A Family of Guanosine Isomers

Product Information

Transposition of certain atoms and/or groups in the nucleobase fragment of guanosine or 2'-deoxyguanosine affords isomers that offer alternative base-pairing modes.

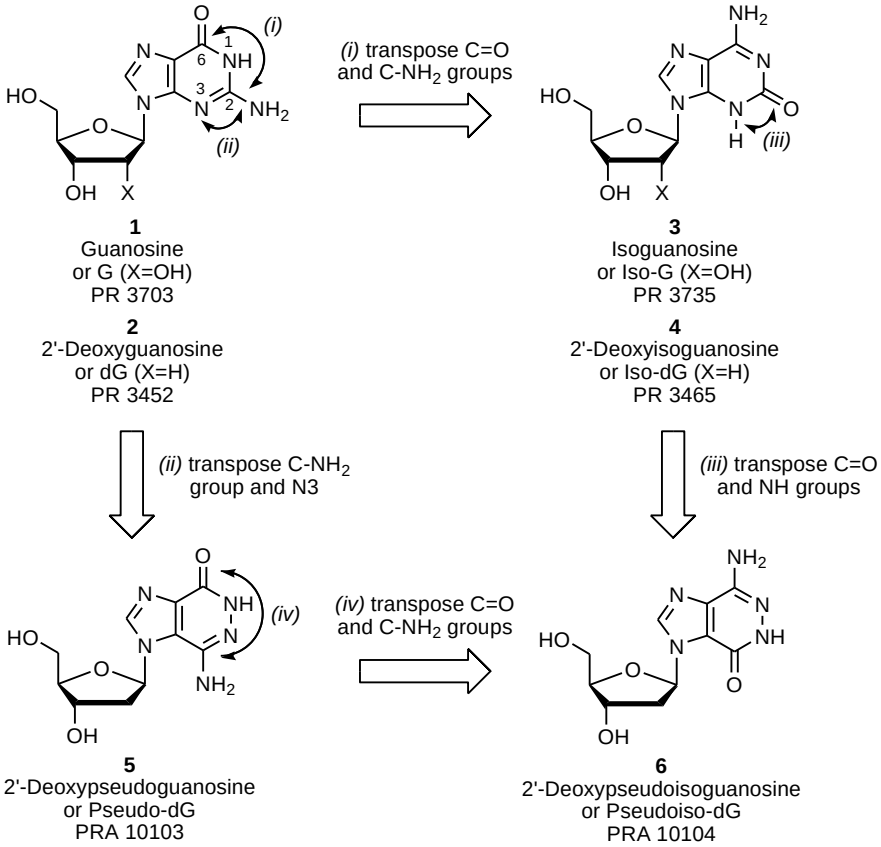

Figure 1. Isomers of guanosine (**1**) and 2'-deoxyguanosine (**2**).

Introduction: Modifications of the nucleobase moiety of guanosine (**1**) and 2'-deoxyguanosine (**2**) can lead to altered base-pairing characteristics. Berry and Associates offer **1**, **2**, and a variety of isomers (**3-6**, Figure 1), as well as the phosphoramidites **7** and **8** (Figure 3 below).

Isoguanosine (Iso-G, 3) and 2'-Deoxyisoguanosine (Iso-dG, 4) are isomeric with G/dG, differing by transposition of the carbonyl group at position 6 of G or dG with the C-NH_2 group at position 2 (transposition *i* in Figure 1). Isoguanosines are important in the field of non-natural base pairing. In 1989, Benner and co-workers[1] reported the enzymatic incorporation of iso-G into RNA and DNA and characterized the distinct non-natural base pairing that resulted, especially pairing involving the similarly transposed isomer of

dC known as iso-dC (not shown; we offer the closely-related compound 5-Methyliso-dC, Product No. PY 7255).

2'-Deoxypseudoguanosine (Pseudo-dG, 5) is the result of the transposition of the C-NH_2 group at position 2 of dG with the nitrogen atom at position 3 (transposition *ii* in Figure 1). Hosmane and co-workers have recently synthesized Pseudo-dG[2] as well as the ribose version, Pseudo-G (not shown).[3]

2'-Deoxypseudoisoguanosine (Pseudoiso-dG, 6) is related to Iso-dG and Pseudo-dG as indicated by the transpositions (*iii*) or (*iv*) as shown in Figure 1, or to dG by a double-transposition (not shown). In 1994, Berry, Townsend, and co-workers reported the synthesis of the ribose version of this compound, Pseudoiso-G (not shown).[4] Hosmane and co-workers have recently synthesized both Pseudoiso-dG[2] and Pseudoiso-G.[3]

Studies on the nucleosides 5, 6, and their ribose versions. The nucleosides **5** and **6** were studied in solution and by computer modeling.[2] Pseudo-dG **5** was found to form homo-pairs (**5 • 5**, see Figure 2), corresponding to what would be an anti-parallel arrangement in a nucleic acid. Evidence for three of the four possible intramolecular hydrogen bonds was obtained. Pseudo-dG **5** also hetero-pairs with pseudoiso-dG **6** as shown, corresponding to a parallel arrangement. Although the nucleosides **5** and **6** were not studied in oligonucleotides, they would be attractive nucleic acid modifications in homo- and hetero-pairing modes. It would also be interesting to study them in pairs with canonical nucleotides. For example, replacing dG with pseudo-dG **5** opposite a dC nucleotide (see Figure 2) may lead to G • C base-pair leveling. Finally, in early 2008, Hosmane and co-workers disclosed results for the inhibition of adenosine deaminase by the nucleosides pseudo-G/dG and pseudoiso-G/dG.[3]

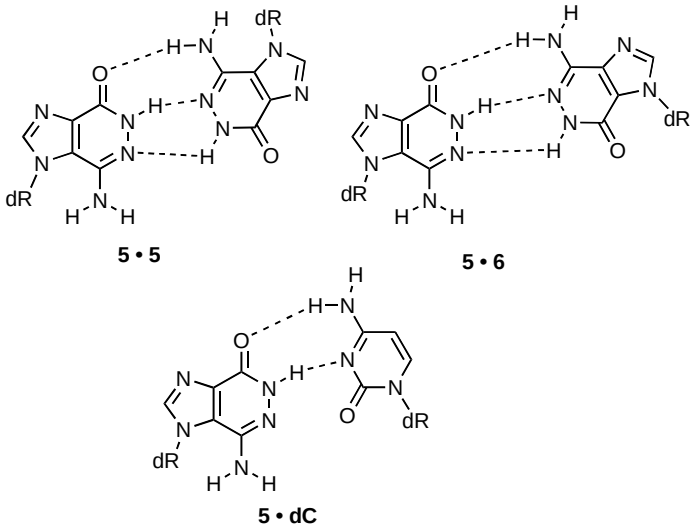

Figure 2. Base-pairing schemes for dG analogs **5** and **6**.

Phosphoramidites of Pseudo-dG and Pseudoiso-dG. We now offer the phosphoramidites Pseudo-dG CEP (**7**, BA 0312) and Pseudoiso-dG (**8**, CEP BA 0314), shown in Figure 3, and we anticipate that these hitherto unknown monomers may be useful for incorporation into nucleic acids to provide novel alternate base-pairing schemes.

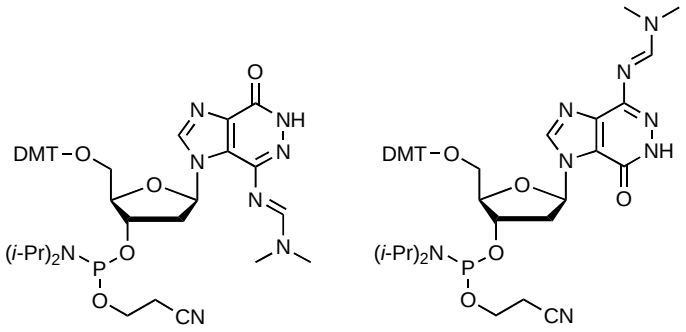

Figure 3. Phosphoramidites for the incorporation of Pseudo-dG and Pseudoiso-dG into oligonucleotides.

Use of Pseudo-dG CEP (7, BA 0312): Employ acetonitrile diluent at the concentration recommended by the synthesizer manufacturer. Use standard coupling protocols; extended coupling times are not required. Cleavage from the solid support may be carried out by standard procedures. Deprotection of the Pseudo-dG residue is slower than the corresponding amidine-protected dG derivative. For best results, use concentrated ammonium hydroxide at 55 °C for 16-18 h. Higher temperatures are not recommended, nor is extended contact with ammonium hydroxide at room temperature, which does not effectively deprotect pseudo-dG. AMA should be avoided, as it gives by-products.

Use of Pseudoiso-dG CEP (8, BA 0314): Employ acetonitrile diluent at the concentration recommended by the synthesizer manufacturer. Use standard coupling protocols; extended coupling times are not required. Cleavage from the solid support may be carried out by standard procedures. Deprotection of the Pseudoiso-dG residue is easier than for Pseudo-dG, and should be carried out using concentrated ammonium hydroxide at 55 °C for 16-18 h or 65 °C for 2 h. Room temperature deprotection is not recommended; only about 1/3 of the amidine protecting group is removed after 24 h. AMA should be avoided, as it gives by-products.

Literature:

1. Switzer, C. Y.; Moroney, S. E.; Benner, S. A. *J. Am. Chem. Soc*. **1989**, *111*, 8322-8323.

2. Ujjinamatada, R. K.; Paulman, R. L.; Ptak, R. G.; Hosmane, R. S. *Bioorg. Med. Chem*. **2006**, *14*, 6359-6367.

3. Ujjinamatada, R. K.; Phatak, P.; Burger, A. M.; Hosmane, R. S. *J. Med. Chem*. **2008**, *51*, 694-698.

4. Berry, D. A.; Wotring, L. L.; Drach, J. C.; Townsend, L. B. *Nucleosides Nucleotides* **1994**, *13*, 2001-2011.