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Use of *O*-glycosylation in total synthesis

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Contents

Keywords: *O*-Glycosylation; Total synthesis.

Abbreviations: Ac, acetyl; ACF, activated carbon fiber; AIBN, 2,2′-azobiisobutyronitrile; Alloc, allyloxycarbonyl; Ar, aryl; AtOH, 7-aza-1-hydroxy-1*H*-benzotriazole; $BF_3(Et_2O)$, boron trifluoride etherate; DMB, 3,4-dimethoxybenzyl; DMTSB, dimethyl(methylthio)sulfonium tetrafluoroborate; Bn, benzyl; Boc, *tert*-butoxycarbonyl; BOP, benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluoride; BOM, benzyloxymethyl; BTOH, 1-hydroxybenzotriazole; Bu, butyl; Bz, benzoyl; CA, chloroacetyl; CAN, ceric ammonium nitrate; Cbz, benzyloxycarbonyl; Cp, cyclopentadienyl; CSA, 10-camphorsulfonic acid; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; DAST, (diethylamino)sulphur trifluoride; Dba, *trans*,*trans*-dibenzylideneacetone; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; DCC, *N*,*N*′-dicyclohexylcarbodiimide; DDQ, 2,3-dichloro-5,6-dicyanobenzoquinone; DECP, diethylcyanophosphate; DHP, 3,4-dihydro-2*H*-pyran; DIAD, diisopropylazodicarboxylate; DIBAL, diisobutylaluminiumhydride; DIPEA, diisopropylethylamine; DISAL, methyl 3,5-dinitrosalicylate; DMAP, 4-dimethylaminopyridine; DMB, 3,4-dimethoxybenzyl; DMDO, 2,2-dimethyldioxirane; DMF, *N*,*N*-dimethylformamide; DMSO, dimethylsulfoxide; DMTr, 4,4′-dimethoxytrityl; DMTSB, dimethyl(methylthio)sulfonium tetrafluoroborate; DMTST, (dimethylthio)methylsulfonium trifluoromethane sulfonate; DNA, desoxyribonucleic acid; DTBMP, 2,6-di-*tert*-butyl-4-methylpyridine; EDC, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide; EDCI, (1-ethyl-3-[3-(dimethylamino)-propyl]carbodiimide hydrochloride; EEDQ, 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline; Et, ethyl; FMOC, 9-fluorenylmethoxycarbonyl; fuc, fucose; Gal, galactose; GDP, guanosine diphosphate; Glc, glucose; GlcNAc, 2-*N*-acetyl-2-deoxyglucose; GPI, glycosylphosphatidylinositol; HMDS, bis(trimethylsilyl)amide; IDCP, iodonium dicollidine perchlorate; im, imidazolyl; imid, imidazole; LDA, lithium diisopropylamide; Lev, levulinoyl; MCPBA, 3-chloroperoxybenzoic acid; Me, methyl; MMTr, 4-methoxytrityl; MOM, methoxymethyl; MOP, 3-methoxypyridyloxy; Ms, mesyl; MP, 4-methoxyphenyl; NB, nitrobenzyl; NBD, nitrobenzoxadiazole; NBS, *N*-bromosuccinimide; NIS, *N*-iodosuccinimide; NMO, 4-methylmorphine-*N*-oxide; PCC, pyridinium chlorochromate; PDC, pyridinium dichromate; PEGA, (polyethylene glycol) polyacrylamide; Pent, 4-pentenyl; Pfp, pentafluorophenyl; Ph, phenyl; Phth, phthalimido; Piv, pivaloyl; PMB, *p*-methoxybenzoyl; PNB, *p*-nitrobenzoyl; PPTS, pyridinium 4-toluenesulfonate; Pr, propyl; py, pyridine; RNA, ribonucleic acid; SEM, [2-(trimethylsilyl)ethoxy]methyl; Ser, serine; SLe^x, sialyl Lewis x; TBAB, tetra-*n*-butylammonium bromide; TBAF, tetra-*n*-butylammonium fluoride; TBDMS, *tert*-butyldimethylsilyl; TBDPS, *tert*-butyldiphenylsilyl; TBS, *tert*-butyldimethylsilyl; TEMPO, 2,2,6,6-tetramethyl-1-piperidinyloxy; TEOC, *N*-trimethylsilylethyloxycarbonyl; TES, triethylsilyl; THF, tetrahydrofuran; THP, tetrahydropyranyl; Thr, threonine; TIPS, triisopropylsilyl; Tf, trifluoromethanesulphonyl; TFA, trifluoroacetic acid; TfOH, triflic acid; Tf_2O, triflic anhydride; Tips, triisopropylsilyl; TMAD, *N*,*N*,*N*′,*N*′-tetramethylazodicarboxamide; TMS, trimethylsilyl; TMSOTf, trimethylsilyl trifluoromethanesulphonate; TMU, *N*,*N*,*N*′,*N*′-tetramethylurea; Tol, toluene; TPS, triphenylsilyl; Tr, triphenylmethyl (trityl); Troc, 2,2,2-trichloroethoxycarbonyl; $TrtClO_4$, triphenylmethyl perchlorate; Ts, 4-toluenesulfonyl (tosyl); TsOH, *p*-toluenesulfonic acid; UDP, uridine-5′-diphosphate.

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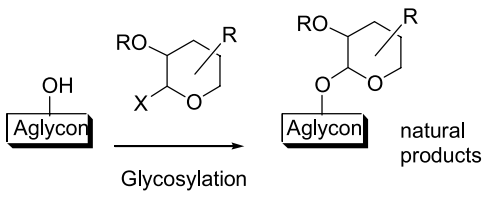
1. Introduction

Carbohydrates are the most abundant group of natural products and the role of sugars as energy and biosynthetic resources (glycolysis, pentose phosphate cycle, etc.), 'energy storage devices' (photosynthesis) and key structural elements in the formation of biological backbones (2-deoxyribose for DNA or *N*-acetylglucosamine for murein) is general knowledge.[1] Carbohydrates and carbohydrate-containing structural moieties are also involved in more active biochemical and bioorganic processes. An enormous amount of precise biological studies of naturally occurring products and the mechanisms of action of these substances have shed light on the biological significance of the glycons of glycoconjugates (glycoproteins, glycolipids) in various domains such as the molecular recognition for the transmission of biological information.[2] Indeed, the presence of the sugars greatly modifies the biological activity of all the drugs. For instance, the glycan chains control the pharmacokinetics of the drugs, such as absorption, distribution, metabolism and excretion. Clearly, the aglycon itself is not active in most instances, as was demonstrated for many antibiotics and antitumour compounds, with erythromycin, daunomycin or amphotericin B being prominent examples. It is now well established that protein- and lipid-bound saccharides play essential roles in many molecular processes impacting eukaryotic biology and disease.[3] Examples of such processes include fertilisation, embryogenesis, neuronal development, hormone activities, the proliferation of cells and their organisation into specific tissues. Carbohydrates are found in nature as monomers, oligomers, or polymers, or as components of biopolymers and other naturally occurring substances. As domains of natural products, they play important roles in conferring certain physical, chemical, and biological properties to their carrier molecules. In addition, they have been implicated in many cellular processes, including cell–cell recognition, cellular transport, and adhesion; they appear in all cells in some form or another, for example, as peptido- and proteoglycans, glycoproteins, nucleic acids, lipopolysaccharides or glycolipids.[4] Indeed, carbohydrates are important elements of recognition and specificity in cell–cell interactions,[5,6] for example, as cell surface oligosaccharides,[7,8] for example, tumour-associated antigens,[9] lectins,[10,11] glycoproteins, glycolipids, and immunodeterminants. They also play a part in the mode of action of many drugs as they contribute to a variety of processes, including active transmembrane transport,[12,13] stabilization of protein folding,[14] and enzyme inhibition.[15,16] With this stimulating biological background, the *O*-glycosylation method, which is a crucial synthetic organic methodology to attach sugars to other sugar moieties or other molecules (aglycon), is again becoming more and more important. Since the major historical advance of the Koenigs–Knorr method was shown in 1901, considerable attention has been directed towards the efficiency of the *O*-glycosylation method.[17] From a synthetic standpoint, the efficiency of the *O*-glycosylation reaction generally involves a high chemical yield, regioselectivity, and stereoselectivity. Among these, the high regioselectivity was easily realised by the selective protection of the hydroxyl group of the glycosyl acceptor. Therefore, many organic chemists have focused on the high chemical yield and high stereoselectivity of this reaction. This review concentrates on the applications of the *O*-glycosylation reaction for the synthesis of biologically attractive natural products and analogues except steroidal glycosides, which have been the subject of a recent review (Scheme 1).[18]



Scheme 1. Glycosylations of aglycons in the formation of natural products and analogues.

This review is an update of the use of *O*-glycosylation in total synthesis covering the literature from 1993 to date, since early work has already been reviewed.[19] For a survey on the applications of the *O*-glycosylation reaction for the total synthesis of natural products and related compounds, glycosyl donors are roughly classified into five groups,