

General rapid C-[¹¹C]Methylation and C-[¹⁸F]Fluoromethylation: Revolutionary advanced method for synthesis of short-lived PET probes

Masaaki Suzuki

RIKEN Center for Molecular Imaging Science, Japan

Positron emission tomography (PET) is a powerful noninvasive method for the investigation of in vivo biochemistry, especially in the human organ. The need for the development of new PET probes has grown with the increase in its use for diagnosis in medicine and for drug development processes in an early stage (microdosing concept). Accordingly, we realized rapid [¹¹C] methylation on various carbon frameworks such as arene, alkyne, alkene, and alkane to establish four kinds of Rapid C-[¹¹C] methylations including heteroaromatics by Pd(0)-mediated reaction of [¹¹C]H₃I and organotributylstannanes or alkoxyborons. Rapid C-[¹⁸F]fluoromethylation were also elaborated by Pd(0)-mediated reactions of [¹⁸F]fluoromethyl iodide (or bromide) using an alkoxyorganoboron precursor. Such methylations would realize ¹¹C and ¹⁸F-labeling of almost any organic compounds, allowing the PD/PK studies by PET in both animals and human to promote "Evidence-based Medicine". Actually, methylation on an arene framework was applied to ¹¹C incorporation into 15R-TIC, a stable prostaglandin analogue, which selectively binds with a novel prostacyclin receptor (IP₂) in the central nervous system. 15R-[¹¹C]TIC methyl ester obtained in high yield was used for PET studies (intravenous administration) to visualize IP₂ receptor distributed in monkey and human brains in addition to the hepatobiliary transport in rat and human abdomens. The talk also includes the syntheses of Celecoxib metabolite [¹¹C]SC-62807, [methyl-¹¹C]thymidine and its stable analogue 4'-[methyl-¹¹C]thiothymidine (biomarker in cancer diagnosis), [¹¹C]all-trans-retinoic acid, ¹¹C-labeled 2-arylpropionic acids and their esters, [¹¹C]acromelic acid A derivative (inhibitor of neuropathic pain), [¹¹C]H-1152, specific Rho-kinase inhibitor, [¹¹C]dehydropravastatin, a probe for transporters in the liver.

Biography

Assistant Professor, Department of Chemistry, Faculty of Science, Nagoya University (collaborated with Prof. Yoshimasa. Hirata and then with Prof. Ryoji Noyori), 1975-1983

Associate Professor (collaborated with Prof. Ryoji Noyori), Department of Chemistry, Faculty of Science, Nagoya University, 1983-1990

Associate Professor, Chemical Instrument Center, Nagoya University, 1990-1993

Professor, Department of Applied Chemistry, Gifu University, 1993-1998

Professor, Department of Biomolecular Science, Faculty of Engineering, Gifu University, 1998-2002

Professor, Regeneration and Advanced Medical Science, Graduate School of Medicine, Gifu University, 2002-2008

Emeritus and visiting Professor of Gifu University, 2008~

Deputy Director, RIKEN Center for Molecular Imaging Science, Molecular Imaging Medicinal Chemistry Laboratory, and Team Leader, 2008~

suzuki.masaaki@riken.jp