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Novel Calix[4]resorcinarene Glycosides

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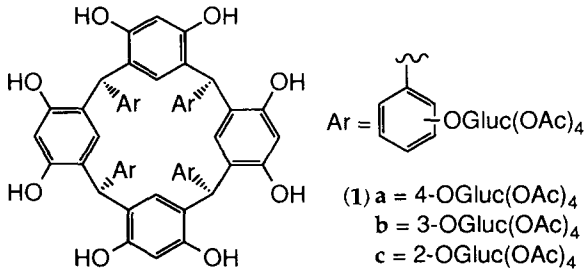
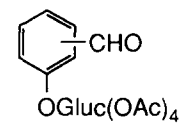
Abstract: Calix[4]resorcinarene glycosides may be prepared using mild conditions by condensing the corresponding glycosidic aldehyde with resorcinol in the presence of a Lewis acid. The protected glycosyl moieties confer enhanced solubility in a number of organic solvents whilst deprotection provides resorcinarenes which are water soluble.

A wealth of knowledge has been amassed concerning calix[n]arenes and the related calix[n]resorcinarenes (resorcinarenes), a recent review detailing the latter's development as useful supramolecular frameworks.[1,2] Resorcinarenes are attractive for investigation as they are prepared with remarkable ease from readily-available materials. This letter describes the synthesis of glycosidic resorcinarenes as exemplified by compounds (**1a-c**).

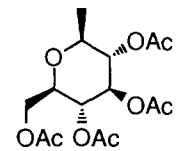


Ar =

(**1**) **a** = 4-OGluc(OAc)$_4$
b = 3-OGluc(OAc)$_4$
c = 2-OGluc(OAc)$_4$



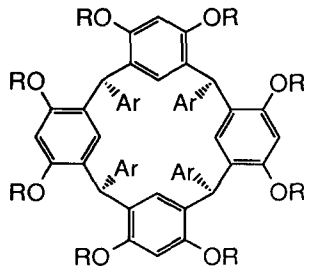
(**2**) **a** = 4-CHO
b = 3-CHO
c = 2-CHO

Gluc(OAc)$_4$ = 

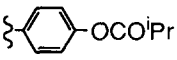
The aforementioned review outlines syntheses of resorcinarenes which have been profitably used by Högberg, Cram and Reinhoudt.[2,3] However, the conditions generally required (alcoholic hydrochloric acid) do not tolerate much variation in functionality of the starting materials. The reviewers note a report in which a simple resorcinarene was prepared using Lewis acid catalysts:[4] this cached report provided the incentive to explore the use of Lewis acids in the preparation of resorcinarenes from acid-sensitive precursors.

Our efforts have been directed towards the synthesis of resorcinarenes (**1a-c**) from glycosidic aldehydes (**2a-c**). The advantages of attaching a glycosidic moiety to the resorcinarene framework are manyfold: the protected carbohydrate confers improved solubility in organic solvents and also aids in the separation of conformational isomers.[3,4] For example, condensation of aldehyde (**2a**) with resorcinol in the presence of aluminium chloride gave a resorcinarene, soluble in a wide variety of organic solvents.[5] Acylation and chromatography enabled the isolation of a major (49%) and a minor (17%) isomer, deduced to be resorcinarenes by analogy with the ^{1}H NMR spectrum of known compound (**4**).[3] The major product is assigned to be the ctt (chair) conformer and the minor the ccc (boat) conformer. MALDI-TOF mass spectral analysis of both butyrated isomers gave a molecular ion at m/z 2736.

Deacylation of the major isomer with $MeOH/H_2O/Et_3N$ (the product of deacylation is water-soluble), followed by hydrolysis and rebutyration yielded derivative (**5**), also accessible from a known resorcinarene aglycone.[6] This enables the positive assignment of structure (**6**) to the major butyrated resorcinarene glycoside and, hence, structure (**1a**) to the condensation product from reaction of glycoside (**2a**) with resorcinol in the presence of aluminium chloride.



(**4**) R = CO^{i}Pr, Ar = Ph

(**5**) R = CO^{i}Pr, Ar = 

(**6**) R = CO^{i}Pr, Ar = 

As stated above, the carbohydrate moieties confer differing solubility in aqueous or non-aqueous media, depending on their state of protection. Glycosylated calix[4]arenes have been previously reported.[7] We are currently investigating the use of resorcinarene glycosides as chiral receptors and in the synthesis of novel supramolecular assemblies.

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5. Representative procedure: Aldehyde (**2a**) (2.26 g, 5 mmol) was dissolved in a mixture of dry Et_2O and dry THF (1:1 ratio, 40 cm^3) under argon. $AlCl_3$ (2.5 mmol, solution in $PhNO_2$) was added and the mixture stirred at room temperature for 15 minutes. Resorcinol (0.55 g, 5 mmol) was added in one portion and stirring continued for a further 20 hours. The mixture was added to Et_2O (100 cm^3); the precipitate obtained was filtered, washed well with Et_2O and resuspended in H_2O (200 cm^3). EtOAc (100 cm^3) was added and the mixture shaken vigorously. The organic layer was separated, washed with H_2O (2 x 100 cm^3), dried ($MgSO_4$) and the solvent removed to deliver resorcinarene (**1a**) as a yellow solid. Acylation, using butyric anhydride (30 cm^3) and pyridine (5 cm^3) at 80 °C for 24 hours, followed by removal of excess reagents by distillation and purification by silica-gel chromatography (EtOAc as eluant) delivered the major and minor butyrated resorcinarenes. All compounds gave satisfactory analyses.
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7. Marra, A.; Dondoni, A.; Sansone, F. *J. Org. Chem.*, **1996**, *61*, 5155; Marra, A.; Scherrmann, M-C.; Dondoni, A.; Casnati, A.; Minari, P.; Ungaro, R. *Angew. Chem. Int. Ed. Engl.*, **1994**, *33*, 2479.

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