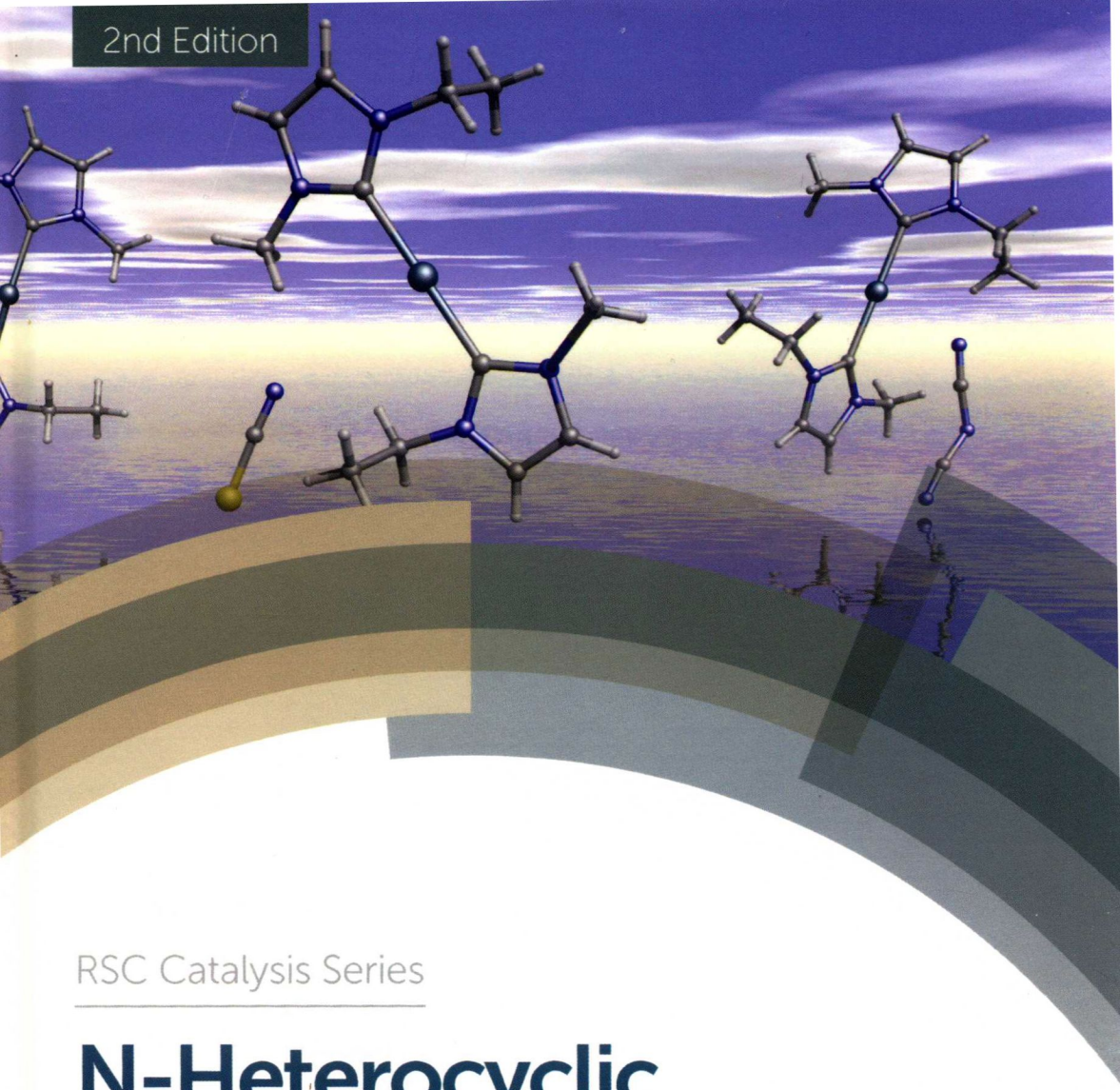
2nd Edition



RSC Catalysis Series

N-Heterocyclic Carbenes

From Laboratory Curiosities to Efficient Synthetic Tools

Edited by Silvia Díez-González

ROYAL SOCIETY OF CHEMISTRY

In less than 20 years N-heterocyclic carbenes (NHCs) have become well-established ancillary ligands for the preparation of transition metal-based catalysts. This is mainly due to the fact that NHCs tend to bind strongly to metal centres, avoiding the need of excess ligand in catalytic reactions. Also, NHC–metal complexes are often insensitive to air and moisture, and have proven remarkably resistant to oxidation.

This book showcases the wide variety of applications of NHCs in different chemistry fields beyond being simple phosphine mimics. This second edition has been updated throughout, and now includes a new chapter on NHC–main group element complexes. It covers the synthesis of NHC ligands and their corresponding metal complexes, as well as their bonding and stereoelectronic properties and applications in catalysis. This is complemented by related topics such as organocatalysis and biologically active complexes.

Written for organic and inorganic chemists, this book is ideal for postgraduates, researchers and industrialists.

Front cover image

Wellens *et al Dalton Trans.*, 2014, **43**, 3443-3452

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Díez-González

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2nd Edition

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Foreword

A journalist recently asked me if I foresaw when my group prepared the first stable carbene that this topic would become a field in its own right. My answer was clear-cut: certainly not! Indeed, in 1988 and even for a few years after, I believed that these species were too fragile to be really useful, and that they would remain laboratory curiosities. I was not totally wrong as far as our group's first stable carbene is concerned, and it is obvious that Arduengo carbenes, the famous NHCs, have been responsible for the fantastic development of this field of chemistry.

As can be seen in this book, during the last 15 years or so, following the pioneering work by Herrmann *et al.*, carbenes have mostly been used as ancillary ligands for the preparation of transition metal-based catalysts. Compared to phosphorus ligands, carbenes tend to bind more strongly to metal centers, avoiding the necessity for the use of excess ligand in catalytic reactions. The corresponding complexes are often less sensitive to air and moisture, and have proven remarkably resistant to oxidation. It is noteworthy that, although the first carbene–transition metal complexes were prepared as early as 1915 by Chugaev (Fischer and Maasböl were the first to fully characterize a carbene–metal species), the recent developments in their application in catalysis have been facilitated considerably by the availability of carbenes stable enough to be bottled. Moreover, the existence of metal-free carbenes has allowed their use as organocatalysts.

It is amazing to realize that the first method of taming a carbene was by attaching it to a transition metal, whereas nowadays carbenes can be used to stabilize transition metal centers that otherwise are not accessible. Similarly striking are some recent developments that show that carbenes, which were considered for years as the prototypes of reactive intermediates, can be used for stabilizing highly reactive main group species.

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For the future, since the robustness of carbene complexes is largely due to the presence of strong carbon–metal bonds, other types of stable low-valent carbon species are highly desirable, and I believe that a second generation of carbon-based L ligands will soon appear.

Lastly, I wish to say here that, for Bo Arduengo and myself, the enormous amount of results summarized in this excellent book is a wonderful gift.

Guy Bertrand
University of California, USA

Preface

I clearly remember ending the preface to the first edition of this book hoping the volume would be soon outdated. And yet, when I was approached by the Royal Society of Chemistry regarding a second edition my very first thought was: be careful what you wish for! Still, this has been an enjoyable journey, particularly thanks to the outstanding group of NHC experts who have agreed to join me in this project. My sincere gratitude goes to all of them for their invaluable contributions to this book.

In this second edition, all 14 chapters from the first edition have been thoroughly revised in order to include the most exciting recent findings, while keeping their main focus on the state of the art. This edition has been completed with the addition of a new chapter on NHC–main group adducts, one of the fastest growing areas of research in this area of chemistry.

Having been considered as transient species, at the most, for long years, nobody could have foreseen the current importance of NHCs at the heart of numerous advances in different chemical fields. In spite of the well-established status of NHCs, there is debate around their Lewis representation and bonding to different elements. A number of representations can be found in the literature (in Figure 1, five-membered ring diaminocarbenes are represented as examples). Representation **A** was soon abandoned, with early data showing the poor π-backdonating ability of NHCs, making the NHC–M bond

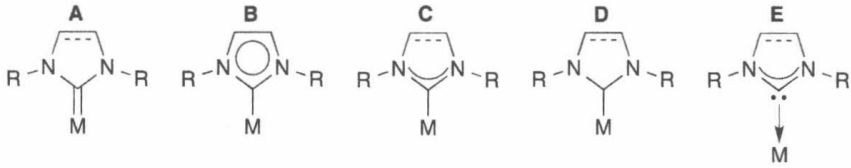

Figure 1 Possible representations of [(NHC)M] complexes.

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single in nature (at least with cyclic diaminocarbenes).[1] Although the current picture of NHCs is far more complex and it is now known that π-back-donation can represent over 30% of the bonding (hardly negligible...),[2] the analytical data still point relentlessly towards NHC–M single bonds. Similarly, the representation of unsaturated NHCs as aromatic derivatives (**B**) has gradually decreased following reports on the predominance of the carbenic form over ylidic resonance structures.[3] Even if subsequent studies pointed towards a cyclic electron stabilization, the resulting aromatic character of

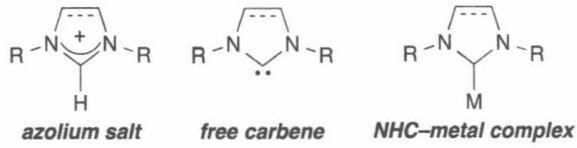

Figure 2 Chosen representations for this book.

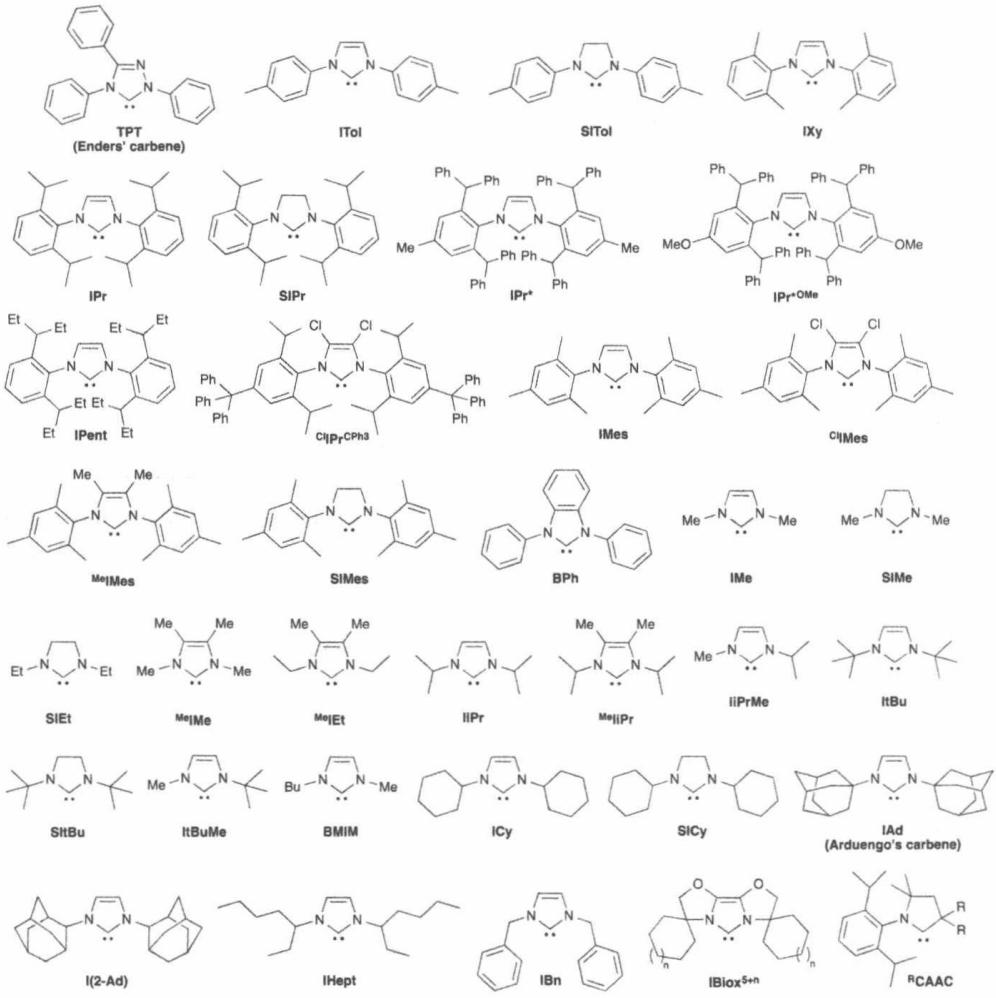

Figure 3 Structures and acronyms of NHCs.

imidazol-2-ylidenes would be substantially smaller than in benzene or imidazolium salts.[4] Most probably, structure **E** might be the one closer to the real bonding situation in these species; however, it is also the least straightforward to use. **C** and **D** are the most popular versions nowadays, despite the fact that they symbolize a trivalent carbon bond (**D**) in a confusing manner for any chemist unfamiliar with the field.

In this book, version **D** has been consistently used all chapters, with two notable exceptions. In Chapter 3, abnormal carbenes are represented in their mesoionic form, whereas in Chapter 5 dative arrow bonds are used in compounds with negligible backbonding and a formal C = E π bond is used for those molecules where substantial multiple bonding has been evidenced. These are arbitrary decisions and do not pretend to make any statement in this debate. For the reader's convenience, the general representations used for azolium salts, free NHCs and NHC–metal complexes are depicted in Figure 2. Also, the structures of NHC acronyms used throughout the different chapters can be found in Figure 3.

Silvia Díez-González

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To those who taught me all the important
things I will ever learn, my parents.

Abbreviations and Acronyms

2M2BN	2-methyl-2-butenenitrile
2M3BN	2-methyl-3-butenenitrile
3D	three-dimensional
3 PN	3-pentenenitrile
9-BBN	9-borabicyclo[3.3.1] nonane
$_{\beta}$MMBL	β-methyl-α-methylene-γ-butyrolactone
$_{\gamma}$MMBL	γ-methyl-α-methylene-γ-butyrolactone
μSR	muon spin resonance
AAAC	acyclic(alkyl)amino carbene
AB	ammonia–borane
Ac	acetyl
acac	acetylacetonato
Ad	adamantyl [tricyclo[3.3.1.1^{3,7}]decyl]
ADC	acyclic diaminocarbene
ADMET	acyclic diene metathesis polymerisation
AdN	adiponitrile
A. fumigatus	*Aspergillus fumigatus*
AIBN	2,2′-azobis(isobutyronitrile)
Am	amyl [2-methylbutyl]
An	*para*-anisyl [4-methoxylphenyl]
aNHC	abnormal N-heterocyclic carbene
aq	aqueous
Ar	aryl
ATH	asymmetric transfer hydrogenation
atm	atmosphere
ATRC	atom transfer radical cyclisation
ATRP	atom transfer radical polymerisation
AYC	amino(ylidene) carbene
BARF	tetrakis[3,5-bis(trifluoromethyl)phenyl] borate
BET	back electron transfer
BINAM	1,1′-bis(2-naphthylamine)
B. mallei	*Burkholderia mallei*
BMIM	1-butyl-3-methylimidazol-2-ylidene
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
bp	boiling point
BPh	1,3-diphenylbenzimidazol-2-ylidene
B. pseudomallei	*Burkholderia pseudomallei*

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bpy	2,2′-bipyridine
B. subtilis	*Bacillus subtilis*
Bu	butyl
Bz	benzoyl
CAAC	cyclic (alkyl) (amino) carbene
C. albicans	*Candida albicans*
CAM	complex-assisted metathesis
CAN	ceric ammonium nitrate
cat	catecholato [1,2-benzenediolate]
Cbz	carboxybenzyl
CHM	Chalk–Harrod mechanism
cin	cinnamyl [3-phenylpropen-2-yl]
CKT	Corriu–Kumada–Tamao
^{Cl}IMes	4,5-dichloro-1,3-bis-(2,4,6-trimethylphenyl) imidazol-2-ylidene
^{Cl}IPr^{CPh3}	4,5-dichloro-1,3-bis[2,6-diisopropyl-4-(triphenylmetyl)phenyl] imidazol-2-ylidene
CM	cross-metathesis
CNT	carbon nanotube
COD	1,5-cyclooctadiene
COE	cyclooctene
conv.	conversion
cot	cyclooctatetraene
Cp	cyclopentadienyl
Cp*	1,2,3,4,5-pentamethyl-cyclopentadienyl
CPME	cyclopentyl methyl ether
Cy	cyclohexyl
DAC	diaminocarbene
dan	1,8-diaminonaphthalene
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0] undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
de	diastereoisomeric excess
DFT	density functional theory
DIPEA	*N*,*N*-diisopropylethylamine
Dipp	2,6-diisopropylphenyl
DKR	dynamic kinetic resolution
DLC	delocalised lipophilic cation
DMA	*N*,*N*-dimethylacetamide
DMAP	4-(dimethyl)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMPU	*N*,*N*′-dimethyl-propylene urea [1,3-dimethyl-3,4,5,6-tetra-hydro-2-pyrimidinone]
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dpe	1,2-diphosphinoethane
dppe	1,2-bis(diphenylphos-phino)ethane
dppp	1,3-bis(diphenylphos-phino)propane
dr	diastereoisomeric ratio
Dur	duryl [2,3,5,6-tetramethylphenyl]
Ec. faecalis	*Enterococcus faecalis*
E. coli	*Escherichia coli*
ee	enantiomeric excess
EPC	endothelial progenitor cells
EPR	electronic paramagnetic resonance
equiv	equivalent
er	enantiomeric ratio
ESI-MS	electrospray ionisation mass spectrometry
ESR	electron spin resonance
Et	ethyl
EWG	electron-withdrawing group
Fc	ferrocenyl
FLP	frustrated Lewis-pair
GC	gas chromatography
GGA	generalised gradient approximation
GO	graphene oxide
h	hour
HDF	hydrodefluorination
Hept	heptyl
HFF	foreskin fibroblasts
HMDS	hexamethyldisilazide
HMPA	hexamethylphosphorus-triamide

HOAt	1-hydroxy-7-azabenzotriazole
HOESY	heteronuclear nuclear overhauser effect spectroscopy
HOMO	highest occupied molecular orbital
i	*iso*
I(2-Ad)	1,3-bis(2-adamantyl) imidazol-2-ylidene
IAd	1,3-bis(1-adamantyl) imidazol-2-ylidene
IBn	1,3-dibenzylimidazol-2-ylidene
IBiox	bisoxazoline-based N-heterocyclic carbene
IC_{50}	half maximal inhibitory concentration
ICAR	initiators for continuous activator regeneration
ICy	1,3-dicyclohexylimidazol-2-ylidene
IH	imidazol-2-ylidene
IHept	1,3-bis(2-heptyl) imidazol-2-ylidene
IiPr	1,3-diisopropylimidazol-2-ylidene
IiPrMe	1-methyl-3-isopropylimidazol-2-ylidene
IL	ionic liquid
IMe	1,3-dimethylimidazol-2-ylidene
IMes	1,3-bis(2,4,6-trimethylphenyl) imidazol-2-ylidene
IPent	1,3-bis(2,6-diisopentylphenyl) imidazol-2-ylidene
IPr	1,3-bis(2,6-diisopropylphenyl) imidazol-2-ylidene
IPr*	1,3-bis[(2,6-diphenylmethyl)-4-methylphenyl] imidazol-2-ylidene
IPr^{*OMe}	1,3-bis[(2,6-diphenylmethyl)-4-methoxyphenyl] imidazol-2-ylidene
IR	infrared
ItBu	1,3-di-*tert*-butylimidazol-2-ylidene
ItBuMe	1-*tert*-butyl-3-methylimidazol-2-ylidene
ITol	1,3-bis(4-methylphenyl) imidazol-2-ylidene
IXy	1,3-bis(2,6-dimethylphenyl)imidazol-2-ylidene
KIE	kinetic isotope effect
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
m	*meta*
MAAC	monoamido(amino) carbene
Mag	magnetite
MAO	methylaluminoxane
MBEC	minimum biofilm eradication concentration
MBL	α-methylene-γ-butyrolactone
MCM	Mobil composition of matter number 41
Me	methyl
MECP	minimum energy crossing point
^{Me}IEt	1,3-diethyl-4,5-dimethylimidazol-2-ylidene
^{Me}IiPr	1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene
^{Me}IMe	1,3,4,5-tetramethylimidazol-2-ylidene
^{Me}IMes	1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene
menthimid	1-methyl-3-(+)-menthylmenthoxide imidazol-2-ylidene
Mes	mesityl [1,3,5-trimethylphenyl]
MIC	mesoionic carbene
MIC	minimum inhibitory concentration
MIDA	*N*-methylimidodiacetate
min	minute
MMA	methyl methacrylate
M_n	number-average molar mass
MOM	methoxymethyl ether
MRSA	methicillin-resistant *Staphylococcus aureus*
MS	molecular sieves
Ms	mesyl [methanesulfonyl]
MTBE	methyl *tert*-butyl ether