Tetrahedron Letters 57 (2016) 4364–4367

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of 8-(1,2,3-triazol-1-yl)-7-deazapurine nucleosides by azide–alkyne click reactions and direct C—H bond functionalization

Sam Kavoosi, Ramanjaneyulu Rayala, Brenna Walsh, Maria Barrios, Walter G. Gonzalez, Jaroslava Miksovska, Logesh Mathivathanan, Raphael G. Raptis, Stanislaw F. Wnuk *

Florida International University, Department of Chemistry and Biochemistry, Miami, FL 33199, United States

ARTICLE INFO

Article history:
Received 5 July 2016
Revised 13 August 2016
Accepted 17 August 2016
Available online 19 August 2016

Keywords:
Azido nucleosides
Click chemistry
Deazapurine nucleosides
Direct C—H functionalization
Fluorescence
Triazoles

ABSTRACT

Treatment of toyocamycin or sangivamycin with 1,3-dibromo-5,5-dimethylhydantoin in MeOH (rt/30 min) gave 8-bromotoyocamycin and 8-bromosangivamycin in good yields. Nucleophilic aromatic substitution of 8-bromotoyocamycin with sodium azide provided novel 8-azidotoyocamycin. Strain promoted click reactions of the latter with cyclooctynes resulted in the formation of the 1,2,3-triazole products. Iodine-mediated direct C8—H bond functionalization of tubercidin with benzotriazoles in the presence of *tert*-butyl hydroperoxide gave the corresponding 8-benzotriazolyltubercidin derivatives. The 8-(1,2,3-triazol-1-yl)-7-deazapurine derivatives showed moderate quantum yields and a large Stokes shifts of ~100 nm.

Synthetic transformations, biological activities, and physicochemical properties of 7-deazapurine derivatives (mainly tubercidin, toyocamycin, and sangivamycin antibiotics) have been extensively studied[1–9] and are subject of the excellent reviews.[10–12] In recent years 7-deazapurine nucleosides have been explored as substrates for 1,4-regioselective copper-catalyzed azide/alkyne cycloaddition (CuAAC), which resulted in developing fluorogenic DNA probes.[13–16] These studies have mainly concentrated on the application of 7-alkynyl derivatives of 7-deazapurines and 7-deazanucleosides for the preparation of the fluorescent 1,2,3-triazol-4-yl probes.[4,17,18] Studies with 7-azido-7-deazapurine nucleosides as well as 8-azido- or 8-alkynyl-7-deazapurine nucleosides have received much less attention due to the lack of availability of the convenient synthetic protocols for their synthesis.[17,19] This is despite the fact that azidonucleosides[20–22] including 8-azido as well as 8-alkynyl purine[23] nucleosides have been used as convenient substrates for CuAAC and strain-promoted azide–alkyne cycloaddition (SPAAC).[24–26] This approach is a rapidly growing field with various applications, including in vivo imaging, of azido/alkyne-modified nucleoside/nucleotides[26,27] or DNA/RNA fragment click adducts.[28–33]

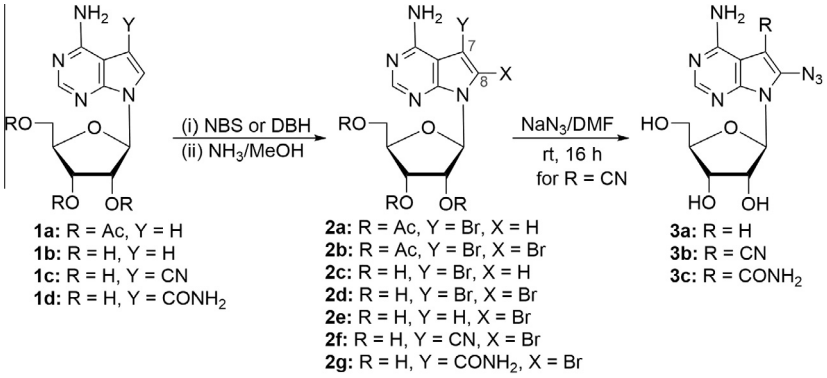
Herein, we report two independent methods for the synthesis of novel 8-triazol-1-yl derivatives of 7-deazapurine nucleosides. One protocol involves strain-promoted click chemistry between 8-azido-7-deazapurine nucleosides and cyclooctynes whereas the second approach explores direct C8—H bond functionalization of 7-deazapurine nucleosides and coupling with benzotriazoles.

The synthesis of the 8-azido-7-deazapurines (**3a**–**c**) was attempted from 8-halo-7-deaza substrates. Thus, bromination of 2′,3′,5′-tri-*O*-acetyltubercidin **1a** using recently reported protocols for the C-8 bromination of purine nucleosides,[34] employing 1,3-dibromo-5,5-dimethylhydantoin (DBH, 0.65 equiv) in CH_2Cl_2 at 0 °C for 40 min, provided 7-bromo **2a** (32%) in addition to 7,8-dibromo **2b** (10%, TLC; Scheme 1). Deacetylation of **2a** and **2b** with methanolic ammonia gave 7-bromotubercidin **2c** (80%) and 7,8-dibromotubercidin **2d** (57%). Treatment of tubercidin **1b** with *N*-bromosuccinimide (NBS, 2 equiv) in the presence of KOAc in DMF yielded 8-bromotubercidin[35] **2e** (34%), whereas attempted bromination of **1b** with DBH in DMF gave a complex reaction mixture.

The 8-bromination of toyocamycin **1c** with 0.75 equiv of DBH in MeOH (30 min.) proceeded efficiently to give after crystallization **2f** (85%). Treatment of **1c** with NBS (1.1 equiv) in DMF at rt for 2.5 h also yielded **2f** (45%) after column chromatography. Replacement of DMF with MeOH gave **2f** (64%) after crystallization, although the reaction took 4 h for completion. The 8-bromotoyocamycin (**2f**) has been previously prepared either by coupling of the corresponding 8-bromo-7-deazapurine with the ribose precursor[36] or by bromination of toyocamycin **1c** with Br_2/H_2O (61%).[37]

* Corresponding author. Tel.: +1 305 348 6195; fax: +1 305 348 3772.
E-mail address: wnuk@fiu.edu (S.F. Wnuk).

http://dx.doi.org/10.1016/j.tetlet.2016.08.053
0040-4039/



Scheme 1. Synthesis of 8-bromo- and 8-azido-7-deazapurine nucleosides.

Thus the DBH/MeOH combination is the most efficient for synthesizing **2f** in terms of yield, reaction time, and product isolation.

Treatment of sangivamycin **1d** with DBH (1.1 equiv) in MeOH (rt, 30 min) yielded **2g** (63%), whereas bromination of **1d** with NBS (1.5 equiv) in DMF for 1.5 h gave **2g** in 40% yield in addition to unidentified byproducts. The synthesis of 8-bromosangivamycin **2g** is usually achieved by the hydrolysis of 8-bromotoyocamycin **2f** with a concentrated NH_4OH and 50% H_2O_2 solution.[36]

Attempts to synthesize 8-azidotubercidin **3a** from 8-bromotubercidin **2e** [NaN_3 (1–5 equiv)/DMF/rt–153 °C; NaN_3 (3 equiv)/TsOH (3 equiv)/EtOH/reflux] were unsuccessful. The higher electron density of π-excessive pyrrole ring most probably prevented the nucleophilic substitution reaction. However, treatment of 8-bromotoyocamycin **2f** with NaN_3 in DMF at room temperature for 16 h produced 8-azidotoyocamycin **3b** in 46% isolated yield (70%, based on TLC and ^{1}H NMR of the crude reaction mixture). Although this azidation reaction was light- and heat-sensitive and required the reaction, purification, and characterization to be carried out in the dark, the isolated 8-azido product **3b** was stable for days when stored in refrigerator at 4 °C.[23,38] The presence of the EWG on the 7-position of the pyrrole ring in toyocamycin, as compared to tubercidin, could be the reason for successful substitution of bromide by azide in **2f**. Treatment of 8-bromosangivamycin **2g** with NaN_3 in DMF (as well as in DMSO or MeOH) at rt or 70 °C failed to produce the desired 8-azidosangivamycin **3c**.

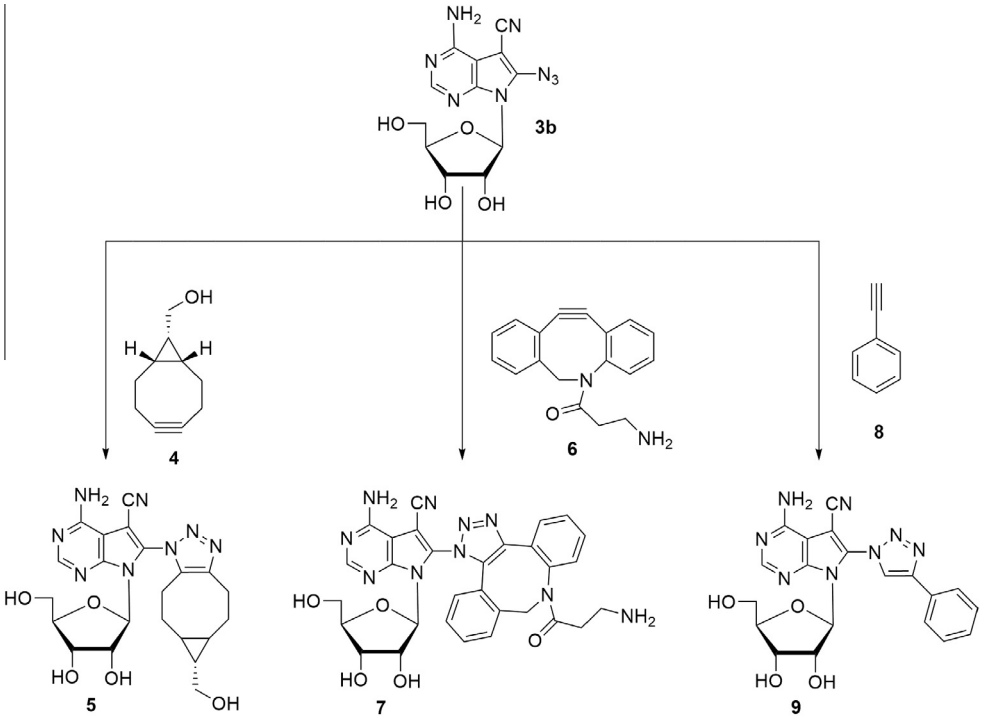
SPAAC reaction of 8-azidotoyocamycin **3b** with symmetrically fused cyclopropyl cyclooctyne **4** (OCT) in an aqueous solution of acetonitrile (ACN) at ambient temperature (4 h) gave the 8-(1,2,3-triazol-1-yl) product **5** as a mixture of two isomers (60%, Scheme 2). Analogous reaction (4 h) of **3b** with a strain modulated dibenzylcyclooctyne **6** (DBCO) produced triazole **7** as a mixture of isomers (47%) after RP-HPLC purification. The resulting triazolyl products have 'light-up' (inherited) fluorescent properties (Table 1), due to increased conjugation in the 7-deazapurine ring, and can therefore be used for fluorescent imaging in cancer cells, as recently reported with 8-triazolyl purine and 5-triazolyl pyrimidine nucleosides.[26,27] CuAAC reaction of 8-azido **3b** with phenylacetylene in aqueous MeOH (4 days/rt) gave 8-(4-phenyl-1*H*-1,2,3-triazol-1-yl)toyocamycin **9** (65%) after silica column purification.

Our attempts to prepare 8-alkynyl-7-dezapurine derivatives, which could serve as substrates for the synthesis of the underdeveloped 8-(1,2,3-triazol-4-yl) adducts via click reactions with organoazides were unsuccessful. Thus, treatment of 8-bromotubercidin (**2e**), 8-bromotoyocamycin (**2f**), 8-bromo-2′,3′,5′-tri-*O*-acetyltoyocamycin,[39] or 8-iodotoyocamycin [prepared by treatment of the silylated toyocamycin with LDA (5 equiv) and iodine (I_2, 1.5 equiv) in THF (16%)] with trimethylsilylacetylene (TMSA) in the presence of TEA and $(PPh_3)_2PdCl_2$/CuI in anhydrous DMF showed mainly unchanged starting material under various reaction conditions. These results are in sharp contrast to 7-halo-7-deazapurines that undergo smooth Sonogashira cross-coupling providing 7-alkynyl analogs, which after further modifications provide derivatives with interesting photophysical and biological properties.[4,17]

Since syntheses of 8-azidotubercidin **3a** for the click reactions were unsuccessful, the possibility to prepare 8-triazolyl adducts of tubercidin **1b**, using a direct C8—H activation of the 7-deazapurine ring, was explored next. Direct C—H fuctionalization of purines and purine nucleosides has recently gained much attention.[19,40–43] The examples include regioselective Pd-catalyzed direct C8—H arylation of the 6-phenyl-7-deazapurines with aryl halides to provide 8-arylated products albeit in low to moderate yields.[44] A regioselective direct C—H amination of the 7-deazapurines to give access to the 8-amino-,[45] or 7-amino-7-deazapurine analogs has also been reported.[46] We found that treatment of tubercidin **1b** with benzotriazole (2 equiv) in the presence of I_2 (0.4 equiv) and *tert*-butylhydroperoxide (TBHP; 5–6 M/decane, 2 equiv)[47] in anhydrous DMF at 35 °C for 96 h showed ~30% conversion (TLC) to 8-(benzotriazol-1-yl)tubercidin **10** which was isolated in 18% yield after column chromatography and HPLC (Scheme 3). Increasing the amount of iodine from catalytic to stoichiometric (3 equiv) afforded **10** in 35% yield after 16 h. ^{1}H NMR data showed that the 7.60 ppm doublet for H7 in **1b** collapsed to a singlet at 7.04 ppm in **10**.

The C8 regioselectivity for the oxidative cross-coupling product **10** was established by an X-ray crystal structure determination (Fig. 1).[48] It is noteworthy that the 7-deazapurine ring and the benzotriazole ring are twisted to each other with an angle of 67.9° between the planes, which does not favor intermolecular π-π interactions. The glycosyl torsion angle C4–N9–C1′–O4′ is 59.8° (*syn* conformation) and the furanose pseudorotation angle[49] is 162.9° (^{2}E conformation). The C3′–C4′–C5′–O5′ torsion angle is 54.1° and is in g^+/gg range.

Treatment of **1b** with 5-methylbenzotriazole [I_2 (0.2 equiv)/TBHP/DMF/rt/5 days] produced a 3:2 mixture of 5-methyl- and 6-methylbenzotriazol-1-yl adducts **11a/11b** (6%). Reaction with stoichiometric amount of iodine (3 equiv) resulted in the efficient conversion to **11a/11b** (48%; ~80% based on TLC after 15 min), showing generality of the iodine-mediated direct activation of tubercidin ring at C8. Analogous treatment of **1b** with 5-chlorobenzotriazole (3 equiv) produced 5/6-chlorobenzotriazol-1-yl adducts **12a/12b** (1:1, 21%; ~60% conversion on TLC). Because 7-deazapurine is structurally similar to indole, the coupling of **1b** with benzotriazole might have occurred *via* initial iodination of the pyrrole ring of 7-deazapurine followed by trapping of the resulting iodonium, or 7-iodo iminium intermediates, with nucleophilic triazole. Subsequent elimination of HI, as proposed for the iodine-catalyzed direct activation of indoles with azoles mediated by TBHP,[47]

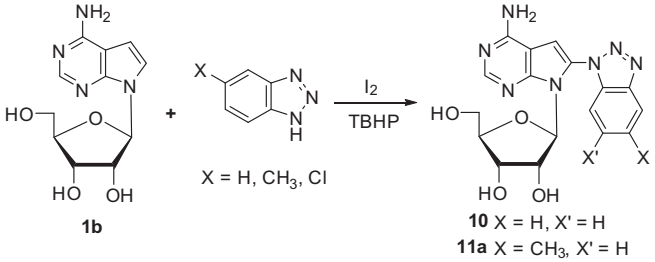


Scheme 2. Click reactions between 8-azidotoyocamycin and cyclooctynes **4**, **6** and phenylacetylene **8**.

Table 1
Photophysical data for 8-(1,2,3-triazol-1-yl)-7-deazapurine nucleosides

	5	**7**	**9**	**10**	**11**[a]	**12**[a]
ε_{max} (M^{-1} cm^{-1})	12,200	12,600	16,000	16,700	17,100	17,700
λ_{max} (abs)[b] (nm)	287	290	295	278	278	276
λ_{max} (exc) [b] (nm)	295	299	301	321	322	343
λ_{max} (emi)[b] (nm)	380	434	412	416	419	480
Stokes shift (nm)	85	135	111	95	97	137
ϕ_F [b] (%)	1.4	0.5	0.4	0.2	0.7	0.8

[a] As mixture of 5- and 6-isomers.
[b] In MeOH.



10 X = H, X' = H
11a X = CH_3, X' = H
11b X = H, X' = CH_3
12a X = Cl, X' = H
12b X = H, X' = Cl

Scheme 3. Iodine-mediated oxidative cross-coupling of tubercidin with benzotriazole.

should yield products **10**–**12**. Subjection of the sangivamycin **1c** and toyocamycin **1b** to direct C8—H functionalization with benzotriazole (rt to 80 °C/48 h) gave unchanged substrate or resulted in rather complex reaction mixture. These results reiterate the literature report that the iodine catalyzed C—H activation of indoles with azoles works rather sluggishly with electron deficient indole substrates.[47]

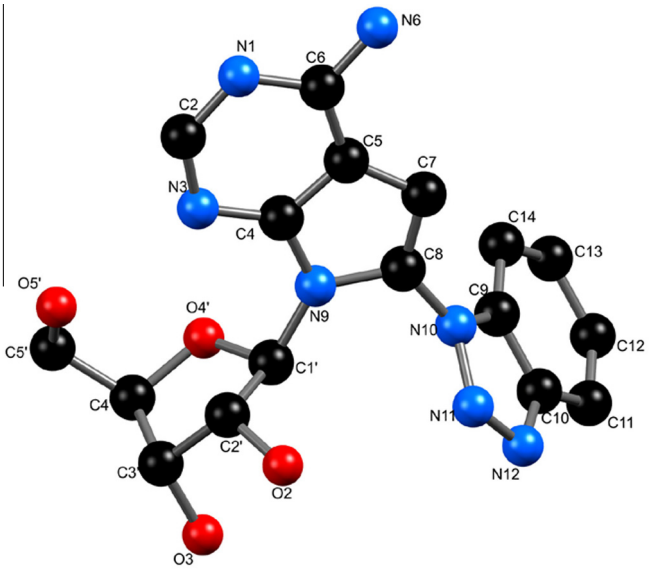


Figure 1. X-ray crystal structure of **10** showing atom labeling. Solvent molecules and H-atoms are omitted for clarity.

The photophysical properties of 8-(1,2,3-triazol-1-yl)-7-deazapurine adducts **5**, **7**, **9**, and **10**–**12** were determined in MeOH. All triazol derivatives have similar absorption and excitation spectra with an absorption maximum between 276 nm and 295 nm and comparable extinction coefficient values (Table 1 and Fig. S2). Moderate quantum yields and a large Stokes shifts of ~100 nm observed here are analogous to the fluorescence properties of aliphatic and benzylic derivatives of 1-(purin-8-yl)triazoles.[23] The emission maximum of triazol **5** (380 nm) is blue shifted compared to other derivatives (412–480 nm), likely due to the absence of an aromatic substituent (Fig. 2). Emission spectrum of chloro substituted benzotriazole **12** is red-shifted compared to benzotriazoles

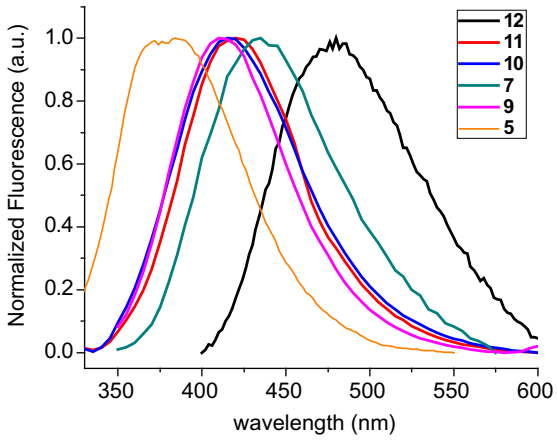


Figure 2. Emission spectra for 8-(1,2,3-triazol-1-yl)-7-deazapurine nucleosides.

10 and **11**, suggesting a resonance conjugation between the aromatic ring and Cl electrons.

Emission properties of the triazole **10** were also investigated in aqueous solutions. Compound **10** is fluorescent at neutral and basic pH (7.0–12.0) and becomes non-fluorescent at acidic pH. Interestingly, compounds **10** and **11** seem to be highly sensitive to UV light, as an increase in emission intensity (8.1 and 2.4 fold) upon irradiation with 280 nm light was observed (Fig. S3). Triazole **10** has an average lifetime about 3.8 ns with two well-defined components 1 ns (10%) and 4.1 ns (90%).

In summary, bromination of 7-deazapurine nucleosides with DBH/MeOH gave 8-bromotoyocamycin and 8-bromosangivamycin in high yields. Treatment of the 8-bromotoyocamycin with sodium azide yielded 8-azidotoyocamycin. Strain promoted click chemistry of 8-azidotoyocamycin with cyclooctynes provided the corresponding 8-triazol-1-yl products. Iodine-mediated direct C—H arylation of tubercidin with benzotriazoles gave the corresponding 8-(benzotriazol-1-yl)tubercidin products. The 8-(1,2,3-triazol-1-yl)-7-deazapurine derivatives showed moderate quantum yields and a large Stokes shifts of ~100 nm.

Acknowledgments

We would like to express our gratitude to Dr. Morris J. Robins for generous donation of 7-deazapurine substrates, NSF-REU (Grant No: CHE1156886 to FIU) for support to BW (James Madison University), FIU MBRS program (NIH/NIGMS R25 GM061347) for support to WGG, and FIU University Graduate School for Dissertation Year Fellowship to RR.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2016.08.053.

References and notes

1. Bookser, B. C.; Ugarkar, B. G.; Matelich, M. C.; Lemus, R. H.; Allan, M.; Tsuchiya, M.; Nakane, M.; Nagahisa, A.; Wiesner, J. B.; Erion, M. D. *J. Med. Chem.* **2005**, *48*, 7808–7820.
2. Kawate, T.; Allerson, C. R.; Wolfe, J. L. *Org. Lett.* **2005**, *7*, 3865–3868.
3. Seela, F.; Xu, K. *Org. Biomol. Chem.* **2008**, *6*, 3552–3560.
4. Bourderioux, A.; Naus, P.; Perlikova, P.; Pohl, R.; Pichova, I.; Votruba, I.; Dzubak, P.; Konecny, P.; Hajduch, M.; Stray, K. M.; Wang, T.; Ray, A. S.; Feng, J. Y.; Birkus, G.; Cihlar, T.; Hocek, M. *J. Med. Chem.* **2011**, *54*, 5498–5507.
5. Naus, P.; Caletkova, O.; Konecny, P.; Dzubak, P.; Bogdanova, K.; Kolar, M.; Vrbkova, J.; Slavetinska, L.; Tloust'ova, E.; Perlikova, P.; Hajduch, M.; Hocek, M. *J. Med. Chem.* **2014**, *57*, 1097–1110.
6. Rayala, R.; Theard, P.; Ortiz, H.; Yao, S.; Young, J. D.; Balzarini, J.; Robins, M. J.; Wnuk, S. F. *ChemMedChem* **2014**, *9*, 2186–2192.
7. Snasel, J.; Naus, P.; Dostal, J.; Hnizda, A.; Fanfrlik, J.; Brynda, J.; Bourderioux, A.; Dusek, M.; Dvorakova, H.; Stolarikova, J.; Zabranska, H.; Pohl, R.; Konecny, P.; Dzubak, P.; Votruba, I.; Hajduch, M.; Rezacova, P.; Veverka, V.; Hocek, M.; Pichova, I. *J. Med. Chem.* **2014**, *57*, 8268–8279.
8. Kielkowski, P.; Fanfrlik, J.; Hocek, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 7552–7555.
9. Takano, S.; Tsuzuki, T.; Murayama, T.; Sakurai, T.; Fukuda, H.; Arisawa, M.; Shuto, S. *J. Org. Chem.* **2015**, *80*, 6619–6627.
10. Seela, F.; Peng, X. *Curr. Top. Med. Chem.* **2006**, *6*, 867–892.
11. Seela, F.; Peng, X.; Budow, S. *Curr. Org. Chem.* **2007**, *11*, 427–462.
12. Seela, F.; Budow, S.; Peng, X. *Curr. Org. Chem.* **2012**, *16*, 161–223.
13. Seela, F.; Ingale, S. A. *J. Org. Chem.* **2010**, *75*, 284–295.
14. Seela, F.; Pujari, S. S. *Bioconjugate Chem.* **2010**, *21*, 1629–1641.
15. Ingale, S. A.; Pujari, S. S.; Sirivolu, V. R.; Ding, P.; Xiong, H.; Mei, H.; Seela, F. *J. Org. Chem.* **2012**, *77*, 188–199.
16. Xiong, H.; Leonard, P.; Seela, F. *Bioconjugate Chem.* **2012**, *23*, 856–870.
17. Tumkevicius, S.; Dodonova, J. *Chem. Heterocycl. Compd.* **2012**, *48*, 258–279.
18. Lawson, C. P.; Dierckx, A.; Miannay, F. A.; Wellner, E.; Wilhelmsson, L. M.; Grotli, M. *Org. Biomol. Chem.* **2014**, *12*, 5158–5167.
19. Klečka, M.; Poštová Slavětínská, L.; Hocek, M. *Eur. J. Org. Chem.* **2015**, *2015*, 7943–7961.
20. Smyslova, P.; Popa, I.; Lycka, A.; Tejral, G.; Hlavac, J. *PLoS ONE* **2015**, *10*, e0144613.
21. Ozols, K.; Cīrule, D.; Novosjolova, I.; Stepanovs, D.; Liepinsh, E.; Bizdēna, Ē.; Turks, M. *Tetrahedron Lett.* **2016**, *57*, 1174–1178.
22. Cīrule, D.; Ozols, K.; Platnieks, O.; Bizdēna, Ē.; Māliņa, I.; Turks, M. *Tetrahedron* **2016**, *72*, 4177–4185.
23. Redwan, I. N.; Bliman, D.; Tokugawa, M.; Lawson, C.; Grøtli, M. *Tetrahedron* **2013**, *69*, 8857–8864.
24. Dyrager, C.; Börjesson, K.; Dinér, P.; Elf, A.; Albinsson, B.; Wilhelmsson, L. M.; Grøtli, M. *Eur. J. Org. Chem.* **2009**, *2009*, 1515–1521.
25. Novosjolova, I.; Bizdēna, Ē.; Turks, M. *Eur. J. Org. Chem.* **2015**, *2015*, 3629–3649.
26. Zayas, J.; Annoual, M. D.; Das, J. K.; Felty, Q.; Gonzalez, W. G.; Miksovska, J.; Sharifai, N.; Chiba, A.; Wnuk, S. F. *Bioconjugate Chem.* **2015**, *26*, 1519–1532.
27. Ito, K.; Liu, H.; Komiyama, M.; Hayashi, T.; Xu, Y. *Molecules* **2013**, *18*, 12909–12915.
28. Gramlich, P. M. E.; Wirges, C. T.; Manetto, A.; Carell, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 8350–8358.
29. Marks, I. S.; Kang, J. S.; Jones, B. T.; Landmark, K. J.; Cleland, A. J.; Taton, T. A. *Bioconjugate Chem.* **2011**, *22*, 1259–1263.
30. Guan, L.; van der Heijden, G. W.; Bortvin, A.; Greenberg, M. M. *ChemBioChem* **2011**, *12*, 2184–2190.
31. Shelbourne, M.; Chen, X.; Brown, T.; El-Sagheer, A. H. *Chem. Commun.* **2011**, 6257–6259.
32. Heuer-Jungemann, A.; Kirkwood, R.; El-Sagheer, A. H.; Brown, T.; Kanaras, A. G. *Nanoscale* **2013**, *5*, 7209–7212.
33. Neef, A. B.; Luedtke, N. W. *ChemBioChem* **2014**, *15*, 789–793.
34. Rayala, R.; Wnuk, S. F. *Tetrahedron Lett.* **2012**, *53*, 3333–3336.
35. Bergstrom, D. E.; Brattesani, A. J. *Nucleic Acids Res.* **1980**, *8*, 6213–6219.
36. Tolman, R. L.; Robins, R. K.; Townsend, L. B. *J. Am. Chem. Soc.* **1969**, *91*, 2102–2108.
37. Tolman, R. L.; Robins, R. K.; Townsend, L. B. *J. Heterocycl. Chem.* **1971**, *8*, 703–706.
38. The 8-azidopurines were reported to be light sensitive and were directly used in coupling with alkynes without prior purification (Ref. 23).
39. Kim, Y.-J.; Kwon, S. H.; Bae, I. H.; Kim, B. M. *Tetrahedron Lett.* **2013**, *54*, 5484–5488.
40. De Ornellas, S.; Storr, T. E.; Williams, T. J.; Baumann, C. G.; Fairlamb, I. J. S. *Curr. Org. Synth.* **2011**, *8*, 79–101.
41. De Ornellas, S.; Williams, T. J.; Baumann, C. G.; Fairlamb, I. J. S. *RSC Catal. Ser.* **2013**, *11*, 409–447.
42. Gayakhe, V.; Sanghvi, Y. S.; Fairlamb, I. J. S.; Kapdi, A. R. *Chem. Commun.* **2015**, 11944–11960.
43. Liang, Y.; Wnuk, S. *Molecules* **2015**, *20*, 4874–4901.
44. Klecka, M.; Pohl, R.; Klepetarova, B.; Hocek, M. *Org. Biomol. Chem.* **2009**, *7*, 866–868.
45. Sabat, N.; Klecka, M.; Slavetinska, L.; Klepetarova, B.; Hocek, M. *RSC Adv.* **2014**, *4*, 62140–62143.
46. Sokolovs, I.; Lubriks, D.; Suna, E. *J. Am. Chem. Soc.* **2014**, *136*, 6920–6928.
47. Beukeaw, D.; Udomsasporn, K.; Yotphan, S. *J. Org. Chem.* **2015**, *80*, 3447–3454.
48. Crystallographic data for 8-(benzotriazol-1-yl)tubercidin **10** have been deposited with the Cambridge Crystallographic Data Center as a supplementary publication No. CCDC-1487054.
49. Altona, C.; Sundaralingam, M. *J. Am. Chem. Soc.* **1972**, *94*, 8205–8212.