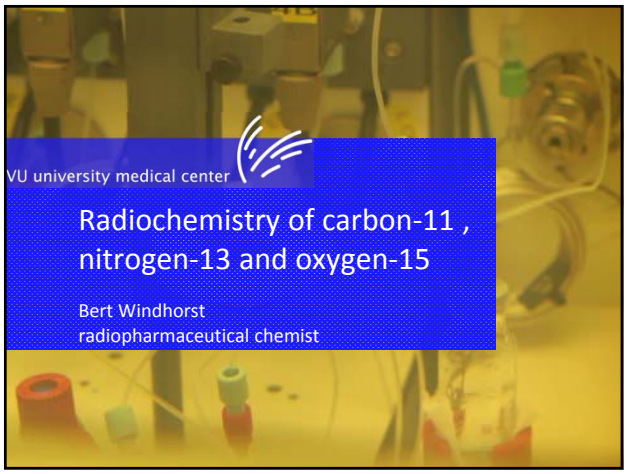

Outline

VUmc

Radiochemistry of carbon-11

Radiochemistry of nitrogen-13

Radiochemistry of oxygen-15

2

Outline

VUmc

Radiochemistry of carbon-11

Radiochemistry of nitrogen-13

Radiochemistry of oxygen-15

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Carbon-11 chemistry

Why is ^{11}C a suitable radionuclide for PET imaging?

- Substitution of ^{12}C with ^{11}C
  - Labeled molecule retains its biological properties
- Decay characteristics: 98.1% β^+, $t_{1/2}$ = 20.4 min
  - Repeated PET studies in same individual
  - Multi step synthesis possible (maximum ~1 h total synthesis time)
- Drawbacks
  - Need 'in-house' cyclotron and advanced lab facilities
  - Sometimes too short half-life (for synthesis and PET application)

4

Carbon-11 chemistry: characteristics

- Position specific labelling
- Remote controlled, automated synthesis devices
- Short reaction times (typically < 5 minutes)
- Late incorporation of carbon-11 in target structure
- Miniaturized scale
- Large stochiometric excess of reagents compared to radioactive precursor
- Diverse chemistry
  - Conventional organic synthesis
  - Organometallic chemistry
  - Enzymatic catalysis
  - Gas phase chemistry
- Solution chemistry in vials & autoclaves
- On column & on-line procedures
- Reactions on solid support
- One-pot reactions
- Attention to specific activity

5

Carbon-11 chemistry: equipment

Automated / remote controlled synthesis equipment
Radiation protection / monitoring
Radiopharmaceutical manufacturing - GMP

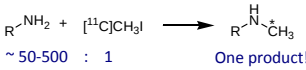
6

Reaction stochiometry

VUmc

selectivity & kinetics

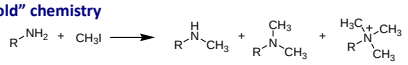
^{11}C chemistry – Generally fast reactions due to large excess of reagents compared to labelled precursor



~ 50-500 : 1 One product!

No double alkylation despite increase in nucleophilicity:
1^0-amine < 2^0-amine < 3^0-amine

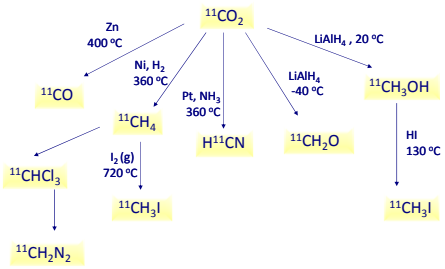
"Cold" chemistry



1 : 1 Product mixture

Carbon-11 diversity

VUmc

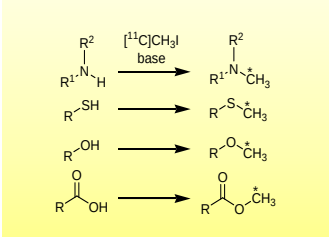


[^{11}C]CH_3I / [^{11}C]$CH_3SO_3CF_3$

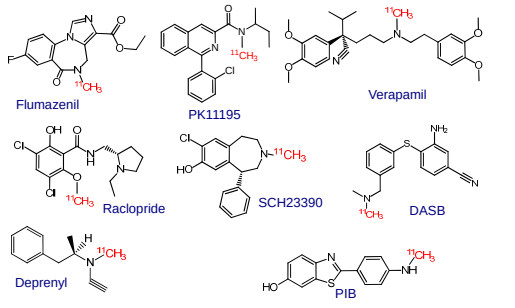
VUmc

Methyl iodide and methyl triflate are by far the most applied carbon-11 labeling agents

The methylation is generally carried out on N-, O and S nucleophiles, most commonly on primary and secondary amines and phenols.



Examples



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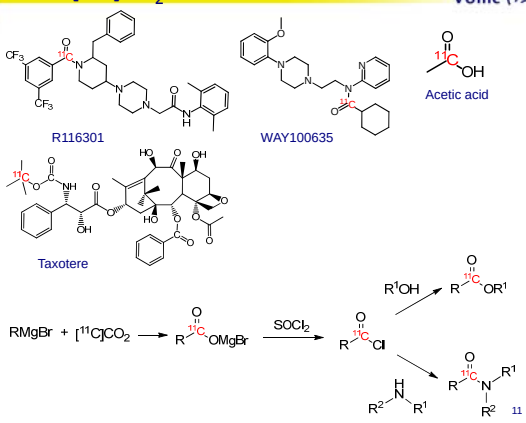
From [^{11}C]CO_2



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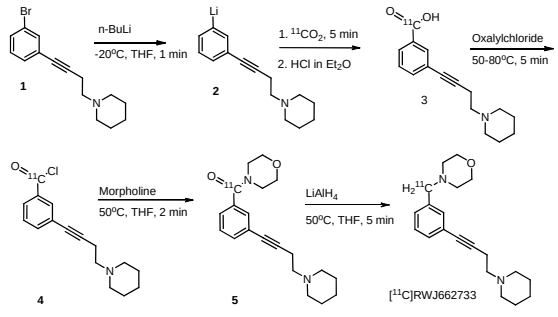
[^{11}C]RWJ662733



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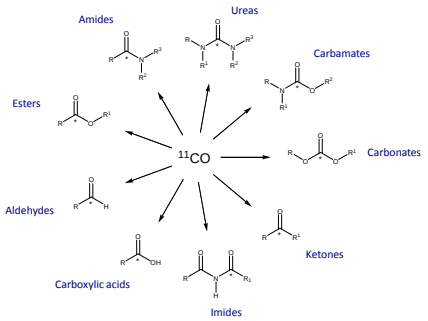
Advanced carbon-11 chemistry

VUmc

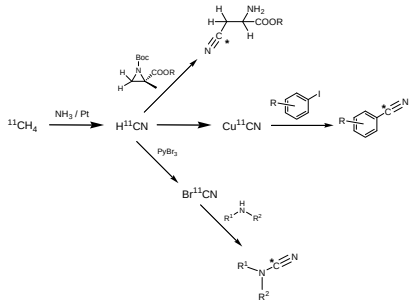
[^{11}C]CO applications



Advanced carbon-11 chemistry

VUmc

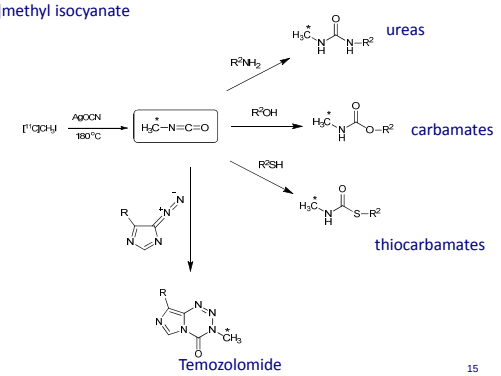
[^{11}C]hydrogencyanide



Advanced carbon-11 chemistry

VUmc

[^{11}C]methyl isocyanate



Temozolomide

Advanced carbon-11 chemistry

VUmc

Other reactions published:

Wittig reaction, Heck reaction, Stille reaction with $[^{11}C]CH_3I$

$[^{11}C]$nitromethane to obtain $[^{11}C]CH_2NO_2$ subsituted compounds

$[^{11}C]$phosgene to obtain amides, cyclic amides

And many more

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Outline

VUmc

Radiochemistry of carbon-11

Radiochemistry of nitrogen-13

Radiochemistry of oxygen-15

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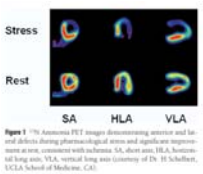
Nitrogen-13 chemistry

VUmc

Half-life 10 minutes: Some applications, fast chemistry required

Most important: ^{13}N labeled Ammonia
In-target chemistry: $^{16}O(p,\alpha)^{13}N$ in natural water
> add ethanol: $[^{13}N]NH_3$ is obtained

used in cardiology to study bloodflow in myocardum



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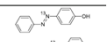
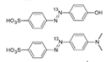
Nitrogen-13 chemistry

VUmc

Also used to obtain ^{13}N labeled amino acids from $[^{13}N]NH_3$

Diazonium salts from $[^{13}N]NO_2$:

Compound	Precursor A (step 1)	Precursor B (step 2)	Structure
1			
2			
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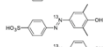
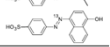
4			
5			

V Gaja *et al*, Mol Imaging Biol (2014) 16:538-549

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Outline

VUmc

Radiochemistry of carbon-11

Radiochemistry of nitrogen-13

Radiochemistry of oxygen-15

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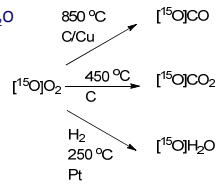
Oxygen-15

VUmc

Half life of 2 minutes

Only very fast chemistry possible

$[^{15}O]CO_2$ or $[^{15}O]CO$ or $[^{15}O]H_2O$



Proces proceeds 'on-line':
conversion direct from the target into administration

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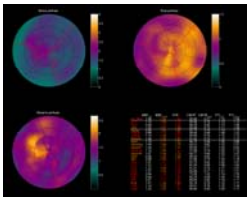
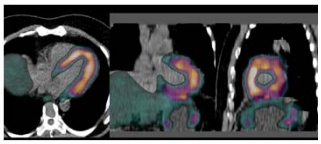
[^{15}O]water

To study bloodflow eg to tumors or myocardium



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Further reading

Molecular Imaging: radiopharmaceuticals for PET and SPECT
by Shankar Vallabhajosula

Chapter 11

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