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DOES REACTION IN CONCENTRATED MIXTURES OF ACTIVATED RIBONUCLEOTIDES FAVOR THE SYNTHESIS OF 3'5'- AS OPPOSED TO 2'5'-LINKED DIMERS?

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We observed intriguing differences in the chemical behavior of activated nucleotides such as 2-MeImpG, 2-MeImpC and 2-MeImpU when left to react by themselves ("selfreaction") compared to when allowed to react as a mixture. These differences refer both to the yield of dimers as well as to the distribution of isomeric forms such as pyrophosphate-, 2'5'- and 3'5'-linked dimers.

The selfreactions were monitored as a function of initial concentration in aqueous solutions at 20°C in the presence of 0.2 M Mg^{2+} and 1.0 M NaCl at pH 7.5 (with 0.5 M HEPES buffer). We find that as the monomer concentration increases, the %age of hydrolysis product formed is lower and the %age of dimers becomes larger. What was unexpected is that regarding the three isomeric dimers, the percent yield of the pyrophosphate remains practically unchanged, whereas the percent yield of the 2'5'- and 3'5'-dimers increases noticeably.

In the selfreactions, even with the highest concentrations of monomer used (≈1.0 M), the amount of naturally linked dimers (pGpG, pUpU and pCpC 3'5') did not exceed 5.4%. However, a mixture of 2-MeImpG, 2-MeImpC and 2-MeImpU yields 12.6 to 17.6% of 3'5' dimers depending on total initial monomer concentration. These results suggest the existence of symbiotic internucleotide interactions. Supporting evidence for such interactions comes from the observation that, whereas 2-MeImpG is insoluble in water at concentrations >0.1 M, it becomes soluble at concentrations up to 0.45 M in a mixture with 2-MeImpC and 2-MeImpU, an increase of more than a factor of four in solubility.

The significance of these findings, if confirmed, is that concentrated solutions of mixtures of nucleotides favor interactions that yield a preponderance of products with 3'5' linkages. These types of experiments could be helpful in understanding the preference of 3'5' internucleotide linkages in a postulated RNA world.

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