Bioorganic & Medicinal Chemistry 20 (2012) 6821–6830

Contents lists available at SciVerse ScienceDirect

Bioorganic & Medicinal Chemistry

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

O-Aryl α,β-D-ribofuranosides: Synthesis & highly efficient biocatalytic separation of anomers and evaluation of their Src kinase inhibitory activity

Raman K. Sharma [a], Sukhdev Singh [a], Rakesh Tiwari [b], Deendayal Mandal [b], Carl E. Olsen [c], Virinder S. Parmar [a], Keykavous Parang [b,*], Ashok K. Prasad [a,*]

[a] *Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi 110 007, India*
[b] *Department of Biomedical and Pharmaceutical Sciences, College of Pharmacy, University of Rhode Island, 41 Lower College Road, Kingston, RI 02881, USA*
[c] *University of Copenhagen, Faculty of Life Sciences, Department of Natural Sciences, DK-1871 Frederiksberg C, Denmark*

ARTICLE INFO

Article history:
Received 10 July 2012
Revised 26 September 2012
Accepted 27 September 2012
Available online 4 October 2012

Keywords:
Lipozyme® TL IM
Regio- and stereoselective deacetylation
Anomers
O-Aryl ribofuranosides
Anticancer activity

ABSTRACT

A series of peracetylated *O*-aryl α,β-D-ribofuranosides have been synthesized and an efficient biocatalytic methodology has been developed for the separation of their anomers which was otherwise almost impossible by column chromatographic or other techniques. The incubation of 2,3,5-tri-*O*-acetyl-1-*O*-aryl-α,β-D-ribofuranoside with Lipozyme® TL IM immobilized on silica led to the selective deacetylation of only one acetoxy group, viz the C-5′-*O*-acetoxy group of the α-anomer over the other acetoxy groups derived from the two secondary hydroxyl groups present in the molecule and also over three acetoxy groups (derived from one primary and two secondary hydroxyls of the β-anomer). This methodology led to the easy synthesis of both, α- and β-anomers of *O*-aryl D-ribofuranosides. All the arylribofuranosides were screened for inhibition of Src kinase. 1-*O*-(3-Methoxyphenyl)-β-D-ribofuranoside exhibited the highest activity for inhibition of Src kinase (IC_{50} = 95.0 μM).

1. Introduction

Acylated and partially acylated carbohydrates are key intermediates in the preparation of oligosaccharides, glycopeptides and modified nucleosides;[1] in particular, sugar monoesters are important as biodegradable surfactants.[2] Moreover, modified nucleosides have been found to be useful therapeutic agents in the treatment of different diseases, such as viral diseases.[3] The majority of these nucleosides are modified natural β-analogues or oligonucleotides assembled from β-nucleosides. On the contrary, the application of unnatural α-nucleosides as therapeutic agents has been limited due to difficulty in their synthesis. Despite these limitations, α-nucleosides continue to be the subject of extreme interest because of their unique properties in some specific applications.[4]

O-Glycosides have been used as antibiotic, antitumor, antifungal, antihypertensive, antiviral and antidiabetic agents.[5] Furthermore, they find applications as substrates for determining the activity of glycosidases, a large subgroup of carbohydrate-processing enzymes that hydrolytically cleave the glycosidic bond within oligo- or polysaccharides or between a glycan and a non-glycan moiety. Oligo/polysaccharides and glycoconjugates are essential for various physiological and pathogenic processes. These glycans are formed by the action of carbohydrate-processing enzymes, such as glycosidases and glycosyltransferases, which assemble and trim carbohydrates to produce bioactive glycans or glycoconjugates.[6] Glycosidases can be classified into a number of subfamilies on the basis of structural similarity.[7] Further, inhibitors of glycosidases can be used as therapeutic agents for the treatment of viral infections, diabetes and cancer.[8] Because glycans formed by the action of glycosidases are involved in a variety of biological processes and exoglycosidases are frequently used as tools for structural analysis of glycans, characterization of catalytic activities of these glycosidases is of considerable importance.

One of the recent applications of *O*-arylribofuranosides is in the detection assay of nucleoside hydrolases or nucleoside phosphorylases in microbial parasites, which have adverse effects on human health and animal population. The *O*-arylribofuranosides are used as chromogenic substrates, which on reaction with nucleoside hydrolases or nucleoside phosphorylases release phenolic chromophore that can be detected spectrophotometrically and thus provides an easy diagnostic method for the presence of enzymes.[9] The *O*-aryl β-D-ribofuranosides have been found to serve as substrates for these enzymes; however most of the synthetic methodologies reported for the preparation of these compounds lead to the formation of mixtures of α,β-anomers. The anomeric separation of *O*-aryl α,β-D-ribofuranosides is almost impossible by conventional chromatographic methods. In this article, we

* Corresponding authors. Tel.: +1 401 874 4471; fax: +1 401 874 5787 (K.P.); tel.: +91 11 27662486 (A.K.P.).
E-mail addresses: kparang@uri.edu (K. Parang), ashokenzyme@yahoo.com (A.K. Prasad).

0968-0896/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.bmc.2012.09.057

report the synthesis of *O*-aryl α,β-D-ribofuranosides and a highly efficient lipase-based separation of the α- and β-anomers using one of the acetoxy functions of peracetylated *O*-aryl α-D-ribofuranoside as handle.

Protein tyrosine kinases (PTKs) are enzymes responsible for the phosphorylation of other proteins and can catalyze the transfer of γ-phosphate group of ATP to the protein phenolic groups (on Tyr). PTKs play a central role in signal transduction pathways and are involved in immune, endocrine, and nervous system physiology and pathology. On the other hand, the abnormal phosphorylation by the PTKs is believed to be important in the development of many types of cancers.[10–12] Src kinase is a member of a structurally homologous group of non-receptor PTKs present in the cytoplasm, known as the 'Src family of kinases'.[13] The Src family of PTKs is divided into nine subfamilies, Src, Yes, Fyn, Frg, Lck, Lyn, Hck, Blk and Frk based on catalytic domain sequence. Src kinases play crucial roles in signal transduction pathways and regulating various cellular functions such as cell proliferation and cell differentiation.[14] Src kinase is a proto-oncogenic tyrosine kinase[15] and has been implicated in the genesis and progression of multiple types of human cancer including colon, breast, lung and other cancers.[16]

The small-molecule inhibitors of this protein are under investigation as potential agents for the treatment of a variety of diseases.[17,18] It is proposed that inhibitors of Src phosphorylation may impede uncontrolled tumor cell growth, and thus function as novel therapeutic agents for cancer. Specifically, Src activity is elevated in breast, pancreatic, ovarian, esophageal, lung, gastric, colon, and head-and-neck cancers.[19–23] A number of planar heteroaromatic small-molecule inhibitor templates have been exploited to identify novel Src kinase inhibitors. To date, purine, pyrrolopyrimidine, pyridopyrimidine, naphthyridone, quinazoline and quinoline-based inhibitors have been reported.[24–27] Most of these compounds are ATP-binding site inhibitors. These N-heteroaromatics lack the carbohydrates and triphosphate groups (ribo-phosphate) present in the ATP. Unfortunately, attempts to improve the biological profile of the latter compounds have so far met with little success. Thus, there is opportunity to identify other small-molecule inhibitors, pharmacophore fragments, or scaffolds that can inhibit Src kinase domain through interaction with ATP-binding site. X-ray studies have revealed a deep, hydrophobic binding pocket near the ATP binding site.[24b] *O*-Arylribofuranosides have a carbohydrate moiety and an aryl group that can mimic ribose and adenine portions of ATP, respectively, in binding to PTKs. Furthermore, these compounds contain aromatic hydrophobic residues that may generate hydrophobic interactions within the hydrophobic pocket of Src ATP binding site. Thus, we screened *O*-arylribofuranosides for their potential inhibitory potency against Src kinase to determine whether these compounds can be used as alternative scaffolds for designing Src kinase inhibitors.

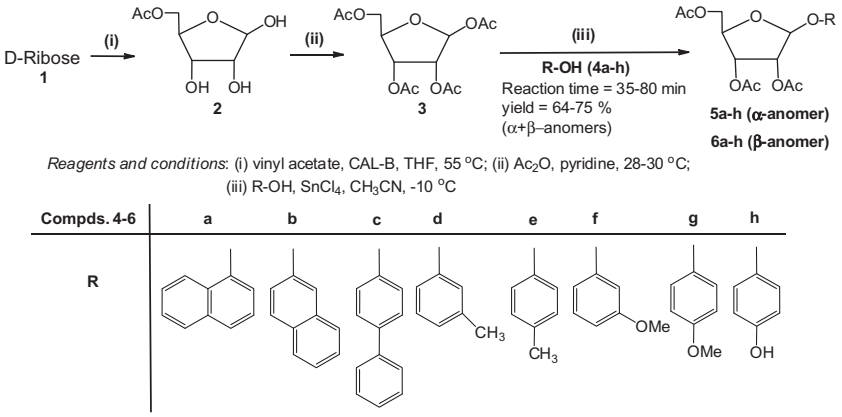
2. Results and discussion

2.1. Chemistry

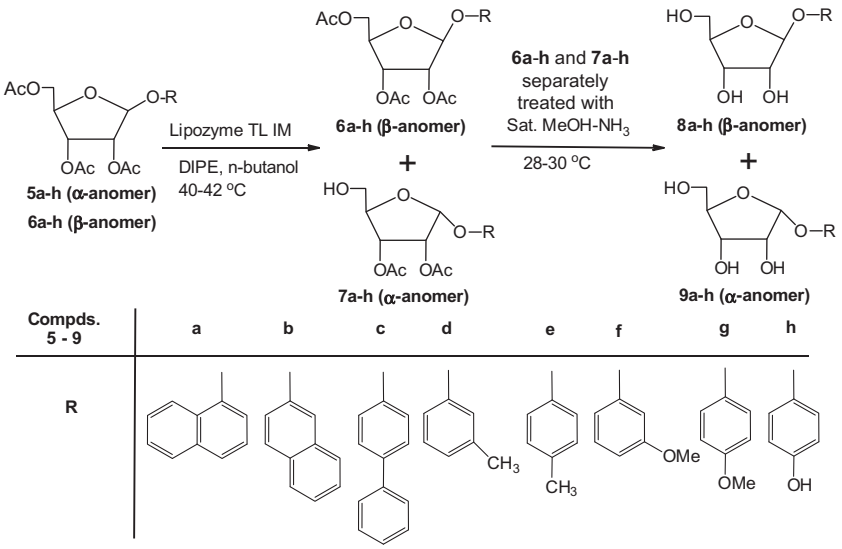
The tetra-*O*-acetylated-α,β-D-ribofuranosides **3** were chemoenzymatically synthesized in two steps from D-ribose in quantitative yields.[28] The coupling of 1,2,3,5-tetra-*O*-acetyl-α,β-D-ribofuranosides (**3**) with different phenols **4a–h** was accomplished according to the modified literature procedure[29] using $SnCl_4$ in acetonitrile at −10 °C to afford a mixture of the corresponding peracetylated *O*-aryl α,β-D-ribofuranosides (**5a** & **6a**, **5b** & **6b**, **5c** & **6c**, **5d** & **6d**, **5e** & **6e**, **5f** & **6f**, **5g** & **6g** and **5h** & **6h**) in different proportions in 64–75% yields (Scheme 1).

All attempts to separate α- and β-anomers from anomeric mixtures of *O*-aryl-D-ribofuranosides **5a** & **6a**, **5b** & **6b**, **5c** & **6c**, **5d** & **6d**, **5e** & **6e**, **5f** & **6f**, **5g** & **6g** and **5h** & **6h** by column chromatography failed, possibly because of the similar nature and almost identical polarity of the two isomers. This led us to explore the possibility of separation of the two anomers by selective deacetylation of acetoxy functions of one of the anomers using lipase-mediated deacetylation reaction.[30]

Recently, Chien and Chern[31] and Fernandez-Lorente et al.[32a] have used native *Candida rugosa* lipase (CRL, Sigma), CRL immobilised on octyl agarose, respectively, to catalyze regioselective deacetylation at C-5 position of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose to afford 1,2,3-tri-*O*-acetyl-β-D-ribofuranose in 80% and 47% yields in phosphate buffer-DMF and phosphate buffer, respectively. Inigo et al.[32b] have studied *Candida antarctica* lipase B catalyzed deacetylation of 1-*O*-methyl-2,3,5-tri-*O*-acetyl-α-ribofuranoside and 1-*O*-methyl-2,3,5-tri-*O*-acetyl-β-D-ribofuranoside, separately and observed regioselective deacetylation in the former compound to afford 2,3-di-*O*-acetyl-α-D-ribofuranoside in 81% yield; selectivity was not observed in β-diastereoisomer. Wengel co workers[33a] have used wheat germ lipase in phosphate buffer for the separation of α,β-anomers of thymidine, albeit in low yields. There is only one report of use of *Pseudomonas cepacia* lipase in organic solvent by Ferrero and Gotor[33b] for the separation of α,β-anomers of thymidine derivatives from an industrial waste stream. Moreover, Gotor co workers[33c] recently reported the concept of regioselective enzymatic acylation or hydrolysis process for the separtion of anomers of α,β-D-nucleosides. To the best of our knowledge, it is the first report on the biocatalytic separation of anomeric mixtures of *O*-arylglycosides.



Scheme 1. Synthesis of αβ-*O*-arylnucleosides.



Scheme 2. Lipase-catalyzed deacylation reaction: separation of anomeric mixtures.

Table 1
Lipozyme® TL IM-catalyzed regio- and chemo selective deacetylation studies on mixture of αβ-anomers of peracetylated ribofuranosides in DIPE at 40–42 °C

Anomeric mixtures[a]	Ratio of α:β anomers	Reaction time (h)	Deacetylated and recovered, unreacted ribofuranosides	Yield[b] (isolated %)
5a & **6a**	1.0:0.9	12.5	**7a**	95
			6a	98
5b & **6b**	1.0:3.8	10.0	**7b**	87
			6b	95
5c & **6c**	1.0:3.3	11.5	**7c**	95
			6c	97
5d & **6d**	1.0:4.1	10.5	**7d**	94
			6d	93
5e & **6e**	1.0:3.6	12.0	**7e**	91
			6e	94
5f & **6f**	1.0:8.8	14.0	**7f**	89
			6f	93
5g & **6g**	1.0:3.2	11.5	**7g**	93
			6g	91
5h & **6h**	1.0:2.9	48.0	**7h**	91
			6h	92

[a] All these reactions did not yield any product when performed in the absence of Lipozyme® TL IM.
[b] The yields reported are calculated by taking α- and β-anomers in the mixture as 100%.

In our present work, four lipases, that is, *Candida rugosa* lipase (CRL), *Candida antarctica* lipase-B immobilized on accurel [CAL-L(A)], *Candida antarctica* lipase-B immobilized on polyacrylate (Lewatit, CAL-B or Novozyme-435) and *Thermomyces lanuginosus* lipase immobilized on silica (Lipozyme® TL IM) were screened for the regioselective deacetylation of acetoxy function of one anomer over the other in different organic solvents, that is, THF, dioxane, acetonitrile, toluene, ethanol and diisopropyl ether (DIPE) at different temperatures. It was observed that Lipozyme® TL IM in DIPE at 40–42 °C selectively and most efficiently deacetylates the acetoxy moiety derived from the C-5′ hydroxyl group of only the α-anomer over the other acetoxy moieties of *O*-aryl-α,β-D-ribofuranosides. Although CAL-B, initially showed selectivity for the deacetylation of C-5′ acetoxy group of α-anomer, it started deacetylation of acetoxy functional groups of the β-anomer as well with time and led to the formation of a mixture of compounds. CRL and CAL-L(A) did not show any appreciable selectivity in the deacetylation studies on anomeric mixture of *O*-aryl D-ribofuranosides.

In a typical reaction, the anomeric mixture of *O*-aryl-D-ribofuranosides **5a** and **6a** (0.5 g, 1.36 mmol) was dissolved in DIPE (20 mL) and incubated with Lipozyme® TL IM (substrate-enzyme ratio, 1:0.5, w/w) and *n*-butanol (0.05 mL) at 40–42 °C. The progress of the reaction was monitored on TLC. On completion of the reaction, enzyme was filtered off and the solvent was removed under reduced pressure. The residue was purified by column chromatography to afford the deacetylated 2,3-di-*O*-acetyl-1-*O*-(1-naphthyl)-α-D-ribofuranoside (**7a**) in 95% yield together with the unreacted, recovered 2,3,5-tri-*O*-acetyl-1-*O*-(1-naphthyl)-β-D-ribofuranoside (**6a**) in 98% yield (Scheme 2, Table 1).

Similarly lipase-catalyzed deacetylation of mixtures of *O*-aryl α,β-D-ribofuranosides **5b** & **6b**, **5c** & **6c**, **5d** & **6d**, **5e** & **6e**, **5f** & **6f**, **5g** & **6g** and **5h** & **6h** led to the formation of deacetylated compounds **7b–h** in high yields, along with the unreacted peracetylated *O*-aryl-β-D-ribofuranosides **6b–h**. It is interesting to note that in all cases the lipase selectively deacetylated the acetoxy function involving primary hydroxyl group of minor α-anomer of *O*-aryl α,β-D-ribofuranosides, except in the case of 2,3,5-tri-*O*-acetyl-1-*O*-(1-naphthyl)-α,β-D-ribofuranosides (**5a** and **6a**), where the amount of the anomers in the mixture is almost same (Table 1). Complete deacetylation of the enzymatically produced partially deacetylated *O*-aryl-α-D-ribofuranosides **7a**–**h** and recovered, unreacted peracetylated *O*-aryl-β-D-ribofuranosides **6a**–**h** with saturated methanolic ammonia afforded *O*-aryl-α-D-ribofuranosides **9a**–**h** and *O*-aryl-β-D-ribofuranosides **8a**–**h** in quantative yields (Scheme 2).

2.2. Src kinase inhibitory activity

Synthesized β- and α-*O*-arylribofuranosides **8a**–**h** and **9a**–**h** were evaluated as Src kinase inhibitors. The results of Src kinase inhibitory activity of these compounds are shown in Table 2. In general the compounds showed weak to modest inhibitory potency against Src kinase. Among all the compounds, 1-*O*-(3-methoxyphenyl)-β-D-ribofuranoside **8f** is the most active and exhibited an IC_{50} value of 95.0 μM. All other derivatives showed weak Src kinase inhibition with IC_{50} values more than 100 μM.

Reported heteroaromatic compounds as Src kinase inhibitors[24a] contain functional groups at appropriate positions for the hydrogen

bonding interactions with specific amino acid residues of Src ATP-binding site.[24b] It appears that these critical bonding interactions are not compensated by the presence of hydrophobic aromatic rings present in these compounds and/or the hydrophobic interactions of the aromatic group with the hydrophobic pocket of Src ATP binding site are modest. As expected the carbohydrate moiety did not provide any additional improvement in the activity of the compounds. The major interactions of ATP with the ATP-binding site are generated through the adenine base contributions.

In most cases α-anomers were less active than the corresponding β-anomer. This is not surprising as ATP has a β-configuration, and β-anomers can mimic the ATP core more efficiently. It is obvious that further optimization of β-anomers with incorporation of appropriate heteroaromatic groups capable of hydrogen bonding interactions is required to generate more potent Src kinase inhibitors. Crystal structure of c-Src with a nonhydrolyzable ATP analog, AMP-PNP (Adenosine 5′-[β,γ-imido]triphosphate, Fig. 1), showed critical hydrogen bonding between the 4-amino group of adenine and Glu339.[34] Similarly, X-ray studies of Src kinases with phenylpyrazolopyrimidines,[35] which resemble the purine core of ATP, have revealed that the 4-amino group of the heteroaromatic group is hydrogen bonded to the side chain of Thr338 as well as the carbonyl of Glu339. This hydrogen bonding interactions contribute significantly to the potency of phenylpyrazolopyrimidines as Src kinase inhibitors.

Molecular modeling was utilized to examine how compounds **8c** and **8f** with modest inhibitory activities (IC_{50} = 95–125 μM) would fit within the ATP-binding site of the enzyme when compared with AMP-PNP (Fig. 2). The modeling studies indicated that the orientation of aromatic groups in **8c** and **8f** is towards the hydrophobic binding pocket versus that of adenine group in AMP-PNP is slightly different (Fig 2a and b). While compound **8f** has an oxygen in methoxy group that may play a role as hydrogen bond acceptor, the aromatic group in **8c** is only capable of hydrophobic interactions deep in the hydrophobic binging pocket of ATP-binding site and does not have any heteroatom in aryl of arylribofuranosides for generating hydrogen bonding (Fig. 2b). The compounds demonstrated only modest inhibitory potency possibly because of mostly hydrophobic interactions and the absence of hydrogen bonding between the base of the arylribofuranosides and the ATP-binding site.

Table 2
IC_{50} values of β- and α-*O*-arylribofuranosides as Src kinase inhibitors

Compounds	IC_{50} (μM)[c]
Staurosporine[a]	0.3 ± 0.0
PP2[b]	2.8 ± 0.0
8a	1370.7
9a	184.7
8b	224.8
9b	297.3
8c	125.0
9c	NA[d]
8d	ND[e]
9d	451.0
8e	143.4
9e	ND
8f	95.0
9f	NA
8g	483.9
9g	NA
8h	272.1
9h	NA

[a] Structure given in Figure 1.
[b] 1-(*tert*-Butyl)-3-(4-chlorophenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-4-amine (structure given in Fig. 1).
[c] The concentration of the compound that inhibited enzyme activity by 50%.
[d] No enzyme inhibitory activity was observed up to the concentration of 100 μM.
[e] Not determined.

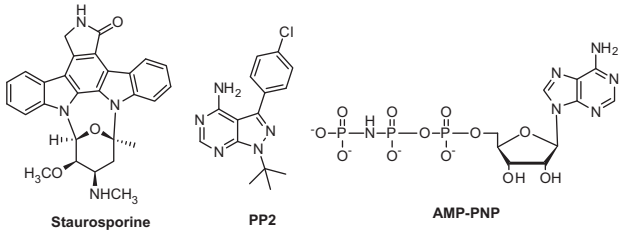


Figure 1. Chemical structure of Staurosporine, PP2 and AMP-PNP.

In conclusion, a highly efficient regio- and stereoselective deacetylation of 2,3,5-tri-*O*-acetyl-1-*O*-aryl-α,β-D-ribofuranosides was achieved by using Lipozyme® TL IM immobilized on silica. Enzymatic deacetylation removed the acetyl moiety from the C-5′ acetoxy group of α-anomer versus the corresponding C-5′ acetoxy function of the β-anomer and the two acetoxy moieties present at the C-2′ and C-3′ position of each of the α- and β-anomers of 2,3,5-tri-*O*-acetyl-1-*O*-aryl-D-ribofuranosides. This methodology enabled us to separate the anomeric mixtures of *O*-arylribofuranosides, which were impossible to separate by normal chromatographic techniques. In this process, simultaneous synthesis of both the anomers, that is, natural β- and unnatural α-anomers of *O*-aryl D-ribofuranosides was achieved. The enzymatic methodology developed herein may find wide applications in the separation of anomeric mixtures of *O*-aryl glycosides, sugars, or nucleosides for the research groups working in these areas. The synthesized compounds were evaluated for the Src kinase inhibitory potency and were found to be weak or modest inhibitors. The data indicate that designing small molecules with modest inhibitory activity against Src kinase is possible by using β-anomer of *O*-aryl-D-ribofuranosides. The compounds may have potential to be used in fragment-based discovery of Src kinase inhibitors. Further optimization by incorporating essential functional groups on the aromatic rings may be required to generate lead compounds with optimal Src inhibitory potency.

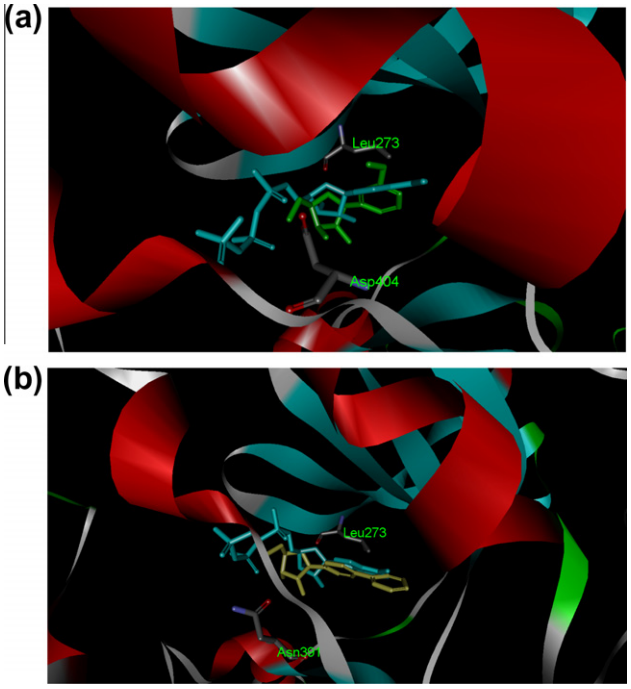


Figure 2. Comparison of structural complexes of Src kinase with different *O*-aryl β-D-ribofuranosides. (a) **8f** (green) and AMP-PNP (blue); (b) **8c** (yellow) and AMP-PNP (blue) based on molecular modeling. The compounds are rendered in stick styles. They are the lowest energy conformers predicted for the compounds.

3. Experimental section

Melting points were determined on a Mettler FP 62 instrument or in a sulfuric acid bath and are uncorrected. The IR spectra were recorded on a Perkin-Elmer model 2000 FT-IR spectrometer by making KBr disc for solid samples and thin film for oils. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-300 Avance spectrometer at 300 and 75.5 MHz, respectively, using TMS as internal standard. The chemical shift values are on δ scale and the coupling constants (J) are in Hz. Signals from OH groups in ^{1}H NMR spectra recorded in $CDCl_3$ were verified by removing them by shaking the solution with D_2O. HR-ESI-TOF-MS analyses were carried out on a micro-TOF-Q instrument from Bruker Daltonics, Bremen. *Thermomyces lanuginosus* lipase immobilized on silica (Lipozyme® TL IM), *Candida antarctica* lipase B immobilized on accurel [CAL-L(A)] and *Candida antarctica* lipase B immobilized on polyacrylate (lewatite, CAL-B or Novozyme-435) were provided by Novozymes Inc. (Copenhagen, Denmark), whereas *Candida rugosa* lipase (CRL) was purchased from Sigma Chemical Co. (USA). All enzymes were used after storing in vacuum over P_2O_5 for more than 24 h. Acetonitrile and diisopropyl ether were distilled and kept over molecular sieves (4 Å) prior to use. Analytical TLCs were performed on precoated Merck silica-gel $60F_{254}$ plates; the spots were detected either under UV light or by charring with 4% alcoholic H_2SO_4. Silica gel (100–200 mesh) was used for column chromatography.

3.1. General procedure for the synthesis of peracetylated 1-*O*-aryl α,β-D-ribofuranosides (5a–h and 6a–h, Scheme 1)

1,2,3,5-Tetra-*O*-acetylribofuranose **3** was chemoenzymatically synthesized from D-ribose (**1**) in two steps in quantitative yields.[28] Compound **3** (2.0 mmol) and the corresponding phenol (**4a–h**, 2.0 mmol) were mixed in dry acetonitrile (10 mL) and stirred under nitrogen atmosphere at −10 °C. After 10 min, tin (IV) chloride (1 M solution in DCM, 2.0 mmol) was added dropwise to the above solution under stirring. The progress of the reaction was monitored by TLC. On completion, the reaction was stopped by pouring the reaction mixture into bicarbonate solution. The reaction mixture was passed through celite and the celite was thoroughly washed with chloroform (3 × 50 mL). The chloroform solution was then washed with water, dried and concentrated to afford the crude products as viscous oils, which were purified by column chromatography to get the anomeric mixtures of the peracetylated 1-*O*-aryl α,β-D-ribofuranosides (**5a** & **6a**, **5b** & **6b**, **5c** & **6c, 5d** & **6d, 5e** & **6e, 5f** & **6f, 5g** & **6g** and **5h** & **6h**) in 64–75% yields by using ethyl acetate and petroleum ether as eluent (Scheme 1). The anomeric mixtures of 1-*O*-aryl D-ribofuranosides were unambiguously identified on the basis of their spectral data analysis and by comparison of chemical shift values of anomeric protons of α- and β-anomers in the mixture with those reported for pure 1-*O*-phenyl-α-D-ribofuranoside and 1-*O*-phenyl-β-D-ribofuranoside.[31,36] The ratio of anomers in the mixtures **5a** & **6a**, **5b** & **6b**, **5c** & **6c, 5d** & **6d, 5e** & **6e, 5f** & **6f, 5g** & **6g** and **5h** & **6h** were calculated based on the integration of corresponding anomeric proton in the ^{1}H NMR spectrum of the mixture (Table 1). The spectral data of the anomeric mixtures are not given here, instead spectral data of enzymatically deacetylated *O*-arylribofuranosides (**7a–h**) and unreacted, recovered *O*-arylribofuranosides (**6a–h**) isolated on incubation of anomeric mixtures with Lipozyme® TL IM are given in the following section.

3.2. General procedure for the Lipozyme® TL IM-catalyzed deacetylation of peracetylated 1-*O*-aryl-α,β-D-ribofuranosides (5a–6a, 5b–6b, 5c–6c, 5d–6d, 5e–6e, 5f–6f, 5g–6g and 5h–6h)

The anomeric mixture of peracetylated 1-*O*-aryl α,β-D-ribofuranoside **5a** & **6a**, **5b** & **6b**, **5c** & **6c**, **5d** & **6d**, **5e** & **6e**, **5f** & **6f**, **5g** & **6g** and **5h** & **6h** (1.5 mmol) was dissolved in diisopropyl ether (25 mL) and incubated with Lipozyme® TL IM (0.23–0.32 g, substrate-enzyme ratio, approximately 1:0.5, w/w) and *n*-butanol (0.05 mL) at 40–42 °C (Scheme 2). The progress of the reaction was monitored by TLC.[37] On completion, the reaction was stopped by filtering off the enzyme and solvent evaporated to dryness under reduced pressure to obtain the crude product. The crude product thus obtained was purified by column chromatography to afford the unreacted, recovered β-anomers **6a–h** and the 5′-*O*-deacetylated compounds **7a–h** in 91–98% and 87–95% yields, respectively. All the unreacted, recovered peracetylated 1-*O*-aryl-β-D-ribofuranosides **6a–h** and enzymatically deacetylated 2,3-di-*O*-acetyl-1-*O*-aryl-α-D-ribofuranoside **7a–h** were unambiguously identified on the basis of their spectral data; the structure of the known compound **6a** was further confirmed on the basis of comparison of its spectral data with that reported in the literature.[38] The details of the Lipozyme® TL IM-catalyzed deacetylation reaction are given in Table 1. All these reactions did not yield any product when performed in the absence of Lipozyme® TL IM.

3.2.1. 2,3,5-Tri-*O*-acetyl-1-*O*-(1-naphthyl)-β-D-ribofuranosides (6a)

It was obtained as semisolid (0.28 g) in 98% yield. R_f = 0.82 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31} = -0.56°$ (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 1746, 1577, 1402, 1238, 1093, 1021 and 779 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74, 2.12 and 2.17 (9H, 3s, 3H each, 3 × COC*H*$_3$), 4.06–4.09 (1H, m, C-5H$_\alpha$), 4.44–4.48 (2H, m, C-4H and C-5H$_\beta$), 5.66–5.70 (2H, m, C-2H and C-3H), 5.84 (1H, s, C-1H), 7.08–7.10, 7.34–7.39, 7.50–7.52, 7.79 and 8.18 (7H; 1H, m; 1H, m; 3H, m; 1H, br s and 1H, br s; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.80 and 21.01 (3 × *C*OC*H*$_3$), 63.66 (C-5), 71.52 (C-3), 75.52 (C-2), 79.74 (C-4), 103.80 (C-1), 108.88, 122.18, 122.59, 126.10, 126.92, 127.97, 134.90 and 152.16 (aromatic carbons), and 170.04 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 425.1214 ([M+Na]$^+$), calcd for [$C_{21}H_{22}O_8$+Na]$^+$ 425.1207.

3.3. 2,3,5-Tri-*O*-acetyl-1-*O*-(2-naphthyl)-β-D-ribofuranoside (6b)

It was obtained as crystalline solid (0.45 g) in 95% yield. R_f = 0.78 (30% ethyl acetate in petroleum ether, v/v); mp 111–112 °C; $[\alpha]_D^{31} = -1.72°$ (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 1743, 1599, 1371, 1245, 1047 and 779 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.92, 2.11 and 2.17 (9H, 3s, 3H each, 3 × COC*H*$_3$), 4.07–4.09 (1H, m, C-5H$_\alpha$), 4.41–4.46 (2H, m, C-4H and C-5H$_\beta$), 5.57–5.59 (2H, m, C-2H and C-3H), 5.80 (1H, s, C-1H), 7.16–7.19, 7.37–7.40, 7.43–7.45 and 7.73–7.79 (7H; 1H, m; 2H, m; 1H, m and 3H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 19.37 (3 × *C*OC*H*$_3$), 62.32 (C-5), 69.98 (C-3), 73.85 (C-2), 78.10 (C-4), 102.11 (C-1), 111.73, 117.50, 123.13, 125.26, 125.95, 126.41, 128.36, 128.53, 133.02 and 152.70 (aromatic carbons), and 168.35 & 169.32 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 425.1213 ([M+Na]$^+$), calcd for [$C_{21}H_{22}O_8$+Na]$^+$ 425.1207.

3.3.1. 2,3,5-Tri-*O*-acetyl-1-*O*-(4-biphenyl)-β-D-ribofuranoside (6c)

It was obtained as semisolid (0.48 g) in 97% yield. R_f = 0.92 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31} = -1.56°$ (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 1747, 1604, 1375, 1237, 1045 and 760 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.96, 2.10 and 2.15 (9H, 3s, 3H each, 3 × COC*H*$_3$), 4.07–4.11 1H, m, C-5H$_\alpha$, 4.43–4.47 (2H, m, C-4H and C-5H$_\beta$), 5.51–5.55 (2H, m, C-2H and C-3H), 5.69 (1H, s, C-1H), 7.06–7.09, 7.31–7.33, 7.39–7.44 and 7.50–7.55 (9H; 2H, m; 1H, m; 2H, m and 4H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.91 and 20.96 (3 × COCH_3), 63.90 (C-5), 71.58 (C-3), 75.44 (C-2), 79.69 (C-4), 103.76 (C-1), 117.10,

127.22, 127.32, 128.61, 129.13, 136.04, 140.95 and 156.09 (aromatic carbons), and 170.00, 170.09 & 170.95 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 451.1358 ([M+Na]$^+$), calcd for [$C_{23}H_{24}O_8$+Na]$^+$ 451.1363.

3.3.2. 2,3,5-Tri-*O*-acetyl-1-*O*-(3-methylphenyl)-β-D-ribofuranoside (6d)

It was obtained as semisolid (0.41 g) in 93% yield. R_f = 0.88 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{24}$ = −2.2° (*c* 0.1, MeOH); IR (Nujol) ν_{max}: 1740, 1518, 1374, 1222, 1038 and 783 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.95, 2.09 and 2.20 (9H, 3s, 3H each, 3 × COC*H*$_3$), 2.31 (3H, s, ArC*H*$_3$), 4.05–4.07 (1H, m, C-5H$_\alpha$), 4.40–4.43 (2H, m, C-4H and C-5H$_\beta$), 5.47–5.52 (2H, m, C-2H and C-3H), 5.64 (1H, s, C-1H), 6.79–6.84 and 7.13–7.15 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 16.20 and 17.08 (3 × COCH$_3$ and ArC*H*$_3$, 59.26 (C-5), 66.90 (C-3), 70.70 (C-2), 74.81 (C-4), 98.91 (C-1), 109.01, 112.75, 118.97, 124.89, 135.26 and 151.81 (aromatic carbons), and 165.21 & 166.23 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 389.1205 ([M+Na]$^+$), calcd for [$C_{18}H_{22}O_8$+Na]$^+$ 389.1207.

3.3.3. 2,3,5-Tri-*O*-acetyl-1-*O*-(4-methylphenyl)-β-D-ribofuranoside (6e)

It was obtained as semisolid (0.40 g) in 94% yield. R_f = 0.79 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = −2.04° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 1746, 1510, 1377, 1218, 1036 and 785 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.95, 2.09 and 2.14 (9H, 3s, 3H each, 3 × COC*H*$_3$), 2.28 (3H, s, ArC*H*$_3$), 4.06 (1H, dd, *J* = 11.2 and 4.2 Hz, C-5H$_\alpha$), 4.37–4.46 (2H, m, C-4H and C-5H$_\beta$), 5.47–5.54 (2H, m, C-2H and C-3H), 5.60 (1H, s, C-1H), 6.88 and 7.07 (4H; 2d, 2H each, *J* = 8.4 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.90 and 21.99 (3 × COC*H*$_3$ and ArC*H*$_3$), 63.95 (C-5), 71.60 (C-3), 75.40 (C-2), 79.48 (C-4), 103.92 (C-1), 116.74, 130.33, 132.29 and 154.45 (aromatic carbons), and 169.94, 170.07 & 170.97 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 389.1208 ([M+Na]$^+$), calcd for [$C_{18}H_{22}O_8$+Na]$^+$ 389.1207.

3.3.4. 2,3,5-Tri-*O*-acetyl-1-*O*-(3-methoxyphenyl)-β-D-ribofuranoside (6f)

It was obtained as semisolid (0.43 g) in 93% yield. R_f = 0.93 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = −0.8° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 1751, 1603, 1370, 1234, 1045, 973 and 769 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 1.90, 2.03 and 2.11 (9H, 3s, 3H each, 3 × COC*H*$_3$), 3.73 (3H, s, OC*H*$_3$), 3.96–4.02 (1H, m, C-5H$_\alpha$), 4.33–4.40 (2H, m, C-4H and C-5H$_\beta$), 5.33–5.36 (2H, m, C-2H and C-3H), 5.82 (1H, s, C-1H), 6.59–6.62 and 7.17–7.23 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-*d*$_6$): δ 20.26 and 20.34 (3 × COCH$_3$, 55.12 OCH$_3$, 62.98 C−5, 70.52 (C-3), 74.06 (C-2), 78.77 (C-4), 102.40 (C-1), 102.42, 108.07, 108.28, 129.99, 156.75 and 160.32 (aromatic carbons), and 169.38, 169.58 & 169.88 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 405.1151 ([M+Na]$^+$), calcd for [$C_{18}H_{22}O_9$+Na]$^+$ 405.1156.

3.3.5. 2,3,5-Tri-*O*-acetyl-1-*O*-(4-methoxyphenyl)-β-D-ribofuranoside (6g)

It was obtained as crystalline solid (0.40 g) in 91% yield. R_f = 0.89 (30% ethyl acetate in petroleum ether, v/v); mp 77–78 °C; $[\alpha]_D^{24}$ = −2.0° (*c* 0.1, MeOH); IR (Nujol) ν_{max}: 1748, 1520, 1380, 1222, 1018 and 786 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.97, 2.09 and 2.14 (9H, 3s, 3H each, 3 × COC*H*$_3$), 3.77 (3H, s, OC*H*$_3$), 4.07 (1H, dd, *J* = 11.7 and 4.5 Hz, C-5H$_\alpha$), 4.38–4.46 (2H, m, C-4H and C-5H$_\beta$), 5.46–5.54 (3H, m, C-1H, C-2H and C-3H), 6.81 and 6.94 (4H; 2d, 2H each, *J* = 8.5 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.90, 20.95 and 21.02 (3 × COCH$_3$, 55.99 (OCH$_3$, 63.94 (C-5), 71.55 (C-3), 75.35 (C-2), 79.43 (C-4), 104.54 (C-1), 114.95, 118.17, 150.63 and 155.53 (aromatic carbons), and 169.95, 170.08 & 170.97 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 405.1162 ([M+Na]$^+$), calcd for [$C_{18}H_{22}O_9$+Na]$^+$ 405.1156.

3.3.6. 2,3,5-Tri-*O*-acetyl-1-*O*-(4-hydroxyphenyl)-β-D-ribofuranoside (6h)

It was obtained as crystalline solid (0.38 g) in 92% yield. R_f = 0.85 (50% ethyl acetate in petroleum ether, v/v); mp 127–128 °C; $[\alpha]_D^{31}$ = −0.4° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3427, 1748, 1511, 1371, 1215, 1044 and 832 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 1.97, 2.09 and 2.14 (9H, 3s, 3H each, 3 × COC*H*$_3$), 4.75 (1H, dd, *J* = 11.7 and 4.5 Hz, C-5H$_\alpha$), 4.36–4.50 (2H, m, C-4H and C-5H$_\beta$), 5.46–5.53 (3H, m, C-1H, C-2H and C-3H), 5.66 (1H, s, -OH), 6.72 and 6.86 (4H; 2d, 2H each, *J* = 8.0 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-*d*$_6$): δ 20.50, 20.57 and 20.65 (3 × COCH$_3$, 63.54 (C-5), 71.14 (C-3), 74.97 (C-2), 79.00 (C-4), 104.16 (C-1), 115.97, 117.94, 150.02 and 151.31 (aromatic carbons), and 169.80, 169.87 & 170.97 (3 × *C*O); HR-ESI-TOF-MS: *m/z* 391.0997 ([M+Na]$^+$), calcd for [$C_{17}H_{20}O_9$+Na]$^+$ 391.1000.

3.3.7. 2,3-Di-*O*-acetyl-1-*O*-(1-naphthyl)-α-D-ribofuranoside (7a)

It was obtained as colorless oil (0.27 g) in 95% yield. R_f = 0.28 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +3.12° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3471, 1745, 1599, 1371, 1232, 1042 and 773 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.14 and 2.23 (6H, 2s, 3H each, 2 × COCH$_3$), 3.86 (2H, br s, C-5H$_{\alpha+\beta}$), 4.37 (1H, d, *J* = 2.8 Hz, C-4H), 5.23 (1H, dd, *J* = 6.8 and 4.3 Hz, C-2H), 5.47 (1H, dd, *J* = 6.8 and 2.7 Hz, C-3H), 6.13 (1H, d, *J* = 4.3 Hz, C-1H), 7.14, 7.36–7.41, 7.47–7.53, 7.80–7.83 and 8.24–8.27 (7H; 1H, d, *J* = 7.6 Hz; 1H, m; 3H, m; 1H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.45 and 21.83 (2 × COCH$_3$), 63.20 (C-5), 71.39 (C-3), 72.59 (C-2), 84.78 (C-4), 99.99 (C-1), 109.93, 122.75, 123.04, 126.35, 126.79, 127.33, 127.62, 128.59, 135.56 and 153.22 (aromatic carbons), and 170.95 & 171.64 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 383.1098 ([M+Na]$^+$), calcd for [$C_{19}H_{20}O_7$+Na]$^+$ 383.1101.

3.3.8. 2,3-Di-*O*-acetyl-1-*O*-(2-naphthyl)-α-D-ribofuranoside (7b)

It was obtained as colorless oil (0.10 g) in 87% yield. R_f = 0.26 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +4.68° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3471, 1743, 1599, 1371, 1245, 1047 and 752 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.15 and 2.19 (6H, 2s, 3H each, 2 × COC*H*$_3$), 3.80–3.86 (2H, m, C-5H$_{\alpha+\beta}$), 4.35 (1H, t, *J* = 3.2 Hz, C-4H), 5.19 (1H, dd, *J* = 7.1 and 4.5 Hz, C-2H), 5.40 (1H, dd, *J* = 7.1 and 3.4 Hz, C-3H), 6.02 (1H, d, *J* = 4.5 Hz, C-1H), 7.21–7.25, 7.36–7.44 and 7.73–7.78 (7H; 1H, m; 3H, m and 3H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-*d*$_6$): δ 20.94, 21.27 (2 × COCH$_3$), 62.45 (C-5), 70.59 (C-3), 71.69 (C-2), 83.72 (C-4), 99.83 (C-1), 112.28, 119.83, 124.79, 126.84, 127.54, 128.03, 129.88, 130.28, 134.67 and 154.88 (aromatic carbons), and 170.45 & 171.19 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 383.1095 ([M+Na]$^+$), calcd for [$C_{19}H_{20}O_7$+Na]$^+$ 383.1101.

3.3.9. 2,3-Di-*O*-acetyl-1-*O*-(4-biphenyl)-α-D-ribofuranoside (7c)

It was obtained as colorless oil (0.13 g) in 95% yield. R_f = 0.43 (20% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +6.24° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3392, 1741, 1517, 1370, 1227, 1041 and 763 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-*d*$_6$): δ 2.09 and 2.13 (6H, 2s, 3H each, 2 × COC*H*$_3$), 3.62 (2H, m, C-5H$_{\alpha+\beta}$), 4.23 (1H, br s, C-4H), 5.05 (1H, t, *J* = 5.4 Hz, –OH), 5.18 (1H, t, *J* = 4.9 Hz, C-2H), 5.32 (1H, t, *J* = 2.4 Hz, C-3H), 5.93 (1H, d, *J* = 4.5 Hz, C-1H), 7.10–7.13, 7.30–7.32, 7.40–7.45 and 7.57–7.59 (9H; 2H, m; 1H, m; 2H, m and 4H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$+DMSO-*d*$_6$): δ 21.09 and 21.40 (2 × COCH$_3$), 61.66 (C-5), 70.73 (C-3), 71.69 (C-2), 84.31 (C-4), 99.58 (C-1), 118.24, 127.11, 127.61, 128.51, 129.54, 135.19, 140.63 and 156.97 (aromatic carbons), and 170.10 & 170.61 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 409.1259 ([M+Na]$^+$), calcd for [$C_{21}H_{22}O_7$+Na]$^+$ 409.1258.

3.3.10. 2,3-Di-*O*-acetyl-1-*O*-(3-methylphenyl)-α-D-ribofuranoside (7d)

It was obtained as colorless oil (0.09 g) in 94% yield. R_f = 0.34 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{24}$ = +8.7° (*c* 0.1, MeOH); IR (Nujol) ν_{max}: 3418, 1746, 1510, 1377, 1218, 1036 and 785 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.06 and 2.10 (6H, 2s, 3H each, 2 × COC*H*$_3$), 2.28 (3H, s, ArC*H*$_3$), 3.55–3.58 (2H, m, C-5H$_{α+β}$), 4.17 (1H, dd, *J* = 6.3 and 3.0 Hz, C-4H), 5.07 (1H, t, *J* = 5.7 Hz, –OH), 5.13 (1H, dd, *J* = 6.8 and 4.8 Hz, C-2H), 5.27 (1H, dd, *J* = 6.8 and 3.3 Hz, C-3H), 5.87 (1H, d, *J* = 4.8 Hz, C-1H), 6.81–6.85 and 7.15–7.20 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 20.25, 20.56 and 20.96 (2 × COC*H*$_3$ and ArC*H*$_3$, 60.74 C–5, 69.82 (C-3), 70.61 (C-2), 83.22 (C-4), 98.55 (C-1), 113.94, 117.63, 122.86, 129.18, 139.01 and 156.48 (aromatic carbons), and 169.45 & 169.96 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 347.1090 ([M+Na]$^+$), calcd for [$C_{16}H_{20}O_7$+Na]$^+$ 347.1101.

3.3.11. 2,3-Di-*O*-acetyl-1-*O*-(4-methylphenyl)-α-D-ribofuranoside (7e)

It was obtained as colorless oil (0.10 g) in 91% yield. R_f = 0.31 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +5.96° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3480, 1746, 1614, 1373, 1224, 1047 and 781 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.15 and 2.17 (6H, 2s, 3H each, COC*H*$_3$), 2.30 (3H, s, ArC*H*$_3$), 3.83–3.85 (2H, m, C-5H$_{α+β}$), 4.31 (1H, d, *J* = 3.3 Hz, C-4H), 5.12 (1H, dd, *J* = 7.2 and 4.5 Hz, C-2H), 5.33 (1H, dd, *J* = 7.2 and 3.6 Hz, C-3H), 5.84 (1H, d, *J* = 4.5 Hz, C-1H), 6.95 and 7.09 (4H; 2d, 2H each, *J* = 8.5 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 21.49, 21.55 and 21.81 (2 × COC*H*$_3$ and ArC*H*$_3$), 63.05 (C-5), 71.03 (C-3), 72.14 (C-2), 83.87 (C-4), 100.74 (C-1), 118.58, 130.90, 154.18 and 164.47 (aromatic carbons), and 170.95 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 347.1106 ([M+Na]$^+$), calcd for [$C_{16}H_{20}O_7$+Na]$^+$ 347.1101.

3.3.12. 2,3-Di-*O*-acetyl-1-*O*-(3-methoxyphenyl)-α-D-ribofuranoside (7f)

It was obtained as colorless oil (0.04 g) in 89% yield. R_f = 0.37 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +2.7° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3487, 1744, 1491, 1372, 1243, 1044 and 770 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.06 and 2.11 (6H, 2s, 3H each, 2 × COC*H*$_3$), 3.55–3.58 (2H, m, C-5H$_{α+β}$), 3.73 (3H, s, OC*H*$_3$), 4.19 (1H, dd, *J* = 6.2 and 3.3 Hz, C-4H), 5.06 (1H, t, *J* = 5.7 Hz, –OH), 5.14 (1H, dd, *J* = 6.7 and 4.5 Hz, C-2H), 5.27 (1H, dd, *J* = 6.7 and 3.3 Hz, C-3H), 5.89 (1H, d, *J* = 4.5 Hz, C-1H), 6.56–6.63 and 7.18–7.23 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 20.26 and 20.56 (2 × COC*H*$_3$, 55.13 OC*H*$_3$ 60.71 (C-5), 69.77 (C-3), 70.58 (C-2), 83.32 (C-4), 98.59 (C-1), 103.15, 107.83, 109.13, 129.95, 157.64 and 160.32 (aromatic carbons), and 169.45 & 169.97 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 363.1045 ([M+Na]$^+$), calcd for [$C_{16}H_{20}O_8$+Na]$^+$ 363.1050.

3.3.13. 2,3-Di-*O*-acetyl-1-*O*-(4-methoxyphenyl)-α-D-ribofuranoside (7g)

It was obtained as colorless oil (0.11 g) in 93% yield. R_f = 0.34 (30% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{24}$ = +5.5° (*c* 0.1, MeOH); IR (Nujol) ν_{max}: 3428, 1738, 1518, 1372, 1236, 1050 and 730 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.05 and 2.10 (6H, 2s, 3H each, 2 × COC*H*$_3$), 3.55–3.58 (2H, m, C-5H$_{α+β}$), 3.70 (3H, s, OC*H*$_3$), 4.18 (1H, dd, *J* = 6.4 and 3.3 Hz, C-4H), 5.04 (1H, t, *J* = 5.7 Hz, –OH), 5.10 (1H, dd, *J* = 6.8 and 4.5 Hz, C-2H), 5.26 (1H, dd, *J* = 6.8 and 3.3 Hz, C-3H), 5.73 (1H, d, *J* = 4.5 Hz, C-1H), 6.84–6.89 and 6.93–6.98 (4H; 2 m, 2H each; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 20.28 and 20.57 (2 × COC*H*$_3$, 55.32 (OC*H*$_3$, 60.74 (C-5), 69.75 (C-3), 70.65 (C-2), 83.07 (C-4), 99.73 (C-1), 114.51, 118.66, 150.33 and 154.63 (aromatic carbons), and 169.48 & 169.97 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 363.1036 ([M+Na]$^+$), calcd for [$C_{16}H_{20}O_8$+Na]$^+$ 363.1050.

3.3.14. 2,3-Di-*O*-acetyl-1-*O*-(4-hydroxyphenyl)-α-D-ribofuranoside (7h)

It was obtained as colorless oil (0.12 g) in 91% yield. R_f = 0.15 (50% ethyl acetate in petroleum ether, v/v); $[\alpha]_D^{31}$ = +4.5° (*c* 0.25, MeOH); IR (Nujol) ν_{max}: 3435, 1742, 1510, 1374, 1225, 1044 and 756 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.16 and 2.17 (6H, 2s, 3H each, 2 × COC*H*$_3$), 3.78–3.91 (2H, m, C-5H$_{α+β}$), 4.32–4.34 (1H, m, C-4H), 5.08 (1H, dd, *J* = 7.2 and 3.0 Hz, C-2H), 5.30–5.33 (2H, m, C-3H and –OH), 5.73 (1H, d, *J* = 4.5 Hz, C-1H), 6.73 and 6.89 (4H; 2d, 2H each, *J* = 8.6 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, CDCl$_3$): δ 20.58 and 20.87 (2 × COC*H*$_3$, 62.08 (C-5), 70.09 (C-3), 71.28 (C-2), 82.26 (C-4), 100.65 (C-1), 116.03, 119.44, 150.45 and 151.63 (aromatic carbons), and 170.34 & 170.95 (2 × *C*O); HR-ESI-TOF-MS: *m/z* 349.0893 ([M+Na]$^+$), calcd for [$C_{15}H_{18}O_8$+Na]$^+$ 349.0894.

3.4. General procedure for the deacetylation of 6a–h and 7a–h: Preparation of 1-*O*-aryl-β-D-ribofuranosides (8a–h) and 1-*O*-aryl-α-D-ribofuranosides (9a–h)

The peracetylated *O*-aryl β-D-ribofuronosides **6a**–**h** and the partially acetylated *O*-aryl α-D-ribofuranosides **7a**–**h** (0.7 mmol) were dissolved in methanol (10 mL) and saturated methanolic ammonia solution (10 mL) was added (Scheme 2). The reaction mixture was stirred for 6–8 h at room temperature to achieve the complete deacetylation as indicated by TLC. The methanol was removed under reduced pressure and the residue was subjected to column chromatography over silica gel with chloroform in methanol as eluent to afford the β- and α-*O*-arylribofuranosides **8a**–**h** and **9a**–**h** in 88–94% and 85–92% yields, respectively. All the compounds, that is, **8a**–**h** and **9a**–**h** were unambiguously identified on the basis of their spectral data; the structures of known compounds **8a**,[9a] **8g**,[39] **8h**[9a] and **9e**[40] were further confirmed on the basis of comparison of their spectral data with those reported in the literature. Only partial spectral data of **8a**, **8g–h** and **9e** were reported in the mentioned references and therefore we report here the complete spectral data of these known compounds as well.

3.4.1. 1-*O*-(1-Naphthyl)-β-D-ribofuranoside (8a)

It was obtained as white solid (0.18 g) in 91% yield. R_f = 0.40 (10% methanol in chloroform, v/v); mp 133–134 °C; $[\alpha]_D^{31}$ = −1.76° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3311, 1581, 1462, 1398, 1264, 1137, 1048 and 764 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$ + DMSO-d_6): δ 3.58 (1H, dd, *J* = 11.7 and 3.6 Hz, C-5H$_α$), 3.71 (1H, dd, *J* =11.7 and 4.8 Hz, C-5H$_β$), 4.05 (1H, t, *J* = 5.7 Hz, C-4H), 4.13 (1H, dd, *J* = 9.5 and 5.6 Hz, C-3H), 4.35-4.38 (2H, m, C-2H and -O*H*), 4.71 and 5.03 (1H, d, *J* = 6.1 Hz and 1H, d, *J* = 3.8 Hz; 2 × -O*H*), 5.75 (1H, s, C-1H), 7.11–7.13, 7.34–7.39, 7.45–7.49, 7.78–7.80 and 8.14–8.16 (7H; 1H, m; 1H, m; 3H, m; 1H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, CDCl$_3$ + DMSO-d_6): δ 63.09 (C-5), 71.04 (C-3), 75.41 (C-2), 85.06 (C-4), 105.76 (C-1), 108.14, 121.17, 121.85, 125.27, 125.90, 126.31, 127.40, 134.36 and 154.02 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 299.0891 ([M+Na]$^+$), calcd for [$C_{15}H_{16}O_5$+Na]$^+$ 299.0890.

3.4.2. 1-*O*-(2-Naphthyl)-β-D-ribofuranoside (8b)

It was obtained as white solid (0.17 g) in 88% yield. R_f = 0.35 (10% methanol in chloroform, v/v); mp 132–134 °C; $[\alpha]_D^{31}$ = −6.32° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3452, 3368, 1626, 1599, 1468, 1389, 1255, 1180, 1027 and 746 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$ + DMSO-d_6): δ 3.46 (1H, br s, C-5H$_α$), 3.63 1H, br s, C-5H$_β$), 4.01 (1H, br s, C-4H), 4.13 (2H, br s, C-2H and C-3H), 4.62, 5.00 and 5.32 (1H, br s; 1H, d, *J* = 4.6 Hz and 1H, br s; 3 × –O*H*), 5.63

(1H, s, C-1H), 7.15–7.17, 7.31–7.43 and 7.75–7.80 (7H; 1H, m; 3H, m and 3H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 63.59 (C-5), 71.42 (C-3), 75.54 (C-2), 85.44 (C-4), 106.06 (C-1), 110.53, 119.66, 124.50, 126.94, 127.48, 128.09, 129.61, 129.84, 134.74 and 155.16 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 299.0899 ([M+Na]$^+$), calcd for [$C_{15}H_{16}O_5$+Na]$^+$ 299.0890.

3.4.3. 1-*O*-(4-Biphenyl)-β-D-ribofuranoside (8c)

It was obtained as white solid (0.19 g) in 90% yield. R_f = 0.52 (10% methanol in chloroform, v/v); mp 122–124 °C; $[\alpha]_D^{31}$ = −5.04° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3345, 1604, 1486, 1235, 1114, 1058 and 769 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 3.39–3.43 (1H, m, C-5H$_\alpha$), 3.58 (1H, dd, *J* = 10.4 and 4.5 Hz, C-5H$_\beta$), 3.94 (1H, dd, *J* = 9.2 and 4.0 Hz, C-4H), 4.03–4.06 (2H, m, C-2H and C-3H), 4.62, 4.96 and 5.27 (1H, t, *J* = 5.5 Hz; 1H, d, *J* = 5.7 Hz and 1H, d, *J* = 4.0 Hz; 3 × –O*H*), 5.50 (1H, s, C-1H), 7.05–7.07, 7.30–7.32, 7.39–7.44 and 7.54–7.59 (9H; 2H, m; 1H, m; 2H, m and 4H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 63.65 (C-5), 71.49 (C-3), 75.57 (C-2), 85.51 (C-4), 106.18 (C-1), 117.47, 127.06, 127.52, 128.48, 129.55, 134.50, 140.71 and 157.09 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 325.1034 ([M+Na]$^+$), calcd for [$C_{17}H_{18}O_5$+Na]$^+$ 325.1046.

3.4.4. 1-*O*-(3-Methylphenyl)-β-D-ribofuranoside (8d)

It was obtained as white solid (0.15 g) in 91% yield. R_f = 0.45 (10% methanol in chloroform, v/v); mp 69–71 °C; $[\alpha]_D^{24}$ = −4.2° (*c* 0.1, MeOH); IR (KBr) ν_{max}: 3442, 3412, 1512, 1370, 1210, 1030 and 780 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 2.29 (s, 3H, ArC*H*$_3$), 3.60–3.64 (2H, m, C-5H$_{\alpha+\beta}$), 3.97–3.98 (1H, m, C-4H), 4.07 (2H, m, C-2H and C-3H), 4.46, 4.87 and 5.15 (1H, d, *J* = 5.3 Hz; 1H, d, *J* = 4.8 Hz and 1H, br s; 3 × –O*H*), 5.46 (s, 1H, C-1H), 6.75–6.78 and 7.09–7.12 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 21.92 (Ar*C*H$_3$, 63.67 (C-5), 71.47 (C-3), 75.60 (C-2), 85.30 (C-4), 106.03 (C-1), 113.90, 117.50, 122.93, 129.69, 139.59 and 157.40 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 263.0895 ([M+Na]$^+$), calcd for [$C_{12}H_{16}O_5$+Na]$^+$ 263.0890.

3.4.5. 1-*O*-(4-Methylphenyl)-β-D-ribofuranoside (8e)

It was obtained as white solid (0.16 g) in 93% yield. R_f = 0.33 (10% methanol in chloroform, v/v); mp 78–80 °C; $[\alpha]_D^{31}$ = −3.16° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3430, 1610, 1509, 1218, 1130, 1051 and 784 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 2.22 (3H, s, Ar-C*H*$_3$), 3.40 (1H, m, C-5H$_\alpha$), 3.51–3.55 (1H, m, C-5H$_\beta$), 3.87 (1H, br s, C-4H), 3.98 (2H, br s, C-2H and C-3H), 4.67, 5.00 and 5.29 (1H, br s; 1H, d, *J* = 3.5 Hz and 1H, br s; 3 × -O*H*), 5.37 (1H, s, C-1H), 6.85 and 7.06 (4H; 2d, 2H each, *J* = 7.2 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 20.96 (Ar*C*H$_3$), 63.70 (C-5), 71.52 (C-3), 75.47 (C-2), 85.33 (C-4), 106.35 (C-1), 117.11, 130.62, 131.18 and 155.37 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 263.0903 ([M+Na]$^+$), calcd for [$C_{12}H_{16}O_5$+Na]$^+$ 263.0890.

3.4.6. 1-*O*-(3-Methoxyphenyl)-β-D-ribofuranoside (8f)

It was obtained as white solid (0.17 g) in 94% yield. R_f = 0.52 (10% methanol in chloroform, v/v); mp 69–71 °C; $[\alpha]_D^{31}$ = −1.1° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3442, 3412, 1512, 1370, 1210, 1030 and 780 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.38–3.40 (1H, m, C-5H$_\alpha$), 3.53–3.57 (1H, m, C-5H$_\beta$), 3.72 (1H, s, OC*H*$_3$), 3.86–3.96 (3H, m, C-2H, C-3H and C-4H), 4.67, 4.99 and 5.29 (1H, t, *J* = 5.1 Hz; 1H, d, *J* = 5.4 Hz and 1H, d, *J* = 3.6 Hz; 3 × –O*H*), 5.42 (1H, s, C-1H), 6.52–6.58 and 7.15–7.20 (4H; 3H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 55.05 (OC*H*$_3$, 62.76 (C-5), 70.58 (C-3), 74.59 (C-2), 84.55 (C-4), 102.45 (C-1), 105.26, 107.21, 108.37, 129.88, 157.79 and 160.30 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 279.0839 ([M+Na]$^+$), calcd for [$C_{12}H_{16}O_6$+Na]$^+$ 279.0839.

3.4.7. 1-*O*-(4-Methoxyphenyl)-β-D-ribofuranoside (8g)

It was obtained as white solid (0.16 g) in 92% yield. R_f = 0.47 (10% methanol in chloroform, v/v); mp 91–93 °C; $[\alpha]_D^{24}$ = −4.9° (*c* 0.1, MeOH); IR (KBr) ν_{max}: 3410, 3387, 1524, 1386, 1224, 1022 and 780 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 3.32–3.36 (1H, m, C-5H$_\alpha$), 3.59–3.62 (1H, m, C-5H$_\beta$), 3.69 (3H, s, OC*H*$_3$), 3.85–3.86 (1H, m, C-4H), 3.97 (2H, br s, C-2H and C-3H), 4.67, 4.97 and 5.25 (1H, t, *J* = 4.0 Hz; 1H, d, *J* = 5.7 Hz and 1H, d, *J* = 4.0 Hz; 3 × –O*H*), 5.30 (1H, s, C-1H), 6.83 and 6.91 (4H; 2d, 2H each, *J* = 9.0 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 54.56 (O*C*H$_3$, 62.08 (C-5), 69.89 (C-3), 73.84 (C-2), 83.66 (C-4), 105.39 (C-1), 113.73, 116.95, 149.79 and 153.41 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 279.0848 ([M+Na]$^+$), calcd for [$C_{12}H_{16}O_6$+Na]$^+$ 279.0839.

3.4.8. 1-*O*-(4-Hydroxyphenyl)-β-D-ribofuranoside (8h)

It was obtained as white solid (0.16 g) in 92% yield. R_f = 0.25 (10% methanol in chloroform, v/v); mp 150–151 °C; $[\alpha]_D^{31}$ = −1.7° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3410, 3387, 1524, 1386, 1224, 1022 and 780 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.40 (1H, br s, C-5H$_\alpha$), 3.51–3.54 (1H, m, C-5H$_\beta$), 3.70 (1H, br s, C-4H), 3.83–3.84 (2H, m, C-2H and C-3H), 4.66 and 4.94 (1H, t, *J* = 6.0 Hz and 1H, d, *J* = 5.7 Hz; 2 × aliphatic –O*H*), 5.30 (2H, br s, C-1H and aliphatic −O*H*), 6.64 and 6.78 (4H; 2d, 2H each, *J* = 9.0 Hz; aromatic protons), and 9.00 (1H, s, ArO*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 63.75 (C-5), 71.52 (C-3), 75.52 (C-2), 85.14 (C-4), 107.25 (C-1), 116.36, 118.55, 150.23 and 152.96 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 265.0688 ([M+Na]$^+$), calcd for [$C_{11}H_{14}O_6$+Na]$^+$ 265.0683.

3.4.9. 1-*O*-(1-Naphthyl)-α-D-ribofuranoside (9a)

It was obtained as white solid (0.17 g) in 87% yield. R_f = 0.38 (10% methanol in chloroform, v/v); mp 99–100 °C; $[\alpha]_D^{31}$ = +3.04° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3520, 3387, 3348, 1593, 1392, 1262, 1228, 1115, 1032 and 782 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.67–3.69 (2H, m, C-5H$_{\alpha+\beta}$), 4.22 1H, t, *J* = 2.9 Hz, C-4H), 4.27 (1H, t, *J* = 3.6 Hz, C-2H), 4.32–4.34 (1H, m, C-3H), 4.38–4.44 and 4.70 (2H, m and 1H, d, *J* = 5.3 Hz; 3 × –O*H*), 5.80 (1H, d, *J* = 4.1 Hz, C-1H), 7.20–7.22, 7.35–7.40, 7.45–7.51, 7.78–7.80 and 8.38 (7H; 1H, m; 1H, m; 3H, m; 1H, m and 1H, br s; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 61.20 (C-5), 69.80 (C-3), 72.24 (C-2), 86.74 (C-4), 101.41 (C-1), 109.80, 121.57, 122.45, 125.22, 125.77, 126.20, 126.42, 127.27, 134.35 and 152.84 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 299.0890 ([M+Na]$^+$), calcd for [$C_{15}H_{16}O_5$+Na]$^+$ 299.0890.

3.4.10. 1-*O*-(2-Naphthyl)-α-D-ribofuranoside (9b)

It was obtained as white solid (0.17 g) in 89% yield. R_f = 0.32 (10% methanol in chloroform, v/v); mp 137–139 °C; $[\alpha]_D^{31}$ = +8.20° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3452, 3368, 1626, 1599, 1468, 1389, 1255, 1180, 1027 and 746 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 3.63 (2H, m, C-5H$_{\alpha+\beta}$), 4.09–4.22 (3H, m, C-2H, C-3H and C-4H), 4.46 and 4.68–4.74 (1H, d, *J* = 9.0 Hz and 2H, m; 3 × –O*H*), 5.72 (1H, br s, C-1H), 7.27–7.47 and 7.72–7.78 (7H; 4H, m and 3H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 60.96 (C-5), 68.67 (C-3), 70.93 (C-2), 85.61 (C-4), 99.96 (C-1), 109.88, 118.60, 122.88, 125.18, 125.80, 126.42, 128.01, 128.20, 133.10 and 154.00 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 299.0880 ([M+Na]$^+$), calcd for [$C_{15}H_{16}O_5$+Na]$^+$ 299.0890.

3.4.11. 1-*O*-(4-Biphenyl)-α-D-ribofuranoside (9c)

It was obtained as white solid (0.19 g) in 89% yield. R_f = 0.51 (10% methanol in chloroform, v/v); mp 64–65 °C; $[\alpha]_D^{31}$ = +3.48° (*c*

0.25, MeOH); IR (KBr) ν_{max}: 3349, 1604, 1486, 1236, 1114, 1032 and 769 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.52 (2H, m, C-5$H_{\alpha+\beta}$), 3.99–4.11 (3H, m, C-2H, C-3H and C-4H), 4.61–4.64 and 4.78–4.86 (1H, m and 2H, m; 3 × –O*H*), 5.62 (1H, br s, C-1H), 7.13–7.15, 7.30–7.32, 7.40–7.44 and 7.55–7.57 (9H; 2H, m; 1H, m; 2H, m and 4H, m; aromatic protons); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 62.47 (C-5), 70.19 (C-3), 72.42 (C-2), 87.09 (C-4), 101.40 (C-1), 118.04, 127.05, 127.49, 128.36, 129.53, 134.51, 140.76 and 157.61 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 325.1035 ([M+Na]$^+$), calcd for $[C_{17}H_{18}O_5+Na]^+$ 325.1046.

3.4.12. 1-*O*-(3-Methylphenyl)-α-D-ribofuranoside (9d)

It was obtained as white solid (0.15 g) in 92% yield. R_f = 0.44 (10% methanol in chloroform, v/v); mp 113–114 °C; $[\alpha]_D^{24}$ = +4.0° (*c* 0.1, MeOH); IR (KBr) ν_{max}: 3452, 1511, 1379, 1218, 1032 and 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 2.30 (s, 3H, ArC*H*$_3$), 3.58 (2H, m, C-5$H_{\alpha+\beta}$), 4.05–4.14 (3H, m, C-2H, C-3H and C-4H), 4.40 and 4.70–4.74 (1H, d, *J* = 9.1 Hz and 2H, m; 3 × –O*H*), 5.54 (1H, d, *J* = 4.4 Hz, C-1H), 6.77–6.79, 6.85–6.89 and 7.10–7.15 (4H; 1H, m; 2H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 21.40 (Ar*C*H$_3$, 62.00 (C-5), 69.72 (C-3), 71.89 (C-2), 86.48 (C-4), 100.87 (C-1), 114.13, 117.76, 122.60, 129.04, 138.96 and 157.29 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 263.0894 ([M+Na]$^+$), calcd for $[C_{12}H_{16}O_5+Na]^+$ 263.0890.

3.4.13. 1-*O*-(4-Methylphenyl)-α-D-ribofuranoside (9e)

It was obtained as white solid (0.15 g) in 91% yield. R_f = 0.31 (10% methanol in chloroform, v/v); mp 103–105 °C; $[\alpha]_D^{31}$ = +4.80° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3475, 3392, 1612, 1513, 1461, 1236, 1142, 1055 and 729 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 2.25 (3H, s, ArC*H*$_3$), 3.54 (2H, m, C-5$H_{\alpha+\beta}$), 3.98–4.10 (3H, m, C-2H, C-3H and C-4H), 4.47 and 4.71–4.77 (1H, d, *J* = 9.0 Hz and 2H, m; 3 × –O*H*), 5.49 (1H, d, *J* = 4.3 Hz, C-1H), 6.94 and 7.05 (4H; 2d, 2H each, *J* = 8.3 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 21.01 (ArCH_3), 62.51 (C-5), 70.22 (C-3), 72.40 (C-2), 86.90 (C-4), 101.72 (C-1), 117.68, 130.30, 131.21 and 155.82 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 263.0882 ([M+Na]$^+$), calcd for $[C_{12}H_{16}O_5+Na]^+$ 263.0890.

3.4.14. 1-*O*-(3-Methoxyphenyl)-α-D-ribofuranoside (9f)

It was obtained as white semisolid (0.18 g) in 85% yield. R_f = 0.50 (10% methanol in chloroform, v/v); $[\alpha]_D^{31}$ = +1.2° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3452, 1511, 1379, 1218, 1032 and 783 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.31 (2H, m, C-5$H_{\alpha+\beta}$), 3.48 (3H, s, OC*H*$_3$), 3.76–3.87 (3H, m, C-2H, C-3H and C-4H), 4.08 and 4.37 (1H, br s and 2H, br s; 3 × -O*H*), 5.28 (1H, d, *J* = 4.0 Hz, C-1H), 6.24–6.27, 6.37–6.40 and 6.84–6.90 (4H; 1H, m; 2H, m and 1H, m; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 60.02 (OCH_3), 66.94 (C-5), 74.64 (C-3), 76.82 (C-2), 91.42 (C-4), 105.83 (C-1), 108.28, 112.40, 114.08, 134.52 and 165.32 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 279.0839 ([M+Na]$^+$), calcd for $[C_{12}H_{16}O_6+Na]^+$ 279.0839.

3.4.15. 1-*O*-(4-Methoxyphenyl)-α-D-ribofuranoside (9g)

It was obtained as white solid (0.16 g) in 90% yield. R_f = 0.25 (10% methanol in chloroform, v/v); mp 60–61 °C; $[\alpha]_D^{24}$ = +6.1° (*c* 0.1, MeOH); IR (KBr) ν_{max}: 3440, 3403, 1520, 1380, 1232, 1014 and 791 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 3.56–3.58 (2H, m, C-5$H_{\alpha+\beta}$), 3.73 (3H, s, OC*H*$_3$), 4.00–4.09 (3H, m, C-2H, C-3H and C-4H), 4.37–4.40 and 4.65–4.70 (1H, m and 2H, m; 3 × –O*H*), 5.43 (1H, d, *J* = 4.3 Hz, C-1H), 6.79 and 7.00 (4H; 2d, 2H each, *J* = 8.9 Hz; aromatic protons); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 55.46 (OCH_3, 62.07 (C-5), 69.79 (C-3), 71.92 (C-2), 86.28 (C-4), 102.07 (C-1), 114.30, 118.69, 151.08 and 154.71 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 279.0852 ([M+Na]$^+$), calcd for $[C_{12}H_{16}O_6+Na]^+$ 279.0839.

3.4.16. 1-*O*-(4-Hydroxyphenyl)-α-D-ribofuranoside (9h)

It was obtained as white solid (0.15 g) in 88% yield. R_f = 0.20 (10% methanol in chloroform, v/v); mp 79–80 °C; $[\alpha]_D^{31}$ = +1.8° (*c* 0.25, MeOH); IR (KBr) ν_{max}: 3440, 3403, 1520, 1380, 1232, 1014, and 791 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.46 (2H, br s, C-5$H_{\alpha+\beta}$), 3.89–3.96 (3H, m, C-2H, C-3H and C-4H), 4.56–4.59 and 4.79–4.84 (1H, m and 2H, m; 3 × aliphatic –O*H*), 5.36 (1H, d, *J* = 4.3 Hz, C-1H), 6.66 and 6.85 (4H; 2d, 2H each, *J* = 8.4 Hz; aromatic protons) and 9.02 (1H, s, ArO*H*); ^{13}C NMR (75.5 MHz, $CDCl_3$ + DMSO-d_6): δ 63.63 (C-5), 71.31 (C-3), 73.48 (C-2), 87.82 (C-4), 103.69 (C-1), 117.44, 120.35, 151.83 and 154.15 (aromatic carbons); HR-ESI-TOF-MS: *m/z* 265.0695 ([M+Na]$^+$), calcd for $[C_{11}H_{14}O_6+Na]^+$ 265.0683.

3.5. c-Src kinase activity assay

The effect of synthesized compounds on the activity of c-Src kinase was determined by HTScan Src Kinase Assay Kit, catalogue number 7776 from Cell Signaling Technology; according to manufacturer's protocol. Streptavidin coated plates was purchased from Pierce. In summary, the kinase reaction was started with the incubation of the 12.5 μL of the reaction cocktail (0.5 ng/μL of GST-Src kinase in 1.25 mM DTT) with 12.5 μL of prediluted compounds (dissolved in 1% DMSO) for 5 min at room temperature. ATP/substrate (25 μL, 20 μM/1.5 μM) cocktail was added to the mixture. The biotinylated substrate (catalogue number 1366) contains the residues surrounding tyrosine 160 (Tyr160) of signal transduction protein with a sequence of EGIYDVP. The reaction mixture was incubated for 30 min at room temperature. The kinase reaction was stopped with the addition of 50 μL of 50 mM EDTA (pH 8.0). The reaction solution (25 μL) was transferred into 96-well streptavidin plates (Pierce, part number 15125), diluted with 75 μL double distilled water, and incubated at room temperature for 60 min. At the end of the incubation, the wells were washed three times with 200 μL of 0.05% Tween-20 in PBS buffer (PBS/T). After that to the each well was added 100 μL of phosphotyrosine antibody (P-Tyr-100) (1:1000 dilution in PBS/T with 1% BSA) and the wells were incubated for another 60 min. After washing three times with 0.05% Tween-20 in PBS/T, the wells were incubated with 100 μL secondary anti-mouse IgG antibody, which was HRP-conjugated (1:500 dilution in PBS/T with 1% BSA) for next 30 min at room temperature. The wells were washed five times with 0.05% Tween-20 in PBS and then were incubated with 100 μL of 3,3′,5,5′-tetramethylbenzidine dihydrochloride (TMB) substrate for 5 min. The reaction was stopped by adding 100 μL/well of stop solution to each well and mixed well and read the absorbance at 450 nm using a microplate reader (Molecular devices, spectra Max M2). IC_{50} values of the compounds were calculated using ORIGIN 6.0 (origin lab) software. IC_{50} is the concentration of the compound that inhibited enzyme activity by 50%. All the experiments were carried out triplicate.

3.6. Molecular modeling

Simulations were performed with the Accelrys Discovery Studio 2.5 modeling package, with the CHARMm-based force field. Model of compounds **8c** and **8f** bound to Src was constructed based on the X-ray crystal structure of AMP-PNP, a nonhydrolyzable ATP analog, bound to c-Src (2SRC) template from RCSB Protein Data Bank. For the molecular modeling of **8c** and **8f**, after initial minimization of the compounds, the coordinates and positions of the backbone atoms of sugar groups were superimposed on the corresponding atoms in AMP-PNP in complex with c-Src after which AMP-PNP was deleted. For refinement, the compound-Src complex underwent CHARMm minimization. All default parameters were used in the minimization process.

Acknowledgments

We acknowledge the financial support from the University of Delhi (DU-DST Purse Grant to AKP and VSP), the Department of Biotechnology (DBT, New Delhi under Indo-German DBT-BMBF collaboration in Biotechnology to AKP and VSP) and the American Cancer Society Grant # RSG-07-290-01-CDD (to KP). RKS and SS thank DBT, New Delhi and UGC, New Delhi for the grant of Senior Research Fellowships, respectively.

References and notes

1. (a) Newman, R. H.; Zhang, J. *Nat. Chem. Biol.* **2008**, *4*, 382; (b) Walsh, G.; Jefferis, R. *Nat. Biotechnol.* **2006**, *24*, 1241.
2. Park, O. J.; Kim, D. Y.; Dordick, J. S. *Biotechnol. Bioeng.* **2000**, *70*, 208.
3. (a) Stephens, A. C.; Rivers, R. P. A. *Curr. Opin. Mol. Ther.* **2003**, *5*, 118; (b) Leumann, C. J. *Bioorg. Med. Chem.* **2002**, *10*, 841; (c) Opalinska, J. B.; Gewirtz, A. M. *Nat. Rev. Drug Disc.* **2002**, *1*, 503; (d) Crooke, S. T. *Antisense Drug Technology Principles, Strategies and Applications*; Marcel Dekker: New York, 2001; (e) Uhlmann, E. *Curr. Opin. Drug Discov. Devel.* **2000**, *3*, 203; (f) Chu, C. K.; Baker, D. C. *Nucleosides and Nucleotides as Antitumor and Antiviral Agents*; Plenum Press: New York, 1993.
4. (a) LePage, G. A.; Khaliq, A. *Cancer Chemother. Rep.* **1979**, *63*, 53; (b) Bretner, M.; Kulikowski, T.; Dzik, J. M.; Balinska, M.; Rode, W.; Shugar, D. *J. Med. Chem.* **1993**, *36*, 3611.
5. Pellissier, H. *Tetrahedron* **2005**, *61*, 2947.
6. (a) Fuster, M. M.; Esko, J. D. *Nat. Rev. Cancer* **2005**, *5*, 526; (b) Smith, A. E.; Helenius, A. *Science* **2004**, *304*, 237; (c) Sears, P.; Wong, C.-H. *Cell. Mol. Life Sci.* **1998**, *54*, 223.
7. (a) Chapman, E.; Best, M. D.; Hanson, S. R.; Wong, C. H. *Angew. Chem., Int. Ed.* **2004**, *43*, 3526; (b) Honke, K.; Taniguchi, N. *Med. Res. Rev.* **2002**, *22*, 637; (c) Henrissat, B.; Davies, G. *Curr. Opin. Struct. Biol.* **1997**, *7*, 637.
8. (a) Kaye, E. M. *Curr. Treat. Options Neurol.* **2001**, *3*, 249; (b) Asano, N. *Glycobiology* **2003**, *13*, 93R; (c) Ganem, B. *Acc. Chem. Res.* **1996**, *29*, 340; (d) Jacob, G. S. *Curr. Opin. Struct. Biol.* **1995**, *5*, 605.
9. (a) Schramm, V. L.; Furneaux, R. H.; Tyler, P. C.; Clinch, K. U.S. Patent, 2002, 6379,911 B2.; (b) Burton, M. WO 2003, 03/035900 A1.; (c) Burton, M. WO 2003, 03/035897 A2.
10. Martin, G. S. *Nat. Rev. Mol. Cell Biol.* **2001**, *2*, 467.
11. Lee, K.; Kim, J.; Jeong, Ki-W.; Lee, K. W.; Lee, Y.; Song, J. Y.; Kim, M. S.; Lee, G. S.; Kim, Y. *Bioorg. Med. Chem.* **2009**, *17*, 3152.
12. Hunter, T. *Cell* **2000**, *100*, 113.
13. Schlessinger, J. *Cell* **2000**, *100*, 293.
14. Al-Obeidi, F. A.; Wu, J. J.; Lam, K. S. *Biopolymers* **1998**, *47*, 197.
15. Parang, K.; Sun, G. *Expert Opin. Ther. Pat.* **2005**, *15*, 1183.
16. Irby, R. B.; Yeatman, T. J. *Oncogene* **2000**, *19*, 5636.
17. Tiwari, R.; Brown, A.; Narramaneni, S.; Sun, G.; Parang, K. *Biochimie* **2010**, *92*, 1153.
18. (a) Boggon, T. J.; Eck, M. J. *Oncogene* **2004**, *23*, 7918; (b) Parsons, S. J.; Parsons, J. T. *Oncogene* **2004**, *23*, 7906.
19. Summy, J. M.; Gallick, G. E. *Cancer Metastasis Rev.* **2003**, *22*, 337.
20. Zhang, Q.; Thomas, S. M.; Xi, S.; Smithgall, T. E.; Siegfried, J. M.; Kamens, J.; Gooding, W. E.; Grandis, J. R. *Cancer Res.* **2004**, *64*, 6166.
21. Golas, J. M.; Lucas, J.; Etienne, C.; Golas, J.; Discafani, C.; Sridharan, L.; Boghaert, E.; Arndt, K.; Ye, F.; Boschelli, D. H.; Li, F.; Titsch, C.; Huselton, C.; Chaudhary, I.; Boschelli, F. *Cancer Res.* **2005**, *65*, 5358.
22. Brunton, V. G.; Avizienyte, E.; Fincham, V. J.; Serrels, B.; Metcalf, C. A., III; Sawyer, T. K.; Frame, M. C. *Cancer Res.* **2005**, *65*, 1335.
23. Lesslie, D. P., III; Summy, J. M.; Parikh, N. U.; Fan, F.; Trevino, J. G.; Sawyer, T. K.; Metcalf, C. A., III; Shakespeare, W. C.; Hicklin, D. J.; Ellis, L. M.; Gallick, G. E. *J. Cancer* **2006**, *94*, 1710.
24. (a) Sawyer, T. K.; Bohacek, R. S.; Metcalf, C. A., III; Shakespeare, W. C.; Wang, Y.; Sundaramoorthi, R.; Keenan, T.; Narula, S.; Weigele, M.; Dalgarno, D. C. *Biotechniques* **2003**, *12*, 2; (b) Zhu, X.; Kim, J. L.; Newcomb, J. R.; Rose, P. E.; Stover, D. R.; Toledo, L. M.; Zhao, H.; Morgenstern, K. A. *Structure Fold Des.* **1999**, *7*, 651.
25. Lombardo, L. J.; Lee, F. Y.; Chen, P.; Norris, D.; Barrish, J. C.; Behnia, K.; Castaneda, S.; Cornelius, L. A. M.; Das, J.; Doweyko, A. M.; Fairchild, C.; Hunt, J. T.; Inigo, I.; Johnston, K.; Kamath, A.; Kan, D.; Klei, H.; Marathe, P.; Pang, S.; Peterson, R.; Pitt, S.; Schieven, G. L.; Schmidt, R. J.; Tokarski, J.; Wen, M. L.; Wityak, J.; Borzilleri, R. M. *J. Med. Chem.* **2004**, *47*, 6658.
26. Hennequin, L. F.; Allen, J.; Breed, J.; Curwen, J.; Fennell, M.; Green, T. P.; Lambert-van der Brempt, C.; Morgentin, R.; Norman, R. A.; Olivier, A.; Otterbein, L.; Ple, P. A.; Warin, N.; Costello, G. J. *J. Med. Chem.* **2006**, *49*, 6465.
27. Boschelli, D. H.; Ye, F.; Wang, Y. D.; Dutia, M.; Johnson, S. L.; Wu, B.; Miller, K.; Powell, D. W.; Yaczko, D.; Young, M.; Tischler, M.; Arndt, K.; Discafani, C.; Etienne, C.; Gibbons, J.; Grod, J.; Lucas, J.; Weber, J. M.; Boschelli, F. *J. Med. Chem.* **2001**, *44*, 3965.
28. Prasad, A. K.; Serensen, M. D.; Parmar, V. S.; Wengel, J. *Tetrahedron Lett.* **1995**, *36*, 6163.
29. Koenigs, W.; Knorr, E. *Chem. Ber.* **1901**, *34*, 957.
30. (a) Prasad, A. K.; Kalra, N.; Yadav, Y.; Kumar, R.; Sharma, S. K.; Patkar, S.; Lange, L.; Wengel, J.; Parmar, V. S. *Chem. Commun.* **2007**, 2616; (b) Prasad, A. K.; Kalra, N.; Yadav, Y.; Singh, S. K.; Kumar, R.; Sharma, S. K.; Patkar, S.; Lange, L.; Wengel, J.; Parmar, V. S. *Org. Biomol. Chem.* **2007**, *5*, 3524; (c) Singh, S. K.; Sharma, R. K.; Maity, J.; Wengel, J.; Parmar, V. S.; Prasad, A. K. *Nucleic Acids Symp. Ser.* **2008**, *52*, 273; (d) Maity, J.; Shakya, G.; Singh, S. K.; Ravikumar, V. T.; Parmar, V. S.; Prasad, A. K. *J. Org. Chem.* **2008**, *73*, 5629; (e) Sharma, R. K.; Aggarwal, N.; Arya, A.; Olsen, C. E.; Parmar, V. S.; Prasad, A. K. *J. Indian Chem., Sect. B* **2009**, *48B*, 1727; (f) Singh, S. K.; Sharma, V. K.; Olsen, C. E.; Wengel, J.; Parmar, V. S.; Prasad, A. K. *J. Org. Chem.* **2010**, *75*, 7932.
31. Chien, T. C.; Chern, J. W. *Carbohydr. Res.* **2004**, *339*, 1215.
32. (a) Fernandez-Lorente, G.; Palomo, J. M.; Cocca, J.; Mateo, J. C.; Moro, P.; Terreni, M.; Fernandez-Lafuente, R.; Guisan, J. M. *Tetrahedron* **2003**, *59*, 5705; (b) Inigo, S.; Porro, M. T.; Montserrat, J. M.; Iglesias, L. E.; Iribarren, A. M. *J. Mol. Catal. B: Enzym.* **2005**, *35*, 70.
33. (a) Damkjaer, D. L.; Petersen, M.; Wengel, J. *Nucleosides Nucleotides* **1994**, *13*, 1801; (b) Ferrero, M.; Gotor, V. *Chem. Rev.* **2000**, *100*, 4319; (c) Garica, J.; Diaz-Rodriguez, A.; Fernandez, S.; Sanghavi, Y. S.; Ferrero, M.; Gotor, V. *J. Org. Chem.* **2006**, *71*, 9765.
34. Xu, W.; Doshi, A.; Lei, M.; Eck, M. J.; Harrison, S. C. *Mol. Cell* **1999**, *3*, 629.
35. Schindler, T.; Sicheri, F.; Pico, A.; Gazit, A.; Levitzki, A.; Kuriyan, J. *Mol. Cell* **1999**, *3*, 639.
36. (a) Boryski, J.; Grynkiewicz, G. *Synthesis* **2001**, *14*, 2170; (b) Stevens, J. D., Jr.; Letcher, H. G. *J. Org. Chem.* **1968**, *33*, 1799.
37. The completion of the reaction was monitored by TLC in ethyl acetate-pet. ether as solvent system. The small separation in α- and β-anomers was observed after three to four runs of the TLC plate. Absence of one anomer and appearance of a slow moving product on TLC indicated completion of the reaction.
38. Antkowiak, W. Z.; Krzyzosiak, W. J.; Biernat, J.; Ciesiolka, J.; Gornicki, P. *Bulletin de l'Academie polonaise des sciences Serie des Sciences Chimiques* **1977**, *25*, 173.
39. Ben-Zeev Efrat, V. J.; Marantz, Y.; Reddy, A. S.; Zhang, Z.; Becker, O.; Mccaulay, D.; Orbach, P.; Shacham, S.; Saha, A.K.; Xie, M. WO 2008, 06032 A2.
40. Dinglinger, F.; Braun, I. *Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie* **1970**, *351*, 1157.