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AN S_N(ANRORC) MECHANISM IN THE AMINO-DEMETHOXYLATION OF 4,6-DIMETHOXYPYRIMIDINES[1]

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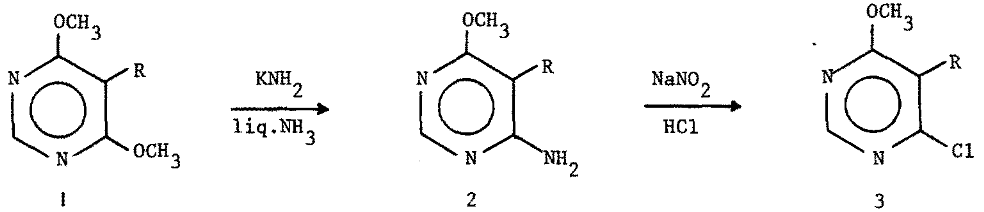
During a recent investigation of the cine-amination of 4-substituted 5-bromopyrimidines by potassium amide in liquid ammonia[2] it was observed that 5-bromo-4,6-dimethoxypyrimidine (1a)[3] undergoes an amino-demethoxylation to 4-amino-5-bromo-6-methoxypyrimidine (2a)[2] on treatment with this reagent at -33° for 24 hours. We observed a similar replacement with 4,6-dimethoxypyrimidine (1b)[4], yielding 4-amino-6-methoxypyrimidine (2b)[4]. The amino compounds 2a and 2b could be diazotized into the corresponding 4-chloropyrimidines 3a[3] and 3b[5] by the action of sodium nitrite in concentrated hydrochloric acid. All products were identified by comparison with authentic samples obtained as cited.



a) R = Br b) R = H

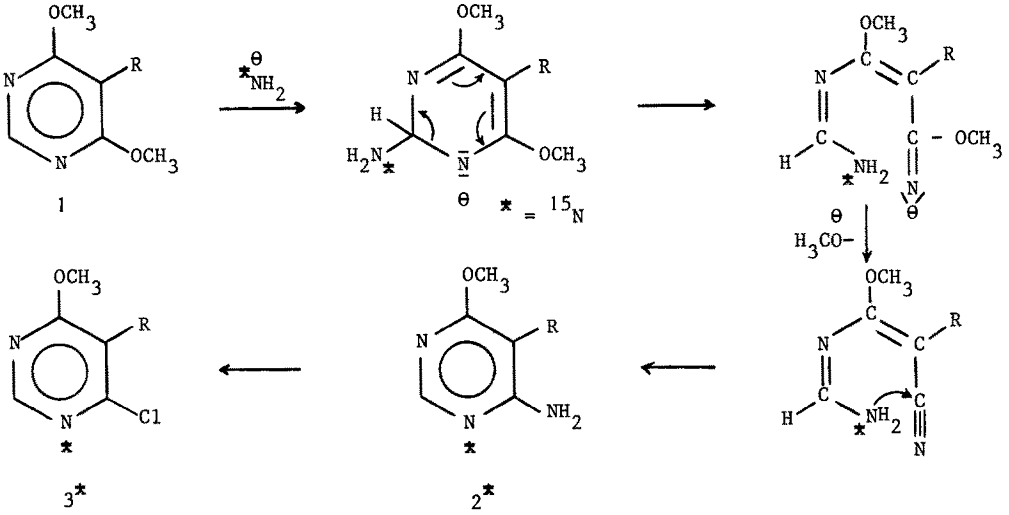
Scheme 1

In view of observations that the amino-dehalogenation of 4-halogenopyrimidines by potassium amide in liquid ammonia frequently occurs via a mechanism involving an open-chain intermediate[1,6,7] - the S_N(ANRORC) mechanism - we studied both replacement reactions with ^{15}N-labelled potassium amide in liquid ammonia. The 4-aminopyrimidines $2a^{*}$[8] and $2b^{*}$ and the corresponding 4-chloropyrimidines $3a^{*}$[8] and $3b^{*}$ were examined for their ^{15}N content by mass spectrometry, comparing the intensities of the M+1 and M peaks. The results are collected in the Table.

Excess of ^{15}N in the pyrimidines $2a^{*}$, $2b^{*}$, $3a^{*}$ and $3b^{*}$[9] and the percentage of S_N(ANRORC) mechanism in the amino-demethoxylation of 1a and 1b

Excess of ^{15}N				% S_N(ANRORC)
$2a^{*}$:	3.9	$3a^{*}$:	3.9	100
$2b^{*}$:	3.4	$3b^{*}$:	3.5	100

The complete retention of the excess of ^{15}N in the 4-chloro derivatives 3a* and 3b* implies that the ^{15}N label is present in the pyrimidine ring and that the amino-demethoxylation of 1a and 1b has completely taken place via an open-chain intermediate. These results constitute the first example of an S_N(ANRORC) process occurring on replacement of a methoxy function by an amino group. The following pathway is proposed for the reaction.



Scheme 2

An addition of a nucleophile to C(2) of 4,6-diethoxypyrimidine has been proposed earlier in the hydrazinolysis of 4,6-diethoxypyrimidine, yielding 3-methyl-1,2,4-triazole[10].

References

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8. * denotes ^{15}N-labelled compound.
9. All experiments were carried out in duplicate; accuracy ± 0.2%.
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