New fluorescent amino carbohydrate derivatives

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Abstract

A series of new fluorescent, *N*-functionalized derivatives of D-glucosamine have been prepared in good yields by nucleophilic attack of the amino group to activated carboxycoumarins, and by reductive amination of fluorescent aldehydes.

Keywords

Carbohydrates, Fluorescent carbohydrates, D-glucosamine, coumarins, reductive amination, fluorescent aldehydes.

Introduction

The interest of fluorescent compounds is due primarily to two facts: their extensive applications[1] and their highly sensitive and specific detection methods.[2] In particular, fluorescent carbohydrates have a wide range of applications in biology and environmental technology. For example, water soluble glucose based imino-anthracenyl derivatives have been shown to recognize specifically Hg^{2+} (which is highly toxic and causes DNA damage and impair mitosis) by *switch-on* fluorescence.[3]

With the aim to generate new derivatives with biological, pharmacological and technological properties, we design the here presented compounds using as diversity point (Scheme 1), the amino group. We have selected coumarins as chromophore units (CU), due to their demonstrated anticoagulant activity and easy availability. On the other hand, fluorescent aldehydes have been chosen as fluorescence sources for their chemosensor potential activity in a wide variety of fields.

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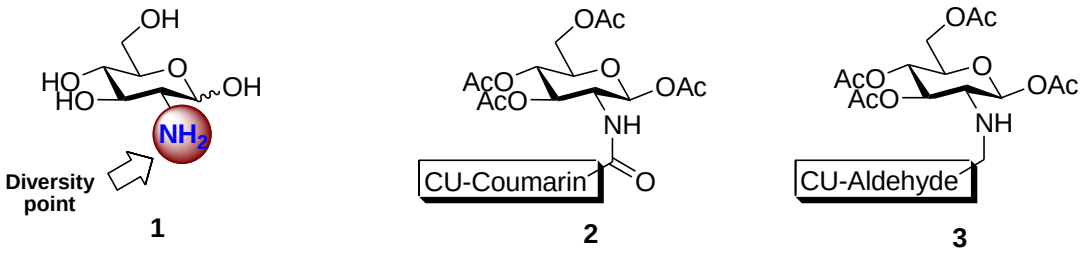
[1] Lee, D.Y.; Singh, N. and Jang, D. O. *Tetrahedron Lett*. **2010**, 51, 1103.
[2] a) Rettig, W. *Applied Fluorescence in Chemistry, Biology and Medicine*; Springer: New York, **1999**. b) Christensen, L.; Norgaard, R.; Bro, S. and Engelsen, B. *Chem. Rev*. **2006**, *106*, 1979.
[3] Mitra, A.; Mittal, K. A. and Rao, P. C. *Chem. Comm.*, **2011**, *47*, 2565 and references therein.

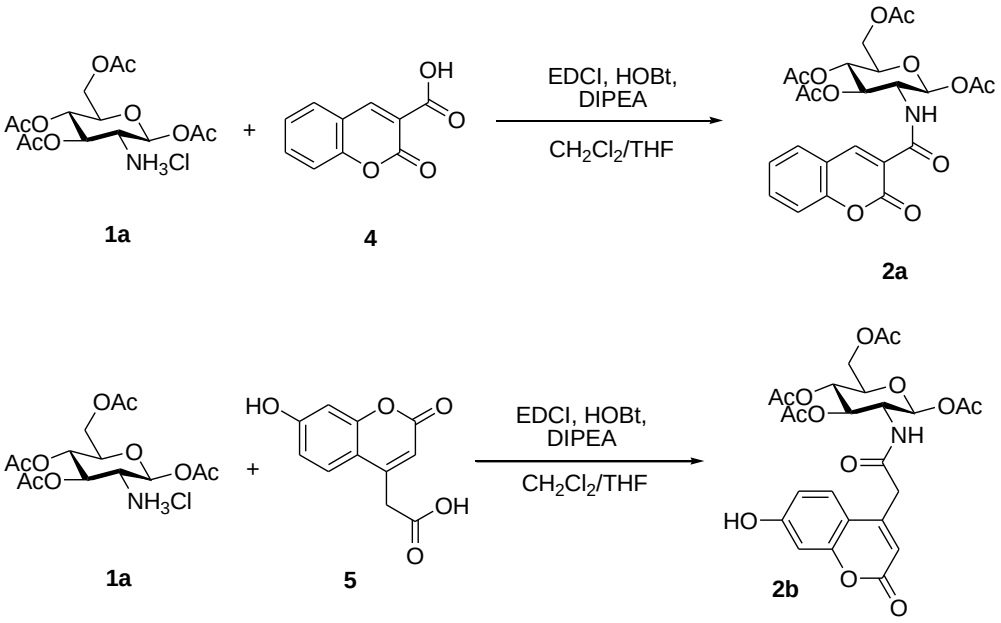


Scheme 1

Results and Discussion

We report here on new fluorescent derivatives of D-glucosamine (**1**) previous protection of its hydroxyl groups. These derivatives having general structures **2** and **3**, have been prepared in good yields by: a) nucleophilic attack of the amino group to activated carboxycoumarins, and b) by reductive amination, respectively.

Two new D-glucosamine derivatives, **2a** and **2b**, containing coumarin as chromophore unit have been prepared by using commercial coumarin-3-carboxylic acid (**4**) and 7-hydoxycoumarin-4-yl acetic acid (**5**),[4] respectively (Scheme 2).

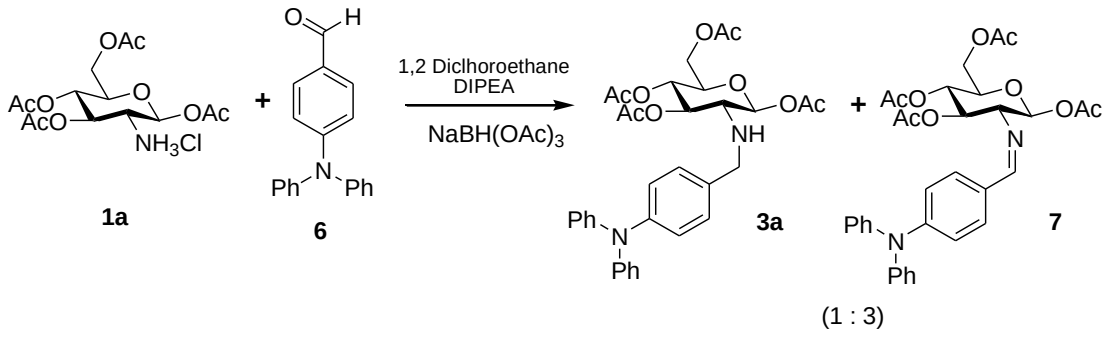


Scheme 2

On the other hand, we have carried out the reaction of tretra-*O*-acetylated D-glucosamine hydrochloride **1a** with a fluorescent aldehyde, 4-diphenylamino benzaldehyde (**6**). Reductive amination was carried out by using sodium triacetoxy

[4] Yao, S.Q. y colaboradores. *Org. Lett.* **2003**, *5*, 1257.

borohydride as reducing agent and DIPEA as a base, in 1,2-dichloroethane,[5] as shown in Scheme 3. ^{1}H-NMR of the obtained product indicated that it was a mixture of the desired product **3a** and the corresponding precursor imine **7** in a 1:3 ratio.



Scheme 3

Experimental

All new compounds were characterized by their IR, ^{1}H-NMR (500 MHz), ^{13}C-NMR (125.7 MHz), and HRMS spectral data.

a) Synthesis of coumarin derivatives of general structure 2.

To a solution of compound **1a** (200 mg, 0.52 mmol) in dry CH_2Cl_2 (10 mL), coumarin acid derivatives **4** or **5** derivatives (0.782 mmol) previously dissolved in THF, and HOBt (1.56 mmol) were added under argon atmosphere. The mixture was cooled to 0ºC. Afer 10 min. 90 μL (0.52 mmol) of DIPEA and 225 mg (1.17 mmol) de EDCI were added. The reaction was allowed to warm to ambience temperatura overnight. The mixture was diluted with CH_2Cl_2 and washed with 1M HCl, aq. sat. K_2CO_3, water and brine. After washing over Na_2SO_4, the solution was evaporated and purified by column chromatography (Hexane/AcOEt) to give **2a** or **2b** in 66% and 68% yield, respectively.

b) Experimental procedure of reductive amination.

4-*N*-Diphenylamino benzaldehyde (**6**, 51,11 mg, 0,187 mmol) was dissolved in 1,2-DCE (5mL). On the other hand, 2-amino-2-deoxy-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (100mg, 0,260 mmol) was dissolved also in 1,2-DCE, and

[5] Vera-Ayoso, Y., Borrachero, P., Cabrera-Escribano, F., Gómez-Guillén, Pierre Vogel. *Synlett* **2006**, *1*, 45.

treated with DIPEA (0,391mmol). Both solutions were joined with stirring and then sodium triacetoxyborohydride (0,200mmol) was added. After 72 h, working up of the reaction by treatment with aq. Sat. $NaHCO_3$, and then extracted with EtOAc, dried, and evaporated to give a product that after purifying gave a chromatographically homogeneous product, whose ^{1}H-RMN indicated to be a 1:3 mixture of compounds **3a** and **7**.

Acknowledgments

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