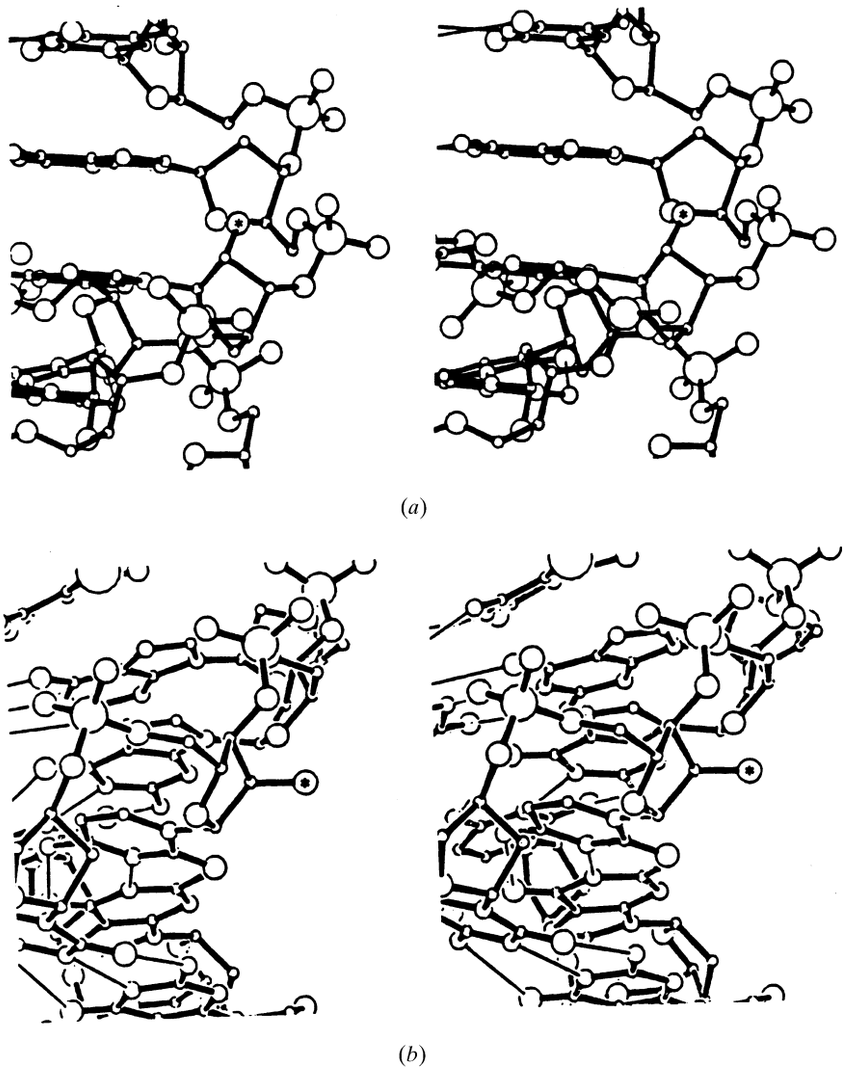

Fig. 23.3.3.5. The role of the C2′-OH in RNA helix geometry. (*a*) Addition of a C2′-OH group (*) to the B-DNA helix leads to close contacts and unallowable steric hindrance with the following O5′ and O4′ atoms and, to a lesser degree, the subsequent base itself. (*b*) A C2′-OH group added to the A-DNA helix extends outward radially from the helix cylinder surface and produces no steric clashes. Hence, A-RNA is quite possible, whereas B-RNA is disallowed.

This packing mode is sufficiently adaptable to accommodate duplexes of lengths four, six, eight, nine, ten and 12 base pairs. Hence, A-DNA does not simulate infinite helices through the crystal lattice, as A-RNA and B- and Z-DNA do.

23.3.3.5. *Allowable RNA helices*

So far this discussion has only been concerned with DNA. Which of the three helix types can be adopted by RNA? Fig. 23.3.3.5 shows that addition of a 2′-OH group to a B-DNA helix [part (*a*)] creates severe steric clash with the phosphate group and sugar ring of the following nucleotide, whereas in an A helix [part (*b*)], the added hydroxyl group extends radially outward from the helix cylinder and causes no steric problems. Hence, the natural helical form for RNA is the A helix, not the B helix. Table A23.3.1.1 shows several single-crystal analyses of A-RNA and RNA/DNA hybrids; Table A23.3.1.2 shows no B-RNA structures. One RNA/DNA hybrid is known as a Z helix: C-G-c-g-C-G (Z24), in which the two central nucleotides are RNA. If one mentally adds an —OH to each C2′ atom in Fig. 23.3.3.3, on the same side of the ring as O3′, it is apparent that the C2′-OH is not inherently incompatible with the Z helix, as it is with the B helix. At guanine sugars, the C2-OH points out and away from the helix, while at cytosine sugars it points away from the base into the spacious minor groove.

23.3.3.6. *Biological applications of A, B and Z helices*

The B helix is the biologically relevant structure for DNA. The A form might logically be adopted at the stage of transient DNA–RNA duplexes during transcription, but elsewhere the B form holds sway. It was once thought that binding of DNA to a protein surface, most particularly nucleosomal winding, might constitute a sufficient dehydration of bound water molecules from the DNA duplex to shift it to the A form. This proved to be false; nucleosomal DNA clearly retains the B conformation. The closest that one comes to biological A-DNA is local deformations upon binding of B-DNA to a few proteins that have been described as ‘A-like distortions’. On the other hand, the A helix has been found repeatedly in RNA duplexes, including tRNA and ribozymes.

The situation is even more restrictive with the Z helix. Although its alternating purine/pyrimidine sequence makes it unusable for genetic *coding*, the suggestion has been made on many occasions that Z-DNA might be an important element in genetic *control* by being involved in negative supercoiling (Herbert & Rich, 1996). It has been shown that a left-handed DNA conformation can be induced by negative superhelical stress, but it is not absolutely clear that this induced, left-handed conformation is the same as the Z helix seen in crystal structures of small oligomers. As noted by Herbert & Rich (1996), after nearly twenty years of enquiry, it is still far from certain that Z-DNA itself has any demonstrable biological role.*

A major stumbling block is the cumbersome mechanism that must be invoked to explain a B-to-Z interconversion. As mentioned previously, a simple twisting of the helix from right to left is not sufficient, because the backbone chains run in opposite directions in the two forms. Fig. 23.3.3.6 demonstrates the steps that must still be undertaken after both B and Z helices have been unwound so as to remove all of their helical character. Note the opposite sense of the backbone strands in B [part (*a*)] and Z [part (*e*)]. In order to accomplish the interconversion, base pairs of B-DNA must be

* Rich and co-workers (Schwartz *et al.*, 1999) have recently solved the crystal structure of the Zα domain of the human editing enzyme ADAR1 in a complex with a six-base-pair Z-DNA helix of sequence CGCGCG. This left-handed hexamer may suffer from the same length *versus* conformation uncertainty mentioned later in this chapter in connection with oligonucleotide crystals, especially since protein–DNA contacts in the Zα complex occur only with the zigzag phosphate backbone, which is not that dissimilar in Z-DNA (Fig. 23.3.3.3) and Z(WC)-DNA (Fig. 23.3.3.7). Nevertheless, it is encouraging to see a short segment of Z actually making contact with its protein in a presumably biologically relevant context.

references