5-Lithio-2,4-bis-*O*-trimethylsilyluracil Rearrangement; Formation of 5-Trimethylsilyluracil

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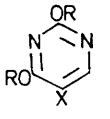
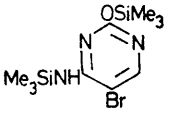
Summary The lithium derivatives prepared from 5-bromo-2,4-bis-*O*-trimethylsilyluracil and 5-bromo-2,4-bis-*NO*-trimethylsilylisocytosine rearrange rapidly to form the corresponding 5-trimethylsilyl compounds, but the lithium derivative from 5-bromo-2,4-bis-*NO*-trimethylsilylcytosine does not.

5-LITHIOPYRIMIDINES *e.g.*, (**1**, X = Li) are versatile synthetic intermediates which have been used effectively for the preparation of *C*-nucleosides related to pseudouridine[1] and for the synthesis of methyl-^{14}C- or ^{3}H-thymine.[2] Protection of functional groups of pyrimidine precursors with trimethylsilyl groups is attractive because (a) these groups are readily introduced and removed and (b) amino groups are as easily protected as hydroxyl which is not the case when alkyl (*e.g.*, t-butyl) protecting groups are used.[1] David and Lubineau[3] successfully coupled the lithium derivative prepared from 5-bromo-bis-*NO*-trimethylsilylcytosine (**2**) with an *aldehydo*-D-ribose derivative to form the corresponding acyclic *C*-nucleoside. This result is in sharp contrast with the work of Pichat and his co-workers[4] who found the lithium derivative prepared from 5-bromo-2,4-bis-*O*-trimethylsilyluracil (**1**, R = $SiMe_3$, X = Br) and the corresponding lithium derivative prepared from pertrimethylsilylated-5-bromouridine to be unreactive toward either methyl iodide or carbon dioxide.



(1)



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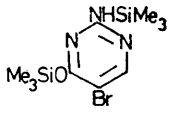

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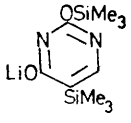

(4)

(5)

(6)

Recent results from our laboratory explain these discrepancies. We have found that the lithium derivative

prepared by treatment of 5-bromo-2,4-bis-*O*-trimethylsilyluracil (**1**, R = $SiMe_3$, X = Br) with n-butyl lithium in tetrahydrofuran at −78 °C rearranges rapidly to (**4**) which upon mild hydrolysis (dilute HCl, room temperature) yields 5-trimethylsilyluracil (**5**, R = OH). A similar rearrangement occurs when 5-bromo-2,4-bis-*NO*-trimethylsilylisocytosine (**3**) is treated with two equivalents of n-butyl lithium yielding, after acidification and hydrolysis, 2-amino-5-trimethylsilyl-4-pyrimidinone (**5**, R = NH_2). In neither of these reactions were other products observed when the addition of n-butyl lithium was carried out at −78 °C or lower; at room temperature however, addition of n-butyl lithium across the 5,6-double bond of the pyrimidine ring[5] competes with the lithium exchange and subsequent rearrangement.

The failure of (**2**) to exhibit a similar rearrangement[3] shows that the high electron density on the amino nitrogen of the dilithio intermediate (**6**) inhibits migration of silicon to the carbanionic centre. In addition, this result indicates the rearrangement to be intramolecular since it is difficult to see how intermolecular attack of a carbanion on the siloxy function of (**6**) would be inhibited. It seems likely that the rearrangement is similar to rearrangements described by Wright and West[6] and proceeds *via* an intramolecular 1,3-anionic shift of silicon from oxygen to carbon.

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