Nitrogen-Centered Radical Mediated Anomeric Specific Cascade Amidoglycosylation of Glycals

Wenbin Shang
  Yunnan University

Chunyu Zhu
  Yunnan University

Fengyuan Peng
  Yunnan University

Zhiqiang Pan
  Yunnan University

Yuzhen Ding
  Yunnan University

Chengfeng Xia (✉ xiacf@ynu.edu.cn)
  Yunnan University   https://orcid.org/0000-0001-5617-5430

Article

Abstract

A nitrogen-centered radical-mediated strategy to prepare 1,2-*trans* 2-amino-2-deoxyglycosides in one step was established. The cascade amidoglycosylation was initiated by a benzenesulfonimide radical generated from NFSI under the catalytic reduction of TEMPO. The benzenesulfonimide radical electrophilic added to the glycals, then the resulted glycosidic radical was converted to oxocarbenium upon oxidation by TEMPO+, and enabled the following anomeric specific glycosylation.

Introduction

2-Amino-2-deoxyglycosides, in particular, 2-*N*-acetamido-2-deoxyglycosides, are widely distributed in living organisms as glycoconjugates and naturally occurring oligosaccharides with important biological roles.[1-3] The 2-amino-2-deoxyglycosides are connected with other carbohydrates, lipids, or amino acids *via* either 1,2-*cis* or, more frequently, 1,2-*trans* glycosidic linkage.[2, 4] Therefore, the stereoselective formation either 1,2-*cis* or 1,2-*trans* glycosidic linkage of 2-amino-2-deoxyglycosides is of high significance due to its essentiality for oligosaccharide assembly.[5-8] A variety of synthetic approaches to 2-amino-2-deoxyglycosides have been developed and considerable progresses have been made.[9-12] Since some of the mono 2-amino-2-deoxysugars are naturally available or easily prepared, they have widely employed in synthesis of 2-amino-2-deoxyglycosides.[5, 13] And many different types of glycosamide precursors, including thioglycoside[14-17], trichloroacetimidate,[18-20] phosphate ester[21, 22], and OABz[23], have been extensively explored. However, these protocols commonly start from glycosamides with masking amino groups[24-26] such as Azide[16, 27-29], PhthN[30], AcNH[21, 31, 32] or TrocNH[33]. Normally, these glycosamide precursors are need to be prepared in multiple steps, including the specific protecting/deprotecting procedures, thus decrease the efficiency of synthesis (Scheme 1a).

Meanwhile glycals are also considered as building blocks for construction of 2-amino-2-deoxyglycosides. In this regard, the applicability of dipolar cycloaddition with azides,[34] [4+2] cycloaddition with azadicarboxylates,[9, 35] or aziridination with *N*-heterocyclic carbine (NHC)[36-39] to the synthesis of 2-amino-2-deoxyglycosides from glycals have been investigated (Scheme 1b, up equation). In the meantime, the installation of an azide moiety at the C-2 position of glycal as a source of an amino group has also been widely applied in preparation of 2-amino-2-deoxyglycosides (Scheme 1b, down equation).[40-46] However, the stereoselectivities at C-1 and C-2 are dependent on the structure of the glycal substrates and glycosylation often proceed nonstereoselectively. In addition, a further C-1 derivatization and construction of stereoselective glycosidic linkage were found to be a considerable challenge.

The N-F reagents, such as Selectfluor[TM] and *N*-fluorobenzenesulfonimide (NFSI), are mild electrophilic fluorinating reagents and well explored.[47] It was reported that when glycals were treated with N-F reagents, the 2-deoxy-2-fluoro carbohydrates were obtained by fluorination of glycals at C2 position (Scheme 1c).[48-50] Recently, nitrogen-centered radicals (NCRs) have aroused increasing concern in synthetic chemistry since NCRs could be used as key intermediates for effective construction of C-N

bonds.[51] Based on considerable synthetic potential of glycals for preparation of 2-amino-2-deoxyglycosides, we proposed that it would be an ideal strategy if the N-F reagents were converted to nitrogen-centered radicals[52, 53] and added to glycal at C-2 position, followed by glycosylation with acceptors at C-1 position. Herein, we reported the nitrogen-centered radical cascade regioselective amination of glycal and anomeric specific glycosylation (scheme 1d).

Results

Radical addition of glycals. As shown in scheme 2, we hypothesized that the nitrogen-centered benzenesulfonimide radical **A**, generated from NFSI by reduction with TEMPO, might regioselectively electrophilic add the alkenyl of glycal to give radical **D**. The radical **D** would then be oxidized by the TEMPO[+] **B** to afford the oxocarbenium **E** and recycle the catalysis TEMPO.[54, 55] We considered that the steric hindrance of benzenesulfonimide and/or the neighboring effects of sulfonyl group would direct the glycosylation in 1,2-trans manner to furnish the anomerically specific product **F**.

Our initial investigation of the nitrogen-centered radical involved amidoglycosylation was conduct between the tri-*O*-benzyl-D-glucal **1** and diisopropylidene-D-glucose **2**. After treatment with NFSI and catalytic amount of TEMPO in DCE at room temperature, the glycosylation product **3** was obtained in 22% yield (Table 1, entry 1). The NMR analysis showed that the acceptor **2** was β-selectively coupled with the glucal **1** as we proposed. We noticed that the glycal **1** was not completely consumed. To accelerate the reaction and increase the yield, the reaction temperature was raised to 50 ^{o}C. The glycosylation was slight improved with 38% yield (entry 2). Screening the solvents, such as DCM, THF, MeNO$_2$, and toluene (entries 3 - 6), identified MeCN as the optimal solvent with 56% yield (entry 7). Meanwhile, a byproduct was also isolated from the reaction mixture as results of Ferrier-rearrangement. According to the mechanism of Ferrier-rearrangement,[56-58] the C-3 elimination was resulted from the HF formation in the reaction. However, attempts to neutralize the HF with base (NaHCO$_3$, Na$_2$CO$_3$, Na$_3$PO$_4$ et al.) did not significantly suppress the Ferrier-rearrangement. Instead, we found that reducing the amount of NFSI considerably decreased the Ferrier-rearrangement byproduct and the glycosylation product **2** was afforded in 75% (Table 1, entry 8 and 9). The amount of catalysis TEMPO was also evaluated and 0.2 equivalent of TEMPO gave the highest yield (entries10 and 11). To demonstrate the practicability of this method, the reaction was conducted in 2 grams scale and 64% yield was achieved.

Scope of glycals. With the optimized reaction conditions established, various glycal donors were examined to explore the scope of the NCR-mediated amidoglycosylation (Scheme 3). Besides the benzyl ether, the methyl ether, benzylidene, and diisopropylidene were also suitable protecting groups and the corresponding disaccharides **4** − **6** were afforded in good yields as well as excellent selectivities (*β/α* > 20:1 or *β* only). However, we found that the glycal with acetyl protecting group only gave the product **7** in 37% yield. The low yield was due to the lower HOMO energies of the double bond.[59] The D-galactals and L-rhamnals were also subjected for the amidoglycosylation. The related disaccharides **8** - **11** were

harvested in good yields too. These results demonstrated that the nitrogen-centered radical was practical protocol for the preparation of β-selective 2-amino-2-deoxyglycosides using glycals as glycosylation donors.

Scope of acceptors. The scope of acceptors for amidoglycosylation was also evaluated (scheme 4). Different monosaccharide acceptors with primary alcohols were subjected for the radical glycosylation. The products **12** – **14** were obtained in good yields and excellent anomeric selectivities. The acceptors with secondary alcohols were then conducted for the glycosylation. But we found that the yields were obviously decreased (30% for **15** and 42% for **16**). We originally considered that the low yield was due to formation Ferrier-rearrangement byproducts too. However only trace amount of the rearrangement byproduct was isolated from the reaction mixture. Instead, we found that a 1-fluorosaccharide was formed as the major byproduct. We reasoned that the formation of 1-fluorosaccharide was due to the competition of NFSI-derived fluoride anion with the bulky secondary saccharide acceptors.[60, 61] It was found that addition of Na_2HPO_4 to the reaction mixture significantly avoided the formation of 1-fluorosaccharide and the yields were increased to 53% and 64%.

Besides the glycosylated serine **17**, a salidroside analog **18** with protective activities against the hypoglycemia and serum limitation induced cell death in rat pheochromocytoma cells,[62, 63] was also synthesized. Finally, the epiandrosterone was subjected as acceptor and the corresponding glycan **19** was furnished in moderate yield as a single anomeric product.

The disulfonyl group is a stable protecting group for subsequent reactions in polysaccharides synthesis. The benzenesulfonimide glycosides also can be easily converted to 2-*N*-acetamido-2-deoxyglycosides by simple treatment. As shown in scheme 5, the disulfonyl group of disaccharide **3** was efficiently removed by treatment with SmI_2.[64] Then the reaction mixture was treated with acetyl anhydride to introduce the acetyl group and gave the NAc-disaccharide **20** in 77% yield in one-pot manner.

In summary, we have established an efficient protocol for cascade synthesis of 1,2-*trans* 2-amino-2-deoxyglycoside, which gives a novel and useful example for radical-mediated glycosylation. The reaction involves a nitrogen-centered radical-mediated amination of glycals and followed by glycosylation. The utilities of this method was illustrated with different glycals and acceptors with highly anomeric selectivities. Moreover, the disulfonyl group was easily converted to acetyl group by one-pot treatment.

Methods

Methods for amidoglycosylation of glycals. To an oven-dried 15 mL reaction tube equipped with a stir bar in the glove box, 0.3 mmol NFSI, 0.3 mmol glycosyl acceptor and 0.05 mmol TEMPO were added. Then dry MeCN (500 μL) was added to dissolve the reactants and reagents. The reaction tube was sealed and moved out of the glove box. Glycal donor (0.25 mmol) was dissolved in dry MeCN (500 μL) and added to the above reaction mixture at a constant speed by a syringe over 2 h at 50°C. Then the reaction was stirred for additional 1 hour at 50°C until glycal donor was completely consumed (monitored by TLC).

The reaction solution was concentrated *in vacuum* to give the residue, which was subjected to flash chromatographic column to afford the corresponding amidoglycosylation products.

References

1. Fiedler, K. & Simons, K. The role of n-glycans in the secretory pathway. *Cell* **81**, 309-312 (1995).
2. Dwek, R.A. Glycobiology: Toward Understanding the Function of Sugars. *Chem. Rev.* **96**, 683-720 (1996).
3. Helenius, A., Aebi & Markus. Intracellular Functions of N-Linked Glycans. *Science* **291**, 2364-2369 (2001).
4. Herzner, H., Reipen, T., Schultz, M. & Kunz, H. Synthesis of Glycopeptides Containing Carbohydrate and Peptide Recognition Motifs. *Chem. Rev.* **100**, 4495-4538 (2000).
5. Bongat, A.F.G. & Demchenko, A.V. Recent trends in the synthesis of O-glycosides of 2-amino-2-deoxysugars. *Carbohydr. Res.* **342**, 374-406 (2007).
6. Banoub, J., Boullanger, P. & Lafont, D. Synthesis of oligosaccharides of 2-amino-2-deoxy sugars. *Chem. Rev.* **92**, 1167-1195 (1992).
7. Beau, J.-M. et al. Glycosylation: The Direct Synthesis of 2-Acetamido-2-Deoxy-Sugar Glycosides. *Eur. J. Org. Chem.* **2018**, 5795-5814 (2018).
8. El Ashry, E.S.H. & Aly, M.R.E. Synthesis and biological relevance of N-acetylglucosamine-containing oligosaccharides. *Pure Appl. Chem.* **79**, 2229-2242 (2007).
9. Griffith, D.A. & Danishefsky, S.J. Sulfonamidoglycosylation of glycals. A route to oligosaccharides with 2-aminohexose subunits. *J. Am. Chem. Soc.* **112**, 5811-5819 (1990).
10. Griffith, D.A. & Danishefsky, S.J. Total synthesis of allosamidin: an application of the sulfonamidoglycosylation of glycals. *J. Am. Chem. Soc.* **113**, 5863-5864 (1991).
11. Leblanc, Y., Fitzsimmons, B.J., Springer, J.P. & Rokach, J. [4 + 2] Cycloaddition reaction of dibenzyl azodicarboxylate and glycals. *J. Am. Chem. Soc.* **111**, 2995-3000 (1989).
12. Fitzsimmons, B.J., Leblanc, Y., Chan, N. & Rokach, J. Preparation of complex aminoglycosides: a new strategy. *J. Am. Chem. Soc.* **110**, 5229-5231 (1988).
13. Nielsen, M.M. & Pedersen, C.M. Catalytic Glycosylations in Oligosaccharide Synthesis. *Chem. Rev.* **118**, 8285-8358 (2018).
14. Geng, Y., Zhang, L.-H. & Ye, X.-S. Pre-activation protocol leading to highly stereoselectivity-controllable glycosylations of oxazolidinone protected glucosamines. *Chem. Commun.* , 597-599 (2008).
15. Geng, Y., Zhang, L.-H. & Ye, X.-S. Stereoselectivity investigation on glycosylation of oxazolidinone protected 2-amino-2-deoxy-d-glucose donors based on pre-activation protocol. *Tetrahedron* **64**, 4949-4958 (2008).
16. Zhang, Y., Zhang, H., Zhao, Y., Guo, Z. & Gao, J. Efficient Strategy for α-Selective Glycosidation of d-Glucosamine and Its Application to the Synthesis of a Bacterial Capsular Polysaccharide Repeating Unit Containing Multiple α-Linked GlcNAc Residues. *Org. Lett.* **22**, 1520-1524 (2020).

17. Manabe, S. et al. Significant Substituent Effect on the Anomerization of Pyranosides: Mechanism of Anomerization and Synthesis of a 1,2-cis Glucosamine Oligomer from the 1,2-trans Anomer. *Chem. Eur. J.* **20**, 124-132 (2014).

18. Mensah, E.A. & Nguyen, H.M. Nickel-Catalyzed Stereoselective Formation of α-2-Deoxy-2-Amino Glycosides. *J. Am. Chem. Soc.* **131**, 8778-8780 (2009).

19. Mensah, E.A., Yu, F. & Nguyen, H.M. Nickel-Catalyzed Stereoselective Glycosylation with C(2)-N-Substituted Benzylidene d-Glucosamine and Galactosamine Trichloroacetimidates for the Formation of 1,2-cis-2-Amino Glycosides. Applications to the Synthesis of Heparin Disaccharides, GPI Anchor Pseudodisaccharides, and α-GalNAc. *J. Am. Chem. Soc.* **132**, 14288-14302 (2010).

20. Kalikanda, J. & Li, Z. Study of the Stereoselectivity of 2-Azido-2-deoxygalactosyl Donors: Remote Protecting Group Effects and Temperature Dependency. *J. Org. Chem.* **76**, 5207-5218 (2011).

21. Arihara, R., Nakamura, S. & Hashimoto, S. Direct and Stereoselective Synthesis of 2-Acetamido-2-deoxy-β-D-glycopyranosides by Using the Phosphite Method. *Angew. Chem. Int. Ed.* **44**, 2245-2249 (2005).

22. Arihara, R., Kakita, K., Suzuki, N., Nakamura, S. & Hashimoto, S. Glycosylation with 2-Acetamido-2-deoxyglycosyl Donors at a Low Temperature: Scope of the Non-Oxazoline Method. *J. Org. Chem.* **80**, 4259-4277 (2015).

23. Wang, X., Wang, P., Li, D. & Li, M. 2,4-Dinitrobenzenesulfonamide-Directed SN2-Type Displacement Reaction Enables Synthesis of β-d-Glycosaminosides. *Org. Lett.* **21**, 2402-2407 (2019).

24. Enugala, R., Carvalho, L.C.R., Dias Pires, M.J. & Marques, M.M.B. Stereoselective Glycosylation of Glucosamine: The Role of the N-Protecting Group. *Chem. Asian J.* **7**, 2482-2501 (2012).

25. Aly, M.R.E.S. & El Ashry, E.S.H. in Advances in Carbohydrate Chemistry and Biochemistry (ed. Baker, D.C.) 117-224 (Academic Press, 2016).

26. Chang, K.-L., Zulueta, M.M.L., Lu, X.-A., Zhong, Y.-Q. & Hung, S.-C. Regioselective One-Pot Protection of d-Glucosamine. *J. Org. Chem.* **75**, 7424-7427 (2010).

27. Vasella, A., Witzig, C., Chiara, J.-L. & Martin-Lomas, M. Convenient Synthesis of 2-Azido-2-deoxy-aldoses by Diazo Transfer. *Helv. Chim. Acta.* **74**, 2073-2077 (1991).

28. Gauffeny, F., Marra, A., Shi Shun, L.K., Sinaÿ, P. & Tabeur, C. A novel and convenient method for the removal of a nitrate group at the anomeric position. *Carbohydr. Res.* **219**, 237-240 (1991).

29. Mong, K.-K.T., Yen, Y.-F., Hung, W.-C., Lai, Y.-H. & Chen, J.-H. Application of 2-Azido-2-deoxythioglycosides for β-Glycoside Formation and Oligosaccharide Synthesis. *Eur. J. Org. Chem.* **2012**, 3009-3017 (2012).

30. Ma, Z., Zhang, J. & Kong, F. A concise synthesis of two isomeric pentasaccharides, the O repeat units from the lipopolysaccharides of P. syringae pv. porri NCPPB 3364T and NCPPB 3365. *Carbohydr. Res.* **339**, 43-49 (2004).

31. Cai, Y., Ling, C.-C. & Bundle, D.R. Facile Approach to 2-Acetamido-2-deoxy-β-d-Glucopyranosides via a Furanosyl Oxazoline. *Org. Lett.* **7**, 4021-4024 (2005).

32. Xolin, A. et al. Glycosylation with N-acetyl glycosamine donors using catalytic iron(iii) triflate: from microwave batch chemistry to a scalable continuous-flow process. *Org. Chem. Front.* **1**, 992-1000 (2014).

33. Gege, C., Geyer, A. & Schmidt, R.R. Synthesis and Molecular Tumbling Properties of Sialyl Lewis X and Derived Neoglycolipids. *Chem. Eur. J.* **8**, 2454-2463 (2002).

34. Dahl, R.S. & Finney, N.S. A Surprising Dipolar Cycloaddition Provides Ready Access to Aminoglycosides. *J. Am. Chem. Soc.* **126**, 8356-8357 (2004).

35. Leblanc, Y., Fitzsimmons, B.J., Springer, J.P. & Rokach, J. [4 + 2] Cycloaddition reaction of dibenzyl azodicarboxylate and glycals. *Journal of the American Chemical Society* **111**, 2995-3000 (1989).

36. Murakami, T., Sato, Y., Yoshioka, K. & Tanaka, M. Convenient stereocontrolled amidoglycosylation of alcohols with acetylated glycals and trichloroethoxysulfonamide. *Carbohydr. Res.* **434**, 121-131 (2016).

37. Murakami, T., Sato, Y., Yoshioka, K. & Tanaka, M. Novel stereocontrolled amidoglycosylation of alcohols with acetylated glycals and sulfamate ester. *RSC Adv.* **4**, 21584-21587 (2014).

38. Nakajima, M. et al. A Direct S0→Tn Transition in the Photoreaction of Heavy-Atom-Containing Molecules. *Angew. Chem. Int. Ed.* **59**, 6847-6852 (2020).

39. Buttar, S. et al. Glycal Metallanitrenes for 2-Amino Sugar Synthesis: Amidoglycosylation of Gulal-, Allal-, Glucal-, and Galactal 3-Carbamates. *J. Org. Chem.* **83**, 8054-8080 (2018).

40. Lemieux, R.U. & Ratcliffe, R.M. The azidonitration of tri-O-acetyl-D-galactal. *Can. J. Chem.* **57**, 1244-1251 (1979).

41. Seeberger, P.H., Roehrig, S., Schell, P., Wang, Y. & Christ, W.J. Selective formation of C-2 azidodeoxy-d-glucose derivatives from d-glucal precursors using the azidonitration reaction. *Carbohydr. Res.* **328**, 61-69 (2000).

42. Czernecki, S., Ayadi, E. & Randriamandimby, D. Seleno glycosides. 2. Synthesis of Phenyl 2-(N-Acetylamino)- and 2-Azido-2-deoxy-1-seleno-.alpha.-D-glycopyranosides via Azido-phenylselenylation of Diversely Protected Glycals. *J. Org. Chem.* **59**, 8256-8260 (1994).

43. Santoyo-Gonzalez, F. et al. Synthesis of phenyl 2-azido-2-deoxy-1-selenoglycosides from glycals. *J. Org. Chem.* **58**, 6122-6125 (1993).

44. Bovin, N.V., Zurabyan, S.É. & Khorlin, A.Y. Addition of halogenoazides to glycals. *Carbohydr. Res.* **98**, 25-35 (1981).

45. Plattner, C., Höfener, M. & Sewald, N. One-Pot Azidochlorination of Glycals. *Org. Lett.* **13**, 545-547 (2011).

46. Chennaiah, A. & Vankar, Y.D. One-Step TEMPO-Catalyzed and Water-Mediated Stereoselective Conversion of Glycals into 2-Azido-2-deoxysugars with a PIFA−Trimethylsilyl Azide Reagent System. *Org. Lett.* **20**, 2611-2614 (2018).

47. Baudoux, J. & Cahard, D. Electrophilic fluorination with N-F reagents. *Org. React. (Hoboken, NJ, U. S.)* **69**, 347-672 (2007).

48. Vincent, S.P., Burkart, M.D., Tsai, C.-Y., Zhang, Z. & Wong, C.-H. Electrophilic Fluorination−Nucleophilic Addition Reaction Mediated by Selectfluor: Mechanistic Studies and New Applications. *J. Org. Chem.* **64**, 5264-5279 (1999).

49. Albert, M., Dax, K. & Ortner, J. A novel direct route to 2-deoxy-2-fluoro-aldoses and their corresponding derivatives. *Tetrahedron* **54**, 4839-4848 (1998).

50. Chen, Z.-M. et al. Organocatalytic Asymmetric Fluorination/Semipinacol Rearrangement: An Efficient Approach to Chiral β-Fluoroketones. *Chem. − Eur. J.* **18**, 12950-12954 (2012).

51. Kärkäs, M.D. Photochemical Generation of Nitrogen-Centered Amidyl, Hydrazonyl, and Imidyl Radicals: Methodology Developments and Catalytic Applications. *ACS Catal.* **7**, 4999-5022 (2017).

52. Miao, Q. et al. Metal-free C−H amination of arene with N-fluorobenzenesulfonimide catalysed by nitroxyl radicals at room temperature. *Chem. Commun.* **55**, 7331-7334 (2019).

53. Li, Y., Hartmann, M., Daniliuc, C.G. & Studer, A. Radical aminooxygenation of alkenes with N-fluoro-benzenesulfonimide (NFSI) and TEMPONa. *Chem. Commun.* **51**, 5706-5709 (2015).

54. Haidasz, E.A. et al. Acid Is Key to the Radical-Trapping Antioxidant Activity of Nitroxides. *J. Am. Chem. Soc.* **138**, 5290-5298 (2016).

55. Hodgson, J.L., Namazian, M., Bottle, S.E. & Coote, M.L. One-Electron Oxidation and Reduction Potentials of Nitroxide Antioxidants: A Theoretical Study. *J. Phys. Chem. A* **111**, 13595-13605 (2007).

56. Balmond, E.I., Coe, D.M., Galan, M.C. & McGarrigle, E.M. α-Selective Organocatalytic Synthesis of 2-Deoxygalactosides. *Angew. Chem. Int. Ed.* **51**, 9152-9155 (2012).

57. Balmond, E.I. et al. A 3,4-trans-Fused Cyclic Protecting Group Facilitates α-Selective Catalytic Synthesis of 2-Deoxyglycosides. *Angew. Chem. Int. Ed.* **53**, 8190-8194 (2014).

58. Zhao, G. & Wang, T. Stereoselective Synthesis of 2-Deoxyglycosides from Glycals by Visible-Light-Induced Photoacid Catalysis. *Angew. Chem. Int. Ed.* **57**, 6120-6124 (2018).

59. Linker, T. et al. Remarkable Oxidation Stability of Glycals: Excellent Substrates for Cerium(IV)-Mediated Radical Reactions. *J. Am. Chem. Soc.* **130**, 16003-16010 (2008).

60. Trainor, G.L. The preparation of O-trifluoromethyl carbohydrates. *J. Carbohydr. Chem.* **4**, 545-563 (1985).

61. Kumar, A., Kumar, V., Dere, R.T. & Schmidt, R.R. Glycoside Bond Formation via Acid-Base Catalysis. *Org. Lett.* **13**, 3612-3615 (2011).

62. Meng, Y. et al. Synthesis and protective effects of aralkyl alcoholic 2-acetamido-2-deoxy-β-d-pyranosides on hypoglycemia and serum limitation induced apoptosis in PC12 cell. *Bioorg. Med. Chem.* **19**, 5577-5584 (2011).

63. Guo, Y. et al. Synthesis and Biological Evaluation of Two Salidroside Analogues in the PC12 Cell Model Exposed to Hypoglycemia and Serum Limitation. *Chem. Pharm. Bull.* **59**, 1045-1047 (2011).

64. Hill, D.C., Flugge, L.A. & Petillo, P.A. SmI2-Promoted Deprotection of N-(Arylsulfonyl)glucosamines. *J. Org. Chem.* **62**, 4864-4866 (1997).

Declarations

Author contributions

W.S. and C.X. conceived this project. W.S., C.Z., F.P., Z.P. and Y.D. carried out the experiments. W.S. and C.X. wrote the paper. All authors discussed the results.

Competing interests

The authors declare no competing interests.

Table And Schemes

The table and schemes are available in the Supplementary Files.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupportingInformation.docx
- SupportingInformation.docx
- SupportingInformation.docx
- Table1.docx
- Table1.docx
- Table1.docx
- Scheme1.png
- Scheme1.png
- Scheme1.png
- Scheme2.png
- Scheme2.png
- Scheme2.png
- Scheme3.png
- Scheme3.png
- Scheme3.png

- Scheme4.png
- Scheme4.png
- Scheme4.png
- Scheme5.png
- Scheme5.png
- Scheme5.png