-stable NHC–nickel(II) complexes efficiently catalyse α-arylation of acyclic ketones, apparently via a radical mechanism.[467]

Carbonyl compounds have been α-functionalized with a range of nucleophiles (N, O, and even C), using an umpolung approach with hypervalent iodine reagents. For example, the reaction of acetophenone with $ClSi(NEt_2)Me_2$ in the presence of base and iodide produces a tethered silyl enol ether Ph–C(=CH_2)–$OSi(NEt_2)Me_2$. Using (diacetoxyiodo)benzene, $PhI(OAc)_2$, the electrophilic enolate structure reacts with the nitrogen to give the α-amino product $PhCOCH_2NEt_2$ in 94% yield in DCM at ambient temperature in a few hours. An enantioselective version is also reported, using chiral iodine reagents.[468] (ee)

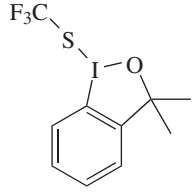
Asymmetric α-amination of β-ketocarbonyls has been achieved using *N*-hydroxycarbamates as nitrogen sources: the approach merges aerobic oxidation with enamine catalysis, using copper(I) and a simple amine (*S*)-*t*-Bu–CH(NH_2)–CH_2NEt_2.[469] (ee)

A computational study has probed the origin of the high enantio- and *N*/*O*-selectivity observed in hydroxyamination of 1,3-dicarbonyls, catalysed by a primary–tertiary diamine derived from *t*-leucine. The reaction, a type of nitroso-aldol, proceeds via *in situ* formed nitrosocarbonyls, and the calculations indicate that the high *N*-selectivity can be ascribed to a bidentate hydrogen-bonding interaction between the tertiary N^+–H and the nitrosocarbonyl group. The enantioselectivity was determined by Si-facial attack on the (*E*)- and (*Z*)-enamines in a Curtin–Hammett-type manner, with this effect being reinforced by the hydrogen bonds.[470] (ee)

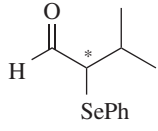
A new nitrosation protocol for 1,3-diketones has been tested on 3-ethyl- and 3-methylpentan-2,4-dione. Formerly, the ketone was added last to nitrous acid solution. In this case, ketone and sodium nitrite were co-dissolved in an alkaline medium, to generate two anions (enolate and nitrite), and the reaction is then initiated with acid. A range of conditions corresponding to conventional and stopped-flow UV–visible spectrophotometry were tested, to confirm that decomposition of nitrous acid was negligible on the nitrosation timescale, and to also compare data with the former protocol.[471]

Asymmetric α-hydrophosphonylation of isatins has been achieved with copper catalysis and a new recyclable fluorous bis(oxazoline) ligand, with yields/*ee* up to 91/92%.[472] (ee)

The hypervalent iodine reagent (**184**) has been used to trifluoromethylthiolate β-ketoesters;[473a] copper(II) catalyses the reaction, with a chiral 'boxmi' ligand (a bisoxazoline 'pincer') rendering it highly enantioselective, with *ee* up to 96%.[473b] The ketone can then be selectively reacted with Grignards, giving α-SCF_3-β-hydroxyesters with *de* >95%. (de) (ee) (de) (ee)



(**184**)



(**185**)

α-Selenylation of aldehydes, such as that of 3-methylbutanal by *N*-phenylselenylphthalimide to give (**185**), is readily performed using the 'general organocatalyst' diphenylprolinol silyl ether, and the high *ee*s are typically rationalized in terms of enamine catalysis, with one face of the prolinol being effectively blocked by the CPh_2OTMS group. However, it is then hard to explain the solvent-induced *ee* inversions observed in some cases, with hexanes and toluene giving high (*S*)-yields, chloroform giving a slight (*R*)-preference, and with increasing amounts of (*R*)-product on going from THF to DCM to acetonitrile. A detailed kinetic, NMR, and labelling investigation supports the carbon–selenium bond-forming step as being highly selective, but then shows this being eroded by the competition between downstream intermediates, reacting at different rates to form opposite enantiomeric products.[474] (ee)

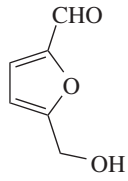
Oxidation and Reduction of Carbonyl Compounds

For other redox reports, see also 'Reactions of Glucosides' and 'Reduction and Oxidation of Imines' sections.

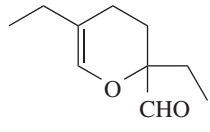
Oxidation of Aldehydes to Acids

The kinetics and mechanisms of the oxidation of 2-furfural in aqueous acetic/hydrochloric acid mixtures have been compared for *N*-bromo- and *N*-chloro-nicotinamide as oxidants. The reactive oxidizing species are proposed to be HOBr and Cl_2, respectively.[475]

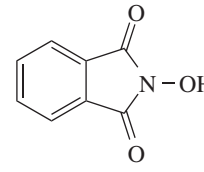
Copper(II) nitrate promotes aerobic oxidation of 5-hydroxymethylfurfural (**186**) to give 2,5-diformylfuran, using $VOSO_4$ catalysis in acetonitrile. An active V^{5+} species is proposed, with NO_x co-forming.[476]



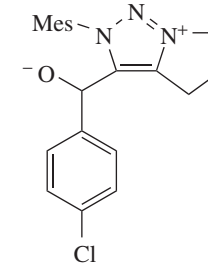
(**186**)



(**187**)



(**188**)



(**189**)

Charge-tagged NHCs have been used for mass spectral detection of intermediates in the NHC-catalysed aerobic oxidation of aldehydes: the technique is particularly useful for studying the otherwise neutral carbene species.[477]

Six aliphatic aldehydes have been studied in their reaction with quinolinium chlorochromate in DMSO solution. Deuterated acetaldehyde (MeCDO) exhibited a primary kinetic isotope effect of 5.78 at 298 K. Solvent effects were also investigated.[478]

The kinetics and mechanism of the oxidation of benzaldehyde by quinolinium chlorochromate in sulfuric acid in the presence of CTAB have been studied.[479]

The kinetics of oxidation of salicylaldehyde by *N*-bromonicotinamide have been measured in aqueous acetic/perchloric acid mixtures, with the conjugate acid of the oxidant postulated as the reactive oxidizing species.[480]

Kinetics of oxidation of benzaldehyde by pyridinium fluorochromate in DMF in the presence of *para*-toluene sulfonic acid were studied from 298 to 328 K: first-order dependence was seen for the substrate, oxidant, and proton.[481]

The kinetics of oxidation of a wide range of positionally substituted benzaldehydes by benzimidazolium dichromate in DMSO have been studied in acid,[482] as well as that of *para*-nitrobenzaldehyde by potassium bromate in perchloric acid.[483]

Cannizzaro disproportionation of 2,5-diethyl-3,4-dihydro-2*H*-pyran-2-carbaldehyde (**187**) in ethanol was studied by quantum chemical modelling, with a hydride-transfer mechanism confirmed.[484]

The use of aldehyde autoxidation as a 'co-oxidation process' has been reviewed, focussing on the use of *N*-hydroxyphthalimide (**188**) catalyst, under mild aerobic conditions. Recent results have used this method for selective epoxidation of olefins and for selective oxidation of alkylaromatics to the corresponding hydroperoxides. Kinetic, activation, and solvent studies support a free-radical mechanism with *in situ* generation of the phthalimido-*N*-oxyl (PINO) radical.[485]

Several half-sandwich complexes of iridium, rhodium, and ruthenium catalyse the conversion of aldehydes in water to carboxylic acids. With some, hydrogen is released (i.e. the 'aldehyde–water shift' reaction), while for others a second molecule of aldehyde intervenes (i.e. aldehyde disproportionation).[486]

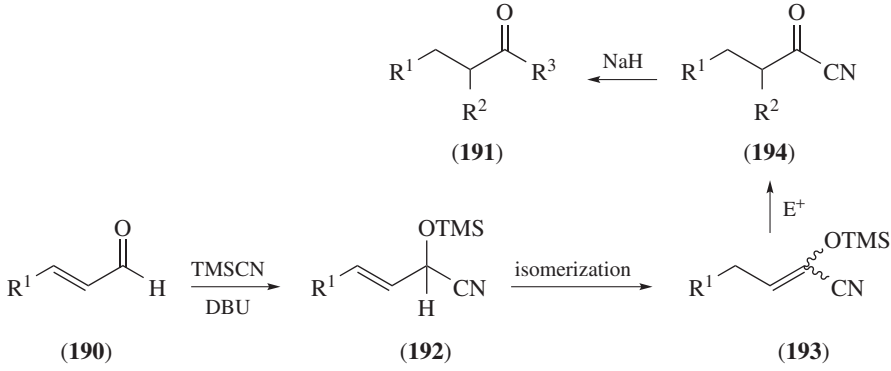
Oxidation of Aldehydes to Esters, Amides, and Related Functional Groups

Tetraphenylphosphonium bromide, under oxidative NHC catalysis, converts aromatic aldehydes directly to phenyl esters. Neither phenol nor benzoic acid is detectible, so the authors propose that the Breslow intermediate – formed from aldehyde and NHC – undergoes a concerted reaction with molecular oxygen and tetraphenylphosphonium bromide, with subsequent loss of triphenylphosphine oxide.[487]

Oxidative esterification of araldehydes using organobromides has been carried out with an NHC catalyst electrogenerated by cathodic reduction of $BMIm^+$ BF_4^- IL.[488]

1,2,3-Triazolyl NHCs catalyse oxidative esterification of aldehydes. In the case of *para*-chlorobenzaldehyde as substrate, an initial carbene–aldehyde adduct (**189**) was isolated and characterized by X-ray crystallography.[489]

A highly versatile redox transformation of enals (**190**) into carboxylic acid derivatives (**191**) uses TMSCN/DBU to generate a cyanohydrin TMS ether (**192**), which isomerizes to the more stable ene-nitrile (**193**). Protonation (or use of another electrophile) gives an acyl cyanide (**194**), and introduction of a nucleophile such as methanol or ammonia gives an ester or amide (**191**; $R^3 = OMe$ or NH_2).[490]



2-Oxoaldehydes have been oxidatively amidated – without the use of metals – to give α-ketoamides. The DMSO-promoted reaction of a cyclic 2° amine (pyrrolidine,

piperidine, or morpholine) gives the ketoamide with DMS as a by-product, taking 1–4 h at 80 °C. The C(1)-oxygen in the product is derived from DMSO (as confirmed by an ^{18}O-label), and it was proposed that an iminium ion intermediate (formed from the substrate and 2° amine) is attacked by DMSO. Aerobic oxidation was ruled out. Acetophenones can be substituted as substrates, using I_2–DMSO to generate the requisite aryl glyoxal (Ar–CO–CHO) *in situ*, giving α-ketoamide in a one-pot process.[491]

A kinetic study of the oxidation of butanone, and of cyclohexanone, by thallium(III) in perchloric acid suggests that enolization is *not* rate-determining, and that the ketone is the reacting tautomer.[492]

An inexpensive, selective, and widely applicable conversion of ketones to esters via cleavage of a C–C bond in air has been reported. Ketones, R^1–CO–alkyl (R^1 = Ar, alkenyl), react with alcohols, R^2–OH, under the influence of CuBr–Py catalyst in air, to give esters, R^1–CO_2R^2 in up to 90% yield. Even the otherwise inactive aryl long-chain-alkyl ketones react, and on the alcohol side, a huge variety is tolerated: 1° and 2°, chiral alcohols (with retention), electron-deficient phenols, bulky sterols, and so on. ^{18}O-labelling studies indicate that oxygenation occurs during the process.[493] (*ee*)

Ketones, ArCOR, have been converted to amides, $ArCONH_2$, by a copper-catalysed aerobic oxidative C–C bond cleavage. Using sodium azide as nitrogen source, a CuI/TEMPO/DMF/H_2O system gives high yields at ~90 °C in less than a day, in air. The utility of the method has been extended to substituted aromatics (including *ortho*-cases, and heteroaromatics), and – on the cleavage side – to sterically hindered alkyl groups. Potential intermediates related to reactants such as ArCHO or ketoacids do not catalyse the process or convert to product, suggesting that the ketone reacts first with the azide nucleophile, followed by oxidative processes. The alkyl group appears to be lost as an aldehyde, which sometimes undergoes a Schmidt reaction to give a nitrile.[494]

The oxidation of 1,4-naphthohydroquinone has been studied in aqueous solution (pH 6.5–7.5) with and without nanomolar copper(II). Mechanisms for auto- and copper-catalysis are proposed.[495]

The mechanism of organocatalytic epoxidation of α,β-unsaturated aldehydes by hydrogen peroxide using diarylprolinol TMS ether catalysts has been investigated in a kinetic study. Unusually, the reaction rate increased as the conversion increased. The hydrate/peroxy hydrate of the product acts as a phase-transfer catalyst, and a new protocol has been developed, in which an achiral additive (chloral hydrate) allows catalyst loading to be decreased while maintaining selectivity.[496] (*de*) (*ee*)

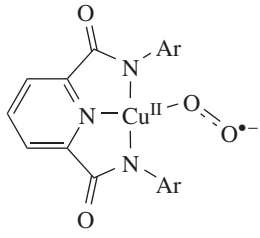
Spiroepoxyoxindoles have been prepared with yields/*de*/*ee* up to 99/90/93%, from isatins; a camphor-derived sulfur ylide is employed.[497] (*de*) (*ee*)

Alkyl and aryl enals, R–CH=CH–CHO, undergo an NHC-catalysed β-hydroxylation via transfer of an oxygen atom from electron-deficient nitroarenes, followed by trapping of the resultant acyl azolium by the solvent (methanol), to give the β-hydroxy ester product R–*CH(OH)–CH_2–CO_2Me. Evidence for a mechanism in which the reaction is initiated by SET, followed by radical recombination, is discussed. Such an SET mechanism would be a significant departure for NHC catalysis. An enantioselective version is also reported.[498] (*ee*)

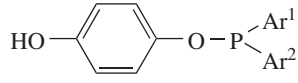
Baeyer–Villiger Oxidation

Transition-metal catalysis of Baeyer–Villiger (BV) oxidation of cyclic ketones in aqueous hydrogen peroxide, to give lactones, has been investigated for the oxides MoO_3, WO_3, TiO_2, Fe_2O_3, Co_3O_4, ZnO, and ZrO_2. The first two give appreciably higher activity, which is ascribed to their strong interactions with H_2O_2.[499]

Tolman's copper(II)–superoxide complex (**195**, Ar = 2,6-diisopropylphenyl) is a very reactive nucleophilic oxidant, proving to be an efficient aldehyde deformylating agent, capable of BV oxidation of electron-rich aldehydes. This and other reactions promoted by the complex have been studied kinetically by UV and NMR spectroscopy, GC–MS, and by ^{18}O-labelling.[500]



(**195**)



(**196**)

Following the development and screening of a peptide catalyst library, a regio- and enantio-selective BV oxidation of cyclic ketones bearing amide, urea, or sulfonamide groups has been developed. Both selectivities can be controlled by changing the catalyst, and both appear to depend on catalyst–substrate hydrogen bonding. These peptide catalysts also overturn the regioselectivity seen with *meta*-chloroperbenzoic acid, suggesting a more general route towards intrinsically disfavoured BV products.[501] (*ee*)

Miscellaneous Oxidative Processes

A DFT investigation of the Algar–Flynn–Oyamada oxidative cyclization of chalcone to give 3-hydroxyflavone supports the belief that epoxide intermediates are not involved and solvation effects are not critical.[502]

Tetra-substituted furans have been prepared by palladium-catalysed oxidative cross-coupling of allenyl ketones with organoboronic acids; palladium–carbene migratory insertion is proposed as the key step.[503]

Alkynylbenziodoxolones (**79**) react with α-unsubstituted aldehydes, R^1–CH_2CHO, to give ynones, R^1–CO–C≡C–R^2, using pyrrolidine and a gold(III) catalyst, in the presence of oxygen. This reaction involves C–C cleavage through aerobic oxidation (the methylene is excised), and proceeds via the trisubstituted allenyl aldehyde, R^2-CH=C=C(R^1)CHO.[504]

Reduction Reactions

DFT has been used to probe the mechanism of Wolff–Kishner reduction in ethylene glycol solvent, using a model ketone, hydrazine, and a water octamer, with and without a base catalyst. The ketone → hydrazone → diimine route fails to extrude N_2 if no base is present. The base-catalysed routes are slightly different for the model aliphatic substrate (acetone) compared to that for acetophenone: in the former, N_2 extrusion and C–H bond formation are concerted, while the latter involves a carbanionic intermediate.[505]

The mechanism of a previously reported transfer hydrogenation by a Cp^*–Rh(III)-bisamide[506a] has been studied by DFT. A series of bisamides have been ranked: the best has an optimal balance of electrophilic metal centre and nucleophilic NH group.[506b]

Acceptorless dehydrogenation of alcohols has been carried out with inexpensive iron catalysts bearing a *PNP*-pincer ligand, with some chemoselectivity.[507]

An iridium(III)–Cp^* catalyst allows acceptorless alcoholic dehydrogenation of aldehydes and ketones, but without discrimination. Further coordination with 6,6′-dihydroxy-2,2′-bipyridine affords selective oxidation of cyclic α,β-unsaturated alcohols over benzylic and aliphatic alcohols, as demonstrated on the A ring of glucocorticoids.[508]

Stereoselective Reduction Reactions

Transfer hydrogenation catalysed by transition-metal complexes has been reviewed (95 references), including tri-, tetra-, and poly-dentate ligands, and enantioselective cases.[509] (*ee*)

A review describes diastereo- and enantio-selective synthesis of *anti*-β-hydroxy-α-amino acid esters by hydrogenation of the corresponding α-amino-β-keto ester hydrochlorides, using transition-metal catalysts complexed with axially chiral bisphosphines. A range of metals were successful (Ru, Rh, Ir, and Ni) in the DKR process employed.[510] (*de*) (*ee*)

A diaryl phosphine, Ar^1Ar^2PH, reacts with a benzoquinone in the presence of a chiral palladium catalyst to give a 4-hydroxyphenyl diaryl phosphinite (**196**) in 98% *ee*, where at least one of the aryls is bulky. Ph_2PH gives the diphosphinite. The products can be converted to phosphinates (using H_2O_2) or sulfides (using S_8).[511] (*ee*)

The mechanism of the catalytic hydrogenation of acetophenone by chiral [RuX_2(diphosphine)-(1,2-diamine)] catalysts has been revised following a DFT study. The reaction carried out with *t*-BuOH/*i*-PrOH had previously been assigned either a six-membered pericyclic TS or a multi-bond concerted TS, but computation favours an outer-sphere hydride transfer to give an ion pair, with the TS both rate- and enantio-determining. The active catalytic complex contains a chiral pocket stabilized by neutral and ionic hydrogen bonding, cation–π interactions, and aryl stacking interactions.[512] (*ee*)

α-Keto esters have been enantio- and chemo-selectively reduced with catecholborane using a BINOL–phosphoric acid/Mg(*n*-Bu)$_2$ catalyst system.[513] (*ee*)

Catalytic asymmetric hydrogenation of ketones has been reviewed (37 references), highlighting ruthenium(II) advances, moves to other precious metals, and more recently to cheaper ones: Fe, Co, Ni, and Cu. Six main classes of *P*- and *N*-ligands are also covered.[514] (*ee*)

A 22-membered *P*,*N*,*N*,*P*,*N*,*N*-chiral macrocycle gives *ee* up to 99% for the hydrogenation of a range of ketones and α-ketoesters using the relatively cheap $Fe_3(CO)_{12}$ as catalyst. Working at <50 atm H_2 in the range 45–65 °C, the *ee* equals or surpasses that of many ruthenium or rhodium species. Some evidence suggests a heterogenous mechanism, with discrete iron particles having their environment modified by the auxiliary.[515] (*ee*)

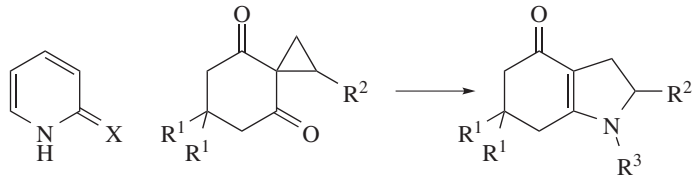
Enones that are sterically congested at the β-position are hydrogenated at the carbonyl group using ruthenium complexed with an achiral diphosphane and a chiral diamine; up to 97% *ee* was achieved, with turnover number of up to 50 000.[516] (*ee*)

The stereoselectivity of borohydride reduction of α,β-epoxy and α,β-aziridinyl ketones is enhanced by the addition of calcium triflate. In cases with no or modest *de* without Lewis acid, $Ca(OTf)_2$ typically gives *anti*-selectivity often equal to or higher than found for the more expensive cerium trichloride.[517] (*de*)

Other Reactions

An unexpected 2:1 reaction of 1,3-dicarbonyls with aldehydes gives spiro-dihydrofuran and cyclopropane derivatives.[518]

DFT calculations indicate that pyridine-2(1*H*)-one (**197**; X = O) can be made from the reaction of cobaltacyclopentadiene with isocyanide; isothiocyanate gives the corresponding thione (**197**; X = S). Hybrid DFT was used to investigate the reaction via singlet and triplet TSs and found both are involved in a two-state mechanism.[519]



(**197**) (**198**) (**199**)

In a novel set of transformations, propargylic amino *N*-oxides have been converted to enones (with good *E*/*Z*-ratios) and to acyloxy ketones using catalysis by silver. *In situ* generated isoxazolinium intermediates have been implicated.[520]

A bifunctional thiourea derived from rosin catalyses direct asymmetric tandem reaction of α-nitro ketones with β,γ-unsaturated α-ketoesters, apparently via a new mechanism involving an inverse-electron-demand Diels–Alder and a retro-Henry reaction.[521] (*ee*)

A DFT examination of solvent effects on the kinetics of Diels–Alder reaction of *N*,*N*-dimethylamino-3-(trimethylsilyl)butadiene with *para*-methoxybenzaldehyde has identified specific hydrogen-bonding effects promoting a highly asynchronous process.[522]

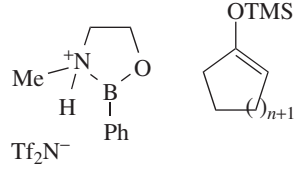
An unusual bis(diguanidinate) ligand has been formed via nucleophilic attack of a guanidate on a carbodiimide.[523]

The kinetics of gas-phase decarbonylation of α-methyl-*trans*-cinnamaldehyde and *E*-2-methylpentenal have been measured around 400 °C, at reduced pressure.[524]

Appropriately substituted aryl alkyl ketones, Ar–CO–CH_2–EWG, undergo a most unusual reaction with TMS-azide, giving carbamoyl azides, Ar–NHCO–N_3. This double C–C cleavage – in which the carbonyl is retained, one nitrogen is inserted, and another substitutes for the alkyl group – is catalysed by ceric ammonium nitrate (CAN). Using 20 mol% CAN, 1 equiv of TEMPO, under O_2 at 60 °C, gives good yields for a wide range of EWG: COR, CO_2R, CONHAr, NO_2, CN, $P(OEt)_2$, and so on, with similar substituent tolerance in the aryl ring, albeit with a preference for donating groups. Evidence for an oxyamination intermediate is presented. The carbamoyl azide products are very useful, providing one-step access to amines, amides, urethanes, and ureas, and a two-step route to amido-tetrazole derivatives.[525]

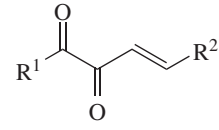
Cyclohexane-1,3-dione-2-spirocyclopropanes (**198**) react with 1° amines (R^3–NH_2) at ambient temperature (without additives) in a ring-opening cyclization to give 2-substituted tetrahydroindol-4-ones (**199**) in up to 98% yield. The regioselective process does not give any 3-substituted product, and bicycles (**199**) are easily converted to 4-hydroxyindoles.[526]

Aryl alkyl ketones are converted to (*Z*)-silyl enol ethers using TMS-diazomethane with a highly stereoselective oxazaborolidinium ion (**200**). The same system converts cycloalkanones to ring-expanded silyl enol ethers (**201**), with both reactions effective in DCM at −78 °C. Several useful onward reactions of the silyl enol ethers are described.[527] (*de*)



(**200**)

(**201**)



(**202**)

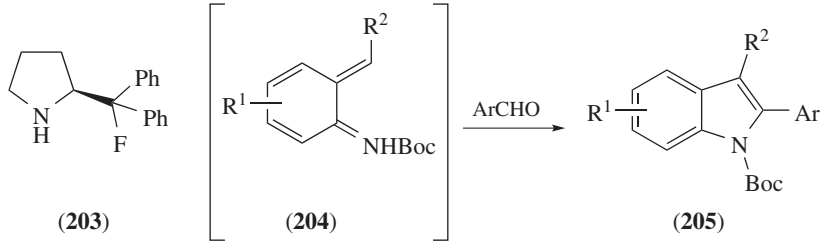
An unexpected synthesis of *E*-1,2-dicarbonyl-3-enes (**202**) from glyoxals (R^1–CO–CHO) and terminal alkynes (R^2–C≡CH) employs a copper(I) catalyst: it represents a formal hydroacylation of a 1-alkyne.[528]

1,2-Diazepines have been prepared via regio- and enantio-selective formal [4 + 3] annulations between enals and azoalkenes formed *in situ* from an α-chloro hydrazone, using a chiral NHC, delivering good yields and often 99% *ee*. Modification of the NHC can switch the reaction to a formal [4 + 1] annulation to give pyrazoles. Careful control of the NHC's steric and electronic properties thus gives control of the reaction path, favouring the enal's homo-enolate over its acyl-anion reactivity. Thus different products have been selectively generated from identical substrates via catalyst rather than substrate control.[529] (*ee*)

Copper(I) catalyses a decarboxylative coupling of a propiolic acid, a 2° amine, and an aldehyde to give a propargylamine.[530]

Cyclic α-diones undergo a one-pot benzannulation with a phosphine-3-alkyl allenoate zwitterion, the latter being generated from an appropriate allene, R^1–CH=C=CH–CO_2R^2.[531]

A fluorine-iminium ion *gauche* effect has been exploited in the aziridination of cyclic enals (with a wide range of ring sizes), achieving *de*/*ee*s of up to 95/99%, using (*S*)-2-(fluorodiphenylmethyl)pyrrolidine (**203**).[532]



(**203**) (**204**) (**205**)

Protected 2-arylindoles (**204**) have been prepared from the appropriate *ortho*-amino benzyl chloride via a highly reactive aza-*ortho*-quinone methide (**205**), which is then intercepted by a suitable benzaldehyde. NHC catalysis obviates the need for transition-metal species.[533]

5-Oxo-1-alkynes have been hydrated to give methyl ketones via a one-pot oxy-iodination/reduction sequence, which uses iodine and is considerably greener than transition-metal catalysis. The 5-keto group is proposed to participate via a 5-*exo*-dig cyclization.[534]

Cyclization of 1-trifluoromethyl-β-dicarbonyls with azides to form 1,2,3-triazoles has been studied by computation: a step-wise mechanism is proposed.[535]

Several reports deal with the activation of C–H bonds, particularly sp^3 cases such as methyl on an aromatic ring, and also sp^2, such as aldehyde-H; some involve activation by *ortho*-substituents, and some have been covered previously under specific functional groups: see in particular 'Insertion Reactions of Imines' and 'Oximes, Oxime Ethers, and Oxime Esters' section. Transition-metal-catalysed, ketone-directed *ortho*-C–H functionalization reactions have been reviewed (34 references), covering Ru-, Rh-, Pd-, and Ir-catalysed processes forming C–C and C–X bonds (X = O, N, Cl, Br, and I) over the last 20 years.[536]

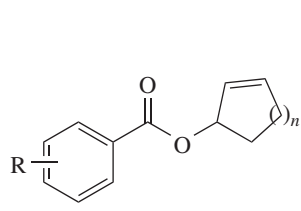
C(sp^3)–H bond functionalization of methyl azaarenes with nucleophilic addition to aldehydes has been carried out using an acid IL, [Hmim][H_2PO_4], and methylimidazolium dihydrogen phosphate. For example, *para*-nitrobenzaldehyde reacts with 2-methylpyridine to give a benzylic alcohol, O_2N–C_6H_4–CH(OH)–CH_2–2-Py. Using 1 equiv of the IL and refluxing water/dioxane, 75% yield is obtained in a day. The aldehyde typically needs an electron-withdrawing substituent (aza-substitution qualifies), while the methyl donor may be an appropriately substituted pyridine, quinoline, or pyrazine. In scoping out the transformation, 1,4-phthalaldehyde only reacted at one formyl group, and the aldehyde does not even have to be aromatic: OHC–CO_2Et reacts as well. Di- and tri-methylheteroaromatics typically react at one methyl only, and 4-methylpyridine does not react. The dihydrogen phosphate anion is likely to carry much of the catalysis, tautomerizing the arene to the enamine form, and also activating the aldehyde by hydrogen bonding.[537]

Bromo- and iodo-difluoromethyl ketones have been prepared from aldehydes using TMS–CF_3X reagents (X = Br or I) in refluxing propionitrile in the presence of Bu_4NX and LiX salts. Evidence is presented for difluorocarbene as an intermediate, with *X*-attack generating a short-lived halodifluorocarbanion as nucleophile, boosted (up to a point) by high concentrations of Bu_4NX. Lithium cation presumably activates the carbonyl.[538]

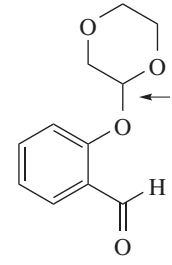
N-Methyl-3-acylindoles have been prepared from *N*-methylindole via palladium(II)-catalysed oxidative C–H bond coupling with benzaldehydes, using *t*-butyl hydroperoxide as oxidant.[539]

Benzimidazoles and aldehydes undergo direct cross-dehydrogenative coupling to give *N*-acylbenzimidazoles using di-*t*-butyl peroxide as oxidant, and no metals. While radicals appear to be involved (TEMPO traps an acyl radical), direct combination of acyl and benzimidazolyl radicals was ruled out by control experiments. Rather, it appears that a *t*-butoxy radical oxidizes the acyl radical to the acyl cation, which is then attacked by the benzimidazole reactant (with proton loss from nitrogen). The process works for aryl, alkenyl, and alkyl aldehydes, and tolerates many functional groups in both reactants.[540]

A dramatic C(sp^3)–H bond activation has been described, in which copper(II) acetate as catalyst and *t*-butyl hydroperoxide as oxidant generate cycloallyl esters (**206**) from benzaldehydes and cycloalkanes. Four C–H bonds are activated: three on adjacent carbons of the cycloalkane, plus the aldehydic C(sp^2)–H. Interesting control experiments have helped to scope out the mechanism: radical traps divert the reaction, and cycloalkanols or cycloalkyl esters are not intermediates, but cycloalkenes are. Using d_{12}-cyclohexane, a kinetic isotope effect of $k_H/k_D = 5.25$ was recorded.[541]



(**206**)



(**207**)

A range of transition-metal-catalysed direct functionalizations of β-C(sp^3)–H bonds of carbonyl compounds have been reviewed, including β-amination of alkyl ketones, β-arylation of aldehydes, ketones, and esters, and β-aldol coupling of cyclic ketones.[542]

Oxidative coupling of salicylaldehydes with cyclic ethers by $Fe_2(CO)_9$/*t*-butyl hydroperoxide results in selective C–O bond formation (**207**, arrowed, from dioxane), via direct α-C–H bond activation in the ether. Neither the transition metal nor the oxidant nor their combination affects the aldehyde group despite the conditions (aqueous medium/110 °C/15–90 min). The reaction works for ethers such as THF and dimethoxyethane: in each case, the product is an acetal.[543]

References

[1] Miyazawa, M., Eizawa, T., Yoshihara, S., Hatanaka, A., Yokoyama, H., and Hirai, Y., *Tetrahedron Lett.*, **55**, 753 (2014).
[2] Lai, J., Du, W., Tian, L., Zhao, C., She, X., and Tang, S., *Org. Lett.*, **16**, 4396 (2014).
[3] Paioti, P. H. S., Ketcham, J. M., and Aponick, A., *Org. Lett.*, **16**, 5320 (2014).
[4] Jiménez-Osés, G., Aydillo, C., Busto, J. H., Zurbano, M. M., Peregrina, J. M., and Avenoza, A., *J. Org. Chem.*, **79**, 2556 (2014).
[5] Meng, S.-S., Liang, Y., Cao, K.-S., Zou, L., Lin, X.-B., Yang, H., Houk, K. N., and Zheng, W.-H., *J. Am. Chem. Soc.*, **136**, 12249 (2014).
[6] Sheng, Y. and Leszczynski, J., *Struct. Chem.*, **25**, 667 (2014).
[7] Yin, Z., Zhang, J., Wu, J., Green, R., Li, S., and Zheng, S., *Org. Biomol. Chem.*, **12**, 2854 (2014).
[8] Maziarz, E. and Furman, B., *Tetrahedron*, **70**, 1651 (2014).
[9] Al-Maksoud, W., Menuel, S., Jahjah, M., Monflier, E., Pinel, C., and Djakovitch, L., *Appl. Catal. A-Gen.*, **469**, 250 (2014).
[10] Korbad, B. L. and Lee, S.-H., *Eur. J. Org. Chem.*, **2014**, 5089.
[11] Michalska, M., Songis, O., Taillier, C., Bew, S. P., and Dalla, V., *Adv. Synth. Catal.*, **356**, 2040 (2014).
[12] Lavinda, O., Tran, V. T., and Woerpel, K. A., *Org. Biomol. Chem.*, **12**, 7083 (2014).
[13] Prévost, M., Dostie, S., Waltz, M.-E., and Guindon, Y., *J. Org. Chem.*, **79**, 10504 (2014).
[14] Shenbagam, K. and Mathiyalagan, N., *Orient. J. Chem.*, **29**, 747 (2013).
[15] Juliá-Hernández, F., Arcas, A., and Vicente, J., *Tetrahedron Lett.*, **55**, 1141 (2014).
[16] (a) Breslow, R., *Tetrahedron Lett.*, **1**, 22 (1959); (b) Ricardo, A., Frye, F., Carrigan, M. A., Tipton, J. D., Powell, D. H. and Benner, S. A., *J. Org. Chem.*, **71**, 9503 (2006); (c) Appayee, C. and Breslow, R., *J. Am. Chem. Soc.*, **136**, 3720 (2014).
[17] Frihed, T. G., Pedersen, C. M., and Bols, M., *Eur. J. Org. Chem.*, **2014**, 7924.
[18] Popik, O., Pasternak-Suder, M., Leśniak, K., Jawiczuk, M., Górecki, M., Frelek, J., and Mlynarski, J., *J. Org. Chem.*, **79**, 5728 (2014).
[19] Jongkees, S. A. K. and Withers, S. G., *Acc. Chem. Res.*, **47**, 226 (2014).
[20] Fan, Q.-H., Striegler, S., Langston, R. G., and Barnett, J. D., *Org. Biomol. Chem.*, **12**, 2792 (2014).
[21] Hosoya, T., Takano, T., Kosma, P., and Rosenau, T., *J. Org. Chem.*, **79**, 7889 (2014).
[22] Mushrif, S. H., Varghese, J. J., and Vlachos, D. G., *Phys. Chem. Chem. Phys.*, **16**, 19564 (2014).
[23] Satoh, H. and Nukada, T., *Trends Glycosci. Glycotech.*, **26**, 11 (2014).
[24] Yasomanee, J. P. and Demchenko, A. V., *Angew. Chem. Int. Ed.*, **53**, 10453 (2014).
[25] Kendale, J. C., Valentín, E. M., and Woerpel, K. A., *Org. Lett.*, **16**, 3684 (2014).
[26] Cox, D. J., Singh, G. P., Watson, A. J. A., and Fairbanks, A. J., *Eur. J. Org. Chem.*, **2014**, 4624.
[27] Cai, F. and Yang, F., *J. Carbohydr. Chem.*, **33**, 1 (2014).
[28] Chen, G., Yin, Q., Yin, J., Gu, X., Liu, X., You, Q., Chen, Y.-L., Xiong, B., and Shen, J., *Org. Biomol. Chem.*, **12**, 9781 (2014).
[29] Chu, A.-H. A., Minciunescu, A., Montanari, V., Kumar, K., and Bennett, C. S., *Org. Lett.*, **16**, 1780 (2014).
[30] Nigudkar, S. S., Stine, K. J., and Demchenko, A. V., *J. Am. Chem. Soc.*, **136**, 921 (2014).
[31] Roy, R., Rajasekaran, P., Mallick, A., and Vankar, Y. D., *Eur. J. Org. Chem.*, **2014**, 5564.
[32] Kimura, H., Hirayama, M., Yoshida, K., Yasuhiro, U., and Nakahara, M., *J. Phys. Chem. A*, **118**, 1309 (2014).
[33] Shi, Y.-H., Xie, Y.-F., Liu, Y.-Q., Wei, Q.-C., Xu, W.-R., Tang, L.-D., and Zhao, G.-L., *Chin. Chem. Lett.*, **25**, 561 (2014).
[34] Nishimura, Y., Yokogawa, D., and Irle, S., *Chem. Phys. Lett.*, **603**, 7 (2014).
[35] Danon, B., Marcotullio, G., and de Jong, W., *Green Chem.*, **16**, 39 (2014).
[36] Amarasekara, A. S. and Razzaq, A., *Carbohydr. Res.*, **386**, 86 (2014).
[37] Qian, X. and Liu, D., *Carbohydr. Res.*, **388**, 50 (2014).
[38] Le, T. X., Papin, C., Doisneau, G., and Beau, J.-M., *Angew. Chem. Int. Ed.*, **53**, 6184 (2014).
[39] Simelane, S. B., Knife, H. H., Muller, A., and Williams, D. B. G., *Org. Lett.*, **16**, 4543 (2014).
[40] Banuelos-Hernandez, A. E. and Mendoza-Espinoza, J. A., *Russ. J. Gen. Chem.*, **84**, 1450 (2014).
[41] Ghosh, M. K. and Rajput, S. K., *Am. Chem. Sci. J.*, **4**, 384 (2014).
[42] Sachdev, N., Singh, A. K., Shrivastava, A., Katre, Y., and Khan, A. A. P., *Arabian J. Chem.*, in press.
[43] Singh, A. K., Singh, R. K., Srivastava, R., Rahmani, S., Srivastava, J., and Singh, M., *Oxid. Commun.*, **37**, 193 (2014).
[44] Pushpalatha, L., *Oxid. Commun.*, **37**, 121 (2014).
[45] Pushpalatha, L., *Oxid. Commun.*, **36**, 901 (2013).

[46] Kumar, A., *Oxid. Commun.*, **37**, 179 (2014).
[47] Singh, A. K., Srivastava, R., Rahmani, S., and Singh, P., *Indian J. Chem. A.*, **52A**, 854 (2013).
[48] Ghosh, M. K. and Rajput, S. K., *Int. Res. J. Pure Appl. Chem.*, **3**, 308 (2013).
[49] Odebunmi, E. O. and Owalude, S. O., *Int. J. Appl. Chem.*, **10**, 51 (2014).
[50] Kumar, A., Bashir, S., and Gani, Z., *Res. J. Chem. Environ.*, **18**, 69 (2014).
[51] Kumar, A., Gani, Z., and Bashir, S., *Orient. J. Chem.*, **29**, 441 (2013).
[52] Laouiti, A., Couty, F., Marrot, J., Boubaker, T., Rammah, M. M., Rammah, M. B., and Evano, G., *Org. Lett.*, **16**, 2252 (2014).
[53] Allen, A. D., Andraos, J., Tidwell, T. T., and Vukovic, S., *J. Org. Chem.*, **79**, 679 (2014).
[54] Mauguiere, F. A. L., Collins, P., Ezra, G. S., Farantos, S. C., and Wiggins, S., *Theor. Chem. Acc.*, **133**, 1 (2014).
[55] Zhang, Z., Li, G., Hu, G., and Sun, Y., *J. Chem.*, Article ID 481586 (5 p.) (2013); available at http://dx.doi.org/10.1155/2013/481586.
[56] Früh, N. and Togni, A., *Angew. Chem. Int. Ed.*, **53**, 10813 (2014).
[57] Drinnan, N. and Wentrup, C., *Aust. J. Chem.*, **67**, 525 (2014).
[58] Chen, N., Zou, M., Tian, X., Zhu, F., Jiang, D., Cheng, J., Shao, X., and Li, Z., *Eur. J. Org. Chem.*, **2014**, 6210.
[59] Lumbroso, A., Catak, S., Sulzer-Mossé, S., and De Mesmaeker, A., *Tetrahedron Lett.*, **55**, 6721 (2014).
[60] Morales, S., Guijarro, F. G., Ruano, J. L. G., and Cid, M. B., *J. Am. Chem. Soc.*, **136**, 1082 (2014).
[61] Chawla, R., Singh, A. K., and Yadav, L. D. S., *Tetrahedron Lett.*, **55**, 3553 (2014).
[62] Keaveney, S. T., McHale, K. S. S., Haines, R. S., and Harper, J. B., *Org. Biomol. Chem.*, **12**, 7092 (2014).
[63] Sindhuja, E. and Ramesh, R., *Tetrahedron Lett.*, **55**, 5504 (2014).
[64] Zhao, G., Liu, H., Zhang, D., Huang, X., and Yang, X., *ACS Catal.*, **4**, 2231 (2014).
[65] Jones, G. O., García, J. M., Horn, H. W., and Hedrick, J. L., *Org. Lett.*, **16**, 5502 (2014).
[66] Siaka, A. A., Uzairu, A., Idris, S. O., and Abba, H., *Chem. Sin.*, **5**, 9 (2014).
[67] Zhang, X., Xu, X., Yu, L., and Zhao, Q., *Tetrahedron Lett.*, **55**, 2280 (2014).
[68] Calow, A. D. J., Carbó, J. J., Cid, J., Fernández, E., and Whiting, A., *J. Org. Chem.*, **79**, 5163 (2014).
[69] Magar, B. K., Kirdant, A. S., and Chondhekar, T. K., *Chem. Sin.*, **5**, 95 (2014).
[70] Magar, B. K., Kirdant, A. S., and Chondhekar, T. K., *J. Chem. Phys. Biol. Sci.*, **4**, 70 (2014).
[71] Magar, B. K., Kirdant, A. S., and Chondhekar, T. K., *Asian J. Biochem. Pharm. Res.*, **3**, 127 (2013).
[72] Magar, B. K., Kirdant, A. S., and Chondhekar, T. K., *Acta Chim. Pharm. Indica*, **4**, 40 (2014).
[73] Pishchugin, F. V. and Tulberdiev, I. T., *Russ. J. Gen. Chem*, **84**, 1362 (2014).
[74] Berski, S. and Ciunik, L. Z., *Mol. Phys.*, **113**, 765 (2015).
[75] Veselý, J. and Rios, R., *Chem. Soc. Rev.*, **43**, 611 (2014).
[76] Ciaccia, M., Pilati, S., Cacciapaglia, R., Mandolini, L., and Di Stefano, S., *Org. Biomol. Chem.*, **12**, 3282 (2014).
[77] Kataja, A. O. and Masson, G., *Tetrahedron*, **70**, 8783 (2014).
[78] Kong, L.-P., Li, N.-K., Zhang, S.-Y., Chen, X., Zhao, M., Zhang, Y.-F., and Wang, X.-W., *Org. Biomol. Chem.*, **12**, 8656 (2014).
[79] Li, Z., Yu, H., Liu, H., Zhang, L., Jiang, H., Wang, B., and Guo, H., *Chem. Eur. J.*, **20**, 1731 (2014).
[80] Soeta, T., Ohgai, T., Sakai, T., Fujinami, S., and Ukaji, Y., *Org. Lett.*, **16**, 4854 (2014).
[81] Zhang, X., Qi, Z., Gao, J., and Li, X., *Org. Biomol. Chem.*, **12**, 9329 (2014).
[82] Wang, M., Huang, Z., Xu, J., and Chi, Y. R., *J. Am. Chem. Soc.*, **136**, 1214 (2014).
[83] Tsymbal, A. V., Kosobokov, M. D., Levin, V. V., Struchkova, M. I., and Dilman, A. D., *J. Org. Chem.*, **79**, 7831 (2014).
[84] (a) Iacobucci, C., Reale, S., Gal, J.-F., and De Angelis, F., *Eur. J. Org. Chem.*, **2014**, 7087; (b) Nicolas, C., Ramozzi, R., El Kaïm, L., Grimaud, L., and Fleurat-Lessard, P., *J. Org. Chem.*, **77**, 1361 (2012).
[85] Belding, L., Zaretsky, S., Rotstein, B. H., Yudin, A. K., and Dudding, T., *J. Org. Chem.*, **79**, 9465 (2014).
[86] Zaretsky, S., Adachi, S., Rotstein, B. H., Hickey, J. L., Scully, C. C. G., St. Denis, J. D., Courtemanche, R., Yu, J. C. Y., Chung, B. K. W., and Yudin, A. K., *J. Org. Chem.*, **79**, 9948 (2014).
[87] Zhao, W., Huang, L., Guan, Y., and Wulff, W. D., *Angew. Chem. Int. Ed.*, **53**, 3436 (2014).
[88] Pramanik, S. and Ghorai, P., *Org. Lett.*, **16**, 2104 (2014).
[89] Tang, W. and Xiao, J., *Synthesis*, **46**, 1297 (2014).
[90] Zhao, Q., Wen, J., Tan, R., Huang, K., Metola, P., Wang, R., Anslyn, E. V., and Zhang, X., *Angew. Chem. Int. Ed.*, **53**, 8467 (2014).
[91] Chakraborty, S., Blacque, O., Fox, T.,, and Berke, H., *Chem. Asian J.*, **9**, 2896 (2014).
[92] Jochmann, P. and Stephan, D. W., *Chem. Eur. J.*, **20**, 8370 (2014).
[93] Šot, P., Vilhanová, B., Pecháček, J., Václavík, J., Zápal, J., Kuzma, M., and Kačer, P., *Tetrahedron: Asymmetry*, **25**, 1346 (2014).

[94] Barrulas, P. C., Genoni, A., Benaglia, M., and Burke, A. J., *Eur. J. Org. Chem.*, **2014**, 7339.
[95] Ge, X., Qian, C., Chen, Y., and Chen, X., *Tetrahedron: Asymmetry*, **25**, 596 (2014).
[96] Ge, X., Qian, C., and Chen, X., *Tetrahedron: Asymmetry*, **25**, 1450 (2014).
[97] Pei, Y.-N., Deng, Y., Li, J.-L., Liu, L., and Zhu, H.-J., *Tetrahedron Lett.*, **55**, 2948 (2014).
[98] (a) Takeda, K., Ohnishi, Y., and Koizumi, T., *Org. Lett.*, **1**, 237 (1999); (b) Kondo, Y., Sasaki, M., Kawahata, M., Yamaguchi, K., and Takeda, K., *J. Org. Chem.*, **79**, 3601 (2014).
[99] Pérez, V. T., de Arriba, Á. L. F., Monleón, L. M., Simón, L., Rub, O. H., Sanz, F., and Morán, J. R., *Tetrahedron*, **70**, 8614 (2014).
[100] Beydoun, K., Ghattas, G., Thenert, K., Klankermayer, J., and Leitner, W., *Angew. Chem. Int. Ed.*, **53**, 11010 (2014).
[101] Mahajan, H. A., Patil, C. J., Nehete, C. A., and Salve, S. B., *Chem. Sin.*, **4**, 62 (2013).
[102] Mahajan, H. A., Patil, C. J., Nehete, C. A., and Salve, S. B., *Chem. Sin.*, **4**, 80 (2013).
[103] Grirrane, A., Álvarez, E., García, H., and Corma, A., *Chem. Eur. J.*, **20**, 14317 (2014).
[104] Wang, Y.-Q., Cui, X.-Y., Ren, Y.-Y., and Zhang, Y., *Org. Biomol. Chem.*, **12**, 9101 (2014).
[105] Azuma, T., Kobayashi, Y., Sakata, K., Sasamori, T., Tokitoh, N., and Takemoto, Y., *J. Org. Chem.*, **79**, 1805 (2014).
[106] Neuvonen, A. J. and Pihko, P. M., *Org. Lett.*, **16**, 5152 (2014).
[107] Zhu, X., Chen, C., Yu, B., Zhang, G., Zhang, W., and Gao, Z., *Chem. Lett.*, **43**, 1832 (2014).
[108] He, H.-X. and Du, D.-M., *Tetrahedron: Asymmetry*, **25**, 637 (2014).
[109] Kano, T., Sakamoto, R., and Maruoka, K., *Chem. Commun. (Cambridge)*, **50**, 942 (2014).
[110] Bonetti, A., Clerici, F., Foschi, F., Nava, D., Pellegrino, S., Penso, M., Soave, R., and Gelmi, M. L., *Eur. J. Org. Chem.*, **2014**, 3203.
[111] Hayashi, M., Iwanaga, M., Shiomi, N., Nakane, D., Masuda, H., and Nakamura, S., *Angew. Chem. Int. Ed.*, **53**, 8411 (2014).
[112] Diosdado, S., López, R., and Palomo, C., *Chem. Eur. J.*, **20**, 6526 (2014).
[113] Wu, L., Xie, C., Mei, H., Soloshonok, V. A., Han, J., and Pan, Y., *Org. Biomol. Chem.*, **12**, 4620 (2014).
[114] Mei, H., Xiong, Y., Xie, C., Soloshonok, V. A., Han, J., and Pan, Y., *Org. Biomol. Chem.*, **12**, 2108 (2014).
[115] Rao, V. U. B., Jadhav, A. P., Garad, D., and Singh, R. P., *Org. Lett.*, **16**, 648 (2014).
[116] Uematsu, R., Maeda, S., and Taketsugu, T., *Chem. Asian J.*, **9**, 305 (2014).
[117] Mondal, B. and Pan, S. C., *Org. Biomol. Chem.*, **12**, 9789 (2014).
[118] Pyne, S. G. and Tang, M., *Org. React.*, **83**, 211 (2014).
[119] Wang, X.-B., Li, T.-Z., Sha, F., and Wu, X.-Y., *Eur. J. Org. Chem.*, **2014**, 739.
[120] Zhang, H.-X., Nie, J., Cai, H., and Ma, J.-A., *Org. Lett.*, **16**, 2542 (2014).
[121] Liu, J., Wang, Z., Levin, A., Emge, T. J., Rablen, P. R., Floyd, D. M., and Knapp, S., *J. Org. Chem.*, **79**, 7593 (2014).
[122] Shengule, S. R. and Karuso, P., *Aust. J. Chem.*, **67**, 184 (2014).
[123] Anderson, J. C., Kalogirou, A. S., and Tizzard, G. J., *Tetrahedron*, **70**, 9337 (2014).
[124] Eisch, J. J., Yu, K., and Rheingold, A. L., *Eur. J. Org. Chem.*, **2014**, 818.
[125] Hirner, S., Kolb, A., Westmeier, J., Gebhardt, S., Middel, S., Harms, K., and von Zezschwitz, P., *Org. Lett.*, **16**, 3162 (2014).
[126] Hennum, M., Fliegl, H., Gundersen, L.-L., and Eisenstein, O., *J. Org. Chem.*, **79**, 2514 (2014).
[127] Soeta, T., Ishizaka, T., Tabatake, Y., and Ukaji, Y., *Chem. Eur. J.*, **20**, 16773 (2014).
[128] Bosque, I., Bagdatli, E., Foubelo, F., and Gonzalez-Gomez, J. C., *J. Org. Chem.*, **79**, 1796 (2014).
[129] Wang, H., Li, Y., and Xu, M.-H., *Org. Lett.*, **16**, 3962 (2014).
[130] Chen, Y.-J., Chen, Y.-H., Feng, C.-G., and Lin, G.-Q., *Org. Lett.*, **16**, 3400 (2014).
[131] Jiang, C., Lu, Y., and Hayashi, T., *Angew. Chem. Int. Ed.*, **53**, 9936 (2014).
[132] Sieber, J. D., Chennamadhavuni, D., Fandrick, K. R., Qu, B., Han, Z. S., Savoie, J., Ma, S., Samankumara, L. P., Grinberg, N., Lee, H., Song, J. J., and Senanayake, C. H., *Org. Lett.*, **16**, 5494 (2014).
[133] Cui, Z., Chen, Y.-J., Gao, W.-Y., Feng, C.-G., and Lin, G.-Q., *Org. Lett.*, **16**, 1016 (2014).
[134] Su, L., Zhu, T.-S., and Xu, M.-H., *Org. Lett.*, **16**, 4118 (2014).
[135] Fukumoto, Y., Daijo, M., and Chatani, N., *Pure Appl. Chem.*, **86**, 283 (2014).
[136] Lemonnier, G., Van Hijfte, N., Poisson, T., Couve-Bonnaire, S., and Pannecoucke, X., *J. Org. Chem.*, **79**, 2916 (2014).
[137] Foubelo, F., and Yus, M., *Eur. J. Org. Chem.*, **2014**, 485.
[138] do Rêgo Barros, O. S., Sirvent, J. A., Foubelo, F., and Yus, M., *Chem. Commun. (Cambridge)*, **50**, 6898 (2014).
[139] Hepburn, H. B. and Lam, H.-W., *Angew. Chem. Int. Ed.*, **53**, 11605 (2014).

[140] Ghosh, D., Bera, P. K., Kumar, M., Abdi, S. H. R., Khan, N.-U. H., Kureshy, R. I., and Bajaj, H. C., *RSC Adv.*, **4**, 56424 (2014).
[141] Gai, R., Prochnow, T., Back, D. F., and Zeni, G., *Tetrahedron*, **70**, 3751 (2014).
[142] Verrier, C., Carret, S., and Poisson, J.-F., *Org. Biomol. Chem.*, **12**, 1875 (2014).
[143] Li, Y., Wu, Z., Shi, J., Pan, Y., Bu, H., Ma, H., Gu, J., Huang, H., Wang, Y., and Wu, L., *Tetrahedron*, **70**, 8971 (2014).
[144] Yang, Z., Yu, H., Zhang, L., Wei, H., Xiao, Y., Chen, L., and Guo, H., *Chem. Asian J.*, **9**, 313 (2014).
[145] Novák, M., Dostál, L., Alonso, M., De Proft, F., Růžička, A., Lyčka, A., and Jambor, R., *Chem. Eur. J.*, **20**, 2542 (2014).
[146] Corre, Y., Iali, W., Hamdaoui, M., Trivelli, X., Djukic, J.-P., Agbossou-Niedercorn, F., and Michon, C., *Catal. Sci. Technol.*, **5**, 1452 (2015).
[147] Mita, T., Sugawara, M., Saito, K., and Sato, Y., *Org. Lett.*, **16**, 3028 (2014).
[148] Jones, S. and Zhao, P., *Tetrahedron: Asymmetry*, **25**, 238 (2014).
[149] Hensel, A., Nagura, K., Delvos, L. B., and Oestreich, M., *Angew. Chem. Int. Ed.*, **53**, 4964 (2014).
[150] Vereshchagina, Y. A., Mironov, V. F., Dimkhametov, M. N., Onys'ko, P. P., Rassukanaya, Y. V., and Chachkov, D. V., *Russ. J. Org. Chem.*, **84**, 969 (2014).
[151] Van Waes, F. E. A., Debrouwer, W., Heugebaert, T. S. A., and Stevens, C. V., *ARKIVOC,* **2014**, 386.
[152] George, J., Sridhar, B., and Reddy, B. V. S., *Org. Biomol. Chem.*, **12**, 1595 (2014).
[153] He, H.-X. and Du, D.-M., *Eur. J. Org. Chem.*, **2014**, 6190.
[154] Wang, X., Qui, G., Zhang, L., and Wu, J., *Tetrahedron Lett.*, **55**, 962 (2014).
[155] Li, J., Zhang, Q., Wu, C., Gu, H., and Yan, B., *Dalton Trans.*, **43**, 55 (2014).
[156] Anderson, J. C., Campbell, I. B., Campos, S., and Shannon, J., *Tetrahedron Lett.*, **55**, 7206 (2014).
[157] Kano, T., Takechi, R., Kobayashi, R., and Maruoka, K., *Org. Biomol. Chem.*, **12**, 724 (2014).
[158] Fujii, S., Konishi, T., Matsumoto, Y., Yamaoka, Y., Takasu, K., and Yamada, K., *J. Org. Chem.*, **79**, 8128 (2014).
[159] Rassukana, Y. V., Yelenich, I. P., Vlasenko, Y. G., and Onys'ko, P. P., *Tetrahedron: Asymmetry*, **25**, 1234 (2014).
[160] Fontenelle, C. Q., Conroy, M., Light, M., Poisson, T., Pannecoucke, X., and Linclau, B., *J. Org. Chem.*, **79**, 4186 (2014).
[161] Milcent, T., Hao, J., Kawada, K., Soloshonok, V. A., Ongeri, S., and Crousse, B., *Eur. J. Org. Chem.*, **2014**, 3072.
[162] Yang, L.-J., Li, S., Wang, S., Nie, J., and Ma, J.-A., *J. Org. Chem.*, **79**, 3547 (2014).
[163] Lu, N., Wang, H., and Wang, Y., *Bull. Korean Chem. Soc.*, **34**, 3591 (2013).
[164] Zhao, X., Li, T.-Z., Qian, J.-Y., Sha, F., and Wu, X.-Y., *Org. Biomol. Chem.*, **12**, 8072 (2014).
[165] Verma, P., Verma, P., and Sunoj, R. B., *Org. Biomol. Chem.*, **12**, 2176 (2014).
[166] Zarei, M., *Tetrahedron Lett.*, **55**, 5354 (2014).
[167] Kim, I., Roh, S. W., Lee, D. G., and Lee, C., *Org. Lett.*, **16**, 2482 (2014).
[168] Tarui, A., Nishimura, H., Ikebata, T., Tahira, A., Sato, K., Omote, M., Minami, H., Miwa, Y., and Ando, A., *Org. Lett.*, **16**, 2080 (2014).
[169] Davis, L. O., Putri, M. A., Meyer, C. L., and Durant, C. P., *Tetrahedron Lett.*, **55**, 3100 (2014).
[170] Tanaka, H., Mizota, I., and Shimizu, M., *Org. Lett.*, **16**, 2276 (2014).
[171] Holmquist, M., Blay, G., and Pedro, J. R., *Chem. Commun. (Cambridge)*, **50**, 9309 (2014).
[172] García-Muñoz, M. J., Dema, H. K., Foubelo, F., and Yus, M., *Tetrahedron: Asymmetry*, **25**, 362 (2014).
[173] Xu, J., Mou, C., Zhu, T., Song, B.-A., and Chi, Y. R., *Org. Lett.*, **16**, 3272 (2014).
[174] Janssen, G. V., Janssen, E., Velde, C. M. L. V., Ehlers, A. W., Slootweg, J. C., Ruijter, E., Lammertsma, K., and Orru, R. V. A., *Org. Lett.*, **16**, 5116 (2014).
[175] Chen, H., Fan, G., Li, S., Mao, K., and Liu, Y., *Tetrahedron Lett.*, **55**, 1593 (2014).
[176] Huang, J.-R., Song, Q., Zhu, Y.-Q., Qin, L., Qian, Z.-Y., and Dong, L., *Chem. Eur. J.*, **20**, 16882 (2014).
[177] Parthasarathy, K., Azcargorta, A. R., Cheng, Y., and Bolm, C., *Org. Lett.*, **16**, 2538 (2014).
[178] Priebbenow, D. L. and Bolm, C., *Org. Lett.*, **16**, 1650 (2014).
[179] Randjelovic, J., Simic, M., Tasic, G., Husinec, S., and Savic, V., *Curr. Org. Chem.*, **18**, 1073 (2014).
[180] Solis-Calero, C., Ortega-Castro, J., Hernandez-Laguna, A., and Munoz, F., *J. Mol. Model.*, **20**, 1 (2014).
[181] Moghaddam, F. M., Khodabakhshi, M. R., and Aminaee, M., *Tetrahedron Lett.*, **55**, 4720 (2014).
[182] Paleta, O., Dolensky, B., Palecek, J., and Kvicala, J., *J. Fluor. Chem.*, **157**, 1 (2014).
[183] Funes-Ardoiz, I. and Sampedro, D., *J. Org. Chem.*, **79**, 11824 (2014).
[184] Knipe, P. C. and Smith, M. D., *Org. Biomol. Chem.*, **12**, 5094 (2014).
[185] Domingo, L. R., Aurell, M. J., Sáez, J. A., and Mekelleche, S. M., *RSC Adv.*, **4**, 25268 (2014).
[186] Ye, W., Zhang, L., Ni, C., Rong, J., and Hu, J., *Chem. Commun. (Cambridge)*, **50**, 10596 (2014).
[187] Nagamoto, M. and Nishimura, T., *Chem. Commun. (Cambridge)*, **50**, 6274 (2014).

188 Zhu, X., Wang, Y.-F., Zhang, F.-L., and Chiba, S., *Chem. Asian J.*, **9**, 2458 (2014).
189 Gao, Z., Zhang, L., Sun, Z., Yu, H., Xiao, Y., and Guo, H., *Org. Biomol. Chem.*, **12**, 5691 (2014).
190 Jia, W.-Q., Chen, X.-Y., Sun, L.-H., and Ye, S., *Org. Biomol. Chem.*, **12**, 2167 (2014).
191 Eschenbrenner-Lux, V., Küchler, P., Ziegler, S., Kumar, K., and Waldmann, H., *Angew. Chem. Int. Ed.*, **53**, 2134 (2014).
192 Pascual-Escudero, A., González-Esguevillas, M., Padilla, S., Adrio, J., and Carretero, J. C., *Org. Lett.*, **16**, 2228 (2014).
193 Qui, L., Gao, L., Tang, J., Wang, D., Guo, X., Liu, S., Yang, L., Li, J., and Hu, W., *J. Org. Chem.*, **79**, 4142 (2014).
194 Zhang, Y., Pan, L., Xu, X., Luo, H., and Liu, Q., *Chem. Commun. (Cambridge)*, **50**, 11039 (2014).
195 Okamoto, K., Shimbayashi, T., Tamura, E., and Ohe, K., *Chem. Eur. J.*, **20**, 1490 (2014).
196 (a) Guan, Y., López-Alberca, M. P., Lu, Z., Zhang, Y., Desai, A. A., Patwardhan, A. P., Dai, Y., Vetticatt, M. J., and Wulff, W. D., *Chem. Eur. J.*, **20**, 13894 (2014); (b) Zhao, Y., Wang, G., Zhou, S., Li, Z., and Meng, X., *Org. Biomol. Chem.*, **12**, 3362 (2014).
197 Uraguchi, D., Tsutsumi, R., and Ooi, T., *Tetrahedron*, **70**, 1691 (2014).
198 Ito, M., Kashiwagi, T., Kotani, S., Nakajima, M., and Sugiura, M., *Tetrahedron Lett.*, **55**, 4082 (2014).
199 Tang, Z., Shi, Y., Mao, H., Zhu, X., Li, W., Cheng, Y., Zheng, W.-H., and Zhu, C., *Org. Biomol. Chem.*, **12**, 6085 (2014).
200 Qian, P., Xie, C., Wu, L., Mei, H., Soloshonok, V. A., Han, J., and Pan, Y., *Org. Biomol. Chem.*, **12**, 7909 (2014).
201 Matsumoto, M., Harada, M., Yamashita, Y., and Kobayashi, S., *Chem. Commun. (Cambridge)*, **50**, 13041 (2014).
202 Lu, B., Wu, J., and Yoshikai, N., *J. Am. Chem. Soc.*, **136**, 11598 (2014).
203 Kumari, P., Bera, P. K., Khan, N.-H., Kureshy, R. I., Abdi, S. H. R., and Bajaj, H. C., *Catal. Sci. Technol.*, **4**, 563 (2014).
204 Perrone, S., Salomone, A., Caroli, A., Falcicchio, A., Citti, C., Cannazza, G., and Troisi, L., *Eur. J. Org. Chem.*, **2014**, 5932.
205 Izadyar, M., *J. Iran. Chem. Soc.*, **11**, 399 (2014).
206 Karimiahmadabadi, M., Erfan, S., Földesi, A., and Chattopadhyaya, J., *J. Org. Chem.*, **79**, 7266 (2014).
207 Kool, E. T., Crisalli, P., and Chan, K. M., *Org. Lett.*, **16**, 1454 (2014).
208 Wang, X. and Yu, X., *J. Org. Chem.*, **79**, 7854 (2014).
209 Zhu, J.-L., Wu, S.-T., and Shie, J.-Y., *J. Org. Chem.*, **79**, 3623 (2014).
210 Zhang, Z.-W., Lin, A., and Yang, J., *J. Org. Chem.*, **79**, 7041 (2014).
211 Zhang, D., Nakamra, I., and Terada, M., *Org. Lett.*, **16**, 5184 (2014).
212 Moilanen, J., Neuvonen, A., and Pihko, P., *J. Org. Chem.*, **79**, 2006 (2014).
213 Du, W., Zhao, M.-N., Ren, Z.-H., Wang, Y.-Y., and Guan, Z.-H., *Chem. Commun. (Cambridge)*, **50**, 7437 (2014).
214 Cho, H., *Tetrahedron*, **70**, 3527 (2014).
215 Wang, X. and Wang, Z., *Tetrahedron*, **70**, 6728 (2014).
216 Subbarao, K. P. V., Reddy, G. R., Muralikrishna, A., and Reddy, K. V., *J. Heterocycl. Chem.*, **51**, 1045 (2014).
217 Nakamura, I., Ishida, Y., and Terada, M., *Org. Lett.*, **16**, 2562 (2014).
218 Bhattarai, B. T., Adhikari, S., Kimball, E. A., Moore, J. N., Shaughnessy, K. H., Snowden, T. S., Fronczek, F. R., and Dolliver, D. D., *Tetrahedron Lett.*, **55**, 4801 (2014).
219 Quartarone, G., Rancan, E., Ronchin, L., and Vavasori, A., *Appl. Catal. A.-Gen.*, **472**, 167 (2014).
220 Kaur, G., Rajput, J. K., Arora, P., and Devi, N., *Tetrahedron Lett.*, **55**, 1136 (2014).
221 Panda, N., Mothkuri, R., and Nayak, D. K., *Eur. J. Org. Chem.*, **2014**, 1602.
222 Faulkner, A., Race, N. J., Scott, J. S., and Bower, J. F., *Chem. Sci.*, **5**, 2416 (2014).
223 Lin, C.-C., Hsieh, T.-H., Liao, P.-Y., Liao, Z.-Y., Chang, C.-W., Shih, Y.-C., Yeh, W.-H., and Chien, T.-C., *Org. Lett.*, **16**, 892 (2014).
224 Bolotin, D. S., Kulish, K. I., Bokach, N. A., Starova, G. L., Gurzhiy, V. V., and Kukushkin, V. Y., *Inorg. Chem.*, **53**, 10312 (2014).
225 Foster, J. C., Powell, C. R., Radzinski, S. C., and Matson, J. B., *Org. Lett.*, **16**, 1558 (2014).
226 Wang, L., Priebbenow, D. L., Dong, W., and Bolm, C., *Org. Lett.*, **16**, 2661 (2014).
227 Chen, B., Scott, M. E., Adams, B. A., Hrovat, D. A., Borden, W. T., and Lautens, M., *Org. Lett.*, **16**, 3930 (2014).
228 Gridnev, I. D., Shastin, A. V., Muzalevskiy, V. M., Balenova, E. S., and Nenajdenko, V. G., *Mendeleev Commun.*, **24**, 340 (2014).
229 Hossain, M. L., Ye, F., Liu, Z., Xia, Y., Shi, Y., Zhou, L., Zhang, Y., and Wang, J., *J. Org. Chem.*, **79**, 8689 (2014).

[230] Hu, F., Xia, Y., Liu, Z., Ma, C., Zhang, Y., and Wang, J., *Org. Biomol. Chem.*, **12**, 3590 (2014).
[231] Barroso, R., Valencia, R. A., Cabal, M.-P., and Valdés, C., *Org. Lett.*, **16**, 2264 (2014).
[232] Ping, W.-W., Jin, L., Wu, Y., Xue, X.-Y., and Zhao, X., *Tetrahedron*, **70**, 9373 (2014).
[233] McSweeney, C. M., Foley, V. M., and McGlacken, G. P., *Chem. Commun. (Cambridge)*, **50**, 14817 (2014).
[234] Gutierrez, O., Strick, B. F., Thomson, R. J., and Tantillo, D. J., *Chem. Sci.*, **4**, 3997 (2013).
[235] Li, B., Bi, S., Liu, Y., Ling, B., and Li, P., *Organometallics*, **33**, 3453 (2014).
[236] Das, A., Alam, R., Eriksson, L., and Szabó, K. J., *Org. Lett.*, **16**, 3808 (2014).
[237] Hong, X., Liang, Y., Griffith, A. K., Lambert, T. H., and Houk, K. N., *Chem. Sci.*, **5**, 471 (2014).
[238] Zhang, X., *Comput. Theor. Chem.*, **1027**, 179 (2014).
[239] Zhao, X., Zhang, L., Li, T., Liu, G., Wang, H., and Lu, K., *Chem. Commun. (Cambridge)*, **50**, 13121 (2014).
[240] Rosselin, M., Choteau, F., Zéamari, K., Nash, K. M., Das, A., Lauricella, R., Lojou, E., Tuccio, B., Villamena, F. A., and Durand, G., *J. Org. Chem.*, **79**, 6615 (2014).
[241] Roca-López, D., Tejero, T., and Merino, P., *J. Org. Chem.*, **79**, 8358 (2014).
[242] Prakash, G. K. S., Zhang, Z., Wang, F., Rahm, M., Ni, C., Iuliucci, M., Haiges, R., and Olah, G. A., *Chem. Eur. J.*, **20**, 831 (2014).
[243] Reeves, J. T., Lorenc, C., Camara, K., Li, Z., Lee, H., Busacca, C. A., and Senanayake, C. H., *J. Org. Chem.*, **79**, 5895 (2014).
[244] Kawade, R. K., Huang, P.-H., Karad, S. N., and Liu, R.-S., *Org. Biomol. Chem.*, **12**, 737 (2014).
[245] Downey, C. W., Maxwell, E. N., and Confair, D. N., *Tetrahedron Lett.*, **55**, 4959 (2014).
[246] Jiang, P., Bao, X., and Salmeron, M., *Acc. Chem. Res.*, **47**, 1524 (2014).
[247] Albrecht, L., Jiang, H., and Jørgensen, K. A., *Chem. Eur. J.*, **20**, 358 (2014).
[248] Sunoj, R. B., *Compr. Enantiosel. Organocatal.*, **2**, 465 (2013).
[249] Parmar, D., Sugiono, E., Raja, S., and Rueping, M., *Chem. Rev.*, **114**, 9047 (2014).
[250] Deng, Y., Kumar, S., and Wang, H., *Chem. Commun. (Cambridge)*, **50**, 4272 (2014).
[251] Valero, G., Ribó, J. M., and Moyano, A., *Chem. Eur. J.*, **20**, 17395 (2014).
[252] (a) Mlynarski, J. and Baś, S., *Chem. Soc. Rev.*, **43**, 577 (2014); (b) Mlynarski, J. and Baś, S., *Chem. Soc. Rev.*, **37**, 1502 (2008).
[253] Landa, A., López, R., Oiarbde, M., and Palomo, C., *Compr. Enantiosel. Organocatal.*, **3**, 841 (2013).
[254] Koeller, S., Thomas, C., Peruch, F., Deffieux, A., Massip, S., Léger, J.-M., Desvergne, J.-P., Milet, A., and Bibal, B., *Chem. Eur. J.*, **20**, 2849 (2014).
[255] Hubin, P. O., Jacquemin, D., Leherte, L., and Vercauteren, D. P., *Chem. Phys.*, **434**, 30 (2014).
[256] Cho, E. and Kim, T. H., *Tetrahedron Lett.*, **55**, 6470 (2014).
[257] Seebach, D., Yoshinari, T., Beck, A. K., and Ebert, M.-O., *Helv. Chim. Acta*, **97**, 1177 (2014).
[258] Huang, X.-R., Liu, Q., Wang, J., Xiao, J.-A., and Yang, H., *Tetrahedron: Asymmetry*, **25**, 1590 (2014).
[259] Guan, Z., Luo, Y., Zhang, B.-Q., Heinen, K., Yang, D.-C., and He, Y.-H., *Tetrahedron: Asymmetry*, **25**, 802 (2014).
[260] Kumar, T. P., Vavle, N. C., Patro, V., and Haribabu, K., *Tetrahedron: Asymmetry*, **25**, 457 (2014).
[261] Eymur, S., Akceylan, E., Sahin, O., Uyanik, A., and Yilmaz, M., *Tetrahedron*, **70**, 4471 (2014).
[262] Patti, A. and Pedotti, S., *Eur. J. Org. Chem.*, **2014**, 624.
[263] Yasui, Y., Benohoud, M., Sato, I., and Hayashi, Y., *Chem. Lett.*, **43**, 556 (2014).
[264] Bhowmick, S., Kunte, S. S., and Bhowmick, K. C., *Tetrahedron: Asymmetry*, **25**, 1292 (2014).
[265] Viswambharan, B., Gori, D., Guillot, R., Kouklovsky, C., and Alezra, V., *Org. Lett.*, **16**, 788 (2014).
[266] Fu, A., Zhao, C., Li, H., Tian, C., Chu, T., Tian, F., Liu, J., Wang, Z., and Duan, Y., *Tetrahedron: Asymmetry*, **25**, 418 (2014).
[267] Barrulas, P., Benaglia, M., and Burke, A. J., *Tetrahedron: Asymmetry*, **25**, 923 (2014).
[268] Yolacan, C., Mavis, M. E., and Aydogan, F., *Tetrahedron*, **70**, 3707 (2014).
[269] Psarra, A., Kokotos, C. G., and Moutevelis-Minakakis, P., *Tetrahedron*, **70**, 608 (2014).
[270] Okumuş, S., Tanyeli, C., and Demir, A. S., *Tetrahedron Lett.*, **55**, 4302 (2014).
[271] Abbaraju, S. and Zhao, J. C.-G., *Adv. Synth. Catal.*, **356**, 2 (2014).
[272] Sakamoto, S., Kazumi, N., Kobayashi, Y., Tsukano, C., and Takemoto, Y., *Org. Lett.*, **16**, 4758 (2014).
[273] Bartrum, H. E., Viceriat, A., Carret, S., and Poisson, J.-F., *Org. Lett.*, **16**, 1972 (2014).
[274] Lin, J., Kang, T., Liu, Q., and He, L., *Tetrahedron: Asymmetry*, **25**, 949 (2014).
[275] Shirakawa, S. and Maruoka, K., *Tetrahedron Lett.*, **55**, 3833 (2014).
[276] Armacost, K. and Acevedo, O., *J. Am. Chem. Soc.*, **136**, 147 (2014).
[277] Weidner, K., Kumagai, N., and Shibasaki, M., *Angew. Chem. Int. Ed.*, **53**, 6150 (2014).
[278] Brady, P. B., Albert, B. J., Akakura, M., and Yamamoto, H., *Chem. Sci.*, **4**, 3223 (2013).

[279] Kumar, M., Kumar, A., Rizvi, M., Mane, M., Vanka, K., Taneja, S. C., and Shah, B. A., *Eur. J. Org. Chem.*, **2014**, 5247.
[280] Ward, D. E., Kundu, D., Biniaz, M., and Jana, S., *J. Org. Chem.*, **79**, 6868 (2014).
[281] Kano, T., Sakamoto, R., and Maruoka, K., *Org. Lett.*, **16**, 944 (2014).
[282] Li, B. and Li, C., *J. Org. Chem.*, **79**, 2242 (2014).
[283] Yanagisawa, A., Miyake, R., and Yoshida, K., *Eur. J. Org. Chem.*, **2014**, 4248.
[284] Roiban, G.-D., Ilie, A., and Reetz, M. T., *Chem. Lett.*, **43**, 2 (2014).
[285] Kitanosono, T. and Kobayashi, S., *Chem. Rec.*, **14**, 130 (2014).
[286] Frings, M., Thomé, I., Schiffers, I., Pan, F., and Bolm, C., *Chem. Eur. J.*, **20**, 1691 (2014).
[287] Sai, M., Akakura, M., and Yamamoto, H., *Chem. Commun. (Cambridge)*, **50**, 15206 (2014).
[288] (a) Zhang, Z. and List, B., *Asian J. Org. Chem.*, **2**, 957 (2013); (b) Honda, K., Mikami, K., and Asian, J., *Org. Chem.*, **3**, 34 (2014).
[289] Curvey, N., Widaman, A. K., Rath, N. P., and Bauer, E. B., *Tetrahedron Lett.*, **55**, 3033 (2014).
[290] Rodríguez-Gimeno, A., Cuenca, A. B., Gil-Tomás, J., Medio-Simón, M., Olmos, A., and Asensio, G., *J. Org. Chem.*, **79**, 8263 (2014).
[291] Tisovský, P., Mečiarová, M., and Šebesta, R., *Org. Biomol. Chem.*, **12**, 9446 (2014).
[292] Li, J.-L., Liu, L., Pei, Y.-N., and Zhu, H.-J., *Tetrahedron*, **70**, 9077 (2014).
[293] Breugst, M. and Houk, K. N., *J. Org. Chem.*, **79**, 6302 (2014).
[294] Huang, H., Zong, H., Bian, G., Yue, H., and Song, L., *J. Org. Chem.*, **79**, 9455 (2014).
[295] Chunhong, Z., Liu, F., and Gou, S., *Tetrahedron: Asymmetry*, **25**, 278 (2014).
[296] Bhosale, D. S., Drabina, P., Palarčik, J., Hanusek, J., and Sedlák, M., *Tetrahedron: Asymmetry*, **25**, 334 (2014).
[297] Kannan, M. and Punniyamurthy, T., *Tetrahedron: Asymmetry*, **25**, 1331 (2014).
[298] Holmquist, M., Blay, G., Muñoz, M. C., and Pedro, J. R., *Org. Lett.*, **16**, 1204 (2014).
[299] Yu, L. and Li, P., *Tetrahedron Lett.*, **55**, 3697 (2014).
[300] Kwiatkowski, P., Cholewiak, A., and Kasztelan, A., *Org. Lett.*, **16**, 5930 (2014).
[301] Xuan, Y., Chen, Z., and Yan, M., *Chem. Commun. (Cambridge)*, **50**, 10471 (2014).
[302] Basavaiah, D., Reddy, G. C., and Bharadwaj, K. C., *Tetrahedron*, **70**, 7991 (2014).
[303] Basavaiah, D., Reddy, G. C., and Bharadwaj, K. C., *Eur. J. Org. Chem.*, **2014**, 1157.
[304] Rodrigues, T. S., Silva, V. H. C., Lalli, P. M., de Oliveira, H. C. B., da Silva, W. A., Coelho, F., Eberlin, M. N., and Neto, B. A. D., *J. Org. Chem.*, **79**, 5239 (2014).
[305] Guillouzic, A.-F., Montel, S., Laborde, C., Volle, J.-N., Pirat, J.-L., and Virieux, D., *Eur. J. Org. Chem.*, **2014**, 788.
[306] Trujillo, C., Sánchez-Sanz, G., Karpavičiené, I., Jahn, U., Čikotiene, I., and Rulíšek, L., *Chem. Eur. J.*, **20**, 10360 (2014).
[307] Zhang, X., An, H., Zhang, H., Zhao, X., and Wang, Y., *Ind. Eng. Chem. Res.*, **53**, 16707 (2014).
[308] Meninno, S., Fuoco, T., Tedesco, C., and Lattanzi, A., *Org. Lett.*, **16**, 4746 (2014).
[309] Ramachandran, P. V., Chanda, P. B., and Otoo, B., *Tetrahedron Lett.*, **55**, 1289 (2014).
[310] Dong, X. and Sun, J., *Org. Lett.*, **16**, 2450 (2014).
[311] Parnes, R., Narute, S., and Pappo, D., *Org. Lett.*, **16**, 5922 (2014).
[312] Yu, H.-Z., Tian, X.-J., Lin, X., Hu, G.-H., and Dang, Z.-M., *Chem. Asian J.*, **9**, 3472 (2014).
[313] Zardoost, M. R., *Russ. J. Phys. Chem. B.*, **7**, 540 (2013).
[314] Zardoost, M. R., *Khim. Fiz.*, **32**, 30 (2013).
[315] Mao, D., Hong, G., Wu, S., Liu, X., Yu, J., and Wang, L., *Eur. J. Org. Chem.*, **2014**, 3009.
[316] (a) Jing, C., Xing, D., and Hu, W., *Chem. Commun. (Cambridge)*, **50**, 951 (2014); (b) Ananthi, N. and Velmathi, S., *J. Chem. Sci.*, **126**, 151 (2014).
[317] Hessler, F., Betík, R., Kadlčíková, A., Belle, R., and Kotora, M., *Eur. J. Org. Chem.*, **2014**, 7245.
[318] Ghosh, D., Sadhukhan, A., Maity, N. C., Abdi, S. H. R., Khan, N.-H., Kureshy, R. I., and Bajaj, H. C., *RSC Adv.*, **4**, 12257 (2014).
[319] Sepúlveda, D., Lu, T., and Wheeler, S. E., *Org. Biomol. Chem.*, **12**, 8346 (2014).
[320] Jindal, G. and Sunoj, R. B., *J. Org. Chem.*, **79**, 7600 (2014).
[321] Nakano, T., Endo, K., and Ukaji, Y., *Org. Lett.*, **16**, 1418 (2014).
[322] Chen, W., Chen, M., and Hartwig, J. F., *J. Am. Chem. Soc.*, **136**, 15825 (2014).
[323] Bhakta, U., Sullivan, E., and Hall, D. G., *Tetrahedron*, **70**, 678 (2014).
[324] Dugas, G. J., Lam, Y., Houk, K. N., and Krauss, I. J., *J. Org. Chem.*, **79**, 4277 (2014).
[325] Deng, H.-P., Eriksson, L., and Szabó, K. J., *Chem. Commun. (Cambridge)*, **50**, 9207 (2014).
[326] Li, G., Gagare, P. D., and Ramachandran, P. V., *Tetrahedron Lett.*, **55**, 5736 (2014).
[327] Joseph, J., Jaroschik, F., Harakat, D., Radhakrishnan, K. V., Vasse, J.-L., and Szymoniak, J., *Chem. Eur. J.*, **20**, 5433 (2014).

[328] Wang, P.-S., Lin, H.-C., Zhai, Y.-J., Han, Z.-Y., and Gong, L.-Z., *Angew. Chem. Int. Ed.*, **53**, 12218 (2014).
[329] Nihei, T., Yokotani, S., Ishihara, T., and Konno, T., *Chem. Commun. (Cambridge)*, **50**, 1543 (2014).
[330] Jadhav, B. D. and Pardeshi, S. K., *Tetrahedron Lett.*, **55**, 4948 (2014).
[331] Roudier, M., Constantieux, T., Quintard, A., and Rodriguez, J., *Org. Lett.*, **16**, 2802 (2014).
[332] Lin, X., Ye, X., Sun, X., Zhang, Y., Gao, L., and Song, Z., *Org. Lett.*, **16**, 1084 (2014).
[333] Utaka, A., Cavalcanti, L. N., and Silva, L. F. Jr., *Chem. Commun. (Cambridge)*, **50**, 3810 (2014).
[334] Karakaya, I., Karabuga, S., Altundas, R., and Ulukanli, S., *Tetrahedron*, **70**, 8385 (2014).
[335] Chen, C., Huang, Q., Zou, S., Wang, L., Luan, B., Zhu, J., Wang, Q., and Pu, L., *Tetrahedron: Asymmetry*, **25**, 199 (2014).
[336] Praveen, C., Leveque, S., Vitale, M. R., Michelet, V., and Ratovelomanana-Vidal, V., *Synthesis*, **46**, 1334 (2014).
[337] Sanz-Marco, A., García-Ortiz, A., Blay, G., Fernández, I., and Pedro, J. R., *Chem. Eur. J.*, **20**, 668 (2014).
[338] Cai, H., Nie, J., Zheng, Y., and Ma, J.-A., *J. Org. Chem.*, **79**, 5484 (2014).
[339] Connon, S. J., *Angew. Chem. Int. Ed.*, **53**, 1203 (2014).
[340] Patra, A., Bhunia, A., and Biju, A. T., *Org. Lett.*, **16**, 4798 (2014).
[341] Takaki, K., Ohno, A., Hino, M., Shitaoka, T., Komeyama, K., and Yoshida, H., *Chem. Commun. (Cambridge)*, **50**, 12285 (2014).
[342] Jang, K. P., Hutson, G. E., Johnston, R. C., McCusker, E. O., Cheong, P. H.-Y., and Scheidt, K. A., *J. Am. Chem. Soc.*, **136**, 76 (2014).
[343] Zhang, Q., Yu, H.-Z., and Fu, Y., *Org. Chem. Front.*, **1**, 614 (2014).
[344] Goodman, C. G. and Johnson, J. S., *J. Am. Chem. Soc.*, **136**, 14698 (2014).
[345] Tong, Y., Mao, J., Wu, S., Zhao, Y., and Cheng, Y., *J. Org. Chem.*, **79**, 2075 (2014).
[346] Wang, Y., Jiang, M., and Liu, J.-T., *Tetrahedron: Asymmetry*, **25**, 212 (2014).
[347] Kamal, A., Sathish, M., Srinivasulu, V., Chetna, J., Shekar, K. C., Nekkanti, S., Tangella, Y., and Shankaraiah, N., *Org. Biomol. Chem.*, **12**, 8008 (2014).
[348] Kumar, T. P., *Tetrahedron: Asymmetry*, **25**, 1286 (2014).
[349] Kumar, T. P. and Haribabu, K., *Tetrahedron: Asymmetry*, **25**, 1129 (2014).
[350] Vinayagam, P., Vishwanath, M., and Kesavan, V., *Tetrahedron: Asymmetry*, **25**, 568 (2014).
[351] Yu, H., Liu, M., and Han, S., *Tetrahedron*, **70**, 8380 (2014).
[352] Wang, Y., Lin, J., and Wei, K., *Tetrahedron: Asymmetry*, **25**, 1599 (2014).
[353] Kumar, T. P. and Balaji, S. V., *Tetrahedron: Asymmetry*, **25**, 473 (2014).
[354] Yoshida, M., Kubara, A., Nagasawa, Y., Hara, S., Yamanaka, M., and Asian, J., *Org. Chem.*, **3**, 523 (2014).
[355] Flores-Ferrándiz, J. and Chinchilla, R., *Tetrahedron: Asymmetry*, **25**, 1091 (2014).
[356] Zhao, H.-W., Yang, Z., Yue, Y.-Y., Li, H.-L., Song, X.-Q., Sheng, Z.-H., Meng, W., and Guo, X.-Y., *Synlett*, **25**, 293 (2014).
[357] Jiang, H., Zhao, H., Zhang, M., Liu, H., and Huang, X., *Struct. Chem.*, **25**, 1343 (2014).
[358] Avila, A., Chinchilla, R., Fiser, B., Gómez-Bengoa, E., and Nájera, C., *Tetrahedron: Asymmetry*, **25**, 462 (2014).
[359] Grošelj, U., *Helv. Chim. Acta*, **97**, 751 (2014).
[360] Sukach, V. A., Tkachuk, V. M., Shoba, V. M., Pirozhenko, V. V., Rusanov, E. B., Chekotilo, A. A., Röschenthaler, G.-V., and Vovk, M. V., *Eur. J. Org. Chem.*, **2014**, 1452.
[361] Bera, S., Samanta, R. C., Daniliuc, C. G., and Studer, A., *Angew. Chem. Int. Ed.*, **53**, 9622 (2014).
[362] Arai, T. and Yamamoto, Y., *Org. Lett.*, **16**, 1700 (2014).
[363] Liang, Q., He, J., and Ni, B., *Tetrahedron: Asymmetry*, **25**, 1146 (2014).
[364] Deredas, D., Huben, K., Maniukiewicz, W., and Krawczyk, H., *Tetrahedron*, **70**, 8925 (2014).
[365] Zhao, B.-L. and Du, D.-M., *Tetrahedron: Asymmetry*, **25**, 310 (2014).
[366] Ramachary, D. B., Reddy, P. S., and Prasad, M. S., *Eur. J. Org. Chem.*, **2014**, 3076.
[367] García-García, C., Redondo, M. C., Ribagorda, M., and Carreño, M. C., *Eur. J. Org. Chem.*, **2014**, 7377.
[368] Wu, L., Wang, Y., and Zhou, Z., *Tetrahedron: Asymmetry*, **25**, 1389 (2014).
[369] Habibi-Khorassani, S. M., Maghsoodlou, M. T., Shahraki, M., Talaiefar, S., Kazemian, M. A., and Aboonajmi, J., *Lett. Org. Chem.*, **11**, 413 (2014).
[370] Alvim, H. G. O., Lima, T. B., de Oliveira, A. L., de Oliveira, H. C. B., Silva, F. M., Gozzo, F. C., Souza, R. Y., da Silva, W. A., and Neto, B. A. D., *J. Org. Chem.*, **79**, 3383 (2014).
[371] Liu, Q., Xu, J., Teng, F., Chen, A., Pan, N., and Zhang, W., *J. Heterocycl. Chem.*, **51**, 741 (2014).
[372] Světlík, J., Prónayová, N., Švorc, L., and Frecer, V., *Tetrahedron*, **70**, 8354 (2014).
[373] An, D., Fan, Y.-S., Gao, Y., Zhu, Z.-Q., Zheng, L.-Y., and Zhang, S.-Q., *Eur. J. Org. Chem.*, **2014**, 301.

374 Reddy, B. V. S., Reddy, S. G., Reddy, M. R., Sridhar, B., and Bhadra, M. P., *Tetrahedron Lett.*, **55**, 4817 (2014).
375 Reddy, B. V. S., Anjum, S. R., Reddy, G. M., and Sridhar, B., *Tetrahedron Lett.*, **55**, 5011 (2014).
376 Colin, O., Greck, C., Prim, D., and Thomassigny, C., *Eur. J. Org. Chem.*, **2014**, 7000.
377 Roßbach, J., Harms, K., and Koert, U., *Eur. J. Org. Chem.*, **2014**, 993.
378 Sarkar, R. and Mukhopadhyay, C., *Tetrahedron Lett.*, **55**, 2618 (2014).
379 Wang, Z. D., Eilander, J., Yoshida, M., and Wang, T., *Eur. J. Org. Chem.*, **2014**, 7664.
380 Kurteva, V. B., Lubenov, L. A., and Antonova, D. V., *RSC Adv.*, **4**, 175 (2014).
381 Chai, H., Li, J., Yang, L., Liu, M., Yang, D., Zhang, Q., and Shi, D., *Chin. J. Chem.*, **32**, 865 (2014).
382 Habibi-Khorassani, S. M., Maghsoodlou, M. T., Shahraki, M., Talaiefar, S., Kazemian, M. A., and Aboonajmi, J., *Res. Chem. Intermed.*, **41**, 5821 (2015).
383 Pan, X., Li, M., and Gu, Y., *Chem. Asian J.*, **9**, 268 (2014).
384 Solé, D. and Fernández, I., *Acc. Chem. Res.*, **47**, 168 (2014).
385 Oudeyer, S., Brière, J.-F., and Levacher, V., *Eur. J. Org. Chem.*, **2014**, 6103.
386 Pratihar, S., *Org. Biomol. Chem.*, **12**, 5781 (2014).
387 Choudhary, A., Newberry, R. W., and Raines, R. T., *Org. Lett.*, **16**, 3421 (2014).
388 Jing, Y., Liu, H., Yu, Y., Tan, X., Wang, H., Wang, F., Du, X., and Chen, Y., *Rev. Roum. Chim.*, **58**, 799 (2013).
389 Ming, J., Han, J., and Lu, X., *Heterocycl. Commun.*, **20**, 243 (2014).
390 Zardoost, M. R., Khalilzadeh, M. A., and Ataei, M. S., *Prog. React. Kinet. Mech.*, **39**, 53 (2014).
391 Wang, M.-C., Huang, P.-J., Yang, X.-C., Song, X., and Lu, H.-J., *Tetrahedron: Asymmetry*, **25**, 781 (2014).
392 Aga, M. A., Kumar, B., Rouf, A., Shah, B. A., and Taneja, S. C., *Tetrahedron Lett.*, **55**, 2639 (2014).
393 Gök, Y. and Kekeç, L., *Tetrahedron Lett.*, **55**, 2727 (2014).
394 Zhang, A., Yang, L., Yang, N., and Liu, Y., *Tetrahedron: Asymmetry*, **25**, 289 (2014).
395 Yi-Shan, S., Boobalan, R., Chen, C., and Lee, G.-H., *Tetrahedron: Asymmetry*, **25**, 327 (2014).
396 Yue, H., Huang, H., Bian, G., Zong, H., Li, F., and Song, L., *Tetrahedron: Asymmetry*, **25**, 170 (2014).
397 Rachwalski, M., *Tetrahedron: Asymmetry*, **25**, 219 (2014).
398 Karabuga, S., Karakaya, I., and Ulukanli, S., *Tetrahedron: Asymmetry*, **25**, 851 (2014).
399 Huang, H., Zong, H., Shen, B., Yue, H., Bian, G., and Song, L., *Tetrahedron*, **70**, 1289 (2014).
400 Calvillo-Barahona, M., Casares, J. A., Cordovilla, C., Genov, M. N., Martínez-Ilarduya, J. M., and Espinet, P., *Chem. Eur. J.*, **20**, 14800 (2014).
401 Pisani, L., Bochicchio, C., Superchi, S., and Scafato, P., *Eur. J. Org. Chem.*, **2014**, 5939.
402 Raders, S. M., Jones, J. M., Semmes, J. G., Kelley, S. P., Rogers, R. D., and Shaughnessy, K. H., *Eur. J. Org. Chem.*, **2014**, 7395.
403 Das, T., Chakraborty, A., and Sarkar, A., *Tetrahedron Lett.*, **55**, 5174 (2014).
404 Kuang, Y. and Wang, Y., *Eur. J. Org. Chem.*, **2014**, 1163.
405 Martins, B. S. and Lüdtke, D. S., *Eur. J. Org. Chem.*, **2014**, 5364.
406 Song, X., Hua, Y.-Z., Shi, J.-G., Sun, P.-P., Wang, M.-C., and Chang, J., *J. Org. Chem.*, **79**, 6087 (2014).
407 Zhang, A.-L., Yang, L.-W., Yang, N.-F., and Liu, D.-C., *J. Organomet. Chem.*, **768**, 50 (2014).
408 Kotani, S., Kukita, K., Tanaka, K., Ichibakase, T., and Nakajima, M., *J. Org. Chem.*, **79**, 4817 (2014).
409 Vidal, C., García-Álvarez, J., Hernán-Gómez, A., Kennedy, A. R., and Hevia, E., *Angew. Chem. Int. Ed.*, **53**, 5969 (2014).
410 Zhang, A., Yang, N., Yang, L., and Peng, D., *Chem. Lett.*, **43**, 462 (2014).
411 Raffier, L., Gutierrez, O., Stanton, G. R., Kozlowski, M. C., and Walsh, P. J., *Organometallics*, **33**, 5371 (2014).
412 Fernández-Mateos, E., Maciá, B., and Yus, M., *Eur. J. Org. Chem.*, **2014**, 6519.
413 Nakakita, T., Miura, M., Toriyama, M., Motohashi, S., and Barybn, M. V., *Tetrahedron Lett.*, **55**, 1090 (2014).
414 Bella, M., Steiner, B., Langer, V., and Koóš, M., *Beilstein J. Org. Chem.*, **10**, 1942 (2014).
415 Bailey, W. F., Wiberg, K. B., and Bartelson, A. L., *Tetrahedron Lett.*, **55**, 4807 (2014).
416 Zhang, X.-S., Chen, K., and Shi, Z.-J., *Chem. Sci.*, **5**, 2146 (2014).
417 Chen, Z., Nieves-Quinones, Y., Waas, J. R., and Singleton, D. A., *J. Am. Chem. Soc.*, **136**, 13122 (2014).
418 Coyle, E. E., Doonan, B. J., Holohan, A. J., Walsh, K. A., Lavigne, F., Krenske, E. H., and O'Brien, C. J., *Angew. Chem. Int. Ed.*, **53**, 12907 (2014).
419 Werner, T., Hoffmann, M., and Deshmukh, S., *Eur. J. Org. Chem.*, **2014**, 6630.
420 Tsai, Y.-L., Syu, S., Yang, S.-M., Das, U., Fan, Y.-S., Lee, C.-J., and Lin, W., *Tetrahedron*, **70**, 5038 (2014).

[421] Barabash, A. V., Butova, E. D., Kanyuk, I. M., Schreiner, P. R., and Fokin, A. A., *J. Org. Chem.*, **79**, 10669 (2014).
[422] Gao, B., Zhao, Y., Hu, M., Ni, C., and Hu, J., *Chem. Eur. J.*, **20**, 7803 (2014).
[423] Wang, X.-P., Lin, J.-H., Xiao, J.-C., and Zheng, X., *Eur. J. Org. Chem.*, **2014**, 928.
[424] Yang, J. and Yoshikai, N., *J. Am. Chem. Soc.*, **136**, 16748 (2014).
[425] Kou, K. G. M., Le, D. N., and Dong, V. M., *J. Am. Chem. Soc.*, **136**, 9471 (2014).
[426] Wang, M., Zhang, X., Chen, Z., Tang, Y., and Lei, M., *Sci. China Chem.*, **57**, 1264 (2014).
[427] Du, X.-W., Ghosh, A., and Stanley, L. M., *Org. Lett.*, **16**, 4036 (2014).
[428] Iglesias, M., Fernandez-Alvarez, F. J., and Oro, L. A., *ChemCatChem*, **6**, 2486 (2014).
[429] Chatterjee, B. and Gunanathan, C., *Chem. Commun. (Cambridge)*, **50**, 888 (2014).
[430] Yumino, S., Hashimoto, T., Tahara, Y., and Nagashima, S., *Chem. Lett.*, **43**, 1829 (2014).
[431] Shinohara, K., Kawabata, S., Nakamura, H., Manabe, Y., and Sakaguchi, S., *Eur. J. Org. Chem.*, **2014**, 5532.
[432] Vergote, T., Nahra, F., Merschaert, A., Riant, O., Peeters, D., and Leyssens, T., *Organometallics*, **33**, 1953 (2014).
[433] Wang, W., Gu, P., Wang, Y., and Wei, H., *Organometallics*, **33**, 847 (2014).
[434] Revunova, K. and Nikonov, G. I., *Chem. Eur. J.*, **20**, 839 (2014).
[435] Hoshimoto, Y., Yabuki, H., Kumar, R., Suzuki, H., Ohashi, M., and Ogoshi, S., *J. Am. Chem. Soc.*, **136**, 16752 (2014).
[436] Gajulapalli, V. P. R., Vinayagam, P., and Kesavan, V., *Org. Biomol. Chem.*, **12**, 4186 (2014).
[437] Sureshkumar, D., Ganesh, V., Kumagai, N., and Shibasaki, M., *Chem. Eur. J.*, **20**, 15723 (2014).
[438] Yang, Z., Son, K.-I., Li, S., Zhou, B., and Xu, J., *Eur. J. Org. Chem.*, **2014**, 6380.
[439] North, M. and Urwin, S., *Tetrahedron*, **70**, 7100 (2014).
[440] Błocka, E., Bosiak, M. J., Wełniak, M., Ludwiczak, A., and Wojtczak, A., *Tetrahedron: Asymmetry*, **25**, 554 (2014).
[441] Wen, Y.-Q., Hertzberg, R., and Moberg, C., *J. Org. Chem.*, **79**, 6172 (2014).
[442] Alegre-Requena, J. V., Marqués-López, E., Miguel, P. J. S., and Herrera, R. P., *Org. Biomol. Chem.*, **12**, 1258 (2014).
[443] Sun, Y.-M., Xin, N., Xu, Z.-Y., Liu, L.-J., Meng, F.-J., Zhang, H., Fu, B.-C., Liang, Q.-J., Zheng, H.-X., Sun, L.-J., Zhao, C.-Q., and Han, L.-B., *Org. Biomol. Chem.*, **12**, 9457 (2014).
[444] Zhang, H., Sun, Y.-M., Yao, L., Ji, S.-Y., Zhao, C.-Q., and Han, L.-B., *Chem. Asian J.*, **9**, 1329 (2014).
[445] Wiktorowicz, J. and Jankowski, S., *Phosphorus, Sulfur Silicon Relat. Elem.*, **189**, 1144 (2014).
[446] (a) Serdiuk, I. E., Wera, M., Roshal, A. S. D., Sowinsky, P., and Zadykowicz, B., *Tetrahedron Lett.*, **52**, 2737 (2011); (b) Hansen, P. E., Kamounah, F. S., Zhiryakova, D., Manolova, Y., and Antonov, L., *Tetrahedron Lett.*, **55**, 354 (2014).
[447] Emamian, S. R., Domingo, L. R., and Tayyari, S. F., *J. Mol. Graph. Model.*, **49**, 47 (2014).
[448] Reeves, C. M., Behenna, D. C., and Stoltz, B. M., *Org. Lett.*, **16**, 2314 (2014).
[449] Xu, Z.-F., Cai, C.-X., Jiang, M., and Liu, J.-T., *Org. Lett.*, **16**, 3436 (2014).
[450] Dong, D.-Q., Hao, S.-H., Wang, Z.-L., and Chen, C., *Org. Biomol. Chem.*, **12**, 4278 (2014).
[451] Zhan, M., Zhang, T., Huang, H., Xie, Y., and Chen, Y., *J. Labelled Compd. Radiopharm.*, **57**, 533 (2014).
[452] Yang, X., Phipps, R. J., and Toste, F. D., *J. Am. Chem. Soc.*, **136**, 5225 (2014).
[453] Lam, Y. and Houk, K. N., *J. Am. Chem. Soc.*, **136**, 9556 (2014).
[454] Gu, X., Zhang, Y., Xu, Z.-J., and Che, C.-M., *Chem. Commun. (Cambridge)*, **50**, 7870 (2014).
[455] Li, Z., Yang, F., Meng, Q., and Gao, Z., *Tetrahedron: Asymmetry*, **25**, 1215 (2014).
[456] Vekariya, R. H. and Patel, H. D., *Tetrahedron*, **70**, 3949 (2014).
[457] List, B., Čorić, I., Grygorenko, O. O., Kaib, P. S. J., Komarov, I., Lee, A., Leutzch, M., Pan, S. C., Tymtsunik, A. V., and van Gemmeren, M., *Angew. Chem. Int. Ed.*, **53**, 282 (2014).
[458] Caruna, L., Kniep, F., Johansen, T. K., Poulsen, P. H., and Jørgensen, K. A., *J. Am. Chem. Soc.*, **136**, 15929 (2014).
[459] Guo, Z.-L., Xue, J.-H., Fu, L.-N., Zhang, S.-E., and Guo, Q.-X., *Org. Lett.*, **16**, 6472 (2014).
[460] Zhu, Y., Cai, C., and Lu, G., *Helv. Chim. Acta*, **97**, 1666 (2014).
[461] Xu, Q., Chen, J., Tian, H., Yuan, X., Li, S., Zhou, C., and Liu, J., *Angew. Chem. Int. Ed.*, **53**, 225 (2014).
[462] Zhang, D.-Y., Zhu, F.-L., Wang, Y.-H., Hu, X.-H., Chen, S., Hou, C.-J., and Hu, X.-P., *Chem. Commun. (Cambridge)*, **50**, 14459 (2014).
[463] Shen, X., Miao, W., Ni, C., and Hu, J., *Angew. Chem. Int. Ed.*, **53**, 775 (2014).
[464] Li, L., Chen, Q.-Y., and Guo, Y., *J. Org. Chem.*, **79**, 5145 (2014).
[465] Fang, Z., Ning, Y., Mi, P., Liao, P., and Bi, X., *Org. Lett.*, **16**, 1522 (2014).
[466] Hashimoto, R., Iida, T., Aikawa, K., Ito, S., and Mikami, K., *Chem. Eur. J.*, **20**, 2750 (2014).
[467] Henrion, M., Chetcuti, M. J., and Ritleng, V., *Chem. Commun. (Cambridge)*, **50**, 4624 (2014).

[468] Mizar, P. and Wirth, T., *Angew. Chem. Int. Ed.*, **53**, 5993 (2014).
[469] Xu, C., Zhang, L., and Luo, S., *Angew. Chem. Int. Ed.*, **53**, 4149 (2014).
[470] Zhang, L., Xu, C., Mi, X., and Luo, S., *Chem. Asian J.*, **9**, 3565 (2014).
[471] Iglesias, E., *RSC Adv.*, **3**, 15192 (2013).
[472] Deng, T., Wang, H., and Cai, C., *Org. Biomol. Chem.*, **12**, 5843 (2014).
[473] (a) Deng, Q.-H., Rettenmeier, C., Wadepohl, H., and Gade, L. H., *Chem. Eur. J.*, **20**, 93 (2014); (b) Shao, X., Wang, X., Yang, T., Lu, L., and Shen, Q., *Angew. Chem. Int. Ed.*, **52**, 3457 (2013).
[474] Burés, J., Dingwall, P., Armstrong, A., and Blackmond, D. G., *Angew. Chem. Int. Ed.*, **53**, 8700 (2014).
[475] Pushpalatha, L., *Oxid. Commun.*, **37**, 155 (2014).
[476] Jia, X., Ma, J., Wang, M., Du, Z., Lu, F., Wang, F., and Xu, J., *Appl. Catal., A.*, **482**, 231 (2014).
[477] Bortolini, O., Chiappe, C., Fogagnolo, M., Giovannini, P. P., Massi, A., Pomelli, C. S., and Ragno, D., *Chem. Commun. (Cambridge)*, **50**, 2008 (2014).
[478] Panwar, S., Pohani, S., Swami, P., Vyas, S., and Sharma, P. K., *Eur. Chem. Bull.*, **2**, 904 (2013).
[479] Rai, K. K., Kannaujia, R. K., Rai, K., and Singh, S., *Orient. J. Chem.*, **29**, 1071 (2013).
[480] Pushpalatha, L., *Oxid. Commun.*, **37**, 148 (2014).
[481] Hiran, B. L., Khuntwal, J., and Malkani, R. K., *Oxid. Commun.*, **36**, 612 (2013).
[482] Kumar, R., Pandey, D., and Kothari, S., *Oxid. Commun.*, **37**, 424 (2014).
[483] Jain, A. K., Meena , and Kumar, D., *Pharm. Chem.*, **6** 187 (2014).
[484] Kovalskyi, Y. P., Marshalok, O. I., Vytrykush, N. M., and Marshalok, G. A., *Chem. Heterocycl. Comp.*, **50**, 7 (2014).
[485] Melone, L. and Punta, C., *New Dev. Aldehydes Res.*, 121 (2013).
[486] Brewster, T. P., Ou, W. C., Tran, J. C., Goldberg, K. I., Hanson, S. K., Cundari, T. R., and Heinekey, D. M., *ACS Catal.*, **4**, 3034 (2014).
[487] Ramanjaneyulu, B. T., Pareek, M., Reddy, V., and Anand, R. V., *Helv. Chim. Acta*, **97**, 431 (2014).
[488] Forte, G., Chiarotto, I., Inesi, A., Loreto, M. A., and Feroci, M., *Adv. Synth. Catal.*, **356**, 1773 (2014).
[489] Berry, M. T., Castrejon, D., and Hein, J. E., *Org. Lett.*, **16**, 3676 (2014).
[490] Kaise, H., Shimokawa, J., and Fukuyama, T., *Org. Lett.*, **16**, 727 (2014).
[491] Mupparapu, N., Khan, S., Battula, S., Kushwaha, M., Gupta, A. P., Ahmed, Q. N., and Vishwakarma, R. A., *Org. Lett.*, **16**, 1152 (2014).
[492] Hemkar, S., Sailani, R., Khandelwal, C. L., and Sharma, P. D., *Am. J. Phys. Chem.*, **2**, 73 (2013).
[493] Huang, X., Li, X., Zou, M., Song, S., Tang, C., Yuan, Y., and Jiao, N., *J. Am. Chem. Soc.*, **136**, 14858 (2014).
[494] Tang, C. and Jiao, N., *Angew. Chem. Int. Ed.*, **53**, 6528 (2014).
[495] Yuan, X., Miller, C. J., Pham, A. N., and Waite, T. D., *Free Radical Biol. Med.*, **71**, 291 (2014).
[496] Davis, R. L., Jensen, K. L., Gschwend, B., and Jørgensen, K. A., *Chem. Eur. J.*, **20**, 64 (2014).
[497] Boucherif, A., Yang, Q.-Q., Wang, Q., Chen, J.-R., Lu, L.-Q., and Xiao, W.-J., *J. Org. Chem.*, **79**, 3924 (2014).
[498] White, N. A. and Rovis, T., *J. Am. Chem. Soc.*, **136**, 14674 (2014).
[499] Ma, Q., Xing, W., Xu, J., and Peng, X., *Catal. Commun.*, **53**, 5 (2014).
[500] Pirovano, P., Magherusan, A. M., McGlynn, C., Ure, A., Lynes, A., and McDonald, A. R., *Angew. Chem. Int. Ed.*, **53**, 5946 (2014).
[501] Romney, D. K., Colvin, S. M., and Miller, S. J., *J. Am. Chem. Soc.*, **136**, 14019 (2014).
[502] Bhattacharyya, S. and Hatua, K., *RSC Adv.*, **4**, 18702 (2014).
[503] Xia, Y., Xia, Y., Ge, R., Liu, Z., Xiao, Q., Zhang, Y., and Wang, J., *Angew. Chem. Int. Ed.*, **53**, 3917 (2014).
[504] Wang, Z., Li, L., and Huang, Y., *J. Am. Chem. Soc.*, **136**, 12233 (2014).
[505] Yamabe, S., Zeng, G., Guan, W., and Sakaki, S., *Beilstein J. Org. Chem.*, **10**, 259 (2014).
[506] (a) Blacker, A. J., Clot, E., Duckett, S. B., Eisenstein, O., Grace, J., Nova, A., Perutz, R. N., Taylor, D. J., and Whitwood, A. C., *Chem. Commun. (Cambridge)*, **45**, 6801 (2009); (b) Nova, A., Taylor, D. J., Blacker, A. J., Duckett, S. B., Perutz, R. N., and Eisenstein, O., *Organometallics*, **33**, 3433 (2014).
[507] Chakraborty, S., Lagaditis, P. O., Forster, M., Bielinski, E. A., Hazari, N., Holthausen, M. C., Jones, W. D., and Schneider, S., *ACS Catal.*, **4**, 3994 (2014).
[508] Ngo, A. H., Adams, M. J., and Do, L. H., *Organometallics*, **33**, 6742 (2014).
[509] Ito, J. and Nishiyama, H., *Tetrahedron Lett.*, **55**, 3133 (2014).
[510] Hamada, Y., *Chem. Rec.*, **14**, 235 (2014).
[511] Huang, Y., Li, Y., Leung, P.-H., and Hayashi, T., *J. Am. Chem. Soc.*, **136**, 4865 (2014).
[512] Dub, P. A., Henson, N. J., Martin, R. L., and Gordon, J. C., *J. Am. Chem. Soc.*, **136**, 3505 (2014).
[513] Enders, D., Stöckel, B. A., and Rembiak, A., *Chem. Commun. (Cambridge)*, **50**, 4489 (2014).
[514] Yoshimura, M., Tanaka, S., and Kitamura, M., *Tetrahedron Lett.*, **55**, 3635 (2014).

[515] Li, Y., Yu, S., Wu, X., Xiao, J., Shen, W., Dong, Z., and Gao, J., *J. Am. Chem. Soc.*, **136**, 4031 (2014).
[516] Chen, X., Zhou, H., Zhang, K., Li, J., and Huang, H., *Org. Lett.*, **16**, 3912 (2014).
[517] Forkel, N. V., Henderson, D. A., and Fuchter, M. J., *Tetrahedron Lett.*, **55**, 5511 (2014).
[518] Sarkar, S., Shil, S., and Misra, A., *J. Indian Chem. Soc.*, **91**, 1289 (2014).
[519] Dahy, A. A. and Koga, N., *J. Organomet. Chem.*, **770**, 101 (2014).
[520] Cui, J.-F., Kung, K. K.-Y., Ko, H.-M., Hui, T.-W., and Wong, M.-K., *Adv. Synth. Catal.*, **356**, 2965 (2014).
[521] Zhang, H.-R., Xue, J.-J., Chen, R., Tang, Y., and Li, Y., *Chin. Chem. Lett.*, **25**, 710 (2014).
[522] Chemouri, H. and Mekelleche, S. M., *Mol. Phys.*, **112**, 601 (2014).
[523] Melen, M. L., Simmonds, H. R., Wadepohl, H., Wood, P. T., Gade, L. H., and Wright, D. S., *Aust. J. Chem.*, **67**, 1030 (2014).
[524] Julio, L. L., Lezama, J., Maldonado, A., Mora, J. R., and Chuchani, G., *J. Phys. Org. Chem.*, **27**, 450 (2014).
[525] Feng, P., Sun, X., Su, Y., Li, X., Zhang, L.-H., Shi, X., and Jiao, N., *Org. Lett.*, **16**, 3388 (2014).
[526] Nambu, H., Fukumoto, M., Hirota, W., and Yakura, T., *Org. Lett.*, **16**, 4012 (2014).
[527] Kang, B. C., Shim, S. Y., and Ryu, D. H., *Org. Lett.*, **16**, 2077 (2014).
[528] Chen, S., Li, X., Zhao, H., and Li, B., *J. Org. Chem.*, **79**, 4137 (2014).
[529] Guo, C., Sahoo, B., Daniliuc, C. G., and Glorius, F., *J. Am. Chem. Soc.*, **136**, 17402 (2014).
[530] Ermolat'ev, D. S., Feng, H., Song, G., and Van der Eycken, E. V., *Eur. J. Org. Chem.*, **2014**, 5346.
[531] Jose, A., Jayakrishnan, A. J., Vedhanarayanan, B., Menon, R. S., Varughese, S., Suresh, E., and Nair, V., *Chem. Commun. (Cambridge)*, **50**, 4616 (2014).
[532] Molnár, I. G., Tanzer, E.-M., Daniliuc, C., and Gilmour, R., *Chem. Eur. J.*, **20**, 794 (2014).
[533] Hovey, M. T., Check, C. T., Sipher, A. F., and Scheidt, K. A., *Angew. Chem. Int. Ed.*, **53**, 9603 (2014).
[534] Trossarello, J., Egunjobi, A., Morgan, W. J., Ahamed, R., and Aiken, K. S., *Curr. Org. Synth.*, **11**, 466 (2014).
[535] Ghadari, R. and Zahedi, M., *Comput. Theor. Chem.*, **1043**, 64 (2014).
[536] Zheng, Q.-Z. and Jiao, N., *Tetrahedron Lett.*, **55**, 1121 (2014).
[537] Zhang, X.-Y., Dong, D.-Q., Yue, T., Hao, S.-H., and Wang, Z.-L., *Tetrahedron Lett.*, **55**, 5462 (2014).
[538] Kosobokov, M. D., Levin, V. V., Struchkova, M. I., and Dilman, A. D., *Org. Lett.*, **16**, 3784 (2014).
[539] Kianmehr, E., Kazemi, S., and Foroumadi, A., *Tetrahedron*, **70**, 349 (2014).
[540] Yu, L., Wang, M., and Wang, L., *Tetrahedron*, **70**, 5391 (2014).
[541] Zhao, J., Fang, H., Han, J., and Pan, Y., *Org. Lett.*, **16**, 2530 (2014).
[542] Yan, G. and Borah, A. J., *Org. Chem. Front.*, **1**, 838 (2014).
[543] Barve, B. D., Wu, Y.-C., El-Shazly, M., Korinek, M., Cheng, Y.-B., Wang, J.-J., and Chang, F.-R., *Org. Lett.*, **16**, 1912 (2014).