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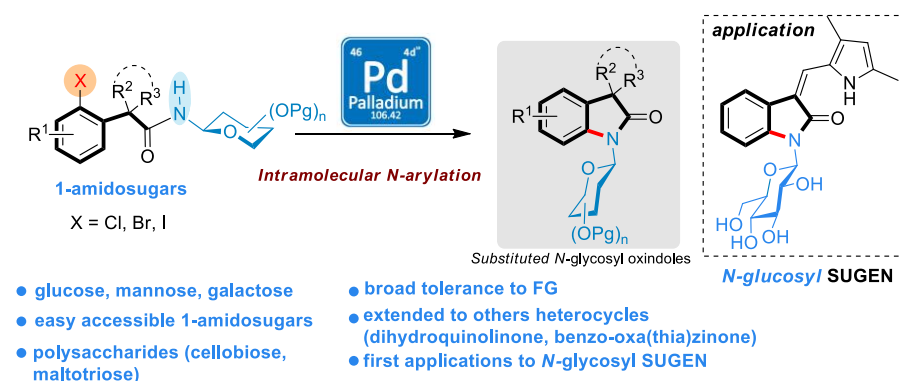
Synthesis of *N*-Glycosyl-2-oxindoles by Pd-Catalyzed *N*-Arylation of 1-Amidosugars

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Supporting Information Placeholder



ABSTRACT: An efficient intramolecular Pd-catalyzed *N*-arylation of *o*-iodo- amidosugars to the synthesis of *N*-glycosylated oxindoles has been reported. The coupling reaction takes place in toluene and involves Pd(OAc)₂/RuPhos catalytic systems in the presence of K₂CO₃. This versatile approach was extended successfully to the synthesis of *N*-glycosylated other heterocycles.

The 2-oxindole scaffold has attracted considerable attention due to its widespread application in organic synthesis, and in the design of pharmaceuticals.¹ This common motif was found in many biological active compounds with applications in various therapeutic areas.² Of the many drugs developed so far containing a 2-oxindole core, four marketed molecules have emerged (Figure 1-A). Sunitinib is used to treat renal cell carcinoma, gastrointestinal stromal and pancreatic neuroendocrine tumours. Ropinirol is recommended in Parkinson's disease, nintedanib is a medication delivered against idiopathic pulmonary fibrosis and ziprasidone is used to treat schizophrenia and bipolar disorder. Other 2-oxindole derivatives are also under clinical trials against various diseases.³

The incorporation of a sugar moiety in bioactive molecules may have several benefits such as enhancing their bioavailability,⁴ their solubility⁵ or their biological activity by targeting for example, selectively cancer tissues through the Warburg effect.⁶ Such a transformation was achieved in the 2-oxindole series, by chemical synthesis,⁷ and recently by biotransformation using *Streptomyces* sp. SANK 60895,⁸ delivering *N*-glycosylated oxindoles which displayed interesting biological activities. Interestingly, these latter structures were also found in the living systems (Figure 1-B) as illustrated by compound **A**, extracted from the seeds of *Ziziphus jujuba* var. *spinosa*⁹ and compound **B**, found in the stems of *Brucea mollis*.¹⁰

Despite the high importance of *N*-glycosyl-2-oxindoles, direct

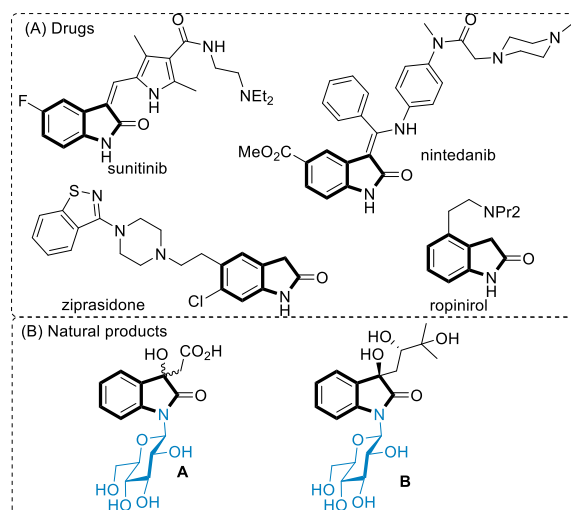
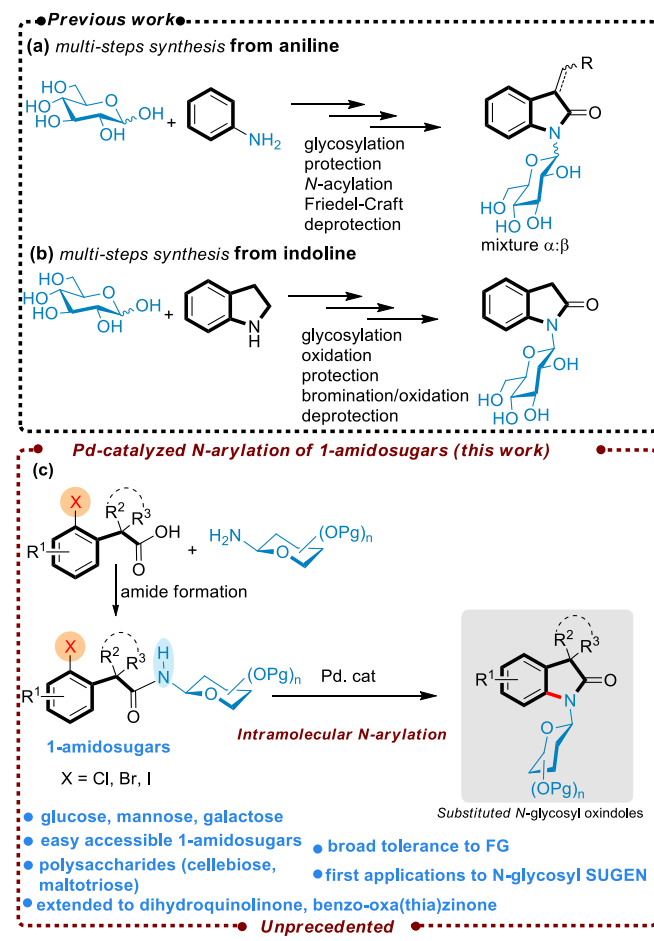


Figure 1. Example of biologically active oxindoles

methods for their synthesis are scarce. To our knowledge, only two methods based on a multi-steps sequence synthesis are reported. The most known one^{7d} relies on a four-steps synthesis (Scheme 1, a) starting from aniline and glucose, to lead to *N*-glycosyl isatines. The extra C3-carbonyl group was used to

Scheme 1. Strategies to the synthesis of *N*-glycosyl oxindoles



further functionalization. This method however, suffers from drawbacks such as low overall yields and difficulties of purification linked to the β/α anomeric composition of the starting materials (up to 2:1). Another approach to *N*-glycosyl-2-oxindoles involves a six-steps procedure including *N*-glycosylation of indoline, oxidation, protection, functionalization and deprotection. Only one unsubstituted oxindole was reported through this procedure in 26% overall yield (Scheme 1, b).¹¹

As part of our continuing effort in functionalizing sugars under transition-metal catalysis,¹² we became interested to develop an efficient and convergent approach to the synthesis of substituted *N*-glycosyl oxindoles. We postulated that these glycosides maybe obtained simply through an intramolecular *N*-arylation of 1-amidosugar using a catalytic amount of palladium (Scheme 1, c). Herein, we report our success in the development of such protocol.

In order to determine optimal conditions for the selective intramolecular arylation of 1-amidosugars, (2-iodophenyl)acetamidoglycopyranose (**3a**, Table 1) was initially selected as a model substrate. This compound was prepared by reacting 2-iodophenylacetic acid (**1a**) with tetraacetylated 1-amino- β -glycopyranose (**2a**) in the presence of hydroxybenzotriazole (HOBt) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl). Under these coupling conditions, compound **3a** was obtained in 67% yield as a β/α mixture in a ratio of 20:1 (determined by ¹H NMR, comparing integrations of the two anomeric protons, see supporting information). With a sub-

sequent amount of **3a** in hand, we turned our attention to examine the intramolecular *N*-arylation of this substrate. The first tentative was accomplished by using our previously reported Pd-catalyzed conditions¹³ for the synthesis of *N*-glycosyl quinolin-2-ones [Pd(OAc)₂ (5 mol%), *n*-Bu₄NOAc (1.5 equiv), dioxane, 100°C, 1 h]. However, under these conditions, even traces of **4a** were not identified by LCMS analysis.

Table 1 Optimization of the coupling reaction of tetraacetylated β -amidoglyucose **3a**^a

entry	Pd.cat	ligand	Solvent	t (h)	yield (%) ^b
1	Pd(dba) ₂ (10 mol%)	DavePhos (10 mol%)	toluene /MeCN (3/1)	24	traces
2	Pd(dba) ₂ (5 mol%)	SPhos (5 mol%)	toluene /MeCN (3/1)	12	15%
3	Pd(dba) ₂ (10 mol%)	SPhos (10 mol%)	toluene /MeCN (3/1)	12	20%
4	Pd(dba) ₂ (10 mol%)	SPhos (10 mol%)	toluene	3	55%
5	Pd(dba) ₂ (10 mol%)	SPhos (20 mol%)	toluene	3	72%
6	Pd(dba) ₂ (10 mol%)	RuPhos (20 mol%)	toluene	3	78%
7	Pd(OAc) ₂ (10 mol%)	RuPhos (20 mol%)	toluene	3	82%
8	Pd(OAc) ₂ (10 mol%)	RuPhos (40 mol%)	toluene	3	90%

^aA sealable tube was charged with 1-amidoglyucose **3a** (1 equiv, 0.2 mmol), [Pd pre-catalyst] (n mol%), ligand (x mol%), K₂CO₃, (2 equiv) in solvent (1.0 mL, 0.015M). ^bYield of isolated product.

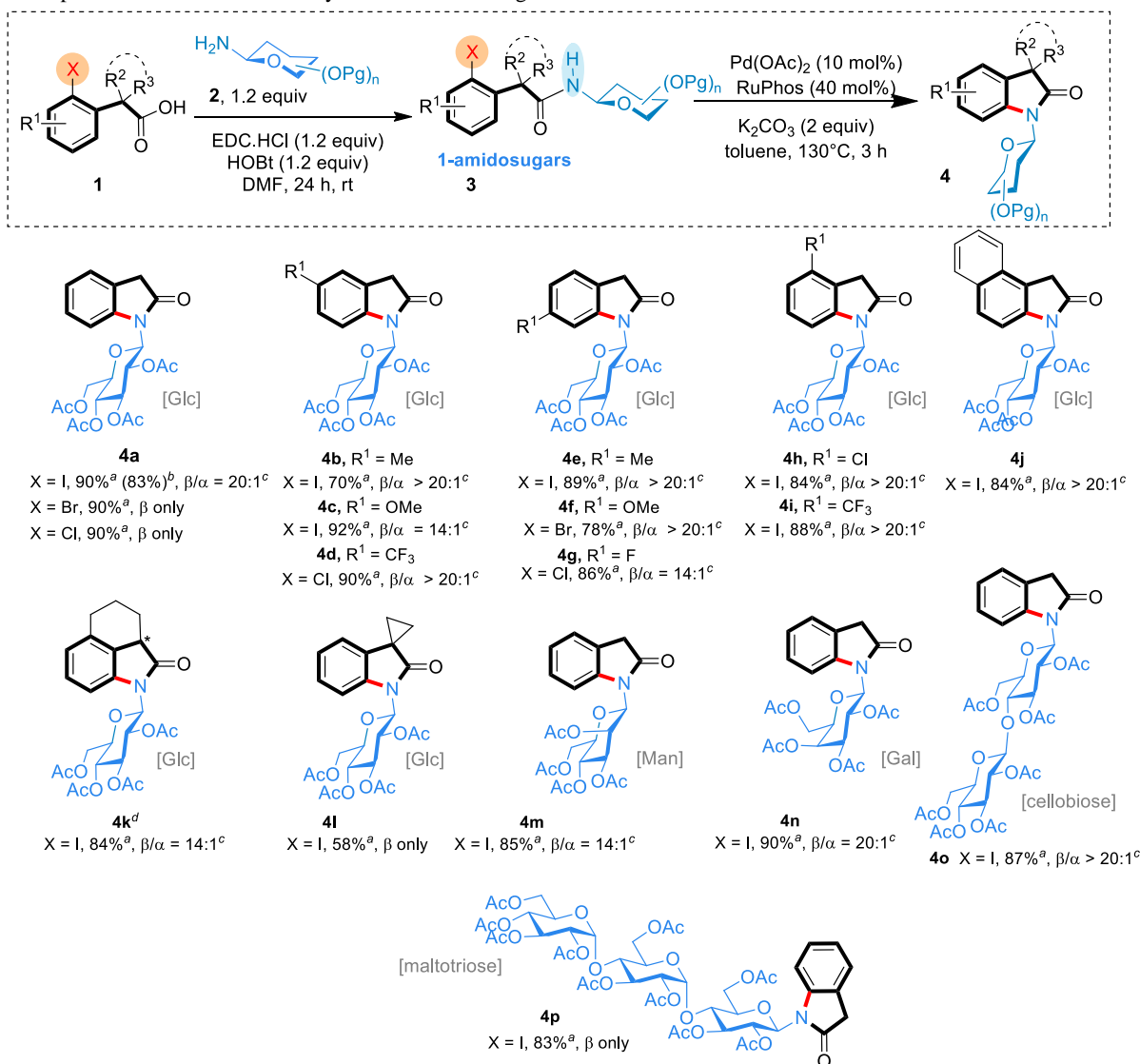
Therefore, we turned our attention toward a systematic screening of literature reaction conditions¹⁴ which have proven their efficiency to accomplish the intramolecular *N*-arylation of secondary amines or amides (Table 1 and SI). Among this series, only conditions using Pd(dba)₂/DavePhos^{14e} (entry 1) provided traces (by LCMS) of the desired cyclized product thus establishing the starting point of our optimizing process. We next evaluated monophosphine SPhos (entry 2) and bidentate phosphine ligand (XantPhos, see SI) usually involved in such pallado-catalyzed coupling reaction type to find that only the SPhos (entry 2) was able, in toluene and acetonitrile solvents, to afford the desired glycoside oxindole **4a** in 15% yield as a β/α mixture (20:1 ratio). Doubling the catalyst ratio to 10 mol% (entry 3) allowed a small improvement of the yield (20%) and gratefully, removing the polar aprotic acetonitrile solvent, the yield of the reaction raised to 55 % in only 3 hours (entry 4). An increase of the Pd/L ratio from 1:1 to 1:2 leads to an improved yield (entry 4, 55% yield vs entry 5, 72% yield). Shifting from SPhos to a more hindered ligand RuPhos allowed a slight improvement of the yield (entry 6, 78%). In addition, performing the reaction with Pd(OAc)₂ pre-catalyst instead of Pd(dba)₂

lead to **4a** in 82% yield (entry 7). We next succeeded in reaching an excellent yield (90%) by combining 10 mol% of Pd(OAc)₂ and 40 mol% of RuPhos (entry 8). It can be noted that **4a** was isolated in all cases as a mixture of β:α anomers in 20:1 ratio, indicating that no anomerization occurred during the process. This was confirmed by conducting the intramolecular coupling reaction from a pure β-anomer **3a** which led to the β-glycosylated oxindole **4a** without traces of the α-anomer.

With optimal conditions in hand, the scalability and robustness of this methodology were demonstrated on 1 mmol scale. As

shown in Scheme 2, **4a** was obtained in 83% yield when the *N*-arylation reaction of **3a** was conducted with 1 mmol scale. Scope and limitations of the reaction were then examined with a diversity of substituted 1-amido-sugars **3** (Scheme 2). These later were prepared from a readily available carboxylic acids **1** and the appropriate 1-amino-β-sugars. In all cases, the expected β-amidosugars **3** were obtained as the major glycosides contaminated in some cases, by a small amount of the α-isomer (see Supporting Information for the β/α ratios), and this mixture was used for the next step.

Scheme 2 Scope of the intramolecular *N*-arylation of 1-amidosugars **3**



Reaction conditions: 1-amidosugar **3** (0.036 to 0.1 mmol), Pd(OAc)₂ (10 mol %), RuPhos (40 mol%), K₂CO₃ (2 equiv) in toluene (0.015 to 0.021 M) at 130 °C for 3 h. ^a Yield of isolated product. ^b reaction was conducted at 1 mmol scale. ^c the β:α ratio was determined by ¹H NMR after purification on flash chromatography. ^d **4k** and his precursor **3k** were obtained as a racemic mixture regarding to the stereogenic center.

We were pleased to note that the coupling conditions were efficient either starting from iodo- or bromo- and chloro-aryl substrates, delivering product **4a** with the same yield (90%). Interestingly, in contrast to the iodide substrate **3a** (β:α = 20:1) used, the bromide **3a'** (β:α = 20:1) or chloride **3a''** (β:α = 9:1) analogues delivered a pure β-*N*-glycosyl oxindole **4a** although they were used as a mixture of β/α anomers. This result indicates

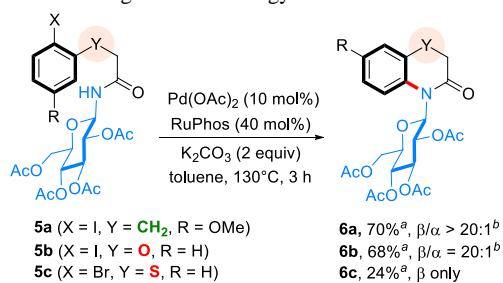
clearly that anomerization occurs during the process when bromide or chloride substrates (**3a'** and **3a''**, respectively) were used. Substrates with electron donating (**3b-c**, **3e-f**) and electron withdrawing (**3d**, **3g-i**) substituents on various positions of the aromatic ring were also successfully converted into the corresponding *N*-glycosyl oxindoles in good to excellent yields (up to 90%). Additionally, the chemoselectivity of this coupling

was examined with the dihalogenated substrate **3h** bearing two different C–X bonds (C–I and C–Cl) at the *ortho-ortho* positions of the benzene ring. Interestingly, under our optimized conditions, only the C–I reacted delivering the corresponding glycoside **4h** in 84% yield and anomeric stereoselectivity $\beta:\alpha$ of 20:1. The presence of aryl fused ring was also well tolerated as shown with compound **4j**. Moreover, the *N*-glycosyl congested tetracycle **4k** was obtained in 84%. In addition, the spiro-oxindole *N*-glycosylated compound **4l** with a cyclopropyl ring on the C3-position was prepared in good 58% yield as a pure β -anomer.

The successful synthesis of *N*-glucosides **4a-l** from 1-amidoglucose **3a-l** encouraged us to investigate other sugar partners on this coupling. Pleasantly, the coupling reaction was extended with success to substrates with various peracetylated mono-, di- and tri-glycosides (**3m-p**). The corresponding oxindoles bearing a mannose (**4m**), a galactose (**4n**), a cellobiose (**4o**) or a maltotriose (**4p**) were all prepared with excellent yields (up to 90%) and high stereoselectivity.

Encouraged by these results, the feasibility of this approach was investigated in the aim to synthesize *N*-glycosylated 6-membered heterocycles (Scheme 3). In this context, we were pleased to see that substrates **5a**, **5b** bearing an ether linkage or their thioether congener **5c** all reacted successfully under our reaction conditions to furnish *N*-glycosylated dihydroquinolinone **6a**, benzoxazinone **6b** and benzothiazinone **6c** in 70%, 68% and 24% yields, respectively. These results represent the first examples of diversification of this family of *N*-heterocycle glycosides through this methodology.

Scheme 3: Extending the methodology to other structures



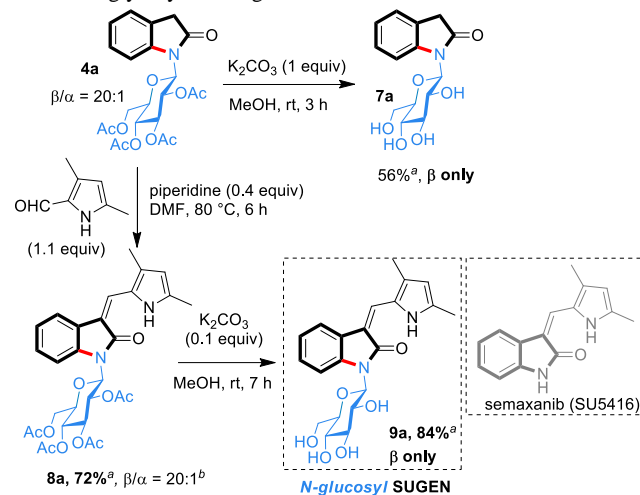
Reaction conditions: 1-amidoglucose **5a-c** (0.08 to 0.11 mmol), Pd(OAc)₂ (10 mol %), RuPhos (40 mol %), K₂CO₃ (2 equiv) in toluene (0.016 to 0.018 M) at 130 °C for 3 h. ^a Yield of isolated product. ^b The $\beta:\alpha$ ratio was determined by ¹H NMR after purification on flash chromatography.

With substantial amounts of **4a** in hand (Scheme 4), we focused our attention on demonstrating whether our method could be employed for molecular diversity. At first, the unprotected glycoside-indolin-2-one **7a** was synthesized by deacetylation of **4a** under Zemplén conditions. This *N*-glucosyloxindole **7a** was thus obtained in a 6-steps procedure, starting from **1a**, in 22% overall yield.

Finally, this methodology was applied to the synthesis of bioactive drug analogues. As shown in Scheme 4, β -*N*-glucosyl SUGEN derivative **8a** which is a *N*-glycosylated analogue of semaxanib (SU5416, a tyrosine-kinase inhibitor drug used as a cancer therapeutic), was obtained in 72% yield by post-functionalization of the *N*-glycosyl oxindole **4a**, *via* condensation with 3,5-dimethyl-1*H*-pyrrole-2-carbaldehyde. As it was previously described,¹⁵ only *Z* isomer of the alkene was observed presumably thanks to the hydrogen bond formed between the nitrogen of the pyrrole and the carbonyl of the oxindole. The deprotected analogue **9a** was further prepared by removal of the

acetate groups in presence of a catalytic amount of potassium carbonate in methanol in 84% yield.

Scheme 4 Further functionalisation of **4a** and application to the synthesis of a glycosylated Sugen derivative **9a**



^a Yield of isolated product. ^b The $\beta:\alpha$ ratio was determined by ¹H NMR after purification on flash chromatography.

In summary, we succeeded the synthesis of *N*-glycosylated oxindoles by intramolecular Pd-catalyzed of *N*-arylation 1-amidoglucose. This is the first methodology reporting an efficient way to prepare a large variety of substituted *N*-glycosyl oxindoles. This coupling reaction tolerates various functional groups and sugar moieties. Moreover, this approach was extended to the synthesis of *N*-glycosylated dihydroquinolinone, benzoxazinone and benzothiazinone. Finally, thanks to this methodology, we described for the first time, the synthesis of a *N*-glycosylated SUGEN derivatives and we expect to apply this general methodology to other therapeutic compounds.

ASSOCIATED CONTENT

Supporting Information

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

Experimental procedures, spectroscopic data and NMR spectra of new compounds.

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Author Contributions

The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript.

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REFERENCES

- (1) Millemaggi, A. & Taylor, R. J. K. 3-Alkenyl-oxindoles: Natural Products, Pharmaceuticals, and Recent Synthetic Advances in Tandem/Telescoped Approaches. *Eur. J. Org. Chem.* 2010, 4527–4547 (2010).
- (2) Kaur, M., Singh, M., Chadha, N.; Silakari, O. Oxindole: A chemical prism carrying plethora of therapeutic benefits. *Eur. J. Med. Chem.* **2016**, *123*, 858.
- (3) Wishart DS, Knox C, Guo AC, Shrivastava S, Hassanali M, Stothard P, Chang Z, Woolsey J. Drugbank: a comprehensive resource for in silico drug discovery and exploration. *Nucleic Acids Res.* 2006 Jan 1;34 (Database issue):D668-72. 16381955.
- (4) Moradi, S. V.; Hussein, W. M.; Varamini, P.; Simerska, P.; Toth, I. Glycosylation, an Effective Synthetic Strategy to Improve the Bioavailability of Therapeutic Peptides. *Chem. Sci.* **2016**, *7*, 2492.
- (5) Cheng, Y.; Zhang, J.; Shao, Y.; Xu, Y.; Ge, H.; Yu, B.; Wang, W. Enzyme-Catalyzed Glycosylation of Curcumin and Its Analogues by Glycosyltransferases from *Bacillus Subtilis* ATCC 6633. *Catalysts* **2019**, *9*, 734.
- (6) (a) Calvaresi, E. C.; Hergenrother, P. J. Glucose conjugation for the specific targeting and treatment of cancer *Chem Sci.* 2013, *4*, 2319–2333; (b) Li, B.; Zhu, M.; Ma, H.; Ma, T.; Dai, Y.; Li, H.; Li, Y.; Wu, C.-Z. Biosynthesis of Novel Shikonin Glucosides by Enzymatic Glycosylation. *Chem. Pharm. Bull.* **2019**, *67*, 1072.
- (7) (a) Sassatelli, M., Saab, E., Anizon, F., Prudhomme, M.; Moreau, P. Synthesis of glycosyl-isoindigo derivatives. *Tetrahedron Lett.* 2004, *45*, 4827; (b) Bouchikhi, F., Anizon, F.; Moreau, P. Synthesis, kinase inhibitory potencies and in vitro antiproliferative activity of isoindigo and 7'-azaisoindigo derivatives substituted by Sonogashira cross-coupling. *Eur. J. Med. Chem.* **2009**, *44*, 2705; (c) Bouchikhi, F., Anizon, F.; Moreau, P. Synthesis and antiproliferative activities of isoindigo and azaisoindigo derivatives. *Eur. J. Med. Chem.* **2008**, *43*, 755–762; (d) Libnow, S.; Methling, K.; Hein, M.; Michalik, D.; Harms, M.; Wende, K.; Flemming, A.; Köckerling, M.; Reinke, H.; Bednarski, P. J.; Lalk, M.; Langer, P. Synthesis of indirubin-*N*-glycosides and their anti-proliferative activity against human cancer cell lines. *Bioorg. Med. Chem.* **2008**, *16*, 5570; (e) Kunz, M.; Driller, K. M.; Hein, M.; Libnow, S.; Hohensee, I.; Ramer, R.; Hinz, B.; Berger, A.; Eberle, J.; Langer, P. Synthesis of Thia-Analogous Indirubin *N*-Glycosides and their Influence on Melanoma Cell Growth and Apoptosis. *ChemMedChem* 2010, *5*, 534; (f) Erben, F. Michalik, D.; Feist, H.; Kleeblatt, D.; Hein, M.; Matin, A.; Iqbal, J.; Langer, P. Synthesis and antiproliferative activity of (Z)-1-glycosyl-3-(5-oxo-2-thioxoimidazolidin-4-ylidene)indolin-2-ones and (Z)-3-(2-glycosylsulfanyl-4-oxo-4,5-dihydro-thiazol-5-ylidene)indolin-2-ones. *RSC Adv.* **2014**, *4*, 10879; (g) Kleeblatt, D. Cordes, C. A.; Lebnrenz, P.; Hein, M.; Feist, H.; Matin, A.; Raza, R.; Iqbal, J.; Munshi, O.; Rahman, Q.; Villinger, A.; Langer, P. Synthesis and antiproliferative activity of *N*-glycosyl-3,3-diaryloxindoles. *RSC Adv.* **2014**, *4*, 22828; (h) Sassatelli, M.; Bouchikhi, F.; Messaoudi, S.; Anizon, F.; Debiton, E.; Barthomeuf, C.; Prudhomme, M.; Moreau, P. Synthesis and Antiproliferative Activities of Diversely Substituted Glycosyl-Isoindigo Derivatives. *Eur. J. Med. Chem.* **2006**, *41*, 88.
- (8) Ohnuki, T.; Ejiri, M.; Kizuka, M.; Fujiwara, M.; Nishi, T. Practical One-Step Glucuronidation via Biotransformation. *Bioorg. Med. Chem. Lett.* **2019**, *29*, 199.
- (9) Li, M.; Wang, Y.; Tsoi, B.; Jin, X.-J.; He, R.-R.; Yao, X.-J.; Dai, Y.; Kurihara, H.; Yao, X.-S. Indoleacetic Acid Derivatives from the Seeds of *Ziziphus Jujuba* Var. *Spinosa*. *Fitoterapia* **2014**, *99*, 48.
- (10) Chen, H.; Bai, J.; Fang, Z.-F.; Yu, S.-S.; Ma, S.-G.; Xu, S.; Li, Y.; Qu, J.; Ren, J.-H.; Li, L.; Si, Y.-K.; Chen, X.-G. Indole Alkaloids and Quassinoids from the Stems of *Bucea Mollis*. *J. Nat. Prod.* **2011**, *74*, 2438.
- (11) Messaoudi, S.; Sancelme, M.; Polard-Housset, V.; Aboab, B.; Moreau, P.; Prudhomme, M. Synthesis and Biological Evaluation of Oxindoles and Benzimidazolinones Derivatives. *Eur. J. Med. Chem.* **2004**, *39*, 453.
- (12) (a) Brachet, E.; Brion, J. D.; Messaoudi, S.; Alami, M. Palladium-Catalyzed Cross - Coupling Reaction of Thioglycosides with (Hetero) aryl Halides. *Adv. Synth. Catal.* **2013**, *355*, 477; (b) Bruneau, A.; Brion, J. D.; Alami, M.; Messaoudi, S. Stereoselective Copper-catalyzed Chan–Lam–Evans *N*-arylation of Glucosamines with Arylboronic Acids at Room Temperature. *Chem. Commun.* **2013**, *49*, 8359; (c) 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; (d) Bruneau, A.; Roche, M.; Hamze, A.; Brion, J. D.; Alami, M.; Messaoudi, S. Stereoretentive Palladium-Catalyzed Arylation, Alkenylation, and Alkynylation of 1-Thiosugars and Thiols Using Aminobiphenyl Palladacycle Precatalyst at Room Temperature. *Chem. Eur. J.* **2015**, *21*, 8375; (e) 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; (f) 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 (g) 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; (h) Probst, N.; Grelier, G.; Dahaoui, S.; Alami, M.; Gandon, V.; Messaoudi, S. Palladium(II)-Catalyzed Diastereoselective 2,3-Trans C(Sp³)-H Arylation of Glycosides. *ACS Catal.* **2018**, *8*, 7781; (i) M. Zhu, G. Dagousset, M. Alami, E. Magnier, S. Messaoudi. Ni/Photoredox-Dual-Catalyzed Functionalization of 1-Thiosugars. *Org. Lett.* **2019**, *21*, 5132; (j) Verdet, T., Benmahdjoub, S., Benmerad, B., Alami, M.; Messaoudi, S. Copper-Catalyzed Anomeric O-Arylation of Carbohydrate Derivatives at Room Temperature. *J. Org. Chem.* **84**, 9226; (k) G. Zhao, M. Zhu, O. Provot, M. Alami, and Messaoudi, S. Synthesis of 2,3-Substituted β-*N*-Glycosyl Indoles through C–H Activation/Annulation Process under Rh(III)-Catalysis, *Org. Lett.* **2020**, *22*, 57.
- (13) Luong, T. T. H., Brion, J.-D., Lescop, E., Alami, M.; Messaoudi, S. Intramolecular Pd-Catalyzed Arylation of 1-Amidosugars: A New Route to *N*-Glycosyl Quinolin-2-ones. *Org. Lett.* **2016**, *18*, 2126.
- (14) (a) Nakazaki, A., Miyagawa, K., Miyata, N.; Nishikawa, T. Synthesis of a C–N Axially Chiral *N*-Arylisatin through Asymmetric Intramolecular *N*-Arylation. *Eur. J. Org. Chem.* **2015**, *2015*, 4603; (b) Harada, R.; Nishida, N.; Uchiito, S.; Onozaki, Y.; Kurono, N.; Senboku, H.; Masao, T.; Ohkuma, T.; Orito, K. Phosphane-Free Pd0-Catalyzed Cycloamination and Carbonylation with Pd(OAc)₂ and Cu(OAc)₂ in the Presence of K₂CO₃: Preparation of Benzocyclic Amines and Benzolactams. *Eur. J. Org. Chem.* **2012**, *2012*, 366; (c) Kukosha, T.; Trufilkina, N.; Katkevics, M. Synthesis of *N*-Alkoxyindol-2-Ones by Copper-Catalyzed Intramolecular *N*-Arylation of Hydroxamates. *Synlett* **2011**, *2011*, 2525; (d) Correa, A.; Elmore, S.; Bolm, C. Iron-Catalyzed *N*-Arylations of Amides. *Chem. Eur. J.* 2008, *14*, 3527; (e) Bonnaterre, F.; Bois-Choussy, M.; Zhu, J. Rapid Access to Oxindoles by the Combined Use of an Ugi Four-Component Reaction and a Microwave-Assisted Intramolecular Buchwald–Hartwig Amidation Reaction. *Org. Lett.* **2006**, *8*, 4351.
- (15) Sun, L.; Tran, N.; Tang, F.; App, H.; Hirth, P.; McMahan, G.; Tang, C. Synthesis and Biological Evaluations of 3-Substituted Indolin-2-Ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases. *J. Med. Chem.* **1998**, *41*, 2588.