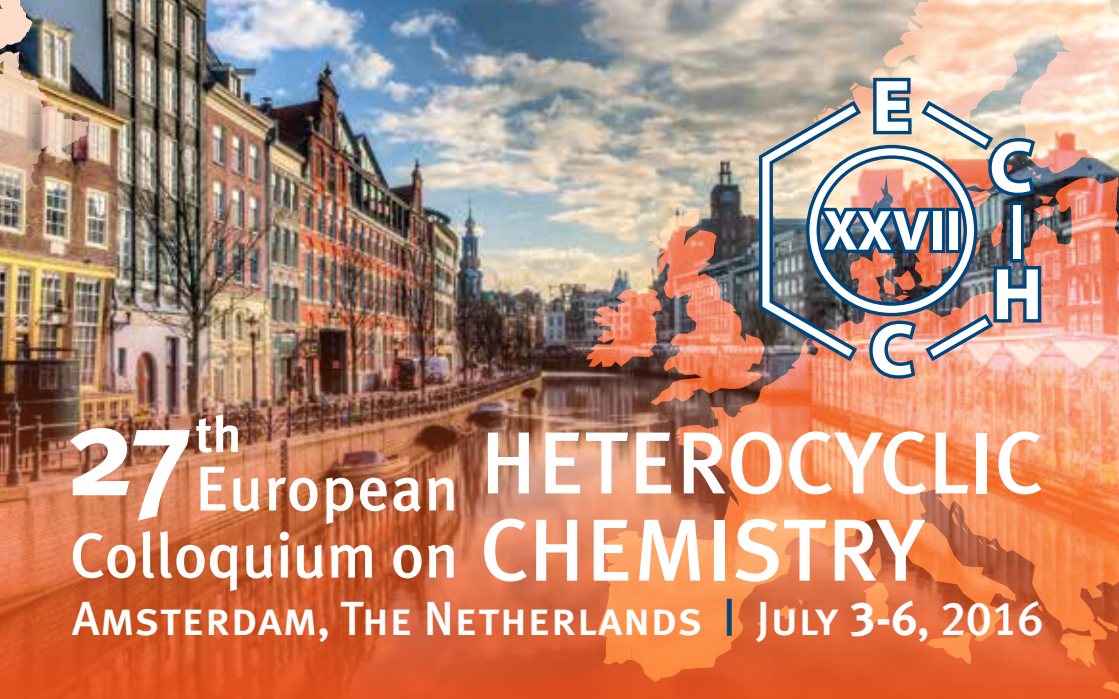

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Book of Abstracts

NEW 9-TERPENYL(7-TERPENYL)PURINES: SYNTHESIS AND CYTOTOXICITY

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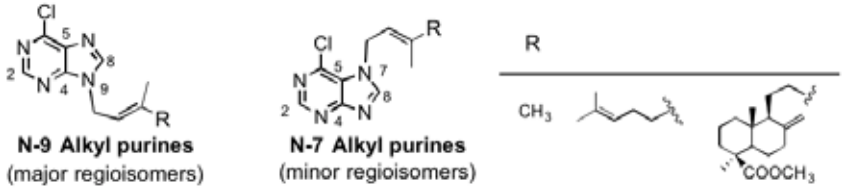
The purine ring system is one of the most widely distributed *N*-heterocycles in Nature [1] and many structurally modified purine nucleosides and nucleotides have activities ranging from antineoplastic and antiviral to antihypertensive, antiasthmatic, antituberculosis, etc [2]. Among the purine derivatives, we have put our attention on natural *N*-alkylpurines such as the asmarines or agelasimines, a group of secondary metabolites isolated from marine sponges with very interesting biological properties [3]. They have a diterpenoid moiety attached to the *N*-7 nitrogen atom of an adenine and are usually isolated in very small quantities, which limited their structure-activity relationship studies.

Our research group has been involved for years in the design, synthesis and biological evaluation of cytotoxic compounds related to natural products, including the chemoinduction of bioactivity on inactive terpenoids [4]. These diterpenoid include compounds such as communic or cupressic acids that bear decaline moieties very close to those present in the above-mentioned marine natural products.

These facts prompted us to design and prepare new terpenylpurine derivatives starting from natural monoterpenoids and diterpenoids, commercially available or isolated from their natural sources and transformed into appropriate alkylated agents.

Thus, we have prepared purines alkylated at *N*-7 and *N*-9 positions with isoprenoids, monoterpenoids and diterpenoids, using two different synthetic approaches: from 6-chloropurine or from 4,5-diamine-6-chloropyrimidine. The structure of the synthesized purines are shown in the following figure.



The purine analogues synthesized have been evaluated for their cytotoxicity against four tumour human cell lines (breast, non-small lung, cervical and hepatocellular carcinoma) and non-tumour cells (porcine liver primary cells). The most cytotoxic derivatives were those with a diterpenoid rest on the purine. The results obtained allowed to draw conclusions on the structure-activity relationship of the compounds in order to evaluate the influence of the terpenyl size on their cytotoxic properties.

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