



# CATALYSTS FOR FINE CHEMICAL SYNTHESIS

Metal Catalysed  
Carbon-Carbon  
Bond-Forming Reactions

3

Editors: Stanley M. Roberts, Jianliang Xiao,  
John Whittall and Tom E. Pickett

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Catalysts for Fine  
Chemical Synthesis

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Volume 3

# Metal Catalysed Carbon-Carbon Bond-Forming Reactions

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**Stanley M. Roberts and Jianliang Xiao**  
*University of Liverpool, UK*

**John Whittall and Tom E. Pickett**  
*The Heath, Runcorn Stylacats Ltd, UK*



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# Catalysts for Fine Chemical Synthesis

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Volume 3

# Catalysts for Fine Chemical Synthesis

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# Catalysts for Fine Chemical Synthesis

## Series Preface

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During the early-to-mid 1990s we published a wide range of protocols, detailing the use of biotransformations in synthetic organic chemistry. The procedures were first published in the form of a loose-leaf laboratory manual and, recently, all the protocols have been collected together and published in book form (*Preparative Biotransformations*, Wiley, Chichester, 1999).

Over the past few years the employment of enzymes and whole cells to carry out selected organic reactions has become much more commonplace. Very few research groups would now have any reservations about using commercially available biocatalysts such as lipases. Biotransformations have become accepted as powerful methodologies in synthetic organic chemistry.

Perhaps less clear to a newcomer to a particular area of chemistry is *when* to use biocatalysis as a key step in a synthesis, and when it is better to use one of the alternative non-natural catalysts that may be available. Therefore we set out to extend the objective of *Preparative Biotransformations*, so as to cover the whole panoply of catalytic methods available to the synthetic chemist, incorporating biocatalytic procedures where appropriate.

In keeping with the earlier format we aim to provide the readership with sufficient practical details for the preparation and successful use of the relevant catalyst. Coupled with these specific examples, a selection of the products that may be obtained by a particular technology will be reviewed.

In the different volumes of this new series we will feature catalysts for oxidation and reduction reactions, hydrolysis protocols and catalytic systems for carbon-carbon bond formation *inter alia*. Many of the catalysts featured will be chiral, given the present day interest in the preparation of single-enantiomer fine chemicals. When appropriate, a catalyst type that is capable of a wide range of transformations will be featured. In these volumes the amount of practical data that is described will be proportionately less, and attention will be focused on the past uses of the system and its future potential.

Newcomers to a particular area of catalysis may use these volumes to validate their techniques, and, when a choice of methods is available, use the background information better to delineate the optimum strategy to try to accomplish a previously unknown conversion.

**S. M. ROBERTS  
I. KOZHEVNIKOV  
E. DEROUANE  
LIVERPOOL, 2002**

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# Preface for Volume 3: Metal Catalysed Carbon-Carbon Bond-Forming Reactions

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Volume 1 in this Series described practical tips for performing some topical oxidation and reduction reactions. This Volume features modern methods for carbon-carbon bond formation, which has always been at the heart of organic synthesis. In recent times, very efficient carbon-carbon bond-forming catalysts have been invented, to assist bench chemists in industry and academia to construct interesting target molecules.

The first Chapter presents a modern overview from an industrial perspective of the employment of catalysts in transformations of commercial importance.

Later Chapters in this Volume describe the use of some of the important catalysts for carbon-carbon bond-forming reactions in detail, often building very significantly on the information available in the primary Journals. Hints and tips on such things as crucial colour changes are included, as well as pointers to potential risks in the procedures. In the cases where the catalyst is not commercially available the preparation of the material is described, again in sufficient detail to make it accessible to the non-expert.

Thus, this Volume is divided into 12 Chapters encompassing different types of carbon-carbon bond forming reactions. The first two experimental Chapters cover alkylation reactions adjacent to carbonyl functionality (Chapter 2) and the asymmetric displacement of acetate groups situated in an allylic position with the resultant formation of optically active product possessing a new carbon-carbon bond (Chapter 3).

The procedures described in Chapters 4–7 all relate to a set of broadly similar transformations that are becoming exceptionally important and well used in laboratories worldwide. In Chapter 4, eight examples of the Suzuki coupling reaction are described; four accounts describe the use on activated alkene (vinyl bromide, triflate or tosylate) as the coupling partner for boronic acid derivatives. The other examples of Suzuki couplings involve aryl bromides and aryl chlorides. It is noteworthy that the methodology introduced by Nolan has been extended to include amination reactions.

Chapter 5 details conditions for performing the Heck reaction (including one asymmetric version) while Chapter 6 describes how Sonogashira reactions can be conducted successfully. (The conditions of Plenio and Luo can be used to perform Heck and/or Suzuki reactions). In Chapter 7 cross-coupling reactions involving



Grignard reagents and organoindium species are reported, together with a variety of cross-couplings invented by Lipshutz, Lautens and colleagues.

The regioselective allylation of selected aldehydes as well as asymmetric carbon-carbon bond-forming reactions using the same carbonyl species are featured in Chapter 8.

Three procedures have been gathered together in Chapter 9 in order to illustrate modern techniques for the use of olefin-methathesis reactions in organic chemistry (Chapter 9). Other cyclisation reactions form the basis of the content of Chapter 10; thus a procedure for the Pauson–Khand reaction is followed by two other methods for producing five-membered rings. In the same Chapter, two procedures leading to six-membered rings are documented, including a  $[2 + 2 + 2]$  reaction.

The final two Chapters contain descriptions of equally important reactions. Chapter 11 has experimental details for two asymmetric coupling reactions leading to aldol products as well as two protocols for performing asymmetric Michael reactions. Asymmetric and diastereoselective hydroformylation reactions form the bulk of Chapter 12; we have joined them together with a modern carbonylation procedure and an intriguing carboxylation reaction.

Last but certainly not least, the Editors wish to thank all the 40+ authors for providing their recipes without fuss and/or delay, according to our prescribed format. We hope the detailed descriptions will allow other scientists to have convenient access to a selection of reactions of ever-growing significance and importance in synthetic chemistry.

**STANLEY M. ROBERTS**  
**LIVERPOOL, 2004**

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# Abbreviations

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|                |   |
|----------------|---|
| Ac             | acetyl  |
| acac           | acetylacetone   |
| Ar             | aryl  |
| b.p.           | boiling point   |
| BINAP          | 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl               |
| BINOL          | <i>to be confirmed</i>                                    |
| BSA            | <i>N,O</i> -bis-(trimethylsilyl)-acetamide                |
| Bu             | butyl   |
| cat            | catalyst  |
| Chsalen        | [N,N'-bis-(2'-hydroxybenzylidene)]-1,2-diaminocyclohexane |
| CLAMPS         | cross-linked aminomethylpolystyrene                       |
| COD            | <i>to be confirmed</i>                                    |
| DBU            | 1,8-diazabicyclo[5.4.0]undec-7-ene                        |
| de             | <i>to be confirmed</i>                                    |
| DEPT           | diethyl tartrate  |
| DIPT           | diisopropyl tartrate                                      |
| DMAP           | 4-dimethylaminopyridine                                   |
| DMF            | Dimethyl formamide  |
| DMM            | dimethoxymethane  |
| DMSO           | dimethyl sulfoxide  |
| dppf [or DPPF] | diphenylphosphinoferrocene                                |
| EDTA           | ethylenediaminetetraacetic acid                           |
| ee             | enantiomeric excess                                       |
| eq             | equivalent  |
| Et             | ethyl   |
| EtOAc          | Ethyl acetate   |
| GC             | gas chromatography  |
| HPLC           | high pressure liquid chromatography                       |
| ID             | internal diameter   |
| IR             | infrared (spectroscopy)                                   |
| L              | ligand  |
| lit.           | literature  |
| M              | metal   |
| m.p.           | melting point   |

|                             |  |
|-----------------------------|--|
| MCPBA }<br><i>m</i> -CPBA } | <i>meta</i> -chloroperbenzoic acid               |
| Me                          | methyl   |
| MTPA                        | methoxy- $\alpha$ -(trifluoromethyl)phenylacetyl |
| NaOMe                       | <i>to be confirmed</i>                           |
| NMR                         | nuclear magnetic resonance                       |
| Ph                          | phenyl   |
| Pr                          | propyl   |
| psi                         | pounds per square inch                           |
| PTC                         | Phase Transfer Catalyst                          |
| r.p.m.                      | rotation per minutes                             |
| $R_f$                       | retention factor                                 |
| $R_t$                       | retention time                                   |
| Salen                       | <i>to be confirmed</i>                           |
| TBHP                        | <i>tert</i> -butyl hydroperoxide                 |
| THF                         | tetrahydrofuran                                  |
| TLC                         | thin layer chromatography                        |
| TMS                         | tetramethylsilane                                |
| UHP                         | urea-hydrogen peroxide                           |
| UV                          | ultraviolet                                      |
| v:v                         | volume per unit volume                           |

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# List of Chemical Names Used

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|                          |                              |
|--------------------------|------------------------------|
| $\text{CaH}_2$           | Calcium hydride              |
| $\text{Ca(OH)}_2$        | Calcium hydroxide            |
| $\text{CH}_2\text{Cl}_2$ | Dichloromethane              |
| $\text{CuCl}$            | Copper (I) chloride          |
| $\text{CuCl}_2$          | Copper (II) chloride         |
| DMF                      | Dimethyl formamide           |
| EtOAc                    | Ethyl acetate                |
| $\text{Et}_2\text{O}$    | Diethyl ether                |
| $\text{Et}_2\text{Zn}$   | Diethyl zinc                 |
| HOAc                     | Acetic acid                  |
| $\text{KHCO}_3$          | Potassium hydrogen carbonate |
| $\text{KHSO}_4$          | Potassium hydrogen sulfate   |
| $\text{NaHCO}_3$         | Sodium hydrogen carbonate    |
| $\text{Na}_2\text{SO}_3$ | Sodium sulfite               |
| $\text{Pd(OAc)}_2$       | Palladium acetate            |

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