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An asymmetric approach to the synthesis of a carbon-11 labelled gliotransmitter D-serine

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Endogenous D-serine is a co-transmitter of glutamate for synaptic N-methyl-D-aspartate receptors (NMDARs). Receptor affinity for binding D-serine versus glycine depends on its GluN2 subunit composition. For the activation of NMDARs glutamate binds to the GluN2 subunit of the receptor and a second ligand binds to the GluN1 subunit. D-serine is an endogenous ligand for the glycine site of the GluN1 subunit receptors in the brain in the case when NMDARs composed of the GluN1 and the GluN2A subunits. NMDARs composed of the GluN1 and the GluN2B subunits preferentially bind glycine at GluN1 sites [Madry, 2007]. Biosynthesis of D-serine requires epimerisation of L-serine in neurones by serine racemase. Resulting D-serine is transported into astrocites for storage. Na+-independent alanine–serine–cystein transporter-1 is found exclusively in neurons, Na+-dependent ASCT1 and ASCT2 are present in both neurons and astrocites. It was demonstrated D-serine plays an important role in the formation and maturation of synaptic contacts and in earlier stages of neuronal circuit construction, as a regulator of neuroblast migration in the developing brain. It has been tested as a therapeutic agent for the treatment of schizophrenia, depression, Parkinson disease and post traumatic stress disorder (PTSD) [Van Horn, 2013].

We performed a key step in the synthesis of carbon-11 labelled D-serine: creation of the chiral centre by the condensation of carbon-11 labelled formaldehyde [Hooker, 2008] with a glycine synthon [Popkov, 2012]. Decay corrected radiochemical yield of the hydroxymethylated complex was above 20%. The observed ratio of diastereomers vary; in the best experiments the d. e. was above 90%. Purification of the L,D diastereomer on a C18 HPLC column takes 8 min. Optimisation of SPE purification is in progress. Hydrolysis of the complex will take up to 3 min.

Literature

J.M. Hooker, M. Schönberger, H. Schieferstein, J.S. Fowler (2008) A simple, rapid method for the preparation of [11C]formaldehyde Angew Chem Int Ed Engl. 47, 5989–5992.

C. Madry, I. Mesic, H. Betz, B. Laube (2007) The N-terminal domains of both NR1 and NR2 subunits determine allosteric Zn2+ inhibition and glycine affinity of N-methyl-D-aspartate receptors. Mol. Pharmacol. 72, 1535–1544.

A. Popkov, B. De Spiegeleer (2012) Chiral nickel (II) complexes in the preparation of 11C- and 18F-labelled enantiomerically pure alpha-amino acids. Dalton Trans. 1430-1440.

M. R. Van Horn, M. Sild, E. D. Ruthazer (2013) D-Serine as a gliotransmitter and its role in brain development and disease 7, doi: 10.3389/fncel.2013.00039

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