Dendritic functionalized pyrenes in arene-ruthenium metalla-prisms as nanomedicine devices

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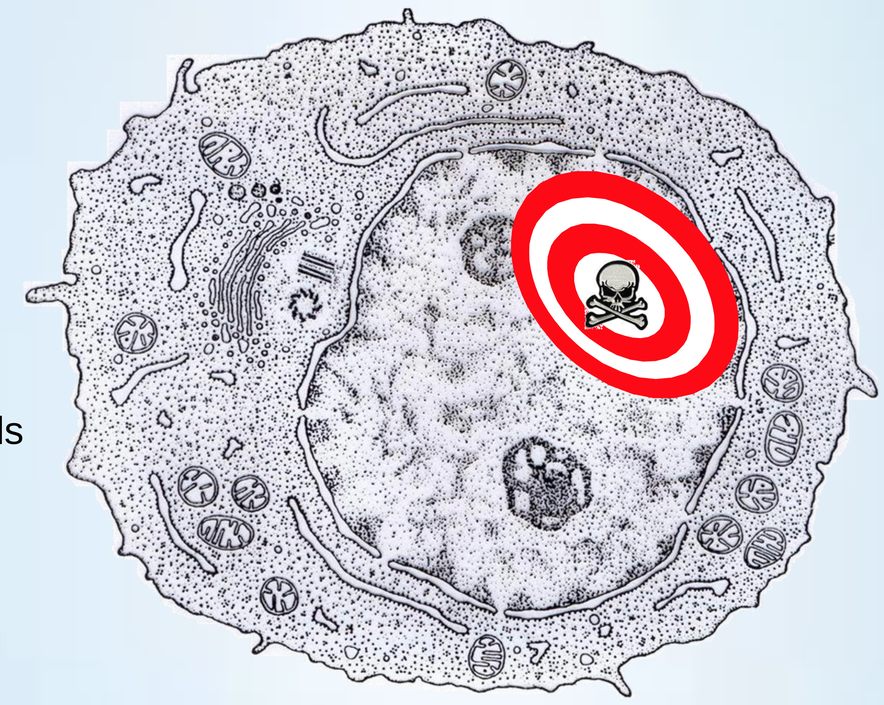
The target: Cancer cells

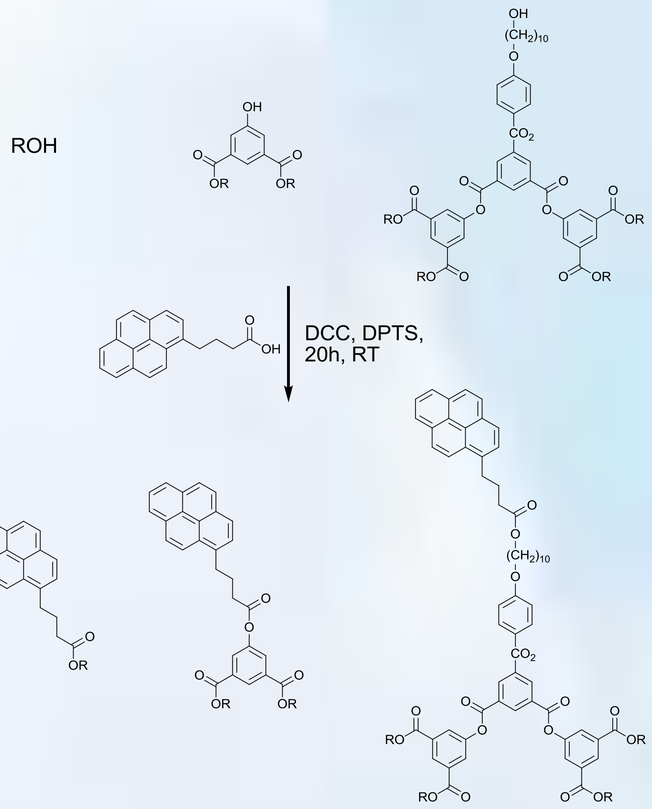
Extravasation of macromolecules is considerably enhanced in tumor tissues due to the "enhanced permeability and retention" (EPR) effect [1]

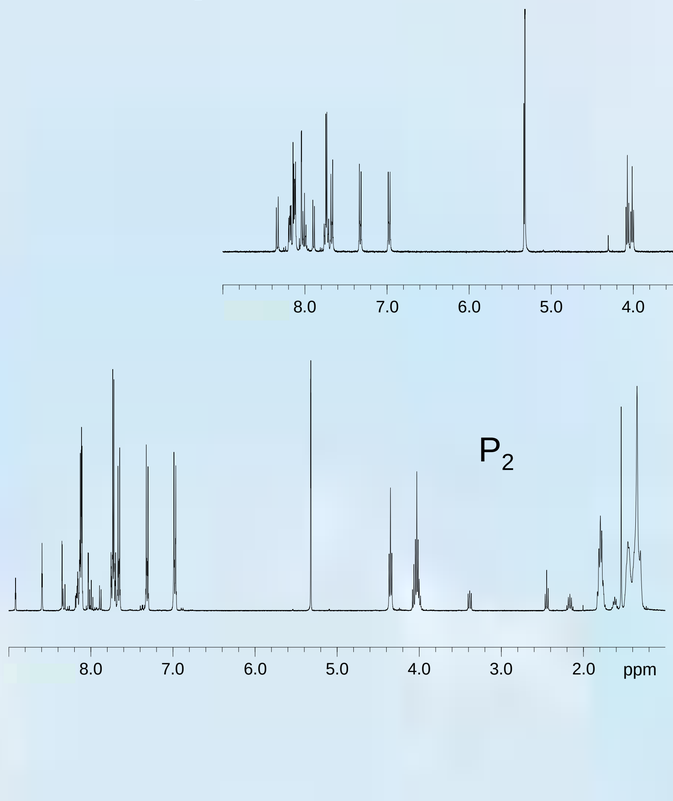
EPR effect is believed to play a major role in selective delivery of nanomedicines

Nanomedicines lead up to 100 times greater intratumor drug delivery efficacy to cancer cells as compared to healthy cells



The weapon: Dendritic functionalized pyrene and ruthenium metalla-prism





P_0 P_1 P_2

R = $-(CH_2)_{10}O-CO_2-$ $-CN$

Pyrenyl-containing dendrimers[2]

High molecular weights

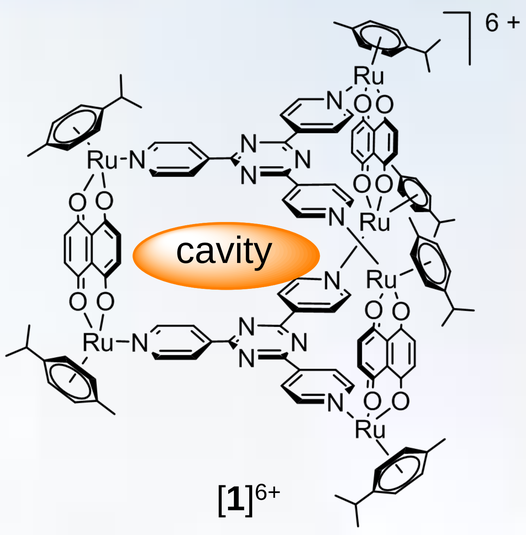
Lipophilic molecules

No cellular internalization

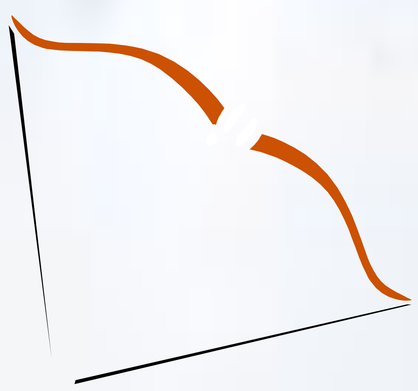
Biological activity on human ovarian cancer cell lines

Complex	A2780 (IC_{50}, μM)	A2780cisR (IC_{50}, μM)
P_0	inactive	inactive
P_1	inactive	inactive
P_2	inactive	inactive
$[\mathbf{1}]^{6+}$	3.1 ± 1.0	4.6 ± 0.5
$[P_0 \subset \mathbf{1}]^{6+}$	0.4 ± 0.1	0.5 ± 0.4
$[P_1 \subset \mathbf{1}]^{6+}$	2.2 ± 1.1	2.4 ± 0.8
$[P_2 \subset \mathbf{1}]^{6+}$	2.6 ± 0.8	2.8 ± 1.0
cisplatin	1.6 ± 0.6	8.6 ± 0.6

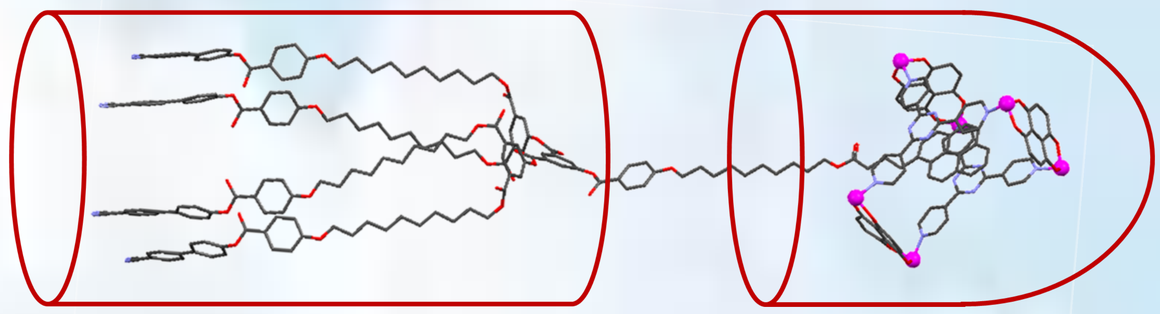
IC_{50} is the drug concentration necessary for 50% inhibition of cell viability



$[\mathbf{1}]^{6+}$



Modelisation of $[P_2 \subset \mathbf{1}]^{6+}$



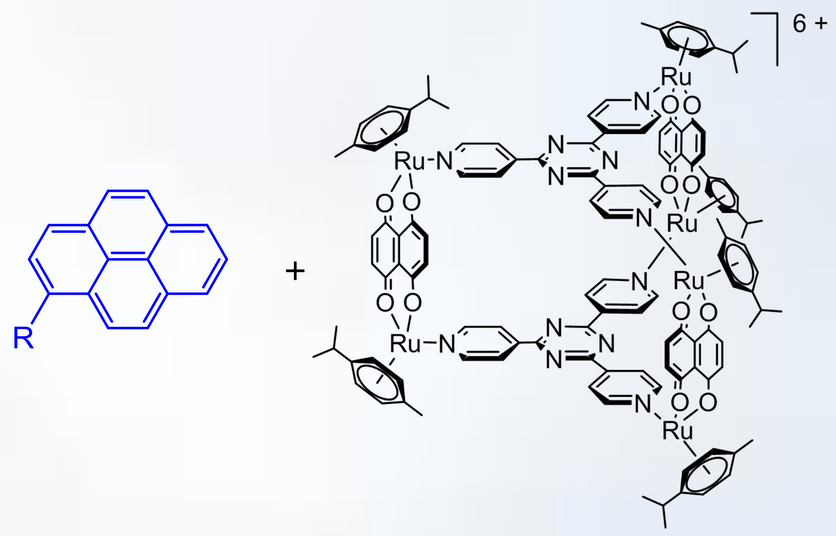
The lipophilic tail — The hydrophilic head

Arene-ruthenium prism[3]

Water soluble

Cytotoxic agent

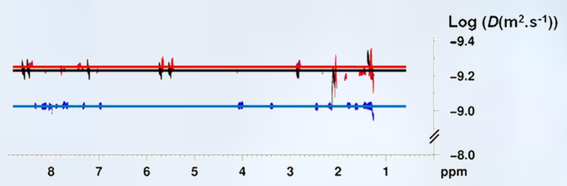
Host-guest system[4]



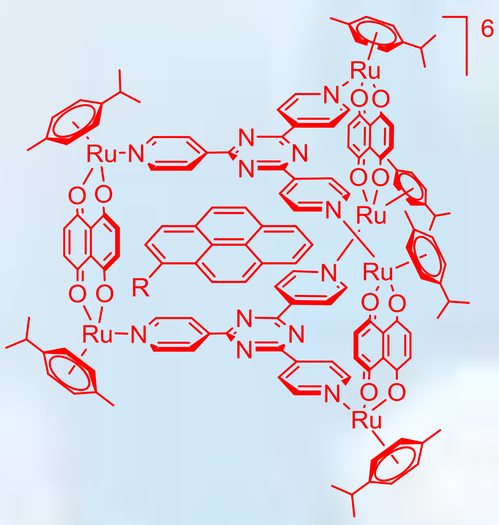
guest — host

1:1 host-guest systems

$K_a > 1.0 \times 10^4\ M^{-1}$



DOSY of $[P_2 \subset \mathbf{1}]^{6+}$



host-guest

1) Y. Matsumura, H. Maeda, *Cancer Res.* **1986**, *46*, 6387-6392; 2) B. Dardel, D. Guillon, B. Heinrich, R. Deschenaux, *J. Mater. Chem.* **2001**, *11*, 2814-2831;
3) B. Therrien, G. Süss-Fink, P. Govindaswamy, A. K. Renfrew, P. J. Dyson, *Angew. Chem. Int. Ed.* **2008**, *47*, 3773-3776; 4) A. Pitto-Barry, N. Barry, O. Zava, R. Deschenaux, P. J. Dyson, B. Therrien, *in preparation*.