

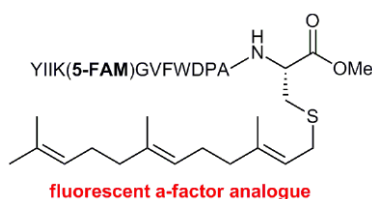
# SYNFORM

People, Trends and Views in Synthetic Organic Chemistry

2013/09

## SYNSTORIES ■ ■ ■ ■

■ **Synthesis of Peptides Containing C-Terminal Methyl Esters Using Trityl Side-Chain Anchoring: Application to the Synthesis of a-Factor and a-Factor Analogues**



■ **Enantioselective Ketone Hydroacylation Using Noyori's Transfer Hydrogenation Catalyst**

■ **Ligand-Controlled  $\beta$ -Selective C(sp<sup>3</sup>)-H Arylation of N-Boc-piperidines**

■ **Preparation and Reactions of Enantiomerically Pure  $\alpha$ -Functionalyzed Grignard Reagents**

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**Dear readers,**

Following a glorious Saturday full of sunshine, this beautiful Scottish summer suddenly switched to a gloomy and rainy Sunday morning, which is the ideal situation for staying home and writing this editorial! Let's have a

look at the articles in this new issue of **SYNFORM** then. The first **SYNSTORY** is about a novel catalytic enantioselective hydroacylation reaction developed by Vy Dong (USA) that converts  $\gamma$ -hydroxy-ketones into the corresponding enantiomerically pure  $\gamma$ -butyrolactones. The next **SYNSTORY** brings us to the realm of peptide chemistry, where Mark Distefano (USA) found an efficient solid-phase method for producing peptides having a C-terminal methyl ester. The third **SYNSTORY** takes us to the highly chemoselective synthesis of  $\beta$ -aryl piperidines developed by Olivier Baudoin (France) which relies on the use of 2-phenyl-pyrrole phosphine ligand. The issue is completed by a report on a very interesting novel use of Grignard reagents which, as demonstrated by Peter O'Brien (UK), can be used as chiral building blocks for the synthesis of stereopure 1,2-diols and rigid amines.

I just had a look outside the window; it's still raining cats and dogs here...

Enjoy your reading!

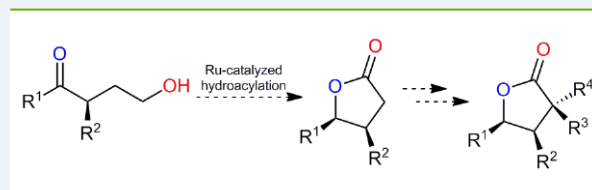
**Matteo Zanda**

*Editor of SYNFORM*

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**CONTACT + + + +**

If you have any questions or wish to send feedback, please write to Matteo Zanda at:  
[Synform@chem.polimi.it](mailto:Synform@chem.polimi.it)

## NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■ NEWS AND VIEWS ■ ■

## Enantioselective Ketone Hydroacylation Using Noyori's Transfer-Hydrogenation Catalyst

*J. Am. Chem. Soc.* **2013**, *135*, 5553–5556

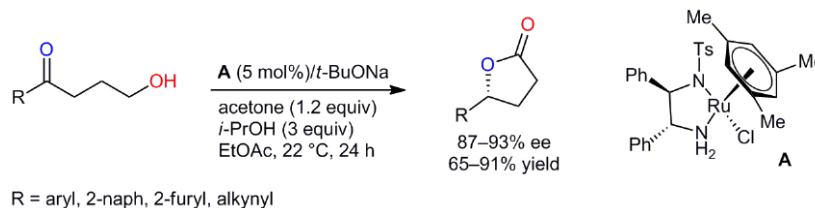
■ The  $\gamma$ -butyrolactone framework is ubiquitous in nature and featured in many bioactive compounds. Recently, Professor Vy Dong and her research team, now at the University of California at Irvine (USA), devised a strategy based on ruthenium catalysis for stereoselective hydroacylation reaction of  $\gamma$ -hydroxy ketones. This reaction occurs via a multistep redox sequence that involves enantioselective reduction of the ketone, oxidation of the primary alcohol to the aldehyde, cyclization to a hemiacetal, and a final oxidation to yield the target  $\gamma$ -butyrolactones in high enantiomeric purity.

This work from Professor Dong's group began at the University of Toronto (Canada) and was completed following the group's move to the University of California at Irvine. Professor Dong said: "Thanks to a great effort from all of our group members, and a welcoming atmosphere from our new hosts, we were able to get the lab and this project back up and running smoothly in Irvine." This paper significantly expanded the scope of enantioselective ketone hydroacylation. Professor Dong explained: "Our group has used the traditional cationic rhodium catalysts developed by Bosnich for our previous ketone hydroacylation methods, but these catalysts

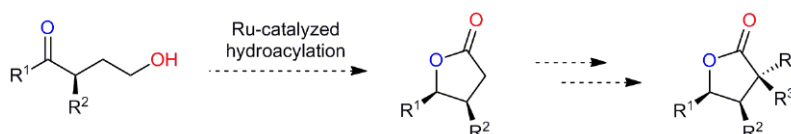
are limited in scope due to competitive decarbonylation. We devised a strategy to get around this side reaction by using a chiral transfer-hydrogenation catalyst – Noyori's catalyst. This was attractive to us based on the lower cost of ruthenium, the accessibility of this commercially available catalyst, and its well-defined properties, and of course, it allows new mechanistic pathways for hydroacylation that avoid decarbonylation altogether." The group was also inspired by previous applications of transfer-hydrogenation catalysts in hydroacylation (for example by Krische and Ryu: *Pure Appl. Chem.* **2012**, *84*, 1729 and *Chem. Commun.* **2009**, 6741).

"Our paper is the first application of a chiral transfer-hydrogenation catalyst for asymmetric hydroacylation," said Professor Dong. She concluded: "Beyond this work, we would love to develop a diastereoselective protocol to make more highly substituted butyrolactones. This would allow access to more complex targets and, hopefully, a variety of natural products." ■

Matteo Zanda



**Scheme 1** The stereoselective Ru-catalyzed hydroacylation



**Scheme 2** Proposed diastereoselective synthesis of highly substituted  $\gamma$ -butyrolactones

*About the authors**Prof. Y. M. Dong*

**Vy Dong** completed her PhD at Caltech (USA). She is currently a Full Professor at the University of California at Irvine (USA).

*S. K. Murphy*

**Stephen Murphy** graduated from Queen's University at Kingston (Canada), and he is currently a doctoral student in Professor Dong's laboratory.

## Synthesis of Peptides Containing C-Terminal Methyl Esters Using Trityl Side-Chain Anchoring: Application to the Synthesis of a-Factor and a-Factor Analogues

*Org. Lett.* **2012**, *14*, 5648–5651

Recently, there has been considerable interest in the synthesis of peptides that contain prenylated C-terminal cysteine methyl esters. A recent paper from the research group of Professor Mark Distefano from the University of Minnesota (Minneapolis, USA) disclosed a new solid-phase synthetic strategy for the preparation of such peptides. Professor Distefano said: “There are a significant number of proteins that have cysteine methyl ester residues on their C-termini. Those proteins include members of the Ras superfamily of monomeric GTP-binding proteins and heterotrimeric G-proteins.<sup>1,2</sup> Since most of those polypeptides are involved in signal transduction pathways within cells, it means that many processes including cell division and control of cell shape are controlled by such proteins.” Professor Distefano explained that to study how those processes work, it is important to be able to synthesize prenylated peptides and proteins. Those processes are also important for therapeutic applications.<sup>3,4</sup> He continued: “There has been considerable interest in developing inhibitors that interfere with enzymes involved in the prenylation pathway, since such inhibitors might stop the growth of cancer cells that undergo rapid cell division, a process that requires the participation of prenylated proteins.”

The paper in *Organic Letters*, however, concerned peptide synthesis rather than proteins. Professor Distefano explained: “There are two reasons why synthetic peptides are important. First, there are naturally occurring prenylated peptides, such as yeast a-factor, that contains a C-terminal-prenylated cysteine methyl ester. The biosynthesis of that peptide and its subsequent interaction with a G-protein-coupled receptor is similar to processes involving larger prenylated proteins. Thus, the a-factor-mediated process is a simplified system for studying protein prenylation in general. The second reason for developing improved peptide-based methods is that synthetic prenylated peptides can be integrated into larger protein fragments using various methods to produce full-length proteins that incorporate non-natural functionality such as fluorophores or photoaffinity labeling groups. Waldmann and co-workers have already done that in a few cases.”<sup>5</sup>

According to Professor Distefano, such peptides have been produced in the past by Fred Naider’s group at the City

University of New York, College of Staten Island (USA), and then Professor Herbert Waldmann’s group at the Max Planck Institute of Molecular Physiology (Germany). Professor Distefano said: “The original method developed by Fred Naider’s group for a-factor synthesis was a fragment condensation approach in which a protected N-terminal decapeptide was coupled to a C-terminal dipeptide containing a farnesylated cysteine methyl ester residue followed by basic deprotection.<sup>6</sup> This is an elegant strategy and has been used extensively for the preparation of many similar peptides. However, it requires unusual side-chain protecting groups and an HF cleavage step to prepare the protected decapeptide piece.” Due to the hazards of working with HF, fewer and fewer laboratories are equipped to use it. Professor Distefano said: “We wanted a method that would be compatible with an Fmoc-based approach for peptide synthesis. Waldmann and co-workers developed a simple method for preparing C-terminal methyl esters based on resin attachment via a hydrazine-based linkage.”<sup>7</sup> Aerobic oxidation of the hydrazine with copper salts in methanol results in solvolytic release of the peptide as the methyl ester that can then be prenylated. “In earlier work, we applied that method to the synthesis of a-factor and related photoactive analogues,” continued Professor Distefano.<sup>8</sup> “While it worked well for those targets, only poor yields were obtained when we tried to incorporate more electron-rich groups such as fluorescein into the desired peptides.”

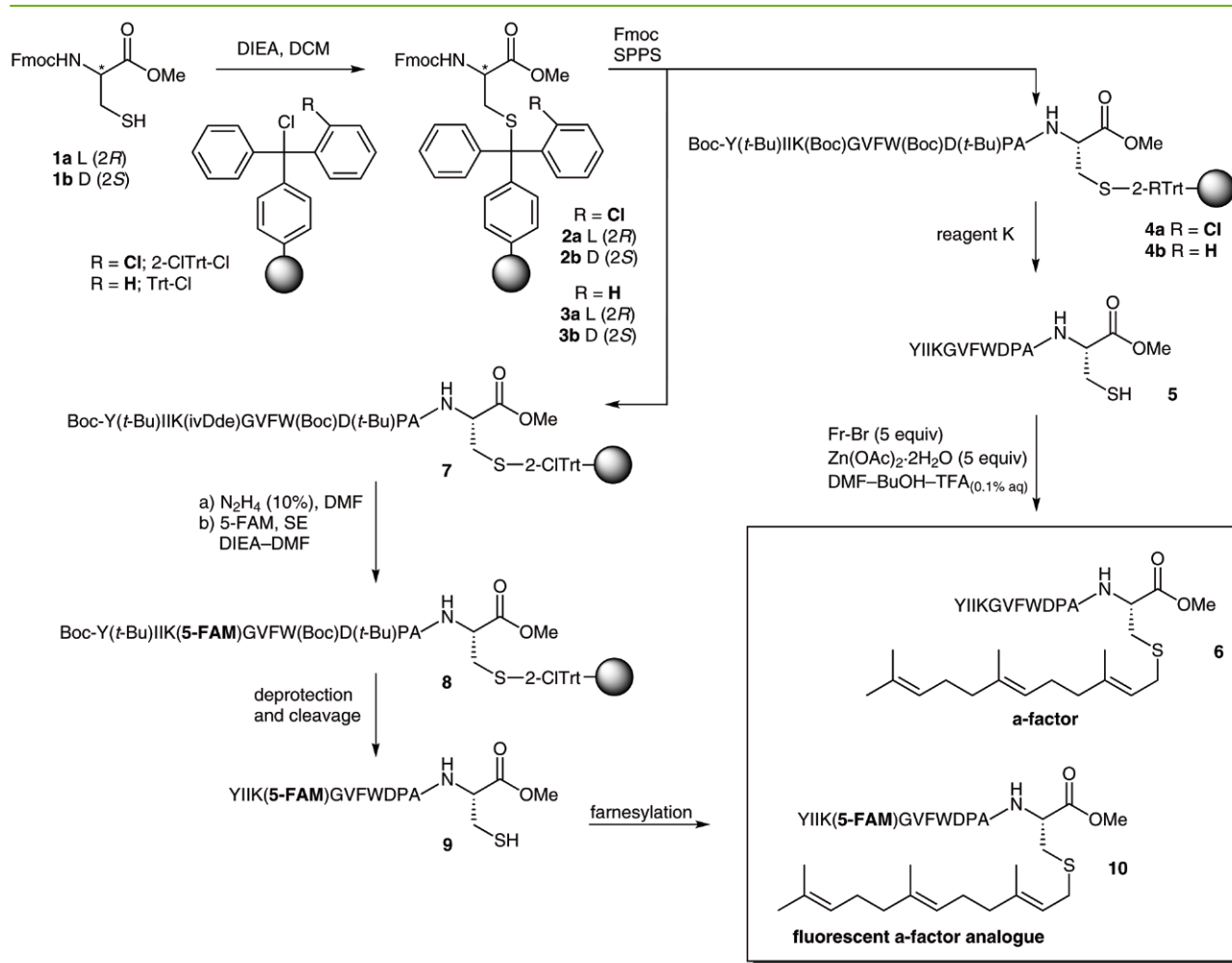
The method described in the recent paper is based on some earlier work carried out by Professor Distefano’s colleague, George Barany.<sup>9</sup> In his approach, Fmoc-Cysteine *tert*-butyl ester was linked to a xanthenyl-based resin via the side-chain thiol group. That strategy allowed the full-length peptides having C-terminal cysteine residues to be assembled on resin. Treatment with TFA resulted in simultaneous side-chain deprotection and resin cleavage due to the acid-labile xanthenyl thioether. “In our method, we replaced the xanthenyl resin, that required a multistep synthesis to prepare, with commercially available trityl-based material,” said Professor Distefano. “That resin initially reacted with Fmoc-Cysteine methyl ester to anchor the cysteine residue to the solid support via its thiol group (see Scheme, **2** and **3**). Standard Fmoc

solid-phase peptide synthesis methods were then used to elongate the peptide." Global side-chain deprotection and resin cleavage afforded the unprenylated form of a-factor that was subsequently alkylated with farnesyl bromide to yield a-factor (**6**). Because the initial cysteine residue contains a methyl ester that is resistant to acid in contrast to the Barany method that uses an acid labile *tert*-butyl ester, the final product contains the desired C-terminal methyl ester.

With regard to the problems encountered using the hydrazide-based resin for synthesis of fluorescein-containing analogues, Professor Distefano commented: "In our method, fluorescein incorporation proceeded smoothly since there were no oxidative conditions." That was accomplished by incorporation of a lysine residue into the growing peptide in which the side chain amino group was protected, using an orthogonal ivDde protecting group. After synthesis of the

complete dodecapeptide (**7**), the  $\epsilon$ -amino group was deprotected with hydrazine and acylated with 5-Fam succinimidyl ester. Professor Distefano continued: "Subsequent global deprotection, resin cleavage and farnesylation were performed as described above for the parent a-factor molecule to yield the desired fluorescent analogue (**10**)."

Racemization and diketopiperazine formation are, however, potential problems with peptides containing C-terminal cysteine residues. Professor Distefano said: "We investigated the possibility of cysteine racemization by preparing the tripeptide NH<sub>2</sub>-Gly-Phe-Cys-OMe using both enantiomers of Fmoc-Cys-OMe. Analysis by HPLC did not show any epimerization of the cysteine residue nor did we observe any evidence for diketopiperazine formation. However, interestingly, significantly higher yields were obtained when the cysteine residue was anchored on trityl resin (**3**) compared with 2-Cl-



**Scheme 1** The new strategy for producing *S*-prenylated C-terminal cysteine methyl ester peptides

trityl resin (**2**). We attribute this difference to loss of the peptide during the synthesis due to  $\beta$ -elimination resulting from exposure to the basic conditions employed for the Fmoc removal. It appears that the electron-withdrawing effect of the chlorine accelerates that side reaction.”

In this work, a fluorescently labeled form of a-factor was produced. Professor Distefano’s group is collaborating with Professor Jeffrey M. Becker from the University of Tennessee (Knoxville, USA), an expert in the biology of a-factor. “We are particularly interested in studying how a-factor, a prenylated molecule, interacts with its receptor,” said Professor Distefano. “The fluorescent a-factor should be useful for measuring the binding affinity between the peptide and the receptor.”

Professor Distefano’s group is currently exploring other uses of the methodology for further applications. He said: “We are going in two directions. First, we are currently expanding the scope of the method to include other esters. The other thing we want to do is to incorporate peptides produced via this method into full-length proteins. That work is ongoing.” ■

Matteo Zanda

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### About the authors



From left: V. Diaz-Rodriguez, Prof. M. Distefano

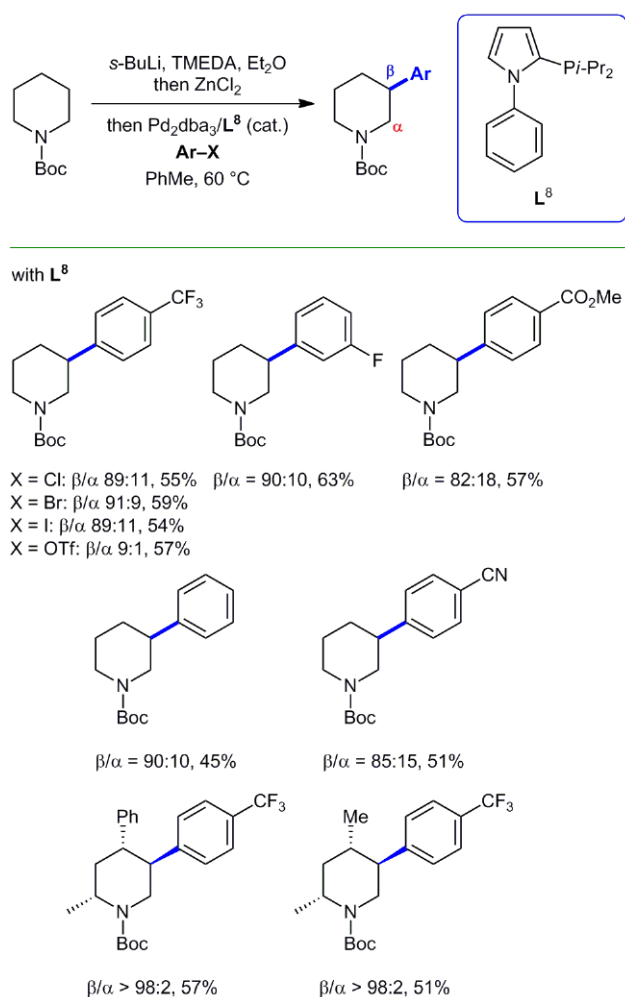


# Ligand-Controlled $\beta$ -Selective C(sp<sup>3</sup>)-H Arylation of *N*-Boc-piperidines

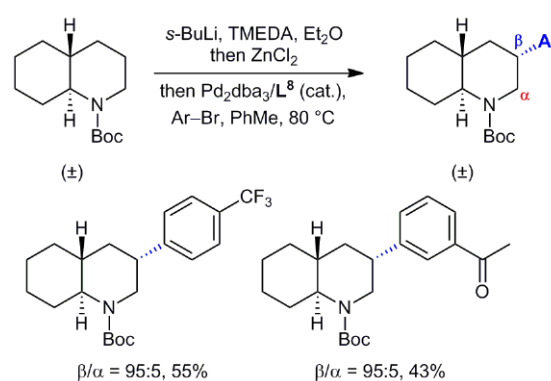
*Chem. Sci.* **2013**, *4*, 2241–2247

3-Arylpiperidines are privileged scaffolds for drug discovery. A number of bioactive compounds incorporate a 3-arylpiperidine subunit, such as preclamol, a dopaminergic autoreceptor agonist, and MK-4827, a poly(ADP-ribose)polymerase (PARP) inhibitor.<sup>1</sup> The synthesis of a 3-arylpiperidine fragment usually involves the construction of the piperidine ring or the partial reduction of a 3-arylpyridine precursor.<sup>2,3</sup> To

date, the inert character of C–H bonds in  $\beta$ -position to the nitrogen atom was deemed to preclude a direct functionalization. Recently, a team led by Professor Olivier Baudoïn, from the Université Claude Bernard Lyon 1 (France), cracked the problem and succeeded in developing such a direct functionalization method, which does not require the additional reduction step. Based on the results obtained by Knochel and co-workers on the *substrate-controlled* arylation of Boc-piperidine,<sup>4</sup> the French researchers developed a *ligand-controlled*  $\beta$ -C(sp<sup>3</sup>)-H arylation of this compound and analogues. Anthony Millet said: “The main idea behind the development of a less bulky and more flexible ligand (Scheme 1, **L**<sup>8</sup>) than Buchwald’s RuPhos was to disfavor the reductive elimination step leading to the  $\alpha$ -arylated product.” This led to a reversal of the  $\alpha/\beta$ -selectivity in favor of the desired  $\beta$ -arylated product. Professor Baudoïn commented: “The use of this Beller-type phosphine, combined with the generation of an organozinc intermediate, allowed us to obtain a wide scope of C3-arylated piperidines and C3-arylated decahydroquinoline” (Scheme 2). Furthermore, this method was applied to the gram-scale formal synthesis of preclamol (Scheme 3).



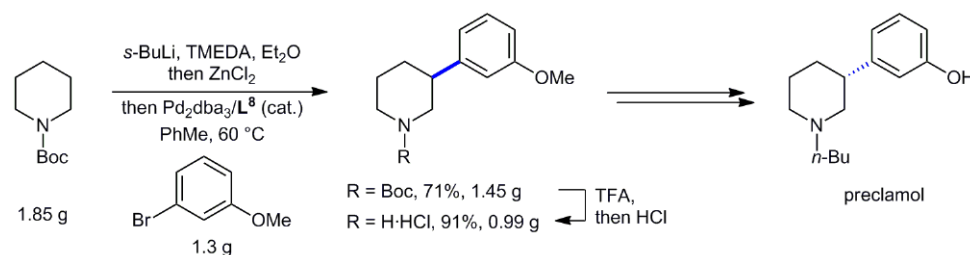
**Scheme 1** Ligand-controlled  $\beta$ -arylation



**Scheme 2**  $\beta$ -Arylation of decahydroquinoline

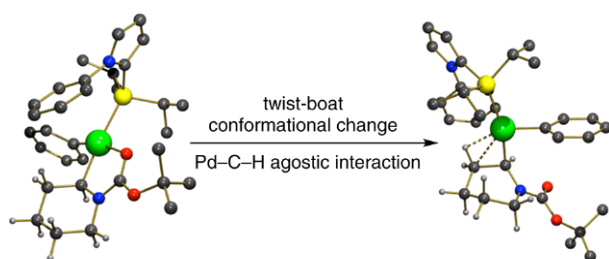
The team assumed that the current reaction involved the same overall mechanism as previously reported with ester enolates.<sup>5</sup> Thus, computational chemistry (DFT) was employed





**Scheme 3** Gram-scale formal synthesis of preclamol

to address the observed  $\alpha/\beta$ -selectivity. Dr. Paolo Larini, who performed these calculations, said: “The pathway leading to the  $\beta$ -arylated product required the establishment of a Pd–C–H agostic intermediate, which forces the piperidine ring to adopt a twist-boat conformation (Figure 1).”



**Figure 1** Pd–C–H agostic intermediate

Professor Baudoin concluded: “The fine-tuning of the phosphine allowed us to develop a *ligand-controlled* migratory arylation. This new  $C(sp^3)$ –H functionalization method represents a direct entry into pharmaceutically relevant 3-aryl-piperidines.” Current developments include the extension of this migrative arylation to acyclic amines. ■

Matteo Zanda

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### About the authors

**Anthony Millet** was born in France in 1986. After a short placement in Dr. Véronique Michelet's group at Chimie Paris-tech (France), he received his MSc in organic chemistry from the Université Pierre et Marie Curie (Paris VI, France). He is currently a PhD student in the group of Professor Olivier Baudoin at the University of Lyon (France). His research interests include the intermolecular functionalization of unactivated C(sp<sup>3</sup>)-H bonds.

**Paolo Larini** was born in 1982 in Florence (Italy). In 2006, he received his MSc in organic chemistry from the University of Florence (Italy) supervised by Professor E. G. Occhiato. He then moved to the University of Turin (Italy) to pursue his PhD (2010) in the group of Professor C. Prandi. During his PhD he spent a period as a visiting scholar at the University of Hawaii (USA) in the group of Professor M. A. Tius. In 2010, he moved to the University of Lyon (France) in the group of Professor O. Baudoin as a postdoctoral researcher working on Pd-catalyzed  $\beta$ -C(sp<sup>3</sup>)-H arylation of esters and amino esters. In 2012, he joined the group of Dr. E. Clot at the University of Montpellier (France) as a postdoctoral fellow. During this stay, he acquired an expertise in computational chemistry and used this tool to understand the selectivities obtained in C-H-activation reactions. In September 2012, he started his academic career as Assistant Professor at the University of Lyon in the group of Professor O. Baudoin. His research focuses on the development of bifunctional ligands for transition metals and the use of computational chemistry to facilitate this research process.

**Eric Clot** was born in 1967 in Marseille (France). After graduating from the Ecole Normale Supérieure de Lyon (France), he obtained the Agrégation de Chimie. After a PhD with Odile Eisenstein and Claude Leforestier in 1995 on the dynamics of metal polyhydrides, he entered the Centre National de la Recherche Scientifique (France) in 1996. He was promoted to Research Director in 2007. He conducts his research in the group headed by Odile Eisenstein in Montpellier (France). He also lectures at Ecole Polytechnique, Palaiseau (France). His research interest focuses on the computational study of the reactivity of transition-metal complexes, with specific interest



From left: Dr. P. Larini, A. Millet, Prof. O. Baudoin, Dr. E. Clot

in the activation of inert bonds and applications to organic reactions. His research is conducted in close collaboration with many experimentalists throughout the world. He is especially happy when they share his keen interest in rugby, a sport for which he is a coach in the Ecole de Rugby du Pic Saint Loup.

**Olivier Baudoin** studied chemistry at the Ecole Nationale Supérieure de Chimie de Paris (ENSCP, France) until 1995. He completed his PhD in 1998 in the group of Professor Jean-Marie Lehn in Paris on the synthesis and study of cyclo-bisintercaland molecules. He then worked as a postdoctoral fellow with Professor K. C. Nicolaou in the Scripps Research Institute (La Jolla, USA). He joined the Institut de Chimie des Substances Naturelles (Gif-sur-Yvette, France) in 1999 as a CNRS researcher and obtained his Habilitation diploma in 2004. In 2006, he was appointed as a Professor at the University of Lyon 1 (France), and was promoted to First Class Professor in 2011. He was the recipient of the CNRS Bronze Medal in 2005, the Scholar Award ("Prix Enseignant-Chercheur") of the French Chemical Society, Organic Division in 2010, and was nominated as a junior member of the Institut Universitaire de France (IUF) in 2009.

# Preparation and Reactions of Enantiomerically Pure $\alpha$ -Functionalized Grignard Reagents

*J. Am. Chem. Soc.* **2013**, *135*, 8071–8077

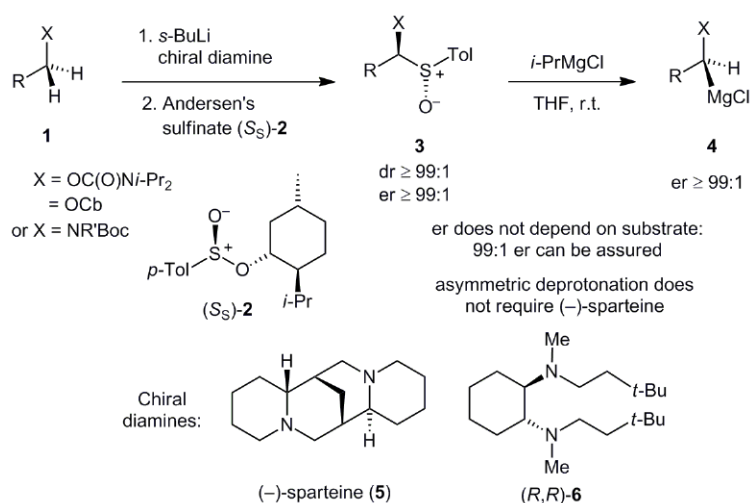
Although Grignard reagents were discovered more than a century ago, chiral non-racemic secondary organomagnesium compounds have remained elusive and only a few examples have been reported in the literature to date, mainly from the work of Satoh (*Tetrahedron* **2003**, *59*, 9803 and references therein), Hoffmann (*Chem. Eur. J.* **2000**, *6*, 3359) and Blakemore (*J. Am. Chem. Soc.* **2007**, *129*, 3068 and references therein).

The O'Brien group at the University of York (UK) has a longstanding interest in asymmetric deprotonation using strong organolithium bases (e.g., *s*-BuLi) and chiral diamines such as (–)-sparteine, an area of chemistry pioneered by Beak and Hoppe. One key limitation of this methodology is that  $\alpha$ -substituted products are generated in widely varying enantioselectivities, and seldom reach 99:1 er. Professor O'Brien said: "To address this, we devised a new approach in which asymmetric deprotonation of substrates **1** would be merged with electrophilic trapping using Andersen's chiral sulfinate ( $S_S$ )-**2** to give  $\alpha$ -functionalized sulfoxides **3** in  $\geq 99:1$  dr and  $\geq 99:1$  er (after separation from the minor diastereomeric sulfoxide). Subsequent sulfoxide  $\rightarrow$  Mg exchange would then generate chiral  $\alpha$ -functionalized Grignard reagents **4** in  $\geq 99:1$

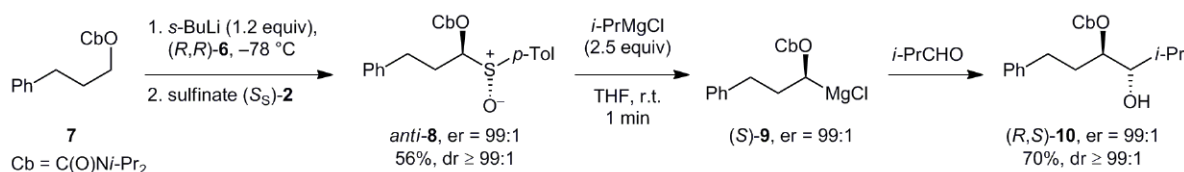
er (Scheme 1) of which only a handful of examples are known in the literature."

"We were also keen to avoid the use of (–)-sparteine as its commercial availability has been highly variable over the last two years," he continued. "Since our approach uses enantiomerically pure chiral sulfinate ( $S_S$ )-**2**, there was also the opportunity to use other diamines such as the Alexakis ligand ( $R,R$ )-**6** which often gives lower enantioselectivity than (–)-sparteine."

Thanks to the sustained efforts from one PhD student in the group, Peter Rayner, and part-funding from GlaxoSmithKline (industrial supervisor: Dr. Richard Horan), the British researchers were able to put this idea into practice with two different series of compounds. The optimized conditions were not easily found, not least because Professor O'Brien and his co-workers encountered an unexpected epimerization in the sulfinate trapping process. In the oxygen series (Scheme 2), asymmetric deprotonation using *s*-BuLi/( $R,R$ )-**6** and trapping with ( $S_S$ )-**2** gave  $\alpha$ -alkoxy sulfoxide *anti*-**8** in  $\geq 99:1$  dr and 99:1 er. Then, the sulfoxide  $\rightarrow$  Mg exchange was carried out at room temperature (for a short reaction time of just one minute) to give enantiomerically pure  $\alpha$ -functionalized



Scheme 1



Scheme 2

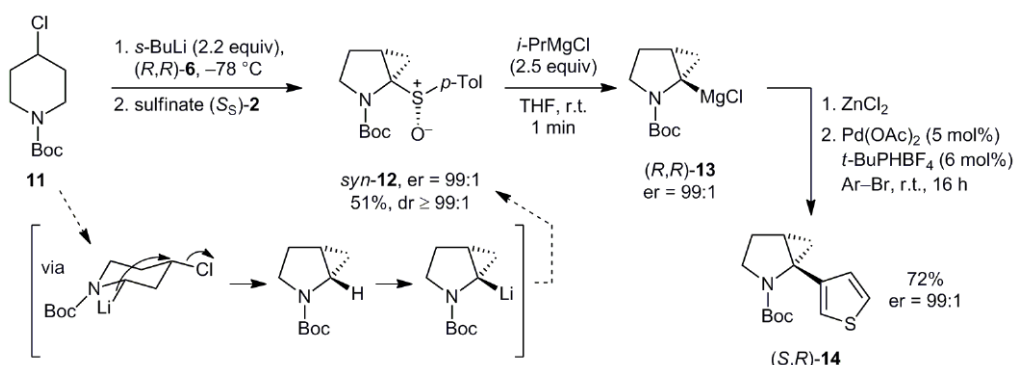
Grignard reagent **(S)-9**. “Trapping with a range of electrophiles was successful – using aldehydes, the reactions were *anti*-stereoselective to give products such as **(R,S)-10** in 99:1 er,” remarked Professor O’Brien. “We were also able to show that the Grignard reagent **(S)-9** was configurationally stable for 30 minutes at room temperature, a remarkable finding.”

The nitrogen series (Scheme 3) proved troublesome for a while. “Despite our best efforts, the  $\alpha$ -amino sulfoxides could not be synthesized from simple *N*-Boc pyrrolidines and piperidines, possibly because they are in fact unstable,” explained Professor O’Brien. “However, we had success with a cyclopropyl system,  $\alpha$ -amino sulfoxide *syn-12*, although optimization was tricky due to some unexpected match/mismatch effects.” Ultimately,  $\alpha$ -amino sulfoxide *syn-12* (of ≥99:1 dr and 99:1 er) was prepared from *N*-Boc chloropiperidine **11** (via lithiation, cyclization and a second lithiation as previously described by Beak). Subsequent sulfoxide → Mg exchange gave Grignard reagent **(R,R)-13** and trapping produced a range of  $\alpha$ -substituted products in 99:1 er. A notable example involved transmetalation to zinc and Negishi coupling to give arylated pyrrolidine **(S,R)-14** in 99:1 er.

“We are convinced that it will be possible to roll out this general approach (asymmetric deprotonation, chiral sulfinat trapping and sulfoxide → Mg exchange) to all types of asymmetric deprotonation reactions,” said Professor O’Brien. “Crucially, our work shows that it is now possible to prepare products from asymmetric deprotonations in 99:1 er without the need to rely on (–)-sparteine, which is difficult to get your hands on at the moment!”

Dr. Richard Horan added: “From an industrial perspective, asymmetric deprotonation is a powerful methodology but the exacting conditions to achieve high yields and enantioselectivities have been a barrier to wider adoption.” He concluded: “Trapping with the chiral sulfinat offers an opportunity to prepare a shelf-stable building block that can be further elaborated in high er under operationally simple conditions, and gives ready access to the complex three-dimensional architectures that are of growing importance in the pharmaceutical industry.”

Matteo Zanda



Scheme 3

### About the authors



*P. Rayner*

**Peter Rayner** is a final-year PhD student in the group of Professor Peter O'Brien. In 2009, he graduated from the University of York (UK) with a 1<sup>st</sup> class MChem degree. He spent the final year of his MChem in industry carrying out a research project with Lubrizol Ltd. During his PhD studies, funded by the EPSRC and GlaxoSmithKline, he has developed a number of novel methods

for the synthesis of chiral organometallic reagents. On completion of his PhD, he will be moving to a postdoctoral research position with Professor Simon Duckett at the University of York.



*Dr. R. Horan*

**Richard Horan** received his MChem at the University of Southampton (UK) in 2001 before moving to the University of Cambridge (UK) for his PhD studies under the supervision of Dr. Darren Dixon. He remained in Cambridge as a postdoctoral researcher in the group of Professor Steven Ley until 2007 when he accepted a position in the process development group at GlaxoSmithKline. Richard is currently a Project Manager in the External Supply group at GlaxoSmithKline, based in Stevenage (UK).



*Prof. P. O'Brien*

**Peter O'Brien** graduated from the University of Cambridge (UK) in 1992 and remained there to carry out a PhD (awarded 1995), supervised by Dr. Stuart Warren. He then moved to The University of York (UK) as a Royal Commission for the Exhibition of 1851 Research Fellow. In 1996, he was appointed as a Lecturer in organic chemistry at The University of York. He was promoted to Senior

Lecturer (July 2002), Reader (July 2005) and Professor (2007). His research interests focus on asymmetric synthesis, especially using organometallic reagents and chiral diamines. In 2013, he was awarded the Royal Society of Chemistry Organic Stereochemistry Award for the development and applications of the (+)-sparteine surrogate.



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