RESEARCH ARTICLE doi.org/10.1002/adsc.70038

ADVANCED SYNTHESIS & CATALYSIS

5,7-Membered Cyclometallated Gold(III) Complexes with Pyridine-Phenyl-Oxazoline N^C^N Ligands as Catalysts for Organic Transformation Reactions Under Silver-Free Conditions

Yosephine Tania Limanto,[a] Karen Ka-Yan Kung,[a] Aries Kwok-Heung Chan,[a] Nathanael Chun-Him Lai,[a,*] and Man-Kin Wong[a,*]

[a] State Key Laboratory of Chemical Biology and Drug Discovery, Research Institute for Future Food, Department of Food Science and Nutrition, The Hong Kong Polytechnic University, Hung Hom, Hong Kong, China
E-mail: chnathanael.lai@polyu.edu.hk; mankin.wong@polyu.edu.hk

Manuscript received: March 7, 2025; Revised manuscript received: June 23, 2025;
Version of record online: August 21, 2025

Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.70038

Abstract: A series of 5,7-membered cyclometallated gold(III) complexes with N^C^N tridentate ligands are developed as catalysts, which are prepared *via* transmetalation of pyridine-phenyl-oxazoline ligand-containing organomercury compounds with potassium gold(III) chloride ($KAuCl_4$) with up to 86% yields. Investigation on the synthesis and catalytic activity of the newly developed gold(III) complexes under silver-free conditions results in >90% conversion for propargylamines and up to >99% conversion for bifunctional modification of oligosaccharides *via* three-component (A^3)-coupling reactions. Employment of the tridentate gold(III) complexes also successfully catalyzes the carboalkoxylation reaction of acetal alkynes. These results reveal potential applications of such 5,7-membered tridentate gold(III) complexes as catalysts for organic transformation reactions and modification of biomolecules.

Keywords: bioconjugations, oligosaccharides, silver-free gold catalysis, three-component coupling, tridentate gold(III) complexes

1. Introduction

Gold catalysis has contributed to a diversity of novel organic transformations and bioconjugations, owing to its superior reactivity and excellent selectivity, with excellent compatibility and functional group tolerance in aqueous medium and mild reaction conditions.[1] Gold complexes are powerful synthetic tools and versatile catalysts toward the π-activation of unsaturated C—C bonds for nucleophilic attack, cross-coupling reactions, oxidative reactions, and photoredox reactions.[2]

Gold(I) complexes exhibit a linear geometry, whereas gold(III) complexes possess a square planar geometry with four coordination sites. The structural differences between gold(I) and gold(III) species remain a significant challenge for ligand design to tune the stability and catalytic activity of gold complexes.[3] With the structural uniqueness of the gold(III) complexes,[4] the use of bidentate chelating ligands for cyclometallated gold(III) complexes with damp,[5] pyridines,[6] quinolines,[6d–e,7] oxazolines,[8] binaphthols (BINOLs),[9] and other aromatic compounds[10] has been reported. For tridentate chelating cyclometallated gold(III) complexes, C^N^C and C^N^N pincer ligands have been established as effective ligands to bind gold(III) species for catalysis, anticancer therapeutics, fluorescent/luminescent imaging, and photochemical reactions.[11] However, the catalytic activity and applications of

gold(III) complexes with N^C^C and N^C^N tridentate ligands remain largely unexplored.[11a,12]

Moreover, a variety of transition metal complexes feature two fused metallacycles, which were prepared from highly symmetrical "ABA"-type ligands to give 5,5- or 6,6-membered rings, and rarely reported 7,7-membered metallacycles (**Figure 1**).[13] However, metallacycles with unsymmetrical tridentate ligands that feature mixed donor atoms or varying ring sizes have been merely studied (i.e., "ABC" type).

For N^C^N tridentate gold(III) complexes, most of the reported gold(III) species adopt either symmetrical 5,5- or 6,6-membered rings (**Figure 2**a).[12,14] Given the scarcity of N^C^N ligands and unsymmetrical tridentate ligands for gold(III) complexes, it is of great importance to develop novel unsymmetrical N^C^N ligands *via* a modular approach with facile ligand design to employ gold(III) complexes as versatile catalysts for organic transformation reactions and bioconjugation.

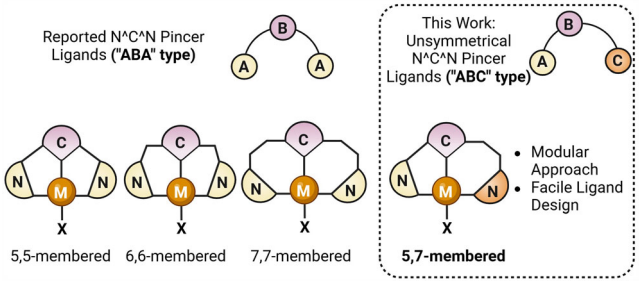


Figure 1. Schematic representation of transition metal complexes with N^C^N pincer ligands in "ABA" and "ABC" types.

In homogeneous gold catalysis, silver salts are usually required for chloride abstraction or dual gold/silver catalysis.[1a,1c,15] However, the "silver effect" may lead to undesired side reactions or interfere with the catalytic activity of gold complexes.[8b,16] Therefore, it is important to develop novel gold catalysts for organic synthesis under silver-free conditions.

Selective modification of biomolecules has become an important tool for developing novel bioconjugates, in which bioconjugation has enabled the attachment of various probes and affinity tags to biomolecules for biological studies and chemical biology research.[17] Glycans and oligosaccharides undertake a variety of vital roles in biological events in living cells, such as protein transportation and folding, inflammation, and immune responses.[18] To achieve site-specific bioconjugation reaction, carbonyl groups (i.e., aldehydes and ketones) are widely employed as bioorthogonal groups for modification of biomolecules such as oligosaccharides, proteins, glycoproteins via periodate- or oxidase-mediated oxidation of alcohols, and genetically encoded and metabolic incorporation of carbonyl-containing amino acids/monosaccharides.[17a] These carbonyl groups can then be condensed through reactions with amines, hydrazines, or aminooxy compounds to form imines, hydrazones, or oximes, respectively. However, slow reaction kinetics at neutral pH and hydrolytic instability of these adducts limit their biological utility.[17a] Therefore, anilines were used as excellent nucleophilic catalysts by Dawson *et al.* to speed up the rates of imine ligations under neutral conditions. This approach has been successfully applied for in vivo labeling of cell surfaces on sialylated glycoproteins and protein receptors.[19] While aniline catalysts enhance the rates of imine ligation, the low hydrolytic

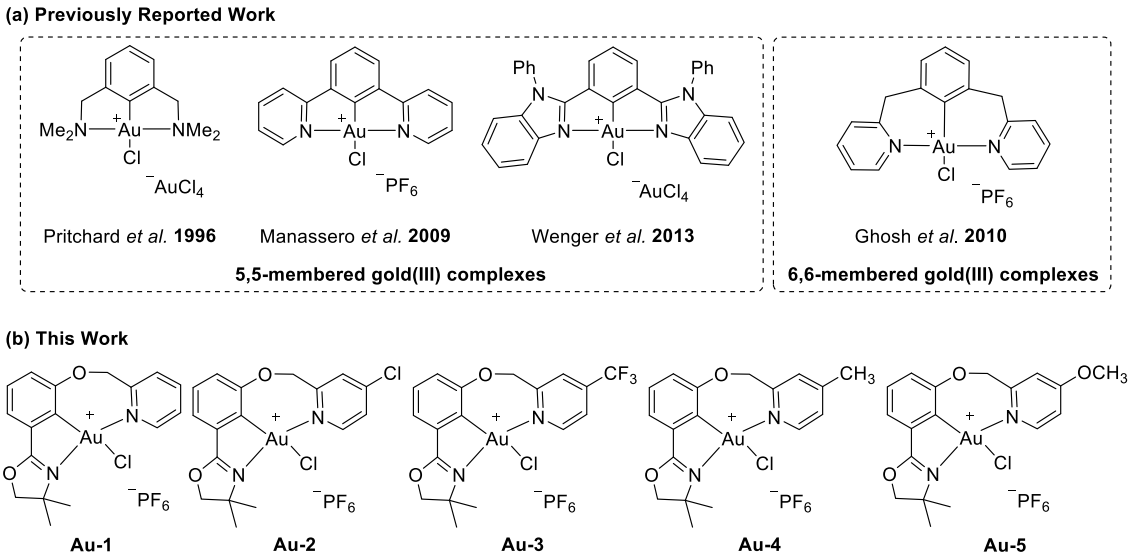


Figure 2. a) Structures of reported tridentate gold(III) complexes. b) Structures of our newly developed 5,7-membered N^C^N tridentate gold(III) complexes (**Au–1** to **Au–5**).

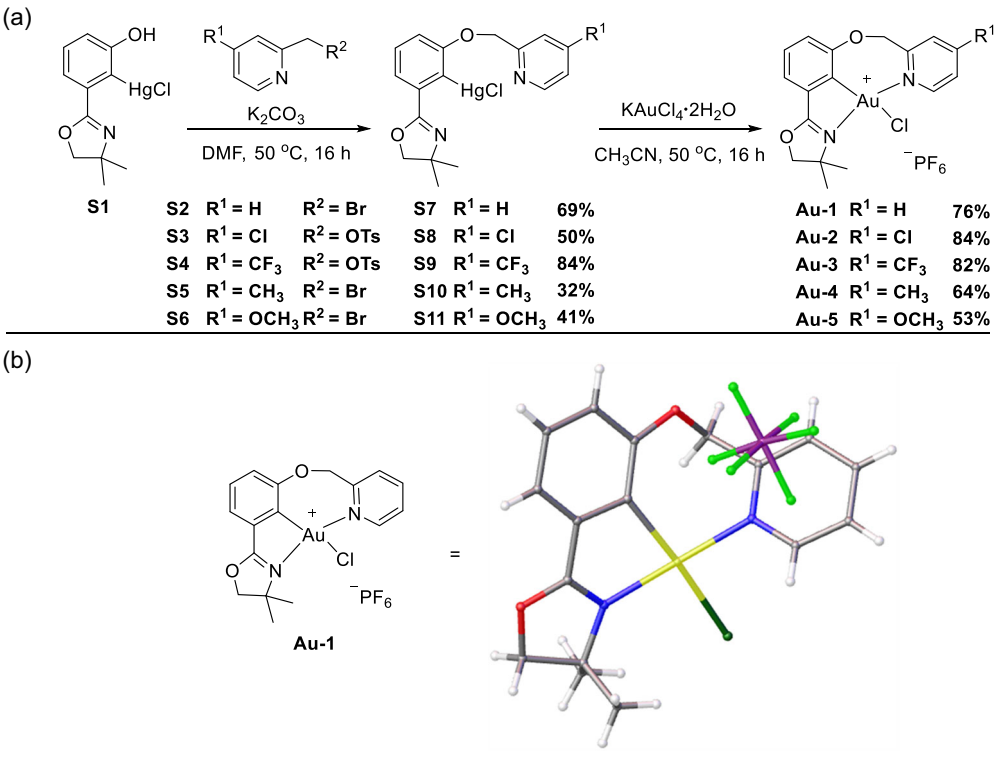
stability of imines remains a significant challenge. The inherent instability and the limitation of incorporating only one functionality per reaction continue to pose obstacles. Thus, it is highly significant to develop new methods and catalysts for selective modification of oligosaccharides. In an effort to develop new approaches for gold catalysis and bioconjugation reactions,[8b,9,20] over the past decade, our group has reported the utilization of gold(III) complexes as versatile and efficient catalysts in three-component (A^3)-coupling reaction between functionalized aldehydes, amines, and alkynes, including aldehyde-containing oligosaccharides.[7,21]

To expand the scope of N^C^N gold(III) complexes for catalysis, in this work, we report a novel series of 5,7-membered N^C^N pyridine-phenyl-oxazoline tridentate gold(III) complexes (**Au–1** to **Au–5**) as efficient catalysts for organic transformation reactions under silver-free reaction conditions (Figure 2b). Kinetic studies of the 5,7-membered gold(III) complexes were conducted, with application in oligosaccharide modification.

2. Results and Discussion

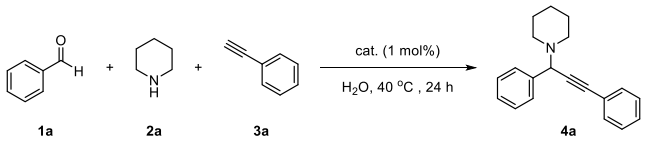
Our studies initiated by preparing the 5,7-membered tridentate ligands *via* a simple S_N2 reaction between the hydroxyl group of organomercury compound **S1** with different substituted methylpyridines that were bromylated or tosylated (**Scheme 1**a). The 5,7-membered gold(III) complexes were obtained by subsequent transmetalation reaction of the corresponding substituted organomercury compounds (**S7–S11**) with $KAuCl_4$ in moderate to good yields (53%–84%). The gold(III) complexes (**Au–1** to **Au–5**) were characterized by NMR and mass spectrometry (Supporting Information). Splitting of the oxazoline proton peaks in the ^{1}H NMR spectra of **S7–11** at δ 4.20–4.22 ppm, and the proton peaks of the 2-picolyl at δ 5.18–5.30 ppm indicated a successful cyclometallation, attaining the gold(III) complexes (Supporting Information).[22] In addition, a crystal structure obtained by X-ray crystallography of **Au–1** confirmed its square planar geometry (Scheme 1b).

To evaluate the catalytic activity of the new series of 5,7-membered gold(III) complexes (**Au–1** to **Au–5**) under silver-free reaction conditions, an A^3-coupling reaction was conducted by treatment of benzaldehyde **1a** (0.2 mmol), piperidine **2a** (1.2 equiv.), phenylacetylene **3a** (1.5 equiv.), and gold(III) catalyst (1 mol%) in H_2O for 24 h at 40 °C. A high yield of 88% of the desired propargylamine **4a** was achieved when **Au–1** was utilized (**Table 1**, entry 1). High to excellent yields of 84% to 90% of the propargylamine **4a** were acquired when **Au–2** to **Au–5** were used (entries 2–5). By comparison with the conversions of our new gold(III) complexes to a similar bidentate phenyl-oxazoline gold(III) analog, **[Au(C^N)Cl$_2$]–1** (C^N = 2-(4,4-dimethyl-4,5-dihydro-2-oxazolyl)phenyl) (entry 6), a slightly higher conversion by using our new gold(III) complexes was observed.

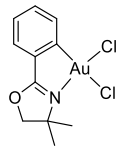


Scheme 1. a) Synthetic route of 5,7-membered gold(III) complexes. b) X-ray crystallographic structure of **Au–1**.

Table 1. Catalytic activity of 5,7-membered gold(III) complexes and **[Au(C^N)Cl_2]–1**.



1a 2a 3a 4a

Entry[a)]	Catalyst	Conversion [%][b)]
1	**Au-1**	88
2	**Au-2**	90
3	**Au-3**	87
4	**Au-4**	84
5	**Au-5**	90
6	**[Au(C^N)Cl_2]–1**	82
		
7	No catalyst	0

[a)] Reactions were carried out with benzaldehyde **1a** (0.2 mmol), piperidine **2a** (0.24 mmol), phenylacetylene **3a** (0.3 mmol), and gold(III) complex (0.002 mmol, 1 mol%) in H_2O (1 mL) at 40 °C for 24 h.
[b)] ^{1}H NMR conversion.

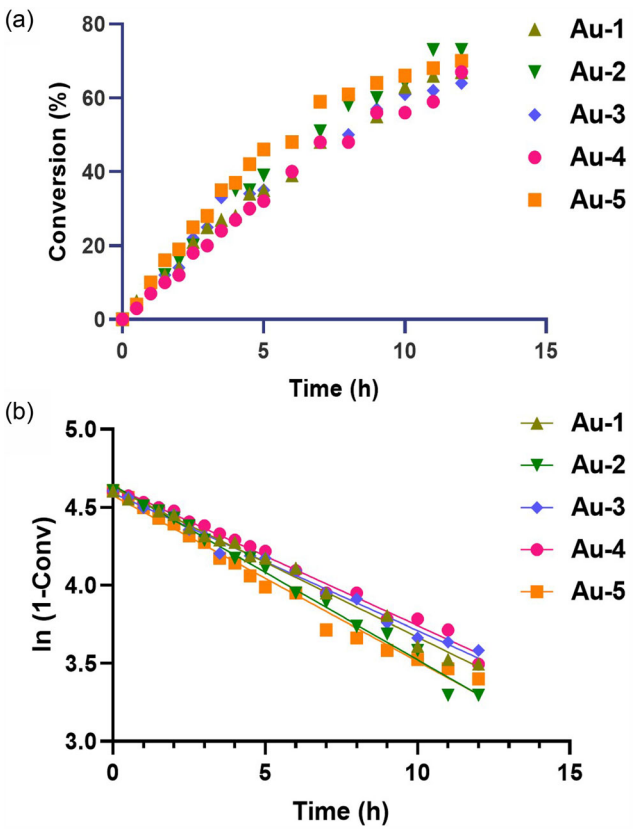


Figure 3. a) Conversion versus time graph of gold(III) catalysts in A^3-coupling reaction for the first 12 h. b) Kinetic study of gold(III) catalysts in A^3-coupling reaction for the first 12 h.

Despite the more steric environment of the tridentate ligand, the observed reactivity and efficiency of all the gold(III) complexes were comparable to the **[Au(C^N)Cl_2]–1** catalyst. No conversion was observed when no catalyst was used (entry 7), indicating that the gold(III) complexes are essential to catalyze the reactions.

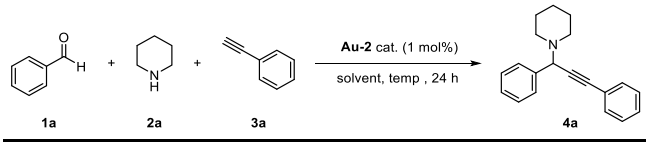
In an effort to study the electronic effect of the substituents of the gold(III) complexes on the catalytic activity, we proceeded with a kinetic study to analyze the reaction rates of the A^3-coupling reactions with catalysts **Au–1** to **Au–5**. The study was conducted under the same reaction conditions as described in Table 1.[16b,21a–b,23] An aliquot was taken out at regular time intervals to determine the conversion of benzaldehyde by ^{1}H NMR analysis, and a graph of conversion against time for the first 12 h was plotted (**Figure 3**a). Similar to a reported literature,[24] the data were fitted to first-order reaction kinetics with rate constant values of k ranging from 0.088 to 0.11 h^{-1} (Figure 3b and Table S2, Supporting Information). The yields were observed to increase up to >90% over a prolonged reaction time of 26 h (Figure S1, Supporting Information). All gold(III) complexes have similar initial reaction rates and conversions (Figure 3), indicating that substituents with strong electron-withdrawing or donating groups exert a slight effect in the reactivity of the gold(III) complexes. **Au–2** was selected for subsequent studies, owing to its higher reaction kinetics with high conversion within 12 h.

Following the study of the catalytic effect of the gold(III) complexes, optimization of **Au–2**-catalyzed A^3-coupling reaction conditions was conducted by screening different solvents. The screening of solvents in the reaction between benzaldehyde **1a** (0.2 mmol), piperidine **2a** (1.2 equiv.), and phenylacetylene **3a** (1.5 equiv.) was conducted first at 40 °C for 24 h (**Table 2**, entries 1–9) with **Au–2** (1 mol%). As shown in Table 2, the highest conversion was attained when H_2O was used (entry 1), followed by a moderate conversion of 72% when no solvent was used (entry 4).

At a lower temperature of 25 °C, the reaction proceeded smoothly to give product **4a** with 33% yield (entry 10). The high yield obtained when H_2O was utilized would be due to the "on-water" effect, wherein the formation of an oily layer above the aqueous layer was observed.[25]

With the optimized conditions at hand, the study of substrate scope was conducted using **Au–2** as catalyst (**Tables 3** and S1, Supporting Information). Apart from **4f**, variation of the aldehyde, amine, and alkyne led to the corresponding propargylamines at moderate to excellent yields. Reaction with morpholine **2b** led to a lower yield of the propargylamine **4b,** with 48% when compared to those using piperidine **2a**. Introduction of a —CH_3 group to pyrrolidine led to an increase in yield from 50% of **4c** to 75% of **4d**. The usage of the aliphatic aldehyde **1b** led to an excellent conversion of 99% of **4e**.

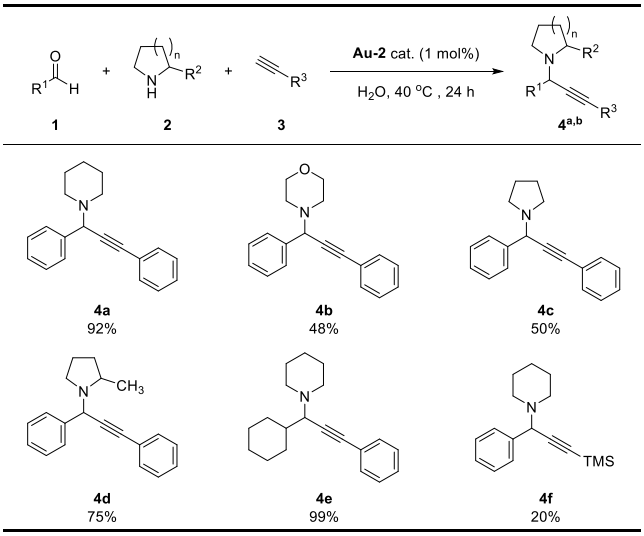
Table 2. Optimization of A^3-coupling reaction conditions.



Entry[a)]	Solvent	Temp. [°C]	Conversion [%][b)]
1	H_2O	40	92 (84)[c)]
2	DCE	40	25
3	Toluene	40	21
4	Neat	40	72
5	H_2O/DMSO (1:1)	40	<5
6	THF	40	0
7	ACN	40	0
8	H_2O/ACN (1:1)	40	9
9	EtOH	40	9
10	H_2O	25	33

[a)] Reactions were carried out with benzaldehyde **1a** (0.2 mmol), piperidine **2a** (0.24 mmol), phenylacetylene **3a** (0.3 mmol), and gold(III) complex **Au–2** (0.002 mmol, 1 mol%) in solvent (1 mL) for 24 h.
[b)] ^{1}H NMR conversion.
[c)] Isolated yield was shown in parentheses.

Table 3. Substrate scope of A^3-coupling reaction using **Au–2** as a catalyst.



[a)] Reactions were carried out with aldehyde **1** (0.2 mmol), amine **2** (0.24 mmol), alkyne **3** (0.3 mmol), and gold(III) complex **Au–2** (0.002 mmol, 1 mol%) in H_2O (1 mL) at 40 °C for 24 h.
[b)] ^{1}H NMR conversion.

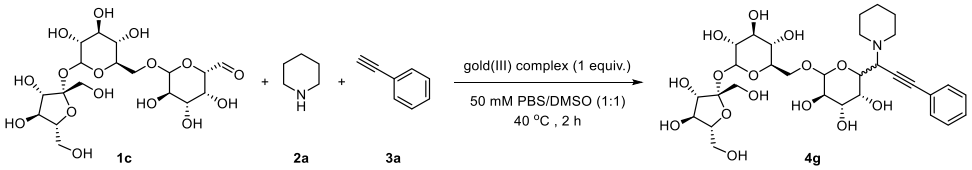
Despite the importance of the synthesis of glycoconjugates, only a limited number of studies have been reported on gold-catalyzed methods for the construction of oligosaccharides and glycoconjugates *via* an aldehyde moiety.[26] Our approach using gold(III)-catalyzed three-component coupling of aldehydes, amines, and alkynes in aqueous media addresses the forementioned limitations by enabling efficient, chemoselective, and bifunctional modification of biomolecules under mild conditions.[7,21b–c] We demonstrated the dual functionalization of unprotected oligosaccharides (i.e., D-raffinose and D-stachyose) at a single aldehyde site. This strategy is particularly attractive in glycoscience for the site-specific and dual labeling of glycans, which can facilitate the study of glycan-mediated biological processes. Our approach also allows for the installation of two distinct functionalities, potentially enabling the development of more sophisticated antibody–drug conjugates and multifunctional therapeutics for targeted drug conjugation. Additionally, the mild and aqueous-compatible reaction conditions would render this method suitable for cell surface labeling applications, where maintaining biomolecule integrity is crucial.

As part of our continuous interest in developing site-selective modification of biomolecules, we envisaged that the newly developed gold(III) complexes can be further explored for bioconjugation reactions. First, the coupling reaction of unprotected trisaccharide D-raffinose aldehyde **1c** (10 mM), piperidine **2a** (10 equiv.), and phenylacetylene **3a** (10 equiv.) using **Au–1** (1 equiv.) in 50 mM PBS (pH 7.4)/DMSO (1:1) was performed at 40 °C for 2 h. We found that the bifunctionally modified D-raffinose **4g** was obtained with 83% aldehyde conversion by LC-MS analysis of the crude reaction mixture (**Table 4**, entry 1). Up to 95% conversion of D-raffinose aldehyde **1c** was observed when **Au–2** to **Au–5** were used for bioconjugation (entries 2-5). Moreover, bifunctional modification of tetrasaccharide D-stachyose **1d** was successfully conducted using **Au–2**, affording 95% of the bifunctionally modified D-stachyose **4h** under the same conditions (Figure S3, Supporting Information).

To investigate the substrate scope, sugar aldehydes **1c** and **1d**, fluorescent dye-containing amine **2e,** and alkyne **3c** were utilized. Under the same conditions of 40 °C for 2 h, 38% to 85% conversion of bi-functionalized oligosaccharides **4i–k** were obtained using **Au–2** (Table S3, Supporting Information). An increase of the reaction temperature to 50 °C for 6 h led to a significant increase of up to >99% conversion for products **4g**, **4i–k** (**Table 5**). These results indicate that these novel 5,7-membered tridentate gold(III) complexes are highly efficient in catalyzing A^3-coupling reactions with excellent compatibility of functionalized substrates.

To further evaluate the catalytic activity of these tridentate complexes, we employed **Au–2** to catalyze the carboalkoxylation reaction of acetal alkyne **5a** (**Table 6**).[8b] The carboalkoxylation reaction was conducted at room temperature for 1.5 h. **Au–2** afforded the product 3-methoxyindanone **6a** with the highest yield of 77% (entry 1). The employment of $\mathbf{KAuCl_4 \cdot 2H_2O}$ led to a low yield of 29% while no target product was observed when **[Au(C^N)Cl$_2$]–1** was utilized (entries 2–3). Additionally, utilization of other previously reported bidentate gold(III) complexes gave lower yields of 50%–58% (entries 4–6). These results demonstrate the

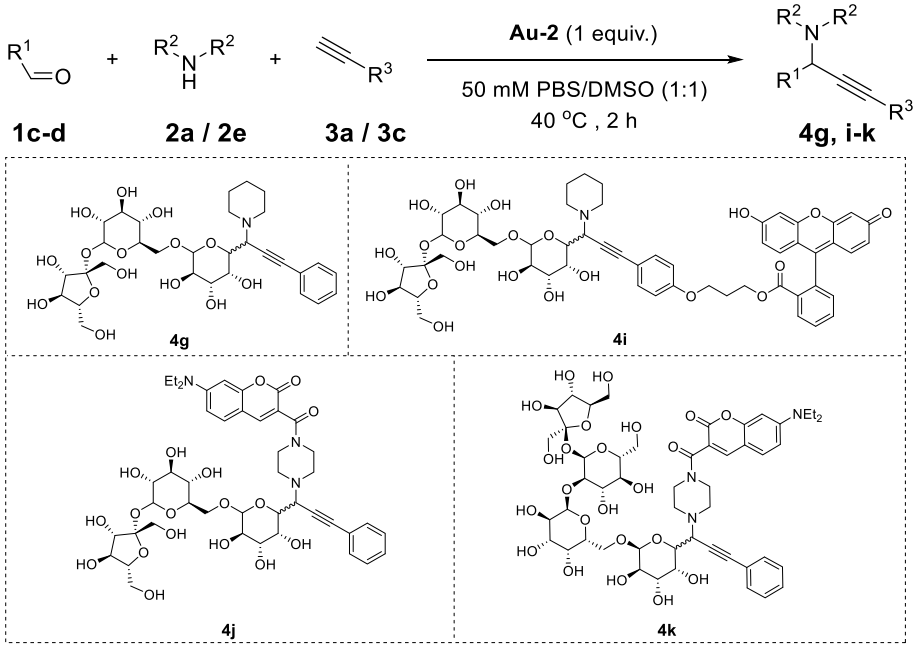
Table 4. Bifunctional modification of D-raffinose aldehyde **1c** using gold(III) complexes.



Entry[a)]	Gold(III) Complex	Conversion [%][b)]
1	**Au−1**	83
2	**Au−2**	95
3	**Au−3**	92
4	**Au−4**	87
5	**Au−5**	91
6	**[Au(C^N)Cl$_2$]−1**	95

[a)] Reactions were carried out with D-raffinose aldehyde **1c** (10 mM), piperidine **2a** (10 equiv.), phenylacetylene **3a** (10 equiv.), and gold(III) complexes (1 equiv.) in 50 mM PBS (pH 7.4)/DMSO (1:1) (90 μL) at 40 °C for 2 h.
[b)] Determined by LC-MS.

Table 5. Substrate scope for multifunctional A^3-coupling reaction.



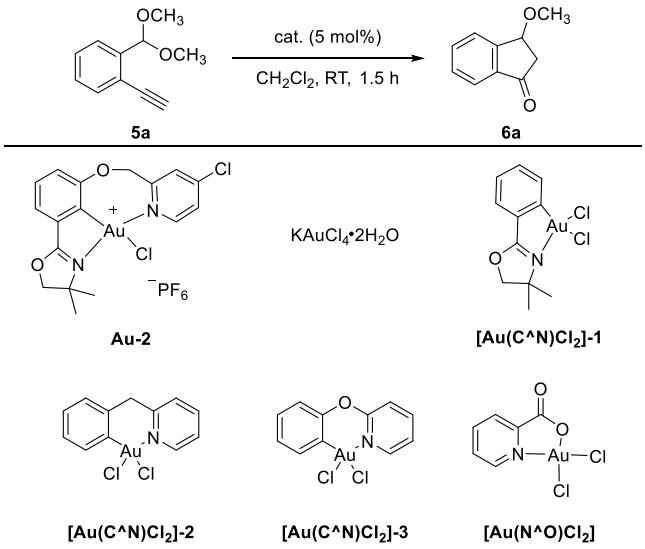
Entry[a)]	Sugar Aldehyde	Amine	Alkyne	Product	Conversion [%][b)]
1	D-raffinose aldehyde **1c**	Piperidine **2a**	Phenylacetylene **3a**	**4g**	>99
2	D-raffinose aldehyde **1c**	Piperidine **2a**	Fluorescein alkyne **3c**	**4i**	>99
3	D-raffinose aldehyde **1c**	Coumarin amine **2e**	Phenylacetylene **3a**	**4j**	56
4	D-stachyose aldehyde **1d**	Coumarin amine **2e**	Phenylacetylene **3a**	**4k**	>99

[a)] Reactions were carried out with sugar aldehyde **1c–d** (10 mM), amine **2a** or **2e** (10 equiv.), alkyne **3a** or **3c** (10 equiv.), and gold(III) complex **Au–2** (1 equiv.) in 50 mM PBS (pH 7.4)/DMSO (1:1) (90 μL) at 50 °C for 6 h.
[b)] Determined by LC-MS.

excellent reactivity of our tridentate complex in comparison to the previously reported C^N and N^O bidentate gold(III) complexes.

Investigation of the substrate scope was then conducted with other acetal alkyne substrates **5**. To assess the reactivity of **Au–2**, the reaction was performed for 1.5 h following the conditions as shown in Table 6. As presented in **Table 7**, substrates with electron-donating groups **5b** and **5e** led to lower yields of 35%–48% compared to the nonsubstituted **5a** and electron-withdrawing

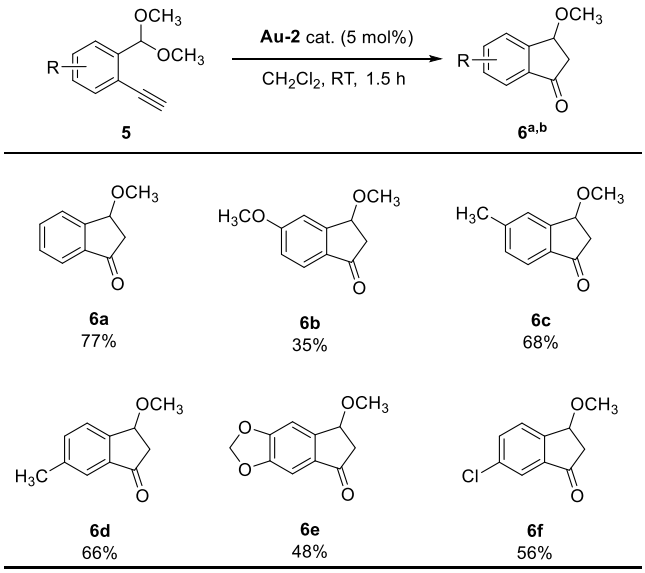
Table 6. Gold(III)-catalyzed carboalkoxylation of acetal alkyne.



Entry[a)]	Catalyst	Yield [%][b)]
1	**Au−2**	77
2	**$KAuCl_4 \cdot 2H_2O$**	29
3	**[Au(C^N)Cl_2]−1**	0
4	**[Au(C^N)Cl_2]−2**	50
5	**[Au(C^N)Cl_2]−3**	55
6	**[Au(N^O)Cl_2]**	58

[a)] Reactions were carried out with acetal alkyne **5a** (0.2 mmol) and gold(III) catalyst (0.01 mmol, 5 mol%) in CH_2Cl_2 (2 mL) at RT for 1.5 h.
[b)] Isolated yield.

Table 7. Substrate scope of carboalkoxylation reaction using **Au–2** as a catalyst.



[a)] Reactions were carried out with acetal alkynes **5** (0.2 mmol) and gold(III) complex **Au–2** (0.01 mmol, 5 mol%) in CH_2Cl_2 (2 mL) at RT for 1.5 h.
[b)] Isolated yield.

substituted **5f** substrates. **6a** was obtained with a good yield of 77% and **6f** with 56%. Substrates with less electron-donating substituent —CH_3 **5c** and **5d** gave the corresponding indanones **6c** and **6d** at yields of 68% and 66%, respectively.

3. Conclusion

To conclude, a series of 5,7-membered N^C^N pyridine-phenyl-oxazoline tridentate gold(III) complexes was successfully developed. These gold(III) complexes demonstrated efficient and versatile catalytic activity for organic synthesis without activation by silver salts. Interestingly, the tridentate gold(III) complexes exhibited excellent activities in catalyzing A^3-coupling reaction and modification of oligosaccharides. Substrate scope studies revealed the high tolerance of the gold(III) complexes towards the complexity and type of substrates, allowing various functionalization of biomolecules. Moreover, in comparison to the previously reported bidentate gold(III) C^N and N^O complexes, the tridentate gold(III) complexes demonstrated higher reactivity in the carboalkoxylation reaction of acetal alkynes.

4. Experimental Section

CCDC 2418508 (for **Au–1**) (https://www.ccdc.cam.ac.UK/structures/search?id=doi:10.5517/ccdc.csd.cc2m5ndw&sid=DataCite) contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.UK/structures.

General Procedure for Synthesis of Gold(III) Complexes: Transmetalation reactions followed previously reported procedures.[27] Using **Au–1** as an example, a solution of **S5** (0.207 g, 0.40 mmol, 1.0 equiv.) and $KAuCl_4.2H_2O$ (0.182 g, 0.44 mmol, 1.1 equiv.) in CH_3CN (4 mL) was stirred at 50 °C for 16 h. Solvent was then removed from the reaction mixture by a rotary evaporator, and the crude mixture was redissolved in CH_2Cl_2. A saturated solution of potassium hexafluorophosphate (10 mL) was prepared and added to the reaction mixture together with tetrabutylammonium bromide (1 mol%). The reaction mixture was stirred at room temperature for 18 h, then extracted by adding H_2O and CH_2Cl_2. The combined organic layer was dried with anhydrous $MgSO_4$, concentrated under vacuum, and the residue was then purified by flash column chromatography using CH_2Cl_2/MeOH (50:1) as eluent to give the desired product **Au–1** (0.200 g, 0.30 mmol, 76% yield). **Au–2** to **Au–5** were prepared according to the above procedure using their corresponding organomercury compounds.

General Procedure for Screening of Cyclometallated Gold(III) Complexes in A^3-Coupling Reaction, Optimization of Reaction Conditions, and Scope Study: A mixture of benzaldehyde **1a** (20.4 μL, 0.2 mmol, 1.0 equiv.), piperidine **2a** (23.8 μL, 0.24 mmol, 1.2 equiv.), phenylacetylene **3a** (31.4 μL, 0.30 mmol, 1.5 equiv.), and gold(III) complexes (**Au–1** to **Au–5**) (0.002 mmol,

1 mol%) in H_2O (1 mL) was stirred at 40 °C for 24 h. An aliquot amount of sample was taken out for ^1H NMR analysis, and the conversion was determined by the ^1H NMR ratio of benzaldehyde to product peak.[21b] Optimization of reaction conditions was conducted by the above procedure using different solvents. Isolation of the product was also done by the following procedure. The reaction mixture was extracted using H_2O and CH_2Cl_2. The combined organic layer was dried with anhydrous $MgSO_4$, concentrated under vacuum, and the residue was purified by flash column chromatography using hexane/EtOAc (80:1) as eluent to obtain the propargylamine **4a** (46.4 mg, 0.17 mmol, 84% yield). A scope study was conducted by the above procedure with varying aldehyde **1**, amine **2,** and alkyne **3**, with gold(III) complex **Au–2** as a catalyst. An aliquot amount of sample was taken out for ^1H NMR analysis, and conversion was determined by ^1H NMR ratio of aldehyde to product peak.

General Procedure for Study of Substrate Scope for Bifunctional Modification of Oligosaccharides: A mixture of D-raffinose aldehyde **1c** or D-stachyose aldehyde **1d** (10 μL of 100 mM in H_2O, 10 mM), amine **2a** or **2e** (10 equiv.), alkyne **3a** or **3c** (10 equiv.), and gold(III) complex **Au–2** (1 equiv.) in 50 mM PBS (pH 7.4)/DMSO (1:1) (90 μL) was conducted at 40 °C for 2 h or at 50 °C for 6 h reaction. After the reaction, the crude mixture (3 μL) was taken out for LC-MS analysis.[21c,21e]

General Procedure for Gold(III)-Catalyzed Carboalkoxylation of Acetal Alkynes and Scope Study: The carboalkoxylation reaction was conducted based on a modification of a previously reported procedure.[8b] To a solution of acetal alkyne **5a** (0.20 mmol, 1.0 equiv.) in 2 mL of CH_2Cl_2, gold(III) complex (0.01 mmol, 5 mol%) was added. The mixture was stirred at room temperature for 1.5 h. The resulting reaction mixture was diluted with 2 mL of CH_2Cl_2. 1 mL of 1.0M HCl solution was then added, followed by stirring for 10 min. The reaction mixture was extracted using H_2O and CH_2Cl_2. The combined organic layer was dried with anhydrous $MgSO_4$, concentrated under vacuum, and the residue was purified by flash column chromatography using hexane/EtOAc (10:1) as eluent to afford the target product **6a**. A scope study was conducted following the same procedures as above, employing various acetal alkynes **5** and **Au–2** as catalysts. All the corresponding target products **6** were identified with reference to the characterization data in the literature.

Acknowledgements

The authors are grateful for the financial support of the Hong Kong Research Grants Council (PolyU15300422), the State Key Laboratory of Chemical Biology and Drug Discovery, the Hong Kong Polytechnic University (P0043816: WZ0Y and P0053072: ZZV2), and the University Research Facility in Life Sciences (ULS) of PolyU.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data supporting the findings of this study are available in the main text or supplementary material.

References

[1] a) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180; b) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266; c) Z. Li, C. Brouwer, C. He, *Chem. Rev.* **2008**, *108*, 3239; d) A. Corma, A. Leyva-Pérez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657; e) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028; f) S. R. Thomas, A. Casini, *Curr. Opin. Chem. Biol.* **2020**, *55*, 103.

[2] a) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*, 3351; b) S. Witzel, A. S. K. Hashmi, J. Xie, *Chem. Rev.* **2021**, *121*, 8868; c) Z. Zheng, X. Ma, X. Cheng, K. Zhao, K. Gutman, T. Li, L. Zhang, *Chem. Rev.* **2021**, *121*, 8979.

[3] a) G. Zuccarello, I. Escofet, U. Caniparoli, A. M. Echavarren, *ChemPlusChem* **2021**, *86*, 1283; b) R. P. Herrera, M. C. Gimeno, *Chem. Rev.* **2021**, *121*, 8311.

[4] a) L. Rocchigiani, M. Bochmann, *Chem. Rev.* **2021**, *121*, 8364; b) M. S. M. Holmsen, A. Nova, M. Tilset, *Acc. Chem. Res.* **2023**, *56*, 3654.

[5] a) R. V. Parish, B. P. Howe, J. P. Wright, J. Mack, R. G. Pritchard, R. G. Buckley, A. M. Elsome, S. P. Fricker, *Inorg. Chem.* **1996**, *35*, 1659; b) R. G. Buckley, A. M. Elsome, S. P. Fricker, G. R. Henderson, B. R. Theobald, R. V. Parish, B. P. Howe, L. R. Kelland, *J. Med. Chem.***1996**, *39*, 5208.

[6] a) M. A. Cinellu, A. Zucca, S. Stoccoro, G. Minghetti, M. Manassero, M. Sansoni, *J. Chem. Soc., Dalton Trans.* **1995**, 2865, https://doi.org/10.1039/DT9950002865; b) Y. Fuchita, H. Ieda, A. Kayama, J. Kinoshita-Nagaoka, H. Kawano, S. Kameda, M. Mikuriya, *J. Chem. Soc., Dalton Trans.* **1998**, 4095, https://doi.org/10.1039/A807108J; c) K. K.-Y. Kung, H.-M. Ko, J.-F. Cui, H.-C. Chong, Y.-C. Leung, M.-K. Wong, *Chem. Commun.* **2014**, *50*, 11899; d) A. C. Reiersølmoen, A. Fiksdahl, *Eur. J. Org. Chem.* **2020**, *2020*, 2867; e) E. M. Laguna, P. M. Olsen, M. D. Sterling, J. F. Eichler, A. L. Rheingold, C. H. Larsen, *Inorg. Chem.* **2014**, *53*, 12231.

[7] H.-M. Ko, K. K.-Y. Kung, J.-F. Cui, M.-K. Wong, *Chem. Commun.* **2013**, *49*, 8869.

[8] a) Y. Miura, T. Mochida, S. Motodate, K. Kato, *Polyhedron* **2016**, *113*, 1; b) J.-J. Jiang, J.-F. Cui, B. Yang, Y. Ning, N. C.-H. Lai, M.-K. Wong, *Org. Lett.* **2019**, *21*, 6289.

[9] J.-F. Cui, H.-M. Ko, K.-P. Shing, J.-R. Deng, N. C.-H. Lai, M.-K. Wong, *Angew. Chem., Int. Ed.* **2017**, *56*, 3074.

[10] A. C. Reiersølmoen, D. Csókás, S. Øien-Ødegaard, A. Vanderkooy, A. K. Gupta, A.-C. C. Carlsson, A. Orthaber, A. Fiksdahl, I. Pápai, M. Erdélyi, *J. Am. Chem. Soc.* **2020**, *142*, 6439.

[11] a) R. Kumar, C. Nevado, *Angew. Chem., Int. Ed.* **2017**, *56*, 1994; b) T. Zou, C. T. Lum, C.-N. Lok, J.-J. Zhang, C.-M. Che, *Chem. Soc. Rev.* **2015**, *44*, 8786; c) R. T. Mertens, S. Gukathasan, A. S. Arojojoye, C. Olelewe, S. G. Awuah, *Chem. Rev.* **2023**, *123*, 6612.

[12] D. Eppel, P. Penert, J. Stemmer, C. Bauer, M. Rudolph, M. Brückner, F. Rominger, A. S. Hashmi, *Chem. – Eur. J.* **2021**, *27*, 8673.
[13] L. González-Sebastián, D. Canseco-González, D. Morales-Morales,in *Pincer Compounds* (Ed: D. Morales-Morales), Elsevier, Amsterdam **2018**, ISBN 9780128129319.
[14] G. Alesso, M. A. Cinellu, S. Stoccoro, A. Zucca, G. Minghetti, C. Manassero, S. Rizzato, O. Swang, M. K. Ghosh, *Dalton Trans.* **2010**, *39*, 10293.
[15] V. K.-Y. Lo, A. O.-Y. Chan, C.-M. Che, *Org. Biomol. Chem.* **2015**, *13*, 6667.
[16] a) D. Weber, M. R. Gagné, *Org. Lett.* **2009**, *11*, 4962; b) A. Franchino, M. Montesinos-Magraner, A. M. Echavarren, *Bull. Chem. Soc. Jpn.* **2021**, *94*, 1099.
[17] a) G. T. Hermanson, in *Bioconjugate Techniques*, *3rd Ed.* (Ed: G. T. Hermanson) Academic Press, Boston **2013**, ISBN 9780123822406; b) E. C. Rodriguez, K. A. Winans, D. S. King, C. R. Bertozzi, *J. Am. Chem. Soc.* **1997**, *119*, 9905; c) H. Zhang, X.-j. Li, D. B. Martin, R. Aebersold, *Nat. Biotechnol.* **2003**, *21*, 660; d) J. M. Gilmore, R. A. Scheck, A. P. Esser-Kahn, N. S. Joshi, M. B. Francis, *Angew. Chem., Int. Ed.* **2006**, *45*, 5307.
[18] a) P. M. Rudd, T. Elliott, P. Cresswell, I. A. Wilson, R. A. Dwek, *Science* **2001**, *291*, 2370; b) C. T. Walsh, S. Garneau-Tsodikova, G. J. Gatto Jr., *Angew. Chem., Int. Ed.* **2005**, *44*, 7342; c) M. He, X. Zhou, X. Wang, *Signal Transduct. Target. Ther.* **2024**, *9*, 194.
[19] a) A. Dirksen, T. M. Hackeng, P. E. Dawson, *Angew. Chem., Int. Ed.* **2006**, *45*, 7581; b) A. Dirksen, S. Dirksen, T. M. Hackeng, P. E. Dawson, *J. Am. Chem. Soc.* **2006**, *128*, 15602; c) A. Dirksen, P. E. Dawson, *Bioconjug. Chem.* **2008**, *19*, 2543; d) Y. Zeng, T. Ramya, A. Dirksen, P. E. Dawson, J. C. Paulson, *Nat. Methods* **2009**, *6*, 207.
[20] a) G.-L. Li, K. K.-Y. Kung, M.-K. Wong, *Chem. Commun.* **2012**, *48*, 4112; b) J.-R. Deng, W.-C. Chan, N. C.-H. Lai, B. Yang, C.-S. Tsang, B. C.-B. Ko, S. L.-F. Chan, M.-K. Wong, *Chem. Sci.* **2017**, *8*, 7537; c) W.-Y. O., J.-F. Cui, Q. Yu, K. K.-Y. Kung, S.-F. Chung, Y.-C. Leung, M.-K. Wong, *Angew. Chem., Int. Ed.* **2023**, *62*, e202218038.
[21] a) V. K.-Y. Lo, Y. Liu, M.-K. Wong, C.-M. Che, *Org. Lett.* **2006**, *8*, 1529; b) V. K.-Y. Lo, K. K.-Y. Kung, M.-K. Wong, C.-M. Che, *J. Organomet. Chem.* **2009**, *694*, 583; c) K. K.-Y. Kung, G.-L. Li, L. Zou, H.-C. Chong, Y.-C. Leung, K.-H. Wong, V. K.-Y. Lo, C.-M. Che, M.-K. Wong, *Org. Biomol. Chem.* **2012**, *10*, 925; d) K.-F. Wong, J.-R. Deng, X.-Q. Wei, S.-P. Shao, D.-P. Xiang, M.-K. Wong, *Org. Biomol. Chem.* **2015**, *13*, 7408; e) H.-Y. Sit, B. Yang, K.-Y. K. Kung, S.-L. J. Tam, M.-K. Wong, *ChemPlusChem* **2019**, *84*, 1739.
[22] E. Tomás-Mendivil, P. Y. Toullec, J. Borge, S. Conejero, V. Michelet, V. Cadierno, *ACS Catal.* **2013**, *3*, 3086.
[23] Y. Rangraz, F. Nemati, A. Elhampour, *Ind. Eng. Chem. Res.* **2019**, *58*, 17308.
[24] Y.-Z. Li, W. K. Leong, *RSC Adv.* **2019**, *9*, 5475.
[25] T. Kitanosono, S. Kobayashi, *Chem.– Eur. J.* **2020**, *26*, 9408.
[26] a) W. Li, B. Yu, *Chem. Soc. Rev.* **2018**, *47*, 7954. b) E. B. Bauer, *Org. Biomol. Chem.* **2020**, *18*, 9160.
[27] A. K.-H. Chan, M.-H. Chau, Y. Ren, J.-J. Jiang, M.-K. Wong, F. K.-C. Leung, *ChemPlusChem* **2023**, *89*, e202300316.