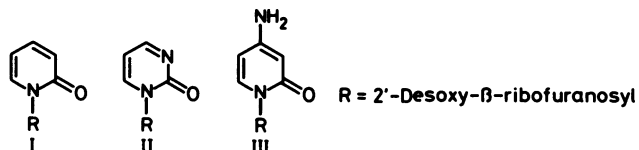


An unusual base pairing between pyrimidine and pyridine nucleotides

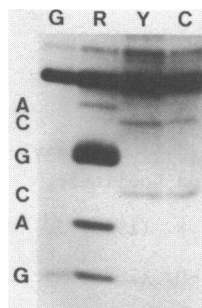
Roland Charczuk, Christoph Tamm*, Bruno Suri¹ and Thomas A. Bickle¹Institut für organische Chemie, Universität Basel, St. Johannis-Ring 19 and ¹Abteilung Mikrobiologie, Biozentrum der Universität Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland

Submitted 31 October 1986

During experiments designed to determine the response of the Klenow fragment of DNA polymerase I to nucleotide analogues in the template strand, we have examined the product of extension of the primer 5'-³²P-GATTTTGA-3' hybridised to a template 5'-TTTCGTCAAAATC-3'. The residue N in the template was either 2-(1H)-pyridinone (I, 1), 2-(1H)-pyrimidone (II, 2) or 4-amino-2-(1H)-pyridinone (III, 3; also known as 3-deazacytosine). All three analogues can be considered to be analogues of cytosine. Products of the reaction were subjected to sequencing according to Maxam and Gilbert (4).



Compound I in the template strand led to non-specific incorporation while compound II caused a block to replication. The most surprising result was obtained with compound III which directed efficient incorporation of cytosine and possibly some thymidine (see the Figure), indicating that dC can hydrogen bond to III and that the geometry is compatible with the phosphodiester backbone of double stranded DNA. The explanation may be that the greater basicity of the 2-carbonyl group of III (compared to dC) stabilises the imino-enol form of the compound which can then base pair with dC (or a tautomer of T). This needs further investigation as does the possible use of III as a C + G transversion mutagen.



*To whom correspondence should be addressed

REFERENCES

- De Bernardini, S., Graf, G., Leach, C.A., Bühlmayer, P., Waldmeier, F. and Tamm, C. (1983) *Helv. Chim. Acta* 66, 639-651.
- Altermatt, R. and Tamm, C. (1985) *Helv. Chim. Acta* 68, 475-483.
- Charczuk, R. and Tamm, C. (1986) *Helv. Chim. Acta*, in press.
- Maxam, A.M. and Gilbert, W. (1980) *Meth. Enzymol.* 65, 499-560.