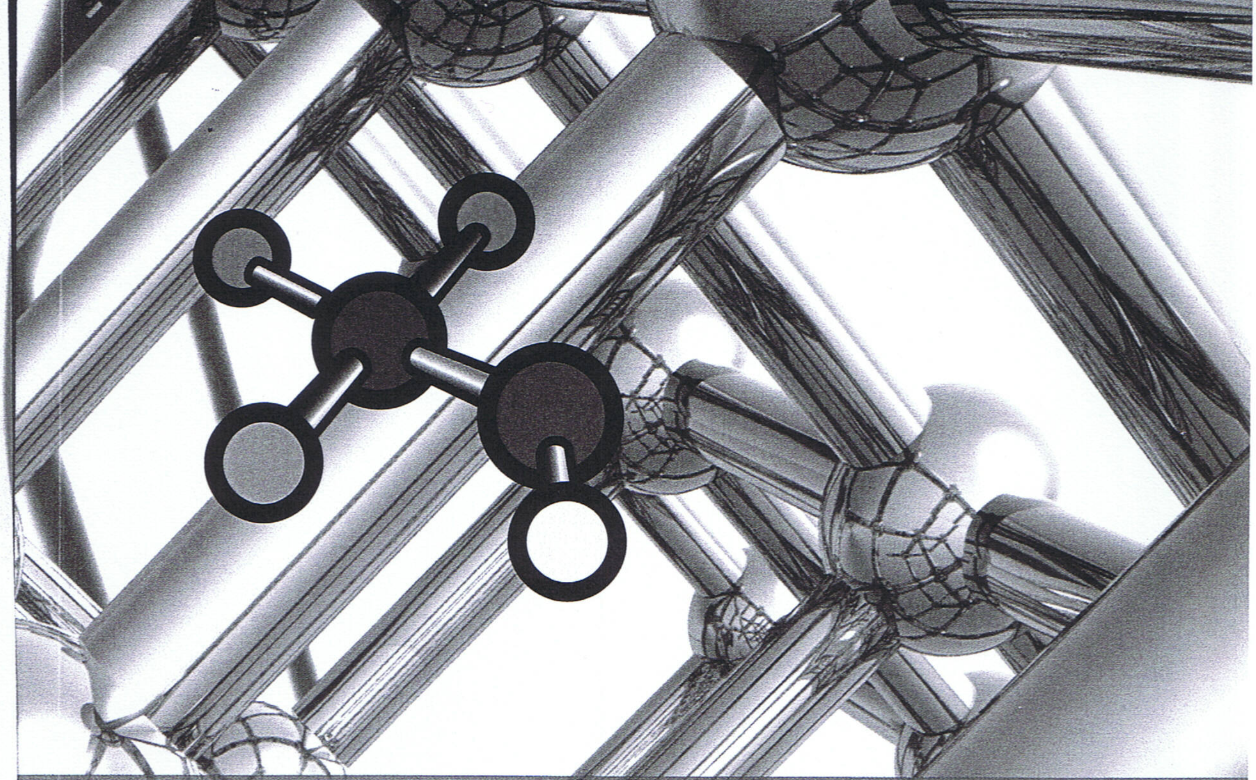

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NEW INDAZOLE AND CONDENSED PYRAZOLE BISPHOSPHONATES

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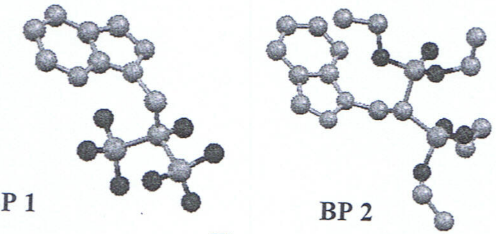
Bisphosphonates (BPs) are synthetic drugs that are effective in treating benign and malignant skeletal diseases characterized by enhanced osteoclast-mediated bone resorption (i.e., osteoporosis, Paget´s disease, and tumor-induced osteolysis). In addition, functional BPs have been also used as novel ligands for well-defined radioactive metal complexes that can be used in imagiology, scintigraphy and radiotherapy applications [1, 2]. BPs are stable, water-soluble, synthetic analogues of naturally occurring pyrophosphonates (P-O-P) in which the central oxygen atom is replaced by a carbon atom (P-C-P), thereby making BPs resistant to enzymatic degradation and usually with low toxicity [1]. The biological activities of these compounds are determined by the nature of the alkyl moiety bound to the bisphosphonic structure as well as the functional groups located on the alkyl chain, with the nitrogen-containing homologues, such as risedronate and zoledronate, amongst the most potent BPs.

Herein, we report the synthesis and characterization of a series of new 1-hydroxybisphosphonates and aminobisphosphonates derived from indazole and condensed pyrazole with potential biological activities. Crystal structures of hydroxybisphosphonate and aminobisphosphonates were determined by X-ray crystallography (Figure 1). The new BPs were evaluated as ligands for complexation with radionuclides and submitted to studies *in vitro* (hydroxyapatite binding studies simulating bone mineral uptake).



BP 1

BP 2

Figure 1

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[1] R.G.G. Russell, M.J. Rogers. *Bone* 25 (1999) 97.
[2] S. Zhang, G. Gangal, H. Uludag. *Chem. Soc. Rev.* 36 (2007) 507.