# SYNTHETIC APPROACHES TO THE PREPARATION OF NATURAL ACYL ARYL GLYCOSIDES

D.L. Avetian
Scientific advisor – Ph.D., Associate Prof. E.V. Stepanova
*National Research Tomsk Polytechnic University*
*634050, Russia, Tomsk, 30, Lenin Avenue, avetyanll@gmail.com*

Acyl aryl glycosides are naturally occurring organic compounds interesting for chemical research. Their bioavailability and activity make them prospective drugs while their wide presence in plants as secondary metabolites makes them useful as chemotaxonomic markers [1].

The structures of acyl aryl glycosides vary at carbohydrate, aglycon and ester parts giving different biological activities [2]. For instance, vanilloloside **1** (Figure 1) lacks anti-cancer activity [3] whilst its 6-*O*-vanilloyl **2** ester shows high antiproliferative effect on cancer cells [4]. There are also natural glycosides acylated at aglycon with prospectively high biological activity [2–4]. The studies also assert aryl glycosides are of low toxicity [5].

Our main research is related to the study of glucopyranosides of vanillyl alcohol and its analogs. We set our goal to obtain acylated derivatives of such substances at aglycon and carbohydrate moieties separately or at the same time. Thus, we de-

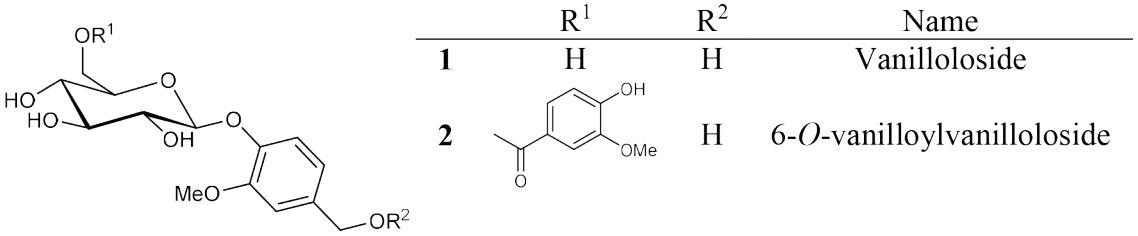


**Fig. 1.** *The structures of vanilloloside **1** and 6-O-vanilloylvanilloloside **2***

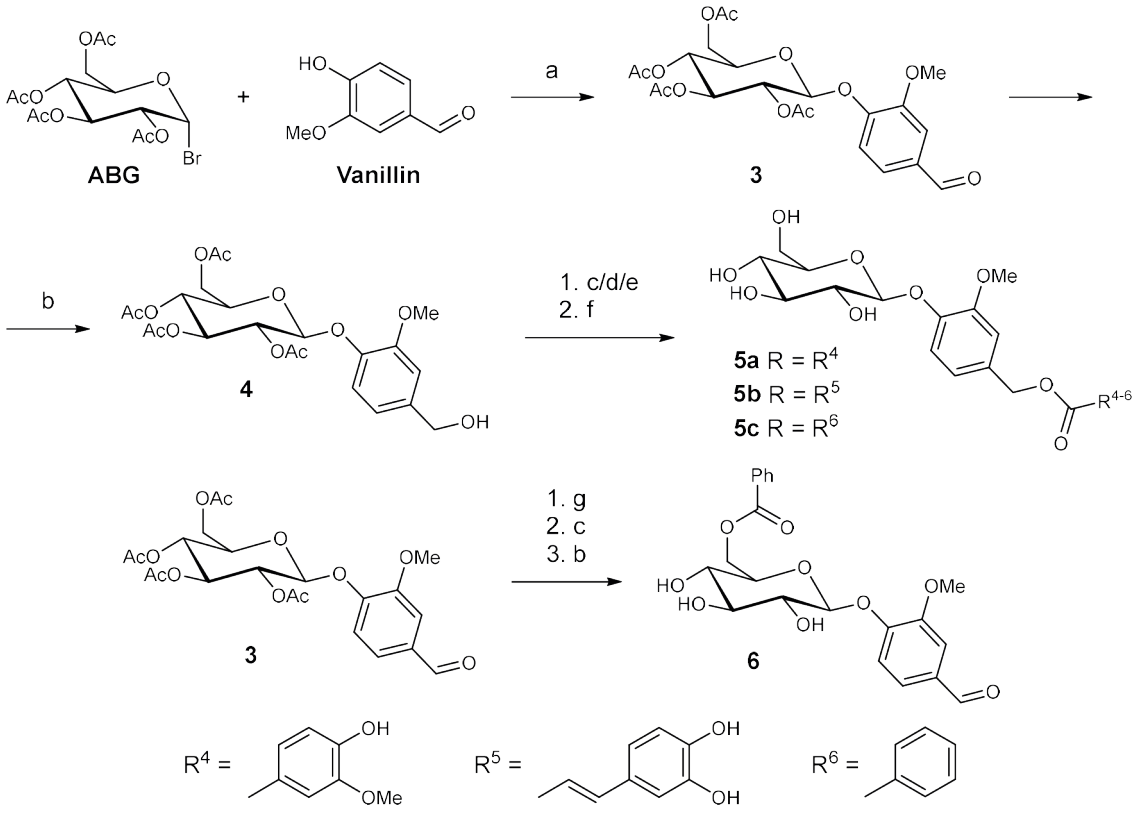


**Fig. 2.** ***a*** *– KOH, acetone/$H_2O$;* ***b*** *– $NaBH_4$, CTMAB, $H_2O/CHCl_3$;* ***c*** *– $R^{4-6}$(O)Cl, Py, DCM;* ***d*** *– $R^{4-6}$(O)OH, DCC/DMAP, DCM;* ***e*** *– 1. $CBr_4$, $PPh_3$, DCM; 2. $R^{4-6}$(O)OH, $K_2CO_3$, DMF;* ***f*** *— HCl/EtOH/$CHCl_3$ (1 : 3 : 1 vol.);* ***g*** *— MeONa, MeOH*

veloped several synthetic approaches to achieve this (Figure 2).

We started with vanillin glycosylation (Figure 2-a) to obtain vanillinoside **3** which was further reducted to the alcohol **4** (Figure 2-b) by $NaBH_4$ in the presence of CTMAB (cetyltrimethylammoniumbromide) as phase-transfer catalyst. Then this glycoside **4** was treated in three different ways to obtain corresponding esters: with benzoyl and acetylated vanilloyl and caffeoyl chlorides and pyridine (Figure 2-c); with acetylated benzoic, caffeic and vanillic acids in DCC/DMAP system (Figure 2-d); with application of an Appel reaction to and further acylation pf the bromide with the same acids in the presence of $K_2CO_3$ (Figure 2-e). The final deacetylation was carried out in selective system of $HCl/EtOH/CHCl_3$ (1 : 3 : 1 vol.) [6] giving products **5a-c** (Figure 2-f).

The aldehyde **3** was also deacetylated with sodium methylate (Figure 2-g). Deprotected carbohydrate then was exposed to esterification with benzoyl chloride. As it could be expected, primary hydroxyl 6-OH showed the highest reactivity giving the ester **6** in yields of approximately 35 % though with several by-products whilst the conversion was not complete.

The reported study was funded by RFBR, project number 19-31-27001.

## References

1. *Lindroth R.L., et al. // Oecologia, 1987. – №70. – P. 144.*
2. *Argyropoulou A., et. al. // Phyther. Res., 2012. – №26. – P. 1800–1806.*
3. *Wang Q.-H., et.al. // J. Mol. Struct., 2014. – №1074. – P. 284–288.*
4. *Rayavarapu S., et.al. // Sci. Rep., 2017. – №7. – P. 8309.*
5. *Itoh A., et. al. // Phytochemistry, 2008. – №69. – P. 1208–1214.*
6. *Stepanova E.V., et al. // Carbohydr. Res., 2014. – №388. – 3. – 105–111.*

# FABRICATION OF BACTERICIDAL 3D GRADIENT MATERIALS BASED ON HYDROXYAPATITE

V.T. Badretdinova[1], T.A. Serykh[1]
Scientific supervisor – PhD, associate research professor S.A. Ulasevich[1];
PhD associate research professor A.P. Chernova[2]

*[1]ITMO University*
*197101, Russia, St Petersburg, Lomonosova St. 9*

*[2]National Research Tomsk Polytechnic University*
*634050, Russia, Tomsk, 30 Lenin Avenue, badretdinova@infochemistry.ru*

Reparation of bone tissue is a topical medical problem. It is so significant due to the spread of bone tissue pathological conditions, caused, in particular, as a result of trauma, tumor (primary and metastatic) lesions, age-related osteoporosis [1]. One of the rational ways to solve the problem is using the synthetic biocompatible materials. The most promising materials are based on calcium phosphates, which are close in composition to the mineral component of bone tissue [2]. The use of chemically synthesized calcium phosphate materials opens up more and more possibilities for eliminating bone defects. Biocompatible and bioactive hydroxyapatite (HA) can be easily integrated into bone tissue and adjacent tissue areas. In addition, HA is able to interact with young bone tissue cells – osteoblasts, positively affecting their growth and division. [3].

In medicine, there is a need for osteoplastic materials, including medicinal substances, which allow targeted action on the identified pathogens. Local delivery of antibacterial substances allows to reduce the toxic effect on the patient, to use antibiotics in smaller quantities than orally, and to deliver stable constant concentrations.

In this regard, the goal of this work is to create calcium phosphate materials that include medicinal substances that will inhibit the growth of bacteria. Such material will have antibacterial properties. First of all, we made gradient samples with calcium phosphate, varying the concentration of antibiotics. Tetracycline and gentamicin were used as model antibiotics. Samples were prepared in six-well plates. We also made a control sample consisting of calcium phosphate without antibiotics. Next, we investigated the biocompatible properties of structures