Title: Synthesis and Preliminary Biological Screening of 6-Aminopyrazolo[3,4-b]pyridine Derivatives

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Source: Der Pharma Chemica, 8 (16), 9-16 (2016)

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6-Chloro-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (1) was utilized as key intermediate for the synthesis of new 6-amino derivatives (2-17) by heating with a number of aliphatic amines. Heating 1 with aromatic amines under similar conditions failed to give the corresponding amino derivatives. The new compounds were fully characterized and some of them were preliminary screened for anticancer, COX inhibition and antimicrobial activities. The compounds are not cytotoxic and some of them are potent and selective COX-2 inhibitors. In particular compound 6-benzylamino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (4) with IC₅₀ = 0.11 µM and SI = 33 for COX-2. 6-Hexylamino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-5-carbonitrile (6) exhibited antifungal and antibacterial activities (Gram -ve) comparable to the reference drugs. The results show clearly that the nature of N-substituent significantly affect the biological activity.
Keywords:
6-Aminopyrazolo[3,4-b]pyridines, Nucleophilic substitution, cytotoxicity, COX inhibition, antimicrobial