s8a.m8.p3 **The first step of tetanus toxin into nerve cell.** C. Fotinou[a], K.A. Shina[b], H. Ando[c], H. Ishida[c], I. Black[a], P. Emsley[a], M. Kiso[c], N. Fairweather[b] and N.W. Isaacs[a]. [a]*Department of Chemistry, University of Glasgow,* [b]*Department of Biochemistry, Imperial College and* [c]*Department of Chemistry, Gifu University.*
Keywords: drug design.

Tetanus toxin (TeNT) and the botulinum toxins (BoNTs) are extremely potent neurotoxins produced by the anaerobic bacteria, C.tetani and C. botulinum respectively. They exhibit zinc endopeptidase activity [1] [2].

Tetanus neurotoxin invades neuronal cells first by binding to the gangliosides on the cell surface. The gangliosides GT1b, and GD1b have been identified as those with the highest affinity. Tetanus toxin consists of two chains, heavy and light, which are disulfide bridged. The C-terminal part of the heavy chain (Hc) has been found to contain the ganglioside binding site(s) which were not well characterized.

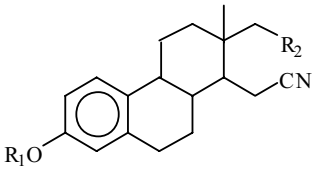
The three-dimensional structure of the complex of Hc plus the carbohydrate part of GT1b has been determined to 2.3 Å. It provides the first direct identification and characterization of the ganglioside binding sites. The involvment of the disialo-group and the external Gal in the binding and the identity of residues of the Hc part of the Tetanus toxin forming the binding sites are consistent with the biochemical evidence that exists to date.

Such information is not only useful in understanding the pathogenesis of Tetanus toxin and designing more efficient vaccines, but also in modelling the ganglioside-botulinum toxins interactions. A side-product of this work is the three-dimensional structure of the heptasaccharide of the GT1b.

[1] C.Montecucco & G.Schiavo, Quarterly Rev. of Biophysics, 28, (4) , 423-472, (1995).
[2] Niemann, H. In Sourcebook of bacterial protein toxins, Alouf, J.E and Freer, J.H., eds, 303- 348, Academic Press, London, (1991).

s8a.m8.p4 **Structure-activity relationships in some D-seco estrone derivatives.** S. Stankovic, D. Lazar, T. Pilati*, S. Jovanovic-Santa, J. Petrovic, R. Kovasevic, *Faculty of Sciences, University of Novi Sad, Trg D. Obradovi}a 4, 21000 Novi Sad, Yugoslavia,* **CNR-Centro per lo Studio delle Relacioni tra Struttura e Reattivita Chimica, via Golgy 19, 20133 Milano, Italy.*
Keywords: antiestrogens, structure, activity.

In the frame of a broader project directed towards obtaining potential antiestrogens, in several steps starting from estrone, four new D-seco estrone derivatives (**1**–**4**) have been synthesized. Biological tests revealed a total loss of estrogenic activity and a moderate antiestrogenic action for all the tested substances.



1 R_1=H R_2=OH
2 R_1=H R_2=Cl
3 R_1=$CH_2C_6H_5$ R_2=Br
4 R_1=H R_2=$OSO_2C_6H_4CH_3$

The compounds have been subjected to X-ray structural analysis to permit structure-activity reltionship studies.

	a (Å)	b (Å)	c (Å)	β (^{0})
1	8.058(1)	9.355(1)	21.129(1)	90.000
2	12.293(1)	8.947(1)	14.635(2)	97.876(5)
3	7.672(1)	14.762(1)	10.123(1)	108.198(6)
4	10.194(1)	7.766(1)	30.158(2)	99.343(7)

R-factors for compounds 1, 2 and 3 are 0.035, 0.031 and 0.035, respectively. For compound 4 in this stage of refinement R-factor is 0.130.

Molecular mechanic calculations were performed to determine minimum energy comformation.