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SYNTHESIS OF 2-AMINO-3-HYDROXYACETOPHENONE-O-β-D-GLUCOPYRANOSIDE : A FLUORESCENT COMPOUND FROM INSOLUBLE PROTEIN FRACTION OF AGING HUMAN LENS

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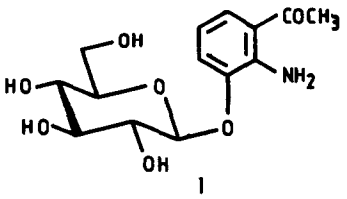
Abstract The synthesis of the title fluorescent glycoside associated with insoluble protein fraction of aging human lens is described.

The physiological and the chemical changes, occurring in the human lens, has been the topic of profound interest for many decades[1]. The yellowing of an aging eye is attributed to the presence of fluorescent substances whose production increases with age. The isolation and structural elucidation formed the basic premise for many investigators who have indeed struggled long in identifying[2] these products. A new fluorescent compound has been recently isolated from the insoluble protein fraction of aging human lens and its structure : 2-amino-3-hydroxyacetophenone-O-β-D-glucopyranoside (**1**) was established[3] by enzymatic degradation and NMR-IR-UV studies. This communication describes for the first time, the total synthesis of this novel fluorescent glycoside (**1**) by involving Schmidt's trichloroacetimidate approach[4] for the stereospecific O-glycosylation.



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The requisite aglycone, namely 2-nitro-3-hydroxyacetophenone (**3**) was prepared by the nitration (HNO_3, AcOH, 70°, 6h) of 3-hydroxyacetophenone (**2**). The required nitroderivative (**3**) was easily isolated from the isomeric mixture by simple crystallization (40%)[5].

2,3,4,6-Tetra-O-acetyl-D-glucopyranosyl-trichloroacetimidate (**6**) was chosen as the glycosyl donor whose preparation from D-glucosepentaacetate (**4**) involved selective deacetylation[6] at 0-1 by using tributyltinethoxide ($ClCH_2CH_2Cl$, Δ, 3h) to afford the hemiacetal derivative (**5**) (85%). Treatment of **5** with trichloroacetonitrile in the presence of DBU (CH_2Cl_2, RT, 15 min) gave **6** (quantitative).

The coupling reaction of **3** and **6** was performed in the presence of a catalytic amount of BF_3:OEt_2 (CH_2Cl_2, -5° to RT, 3h) to afford the β-glycoside (**7**) (70%) confirmed by ^1H NMR and ^{13}C NMR spectroscopies. The catalytic reduction (PtO_2, MeOH, 45 psi, H_2 30 min) of the nitro-group in **7** then gave the amine **8** which was finally deacetylated (MeOH, NaOMe, RT,

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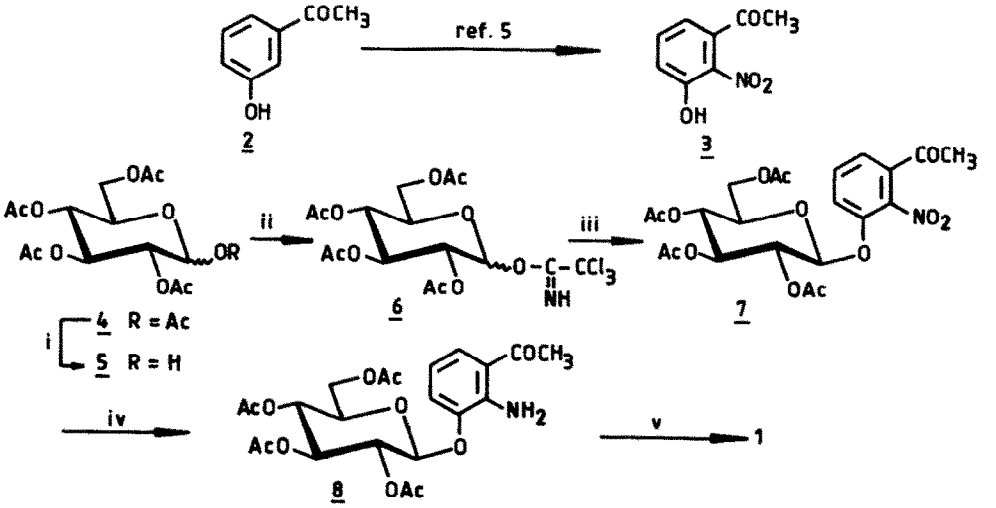

i) Bu_3SnOEt, $ClCH_2CH_2Cl$, 3h ; ii) CCl_3CN, DBU, CH_2Cl_2, R T, 15 min. ; iii) $BF_3:OEt_2$, CH_2Cl_2, -5°–R T, 3h ; iv) PtO_2, H_2, MeOH, 45psi, 30min. ; v) NaOMe, MeOH, R T, 1h

1h) to provide the title product (**1**) (70% from **7**). The spectral properties[7] of **1** were identical with those reported[3] for the natural product.

References and Footnotes

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7. Spectral properties of **1** : ^1H NMR (D_2O, 200 MHz): δ 2.65 (s, 3H), 3.63 (m, 4H), 3.81 (dd, 1H, J=4.5, 11.4 Hz), 3.97 (dd, 1H, J 2.3, 11.4 Hz), 5.07 (d, 1H, J=8.0 Hz), 6.79 (t, 1H, J=8.0 Hz), 7.36 (d, 1H, J=8.0 Hz), 7.70 (d, 1H, J=8.0 Hz), UV (H_2O)λ_{max} 261 (ε = 4500) and 361 (ε = 3500), IR (KBr) : 3450 and 1180 cm^{-1}, MS : m/z 312 (M^++1). All new compounds exhibit satisfactory spectral and elemental/mass analysis.

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