TSE-LOK HO

Fiesers' Reagents for Organic Synthesis

VOLUME
29

WILEY

Fiesers' Reagents for Organic Synthesis

Fiesers'

Reagents for Organic Synthesis

VOLUME TWENTY NINE

Tse-Lok Ho

WILEY

This edition first published 2020

Registered Office
John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA

Editorial Office
111 River Street, Hoboken, NJ 07030, USA

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

ISBN: 9781119413035
ISSN: 0271-616X

Cover design by Wiley

Set in 9/12pt Times by SPi Global, Pondicherry, India

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

CONTENTS

PREFACE

This volume covers mostly progress of synthetic organic methodologies for the period from the beginning of 2013 to mid-2014. The major advances have been refinements of reagent applications and expansion of the scope.

The author thanks Jeffrey Ho, Dr. Sheng-Ying Hsieh, Prof. Yun Li, and Dr. Geoff T'so for some indispensable literature help.

GENERAL ABBREVIATIONS

Ac	acetyl
acac	acetylacetonate
Ad	1-adamantyl
AIBN	2,2'-azobisisobutyronitrile
aq	aqueous
Ar	aryl
BARF	tetrakis[3,5-bis(trifluoromethy)phenyl]borate
9-BBN	9-borabicyclo[3.3.1]nonane
BHT	butylated hydroxytoluene = (2,6-di-*t*-butyl-4-methylphenol)
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-binaphthalene-2,2'-diol
Bmim	*N*-butyl-*N*'-methylimidazolium
Bn	benzyl
Boc	*t*-butoxycarbonyl
bpy	2,2'-bipyridyl
bpz	2,2'-bipyrazine
BQ	1,4-benzoquinone
Bs	benzenesulfonyl
Bu	*n*-butyl
Bz	benzoyl
18-c-6	18-crown-6
c-	cyclo-
CAN	cerium(IV) ammonium nitrate
cap	caprolactamate
cat	catecholate
Cbz	benzyloxycarbonyl
cod	1,5-cyclooctadiene
Cp	cyclopentadienyl
*Cp**	1,2,3,4,5-pentamethylcyclopentadienyl
CPME	cyclopentyl methyl ether
CSA	10-camphorsulfonic acid
CuTC	copper(I) thienylcarboxylate
Cy	cyclohexyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DAST	(diethylamino)sulfur trifluoride

dba	dibenzylideneacetone
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	1,3-dicyclohecylcarbodiimide
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DIAD	diisopropyl azodicarboxylate
Dibal-H	diisobutylaluminum hydride
DMA	*N,N*-dimethylacetamide
DMAP	4-dimethylaminopyridine
DMDO	dimethyldioxirane
DME	1,2-dimethoxyethene
DMF	*N,N*-dimethylformamide
DMPU	*N,N*'-dimethylpropyleneurea
DMSO	dimethyl sulfoxide
DPM	dipivaloylmethane
DPPB	1,4-bis(diphenylphosphino)butane
DPPE	1,2-bis(diphenylphosphino)ethane
DPPF	1,1'-bis(triphenylphosphino)ferrocene
DPPP	1,3-bis(diphenylphosphino)propane
DTTB	4,4'-di-*t*-butylbiphenyl
ee	enantiomer excess
Et	ethyl
Fc	ferrocenyl
Fmoc	9-fluorenylmethoxycarbonyl
Fu	2-furyl
HFIP	hexafluoroisopropanol
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoric amide
Hx	*n*-hexyl
Ipc	isopinocampheyl
L	ligand
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
LED	light-emitting diode
LHMDS	lithium hexamethyldisilazide
LiDBB	lithium 4,4'-di-*t*-butylbiphenylide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
LN	lithium naphthaleneide
MCPBA	*m*-chloroperbenzoic acid
Me	methyl
MEM	methoxyethoxymethyl

Mes	mesityl
MOM	methoxymethyl
Ms	methanesulfonyl
MS	molecular sieve
MTO	methyltrioxorhenium
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NHC	*N*-heterocyclic carbene
NIS	*N*-iodosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methylpyrrolidone
Np	naphthyl
Ns	*p*-nitrobenzenesulfonyl
Nu	nucleophile
Oc	*n*-octyl
PEG	poly(ethylene glycol)
Ph	phenyl
phen	1,10-phenanthroline
Pht	phthaloyl
pic	2-picoline
pin	pinacolato
Piv	pivaloyl
PMB	*p*-methoxybenzyl
PMHS	poly(methylhydrosiloxane)
PMP	*p*-methoxyphenyl
Pr	*n*-propyl
Py	pyridine
RaNi	Raney nickel
RCM	ring-closing metathesis
R^F	perfluoroalkyl
ROMP	ring opening methathesis polymerization
s-	secondary
salen	*N,N*'-ethenebis(salicylideneiminato)
SAMP	(*S*)-1-amino-2-methoxymethylpyrrolidine
SEM	2-(trimethylsilyl)ethoxymethyl
SES	2-[(trimethylsilyl)ethyl]sulfonyl
TBAF	tetrabutylammonium fluoride
TBDPS	*t*-butyldiphenylsilyl
TBS	*t*-butyldimethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidinoxy
TES	triethylsilyl
Tf	trifluoromethanesulfonyl

TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
THP	tetrahydropyranyl
TIPS	triisopropylsilyl
TMEDA	*N,N,N',N'*-tetramethylethanediamine
TMS	trimethylsilyl
Tol	*p*-tolyl
tpp	tetraphenylporphyrin
tpy	terpyridyl
Ts	*p*-toluenesulfonyl
TSE	2-(trimethylsilyl)ethyl
Z	benzyloxycarbonyl
Δ	heat
))))	ultrasound

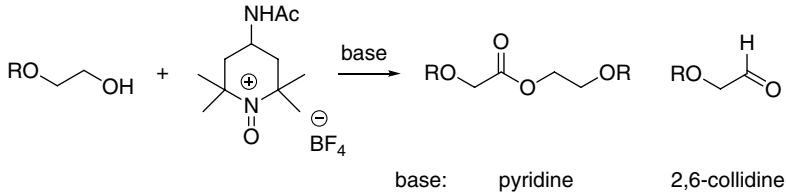
REFERENCE ABBREVIATIONS

ACIE	Angew. Chem. Inter. Ed.
ASC	Adv. Synth. Catal.
CAJ	Chem. Asian J.
CC	Chem. Commun.
CEJ	Chem. Eur. J.
ChJC	Chinese J. Chem.
CL	Chem. Lett.
CO	ChemistryOpen
CS	Chem. Science
CSR	Chem. Soc. Rev.
EJOC	Eur. J. Org. Chem.
HCA	Helv. Chim. Acta
JACS	J. Am. Chem. Soc.
JCCS	J. Chinese Chem. Soc.
JOC	J. Org. Chem.
OBC	Org. Biomol. Chem.
OL	Org. Lett.
S	Synthesis
SL	Synlett
T	Tetrahed.
TL	Tetrahed. Lett.

A

4-Acetamido-2,2,6,6-tetramethyl-1-oxopiperidinium tetrafluoroborate

Oxidation. Hexafluoroisopropyl ester of aroic acids are generated by oxidation of mixtures of ArCHO and $(CF_3)_2CHOH$.[1] Probably the hemiacetals are the critical substrates. As for acquiring aldehydes from oxidation of primary alcohols, the base must be carefully selected. Thus, in the case of 2-alkoxyethanols, 2,6-lutidine should be used.[2]



Alkyl perfluoroalkyl ketones undergo dehydrogenation on treatment with the oxopiperidinium salt and 2,6-collidine to furnish alkenyl perfluoroalkyl ketones.[3]

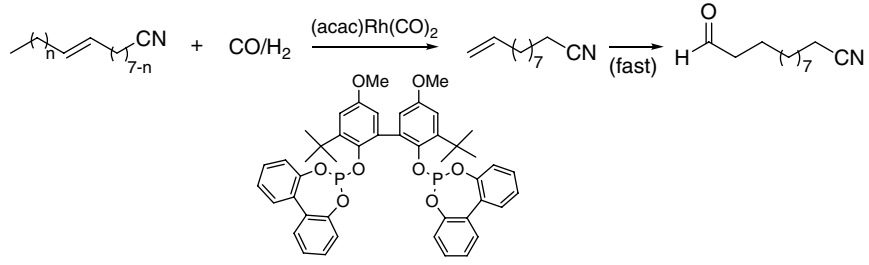
[1] Kelly, C.B., Mercadante, M.A., Wiles, R.J., Leadbeater, N.E. *OL* **15**, 2222 (2013)
[2] Bobbitt, J.M., Bartelson, A.L., Bailey, W.F., Hamlin, T.A., Kelly, C.B. *JOC* **79**, 1055 (2014)
[3] Hamlin, T.A., Kelly, C.B., Leadbeater, N.E. *EJOC* 3658 (2013)

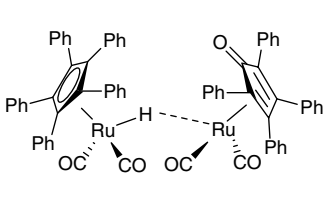
Acetylacetonato(dicarbonyl)rhodium(I)

Addition. The Rh(I) complex is the most reliable catalyst for hydroformylation, and research in the area concerns chiefly with ligands to modify its activity and robustness, although catalysts based on other metals such as Ru, Ir, Pd, and Fe have shown activities.[1] Libraries of bisdiazophospholanes have been compiled regarding optimization of conditions for hydroformylation with the Rh chelate.[2]

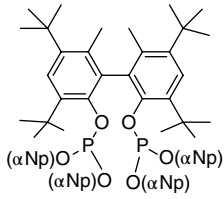
Linear hydroformylation of functionalized alkenes at room temperature is benefited by 6-diphenylphosphino-2-pyridone as ligand.[3] Alkenenitriles with an internal double bond and no obstruction to its isomerization toward the far terminus would undergo hydroformylation. The bond migration step is rate-determining.[4] When the reaction is carried out in the presence of $(acac)Rh(CO)_2$, Ru complex **1** and ligand **2**, internal alkenes produce primary alcohols, as hydrogenation occurs succeeding hydroformylation.[5]

Fiesers' Reagents for Organic Synthesis, First Edition. Tse-Lok Ho.



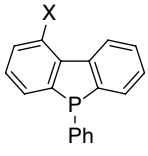


(**1**)

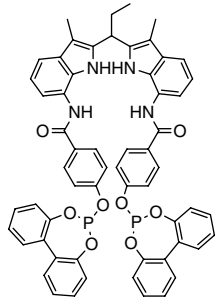


(**2**)

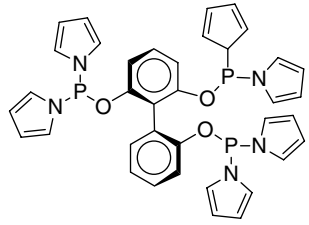
Control for production of linear vs branched aldehydes is of great interest. The dibenzophosphole ligand **3** favors formation of the branched aldehyde from styrene to the extent of 95:5.[6] A more elaborate ligand construct is to coordinate each of the three nitrogen atoms of tri(3-pyridyl)phosphine to tetraphenylporphyrinatozinc(II). On exchange of the huge ligand with one CO on the rhodium center a catalyst that favors branched hydroformylation is created.[7] The ligand **4** has a pocket for binding and preorganization in close proximity to the metal-coordination site, with it the reaction occurs predominantly in a way contrary to the usual trend.[8] Ligand **5** for the Rh complex favors linear hydroformylation.[9]



(**3**) = F, Cl



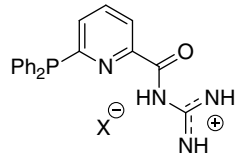
(**4**)



(**5**)

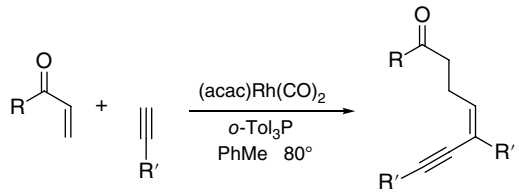
A method for catalyst recycling after hydroformylation of long-chain alkenes involves temperature manipulation.[10] A multicomponent solvent system consisting of PEG-400, dioxane, and *n*-heptane is crucial. The reaction is made heterogeneous afterward by cooling for facile recovery of the catalyst and ligand (Biphephos).

2-Alkenoic acids are converted to saturated primary alcohols of the same carbon chain length by a process that involves decarboxylation, hydroformylation and hydrogenation.[11]

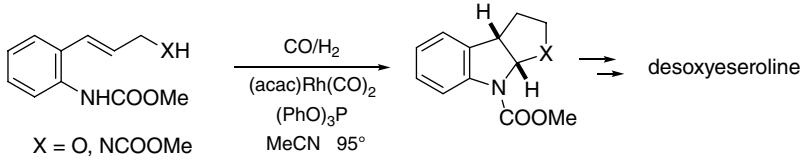


(**3**)

Addition. Exposure of 1-alken-3-ones and 1-alkynes to (acac)$Rh(CO)_2$ and (*o*-Tol)$_3$P in toluene at 80° leads to adducts containing a saturated ketone and a conjugated enyne unit.[12] The reaction proceeds via dimerization of the alkynes before the conjugate addition.



Cyclization. *o*-Aryloxybenzoic acids form dibenzofurans with loss of the carboxyl group and two hydrogen atoms on heating with (acac)Rh(cod), an analog of (acac) $Rh(CO)_2$, in Ac_2O containing KI.[13] *o*-(Methoxycarbonylamino)cinnamyl alcohols and analogs undergoes hydroformylation at the benzylic position which is amenable to a short synthesis ot desoxyeseroline.[14]



[1] Pospech, J., Fleischer, I., Franks, R., Buchholz, S., Beller, M. *ACIE* **52**, 2852 (2013)
[2] Adint, T.T., Wong, G.W., Landis, C.R. *JOC* **78**, 4231 (2013)
[3] Straub, A.T., Otto, M., Usui, I., Breit, B. *ASC* **355**, 2071 (2013)
[4] Ternel, J., Couturier, J.-L., Dubois, J.-L., Carpentier, J.-F. *ASC* **355**, 3191 (2013)
[5] Yuki, Y., Takahashi, K., Tanaka, Y., Nozaki, K. *JACS* **135**, 17393 (2013)
[6] Oukhrib, A., Bonnafoux, B., Panossian, A., Waifang, S., Nguyen, D.H., Urrutigoity, M., Colobert, F., Gouygou, M., Leroux, F.R. *T* **70**, 1431 (2014)
[7] Besset, T., Norman, D.W., Reek, J.N.H. *ASC* **355**, 348 (2013)
[8] Dydio, P., Reek, J.N.H. *ACIE* **52**, 3878 (2013);X Dydio, P., Detz, R.J., de Bruin, B., Reek, J.N.H. *JACS* **136**, 8418 (2014)
[9] Chen, C., Qiao, Y., Geng, H., Zhang, X. *OL* **15**, 1048 (2013)

[10] Brunsch, Y., Behr, A. *ACIE* **52**, 1586 (2013)
[11] Diab, L., Gellrich, U., Breit, B. *CC* **49**, 9737 (2013)
[12] Lerum, R.V., Russo, C.M., Marquez, J.E., Chisholm, J.D. *ASC* **355**, 3485 (2013)
[13] Maetani, S., Fukuyama, T., Ryu, I. *OL* **15**, 2754 (2013)
[14] Chiou, W.-H., Kao, C.-L., Tsai, J.-C., Chang, Y.-M. *CC* **49**, 8232 (2013)

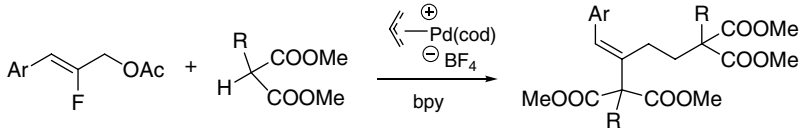
Alkynyl(*o*-methoxyphenyl)iodonium salts

Alkynyl group transfer. In comparison with those with an unsubstituted phenyl group the methoxy substituent improves reactivity of the reagents.[1]

[1] Hamnett, D.J., Moran, W.J. *OBC* **12**, 4156 (2014)

η³-Allyl(cyclopentadienyl)palladium

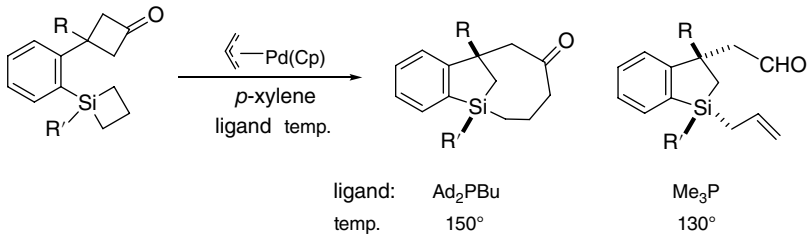
Substitution. Cinnamyloxy derivatives with a β-fluoro substituent undergo double substitution by malonic esters.[1] The Pd complex is able to activate the alkenyl fluorine.



Addition. A metathetic cyclization involving an *N*-cyanoanilide unit and a double bond of an *o*-methallyl side chain generates 2-cyanomethylindoline derivatives.[2]

An access to 3-arylidenepyrrolidines by *syn*-addition of the aryl group from $ArB(OH)_2$ and the iminium species derived from a homopropargylamine and formaldehyde is promoted by $CpPd(\eta^3\text{-}C_3H_5)$.[3]

Cyclic shuffle. A remarkable transformation mediated by $CpPd(\eta^3\text{-}C_3H_5)$ is the breaking of the 3-[*o*-(1-silacyclobutyl)phenyl]cyclobutanone system to create benzosiloles.[4]



[1] Yamamoto, M., Hayashi, S., Isa, K., Kawatsura, M. *OL* **16**, 700 (2014)
[2] Miyazaki, Y., Ohta, N., Semba, K., Nakao, Y. *JACS* **136**, 3732 (2014)
[3] Tsukamoto, H., Shiraishi, M., Doi, T. *OL* **15**, 5932 (2013)
[4] Ishida, N., Ikemoto, W., Murakami, M. *JACS* **136**, 5912 (2014)

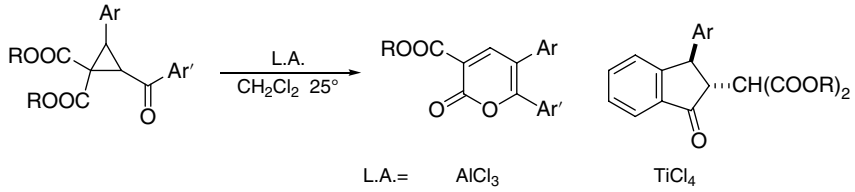
Aluminum bromide

Substitution. Hydride abstraction from C-1 of adamantane on grinding with $AlBr_3$ and CBr_4 occurs; when an amine is also present the bridgedhead cation is trapped to produce the 1-aminoadamantane.[1]

[1] Wei, Z., Li, J., Wang, N., Zhang, Q., Shi, D., Sun, K. *T* **70**, 1395 (2014)

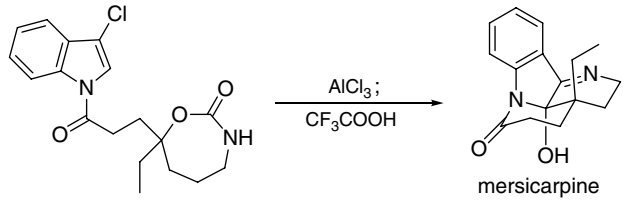
Aluminum chloride

Isomerization. 2-Aroylcyclopropane-1,1-dicarboxylic esters are subject to ring-opening isomerization by action of Lewis acids. Interestingly, different types of product are obtained from treatment with $AlCl_3$, and $TiCl_4$.[1]

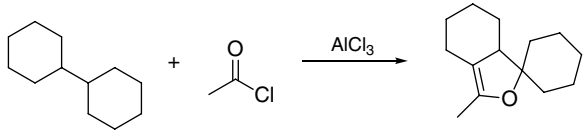


Substitution. Deoxygenative arylation of phloroglucinol is a convenient method for synthesis of 5-arylresorcinols.[2] It is thought that all three oxygen atoms are coordinated to $AlCl_3$ to expose a highly electrophilic cyclohexadienone for bonding with arenes.

The conclusion of a mersicarpine synthesis[3] involves an intramolecular alkylation and imination.[3]

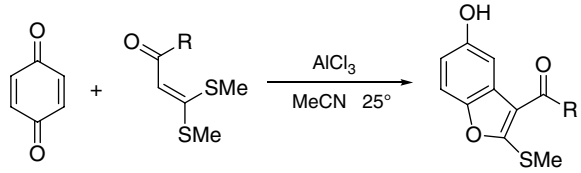


The reaction of 1,1'-bicyclohexyl with acetyl chloride in the presence of $AlCl_3$ is fascinating, as C-H acetylation occurs in one ring and oxygen atom insertion to a C-H bond of the other ring are involved.[4]



Electrophilic attack by aroyldithioacetic esters on phenols results in the formation of 4-aryl-2*H*-chromene-2-thiones.[5]

Cycloaddition. Role reversal for nucleophile and electrophile is witnessed in the reaction of benzoquinone with acylketene dithioacetals.[6] Still, $AlCl_3$ is the essential mediator.



Ionization of a benzylic tosylamino group induced by $AlCl_3$ in the presence of cyclopropane-1,1-dicarboxylic esters triggers indan formation.[7]

O-C bond cleavage. Catechols protected as benzodioxepanes are recovered by heating with $AlCl_3$ in benzene.[8]

[1] Sathishkannam, G., Srinivasan, K. *ASC* **356**, 729 (2014)
[2] Gulyas-Fekete, G., Boluda, C.J., Westermann, B., Wessjohann, L.A. *S* **45**, 3038 (2013)
[3] Lv, Z., Li, Z., Liang, G. *OL* **16**, 1653 (2014)
[4] Lyall, C.L., Uosis-Martin, M., Lowe, J.P., Mahon, M.F., Pantos, G.D., Lewis, S.E. *OBC* **11**, 1468 (2013)
[5] Devi, N.S., Singh, S.J., Devi, L.R., Singh, O.M. *TL* **54**, 183 (2013)
[6] Verma, G.K., Verma, R.K., Shukla, G., Anugula, N., Srivastava, A., Singh, M.S. *T* **69**, 6612 (2013)
[7] Zhu, M., Liu, J., Yu, J., Chen, L., Zhang, C., Wang, L. *OL* **16**, 1856 (2014)
[8] Huang, W.-B., Guo, Y., Jiang, J.-A., Pan, X.-D., Liao, D.-H., Ji, Y.-F. *SL* **24**, 741 (2013)

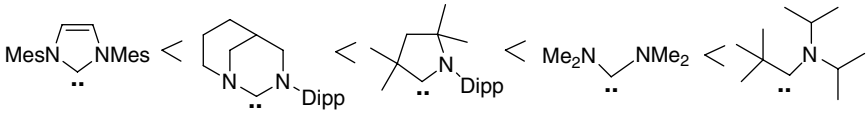
Aluminum phenoxides

Cycloaddition. Derived from tris(2-hydroxy-3,5-dichlorobenzyl)amine and Me_3Al the tetracoordinated aluminum phenoxide is a highly active catalyst (in combination with Bu_4NI) for transforming epoxides and oxetanes into cyclic carbonates by incorporating CO_2.[1]

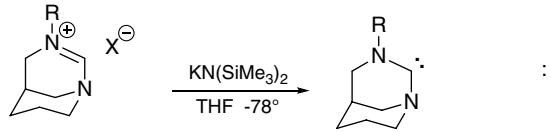
[1] Whiteoak, C.J., Kielland, N., Laserna, V., Castro- Gómez, F., Martin, E., Escudero-Adán, E.C., Bo, C., Kleij, A.W. *CEJ* **20**, 2264 (2014)

Aminocarbenes

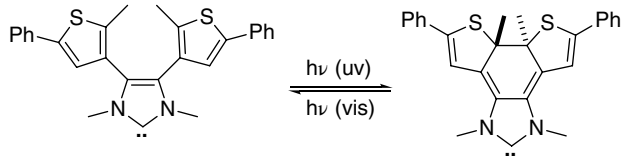
Structural variations. By comparing reactions with isonitriles, PhCHO, and methyl acrylate, ranking in both electrophilicity and nucleophilicity for a series of aminocarbenes has been determined.[1]



Synthesis of carbene (**1**) derived from 1-aza-3-azoniabicyclo[3.3.1]non-2-enes show limited participation of the bridgehead nitrogen lone-pair; such carbenes are electrophilic, and have more iminium characters.[2] The photoswitchable carbene **2A/2B** can be used to promote ring-opening polymerization of lactones.[3]

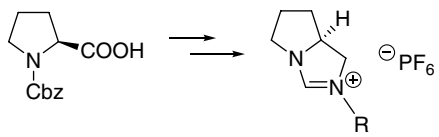


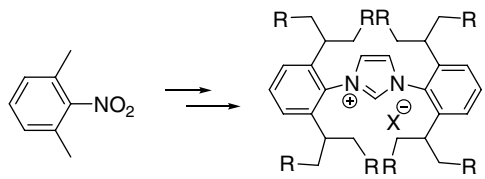
(**1**)



(**2A**) (**2B**)

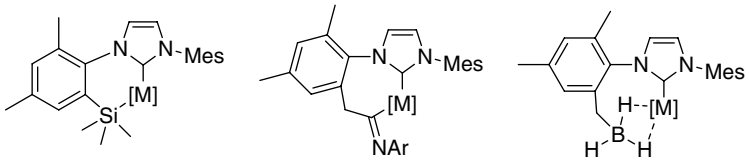
Preparation. A series of bicyclic carbene precursors are obtained from (*S*)-proline.[4] From triflate of a 4-hydroxyproline derivative imidazolium salt is readily obtained, and the ester group of the proline residue can be engaged in peptide synthesis prior to the access of the carbenes.[5] Access to the imidazolium salts **2** related to [IPr] is gained in an 8-step operation from 2,6-dimethylnitrobenzene.[6] There is also a report on multicomponent synthesis of symmetrical and unsymmetrical *N*-heterocyclic carbene (NHC) precursors, as well as their metal complexes.[7] A summary outlines various synthetic routes and applications of water-soluble NHC-transitional metal complexes.[8]



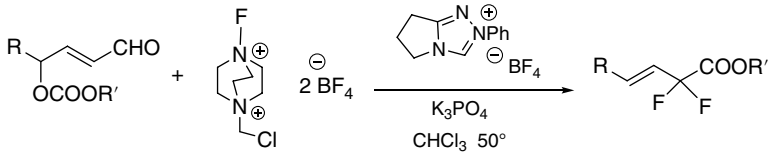


(**2**)

The borane complex of *N,N'*-dimethylimidazolidene is subject to photodecomposition to supply initiator for radical generation from alkyl iodides.[9a] Hybrid Rh(I)-porphyrin complexes also bearing two NHC units release the carbenes for aerobic oxidation of alcohols, and the decomposition is enhanced by irradiation.[9] NHC metal complexes with special internal ligands are those shown below.[9b]



Substitution. Redox transformation of 2-alkenals into saturated acyl electrophiles by NHC is well exploited. Based on this property oxime esters[10] and thioesters[11] are prepared. A synthesis of 2,2-difluoro-3-alkenoic esters from reaction of 4-alkoxycarboxy-2-alkenals with selecfluor.[12] Acquisition of *N*-carboxylanilines from RCHO and ArNO is ascribable to the formation of α-hydroxyalkylidene derivatives H-bonded to the nitrogen atom of the nitrosoarenes, from which C-O bond formation is favored via a five-atom transition state.[13]

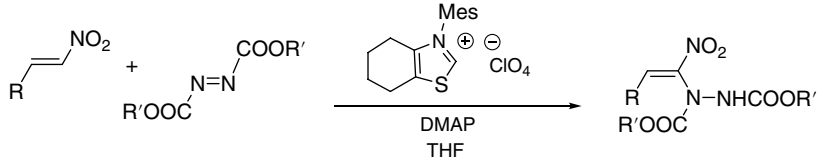


A synthetic approach to 3-ethylidenebenzopyranone and heterologs is based on the intramolecular S_N2' reaction on *o*-(4-halo-2-alkenoxy)benzaldehydes by treatment with an NHC.[14] Diheteroaryl ketones can be assembled from formyl-substituted heteroarenes and aryl heteroaryl iodonium triflates by virtue of NHC-activation of the aldehydes and the selective surrender of the heteraryl group from the iodonium salt.[15]

In the replacement of the tertiary carbonato group of 3-pivalyloxy-3-methyl-1-butene by an aryloxy residue on catalysis of a carbene derived from 1,2,3-triazolium salt, the oxygenation pattern does not change.[16] More straightforward is the formation of the 5-membered cyclic carbonate from reaction of glycerol with dimethyl carbonate; the catalyst used is an imidazolium salt-derived NHC in which the two *N*-substituents are 2,6-dimethylphenyl and *n*-hexadecyl groups.[17]

Arylation of unactivated arenes draws the benefit from participation of an NHC.[18]

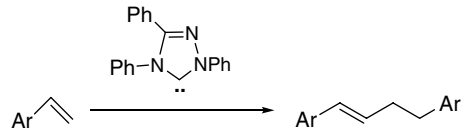
Addition. Quite unusual is the activation of nitroalkenes and azodicarboxylic esters to form adducts.[19] Acyl anion equivalents are created from certain 2-aroyloxyalkanals which can add to aroylazoarenes to furnish six-membered heterocyclic lactones.[20]



An NHC causes the combination of aldehydes with carbodiimides in air to form *N*-acylureas.[21] Phthalides are formed when *o*-formylcinnamonitrile and related alkenes are treated with an NHC in air.[22]

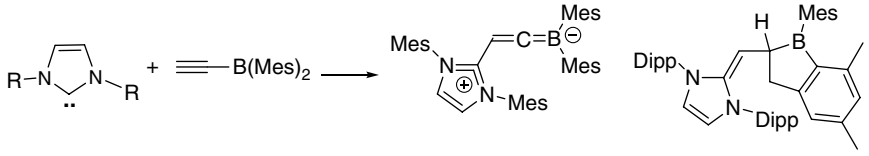
In view of the extensive activities concerning the application of NHC to organic synthesis periodic review of certain area is always welcome. There is now one publication addressing bond formation reactions that involve alkenes and alkynes.[23] Adducts of NHC and CO_2 serve as precatalysts for activating Michael donors.[24] Interestingly, glucose and other simple sugars have found use as a nucleophilic formyl synthon for conjugate addition to α,β-unsaturated ketones in the presence of a thiazolylene species.[25]

3-Acyl-3-aminooxindoles are prepared from the 3-imino precursors by reaction with 2-alkenals.[26] Intramolecular hydroacylation is often a favorable method to synthesize cyclic ketones by union of aldehydes and an enone system, with mediation of of an NHC. Steric constraint dictates the formation of a common ring.[27] Styrenes are receptive to hydroacylation by aldehydes therefore arylethyl ketones are readily prepared from their reaction with aldehydes.[28] However, the dimerization of styrenes to give 1,4-diaryl-1-butenes is quite surprising.[29]

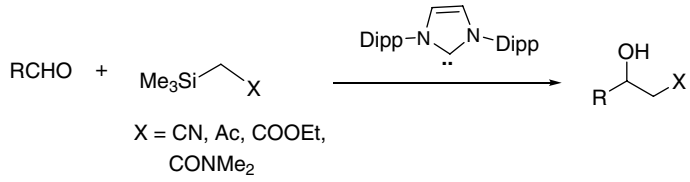


The dicationic adduct of [SIMes] and fluorodiphenylphosphine is a strong Lewis acid that catalyzes hydrosilylation of alkenes and hydrodefluorination of alkyl fluorides.[30] Hydroboration of various unsaturated compounds, including alkynes, enones, imines, and azadienes, is effective using $B_2(pin)_2$ in methanol, provided that a benzoimidazolylene is present as catalyst.[31]

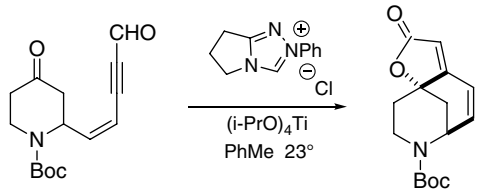
The bulkiness of the *N*-substituents in NHC influences the interaction with compounds such as ethynyldimesitylborane.[32]



Aldehydes do not always play the acyl addend role, as exemplified by the following reaction.[33] The same NHC catalyst is used to derivatize carbonyl compounds with cyanophosphates.[34]



Synthetcally the most significant application is the intramolecular addition of an ynal unit to a ketone to form the butenolide product, as it is well suited for the construction of the complete skeleton of securinine.[35]

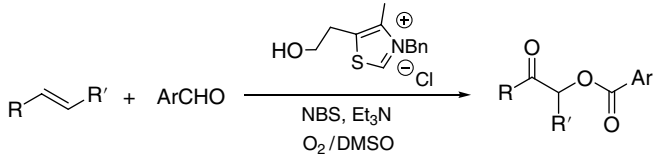


Oxidation. The cyclic carbenes based on the ring structure of Meldrum's acid serve as hydrogen acceptors (e.g., in converting 1,4-dihydrocyclohexadiene to benzene).[36] They can also insert into C-H bonds.

A triazolium salt-derived NHC and DBU converts ArCHO in hydroxylic solvents in the air to aroic acids or esters.[37] Benzils are probably the initial products which are susceptible to oxidative cleavage.

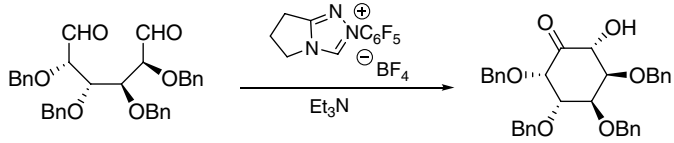
Condensation. Oxidative condensation of aldehydes and thiols to give thioesters takes full advantage of the selective activation of aldehydes by NHC.[38]

Functionalization of a double bond by ArCHO under oxidative conditions gives aroates of α-ketols.[39]

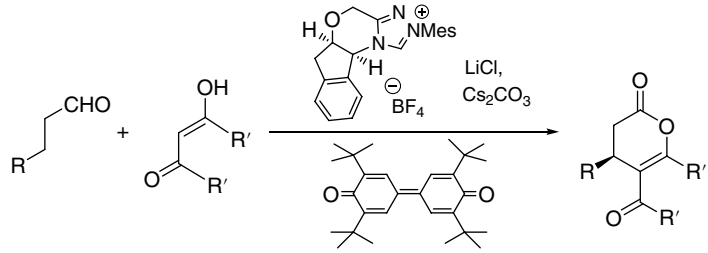


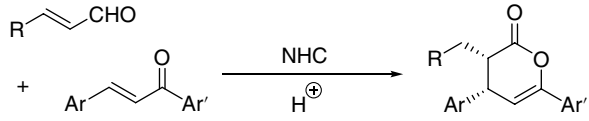
While 1,4-dimethyl-1,2,4-triazolium iodide is an excellent catalyst for monoacetalization of terephthalaldehyde, the derived NHC is useful for promoting benzoin condensation.[40] Mixed acyloin condensation between aromatic and aliphatic aldehydes favors the formation of α-ketols in which the ketone group is adjacent to the alkyl chain.[41,42] An approach to unsymmetrical benzils is based on the diverse reactivities of ArCHO and Ar'C(=NPh)Cl, namely the vigorous attack of the imino chlorides on the aldehyde adducts of NHC.[43]

The intramolecular condensation of substituted adipaldehydes is well suited to deliver precursors of stereoisomeric inositols.[44]



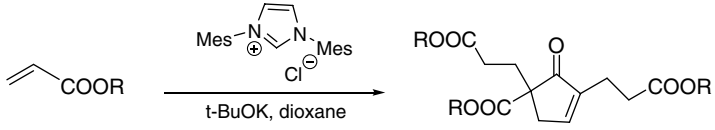
Conditions for converting alkanals into β-electrophilic acyl synthons in situ by NHC and an oxidant have been established.[45] Thus the active species can be trapped by β-dicarbonyl compounds to form 5-acyl-3,4-dihydro-2-pyrones. A simpler cycloaddition route involves the employment of alkenals, chalcones, and an acid besides the NHC.[46]



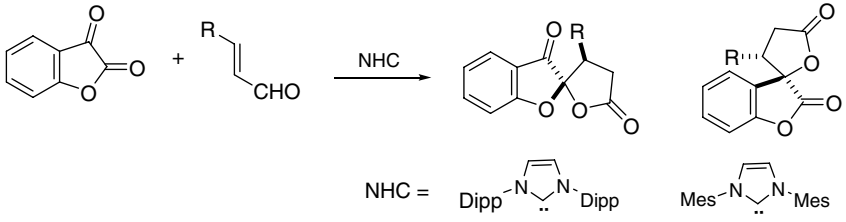


Simultaneous generation of acyl electrophiles from 2-alkenals and *N*-arylhydroxamic acids from aldehydes and nitrosoarenes by NHC provides reactive species that their mutual fates to form hydroxamic esters are ordained.[47]

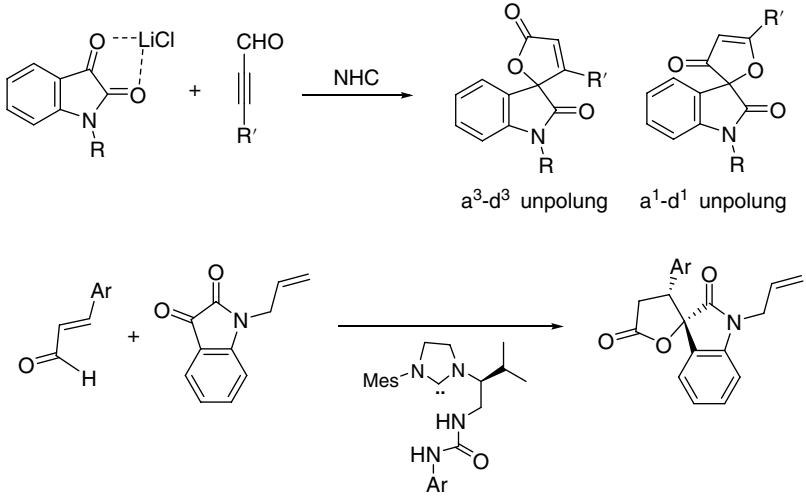
Cycloaddition. A polymer-linked NHC has been synthesized starting from histidine via 4-vinyl-1,3-dimethylimidazolium iodide. The catalyst directs the insertion of CO_2 into an epoxide ring.[48] A 2,5,5-trisubstituted 2-cyclopentenone is produced from [IMes]-catalyzed tetramerization of an acrylic ester.[49] The dimer, a 2-methyleneglutaric ester, appears to be the intermediate.



2-Haloalkanals behave as active acyl α−carbanion synthons, therefore they find ready use in annulating 2-nitroethenylindole.[50] The NHC adducts with 2-alkynals show nucleophilic character at the β-carbon site, their reaction with α-keto esters leads to butenolide-γ-carboxylic esters.[51] The regioselectivity of the [3+2]cycloaddition of 2-alkenals to 2,3-dihydrobenzofurandione varies with the structure of the NHC catalyst.[52] Most likely it is the consequence of steric factors.

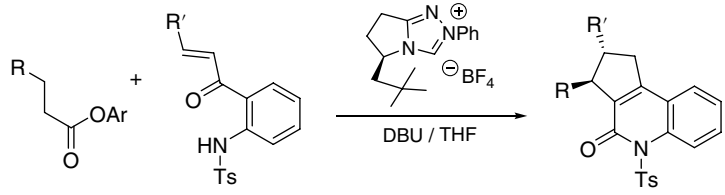


Spiroannulation of isatins by combining with 2-alkynals is subject to change by adding a Lewis acid (e.g., LiCl) as cocatalyst, which coordinates with the carbonyl groups.[53] A shift between the mode of a^3-d^3 umpolung and a^1-d^1 umpolung is recognized. The NHC with a urea subunit in of of the *N*-substituents for H-bonding shows catalytic activity for spiroannulation of isatins on reaction with cinnamaldehydes.[54]

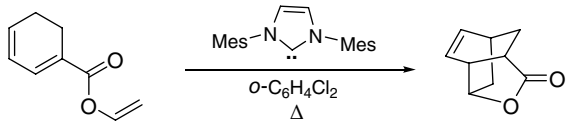


The formal oxidative hydroacylation of 2-alkenals to afford γ-keto esters is accomplished via a [3+2]cycloaddition with acyphosphonates. Alcoholysis opens the lactone ring and liberates the phosphonic diesters.[55]

In rendering the β-carbon of aryl alkanoates nucleophilic by NHC for reaction with conjugated ketones, cyclopentenes with an acyl pendant are formed.[56]



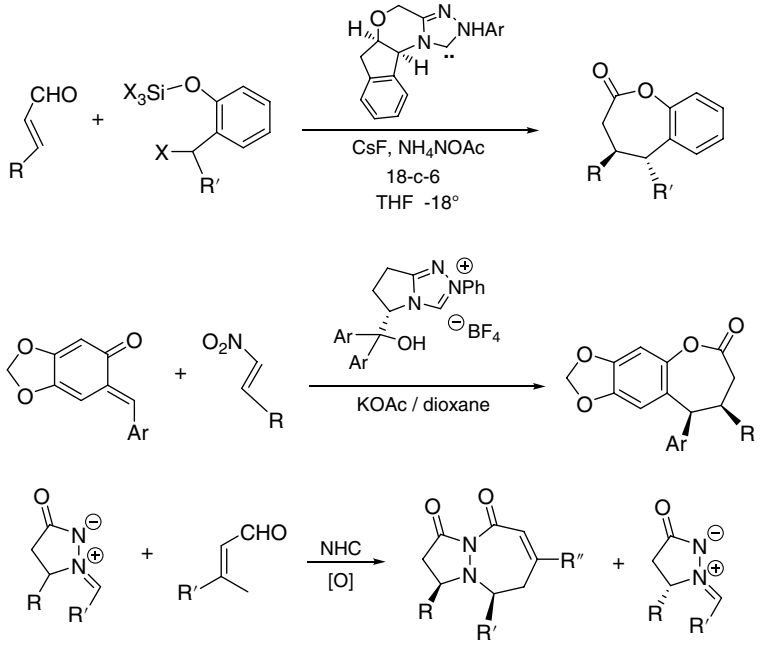
Deconjugation of the diene unit from the ester carbonyl is responsible for the occurrence of the intramolecular Diels-Alder reaction described in the following equation.[57] It seems energetically feasible only after the addition of the NHC to induce an allylic strain.



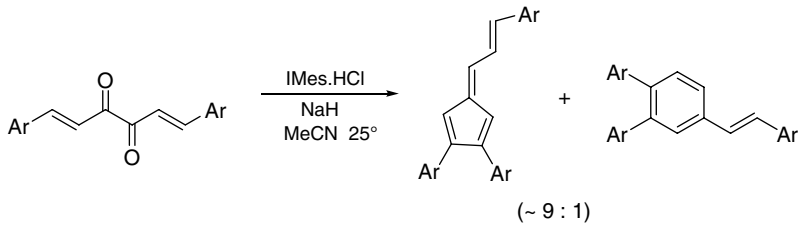
Facilitated generation of the hydroxyquinodimethane form of 2-methyl-3-formylbenzofuran and the *S*- and *N*-analogs by NHC is readily conceived. Fused dihydropyrones are synthesized by trapping the reactive species with carbonyl compounds.[58] Incorporating the ketone group of isatin into a spiropyrone is accomplished on reaction with α-bromo-α, β-unsaturated aldehydes with the latter reactants acting as conjugated ketene equivalents.[59] Carbonates of 4-hydroxy-2-alkenals also deliver such ketene equivalents by a 1,4-elimination process, as demonstrated in the reaction with azodicarboxylic esters.[60]

When both α-bromo-α,β-unsaturated aldehydes and simple alkanals are treated with an NHC, redox transformation of the former into Michael acceptors with an activated acyl group and the latter into the nucleophilic form, formation of 3,4-dihydropyrones is bound to happen.[61] 4-Nitrophenyl esters of 2-alkenoic acids undergo dearyloxylation on reaction with NHC, and become susceptible to transacylation with enamides. An ensuing [3,3] sigmatropic rearrangement gets the molecules ready for ring closure to regenerate the NHC catalyst and complete the synthesis of *N*-substituted 3,4-dihydro-2-pyridones.[62]

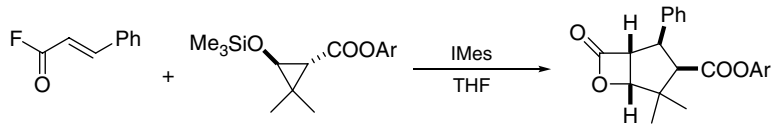
Representatives of [4+3]cycloaddition mediated by NHC include synthesis of lactones[63,64] and bicyclic ureas.[65]



Biscinnamoyls form cinnamylidenefulvenes as the major products on treatment with 1,3-dimesitylimidazolidene.[66]



Rearrangement. Although the formation of a β-lactone fused to a cyclopentane ring from a push-pull cyclopropanecarboxylic ester and cinnamoyl fluoride appears to be the result of sequential [3+2]- and [2+2]cycloadditions, involvement of an Ireland-Claisen rearrangement was formulated.[67]



Reduction. The readily available *N*-benzyl analog of thiamine is often used as an NHC precursor. Its application as a mediator of aryl azide decomposition under basic conditions to afford arylamines is apparent.[68]

[1] Martin, D., Canac, Y., Lavallo, V., Bertrand, G. *JACS* **136**, 5023 (2014)
[2] Martin, D., Lassauque, N., Steinmann, F., Manuel, G., Bertrand, G. *CEJ* **19**, 14895 (2013)
[3] Neilson, B.M., Bielawski, C.W. *CC* **49**, 5453 (2013)
[4] Thomasset, A., Bouchardy, L., Bouraud, C., Guillot, R., Toffano, M., Vo-Thanh, G. *S* **46**, 242 (2014)
[5] Zhao, Y., Gilbertson, S.R. *OL* **16**, 1033 (2014)
[6] Meiries, S., Le Duc, G., Chartoire, A., Collado, A., Speck, K., Arachchige, K.S.A., Slawin, A.M.Z., Nolan, S.P. *CEJ* **19**, 17358 (2013)
[7] Queval, P., Jahier, C., Rouen, M., Artur, I., Legeay, J.-C., Falivene, L., Toupet, L, Crévisy, C., Cavallo, L., Baslé, O., Mauduit, M. *ACIE* **52**, 14103 (2013)
[8] Schaper, L.-A., Hock, S.J., Herrmann, W.A., Kühn, F.E. *ACIE* **52**, 270 (2013)
[9] Olguín, J., Müller-Bunz, H., Albrecht, M. *CC* **50**, 3488 (2014)
[9a] Pan, X., Lalevée, J., Lacôte, E., Curran, D.P. *ASC* **355**, 3522 (2013)
[9b] Mo, Z., Deng, L. *SL* **25**, 1045 (2014)
[10] Enders, D., Grossmann, A., Van Craen, D. *OBC* **11**, 138 (2013)
[11] He, L., Guo, H., Li, Y.-Z., Du, G.-F., Dai, B. *CC* **50**, 3719 (2014)
[12] Dong, X., Zhao, Y.-M., Sun, J. *SL* **24**, 1221 (2013)
[13] Wang, G., Chen, X., Zhang, Y., Yao, W., Ma, C. *OL* **15**, 3066 (2013)
[14] Zhao, M., Yang, H., Li, M.-M., Chen, J., Zhou, L. *OL* **16**, 2904 (2014)
[15] Toh, Q.Y., McNally, A., Vera, S., Erdmann, N., Gaunt, M.J. *JACS* **135**, 3772 (2013)