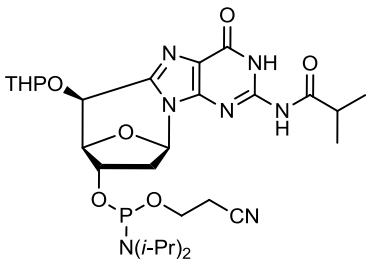
(5′S)-8,5′-Cyclodeoxyguanosine (THP) CEP
Product No. BA 0382

Product Information



$C_{28}H_{42}N_7O_7P$
Mol. Wt.: 619.65

This phosphoramidite is used for standard 3' to 5' oligonucleotide synthesis.

The naturally occurring nucleosides, cyclo-dG and cyclo-dA are bridged cyclonucleosides that result from oxidative free radical damage to DNA. This specialized "tandem lesion" encompasses damage to both the sugar and the base moiety of the same purine nucleoside. This oxidative damage plays a significant role in mutagenesis, carcinogenesis and aging.[1] Both of the bulky 8,5'-Cyclodeoxyadenosine (cyclo-dA) and the 8,5'-Cyclodeoxyguanosine (cyclo-dG) lesions have been shown to be present in human cells.[1,2] Cyclo-dA and Cyclo-dG are both strong blockers of gene expression in CHO and human cells. These lesions can be repaired *via* nucleoside excision repair mechanisms, but not by base excision repair mechanisms.[3] Structural investigations have shown that when incorporated into DNA, cyclo-dG stacks in the DNA duplex, retains Watson-Crick hydrogen bonding with dC, but significantly perturbs the helix structure near the lesion.[4]

Both cyclo- dA and cyclo-dG are valuable tools for investigations into DNA damage and repair. We offer the traditionally DMT protected cyclo-dA CEP (BA 0329), but the difficulties encountered when developing a practical synthesis for a cyclo-dG phosphoramidite that would be applicable to automated DNA synthesis led us away from the conventional 5'-DMT protection. A better alternative, which dramatically increases the overall yield of the synthesis, is to utilize a 5'-tetrahydropyranyl (THP) protecting group. We have found that BA 0382 couples efficiently in automated oligonucleotide synthesis. Furthermore, the THP protection is cleanly removed by treatment with 3%

TCA in CH_2Cl_2, however the standard DMT deprotect conditions are insufficient. We found that THP deprotection was readily accomplished by adding two or three 15-minute deprotect steps at the end of the cyclo-dG cycle. A slight disadvantage of the 5'-THP is that the characteristic orange color that is seen with DMT deprotection is not observed with THP deprotection.

Use: Dissolve the CEP acetonitrile at concentrations recommended by the synthesizer manufacturer. Coupling should be carried out using standard instrument protocols modified for extended detrotection. On our Expedite 8909, excellent coupling efficiencies and yields could be obtained with either 2 or 3 900 second deprotect cycles after the incorporation of BA 0382. Cleavage from the solid support can be carried out under standard conditions, and the (5′S)-8,5′-cyclodeoxyguanosine residue is stable to standard deprotection conditions.

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2. Dizdaroglu, M.; Dirksen, M.L.; Jiang, H.X.; Robbins, J.H.*J. Biochem*. **1987**, *241*, 929-932.
3. a) Brooks, P.J.; Wise, D.S.; Berry, D.A.; Kosmoski, J.V.; Smerdon, M.J.; Somers, R.L.; Mackie, H.; Spoonde, A.Y.; Ackerman, E.J.; Coleman, K.; Tarone, R.E.; Robbins, J.H. *J. Biol. Chem*. **2000**, *275* , 22355-22362. b) Swanson, A. L.; Wang, J.; Wang, Y. *Chem. Res. Toxicol.* **2012**, *25*, 1682-1691. c) Pande, P.; Das, R.S.; Sheppard, C.; Kow, Y.W.; Basu, A.K. *DNA Repair*, **2012**, *11*, 926-931.
4. Huang, H.; Das, R.S.; Basu, A.K.; Stone, M.P. *J. Am. Chem. Soc.* **2011**, *133*, 20357-20368.