Homogeneous deuteriodeiodination of iodinated tyrosine in angiotensin-I using synthesized triethyl[H-2]silane and Pd(0)

In our efforts to develop new reactions for the efficient labelling of peptides and proteins with tritium, we now report the use of silane hydrides together with homogenous Pd(0) catalysis for the protio- and deuteriodeiodination of an α-iodo-tyrosine containing peptide (angiotensin-I) performed at room temperature.

Synthesis and biological evaluation of I-125/I-123-labelled analogues of citalopram and escitalopram as potential radioligands for imaging of the serotonin transporter

Two novel radioligands for the serotonin transporter (SERT), [I-125][3-[5-iodo-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl]-propyl]-dimethylamine ([I-125]-2) and S-[I-125][3-[5-iodo-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl]-propyl]-dimethylamine ([I-125]-(S)-2) were synthesized in a Br/I-125 exchange reaction. Binding experiments in rats yielded K-d values of 0.7 +/- 0.06 and 0.52 +/- 0.02nM for [I-125]-2 and [I-125]-(S)-2,
respectively. One hour after intravenous injection of [I-125]-2, 0.34% of the injected dose had accumulated in the brain. The highest hypothalamus-to-cerebellum ratio was reached 2 h after injection of [I-125]-(S)-2 and amounted to 2.4. Pretreatment experiments with paroxetine resulted in effective reduction of the target-to-cerebellum ratios. The corresponding iodine-123 labelled compound S-[I-123][3-[5-iodo-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl]propyl]- dimethylamine [I-123]-S-2 was investigated in a pig single photon emission computed tomography (SPECT) study. Between 60 and 110 min after IV injection, the midbrain-to-cerebellum ratio was 1.2. However, the uptake did not differ between high-density and medium-density regions questioning the feasibility of the radioligand in imaging cortical SERT distribution in vivo. These data suggest that the iodine-labelled derivatives of citalopram and escitalopram are not superior to another SPECT tracer for the SERT, namely [I-123] ADAM.
Novel Radiolabeled γ-Hydroxybutyric Acid Analogues for Radiolabeling and Photolinking of High-Affinity γ-Hydroxybutyric Acid Binding Sites

γ-Hydroxybutyric acid (GHB) is a therapeutic drug, a drug of abuse, and an endogenous substance that binds to low- and high-affinity sites in the mammalian brain. To target the specific GHB binding sites, we have developed a 125I-labeled GHB analog and characterized its binding in rat brain homogenate and slices. Our data show that [125I]4-hydroxy-4-[4-(2-iodobenzyloxy)phenyl]butanoate ([125I]BnOPh-GHB) binds to one site in rat brain cortical membranes with low nanomolar affinity (Kd, 7 nM; Bmax, 61 pmol/mg protein). The binding is inhibited by GHB and selected analogs, but not by γ-aminobutyric acid. Autoradiography using horizontal slices from rat brain demonstrates the highest density of binding in hippocampus and cortical regions and the lowest density in the cerebellum. Altogether, the findings correlate with the labeling and brain regional distribution of high-affinity GHB sites or [3H](E,RS)-(6,7,8,9-tetrahydro-5-hydroxy-5H-benzocyclohept-6-ylidene)acetic acid ([3H]NCS-382) binding sites. Using a 125I-labeled photoaffinity derivative of the new GHB ligand, we have performed denaturing protein electrophoresis and detected one major protein band with an apparent mass of 50 kDa from cortical and hippocampal membranes. [125I]BnOPh-GHB is the first reported 125I-labeled GHB radioligand and is a useful tool for in vitro studies of the specific high-affinity GHB binding sites. The related photoaffinity linker [125I]4-hydroxy-4-[4-(2-azido-5-iodobenzyloxy)phenyl]butanoate can be used as a probe for isolation of the elusive GHB binding protein.

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Radioliodestannyllation of Novel GHB Neuroreceptor Ligands

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Radionuklidbehandling af neuroendokrine tumorer
Peptide receptor radionuclide therapy using somatostatin analogues labelled with beta-emitting isotopes can be given to patients with metastasized or inoperable neuroendocrine tumours provided these have increased uptake on octreotide scintigraphy. This is a brief review of the treatment principle, indications and contraindications and practices with 177 Lu-DOTATATE treatment used at Rigshospitalet. Side effects are generally mild and reversible. Severe long-term side effects are rare. The majority of patients will experience increased quality of life and partial tumour reduction or stabilization for a period of time. However, up to 20% will experience no treatment effect.

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Paradigm Shift in the Regulatory Environment for Rapid Human Proof of Concept - Microdosing

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Labelling of a potent glucaton receptor antagonist with tritium, carbon-14 and stable isotopes

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Synthesis of 4-substituted tetrahydropyridines by cross-coupling of enol phosphates

Enol phosphates, synthesized from 4-piperidone, react by palladium catalyzed cross-coupling with arylboronic acids and by iron and palladium catalyzed cross-coupling with Grignard reagents to give 4-substituted tetrahydropyridines. (c) 2005 Elsevier Ltd. All rights reserved.

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