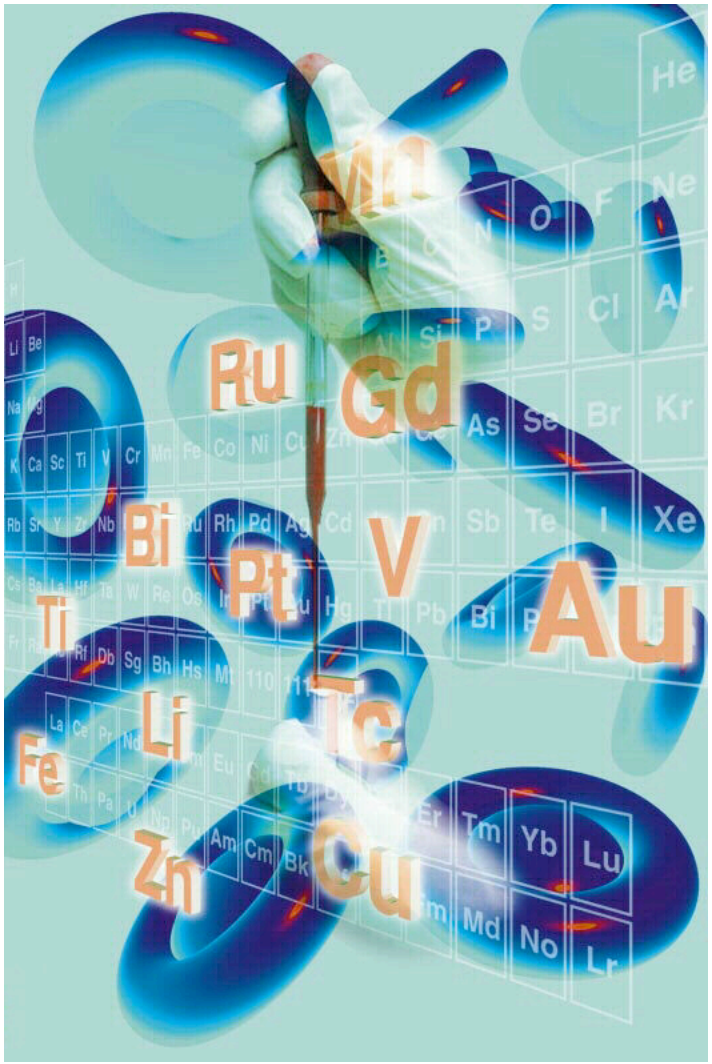

Dr. Bernard BOITREL

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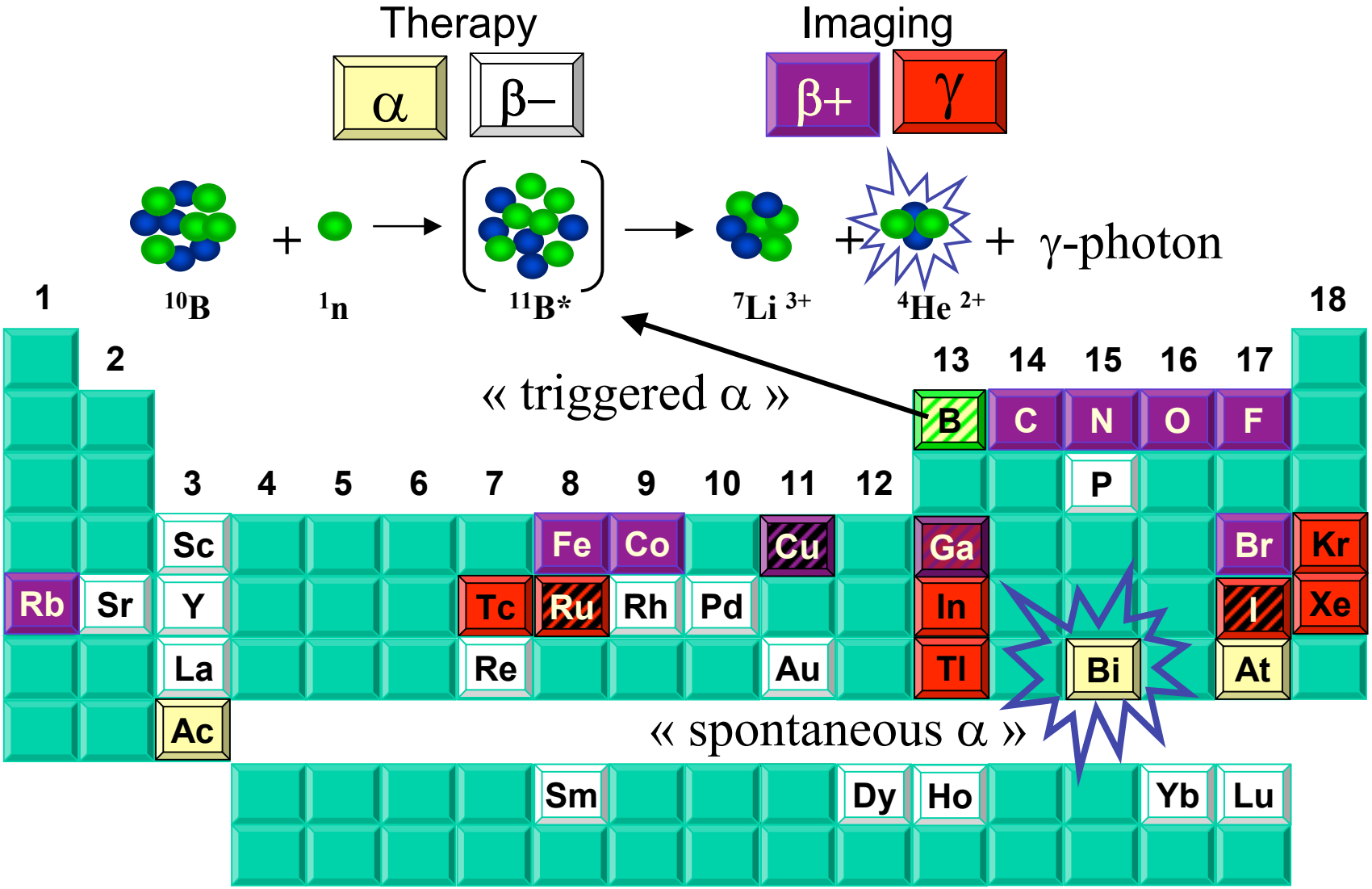
FUNCTIONALIZED BISMUTH PORPHYRINS :

A ROUTE FOR ALPHA-RADIOTHERAPY ?

Illustration from *Angew. Chem. Int. Ed.* **1999**, *38*, 1512-1531

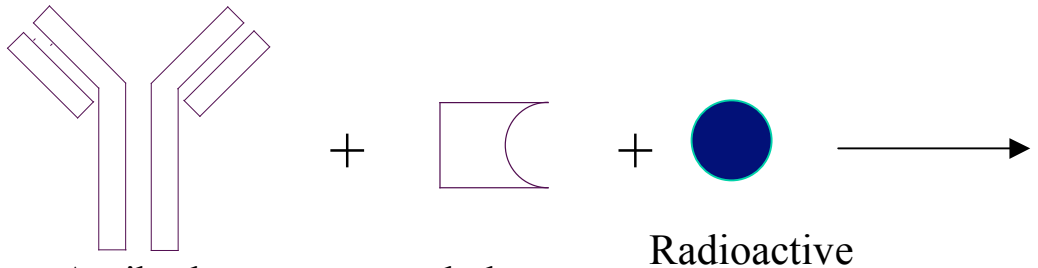
RADIOISOTOPES IN NUCLEAR MEDICINE

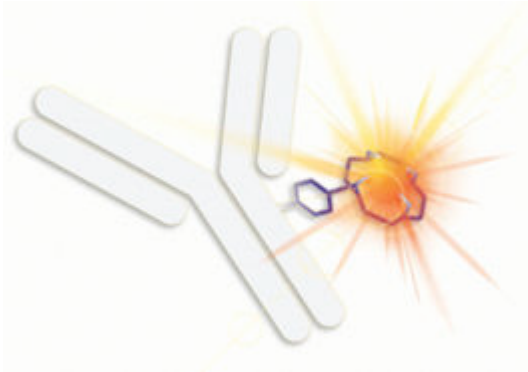


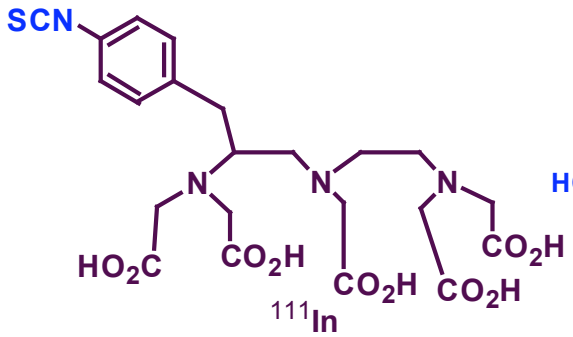
According to McDevitt; M.R. *et al. Eur. J. Nucl. Med.* **1998**, *25*, 1341-1351

Illustration adapted from Dr. N. Noiret (ENSCR, Rennes)

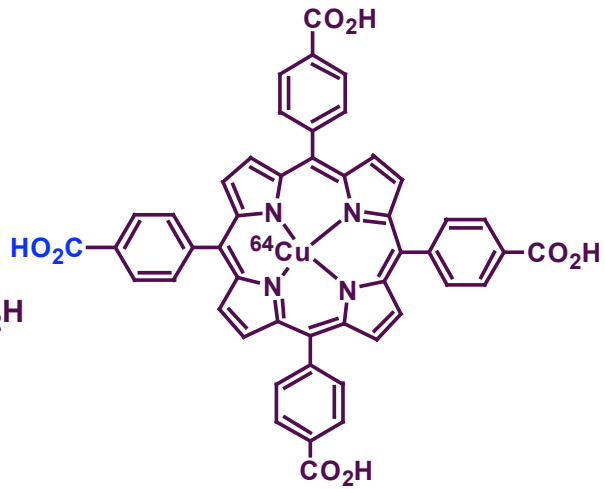
BASIS OF RADIO-IMMUNOTHERAPY



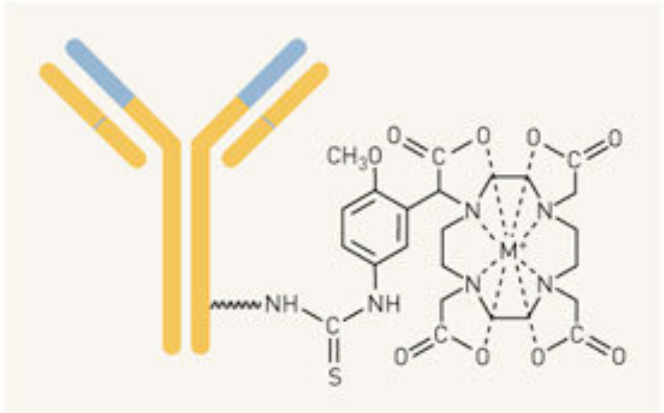




Gansow, O. A *et al.*
Inorg. Chem. **1986**, *25*, 2772-2781.



Lavallee, D. K *et al*. *J. Nucl. Med. (abstracts)*
1985, *26*, 437-438.



Ehrlich's magic bullets :
Modified Antibody
(e.g. Mabthera (rituximab, anti-CD20)

One of the first uses of anti-tumor antibody as carriers of radioactive molecules:
Korngold and Pressman, Cancer Res. **1953**, *14*, 96-99

CHOICE OF THE RADIONUCLIDE

Isotopes	LET	Half-time life
	β emitters	
^{131}I		8,2 days
^{90}Y	(0.2 Kev/µm)	2,7 days
	α emitters	
^{225}Ac		10 days
^{211}At	(97 Kev/µm)	7.2 hours
^{212}Bi		60.6 min
^{213}Bi		45.6 min

Basic requirements

- Short half-life time
- No other emission, if possible
- Stable Chelates

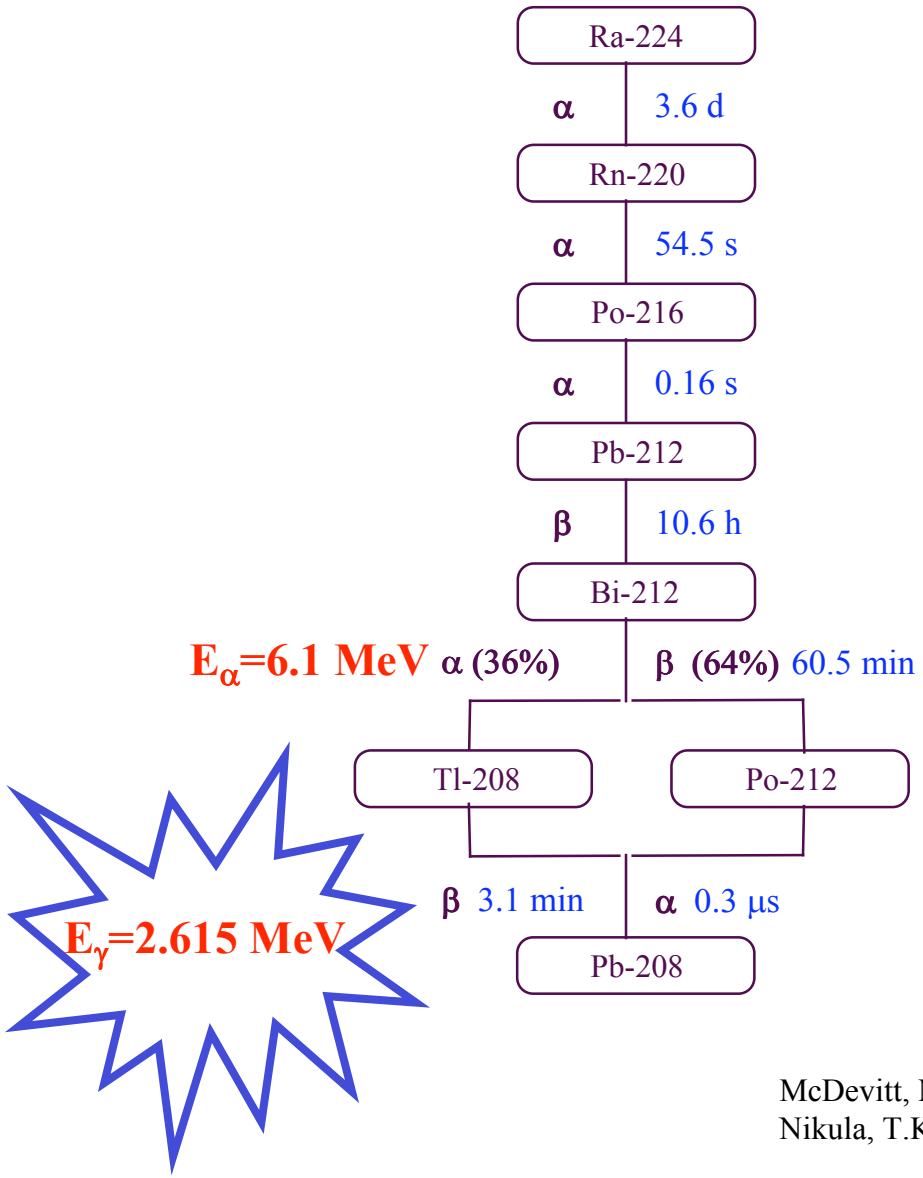
Advantages of α emitters

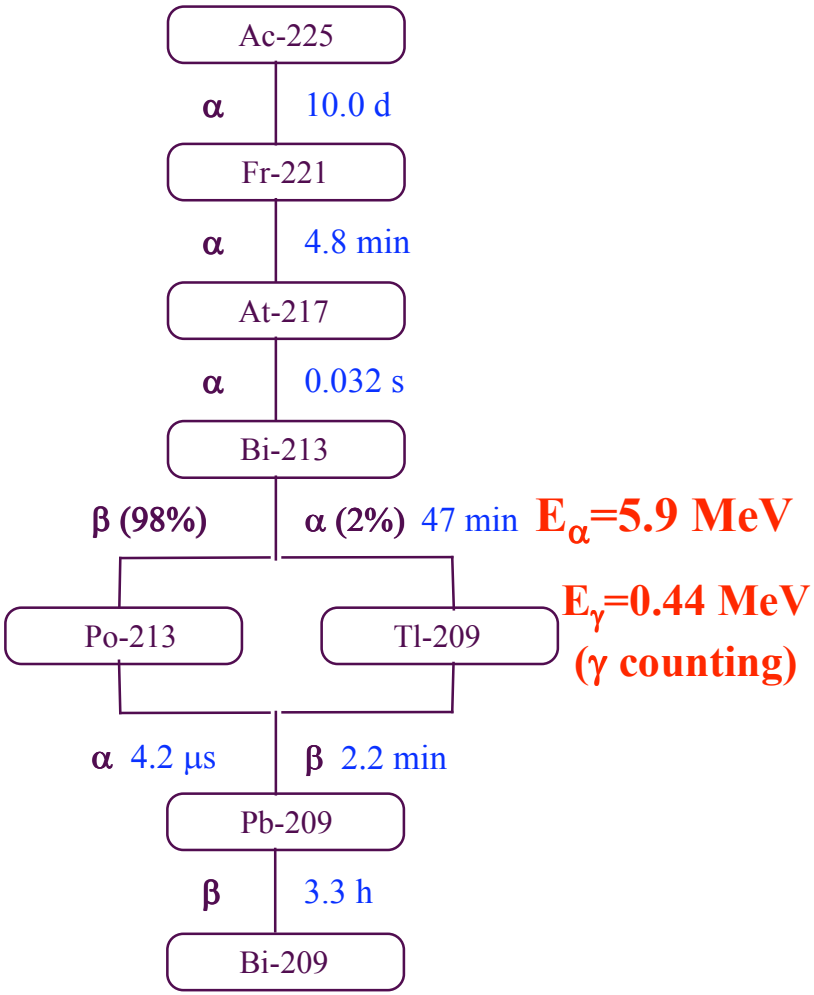
High Linear Energy Transfer (60-230 Kev/µm)

=> A few hundred decay to achieve 99.99% of cell death

Short mean range in tissue (1-5 cells, around 70 µm)

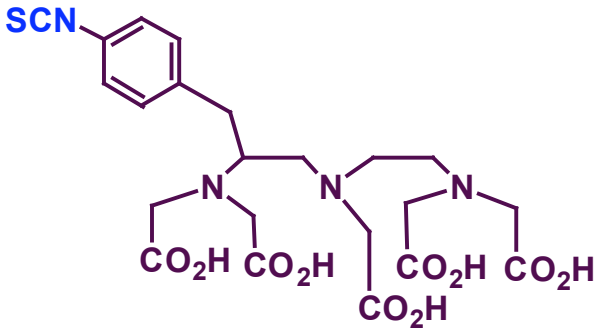
^{224}Ra AND ^{225}Ac DECAY SCHEMES





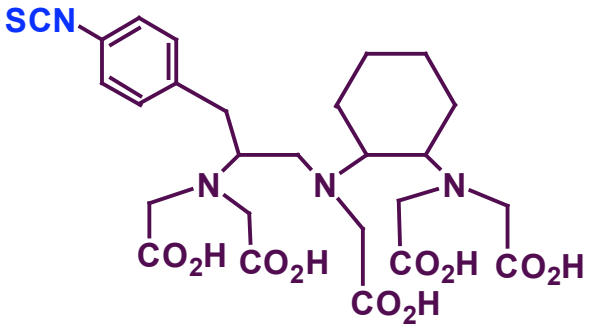
McDevitt, M.R. *et al. Eur. J. Nucl. Med.* **1998**, *25*, 1341-1351
Nikula, T.K. *et al. J. Nucl. Med.*. **1999**, *40*, 166-176

CHELATES ALREADY KNOWN TO COORDINATE ^{213}Bi or ^{212}Bi



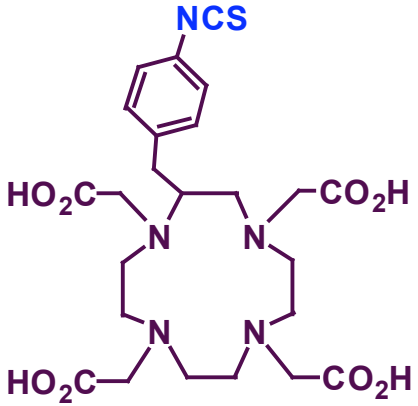
Related to DTPA

Gansow, O. A *et al.*
Inorg. Chem. **1986**, *25*, 2772-2781.



Related to cyDTPA

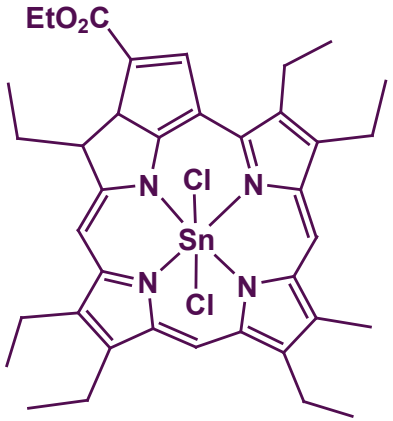
Brechbiel, M. W.; Gansow, O. A. *J. Chem. Soc. Perkin Trans. I* **1992**, 1173-1178.



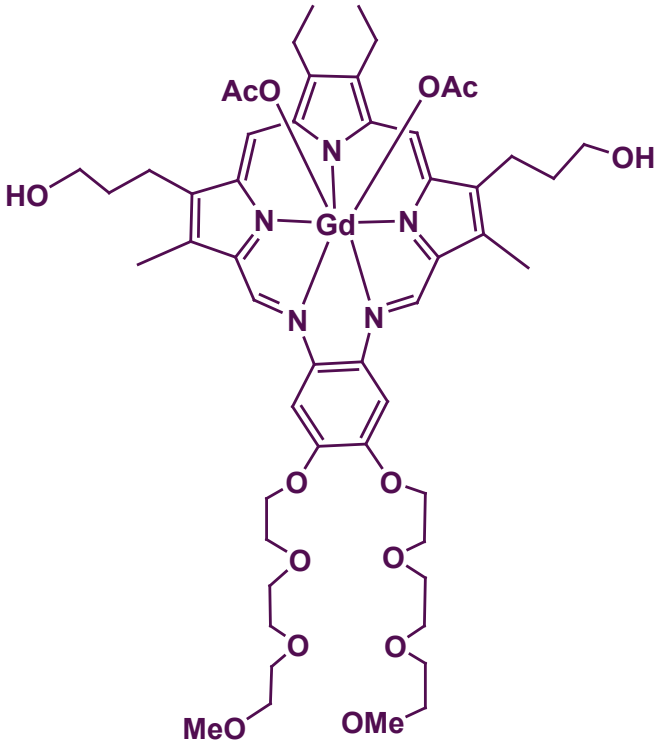
Related to DOTA

Strand, M. *et al. Cancer Res.* **1990**, *50*, 4221-4226.

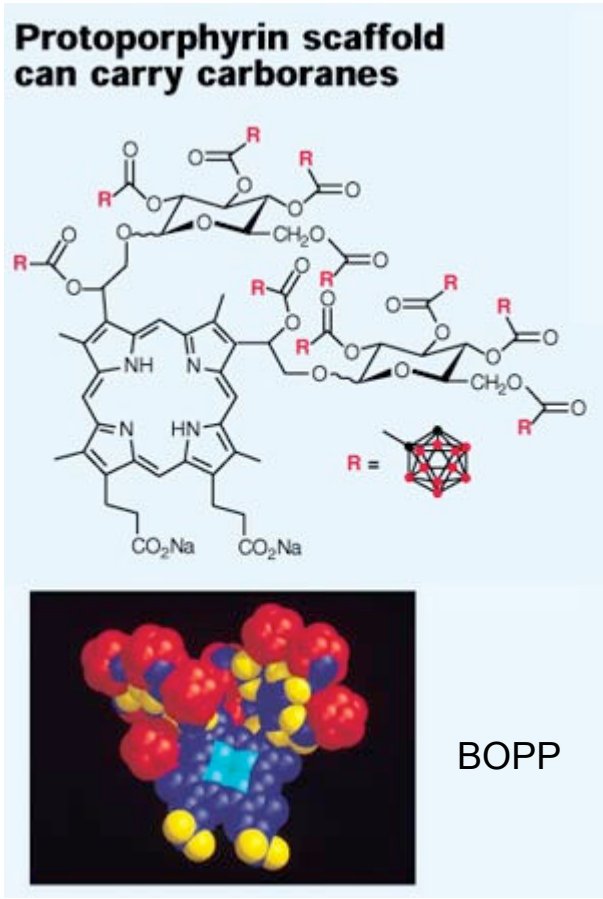
PORPHYRINS OF POTENTIAL INTEREST IN MEDICINE



Tin(IV) etiopurpurin
(PDT)

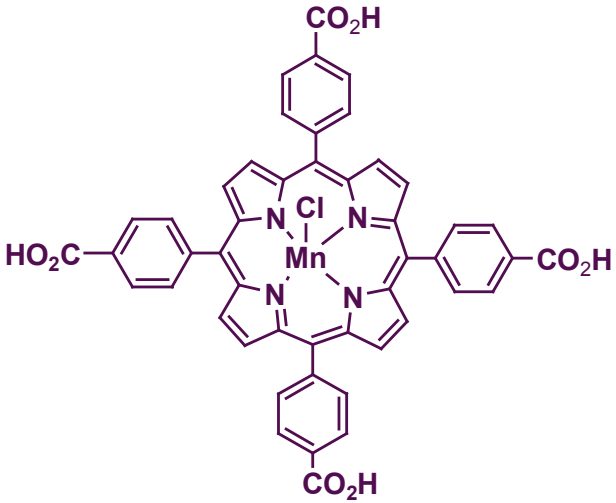


Gd-Tex $^{2+}$
(radiosensitizer)



BOPP

(BNCT)

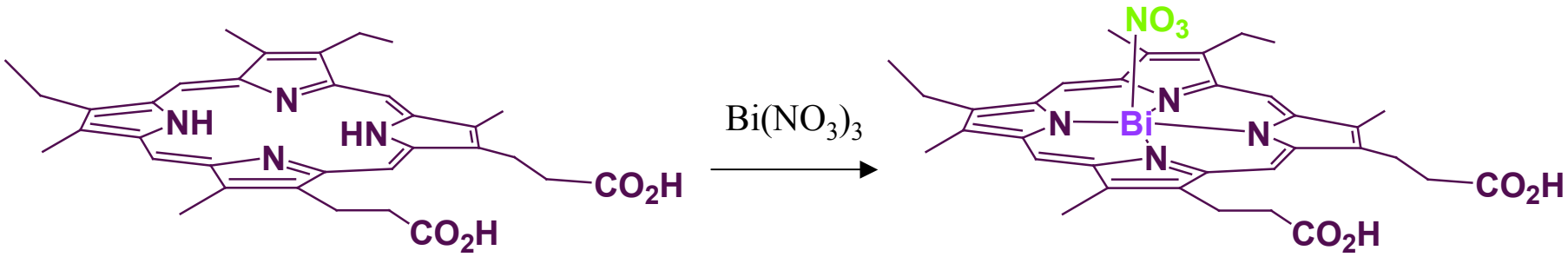


MnTBAP (brain deseases)

H. Ali; J. E. van Lier *Chem. Rev.* **1999**, *99*, 2379-2450.

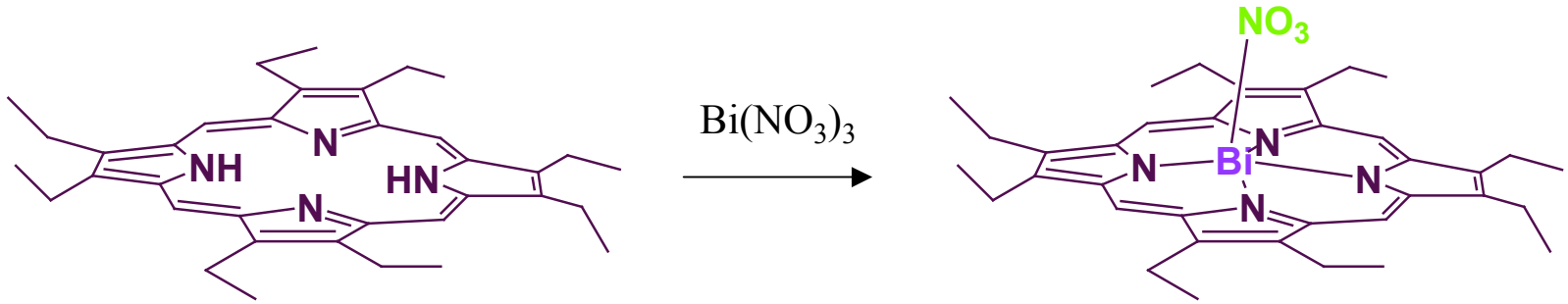
B. Kahl *et al*. *Cancer Res.* **1990**, *50*, 4860.
M. Graça H. Vincente *et al*. *Chem. Commun.* **2001**, 483.

FIRST COMPLEXES OF BISMUTH WITH PORPHYRINS



Mesoporphyrin IX

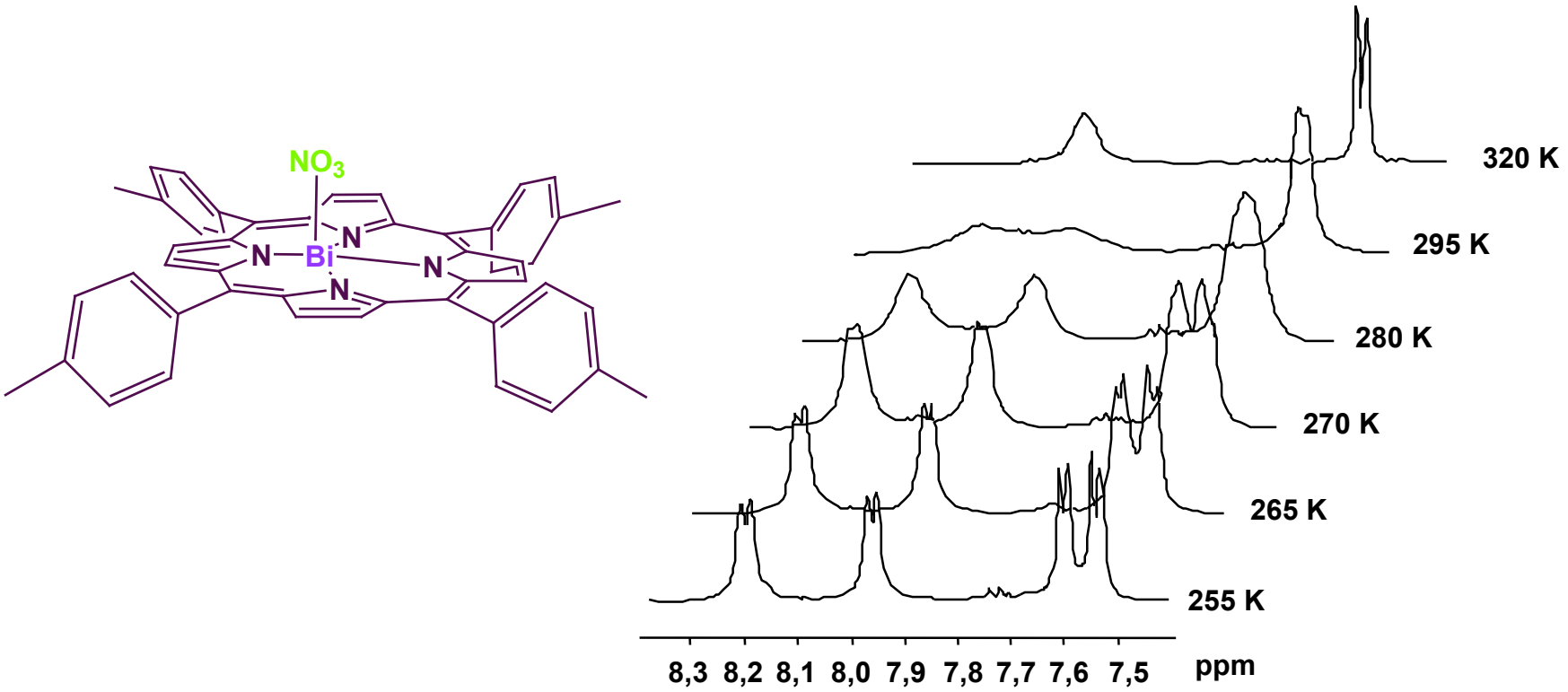
Treibs, A. *Liebigs Ann. Chem.* **1969**, *728*, 115.



Octaethylporphyrin

Buchler, J. W.; Lay, K. L. *Inorg. Nucl. Chem. Lett.* **1974**, *10*, 297-300.

PROTON NMR SPECTROSCOPY OF (TTP)Bi(NO_3)



Barbour, J.; Belcher, W. J.; Brothers, P. J.; Rickard, C. E. F.; Ware, D. C. *Inorg. Chem.* **1992**, *31*, 746-754.