

Synthesis and theoretical studies of gallium complexes back-shielded by a cage-shaped framework of tris(*m*-oxybenzyl)arene†

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Cage-shaped gallium complexes with a back-shielding framework of tris(*m*-oxybenzyl)arene were synthesized, their bottom arene rings tuned their characteristic Lewis acidity, which was supported by theoretical calculation as well as catalytic application in a hetero Diels–Alder reaction.

The chemistry of Lewis acids has been developed quite extensively because of their effective activation of reactant reagents.¹ A representative class of Lewis acids contains group 13 elements because they have a vacant p-orbital to contribute to an accepting basic substrate.² Recently, we designed tris(*o*-hydroxyphenyl)methane **1H₃** and tris(*o*-hydroxyphenyl)silane **2H₃** as ligands to synthesize cage-shaped borates **1B** and **2B** (Scheme 1a).^{3,4} The cage-shaped geometry created a highly accessible vacant molecular orbital (MO) on boron in **1B** and **2B** and enhanced catalytic activity. We expected this cage-shape concept to lend a greater advantage for larger group 13 metal compounds. In contrast to boron complexes, the open shape of ML₃, having either a Ga or an In center, has four, or more, coordinated spheres⁵ and easily accepts an external ligand (L_{ex}) to lower the Lewis acidity (Scheme 2a). That is a disadvantage for activation of the substrate as a Lewis acid. It was suggested that the cage-shaped framework could overcome this problem by inhibiting the external ligand (L_{ex}) coordination (Scheme 2b). Herein, we report a new type of cage-shaped gallium complex, **3aGa**, with a back-shielding framework (Scheme 1b) and interesting properties.

First, we attempted to synthesize cage-shaped gallium complexes with the previously reported ligands **1H₃** and **2H₃**, but no desired complexes were obtained due to their narrow space. Therefore, we designed new ligands **3H₃**, as shown in Scheme 3, in which three oxybenzyl moieties were linked to a benzene ring.⁶ The Cu(I)-catalyzed coupling between the Grignard reagent **4a** and 1,3,5-tris(bromomethyl)benzene **5a** gave the compound **6a** bearing three *m*-methoxybenzyl moieties. Treatment of **6a** with BBr₃ afforded the compound **3aH₃**. Three more types of **3b–dH₃** derivatives bearing substituents on benzene rings were similarly synthesized. The reaction of **3aH₃** with GaCl₃ in the presence of pyridine gave the cage-shaped

gallium complex **3aGa·Py**.⁷ In the ¹H NMR of **3aGa·Py**, the upfield-shift of the proton at the *m*- and *p*-positions of the oxygen moiety relative to that of **3aH₃** was confirmed (*m*-position, 7.15 → 7.07 ppm; *p*-position, 6.78 → 6.68 ppm). Analogous results for spectral analysis were obtained for **3b–3dGa·Py**.

The structure of gallium complex **3bGa·Py** was analyzed by X-ray crystallography.⁸ Considering the occupancy factor of the gallium atom was 0.44, the refinement of the crystal structure was carried out successfully by using disorder modeling. We think that a part of the complex was decomposed by pyridine hydrochloride during recrystallization because it took several months to obtain a crystal which was suitable for X-ray analysis. The structure shown in Fig. 1 supports the generation of **3bGa·Py**. The top view shows that the Ga atom lies above the center of the benzene ring (Fig. 1b). The average lengths of the Ga–O bond, 3.06 Å, and of the Ga–N1 bond, 3.28 Å, were considerably longer than usual (1.94 Å and 2.02 Å, respectively),⁹ because of a deficiency of *ca.* half the gallium atoms in the crystal.

Theoretical calculations were performed to investigate the properties of the cage-shaped gallium complex, **3bGa**, in comparison with the open-shaped one, Ga(OPh)₃, **7**, using the hybrid density functional theory B3PW91/6-31+G(d,p) method with the Gaussian 03 program.¹⁰ The stabilization energies in pyridine complexation reveal that the back-shielding effect of the cage-shaped structure should be effective for keeping Lewis acidity high (Scheme 4). The open-shaped gallium complex **7·Py** coordinated by pyridine has a stabilization energy of 39.2 kcal mol⁻¹ (*path a*), and coordination of the second pyridine leads to additional stabilization of 14.2 kcal mol⁻¹ (*path b*), as shown in Scheme 4a. These results show that the second ligand coordination-dissociation step (*path b*) mainly contributes to Lewis acidity. However, the cage-shaped gallium complex, **3bGa**, disturbs the second coordination to get one stabilization energy of 39.3 kcal mol⁻¹ that contributes to Lewis acid-mediated reactions (*path c*), as shown in Scheme 4b. This is the reason the cage-shaped complex has high potential as a Lewis acid.

The optimized structures and the MO diagrams of **3bGa**, **7** and **7·Py** are shown in Scheme 5.¹¹ The complex **3bGa** has a

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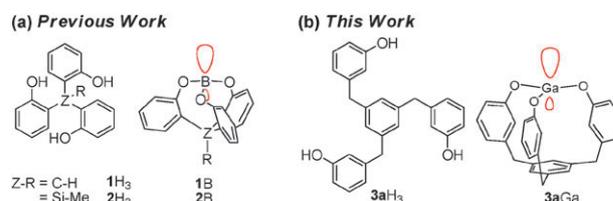
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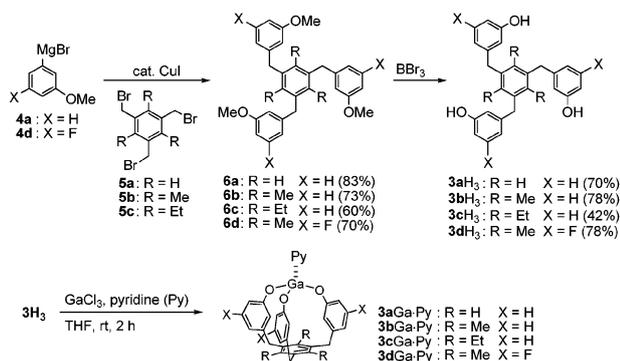
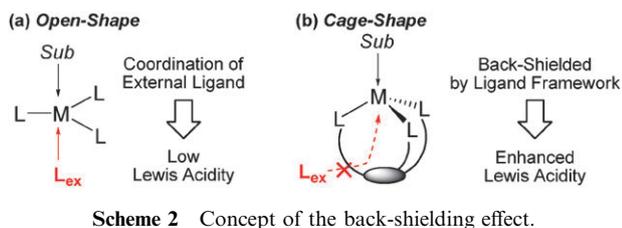
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Scheme 1 Cage-shaped metal complexes and their ligands.



Scheme 3 Preparation of ligands **3H₃** and their gallium complexes **3Ga-Py**.

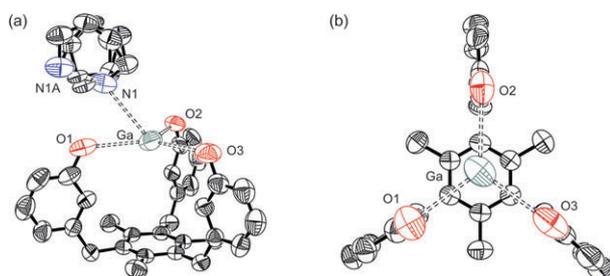
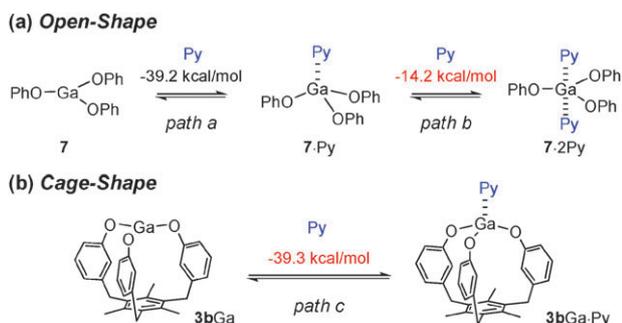
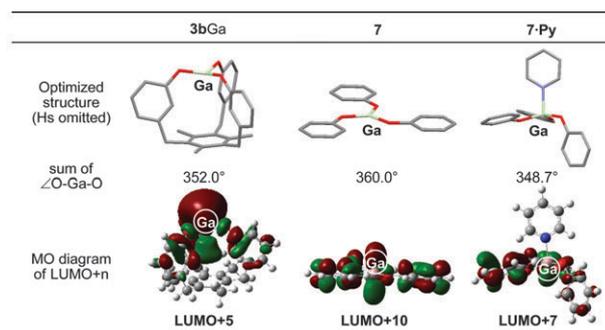


Fig. 1 ORTEP drawing of **3bGa-Py** with disorder modelled in (thermal ellipsoids are at 50% probability level. Hydrogens are omitted for clarity. The occupancy factor of the gallium atom is 0.44): (a) side view and (b) top view (pyridine is omitted for clarity).



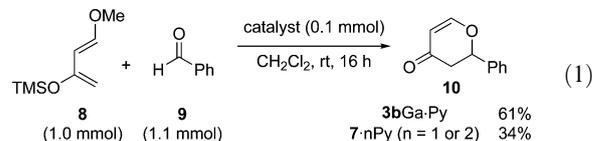
Scheme 4 Stabilization energy of **7** and **3bGa** in a pyridine complexation (Gaussian03 D.01, B3PW91/6-31+G(d,p), gas phase).

small concave geometry around gallium while **7** has a planar geometry (sum of $\angle \text{OGaO}$: **3bGa**, 352.0°; **7**, 360.0°). The diagram of the unoccupied orbital of **3bGa**, which contributes to Lewis acidity (corresponding to LUMO + *n*),¹² shows a large and accessible lobe on gallium, while the corresponding lobes in **7** and **7-Py** are small and buried. These results indicate that the MO of **3bGa** is more suited to accepting a reagent than that of either **7** or **7-Py**.

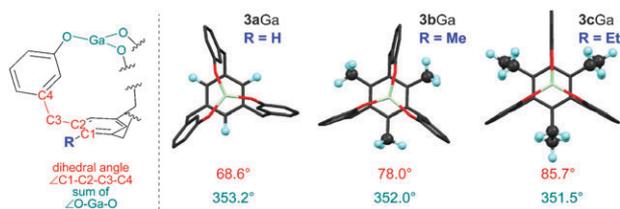


Scheme 5 Comparison of open- and cage-shaped gallium complexes (**3bGa**, **7** and **7-Py**) by first principles calculations (B3PW91/6-31+G(d,p)).

We examined the catalytic activity of the gallium complexes during the hetero Diels–Alder reaction of Danishefsky's diene **8** with benzaldehyde **9** to give pyran **10** (eqn (1)).^{13,14} The open-shaped gallium complex **7-nPy** (*n* = 1 or 2) afforded **10** in only 34% yield. In contrast, the cage-shaped gallium complex **3bGa-Py** gave **10** in a higher yield of 61%. The cage-shaped structure apparently enhanced catalytic activity of the complex.



Next, we examined the effect of the substituents on the cage-shaped gallium complexes **3a–dGa** by theoretical calculation (Scheme 6 and 7). The substituents, R, on the bottom benzene ring changed the geometry around the gallium as shown in Scheme 6. In the complex with bulky substituents, both the benzene rings of the arm and the bottom benzene ring approach a perpendicular state because of the steric hindrance between the substituents (dihedral angle (C1–C2–C3–C4): **3aGa**, 68.6°; **3bGa**, 78.0°; **3cGa**, 85.7°). The large dihedral angle of **3cGa** creates a more concave geometry around gallium than those of **3aGa** and **3bGa** (sum of $\angle \text{OGaO}$: **3aGa**, 353.2°; **3bGa**, 352.0°; **3cGa**, 351.5°). These geometric changes produce differences in the energy levels of the LUMOs and LUMOs + *n*¹² of **3a–cGa**, as shown in Scheme 7.¹⁵ These orbitals are the unoccupied orbitals to which gallium *p_z* orbitals contribute. LUMOs + *n* have upward lobes on gallium, which contribute to Lewis acidity, while LUMOs have downward lobes that are not suitable for accepting a nucleophile. The order of energy levels for LUMOs + *n*, **3aGa** < **3bGa** < **3cGa**, is reverse to that of LUMOs, **3aGa** > **3bGa** > **3cGa**. Although the reason for this relationship is not yet clear, the bulkiness of the substituents on the bottom benzene ring would finely tune the eigenvalue of the orbital to which the gallium *p_z* orbitals contribute. The pyridine-complexation energy also showed the same order for the eigenvalue of LUMO + *n*. On the other hand, the electron withdrawing character of the fluoro groups on the benzene rings of the arm led to larger pyridine-complexation energy and lower energy levels for LUMO and LUMO + *n* than for **3bGa**. These results reveal that the steric substituents on the



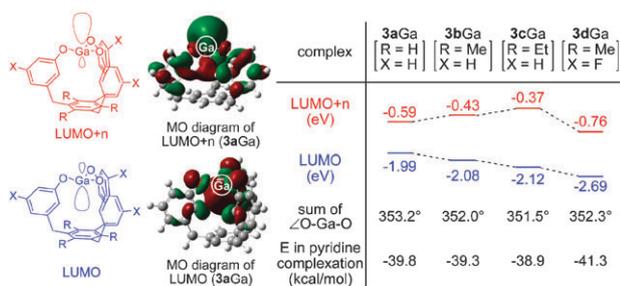
Scheme 6 Structural change caused by the substituents on the bottom benzene ring.

bottom benzene ring and the strongly electronegative substituents on the benzene arm affect the Lewis acidity of the gallium complexes.

The results of the hetero Diels–Alder reaction using the cage-shaped derivatives **3b–dGa**·Py are summarized in Table 1. The unsubstituted **3aGa**·Py gave a lower yield than the methyl-substituted **3bGa**·Py despite having almost the same pyridine complexation energy. This result suggests that methyl groups on the bottom benzene ring disturbed the inversion of the benzene rings on the arm to keep them on the same side as the gallium metal even when the Ga–O bond was cleaved, consequently preventing the decomposition of the complex. The bulkier ethyl group provided no improvement, likely due to the high energy level of its LUMO + *n*. The fluoro derivative **3dGa**·Py showed lower catalytic activity than **3bGa**·Py. The larger stabilization energy in the pyridine complexation of **3dGa** probably inhibits the release of an original pyridine and a product from the gallium metal at the start and at the end of the reaction. The generation and regeneration of an active catalyst are important in this case, and **3bGa**·Py was the best catalyst among **3a–dGa**·Py.

In summary, we synthesized gallium complexes with Lewis acidity enhanced by a cage-shaped structure. Theoretical calculations and application to a hetero Diels–Alder reaction suggest that the back-shielding framework shows promise for the high activation of carbonyl compounds. The substituents on the bottom benzene ring finely tuned the energy level and controlled the stability of the complexes.

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Scheme 7 Theoretical calculation of **3a–dGa**.

Table 1 Hetero Diels–Alder reaction using cage-shaped derivatives

Entry	Catalyst	Yield/%
1	3aGa ·Py	42
2	3bGa ·Py	61
3	3cGa ·Py	57
4	3dGa ·Py	46

^a All reaction were performed under the same conditions with eqn (1).

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- Gaussian 03, Revision D.01; Gaussian, Inc.: Wallingford CT, 2004. See ESI for the full list of authors.
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