



Universiteit
Leiden
The Netherlands

Mimetics of ADP-ribosylated histidine through copper(I)-catalyzed click chemistry

Minnee, H.; Rack, J.G.M.; Marel, G.A. van der; Overkleeft, H.S.; Codee, J.D.C.; Ahel, I.; Filippov, D.V.

Citation

Minnee, H., Rack, J. G. M., Marel, G. A. van der, Overkleeft, H. S., Codee, J. D. C., Ahel, I., & Filippov, D. V. (2022). Mimetics of ADP-ribosylated histidine through copper(I)-catalyzed click chemistry. *Organic Letters*, 24(21), 3776-3780. doi:10.1021/acs.orglett.2c01300

Version: Publisher's Version

License: [Creative Commons CC BY 4.0 license](#)

Downloaded from: <https://hdl.handle.net/1887/3453567>

Note: To cite this publication please use the final published version (if applicable).

Mimetics of ADP-Ribosylated Histidine through Copper(I)-Catalyzed Click Chemistry

Hugo Minnee, Johannes G. M. Rack, Gijsbert A. van der Marel, Herman S. Overkleeft, Jeroen D. C. Codée, Ivan Ahel, and Dmitri V. Filippov*



Cite This: *Org. Lett.* 2022, 24, 3776–3780



Read Online

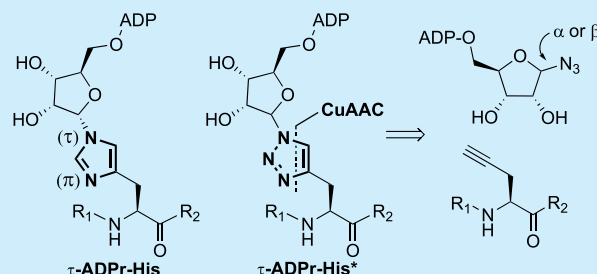
ACCESS |

Metrics & More

Article Recommendations

Supporting Information

ABSTRACT: A convergent synthesis provided nearly perfect τ -ADP-ribosylated histidine isosteres (His*- τ -ADPr) via a copper(I)-catalyzed cycloaddition between an azido-ADP-ribosyl analogue and an oligopeptide carrying a propargyl glycine. Both α - and β -configured azido-ADP-ribosyl analogues have been synthesized. The former required participation of the C-2 ester functionality during glycosylation, while the latter was obtained in high stereoselectivity from an imidate donor with a nonparticipating *para*-methoxy benzyl ether. Four His*- τ -ADPr peptides were screened against a library of human ADP-ribosyl hydrolases.



A wide array of posttranslational modifications (PTMs), varying from small alterations (e.g., methylation) to the introduction of complete proteins (e.g., ubiquitination), are essential for regulatory control of protein activity. Although nicotinamide adenine dinucleotide (NAD⁺) is commonly known for its role as a redox cofactor, it also participates in a PTM called adenosine diphosphate-ribosylation (ADP-ribosylation). In this PTM, the adenosine diphosphate ribose (ADPr) moiety is covalently attached to specific amino acid side chains of the targeted protein by substitution of the nicotinamide residue. In humans, this process is primarily facilitated by ADP-ribosyl transferases termed PARPs,¹ and the resulting modification can be either mono-ADP-ribosylation (MARylation) when a single ADPr molecule is introduced or poly-ADP-ribosylation (PARylation) when longer linear or branched ADPr polymers are formed. The latter process can be mediated by only a small subset of PARPs: PARP1, PARP2, PARP5a, and PARP5b. Ever since the first isolation of poly-ADPr chains² and the identification of the transferase enzyme,³ this PTM has received ever increasing attention because of the many roles it plays in various biological events. However, progress has been slowed down due to the lack of appropriate tools to study this modification. Advances in mass spectrometry revealed the breadth of possible amino acid acceptors, including glutamate, aspartate, arginine,⁴ lysine,⁵ cysteine,⁶ histidine,^{7,8} tyrosine,^{9,10} and serine.¹¹ A complex regulatory network of proteins “writing”, “reading”, and “erasing” the ADP-ribosylation^{12,13} is responsible for the huge structural diversity of the “ADP-ribosylome”. Due to such structural diversity, ADP-ribosylation allows for the spatiotemporal and context specific regulation of a wide variety of cellular processes including DNA damage response, replication, transcription, and cellular signaling (e.g., WNT signaling).^{14–17}

Among the different acceptor residues, serine has emerged as the primary target in DNA damage-induced ADP-ribosylation.^{18–20} Recent proteomic studies have also drawn attention toward the occurrence of lower-frequency modifications at tyrosine and histidine sites.^{7,8,21} The identification of these new flavors of stress-induced ADP-ribosylation is suggestive of a specialized control mechanism for subprocesses within the DNA-damage response (DDR). For an identification and characterization of the responsible “writers”, “readers”, and “erasers” as well as an examination of their cellular function, well-defined molecular tools are indispensable.

To generate tools to study histidine ADP-ribosylation, we reasoned that click chemistry could be exploited to create a nearly perfect isostere of ADP-ribosylated histidine (Figure 1A). Although the exact structure of ADP-ribosylated histidine (His-ADPr) has not yet been determined, we hypothesize here that ADPr is introduced at the τ -position of the imidazole functionality, most likely via an α -configured linkage. This hypothesis is based on the isolation of ribosylated and ADP-ribosylated histidine metabolites^{22,23} combined with the known stereospecificity of PARP enzymes. The suspected 1,4-substitution pattern can be mimicked via a Cu(I)-catalyzed azide–alkyne cycloaddition (CuAAC), known for its high regioselectivity, with an azido-ADPr analogue and an oligopeptide carrying a propargyl click handle at a specific

Received: April 13, 2022

Published: May 19, 2022



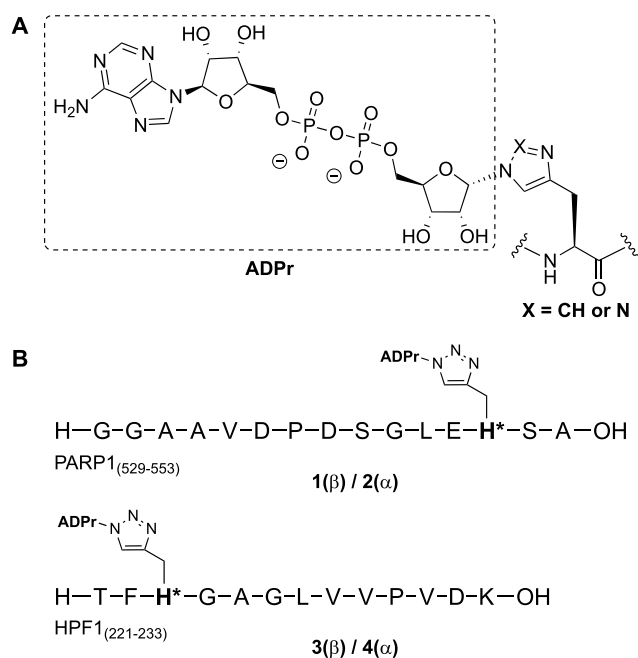


Figure 1. (A) Proposed structure of ADP-ribosylated histidine ($X = \text{CH}$) under physiological conditions. Based on histidine metabolites and the α -selective introduction of PARPs, it is suggested that ADPr is attached to the imidazole functionality at the τ -nitrogen through an α -configured glycosidic bond. An ADP-ribosylated histidine isostere ($X = \text{N}$) can be obtained through CuAAC, where the imidazole functionality is replaced by a triazole moiety. (B) Structures of the ADP-ribosylated histidine mimetics described in this paper.

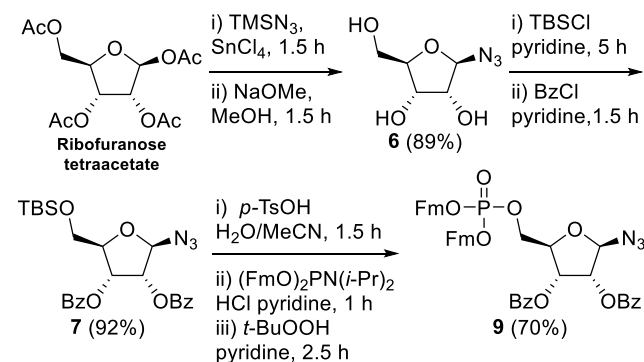
position. The use of CuAAC has been successfully implemented before in the synthesis of ADP-ribosylated oligopeptides and proteins.^{24–26} Here, the convergent syntheses of both α - and β -configured ADP-ribosylated histidine mimetics 1–4 (Figure 1B) are described.

The target oligopeptides 1–4 are based on two potential His-ADPr sites, located on histone PARylation factor 1 (HPF1) and PARP1, respectively, that have been identified in recent proteomic studies.²⁷ We aimed to assemble the peptides by a late-stage click reaction between the fully deprotected propargyl-glycine containing peptides and the α - and β -ADP-ribosyl azides 22 and 25, which in turn can be obtained from the two anomeric azido ribose 5-phosphates (9 and 17) and known adenosine phosphoramidite 20 using our P(III)–P(V) coupling method.²⁸

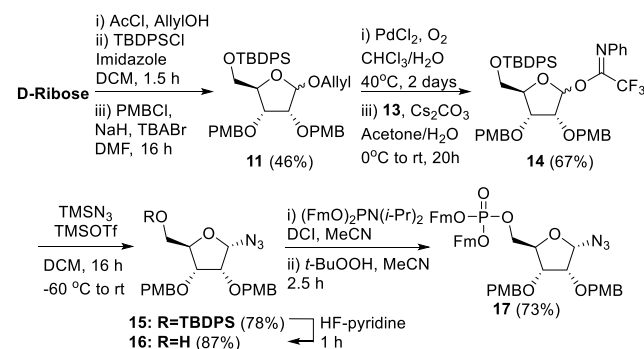
Synthesis of the β -configured 5-phosphorylribofuranoside 9 started with commercially available ribofuranose tetraacetate (Scheme 1). Owing to neighboring group participation of the C-2-O-acetyl, the desired β -azide was acquired with excellent stereoselectivity.²⁹ After a series of standard protecting group manipulations, the fully protected azidoribofuranoside 7 was obtained, of which the silyl ether was selectively removed under acidic conditions. Phosphitylation with bis-(fluorenylmethyl)- N,N -diisopropyl phosphoramidite under influence of pyridine-1-ium chloride as an activator provided the corresponding phosphite which was oxidized with t -BuOOH to yield 1- β -azido-5-phosphorylribofuranoside 9.

The assembly of the α -configured 1-azido-5-phosphorylribofuranoside requires a nonparticipating protection group at the C-2-hydroxyl to stereoselectively introduce the α -azido group. To this end, suitably protected imidate 14 was prepared from D-ribose in 5 steps (Scheme 2).³⁰ Activation of the ribosyl

Scheme 1. Synthesis of the β -Configured 1-Azido-5-phosphorylribofuranoside 9



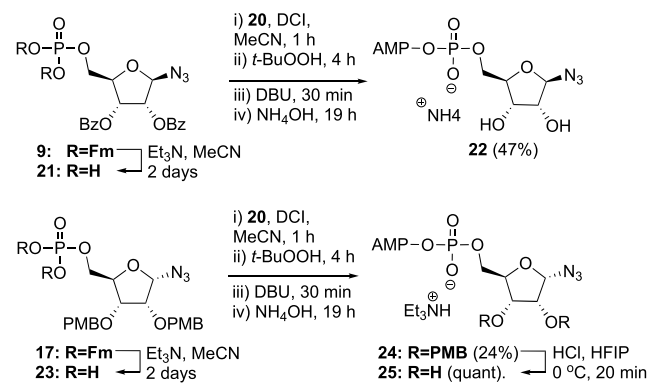
Scheme 2. Synthesis of the α -Configured 1-Azido-5-phosphorylribofuranoside 17



donor 14 with trimethylsilyl triflate at -60 °C in the presence of trimethylsilyl azide provided ribosyl azide 15 with excellent stereoselectivity ($\alpha/\beta = 14:1$, Scheme 1B). Removal of the PMB protecting groups proved difficult at this point using either oxidative or acidic conditions, which resulted in the formation of 2,3- O - p -methoxybenzylidene products or degradation of the compound, respectively. We therefore decided to postpone the removal of the PMB ethers to a later stage and first removed the C-5- O -silyl group in 15 with HF-pyridine as a fluorine source. Then, phosphitylation and subsequent oxidation, as described above for β -ribosyl azide 9, provided α -azido-5-phosphorylribofuranoside 17.

The pyrophosphate linkage in the target α - and β -azido ADP-ribose building blocks was installed using our P(III)–P(V) coupling method (Scheme 3).²⁸ The required adenosine

Scheme 3. Synthesis of the 1'-Azide ADPr Analogues 22 and 25 Using Phosphoramidite Chemistry

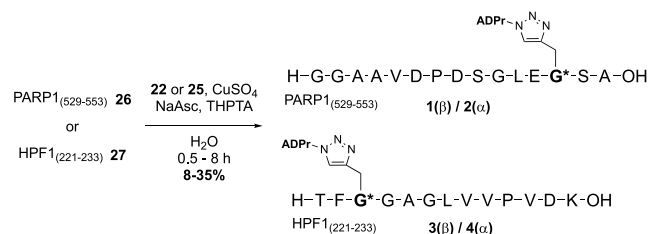


phosphoramidite **20** was synthesized from adenosine in 6 steps according to a previously reported method (Scheme S3).³¹ First the phosphates in **9** and **17** were liberated by removal of the Fm-groups with triethylamine. Next, the phosphates **21** and **23** were coupled with adenosine amidite **20** upon activation with dicyanoimidazole (DCI). Subsequent *t*-BuOOH mediated oxidation of the P(III)–P(V) intermediate provided the partially protected pyrophosphates. Deprotection of these building blocks started with the removal of the cyanoethyl groups with DBU, after which treatment with aqueous ammonia provided the fully deprotected β -azido-ADPr **22** and α -azido-ADPr **24**, carrying the two PMB ethers. β -Azido-ADPr **22** could be purified by size exclusion chromatography (SEC) and was isolated as the ammonium salt. On the contrary, due to hydrophobic interactions of the C-2- and C-3-O-PMB groups of α -azido-ADPr **25**, SEC was not efficient, and preparative reversed-phase high-performance liquid chromatography (RP-HPLC) was required to obtain the pure compound. Final removal of the PMB groups was executed using a catalytic amount of HCl in hexafluoro-2-propanol³² to yield **25** as triethylammonium salt after workup and lyophilization.

The required peptides **26** and **27** were synthesized using Fmoc-based solid phase peptide synthesis (SPPS), incorporating propargyl glycine at the positions that are to carry the Hist-type ADPr modification. Both peptides were obtained in good yield and purity after RP-HPLC purification using an NH₄OAc buffered eluent system.

For the final Cu(I)-catalyzed conjugation, a 1.5-fold molar excess of the azido-ADPr analogue (**22** or **25**) was added to an aqueous solution of the oligopeptide (**26** or **27**) after which the solution was degassed with argon (Scheme 4). In parallel, a

Scheme 4. Synthesis of ADP-Ribosylated Histidine Mimetics via Copper(I) Click Chemistry^a



^aTwo oligopeptides originating from PARP1 (**26**) and HPF1 (**27**) have been selected and synthesized with a propargylglycine incorporated at the location of the histidine. Depending on the ADPr analogue used, an α - or β -configured conjugate is formed. Hence, a total of four ADPr conjugates **1–4** are obtained.

fresh “click mixture” was prepared for every reaction by adding an aqueous solution of sodium ascorbate to CuSO₄ directly followed by tris(3-hydroxypropyltriazolylmethyl)amine (THPTA). After addition of this mixture to the solution of the azide and the alkyne, the conversion of the oligopeptide was monitored with liquid chromatography–mass spectrometry (LC-MS). Upon complete conversion, the crude products were desalted by SEC and subsequently purified by preparative HPLC. Unfortunately, this tandem purification method provided the desired products in moderate yields. Direct preparative RP-HPLC proved to be more efficient and provided the desired products in high purity.

Having obtained the triazole mimetics of ADP-ribosylated histidine peptides, we set out to investigate the enzymatic turnover of this modification (Figure 2A). Peptides **1–4** were

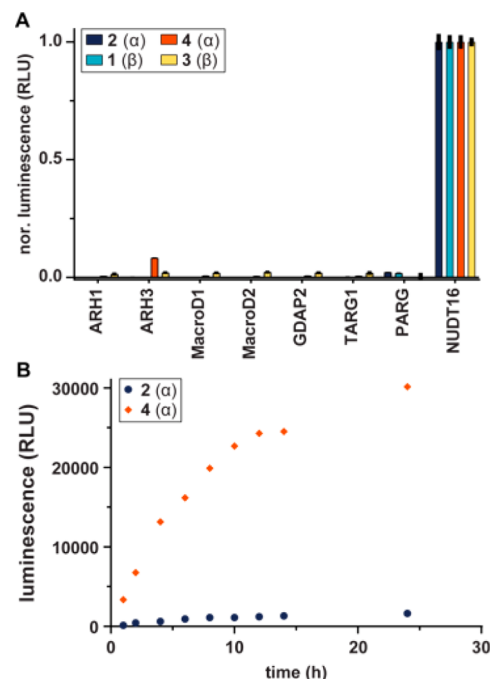


Figure 2. Enzymatic hydrolysis of interglycosidic linkages in ADP-ribosylated histidine mimetic peptides **2**(α), **1**(β), **4**(α), and **3**(β). (A) Hydrolase activity against the various peptides was assessed by monitoring AMP release directly (NudT16) or converting released ADPr via NudT5 to AMP. AMP was measured using the AMP-Glo assay (Promega). Samples are background corrected and normalized to NudT16 activity. (B) Time-course experiment of histidine isosteres **2**(α) and **4**(α) with ARH3. Time points taken up to 24 h. Data of both experiments represent mean values $\pm$ SD measured in triplicates.

incubated in the presence of different human (ADP-ribosyl)-hydrolases and nudix hydrolase 5 (NudT5) for 1 h at 30 °C. The former may catalyze the breakage of the *N*-glycosidic bond of the ribosyltriazole, while the latter converts the released ADPr into adenosine monophosphate (AMP), which was quantified using the AMP-Glo assay.³³ As a positive control, the samples were incubated in the presence of NudT16, which in contrast to NudT5 can hydrolyze ADPr that is conjugated to a peptide.³⁴ Although most human hydrolases were unable to remove ADPr from the peptides, we observed a consistent minor turnover ($\sim$ 8.2%) for the HPF1- α peptide **4**, indicating that our developed isostere is indeed a functional mimic of ADP-ribosylated histidine. Interestingly, ARH3 appeared unable to convert PARP1- α (**2**), which could suggest that the removal of His-ADPr modifications is sequence-dependent.³⁵ These findings were substantiated in a time-course experiment (Figure 2B), which showed the steady enzymatic conversion of **4** and the resistance of **2** toward enzymatic turnover.

In conclusion, we have described the synthesis of both α - and β -configured ADPr-azide analogues that were successfully used to prepare mimetics of ADP-ribosylated histidine using CuAAC. Initial screening of the peptides against a collection of human ADPr hydrolases revealed that ARH3 is able to hydrolyze the *N*-glycosidic triazole-ribose linkage of HPF1- α **4**, while PARP1- α **2** remained unscathed. Not only do these

results suggest that ARH3 is likely able to remove the ADPr modification from histidine residues in the right sequential context,³⁵ but it also demonstrates that the peptides presented here provide useful tools for the further study of the interactions of the His-ADPr modification with either binders or hydrolases. Our current efforts in the synthesis of peptides with native ADP-ribosylated histidine will hopefully further elucidate the process of His-ADPr demodification in the near future.

■ ASSOCIATED CONTENT

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.2c01300>.

Syntheses of β -configured ribose 5-phosphate **9**, α -configured ribose 5-phosphate **17**, and phosphoramidite **20**; procedures for pyrophosphate construction, final CuAAC conjugation, solid-phase peptide synthesis of **26** and **27**, plasmid expression, protein purification, and (ADP-ribosyl)hydrolase activity screening; general experimental procedures; and copies of IR and NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Dmitri V. Filippov – Bio-Organic Synthesis, Leiden Institute of Chemistry, Leiden University, 2300 RA Leiden, The Netherlands; orcid.org/0000-0002-6978-7425; Email: filippov@chem.leidenuniv.nl

Authors

Hugo Minnee – Bio-Organic Synthesis, Leiden Institute of Chemistry, Leiden University, 2300 RA Leiden, The Netherlands

Johannes G. M. Rack – Sir William Dunn School of Pathology, University of Oxford, Oxford OX1 3RE, United Kingdom

Gijsbert A. van der Marel – Bio-Organic Synthesis, Leiden Institute of Chemistry, Leiden University, 2300 RA Leiden, The Netherlands

Herman S. Overkleef – Bio-Organic Synthesis, Leiden Institute of Chemistry, Leiden University, 2300 RA Leiden, The Netherlands; orcid.org/0000-0001-6976-7005

Jeroen D. C. Codée – Bio-Organic Synthesis, Leiden Institute of Chemistry, Leiden University, 2300 RA Leiden, The Netherlands

Ivan Ahel – Sir William Dunn School of Pathology, University of Oxford, Oxford OX1 3RE, United Kingdom

Complete contact information is available at:

<https://pubs.acs.org/doi/10.1021/acs.orglett.2c01300>

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

■ REFERENCES

- (1) Lüscher, B.; Ahel, I.; Altmeyer, M.; Ashworth, A.; Bai, P.; Chang, P.; Cohen, M.; Corda, D.; Dantzer, F.; Daugherty, M. D.; Dawson, T. M.; Dawson, V. L.; Deindl, S.; Fehr, A. R.; Feijs, K. L. H.; Filippov, D. V.; Gagné, J.-P.; Grimaldi, G.; Guettler, S.; Hoch, N. C.; Hottiger, M. O.; Korn, P.; Kraus, W. L.; Ladurner, A.; Lehtiö, L.; Leung, A. K. L.; Lord, C. J.; Mangerich, A.; Matic, I.; Matthews, J.; Moldovan, G.-L.; Moss, J.; Natoli, G.; Nielsen, M. L.; Niepel, M.; Nolte, F.; Pascal, J.; Paschal, B. M.; Pawlowski, K.; Poirier, G. G.; Smith, S.; Timinszky, G.; Wang, Z.-Q.; Yélamos, J.; Yu, X.; Zaja, R.; Ziegler, M. ADP-Ribosyltransferases, an Update on Function and Nomenclature. *FEBS J.* **2021**, in press. DOI: 10.1111/febs.16142.
- (2) Chambon, P.; Weill, J. D.; Doly, J.; Strosser, M. T.; Mandel, P. On the Formation of a Novel Adenylate Compound by Enzymatic Extracts of Liver Nuclei. *Biochem. Biophys. Res. Commun.* **1966**, *25* (6), 638–643.
- (3) Okayama, H.; Edson, C. M.; Fukushima, M.; Ueda, K.; Hayaishi, O. Purification and Properties of Poly(Adenosine Diphosphate Ribose) Synthetase. *J. Biol. Chem.* **1977**, *252* (20), 7000–7005.
- (4) Vandekerckhove, J.; Schering, B.; Bärmann, M.; Aktories, K. Botulinum C2 Toxin ADP-Ribosylates Cytoplasmic Beta/Gamma-Actin in Arginine 177. *J. Biol. Chem.* **1988**, *263* (2), 696–700.
- (5) Altmeyer, M.; Messner, S.; Hassa, P. O.; Fey, M.; Hottiger, M. O. Molecular Mechanism of Poly(ADP-Ribosyl)ation by PARP1 and Identification of Lysine Residues as ADP-Ribose Acceptor Sites. *Nucleic Acids Res.* **2009**, *37* (11), 3723–3738.
- (6) Vyas, S.; Matic, I.; Uchima, L.; Rood, J.; Zaja, R.; Hay, R. T.; Ahel, I.; Chang, P. Family-Wide Analysis of Poly(ADP-Ribose) Polymerase Activity. *Nat. Commun.* **2014**, *5* (1), 1–13.
- (7) Buch-Larsen, S. C.; Rebak, A. K. L. F. S.; Hendriks, I. A.; Nielsen, M. L. Temporal and Site-Specific ADP-Ribosylation Dynamics upon Different Genotoxic Stresses. *Cells* **2021**, *10* (11), 2927.
- (8) Larsen, S. C.; Hendriks, I. A.; Lyon, D.; Jensen, L. J.; Nielsen, M. L. Systems-Wide Analysis of Serine ADP-Ribosylation Reveals Widespread Occurrence and Site-Specific Overlap with Phosphorylation. *Cell Rep.* **2018**, *24* (9), 2493–2505.
- (9) Bartlett, E.; Bonfiglio, J. J.; Prokhorova, E.; Colby, T.; Zobel, F.; Ahel, I.; Matic, I. Interplay of Histone Marks with Serine ADP-Ribosylation. *Cell Rep.* **2018**, *24* (13), 3488–3502.
- (10) Leslie Pedrioli, D. M.; Leutert, M.; Bilan, V.; Nowak, K.; Gunasekera, K.; Ferrari, E.; Ralph, I.; Malmström, L.; Hottiger, M. O. Comprehensive ADP-Ribosylome Analysis Identifies Tyrosine as an ADP-Ribose Acceptor Site. *EMBO Rep.* **2018**, *19* (8), e45310.
- (11) Leidecker, O.; Bonfiglio, J. J.; Colby, T.; Zhang, Q.; Atanassov, I.; Zaja, R.; Palazzo, L.; Stockum, A.; Ahel, I.; Matic, I. Serine Is a New Target Residue for Endogenous ADP-Ribosylation on Histones. *Nat. Chem. Biol.* **2016**, *12* (12), 998–1000.
- (12) Rack, J. G. M.; Palazzo, L.; Ahel, I. (ADP-Ribosyl)Hydrolases: Structure, Function, and Biology. *Genes Dev.* **2020**, *34* (5–6), 263–284.
- (13) Liu, C.; Yu, X. ADP-Ribosyltransferases and Poly ADP-Ribosylation. *Curr. Protein Pept. Sci.* **2015**, *16* (6), 491–501.
- (14) Lüscher, B.; Bütepage, M.; Eckei, L.; Krieg, S.; Verheugd, P.; Shilton, B. H. ADP-Ribosylation, a Multifaceted Posttranslational Modification Involved in the Control of Cell Physiology in Health and Disease. *Chem. Rev.* **2018**, *118* (3), 1092–1136.
- (15) Slade, D. PARP and PARP Inhibitors in Cancer Treatment. *Genes Dev.* **2020**, *34* (5–6), 360–394.
- (16) Dantzer, F.; Santoro, R. The Expanding Role of PARPs in the Establishment and Maintenance of Heterochromatin. *FEBS J.* **2013**, *280* (15), 3508–3518.
- (17) Szántó, M.; Bai, P. The Role of ADP-Ribose Metabolism in Metabolic Regulation, Adipose Tissue Differentiation, and Metabolism. *Genes Dev.* **2020**, *34* (5–6), 321–340.
- (18) Schützenhofer, K.; Rack, J. G. M.; Ahel, I. The Making and Breaking of Serine-ADP-Ribosylation in the DNA Damage Response. *Front. Cell Dev. Biol.* **2021**, *9*, DOI.
- (19) Palazzo, L.; Suskiewicz, M. J.; Ahel, I. Serine ADP-Ribosylation in DNA-Damage Response Regulation. *Curr. Opin. in Genet. Dev.* **2021**, *71*, 106–113.

(20) Voorneveld, J.; Rack, J. G. M.; van Gijlswijk, L.; Meeuwenoord, N. J.; Liu, Q.; Overkleeft, H. S.; van der Marel, G. A.; Ahel, I.; Filippov, D. V. Molecular Tools for the Study of ADP-Ribosylation: A Unified and Versatile Method to Synthesize Native Mono-ADP-Ribosylated Peptides. *Chemistry* **2021**, *27* (41), 10621–10627.

(21) Buch-Larsen, S. C.; Hendriks, I. A.; Lodge, J. M.; Rykær, M.; Furtwängler, B.; Shishkova, E.; Westphall, M. S.; Coon, J. J.; Nielsen, M. L. Mapping Physiological ADP-Ribosylation Using Activated Ion Electron Transfer Dissociation. *Cell Rep.* **2020**, *32* (12), 108176.

(22) Imamura, I.; Watanabe, T.; Sakamoto, Y.; Wakamiya, T.; Shiba, T.; Hase, Y.; Tsuruhara, T.; Wada, H. N. Tau-Ribosylhistidine, a Novel Histidine Derivative in Urine of Histidinemic Patients. Isolation, Structure, and Tissue Level. *J. Biol. Chem.* **1985**, *260* (19), 10526–10530.

(23) Oppenheimer, N. J.; Bodley, J. W. Diphtheria Toxin. Site and Configuration of ADP-Ribosylation of Diphthamide in Elongation Factor 2. *J. Biol. Chem.* **1981**, *256* (16), 8579–8581.

(24) Zhu, A.; Li, X.; Bai, L.; Zhu, G.; Guo, Y.; Lin, J.; Cui, Y.; Tian, G.; Zhang, L.; Wang, J.; Li, X. D.; Li, L. Biomimetic α -Selective Ribosylation Enables Two-Step Modular Synthesis of Biologically Important ADP-Ribosylated Peptides. *Nat. Commun.* **2020**, *11* (1), 5600.

(25) Liu, Q.; Kistemaker, H. A. V.; Bhogaraju, S.; Dikic, I.; Overkleeft, H. S.; van der Marel, G. A.; Ova, H.; van der Heden van Noort, G. J.; Filippov, D. V. A General Approach Towards Triazole-Linked Adenosine Diphosphate Ribosylated Peptides and Proteins. *Angew. Chem., Int. Ed.* **2018**, *57* (6), 1659–1662.

(26) Kim, R. Q.; Misra, M.; Gonzalez, A.; Tomašković, I.; Shin, D.; Schindelin, H.; Filippov, D. V.; Ova, H.; Đikić, I.; van der Heden van Noort, G. J. Development of ADP-Ribosyl Ubiquitin Analogues to Study Enzymes Involved in Legionella Infection. *Chemistry* **2021**, *27* (7), 2506–2512.

(27) Hendriks, I. A.; Larsen, S. C.; Nielsen, M. L. An Advanced Strategy for Comprehensive Profiling of ADP-Ribosylation Sites Using Mass Spectrometry-Based Proteomics. *Mol. Cell Proteomics* **2019**, *18* (5), 1010–1026.

(28) Gold, H.; van Delft, P.; Meeuwenoord, N.; Codée, J. D. C.; Filippov, D. V.; Eggink, G.; Overkleeft, H. S.; van der Marel, G. A. Synthesis of Sugar Nucleotides by Application of Phosphoramidites. *J. Org. Chem.* **2008**, *73* (23), 9458–9460.

(29) Štimac, A.; Kobe, J. An Improved Preparation of 2,3,5-Tri-O-Acyl- β -D-Ribofuranosyl Azides by the Lewis Acid-Catalysed Reaction of β -D-Ribofuranosyl Acetates and Trimethylsilyl Azide: An Example of Concomitant Formation of the α Anomer by Trimethylsilyl Triflate Catalysis. *Carbohydr. Res.* **1992**, *232* (2), 359–365.

(30) Kistemaker, H. A. V.; Nardoza, A. P.; Overkleeft, H. S.; van der Marel, G. A.; Ladurner, A. G.; Filippov, D. V. Synthesis and Macrodomein Binding of Mono-ADP-Ribosylated Peptides. *Angew. Chem., Int. Ed.* **2016**, *55* (36), 10634–10638.

(31) Kistemaker, H. A. V.; Meeuwenoord, N. J.; Overkleeft, H. S.; Marel, G. A. v. d.; Filippov, D. V. Solid-Phase Synthesis of Oligo-ADP-Ribose. *Curr. Prot. Nucleic Acid Chem.* **2016**, *64* (1), 4.68.1.

(32) Volbeda, A. G.; Kistemaker, H. A. V.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V.; Codée, J. D. C. Chemoselective Cleavage of P-Methoxybenzyl and 2-Naphthylmethyl Ethers Using a Catalytic Amount of HCl in Hexafluoro-2-Propanol. *J. Org. Chem.* **2015**, *80* (17), 8796–8806.

(33) Voorneveld, J.; Rack, J. G. M.; Ahel, I.; Overkleeft, H. S.; van der Marel, G. A.; Filippov, D. V. Synthetic α - and β -Ser-ADP-Ribosylated Peptides Reveal α -Ser-ADPr as the Native Epimer. *Org. Lett.* **2018**, *20* (13), 4140–4143.

(34) Palazzo, L.; Thomas, B.; Jemth, A.-S.; Colby, T.; Leidecker, O.; Feijs, K. L. H.; Zaja, R.; Loseva, O.; Puigvert, J. C.; Matic, I.; Hellday, T.; Ahel, I. Processing of Protein ADP-Ribosylation by Nudix Hydrolases. *Biochem.* **2015**, *468* (2), 293–301.

(35) Hendriks, I. A.; Buch-Larsen, S. C.; Prokhorova, E.; Elsborg, J. D.; Rebak, A. K. L. F. S.; Zhu, K.; Ahel, D.; Lukas, C.; Ahel, I.; Nielsen, M. L. The Regulatory Landscape of the Human HPF1- and

ARH3-Dependent ADP-Ribosylome. *Nat. Commun.* **2021**, *12* (1), 5893.

Recommended by ACS

Peptide Ligation via the Suzuki–Miyaura Cross-Coupling Reaction

Tae-Kyung Lee, Jung-Mo Ahn, *et al.*

NOVEMBER 27, 2019
THE JOURNAL OF ORGANIC CHEMISTRY

READ 

Electrophilic Sulfonium-Promoted Peptide and Protein Amidation in Aqueous Media

Chuan Wan, Zigang Li, *et al.*

DECEMBER 30, 2021
ORGANIC LETTERS

READ 

Expansion of Phosphane Treasure Box for Staudinger Peptide Ligation

Kiran Bajaj, Dalip Kumar, *et al.*

SEPTEMBER 04, 2021
THE JOURNAL OF ORGANIC CHEMISTRY

READ 

Prebiotic Catalytic Peptide Ligation Yields Proteinogenic Peptides by Intramolecular Amide Catalyzed Hydrolysis Facilitating Regioselective Lys...

Jyoti Singh, Matthew W. Powner, *et al.*

MAY 31, 2022
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

READ 

Get More Suggestions >