ChemPubSoc Europe

DOI: 10.1002/chem.201405516

CHEMISTRY
A European Journal
Communication

Photocatalysis

Stereoselective Synthesis of α-Linked 2-Deoxy Glycosides Enabled by Visible-Light-Mediated Reductive Deiodination

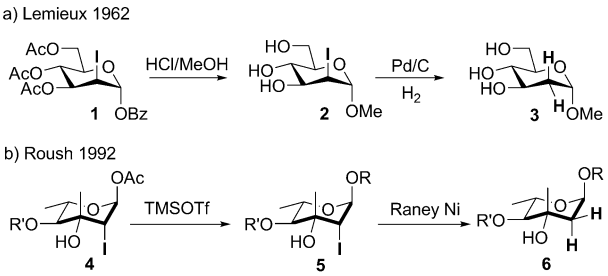
Hao Wang,[a] Jinyi Tao,[a] Xinpei Cai,[a] Wei Chen,[a] Yueqi Zhao,[a] Yang Xu,[a] Wang Yao,[a] Jing Zeng,[a] and Qian Wan*[a, b]

Dedicated to the memory of Professor André Lubineau

Abstract: 2-Deoxy sugars and their derivatives occur abundantly in many pharmaceutically important natural products. However, the construction of specific 2-deoxy-glycosidic bonds remains as a challenge. Herein, we report an efficient way to prepare 2-deoxy-α-glycosides by glycosylation of 2-iodo-glycosyl acetate and subsequent visible-light-mediated tin-free reductive deiodination. We have successfully applied the postglycosylational-deiodination strategy in the synthesis of more than 30 mono-, di-, tri-, tetra- and pentadeoxysaccharides with excellent stereoselectivity and efficiency. This method has also been applied to the synthesis of a 2-deoxy-tetrasaccharide containing four α-linkages.

Many biologically active natural products contain α- or/and β-linked 2-deoxy sugar moieties.[1] The occurrence of the deoxy sugar components may influence the biological or/and pharmacological properties of these natural products and drugs. Consequently, the synthesis of deoxy sugars and their derivatives has become an important yet challenging field in carbohydrate chemistry and natural-product synthesis.[2] However, the creation of 2-deoxy sugar linkages directly from 2-deoxy-glycosyl donors is more challenging than other glycosidic bond formation due to the lack of a stereodirecting group at the C-2 position.[3] Recently, Zhu[4] and Bennett[5] have succeeded in constructing 2-deoxy glycosides with excellent α-selectivity by anomeric *O*-alkylation and a reagent-controlled strategy under strong basic conditions, respectively. Despite the remarkable progress made in the past few years, moderate yields, poor stereoselectivity, substrate dependence, and the requirement of orthogonal sets of protecting groups are usually encountered in the practice.[6] Moreover, the inherent susceptibility of 2-deoxy sugar is another major concern. A number of 2-deoxy sugar linkages exhibited poor tolerance during multistep synthesis. As a result, the utilizations of direct glycosylation in the preparation of complex 2-deoxy glycosides or natural products are rarely reported in the literature,[7] while the most effective way to synthesize biologically active targets containing deoxy sugar component relies on an indirect glycosylation strategy.[8]

A commonly used indirect method involves pre-installation of a temporary directing group at the C-2 position, followed by its reductive removal after glycosylation.[3] In 1962, Lemieux et al. found methanolysis of a 2-deoxy-2-iodo-mannosyl benzoate **1** yielded a methyl 2-deoxy-2-iodo-α-glycoside **2**, and the resulting product was converted to the corresponding α-linked 2-deoxy sugar **3** by using a palladium-catalyzed reduction (Scheme 1a).[9] In 1992, Roush et al. reported that *trans*-di-



Scheme 1. Selected indirect approaches to 2-deoxy-α-glycosides.

axial 2-iodo glycosyl acetate **4** was successfully used as a glycosyl donor in their synthesis of trisaccharide of olivomycin A (Scheme 1b).[10] Later, Roush et al. further demonstrated that the iodo-substituent at the C-2 position well controlled the stereochemistry of the newly formed glycosidic bond.[11] This character was further illustrated in the glycosylation of 2-deoxy-2-halo-glycosyl trifluoroacetimidtaes,[8a] trichloroacetimidates,[12a–c] thioethers,[12d,e] and fluorides,[12f,g] which provided the corresponding 2-deoxy-2-halo-glycosides, and after reductive removal, the 2-deoxy-glycosides with high stereroselectivity. Meanwhile, the use of oxidative coupling of glycals in the preferential synthesis of 2-deoxy-2-halo-α-glycosides was developed by Lemieux,[13a] Tatsuta,[13b] Thiem,[13c,d] Kessler,[13e] and Danishefsky,[13f] respectively. The C-2 auxiliary substituents may not only control the stereoselectivity of glycosylation, but also

[a] *H. Wang, J. Tao, X. Cai, W. Chen, Y. Zhao, Y. Xu, W. Yao, Prof. Dr. J. Zeng, Prof. Dr. Q. Wan*
Tongji School of Pharmacy
Huazhong University of Science and Technology
13 Hangkong Road, Wuhan, Hubei, 430030 (P. R. China)
E-mail: wanqian@hust.edu.cn

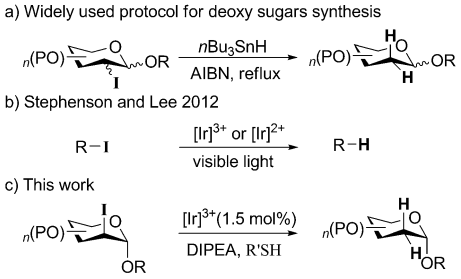
[b] *Prof. Dr. Q. Wan*
Institute of Brain Research
Huazhong University of Science and Technology
13 Hangkong Road, Wuhan, Hubei, 430030 (P. R. China)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201405516.

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

stabilize the resulting glycosidic linkages. The latter feature would provide synthetic chemists more flexibility to conquer target molecules, and the introduction of the desired 2-deoxy function(s) in the later stage could significantly improve the overall efficiency of the synthesis.

The most widely used deiodination reaction involves the toxic organotin-mediated radical reduction (Scheme 2a).[14] Despite the development of several improved methods to avoid the use of potentially explosive initiators and toxic hydrogen atom donors,[15] the successful applications of those methods

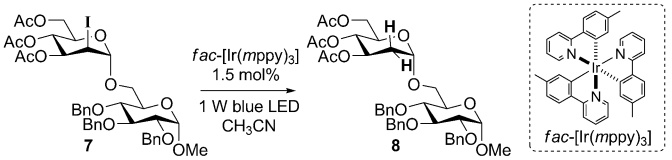


Scheme 2. Reductive deiodinations.

in the synthesis of complex targets were rare.[16] Recently, studies on visible-light-induced photocatalytic reactions have received considerable attention.[17] In 2012, Stephenson[18a] and Lee[18b] reported a highly efficient way to remove an iodo-group by using a photocatalyst and readily available amine under visible-light irradiation, respectively (Scheme 2b).[19] We envisioned that the combination of such an advance with Roush's strategy[10] would be beneficial to solve the challenging problem involving the synthesis of 2-deoxy sugars. Herein, we report an efficient way to prepare 2-deoxy-α-glycoside by glycosylation of 2-iodo-glycosyl acetate and subsequent visible-light-mediated tin-free reductive deiodination (Scheme 2c).[20,21]

Initially, we selected the deiodination of the known 2-deoxy-2-iodo-α-mannosyl disaccharide **7** as the model study. An encouraging result was obtained upon submitting **7** to irradiation by a 1 W blue LED with *fac*-[Ir(*m*ppy)$_3$] (*fac*-[Ir(*m*ppy)3] = *fac*-tris[2-(*p*-tolyl)pyridinato-C^2,N']iridium(III)) (1.5 mol%) as a photosensitizer or catalyst in Stephenson reported conditions (Table 1, entries 1–6).[18a,22] Early studies revealed that the blend of *n*Bu$_3$N (2 equiv) and Hantzsch ester (2 equiv) in the presence of the *fac*-[Ir(*m*ppy)$_3$] (1.5 mol%) in CH$_3$CN might reduce secondary iodide efficiently within a couple of hours (entry 6). Subsequent optimization revealed that the replacement of expensive Hantzsch ester with inexpensive *p*-toluenethiol afforded an excellent yield (entries 7, 8).[23] Other thiols were also tested for the reduction and were found to be inferior to *p*-toluenethiol.[23] In the absence of the reducing reagent (amine), the reduction became less efficient and the 2-deoxyl glycoside **8** was isolated with 39% yield (entry 10). Although the role of *p*-toluenethiol in this transformation is not fully understood at this moment, it may act as a hydrogen-atom shuttle, electron donor, or hydrogen donor.[24]

Table 1. Optimization of visible-light-mediated deiodination.



Entry	Conditions	Yield [%][a]
1	*n*Bu$_3$N (10 equiv), 1.5 h	84
2	*n*Bu$_3$N (2 equiv), 3 h	69
3	DIPEA (10 equiv), 1.5 h	80
4	DIPEA (2 equiv), 1.5 h	60
5	*n*Bu$_3$N (10equiv), HCOOH(10 equiv), 1.5 h	86
6	*n*Bu$_3$N (2 equiv), Hantzsch ester (2 equiv), 1.5 h	91
7	*n*Bu$_3$N (2 equiv), *p*-toluenethiol (2 equiv), 1.5 h	93
8	DIPEA (2 equiv), *p*-toluenethiol (2 equiv), 1.5 h	**95**
9	DIPEA (2 equiv), *p*-toluenethiol (1 equiv), 1.5 h	42
10	*p*-toluenethiol (5 equiv), 4 h	39

[a] Isolated yield after purification by column chromatography on SiO$_2$. DIPEA = *N*,*N*-diisopropylethylamine.

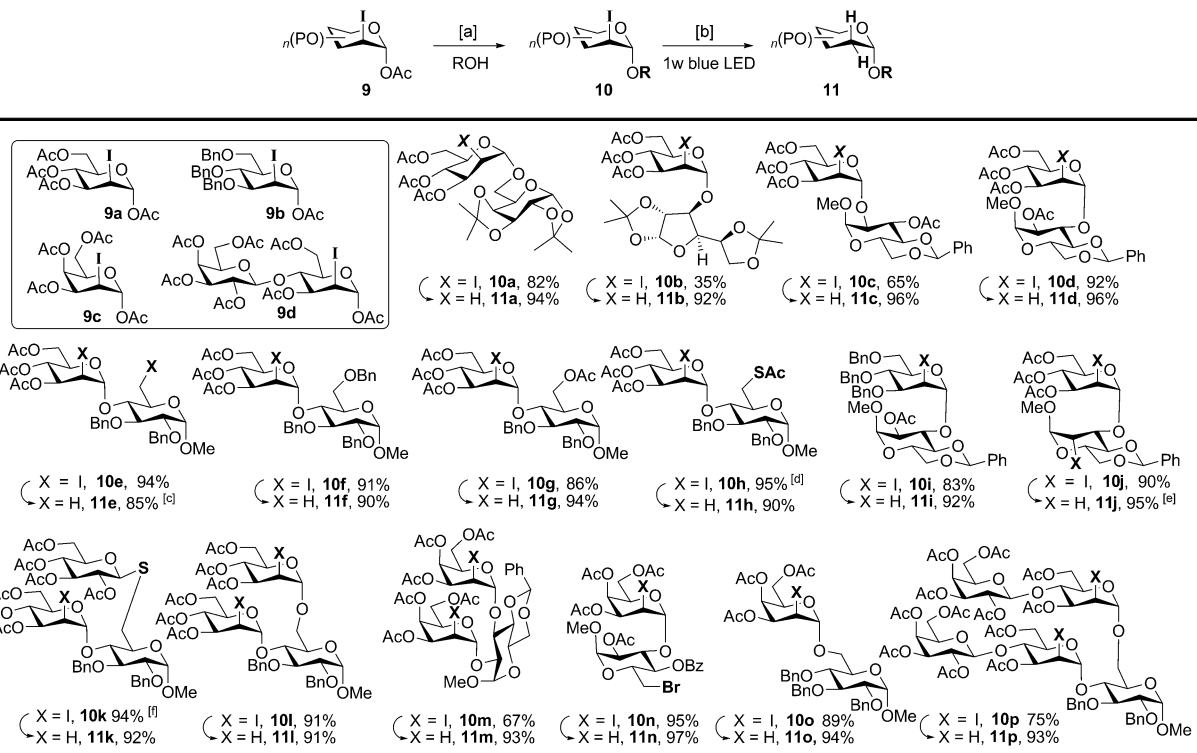
In view of the synthetic potential of deiodination, the scope of this newly uncovered protocol in 2-deoxy-α-glycoside synthesis was next explored. As summarized in Table 2, from the known corresponding glycosyl acetates **9a–d**,[6b,25] α-linked 2-iodo-2-deoxy glycosides **10a–p** were accessed under the modified Roush's conditions in good to excellent yield with exclusive stereochemistry. The optimal deiodination condition from Table 1 (entry 8) was adopted to examine the scope of functionalization of the C-2-position of newly formed glycosides. The visible-light-mediated reduction was found to reduce mono-/di-, primary, or/and secondary iodides within two hours, and the desired 2-deoxy-α-di-, tri-, and pentasaccharides **11a–p** were obtained with good to excellent yields. Both glycosylation and deiodination demonstrated excellent functional-group tolerance, in which thioether **11k** (*S*-glycoside), thioester **11h**, ester, benzylideneacetals, acetonide, silyl-ether, ally ether, glycan, and benzyl ethers remained untouched.[26] We were also delighted to discover the remarkable chemoselectivity during the reduction between alkyl iodide and alkyl bromide **11n**, which was difficult to achieve under conventional conditions.[8a]

Compared to the conventional deiodination conditions, these photoinduced dieodination reaction conditions displayed a great advantage (Table 3). Among the reported methods, the combination of Bu$_3$SnH and AIBN exhibited the best efficiency, which produced 2-deoxy disaccharide **8** in 81% yield (Table 3, entry 1).[16a] $Na_2S_2O_4$ (entry 2) VA-061 and H_3PO_2 (entry 3), and Et_3B (entry 4)[16b–d] also generated **8** in moderate yields. However, the rest conditions showed lesser efficiency under the current circumstance.[16e–i]

To further demonstrate the synthetic potential of this methodology in the construction of complex targets, we decided to synthesize 2-dexoy-α-tetrasaccharide **14** containing four α-linkages by two routes (Scheme 3). The diiododisaccharide **10j** underwent a sequential removal of benzylideneactetal (90%), TMSOTf-mediated glycosylation (70%), and global reduction

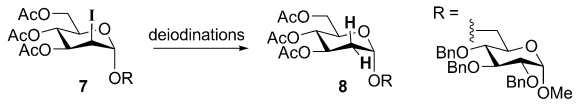
© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Table 2. Synthesis of α-linked-2-deoxy-glycosides.



[a] **9a–d** (1.1 equiv), TMSOTf (0.5 equiv) for each alcohol, 0 °C, toluene. [b] *fac*-Ir(*m*ppy)$_3$ (1.5 mol%), DIPEA (2.0 equiv), *p*-toluenethiol (2.0 equiv) for each iodine, CH_3CN, RT. [c] *fac*-[Ir(*m*ppy)$_3$] (3.0 mol%), DIPEA (20.0 equiv), *tert*-butyl mercaptan (4.0 equiv), CH_3CN. [d] **10e**, KSAc (1.2 equiv), DMF, 30 °C. [e] CH_2Cl_2 was used as the solvent. [f] **10e**, DIPEA, RSH (1.5 equiv), CH_3CN, RT.

Table 3. Comparison among different deiodination reaction conditions.



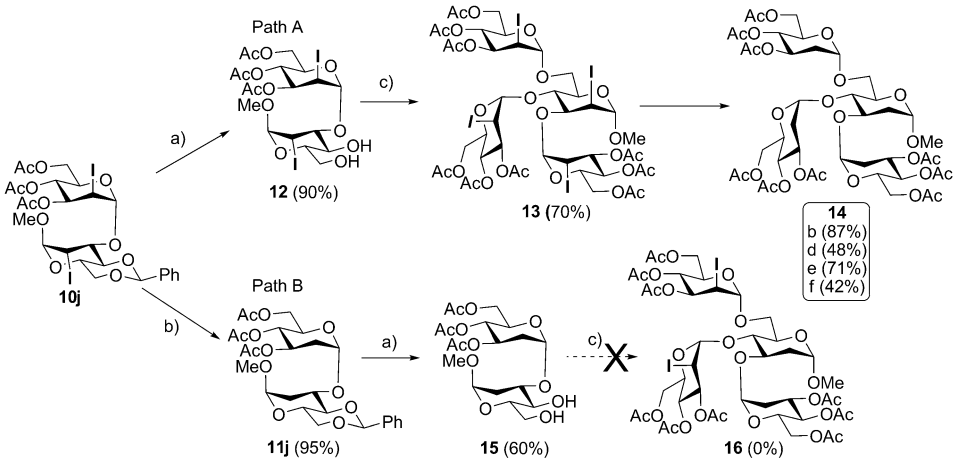
Entry	Conditions	Yield [%][a]
1	Bu_3SnH (3.0 equiv), AIBN (0.1 equiv), toluene, 100 °C, 2 h	81
2	$Na_2S_2O_4$ (8 equiv), $NaHCO_3$ (10 equiv), 40 °C, DMF/H_2O, 21 h	66
3	VA-061 (0.5 equiv), aq. H_3PO_2 (10 equiv), NEt_3 (10 equiv), *i*PrOH, 80 °C, 1 h	72
4	Et_3B (24 equiv), THP, air, 0 °C, 3 h	79
5	diauroyl peroxide (0.017 equiv), reflux, cyclohexane, 23 h	42
6	$(TMS)_3SiH$ (1.5 equiv), ACCN (0.3 equiv), reflux, H_2O, 8 h	36
7	$(TMS)_3SiH$ (2 equiv), air, CH_3CN, 50 °C, 20 h	10
8	$InCl_3$ (1.0 equiv), $NaBH_4$ (1.5 equiv), CH_3CN, RT, 8 h	43
9	$(TMS)_3SiH$ (2.0 equiv), AIBN (0.2 equiv), toluene, 75 °C, 5 h	30
10	DIEPA (2 equiv), *p*-toluenethiol (2 equiv), 1 W blue LED, *fac*-[Ir(*m*ppy)$_3$] (1.5 mol%), 1.5 h.(this work)	**95**

[a] Isolated yield after purification by coloumn chromatography on SiO_2. ACCN = 1,1′-azobis(cyclohexane-carbonitrile); VA-061 = 2,2′-azobis[2-(2-imidazolin-2-yl)propane]; AIBN = azobisisobutyronitrile; *fac*-[Ir(*m*ppy)$_3$] = *fac*-tris(2-(*p*-tolyl)pyridine-C^2, N')iridium(III).

(87%) to afford terasaccharide **14** bearing four α-linkages with good yield (Scheme 3, Path A). It should be noted that the global deiodinations were less efficient without the addition of thiol (Scheme 3, conditions d and e) or with a lower catalyst loading (conditions f).[27] Alternatively, the 2-deoxy disaccharide **11j**, obtained from deiodinations of **10j**, was subjected to the optimal debenzylidenation to afford the corresponding diol **15** in moderate yield. However, subsequently, we failed to isolate the diiodotetrasccharide **16** according to our standard glycosylation conditions (Scheme 3, Path B), probably due to the sensitive nature of the 2-deoxy glycosidic bond. This comparative study clearly demonstrated the advantages of an indirect synthesis strategy. The iodo group at the C-2 position has been used as a temporary directing group as well as an impermanent stabilizing group during the multistep transformations.

In conclusion, an efficient approach for stereospecific synthesis of 2-deoxy-α-(1→2), (1→3), (1→4), and (1→6)-linked glycosides by the postglycosylational-deiodination strategy has been reported. The 2-, 3-, 4-, and 6-iodo group can be reduced efficiently under visible-light irradiation. Further applications of this protocol to the synthesis of α-linked 2-deoxy glycosides and synthesis of naturally occurring therapeutic molecules bearing 2-deoxy sugar components as well as mechanistic studies are currently under investigation and will be reported in due course.

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 3. Synthesis of α-linked-2-deoxy tetrasaccharide by later-stage deiodination. a) *p*-TsOH·H_2O (1.5 equiv), MeOH/CH_2Cl_2 (1:1), 40 °C. b) *fac*-[Ir(*m*ppy)$_3$] (1.5 mol%), DIPEA (2.0 equiv), *p*-toluenethiol (2.0 equiv) for each iodine, RT. c) **9a** (2.2 equiv), TMSOTf (1.0 equiv), CH_2Cl_2, 0 °C. d) *fac*-[Ir(*m*ppy)$_3$] (6.0 mol%), DIPEA (40.0 equiv). e) *fac*-[Ir(*m*ppy)$_3$] (6.0 mol%), *n*Bu_3N (8.0 equiv), Hantzsch ester (8.0 equiv). f) *fac*-[Ir(*m*ppy)$_3$] (1.5 mol%), DIPEA (40.0 equiv), *p*-toluenethiol (2.0 equiv).

Acknowledgements

We thank the National Natural Science Foundation of China (21272082, 21402055, 21472054), the Recruitment Program of Global Youth Experts of China, the State Key Laboratory of Bioorganic and Natural Products Chemistry (SKLBNPC13425), the Specialized Research Fund for the Doctoral Program of Higher Education (20120142120092), and the Huazhong University of Science and Technology (2014ZZGH015) for support.

Keywords: deiodination · glycosides · glycosylation · photocatalysis · radical reaction

[1] a) R. M. De Lederkremer, C. Marino, *Adv. Carbohydr. Chem. Biochem.* **2007**, *61*, 143 – 216; b) A. Kirschning, A. F.-W. Bechthold, J. Rohr, *Top. Curr. Chem.* **1997**, *188*, 1 – 84.

[2] a) V. Křen, T. řezanka, *FEMS Microbiol. Rev.* **2008**, *32*, 858 – 889; b) J. M. Langenhan, B. R. Griffith, J. S. Thorson, *J. Nat. Prod.* **2005**, *68*, 1696 – 1711.

[3] For recent reviews on the synthesis of 2-deoxy glycosides, see: a) D. Takahashi, K. Toshima, In *Stereoselective Synthesis of Drugs and Natural Products*, 2 V set, first edition (Eds.: V. Andrushko, N. Andushko), John Wiley & Sons Inc. **2013**, pp. 1137; b) A. Borovika, P. Nagorny, *J. Carbohydr. Chem.* **2012**, *31*, 255 – 283; c) Z. Li, N. Ding, W. Zhang, P. Wang, M. Li, Y. Li, *Chin. J. Org. Chem.* **2012**, *32*, 1812 – 1826; d) D. Hou, T. L. Lowary, *Carbohydr. Res.* **2009**, *344*, 1911 – 1940; e) J. Thiem, W. Klaffke, *Comprehensive Glycoscience: From Chemistry to Systems Biology* **2007**, ##*vol 1*, 313; f) C. H. Marzabadi, R. W. Franck, *Tetrahedron* **2000**, *56*, 8385 – 8417.

[4] a) D. Zhu, K. N. Baryal, S. Adhikari, J. Zhu, *J. Am. Chem. Soc.* **2014**, *136*, 3172 – 3175; b) K. N. Baryal, D. Zhu, X. Li, J. Zhu, *Angew. Chem. Int. Ed.* **2013**, *52*, 8012 – 8016; *Angew. Chem.* **2013**, *125*, 8170 – 8174.

[5] a) J. P. Issa, C. S. Bennett, *J. Am. Chem. Soc.* **2014**, *136*, 5740 – 5744; b) J. P. Issa, D. Lloyd, E. Steliotes, C. S. Bennett, *Org. Lett.* **2013**, *15*, 4170 – 4173.

[6] Selected recent synthesis of 2-deoxy glycosides, see: a) D. Zhu, S. Adhikari, K. N. Baryal, B. N. Abdullah, J. Zhu, *J. Carbohydr. Chem.* **2014**, *33*, 438 – 451; b) D. Liu, S. Sarrafour, W. Guo, B. Goulart, C. S. Bennett, *J. Carbohydr. Chem.* **2014**, *33*, 423 – 434; c) E. I. Balmond, D. Benito-Alifonso, D. M. Coe, R. W. Alder, E. M. McGarrigle, M. C. Galan, *Angew. Chem. Int. Ed.* **2014**, *53*, 8190 – 8194; *Angew. Chem.* **2014**, *126*, 8329 – 8333; d) T. M. Beale, P. J. Moon, M. S. Taylor, *Org. Lett.* **2014**, *16*, 3604 – 3607; e) M. Kaneko, S. B. Herzon, *Org. Lett.* **2014**, *16*, 2776 – 2779; f) M. Islam, N. D. Tirukoti, S. Nandi, S. Hotha, *J. Org. Chem.* **2014**, *79*, 4470 – 4476; g) S. Adhikari, K. N. Baryal, D. Zhu, X. Li, J. Zhu, *ACS Catal.* **2013**, *3*, 57 – 60; h) V. P. Verma, C.-C. Wang, *Chem. Eur. J.* **2013**, *19*, 846 – 851; i) J. M. Nogueira, J. P. Issa, A. A. Chu, J. A. Sisel, R. S. Schum, C. S. Bennett, *Eur. J. Org. Chem.* **2012**, *77*, 4927 – 4936; j) E. I. Balmond, D. M. Coe, M. C. Galan, E. M. McGarrigle, *Angew. Chem. Int. Ed.* **2012**, *51*, 9152 – 9155; *Angew. Chem.* **2012**, *124*, 9286 – 9289; k) J. M. Nogueira, S. H. Nguyen, C. S. Bennett, *Org. Lett.* **2011**, *13*, 2814 – 2817; l) Y. Li, X. Yang, Y. Liu, C. Zhu, Y. Yang, B. Yu, *Chem. Eur. J.* **2010**, *16*, 1871 – 1882; m) Y.-S. Lu, Q. Li, Y. Wang, X.-S. Ye, *Synlett* **2010**, 1519 – 1524; n) Y.-S. Lu, Q. Li, L.-H. Zhang, X.-S. Ye, *Org. Lett.* **2008**, *10*, 3445 – 3448; o) J. Park, T. J. Boltje, G.-J. Boons, *Org. Lett.* **2008**, *10*, 4367 – 4370; p) H. Tanaka, A. Yoshizawa, T. Takahashi, *Angew. Chem. Int. Ed.* **2007**, *46*, 2505 – 2507; *Angew. Chem.* **2007**, *119*, 2557 – 2559; q) B. D. Sherry, R. N. Loy, F. D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 4510 – 4511; r) K. S. Kim, J. Park, Y. J. Lee, Y. S. Seo, *Angew. Chem. Int. Ed.* **2003**, *42*, 459 – 462; *Angew. Chem.* **2003**, *115*, 475 – 478.

[7] For selected direct synthesis of digitoxin, see: a) F. E. McDonald, K. S. Reddy, *Angew. Chem. Int. Ed.* **2001**, *40*, 3653 – 3655; *Angew. Chem.* **2001**, *113*, 3765 – 3767; b) K. N. Baryal, S. Adhikari, J. Zhu, *J. Org. Chem.* **2013**, *78*, 1246912476.

[8] a) X. Yang, B. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 12433 – 12435; b) W. R. Roush, R. A. Hartz, D. J. Gustin, *J. Am. Chem. Soc.* **1999**, *121*, 1990 – 1991; c) W. R. Roush, C. E. Bennett, *J. Am. Chem. Soc.* **2000**, *122*, 6124 – 6125; d) T. B. Durham, N. Blanchard, B. M. Savall, N. A. Powell, W. R. Roush, *J. Am. Chem. Soc.* **2004**, *126*, 9307 – 9317; e) S. J. Danishefsky, H. G. Selnick, D. M. Armistead, F. E. Wincott, *J. Am. Chem. Soc.* **1987**, *109*, 8119 – 8120; f) K. C. Nicolaou, Y. Li, K. C. Fylaktakidou, H. J. Mitchell, H.-X. Wei, B. Weyershausen, *Angew. Chem. Int. Ed.* **2001**, *40*, 3849 – 3854; *Angew. Chem.* **2001**, *113*, 3968 – 3972.

[9] a) R. U. Lemieux, S. Levine, *Can. J. Chem.* **1962**, *40*, 1926 – 1932; b) J. Stanek, V. Schwarz, *Collect. Czech. Chem. Commun.* **1955**, *20*, 42 – 45. The authors mis-characterized compound **1**.

[10] D. P. Sebesta, W. R. Roush, *J. Org. Chem.* **1992**, *57*, 4799 – 4802.

[11] a) W. R. Roush, X.-F. Lin, *J. Am. Chem. Soc.* **1995**, *117*, 2236 – 2250; b) J. A. Hunt, W. R. Roush, *J. Am. Chem. Soc.* **1996**, *118*, 9998 – 9999; c) A. Kirschning, *Eur. J. Org. Chem.* **1998**, 2267 – 2274; d) W. R. Roush, C. E. Bennett, *J. Am. Chem. Soc.* **1999**, *121*, 3541 – 3542; e) W. R. Roush, S. Narayan, *Org. Lett.* **1999**, *1*, 899 – 902; f) A. Kirschning, M. Jesberger, A. Schönberger, *Org. Lett.* **2001**, *3*, 3623 – 3626; h) T. B. Durham, W. R. Roush, *Org. Lett.* **2003**, *5*, 1871 – 1874.

[12] a) W. R. Roush, B. W. Gung, C. E. Bennett, *Org. Lett.* **1999**, *1*, 891 – 893; b) T. B. Durham, W. R. Roush, *Org. Lett.* **2003**, *5*, 1875 – 1878; c) P. Y. Chong, W. R. Roush, *Org. Lett.* **2002**, *4*, 4523 – 4526; d) M. Á. Rodríguez, O. Boutureira, X. Arnés, M. I. Matheu, Y. Díaz, S. Castillón, *J. Org. Chem.* **2005**, *70*, 10297 – 10310; e) A. Kövér, O. Boutureira, M. I. Matheu, Y. Díaz, S. Castillón, *J. Org. Chem.* **2014**, *79*, 3060 – 3068; f) N. Blanchard, W. R. Roush, *Org. Lett.* **2003**, *5*, 81 – 84; g) K. Toshima, K. Uehara, H. Nagai, S. Matsumura, *Green Chem.* **2002**, *4*, 27 – 29.

[13] a) R. U. Lemieux, A. Morgan, *Can. J. Chem.* **1965**, *43*, 2190 – 2198; b) K. Tatsuta, K. Fujimoto, M. Kinoshita, S. A. Umezawa, *Carbohydr. Res.* **1977**, *54*, 85 – 104; c) J. Thiem, H. Karl, J. Schwentner, *Synthesis* **1978**, *9*, 696 – 698; d) J. Thiem, H. Karl, *Tetrahedron Lett.* **1978**, *19*, 4999 – 5002; e) H. Kessler, M. Kottenhahn, A. Kling, C. Kolar, *Angew. Chem. Int. Ed. Engl.*

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

1987, *26*, 888 – 890; *Angew. Chem.* **1987**, *99*, 919 – 921; f) R. W. Friesen, S. J. Danishefsky, *J. Am. Chem. Soc.* **1989**, *111*, 6656 – 6660.

[14] a) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2002**, *102*, 4009 – 4091; b) W. P. Neumann, *Synthesis* **1987**, *8*, 665 – 683.

[15] For the review on tin free reduction, see: P. A. Baguley, J. C. Walton, *Angew. Chem. Int. Ed.* **1998**, *37*, 3072 – 3082; *Angew. Chem.* **1998**, *110*, 3272 – 3283.

[16] a) D. H. R. Barton, S. W. McCombie, *J. Chem. Soc. Perkin Trans. 1* **1975**, *16*, 1574 – 1585; b) V. Costantino, E. Fattorusso, C. Imperatore, A. Mangoni, *Tetrahedron Lett.* **2002**, *43*, 9047 – 9050; c) H. Nambu, A. H. Alinejad, K. Hata, H. Fujioka, Y. Kita, *Tetrahedron Lett.* **2004**, *45*, 8927 – 8929; d) T. Muraki, M. Yokoyama, H. Togo, *J. Org. Chem.* **2000**, *65*, 4679 – 4684; e) J. Boivin, B. Quiclet-Sire, L. Ramos, S. Z. Zard, *Chem. Commun.* **1997**, *4*, 353 – 354; f) A. Postigo, S. Kopsov, C. Ferreri, C. Chatgilialogu, *Org. Lett.* **2007**, *9*, 5159 – 5162; g) H. Jiang, J. R. Bak, F. J. López-Delgado, K. A. Jørgensen, *Green Chem.* **2013**, *15*, 3355 – 3359; h) K. Inoue, A. Sawada, I. Shibata, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 906 – 907; i) M. Shan, E. U. Sharif, G. A. O'Doherty, *Angew. Chem. Int. Ed.* **2010**, *49*, 9492 – 9495; *Angew. Chem.* **2010**, *122*, 9682 – 9685.

[17] For selected reviews, see: a) D. M. Schultz, T. P. Yoon, *Science* **2014**, *343*, 985; b) X.-J. Dai, X.-L. Xu, X.-N. Li, *Chin. J. Org. Chem.* **2013**, *33*, 2046 – 2062; c) Y. Xi, H. Yi, A. Lei, *Org. Biomol. Chem.* **2013**, *11*, 2387 – 2405; d) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322 – 5363; e) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828 – 6838; *Angew. Chem.* **2012**, *124*, 6934 – 6944; f) J. W. Tucker, C. R. J. Stephenson, *J. Org. Chem.* **2012**, *77*, 1617 – 1622; g) F. Teplý, *Collect. Czech. Chem. Commun.* **2011**, *76*, 859 – 917; h) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102 – 113; i) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527 – 532.

[18] a) J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.* **2012**, *4*, 854 – 859; b) H. Kim, C. Lee, *Angew. Chem. Int. Ed.* **2012**, *51*, 12303 – 12306; *Angew. Chem.* **2012**, *124*, 12469 – 12472.

[19] For selected visible-light-mediated radical reduction, see: a) G. L. Lackner, K. W. Quasdorf, L. E. Overman, *J. Am. Chem. Soc.* **2013**, *135*, 15342 – 15345; b) J. D. Nguyen, B. Reiß, C. Dai, C. R. J. Stephenson, *Chem. Commun.* **2013**, *49*, 4352 – 4354.

[20] Key intermediates, 2-or 3-iodo-glycosides, can be prepared in different ways, for selected references, see: a) C.-F. Liu, D.-C. Xiong, X.-S. Ye, *J. Org. Chem.* **2014**, *79*, 4676 – 4686; b) T. K. Pradhan, C. C. Lin, K.-K. T. Mong, *Org. Lett.* **2014**, *16*, 1474 – 1477; c) H. Tanaka, D. Takahashi, T. Takahashi, *Angew. Chem. Int. Ed.* **2006**, *45*, 770 – 773; *Angew. Chem.* **2006**, *118*, 784 – 787; d) K. Suzuki, T. Mukaiyama, *Chem. Lett.* **1982**, 1525 – 1528.

[21] a) W. J. Wever, M. A. Cinelli, A. A. Bowers, *Org. Lett.* **2014**, *16*, 30 – 33; b) R. S. Andrews, J. J. Becker, M. R. Gagné, *Angew. Chem. Int. Ed.* **2010**, *49*, 7274 – 7276; *Angew. Chem.* **2010**, *122*, 7432 – 7434.

[22] The photosensitizer, *fac*-[Ir(*m*ppy)$_3$], was purchased from Wuhan Zhuoxin Technology, Wuhan, China. In the laboratory, we used *fac*-[Ir(*m*ppy)$_3$] instead of *fac*-[Ir(ppy)$_3$] (*fac*-[Ir(ppy)$_3$ = tris[2-phenylpyridinato-C^2,N']iridium(III)) due to the cost issue. Note: *fac*-[Ir(ppy)$_3$] can also reduce iodo-glycosides efficiently in the presence of thiol (see the Supporting Information).

[23] More details about optimizations (light resource, solvents, additives, catalysts etc.) can be found in the Supporting Information.

[24] For the utilization of thiols in radical reactions, see: a) X. Pan, E. Lacôte, J. Lalevée, D. P. Curran, *J. Am. Chem. Soc.* **2012**, *134*, 5669 – 5674; b) R. S. Andrews, J. J. Becker, M. R. Gagné, *Org. Lett.* **2011**, *13*, 2406 – 2409; c) T. M. Nguyen, N. Manohar, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2014**, *53*, 6198 – 6201; *Angew. Chem.* **2014**, *126*, 6312 – 6315; d) T. M. Nguyen, D. A. Nicewicz, *J. Am. Chem. Soc.* **2013**, *135*, 9588 – 9591; e) D. J. Wilger, N. J. Gesmundo, D. A. Nicewicz, *Chem. Sci.* **2013**, *4*, 3160 – 3165; f) K. Qvortrup, D. A. Rankic, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2014**, *136*, 626 – 629; g) F. Dénès, M. Pichowicz, G. Povie, P. Renaud, *Chem. Rev.* **2014**, *114*, 2587 – 2693.

[25] a) W. R. Roush, S. Narayan, C. E. Bennett, K. Briner, *Org. Lett.* **1999**, *1*, 895 – 897; b) D. Lafont, P. Boullanger, M. Rosenzweig, *J. Carbohydr. Chem.* **1998**, *17*, 1377 – 1393; c) S. Kopitzki, K. J. Jensen, J. Thiem, *Chem. Eur. J.* **2010**, *16*, 7017 – 7029; d) Y. Yang, X.-C. Xue, X.-F. Jin, L.-J. Wang, Y.-L. Sha, Z.-J. Li, *Tetrahedron* **2012**, *68*, 7148 – 7154; e) Y. Zhang, Y. Liu, Z. Wang, Z. Wang, L. Huang, *J. Chem. Res.* **2012**, *36*, 244 – 246; f) R. Saeeng, U. Sirion, Y. Sirichan, T. Trakulsujaritchok, P. Sahakitpichan, *Heterocycles* **2010**, *81*, 2569 – 2580; g) D. W. Gammon, H. H. Kinfe, D. E. De Vos, P. A. Jacobs, B. F. Sels, *J. Carbohydr. Chem.* **2007**, *26*, 141 – 157; h) A. J. Janczuk, W. Zhang, P. R. Andreana, J. Warrick, P. G. Wang, *Carbohydr. Res.* **2002**, *337*, 1247 – 1259.

[26] Additional 13 deiodination reactions of monosaccharide can be found in the Supporting Information.

[27] Visible-light-mediated radical reactions in a flow reactor needes less catalyst, see: a) J. W. Tucker, Y. Zhang, T. F. Jamison, C. R. J. Stephenson, *Angew. Chem. Int. Ed.* **2012**, *51*, 4144 – 4147; *Angew. Chem.* **2012**, *124*, 4220 – 4223; b) F. R. Bou-Hamdan, P. H. Seeberger, *Chem. Sci.* **2012**, *3*, 1612 – 1616.

Received: October 3, 2014
Published online on November 5, 2014

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim