AUTHOR QUERY FORM

ELSEVIER

Journal: CAR

Article Number: 6384

Please e-mail or fax your responses and any corrections to:

E-mail: corrections.essd@elsevier.sps.co.in

Fax: +31 2048 52799

Dear Author,

Please check your proof carefully and mark all corrections at the appropriate place in the proof (e.g., by using on-screen annotation in the PDF file) or compile them in a separate list. Note: if you opt to annotate the file with software other than Adobe Reader then please also highlight the appropriate place in the PDF file. To ensure fast publication of your paper please return your corrections within 48 hours.

For correction or revision of any artwork, please consult http://www.elsevier.com/artworkinstructions.

Any queries or remarks that have arisen during the processing of your manuscript are listed below and highlighted by flags in the proof. Click on the 'Q' link to go to the location in the proof.

Location in article	Query / Remark: click on the Q link to go Please insert your reply or correction at the corresponding line in the proof
Q1	Please confirm that given names and surnames have been identified correctly.
Q2	Please check the edit(s) made in the sentence 'The...benzothiazole 1E', and correct if necessary.
Q3	Please check the edit(s) made in the sentence 'Additionally...discovered', and correct if necessary.
Q4	Please check the edit(s) made in the sentence 'With...compounds', and correct if necessary.
Q5	Please check the edit made in the sentence 'Purified...fraction', and correct the subsequent occurences also if necessary.
Q6	Please check page range in Ref. 10.

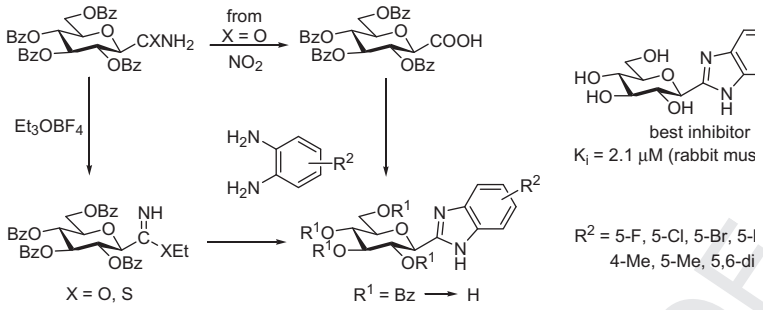
Please check this box if you have no corrections to make to the PDF file ☐

Thank you for your assistance.

Graphical abstract

Synthesis of substituted 2-(β-D-glucopyranosyl)-benzimidazoles and their evaluation as inhibitors of glycogen phosphorylase pp xxx–xxx

Éva Bokor, Enikő Szilágyi, Tibor Docsa, Pál Gergely, László Somsák *



Highlights

► Synthesis of *C*-(β-D-glucopyranosyl)formimidates and -thioformimidates. ► New synthesis of *C*-(β-D-glucopyranosyl)-benzimidazoles. ► Low micromolar inhibitors of glycogen phosphorylase.

Carbohydrate Research xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Synthesis of substituted 2-(β-D-glucopyranosyl)-benzimidazoles and their evaluation as inhibitors of glycogen phosphorylase

Q1 Éva Bokor[a], Enikő Szilágyi[a], Tibor Docsa[b], Pál Gergely[b], László Somsák[a,*]

[a] Department of Organic Chemistry, University of Debrecen, POB 20, H-4010 Debrecen, Hungary
[b] Department of Medical Chemistry, Medical and Health Science Centre, University of Debrecen, Egyetem tér 1, H-4032 Debrecen, Hungary

ARTICLE INFO

Article history:
Received 3 November 2012
Received in revised form 15 January 2013
Accepted 16 January 2013
Available online xxxx

Keywords:
C-Glycopyranosyl-formimidate
C-Glycopyranosyl-thioformimidate
2-C-Glycopyranosyl benzimidazole
Glycogen phosphorylase
Inhibitor

ABSTRACT

Microwave assisted condensation of O-perbenzoylated C-(β-D-glucopyranosyl)formic acid with 1,2-diaminobenzenes in the presence of triphenylphosphite gave the corresponding O-protected 2-(β-D-glucopyranosyl)-benzimidazoles in moderate yields. O-Perbenzoylated C-(β-D-glucopyranosyl) formamide and -thioformamide were transformed into the corresponding ethyl C-(β-D-glucopyranosyl) formimidate and -thioformimidate, respectively, by $Et_3O{\cdot}BF_4$. Treatment of the formimidate with 1,2-diaminobenzenes afforded O-protected 2-(β-D-glucopyranosyl)-benzimidazoles-in good to excellent yields. Similar reaction of the thioformimidate gave these compounds in lower yields. The O-benzoyl protecting groups were removed by the Zemplén protocol. These test compounds were assayed against rabbit muscle glycogen phosphorylase (GP) *b*, the prototype of liver GP, the rate limiting enzyme of glycogen degradation. The best inhibitors were 2-(β-D-glucopyranosyl)-4-methyl-benzimidazole (K_i = 2.8 μM) and 2-(β-D-glucopyranosyl)-naphtho[2,3-*d*]imidazole (K_i = 2.1 μM) exhibiting a ~3–4 times stronger binding than the unsubstituted parent compound.

1. Introduction

Inhibition of glycogen phosphorylase (GP) has been considered as an effective therapeutic approach in combating type 2 diabetes (for the biochemical and pharmacological background of targeting liver GP as a validated concept for lowering blood glucose levels, please survey recent review articles[1–6]). Furthermore, the pharmaceutical utility of GP inhibitors in the intervention of other diseased states associated with GP activity (e.g., cardiovascular disorders,[7–9] ischaemic lesions,[10–13] and tumorous growth[11,14–16]) has also been under investigation.

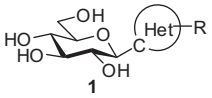
A large array of compounds were shown to have an inhibitory effect against this enzyme[17–19] including glucose derivatives[20,21] which primarily bind to the catalytic site of the enzyme. In the course of searching for potent glucose based inhibitors, several C-β-D-glucopyranosyl heterocycles (Chart 1), such as tetrazole[22] **1A**, 1,3,4-oxadiazoles[22–24] **1B**, 1,2,4-oxadiazoles[23,25,26] **1C**,**D**, benzothiazole[22] **1E** and benzimidazole[22] **1F** have been synthesized and some of them proved to be efficient against rabbit muscle glycogen phosphorylase *b* (RMGP*b*, the prototype of GP enzymes for enzymatic tests[2]). In this class, 2-(β-D-glucopyranosyl)-benzimidazole (**1F**) was the first compound to have a K_i value in the low micromolar range.[22,27] As evidenced by X-ray crystallography, the strong binding in the catalytic centre is the result of direct and water mediated H-bonds between the protein and the heteroaromatic ring, and van der Waals interactions of the large aromatic part in the so-called β-channel of the enzyme.[27] The higher affinity of **1F** Q2 in comparison with its thio counterpart **1E** can be attributed to the direct H-bond of the imidazole NH with the His377 main chain carbonyl group of the enzyme which is certainly absent for benzothiazole **1E**.[27] Analogous NH-(His377)CO interactions were identified in other GP enzyme-inhibitor complexes (e.g., in cases of spiro(thio)hydantoin[28,29] and *N*-acyl-β-D-glucopyranosylamine type inhibitors[30]) indicating the prominent importance of this special H-bridge, as well. Additionally, X-ray crystallographic investi- Q3 gation of **1F** in complex with RMGP*b* revealed that besides the active site the compound also occupied the new allosteric site, and a new binding cleft called the benzimidazole site was also discovered.[27]

To get an insight into the structure–activity relationship of this type of inhibitor the aim of our present work has been to synthesize a series of substituted 2-(β-D-glucopyranosyl)-benzimidazoles and to evaluate their effect on RMGP*b*.

For the formation of 2-*C*-glycosyl-benzimidazoles several synthetic methods are known from the literature most of which have been described for furanose based derivatives. Furanosyl benzimidazoles were prepared (a) by acid catalysed condensation of *C*-glycofuranosyl formic acids and *o*-phenylenediamine (OPD),[31,32] (b) by coupling of *C*-glycofuranosyl formic acids or their chlorides with 1,2-diaminobenzenes, followed by acid or $POCl_3$ mediated ring closure of the resulting amide type intermediates,[33,34] (c) in the

* Corresponding author. Tel.: +36 52512900x22348; fax: +36 52512744.
E-mail address: somsak@tigris.unideb.hu (L. Somsák).

0008-6215/$ - see front matter © 2013 Published by Elsevier Ltd.
http://dx.doi.org/10.1016/j.carres.2013.01.011



1

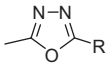
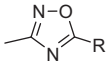
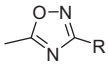
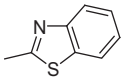
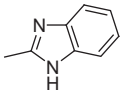
	Het	R	K_i [μM]
A		-	No inhibition[22]
B		CH_3	145[27] 212[22]
		2-naphthyl	10 % at 625 μM[23]
C		2-naphthyl	38[25]
D		2-naphthyl	2.4[23]
E		-	76[27] 229[22]
F		-	8.6[27] 11[22]

Chart 1. Inhibitory potency (K_i) of *C*-glucosyl heterocyclic derivatives against rabbit muscle glycogen phosphorylase *b* (RMGP*b*).

reaction of *C*-glycofuranosyl formaldoximoyl chlorides (actually the nitrile oxide obtained by base induced dehydrochlorination) with OPD,[35] (d) by intramolecular ring closure of suitably protected 2-(pentitol-1′-yl)-benzimidazoles obtained from 2-lithiated benzimidazoles and sugar lactone or acyclic pentose derivatives,[36–38] and (e) by acid induced cyclodehydration of unprotected 2-(tetritol-1′-yl)-benzimidazoles.[39]

For the synthesis of 2-*C*-glycopyranosyl-benzimidazoles three procedures were reported: (a) acid catalysed condensation of unprotected *C*-glycopyranosylmethanals (generated in situ from the appropriate dimethyl acetals) with OPD, followed by spontaneous oxidation of the intermediate benzimidazolines,[40] (b) reaction of O-perbenzoylated ethyl (*C*-β-D-glucopyranosyl)thioformimidate hydrochloride (prepared from the corresponding glycosyl cyanide) with OPD,[22] and (c) treatment of O-peracetylated *C*-glycopyranosyl formaldoximoyl chlorides with OPD.[41] In addition, a 2-benzimidazolyl moiety was also attached to C-1 of D-galactal in the reaction of methyl *C*-(2-deoxy-D-*lyxo*-hex-1-enopyranosyl)formimidate and the dihydrochloride salt of OPD.[42]

In this paper, we disclose further synthetic possibilities to construct benzimidazole at the anomeric centre of the pyranose unit.

2. Results and discussion

2.1. Syntheses

C-(β-D-Glucopyranosyl)formic acid **5**, prepared from cyanide **2** via amide **3**[43] by the literature protocol[44] (Table 1), was reacted with 1,2-diaminobenzenes (**a**, **f**, **h**) in the presence of triphenylphosphite in pyridine under microwave irradiation (conditions were adapted from a published procedure applied for non-sugar based compounds[45]). Although the conversions were complete at 140 °C in 20 min, the desired products could be isolated only in moderate yields (**8a**: 45%, **8f**: 53%, **8h**: 43%). Nevertheless, it has to be noted, that earlier attempts to transform **5** into benzimidazole **8a** by the classical acid catalysed procedure with conventional heating brought about no reaction even at elevated temperatures.[22] Therefore, application of the more reactive iminoesters **6** and **7** was envisaged for the construction of benzimidazoles.

Previously, hydrochloride salt of O-perbenzoylated ethyl *C*-(β-D-glucopyranosyl)thioformimidate obtained from glucopyranosyl cyanide **2** by an acid catalysed addition of EtSH to the nitrile group was used for this purpose.[22] Since these conditions were rather unpleasant and subsequent transformation of the salt gave benzimidazole **8a** in a 34% yield only, we set out to produce and use the free form of this type of precursor. Free thioimidate **7** was obtained from thioamide **4** by $Et_3O{\cdot}BF_4$. The preparation of **4**[46] was also modified to avoid the use of H_2S; thus, cyanide **2** was reacted with P_4S_{10} in refluxing EtOH as described for the synthesis of aliphatic and aromatic thioamides.[47] Similarly to **7**, imidate **6** was obtained from amide **3** by $Et_3O{\cdot}BF_4$.

Next, the preparation of benzimidazole **8a** from either **6** or **7** was compared in preliminary experiments. Reaction of **6** or **7** with OPD gave **8a** in 89% and 62% yields, respectively. Therefore, also taking into account the instability of **7** (decomposition was observed on storage at rt after a few days), further reactions to get the desired benzimidazoles were performed with **6**.

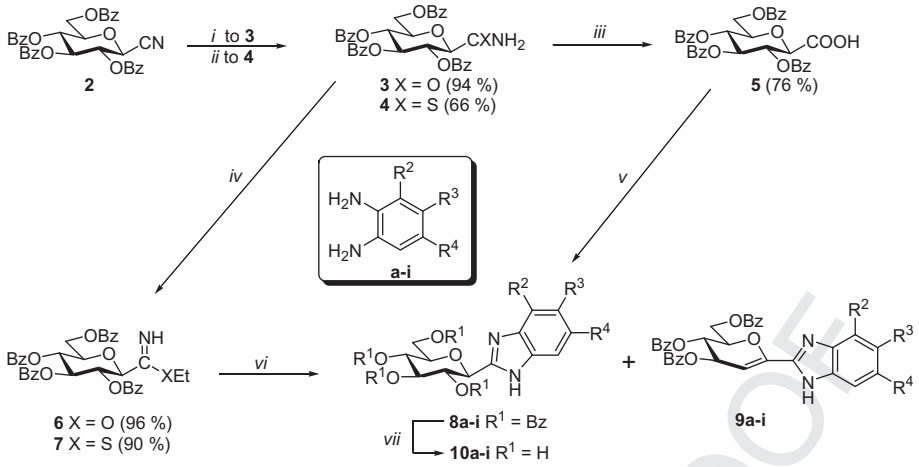
Similarly to **8a**, high yields were also achieved in reactions of **6** with methyl-substituted 1,2-diaminobenzenes **f–h** and 2,3-diaminonaphthalene **i**, respectively (Table 1). A comparison of the yields for **8a**,**f**,**h** obtained from acid **5** under conditions *v* and from imidate **6** under conditions *vi*, respectively, showed the ring closure of **6** with 1,2-diaminobenzenes to be superior to that of **5**.

On treatment of imidate **6** with 1,2-diaminobenzenes containing electron withdrawing substituents (**b–e**) benzoic acid elimination was also observed, and beside the 2-glucopyranosyl benzimidazoles **8b–e** 4-substituted-2-(3′,4′,6′-tri-*O*-benzoyl-2′-deoxy-D-*arabino*-hex-1-enopyranosyl)-benzimidazoles (1-*C*-benzimidazolyl glucals, **9b–e**) were also isolated. Furthermore, total consumption of the starting material **6** in reaction with 4-nitro-1,2-diaminobenzene (**e**) required higher temperature, thus cyclization was performed in boiling ethanol to yield benzimidazole **8e** together with **9e**. This tendency for elimination might be attributed to an increased acidity of the C-1–H proton in the 2-glucosyl-benzimidazoles probably due to the presence of the electron withdrawing substituent in the aromatic ring system.

For enzymatic studies removal of the benzoyl protecting groups of **8b–i** was effected by the Zemplén method to give test compounds **10b–i** in good yields.

The structure of the new compounds was determined by ^1H and ^{13}C NMR spectroscopy. The presence of a β-D-configured glucopyranosyl moiety in the $^4C_1$ conformation was confirmed by the vicinal proton–proton coupling constants for compounds **6**, **7**, **8b–i** and **10b–i**, respectively. In the ^1H NMR spectra of 1-*C*-hetaryl glucals **9b–e** the observed small couplings between the vicinal ring protons (3–6 Hz) suggested a conformational change of the pyranose ring (from chair to half chair).[48] In the ^{13}C NMR spectra of **9b–e** characteristic resonances appeared for C-1′ (143–145 ppm) and C-2′ (99–101 ppm) providing evidence for the unsaturated nature of the pyranoid ring.[48] Among ^{13}C NMR signals of the benzimidazole units only those for C-2 appeared as sharp peaks at 146–158 ppm, the others usually gave broad signals. These observations are in accord with the literature experiences,[35,41] and may be explained by the rapid proton exchange between N-1 and N-3 of the benzimidazole moiety.[35,41,49] Additionally, in the ^{13}C NMR spectra duplication of certain carbon peaks was also observed (primarily for the benzimidazole carbon signals for example, in **8b**, **9c**, **9e** and **10b**), which may refer to the coexistence of the tautomeric pairs. For the fluoro-benzimidazole **8b** this phenomenon seemed quite clear as 14 resonances were observed in the ^{13}C NMR spectrum which could be tentatively assigned on the basis of the characteristic C–F couplings[50] as illustrated in Figure 1.

Table 1
Synthesis of 2-(β-D-glucopyranosyl)-benzimidazoles



i) HBr-AcOH, rt;[43] *ii*) P_4S_{10}, abs. EtOH, reflux; *iii*) NO_2, abs. CH_2Cl_2, rt;[44] *iv*) $Et_3O{\cdot}BF_4$, abs. CH_2Cl_2, Ar, rt; *v*) $P(OPh)_3$ (1.2 equiv.), **a** or **f** or **h** (1.0 equiv), abs. pyridine, μW, 140 °C, 20 min; *vi*) **a-i** (2 equiv.), abs. CH_2Cl_2, reflux; *vii*) ~1 M NaOMe in abs. MeOH, rt.

Reagent	R^2	R^3	R^4	Conditions and yields (%)				
				8		**9**		**10**
a	H	H	H	*v*	45	–	*vii*	–[c,d]
				vi	89 (from **6**)	–		
				vi	62[a] (from **7**)			
b	H	F	H	*vi*	46	35	*vii*	54
c	H	Cl	H	*vi*	76	24	*vii*	89
d	H	Br	H	*vi*	54	29	*vii*	58
e	H	NO_2	H	*vi*[b]	46	20	*vii*	53
f	H	Me	H	*v*	53	–	*vii*	87
				vi	83	–		
g	Me	H	H	*vi*	79	–	*vii*	73
h	H	Me	Me	*v*	43	–	*vii*	78
				vi	81	–		
i	H			*vi*	79	–	*vii*	77

[a] Reported yield of **8a** by the earlier method from perbenzoylated β-D-glucopyranosyl cyanide via the thioimidate hydrochloride salt: 34%.[22]
[b] Modified reaction conditions were necessary for complete consumption of the starting material **6**: abs. EtOH, reflux.
[c] Debenzoylation of **8a** by the Zemplén protocol was carried out earlier. Reported yield of **10a**: 84%.[22]
[d] Reported yield of **10a** by a different method: 54%.[40]

2.2. Enzyme kinetic studies

Enzyme kinetic measurements with rabbit muscle glycogen phosphorylase *b* were performed as described previously,[51,52] and the obtained inhibitor constants are given in Table 2. The new compounds showed inhibitory effects in the micromolar range and some of them proved equivalent or somewhat better inhibitors than **10a** (=**1F** in Chart 1).

Among benzimidazoles with a halogen substituent in the 5-position fluoro derivative **10b** exhibited modest activity, while the chloro (**10c**) as well as bromo (**10d**) compounds were as good inhibitors as **10a**. Substitution of the benzimidazole ring in the same position by a nitro group (**10e**) brought about a significant decrease of the inhibition. Among the alkyl substituted derivatives the 5-methyl- (**10f**) and 4-methyl-benzimidazoles (**10g**) displayed similar and slightly better (~3-fold increase) potency than **10a**, respectively. However, introduction of two methyl groups into the 5- and 6-positions of the heterocycle (**10h**) resulted in a remarkable weakening of the inhibition. Finally, the naphtho[2,3-*d*]imidazole **10i** showed ~4 times stronger binding than **10a** and proved to be the most effective inhibitor of this series. To elucidate the nature of the binding modes of the new compounds to GP enzyme X-ray crystallographic studies are in progress and will be reported elsewhere.

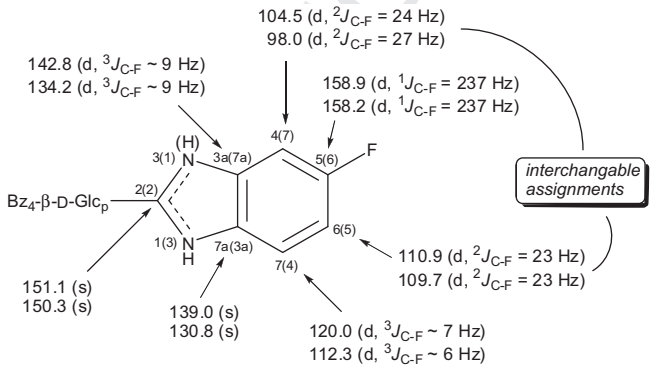
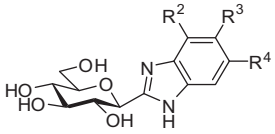


Figure 1. Tentative assignment of ^{13}C NMR signals for tautomers of compound **8b**.

Table 2
Kinetic data on the inhibition of rabbit muscle glycogen phosphorylase *b* by the new compounds **10b–i**



10	R^2	R^3	R^4	K_i (μM)
a	H	H	H	8.6[27] 11[22]
b	H	F	H	55
c	H	Cl	H	9.7
d	H	Br	H	7.5
e	H	NO_2	H	179
f	H	Me	H	12
g	Me	H	H	2.8
h	H	Me	Me	152
i	H			2.1

3. Conclusion

New synthetic pathways were elaborated for the formation of substituted 2-(β-D-glucopyranosyl)-benzimidazoles by heterocyclizations of 2,6-anhydro-aldonic acid derivatives as precursors. Condensation of O-perbenzoylated *C*-(β-D-glucopyranosyl)formic acid with 1,2-diaminobenzenes in the presence of $P(OPh)_3$ under microwave irradiation gave the desired benzimidazoles in moderate yields. Ring closure of O-perbenzoylated ethyl *C*-(β-D-glucopyranosyl)formimidate, prepared from the corresponding formamide by $Et_3O{\cdot}BF_4$, with the 1,2-diaminobenzenes afforded a more efficient procedure. With electron depleted aromatic diamines undesirable β-elimination of benzoic acid from the 1,2-positions of the glucopyranosyl moiety also took place to yield 1-*C*-benzimidazolyl glucals besides the target compounds. Enzyme kinetic studies with the new 2-(β-D-glucopyranosyl)-benzimidazoles showed the compounds to inhibit RMGP*b* in the low micromolar range. Substitution of the benzimidazole moiety by a methyl group in the 4-position or further annelation of a benzene ring provided more efficient inhibitors than the unsubstituted parent compound.

4. Experimental

4.1. General methods

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at rt. NMR spectra were recorded with Bruker 360 (360/90 MHz for $^1H/^{13}C$) spectrometer. Chemical shifts are referenced to Me_4Si (^1H), or to the residual solvent signals (^{13}C). Microwave assisted procedures were performed in a CEM-Discover Focused Microwave Synthesis System (2450 MHz) with a built-in infrared temperature sensor and a CEM-Explorer computer controlled robotic sampler.

TLC was performed on DC-Alurolle Kieselgel 60 F_{254} (Merck), and the plates were visualized under UV light and by gentle heating. For column chromatography Kieselgel 60 (Merck, particle size 0.063–0.200 mm) was used. Dichloromethane was distilled from P_4O_{10} and stored over 4 Å molecular sieves. 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide,[43] *C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formamide[43] and *C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formic acid[44] were synthesized according to published procedures.

4.2. *C*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl) thioformamide (4)

A solution of phosphorus pentasulfide (2.23 g, 10 mmol) in anhydrous EtOH (20 mL) was stirred at rt for 1.5 h, then 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl cyanide[43] (**2**, 3.02 g, 5 mmol) was added and the mixture was heated at reflux temperature for 2 h. After cooling the heterogenous mixture to rt, the precipitate was filtered off and washed with EtOH to yield 2.1 g (66%) of **4** as a pale yellowish solid. Mp: 199–201 °C (Lit.[46] mp: 198–200 °C). ^1H and ^{13}C NMR data correspond to the reported spectra.[46]

4.3. Ethyl *C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl) formimidate (6)

C-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl)formamide[43] (**3**, 1.0 g, 1.60 mmol) and $Et_3O{\cdot}BF_4$ (0.91 g, 4.80 mmol) were dissolved in anhydrous CH_2Cl_2 (15 mL), the mixture was stirred at rt under Ar and monitored by TLC (1:1 EtOAc–hexane). After completion of the reaction (2 days), the mixture was diluted with CH_2Cl_2 (30 mL), extracted with satd aq $NaHCO_3$ solution (30 mL) and then with water (30 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude pale yellow amorphous product (1.0 g, 96%) was used without further purification. R_f: 0.55 (1:1 EtOAc–hexane); ^1H NMR ($CDCl_3$) δ (ppm): 8.06–7.25 (21H, m, aromatics, NH), 5.99, 5.72, 5.55 (3 × 1H, 3 pseudo t, J = 10.6, 9.2 Hz in each, H-2, H-3, H-4), 4.70 (1H, dd, J = 11.9, 2.6 Hz, H-6a), 4.52 (1H, dd, J = 11.9, 5.3 Hz, H-6b), 4.25 (1H, ddd, J = 9.2, 5.3, 2.6 Hz, H-5), 4.21 (1H, d, J = 9.2 Hz, H-1), 4.12–3.91 (2H, m, CH_2), 0.84 (3H, t, 6.6 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ (ppm): 167.5, 166.1, 165.7, 165.1 (2) (CO, CNH), 133.5–128.2 (aromatics), 75.8, 74.6, 73.6, 70.7, 69.1 (C-1–C-5), 62.8, 62.1 (C-6, CH_2), 13.4 (CH_3).

4.4. Ethyl *C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl) thioformimidate (7)

C-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl)thioformamide (**4**, 0.2 g, 0.31 mmol) and $Et_3O{\cdot}BF_4$ (0.18 g, 0.94 mmol) were dissolved in anhydrous CH_2Cl_2 (4 mL), the mixture was stirred at rt under Ar and monitored by TLC (1:1 EtOAc–hexane). After completion of the reaction (2 days), the mixture was diluted with CH_2Cl_2 (10 mL), extracted with satd aq $NaHCO_3$ solution (15 mL), then with water (15 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was evaporated. The crude pale yellow amorphous product (0.19 g, 90%) was used without further purification. R_f: 0.62 (1:1 EtOAc–hexane); ^1H NMR ($CDCl_3$) δ (ppm): 8.06–7.24 (21H, m, aromatics, NH), 5.95, 5.74, 5.70 (3 × 1H, 3 pseudo t, J = 9.8, 9.1 Hz in each, H-2, H-3, H-4), 4.68 (1H, dd, J = 11.9, 2.8 Hz, H-6a), 4.51 (1H, dd, J = 11.9, 4.9 Hz, H-6b), 4.39 (1H, d, J = 9.1 Hz, H-1), 4.22 (1H, ddd, J = 9.1, 4.9, 2.8 Hz, H-5), 2.88–2.71 (2H, m, CH_2), 1.17 (3H, pseudo t, 7.7, 7.0 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ (ppm): 172.7 (CNH), 166.1, 165.7, 165.1, 164.9 (CO), 133.4–128.2 (aromatics), 80.6, 76.1, 73.9, 70.9, 69.1 (C-1–C-5), 62.8 (C-6), 23.1 (CH_2), 13.1 (CH_3).

4.5. General procedure I for the synthesis of substituted 2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazoles from O-perbenzoylated *C*-(β-D-glucopyranosyl)formic acid (5)

C-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl)formic acid[44] (**5**, 0.1 g, 0.16 mmol), a 1,2-diaminobenzene (**a** or **f** or **h**, 0.16 mmol, 1 equiv) and triphenyl phosphite (50 μl, 0.19 mmol, 1.2 equiv) were dissolved in anhydrous pyridine (2 mL). The closed vial was irradiated by microwaves for 20 min at 140 °C (maximum pres-

sure: 20 bar, power 220 W). The completion of the reaction was monitored by TLC (1:1 EtOAc–hexane). The reaction mixture was concentrated under reduced pressure, traces of pyridine were removed by repeated co-evaporations with toluene. The crude product was purified by column chromatography (2:3 EtOAc–hexane).

4.6. General procedure II for the synthesis of substituted 2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazoles from O-perbenzoylated ethyl (*C*-β-D-glycopyranosyl) formimidate (6)

Ethyl *C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glycopyranosyl)formimidate (**6**, 0.1 g, 0.15 mmol) and a 1,2-diaminobenzene (**a–i**, 0.30 mmol, 2 equiv) were dissolved in anhydrous CH_2Cl_2 (3 mL). The mixture was refluxed and monitored by TLC (2:3 EtOAc–hexane). After completion of the reaction the solvent was evaporated, and the residue was purified by column chromatography.

4.7. General procedure III for the Zemplén-deacylation

A benzoylated compound was dissolved in dry MeOH (5 mL/100 mg, a few drops of $CHCl_3$ were added in case of incomplete dissolution) and a catalytic amount of a NaOMe solution (~1 M in MeOH) was added. The mixture was kept at rt and monitored by TLC (7:3 $CHCl_3$–MeOH). When the starting material was consumed the mixture was neutralised with a cation exchange resin Amberlyst 15 (H^+ form), then the resin was filtered off and the solvent removed. The residue was purified by column chromatography.

4.8. 2-(2′,3′,4′,6′-Tetra-O-benzoyl-β-D-glucopyranosyl)-benzimidazole (8a)

A: From acid **5** (0.1 g, 0.16 mmol) and *o*-phenylenediamine (**a**, 0.02 g, 0.16 mmol) according to General procedure **I.** Yield: 0.05 g (45%).

B: From imidate **6** (0.10 g, 0.15 mmol) and *o*-phenylenediamine (**a**, 0.04 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 3 h. Purified by column chromatography (2:3 EtOAc–hexane) to yield 0.09 g (89%) of white solid. Mp: 122–124 °C (Lit.[22] mp: 120–123 °C). ^{1}H and ^{13}C NMR data correspond to the reported spectra.[22]

4.9. 5(6)-Fluoro-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8b) and 5(6)-fluoro-2-(3′,4′,6′-tri-*O*-benzoyl-2′-deoxy-D-arabino-hex-1-enopyranosyl)-benzimidazole (9b)

From imidate **6** (0.10 g, 0.15 mmol) and 1,2-diamino-4-fluorobenzene (**b**, 0.04 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 5 h. Purified by column chromatography (1:2, then 2:3 EtOAc–hexane) to give **9b** as the first than **8b** as the second fraction.

Compound **8b**: Yield: 0.051 g (46%) pale yellow solid; R_f: 0.31 (2:3 EtOAc–hexane); mp: 124–126 °C; $[\alpha]_D$ = −39 (*c* 0.5, DMSO); ^{1}H NMR ($CDCl_3$) δ (ppm): 11.58 (1H, br s, benzimidazole NH), 7.96–6.76 (23H, m, aromatics), 6.30–6.21, 6.02 (3 × 1H, 3 pseudo t, J = 9.2, 9.2 Hz in each, H-2′, H-3′, H-4′), 5.36 (1H, d, J = 9.2 Hz, H-1′), 4.69 (1H, dd, J = 12.3, <1 Hz, H-6′a), 4.57 (1H, dd, J = 12.3, 5.3 Hz, H-6′b), 4.52 (1H, ddd, J = 9.2, 5.3, <1 Hz, H-5′); ^{13}C NMR (DMSO-d_6) δ (ppm): 165.4, 165.1, 164.8, 164.3 (CO), 158.9 (d, $^1J_{C\text{-}F}$ = 237 Hz, benzimidazole), 158.2 (d, $^1J_{C\text{-}F}$ = 237 Hz, benzimidazole), 151.1, 150.3 (benzimidazole), 142.8 (d, $^3J_{C\text{-}F}$ = 9 Hz, benzimidazole), 139.0 (br s, benzimidazole), 134.2 (d, $^3J_{C\text{-}F}$ = 9 Hz, benzimidazole), 133.7–133.3 (aromatics), 130.9 (br s, benzimidazole), 129.3–128.5 (aromatics), 120.0 (d, $^3J_{C\text{-}F}$ = 7 Hz, benzimidazole), 112.3 (d, $^3J_{C\text{-}F}$ = 6 Hz, benzimidazole), 110.9 (d, $^2J_{C\text{-}F}$ = 23 Hz, benzimidazole), 109.7 ($^2J_{C\text{-}F}$ = 23 Hz, benzimidazole), 104.5 (d, $^2J_{C\text{-}F}$ = 24 Hz, benzimidazole), 98.0 (d, $^2J_{C\text{-}F}$ = 27 Hz, benzimidazole), 79.1, 74.8, 74.2, 73.4, 71.5, 69.0 (C-1′–C-5′), 62.8 (C-6′). Anal. Calcd for $C_{41}H_{31}FN_2O_9$ (714.69): C, 68.90; H, 4.37; N, 3.92. Found: C, 68.84; H, 4.29; N, 4.03.

Compound **9b**: Yield: 0.032 g (35%), pale yellow syrup; R_f: 0.58 (2:3 EtOAc–hexane); $[\alpha]_D$ = −7 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 10.41 (1H, br s, benzimidazole NH), 8.02–6.94 (18H, m, aromatics), 6.43 (1H, br s, H-2′), 5.95–5.92 (2H, m, H-3′, H-4′), 4.88 (1H, ddd, J = 4.0, <1 Hz, H-5′), 4.79 (2H, s, H-6′a, H-6′b); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.2, 165.6, 165.0 (CO), 159.8 (d, $^1J_{C\text{-}F}$ = 239 Hz, benzimidazole C-5), 146.8 (benzimidazole C-2), 145.0 (C-1′), 143.1, 139.8 (2 br s, benzimidazole C-3a, C-7a), 133.5–128.4 (aromatics), 120.2 (br s, benzimidazole C-4 or C-7), 111.9 (d, $^2J_{C\text{-}F}$ = 25 Hz, benzimidazole C-6), 104.4 (br s, benzimidazole C-4 or C-7), 99.4 (C-2′), 75.2, 67.9, 67.3 (C-3′–C-5′), 61.7 (C-6′). Analysis: $C_{34}H_{25}FN_2O_7$ (592.57), ESI-MS (positive mode) *m/z*: 615.157 $[M+Na]^+$, 1207.327 $[2\,M+Na]^+$.

4.10. 5(6)-Chloro-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8c) and 5(6)-chloro-2-(3′,4′,6′-tri-O-benzoyl-2′-deoxy-D-arabino-hex-1-enopyranosyl)-benzimidazole (9c)

From imidate **6** (0.10 g, 0.15 mmol) and 1,2-diamino-4-chlorobenzene (**c**, 0.04 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 5 h. Purified by column chromatography (2:3 EtOAc–hexane) to give **9c** as the first and **8c** as the second fraction.

Compound **8c:** Yield: 0.085 g (76%), pale yellow solid; R_f: 0.29 (2:3 EtOAc–hexane); mp: 123–125 °C; $[\alpha]_D$ = −61 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 11.33 (1H, br s, benzimidazole NH), 7.94–6.95 (23H, m, aromatics), 6.21, 6.14, 6.00 (3 × 1H, 3 pseudo t, J = 9.4, 9.4 Hz in each, H-2′, H-3′, H-4′), 5.31 (1H, d, J = 9.4 Hz, H-1′), 4.72 (1H, dd, J = 12.3, <1 Hz, H-6′a), 4.60 (1H, dd, J = 12.3, 4.4 Hz, H-6′b), 4.50 (1H, ddd, J = 9.4, 4.4, <1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.5, 166.0, 165.1 (2) (CO), 149.8 (benzimidazole C-2), 142.0, 137.8 (2 br s, benzimidazole C-3a, C-7a), 133.3–127.8 (aromatics), 126.9, 123.3, 119.3 (br s), 112.4 (br s) (benzimidazole C-4–C-7), 77.0, 75.5, 74.1, 71.7, 69.5 (C-1′–C-5′), 63.4 (C-6′). Anal. Calcd for $C_{41}H_{31}ClN_2O_9$ (731.15): C, 67.35; H, 4.27; N, 3.84. Found: C, 67.47; H, 4.13; N, 3.90.

Compound **9c:** Yield: 0.022 g (24%), pale yellow syrup; R_f: 0.59 (2:3 EtOAc–hexane); $[\alpha]_D$ = −5 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 11.40 (1H, br s, benzimidazole NH), 8.00–7.07 (18H, m, aromatics), 6.45 (1H, d, J = 4.0 Hz, H-2′), 5.98 (1H, pseudo t, J = 6.6, 5.9 Hz, H-3′ or H-4′), 5.94 (1H, pseudo t, J = 5.9, 4.0 Hz, H-3′ or H-4′), 4.81 (1H, ddd, J = 6.6, 4.6, 4.0 Hz, H-5′), 4.71–4.70 (2H, m, H-6′a, H-6′b); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.1, 165.6, 164.9 (CO), 146.8 (br s, benzimidazole C-2), 145.0 (C-1′), 144.1, 141.8 (2 br s, benzimidazole C-3a, C-7a), 133.6–133.2 (aromatics), 132.0 (br s, benzimidazole C-5), 129.8–128.3 (aromatics), 123.9, 120.3, 119.1, 112.2, 111.3 (br s for each, benzimidazole C-4, C-6, C-7), 99.8 (C-2′), 75.2, 68.1, 67.3 (C-3′–C-5′), 61.7 (C-6′). Analysis: $C_{34}H_{25}ClN_2O_7$ (609.02), ESI-MS (positive mode) *m/z*: 631.123 $[M+Na]^+$, 1239.257 $[2M+Na]^+$.

4.11. 5(6)-Bromo-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8d) and 5(6)-bromo-2-(3′,4′,6′-tri-*O*-benzoyl-2′-deoxy-D-arabino-hex-1-enopyranosyl)-benzimidazole (9d)

From imidate **6** (0.10 g, 0.15 mmol) and 1,2-diamino-4-bromobenzene (**d**, 0.06 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 3 h. Purified by column chromatography (2:3 EtOAc–hexane) to give **9d** as the first and **8d** as the second fraction.

Compound **8d**: Yield: 0.064 g (54%) pale yellow solid; R_f: 0.31 (2:3 EtOAc–hexane); mp: 126–128 °C; $[\alpha]_D$ = –62 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 8.02–6.76 (23H, m, aromatics), 6.42, 6.29, 6.14 (3 × 1H, 3 pseudo t, *J* = 9.6, 9.6 Hz in each, H-2′, H-3′, H-4′), 5.39 (1H, d, *J* = 9.6 Hz, H-1′), 4.72 (1H, dd, *J* = 12.3, 2.2 Hz, H-6′a), 4.63 (1H, dd, *J* = 12.3, 4.9 Hz, H-6′b), 4.56 (1H, ddd, *J* = 9.6, 4.9, 2.2 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.4, 166.0, 165.0 (2) (CO), 149.6 (benzimidazole C-2), 140.9, 138.1 (2 br s, benzimidazole C-3a, C-7a), 133.3–127.7 (aromatics), 125.9, 119.0 (br s), 117.3 (br s), 115.9 (benzimidazole C-4, C-5, C-6, C-7), 77.0, 75.5, 74.1, 71.7, 69.4 (C-1′–C-5′), 63.4 (C-6′). Analysis: $C_{41}H_{31}BrN_2O_9$ (775.60), ESI-MS (positive mode) *m/z*: 799.112 $[M+Na]^+$, 1573.242 $[2M+Na]^+$.

Compound **9d**: Yield: 0.029 g (29%) pale yellow syrup; R_f: 0.61 (2:3 EtOAc–hexane); $[\alpha]_D$ = –4 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 10.06 (1H, br s, imidazole NH), 8.04–7.33 (18H, m, aromatics), 6.46 (1H, br s, H-2′), 5.97–5.93 (2H, m, H-3′, H-4′), 4.91 (1H, ddd, *J* = 4.0, <1 Hz, H-5′), 4.81 (2H, s, H-6′a, H-6′b). Analysis: $C_{34}H_{25}BrN_2O_7$ (653.48), ESI-MS (positive mode) *m/z*: 677.074 $[M+Na]^+$, 1329.197 $[2M+Na]^+$.

4.12. 5(6)-Nitro-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8e) and 5(6)-nitro-2-(3′,4′,6′-tri-*O*-benzoyl-2′-deoxy-D-arabino-hex-1-enopyranosyl)-benzimidazole (9e)

From imidate **6** (0.10 g, 0.15 mmol) and 1,2-diamino-4-nitrobenzene (**e**, 0.05 g, 0.30 mmol) according to General procedure **II.** in anhydrous ethanol. Reaction time: 1 day. Purified by column chromatography (1:2 EtOAc–hexane) to give **9e** as the first and **8e** as the second fraction.

Compound **8e**: Yield: 0.052 g (46%) yellow solid; R_f: 0.25 (2:3 EtOAc–hexane); mp: 134–136 °C; $[\alpha]_D$ = –65 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 12.87 (1H, br s, benzimidazole NH), 8.45–6.96 (23H, m, aromatics), 6.20, 6.12, 6.01 (3 × 1H, 3 pseudo t, *J* = 9.4, 9.4 Hz in each, H-2′, H-3′, H-4′), 5.33 (1H, d, *J* = 9.4 Hz, H-1′), 4.77 (1H, dd, *J* = 11.8, <1 Hz, H-6′a), 4.63 (1H, dd, *J* = 11.8, <1 Hz, H-6′b), 4.51 (1H, ddd, *J* = *J* = 9.4, <1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.3, 165.8, 165.1, 164.8 (CO), 152.7 (benzimidazole C-2), 143.3 (benzimidazole C-5), 141.6, 138.0 (2 br s, benzimidazole C-3a, C-7a), 133.5–127.6 (aromatics), 118.9, 116.1, 111.6 (br s for each, benzimidazole C-4, C-6, C-7), 77.1, 75.4, 74.0, 71.7, 69.0 (C-1′–C-5′), 63.2 (C-6′). Anal. Calcd for $C_{41}H_{31}N_3O_{11}$ (741.70): C, 66.39; H, 4.21; N, 5.67. Found: C, 66.26; H, 4.13; N, 5.79.

Compound **9e**:Yield: 0.019 g (20%) yellow syrup; R_f: 0.39 (2:3 EtOAc–hexane); $[\alpha]_D$ = +1 (*c* 0.5, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ (ppm): 13.51 (1H, br s, benzimidazole NH), 8.13–7.48 (18H, m, aromatics), 6.40 (1H, br s, H-2′), 6.02 (1H, pseudo t, *J* = 5.3, 4.0 Hz, H-3′ or H-4′), 5.93 (1H, pseudo t, *J* = 6.6, 5.9 Hz, H-3′ or H-4′), 5.23 (1H, ddd, *J* = 5.9, 5.3, 3.3 Hz, H-5′), 4.89 (1H, dd, *J* = 12.6, 5.3 Hz, H-6′a), 4.78 (1H, dd, *J* = 12.6, 3.3 Hz, H-6′b); ^{13}C NMR (DMSO-d_6) δ (ppm): 165.3, 165.0, 164.5 (CO), 150.5 (br s), 149.7 (br s), 147.5 (br s), 145.0, 143.0, 142.3 (br s), 138.7 (br s) (benzimidazole, C-1′), 133.8–128.7 (aromatics), 119.2, 118.5, 117.8, 115.2, 112.3, 108.4 (br s for each, benzimidazole), 100.5 (C-2′), 74.6, 67.9, 67.0 (C-3′–C-5′), 61.5 (C-6′). Analysis: $C_{34}H_{25}N_3O_9$ (619.58), ESI-MS (positive mode) *m/z*: 642.148 $[M+Na]^+$, 1261.309 $[2M+Na]^+$.

4.13. 5(6)-Methyl-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8f)

A: From acid **5** (0.1 g, 0.16 mmol) and 3,4-diaminotoluene (**f**, 0.02 g, 0.16 mmol) according to General procedure **I.** Yield: 0.06 g (53%).

B: From imidate **6** (0.10 g, 0.15 mmol) and 3,4-diaminotoluene (**f**, 0.04 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 2 h. Purified by column chromatography (2:3 EtOAc–hexane) to yield 0.09 g (83%) of pale yellow syrup. R_f: 0.41 (1:1 EtOAc–hexane); $[\alpha]_D$ = –65 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 10.73 (1H, br s, benzimidazole NH), 7.92–6.90 (23H, m, aromatics), 6.19, 6.11, 5.96 (3 × 1H, 3 pseudo t, *J* = 9.2, 9.2 Hz in each, H-2′, H-3′, H-4′), 5.32 (1H, d, *J* = 9.2 Hz, H-1′), 4.68 (1H, dd, *J* = 12.2, 2.6 Hz, H-6′a), 4.54 (1H, dd, *J* = 12.2, 5.3 Hz, H-6′b), 4.44 (1H, ddd, *J* = 9.2, 5.3, 2.6 Hz, H-5′), 2.32 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.4, 165.9, 165.2 (2) (CO), 148.1 (benzimidazole C-2), 142.4, 138.8 (2 br s, benzimidazole C-3a, C-7a), 133.4–128.0 (aromatics, benzimidazole C-5), 124.4, 118.9, 111.1 (br s for each, benzimidazole C-4, C-6, C-7), 76.8, (C-1′), 75.3, 74.1, 71.5, 69.5 (C-1′–C-5′), 63.4 (C-6′), 21.5 (CH_3). Anal. Calcd for $C_{42}H_{34}N_2O_9$ (710.73): C, 70.98; H, 4.82; N, 3.94. Found: C, 70.83; H, 4.96; N, 4.09.

4.14. 4(7)-Methyl-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8g)

From imidate **6** (0.10 g, 0.15 mmol) and 2,3-diaminotoluene (**g**, 0.04 g, 0.30 mmol) according to General Procedure **II.** Reaction time: 5 h. Purified by column chromatography (1:2 EtOAc–hexane) to yield 0.087 g (79%) of yellow solid. Mp: 117–119 °C; $[\alpha]_D$ = –43 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 10.88 (1H, br s, benzimidazole NH), 7.96–6.88 (23H, m, aromatics), 6.18, 6.06, 5.92 (3 × 1H, 3 pseudo t, *J* = 9.2, 9.2 Hz in each, H-2′, H-3′, H-4′), 5.38 (1H, d, *J* = 9.2 Hz, H-1′), 4.69 (1H, dd, *J* = 11.7, <1 Hz, H-6′a), 4.51 (1H, dd, *J* = 11.7, 5.3 Hz, H-6′b), 4.44 (1H, ddd, *J* = 9.2, 5.3, <1 Hz, H-5′), 2.33 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.3, 165.8, 165.3, 165.2 (CO), 147.7 (benzimidazole C-2), 142.1 (br s, benzimidazole C-3a, C-7a), 133.4–128.0 (aromatics), 123.1, 122.4, 116.8, 108.8 (br s for each, benzimidazole C-4–C-7), 76.8, 75.2, 73.9, 71.4, 69.5 (C-1′–C-5′), 63.3 (C-6′), 16.5 (CH_3). Anal. Calcd for $C_{42}H_{34}N_2O_9$ (710.73): C, 70.98; H, 4.82; N, 3.94. Found: C, 70.87; H, 4.90; N, 3.85.

4.15. 5,6-Dimethyl-2-(2′,3′,4′,6′-tetra-*O*-benzoyl-β-D-glucopyranosyl)-benzimidazole (8h)

A: From acid **5** (0.1 g, 0.16 mmol) and 1,2-diamino-4,5-dimethylbenzene (**h**, 0.02 g, 0.16 mmol) according to General procedure **I.** Yield: 0.05 g (43%).

B: From imidate **6** (0.10 g, 0.15 mmol) and 1,2-diamino-4,5-dimethylbenzene (**h**, 0.04 g, 0.30 mmol) according to General procedure **II.** Reaction time: 3 h. Purified by column chromatography (2:3 EtOAc–hexane) to yield 0.09 g (81%) of pale yellow solid. Mp: 207–209 °C; $[\alpha]_D$ = –64 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ (ppm): 11.00 (1H, br s, benzimidazole NH), 7.98–6.92 (22H, m, aromatics), 6.27, 6.21, 6.05 (3 × 1H, 3 pseudo t, *J* = 9.2, 9.2 Hz in each, H-2′, H-3′, H-4′), 5.34 (1H, d, *J* = 9.2 Hz, H-1′), 4.67 (1H, dd, *J* = 11.9, 2.6 Hz, H-6′a), 4.54 (1H, dd, *J* = 11.9, 5.3 Hz, H-6′b), 4.48 (1H, ddd, *J* = 9.2, 5.3, 2.6 Hz, H-5′), 2.17 (6H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.3, 165.9, 165.1, 165.0 (CO), 147.5 (benzimidazole C-2), 141.1 (br s, benzimidazole C-3a, C-7a), 133.2–127.9 (aromatics, benzimidazole C-5, C-6), 119.5, 111.6 (2 br s, benzimidazole C-4, C-7), 76.8, 75.6, 74.3, 71.7, 69.5 (C-1′–C-5′), 63.3 (C-6′), 20.2 (2 × CH_3). Anal: Calcd for $C_{43}H_{36}N_2O_9$ (724.75): C, 71.26; H, 5.01; N, 3.87. Found: C, 71.15; H, 4.92; N, 3.99.

4.16. 2-(2′,3′,4′,6′-Tetra-*O*-benzoyl-β-D-glucopyranosyl)-naphtho[2,3-*d*]imidazole (8i)

From imidate **6** (0.10 g, 0.15 mmol) and 2,3-diamino-naphthalene (**i**, 0.05 g, 0.30 mmol) according to General procedure **II.**

Reaction time: 4 h. Purified by column chromatography (4:5 EtOAc–hexane) to yield 0.091 g (79%) of pale brown solid. Mp: 184–186 °C; $[\alpha]_D = -113$ (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$) δ (ppm): 10.64 (1H, br s, naphthoimidazole NH), 7.81–6.92 (26H, m, aromatics), 6.14, 6.05, 5.90 (3 × 1H, 3 pseudo t, $J = 9.6$, 9.6 Hz in each, H-2′, H-3′, H-4′), 5.29 (1H, d, $J = 9.6$ Hz, H-1′), 4.64 (1H, dd, $J = 12.3$, <1 Hz, H-6′a), 4.49 (1H, dd, $J = 12.3$, 5.3 Hz, H-6′b), 4.39 (1H, ddd, $J = 9.6$, 5.3, <1 Hz, H-5′); ^{13}C NMR ($CDCl_3$) δ (ppm): 166.2, 165.9, 165.1 (2) (CO), 152.9 (naphthoimidazole C-2), 142.7 (br s, naphthoimidazole C-3a, C-9a), 133.2–127.8, 123.6 (aromatics), 116.2, 107.8 (2 br s, naphthoimidazole C-4, C-9), 76.9, 75.6, 74.2, 71.7, 69.5 (C-1′–C-5′), 63.4 (C-6′). Analysis: $C_{45}H_{34}N_2O_9$ (746.76), ESI-MS (positive mode) *m/z*: 769.219 $[M+Na]^+$, 1516.457 $[2M+Na]^+$.

4.17. 5(6)-Fluoro-2-(β-D-glucopyranosyl)-benzimidazole (10b)

From **8b** (0.22 g, 0.30 mmol) according to General Procedure **III.** Reaction time: 3.5 h. Purified by column chromatography (4:1 $CHCl_3$–MeOH) to yield 0.048 g (54%) of pale yellow syrup. R_f: 0.19 (10:3 $CHCl_3$–MeOH); $[\alpha]_D = +9$ (*c* 0.2, DMSO); ^1H NMR (CD_3OD) δ (ppm): 7.48 (1H, s, benzimidazole H-4), 7.21 (1H, d, $J = 8.7$ Hz, benzimidazole H-7), 6.97 (1H, t, $J = 8.7$ Hz, benzimidazole H-6), 4.46 (1H, d, $J = 9.4$ Hz, H-1′), 3.88 (1H, dd, $J = 11.8$, <1 Hz, H-6′a), 3.73 (1H, dd, $J = 11.8$, <1 Hz, H-6′b), 3.61 (1H, pseudo t, $J = 9.8$, 9.8 Hz, H-2′ or H-3′or H-4′), 3.52–3.47 (3H, m, H-2′ and/or H-3′ and/or H-4′, H-5′); ^{13}C NMR (DMSO-d_6) δ (ppm): 158.3 (d, $^1J_{C-F} = 236$ Hz, benzimidazole C-5,), 153.9, 143.2, 138.9, 133.7, 130.6, 119.7, 112.0, 109.7, 104.0, 98.0 (br s for each, benzimidazole), 81.4, 77.8, 75.9, 72.7, 70.0 (C-1′–C-5′), 61.3 (C-6′). Anal. Calcd for $C_{13}H_{15}FN_2O_5$ (298.27): C, 52.35; H, 5.07; N, 9.39. Found: C, 52.26; H, 5.21; N, 9.33.

4.18. 5(6)-Chloro-2-(β-D-glucopyranosyl)-benzimidazole (10c)

From **8c** (0.24 g, 0.33 mmol) according to general procedure **III.** Reaction time: 5 h. Purified by column chromatography (4:1 $CHCl_3$–MeOH) to yield 0.092 g (89%) of colourless syrup. R_f: 0.23 (4:1 $CHCl_3$–MeOH); $[\alpha]_D = +23$ (*c* 0.5, DMSO); ^1H NMR (CD_3OD) δ (ppm): 7.50 (1H, d, $J = 1.4$ Hz, benzimidazole H-4), 7.45 (1H, d, $J = 8.9$ Hz, benzimidazole H-7), 7.15 (1H, dd, $J = 8.9$, 1.4 Hz, benzimidazole H-6), 4.47 (1H, d, $J = 8.9$ Hz, H-1′), 3.88 (1H, dd, $J = 11.6$, <1 Hz, H-6′a), 3.73 (1H, dd, $J = 11.6$, 4.8 Hz, H-6′b), 3.61 (1H, pseudo t, $J = 8.9$, 8.9 Hz, H-2′or H-3′ or H-4′), 3.55–3.45 (3H, m, H-2′ and/or H-3′ and/or H-4′, H-5′); ^{13}C NMR (CD_3OD) δ (ppm): 155.2 (benzimidazole C-2), 140.3, 138.1 (2 br s, benzimidazole C-3a, C-7a), 129.2 (benzimidazole C-5), 124.1, 117.1 (br s), 115.9(br s) (benzimidazole C-4, C-6, C-7), 82.2, 79.2, 77.3, 74.8, 71.2 (C-1′–C-5′), 62.8 (C-6′). Anal. Calcd for $C_{13}H_{15}ClN_2O_5$ (314.72): C, 49.61; H, 4.80; N, 8.90. Found: C, 49.72; H, 4.87; N, 8.75.

4.19. 5(6)-Bromo-2-(β-D-glucopyranosyl)-benzimidazole (10d)

From **8d** (0.27 g, 0.35 mmol) according to General procedure **III.** Reaction time: 6 h. Purified by column chromatography (8:1 $CHCl_3$–MeOH) to yield 0.073 g (58%) of colourless syrup. R_f: 0.23 (10:3 $CHCl_3$–MeOH); $[\alpha]_D = +21$ (*c* 0.43, DMSO); ^1H NMR (CD_3OD) δ (ppm): 7.65 (1H, s, benzimidazole H-4), 7.41, 7.29 (2 × 1H, 2d, $J = 8.4$ Hz, benzimidazole H-6, H-7), 4.47 (1H, d, $J = 9.4$ Hz, H-1′), 3.88 (1H, dd, $J = 11.8$, <1 Hz, H-6′a), 3.74 (1H, dd, $J = 11.8$, <1 Hz, H-6′b), 3.61 (1H, pseudo t, $J = 9.4$, 8.4 Hz, H-2′or H-3′ or H-4′), 3.53–3.46 (3H, m, H-2′ and/or H-3′ and/or H-4′, H-5′); ^{13}C NMR (DMSO-d_6) δ (ppm): 153.8 (benzimidazole C-2), 141.5, 134.8 (2 br s, C-3a, C-7a), 124.5, 121.0, 113.9, 113.8 (br s for each, benzimidazole C-4–C-7), 81.5, 77.8, 75.9, 72.8, 70.0 (C-1′–C-5′), 61.3 (C-6′). Anal. Calcd for $C_{13}H_{15}BrN_2O_5$ (359.17): C, 43.47; H, 4.21; N, 7.80. Found: C, 43.43; H, 4.34; N, 7.93.

4.20. 2-(β-D-Glucopyranosyl)-5(6)-nitro-benzimidazole (10e)

From **8e** (0.30 g, 0.40 mmol) according to General procedure **III.** Reaction time: 1 day. Purified by column chromatography (85:15 $CHCl_3$–MeOH) to yield 0.07 g (53%) of yellow syrup. R_f: 0.27 (4:1 $CHCl_3$–MeOH); ^1H NMR (DMSO-d_6) δ (ppm): 13.03 (1H, br s, benzimidazole NH), 8.44 (1H, d, $J = 1.3$ Hz, benzimidazole H-4), 8.11 (1H, dd, $J = 9.2$, 1.3 Hz, benzimidazole H-6), 7.70 (1H, d, $J = 9.2$ Hz, benzimidazole H-7), 5.14 (3H, br s, 3 × OH), 4.60 (1H, br s, OH), 4.42 (1H, d, $J = 9.2$ Hz, H-1′), 3.74 (1H, dd, $J = 11.9$, <1 Hz, H-6′a), 3.63 (1H, pseudo t, $J = 9.2$, 9.2 Hz, H-2′or H-3′ or H-4′), 3.49 (1H, dd, $J = 11.9$, 5.3 Hz, H-6′b), 3.39–3.34 (2H, m, H-2′ or H-3′ or H-4′, H-5′), 3.24 (1H, pseudo t, $J = 9.2$, 9.2 Hz, H-2′or H-3′ or H-4′); ^{13}C NMR (DMSO-d_6) δ (ppm): 157.3 (benzimidazole C-2), 142.5 (benzimidazole C-5), 141.4, 138.8 (2 br s, benzimidazole C-3a, C-7a), 117.7, 114.3 (br s), 112.6 (br s) (benzimidazole C-4, C-6, C-7), 81.6, 77.7, 76.0, 72.8, 70.0 (C-1′–C-5′), 61.2 (C-6′). Anal. Calcd for $C_{13}H_{15}N_3O_7$ (325.27): C, 48.00; H, 4.65; N, 12.92. Found: C, 47.87; H, 4.56; N, 12.96.

4.21. 2-(β-D-Glucopyranosyl)-5(6)-methyl-benzimidazole (10f)

From **8e** (0.27 g, 0.38 mmol) according to General procedure **III.** Reaction time: 3 h. Purified by column chromatography (85:15 $CHCl_3$–MeOH) to yield 0.10 g (87%) of colourless syrup. R_f: 0.42 (7:3 $CHCl_3$–MeOH); $[\alpha]_D = +18$ (*c* 0.5, MeOH); ^1H NMR (CD_3OD) δ (ppm): 7.41 (1H, d, $J = 7.9$ Hz, benzimidazole H-6 or H-7), 7.32 (1H, s, benzimidazole H-4), 7.03 (1H, d, $J = 7.9$ Hz, benzimidazole H-6 or H-7), 4.49 (1H, d, $J = 9.2$ Hz, H-1′), 3.91 (1H, dd, $J = 11.9$, <1 Hz, H-6′a), 3.76 (1H, dd, $J = 11.9$, 4.0 Hz, H-6′b), 3.66 (1H, pseudo t, $J = 9.2$, 9.2 Hz, H-2′ or H-3′ or H-4′), 3.61–3.49 (3H, m, H-2′and/or H-3′ and/or H-4′, H-5′), 2.42 (3H, s, CH_3); ^{13}C NMR (CD_3OD) δ (ppm): 153.4 (benzimidazole C-2), 139.0, 137.6 (benzimidazole C-3a, C-7a), 133.6 (benzimidazole C-5), 125.2, 115.9, 115.4 (benzimidazole C-4, C-6, C-7), 82.1, 79.3, 77.3, 74.8, 71.2 (C-1′–C-5′), 62.7 (C-6′), 21.7 (CH_3). Anal. Calcd for $C_{14}H_{18}N_2O_5$ (294.30): C, 57.13; H, 6.16; N, 9.52. Found: C, 57.29; H, 6.07; N, 9.39.

4.22. 2-(β-D-Glucopyranosyl)-4(7)-methyl-benzimidazole (10g)

From **8g** (0.25 g, 0.35 mmol) according to General Procedure **III.** Reaction time: 4 h. Purified by column chromatography (4:1 $CHCl_3$–MeOH) to give 0.075 g (73%) of colourless syrup. R_f: 0.20 (4:1 $CHCl_3$–MeOH); $[\alpha]_D = +13$ (*c* 0.5, DMSO); ^1H NMR (DMSO-d_6) δ (ppm): 12.46 (1H, br s, benzimidazole NH), 7.32, 7.04, 6.95 (3 × 1H, benzimidazole), 5.14 (3H, br s, 3 × OH), 4.64 (1H, br s, OH), 4.36 (1H, d, $J = 10.2$ Hz, H-1′), 3.73–3.24 (6H, m, H-2′, H-3′, H-4′, H-5′, H-6′a, H-6′b), 2.50 (3H, s, CH_3); ^{13}C NMR (DMSO-d_6) δ (ppm): 151.9 (benzimidazole C-2), 141.8, 133.5, 128.4, 121.6, 115.6, 109.0 (br s for each, benzimidazole C-3a, C-7a, C-4–C-7), 81.3, 77.9, 75.9, 72.7, 70.0 (C-1′–C-5′), 61.2 (C-6′). Anal. Calcd for $C_{14}H_{18}N_2O_5$ (294.30): C, 57.13; H, 6.16; N, 9.52. Found: C, 57.18; H, 6.05; N, 9.64.

4.23. 5,6-Dimethyl-2-(β-D-glucopyranosyl)-benzimidazole (10h)

From **8h** (0.27 g, 0.37 mmol) according to General procedure **III.** Reaction time: 3 h. Purified by column chromatography (85:15 $CHCl_3$–MeOH) to yield 0.09 g (78%) of colourless syrup. R_f: 0.42 (7:3 $CHCl_3$–MeOH); $[\alpha]_D = +24$ (*c* 0.5, MeOH); ^1H NMR (CD_3OD) δ (ppm): 7.28 (2H, s, benzimidazole H-4, H-7), 4.47 (1H, d, $J = 9.2$ Hz, H-1′), 3.91 (1H, dd, $J = 11.9$, <1 Hz, H-6′a), 3.76 (1H, dd,

J = 11.9, 5.3 Hz, H-6′b), 3.67 (1H, pseudo t, J = 9.2, 9.2 Hz, H-2′ or H-3′ or H-4′), 3.59–3.49 (3H, m, H-2′ and/or H-3′ and/or H-4′, H-5′), 2.31 (6H, s, CH_3); ^{13}C NMR (CD_3OD) δ (ppm): 152.7 (benzimidazole C-2), 137.6 (benzimidazole C-3a, C-7a), 132.7 (benzimidazole C-5, C-6), 115.9 (benzimidazole C-4, C-7), 82.1, 79.3, 77.3, 74.7, 71.2 (C-1′–C-5′), 62.7 (C-6′), 20.5 (CH_3). Anal. Calcd for $C_{15}H_{20}N_2O_5$ (308.34): C, 58.43; H, 6.54; N, 9.09. Found: C, 58.56; H, 6.59; N, 8.95.

4.24. 2-(β-D-Glucopyranosyl)-naphtho[2,3-*d*]imidazole (10i)

From **8i** (0.25 g, 0.33 mmol) according to General Procedure **III.** Reaction time: 4 h. Purified by column chromatography (4:1 $CHCl_3$–MeOH) to yield 0.085 g (77%) of colourless syrup. R_f: 0.17 (4:1 $CHCl_3$–MeOH); $[\alpha]_D$ = +10 (*c* 0.6, DMSO); ^1H NMR (DMSO-d_6) δ (ppm): 12.47 (1H, br s, naphthoimidazole NH), 8.06–7.99 (4H, m, aromatics), 7.38–7.36 (2H, m, aromatics), 5.20 (2), 5.11 (3H, br s, 3 × OH), 4.59 (1H, br s, OH), 4.46 (1H, d, J = 9.9 Hz, H-1′), 3.77 (1H, dd, J = 11.2, <1 Hz, H-6′a) 3.71 (1H, pseudo t, J = 9.2, 9.2 Hz, H-2′ or H-3′ or H-4′), 3.51 (1H, dd, J = 11.2, 6.6 Hz, H-6′b) 3.46–3.36 (2H, m, H-2′ or H-3′ or H-4′, H-5′), 3.26 (1H, pseudo t, J = 9.2, 9.2 Hz, H-2′ or H-3′ or H-4′); ^{13}C NMR (DMSO-d_6) δ (ppm): 157.0 (naphthoimidazole C-2), 138.7 (br s), 129.6, 127.7, 123.3, 110.7 (br s) (naphthoimidazole), 81.6, 77.8, 76.1, 72.8, 70.1 (C-1′–C-5′), 61.3 (C-6′). Anal. Calcd for $C_{17}H_{18}N_2O_5$ (330.34): C, 61.81; H, 5.49; N, 8.48. Found: C, 61.74; H, 5.60; N, 8.55.

Acknowledgements

This work was supported by the Hungarian Scientific Research Fund (OTKA CK77712, CNK80709) and TÁMOP 4.2.1./B-09/1/KONV-2010-0007 project implemented through the New Hungary Development Plan, co-financed by the European Social Fund.

References

1. Treadway, J. L.; Mendys, P.; Hoover, D. J. *Expert Opin. Invest. Drugs* **2001**, *10*, 439–454.
2. Oikonomakos, N. G. *Curr. Protein Pept. Sci.* **2002**, *3*, 561–586.
3. Kurukulasuriya, R.; Link, J. T.; Madar, D. J.; Pei, Z.; Richards, S. J.; Rohde, J. J.; Souers, A. J.; Szczepankiewicz, B. G. *Curr. Med. Chem.* **2003**, *10*, 123–153.
4. Barf, T. *Mini-Rev. Med. Chem.* **2004**, *4*, 897–908.
5. Ross, S. A.; Gulve, E. A.; Wang, M. H. *Chem. Rev.* **2004**, *104*, 1255–1282.
6. Agius, L. *Best Pract. Res. Clin. Endocrinol. Metab.* **2007**, *21*, 587–605.
7. Tracey, W. R.; Treadway, J. L.; Magee, W. P.; Sutt, J. C.; McPherson, R. K.; Levy, C. B.; Wilder, D. E.; Yu, L. J.; Chen, Y.; Shanker, R. M.; Mutchler, A. K.; Smith, A. H.; Flynn, D. M.; Knight, D. R. *Am. J. Physiol. Heart Circ. Physiol.* **2004**, *286*, H1177–H1184.
8. Treadway, J. L.; Magee, W. P.; Hoover, D. J.; McPherson, R. K.; Martin, W. H.; Zavadoski, W. J.; Gibbs, E. M.; Tracey, W. R. *Diabetes* **2000**, *49*, A127.
9. Baker, D. J.; Greenhaff, P. L.; Timmons, J. A. *Expert Opin. Ther. Patents* **2006**, *16*, 459–466.
10. Tracey, W.; Treadway, J.; Magee, W.; McPherson, R.; Levy, C.; Wilder, D.; Li, Y.; Yue, C.; Zavadoski, W.; Gibbs, E.; Smith, A.; Flynn, D.; Knight, D. *Diabetes* **2003**, *52*, A135.
11. Henke, B. R.; Sparks, S. M. *Mini-Rev. Med. Chem.* **2006**, *6*, 845–857.
12. Guan, T.; Qian, Y. S.; Tang, X. Z.; Huang, M. H.; Huang, L. F.; Li, Y. M.; Sun, H. B. *J. Neurosci. Res.* **2011**, *89*, 1829–1839.
13. Sun, H.; Xu, L. *Mini-Rev. Med. Chem.* **2010**, *10*, 1188–1193.
14. Schnier, J. B.; Nishi, K.; Monks, A.; Gorin, F. A.; Bradbury, E. M. *Biochem. Biophys. Res. Commun.* **2003**, *309*, 126–134.
15. Geschwind, J.-F.; Georgiades, C. S.; Ko, Y. H.; Pedersen, P. L. *Expert Rev. Anticancer Ther.* **2004**, *4*, 449–457.
16. Lee, W. N. P.; Guo, P.; Lim, S.; Bassilian, S.; Lee, S. T.; Boren, J.; Cascante, M.; Go, V. L. W.; Boros, L. G. *Br. J. Cancer* **2004**, *91*, 2094–2100.
17. Somsák, L.; Czifrák, K.; Tóth, M.; Bokor, É.; Chrysina, E. D.; Alexacou, K. M.; Hayes, J. M.; Tiraidis, C.; Lazoura, E.; Leonidas, D. D.; Zographos, S. E.; Oikonomakos, N. G. *Curr. Med. Chem.* **2008**, *15*, 2933–2983.
18. Oikonomakos, N. G.; Somsák, L. *Curr. Opin. Invest. Drugs* **2008**, *9*, 379–395.
19. Loughlin, W. A. *Mini-Rev. Med. Chem.* **2010**, *10*, 1139–1155.
20. Somsák, L. *C. R. Chim.* **2011**, *14*, 211–223.
21. Praly, J. P.; Vidal, S. *Mini-Rev. Med. Chem.* **2010**, *10*, 1102–1126.
22. Hadady, Z.; Tóth, M.; Somsák, L. *Arkivoc* **2004**, *vii*, 140–149.
23. Tóth, M.; Kun, S.; Bokor, É.; Benltifa, M.; Tallec, G.; Vidal, S.; Docsa, T.; Gergely, P.; Somsák, L.; Praly, J.-P. *Bioorg. Med. Chem.* **2009**, *17*, 4773–4785.
24. Kun, S.; Nagy, G. Z.; Tóth, M.; Czecze, L.; Nguyen van Nhien, A.; Docsa, T.; Gergely, P.; Charavgi, M.-D.; Skourti, P. V.; Chrysina, E. D.; Patonay, T.; Somsák, L. *Carbohydr. Res.* **2011**, *346*, 1427–1438.
25. Benltifa, M.; Vidal, S.; Fenet, B.; Msaddek, M.; Goekjian, P. G.; Praly, J.-P.; Brunyánszki, A.; Docsa, T.; Gergely, P. *Eur. J. Org. Chem.* **2006**, 4242–4256.
26. Benltifa, M.; Vidal, S.; Gueyrard, D.; Goekjian, P. G.; Msaddek, M.; Praly, J.-P. *Tetrahedron Lett.* **2006**, *47*, 6143–6147.
27. Chrysina, E. D.; Kosmopoulou, M. N.; Tiraidis, C.; Kardarakis, R.; Bischler, N.; Leonidas, D. D.; Hadady, Z.; Somsák, L.; Docsa, T.; Gergely, P.; Oikonomakos, N. G. *Protein Sci.* **2005**, *14*, 873–888.
28. Gregoriou, M.; Noble, M. E. M.; Watson, K. A.; Garman, E. F.; Krülle, T. M.; Fuente, C.; Fleet, G. W. J.; Oikonomakos, N. G.; Johnson, L. N. *Protein Sci.* **1998**, *7*, 915–927.
29. Oikonomakos, N. G.; Skamnaki, V. T.; Ősz, E.; Szilágyi, L.; Somsák, L.; Docsa, T.; Tóth, B.; Gergely, P. *Bioorg. Med. Chem.* **2002**, *10*, 261–268.
30. Anagnostou, E.; Kosmopoulou, M. N.; Chrysina, E. D.; Leonidas, D. D.; Hadjiloi, T.; Tiraidis, C.; Zographos, S. E.; Györgydeák, Z.; Somsák, L.; Docsa, T.; Gergely, P.; Kolisis, F. N.; Oikonomakos, N. G. *Bioorg. Med. Chem.* **2006**, *14*, 181–189.
31. Bobek, M.; Farkas, J. *Collect. Czech. Chem. Commun.* **1968**, *34*, 247–252.
32. Ricciardi, F.; Joullie, M. M. *Synth. Commun.* **1986**, *16*, 35–42.
33. Jazouli, M.; Guianvarc'h, D.; Soufiaoui, M.; Bougrin, K.; Vierling, P.; Benhida, R. *Tetrahedron Lett.* **2003**, *44*, 5807–5810.
34. Davenport, R. J.; Diaz, P.; Galvin, F. C. A.; Lloyd, S.; Mack, S. R.; Owens, R.; Sabin, V.; Wynn, J. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 558–561.
35. Smellie, I. A. S.; Paton, R. M. *Arkivoc* **2012**, *ix*, 49–61.
36. Guianvarc'h, D.; Benhida, R.; Fourrey, J. L. *Tetrahedron Lett.* **2001**, *42*, 647–650.
37. Guianvarc'h, D.; Fourrey, J. L.; Dau, M.; Guerineau, V.; Benhida, R. *J. Org. Chem.* **2002**, *67*, 3724–3732.
38. Guianvarc'h, D.; Fourrey, J. L.; Maurisse, R.; Sun, J. S.; Benhida, R. *Org. Lett.* **2002**, *4*, 4209–4212.
39. Sallam, M. A. E.; Ibrahim, E. S. I.; ElEter, K. A. A.; Cassady, J. M. *Carbohydr. Res.* **1997**, *298*, 93–104.
40. Vojtech, M.; Petrusova, M.; Slavikova, E.; Bekesova, S.; Petrus, L. *Carbohydr. Res.* **2007**, *342*, 119–123.
41. Smellie, I. A. S.; Fromm, A.; Fabbiani, F. P. A.; Oswald, I. D. H.; White, F. J.; Paton, R. M. *Tetrahedron* **2010**, *66*, 7155–7160.
42. Somsák, L. *Carbohydr. Res.* **1996**, *286*, 167–171.
43. Somsák, L.; Nagy, V. *Tetrahedron: Asymmetry* **2000**, *11*, 1719–1727. Corrigendum 2247.
44. Czifrák, K.; Szilágyi, P.; Somsák, L. *Tetrahedron: Asymmetry* **2005**, *16*, 127–141.
45. Lin, S. Y.; Isome, Y.; Stewart, E.; Liu, J. F.; Yohannes, D.; Yu, L. B. *Tetrahedron Lett.* **2006**, *47*, 2883–2886.
46. Ősz, E.; Czifrák, K.; Deim, T.; Szilágyi, L.; Bényei, A.; Somsák, L. *Tetrahedron* **2001**, *57*, 5429–5434.
47. Kaboudin, B.; Elhamifar, D. *Synthesis* **2006**, 224–226.
48. Mahmoud, S. H.; Somsák, L.; Farkas, I. *Carbohydr. Res.* **1994**, *254*, 91–104.
49. Grimmet, M. R. Imidazoles and their Benzo Derivatives *Comprehensive Heterocyclic Chemistry* **1984**, *Vol. 5*, 345–498.
50. Hesse, M.; Meier, H.; Zeeh, B. *Spectroscopic Methods in Organic Chemistry*; Georg Thieme Verlag Stuttgart: New York, 1997.
51. Ősz, E.; Somsák, L.; Szilágyi, L.; Kovács, L.; Docsa, T.; Tóth, B.; Gergely, P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1385–1390.
52. Somsák, L.; Kovács, L.; Tóth, M.; Ősz, E.; Szilágyi, L.; Györgydeák, Z.; Dinya, Z.; Docsa, T.; Tóth, B.; Gergely, P. *J. Med. Chem.* **2001**, *44*, 2843–2848.