DOI: 10.1002/adsc.202((will be filled in by the editorial staff))

Use of Imidazo[1,5-*a*]pyridin-3-ylidene as a Platform for Metal-Imidazole Cooperative Catalysis: Silver-Catalyzed Cyclization of Alkyne-Tethered Carboxylic Acids

Vishal Kumar Rawat,[a] Kosuke Higashida,[a,b,*] and Masaya Sawamura[a,b,*]

[a] Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810, Japan
[E-mail: sawamura@sci.hokudai.ac.jp, higashida@icredd.hokudai.ac.jp]
[b] Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Sapporo 001-0021, Japan

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. Silver complexes with 5-(4-*(tert*-butyl)-1*H*-imidazol-1-yl)-imidazo[1,5-*a*]pyridin-3-ylidene ligands were synthesized as metal-imidazole acid-base cooperative catalysts. Single crystal XRD analysis revealed that the silver atom was located in the vicinity of the imidazole ring and that cationic silver complexes formed dimers through coordination between the silver metal and the imidazole pendant. These cationic silver complexes served as catalysts for cyclization of alkyne-tethered carboxylic acids. NMR experiments indicated that the dimeric cationic silver complex dissociated to a monomer upon protonation of the imidazole moiety, resulting in coordination of an acetonitrile to the silver atom. DFT calculations supported the acid-base cooperative action of the silver-imidazole for the efficient alkyne-carboxylic acid cyclization.

Keywords: Silver catalyst; Cooperative catalysis; *N*-Heterocyclic carbene; Cyclization

N-Heterocyclic carbenes (NHCs) are strong σ-donating ligands, and their transition metal complexes have been widely investigated as catalysts for reaction development due to their robustness and tunability. [1] To date, a broad spectrum of NHC ligands with different electronic and steric properties have been synthesized and evaluated. Imidazo[1,5-*a*]pyridin-3-ylidene (Figure 1a) is an NHC scaffold with a rigid bicyclic framework, introduced independently by Lassaletta[2] and Glorius. [3] Since the substituent at the C5 position of the imidazo[1,5-*a*]pyridin-3-ylidene projects into the catalytic environment around the NHC-bound metal center, it is expected that ligand modification at this position would have great impact on the nature of the catalyst not only through steric effect but also through a coordinative interaction. In fact, imidazo[1,5-*a*]pyridin-3-ylidene ligands have been modified at the C5 position with sterically bulky aromatic rings, [4] coordinative substituents, [5] chiral auxiliaries, [6] and other substituents. [7]

Therefore, we envisioned that imidazo[1,5-*a*]pyridin-3-ylidene could be used as a robust template for producing acid-base cooperative catalysts[8] by locating a Lewis acidic transition metal center and a basic functional group such as imidazole at the C3 carbene carbon and the C5 position, respectively (Figure 1b). More specifically, we chose the 4-(*tert*-butyl)-1*H*-imidazol-1-yl group as the rigid basic substituent at the C5 position so as to spatially separate the Lewis acidic center and the basic center in the catalytic region. Here, we report the synthesis of protonated precursors for such imidazo[1,5-*a*]pyridin-3-ylidene ligands, their conversion to the corresponding silver(I) complexes, and their application to the silver-catalyzed cyclization of alkyne-tethered carboxylic acids (Figure 1c). [9,10]

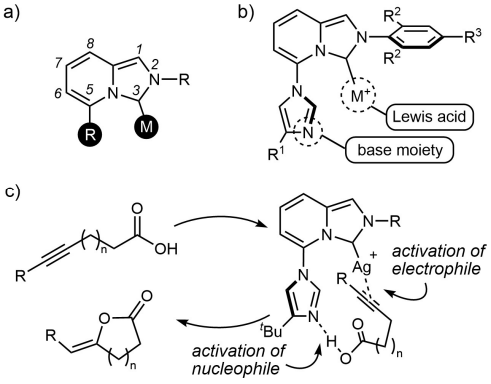
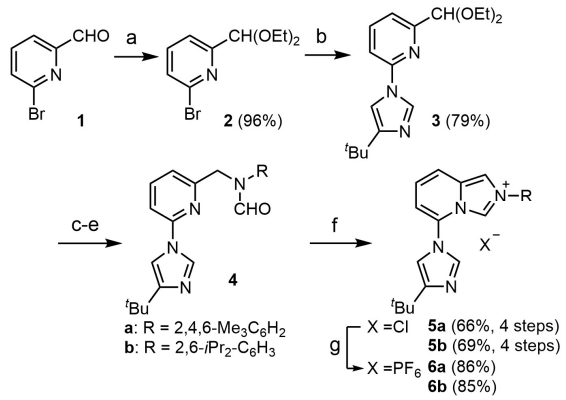


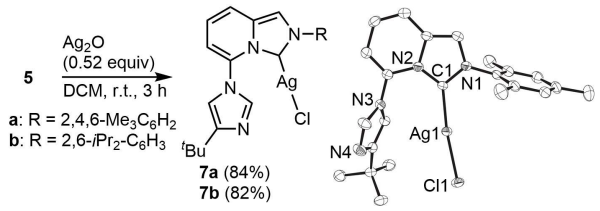
Figure 1. General chemical diagrams for a) imidazo[1,5-*a*]pyridin-3-ylidene metal complexes and b) Lewis acid-base cooperative catalysts with an imidazo[1,5-*a*]pyridin-3-ylidene platform. c) Cyclization of alkyne-tethered carboxylic acids through Lewis acid-base cooperative catalysis.

The synthesis of 5-(4-*(tert*-butyl)-1*H*-imidazol-1-yl)-imidazo[1,5-*a*]pyridinium salt as an NHC precursor is outlined in Scheme 1. Acetal protection of commercially available 6-bromo-2-pyridinecarboxaldehyde (**1**) gave 2-bromo-6-(diethoxymethyl)pyridine (**2**) in 96% yield. The 4-*(tert*-butyl)-1*H*-imidazolyl substituent was introduced through copper-catalyzed coupling between **2** and 4-*(tert*-butyl)-1*H*-imidazole to give 2-(4-(*tert*-butyl)-1*H*-imidazol-1-yl)-6-(diethoxymethyl)pyridine (**3**) in 79% yield. In this coupling, using benzotriazole[11] as a ligand for the copper catalyst was crucial for obtaining **3** in a reasonable yield. After removing the acetal protection under acidic conditions, reductive amination with 2,4,6-trimethylphenylmethylamine or 2,6-diisopropylphenylmethylamine followed by *N*-formylation[12] produced the corresponding *N*-aryl formamides (**4a**: R = 2,4,6-trimethylphenyl; **4b**: R = 2,6-diisopropylphenyl). Next, dehydrative cyclization[2] of **4a** and **4b** furnished 5-(4-*(tert*-butyl)-1*H*-imidazol-1-yl)-imidazo[1,5-*a*]pyridinium salts **5a** (69%) and **5b** (66%), respectively. The chloride anions on the imidazolium salts **5a** and **5b** were replaced with a weakly coordinating PF_6 anion through salt metathesis with KPF_6, yielding **6a** and **6b** in 86% and 85% yields, respectively.



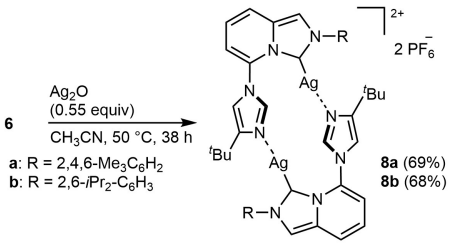
Scheme 1. Synthesis of NHC precursors **5** and **6**. (a) $TsOH{\cdot}H_2O$ (7 mol%), $HC(OEt)_3$ (1.2 equiv), EtOH, r.t., 3 h; (b) CuI (10 mol%), benzotriazole (20 mol%), 4-(*tert*-butyl)-1*H*-imidazole (1 equiv), KO^{t}Bu (1.4 equiv), DMSO, 110 °C, 14 h; (c) 1 M HCl aq., acetone, 60 °C, 3 h; (d) RNH_2 (1.2 equiv), AcOH (1 equiv), $NaBH(OAc)_3$ (1.5 equiv), DCM, r.t., 14 h; (e) HCOOH (excess), Ac_2O (excess), THF, 0 °C, 3 h; (f) $POCl_3$ (1.3 equiv), toluene, 100 °C, 38 h; (g) KPF_6 (2 equiv), H_2O, r.t., 18 h.

Silver(I) chloride complexes **7a** and **7b** bearing the 5-(4-*(tert*-butyl)-1*H*-imidazol-1-yl)-imidazo[1,5-*a*]pyridin-3-ylidene framework were synthesized through the reaction of Ag_2O and imidazolium salts **5a** or **5b** in 84% and 82% yields, respectively (Scheme 2). Single crystals of **7a** and **7b** suitable for XRD analysis were grown from DCM/Et_2O and DCE/Et_2O solutions, respectively. XRD analysis gave the mononuclear structures of complexes **7a** and **7b**. An ORTEP drawing of **7a** is shown in Scheme 2 (see Supporting Information for ORTEP drawing of **7b**). As expected, the silver atom is located in the vicinity of the imidazole ring uncoordinated to the N(4) atom.



Scheme 2. Synthesis of neutral silver complexes **7a** and **7b**. ORTEP drawing of **7a** is described with 50% probability thermal ellipsoids. Hydrogen atoms are omitted for clarity.

Cationic silver(I) complexes **8a** and **8b** were prepared from imidazolium salts **6a** and **6b**, respectively. Specifically, the reaction between Ag_2O and the imidazolium salts (**6a** or **6b**) in acetonitrile at 50 ºC for 38 hours gave the desired complexes **8a** and **8b** in 69% and 68% yields, respectively (Scheme 3). XRD analysis of single crystals of **8a** and **8b** obtained through recrystallization from a DCM/Et_2O solution indicated that both complexes existed as dimers with intermolecular coordination between the pendant imidazole and the silver atom (see Supporting Information for ORTEP drawings for **8a** and **8b**). The average $C_{carbene}$–Ag interatomic distance was 2.08 Å for both **8a** and **8b**, which is comparable to those for known silver NHC complexes. [13] In the $^{13}C\{^1H\}$ NMR spectra of **8a** and **8b** in CD_2Cl_2, resonances for the carbene carbon bound to the silver metal were observed as a pair of doublets at 167.3 ppm $\{^1J(^{13}C–^{107}Ag) = 287.1$ Hz, $^1J(^{13}C–^{109}Ag) = 248.5$ Hz$\}$ for **8a** and at 167.3 ppm $\{^1J(^{13}C–^{107}Ag) = 289.0$ Hz, $^1J(^{13}C–^{109}Ag) = 249.5$ Hz$\}$ for **8b**. The appearance of C–Ag coupling indicated that dissociation of the silver metal from the carbene is much slower than the NMR time scale. [14,15]



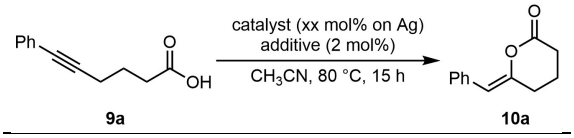
Scheme 3. Synthesis of silver complexes **8a** and **8b**.

Next, we evaluated the neutral and cationic silver complexes **7a**, **7b**, **8a**, and **8b** (2 mol% Ag) for catalytic activity in the cyclization of 6-phenylhex-5-ynoic acid (**9a**) in acetonitrile at 80 °C for 15 hours. When we applied the cationic complex (**8a**) with the N(1)-mesityl-substituted NHC ligand, the starting material was fully consumed to afford 6-*exo-dig* lactonization product **10a** in 98% isolated yield with exclusive *Z*-selectivity (Table 1, entry 1). Meanwhile, the cyclization of **9a** with **8a** in toluene, 1,4-dioxane,

and 1,2-dichloroethane gave only trace amounts of the product (see Supporting Information). The cationic silver complex (**8b**) having the NHC ligand subsituted with a bulkier N(1)-aryl group (2,6-diisopropylphenyl) was much less active, yielding (*Z*)-**10a** in only 21% yield (entry 3). The neutral silver chloride complexes **7a** and **7b** gave only a trace or none of the cyclization product (entries 4 and 5). In accordance with the literature, [9] Ag_2CO_3 as a basic silver complex also promoted this cyclization to give **10a** (83%), albeit with lower efficiency than **8a** (entry 6). Using ligand-free cationic silver(I) salt $AgPF_6$ as a catalyst resulted in only 12% yield (entry 8).

Combinations of $AgPF_6$ and conventional NHC ligands such as IMes (**L1**)[16] and IPr (**L2**)[17] gave **10a** in 27% and 16% yields, respectively (Table 1, entries 9 and 10). Imidazo[1,5-*a*]pyridin-3-ylidene ligand **L3** with a phenyl group at the C5 position gave even lower yield (13%, entry 11). The addition of 1-phenylimidazole (**11**) as an exogenous organic base to the reaction systems with **L1**, **L2**, or **L3** led to substantial increases in the yield of **10a** to 62%, 44%, or 18%, respectively (entries 12-14). These results suggest cooperative action of the cationic silver center and the imidazole derivative (**11**) as a Lewis acid and a Brønsted base, respectively. Furthermore, comparison of these results with those for the cationic silver complex (**8a**) with the imidazole-functionalized NHC ligand (entry 1) confirms that the expected acid-base cooperative catalysis with the intramolecularly arranged cationic Ag center and imidazole moiety has been achieved.

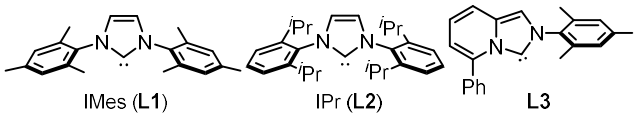
Table 1. Silver-Catalyzed Cyclization of **9a**



9a **10a**

entry	catalyst (xx mol% Ag)	additive	yield [%][a]
1	**8a** (2)	none	98[b]
2	**8a** (1)	none	94[c]
3	**8b** (2)	none	21
4	**7a** (2)	none	trace
5	**7b** (2)	none	0
6	Ag_2CO_3 (2)	none	83
7	Ag_2CO_3 (1)	none	25[d]
8	$AgPF_6$ (2)	none	12
9	$AgPF_6$ (2)	**L1**	27
10	$AgPF_6$ (2)	**L2**	16
11	$AgPF_6$ (2)	**L3**	13
12	$AgPF_6$ (2)	**L1**+**11**	62
13	$AgPF_6$ (2)	**L2**+**11**	44
14	$AgPF_6$ (2)	**L3**+**11**	18

Reaction conditions: **9a** (0.10 mmol) and Ag catalyst (1-2 mol% on Ag atom) in CH_3CN (0.5 mL) at 80 °C for 15 h. **11**: 1-Phenylimidazole. [a]Yield was determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. [b]Isolated yield. [c]Reaction over 50 h. [d]Reaction over 30 h.



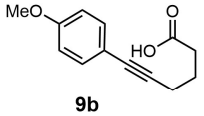
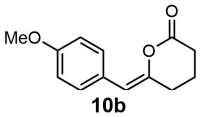
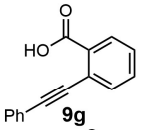
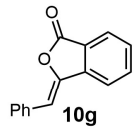
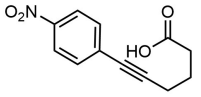
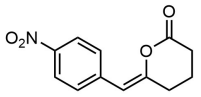
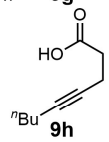
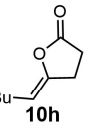
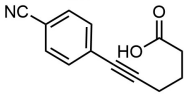
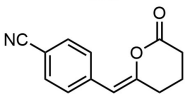
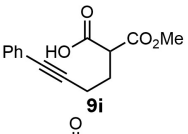
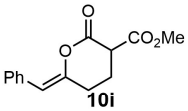
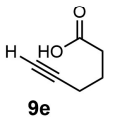
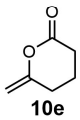
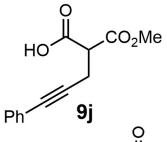
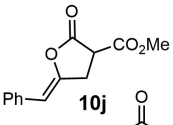
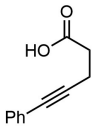
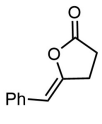
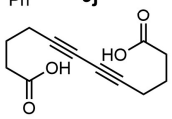
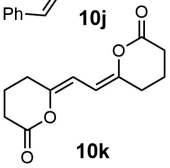
The catalyst loading could be reduced to 1 mol% on the Ag atom using **8a** as the catalyst for the reaction of **9a** over an extended reaction time (50 h) with the product yield nearly unchanged (Table 1, entry 2). In contrast, the reaction of **9a** catalyzed by the reduced amount of Ag_2CO_3 (1 mol% Ag) remained at only 25% even with the extended reaction time (entry 7). A time-course profile for the Ag_2CO_3-catalyzed reaction indicated that Ag_2CO_3 was more active than **8a** but lost its activity at 10 h (see Supporting Information for time-yield profiles). Thus, the NHC ligand (**8a**) with the basic pendant is useful for maintaining the activity of the cationic silver catalyst.

With the optimal conditions in hand using **8a** as the acid-base cooperative catalyst, the scope of alkyne-tethered carboxylic acids (**9**) was explored (Table 2). Both electron-donating (-OMe; **9b**) and withdrawing groups (-NO_2 and -CN: **9c**,**d**) were competent substituents at the *para* position of the aromatic ring of the phenylacetylene derivatives to afford the cyclized products **10b**–**d** in high yields (94–99%, entries 1-3). Terminal alkyne **9e** was less reactive (25%, entry 4). 5-Phenyl-4-pentynoic acid (**9f**) underwent 5-*exo*-*dig* cyclization with exclusive regio- and stereoselectivities to produce (*Z*)-γ-benzylidenebutyrolactone (**10f**) in 93% yield (entry 5). The reaction of 2-(phenylethynyl)benzoic acid (**9g**) occurred preferentially in 5-*exo*-*dig* cyclization mode to afford (*Z*)-3-benzylideneisobenzofuran-1(3*H*)-one (**10g**) as the major product, while the competitive 6-*endo*-*dig* cyclization formed the corresponding δ-lactone (1%) as an inseparable by-product (entry 6). 4-Nonynoic acid **9h** was transformed to an *E*/*Z* mixture (13/87) of the corresponding γ-lactone **10h** in 88% yield (entry 7). Similar erosion of stereoselectivity on the cyclization of **9h** was reported for other silver(I) and gold(I) catalytic systems.[9b,18] Monomethyl malonate derivatives **9i** and **9j** were suitable substrates for the *exo* cyclization, giving the corresponding six- (**10i**) and five-membered (**10j**) lactones in 87% and 84% yields, respectively (entries 8 and 9). Twofold cyclization of dodeca-5,7-diynedioic acid **9k** occurred cleanly to furnish the bislactone **10k** in 98% yield (entry 10).

To gain insight into the reaction mechanism, the interactions between **8a** and **9a** were investigated by ^1H NMR titration with varying amounts of carboxy-tethered alkyne **9a** (**9a**/Ag: 0–4 equiv) in CD_3CN at 25 °C. Only a trace of cyclization was observed at this temperature. Upon addition of the alkyne (**9a**), signals for a new species appeared and their intensities

increased gradually as the **9a**/Ag ratio increased (see Supporting Information for details of the titration). Figure 2 shows aromatic regions of the spectra of **8a** in CD_3CN and the mixture of **8a** and **9a** at **9a**/Ag = 4, where the ratio between the new species and **8a** is 19:81. [19] The most significant spectral change upon addition of **9a** is the downfield shift of the signals arising from the imidazole pendant. This is likely due to protonation of the imidazole at the N(4) atom by the carboxyl group of **9a**, resulting in dissociation of the intermolecular N–Ag interactions and monomerization of the silver complex. Since no significant chemical shift change was observed at the propargylic methylene protons of **9a**, its alkyne moiety should be virtually uncoordinated with the silver atom. Instead, coordination of CD_3CN to the vacant site of the silver atom is reasoned (see Supporting Information for ^{1}H NMR titrations). [20]

Table 2. Cyclization of Alkyne-Tethered Carboxylic Acids (**9**) Catalyzed by **8a**

entry	substrate	product	yield	entry	substrate	product	yield
1	 **9b**	 **10b**	98%	6	 **9g**	 **10g**	97%[b]
2	 **9c**	 **10c**	99%	7	 **9h**	 **10h**	88% (E/Z=13/87)
3	 **9d**	 **10d**	94%	8	 **9i**	 **10i**	87%
4	 **9e**	 **10e**	25%[a]	9	 **9j**	 **10j**	84%
5	 **9f**	 **10f**	93%	10	 **9k**	 **10k**	98%

Reaction conditions: **9** (0.1 mmol) and **8a** (0.001 mmol, 2 mol% on Ag atom) in CH_3CN (0.5 mL) at 80 ºC for 15 h. [a]Determined by ^{1}H NMR analysis using phenanthrene as an internal standard due to the volatility of the product. [b]Including 1% of 3-phenyl-1*H*-isochromen-1-one.

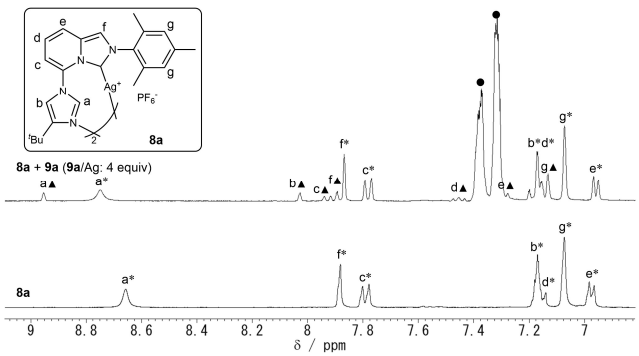


Figure 2. ^{1}H NMR spectra of **8a** (bottom) and **8a**+**9a** (**9a**/Ag: 4 equiv) (top). *: **8a**; ●: **9a**; ▲: new species.

Density functional theory (DFT) calculations were conducted to investigate the mechanism of the Ag-catalyzed cyclization. The geometry optimizations as well as frequency calculations were performed at the M06/lanl2dz (for silver) and 6-31+G(d,p) (for other elements) levels of theory[21,22] using Gaussian 16, [23] and the solvation effect of acetonitrile was introduced using the CPCM model. [24] The relative energies were corrected for the Gibbs free energies and given in kcal mol^{-1} (Figure 3).

A mononuclear silver-alkyne π complex (**Int-A**) with an interaction between imidazole and the carboxylic acid is proposed as a plausible precursor for the cyclization. Nucleophilic *anti*-attack of the carboxy group to the alkyne moiety in the 6-*exo*-*dig* mode occurs through **TS-A** to form a six-membered lactone (**Int-B**) hydrogen-bonded with the protonated imidazole moiety. This step has an energy barrier of 21.4 kcal/mol and is 15.7 kcal mol^{-1} endothermic. After dissociation of the hydrogen bond leading to the more stable intermediate **Int-C**, protonation of the Ag–C bond through **TS-B** gives the lactone (**Int-D**) π-coordinated to the Ag atom at the *exo* alkene moiety. These results support our expectation that the Brønsted base moiety of the NHC ligand would participate cooperatively in the silver-catalyzed cyclization of the alkyne-tethered carboxylic acid.

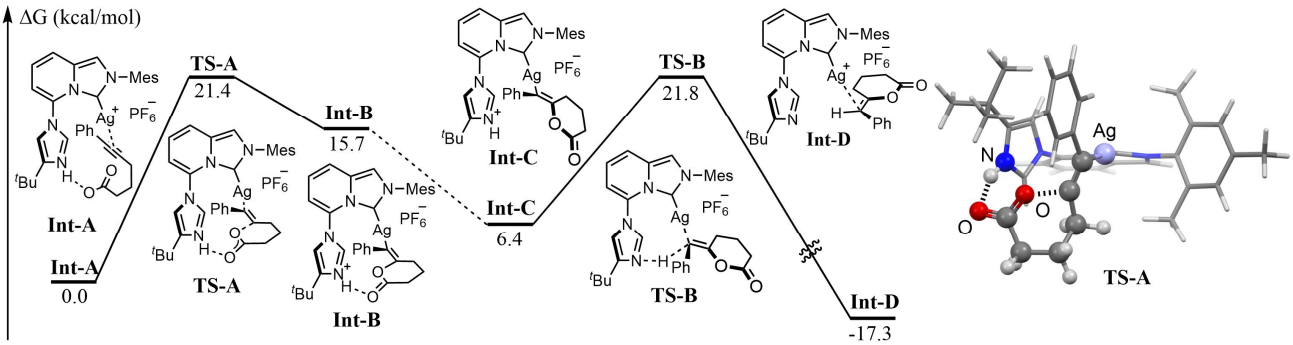


Figure 3. Energy diagram for cyclization of **9a** catalyzed by silver complex **8a**. Calculations were performed at M06/ lanl2dz (for silver) and 6-31+G(d,p) (for other elements) levels of theory. The counter anion (PF_6^-) of 3D model of **TS-A** is omitted for clarity.

In conclusion, we synthesized neutral and cationic silver(I) complexes with 5-(4-*(tert*-butyl)-1*H*-imidazol-1-yl)-imidazo[1,5-*a*]pyridin-3-ylidene ligands. Single-crystal XRD analysis showed that the neutral and cationic complexes existed as monomers or dimers. The cationic silver complexes showed catalytic activity for the cyclization of alkyne-tethered carboxylic acids. NMR experiments and DFT calculations indicated that an *in situ* generated monomeric cationic silver complex with an imidazole pendant acts as a cooperative Lewis acid-base catalyst. Exploration toward the development of other cooperative NHC-metal catalysis is underway.

Experimental Section

General Procedure for Silver-Catalyzed Cyclization of 9

In a nitrogen-filled glove box, alkynoic acid (**9**, 0.1 mmol) was placed in a vial containing a magnetic stirring bar. A solution of cationic silver complex **8a** (1.2 mg, 0.001 mmol, 2 mol% on Ag) in dry CH_3CN (0.5 mL) was added to the vial, and the vial was sealed with a screw-cap and removed from the glove box. After stirring at 80 °C for 15 hours, the mixture was cotton-filtered, and the resulting solution was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography to afford alkylidenelactone **10**.

Crystal Structures

CCDC-2045683-2045686 for **7a**, **7b**, **8a**, and **8b** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

This work was supported by JSPS KAKENHI Grant No. JP20K15268 in Grant-in-Aid for Early-Career Scientists to K.H. and No. JP18H03906 in Grant-in-Aid for Scientific Research (A) to M.S.

References

[1] a) W. A. Herrmann, C. Köcher, *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2162–2187; b) W. A. Herrmann, *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309; c) C. M. Crudden, D. P. Allen, *Coord. Chem. Rev.* **2004**, *248*, 2247–2273; d) O, Kühl, *Chem. Soc. Rev.* **2007**, *36*, 592–607; e) F. E. Hahn, M. C. Jahnke, *Angew. Chem., Int. Ed.* **2008**, *47*, 3122–3172; f) M. H. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485-496.

[2] M. Alcarazo, S. J. Roseblade, A. R. Cowley, R. Fernández, J. M. Brown, J. M. Lassaletta, *J. Am. Chem. Soc.* **2005**, *127*, 3290–3291.

[3] C. Burstein, C. W. Lehmann, F. Glorius, *Tetrahedron* **2005**, *61*, 6207–6217.

[4] a) M. Espina, I. Rivilla, A. Conde, M. M. Díaz-Requejo, P. J. Pérez, E. Álvarez, R. Fernández, J. M. Lassaletta, *Organometallics* **2015**, *34*, 1328–1338; b) Y. Kim, Y. Kim, M. Y. Hur, E. Lee, *J. Organomet. Chem*. **2016**, *820*, 1–7; c) D.-A. Park, J. Y. Ryu, J. Lee, S. Hong, *RSC Adv.* **2017**, *7*, 52496–52502; d) M. Kashihara, R.-L. Zhong, K. Semba, S. Sakaki, Y. Nakao, *Chem. Commun*. **2019**, *55*, 9291–9294; e) X. Yi, K. Chen, J. Guo, W. Chen, W. Chen, *Adv. Synth. Catal.* **2020**, *362*, 4373–4377.

[5] a) C. Grohmann, T. Hashimoto, R. Fröhlich, Y. Ohki, K. Tatsumi, F. Glorius, *Organometallics* **2012**, *31*, 8047–8050; b) E. Y. Tsui, T. Agapie, *Polyhedron* **2014**, *84*, 103–110; c) R. Nakao, K. Nozaki, *J. Am. Chem. Soc*. **2015**, *137*, 10934–10937; d) W. Tao, R. Nakano, S. Ito, K. Nozaki, *Angew. Chem., Int. Ed.* **2016**, *55*, 2835–2839; e) W. Tao, S. Akita, S. Ito, Y. Hoshimoto, S. Ogoshi, K. Nozaki, *Chem. Commun.* **2017**, *53*, 2630–2633; f) G. Liu, C. Liu, F. Han, Z. Wang, J. Wang, *Tetrahedron Lett.* **2017**, *58*, 726–731; g) K. Azouzi, C. Duhayon, I. Benaissa, N. Lugan, Y. Canac, S. Bastin, V. César, *Organometallics* **2018**, *37*, 4726–4735.

[6] a) F. Grande-Carmona, J. Iglesias-Sigüenza, E. Álvarez, E. Díez, R. Fernández, J. M. Lassaletta, *Organometallics* **2015**, *34*, 5073–5080; b) C. T. Check, K. P. Jang, C. B. Schwamb, A. S. Wang, M. H. Wang,

K. A. Scheidt, *Angew. Chem., Int. Ed.* **2015**, *54*, 4264–4268; c) J. Iglesias-Sigüenza, C. Izquierdo, E. Díez, R. Fernández, J. M. Lassaletta, *Dalton. Trans.* **2016**, *45*, 10113-10117; d) J.-Q. Zhang, Y. Liu, X.-W. Wang, L. Zhang, *Organometallics* **2019**, *38*, 3931–3938; e) C. A. Swamy P, A. Varenikov, G. de Ruiter, *Chem. Eur. J.* **2020**, *26*, 2333–2337.

[7] a) A. Fürstner, M. Alcarazo, H. Krause, C. W. Lehmann, *J. Am. Chem. Soc.* **2007**, *129*, 12676–12677; b) S. J. Roseblade, A. Ros, D. Monge, M. Alcarazo, E. Álvarez, J. M. Lassaletta, R. Fernández, *Organometallics* **2007**, *26*, 2570–2578; c) M. Alcarazo, T. Stoke, A. Anoop, W. Thiel, A. Fürstner, *Angew. Chem., Int. Ed.* **2010**, *49*, 2542–2546; d) Y. Tang, I. Benaissa, M. Huynh, L. Vendier, N. Lugan, S. Bastin, P. Belmont, V. César, V. Michelet, *Angew. Chem., Int. Ed.* **2019**, *58*, 7977–7981; S. Byun, H. Seo, J.-H. Choi, J. Y. Ryu, J. Lee, W. Chung, S. Hong, *Organometallics* **2019**, *38*, 4121–4132.

[8] a) H. Nogami, M. Kanai, M. Shibasaki, *Chem. Pharm. Bull.* **2003**, *51*, 702–709; b) D. H. Paull, C. J. Abraham, M. T. Scerba, E. Alden-Danforth, T. Lectka, *Acc. Chem. Res.* **2008**, *41*, 655–663; c) E. L. Margelefsky, R. K. Zeidan, M. E. Davis, *Chem. Soc. Rev.* **2008**, *37*, 1118–1126; d) D. W. Stephan, *Acc. Chem. Res.* **2015**, *48*, 306–316; e) S. Afewerki, A. Córdova, *Chem. Rev.* **2016**, *116*, 13512–13570; f) G. J. Knox, L. S. Hutchings-Goetz, C. M. Pearson, T. N. Snaddon, *Top. Curr. Chem.* **2020**, *378*, 16.

[9] Silver-catalyzed cyclization of alkynoic acids, see: a) K. Schötz, T. Clark, H. Schaller, P. von R. Schleyer, *J. Org. Chem.* **1984**, *49*, 735–736; b) P. Pale, J. Chuche, *Tetrahedron Lett.* **1987**, *28*, 6447–6448; c) V. Dalla, P. Pale, *Tetrahedron Lett.* **1994**, *35*, 3525–3528; d) J. A. Marshall, M. A. Wolf, E. M. Wallace, *J. Org. Chem.* **1997**, *62*, 367–371; e) R. Rossi, F. Bellina, C. Bechini, L. Mannina, P. Vergamini, *Tetrahedron* **1998**, *54*, 135–156; f) V. Dalla, P. Pale, *New. J. Chem.* **1999**, *23*, 803–805; g) F. Bellina, D. Ciucci, P. Vergamini, R. Rossi, *Tetrahedron* **2000**, *56*, 2533–2545; h) T. Yoshikawa, M. Shindo, *Org. Lett.* **2009**, *11*, 5378–5381; i) R. Nolla-Saltiel, E. Robles-Marín, S. Porcel, *Tetrahedron Lett*. **2014**, *55*, 4484–4488; j) I. J. Barve, T. U. Thikekar, C.-M. Sun, *Org. Lett.* **2017**, *19*, 2370–2373.

[10] For cyclization of alkynoic acids catalyzed by acid-base cooperative catalysts, see: a) N. Á. Espinosa-Jalapa, D. Ke; N. Nebra, L. L. Goanvic, S. Mallet-Ladeira, J. Monot, B. Martin-Vaca, D. Bourissou, *ACS Catal.* **2014**, *4*, 3605–3611; b) J. Monot, P. Brunel, C. E. Kefalidis, N. Á. Espinosa-Jalapa, L. Maron, B. Martin-Vaca, D. Bourissou, *Chem. Sci.* **2016**, *7*, 2179–2187.

[11] A. K. Verma, J. Singh, V. K. Sankar, R. Chaudhary, R. Chandra, *Tetrahedron Lett.* **2007**, *48*, 4207–4210.

[12] A. Fürstner, M. Alcarazo, V. César, C. W. Lehmann, *Chem. Commun.* **2006**, 2176–2178.

[13] J. C. Garrison, W. J. Youngs, *Chem. Rev.* **2005**, *105*, 3978–4008.

[14] a) P. de Frémont, N. M. Scott, E. D. Stevens, T. Ramnial, O. C. Lightbody, C. L. B. Macdonald, J. A. C. Clyburne, C. D. Abernethy, S. P. Nolan, *Organometallics* **2005**, *24*, 6301–6309; b) H.-L. Su, L. M. Pérez, S.-J. Lee, J. H. Reibenspies, H. S. Bazzi, D. E. Bergbreiter, *Organometallics* **2012**, *31*, 4063–4071.

[15] In the $^{13}C\{^{1}H\}$ NMR spectra of the neutral AgCl complexes **7a** and **7b** in CD_2Cl_2, resonances for the carbene carbon were not observed. This is likely due to line-broadening of the signals, reflecting labile nature of the coordination of the carbene carbon atom to the Cl-bound silver atom. See: M. E. Garner, W. Niu, X. Chen, I. Ghiviriga, K. A. Abboud, W. Tan, A. S. Veige, *Dalton. Trans.* **2015**, *44*, 1914–1923.

[16] 1,3-Dimesitylimidazol-2-ylidene (IMes) was purchased from Sigma-Aldrich Co. LLC: A. J. Arduengo III, H. V. R. Dias, R. L. Harlow, M. Kline, *J. Am. Chem. Soc.* **1992**, *114*, 5530–5534.

[17] 1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) was purchased from Tokyo Chemical Industry Co.: A. J. Arduengo III, R. Krafczyk, R. Schmutzler, *Tetrahedron* **1999**, *55*, 14523–14534.

[18] a) H. Harkat, J.-M. Weibel, P. Pale, *Tetrahedron Lett.* **2006**, *47*, 6273-6276; b) H. Harkat, A. Y. Dembelé, J.-M. Weibel, A. Blanc, P. Pale, *Tetrahedron* **2009**, *65*, 1871-1879.

[19] The apparent chemical shift change was observed for H_a* upon the addition of **9a**. It may be due to weak interaction between H_a* and **9a**.

[20] ^{1}H NMR titration of **8a** with benzoic acid in CD_3CN produced new signals similar to those detected in the titration of **8a** with **9a** in CD_3CN. In contrast, no new species appeared in the titration of **8a** with benzoic acid in CD_2Cl_2. This suggests that acetonitrile coordinates to the cationic silver complex, facilitating the monomerization of the complex with simultaneous protonation of the imidazole moiety. This behavior is consistent with the low catalytic activity of **8a** in toluene, 1,4-dioxane, and 1,2-dichloroethane.

[21] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215–241.

[22] a) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299–310; b) R. Ditchfield, W. J. Hehre, J. A. Pople, *J. Chem. Phys*. **1971**, *54*, 724–728; c) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257-2261; d) P. C. Hariharan, J. A. Pople, *Theoret. Chim. Acta.* **1973**, *28*, 213–222.

[23] Gaussian 16, Revision C.01: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J.

Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2019.

[24] V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995–2001.

Use of Imidazo[1,5-*a*]pyridin-3-ylidene as a Platform for Metal-Imidazole Cooperative Catalysis: Silver-Catalyzed Cyclization of Alkyne-Tethered Carboxylic Acids

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Vishal Kumar Rawat, Kosuke Higashida,* Masaya Sawamura*