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Synthesis and Antiviral Evaluation of Imidazo[1,5-a]-1,3,5--triazine (5,8-diaza-7,9-dideazapurine) Derivatives

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A series of imidazo[1,5-a]-1,3,5-triazines substituted in the 2,4,6 and 8-positions were synthesized and examined for their inhibitory effects on the replication of orthomyxoviruses (influenza virus A and B) and paramyxoviruses (respiratory syncytial virus, parainfluenza virus type 3) in MDCK, HeLa or Vero cells. Some 2-thiosubstituted compounds, e.g. 8-(4-methylbenzyl)-2-thioxoimidazo[1,5-a]-1,3,5-triazine-4-one, were found to inhibit influenza A virus replication at a concentration (10-20 μg/ml) that was > 10-fold lower than the cytotoxic concentration. 4-Thiosubstituted derivatives, e.g. 8-(4-methylbenzyl)imidazo-[1,5-a]-1,3,5-triazine-4-thione were inhibitory to the ortho- and paramyxoviruses at a concentration (0.16-1.6 μg/ml) that coincided with their cytotoxic concentration. The compounds need further to be evaluated for their activity against viruses other than ortho- and paramyxoviruses.