

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.

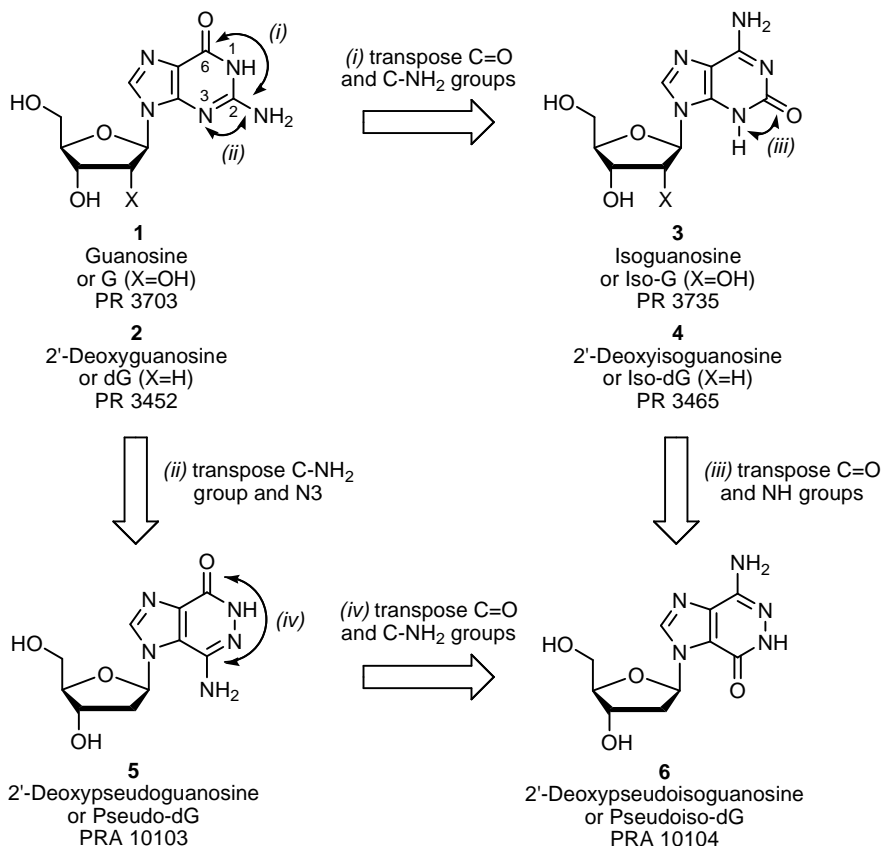


Figure 1. Isomers of guanosine (1) and 2'-deoxyguanosine (2).

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-NH₂ 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-workers¹ 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-NH₂ 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-dG² 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-dG² 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

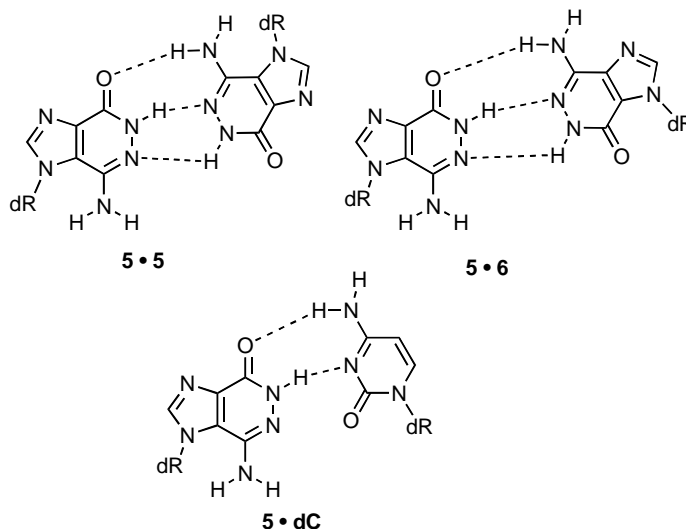


Figure 2. Base-pairing schemes for dG analogs **5** and **6**.

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.

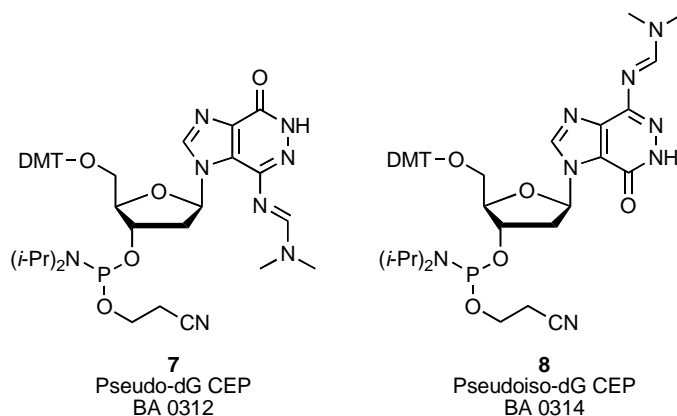


Figure 3. Phosphoramidites for the incorporation of Pseudo-dG and Pseudoiso-dG into oligonucleotides.

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.

Note: Pseudo-dG CEP (BA 0312) and Pseudoiso-dG CEP (BA 0314) are from our Experimental Grab Bag. The compounds in this unique collection have met all of Berry and Associates' purity standards, but have not been validated for any particular purpose.

We hope that you may find them interesting, but please be aware that their purchase and use is at your own risk.

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.