Carbometalation and Heterometalation of Carbon-Carbon Multiple-Bonds Using Group-13 Heavy Metals: Carbogallation, Carboindation, Heterogallation, and Heteroindation

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Abstract: Organogallium and -indium compounds are useful reagents in organic synthesis because of their moderate stability, efficient reactivity and high chemoselectivity. Carbogallation and -indation of a carbon-carbon multiple bond achieves the simultaneous formation of carbon-carbon and carbon-metal bonds. Heterogallation and -indation construct carbon-heteroatom and carbon-metal bonds. Therefore, these reaction systems represent a significant synthetic method for organogalliums and -indiums. Many chemists have attempted to apply various types of unsaturated compounds such as alkynes, alkenes, and allenes to these reaction systems. This minireview provides an overview of carboindation and -gallation as well as heteroindination and -gallation.

1. Introduction

Carbometalation of a carbon-carbon multiple-bond is an important and powerful method for the synthesis of organometallic compounds because organometallics are produced by the formation of a new carbon-carbon bond.[1] There are many types of transition metal-catalyzed carbometalations, and most of them occur in a syn-addition fashion. Transition metal catalyst-free carbometalation is also an attractive reaction because toxic and expensive transition metals are not required. In several reports, highly reactive organometallic compounds such as organolithiums and Grignard reagents have been added directly to alkynes and alkenes. However, the high nucleophilicity of the organometallics that were used led to a lack of functional group tolerance. On the other hand, carbometalation using group-13 heavy metal species such as organogalliums and -indiums is a diverse reaction system with high chemoselectivity. This is because the Ga(III) and In(III) centers possess moderate Lewis acidity and high π-electron affinity that is caused by the large ionic radius, which leads to a compatibility with functional groups and to the activation of carbon-carbon multiple bonds, respectively.[2] Moderate reactivity of organogalliums and -indiums enables chemoselective reactions, and the organometallics produced by carbometalation are applicable to sequential reactions.[1][1] Carboindation via a radical mechanism is possible due to the stability of low-valent indium species. Therefore, the importance of carbogallation and carboindation has increased because of their usability and diversity. This review focuses on stoichiometric carbogallation and carboindation to synthesize organogalliums and organoindiums, respectively, and the application of these organometallic compounds to organic synthesis. Many excellent catalytic reactions, in which the catalytic cycle involves carbogallation and -indation, have been reported. In these cases, organogalliums and indium species are generated as transient intermediates, but are not afforded as final products. Therefore, the catalytic reactions are excluded in this review.[2]

2. Carbogallation of Carbon–Carbon Multiple-Bonds

2.1. Carbogallation with Organogalliums

The first carbogallation of alkynes was reported by Yamaguchi.[4] Treatment of alkynyltrimethylsilane with GaCl₃ in the presence of a catalytic amount of pyridine 2 gave dimeric product 4 after a workup with D₂O, and two deuterium atoms were introduced at an exo-methylene moiety of 4, which suggested the possibility of a generation of 3 via carbogallation (Scheme 1a).

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\text{Scheme 1. Carbogallation between alkynylgalliums generated by transmetalation and \textit{exo}-methylene moiety of } \text{allylsilane 1 and GaCl}_3 \text{ in the presence of pyridine gives dimeric product 4 after a workup with } D_2O, \text{ and two deuterium atoms were introduced at an exo-methylene moiety of 4, which suggested the possibility of a generation of 3 via carbogallation.}
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The addition of pyridine prevented origomerization of 4. The reaction mechanism is shown in Scheme 1b. Transmetalation between 5 and GaCl₃ produces alkynylgallium 6, and then carbogallation between two alkynylgallium 6 yields digallium compound 8.

Allylgallium species generated by transmetalation between allylsilane 9 and GaCl₃ underwent syn-carbogallation (13) of alkynylsilsane 1 (Scheme 2).[1] Takai reported that an allylgallium generated from allyl bromide 16 and Ga(0) was applicable to...
carbogallation of terminal alkynes (Scheme 3). After alkyne 14 was reacted with allylic gallium 15, quenching with I₂ gave 1,1-diiodoalkene 18. Authors proposed the Ga(III)-assisted carbogallation of allyl alkyne gallium species 19.

Yamaguchi reported that carbogallations of silyl acetylene 20 proceeded using GaCl₃ and silyl enolates (Scheme 4). Carbogallation of silylacetylene 17 with GaCl₃ and silyl enol ether was discovered. Quenching with NBS (24) gave 1,1-dibromoalkene 23 (Scheme 4), which indicated the production of 1,1-dimetalated alkene 19 by carbogallation.

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Carbogallation using silyl enol ether 25, which is derived from a six-membered cyclic ketone, predominantly provided ethenylated cyclic ketone 26 with a equatorial vinyl group (Scheme 5). Enolate ethenylation and alkylation display equatorial stereochemistry and axial stereochemistry, respectively. It is proposed that α-galliokeketone is the reactive species rather than gallium enolate (Scheme 6). 25 and silyl acetylene 17 transmetallate with GaCl₃ to provide gallium enolate 28 and gallium acetylide 27, respectively. 28 isomerizes to α-galliokeketones 29 and 32. There is an equilibrium between 29 and 32, and 29 has a bulky GaCl₃ group at the equatorial position, which makes it more stable than 32. Then, carbogallation of 27 with 29 preferentially proceeds to give 1,1-digallioalkene 31.

Yorimitsu and Oshima disclosed carbogallation of alkynes using allylic galliums generated by retro-allylation (Scheme 7a). Allylic gallium 36 was produced by retro-allylation between homoallyl alkoxide 41 and GaCl₃, and then reacted with alkyne 35 to give product 37 after quenching with an aqueous solution of HCl. Quenching with DCCI instead of HCl afforded di- and monodeuterated products (37- and (E)-37-). Based on a DCCI-quenching experiment, a syn-addition mechanism was proposed (Scheme 7b). Allylgallation of alkyne 35 with 36 proceeds via a six-membered transition state to give

**Scheme 2. Allylgallation of alkynylsilane with allylic gallium generated by transmetalation between allylic silane and GaCl₃.**

**Scheme 3. Allylgallation of terminal alkynes with allylic gallium generated from allylbromide and Ga(0).**

**Scheme 4. Allylgallation of alkynylsilane with allylic gallium generated by transmetalation between allylic silane and GaCl₃.**

**Scheme 5. Carbogallation using silyl enol ether 25 derived from a six-membered cyclic ketone.**
alkenylgallium 39. Meanwhile, deprotonation of alkyne 35 by basic allylic gallium gives alkenylgallium 38. The syn-addition of 36 to 38 yields 1,1-metalated alkene 40.

1,2-Bis(arylimino)acenaphthene (bian) ligands have attracted much attention. The synthesis of (dpp-bian)Ga–Ga(dpp-bian) complex 41 and reversible carbogallation of alkynes with 41 was reported (Scheme 8).[11] When treatment of a solution of 41 with acetylene or phenylacetylene was carried out, the Ga–N–C fragment was added to the alkynes to provide carbon-carbon and carbon-gallium bonds and to give alkenyl gallium 42 or 43, respectively. These organogalliums were identified by single-crystal X-ray analysis. The carbogallation was reversible, and the equilibrium between 43 and 41 + phenyl acetylene was studied by ¹H NMR spectroscopy.

Carbogallation of a carbon-carbon double bond was established using allylgallium species. Araki reported a regioselective allylgallation of cyclopropenes (Scheme 9).[12] The reaction of the allylic gallium with cyclopropane 44 bearing a hydroxalkyl group on the C₁ carbon gave cyclopropylgallium products 47 and 48. The structure of 47 was revealed by X-ray diffraction analysis. Therefore, the coordination of the hydroxy group to a Ga atom in the allylic gallium was classified as anti-Markovnikov regioselectivity (TS 45 and TS 46).

2.2. Carbogallation of Gallium Trihalide-Activated Carbon-Carbon Multiple-Bond

A reaction of silyl acetylene with GaCl₃ and nucleophilic arenes was carried out, followed by treatment with MeLi to give alkenylidimethylgallium 52 (Scheme 10a).[14] The complex 53 was formed from GaCl₃ and vinyl tert-butyldimethylsilylane and identified at −78 °C via NMR spectroscopy (Scheme 10b). Carbogallation proceeds via the regioselective nucleophilic attack of an arene at the β-carbon atom of a silyl group to give zwitterion intermediate 54. Finally, a proton abstract and ligand exchange by MeLi produce alkenylgallium 52. In the absence of nucleophilic arenes, ethynylsilane 55 was trimerized via alkenylgallation caused by GaCl₃ (Scheme 11a).[15] The reaction of GaCl₃ with 3 equivalents of 55 in CH₂Cl₂ and methylcyclohexane at −78 °C gave trienyl cation 56. Interestingly, the cation intermediate 56 was identified by ¹H and ¹³C NMR spectroscopics. MeMgBr in Et₂O was then added to the solution of 56 to
produce alkenylgallium 57. Proposed mechanism is shown in Scheme 11b. The reaction is initiated with the activation of 55 by GaCl₃, and then the nucleophilic addition of another 55 gives alkenyl cation 59. The cation 59 is converted to trienyl cation 56 by the addition of 55. Finally, the treatment of MeMgBr produces trienylgallium compound 57.

Silyl allene 60 also underwent carbogallation with GaCl₃ and p-xylene (Scheme 12). In this case, however, an intramolecular proton transfer in zwitterion alkylgallium species 61, which was formed by the carbogallation, occurred to give allenysilane 62 and GaCl₃, so a stable organogallium product was not obtained.

We reported the regio- and stereoselective anti-carbogallation of alkynes using GaBr₃ and silyl ketene acetal 64 (Scheme 13). Alkyne 63 was treated with GaBr₃ and silyl ketene acetal 64 to give dialkenylgallium 65 (Scheme 13a). The structure of 65 was determined by X-ray diffraction analysis after complexation with pyridine (65-pyridine). That result suggested carbogallation occurred as shown in Scheme 13b. The interaction between GaBr₃ and a carbon-carbon triple bond of alkyne 63 causes the regioselective nucleophilic attack of 64 from the opposite site of GaBr₃ to provide monoalkenylgallium 64 and Me₃SiBr.

Synthesized alkenylgalliums were directly applied to Pd-catalyzed cross-coupling with aryl iodides (Scheme 14). Various types of functional groups were compatible with alkenylgalliums, and 4-acetyliodobenzene, 2-iodopyridine as well as iodobenzene smoothly coupled with alkenylgalliums (65 or 66) to give the corresponding trisubstituted alkene products (67, 68, and 69). The use of phosphine ligands for a Pd-catalyst is not necessary to the cross-coupling of organogalliums (and organoindiums) in highly-coordinative solvents such as DMF perhaps because the solvents could work as efficient ligands.

The developed process for trisubstituted alkene synthesis via carbogallation/cross-coupling was employed for the first total synthesis of nodosol 75 (Scheme 15). The key synthetic intermediate, diene 72, was regio- and stereoselectively prepared by carbogallation of enyne 70 followed by cross-coupling using 4-bromoiodobenzene.

We discovered that vinyl ether 76 underwent carbogallation with GaBr₃ and silyl ketene acetal 77 at low temperature to give β-phenoxyalkylgallium species 78 (Scheme 16). Interestingly, the syn-elimination of phenoxygallium from 78 via transition state 79 occurred at room temperature to give α-vinyl ester 80.
Therefore, the authors established the first catalytic cross-coupling of alkenyl ethers with silyl ketene acetal. Vinyl ether 81 was coupled with silyl ketene acetal 82 in the presence of GaBr₃ catalyst to produce α-vinyl ester 83 (Scheme 17). Silyl ketene imines were also applicable to this cross-coupling system.19 A proposed catalytic cycle is shown in Figure 1. GaBr₃ is coordinated by alkenyl ether 1, and then the anti-carbogallation of the activated 81 with silyl ketene acetal 82 occurs regioselectively to give alkylgallium 85 and Me₂SiBr. After conformation change from six-membered 85 to four-membered 86, syn-elimination of Br₂GaOBu proceeds to give coupling product 83. Finally, GaBr₃ is regenerated by transmetalation between Br₂GaOBu and Me₂SiBr.

3. Heterogallation of Carbon-Carbon Multiple-Bonds

Zheng and Yang demonstrated the first synthesis and characterization of pyrazolato gallium dichlorides and its application to azagallation of alkynes.20 When pyrazolato gallium dichloride 88 was mixed with silyl acetylene, azagallation of the carbon-carbon triple bond gave pyrazolato alkenylgallium 89 (Scheme 18a). The reaction mechanism remains unclear, but the more reactive three-coordinated gallium species 91 is proposed (Scheme 18b). The gallium center of 91 activates silyl acetylene by π-coordination, and the intramolecular nucleophilic attack by a β-nitrogen of the Ga atom causes azagallation.

Uhl synthesized Ga/P complex 93 with the geminal arrangement of coordinatively unsaturated Ga and P atoms.21 When 93 was mixed with alkyne 94, phosphagallation of a carbon-carbon triple bond occurred to give five-membered heterocycle 95 involving P and Ga atoms (Scheme 19). The terminal C atom of alkyne 94 has its relatively high negative partial charge to bind to the electropositive Ga atom, and the relatively positive internal C atom binds to the electronegative P atom.

![Scheme 16](image-url)  
**Scheme 16.** Carbogallation of vinyl ether 76 with GaBr₃ and silyl ketene acetal 77, and β-elimination of phenoxygallium to give α-vinyl ester 80.

![Scheme 17](image-url)  
**Scheme 17.** Catalytic coupling reaction of vinyl ether 81 with silyl ketene acetal 82.

![Scheme 18](image-url)  
**Scheme 18.** Azagallation of alkyne with pyrazolato gallium dichloride 88.

![Scheme 19](image-url)  
**Scheme 19.** Phosphagallation of a carbon-carbon triple bond by Ga/P FLPs complex.
4. Carboindation of Carbon-Carbon Multiple-Bonds

4.1. Carboindation with Organoindiums

Various carboindations using allylindiums generated by the reaction of In(0) with allylic halides have been reported. Butsugan developed the first carboindation of alkynols in 1992 (Scheme 20).[22] The carboindation of alkynol 96 with allylic indium 97 proceeded via a syn addition mechanism to give anti-Markovnikov adduct 98 and Markovnikov adduct 99. The reaction using 3-butyn-1-ol 100 gave a high yield, but 4-pentyn-1-ol 101, 3-methoxy-1-propyne 102, 1-octyne 103, and phenylacetylene 104 were not suitable to these conditions. Therefore, a hydroxy group near the triple bond is important in the carboindation.

The regioselectivity depended on the structures of alkynols and allylic indiums (Scheme 21a). The reaction using sterically hindered alkynol 105 and allylic indium 106 showed perfect regioselectivity. A proposed reaction mechanism is shown in Scheme 21b. A hydroxy group coordinates to an indium atom of allylic indium 97. The allyl group on the coordinated indium atom adds to the terminal carbon of alkynol 96 and the indium adds to the inner carbon.[23]

Yamamoto[24] and Ranu[25] independently reported the carboindation of unactivated alkynes using allylic indiums (Scheme 22). In contrast to the DMF solvent conditions, aromatic alkyne 111 and aliphatic alkyne 114 without a directing group such as a hydroxy group smoothly underwent carboindation using an allylic indium under THF solvent conditions to give dienes 113 and 115, respectively (Scheme 22a and 22b). Quenching with DCl/D2O afforded an E/Z mixture of deuterated diene product 115 (Scheme 22b). Therefore, the carboindation of an alkyne with an allylic indium proceeds via syn-addition fashion (116) to produce alkenylnium 117, which undergoes E-Z isomerization (Scheme 22c).

Carboindation of alkyne using benzylic indiums was also reported by Yamamoto (Scheme 23).[24b] The benzyllination of aromatic alkyne 111 occurred in an anti-addition manner (Scheme 23a), while that of aliphatic alkyne 114 took place in a nonstereoselective fashion (Scheme 23b). As in the case of allylindination, syn-addition followed by E-Z isomerization occurred. The produced alkenylnium 122 coupled with benzyl iodide in the presence of a palladium catalyst to give three-component coupling product 123 in 49% yield (Scheme 23c).

Intramolecular cyclizations of alkyne bearing an allylic bromide moiety via allylindation were reported. Salter discovered that In(0) mediated the cyclization of 123 to give cyclic compound 124 (Scheme 24a).[26] The allylic indium moiety of 125, which generated by the reaction of allylic bromide 123 with In(0), adds to an intramolecular carbon-carbon triple bond in a syn fashion, giving alkenylnium 126, regio- and stereo-
selectively (Scheme 24b). Actually, the use of D$_2$O instead of H$_2$O stereoselectively gave deuterated product 124-d. Lee reported an improved intramolecular cyclization system (Scheme 24c).

The cyclization of 127 in DMF smoothly proceeded without an H$_2$O co-solvent, and the addition of KI was a key factor. The produced alkenylindium 128 was successfully coupled with an aryl iodide or I$_2$.

Araki and Butsugan discovered the stereodivergent allylindation of cyclopropene derivatives (Scheme 25).

In a reaction of cyclopropene 131 with allylic indium 132, the allylic indium was added preferentially from the anti-face of the acetoxymethyl group (TS 133) to avoid steric repulsion with the acetoxymethyl group, and the allylic group was introduced to the substituted carbon of the cyclopropene double bond to give product 134. In contrast, the stereoselectivity of allylindation into cyclopropene 135 was reversed to that of acetate 131, although the regioselectivity was not changed. This result suggested that the coordination of the hydroxy group to an allylic indium species led to allylindation from the cis face of the hydroxymethyl group (TS136).

The generated cyclopropylindiums were applicable to further transformations (Scheme 26).

Interestingly, the allylindation of cyclopropene 142 bearing a hydroxyalkyl group at a 1-position as well as at a 2-position took place with the opposite regioselectivity in the reaction of 135 (Scheme 27a).

Other strained olefins underwent carboindation with allylic indium reagents. Allylindation of norbornenol 147 regio- and...
stereoselectively proceeded to give allylated product 148, and the allylic group was installed exclusively from the exo face (Scheme 28). Therefore, the hydroxy group of 147 acts as a director to lead the carboallylation on the exo face (TS 149).

The reaction of methylenecyclopropane 151 with allylic indium species 138 exclusively gave deuterated cyclopropane 152 after carrying out a 1 M DCl/D₂O quench (Scheme 29). Regio- and stereoselective allylation occurred owing to the coordination of a hydroxyl of 151 to an indium center (TS153).

Araki and Butsugan developed carboindation of allenols using an allylic indium species.[33,34] The regio- and stereoselective addition of prenylindium species 156 to an allene moiety of allenol 155 proceeded to afford product 157 (Scheme 30a). O-protected allenols were not applicable to this carboindation system, which suggested the importance of an hydroxy group for effective carboallylation. A plausible reaction mechanism is shown in Scheme 30b. The carboindation regio- and stereoselectively proceeds through hydroxyl-chelated bicyclic transition state TS158 to give alkenylindium 159, and 159 was protonated by an internal hydroxy group to afford indium alkoxide 160.

4.2. Carboindation of Indium Trihalide-Activated Carbon-Carbon Multiple-Bond

We reported the carboindation of alkynes using InBr₃ and silyl ketene acetal.[35] When alkyne 161 was treated with InBr₃ and silyl ketene acetal 162, carboindation regio- and stereoselectively occurred to give alkenylindiums 163 and 164 (Scheme 30). The treatment of 163 and 164 with D₂O afforded deuterated 165. The reaction mechanism is illustrated in Scheme 31. The activation of alkyne 161 by InBr₃ increase the positive charge on the internal carbon of 161. The nucleophilic attack by silyl ketene acetal 162 to the internal carbon from the opposite side of the coordinated InBr₃ to give monoalkenylindium 163. The successive addition of the resulting 163 to another 161 afforded dialkenylindium 164 with the same selectivity. The moderate Lewis acidity and high π-electron affinity of InBr₃ plays an important role in the effective activation of alkynes in the presence of coordinative ketene silyl acetal. In contrast, the use of strong Lewis acids such as AlCl₃ and BF₃·OEt₂ strongly interacted with an oxygen atom of ketene silyl acetal, which resulted in no reaction.

Scheme 32 illustrates the anti-carboindation mechanism. The activation of alkyne 161 by InBr₃ takes place to increase the positive charge on the internal carbon of the alkyne. Ketene silyl acetal 162 attacks the internal carbon from the opposite side of the InBr₃ to give monoalkenylindium 163. The successive addition of 163 to another alkyne 161 produces dialkenylindium 164. Quenching with D₂O affords deuterated compound 165.

The treatment with I₂ gave iodinated β,γ-unsaturated ester 166, and Pd-catalyzed cross-coupling of the synthesized alkenylindium with iodobenzene in a one-pot manner gave
coupling product 167 (Scheme 33). In both reactions, the configuration of the corresponding alkenylindium was retained.

The regio- and stereoselective carboindation of alkynes using InBr₃ and allylic silanes was developed.¹⁶ This is the first report of the stereoselective anti-allylindation of alkynes. The carboindation of 1-decyne 168 followed by the quenching of alkenylindium 170 with I₂ gave 171, regio- and stereoselectively (Scheme 34a). The produced 1,4-dienylindium 172 was applicable to Pd-catalyzed cross-coupling (Scheme 34b).

We also established anti-carboindation of alkynyl ethers using InI₃ and organosilicon or –stannanes (Scheme 35).³⁷ The interaction between InI₃ and an alkynyl ether is accelerated by the conjugative electron-donation of an oxygen atom bonding an alkyne moiety, which revealed by DFT calculations. The carboindation of alkynyl ether 174 using InI₃ and silyl ketene acetal 175 gave metalated enol ether 176 (Scheme 35a). The iodination of 176 afforded trisubstituted enol ether 178 regio- and stereoselectively (Scheme 35b), as well as various nucleophiles such as silyl ketene imine 179, alkynyl stannane 182 (Scheme 35c and 35d).

An indium trihalide effectively activates simple alkenes (Scheme 36). The regioselective carboindation of 1-hexene 185 using InBr₃ and silyl ketene acetal 162 proceeded to give alkylindium 186 (Scheme 36a). The structure of 186 was revealed by X-ray diffraction analysis. The crystal structure of alkylindium 188 was afforded by the carboindation of cyclohexene 187 and showed an anti-addition mechanism (TS 189) (Scheme 36b). Alkylindium 191 was treated with 1 M HBr and PhI(OAc)₂ to give the corresponding protonated product 192 and brominated product 193, respectively (Scheme 36c).

### 4.2. Carboindation via Radical Mechanism

Takemoto discovered indium-mediated reductive radical cyclization of alkynes bearing an iodoalkane moiety by using a low-valent indium species (Scheme 35). Treatment of alkyne 194 with In(0) and I₂ promoted 5-exo cyclic carboindation to give alkylindium 195 (Scheme 37a).³⁹ The generated alkylindium 195 was coupled with iodosobenzene in the presence of a Pd catalyst to give an E/Z isomer mixture 196. A proposed
reduced by reduction of alkyl iodide with row-valent indium species. 

The radical 

produced by reduction of alkyl iodide with row-valent indium species. 

mechanism is illustrated in Scheme 37b. The single electron transfer (SET) from a low-valent indium iodide species, which is generated from In(0) and I₂ to 194 provides alkyl radical 197. The radical 197 then undergoes a radical cyclization to produce alkényl radical 198, and then the radical reductively combines with an indium cation (InX₃) to give the E/Z-mixture of alkénylindium 199. Alkene 199 with an iodoalkyl moiety was also applicable to this reductive radical cyclization, and stable alkénylindium 200 was isolated (Scheme 37c). The alkénylindium 200 underwent oxidation by H₂O₂ to give the corresponding primary alcohol 201.

A reductive radical cyclization of iodoarene bearing an alkénylindium species by using In(0)/pyridinium tribromide (PyHBr₃) occurred regio- and stereoselectively to produce 3-alkénylideneoxindoles 203 (Scheme 36a). In the reaction mechanism (Scheme 38b), either InBr generated from In(0) or InBr₂ generated from PyHBr could mediate the radical carboindation of iodoarene 202, and the coordination of the amide group to an indium atom led to the high stereoselectivity. 202 underwent SET from a low-valent indium species to afford sp²-carbon radical 205. The radical 205 produces alkenyl radical 206 via radical cyclization, and then the radical exclusively gives an E-isomer of alkenykindium 203 due to the strong coordination of the amido moiety to the indium center. The generated alkenykindium 203 was applied to Pd-catalyzed cross-coupling with 4-iodo toluene.

Ranu reported the InI-mediated cyclization of α-carbonyl bromoalkynes (Scheme 39). The treatment of α-carbonyl bromoalkyne 207 with InI gave 4-methylene-tetrahydropyran 208 via 5-exo cyclization. Alkenykindium 209 would be produced via InI-mediated reductive radical carboindation.

Shibata and Baba established the carboindation of alkynes and alkenes via indium hydride-mediated radical cyclization. Enyne 210 underwent cyclization in the presence of HInCl₂, which was generated from InCl₃ and Et₃SiH, to give exo-methylene compound 212 through alkénylindium 211 (Scheme 40a). A proposed mechanism is shown in Scheme 40b. Transmetalation between InCl₃ and Et₃SiH gives HInCl₂, and then the Et₂B/Oₜ-B system generates a dichloroindium radical (InCl₂) from HInCl₂. The indium radical adds to an alkene moiety of 210 to produce alkényl radical 213. Alkyl radical 214 is produced by the 5-exo cyclization of 213, and then abstracts a hydrogen atom from HInCl₂ to give alkénylindium 211.

Carboindation of alkenes by radical cyclization was also developed (Scheme 41a). When allenene 215 was treated with In(OMe)Cl₂ and PhSiH₃, carboindation of an allene moiety and 5-exo cyclization proceeded to give alkenykindium 216. In this case, an indium radical selectively adds to a central carbon of an allene moiety to provide allylic radical 218 (Scheme 41b).
The 5-exo cyclization of 218 followed by the hydrogen abstraction of alkyl radical 219 from HInCl affords alkenylindium 216. Then, Pd-catalyzed cross-coupling of the alkenylindium 216 with an iodoarene successfully proceeds to yield 217.

5. Heteroindation of Carbon-Carbon Multiple-Bonds

We reported the regioselective oxyindation of a terminal alkyne moiety in a 2-alkynyl benzoic ester.\(^{[45]}\) The reaction of 2-alkynyl benzoic ester 220 with InI\(_3\) at 50 °C exclusively gave 4-metalated isocoumarin 221 via oxyindation of an alkyne moiety (Scheme 42a). The 6-endo cyclization contrasts with the 5-exo cyclization caused by B-chlorocatecholborane (Scheme 42b), which was reported by Blum.\(^{[46]}\) The obtained organooindium 221 was characterized by X-ray diffraction analysis.

A reaction mechanism of the oxyindation was revealed by both experimental and theoretical studies. When the reaction of 222 with InI\(_3\) was carried out at room temperature, zwitterion intermediate 224 with a new carbon-indium and carbon-carbon bonds was obtained and identified by X-ray diffraction analysis (Scheme 43a). Zwitterion 224 was heated at 50 °C, and then elimination of Mel occurred to give isocoumarin 225 bearing a carbon-indium bond at the 4-position (Scheme 43b). Based on experimental results, the details of the reaction mechanism were examined using theoretical calculation (Scheme 44), which showed that the activation energy of 5-exo cyclization is much smaller than that of the elimination of Mel so that 5-exo cyclization is reversible. Eventually, selective production of the thermodynamically stable 6-membered zwitterion 224 produced a remarkable level of 6-endo selectivity.

Alkenyl indium 229 was synthesized by the oxyindation of 222 using InBr\(_3\) and applied to Pd-catalyzed cross-coupling with iodo benzene or benzoic chloride in a one-pot manner to afford 4-substituted isocoumarin 230 or 231, respectively (Scheme 45).

The formal total synthesis of oosponol was demonstrated by the present oxyindation (Scheme 46). Alkenylindium 234 was synthesized via the oxyindation of 233 with InBr\(_3\), and then a one-pot process for the Pd-catalyzed cross-coupling of 2-
(acetyloxy)acetyl chloride provided a key isocoumarin precursor, 235, for Oosponol.\(^{[47]}\)

Carbonyl-ene-yne compounds are also applicable to oxyindation with indium trihalides to give 2-pyrones bearing a carbon-indium bond (Scheme 47).\(^{[50]}\) The oxyindation of 236 using \(\text{InI}_3\) produced tetrasubstituted metalated isocumarin 237. Subsequently, the coupling reaction of 237 with either an aryl iodide or an aryl chloride in the presence of a palladium catalyst led to 2-pyrones 238 or 239 bearing four different substituents, respectively. Tetrasubstituted 2-pyrones 240 and 241 exhibited an aggregation-induced emission (AIE) in the solid state (Scheme 48). It is noted that 240 and 241 exhibit greater quantum yields than triphenylated 2-pyrone 242.\(^{[49]}\)

Gomez-Bengoa and Sestelo reported that cyclic oxyindation of lithium \(\alpha\)-phenylethynylphenoxide 243 with \(\text{InCl}_3\) proceeded to give alkenylindium 244 (Scheme 49).\(^{[50]}\) In this case, the \(\pi\)-coordination of an alkyne moiety to \(\text{InCl}_3\) followed by \(\text{endo}\)-cyclization induced by the nucleophilic attack of a lithium alkoxide moiety occurs (TS 245). Organoindium 244 underwent Pd-catalyzed cross-coupling with 4-iodotoluene to afford benzo [b]furan 246. The discovery of oxyindation provided important insight into the reaction mechanism of the In-catalyzed hydroalkoxylation of \(\alpha\)-alkynylphenol derivatives.
6. Conclusions and Outlook

We briefly summarized the history of carbogallation and -indation, and heterogallation and -indation of carbon-carbon multiple bonds. Carbogallation is divided into two main systems that are the addition of organogallium species and the addition of an external nucleophile to a gallium-activated alkyne. In the former system, allylgalliums, alkynylgalliums, and gallium enolates were used as organogallium species. In the latter, a gallium trihalide activates a carbon-carbon multiple bond of alkynes, alkenes, and alkenyl ethers, and carbogallation is then completed by the nucleophilic addition of various carbon nucleophiles. On the other hand, there are three types of carboindation. Two types are the same as carbogallation. A third type includes a radical pathway, which gives it a broader diversity than carbogallation. A third type of carboindation involves a radical mechanism due to the stability of low-valent indium species. A few types of fascinating azagallation and oxyindation have been established. The moderate reactivity and stability of organogallium and -indium has resulted in high levels of compatibility with functional groups. Carbogallation, carboindation, heterogallation, and heteroindation are powerful tools available for the synthesis of highly funcionalized organometallic compounds, and further development of this field of study will be extremely useful as more sophisticated organic syntheses are required in the near future.

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Conflict of Interest

The authors declare no conflict of interest.

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