TSE-LOK HO

Fiesers' Reagents for Organic Synthesis

VOLUME
27

WILEY

Reagents for Organic Synthesis

Fiesers'

Reagents for Organic Synthesis

VOLUME TWENTY SEVEN

Tse-Lok Ho

WILEY

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PREFACE

行萬里路　　Ten thousand miles to tread
讀萬卷書　　Ten thousand volumes to read

The old Chinese saying encourages lover of knowledge to broaden his vista by extensive reading and exploration of the surrounding world. While I do not expect to be able to fulfil such lofty objectives during my lifetime, engaging the work on the ROS series definitely has set me along the right path.

My initial spiritual contact with the Fiesers was made through their excellent textbooks and experimental manual that formed part of my education in college. Of course I never had any idea that I shall follow their footsteps in one of their endeavors yet through thick and thin I have now produced ten volumes of the ROS series. This work always puts me in the mindset of another Chinese idiom: Edging towards a deep chasm and stepping on thin ice,* because of the very high standard the Fiesers set for the series. On reflection I can only say I have tried to do my very best.

Professor Louis Frederick Fieser died in 1977, therefore the time I completed this volume marks the 35th anniversary of his death. He and his wife Mary were innovative educators to whom our generation and perhaps several others owe much; they have left a legacy far beyond the ROS series. Individuals born in 1977 and decided to pursue a career in organic chemistry should be in the position of establishing themselves, so it is appropriate to dedicate this Volume in Professor Fieser's memory. And what would be more appropriate to ask Professor Koji Nakanishi to write a Foreword on this occasion?

Professor Nakanishi is one of the most distinguished organic chemists now living. When he went to Harvard to study under Professor Fieser, he immediately proved his exquisite experimental prowess in the annual competition of organic preparation (Martius Yellow) among graduate students in the Fieser laboratory he beat everyone, including the greatly experienced LFF, in finishing the series in terms of highest product yield and purity, as well as shortest time. During his career his contributions to natural products chemistry and biophysical/biochemical investigations are admirable, enviable, and universally recognized.

The tradition in the Fieser laboratory led me to examine the general comparison of experimental chemistry to cooking. The Fieser lab must be likened to a Cordon Bleu school in which youngsters honed their skills. It was also quite natural that the Fiesers eventually developed the ROS series for the service of a wider community. As preparation of dishes manifests the ingenuity of a chef, the same ingredients can yield products with tastes and appearances poles apart, by artful use of condiments and handling. I am reminded of the popular contests on TV shows of Japan and China in which accomplished chefs are

crowned champions at the end. The role the Fiesers played in the collection and evaluation of “recipes” from organic literature was somewhat like that of the judges for the chef contests.

This Volume includes survey of the most important synthetic methodologies announced during 2010 and the first half of 2011. Continuing emphasis on chiral catalysis, and particularly organocatalysis, is still evident, although catalytic reactions by derivatives of noble metals (gold, palladium, platinum, ruthenium, rhodium) as well as reactions mediated by salts of copper, iron and indium are still being actively developed. A very important area is concerned with C-H bond activation by metal species.

Tse-Lok Ho

* 如臨深淵 如履薄冰

FOREWORD

I congratulate Professor Tse-Lok Ho for his efforts to continue publishing *Fiesers' Reagents for Organic Synthesis*, which has reached Volume 27. Although not a synthetic chemist, I have all earlier volumes in my laboratory, which judging from their pathetic shapes on the bookshelf have all been very well used by group members. It is incredible that the Fieser / Fieser team published so many monographs in addition to their research results—*Natural Products Related to Phenanthrene* 3rd Edition (1949), *Steroids* (1959), *Advanced Organic Chemistry* (1961), *Topics in Organic Chemistry* (1963)—before starting the *Reagents for Organic Synthesis* series in 1967. This was the era before computers, when manuscripts were truly manuscripts or typewritten.

The period 1950–1952 spent during my graduate student years in the Fieser group at Harvard University had a profound effect on my career. I had come from Nagoya University as a GARIOA student (predecessor of Fulbright) soon after WWII. I remember Mary Fieser always set herself up at a particular desk in the library of the Chemistry department in the Converse Laboratory surrounded by journals and books while hand-writing one book manuscript or another.

In those years Professor Louis Fieser gave his famous undergraduate organic chemistry course — Chem 20, and constantly worked by his desk in his office with a dirty lab towel dangling from his lab coat. He was an exquisite classical experimentalist. Mary Fieser, very knowledgeable and energetic, used to come to the lab to attend weekly colloquia and group seminars to keep up her outlook on new developments of chemical research.

While nowadays one can secure full information on a reagent through the internet, browsing through the pages of *Fiesers' Reagents* series allows one to pick up unexpected information and/or ideas for ongoing research—a bonus that might not have been gained from looking up a specific reagent on the computer. It is wonderful news that this classic series continues to be published.

KOJI NAKANISHI

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New York, NY

GENERAL ABBREVIATIONS

Ac	acetyl
acac	acetylacetonate
Ad	1-adamantyl
AIBN	2,2′-azobisisobutyronitrile
aq	aqueous
Ar	aryl
9-BBN	9-borabicyclo[3.3.1]nonane
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BINOL	1,1′-binaphthalene-2,2′-diol
Bn	benzyl
Boc	*t*-butoxycarbonyl
bpy	2,2′-bipyridyl
Bs	benzenesulfonyl
Bu	*n*-butyl
Bz	benzoyl
18-c-6	18-crown-6
c-	cyclo-
CAN	cerium(IV) ammonium nitrate
Cbz	benzyloxycarbonyl
cod	1,5-cyclooctadiene
Cp	cyclopentadienyl
*Cp**	1,2,3,4,5-pentamethylcyclopentadienyl
CSA	10-camphorsulfonic acid
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-dicyclohexylcarbodiimide
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-dimethoxyethane
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
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoric amide
Hx	*n*-hexyl
L	ligand
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
LHMDS	lithium hexamethyldisilazide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
LN	lithium naphthalenide
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
NIS	*N*-iodosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methylpyrrolidone
Np	naphthyl
Nu	nucleophile
Oc	*n*-octyl

PEG	poly(ethylene glycol)
Ph	phenyl
Phen	1,10-phenanthroline
Pht	phthaloyl
Pin	pinacolato
Piv	pivaloyl
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
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.
CL	Chem. Lett.
CSR	Chem. Soc. Rev.
EJOC	Eur. J. Org. Chem.
H	Heterocycles
HCA	Helv. Chim. Acta
JACS	J. Am. Chem. Soc.
JHC	J. Heterocycl. Chem.
JOC	J. Org. Chem.
OBC	Org. Biomol. Chem.
OL	Org. Lett.
OM	Organometallics
S	Synthesis
SL	Synlett
T	Tetrahed.
TL	Tetrahed. Lett.

A

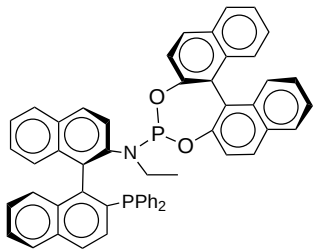
Acetylacetonato(1,5-cyclooctadiene)rhodium(I).

Hydroformylation. In the presence of Ph_3P, (acac)Rh(cod) acts as catalyst for hydroformylation of 1-alkenes giving an n/iso ratio of 3:1 or higher.[1]

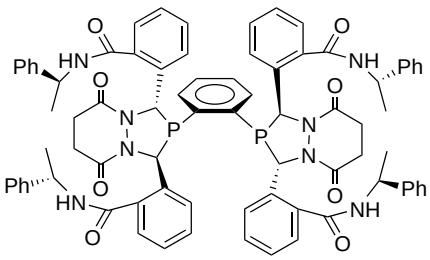
[1]Piras, I., Jennerjahn, R., Jackstell, R., Spannenberg, A., Franke, R., Beller, M. *ACIE* **50**, 280 (2011).

Acetylacetonato(dicarbonyl)rhodium(I).

Hydroformylation. The binol-based ligand **1** forms a formylation catalyst with the Rh(I) complex in syngas to transform 1-alkenes into optically active branched aldehydes.[1] Enamides and allylic ethers and amine derivatives are homologated at the sp^2 site closer to the functional group; the diazaphospholane ligand **2** directs the asymmetric reaction course.[2]

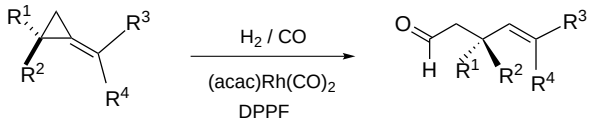


(**1**)



(**2**)

A directed hydroformylation of 4-alkenols to form 3-substituted 2-tetrahydropyranols is realized using Ph_2POMe as the ligand.[3] Alkoxy group exchange precedes hydrorhodation of the double bond. Regioselective and stereoselective ring opening of alkylidenecyclopropanes involving the less substituted CC bond is observed during the hydroformylation.[4]



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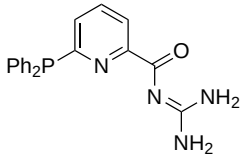
For achieving reduction in tandem with hydroformylation conditions such as having Xantphos and Et_3P,[5] or Xantphos and Shvo complex[6] have been established.

Two-carbon homologation of an aldehyde occurs when the guanidine derivative **3** is present.[7] One-pot homologation via hydroformylation and Knoevenagel reaction is also achievable.



(**3**)

Decarbonylative hydroarylation. Hydroarylation of norbornenes introduces an aryl group from ArCHO to the exo side of the bridged system.[8] The Rh(I)-catalyzed reaction requires also $Co(acac)_3$. With acrylic esters the analogous reaction is conducted in the presence of $Ni(acac)_2$. The decarbonylative Heck reaction products are formed in various ratios.[9]

Arylation of 2-arylpyridines by Rh(I)-catalysis[10] offers an alternative method to the Pd-catalyzed process.

Acylchlorination. 1-Alkynes and ArCOCOCl readily combine to afford (*Z*)-ArCOCOCH=C(Cl)R, by catalysis of $(acac)Rh(CO)_2$.[11]

[1]Zhang, X., Cao, B., Yan, Y., Yu, S., Ji, B., Zhang, X. *CEJ* **16**, 871 (2010).
[2]McDonald, R.I., Wong, G.W., Neupane, R.P., Stahl, S.S., Landis, C.R. *JACS* **132**, 14027 (2010).
[3]Grünanger, C.U., Breit, B. *ACIE* **49**, 967 (2010).
[4]Simaan, S., Marek, I. *JACS* **132**, 4066 (2010).
[5]Boogaerts, I.I.F., White, D.F.S., Cole-Hamilton, D.J. *CC* **46**, 2194 (2010).
[6]Takahashi, K., Yamashita, M., Ichihara, T., Nakano, K., Nozaki, K. *ACIE* **49**, 4488 (2010).
[7]Kemme, S.T., Smejkal, T., Breit, B. *CEJ* **16**, 3423 (2010).
[8]Yang, L., Guo, X., Li, C.-J. *ASC* **352**, 2899 (2010).
[9]Yang, L., Correia, C.A., Guo, X., Li, C.-J. *TL* **51**, 5486 (2010).
[10]Shuai, Q., Yang, L., Guo, X., Basle, O., Li, C.-J. *JACS* **132**, 12212 (2010).
[11]Kashiwabara, T., Tanaka, M. *ASC* **353**, 1485 (2011).

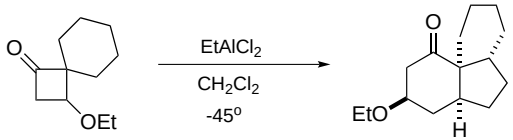
1-Acylimidazoles.

Derivatization of carboxylic acids. Carbamates and *N'*-methoxyureas derived from imidazole are excellent reagents for converting RCOOH into esters and Weinreb amides, respectively.[1]

[1]Heller, S.T., Sarpong, R. *OL* **12**, 4572 (2010).

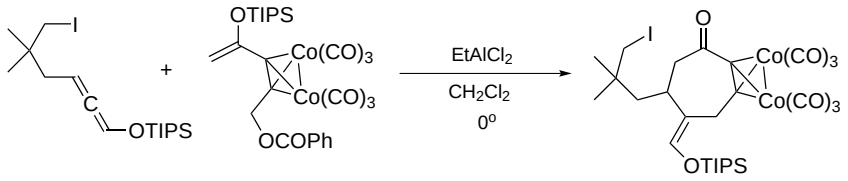
Alkylaluminum chlorides.

Annulation. 3-Alkoxycyclobutanones undergo ring expansion by incorporation of an alkene, in the presence of $EtAlCl_2$. An intramolecular version delivering a single product from a mixture of four diastereoisomers is most impressive.[1]



87%

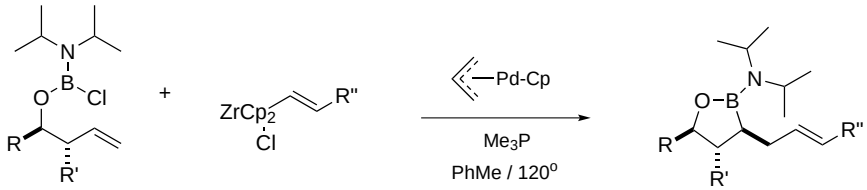
Involvement of the remote double bond of an allenyl silyl ether in the elaboration of 4-siloxymethylenecycloheptanones is synthetically expedient for elaboration of some sesquiterpenes.[2]



[1]Matsuo, J., Sasaki, S., Hoshikawa, T., Ishibashi, H. *CC* **46**, 934 (2010).
[2]Mitachi, K., Yamamoto, T., Kondo, F., Shimizu, T., Miyashita, M., Tanino, K. *CL* **39**, 630 (2010).

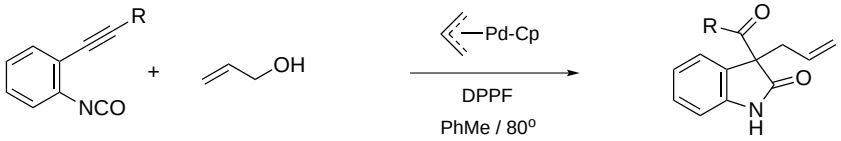
η^3-Allyl(cyclopentadienyl)palladium.

Alkenylboration.[1] Coupling with alkenylzirconocene chlorides of homoallyloxychloroboranes is promoted by the π-allylcomplex of Pd.

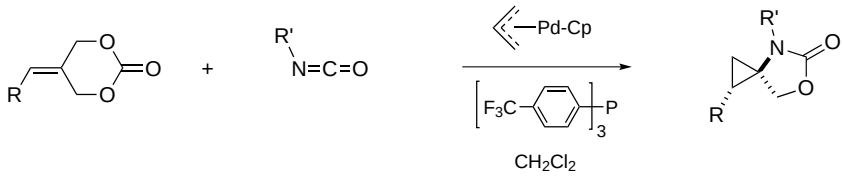


Cycloaddition. Isochromans are formed[2] on mixing *o*-trimethylsilylbenzyl carbonates with η-keto esters in the presence of η^3-C_3H_5Pd-Cp, in a simple extension of the reaction involving imines.

Other cycloaddition reactions include those between *N*-tosylimines and 2-acetoxy-3-trimethylsilylmethyl-3-butenenitrile to form *N*-tosyl-3-cyano-4-methylenepyrrolidines.[3] 3-Acyloxindoles are readily assembled from *N*-(2-alkynylaryl) isocyanates and allylic or benzylic alcohols.[4]



Benzotriazinones and sulfonyl analogs undergo elimination of dinitrogen on reaction with aryl isocyanides.[5] From cyclic allylic carbonates condensation with *N*-tosylaziridines to furnish 9-membered N,O-heterocycles has been observed.[6] The reaction of 5-alkylidene-1,3-dioxan-2-ones with RNCO is more interesting as it affords spirocyclic products.[7]



[1]Daini, M., Suginome, M. *JACS* **133**, 4758 (2011).
[2]Ueno, S., Ohtsubo, M., Kuwano, R. *OL* **12**, 4332(2010).
[3]Trost, B.M., Silverman, S.M. *JACS* **132**, 8238 (2010).
[4]Toyoshima, T., Mikano, Y., Miura, T., Murakami, M. *OL* **12**, 4584 (2010).
[5]Miura, T., Nishida, Y., Morimoto, M., Yamauchi, M., Murakami, M. *OL* **13**, 1429 (2011).
[6]Shintani, R., Ikehata, K., Hayashi, T. *JOC* **76**, 4776 (2011).
[7]Shintani, R., Moriya, K., Hayashi, T. *CC* **47**, 3057 (2011).

Allylsilanes.

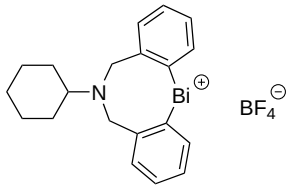
Activation. In allylation of RCHO with allyltrichlorosilanes the latter reagents are activated by aryl methyl sulfoxides.[1] For reaction of allylsilanes with tetrahydropyranyl ethers to replace the alkoxy group of the latter substances, $BiBr_3$ is a mild catalyst.[2]

Supersilyl group effects. Comparing with the more common allyltriorganosilanes those bearing the tris(trimethylsilyl)silyl group enjoy special reactivities in aldol reaction, [2+2]cycloaddition and many others due to steric influences.[3] Similar trends are found in tris(trimethylsilyl)siloxy derivatives as compared with the simpler analogs.

[1]De Sio, V., Massa, A., Scettri, A. *OBC* **8**, 3055 (2010).
[2]Krabbe, S.W., Angeles, V.V., Mohan, R.S. *TL* **51**, 5643 (2010).
[3]Laub, H.A., Yamamoto, H., Mayr, H. *OL* **12**, 5206 (2010).

Allylstannanes.

Allylation. For the reaction of tetrallylstannane with aldehydes at room temperature, a reusable catalyst **1** is reported.[1]



(**1**)

[1]Zhang, X., Qiu, R., Tan, N., Yin, S., Xia, J., Luo, S., Au, C.-T. *TL* **51**, 153 (2010).

Aluminum.

Lewis acids. Lewis catalysts are formed when aluminum is heated with ArI in the presence of $HgCl_2$ or Ga at 120°.[1]

Reduction. Recovery of triphenylphosphine from triphenylphosphine oxide at room temperature is accomplished in two steps: treatment with oxalyl chloride then aluminum and $PbCl_2$. The conversion takes only a short time.[2]

[1]Tang, X., Rawson, D., Woodward, S. *SL* 636 (2010).
[2]Yano, T., Hoshino, M., Kuroboshi, M., Tanaka, H. *SL* 801 (2010).

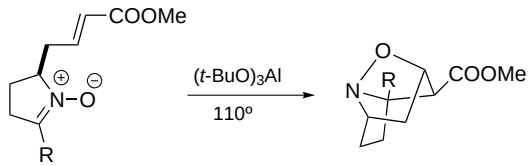
Aluminum bromide.

Carboxylation. Arenes are converted into ArCOOH when $AlBr_3$ and R_3SiCl are present.[1]

[1]Nemoto, K., Yoshida, H., Egusa, N., Morohashi, N., Hattori, T. *JOC* **75**, 7855 (2010).

Aluminum *t*-butoxide.

Cycloaddition. Intramolecular [3+2]cycloaddition of nitrone and conjugated ester subunits is promoted by $(t\text{-BuO})_3Al$.[1]

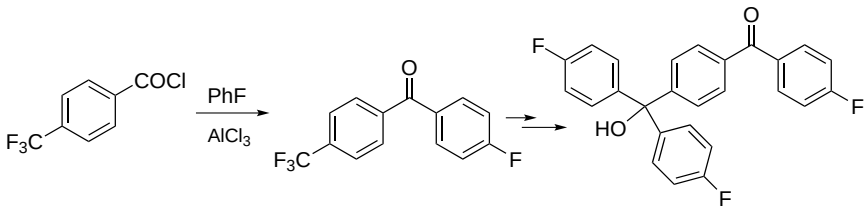


[1]Davis, F.A., Theddu, N., Edupuganti, R. *OL* **12**, 4118 (2010).

Aluminum chloride.

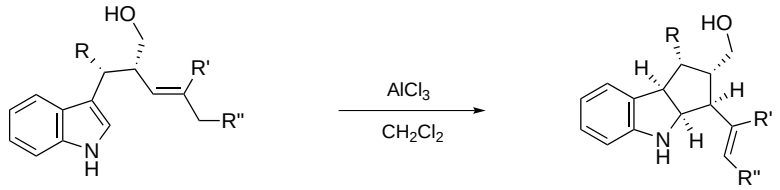
Electrophilic reactions. Sterically hindered diaryl ketones are accessible at room temperature by reaction of ArCOCl and ArSnR and catalyzed by $AlCl_3$.[1] (Using indium metal under solvent-free conditions is an alternative method.)

There is a rather unusual display of electrophilicity of the trifluoromethyl group in 4-fluoro-4′-trifluoromethylbenzophenone. The latter is the initial product of the Friedel-Crafts reaction between 4-trifluoromethylbenzoyl chloride and fluorobenzene.[2]



The Friedel-Crafts reaction is now extended to sulfinylation of electron-rich arenes with RS(O)OMe, to give ArS(O)R.[3]

Ene reaction. [*b*]Cyclopentanoindolines arise on treatment of 3-(3-alkenyl)indoles with $AlCl_3$.[4]



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Aluminum oxide.

Oxidative dimerization. γ-Alumina is a useful support for oxidants used in converting anilines into azoarenes or azoxyarenes, by the ball milling technique.[1]

[1]Thorwirth, R., Bernhardt, F., Stolle, A., Ondruschka, B., Asghari, J. *CEJ* **16**, 13236 (2010).

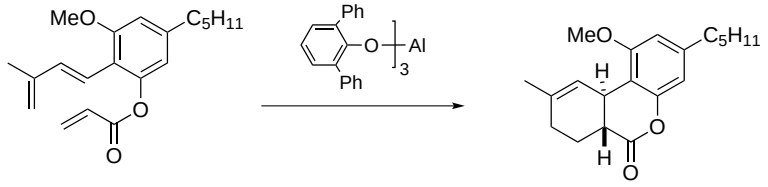
Aluminum triflate.

Bisannulation.[1] In a formal synthesis of (-)-haouamine A one of the critical steps is the elaboration of an indanopiperidine by a tandem Prins reaction and Friedel-Crafts cyclization, which is achievable with $Al(OTf)_3$ in $MeNO_2$.

[1]Fenster, E., Fehl, C., Aube, J. *OL* **13**, 2614 (2011).

Aluminum tris(2,6-diphenylphenoxide), ATPH.

Cycloaddition.[1] A highly stereoselective intramolecular Diels-Alder reaction is induced to provide an intermediate of Δ^1-tetrahydrocannabinol, using ATPH as catalyst.

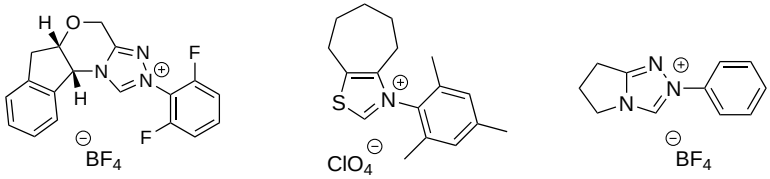


[1]Pearson, E.L., Kanizaj, N., Willis, A.C., Paddon-Row, M.N., Sherburn, M.S. *CEJ* **16**, 8280 (2010).

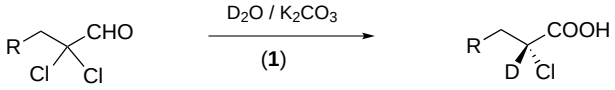
Aminocarbenes.

Modification. 4-Functionalized 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene species are synthesized from the parent carbene on reaction with electrophiles and subsequent treatment with $KN(SiMe_3)_2$.[1]

2-Deutero-2-haloalkanoic acids. The carbene derived from **1** effects transformation of 2,2-dichloro aldehydes and 2-fluoro-2-alkenals into chiral 2-deutero-2-haloalkanoic acids.[2] Heavy water is the source of deuterium.



(**1**) (**2**) (**3**)



Transforming ArCHO into acylators. Formation of aryl ketones is observed on mixing ArCHO and activated RBr with **2** and Cs_2CO_3 at room temperature.[3] The carbene from 1,3-dibenzylbenzimidazolium chloride exposes the acyl anion property of cinnamaldehyde and the reaction with *N*-tosylaziridines leads to CC bond formation and CN bond cleavage.[4] The umpolung alkylation method is applicable to the preparation of 1,3-diaryl-1,3-propanediones from ArCHO and $Ar'COCH_2X$.[5]

The bicyclic triazolium salt **3** forms a carbene which is capable of promoting cyclization of 2-cyanomethoxybenzaldehyde and congeners to give 3-aminochromen-4-ones.[6]

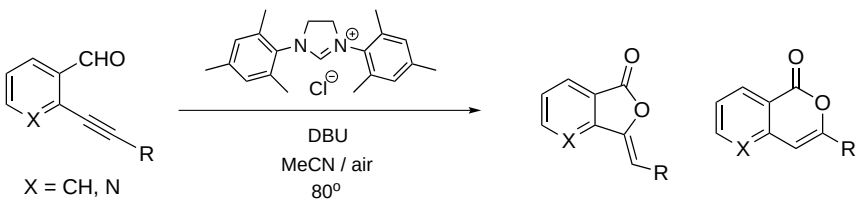
Aldehydes behave as acylating agents for alcohols in the presence of an *N*-heterocyclic carbene under oxidative conditions.[7] However, no amides are formed when the alcohols are replaced by amines.

Lactone formation is also accomplishable by this approach.[8] Several oxidants can be employed in this oxidative esterification process, e.g., the effectiveness of Fe(III) species appear to be quite effective in the preparation of aryl carboxylates.[9] In the air benzyl and cinnamyl esters are readily formed from mixtures of RCHO and benzyl and cinnamyl bromides,[10] perhaps by involving in situ hydrolysis of the activated bromides.

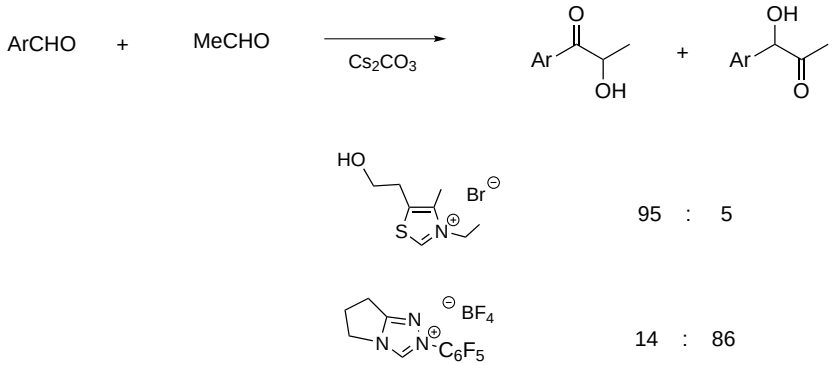
Addition reactions. Under the influence of an *N*-heterocyclic carbene $Me_3SiSnBu_3$ adds to RCHO to afford $Me_3SiOCHR(SnBu_3)$. Conjugated aldehydes undergo 1,4-additions under such conditions.[11] 1,3-Dimesitylimidazol-2-ylene is shown to promote aldol-type reaction between 2-trimethylsiloxyfuran and aldehydes, to afford as major products the *anti*-4-(α-hydroxyalkyl)-2-butenolides.[12]

A procedure for conjugate addition of alcohols has also been developed.[13] Certain cyclopropenes are receptive to ArCHO, therefore a novel route to aryl cyclopropyl ketones is based on the carbene-catalyzed addition.[14] By the same token, aldehydes (and enals) add to benzynes.[15,16]

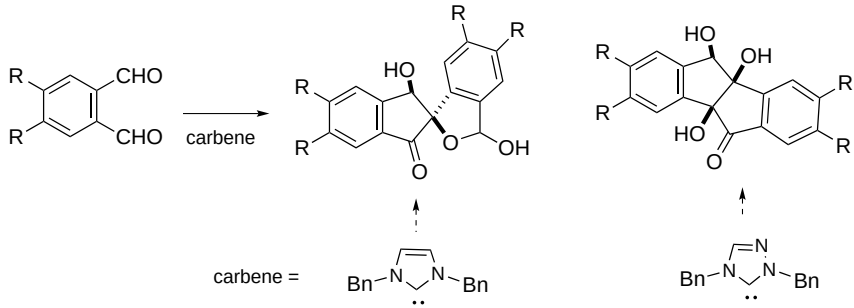
An intramolecular hydrocarboxylation occurs when 2-alkynylbenzaldehydes are heated with 1,3-dimesitylimidazol-2-ylene.[17]



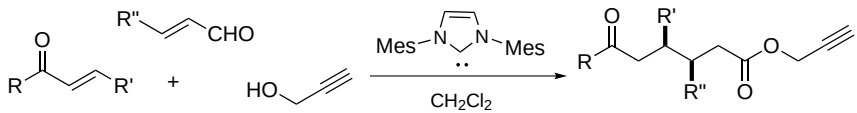
Benzoin condensation. Selective cross-condensation of ArCHO and RCHO has been accomplished (**3** and Rb_2CO_3 in THF) yielding mainly α-ketols in which the hydroxyl group is benzylic.[18] By changing the carbene a regiochemical reversal is realized.[19]



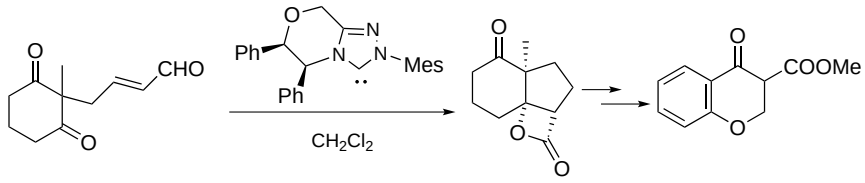
Phthaldehydes give dimeric products, and again the carbene catalyst is determinative of product structure.[20]



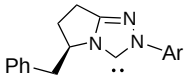
α-Keto esters and ArCHO also combine in a redox process to furnish α-aroyloxy esters.[21] More useful reactions are those involving (1) salicylaldehydes and enals to assemble 3-substituted coumarins[22] and (2) enones, enals and propargyl alcohol, leading to the formation of propargyl 6-oxoalkanoates.[23]



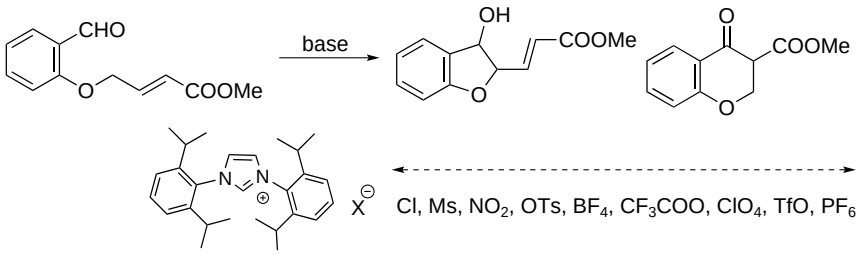
Still more intriguing is the condensation of enones with enals that forms β-lactones fused to a cyclopentane ring (cyclopentenes are often the isolated products).[24,25] Intramolecular reaction occurs between ketone and enal when both functions are present.[26]



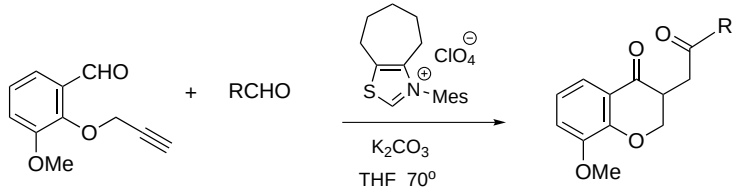
Stetter and Michael reactions. Carbene **4** is capable of inducing an intramolecular Stetter reaction resulting in chiral products.[27] The counterions of the imidazolium salt precursors play a role in the course of the reaction, i.e., to favor Stetter reaction or vinylogous aldol reaction.[28]



(**4**)



2-Propargyloxybenzaldehyde and congeners undergo condensation with RCHO to afford diketones.[29] It appears that adduct formation precedes cyclization.

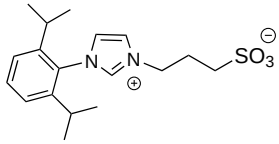


It is also possible to perform benzoin condensation of ArCHO then a Stetter reaction with Ar′CH=CHCHO to follow. An internal imidazolium salt **5** is a useful precursor of the carbene catalyst.[30]

Michael reaction catalyzed by carbene species proceed under mild conditions.[31] A synthesis of 5-acyl-2,3-dihydro-2-pyrones from β-dicarbonyl compounds and enals is

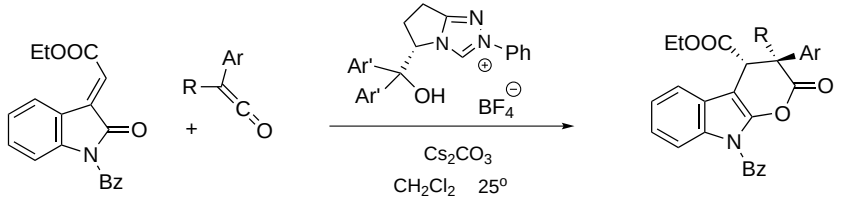
conducted in the presence of an oxidant.[32] Evidently, no oxidant is required when the enals are replaced with 2-alkynals.[33]

Cyclization of a methyl 3-(1-cyclopentenylcarboxy)-2-propenoate involves an intramolecular Michael reaction. The product is suitable for elaboration of 7-deoxyloganin.[34]



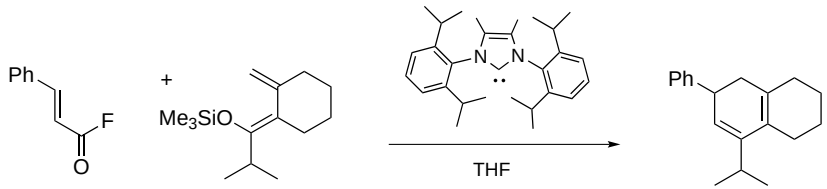
(**5**)

Cycloaddition reactions. The employment of these carbenes for promoting cycloadditions has met with different degrees of success. β-Lactones spiroannulated to an oxindole nucleus are formed from aryl ketenes and isatins.[35] Such ketenes also add to *N*-tosylcarboxamides to afford oxazolin-4-ones; but a reliable synthesis of chiral products is elusive (by using a chiral carbene).[36] Ketenes act as dienophiles in a hetero-Diels-Alder reaction with 3-alkylideneoxindoles.[37]

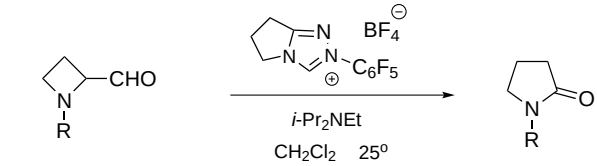


Ar' = 3,5-$(CF_3)_2C_6H_3$

The Diels-Alder reaction of 1-siloxy-1,3-dienes with 2-alkenoyl fluorides delivers 1,3-cyclohexadienes. In situ decarboxylation of the fused β-lactones results in such products.[38]



Rearrangement. Two types of molecular rearrangement reactions have been achieved by the agency of *N*-heterocyclic carbenes: mixed carbonates of enolized oxindoles to oxindole-3-carboxylic esters[39] and 2-formylazetidines and pyrrolidines to the ring-enlarged lactams.[40]



R = Bn, Boc, Ac, Ts

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