SCIENCE CHINA
Chemistry

•ARTICLES•

April 2021 Vol.64 No.4: 552–557
https://doi.org/10.1007/s11426-020-9930-7

Stereodivergent synthesis of *C*-glycosamino acids *via* Pd/Cu dual catalysis

Xiaoxiao Yan[1†], Feng Feng[1†], Lin Zhou[1], Linrong Chen[1], Shouchu Tang[1], Jian Liu[1*], Feng Cai[2] & Xiaolei Wang[1*]

[1]*State Key Laboratory of Applied Organic Chemistry, Department of Chemistry and School of Pharmacy, Lanzhou University, Lanzhou 730000, China;*
[2]*The National Glycoengineering Research Center and Shandong Provincial Key Laboratory of Carbohydrate Chemistry and Glycobiology, Shandong University, Qingdao 266237, China*

Received September 25, 2020; accepted December 29, 2020; published online February 9, 2021

Herein, we reported the stereodivergent synthesis of *C*-glycosamino acids *via* Pd/Cu dual catalysis and found a suitable system to resolve many challenges, such as the tolerance towards the density of functional groups, the variability of the anomeric position, the compatibility of appropriate catalyst combinations, the regioselectivity of nucleophiles, and the match/mismatch problems between chiral substrates and chiral ligand-metal complexes. The method enables the efficient preparation of a series of unnatural *C*-glycosamino acid skeletons bearing two contiguous stereogenic centers in good yields with excellent diastereoselectivity. From this crucial precursor, various *C*-glycosamino acid derivatives have been achieved diversely. The readily prepared *C*-glycosamino acid hybrids will meet the growing demands for the development of new molecular entities for discovering new drugs and materials. This stereodivergent synthesis of *C*-glycosamino acids will further accelerate the study of their structural features, mode of action, and potential biological applications in the near future.

***C*-glycosamino acid, glycomimetics, peptidomimetics, stereodivergent, dual catalysis**

Citation: Yan X, Feng F, Zhou L, Chen L, Tang S, Liu J, Cai F, Wang X. Stereodivergent synthesis of *C*-glycosamino acids *via* Pd/Cu dual catalysis. *Sci China Chem*, 2021, 64: 552–557, https://doi.org/10.1007/s11426-020-9930-7

1 Introduction

Glycosamino acids are hybrid structures of carbohydrates and amino acids that can be utilized to generate potent glycomimetics and peptidomimetics (Figure 1) [1]. Incorporating glycosamino acids into peptides could allow the engineering of carbohydrate-binding sites into synthetic polypeptides, which can further modify the pharmacokinetics and dynamic properties of the peptides in a drug-like manner [2]. There are many different types of naturally occurring glycosamino acids, such as sialic acid and *O*/*N*-glycans, which play essential roles in many biological processes, including cell-cell interactions, tumor metastasis, infection, inflammation, and cancers [3]. However, *O*/*N*-glycans are unstable under glycosidases or acidic physiological environments. Thus, *C*-glycosamino acids, in which the α-position of amino acids is connected to the anomeric carbon atom of a sugar motif through carbon-carbon bond linkages, were developed to address these issues [4,5]. Related investigations have shown that many *C*-glycosamino acids and *C*-glycopeptides have interesting solution conformations, and their biological activities are similar to those of naturally occurring analogs [6]. In particular, some *C*-glycosamino acids depict significantly improved biological prosperity and have been successfully employed in specific therapeutics [7], such as the anti-influenza drug oseltamivir.

†These authors contributed equally to this work.
*Corresponding authors (email: jianliu@lzu.edu.cn; wangxiaolei@lzu.edu.cn)

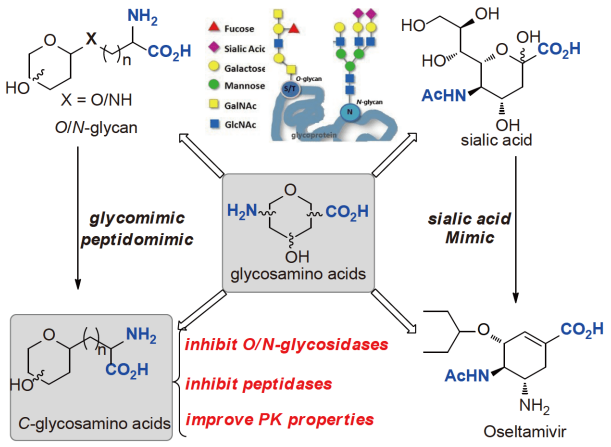
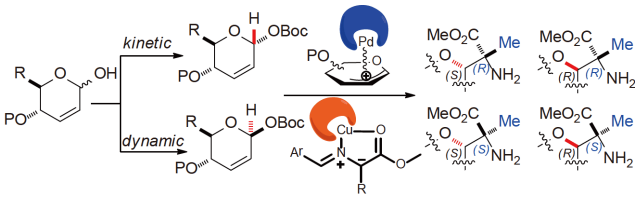


Figure 1 General structures of glycosamino acids (color online).

Given their tremendous structural and functional diversity, unfortunately, *C*-glycosamino acid hybrids do not yet to be fully explored due to the limited availability of these structurally complex compounds [4].

The limited availability of *C*-glycosamino acid blocks has significantly restricted the research of their structural features and mode of action. To date, only a few reports have addressed the synthesis of *C*-glycosamino acids. Most of these synthetic strategies have significant drawbacks, such as low diastereoselectivity [8a], multistep synthesis [8a–8f], unspecified stereochemistry [8d], and lack of stereodivergence [1,8]. However, efficient and diverse preparation of *C*-glycosamino acid building blocks remains quite challenging.

With the development of dual catalysis in recent years [9], we speculated that the *C*-glycosamino acid skeleton might be constructed *via* a dual catalytic system in a diverse manner. As shown in Scheme 1, the stereocenter of the anomeric position can be controlled *via* the substrate-palladium complex, and the other chiral center close to the *α*-amino acid motif can be elegantly controlled *via* the metal-chiral ligand complex. The applications of transition metal catalysis for constructing *C*-glycosyl linkages have significantly increased in recent years [10,11]. However, the dual catalysis strategy has never been successfully applied in the synthesis of *C*-glycosamino acids due to the difficulty in controlling the remote formation of glycosidic bonds with high diastereoselectivity and regioselectivity. In this area, one must address the density of functional groups of carbohydrates, the variability of the anomeric position, the judicious selection of appropriate catalyst combinations, the regioselectivity of nucleophiles, and the match/mismatch problems between chiral substrates and chiral ligand-metal complexes. Herein, we describe the regio- and diastereodivergent synthesis of *C*-glycosamino acids *via* bimetallic catalyzed Heck-type glycosylation [12,13], a protocol that is highly desired from a synthetic efficiency perspective (Scheme 1).



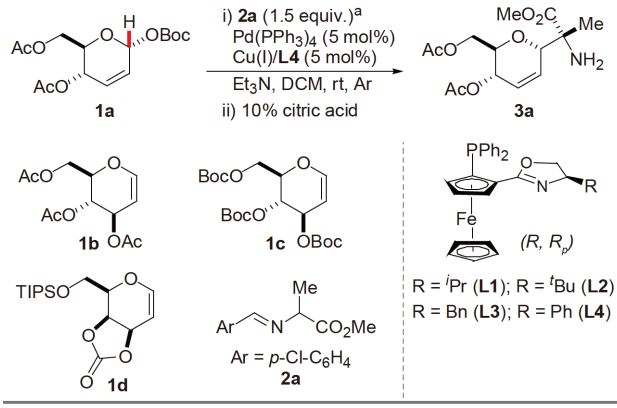
Scheme 1 Planned synthesis of *C*-glycosamino acid hybrids (color online).

2 Experimental

General procedure for the synthesis of *C*-glycosamino acid **3a**–**3m**. To a well-dried 10-mL seal tube with $Cu(MeCN)_4BF_6$ (1.5 mg, 0.005 mmol, 0.05 equiv.) and **L4** (2.8 mg, 0.005 mmol, 0.05 equiv.), dichloromethane (DCM) (0.5 mL) was then added under Ar and stirred for 30 min at room temperature (rt). Then the above mixture was transferred to another well-dried 10-mL seal tube containing *tert*-butyl carbonate glucenose **1** (33.0 mg, 0.1 mmol, 1.0 equiv.), aldimine ester **2** (0.15 mmol, 1.5 equiv.), $Pd(PPh_3)_4$ (5.5 mg, 0.005 mmol, 0.05 equiv.) and DCM (0.5 mL) under Ar at rt. The reaction was monitored by thin layer chromatography (TLC). About 5 h, the solvent dichloromethane was concentrated *in vacuo*. The residue was then diluted with tetrahydrofuran (1 mL) and 10% citric acid solution (4 mL). After 2 h at room temperature, saturated sodium bicarbonate solution was added to adjust the pH to neutral and extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by flash column chromatography (PE/EtOAc) to afford the desire products.

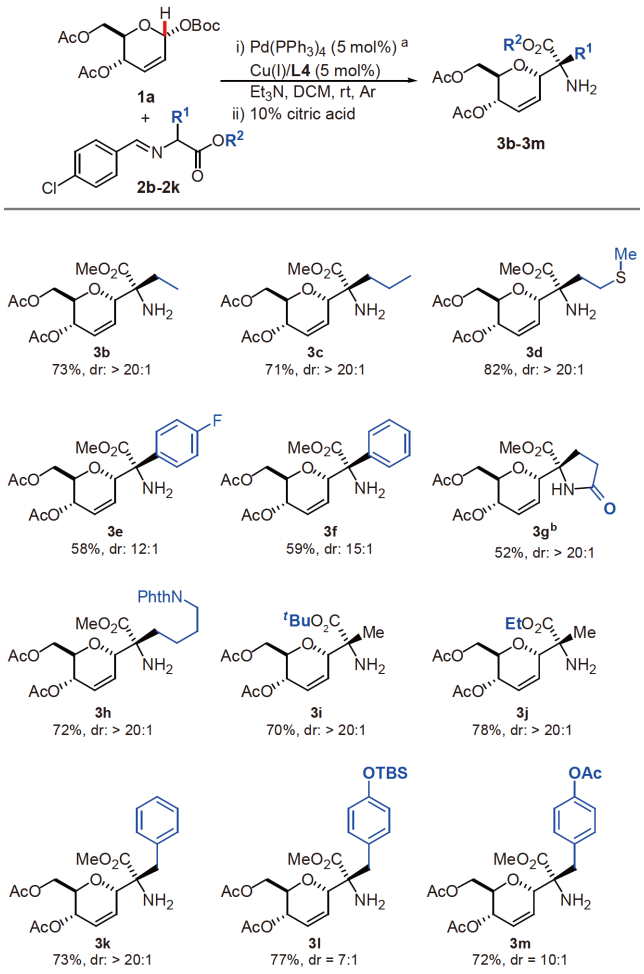
3 Results and discussion

After extensive exploration of the reaction conditions (Tables S1–S3, Supporting Information online), glycal donor **1a** [14] was found to react with *α*-substituted aldimine esters **2a** under $Pd(PPh_3)_4$ and $Cu(MeCN)_4BF_4$/phosferrox (**L4**) [15] conditions to afford **3a** in 85% yield with >20:1 *dr* (Scheme 2, entry 1). The detailed reaction conditions were as follows: the coupling reaction was performed with **1a** (1.0 equiv.), **2a** (1.5 equiv.), Et_3N (1.5 equiv.), $Pd(PPh_3)_4$ (0.05 equiv.), $Cu(MeCN)_4BF_4$ (0.05 equiv.) and phosferrox-**L4** (0.05 equiv.) in dichloromethane (1.0 mL) at room temperature for 5 h. No reaction was observed when using glycal donors **1b** and **1c** (entries 2 and 3). The product was generated with only 50% yield using glycal donor **1d** (entry 4). The reaction yield was considerably diminished using other phosferrox ligands (**L1**–**L3**, entries 5–7) or different palladium catalysts (entries 8–12). Reducing the reaction temperature to 0 °C for a prolonged time did not further improve the diastereoselectivity while maintaining the yield (entry 13). The control



entry	variations from standard conditions	yield (%)[b]	*dr*.[c]
1	none	85	>20:1
2	**1b**	0	n.d.
3	**1c**	0	n.d.
4[d]	**1d**	50	>20:1
5	**L1**	46	>20:1
6	**L2**	43	2:1
7	**L3**	42	>20:1
8	$Pd(OAc)_2$/dppe	20	>20:1
9	$Pd_2(dba)_3$/dppe	<5	n.d.
10	$Pd_2(dba)_3 \cdot CHCl_3$/dppe	50	>20:1
11	$Pd(dppf)Cl_2$	0	n.d.
12	$Pd(PPh_3)_2Cl_2$	0	n.d.
13[e]	at 0 °C	85	>20:1
14	without $Cu(MeCN)_4BF_4$/**L4**	0	n.d.
15	without $Pd(PPh_3)_4$	0	n.d.

Scheme 2 a) Optimization of reaction conditions. Unless otherwise noted, the reaction of **1** (0.10 mmol) with **2a** (1.5 equiv.) was carried out using a catalytic system consisting of a palladium catalyst (0.05 equiv.), $Cu(MeCN)_4BF_4$ (0.05 equiv.), and (R,R_p)-L (0.05 equiv.) under an Ar atmosphere in the presence of triethylamine (1.5 equiv.) in CH_2Cl_2 (1.0 mL) at room temperature for 5 h. b) Isolated yields. c) The *dr* value was determined by crude ^{1}H NMR. d) the related product **3w** in scheme 4. e) At 0 °C for 14 h (color online).



Scheme 3 Substrate scope of aldimine esters. a) **1a** (0.10 mmol), **2a** (1.5 equiv.), $Pd(PPh_3)_4$ (0.05 equiv.), $Cu(MeCN)_4BF_4$ (0.05 equiv.), (R,R_p)-**L4** (0.05 equiv.), and triethylamine (1.5 equiv.) in CH_2Cl_2 (1.0 mL) at room temperature for 5 h; then, the reaction system was treated with 10% citric acid. b) Lactam was formed when treated with 10% citric acid (color online).

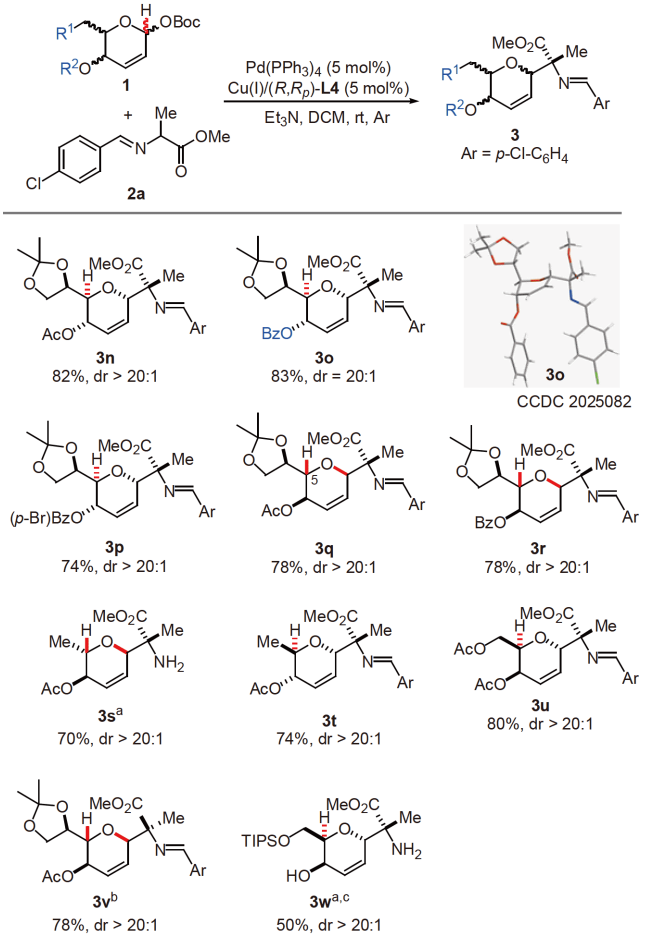
experiments suggested that both copper and palladium catalysts were indispensable for this chemical transformation (entries 14 and 15).

With optimized reaction conditions in hand, the scope of the α-substituted aldimine esters was evaluated. As shown in Scheme 3, we were pleased to find that both natural and unnatural α-amino acid-derived aldimine esters were suitable in this reaction system, yielding the precursors of *C*-glycosamino acids. Diverse substituents, including alkyl (**3b**, **3c**), thioether (**3d**), (substituted) phenyl (**3e**, **3f**), ester (**3g**), and protected amine (**3h**) groups, are all well tolerated in this reaction system, giving desired *C*-glycosamino acid derivatives in good yields with excellent diastereoselectivity. In addition, other aldimine esters (**2i**, **2j**) also gave the desired products (**3i**, **3j**) without losing diastereoselectivity. Significantly, the *tert*-butyl masked ester will provide an opportunity for further peptide ligation. The phenylalanine-type aldimine ester also provided the desired product (**3k**). However, the *dr* value decreased to 7:1 due to the bulky protecting group of the tyrosine-type aldimine ester (**2l**). The bulky *tert*-butyldimethylsilyl (TBS) protecting group might come from the less approachable of two metal-chelated coupling partners, which further decreases the diastereoselectivity [15f–15j]. To further clarify the decrease of *dr*, we prepared a less hinderance substrate containing OAc group, and the related product's *dr* restored to 10:1.

Subsequently, the scope of the glycone part was explored (Scheme 4). First, we assessed aldimine esters **2a** with different glycosyl donors [16]. The reaction system shows good tolerance toward both substituted (**3n**–**3p**) and deoxygenated substrates (**3s**, **3t**) with different protecting groups. Even changing the absolute configuration of the anomeric position and epimerization of the C5 position had no influence on the diastereoselectivity and yield (**3q**–**3s**). For the galactose-type carbohydrate donor, we also obtained the corresponding product in good yield and excellent diastereoselectivity (**3u**).

While using (S,S_p)-**L4**, we can still obtain the target molecule (**3v**) without losing yield and diastereoselectivity. As mentioned in Scheme 2, we obtained a free alcohol product (**3w**) while using glycosyl donor **1d** in 50% yield. Finally, the absolute configuration of compound **3o** was determined by X-ray analysis (CCDC 2025082).

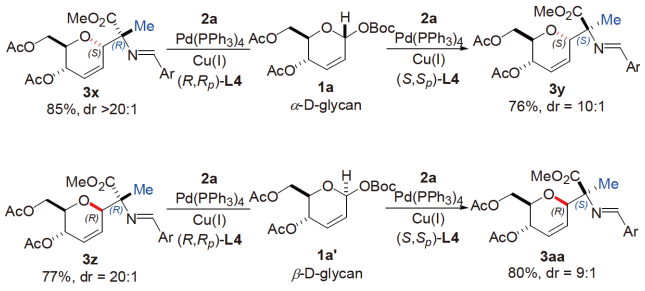
After examining the substrate scope of both aldimine esters and glycosyl donors, we further explored the stereodivergence of the current method with aldimine esters **2a** under standard reaction conditions. As shown in Scheme 5, the configuration of the anomeric position might have stereomatch or mismatch issues with the chiral Cu(I)/**L4**/**2a** complex. Thus, changing the absolute configuration of ligand **L4** might influence the reactivity, diastereoselectivity and yield. Under the optimized conditions, the reaction of α-D-glycoside **1a** and (S,S_p)-**L4** proceeded smoothly, affording **3y** in good yields with 10:1 *dr*. The reaction of β-D-glycoside **1a′** with (R,R_p)-**L4** and (S,S_p)-**L4** also went smoothly, giving **3z** and **3aa** in good yields with acceptable *dr* values. These results indicated that the two distinct metal-substrate complexes play an essential role in the formation of the corresponding two new continuous stereogenic centers.



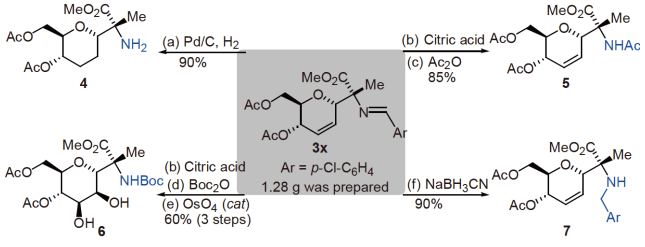
Scheme 4 Substrate scope of glycal donors. a) The reaction mixture was treated with 10% citric acid. b) (S,S_p)-**L4** was used. c) Glycal donor **1d** was used (color online).

To show the utility of this methodology, a gram-scale reaction was tested, as shown in Scheme 6. When the reaction was scaled up to gram-scale, this reaction proceeded smoothly without a notable change in terms of the isolated yield and diastereoselectivity (see Supporting Information online for details). With gram-scale **3x** in hand, further chemical transformations were conducted. For the glycone motif, the double bond was then either reduced to saturated alkane (**4**) or oxidized to mannose-type amino acid building blocks (**6**) under OsO_4 [8e,17]. For the transformation of the aldimine ester part, we can obtain amide (**5**) after treatment with acetic anhydride or benzylamine (**7**) with $NaBH_3CN$.

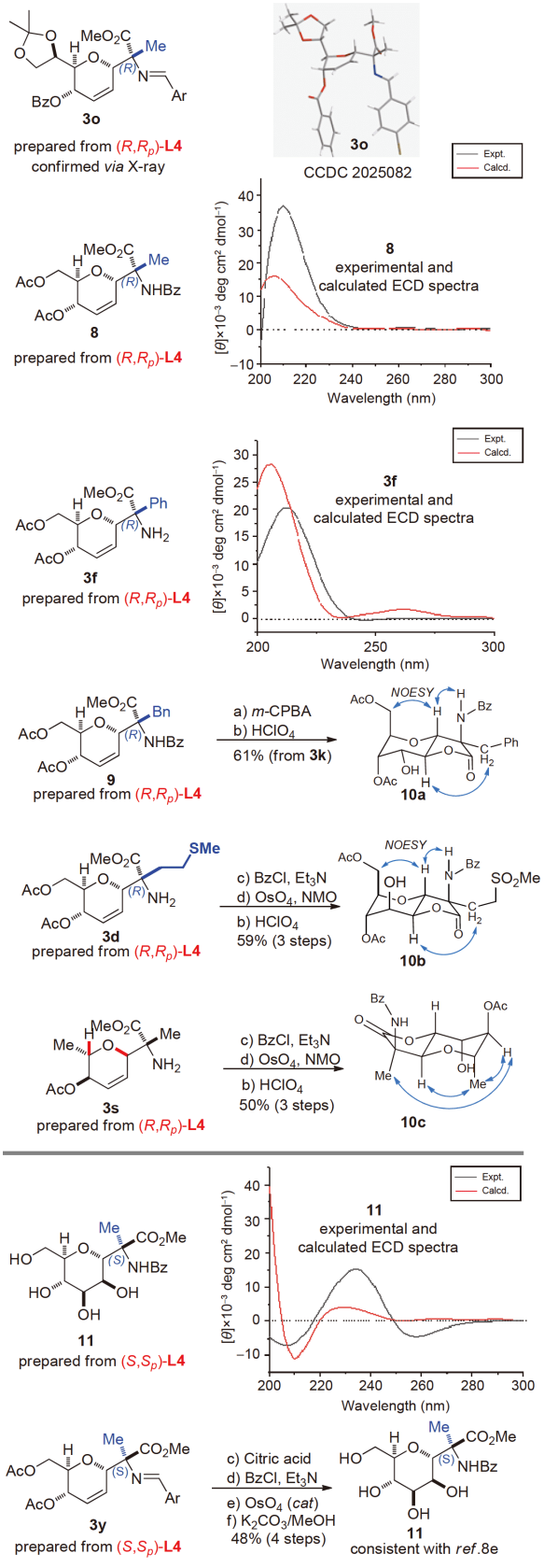
To further confirm the absolute configuration, we obtained a crystal for **3o** as shown in Scheme 4. After extension efforts, we could not obtain any other crystal of products and their derivatives as shown in Schemes 3 and 4. As is known to us, the circular dichroism (CD) spectra have emerged as a promising tool for the determination of absolute configurations and predominant conformations of chiral molecules in academic laboratories [18]. We can use this spectroscopy to deduce the absolute configuration *via* comparing the experimental with calculated CD spectra. Guided by this technology, we prepared **8**, **3f** and **10c** (see Supporting Information online) containing a UV sensitive protecting group, the experimental CD spectra totally agree with calculated *via* Gaussian. Thus the absolute configuration of these products can be confirmed through comparing the



Scheme 5 Stereodivergence study. **1a** or **1a′** (0.10 mmol), **2a** (1.5 equiv.), $Pd(PPh_3)_4$ (0.05 equiv.), $Cu(MeCN)_4BF_4$ (0.05 equiv.), **L4** (0.05 equiv.), and triethylamine (1.5 equiv.) in CH_2Cl_2 (1.0 mL) at room temperature for 5 h (color online).



Scheme 6 Gram-scale synthesis and chemical transformation study of **3a**. (a) Pd/C (*cat.*) under H_2 (balloon) in methanol; (b) 10% citric acid in THF; (c) Ac_2O (1.5 equiv.) in pyridine; (d) Boc_2O (1.5 equiv.), $NaHCO_3$ (s, 1.2 equiv.) in DCM; (e) OsO_4 (5% *cat.*) with NMO (3.0 equiv.) in acetone/H_2O = 4/1 (color online).



Scheme 7 The determination of the absolute configuration. a) *m*-CPBA (1.5 equiv.) in DCM; b) $HClO_4$ in THF; c) BzCl (1.5 equiv.), Et_3N (3.0 equiv.) in DCM; d) OsO_4 (10% *cat.*) with NMO (3.0 equiv.) in acetone/H_2O=4/1; e) 10% citric acid in THF; f) K_2CO_3 in MeOH (color online).

experimental with calculated CD spectra.

We then obtained **10a–10c** *via* three steps chemical transformation. From the key NOESY signal, we can also confirm the absolute configuration of **10a–10c**. After this, we then compared the experimental with calculated CD spectra of **11**, prepared from (S,S_p)-**L4** ligand. As is shown in Scheme 7, the experimental CD spectra is also consistent with the calculated CD spectra. And also the analytical and spectral data of **11** was in good agreement with previous report [8e].

4 Conclusions

In conclusion, we have developed the stereodivergent Pd/Cu dual catalyzed α-glycosylation of aldimine esters *via* the combination of two chiral metal complexes, we can access all possible stereoisomers under identical conditions. According to the results, the reaction between D-glycal donors and (R,R_p)-**L4**-Cu complex is more favorable, giving *C*-glycosamino acid skeleton with excellent diastereoselectivity. The diverse preparation of unnatural *C*-glycosamino acid derivatives will further facilitate the biological study of these glycomimetics and peptidomimetics. Ongoing studies are focused on the synthesis and biological evaluation of *C*-mannose-amino acids as novel fimH antagonists towards uropathogenic *Escherichia coli* for the treatment of urinary tract infections [19].

Acknowledgements This work was supported by the National Natural Science Foundation of China (051170001, 21772084, 22071087), the Fundamental Research Funds for the Central Universities (lzujbky-2017-k06) and the Open Projects Funds of Shandong Key Laboratory of Carbohydrate Chemistry and Glycobiology, Shandong University (2019CCG05). Xiaolei Wang thanks the Thousand Young Talents Program for financial support. We also thank Sumit O. Bajaj (Corden Pharma Boulder) for language polishing and Prof. Quanxiang Wu & Ya Li for giving suggestion towards the absolute configuration determining *via* CD spectra.

Conflict of interest The authors declare no conflict of interest.

Supporting information The supporting information is available online at http://chem.scichina.com and http://link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

1 Schweizer F. *Angew Chem Int Ed*, 2002, 41: 230–253
2 von Roedern EG, Kessler H. *Angew Chem Int Ed Engl*, 1994, 33: 687–689
3 Kobata A. *Acc Chem Res*, 1993, 26: 319–324
4 For selected reviews on glycosamino acids, see: (a) Dondoni A, Marra A. *Chem Rev*, 2000, 100: 4395–4422; (b) Chakraborty T, Ghosh S, Jayaprakash S. *Curr Med Chem*, 2002, 9: 421–435; (c) Chakraborty TK, Srinivasu P, Tapadar S, Mohan BK. *J Chem Sci*, 2004, 116: 187–207; (d) Tian GZ, Wang XL, Hu J, Wang XB, Guo XQ, Yin J. *Chin Chem Lett*, 2015, 26: 922–930

5 Only a few cases *C*-glycopeptides were isolated from natural sources: (a) Hofsteenge J, Mueller DR, de Beer T, Loeffler A, Richter WJ, Vliegenthart JFG. *Biochemistry*, 1994, 33: 13524–13530; (b) de Beer T, Vliegenthart JFG, Loeffler A, Hofsteenge J. *Biochemistry*, 1995, 34: 11785–11789; (c) Löffler A, Doucey MA, Jansson AM, Müller DR, de Beer T, Hess D, Meldal M, Richter WJ, Vliegenthart JFG, Hofsteenge J. *Biochemistry*, 1996, 35: 12005–12014; (d) Doucey M. *Glycobiology*, 1999, 9: 435–441

6 (a) Moos E, Ben R. *Curr Topic Med Chem*, 2005, 5: 1351–1361; (b) Gustafsson T, Saxin M, Kihlberg J. *J Org Chem*, 2003, 68: 2506–2509

7 (a) Yang G, Schmieg J, Tsuji M, Franck RW. *Angew Chem Int Ed*, 2004, 43: 3818–3822; (b) Laurent X, Bertin B, Renault N, Farce A, Speca S, Milhomme O, Millet R, Desreumaux P, Hénon E, Chavatte P. *J Med Chem*, 2014, 57: 5489–5508

8 (a) Dondoni A, Junquera F, Merchán FL, Merino P, Scherrmann MC, Tejero T. *J Org Chem*, 1997, 62: 5484–5496; (b) McDevitt JP, Lansbury PT. *J Am Chem Soc*, 1996, 118: 3818–3828; (c) Andrews RS, Becker JJ, Gagné MR. *Angew Chem Int Ed*, 2012, 51: 4140–4143; (d) Colombo L, Casiraghi G, Pittalis A, Rassu G. *J Org Chem*, 1991, 56: 3897–3900; (e) Di Giacomo M, Serra M, Brusasca M, Colombo L. *J Org Chem*, 2011, 76: 5247–5257; (f) Schweizer F, Inazu T. *Org Lett*, 2001, 3: 4115–4118

9 For reviews on dual catalysis, see: (a) Allen AE, MacMillan DWC. *Chem Sci*, 2012, 3: 633–658; (b) Zhang HH, Chen H, Zhu C, Yu S. *Sci China Chem*, 2020, 63: 637–647; (c) Skubi KL, Blum TR, Yoon TP. *Chem Rev*, 2016, 116: 10035–10074; For selected examples on dual catalysis, see: (d) Krautwald S, Sarlah D, Schafroth MA, Carreira EM. *Science*, 2013, 340: 1065–1068; (e) Zuo Z, Ahneman DT, Chu L, Terrett JA, Doyle AG, MacMillan DWC. *Science*, 2014, 345: 437–440; (f) Shin NY, Ryss JM, Zhang X, Miller SJ, Knowles RR. *Science*, 2019, 366: 364–369

10 For reviews on *C*-glycoside synthesis, see: (a) Lee D, He M. *Curr Topic Med Chem*, 2005, 5: 1333–1350; (b) Bokor É, Kun S, Goyard D, Tóth M, Praly JP, Vidal S, Somsák L. *Chem Rev*, 2017, 117: 1687–1764; (c) Yang Y, Yu B. *Chem Rev*, 2017, 117: 12281–12356; (d) Leng WL, Yao H, He JX, Liu XW. *Acc Chem Res*, 2018, 51: 628–639; (e) Kitamura K, Ando Y, Matsumoto T, Suzuki K. *Chem Rev*, 2018, 118: 1495–1598

11 For selected examples of the transition-metal-catalyzed *C*-glycosylation, see: (a) Gong H, Sinisi R, Gagné MR. *J Am Chem Soc*, 2007, 129: 1908–1909; (b) Gong H, Gagne MR. *J Am Chem Soc*, 2008, 130: 12177–12183; (c) Nicolas L, Angibaud P, Stansfield I, Bonnet P, Meerpoel L, Reymond S, Cossy J. *Angew Chem Int Ed*, 2012, 51: 11101–11104; (d) Zhao C, Jia X, Wang X, Gong H. *J Am Chem Soc*, 2014, 136: 17645–17651; (e) Zhu F, Rourke MJ, Yang T, Rodriguez J, Walczak MA. *J Am Chem Soc*, 2016, 138: 12049–12052; (f) Zhu F, Rodriguez J, Yang T, Kevlishvili I, Miller E, Yi D, O'Neill S, Rourke MJ, Liu P, Walczak MA. *J Am Chem Soc*, 2017, 139: 17908–17922; (g) Badir SO, Dumoulin A, Matsui JK, Molander GA. *Angew Chem Int Ed*, 2018, 57: 6610–6613; (h) Dumoulin A, Matsui JK, Gutiérrez-Bonet Á, Molander GA. *Angew Chem Int Ed*, 2018, 57: 6614–6618; (i) Dai Y, Tian B, Chen H, Zhang Q. *ACS Catal*, 2019, 9: 2909–2915

12 For reviews on *C*-Glycosylation *via* Heck reaction, see: (a) Wellington KW, Benner SA. *Nucleosides Nucleotides Nucleic Acids*, 2006, 25: 1309–1333; (b) Mabit T, Siard A, Legros F, Guillarme S, Martel A, Lebreton J, Carreaux F, Dujardin G, Collet S. *Chem Eur J*, 2018, 24: 14069–14074

13 (a) Babu RS, O'Doherty GA. *J Am Chem Soc*, 2003, 125: 12406–12407; (b) Babu RS, Zhou M, O'Doherty GA. *J Am Chem Soc*, 2004, 126: 3428–3429; (c) Guo H, O'Doherty GA. *Angew Chem Int Ed*, 2007, 46: 5206–5208; (d) Bajaj SO, Sharif EU, Akhmedov NG, O'Doherty GA. *Chem Sci*, 2014, 5: 2230–2234

14 Gomez A, Lobo F, Miranda S, Lopez J. *Molecules*, 2015, 20: 8357–8394

15 (a) Richards CJ, Damalidis T, Hibbs DE, Hursthouse MB. *Synlett*, 1995, 1995(01): 74–76; (b) Richards CJ, Mulvaney AW. *Tetrahedron-Asymmetry*, 1996, 7: 1419–1430; (c) Stangeland EL, Sammakia T. *Tetrahedron*, 1997, 53: 16503–16510; (d) Gao W, Zhang X, Raghunath M. *Org Lett*, 2005, 7: 4241–4244; (e) Yan XX, Peng Q, Zhang Y, Zhang K, Hong W, Hou XL, Wu YD. *Angew Chem Int Ed*, 2006, 45: 1979–1983; (f) Tong MC, Chen X, Tao HY, Wang CJ. *Angew Chem Int Ed*, 2013, 52: 12377–12380; (g) Tong MC, Chen X, Li J, Huang R, Tao H, Wang CJ. *Angew Chem Int Ed*, 2014, 53: 4680–4684; (h) Wei L, Zhu Q, Xu SM, Chang X, Wang CJ. *J Am Chem Soc*, 2018, 140: 1508–1513; (i) Zhang Q, Yu H, Shen L, Tang T, Dong D, Chai W, Zi W. *J Am Chem Soc*, 2019, 141: 14554–14559

16 (a) Zheng LS, Llopis Q, Echeverria PG, Férard C, Guillamot G, Phansavath P, Ratovelomanana-Vidal V. *J Org Chem*, 2017, 82: 5607–5615; (b) Guo H, O'Doherty GA. *Org Lett*, 2005, 7: 3921–3924; (c) Suzuki K, Yuki Y, Mukaiyama T. *Chem Lett*, 1981, 10: 1529–1532; (d) Tsubuki M, Kanai K, Nagase H, Honda T. *Tetrahedron*, 1999, 55: 2493–2514; (e) Dai Y, Zheng J, Zhang Q. *Org Lett*, 2018, 20: 3923–3927

17 (a) Colombo L, di Giacomo M, Ciceri P. *Tetrahedron*, 2002, 58: 9381–9386; (b) Guaragna A, D'Alonzo D, Paolella C, Napolitano C, Palumbo G. *J Org Chem*, 2010, 75: 3558–3568; (c) Ansari AA, Rajasekaran P, Khan MM, Vankar YD. *J Org Chem*, 2014, 79: 1690–1699; (d) Bataille C, Bégin G, Guillam A, Lemiègre L, Lys C, Maddaluno J, Toupet L. *J Org Chem*, 2002, 67: 8054–8062; (e) Hong BC, Chen ZY, Nagarajan A, Rudresha K, Chavan V, Chen WH, Jiang YF, Zhang SC, Lee GH, Sarshar S. *Tetrahedron Lett*, 2005, 46: 1281–1285

18 Berova N, Bari LD, Pescitelli G. *Chem Soc Rev*, 2007, 36: 914–931

19 Mydock-McGrane LK, Hannan TJ, Janetka JW. *Expert Opin Drug Discovery*, 2017, 12: 711–731