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STEREOCONTROLLED SYNTHESES OF PHYTOALEXIN ELICITOR-ACTIVE β-D-GLUCOHEXAOSIDE AND β-D-GLUCONONAOSIDE[1]

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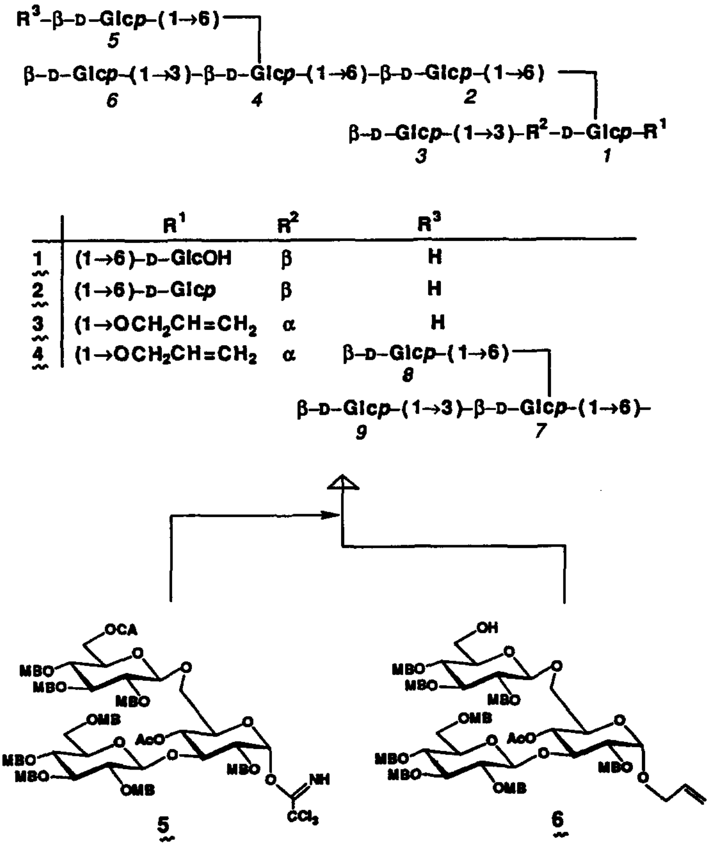
Abstract: Unambiguous synthetic routes to elicitor-active β-D-glucohexaoside as well as β-D-gluconoaoside were described in a stereocontrolled manner. Minimum structure required for the elicitor activity is β-D-glucohexaoside.

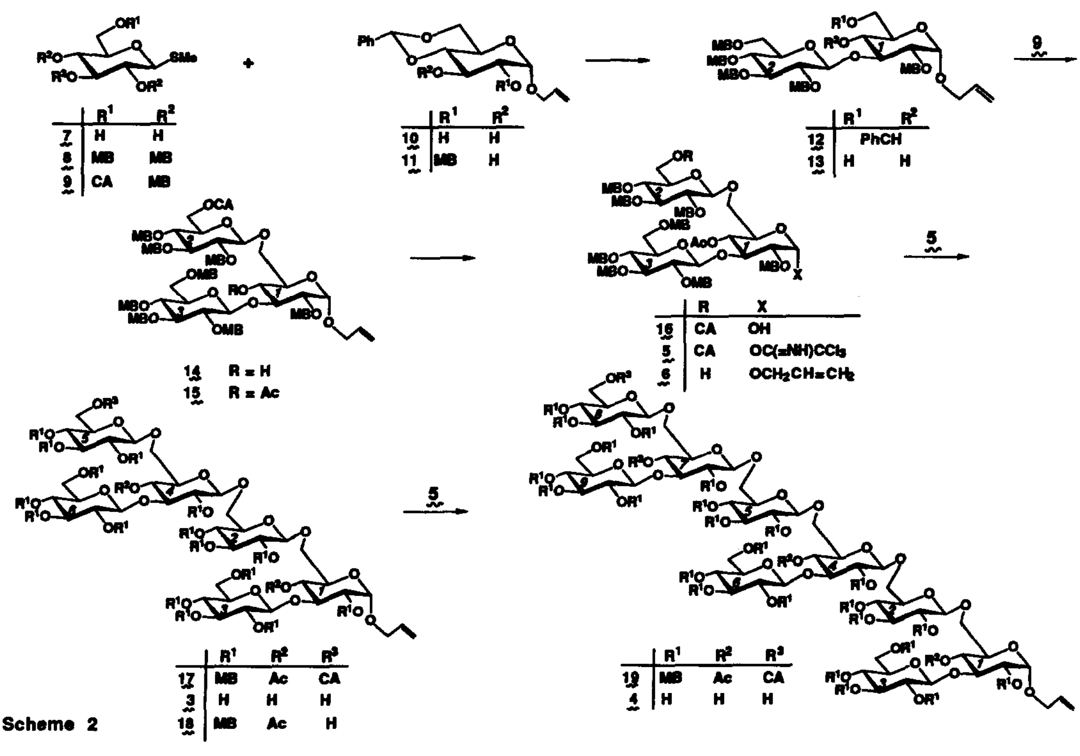
Plants respond to invasive microbes at the site of infection by the accumulation of phytoalexins[2], the biosynthesis of which is induced by molecules called elicitors[3].



Scheme 1 (MB = 4-Me-Bz, CA = ClCH$_2$CO)

In 1984, Sharp and co-workers[4] purified and characterized an elicitor-active β-D-glucohexaosyl glucitol **1** after partial hydrolysis of the mycelial walls of the fungal pathogen *phytophthora megasperma f. sp. glycinea.* The proposed structure **1** was confirmed by Garegg and co-workers[5] through the unambiguous synthesis of β-D-glucohepatose **2** that had elicitor-activity equivalent to that of natural product. As part of our experiments directed toward the elucidation of structure-activity relationship of these β-D-glucooligoses, we now describe the unambiguous synthesis of β-D-glucohexaoside **3** and its higher homologue gluconaoside **4**, which eventually showed the minimum structural requirement for the phytoalexin elicitor-activity is glucohexaoside **3**.

A retrosynthetic consideration of the targets **3** and **4** led us to design a β-D-glucotriosyl donor **5** and a glucotriosyl acceptor **6** as two key intermediates which were prepared in a straightforward manner. Glycosylation of a glucosyl acceptor **11** (83% from **10**[6], *1* Bu_2SnO, *2* MeBzCl) with a donor **8**[7] (87% from **7**, MBzCl in Py) in the presence of MeOTf[8] and powdered molecular sieves 4A (MS4A) in CH_2Cl_2 gave 87% of **12**, which was hydrolysed to diol **13** (90%, 7:3 AcOH-H_2O at 80°). Methyl thioglucoside **7** was converted to a glucosyl donor **9** in 4 steps (*1* TrCl, Py, *2* MeBzCl, *3* 8:2 AcOH-H_2O, *4* $(ClCH_2CO)_2O$, DMAP in Py, overall 49%). MeOTf-MS4A Promoted glycosylation of **13** with **9** gave 80% of **14** which was further converted into a glycotriosyl donor **5** via **15** and **16** in 3 steps (*1* Ac_2O in Py, *2* $PdCl_2$-AcONa-AcOH-



Scheme 2

H_2O[9], *3* Cl_3CCN, DBU in Cl_2CH_2[10], overall 26%). Another key intermediate **6** was readily prepared from **15** in 93% by treatment with NH_2CSNH_2 in EtOH[11].

Crucial coupling between **5** and **6** was achieved in the presence of $BF_3 \bullet OEt_2$ and MS AW-300 in $(CH_2Cl)_2$ to give 74% of **17** which was quantitatively deprotected by NaOMe in MeOH and purified by Sephadex G10 in H_2O to give **3**. On the other hand, selective deprotection of **17** afforded 70% of a glucohexaosyl acceptor **18** which was again glycosylated with **5** under the same condition as above to give 18%[12] of **19**. Deacylation of **19** in NaOMe-MeOH afforded **4**. Both synthetic β-D-glucooligosides **3** and **4** have elicitor-activity equivalent[13] to that of **1**, hence glucohexaoside **3** is at the moment a mininum necessary unit for the elicitor-activity. In addition, it is to be noted that the β-D configuration at C-1*1* in the original elicitor molecule **1** is not required for the elicitor-activity. It may be postulated that in the molecule **3** D-glucosyl residues *1*, *2* and *4* play roles as the scaffolding while the residues *3*, *5*, and *6* as the biological signals which interact with a putative receptor protein. Based on this line of reasoning, further modification of structure **3** is under current investigation.

In summary, an unambiguous synthetic routes to the targets **3** and **4** were developed and the minimun structural requirement for the elicitor-activity is now regarded as a glucohexaoside **3**.

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References and Notes

1 Part 9 in the series "Synthetic studies on plant cell wall glycans". For part 8, see K. Sakai, Y. Nakahara, and T. Ogawa, submitted for publication.

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7 Physical data for key compounds are described below. Values of $[\alpha]_D$ and $\delta_{H,C}$ were measured for $CHCl_3$ and $CDCl_3$ solution, respectively, at 23°±3°, unless noted otherwise. **3**: $[\alpha]_D$ +65.0° (c 0.1, H_2O); δ_H (D_2O, 60°) 4.986 (d, 3.8 Hz, 1^{1}), 4.726 and 4.704 (2d, 7.9 Hz, $1^{3,6}$), 4.563, 4.511 and 4.505 (3d, 7.9 Hz, $1^{2,4,5}$). **4**: $[\alpha]_D$ -184° (c 0.08, H_2O); δ_H (D_2O, 60°) 4.988 (d, 4.0 Hz, 1^{1}), 4.730, 4.726 and 4.705 (3d, 7.9 Hz, $1^{3,6,9}$), 4.569, 4.556, 4.523, 4.513 and 4.508 (5d, 7.6~7.9 Hz, $1^{2,4,5,7,8}$). **5**: $[\alpha]_D$ +25.0° (c 0.9); δ_H 8.11 (s, C=NH), 6.34 (d, 3.7 Hz, 1^{1}), 4.95 and 4.90 (2d, 7.6 Hz, $1^{2,3}$), 2.46, 2.40, 2.35, 2.34, 2.30, 2.29, 2.27 and 2.25 (8s, 8 x MePh), 1.99 (s, Ac). **6**: $[\alpha]_D$ +33.4° (c 1.0); δ_H 4.99 and 4.85 (2d, 7.9 Hz, $1^{2,3}$), 2.48, 2.42, 2.35, 2.33, 2.30, 2.28, 2.27 and 2.25 (8s, 8 x MePh), 2.00 (s, Ac). **8**: $[\alpha]_D$ +34.6° (c 1.0); δ_H 4.72 (d, 9.8 Hz, 1), 2.39, 2.35, 2.34, 2.31 and 2.28 (5s, 4 x MePh and MeS). **9**: $[\alpha]_D$ +8.2° (c 1.0); δ_H 4.70 (d, 10.1 Hz, 1), 2.35, 2.35, 2.28 and 2.25 (3s, 3 x MePh and MeS). **11**: $[\alpha]_D$ +111° (c 1.0); δ_H 5.58 (s, CHPh), 5.20 (d, 3.9 Hz, 1), 2.41 (s, MePh). **12**: $[\alpha]_D$ +44.6° (c 1.0); δ_H 5.13 (d, 4.0 Hz, 1^{1}), 5.10 (d, 7.9 Hz, 1^{2}), 2.44, 2.36, 2.33, 2.30 and 2.24 (5s, 5 x MePh). **13**: $[\alpha]_D$ +64.7° (c 1.0); m.p. 211-213° (EtOAc-hexane); δ_H 5.09 (d, 4.0 Hz, 1^{1}), 4.99 (d, 7.9 Hz, 1^{2}), 2.43, 2.41, 2.35, 2.24 and 2.23 (5s, 5 x MePh). **14**: $[\alpha]_D$ +26.6° (c 1.0); δ_H 4.92 and 4.89 (2d, 7.9 Hz, $1^{2,3}$), 4.83 (d, 4.0 Hz, 1^{1}), 2.44, 2.42, 2.36, 2.36, 2.30, 2.28, 2.25 and 2.23 (7s, 8 x MePh). **15**: $[\alpha]_D$ +36.4° (c 1.0); δ_H 4.99 and 4.83 (2d, 8.0 Hz, $1^{2,3}$), 2.48, 2.43, 2.35, 2.34, 2.30, 2.28, 2.27 and 2.25 (8s, 8 x MePh), 1.98 (s, Ac). **17**: $[\alpha]_D$ +23.0° (c 1.0); δ_H 2.512, 2.417, 2.417, 2.379, 2.362, 2.334, 2.334, 2.327, 2.314, 2.295, 2.257, 2.257, 2.218, 2.182, 2.145 and 2.102 (13s, 16 x MePh), 1.882 and 1.798 (2s, 2 x Ac). **18**: $[\alpha]_D$ +31.1° (c 0.5); δ_H 2.505, 2.438, 2.406, 2.377, 2.356, 2.350, 2.338, 2.330, 2.305, 2.290, 2.290, 2.266, 2.260, 2.225, 2.154 and 2.120 (15s, 16 x MePh), 1.923 and 1.911 (2s, 2 x Ac). **19**: δ_H 2.515, 2.407 (x2), 2.382, 2.371, 2.360 (x2), 2.337 (x2), 2.312, 2.307 (x3), 2.282, 2.256 (x3), 2.230, 2.219, 2.200, 2.190 (x2), 2.145 and 2.083 (16s, 24 x MePh), 1.896, 1.846 and 1.796 (3s, 3 x Ac).

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