*N*2-Substituted 2′-Deoxyguanosine Triphosphate Derivatives, Selective Substrates for Human DNA Polymerase κ.

A. S. Prakasha Gowda, Marietta Lee, and Thomas E. Spratt\*[a]

[a] A. S. Prakasha Gowda, Thomas E. Spratt  
Department of Biochemistry and Molecular Biology  
Pennsylvania State University  
500 University Dr.  
Hershey, PA 17033  
tes13@psu.edu

[b] Mariatta Y.Lee  
Department of Biochemistry and Molecular Biology  
New York Medical College  
Valhalla, NY 10595

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**Abstract:** *N*2-Alkyl-2’-deoxyguanosine triphosphate (*N*2-alkyl-dGTP) derivatives with methyl, butyl, benzyl, 4-ethynylbenzyl substituents were prepared and tested for substrates for human DNA polymerases. *N*2-Benzyl-dGTP was equal to dGTP as a substrate for DNA polymerase κ, but was a poor substrate for pol β ,δ, η, ι ,or ν. In vivo reactivity was evaluated by incubation of *N*2-4-ethynylbenzyl-dG with wild-type and pol κ deficient mouse embryonic fibroblasts. CuAAC click reaction with 5(6)-FAM-azide demonstrate that only pol κ containing cells were able to incorporate *N*2-4-ethynylbenzyl-dG into the nucleus. This is the first instance of a Y-family-polymerase-specific dNTP and this method can be used to probe the activity of pol κ in vivo.

Synthetic nucleotide analogs are widely used tools in chemical biology, diagnostics, and therapeutics. Modifications on the Watson-Crick hydrogen-bonding face have been employed to probe the value of Watson-Crick hydrogen bonds in DNA replication,[[1](#_ENREF_1)] and create extra-biological base pairs.[[2](#_ENREF_4" \o "Sefah, 2014 #6665)] Minor groove modifications are used to elucidate critical protein-DNA interactions,[[3](#_ENREF_8)] while major groove modifications have proved to be useful in exploring polymerase enzymology[[4](#_ENREF_11)] and cellular reactivity.[[5](#_ENREF_13" \o "Sirbu, 2012 #6616)] Inhibitors of viral reverse transcriptases are in clinical use for HIV, hepatitis B, and hepatitus C therapy.[[6](#_ENREF_16" \o "Clark, 2015 #6768)] Human DNA polymerase inhibitors are also in use for cancer chemotherapy. Gemcitabine, a cytidine analog that is incorporated into the DNA but then inhibits DNA synthesis, is used to treat pancreatic cancer, non-small cell lung cancer, breast cancer, and bladder cancer.[[6c](#_ENREF_18" \o "Jordheim, 2013 #6764)] Gemcitabine is effective because it affects rapidly growing tumor cells more than normal tissue. More recently, specialized polymerases that are over expressed in tumors have been the target of inhibition studies.[[7](#_ENREF_21" \o "Korzhnev, 2016 #6767)] Identification of nucleotide analogs as selective substrates or inhibitors for specific polymerases is challenging because all polymerases utilize the four cononocial dNTPs, and correct base pairing is mostly dependent on the polymerase recognizing Watson-Crick geometry. Recently, engineered polymerases were utilized to create a modifed nucleotide that can recognize a carcinogen-modified DNA template,[[8](#_ENREF_22)] and expanded size dNTPs (dxNTPs) have been shown to have some selectivity for human DNA polymerase θ.[[9](#_ENREF_24" \o "Kent, 2016 #6763)] In this report, we utilize the known reactivity of DNA polymerase κ to rationally design *N*2-benzyl-dGTPs that are highly specific substrates for pol κ. These triphosphates are the first reports of nucleotide triphosphates that are highly selective substrates for a human Y-family polymerase. These compounds can be utilized to probe for the reactivity of pol κ in vivo, and potentially be modified to be selective inhibitors of pol κ .

The mammalian cell utilizes sixteen DNA polymerases to replicate DNA, the four high-fidelity enzymes that duplicate the bulk of genomic and mitochondrial DNA, together with specialized DNA polymerases that perform roles in the DNA damage response. Translesion DNA synthesis (TLS) polymerases are a subset of the specialized polymerases that are involved in the bypass of DNA damage.[[10](#_ENREF_26)] TLS polymerases include the Y-family DNA polymerases, pol η, pol ι, pol κ, and REV1, the B-family pol ζ, [[10b](#_ENREF_27)] and perhaps other pols such as λ, ν, θ, and PrimPol.[[11](#_ENREF_30)] These polymerases have unique DNA binding sites that enable the polymerases to bypass a variety of DNA damage. However, polymerases that participate in lesion bypass also perform other functions. For example, while DNA polymerase κ (pol κ) is the most active polymerase in the accurate bypass of bulky *N*2-dG adducts,[[12](#_ENREF_34)] pol κ also bypasses the structurally divergent 8-oxo-dG,[[13](#_ENREF_35)] participates in nucleotide excision repair,[[14](#_ENREF_36)] replicates non-B-DNA sequences,[[15](#_ENREF_37)] and it’s polymerase activity is involved in the initiation of the ATR checkpoint signal.[[16](#_ENREF_39)] In addition, abnormal expression of pol κ correlates with increased mutations in tumors.[[17](#_ENREF_40)] Further complicating the matter, many of these function are not unique to pol κ, as both pol ι and η[[18](#_ENREF_41)] can bypass *N*2-dG adducts, pol δ is the major NER polymerase, and pol η can also replicate non-B-DNA sequences.[[19](#_ENREF_43)]

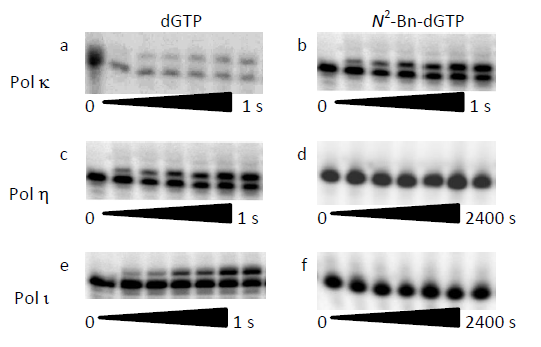
The roles of individual polymerases in the cell are difficult to resolve, in part, because all polymerases utilize undamaged DNA and the four dNTPs as substrates. To help elucidate the many roles of pol κ, we have designed a triphosphate that is a highly specific substrate for pol κ. Here we describe the synthesis of *N*2-benzyl-dGTP (*N*2-Bn-dGTP), and show that it is a substrate for purified pol κ but a very poor substrate for pol β, δ, η, ι, and ν. We also show that *N*2-*p*-ethynylbenzyl-dG (EBndG), when given to cells, is incorporated into the DNA only in the presence of pol κ.

The rationale for the design of a pol κ-specific dNTP substrate is illustrated in . Pol κ bypasses hydrophobic *N*2-alkyl-dG adducts ranging from methyl to (benzo[a]pyren-6-yl)methyl,[[20](#_ENREF_44)] as well as the carcinogenic *N*2-7,8,9-trihydroxy-7,8,9,10-tetrahydro­benzo­[a]­pyren-10-yl-dG (*N*2-BP-dG) (a) with kinetic parameters approaching those of undamaged DNA.[[21](#_ENREF_45)] While high fidelity polymerases utilize interactions with the minor groove of the DNA to enhance fidelity, pol κ has an opening on the minor groove side of the DNA that can accommodate bulky alkyl groups attached to the *N*2-position of dG in the template base.[[22](#_ENREF_46)] We hypothesized that this binding pocket can also accommodate the *N*2-alkyl groups when bound to the incoming dGTP (b). We investigated the specificity of the dNTPs by examining the in vitro reactivity with an array of human polymerases that includes pols κ, β, δ, η, ι, and ν. These enzymes include members of the A-, B-, X- and Y-polymerase families.



**Figure 1.** Rationale for design of pol κ specific dNTP substrate. a, Incorporation of dCTP opposite *N*2-BP-dG. b, Incorporation of *N*2-Bn-dGTP opposite dC .

The in vitro activities of purified human polymerases with *N*2-alkyl-dGTPs were analyzed by primer extension assays, as illustrated in Figure 2. The panels on the left show that pol κ, η and ι readily inserted dGTP opposite dC. The panels on the right demonstrate that only pol κ rapidly incorporated *N*2-Bn-dGTP. Even at a higher *N*2-Bn-dGTP concentration and longer time periods, pol η and ι were much less efficient at utilizing *N*2-Bn-dGTP. Figure S1 (Supporting Information) shows representative gel images of all the polymerases examined. The in vitro reactivity of six purified polymerases were examined as described in the Supporting Information. The kinetic parameters are presented in Table S1 and the reactivities are summarized in Figure 3**.**



**Figure 2.** Comparison of the reactivity of pol κ, η and ι with *N*2-Bn-dGTP. In the primer extension assay, DNA (10 nM) and the polymerase (100 nM) were reacted with 5 μM dGTP (a, c, e) or *N*2-Bn-dGTP (b, d, f) at a concentration of 5 μM (b), or 25 μM (d, f) for the indicated amount of time. The substrates and products were separated by PAGE. The lower bands on the polyacrylamide gels are the 15-mer starting material, while the upper bands are the 16-mer products.

Pol κ reacted rapidly with the three dGTP analogs (Figure S2, S3). The methyl and benzyl substitutions did not impact the kpol, while the Kd rose by a factor of 2. *N*2-butyl-dGTP was a slightly poorer substrate than dGTP, with a 20-fold decrease in kpol. The Y-family pols η and ι, while not affected by the methyl substitutions, experienced a 10,000-fold reduction in kpol with the butyl substitution (Figures S4-S7). Pol ι reacted poorly with *N*2-Bn-dGTP, while the reactivity of pol η further decreased due to a decrease in kpol and an increase in Kd. In spite of the ability of pol η to bypass *N*2-(2-naphthyl)methyl-dG in the template, the polymerase in unable to utilize *N*2-Bu-dGP or *N*2-Bn-dGTP as substrates. Of the Y-family polymerases, only pol κ reacts with *N*2-Bn-dGTP at rates similar to unmodified dNTPs.



**Figure 3**. Reactivity of dGTP (H), *N*2-methyl-dGTP (Me), *N*2-butyl-dGTP (Bu) and *N*2-Bn-dGTP (Bn) with DNA polymerase κ. ι, η, β, ν, and δ/PCNA.

Next, we examined the reactivity with representatives of the A-, B- and X-polymerase families. Humans have three A-family polymerases, the high fidelity pol γ, responsible for mitrochondirial replication, and the low fidelity pol θ and ν. Pol θ has a role in alternative NHEJ while pol ν is implicated in the repair of intrastrand crosslinks and translesion DNA synthesis. Despite the fact that pol ν has low fidelity, it incorporated the *N*2-alkyl-dGTPs very poorly (Figure S10, S11). The kpol/Kd for *N*2-Bn-dGTP is decreased > 105 –fold when compared with dGTP. The reactivity of *N*2-Bn-dGTP with pol γ and θ still needs to be determined. Humans have four B-family polymerases α, δ and ε are involved in high fidelity DNA replication, while pol ζ is involved in TLS. Pol δ is a B-family polymerase implicated in lagging strand replication. We examined the reactivity of pol δ/PCNA in steady-state kinetics (Figure S12). The reaction is sensitive to small modifications as demonstrated by the 300-fold decreased in kcat/Km for *N*2-Me-dGTP relative to dGTP (Table S1). Increasing the size of the substitution further decreased reactivity, with a 105-fold decrease in kcat/Km for pol δ with *N*2-Bn-dGTP. Similarities among B-family polymerases suggest that both pol α and ε will be equally poor at utilizing *N*2-Bn-dGTP as a substrate. It was previously shown that *N*2-butylphenyl-dGTP was not a substrate for pol α, γ and β, but was an inhibitor of pol α.[[23](#_ENREF_47)] Humans have three X-family polymerases, β, λ, and μ. Pol β is the primary polymerase involved in base excision repair, while pol λ and μ are involved in NHEJ. The preferred substrate for pol β is a duplex DNA with a single-nucleotide gap. Pol β was very inefficient at the incorporation of nucleotides opposite the *N*2-BP-dG.[[24](#_ENREF_49)] Unsurprisingly, we found that pol β did not accommodate steric bulk at the *N*2-position of the dNTP (Figures S8, S9). Methyl substitution decreased kpol/Kd values over 1000-fold. Further increases in size of the alkyl group lead to a decrease in kpol/Kd of greater than 6-orders of magnitude.

The fidelity of the pol κ with *N*2-Bn-dGTP is slightly better than for dGTP. We investigated the fidelity of the incorporation of *N*2-Bn-dGTP opposite dA, dC, dG, and dT as the template base with Michaelis-Menten kinetics. As summarized inTable S2, the preference for dC is higher with *N*2-Bn-dGTP than for dGTP. The increased selectivity for dC as template is due to the decreased rate of mispair formation. The finc for dGTP was 0.07 for each nucleotide, while finc averaged 0.015 for *N*2-Bn-dGTP.

The in vitro reactions have shown that *N*2-Bn-dGTP reacts with pol κ, but not pol β, δ, η, ι, or ν. To determine if this reaction occurs in vivo, we synthesized *N*2-(4-ethynylbenzyl)-dG (EBdG) as described in the Supplementary Information. Attachment of the ethynyl moiety to the benzyl group enables the use of copper(I)-catalyzed azide-alkyne cycloaddition chemistry to attach a fluorescent group to the nucleoside and thus determine the amount and location of EBdG in the cell.[[5](#_ENREF_13)] The labelling of the nuclei is shown in Figure 4a-c, in which mouse embryonic fibroblasts (MEF) were incubated with 10 μM EBdG for 24h. The cells were fixed and the ethynyl groups were reacted with azido-FAM, and the nuclei identified with DAPI-staining of the DNA. The complete overlap DAPI (Figure 4a) and FAM (Figure 4b) signals indicates that the cells incorporated EBdG into the nucleus.



**Figure 4** Detection of EBdG in nucleus of pol κ containing cells. Wild-type (a-c) and POLK(-/-) (d-f) cells were treated with 10 μM EBdG for 24 h. DNA is visualized with DAPI-staining (a,d) and EBdG visualized by Click reaction with FAM-N3 (b,e). The white bar is 40 µm. g, Levels of FAM-EBdG conjugate in nuclei of MEF POLK(+/+) (black) and POLK(-/-) (red) cells. The incubation with EBdG was performed three times. The total number of cells in violin plots are described for wildtype (black) and POLK(-/-)(red) cells.

To determine if pol κ is the polymerase that incorporates EBdG into DNA in mammalian cells we incubated POLK deficient MEF cells with the nucleoside and then analyzed the incorporation by visualization after the Click reaction. Figure 4d-f shows that POLK deficient MEF cells were unable to incorporate EBdG into the nucleus. The relative intensities of FAM signal to the DAPI signal was measured for each nucleus. The first lane of Figure 4g shows the background level of FAM fluorescence in the nucleus. At 10 nM EBdG, approximately half of the wild-type cells incorporated a small amount of the nucleoside. Above this concentration, all cells incorporated EBdG. In cells without pol κ, EBdG is not incorporated into the DNA. These results indicate that EBdG is able to diffuse into the nucleus, be converted into the triphosphate, and be incorporated into the DNA. In addition, the incorporation into the DNA is dependent on the presence of pol κ.

In conclusion, we have found that *N*2-alkyl-dGTPs are substrates for DNA pol κ. The kinetic parameters for *N*2-Bn-dGTP are only slightly slower than dGTP. The fidelity of the pol κ catalyzed incorporation is slightly better for *N*2-Bn-dGTP than it is for dGTP. We also found that *N*2-Bn-dGTP reacted slowly with representatives from the A-family (ν), B-family (δ), or an X-family (β); the kpol/Kd or kcat/Km values are <105 that of pol κ. We also found that the ethynyl nucleoside, *N*2-EBn-dG is incorporated into the DNA by cells by pol κ. These reagents will be very useful at elucidating the cellular activities of pol κ, and can be the basis for the selective inhibition of pol κ.

**Note added in proof.**

In the course preparing this manuscript, Matyasovsky et al published their discovery that 2-methyl-, 2-vinyl, and 2-ethynyl- but not 2-phenyl-dATP analogs are incorporated into DNA by prokaryotic polymerases.[[25](#_ENREF_50)] This discovery leads to the possibility that dATP analogs can also be designed to probe pol κ activity

Acknowledgements

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**Keywords:** DNA polymerase • DNA modification • fluorescent labelling • nucleotides • bioconjugation

[1] a) E. T. Kool, H. O. Sintim, *Chem.Commun.(Camb.)* **2006**, 3665-3675; b) T. W. Kim, J. C. Delaney, J. M. Essigmann, E. T. Kool, *Proc.Natl.Acad.Sci.U.S.A.* **2005**, *102*, 15803-15808; c) E. T. Kool, *Annu. Rev. Biochem* **2002**, *71*, 191-219.

[2] a) K. Sefah, Z. Yang, K. M. Bradley, S. Hoshika, E. Jiménez, L. Zhang, G. Zhu, S. Shanker, F. Yu, D. Turek, W. Tan, S. A. Benner, *Proceedings of the National Academy of Sciences* **2014**, *111*, 1449-1454; b) T. Lavergne, M. Degardin, D. A. Malyshev, H. T. Quach, K. Dhami, P. Ordoukhanian, F. E. Romesberg, *J. Am. Chem. Soc.* **2013**, *135*, 5408-5419; c) S. A. Benner, *Acc. Chem. Res.* **2004**, *37*, 784-797; d) L. Li, M. Degardin, T. Lavergne, D. A. Malyshev, K. Dhami, P. Ordoukhanian, F. E. Romesberg, *J. Am. Chem. Soc.* **2014**, *136*, 826-829.

[3] a) A. S. Meyer, M. Blandino, T. E. Spratt, *J. Biol. Chem.* **2004**, *279*, 33043-33046; b) J. C. Morales, E. T. Kool, *Biochemistry* **2000**, *39*, 12979-12988; c) S. Xia, T. D. Christian, J. Wang, W. H. Konigsberg, *Biochemistry* **2012**, *51*, 4343-4353.

[4] a) A. Hottin, A. Marx, *Acc. Chem. Res.* **2016**, *49*, 418-427; b) M. Hocek, *J. Org. Chem.* **2014**, *79*, 9914-9921.

[5] a) B. M. Sirbu, F. B. Couch, D. Cortez, *Nat. Protocols* **2012**, *7*, 594-605; b) B. M. Sirbu, W. H. McDonald, H. Dungrawala, A. Badu-Nkansah, G. M. Kavanaugh, Y. Chen, D. L. Tabb, D. Cortez, *J. Biol. Chem.* **2013**, *288*, 31458-31467; c) K. Bergen, A.-L. Steck, S. Strütt, A. Baccaro, W. Welte, K. Diederichs, A. Marx, *J. Am. Chem. Soc.* **2012**, *134*, 11840-11843.

[6] a) D. N. Clark, J. Hu, *Antiviral Res* **2015**, *123*, 132-137; b) A. M. Margolis, H. Heverling, P. A. Pham, A. Stolbach, *J. Med. Toxicol.* **2014**, *10*, 26-39; c) L. P. Jordheim, D. Durantel, F. Zoulim, C. Dumontet, *Nature Reviews Drug Discovery* **2013**, *12*, 447-464; d) E. J. Gane, C. A. Stedman, R. H. Hyland, X. Ding, E. Svarovskaia, W. T. Symonds, R. G. Hindes, M. M. Berrey, *N. Engl. J. Med.* **2013**, *368*, 34-44; e) M. J. Sofia, D. Bao, W. Chang, J. Du, D. Nagarathnam, S. Rachakonda, P. G. Reddy, B. S. Ross, P. Wang, H. R. Zhang, S. Bansal, C. Espiritu, M. Keilman, A. M. Lam, H. M. Steuer, C. Niu, M. J. Otto, P. A. Furman, *J. Med. Chem.* **2010**, *53*, 7202-7218.

[7] D. M. Korzhnev, M. K. Hadden, *J. Med. Chem.* **2016**, *59*, 9321-9336.

[8] a) L. A. Wyss, A. Nilforoushan, F. Eichenseher, U. Suter, N. Blatter, A. Marx, S. J. Sturla, *J Am Chem Soc* **2015**, *137*, 30-33; b) L. A. Wyss, A. Nilforoushan, D. M. Williams, A. Marx, S. J. Sturla, *Nucleic Acids Res* **2016**, *44*, 6564-6573.

[9] a) T. Kent, T. D. Rusanov, T. M. Hoang, W. A. Velema, A. T. Krueger, W. C. Copeland, E. T. Kool, R. T. Pomerantz, *Nucleic Acids Res.* **2016**, *44*, 9381-9392; b) M. Winnacker, E. T. Kool, *Angew. Chem. Int. Ed.* **2013**, *52*, 12498-12508.

[10] a) W. Yang, R. Woodgate, *Proc.Natl.Acad.Sci.U.S.A.* **2007**, *104*, 15591-15598; b) S. Prakash, R. E. Johnson, L. Prakash, *Annu. Rev. Biochem* **2005**, *74*, 317-353; c) S. S. Lange, K. Takata, R. D. Wood, *Nat. Rev. Cancer* **2011**, *11*, 96-110; d) J. E. Sale, A. R. Lehmann, R. Woodgate, *Nat Rev Mol Cell Biol* **2012**, *13*, 141-152.

[11] a) L. V. Skosareva, N. A. Lebedeva, N. I. Rechkunova, A. Kolbanovskiy, N. E. Geacintov, O. I. Lavrik, *DNA Repair (Amst)* **2012**, *11*, 367-373; b) K.-i. Takata, T. Shimizu, S. Iwai, R. D. Wood, *J. Biol. Chem.* **2006**, *281*, 23445-23455; c) M. J. Yousefzadeh, R. D. Wood, *DNA Repair (Amst)* **2013**, *12*, 1-9; d) J. Bianchi, S. G. Rudd, S. K. Jozwiakowski, L. J. Bailey, V. Soura, E. Taylor, I. Stevanovic, A. J. Green, T. H. Stracker, H. D. Lindsay, A. J. Doherty, *Mol. Cell* **2013**, *52*, 566-573.

[12] S. Avkin, M. Goldsmith, S. Velasco-Miguel, N. Geacintov, E. C. Friedberg, Z. Livneh, *J. Biol. Chem.* **2004**, *279*, 53298-53305.

[13] R. Vasquez-Del Carpio, T. D. Silverstein, S. Lone, M. K. Swan, J. R. Choudhury, R. E. Johnson, S. Prakash, L. Prakash, A. K. Aggarwal, *PLoS.One.* **2009**, *4*, e5766.

[14] T. Ogi, A. R. Lehmann, *Nature Cell Biol.* **2006**, *8*, 640-642.

[15] a) B. A. Baptiste, K. A. Eckert, *Environ Mol Mutagen* **2012**, *53*, 787-796; b) E. Walsh, X. Wang, M. Y. Lee, K. A. Eckert, *J Mol Biol* **2013**, *425*, 232-243.

[16] R. Bétous, M. J. Pillaire, L. Pierini, S. van der Laan, B. Recolin, E. Ohl‐Séguy, C. Guo, N. Niimi, P. Grúz, T. Nohmi, E. Friedberg, C. Cazaux, D. Maiorano, J. S. Hoffmann, *The EMBO Journal* **2013**, *32*, 2172-2185.

[17] M.-J. Pillaire, R. Betous, C. Conti, J. Czaplicki, P. Pasero, A. Bensimon, C. Cazaux, J.-S. Hoffmann, *Cell Cycle* **2007**, *6*, 471-477.

[18] a) J. Y. Choi, F. P. Guengerich, *J. Biol. Chem.* **2006**, *281*, 12315-12324; b) J. Y. Choi, F. P. Guengerich, *J. Mol. Biol.* **2005**, *352*, 72-90.

[19] L. Rey, J. M. Sidorova, N. Puget, F. Boudsocq, D. S. Biard, R. J. Monnat, Jr., C. Cazaux, J. S. Hoffmann, *Mol Cell Biol* **2009**, *29*, 3344-3354.

[20] J. Y. Choi, K. C. Angel, F. P. Guengerich, *J. Biol. Chem.* **2006**, *281*, 21062-21072.

[21] O. Rechkoblit, Y. Zhang, D. Guo, Z. Wang, S. Amin, J. Krzeminsky, N. Louneva, N. E. Geacintov, *J. Biol. Chem.* **2002**, *277*, 30488-30494.

[22] V. Jha, C. Bian, G. Xing, H. Ling, *Nucleic Acids Res.* **2016**, *44*, 4597-4967.

[23] a) N. N. Khan, G. E. Wright, L. W. Dudycz, N. C. Brown, *Nucleic Acids Res* **1984**, *12*, 3695-3706; b) N. N. Khan, G. E. Wright, L. W. Dudycz, N. C. Brown, *Nucleic Acids Res* **1985**, *13*, 6331-6342.

[24] P. Chary, W. A. Beard, S. H. Wilson, R. S. Lloyd, *Chem. Res. Toxicol.* **2012**, *25*, 2744-2754.

[25] J. Matyašovský, P. Perlíková, V. Malnuit, R. Pohl, M. Hocek, *Angew. Chem. Int. Ed.* **2016**, *55*, 15856-15859.

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