

TSE-LOK HO



Fiesers'
Reagents for
Organic Synthesis

VOLUME

28

WILEY

Reagents for Organic Synthesis

Fiesers'

Reagents for Organic Synthesis

VOLUME TWENTY EIGHT

Tse-Lok Ho

WILEY

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PREFACE

This volume covers progress of synthetic organic methodologies for the period between the second half of 2011 and the end of 2012, also a few items of yester-years. The major advances have been refinements of reagent applications and expansion of the scope. Although ligands still figure prominently in affecting reactivities of transition metal ions, work aiming at finding ligand-free reactions remains an honorable goal. Fruitful developments concerning oxidative coupling reactions that eschew halogen compounds are also in evidence. It is noted that burgeoning contributions to synthetic methodology are coming from Chinese chemists, perhaps reflecting societal changes from one of most populous nations. Or they are spiritually ingrained in the expostulation of the benevolent Han tribe leader, King Tang of the Shang Dynasty (商湯), who had a bath tub engraved to remind himself to refine his character while cleansing:

REINVIGORATE TODAY 苟日新
REINVIGORATE EVERY DAY 日日新

Doesn't this maxim somehow coincide with the effort of synthetic organic chemists?

GENERAL ABBREVIATIONS

<i>Ac</i>	acetyl
<i>acac</i>	acetylacetonate
<i>Ad</i>	1-adamantyl
<i>AIBN</i>	2,2'-azobisisobutyronitrile
<i>aq</i>	aqueous
<i>Ar</i>	aryl
<i>9-BBN</i>	9-borabicyclo[3.3.1]nonane
<i>BINAP</i>	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
<i>BINOL</i>	1,1'-binaphthalene-2,2'-diol
<i>Bn</i>	benzyl
<i>Boc</i>	<i>t</i> -butoxycarbonyl
<i>bpy</i>	2,2'-bipyridyl
<i>bpz</i>	2,2'-bipyrazine
<i>BQ</i>	1,4-benzoquinone
<i>Bs</i>	benzenesulfonyl
<i>Bu</i>	<i>n</i> -butyl
<i>Bz</i>	benzoyl
<i>18-c-6</i>	18-crown-6
<i>c-</i>	cyclo-
<i>CAN</i>	cerium(IV) ammonium nitrate
<i>cap</i>	caprolactamate
<i>Cbz</i>	benzyloxycarbonyl
<i>cod</i>	1,5-cyclooctadiene
<i>Cp</i>	cyclopentadienyl
<i>Cp*</i>	1,2,3,4,5-pentamethylcyclopentadienyl
<i>CSA</i>	10-camphorsulfonic acid
<i>Cy</i>	cyclohexyl
<i>DABCO</i>	1,4-diazabicyclo[2.2.2]octane
<i>DAST</i>	(diethylamino)sulfur trifluoride
<i>dba</i>	dibenzylideneacetone
<i>DBN</i>	1,5-diazabicyclo[4.3.0]non-5-ene
<i>DBU</i>	1,8-diazabicyclo[5.4.0]undec-7-ene
<i>DCC</i>	1,3-dicyclohexylcarbodiimide
<i>DDQ</i>	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
<i>DEAD</i>	diethyl azodicarboxylate

<i>DIAD</i>	diisopropyl azodicarboxylate
<i>Dibal-H</i>	diisobutylaluminum hydride
<i>DMA</i>	<i>N,N</i> -dimethylacetamide
<i>DMAP</i>	4-dimethylaminopyridine
<i>DMDO</i>	dimethyldioxirane
<i>DME</i>	1,2-dimethoxyethane
<i>DMF</i>	<i>N,N</i> -dimethylformamide
<i>DMPU</i>	<i>N,N'</i> -dimethylpropyleneurea
<i>DMSO</i>	dimethyl sulfoxide
<i>DPM</i>	dipivaloylmethane
<i>DPPB</i>	1,4-bis(diphenylphosphino)butane
<i>DPPE</i>	1,2-bis(diphenylphosphino)ethane
<i>DPPEF</i>	1,1'-bis(diphenylphosphino)ferrocene
<i>DPPP</i>	1,3-bis(diphenylphosphino)propane
<i>DTTB</i>	4,4'-di- <i>t</i> -butylbiphenyl
<i>ee</i>	enantiomer excess
<i>Et</i>	ethyl
<i>Fc</i>	ferrocenyl
<i>Fmoc</i>	9-fluorenylmethoxycarbonyl
<i>Fu</i>	2-furyl
<i>HMDS</i>	hexamethyldisilazane
<i>HMPA</i>	hexamethylphosphoric amide
<i>Hx</i>	<i>n</i> -hexyl
<i>L</i>	ligand
<i>LAH</i>	lithium aluminum hydride
<i>LDA</i>	lithium diisopropylamide
<i>LHMDS</i>	lithium hexamethyldisilazide
<i>LiDBB</i>	lithium 4,4'-di- <i>t</i> -butylbiphenylide
<i>LTMP</i>	lithium, 2,2,6,6-tetramethylpiperidide
<i>LN</i>	lithium naphthalenede
<i>MCPBA</i>	<i>m</i> -chloroperbenzoic acid
<i>Me</i>	methyl
<i>MEM</i>	methoxyethoxymethyl
<i>Mes</i>	mesityl
<i>MOM</i>	methoxymethyl
<i>Ms</i>	methanesulfonyl
<i>MS</i>	molecular sieve
<i>MTO</i>	methyltrioxorhenium
<i>NBS</i>	<i>N</i> -bromosuccinimide
<i>NCS</i>	<i>N</i> -chlorosuccinimide
<i>NIS</i>	<i>N</i> -iodosuccinimide

<i>NMO</i>	<i>N</i> -methylmorpholine <i>N</i> -oxide
<i>NMP</i>	<i>N</i> -methylpyrrolidone
<i>Np</i>	naphthyl
<i>Ns</i>	<i>p</i> -nitrobenzenesulfonyl
<i>Nu</i>	nucleophile
<i>Oc</i>	<i>n</i> -octyl
<i>PEG</i>	poly(ethylene glycol)
<i>Ph</i>	phenyl
<i>Phen</i>	1,10-phenanthroline
<i>Phl</i>	phthaloyl
<i>Pin</i>	pinacolato
<i>Piv</i>	pivaloyl
<i>PMB</i>	<i>p</i> -methoxybenzyl
<i>PMHS</i>	poly(methylhydrosiloxane)
<i>PMP</i>	<i>p</i> -methoxyphenyl
<i>Pr</i>	<i>n</i> -propyl
<i>Py</i>	pyridine
<i>RaNi</i>	Raney nickel
<i>RCM</i>	ring-closing metathesis
<i>R^F</i>	perfluoroalkyl
<i>ROMP</i>	ring opening metathesis polymerization
<i>s-</i>	secondary
<i>salen</i>	<i>N,N'</i> -ethenebis(salicylideneiminato)
<i>SAMP</i>	(<i>S</i>)-1-amino-2-methoxymethylpyrrolidine
<i>SEM</i>	2-(trimethylsilyl)ethoxymethyl
<i>SES</i>	2-[(trimethylsilyl)ethyl]sulfonyl
<i>TBAF</i>	tetrabutylammonium fluoride
<i>TBDPS</i>	<i>t</i> -butyldiphenylsilyl
<i>TBS</i>	<i>t</i> -butyldimethylsilyl
<i>TEMPO</i>	2,2,6,6-tetramethylpiperidinoxyl
<i>TES</i>	triethylsilyl
<i>Tf</i>	trifluoromethanesulfonyl
<i>TFA</i>	trifluoroacetic acid
<i>TFAA</i>	trifluoroacetic anhydride
<i>THF</i>	tetrahydrofuran
<i>THP</i>	tetrahydropyran
<i>TIPS</i>	triisopropylsilyl
<i>TMEDA</i>	<i>N,N,N',N'</i> -tetramethylethanediamine
<i>TMS</i>	trimethylsilyl
<i>Tol</i>	<i>p</i> -tolyl
<i>tpP</i>	tetraphenylporphyrin

<i>Ts</i>	<i>p</i> -toluenesulfonyl
<i>TSE</i>	2-(trimethylsilyl)ethyl
<i>Z</i>	benzyloxycarbonyl
Δ	heat
))))	ultrasound

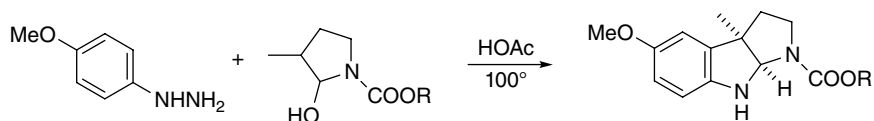
REFERENCE ABBREVIATIONS

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

A

Acetic acid

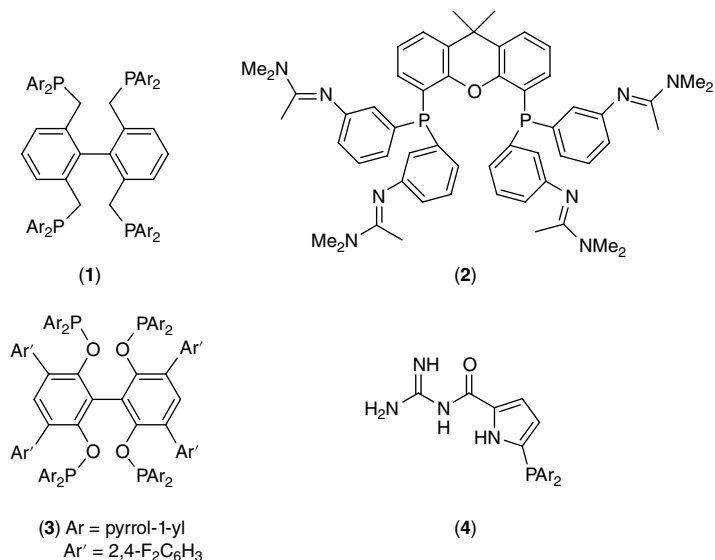
Fischer indole synthesis. The pyrroloindole ring system characterized of the physostigmine alkaloids is formed in the interrupted indolization between an arylhydrazine and *N*-protected 2-hydroxy-3-methylpyrrolidine, and it is accomplished in hot HOAc.¹



¹ Schammel, A.W., Chiou, G., Garg, N.K. *JOC* **77**, 725 (2012)

Acetylacetonato(dicarbonyl)rhodium(I)

Addition. With ligand **1** hydroformylation of 2-alkenes catalyzed by (acac)Rh(CO)₂ proceeds via a double bond shift.¹ In the presence of an amine the reaction becomes a hydroamination process (amino group introduced at the carbon chain terminus).²

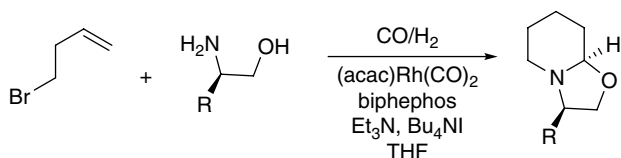


2 Acetyl bromide

Ligand **2** is for linear hydroformylation of 1-alkenes, in which the amidate groups bring the catalyst into the aqueous phase as the bicarbonate salt is formed.³ Developed for highly linear hydroformylation of 1-alkenes, including allyl cyanides, is a ligand series represented by **3**.⁴

When ligands such as **4** for the Rh catalyst are used the aldehyde products undergo reduction to yield primary alcohols.⁵ Simpler ligands such as $(4\text{-FC}_6\text{H}_4)_3\text{P}$ can be used in the hydroacylation of enamides to form 1,4-dicarbonyl compounds.⁶

Homoallylic alcohols form 5-membered cyclic products even if the new CC bond formation is with the internal sp^2 -carbon atom.⁷ Double trapping of the homologous aldehyde derived from 4-bromo-1-butene with 2-phenyl-2-aminoethanol leads to a bicyclic heterocycle which is amenable to substitution at the α -carbon to the nitrogen atom.⁸



Under normal hydroformylation condition but with addition of a secondary amine and 2,2',6,6'-tetrakis(diphenylphosphinomethyl)biphenyl to the reaction mixture, Schiff bases are formed and then reduced.⁹

Decarbonylation. The removal of CO from 2-(2-acylaryl)pyridines by heating with (acac)Rh(CO)₂ is of synthetic interests because the ketone substrates are generally more readily accessible.¹⁰

¹ Cai, C., Yu, S., Liu, G., Zhang, X., Zhang, X. *ASC* **353**, 2665 (2011)

² Liu, G., Huang, K., Cao, B., Chang, M., Li, S., Yu, S., Zhou, L., Wu, W., Zhang, X. *OL* **14**, 102 (2012)

³ Mokhadinyana, M., Desset, S.L., Williams, D.B.G., Cole-Hamilton, D.J. *ACIE* **51**, 1648 (2012)

⁴ Cai, C., Yu, S., Cao, B., Zhang, X. *CEJ* **18**, 9992 (2012)

⁵ Fuchs, D., Rousseau, G., Diab, L., Gellrich, U., Breit, B. *ACIE* **51**, 2178 (2012)

⁶ Zhang, H.-J., Bolm, C. *OL* **13**, 3900 (2011)

⁷ Ueki, Y., Ito, H., Usui, I., Breit, B. *CEJ* **17**, 8555 (2011)

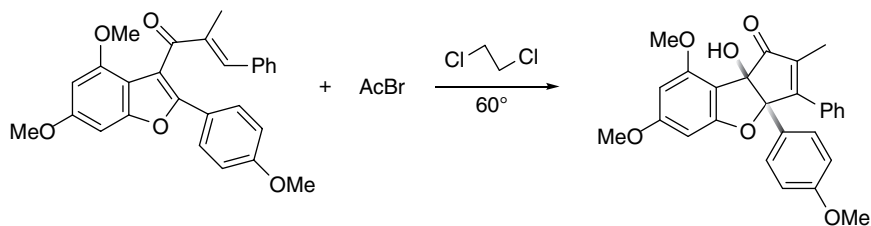
⁸ Zill, N., Schoenfelder, A., Girard, N., Taddei, M., Mann, A. *JOC* **77**, 2246 (2012)

⁹ Liu, G., Huang, K., Cai, C., Cao, B., Chang, M., Wu, W., Zhang, X. *CEJ* **17**, 14559 (2011)

¹⁰ Lei, Z.-Q., Li, H., Li, Y., Zhang, X.-S., Chen, K., Wang, X., Sun, J., Shi, Z.-J. *ACIE* **51**, 2690 (2012)

Acetyl bromide

Nazarov cyclization. Cross-conjugated ketones in which one of the double bonds belongs to a benzofuran nucleus undergo Nazarov cyclization.¹ Enolacetylation to create a highly electrophilic moiety for the reaction to proceed is most likely.



¹Magnus, P., Freund, W.A., Moorhead, E.J., Rainey, T. *JACS* **134**, 6140 (2012)

1-Acyl-1,5-diazabicyclo[4.3.0]non-5-ene tetraphenylborates

O-Acylation. These reagents are excellent acyl donors to OH-compounds.¹

¹Taylor, J.E., Williams, J.M.J., Bull, S.D. *TL* **53**, 4074 (2012)

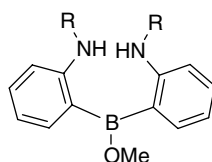
1-Acylpyrazoles

Acylation. A review of the acylating capability of 1-acylpyrazoles has been published.¹

¹Goldys, A.M., McErlean, C.S.P. *EJOC* 1877 (2012)

Alkoxybis(2,2'-aminomethylphenyl)boranes

Alcoholysis. Alkoxyboranes **1** are useful catalysts for cleavage of 1,3-dicarbonyl compounds such as β -keto esters and *N*-acylamides by alcohols under essentially neutral conditions. These boranes perform activation on both reactants.¹



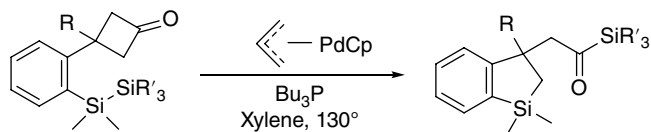
(1) R = Me, Cy

¹Oishi, S., Saito, S. *ACIE* **51**, 5395 (2012)

η^3 -Allyl(cyclopentadienyl)palladium

Cyclomutation.¹ Cleavage of the small ring of 3-arylcyclobutanones that is *o*-substituted by a heteroatom group such as disilane is attended by heterocyclization.

4 Aluminum chloride



Decarboxylation. Benzyl cyanoacetates extrude CO_2 while the remaining parts recombine to afford 3-arylpentanitriles. In the case of 2-furylmethyl cyanoacetates the choice of the phosphine ligand affects the recombination step. It can be coaxed toward formation of 2-cyanomethyl-5-methylfurans.²

¹Ishida, N., Ikemoto, W., Murakami, M. *OL* **14**, 3230 (2012)

²Recio III, A., Heinzman, J.D., Tunge, J.A. *CC* **48**, 142 (2012)

η^3 -Allylpalladium molybdosulfide

Allylation.¹ In the presence of $(\eta^3\text{-C}_3\text{H}_5)\text{Pd}(\text{S}_4\text{Mo}_3)$ the allylation of arylamines can use allyl alcohol. The allyl group is to be attached to C-3 of an indole nucleus.

¹Tao, Y., Wang, B., Zhao, J., Song, Y., Qu, L., Qu, J. *JOC* **77**, 2942 (2012)

Aluminum chloride

Group migration. On treatment with AlCl_3 , the protecting group of *N*-mesylindeles migrates to C-7.¹



Mannich reaction.² Condensation of ArCHO , MeCN and MeCOAr' to afford $\text{ArCH}(\text{NHAc})\text{CH}_2\text{COAr}'$ is observed on treatment with AlCl_3 and AcCl . β -Keto esters undergo a similar reaction.

Cyclization. γ,δ -Unsaturated ketones cyclize to form a benzene ring in the presence of AlCl_3 in dioxane.³

Ether cleavage.⁴ Ethers are split by silyldealkylation of ethers using R_3SiCl , with AlCl_3 or FeCl_3 or BiCl_3 as promoter. The other products are RCl .

¹Prasad, B., Adepu, R., Sandra, S., Rambabu, D., Krishna, G.R., Reddy, C.M., Deora, G.S., Misra, P., Pal, M. *CC* **48**, 10434 (2012)

²Ali, Z.M., Ardeshir, K., Mohammad, M., Abdolkarim, Z., Maliheh, S., Fatemeh, D.-P., Hassan, K., Ahmad, A.D.-F., Maria, M. *ChJC* **30**, 345 (2012)

³Narender, T., Sarkar, S., Rajendar, K., Tiwari, S. *OL* **13**, 6140 (2011)

⁴Wakabayashi, R., Sugiura, Y., Shibue, T., Kuroda, K. *ACIE* **50**, 10708 (2011)

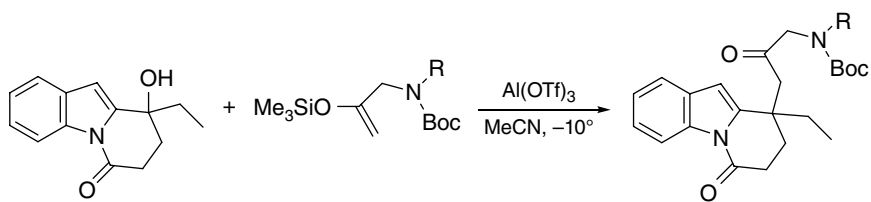
Aluminum fluoride

CH activation. High-surface AlF_3 is able to activate aliphatic C-H bond under very mild conditions (at 40°), and this property can be exploited by deuteration.¹

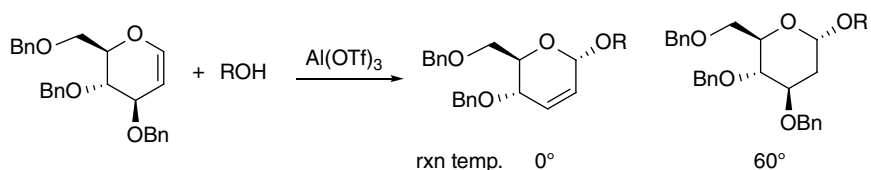
¹Prechtl, M.H.G., Teltewskoi, M., Dimitrov, A., Kemnitz, E., Braun, T. *CEJ* **17**, 14385 (2011)

Aluminum triflate

Substitution. Benzyl and cinnamyl alcohols are easily converted into the corresponding amines with the aid of $\text{Al}(\text{OTf})_3$.¹ Substitution using other nucleophiles are equally smooth, as exemplified in the construction of an intermediate for a synthesis of mersicarpine.²



The reaction of tri-*O*-benzylglucal with an alcohol on catalysis by $\text{Al}(\text{OTf})_3$ temperature can change the reaction mechanism.³ At 0° Ferrier rearrangement products are formed but at 60° addition to the double bond is favored.



¹Ohshima, T., Ipposhi, J., Nakahara, Y., Shibuya, R., Mashima, K. *ASC* **354**, 2447 (2012)

²Zhong, X., Li, Y., Han, F.-S. *CEJ* **18**, 9784 (2012)

³Williams, D.B.G., Simelane, S.B., Kinfie, H.H. *OBC* **10**, 5636 (2012)

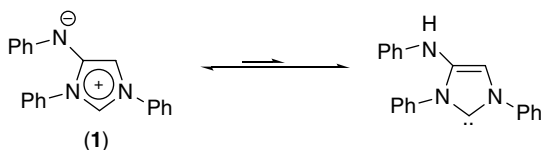
Aluminum tris(2,6-di- β -naphthoxide)

Vinylogous aldol reaction.¹ The title reagent is a more bulky analog of ATPH and perhaps more sensitive to steric effects. Its application as catalyst in site-selective condensation such as reaction between crotonic esters and aldehydes to form 5-hydroxy-2-alkenoates has been demonstrated.

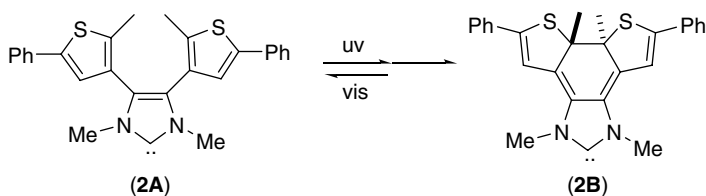
¹Gazaille, J.A., Sammakia, T. *OL* **14**, 2678 (2012)

Aminocarbenes

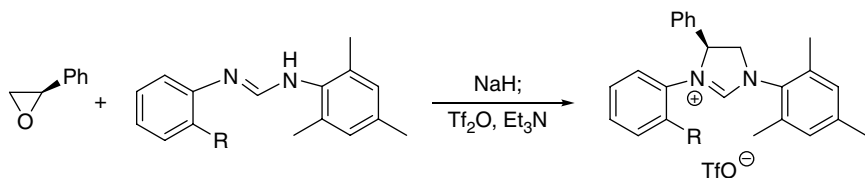
Structural variations. The commercially available mesionic “Nitron” has an *N*-heterocyclic carbene (NHC) tautomer, but its application in directing reactions has yet to be explored.¹ Electron properties and stability of imidazole-based mesionic carbenes (imidazol-5-ylidenes) are found to be inversely correlated.²



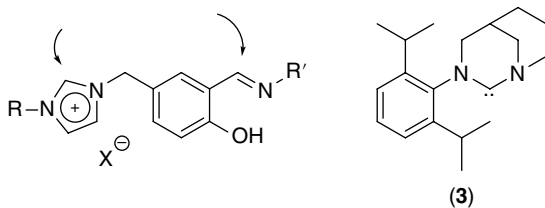
Imidazolium and imidazolium bicarbonate salts are air-stable precursors of NHC’s.³ 1,3-Bis(2,6-dimethoxyphenyl)imidazol-2-ylidene is a typical electron-rich carbene.⁴ A photoswitchable NHC pair is **2A** and **2B**, interconverted by uv and visible lights.⁵



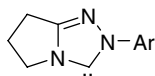
A convenient method for synthesis of chiral imidazolium salts, precursors of NHC’s, is based on reaction of *N,N*-disubstituted amidines and chiral oxiranes.⁶



Imidazolium salts that bear an *N*-substituent extended to a salicyldiminato function are versatile precursors of multipurpose and tunable catalysts. Two sites for metal bonding are obvious.⁷ A new type of the carbene is represented by **3** which in placing one of the nitrogen atoms at a bridgehead prevents its lone pair electrons to delocalize and therefore increases the electrophilicity of the carbene center while keeping nucleophilicity the same.⁸



Reduction. Transfer reduction of carbonyl compounds by *i*-PrOH is effected with 1,3-diarylimidazolium tetrafluoroborate (each aryl group being 4-substituted) and KOH.⁹ Ketones and imines are reduced via hydrosilylation, with **4A** as catalyst.¹⁰ By this procedure the multiple bond of propargylic alcohols and cinnamyl alcohols are reduced, the former class of compounds to be converted into allylic alcohols.¹¹



(**4A**) Ar = Ph

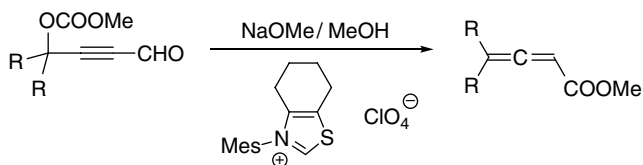
(**4B**) Ar = Mes

(**4C**) Ar = C₆F₅

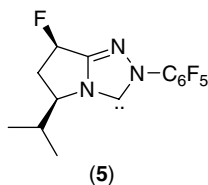
Formation of 3-acyloxy-2-indolinones from isatins and aldehydes is achieved by heating with **4B** and *t*-BuOK in toluene.¹² The aldehydes become the acyl moiety. The effect of **4B** on tri-*O*-benzylfuranoses such as the ribose derivative is that debenzoyloxyl-ation occurs at C-2 while oxidation to the γ -lactones is the complementary reaction.¹³

Oxidative functionalization of aldehydes. The most extensive uses of NHC's appear to involve transformation of aldehydes. For example, under oxygen aldehydes and alkyl halides form esters under the influence of the ylide (carbene) derived from 3,4-dimethylthiazole iodide.¹⁴ Type **4** NHC unites aldehydes and thiols to give thioesters,¹⁵ and carboxylic acids are obtained when **4C** exerts its effect.¹⁶ Aldehydes and ArB(OH)₂ also combine to yield aryl esters,¹⁷ otherwise anodic oxidation of aldehydes in alcohols to furnish esters is catalyzed by a thiazole carbene.¹⁸

α -Halocinnamaldehydes lose the halogen substituent during conversion to the cinnamic esters,¹⁹ and an intramolecular redox transformation of 2-alkynals with a carbonato substituent at C-4 leads to 2,3-alkadienoic esters.²⁰

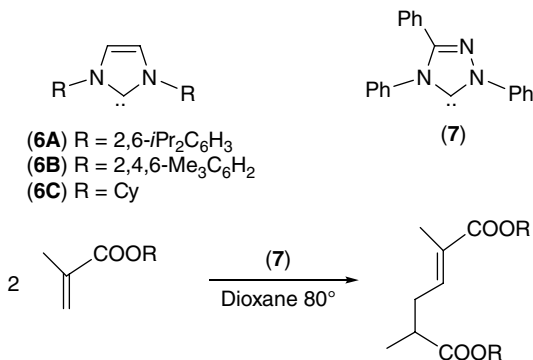


Addition. α -Cyanohydrin ester formation²¹ from aldehydes on NHC-catalyzed reaction with acetyl cyanide or ethyl cyanofornate is somewhat unusual. The fluorinated carbene **5** is useful for promoting hydroacylation of cinnamic esters by aldehydes.²²



Perhaps the perennial favorite among NHC's, **6A** (often called IPr), helps the union of dimethylamine and CO to form DMF.²³ Actually a general procedure for formylation of amines is that involving a polysiloxane.²⁴

The triazole-based carbene **7** can cause tail-to-tail dimerization of methacrylic esters²⁵ because it confers the β -carbon of the ester with anionic properties.²⁶

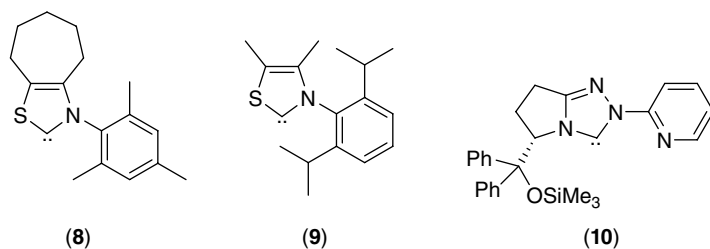


Conjugate addition of aldehydes to vinyl sulfones is akin to the Stetter reaction. A bicyclic thiazole carbene **8** is an active catalyst.²⁷ However, a carbene can transform α -bromo enals into acylate azolium salts which act as Michael acceptors for β -keto esters.²⁸

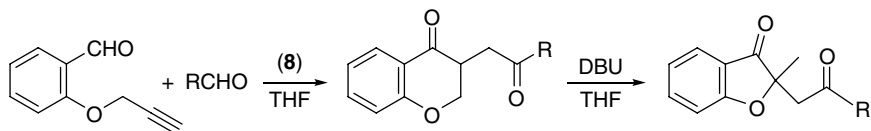
Stable esters can be activated by carbenes to form enolates (not involving ketene intermediates), as shown by a synthesis of 3,4-dihydropyridones from reaction with conjugated imines.²⁹

In conjunction with metallic catalysts that fashion and combine a 2-diazo-1,3-diketone and a functionalized alkene ready for Michael addition, an NHC effectively completes the final step leading to a spirolactone or lactam.³⁰

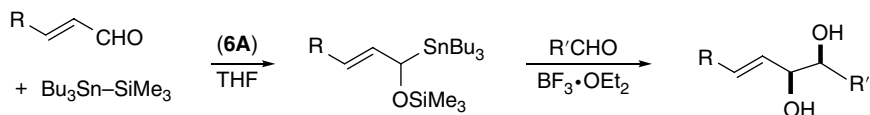
Benzoin condensation and related reactions. Cross-benzoin condensation using **9** which is generated in situ also from a perchlorate salt is successful.³¹ As for asymmetric benzoin condensation, **10** has been developed.³²



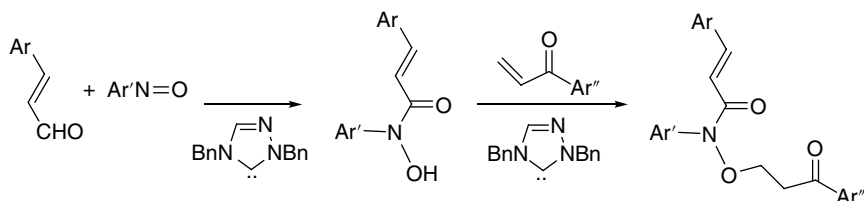
It is quite remarkable that two research groups reported at about the same time the same kind of transformation using the same bicyclic thiazole carbene **8**.^{33,34}



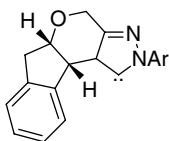
Conjugated aldehydes form 1-tributylstannyl-1-trimethylsiloxy-2-alkenes in a carbene-mediated reaction. The adducts are useful for synthesis of unsaturated diols by further reaction with R'CHO in the presence of $\text{BF}_3 \cdot \text{OEt}_2$.³⁵



N-(2-Aroylolethoxyl) cinnamides are assembled from cinnamaldehydes, nitrosoarenes and aryl vinyl ketones. The first step which forms the hydroxamic acids can be considered as an aza-benzoin condensation.³⁶

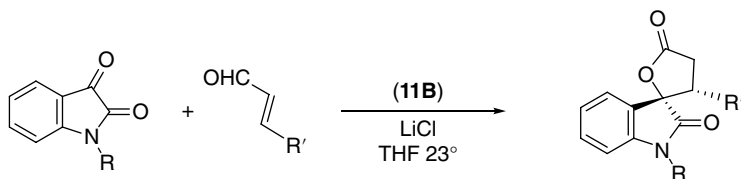
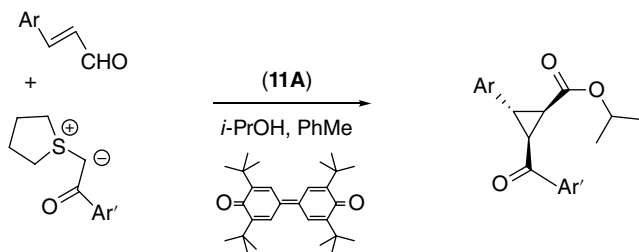


Annulation. The sulfur ylide reaction with electron-deficient alkenes to form cyclopropane derivatives as applied to conjugated aldehydes can give ester products by intervention of carbene **11A**.³⁷ In the case of spirallactonization of isatin a conjugated aldehyde is transformed into an equivalent of a chiral carboxylic acid β -anion by *ent*-**11B**.³⁸ Oxindole-3-imines form spirolactams on reaction with conjugated aldehydes.³⁹

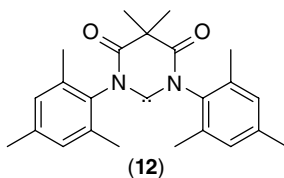


(**11A**) Ar = Mes

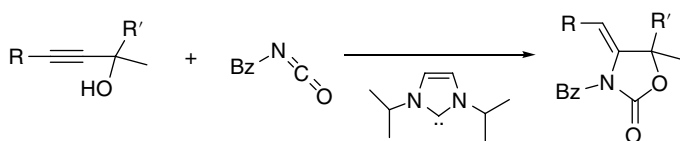
(**11B**) Ar = 2,6-Et₂C₆H₃



Total consumption of **12** on reaction with alkynes is as expected, adducts of which afford cyclopropenones on hydrolysis.⁴⁰ Nitriles also undergo cycloaddition with **12**.



Along with a Lewis acid, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene **6A** or its dihydro derivative is capable of mediating insertion of CO₂ into oxiranes to yield dioxolan-2-ones.⁴¹ A similar transformation is the formation of 4-alkylidene-oxazolidin-2-ones where a carbene serves as a Brønsted base.⁴²

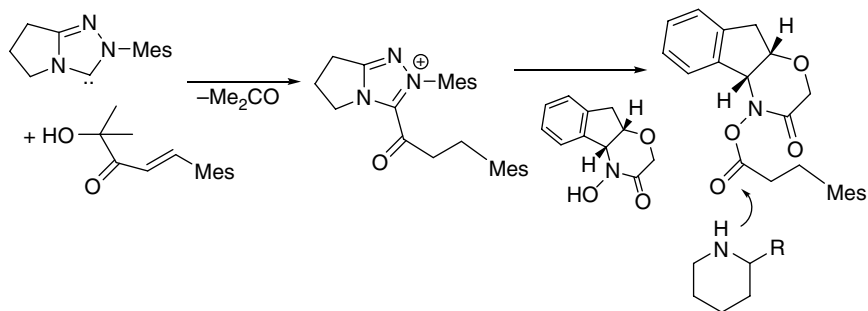


NHC's help unfold the nucleophilicity of saturated aldehydes, as seen in the facile assemblage of 3,4-dihydro-2-pyrones and 2-pyridones.⁴³ A formal [3+2]cycloaddition between conjugated aldehydes and isatin imines leads to spiroannulated oxindoles, with the formyl group being converted into a lactamic carbonyl by intervention of **6B**.⁴⁴

Decomposition of the Diels-Alder adduct of 1-trimethylsiloxy-1,3-butadiene and acrylyl fluoride to afford 1,3-cyclohexadiene is a favorable reaction, in which Me₃SiF and CO₂ are eliminated.⁴⁵ The role of carbene for the two-step process is not clear.

A theoretical study (DFT calculation) indicates the cocatalytic NHC and Ti(OR)₄ to develop *cis*-3,4-disubstituted cyclopentenes is due to involvement of a chelated intermediate.⁴⁶

Kinetic resolution. 2-Substituted cyclic amines are resolved via *N*-acylation. The acylating agent is derived from a chiral *O*-acylhydroxamate.⁴⁷



¹Färber, C., Leibold, M., Bruhn, C., Maurer, M., Siemeling, U. *CC* **48**, 227 (2012)

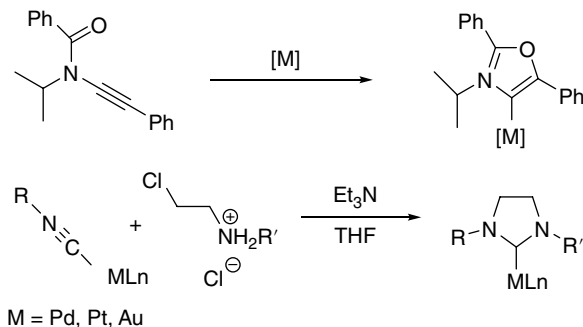
²Ung, G., Bertrand, G. *CEJ* **17**, 8269 (2011)

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- ¹³ Wendeborn, S., Mondière, R., Keller, I., Nussbaumer, H. *SL* 541 (2012)
- ¹⁴ Li, Y., Du, W., Deng, Q.-P. *T* **68**, 3611 (2012)
- ¹⁵ Uno, T., Inokuma, T., Takemoto, Y. *CC* **48**, 1901 (2012)
- ¹⁶ Kuwano, S., Harada, S., Oriez, R., Yamada, K. *CC* **48**, 145 (2012)
- ¹⁷ Meng, J.-J., Gao, M., Wei, Y.-P., Zhang, W.-Q. *CAJ* **7**, 872 (2012)
- ¹⁸ Finney, E.E., Ogawa, K.A., Boydston, A.J. *JACS* **134**, 12374 (2012)
- ¹⁹ Wang, X.-B., Zou, X.-L., Du, G.-F., Liu, Z.-Y., Dai, B. *T* **68**, 6498 (2012)
- ²⁰ Zhao, Y.-M., Tam, Y., Wang, Y.-J., Li, Z., Sun, J. *OL* **14**, 1398 (2012)
- ²¹ Zhang, J., Du, G.F., Xu, Y.K., He, L., Dai, B. *TL* **52**, 7153 (2011)
- ²² Sanchez-Larios, E., Thai, K., Bilodeau, F., Gravel, M. *OL* **13**, 4942 (2011)
- ²³ Li, X., Liu, K., Xu, X., Ma, L., Wang, H., Jiang, D., Zhang, Q., Lu, C. *CC* **47**, 7860 (2011)
- ²⁴ Jacquet, O., Gomes, C.D.N., Ephritikhine, M., Cantat, T. *JACS* **134**, 2934 (2012)
- ²⁵ Biju, A.T., Padmanaban, M., Wurz, N.E., Glorius, F. *ACIE* **50**, 8412 (2011)
- ²⁶ Matsuoka, S., Ota, Y., Washio, A., Katada, A., Ichioka, K., Takagi, K., Suzuki, M. *OL* **13**, 3722 (2011)
- ²⁷ Bhunia, A., Yetra, S.R., Bhojgude, S.S., Biju, A.T. *OL* **14**, 2830 (2012)
- ²⁸ Yao, C., Wang, D., Lu, J., Li, T., Jiao, W., Yu, C. *CEJ* **18**, 1914 (2012)
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- ³¹ Piel, I., Pawelczyk, M.D., Hirano, K., Fröhlich, R., Glorius, F. *EJOC* 5475 (2011)
- ³² Soeta, T., Tabatake, Y., Inomata, K., Ukaji, Y. *T* **68**, 894 (2012)
- ³³ Padmanaban, M., Biju, A.T., Glorius, F. *OL* **13**, 5624 (2011)
- ³⁴ Franz, J.F., Fuchs, P.J.W., Zeitler, K. *TL* **52**, 6952 (2011)
- ³⁵ Blanc, R., Nava, P., Rajzman, M., Commeiras, L., Parrain, J.-L. *ASC* **354**, 2038 (2012)
- ³⁶ Sun, Z.-X., Cheng, Y. *EJOC* 4982 (2012)
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- ³⁸ Dugal-Tessier, J., O'Bryan, E.A., Schroeder, T.B.H., Cohen, D.T., Scheidt, K.A. *ACIE* **51**, 4963 (2012)
- ³⁹ Lv, H., Tiwari, B., Mo, J., Xing, C., Chi, Y.R. *OL* **14**, 5412 (2012)
- ⁴⁰ Moerdyk, J.P., Bielawski, C.W. *JACS* **134**, 6116 (2012)
- ⁴¹ Liu, X., Cao, C., Li, Y., Guan, P., Yang, L., Shi, Y. *SL* 1343 (2012)
- ⁴² Jo, K.A., Maheswara, M., Yoon, E., Lee, Y.Y., Yun, H., Kang, E.J. *JOC* **77**, 2924 (2012)
- ⁴³ Zhao, X., Ruhl, K.E., Rovis, J. *ACIE* **51**, 12330 (2012)
- ⁴⁴ Zhang, B., Feng, P., Sun, L.-H., Cui, Y., Ye, S., Jiao, N. *CEJ* **18**, 9198 (2012)
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- ⁴⁶ Domingo, L.R., Zaragoza, R.J., Arnó, M. *OBC* **9**, 6616 (2011)
- ⁴⁷ Binanzer, M., Hsieh, S.-Y., Bode, J.W. *JACS* **133**, 19698 (2011)

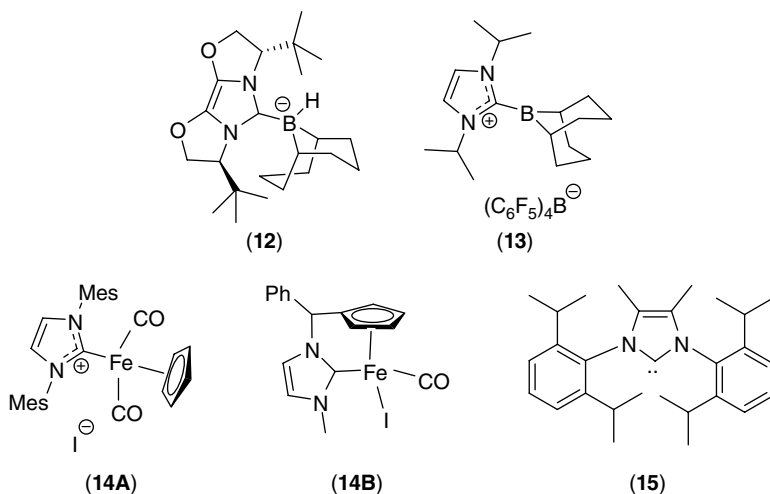
Aminocarbene - metal complexes

The more extensively employed metal-carbene complexes are grouped and discussed individually.

Preparation. Ynamides are useful precursors of unstable NHC's.¹

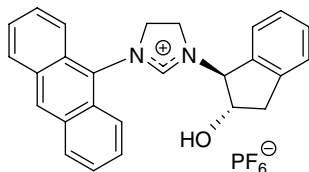


Reduction. Ligand exchange removes Me₂S from borane and the boron atom is linked to a carbene center, the resulting stable solid (to air, water and chromatography) retains power of reducing the carbonyl group with silica promotion.² One, two or all three hydrides is transferrable, and no quench or workup is needed. Furthermore, aldehydes can be reduced selectively in the presence of ketones. The use of a more complex entity **12** for asymmetric reduction also has been reported.³ The salt **13** is a catalyst for hydrogenation of imines and enamines,⁴ whereas the iron complex **14A** is active in hydrosilylation of imines under visible light.⁵ Complex **14B** is prepared from the imidazolium iodide with an N-substituent bearing a terminal cyclopentadiene unit and Fe₃(CO)₁₂, and it serves as a catalyst for sulfoxide reduction.⁶



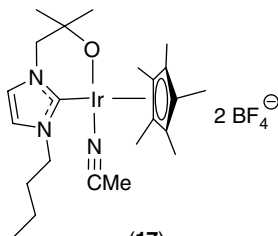
Catalyzing semihydrogenation of alkynes, allenes and dienes with hydrosilane assisted by the complex **15** is a pleasing discovery.⁷

Substitution. Regioselective S_N2' displacement of allyl phosphates with organoborates is achieved, using the unsymmetrical carbene complex generated from **16** and CuCl.⁸ For carboxylation of benzoxazole and benzothiazole the effectiveness of a 1,2,3-triazol-5-ylidene CuCl is recognized.⁹



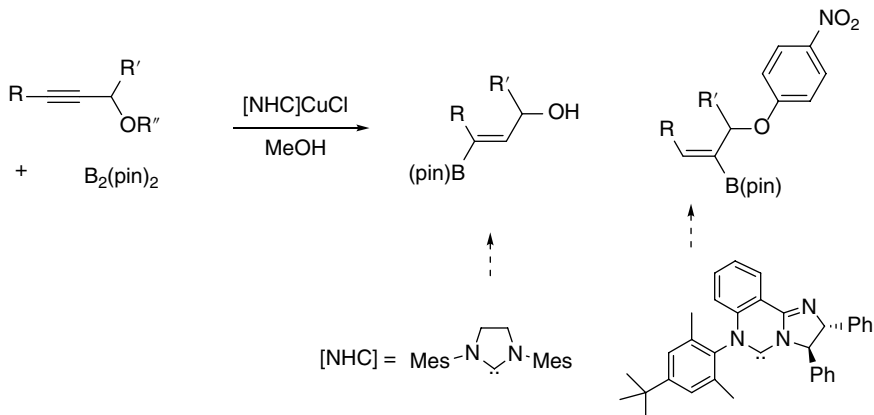
(16)

Primary alcohols are viable substrates for *N*-alkylation of amines, when the iridium complex **17** is present in the reaction media.¹⁰



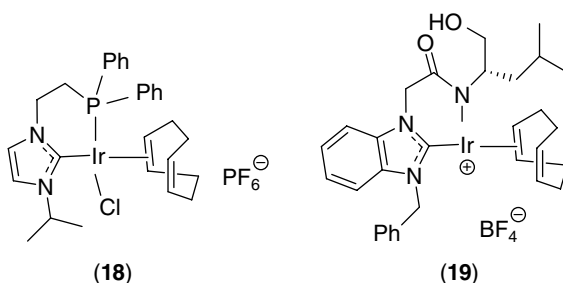
(17)

Addition. Hydroboration of propargylic alcohols with (bispinacolato)diboron places the boryl group at the carbon farther from the hydroxyl function, but that of their *p*-nitrophenyl ethers shows an opposite regioselectivity, although different Cu-carbenoids are involved.¹¹

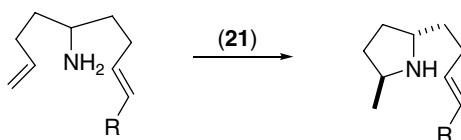
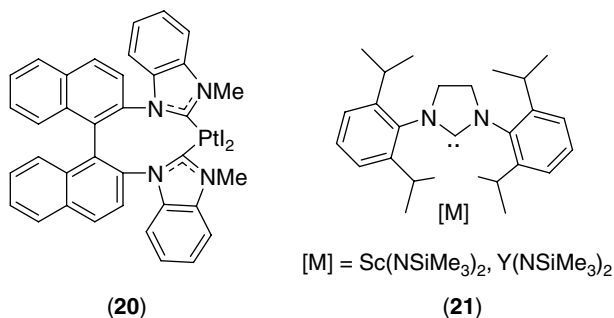


Alkylboranes obtained from hydroboration with 9-BBN deliver 1-aminoalkanes on reaction with hydroxylamine *O*-benzoates in the presence of **5C**-CuCl.¹² Carboxylation is done with CO₂ (catalyst from **6A**-CuCl and MeOLi).¹³ Borylcarboxylation of alkynes catalyzed by a copper(I)-carbene provides 4-borato-2-buten-4-olides which are valuable substrates for Suzuki coupling.¹⁴

An iridium(I) salt in which the metal center is surrounded by **6B**, 1,5-cyclooctadiene, and Bn₃P is serviceable for hydrogenation of alkenes.¹⁵ Another complex (**18**) that one of the imidazoline nitrogen atoms is connected to a phosphinated sidechain is able to catalyze transfer hydrogenation of conjugated ketones (to give saturated alcohols), as well as alkylation of α-arylethanol with primary alcohols [to yield ArCH(OH)CH₂CH₂R],¹⁶ hydrosilylation to produce chiral benzylic alcohols is effected in the presence of **19**.¹⁷



An ionic Pt-complex derived from **20** and AgBF₄ is shown to promote intramolecular hydroamination.¹⁸ For accomplishing selective cyclization involving one of two double bonds a lanthanide complex (**21**) proves its value.¹⁹



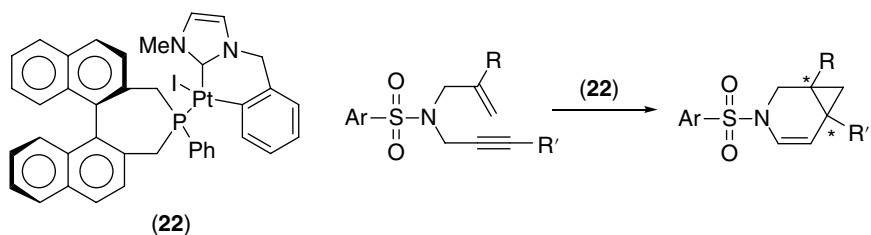
Condensation of RCHO, amines and 1-alkynes to form propargylic amines is also effected by a carbene-AgOAc complex.²⁰

(*E*)-3-Chloro-2-alkenoylarenes are adducts of ArCOCl and 1-alkynes, formed in a reaction catalyzed by **6A**-Ir(cod)Cl.²¹

Upon conversion of the type **6** carbene-bound CuCl to CuF·HF by AgHF₂ or Et₃N(HF)₃ - *t*-BuOK, a catalytic activity for promoting diastereoselective allylation of *N*-*t*-butanesulfinyl aldimines is revealed.²²

Change of a non-carbene ligand to modify properties of the complex is also the case of **6A**-GaCl₃, the replacement of a chlorine atom with a 2,4,6-trifluorophenylcyanide ligand renders the resulting complex more active as a π -Lewis acid with increasing resistance to hydrolysis.²³

Cycloisomerization. The Pt-carbenoid **22** is the motivator for transforming 1,6-enynes to bicycle[4.1.0]heptenes.²⁴



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⁹ Inomata, H., Ogata, K., Fukuzawa, S., Hou, Z. *OL* **14**, 3986 (2012)

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¹⁷ Kawabata, S., Tokura, H., Chiyojima, H., Okamoto, M., Sakaguchi, S. *ASC* **354**, 807 (2012)

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¹⁹ Jiang, T., Livinghouse, T., Lovick, H.M. *CC* **47**, 12861 (2011)

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O-(2-Aminoethyl)diphenylborinate

Alcohol functionalization. With the title reagent as catalyst, regioselectivity for mono-acylation, sulfonylation and alkylation of diols and sugars is observed.¹ It can also be used in Koenigs-Knorr glycosylation.²

¹Lee, D., Williamson, C.L., Chan, L., Taylor, M.S. *JACS* **134**, 8260 (2012)

²Gouliaras, C., Lee, D., Chan, L., Taylor, M.S. *JACS* **133**, 13926 (2011)

Antimony(III) chloride

Benzylation. Friedel-Crafts benzylation with ArCH(OH)R succeeds by using SbCl₃ as catalyst.¹

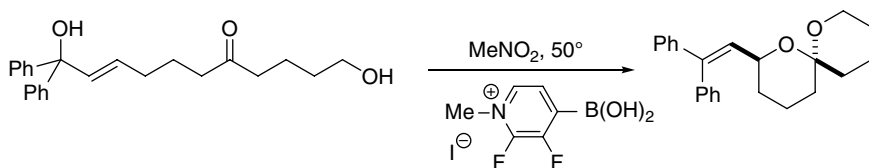
¹Shukla, P., Choudhary, M.K., Nayak, S.K. *SL* 1585 (2011)

Arylboronic acids

Functionalization. For conversion of ArB(OH)₂ into ArNH₂, 2,4-dinitrophenoxyamine is an adequate reagent,¹ and phenols are produced by oxidation with tolyldimethylamine oxide.²

Condensation. 2-Iodo-5-methoxyphenylboronic acid acts as a stable and recyclable catalyst for the direct amidation of carboxylic acids at room temperature, 4A-MS is also required for the dehydration.³

Friedel-Crafts reaction. 2,3-Difluoro-1-methylpyridinium-4-boronic acid iodide is a useful activator of allylic alcohols for cyclization onto an aromatic ring and formation of spiroacetals.⁴ Friedel-Crafts alkylation of arenes with propargylic alcohols is catalyzed by C₆F₅B(OH)₂.⁵



Suzuki coupling. Coupling procedures using ArBF₃K are now recognized as providing the same results as with ArB(OH)₂. It is due to hydrolysis of the aryltrifluoroborate salts.⁶

¹Zhu, C., Li, G., Ess, D.H., Falck, J.R., Kürti, L. *JACS* **134**, 18253 (2012)

²Zhu, C., Wang, R., Falck, J.R. *OL* **14**, 3494 (2012)

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⁶Butters, M., Harvey, J.N., Jover, J., Lennox, A.J.J., Lloyd-Jones, G.C., Murray, P.M. *ACIE* **49**, 5156 (2010)