ABNORMAL NUCLEOPHILIC SUBSTITUTION AND RING TRANSFORMATION OF 5- BROMO-6-METHYLURACIL DERIVATIVES WITH AMINES

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Reaction of N-substituted-5-bromo-6-methyluracil derivatives with a variety of amines or hydrazines was investigated.

Refluxing 1-substituted or 1,3-disubstituted 5-bromo-6-methyluracils(I) with aromatic amines in DMF caused a new type of nucleophilic substitution with a concomitant migration to an allylic position to give 6-arylaminomethyluracil derivatives(II). Furthermore, (I) reacted with sodium acetate and sodium benzoate, instead of aromatic amines, under the same conditions to afford the 6-acetoxymethyl and 6-benzoxymethyluracils, respectively.

Next, we found that 3-substituted 5-bromo-6-methyl-1-phenyluracil derivatives (III) react with methylamine and hydrazine caused ring transformation to give the hydantoins and the triazines, respectively.

Thus, 5-bromo-3,6-dimethyl-6-phenyluracil(IIIa) in DMF was heated with 30% aqueous solution of methylamine in a sealed tube at 100° for 18 hours to give a normal substitution product, 3,6-dimethyl-5-methylamino-1-phenyluracil(IVa) and an abnormal product, 3-methyl-1-phenylhydantoin(Va) in 21% and 30% yields respectively Similar treatment of 3-substituted (ethyl or allyl) 5-bromo-6-methyluracil derivatives bearing a phenyl group at 1-position with methylamine gave the corresponding hydantoin derivatives.

When the 5-bromo compound(IIIa) was heated at 100° for 2 hours in excess hydrazine hydrate, the ring transformation product, 6-carboxy-5-methyl-3-methylamino-4-phenyl-1,4-dihydro-as-triazine was obtained.