T. KAN,* Y. KITA, Y. MOROHASHI, Y. TOMINARI, S. HOSODA, T. TOMITA, H. NATSUGARI, T. IWATSUBO, T. FUKUYAMA* (UNIVERSITY OF SHIZUOKA AND THE UNIVERSITY OF TOKYO, JAPAN)

Convenient Synthesis of Photoaffinity Probes and Evaluation of Their Labeling Abilities
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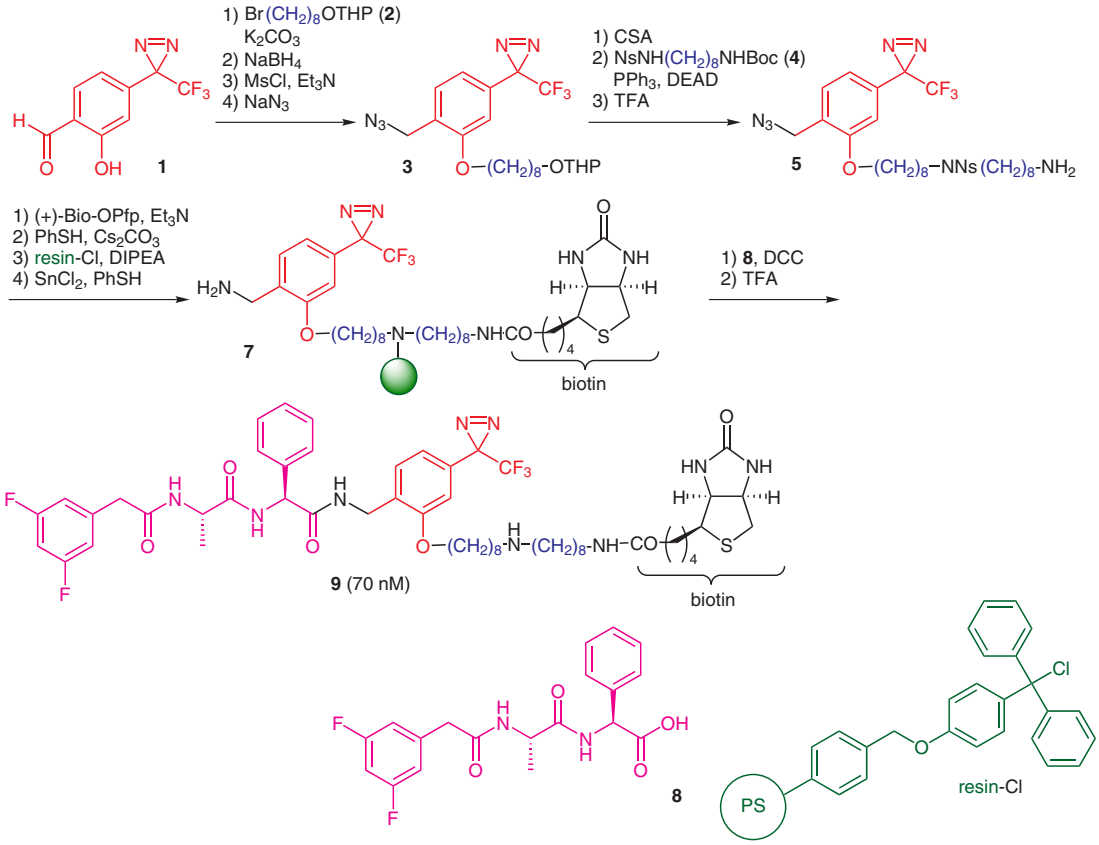
Photoaffinity Probes for Alzheimer's Disease



Significance: A convenient solid-phase synthesis of a variety of photoaffinity probes was achieved by utilizing the Ns (Ns = Nosyl) strategy. Thus, the synthesis of the photoaffinity probe **9** was achieved in 47% overall yield from diazirine **1** and alkyl bromide **2**. The carbon–nitrogen bond formation at the side chain was accomplished by the Mitsunobu reaction of the Ns amines (e.g. **4**; Ns strategy). By using a similar synthetic route, six photoaffinity probes were prepared. The synthetic probes were evaluated via the labeling ability with the preseniline 1 C-terminal fragments (PS 1 CTFs), and **9** exhibited inihibitory activity of Ab40 (IC_{50} = 70 nM).

Comment: The authors have developed the Ns strategy for the convenient preparation of di- and trialkyl amines (see review below). PS 1 CTFs were identified as therapeutic targets for Alzheimer's disease. To the authors' knowledge, there have been no or only few systematic studies on the structure and labeling-ability relationship (SAR) of photoaffinity probes.

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SYNFACTS Contributors: Yasuhiro Uozumi, Yoichi M. A. Yamada
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