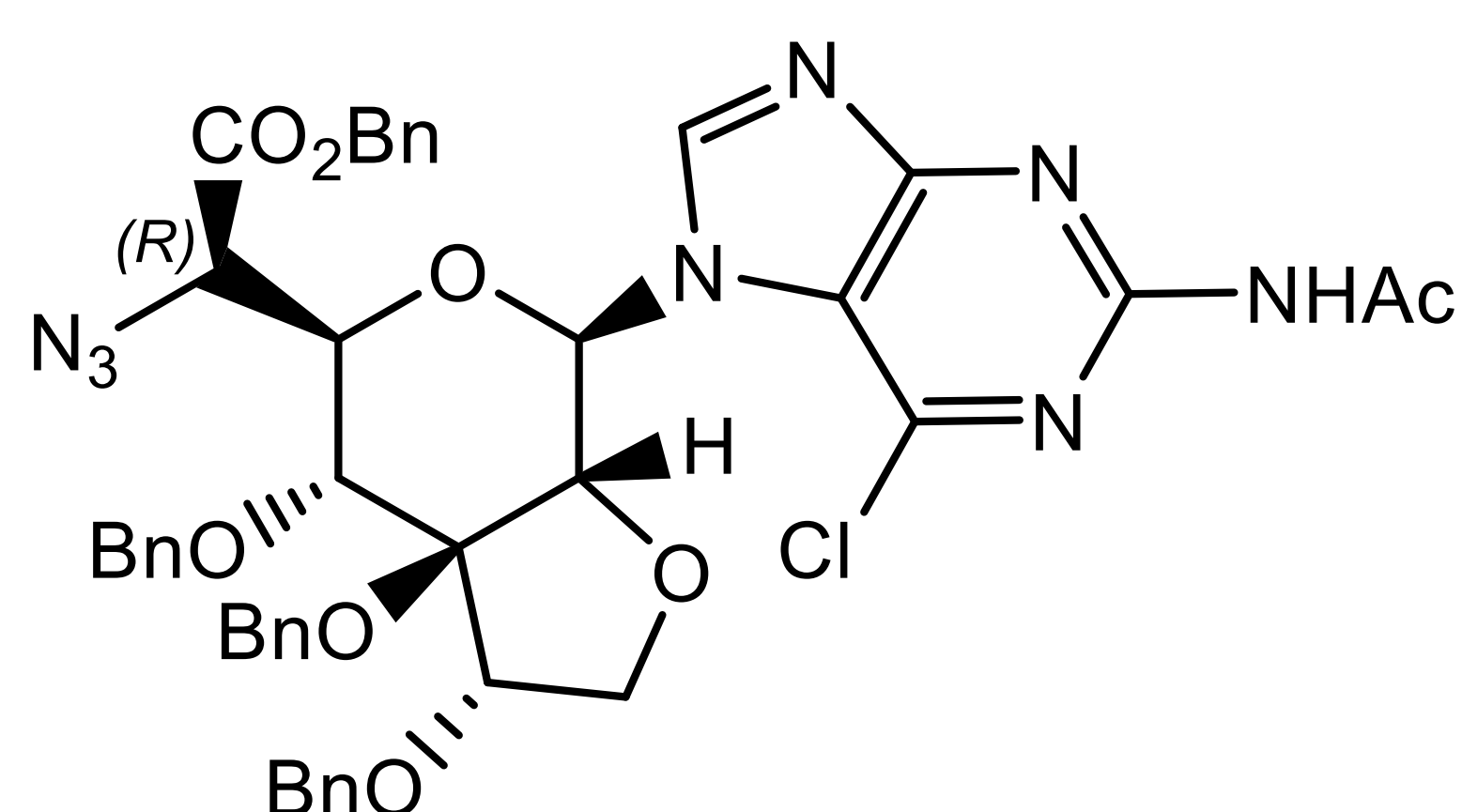


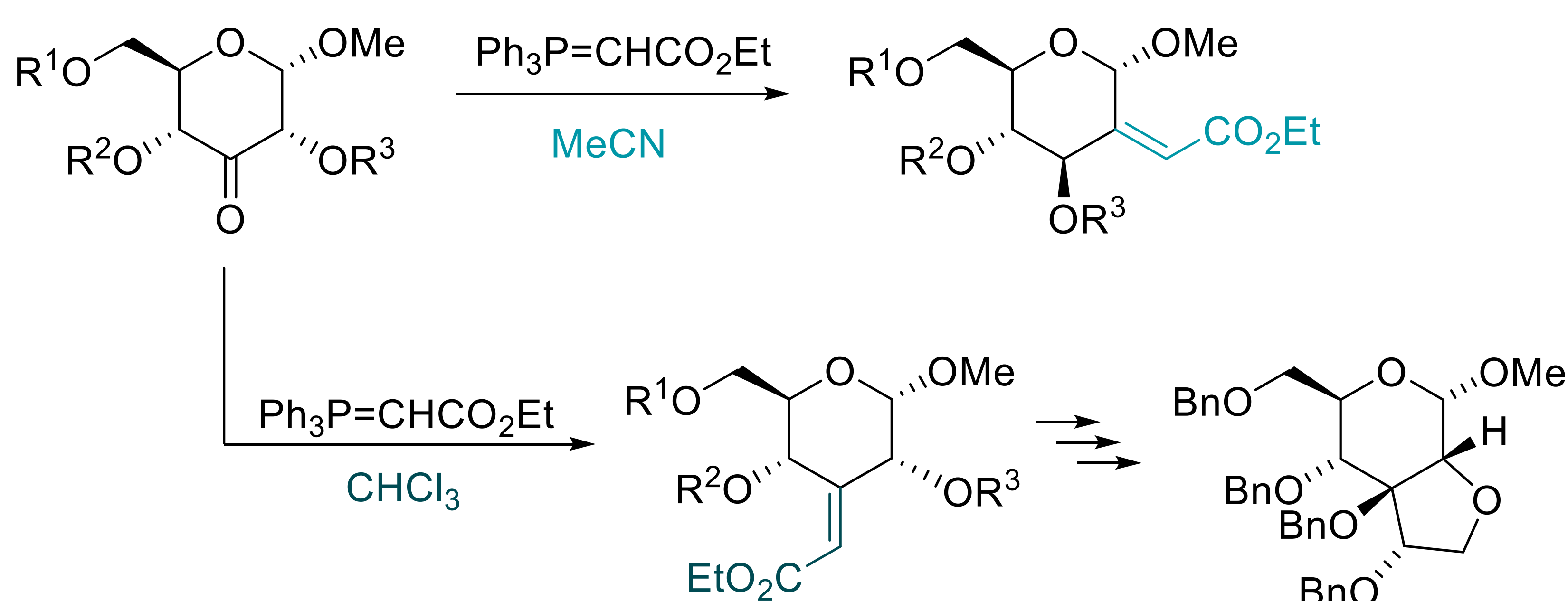
Introduction



- Alzheimer's Disease is the leading cause of dementia
- Current treatment options are not viable for long-term illness
- Studies suggest that selective butyrylcholinesterase (BChE) inhibition might provide better therapies

- Potent and selective BChE inhibitor (IC₅₀ 140 nM)
- Rauter *et al. Bioorg. Med. Chem.* **2009**, *17*(14), 5106

New synthetic strategies for the synthesis of bicyclic sugar moieties

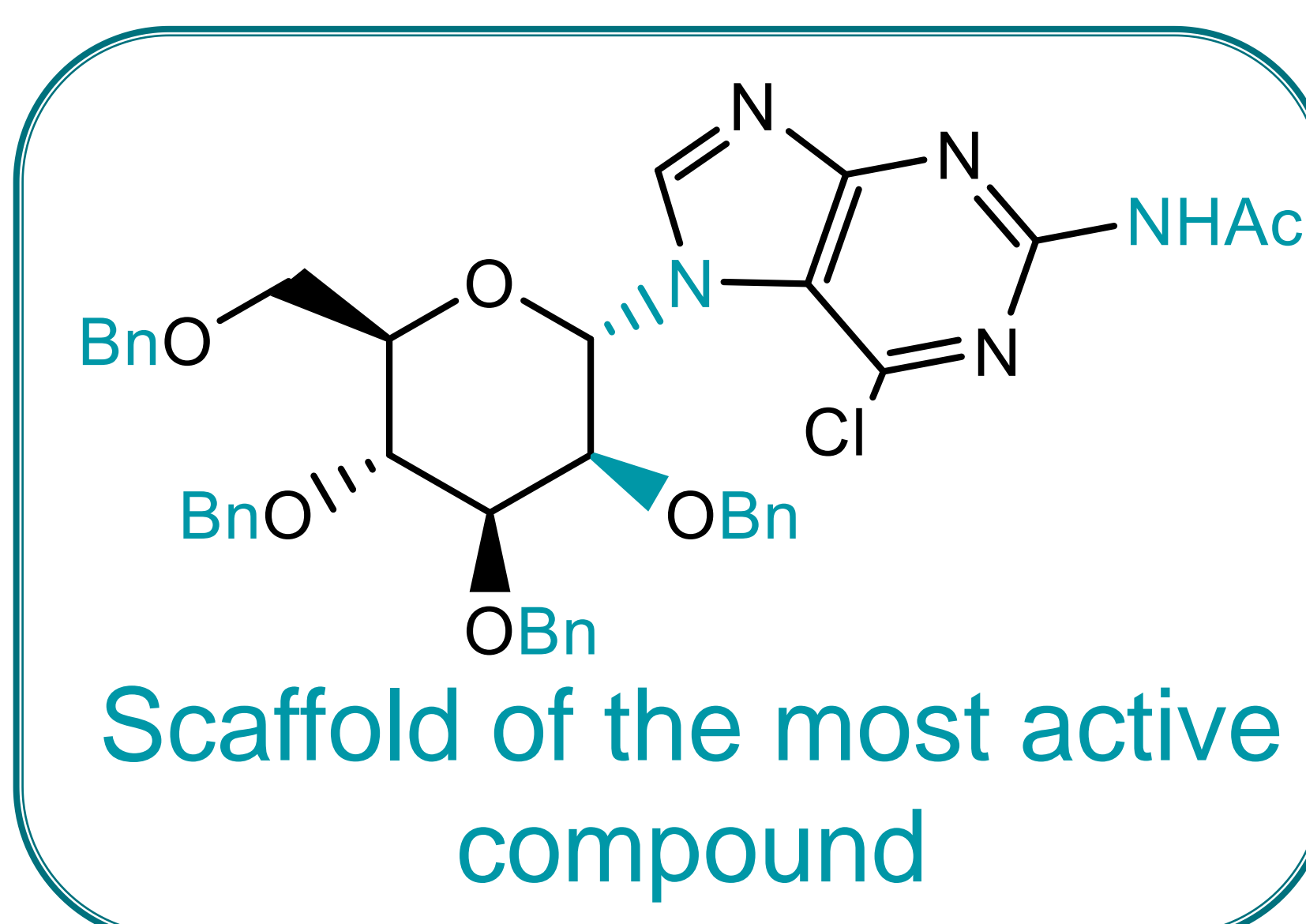


- Strategy based on stereoselective reactions
- Wittig reaction as key step
- Stereocontrol of olefin based on sugar protection
- Regiocontrol of olefin based on solvent of the reaction
- Cachatra *et al. Org Lett* **2015**, *17*(22), 5622

First approach

Second approach

Structure optimization for increased activity



Changing structural features:

- Replacing the benzyl by methyl groups
- Deoxygenation at different positions of the sugar moiety

**Alzheimer's
Disease**

Selective inhibitor of BChE (IC₅₀ 49 nM)

- Rauter *et al. Org. Biomol. Chem.* **2014**, *12*(15), 2446
- Rauter *et al. Eur. J. Org. Chem.* **2014**, *13*, 2770

Cancer

Active against several cancer cell lines (PC3, MCF7, A375, HeLa, A2780, U87)
Rauter *et al. Eur. J. Med. Chem.* **2015**, *90*, 595

Collaborations:



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This work was supported by Fundação para a Ciência e a Tecnologia (FCT), Portugal (Projects UID/MULTI/00612/2013 and PhD fellowship SFRH/BD/90359/2013) and the EU (project D3i4AD – IAPP Grant No. 612347)

