



HAL
open science

Visible-Light-Mediated Stadler–Ziegler Arylation of Thiosugars with Anilines

Mingxiang Zhu, Juba Ghouilem, Samir Messaoudi

► **To cite this version:**

Mingxiang Zhu, Juba Ghouilem, Samir Messaoudi. Visible-Light-Mediated Stadler–Ziegler Arylation of Thiosugars with Anilines. *ACS Organic & Inorganic Au*, 2022, 2 (4), pp.351-358. <10.1021/acsorginorgau.2c00006>. <hal-03855500>

HAL Id: hal-03855500

<https://hal.science/hal-03855500v1>

Submitted on 16 Nov 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

Visible-Light-Mediated Stadler-Ziegler Arylation of Thiosugars with Anilines

Mingxiang Zhu, Juba Ghouilem, and Samir Messaoudi*

Université Paris-Saclay, CNRS, BioCIS, 92290, Châtenay-Malabry, France.

Supporting Information Placeholder

ABSTRACT: Here we report a one-pot Stadler-Ziegler reaction towards the synthesis of 1-thioglycosides in good yield from commercially available anilines and (un)protected 1-glycosyl thiols. This simple and mild approach employs the photoredox catalyst [Ru(bpy)₃](PF₆)₂ under visible light. **KEYWORDS:** Photoredox, thiosugars, aryl diazoniums, Stadler-Ziegler reaction, thioglycosides, anilines, C-glycosides

Many glycosides containing a C–S anomeric bond display properties offering access to a broad array of fields, including drug discovery and chemical biology.^{1–14} These glycomimetics are known to be more resistant to the metabolic hydrolysis than their *O*-glycoside congeners under biological conditions.^{15–17} Figure 1A displays representative examples of bioactive 1-thioglycosides including FDA-approved antibiotic Clindamycin used in the treatment of a variety of serious infections¹⁸ and GB1107, an orally active inhibitor of Galectin-3 which reduces lung adenocarcinoma growth and blocks metastasis.¹⁹ Besides, different other biological activities are well explored with thioglycosides including hSGLT1,²⁰ lectine A²¹ and Hsp90 inhibitions.^{22–23} On the other side, thioglycosides are largely used as versatile and reactive intermediates in polysaccharide assembly tactics through iterative glycosylations (Figure 1B).^{24–32}

Due to their key role in many biological processes, the development of methods towards an efficient and stereoselective synthesis of 1-arylthioglycosides is considered to be of great importance.^{33–34} A well-known strategy largely applied toward these target *S*-arylated glycosides is the cross-coupling reaction typically catalyzed by the Pd^{35–38}, Ni,³⁹ Cu^{40–43} transition metals, in which an aryl halide reacts with a glycosyl thiols leading to the desired thioglycoside derivative (Figure 1C). Despite their high interest, these methods required the use of expensive catalysts or a high temperature and a long reaction time, limiting thus the practicability or the scope of substrates. Liao and Yan reported an efficient transition-metal-free protocol for the synthesis of aryl 1-thioglycosides *via* an *in situ* arynes generation (Figure 1C).⁴⁴ Although efficient, some limitations persisted such as a lack of regioselectivity with non-symmetrical arynes or the limited tolerance for functional groups. Recently, our group developed the first electrochemical method for coupling various glycosyl thiols with aryl iodides and bromides under base-free conditions (Figure 1C).⁴⁵ Highly complex thioglycosides could be prepared under this ecofriendly method including unprotected thiosugars. In addition, we developed another protocol for the synthesis of aryl 1-thioglycosides *via* a Ni/Ru photoredox dual catalyzed cross-coupling of thiosugars with aryl iodides (Figure 1C).⁴⁶ Suitable for only protected thiosugars, this method did not also tolerate the more available and less expensive aryl bromides are still non-suitable partners under these photoredox conditions.

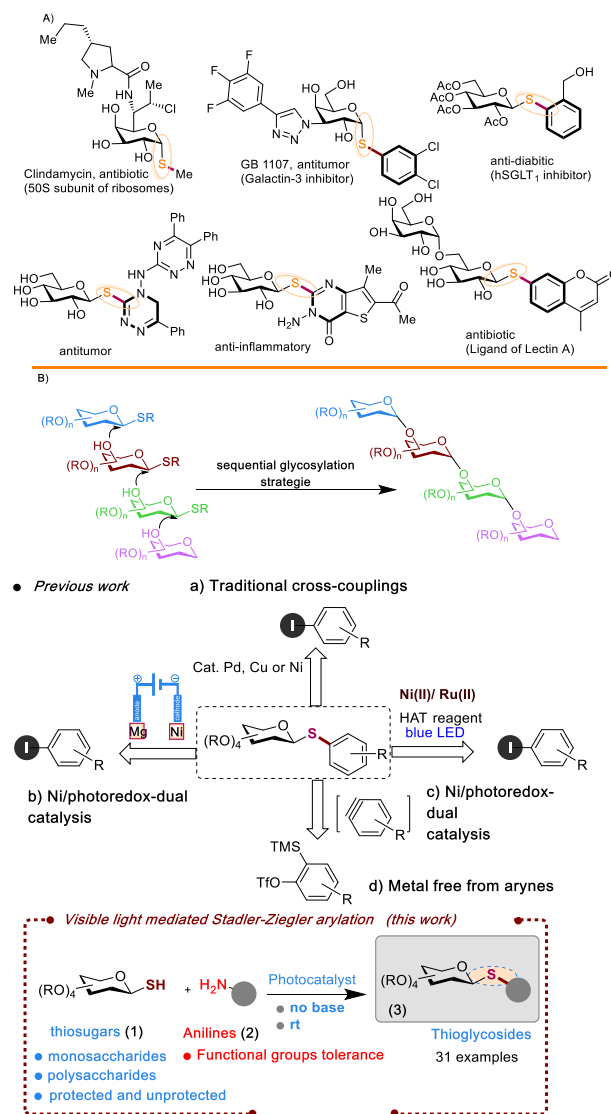


Figure 1. (A) Examples of bioactive thioglycosides, (B) Utility of thioglycosides in sequential glycosylation reaction (C) catalytic strategies to access to thioglycosides **3**.

Owing to the high importance of thioglycosides, there is a strong impetus to develop a mild and general photoredox reaction for their efficient synthesis. We wish to identify more suitable partners than bromides and iodides able to react efficiently with thiosugars under a simple photoredox protocol to generate the desired thioglycoside. Specifically, we focused our attention on the introduction of an approach that tolerates reactive functions on the aryl partners such as

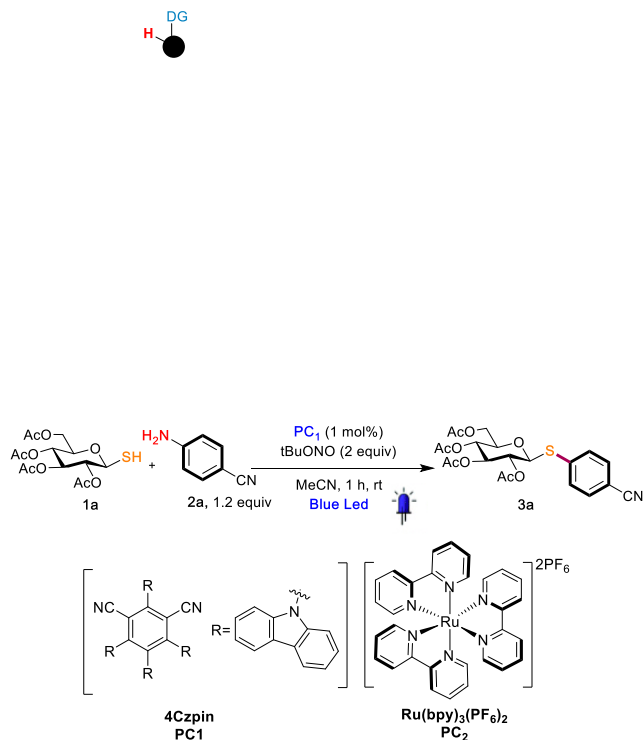
halogens, carboxylic acids, or alcohols, which may be subjected to further functionalization. Since arylamines are usually more readily available and less expensive than the corresponding aryl halides, we were interested in using them as coupling partners in the famous Stadler–Ziegler reaction.^{47–50} We hypothesized that highly reactive aryl diazonium salts generated from arylamines would be suitable as arylating agents, able to easily generate aryl radicals which could then be trapped by the thiosugar nucleus. Since the pioneering work by Stadler⁴⁷ and by Ziegler,⁴⁸ this process has been used in various applications for the synthesis of arylsulfides including industrial manufacturing.^{51–59} Recently, various groups reported modifications of this protocol to achieve improved yields and milder reaction conditions. Among them, the group of Noël reported a mild procedure for the synthesis of arylsulfides by using photoredox catalysis.^{60–62} To avoid the isolation of diazonium salts and to enhance the reaction efficiency, the authors established an elegant one-pot protocol from aryl amines combining the diazotization and coupling steps.^{60–61}

Based on these recent achievements, and on our ongoing interests in metal-catalyzed functionalization of thiosugars,^{63–67} we propose herein a catalytic photoredox method for the arylation of protected and unprotected thiosugars with various anilines (Figure 1C). If successful, this approach would provide not only an excellent complementary pathway to the established S-arylation methods but also immediate access to a reactive platform that can be engaged in numerous postfunctionalizations.

To examine the feasibility of this study, we chose the coupling of tetra-*O*-acetylated 1-thio-β-D-glucopyranose **1a** with a commercially available 4-cyanoaniline **2a** as a model study under various reaction conditions (Table 1 and Table S1 in SI). The reaction of **1a** (1 equiv.) with **2a** (1.2 equiv) was first investigated by using 1 mol% of a commercially available Ru(bpy)₂PF₆ photocatalyst in the presence of *t*BuONO (2 equiv) as a diazotization reagent in acetonitrile under a white light-emitting diode (LED) irradiation at room temperature for 24 h (Table S1, entry 1, ESI). Accordingly, these conditions afforded the expected product **3a** in an encouraging 67% yield as a single β-anomer (*J*_{1,2} = 9.0 Hz) (See ESI). Increasing the amount of the aniline partner **2a** from 1.2 equiv to 2 equiv furnished **3a** in a slightly lower yield (57%, Table S1, entry 2, ESI). Pleasantly, switching from white to blue light furnished **3a** in 77% yield (Table S1, entry 3, ESI). Interestingly, reducing the reaction time to only 1 h instead of 24 h led to the thioglucoside **3a** in a good 77% yield (Table 1, entry 1). The reaction time was fixed at 1 h and we decided to examine the other reaction parameters. The reaction with the organophotocatalyst 4CzIPN (*E*_(PC^{•+}/PC^{•-}) = +1.43 V) instead of Ru(bpy)₂PF₆ was less efficient and gave **3a** in a 66% yield (entry 2). Decreasing amounts of the photocatalyst to 0.5 mol% gave **3a** in a still good yield of 70% (entry 3). However, tentative to remove traces of water from the reaction medium by adding molecular sieves (4 Å) led to complete inhibition of any reactivity (entry 4). The influence of the solvent was also examined and revealed that MeCN was the solvent of choice since the other solvents such as DMSO, DMA, DMF and MeOH were completely incompatible with this coupling (entry 5) or less efficient in the case of dioxane (43%, entry 6). Negative controlling experiments demonstrated that both the Ru-photocatalyst and light are crucial for this reaction (entries 7–9).

With these encouraging results, we investigated next, the scope and limitations for this Stadler–Ziegler reaction by using a series of commercially available aryl amines **2** bearing different functional groups. As showed in Scheme 1, cross-couplings of tetra-*O*-acetylated 1-thio-β-D-glucopyranose **1a** with aryl amines bearing various functions (–CN, –Cl, –Br, –I, –CF₃, –NO₂, –CO₂Me, –C(O)Me, –OMe, –Me, –*t*Bu, –Ph) at *para* or *meta* positions have been successfully achieved to afford the corresponding thioglycosides (**3a–j** and **3o–s**) in yields up to 85%. Interestingly, reactive C-halogen

Table 1. Optimization of the coupling reaction of **1a** with **2a**^[a]

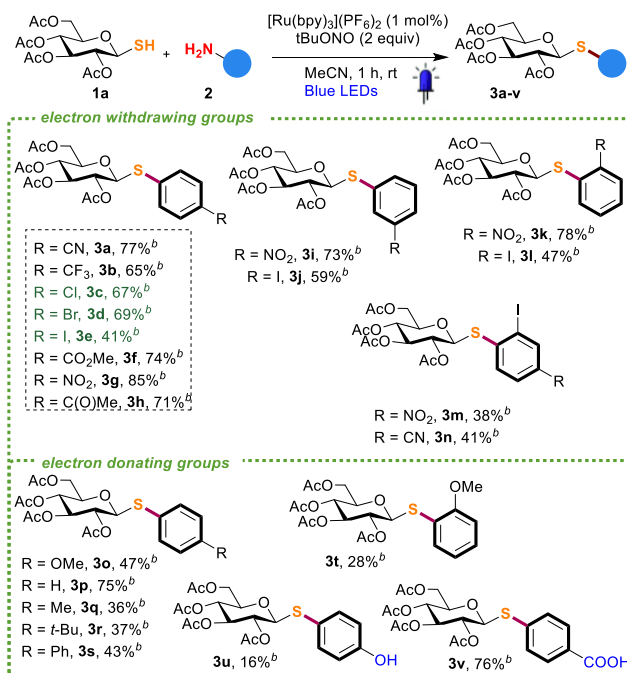


Entry	Deviation from the standard conditions	Yield 3a (%) ^b
1	none	77
2	PC1 instead PC2	66
3	PC2 0.5 mol%	70
4	+ molecular sieves 4 Å	trace
5	DMSO or DMF or DMA or MeOH instead of MeCN	traces
6	Dioxane instead of MeCN	43
7	No photocatalyst PC1	17
8	No LED	17
9	No photocatalyst PC1 and LED	17

^a Reactions conditions: **1a** (0.3 mmol), **2a** (0.36 mmol), *t*BuONO (0.6 mmol), MeCN (2.0 mL), blue LEDs (4.5 W, irradiation). ^b Isolated yield.

bonds (e.g., I, Br, Cl) were tolerated in this photoredox reaction affording compounds **3c–e**, **3j**, **3l**, **3m**, **n** in acceptable yields. The presence of halogen substituents in these products provided a handle for further structural diversifications using metal-catalyzed cross-coupling reactions. In addition, the presence of an *ortho* substitution at the aromatic ring of the aniline partner affects slightly but doesn't inhibit completely the coupling process, as compounds **3k–n** were obtained in yields ranging between 28% and 78% depending on the electronic effect of the functional group.

Scheme 1. Scope and limitation of the coupling of **1a** with arylamines **2**.^a

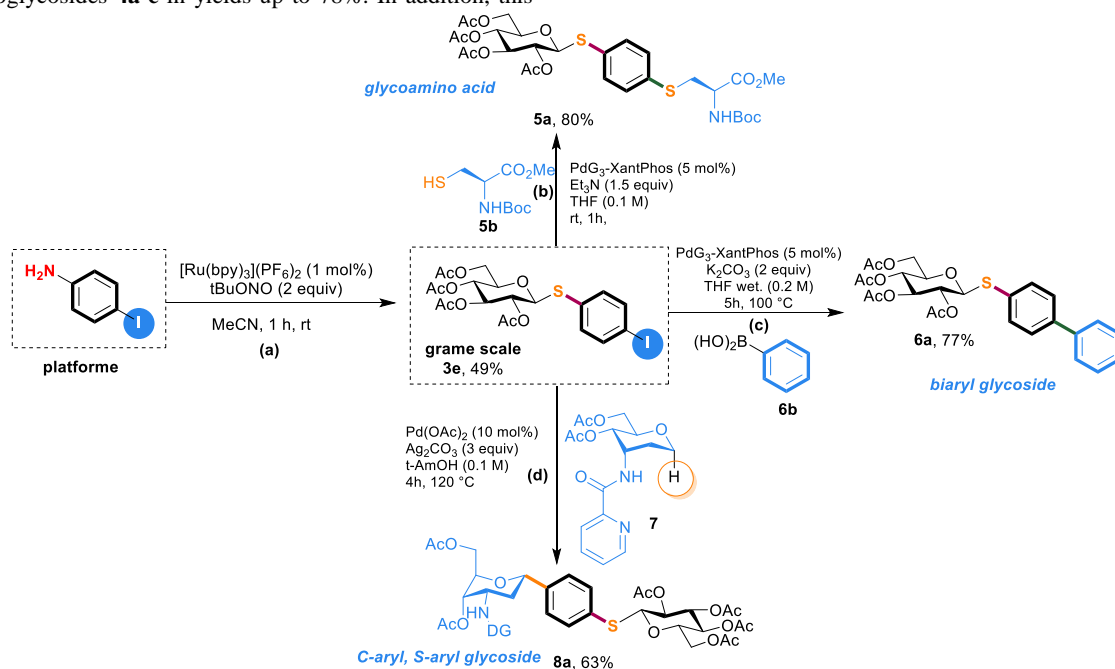
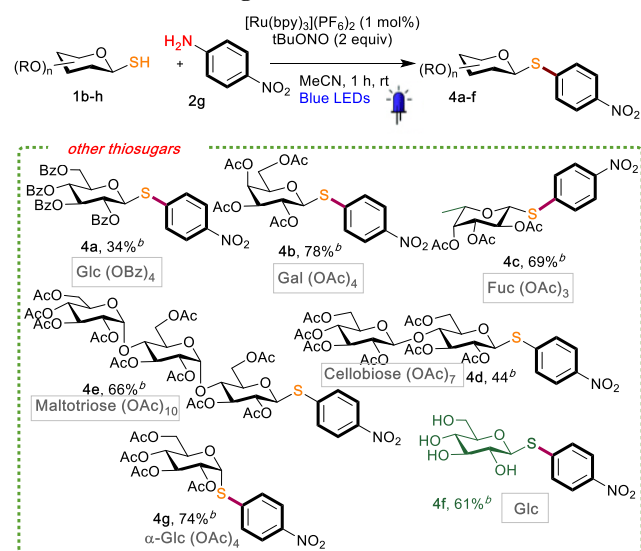


Of note, the presence of a polar function on the aniline such as a carboxylic acid **2v** is well tolerated furnishing the desired compound **3v** in 76% yield. However, the yield drops down to only 16% when the coupling of **1a** was conducted with a *p*-hydroxy aniline (compound **3u**).

This successful study with the tetra-*O*-acetylated 1-thio-β-D-glucopyranose **1a** encouraged us to examine the feasibility of this coupling with different other glycosyl thiols **1b-h**. As depicted in Scheme 2, this coupling reaction tolerates different glycosylthiols such as *O*-benzoylated 1-thio-β-D-glucopyranose **1b**, *O*-acetylated 1-thio-β-D-galactopyranose **1c**, and *O*-acetylated 1-thio-β-D-fucopyranose **1d** which react smoothly with the *p*-nitro aniline **2g** to lead to thioglycosides **4a-c** in yields up to 78%. In addition, this

protocol could be extended to more complex and biologically relevant saccharide derivatives such as thio-β-D-cellobiose disaccharide **1e** and thio-β-D-maltotriose trisaccharide **1f** delivering **4d** and **4e** in 44% and 66% yields, respectively. More interestingly, we observed that our protocol is compatible with unprotected thiosugars since the reaction of unprotected thio-β-D-glucose **1g** with **2g** yielded the thioglycoside **4f** in a good 61% yield, and no side products arising from the *O*-arylation were observed (Scheme 1). This is another important input compared to our previously reported photoredox approach to functionalize thiosugars with aryl halides. Finally, besides β-glycosyl thiols, α-anomers are also effective coupling partners for this photoredox coupling as the α-thioglycoside furnishes the α-thioglycosides **4g** in 74% yield.

Scheme 2. Scope and limitation of the coupling of glycosyl thiols **1b-h** with the aniline **2g**.



Scheme 3. ^aReactions conditions: (a) **1a** (3 mmol), **2e** (1.2 eq), [Ru(bpy)₃](PF₆)₂ (1 mol%), MeCN 20 mL, *t*BuONO (2 eq), Blue led, rt, 1 h. (b) **3e** (0.1 mmol), **5b** (0.1 mmol), PdG3 XantPhos (5 mol%), Et₃N (1.5 equiv), in THF (0.1 M) at rt for 1 h. (c) **3e** (0.1 mmol), **6b** (0.2 mmol), PdG3 XantPhos (5 mol%), K₂CO₃ (2 equiv), in wet THF (0.2 M) at 100% for 5 h. (d) **3e** (0.2 mmol), **7** (0.4 mmol), Pd(OAc)₂ (10 mol%), Ag₂CO₃ (3 equiv), in *t*-AmOH (0.1 M) at 120 for 4 h. ^bIsolated yield.

To further show the synthetic utility of our protocol, we carried out studies on whether the iodinated substrate **3e** could be used as a platform to access more complex thioglycosides through metal-catalyzed transformations of the C–I bond (Scheme 2). To this end, **3e** was firstly prepared on a gram scale with a slightly higher yield demonstrating the scalability of our protocol. Thus, with substantial amounts of **3e** in hand, we examined next its coupling with the cysteine substrate under our previously reported Pd-catalyzed methodology.⁶⁸ When PdG3-XantPhos was used as a catalyst in the presence of Et₃N, the glycoamino acid **5a** was isolated in an excellent yield. This later may be used as a building block in the SPPS peptide synthesis (Scheme 3). In addition, **3e** was converted to the biaryl **5b** in good yield through a Suzuki-Miyaura cross-coupling with the phenylboronic⁶⁹ (Scheme 3). Finally, **3e** was engaged in a Csp³–H activation process of the anomeric C–H bond of substrate **7** under our recently reported protocol.⁷⁰ The di-glycoside **8a** bearing two different sugars linked through C–C and C–S bonds was obtained in 63 % yield (Scheme 3).

From the point of view of mechanistic considerations, based on the literature reports we may assume that the reaction starts by the *in situ* formation of the diazo salt from aniline and *t*BuONO reagent, followed by the formation of the diazosulfide (I) (Figure 2). Noël and co-workers suggested in their early mechanistic studies that this intermediate is the reactive photo-labile species in the photocatalytic cycle of the photocatalyzed Stadler-Ziegler process.⁶⁰ A single electron transfer (SET) from the excited state Ru photocatalyst to the diazosulfide (I) leads to N₂ extrusion and the formation of the thiolate (III) and aryl radical (II). These two intermediates evolve into the formation of the thioether radical anion (IV) which produces the final thioglycoside and close the Ru-catalytic cycles by a final SET.

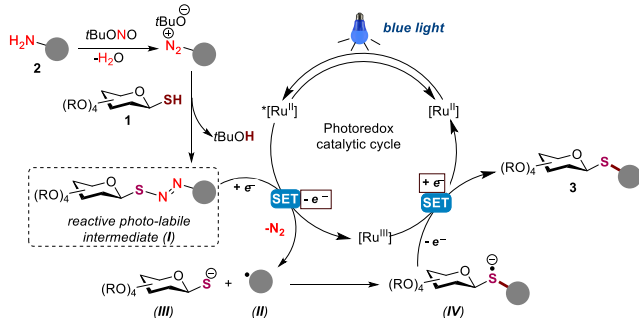


Figure 2. A proposed mechanism

In summary, we reported here a new approach for the S-arylation of anomeric glycosyl thiols with various aryl amines *via* a cooperative photoredox strategy. This method provides unprecedented access to functionalized thioglycosides under mild conditions with high efficiency and selectivity. We anticipate that this mild synthetic protocol will find numerous applications in organic synthesis as well as in medicinal chemistry.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures and analytical data (PDF)

AUTHOR INFORMATION

Corresponding Author

Samir Messaoudi-Université Paris-Saclay, CNRS, BioCIS, 92290, Châtenay-Malabry, France

http://orcid.org/0000-0002-4994-9001

Email : samir.messaoudi@universite-paris-saclay.fr

Authors

Université Paris-Saclay, CNRS, BioCIS, 92290, Châtenay-Malabry, France

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

Authors acknowledge support of this project by CNRS, University Paris-Saclay and ANR (SelfSuChi, ANR-18-CE07-0012). The ANR is gratefully acknowledged for a doctoral fellowship to J. G the China Scholarship Council for a fellowship (CSC) to Mingxiang Zhu.

REFERENCES

- (1) Driguez, H. Thiooligosaccharides in glycobiology. In *Glycoscience Synthesis Of Substrate Analogs And Mimetics*; Springer Verlag: Berlin, **1997**; 187, 85-116.
- (2) Witczak, Z. J. Thio sugars: biological relevance as potential new therapeutics. *Curr. Med. Chem.* **1999**, *6*, 165–178;
- (3) Pachamuthu, K.; Schmidt, R. R. Synthetic routes to thiooligosaccharides and thioglycopeptides. *Chem. Rev.* **2006**, *106*, 160–187;
- (4) Samuni-Blank, M.; Izhaki, I.; Dearing, M. D.; Gerchman, Y.; Trabelcy, B.; Karasov, A. L. W. H.; Arad, Z. Intraspecific directed deterrence by the mustard oil bomb in a desert plant. *Curr. Biol.* **2012**, *22*, 1218–1220;
- (5) Lian, G.; Zhang, X.; Yu, B. Thioglycosides in carbohydrate research. *Carbohydr. Res.* **2015**, *403*, 13–22.
- (6) Castaneda, F.; Burse, A.; Boland, W.; Kinne, R. K. H. Thioglycosides as inhibitors of hSGLT1 and hSGLT2: potential therapeutic agents for the control of hyperglycemia in diabetes. *Int. J. Med. Sci.* **2007**, *4*, 131-139;
- (7) Rodrigue, J.; Ganne, G.; Blanchard, B.; Saucier, C.; Giguere, D.; Shiao, T. C.; Varrot, A.; Imbert, A.; Roy, R. Aromatic thioglycoside inhibitors against the virulence factor LecA from *Pseudomonas aeruginosa*. *Org. Biomol. Chem.* **2013**, *11*, 6906–6918;
- (8) Elgemeie, G. H.; Farag, A. B.; Amin, K. M.; El-Badry, O. M.; Hassan, G. S. Design, Synthesis and Cytotoxic Evaluation of Novel Heterocyclic thioglycosides. *Eur. J. Med. Chem.* **2014**, *4*, 814–833;
- (9) Aouad, M. R. Synthesis and Antimicrobial Screening of Novel Thioglycosides and Acyclonucleoside Analogs Carrying 1,2,3-Triazole and 1,3,4-Oxadiazole Moieties. *Nucleos. Nucleot. Nucl.* **2016**, *35*, 1–15;
- (10) Kato, E.; Nagano, H.; Yamamura, S.; Ueda, M. Synthetic inhibitor of leaf-closure that reveals the biological importance of leaf-movement for the survival of leguminous plants. *Tetrahedron* **2003**, *59*, 5909-5917;
- (11) Schnabelrauch, M.; Vasella, A.; Withers, S. G. Synthesis and Evaluation as Irreversible Glycosidase Inhibitors of Mono- and Oligo (glycosylthio) benzoquinones. *Helv. Chim. Acta.* **1994**, *77*, 778-799;
- (12) Adinolfi, M.; d'Ischia, M.; Iadonisi, A.; Leone, L.; Pezzella, A.; Valerio, S. Glycosylated eumelanin building blocks by thioglycosylation of 5, 6-diacetoxyindole with an expedient selenium-based dynamic-mixture methodology. *Eur. J. Org. Chem.* **2012**, *23*, 4333-4338;
- (13) Shirota, K.; Kato, Y.; Suzuki, K.; Sugiyama, Y. Characterization of novel kidney-specific delivery system using an alkylglucoside vector. *J. Pharmacol. Exp. Ther.* **2001**, *299*, 459–467;
- (14) Caraballo, R.; Sakulsombat, M.; Ramström, O. Towards dynamic drug design: identification and optimization of β -galactosidase inhibitors from a dynamic hemithioacetal system. *ChemBioChem* **2010**, *11*, 1600–1606.
- (15) a) Rye, C. S.; Withers, S. G. The synthesis of a novel thio-linked disaccharide of chondroitin as a potential inhibitor of polysaccharide lyases. *Carbohydr. Res.* **2004**, *339*, 699–703;
- (16) Metaferia, B. B.; Fetterolf, B. J.; Shazad-ul-Hussan, S.; Moravec, M.; Smith, J. A.; Ray, S.; Gutierrez-Lugo, M. -T.; Bewley, C. A. Synthesis of Natural Product-Inspired Inhibitors of Mycobacterium tuberculosis Mycothiol-Associated Enzymes: The First Inhibitors of GlcNAc-Ins Deacetylase. *J. Med. Chem.* **2007**, *50*, 6326–6336;
- (17) Castaneda, F.; Burse, A.; Boland, W.; Kinne, R. K.-H. Thioglycosides as inhibitors of hSGLT1 and hSGLT2: potential therapeutic agents for the control of hyperglycemia in diabetes. *Int. J. Med. Sci.* **2007**, *4*, 131–139.
- (18) Matzov, D.; Eyal, Z.; Benhamou, R. I.; Shalev-Benami, M.; Halfon, Y.; Krupkin, M.; Zimmerman, E.; Rozenberg, H.; Bashan, A.; Fridman, M.;

- Yonath, A. Structural insights of lincosamides targeting the ribosome of *Staphylococcus aureus*. *Nucleic Acids Res.* **2017**, *45*, 10284–10292.
- (19) Delaine, T.; Collins, P.; MacKinnon, A.; Sharma, G.; Stegmayr, Rajput, J.; V. K.; Mandal, S.; Cumpstey, I.; Larumbe, A.; Salameh, B. A.; Kahl-Knutsson, B.; vanHattum, H.; vanScherpenzeel, M.; Pieters, R. J.; Sethi, T.; Schambye, H.; Oredsson, S.; Leffler, H.; Blanchard, H.; Nilsson, J. Galectin-3-Binding Glycomimetics that Strongly Reduce Bleomycin-Induced Lung Fibrosis and Modulate Intracellular Glycan Recognition. *ChemBioChem* **2016**, *17*, 1759–1770.
- (20) Feng, G.; Wang, S.; Lv, J.; Luo, T.; Wu, Y.; Dong, H. Improved Synthesis of 1-Glycosyl Thioacetates and Its Application in the Synthesis of Thioglycoside Gliflozin Analogues. *Eur. J. Org. Chem.* **2021**, *2021*, 2940–2949.
- (21) Rodrigue, J.; Ganne, G.; Blanchard, B.; Saucier, C.; Giguere, D.; Shiao, T. C.; Varrot, A.; Imbert, A. Roy, R. Aromatic thioglycoside inhibitors against the virulence factor LecA from *Pseudomonas aeruginosa*. *Org. Biomol. Chem.* **2013**, *11*, 6906.
- (22) Mielczarek-Lewandowska, A.; Hartman, M. L.; Czyz, M. Inhibitors of HSP90 in melanoma. *Apoptosis* **2020**, *25*, 12–28.
- (23) Li, L.; Chen, N.-N.; You, Q.-D.; Xu, X.-L. An updated patent review of anticancer Hsp90 inhibitors (2013-present). *Expert Opin. Ther. Pat.* **2021**, *31*, 67–80.
- (24) Codee, J. D. C.; Litjens, R. E. J. N.; van den Bos, L. J.; Overkleeft, H. S.; van der Marel, G. A. Thioglycosides in sequential glycosylation strategies. *Chem. Soc. Rev.* **2005**, *34*, 769–782;
- (25) Johannes, M.; Reindl, M.; Gerlitzki, B.; Schmitt, E.; Hoffmann-Röder, A. Synthesis and biological evaluation of a novel MUC1 glycopeptide conjugate vaccine candidate comprising a 4'-deoxy-4'-fluoro-Thomson-Friedenreich. *Beilstein J. Org. Chem.* **2015**, *11*, 155–161;
- (26) Budhadev, D.; Mukhopadhyay, B. Synthesis of two trisaccharides related to the hepatoprotective phenylethanoids leonoside E and F isolated from *Leonurus japonicus* Houtt. *Carbohydr. Res.* **2014**, *384*, 51–55;
- (27) Basu, N.; Maity, S. K.; Ghosh, R. Trichloroisocyanuric acid (TCCA)-TMSOTf: an efficient activator system for glycosylation reactions based on thioglycosides. *RSC Adv.* **2012**, *2*, 12661–12664;
- (28) Verma, P.; Raj, R.; Roy, B. Synthesis of a tetrasaccharide related to the triterpenoid saponin isolated from *Schima noronhae*. *Tetrahedron: Asymmetry* **2010**, *21*, 2413–2418; (
- (29) Xiong, C. D.; Zhang, L. H.; Ye, X. S. Bromodimethylsulfonium Bromide-Silver Triflate: A New Powerful Promoter System for the Activation of Thioglycosides. *Adv. Synth. Catal.* **2008**, *350*, 1696–1700;
- (30) Roy, B.; Pramanik, K.; Mukhopadhyay, B. Synthesis of a tetra- and a trisaccharide related to an anti-tumor saponin “Julibroside J 28” from *Albizia julibrissin*. *Glycoconjugate J.* **2008**, *25*, 157–166;
- (31) Zeng, Y.; Wang, Z.; Whitfield, D.; Huang, X. Installation of Electron Donating Protective Groups, a Strategy for Glycosylating Unreactive Thioglycosyl Acceptors using the Pre-activation Based. *J. Org. Chem.* **2008**, *73*, 7952–7962;
- (32) Fridman, M.; Belakhov, V.; Lee, L. V.; Liang, F. -S.; Wong, C. -H.; Baasov, T. Dual Effect of Synthetic Aminoglycosides: Antibacterial Activity against *Bacillus anthracis* and Inhibition of Anthrax Lethal Factor. *Angew. Chem. Int. Ed.* **2005**, *44*, 447–452.
- (33) Ibrahim, N.; Alami, M.; Messaoudi, S. Recent Advances in Transition-Metal-Catalyzed Functionalization of 1-Thiosugars. *Asian. J. Org. Chem.* **2018**, *7*, 2026–2038.
- (34) Qiao, M.; Zhang, L.; Jiao, R.; Zhang, S.; Li, B.; Zhang, X. Chemical and enzymatic synthesis of S-linked sugars and glycoconjugates. *Tetrahedron* **2021**, *81*, 13192;
- (35) Brachet, E.; Brion, J. -D.; Messaoudi, S.; Alami, M. Stereoselective Palladium-Catalyzed Alkenylation and Alkynylation of Thioglycosides. *Adv. Synth. Catal.* **2013**, *355*, 2627–2636;
- (36) Brachet, E.; Brion, J. -B.; Messaoudi, S.; Alami, M. Palladium-Catalyzed Cross-Coupling Reaction of Thioglycosides with (Hetero) aryl Halides. *Adv. Synth. Catal.* **2013**, *355*, 477–490;
- (37) Ding, Y.; Huang, Y.; Shi, W.; Zheng, N.; Wang, C.; Chen, X.; An, Y.; Zhang, Z.; Liang, Y. Modular Synthesis of Aryl Thio/Selenoglycosides via the Catellani Strategy. *Org. Lett.* **2021**, *23*, 5641–5646;
- (38) Li, J.; Wang, M.; Jiang, X. Diastereoselective Synthesis of Thioglycosides via Pd-Catalyzed Allylic Rearrangement, *Org. Lett.* **2021**, *23*, 9053–9057.
- (39) Brachet, E.; Brion, J. D.; Alami, M.; Messaoudi, S. Nickel-Catalyzed Arylation, Alkenylation, and Alkynylation of Unprotected Thioglycosides at Room Temperature. *Chem.-Eur. J.* **2013**, *19*, 15276–15280.
- (40) Chabrier, A.; Bruneau, A.; Benmahdjoub, S.; Benmerad, B.; Belaid, S.; Brion, J. D.; Alami, M.; Messaoudi, S. Stereoretentive Copper-Catalyzed Directed Thioglycosylation of C(sp²)-H Bonds of Benzamides. *Chem.-Eur. J.* **2016**, *22*, 15006–15010;
- (41) Nauš, P.; Lešetický, L.; Smrček, S.; Tišlerová, I.; Štícha, M. Copper-Assisted Arylation of 1-Thiosugars: Efficient Route to Triazine Substituted Arylthioglycosides. *Synlett* **2003**, *14*, 2117–2122;
- (42) Yuan, X.; Kou, Y.; Yu, L.; Zhang, Z.-X.; Xue, W. 2'-Cyanoethyl thioglycosides: effective nucleophiles for synthesis of (hetero)aryl thioglycosides under the catalysis of Cu. *Org. Chem. Front.* **2015**, *2*, 1604–1607;
- (43) Zhu, F.; Miller, E.; Zhang, S. Q.; Yi, D.; O'Neill, S.; Hong, X.; Walczak, M. A. Stereoretentive C(sp³)-S Cross-Coupling. *J. Am. Chem. Soc.* **2018**, *140*, 18140–18150.
- (44) Liu, Y.; Yu, X.; Zhang, X.; Zhong, Q.; Liao, L.; Yan, N. Transition-metal-free synthesis of aryl 1-thioglycosides with arynes at room temperature. *RSC Adv.* **2021**, *11*, 26666–26671.
- (45) Zhu, M.; Alami, M.; Messaoudi, S. Electrochemical nickel-catalyzed Migita cross-coupling of 1-thiosugars with aryl, alkenyl and alkynyl bromides. *Chem. Commun.*, **2020**, *56*, 4464–4467.
- (46) Zhu, M.; Dagousset, G.; Alami, M.; Magnier, E.; Messaoudi, S. Ni/Photoredox-Dual-Catalyzed Functionalization of 1-Thiosugars. *Org. Lett.* **2019**, *21*, 5132–5137.
- (47) Stadler, O. Zur Kenntniss der Mercaptane. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2075–2081;
- (48) Ziegler, J. H., Ueber eine Methode zur Darstellung aromatischer Sulfide von bestimmter Constitution und das Thioxanthon. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 2469–2472;
- (49) Abeywickrema, A. N.; Beckwith, A. L. J. Mechanistic and kinetic studies of the thiodiazonium reaction. *J. Am. Chem. Soc.* **1986**, *108*, 8227–8229;
- (50) Hilbert, G. E.; Johnson, T. B. A study of the germicidal activity of diaryl-sulfide phenols. *J. Am. Chem. Soc.*, **1929**, *51*, 1526–1536.
- (51) Barbero, M.; Degani, I.; Diulgheroff, N.; Dughera, S.; Fochi, R.; Migliaccio, M. Alkyl- and Arylthiodiazoniumations of Dry Arenediazonium o-Benzenedisulfonimides. Efficient and Safe Modifications of the Stadler and Ziegler Reactions to Prepare Alkyl Aryl and Diaryl Sulfides. *J. Org. Chem.* **2000**, *65*, 5600–5608;
- (52) Petrillo, G.; Novi, M.; Garbarino, G.; Carlo, D. E. A mild and efficient SRN1 approach to diaryl sulfides from arenediazonium tetrafluoroborates. *Tetrahedron* **1986**, *42*, 4007–4016;
- (53) Perumal, S.; Chandrasekaran, R.; Vijayabaskar, V.; Wilson, D. A. ¹H and ¹³C NMR study of substituent effects in 2- and 3-substituted diphenyl sulphides and sulphones and 4-substituted 2',6'-dimethyldiphenyl sulphides. *Magn. Reson. Chem.* **1995**, *33*, 779–790;
- (54) Smith, G.; Ruhland, T.; Mikkelsen, G.; Andersen, K.; Christoffersen, C. T.; Alifrangis, L. H.; Mørk, A.; Wren, S. P.; Harris, N.; Wyman, B. M.; Brandt, G. The synthesis and SAR of 2-arylsulfanyl-phenyl piperazinyll acetic acids as glyT-1 inhibitors. *Bioorg. Med. Chem.* **2004**, *14*, 4027–4030;
- (55) Smith, G.; Mikkelsen, G.; Eskildsen, J.; Bundgaard, C. The synthesis and SAR of 2-arylsulfanylphenyl-1-oxyalkylamino acids as GlyT-1 inhibitors. *Bioorg. Med. Chem.* **2006**, *16*, 3981–3984.
- (56) Subir, P.; Puneshwar, S.; Brindaban C, R. Visible light photoredox catalyzed one pot Stadler-Ziegler reaction of heteroaryl amines with heteroaryl thiols at room temperature: An efficient synthesis of diheteroaryl sulphides. *Indian J. Chem.* **2019**, *58B*, 183–191;
- (57) Jiang, M.; Li, H.; Yang, H.; Fu, H. Room-Temperature Arylation of Thiols: Breakthrough with Aryl Chlorides. *Angew. Chem. Int. Ed.* **2017**, *56*, 874–879;
- (58) Naveen, N.; Sengupta, S.; Chandrasekaran, S. Metal-Free S-Arylation of Cysteine Using Arenediazonium Salts. *J. Org. Chem.* **2018**, *83*, 3562–3569;
- (59) Sengupta, S.; Chandrasekaran, S. Modifications of amino acids using arenediazonium salts. *Org. Biomol. Chem.* **2019**, *17*, 8308–8329.
- (60) Wang, X.; Cuny, G. D.; Noël, T. A Mild, One-Pot Stadler-Ziegler Synthesis of Arylsulfides Facilitated by Photoredox Catalysis in Batch and Continuous-Flow. *Angew. Chem. Int. Ed.* **2013**, *52*, 7860–7864.
- (61) Bottecchia, C.; Rubens, M.; Gunnoo, S.; Hessel, V.; Madder, A.; Noël, T. Visible Light-Mediated Selective Arylation of Cysteine in Batch and Flow. *Angew. Chem. Int. Ed.* **2017**, *56*, 12701–12707.
- (62) Bartolomeu, A. de A.; Silva, R. C.; Brocksom, T. J.; Noël, T.; de Oliveira, K. T. Photoarylation of Pyridines Using Aryldiazonium Salts and Visible Light: An EDA Approach. *J. Org. Chem.* **2019**, *84*, 10459–10471.
- (63) AL-Shuaeeb, R. A. A.; Montoir, D.; Alami, M.; Messaoudi, S. Synthesis of (1 → 2)-S-linked saccharides and S-linked glycoconjugates via a

Palladium-G3-XantPhos precatalyst catalysis. *J. Org. Chem.* **2017**, *82*, 6720–6728;

(64) Probst, N.; Lartia, R.; Théry, O.; Alami, M.; Defrancq, E.; Messaoudi, S. Efficient Buchwald-Hartwig-Migita cross-coupling for DNA thio-glycoconjugation. *Chem. Eur. J.* **2018**, *24*, 1795–1800;

(65) Montoir, D.; Amoura, M.; Ababsa, Z. E. -A.; Vishwanath, T. M.; Yen-Pon, E.; Robert, V.; Beltramo, M.; Piller, V.; Alami, M.; Aucagne, A.; Messaoudi, S. Synthesis of aryl-thioglycopeptides through chemoselective Pd-mediated conjugation. *Chem. Sci.* **2018**, *9*, 8753–8759.

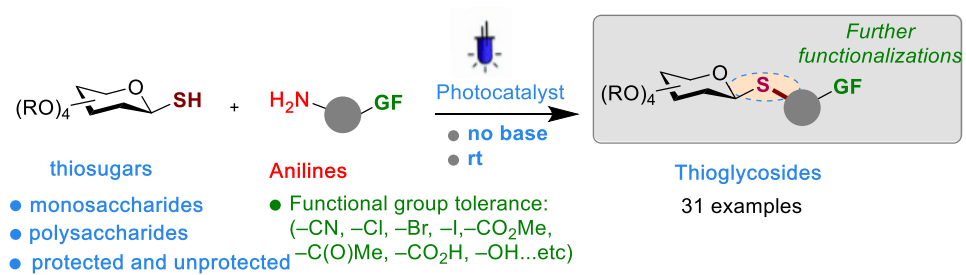
(66) M. Zhu, M. Alami, S. Messaoudi, *Room Temperature Pd-Catalyzed Synthesis of 1-(Hetero)aryl Selenoglycosides*, *Org. Lett.* **2020**, *22*, 6584–6589;

(67) N. Bennai, N. Ibrahim, J. Marrot, M. Belkadi, M. Alami, E. Magnier, E. Anselmi, S. Messaoudi, *Synthesis of S-Trifluoromethyl S-Arylsulfoximine Thioglycosides through Pd-Catalyzed Migita Cross-Coupling*, *Eur. J. Org. Chem.* **2020**, 4972–4981.

(68) Al-Shuaeeb, A. A.; Kolodych, S.; Koniev, O.; Delacroix, S.; Erb, S.; Nicolaÿ, S.; Cintrat, J.-C.; Brion, J.-D.; Cianféroni, S.; Alami, M.; Wagner, A.; Messaoudi, S. Palladium Catalyzed Chemoselective and Biocompatible Functionalization of Cysteine-Containing Molecules at Room Temperature. *Chem. Eur. J.* **2016**, *22*, 11365–11370.

(69) Benmahdjoub, S.; Ibrahim, N.; Benmerad, B.; Alami, M.; Messaoudi, S. One-Pot Assembly of Unsymmetrical Biaryl Thioglycosides through Chemoselective Palladium-Catalyzed Three-Component Tandem Reaction. *Org. Lett.* **2018**, *20*, 4067–4071.

(70) Ghouilem, G.; Tran, C.; Grimblat, N.; Retailleau, P.; Alami, M.; Gandon, V.; Messaoudi, S. Diastereoselective Pd-Catalyzed Anomeric C(sp³)H Activation: Synthesis of (hetero)aryl C-Glycosides. *ACS Catalysis* **2021**, *11*, 1818–1826.



Insert Table of Contents artwork here
