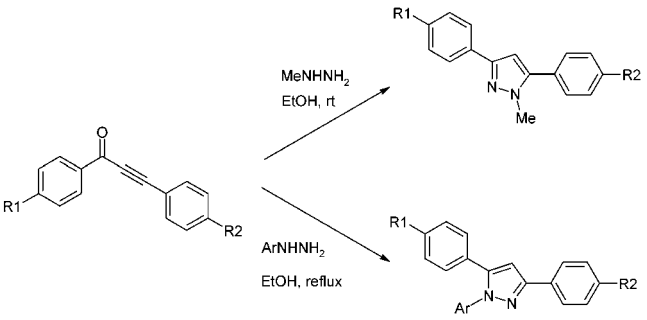
Organic Process Research & Development **2004**, *8,* 303−310

Highlights from the Literature

Some Items of Interest to Process R&D Chemists and Engineers

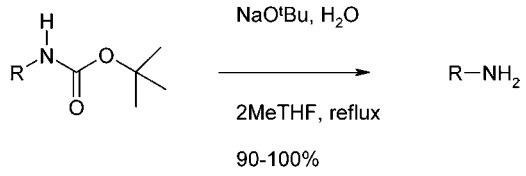
1,3,5-Substituted Pyrazoles

As part of a drug candidate development programme researchers at Merck have recently reported (*Synthesis* **2004**, 43) their efforts towards the synthesis of diversely substituted 1,3,5-substituted pyrazoles from the reaction of acetylenic ketones with substituted hydrazines. A number of methods for the construction of this heterocycle exist; however, varying degrees of regioisomeric pyrazole products are produced. Their method exhibits high and predictable regioselectivity regardless of the nature of the substituents in the substrates and affords essentially single pyrazole isomers in excellent yields.



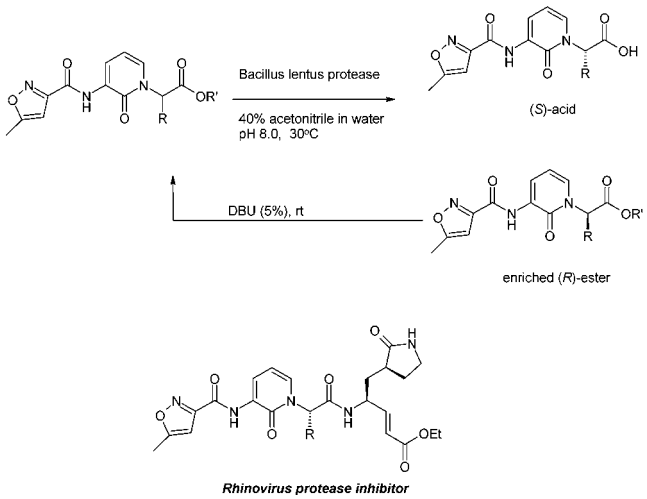
Deprotection of BOC under Basic Conditions

The *tert*-butyl carbamate (BOC) group is a common protecting group for amines. Liberation of the amine via deprotection is commonly performed using acid; however, Tom and co-workers at Pfizer describe (*Tetrahedron Lett.* **2004**, 905) how treatment of primary BOC amines with excess sodium *tert*-butoxide in slightly wet tetrahydrofuran or 2-methyltetrahydrofuran yields the corresponding primary amine in excellent yield. The group postulate that the reaction proceeds through an isocyanate intermediate.



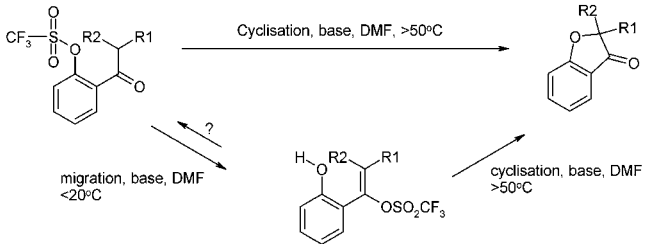
Enzymatic Resolution

Tao and colleagues report (*Tetrahedron* **2004**, 759) the development of an efficient synthesis for the preparation of (2*S*)-2-[3-{[(5-methylisoxazol-3-yl)carbonyl]amino}-2-oxopyridin-1(2*H*)-yl]pent-4-ynoic acid (see below) as a key intermediate in the synthesis of a human rhinovirus (HRV) protease inhibitor. In the presence of 40% acetonitrile, the alkaline protease from *Bacillus lentus* was shown to catalyse the kinetic resolution of racemic ester (see below) to afford (*S*)-acid in 49% chemical yield/per cycle with excellent chiral purity. Epimerisation of the (*R*)-ester was achieved via a DBU-catalysed epimerization. Interestingly, the group draw a comparison between the enzymatic preparation and an existing chemical resolution route. The biotransformation protocol exhibits lower costs as well as higher yields, enantioselectivity, and substrate loads.



Reactions of Substituted 2-Acetophenone Triflates

Coe and co-workers at Pfizer report (*J. Org. Chem.* **2003**, *68*, 9964) an unexpected, yet facile, conversion of mono- and dialkyl-substituted ketones to 2-substituted benzofuran-3-ones. This oxidative ring closure of alkyl-substituted 2-hydroxyacetophenone trifluoromethanesulfonate esters (triflates) occurs upon exposure to base in anaerobic DMF at 20−90 °C. Potential mechanistic pathways are described in the paper.



N-Acyl-Substituted Sulfamides

N-Alkoxycarbonyl- or *N*-aryloxycarbonyl-substituted sulfamides have been prepared by Masui and colleagues from Shionogi (*Tetrahedron Lett.* **2004**, 1853) using a one-pot method in efficient yields from chlorosulfonyl isocyanate (CSI), alcohols, and aqueous (or dry) amines via the corresponding water-resistant carboxysulfamoylammonium salts (Burgess-type reagents), which are generated in situ by the

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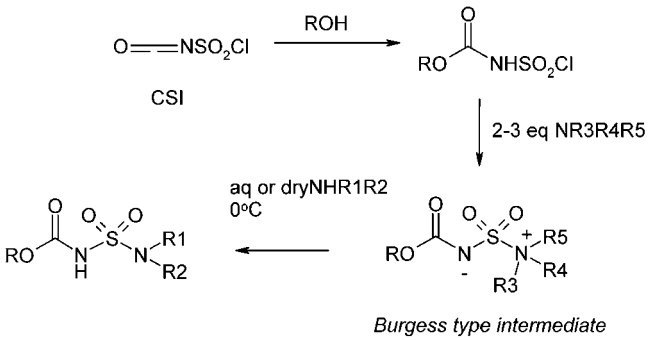
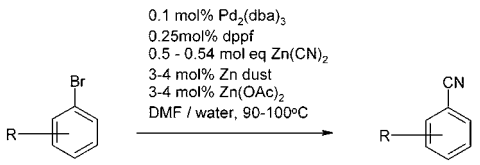
deactivation of the corresponding water-sensitive *N*-(chlorosulfonyl)carbamates with tertiary amines.



Burgess type intermediate

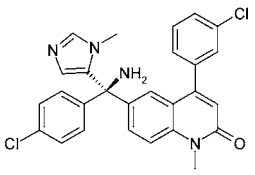
Robust Pd-Catalysed Cyanation Procedure

Conditions have been developed at Bristol Myers Squibb to ensure a more robust Pd(0)-mediated procedure to convert aryl bromides to aryl cyanides and have been reported by Chidambaram (*Tetrahedron Lett.* **2004**, 1441). The method uses zinc dust to keep the Pd in the zero oxidation state and zinc acetate to ensure high catalytic activity. This procedure is applicable to a wide range of substrates and enables reactions to be performed where reagent-grade DMF is used without stringent deoxygenation controls.



Zarnestra (R115777)

R115777 (Zarnestra) is currently undergoing clinical evaluation as an orally active antitumor agent with low toxicity. In a recent communication (*Eur. J. Org. Chem.* **2004**, 479) Angibaud and colleagues describe their efforts in defining and developing a synthetic route to access Zarnestra.



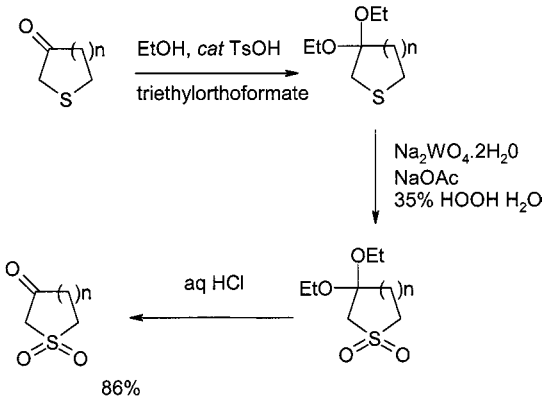
R115777

Multigram Synthesis of Tetrahydrothiophene-3-one-1,1-dioxide

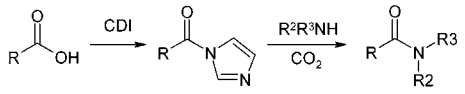
A short and efficient multigram-scale synthesis of tetrahydrothiophene-3-one-1,1-dioxide is described by Altenbach and colleagues from Abbott and Synlab (*Synth. Commun.* **2004**, 567). Their method (see below) requires no chromatography and avoids the use of environmentally hazardous oxidants such as the Jones reagent.

Amidination Using CDI, Rate Enhancement with CO_2

In a fascinating paper by Vaidyanathan and co-workers at Pfizer (*J. Org. Chem.* **2004**, 2565) a description of how



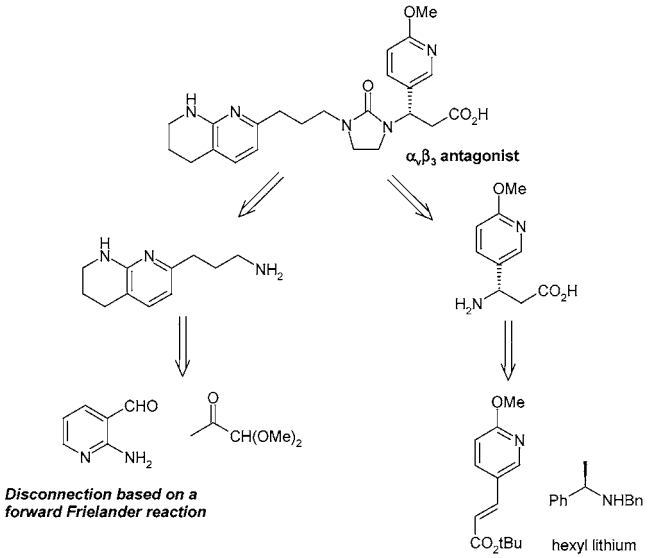
carbon dioxide catalyses the reaction of imidazolides with amines to form amides is described. A substantial rate enhancement of this reaction is observed in the presence of CO_2 compared to the CO_2-free case. In fact the group establish that sparging of CO_2 can effectively "jump start" slow amidination reactions. The scope, postulated mechanism, and limitations of this reaction are discussed.



rate enhancement

$\alpha_v\beta_3$ Antagonist

Workers from Merck outline a practical preparation of an $\alpha_v\beta_3$ antagonist in a recent article (*J. Org. Chem.* **2004**, *68*, 1959). The synthesis comprises three key fragments, a tetrahydronaphthyridine moiety, a β-alanine moiety, and a central imidazolidone core. The tetrahydronaphthyridine component was prepared using two different methods, both of which relied on variations of the Friedländer reaction to establish the desired regiochemistry. The β-alanine component was prepared using Davies' asymmetric 1,4-addition methodology as the key stereodefining step. Construction of the central imidazolidone portion was created from these two intermediates using an effective three-step cyclization protocol.

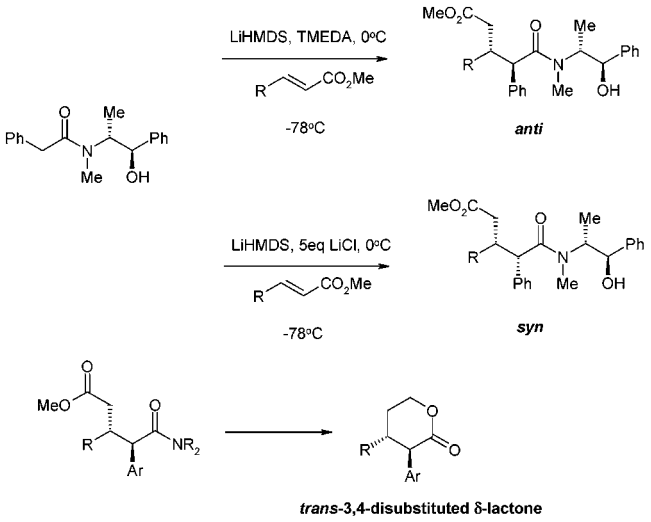


Disconnection based on a forward Frielander reaction

Disconnection based on a forward reaction using Davies methodology

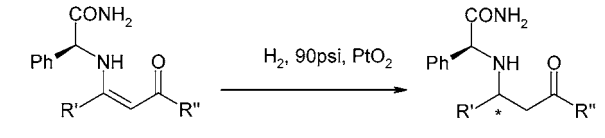
Michael Reactions of Pseudoephedrine Amide Enolates

Smitrovich and colleagues at Merck report (*J. Org. Chem.* **2004**, 1903) how the stereochemical outcome of the asymmetric Michael reaction of pseudoephedrine amide enolates changes dramatically in the presence of LiCl. Reaction of the enolate in the absence of LiCl results in formation of the *anti* Michael adduct with high selectivity, whereas in the presence of lithium chloride the *syn* adduct is favored. This method provides access to enantiomerically enriched *trans*-3,4-disubstituted δ-lactones from the *anti* Michael adducts by a two-step reduction/lactonization sequence. Information obtained from NMR studies indicates that, under both enolization conditions, the (*Z*)-enolate is formed. Rationalisation of the selectivity is presented in the article.



Diastereoselective Hydrogenation

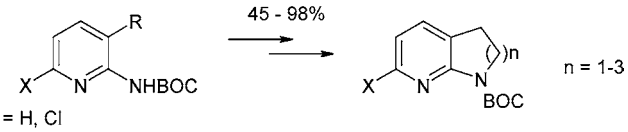
In a communication from Merck (*J. Am. Chem. Soc.* **2004**, *126*, 3048) pure (*Z*)-enamines (readily prepared from β-ketoesters and amides using (*S*)-phenylglycine amide) were hydrogenated with very high diastereoselectivities (up to 200:1) using heterogeneous catalysis. Hydrogenolytic cleavage of the (*S*)-phenylglycine amide afforded the corresponding chiral β-aminoesters and amides. The high geometrical purity of the (*Z*)-enamine and a simple activation procedure for the PtO_2 catalyst were essential in achieving the high selectivity.



R' = alkyl or aryl
R" = alkoxy or amido

Synthesis of Annulated Pyridines

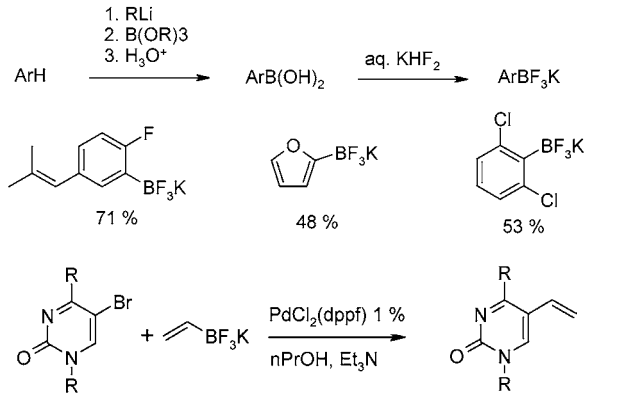
Davies and colleagues from Merck describe (*Tetrahedron Lett.* **2004**, 1721) how the ortho-alkylation of Boc-protected aminopyridines with α,ω-dihaloalkanes followed by in situ cyclisation, resulted in the corresponding annulated pyridine derivatives in good to excellent yields. Factors such as the nature of alkylating agent, chelating agent, transmetalation additive, and directing group are presented in the communication. Since the 6-chloro derivative may be processed through this sequence, there exists an opportunity to further functionalise the annulated pyridines.



X = H, Cl
R = H, Me

Potassium Trifluoro(organo)borates: New Perspectives in Organic Chemistry

S. Darses and J.-P. Genet (*Eur. J. Org. Chem.* **2003**, 4313) have summarised recent achievements concerning the chemistry of potassium trifluoro(organo)borates, which are highly stable organoboron derivatives. These salts have lately emerged as promising alternatives to other organoboron reagents and have shown interesting reactivity, not only through intermediate formation of difluoroboranes but also in transmetalation reactions with transition metals where they have proven to be more reactive than boronic acids and esters. Thanks to the filling of the vacant orbitals of the trivalent boron atom, these -ate complexes are much more stable towards oxygen or moisture than other organoboron derivatives. The authors have also summarised the potential synthesis of compounds of this type, which is reported to be a straightforward process after preparation of the boronic acid derivatives; these are treated in situ with potassium hydrogen difluoride. Their isolation and purification are also reported to be straightforward in comparison to methods available for boronic acids and esters.



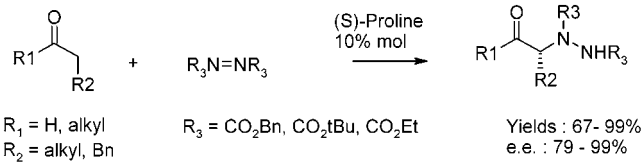
Molybdenum-Catalysed Asymmetric Allylic Alkylations

O. Belda et al. (*Acc. Chem. Res.* **2004**, *37*, 159) have described the achievements gained thus far in the area of highly regio- and enantioselective molybdenum-catalysed allylic alkylation reactions, which have become a powerful synthetic tool during the past few years. Several metals catalyse asymmetric allylic alkylations, each particular metal exhibiting its own reactivity and preference for products with different regio- and stereochemistries. The Mo-catalysed reaction is characterised by its high tendency to form the more substituted products from unsymmetrical substrates. Recent developments allow these products to be obtained in high yields with very high enantioselectivity. Along with accumulating mechanistic information, conditions permitting a wider range of substrates giving products in high yield and purity are expected to be found. This is important, since the reaction

is robust and $Mo(CO)_6$ used as the Mo source is cheap, rendering the process suitable also for large-scale synthesis.

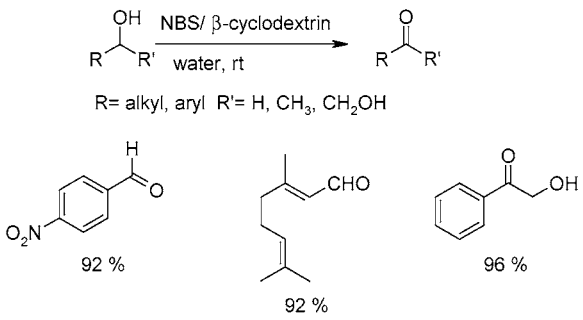
Asymmetric Electrophilic α-Amination of Carbonyl Groups

The electrophilic amination based on the "umpolung" methodology constitutes an unconventional C−N bond-forming reaction. C. Greck et al. (*Eur. J. Org. Chem.* **2004**, 1377) have given a concise overview of this interesting topic, focusing on asymmetric versions, which have been developed using chiral reagents or catalysts. The aminated products can be obtained with high stereoselectivities. The methodology is very useful for synthesis of α-amino acids and their derivatives. For instance, proline has been found to catalyse direct asymmetric α-amination of various carbonyl compounds with azadicarboxylates in medium to high yields and with good to excellent enantioselectivities.



A Simple and Selective Oxidation of Alcohols and Epoxides with NBS in the Presence of β-Cyclodextrin in Water

K. Rama Rao et al. (*Adv. Synth. Catal*. **2004**, *346*, 346) have developed a simple and mild oxidation of various alcohols and epoxides with NBS catalysed by β-cyclodextrin in water. The reaction is performed at room temperature, and the products are obtained in high to excellent yields. From primary alcohols only the corresponding aldehydes were obtained; no further oxidation of the product was observed.



Catalytic, Asymmetric Sulfur Ylide-Mediated Epoxidation of Carbonyl Compounds

The reaction of sulfur ylides with carbonyl compounds to give epoxides is an important synthetic method. V. K. Aggarwal and C. L Winn (*Acc. Chem. Res*. **2004**, Advanced Articles) have summarised the recent advances in rendering this process both asymmetric and catalytic. Two catalytic processes have been developed, the first involving the reaction of a sulfide with an alkyl halide in the presence of base and aldehyde and the second involving the reaction of a sulfide with a diazo compound or diazo precursor in the presence of a metal catalyst and aldehyde. These catalytic methods coupled with suitable chiral sulfides provide a new catalytic method for the preparation of epoxides.

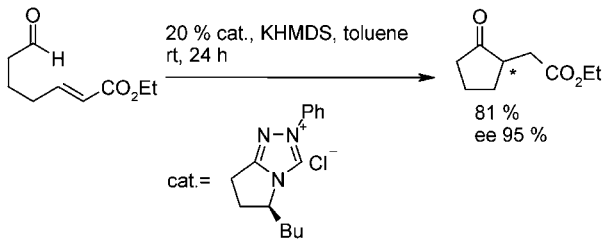
The method involving reaction of a chiral sulfide with an alkyl halide and base in the presence of an aldehyde is generally limited to the synthesis of stilbene oxide derivatives. The method involving reaction of a chiral sulfide and a diazo precursor in the presence of a PTC, metal catalyst, and aldehyde shows broader scope.

The Complex Synergy of Water in the Metal/Bromide Autoxidation of Hydrocarbons

One of the most active and selective catalysts in homogeneous liquid-phase oxidation using molecular oxygen is a mixture of cobalt, manganese, and bromide salts in acetic acid. It has been used for the production of hundreds of different carboxylic acids in high yields and purity. Water is normally a byproduct in these reactions, and W. Partenheimer (*Adv. Synth. Catal*. **2004**, *346*, 297) has found that its concentration is an important variable. In anhydrous acetic acid, with substrates with sufficiently strong electron-withdrawing groups, all of the active bromide becomes inactive via benzylic bromide formation. For 4-chlorotoluene increasing the water concentration to 5 wt % initially decreases the reaction but is more active and selective because the oxidation and the hydrolysis of the benzylic bromide allows for sufficient active bromide catalyst. It is shown that benzylic bromides do not promote the reaction. However, there are also other factors; for example, the reactivity of peroxy radicals of aldehydes are higher at low water content, the formation of Mn(IV) is also less with low amounts of water which prevents MnO_2 to be formed and precipitated.

Nucleophilic Carbenes in Asymmetric Organocatalysis

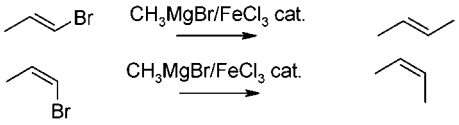
The coenzyme thiamine (vitamin B1), a natural thiazolium salt, is involved in many enzymatic catalyses. Since it has been proposed that the catalytically active species of these reactions is a nucleophilic carbene, many chemists have tried to perform enzyme mimetic asymmetric carbene catalysis. D. Enders and T. Balensiefer (*Acc. Chem. Res*. **2004**, Advanced Articles) have summarised the long and hard search for stable carbenes useful as biomimetic catalysts. It has finally been possible to develop an enantioselective benzoin condensation as well as an enantioselective intramolecular Stetter reaction utilizing stable carbenes as organocatalysts. The reactions reported so far are selective but restricted in scope and conditions. There have also been recent reports on transesterifications, ring-opening polymerizations catalysed by N-heterocyclic carbenes.



Transition Metal-Catalysed Carbon−Carbon Bond Formation with Grignard Reagents

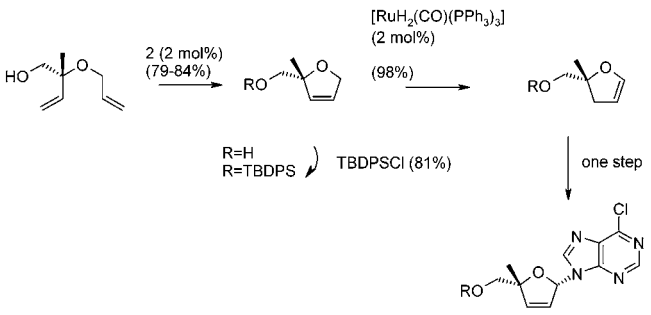
Organomagnesium compounds are among the most versatile organometallic reagents in organic synthesis. Besides

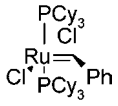
their classical nucleophilic reactions to carbonyl compounds, Grignard reagents gain useful reactivity when combined with various transition metal salts. H. Shinokubo and K. Oshima (*Eur. J. Org. Chem.* **2004**, Advanced Article) have summarised the carbon−carbon bond-forming reaction with Grignard reagents through catalysis with iron, manganese, chromium, and cobalt salts. A wide range of reactions has been developed; in particular, efficient cross-coupling reactions of organic halides, including alkyl halides with Grignard reagents, have been performed effectively under, for instance, iron catalysis. One of the characteristics of these reactions is the involvement of a carbon-centered radical species. Soon, other nontoxic and economical metals, such as iron, may substitute palladium and nickel catalysts.



Catalysis at the Interface of Ruthenium Carbene and Ruthenium Hydride Chemistry

Soon after the introduction of stable and well-defined ruthenium precatalysts for olefin metathesis it was discovered that double bond migrations may interfere with the metathesis reaction. This undesired side reaction has been attributed to the formation of ruthenium hydride species in situ. B Schmidt (*Eur. J. Org. Chem.* **2004**, Advanced Articles) has summarised recent findings where typical ruthenium metathesis precatalysts have been shown to promote nonmetathesis transformations efficiently in preparatively useful yields and selectivities, presumably via the in situ formation of ruthenium hydride species. These findings open up a pathway to development of novel catalysed reaction sequences that combine ruthenium carbene- and ruthenium hydride-mediated steps.





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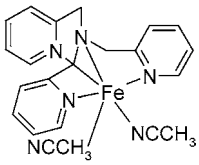
In Situ Formation of Peracetic Acid in Iron-Catalysed Epoxidations by Hydrogen Peroxide in Acetic Acid

M. Fujita et al. (*Adv. Synth. Catal*. **2004**, *346*, 190) have reported that iron complexes such as **1** have been found to catalyse the in situ formation of peracetic acid from hydrogen peroxide and acetic acid in the course of olefin oxidations. While oxidation of cyclooctene by hydrogen peroxide catalysed by **1** gives nearly equimolar epoxide and *cis*-diol products, the introduction of acetic acid to the reaction greatly enhances the selectivity for epoxidation. The resulting product distribution is nearly identical to that of cyclooctene oxidation by peracetic acid catalysed by **1**. Such in situ conversion of hydrogen peroxide to peracetic acid is not commonly observed in oxidation catalysis but has been reported for metal-free haloperoxidases in acetate buffer.

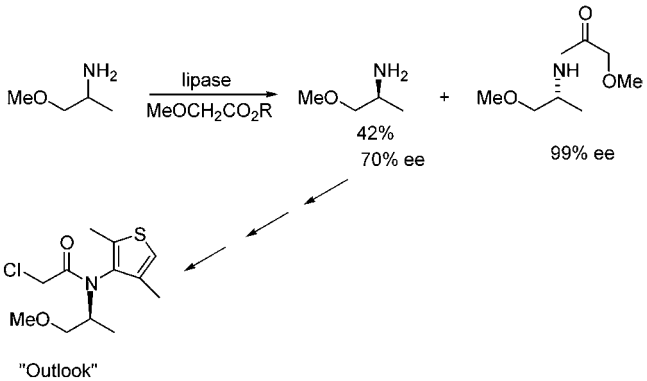


1

Industrial Methods for the Production of Optically Active Intermediates

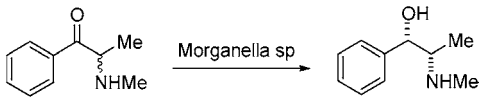
A group from BASF, led by Bernard Hauer, has produced an excellent 36-page review of the current state of the art in large-scale synthesis of optically active molecules (Breuer, M. et al. *Angew. Chem., Int. Ed.* **2004**, *43*, 788). The review compares different routes and technologies for the preparation of amino acids, amines, acids, epoxides, alcohols, etc. and focuses on industrial issues such as efficiency, environment, space-time-yield, as well as chemical yield and enantiomeric purity.

The patent literature is covered, and the review emphasizes, through personal knowledge as well as the literature, which processes are used commercially and on what tonnage. Thus, it is revealed that BASF uses the process below to produce (*S*)-1-methoxy-2-propylamine, an intermediate in the herbicide for corn (named Outlook), on a scale of 2500 t/a.



"Outlook"

The review emphasizes that biotransformations can be very efficient when compared to other methods. A recent Fuji process to produce ephedrine relies on an asymmetric reduction of a carbonyl group by microorganisms. The enantiomer that is not reduced racemises “in-situ” in this dynamic kinetic resolution.



However, the review indicates that for the production of enantiomers of epichlorohydrin and glycidol, Daiso in Japan have switched from microbial resolution to Jacobsen hydrolytic kinetic resolution and have obtained a license from Rhodia-Chirex. Production capacity is said to be expanding to 50 t/a by 2004.

Resolution methods, whether chemical or enzymatic, still play an important role in production processes, whereas the future should lie with catalytic processes, once the turnover number and turnover frequency have improved sufficiently to make the cost of catalyst metal and complex ligand less significant (see *Asymmetric Catalysis on Industrial Scale: Challenges, Approaches and Solutions*; Blaser, H. U., Schmidt, E., Eds.; Wiley VCH: Weinheim, 2004, ISBN 3-527-30631-5).

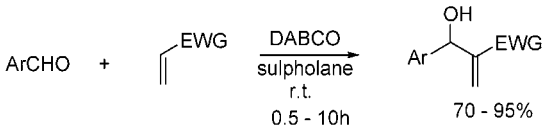
Amination by Addition of Arylmagnesium Reagents to Arylazotosylates

The group of Knochel at Munich is expanding the repertoire of Grignard reagent reactions. For example, the reaction with nitro compounds to produce diarylamines has recently been highlighted (Sapountzis, I. et al. *J. Am. Chem. Soc*. **2002**, *124*, 9390). The drawback is the need to use 2 mol of Grignard, since one equivalent is used in the reduction of the nitro to nitroso. The obvious alternative of using the nitroso compound directly suffers from the disadvantage that nitroso compounds are not very stable and tend to dimerise (Kopp, F. et al. *SynLett* **2003**, 885).

The latest publication from the group (Sapountzis, I. et al. *Angew. Chem., Int. Ed*. **2004**, *43*, 897) uses arylazotosylates as substrate. These are easily made from arylamines by diazotisation and reaction of the crude diazonium fluoroborate salt with sodium toluenesulphinate in dichloromethane. Reaction of the ArN═NTS with Grignard reagents gives, after allylation and zinc reduction, the desired diarylamine. The procedure works for a wide variety of compounds. From a process viewpoint the atom efficiency is still a problem, and the current experimental procedure would need some modification (e.g. evaporation to dryness of a solution which may contain some Grignard).

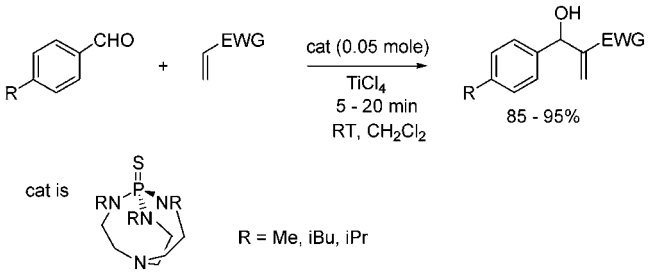
Sulpholane: A New Solvent for the Baylis−Hillman Reaction

The Baylis−Hillman reaction is notoriously sluggish, and various methods have been used to overcome the slow reaction rates, including the use of high pressure (for a review, see Ciganek, E. *Org. React.* **1997**, *51*, 201). A recent publication from a group at the Indian Institute of Technology (Krishna, P. R. et al. *Tetrahedron Lett.* **2004**, *45*, 1183) describes the use of sulpholane as solvent; moderate to high yields of products are obtained with DABCO as base on a variety of aromatic aldehydes and Michael acceptors. Even less reactive acceptors such as acrylamide react in 10 h at room temperature in sulpholane. The authors used an excess of Michael acceptor (3 equiv), but this may not be necessary and, in fact, may make the work up more difficult—they used dilution with water, extraction, and chromatography to isolate the products.



Highly Active Catalyst for the Baylis−Hillman Reaction

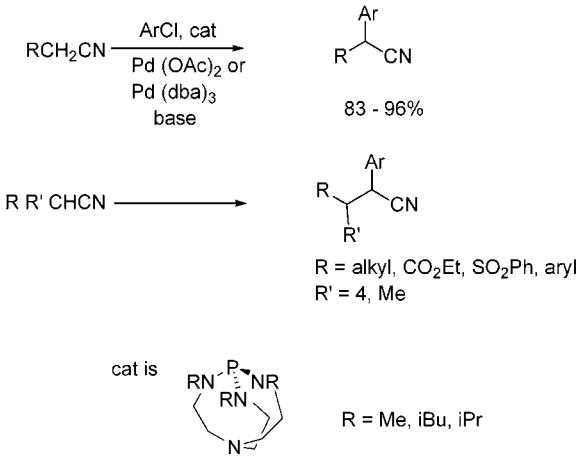
Although DABCO is the most popular choice of base for the B−H reaction, rates can still be slow with some substrates. It has now been found that proazaphosphatrane sulphides, easily prepared from the commercially available proazaphosphatranes, facilitate the B−H reaction when titanium tetrachloride is used as cocatalyst (Verkade, J. G. et al. *Angew. Chem., Int. Ed*. **2003**, *42*, 5054).



Aliphatic aldehydes and cyclic enones give good yields under similar conditions. Ortho-substituted benzaldehydes, which give poor yields under standard conditions, also work well. I wonder what happens when sulpholane is used as solvent.

Arylation of Nitriles with Aryl Chlorides

In a paper from the same group, the bicyclic proazaphosphatranes, which are nonionic, very strong bases, have been found to catalyse a number of reactions, including the arylation of nitriles (Verkade, J. G. et al. *Angew. Chem., Int. Ed*. **2003**, *42*, 5051).



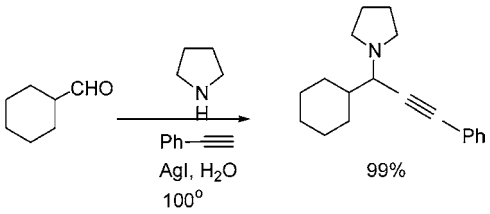
2-Pyridyl Boronates: A Practical Solution to a Longstanding Problem

While 3- and 4-pyridyl boronic acids are commercially available, 2-pyridyl boronate species have proved to be a significant challenge to chemists wishing to do Suzuki chemistry to construct 2-substituted pyridines. Now, Hodgson and co-workers at Pfizer have published a scalable process for the formation of a stable 2-pyridylboronate (an *N*-

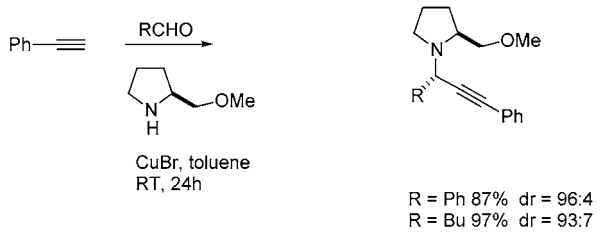
phenyldiethanolamine adduct) and have described its successful application in Suzuki-style palladium-catalysed couplings. (Hodgson, P. D. et al. *Tetrahedron Lett.* **2004**, *45*, 685).

Silver- and Copper-Catalysed Three-Component Coupling of Aldehydes, Alkynes, and Amines

Previous studies have shown that aromatic aldehydes/imines react with terminal alkynes to produce propagyl alcohols and propargylamines and that use of copper(I)-pybox catalyst leads to an enantioselective process (Wei, C. M. et al. *J. Am. Chem. Soc*. **2002**, *124*, 5638 and Koradin, C. et al. *Angew. Chem., Int. Ed*. **2002**, *41*, 2535). It has now been shown that silver iodide catalysis allows the reaction of both aliphatic and aromatic aldehydes to take place in water in a three-component reaction to yield propargylamines. Whereas trimerisation of the aldehyde was a major limitation in previous studies with aliphatic aldehydes, in this study virtually no trimerisation was seen (Wei, C. M. et al. *Org Lett*. **2003**, *5*, 4473). A limitation is that cyclic amines must be used—simple dialkylamines do not work.

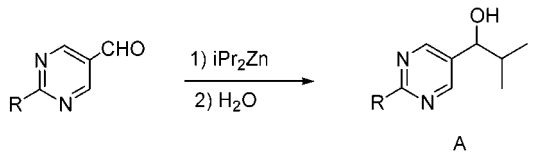


A more recent paper from the Knochel group (Gommermann, N. et al. *Angew. Chem., Int. Ed*. **2003**, *42*, 5763) describes a copper-catalysed enantioselective three-component coupling of aldehydes, amines, and alkynes using CuBr and *R*-quinap. Yields are high (up to 99%), and enantioselectivities are also excellent (up to 96% ee). The reaction shows nonlinear effects, giving high ee with relatively low ee catalyst. If a chiral amine is used, the reaction is highly diastereoselective with only CuBr as catalyst.



Absolute or Spontaneous Asymmetric Synthesis and Asymmetric Amplification

A recent report (Soai, K. et al. *Tetrahedron Asymmetry* **2003**, *14*, 185) indicated that an asymmetric autocatalytic reaction of diisopropylzinc to a heterocyclic aromatic aldehyde leads to increased ee as the reaction proceeds, since the product is a catalyst for its own formation. In the absence of any discrete optically active additives, Soia carried out 37 reactions (see Scheme) in a 80:20 toluene—ether solvent mixture in new and clean equipment, and 19 reactions gave the S-enantiomer, whereas 18 gave the R-enantiomer. The authors concluded that this constitutes one of the conditions necessary for spontaneous asymmetric synthesis.



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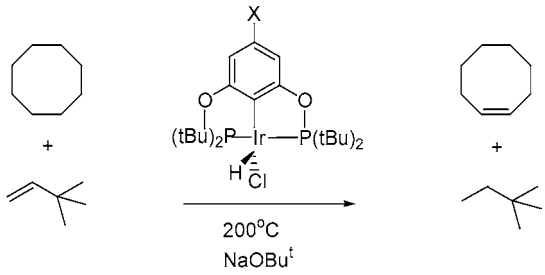
This work has been repeated by a group at Texas A&M University (Singleton, D. A. et al. *Org. Lett*. **2003**, *5*, 4337) who in 54 experiments obtained 27 R-products and 27 S-products. In a test of the mechanistic viability of a random-chance process, the authors found that a very small number of molecules of the catalyst A (60 000 i.e., 10^{-16} M) catalysed the process. In 13 out of 13 experiments, the resulting product had the same configuration as the catalyst, whereas simultaneously performed reactions lacking A afforded a mixture of enantiomers. In a control study, when the catalyst A level was reduced to 10^{-23} M, a mixture of enantiomers also ensued.

The conclusion is that in both the Soai and the Singleton experiments, amplification of the random-chance excess of one enantiomer in the initial "racemic" product takes place. The implications for process chemistry, where a trace impurity may have an enormous effect on a reaction, may be quite significant.

Transfer Dehydrogenation of Alkanes

The catalytic functionalisation of alkanes remains a challenging task, its value being the conversion of inexpensive hydrocarbon feedstocks to higher-added-value products. Catalytic dehydrogenation is a useful first-step process since the resultant alkenes can be easily functionalised. In the past iridium phosphine complexes have catalysed the transfer dehydrogenation of cyclooctane with *tert*-butyl ethylene, but temperatures of 200 °C were required. Turnover numbers of up to 1000 were achieved, but catalyst inhibition was a problem.

It has now been shown that iridium bis-phosphinite complexes have a much higher activity in this reaction, although temperatures of 200 °C are still required (Gökker-Schnetmann, I. et al. *J. Am. Chem. Soc*. **2004**, *126*, 1804). The catalysts are easily prepared from substituted resorcinols.



Environmentally Friendly Non-Phosgene Process for Polycarbonate Production

Workers from Asahi Kasei Corporation in Japan have developed a new green process for producing an aromatic polycarbonate based on bisphenol A without using phosgene

and methylene chloride. The new production process is claimed to be the first to use carbon dioxide as a raw material. It also has other environmental advantages as well as being more economic. A 50 000 t/a plant in Taiwan has been operating since June 2002, and the process has received a Green and Sustainable Chemistry award in Japan. Details are described in a paper in *Green Chemistry* (Fukuoka, S. et al. *Green Chem.* **2003**, *5*, 497).

The multistep process begins with the reaction of ethylene oxide with carbon dioxide to produce ethylene carbonate which is then reacted with methanol to give dimethyl carbonate and ethylene glycol. Transesterification with phenol then gives the high-purity diphenyl carbonate, which is necessary for polycarbonate production. This process uses a novel reactive distillation technology, patented by Asahi Kasei, in a continuous process which uses two columns, one operated under pressure and one under reduced pressure.

After a prepolymerisation step between the diphenyl carbonate and bisphenol A, the prepolymer is subjected to continuous melt polymerization using a specially designed reactor. The product is a high-purity and high-performance engineering plastic with a good colour tone.

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