

Pyrazoloquinazolinones and benzimidazoquinazolinones via a 3 + 3 N-acylation-S_NAr strategy

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An efficient synthesis of pyrazolo[1,5-*a*]quinazolin-5(4*H*)-ones and pyrazolo[1,5-*a*]pyrido[3,2-*e*]pyrimidin-5(4*H*)-ones is reported from the reaction of 2-haloaroyl chlorides with 5-amino-1*H*-pyrazoles. A similar preparation of benzo[4,5]imidazo[1,2-*a*]quinazolin-5(6*H*)-ones and benzo-[4,5]imidazo[1,2-*a*]pyrido[3,2-*e*]pyrimidin-5(6*H*)-ones results from the reaction of 2-haloaroyl chlorides with 2-aminobenzimidazoles. These syntheses take advantage of the 1,3-disposition of electrophilic centers in the acid chloride and a similar arrangement of nucleophilic sites in 5-amino-1*H*-pyrazole and 2-aminobenzimidazole to form the central six-membered ring by a 3 + 3 strategy. Initial acylation of the amino group of the pyrazole or benzimidazole occurs in DMF containing carbonate base at -10 °C. Subsequent heating, in the same reaction vessel, completes the synthesis via an S_NAr ring closure between N1 of the pyrazole or benzimidazole and the 2-haloarylamide. The reaction gives 66–93% yields for the two-step sequence. These compounds are known to intercalate into DNA, and thus, may be useful as antiproliferative agents for cancer treatment. Mechanistic and spectral aspects of the project will also be presented.

