Catalysis-Enabled Access to Cryptic Geldanamycin Oxides

Margaret J. Hilton, Christopher Brackett, Brandon Q. Mercado, Brian S. J. Blagg, **Scott Miller**

Submitted date: 08/01/2020 • Posted date: 09/01/2020

Licence: CC BY-NC-ND 4.0

Citation information: Hilton, Margaret J.; Brackett, Christopher; Mercado, Brandon Q.; Blagg, Brian S. J.; Miller, Scott (2020): Catalysis-Enabled Access to Cryptic Geldanamycin Oxides. ChemRxiv. Preprint.
<https://doi.org/10.26434/chemrxiv.11550714.v1>

Catalytic, selective modifications of natural products can be a fertile platform for unveiling not only new natural product analogs with altered biological activity, but also for revealing new reactivity and selectivity hierarchies for embedded functional groups in complex environments. Motivated by these intersecting aims, we report site and stereoselective oxidation reactions of geldanamycin facilitated by aspartyl-peptide catalysts. Through the isolation and characterization of four new geldanamycin oxides, we discovered a synergistic effect between lead peptide-based catalysts and geldanamycin, resulting in an unexpected reaction pathway. Curiously, it seems unlikely that our discoveries would not have been possible absent the outer sphere interactions intrinsic to both the catalyst and the natural product. The result is a set of new “meta” catalytic reactions that deliver both unknown and previously incompletely characterized geldanamycin analogs. Enabled by the catalytic, site-selective epoxidation of geldanamycin, biological assays were carried out to document the bioactivities of the new compounds.

File list (2)

(b)-Manuscript.pdf (1.08 MiB)

[view on ChemRxiv](#) • [download file](#)

(c)-SI.pdf (2.66 MiB)

[view on ChemRxiv](#) • [download file](#)

Catalysis-Enabled Access to Cryptic Geldanamycin Oxides

Margaret J. Hilton,[†] Christopher Brackett,[‡] Brandon Q. Mercado,[†] Brian S. J. Blagg,[‡] Scott J. Miller^{†*}

[†]Department of Chemistry, Yale University, New Haven, Connecticut 06520, United States

[‡]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States

Supporting Information Placeholder

ABSTRACT: Catalytic, selective modifications of natural products can be a fertile platform for unveiling not only new natural product analogs with altered biological activity, but also for revealing new reactivity and selectivity hierarchies for embedded functional groups in complex environments. Motivated by these intersecting aims, we report site and stereo-selective oxidation reactions of geldanamycin facilitated by aspartyl-peptide catalysts. Through the isolation and characterization of four new geldanamycin oxides, we discovered a synergistic effect between lead peptide-based catalysts and geldanamycin, resulting in an unexpected reaction pathway. Curiously, it seems unlikely that our discoveries would not have been possible absent the outer sphere interactions intrinsic to both the catalyst and the natural product. The result is a set of new “meta” catalytic reactions that deliver both unknown and previously incompletely characterized geldanamycin analogs. Enabled by the catalytic, site-selective epoxidation of geldanamycin, biological assays were carried out to document the bioactivities of the new compounds.

INTRODUCTION

Catalysis in chemistry and biochemistry is founded upon accelerating reaction rates and achieving control over some selectivity issue.^{1,2} Accordingly, the field of “asymmetric catalysis” continues to blossom as an ever more powerful way of producing stereochemically homogeneous building blocks with high efficiency.³ Directing chiral catalysts towards complex substrates, such as bioactive natural products, creates a further challenge in addition to enantioselectivity, involving the differentiation of functional groups within the same compound.^{4,5} If more than one copy of the same reactive functional group exists in the structure, then the issue of stereoselectivity is compounded by that of site selectivity, resulting in a demanding landscape of partitioned pathways that lead to many different products to traverse. As a pragmatic solution to these multifaceted selectivity challenges, the application of a diverse catalyst library to a given scaffold offers the opportunity to simultaneously assess (a) multi-product reaction outcomes and (b) to achieve analogs that might not be available in a straightforward manner by either biosynthetic or chemical methods. In addition, and perhaps most alluringly, subjecting complex molecules to catalyst libraries also creates the opportunity to unveil unexpected reactivity, leading to compounds that might not be targeted at all based on canonical reactivity patterns. This paper discloses findings along all of these lines, wherein we have observed an unanticipated cooperativity between a complex substrate of interest and various catalysts. Accordingly, our study has provided a number of perhaps “cryptic” natural product analogs.

In terms of project design, we were curious about expanding the breadth of aspartic acid-based peptides in the context of natural product derivatization. In the field of asymmetric catalysis, for small molecule functionalization, we had previously demonstrated that Asp-containing peptides are efficient and selective catalysts for

Figure 1. Overview of Aspartyl-Peptide Catalyzed Reactions and Geldanamycin

both enantioselective alkene epoxidation (Figure 1a),^{6,7} as well as Baeyer Villiger oxidation^{8,9} with then-unprecedented catalyst-controlled reversals of intrinsic migratory aptitude tendencies (Figure 1b). Mechanistically, the key has been a catalytic shuttle between the aspartic acid catalyst, and its reactive aspartyl peracid form (**1**), which transfers the O-atom in each scenario. We had also shown that a predictive choice of catalyst (i.e., peptide-sequence-selected) could be employed to predetermine whether epoxidation or Baeyer-Villiger oxidation would occur, at least with a carefully designed, admittedly “rigged” substrate **2** (Figure 1c).⁹ Accordingly, a critical next step for the advancement of catalyst-dependent, site-selective diversification of complex natural products with the Asp-based catalyst paradigm is to demonstrate feasibility with genuinely complex bioactive structures. For this purpose, we chose to explore the catalyst-dependent diversification of geldanamycin using Asp-containing peptides (Figure 1d).

Geldanamycin exhibits profound biological activity, targeting Hsp90,^{10,11} a molecular chaperone responsible for folding, stabilization, and maturation of many client proteins, and has shown promise as an anti-cancer therapeutic.¹²⁻¹⁵ However, geldanamycin exhibits poor bioavailability and hepatotoxicity,¹⁶ stimulating the pursuit of new analogues to address these issues via total^{17,18} and semi-synthetic methods.¹⁹⁻²² In fact, geldanamycin derivatives, such as 17-allylamino-17-demethoxygeldanamycin (**17-AAG**),²³ have reached clinical trials for the treatment of many types of cancer, including colorectal, breast, ovarian, lung, multiple myeloma, and leukemia.²⁴ In addition, geldanamycin is a challenge for confronting chemoselectivity, as it contains two alkenyl regions for epoxidation — a diene and an isolated trisubstituted alkene, along with quinoid functionality replete with unsaturation. There-

fore, multiple alkene sites may be subject to functionalization, along with the consideration of π -facial selectivity that could lead to various diastereomers from the epoxidation of each alkene site. Finally, practical considerations were also favorable, such as accessibility to the compound and solubility in a variety of reaction-compatible solvents.

RESULTS AND DISCUSSION

Our survey of aspartyl peptide-based catalysts produced interesting and unexpected results immediately. As is discussed in detail below, four principle mono-oxide products of geldanamycin are observed in these reactions, and their ratios may be extensively modulated with catalyst-dependent kinetic control. Two of the compounds resolve long-standing ambiguities regarding diastereomerism of the geldanamycin-derived epoxides,^{14,21} one of which is efficiently accessed for the first time based on a unique, peptide-based catalyst. Two other compounds, each also unveiled for the first time as a result of a specific aspartyl peptide-based catalyst, are the products of an unanticipated reaction pathway. Moreover, observation of these compounds emerges from an unanticipated cooperation between the complexity of the peptide-based chiral catalysts and the embedded functional group arrays within the macrocyclic molecular scaffold of geldanamycin. This symbiosis, between complex chiral catalysts and complex substrates, enables explicit biological testing of these new and fully characterized compounds, several of which represent structures that were outside of our original conception, grounded in either rational design or traditional scaffold diversification analysis.

Chemistry. Initiating our investigations, geldanamycin oxidation was tested using *m*-CPBA to establish inherent reactivity

Figure 2. Initial Peptide Evaluation^{a,b} and Structure Determination

^aStandard conditions: Geldanamycin (2.8 mg, 5 μ mol, 1 equiv), peptide (50 mol %), 4-dimethylaminopyridine (DMAP, 50 mol %), aqueous H₂O₂ (30 wt %; 5.0 equiv), N,N'-diisopropylcarbodiimide (DIC, 5.0 equiv), CHCl₃ (0.01 M), 22 $^{\circ}$ C, 24 h. ^bAverage from two trials. Determined using UPLC from crude reaction mixtures with an internal standard and calibration curve. Product distributions are corrected to total 100%. See SI for yields. ^cConditions: Geldanamycin (2.8 mg, 5 μ mol, 1 equiv), *m*-chloroperoxybenzoic acid (*m*-CPBA, 2 equiv), CHCl₃ (0.01 M), 22 $^{\circ}$ C, 24 h. (Abbreviations: Boc = *tert*-butoxycarbonyl; Aic = 2-aminoinane carboxyl; Z = Cbz = carboxybenzyl; Acpc = 1-aminocyclopropane carboxyl; EBA = ethylbenzylamine; trt = trityl)

and selectivity, as these results are likely to be minimally biased by outer sphere noncovalent interactions between the reactive species and substrate, beyond the traditional Henbest paradigm.²⁵ Reaction of geldanamycin with *m*-CPBA cleanly yielded two mono-oxidized products in a 15:85 ratio (**A**:**B**, Figure 2, entry 1), strongly favoring compound **B**. Upon isolation and characterization by NMR spectroscopy, it was determined that **A** and **B** are diastereomeric epoxides, derived from reaction of the 8,9-trisubstituted alkene. These compounds have been reported previously, albeit in the absence of either a relative or absolute stereochemical assignment.^{14,21} Nor had either been produced with catalyst-dependent selectivity, to our knowledge. In our hands, we were delighted to achieve X-ray quality crystals of **A**. Analysis of the X-ray crystal structure revealed the complete stereochemistry of the compound, displaying that epoxidation occurs from the “bottom” face, as drawn, to yield **A**, implying that the *m*-CPBA-favored product **B** is the result of epoxidation of the “top” alkene face.

The coin of the realm in studies of site-selective catalysis is the catalyst-dependent reversal of the intrinsic selectivity patterns observed with simple reagents and catalysts. Thus, we then transitioned to the exploration of Asp-based catalysts. Rather surprisingly, results divergent from those observed with *m*-CPBA surfaced immediately. Using the monomeric Boc-Asp-OMe, the *m*-CPBA-favored product **B** is still favored over **A**, although to a lesser degree, and a new product (**C**) is now observed (Figure 2, entry 2). Interestingly, **C** results from epoxidation of the quinone at the 16,17-position, a result also confirmed by X-ray crystallography analysis. Further evaluation of catalysts (*vide infra*) led to the observation of product **D**, which also results from quinone epoxidation at the 16,17-position, yet from the alternate π face in comparison to **C**. This structure was also established by X-ray crystallography analysis. In general, other minor products, such as from bis-oxidation or diene epoxidation, may be produced, yet low yields (<5%) excluded these from our analysis. These observations alone struck us as quite noteworthy. The most preliminary survey of Asp-based catalysts rapidly delivered three alternative products relative to the major compound produced by *m*-CPBA. Two of these geldanamycin oxides resolved long-standing structural ambiguity (**A** and **B**), and two (**C** and **D**) proved to be new geldanamycin scaffolds, unknown prior to the present studies, to our knowledge. Overall, all four compounds provided new insight into reactivity trends of both geldanamycin and Asp-containing peptide catalysts.

To assess the extent to which these catalyst-dependent product ratios could be varied, a library of 14 Asp-containing peptides was selected from previous projects and was then evaluated (Figure 2, select results shown; for full list, see SI). Low selectivities were measured for predictable β -turn-biased and/or β -hairpin-biased sequences²⁶⁻²⁸ (entries 3-4), including two peptides with C-terminal amide caps (entries 5-6). A legacy catalyst for allylic alkene epoxidation⁷ slightly favors product **C** (entry 7, **P2**). Both reactivity and selectivity for 8,9-epoxidation improved significantly when Boc-Asp-Aic-D-Asp(*t*-Bu)-Val-OMe (**P8**) was employed (entry 8). The formation of products **C** and **D** is largely suppressed with this more reactive peptide, resulting in a distribution of 68%, 25%, 5%, and 1%, respectively (**A**, **B**, **C**, and **D**, entry 8). In contrast to the reaction using *m*-CPBA, which yielded **A** and **B** in a 1:5.7 dr, **P8** provides a coveted reversal of diastereoselectivity, delivering a 2.7:1 dr (**A**:**B**). Finally, legacy catalyst **P1**, which was previously reported to promote Baeyer Villiger oxidation (Figure 1b),⁸ provides the most striking catalyst-dependent diversion from conventional reactivity, exhibiting 98% selectivity for quinone epoxidation, affording products **C** and **D** in a 3.5:1 diastereomeric ratio (entry 9).

Thus, our initial examination of Asp-based peptides (Figure 2), yielded two catalysts that favor two distinct products, alternative

to that favored by *m*-CPBA: **P8**, favoring 8,9-epoxide **A**; and **P1**, favoring 16,17-epoxide **C**. Moreover, the screening provides catalyst-dependent access to the unique epoxyquinones **C** and **D**, which are not detected to an appreciable extent with *m*-CPBA. As these catalysts provide stark contrasts to the outcomes induced by *m*-CPBA, we wished to understand further the basis of these catalyst-controlled outcomes in hopes of some degree of further optimization.

To this end, several new catalysts were explored in the context of attempted optimization for product **A** (Figure 3). Relative to catalyst **P8**, exchanging Aic at the *i*+1 position for Acpc, D-Phe, or D-Val resulted in similar product distributions (entries 1-3, respectively). However, **P10** with Acpc in the *i*+1 position does provide a modest enhancement of **A**:**B** ratio (3.1:1 dr), which could be further optimized (*vide infra*). On the other hand, if the *i*+1 residue is converted to an L-amino acid (Phe, Val, or Pro), the selectivity for **A** consecutively diminishes (entries 4-6, respectively). For example, with **P15** (Pro at *i*+1), almost equal amounts of **A**, **B**, and **C** are observed (entry 6), as is seen with other peptides containing the sequence Asp-Pro (**P2**, **P4**, **P6**, Figure 2).

Figure 3. Point mutations of lead catalyst, A-Selective Catalyst, P10^{a,b}

^aStandard conditions: Geldanamycin (2.8 mg, 5 μ mol, 1 equiv), peptide (50 mol %), 4-dimethylaminopyridine (DMAP, 50 mol %), aqueous H₂O₂ (30 wt %; 5.0 equiv), *N,N'*-diisopropylcarbodiimide (DIC, 5.0 equiv), CHCl₃ (0.01 M), 22 $^{\circ}$ C, 24 h. ^bAverage from two trials. Determined using UPLC from crude reaction mixtures with an internal standard and calibration curve. Product distributions are corrected to total 100%. (Abbreviations: Boc = *tert*-butoxycarbonyl; Acpc = 1-aminocyclopropane carboxyl; Dap = L-2,3-diaminopropionic acid)

As shown in Figure 3, additional changes at the *i*+2 position provided generally decreases in the selectivity for **A**. When D-Asp(*t*-Bu) is replaced with D-Asn(trt) at *i*+2, thus adding a hydrogen-bond donor in place of an acceptor, selectivity for **A** decreases (entry 7). Intriguingly, when the possibility for

hydrogen-bonding at this position is removed through insertion of a D-Leu residue, selectivity for **A** is restored to a small degree (entry 8). Finally, low steric bulk at *i*+3 (Gly, entry 9) causes diminished selectivity for product **A**, yet a polar aromatic group (Tyr(*t*-Bu), entry 10) did not significantly modulate the product distributions in comparison to **P10**. However, including a hydrogen-bond donor (Dap(Boc)) at *i*+3 produces a lower amount of **A**, and a greater amount of **C** now emerges, affording almost equal yields of **A**, **B**, and **C** (entry 11). Overall, this series of peptide mutations revealed that most sequences, except those with additional hydrogen-bond donors, are likely accessing similar transition state ensembles, resulting in comparable energetic landscapes for the production of the major product, **A**.

To gain additional structural information concerning both **A**-selective **P10** and **C**-selective **P1**, peptide truncation studies were performed. When **A**-selective catalyst **P10** is shortened to the trimer Boc-Asp-Acpc-D-Asp(OMe)-OMe, ~8-9% selectivity is lost for the formation of product **A** (Figure 4a, entry 2). However, the product ratios are well within the range observed for other tetrameric peptides, reinforcing the observation that the *i*+3 residue is not the most influential position in guiding selectivity profiles (e.g., **P18** and **P19** in Figure 3). The dimer, Boc-Asp-Acpc-OMe, reveals a much more significant perturbation on product selectivity, providing approximately equal amounts of **A**, **B** and **C** (entry 3), suggesting that a β -turn-biased structure of **P10** may be the source of the observed preference for **A** in the optimal tetrameric peptides. Indeed, the dimer results in similar product distributions in comparison to the monomer, Boc-Asp-OMe (entry 4). All of these data, including insight from the crystal structures,

Figure 4. Mechanistic considerations for A-selective catalyst P10^{a,b}

4b) Plausible Model for Selective Formation of A

^aStandard conditions: Geldanamycin (2.8 mg, 5 μ mol, 1 equiv), peptide (50 mol %), 4-dimethylaminopyridine (DMAP, 50 mol %), aqueous H₂O₂ (30 wt %; 5.0 equiv), *N,N'*-diisopropylcarbodiimide (DIC, 5.0 equiv), CHCl₃ (0.01 M), 22 $^{\circ}$ C, 24 h. ^bAverage from two trials. Determined using UPLC from crude reaction mixtures with an internal standard and calibration curve. Product distributions are corrected to total 100%. See SI for yields.

led us to consider a selectivity model, wherein the carbamate at C7 in geldanamycin could be engaged in a directing hydrogen-bond with the peptide backbone, guiding epoxidation to the "bottom" alkene face (Figure 4b).

The truncation study for **C**-selective **P1**, which favors quinone epoxidation (**C** and **D**), resulted in a much less drastic attenuation in product selectivity (Figure 5a). Surprisingly, each truncate resulted in similar product ratios to **P1**, all favoring the formation of **C** and **D**. Even the dimer Boc-Asp-Pro-OMe (entry 3) provides **C** and **D** in 69% and 27%, respectively, in comparison to **P1**, yielding **C** and **D** in 76% and 22%, respectively. A particularly remarkable comparison is that between two dimers, with only one residue changed: the dimer Boc-Asp-Acpc-OMe (Figure 4a, entry 3) favors 8,9-epoxidation overall (74:26 = **A**+**B** : **C**+**D**), while Boc-Asp-Pro-OMe remains selective for quinone oxidation (4:96 = **A**+**B** : **C**+**D**). Thus, it appears that the first two residues of **P1** (Asp-Pro) are primarily responsible for directing the reaction towards the quinone epoxidation pathway.

Figure 5. Data-guided mechanistic speculation into quinone oxidation to form C and D^{a,b}

^aStandard conditions: Geldanamycin (2.8 mg, 5 μ mol, 1 equiv), peptide (50 mol %), 4-dimethylaminopyridine (DMAP, 50 mol %), aqueous H₂O₂ (30 wt %; 5.0 equiv), *N,N'*-diisopropylcarbodiimide (DIC, 5.0 equiv), CHCl₃ (0.01 M), 22 $^{\circ}$ C, 24 h. ^bAverage from two trials. Determined using UPLC from crude reaction mixtures with an internal standard and calibration curve. Product distributions are corrected to total 100%. See SI for yields.

Notably, any perturbation to the L-Asp-L-Pro dipeptide stereochemistry supports this assertion (Figure 5a, entries 5-7). In each case, any other stereochemical dyad results in diversion of the reaction pathway towards 8,9-epoxidation (formation of **A** and **B**). Furthermore, peptides containing the Asp-Pro sequence tend to provide a higher yield of products **C** and **D**, but the overall product distribution is dependent on the remaining residues (e.g., **P2**, **P4**, **P6**, **P15**). The subtle yet complex influence of the peptide sequence on the reaction outcome reinforces the synergistic nature of attractive interactions between the substrate and catalyst.

As quinone-selective catalyst **P1** promotes a distinct reaction pathway, any selectivity model for the formation of **C** and **D** will differ substantially from that shown in Figure 4b. Thus, shown in Figure 5b is an alternative scenario that may account for the strict requirement for L-Asp-L-Pro chirality, with further selectivity tuning by distal residues. Accordingly, it is possible that the peracid and Pro carbonyl (blue circle) are oriented in the same direction,²⁹ such that interactions with the Pro(C=O) are responsible for this selectivity. The hydroxyl group at C11, which is situated near the back of the quinone, as drawn, could be involved in directing the peptide via hydrogen-bonding with Pro(C=O) towards product **C**. Formation of the minor epoxyquinone **D** could then result from conformational inversion of the quinone π -face, or even be directed by hydrogen-bonding with the amide at C1.

Regarding the plausible selectivity models presented in Figures 4b and 5b, it is absolutely essential to acknowledge that mechanistic rationalizations for selectivity outcomes with ratios at these levels must be realized with an abundance of mechanistic caveats. However, at the global level of these observed reversals of product selectivity, in situations in which multiple, non-stereoisomeric products are formed, we contend that the state of the art is limited and that these heuristic models may guide the field forward. Computational studies (and even empirical studies^{29,30}) of problems of this complex nature are also a frontier-level, extensive endeavor,³¹⁻³³ and ongoing efforts along these lines will no doubt add further insight.

As we did not anticipate formation of the epoxyquinones **C** and **D** from these studies, we wondered if their formation was a particular function of the catalysts, the secondary structure of geldanamycin and its epoxyquinone adducts, or a synergistic result of both features. Therefore, we examined the reactions of several model quinones (**3-6**; Figure 6) under analogous conditions. In all cases, no detectable reactions were observed using *m*-CPBA, and decomposition of the model quinones was detected under standard reaction conditions with **P1**, or when nucleophilic epoxidation conditions were tested (e.g., *t*BuOOH, base). In contrast, compounds **C** and **D** seem to be quite stable when formed under conditions of catalytic **P1**. These realizations further bolster the symbiotic relationship between these catalysts and their substrates. These findings may well suggest that **P1**, originally discovered as a nucleophilic peracid and Baeyer-Villiger oxidation catalyst,⁸ may well be functioning once again in a peptide-tuned nucleophilic manner in the presence of the specific functionality-adorned geldanamycin scaffold. This assertion is supported by the fact that, subsequent to the discovery of **P1**, and based on its behavior, we also found the classical, stoichiometric nucleophilic epoxidation conditions (*t*BuOOH, base; see SI for details) allow the formation of **C** and **D** with yields and selectivities comparable to catalytic **P1**. Since these conditions fail to deliver efficient epoxidation of the model quinones further underscores the importance of the global functionality of the natural product, rather than simply its local structural environment.

Figure 6. Evaluation of Model Quinones

Having identified the selective peptide catalysts **P10** and **P1** for geldanamycin oxidation, and in pursuit of ample quantities for characterization and biological evaluation, several optimized experiments were carried out (Scheme 1). Fortuitously, higher reactivity was observed as a function of higher reagent loadings/lower peptide catalyst loadings. With **P10**, **A** and **B** were

favoured in slightly higher ratios than at the microscale, resulting in a 3.9:1 dr of **A:B** (74:19:6:1 of **A:B:C:D**). Products **A** and **B** were isolated in 39% and 10% yields, respectively. With **P1**, higher conversion could be achieved through use of stoichiometric DMAP, resulting in an **A:B:C:D** ratio of 0:0:76:24, from which **C** and **D** were isolated in 32% and 14% yields, respectively. Taken together, a comparison of catalysts **P10** to **P1** on somewhat larger scale reveals that the C8,9 (**A+B**) versus C16,17 (**C+D**) functionalization ratios can swing from 93:7 to 0:100 as a function of the peptide-based catalyst, of course with attendant tuning of the diastereoselectivity in each series.

Scheme 1. Isolation of geldanamycin analogues

As 17-substituted geldanamycin derivatives have demonstrated improved bioactivity and bioavailability,^{23,34,35} we sought to test these optimal peptide sequences and reaction conditions with **17-AAG** to access additional analogs. We predicted that **P10** would likely lead to the same mode of epoxidation, as the local environment near the 8,9-position is unchanged. However, we were uncertain if adjusting the electronic nature of the quinone would disrupt or enhance quinone epoxidation with **P1**. With the scaled reaction conditions shown in Scheme 1, **P10** indeed affords the expected product, in fact with elevated selectivity compared to geldanamycin, resulting in **17-A** in 93% selectivity and 33% isolated yield. The same epoxide diastereomer as in **A** was confirmed by X-ray crystallography analysis (See SI). Yet, *m*-CPBA was less effective with **17-AAG** than geldanamycin, providing only 30% conversion and favoring the same product as **P10** in a 2:1 ratio (See SI). Finally, reaction of **17-AAG** with **P1** resulted in only 10% conversion of the starting material and detection of one new mono-oxidized product by UPLC-MS (See SI). While we have not definitively assigned the structure of this compound, the low reactivity of this modified

quinone core in **17-AAG** reflects the significant influence of the substituents on accessing quinone oxidation. No further optimization or isolation of this product was attempted.

Biology. Intrigued by these novel epoxy-geldanamycin and **17-AAG** analogues, their biological activity was investigated. As previously mentioned, geldanamycin is a well characterized Hsp90 inhibitor and has shown promising anticancer activity. Therefore, the anti-proliferative activity manifested by these analogs was determined against two breast cancer cell lines, MCF-7 and SKBr-3. Only one of the new compounds inhibited the growth of these cancer cells at 10 μ M. Compound **B**, which resulted from the reaction of geldanamycin and *m*-CPBA, retained the majority of the parent compound's anti-proliferative activity. In fact, compound **B** manifested an EC₅₀ value of 338.1 ± 160.2 and 28.7 ± 14.3 nM against MCF-7 and SKBr-3 cell lines, respectively. This activity was similar (albeit less active) to geldanamycin's EC₅₀ values of 19.9 and 24 nM, respectively (NCI ID: 122750).

In addition to the anti-proliferative activity manifested by these compounds, the molecules were evaluated for direct binding to Hsp90 isoforms. The affinity of these epoxide analogues was determined for the individual isoforms of Hsp90 to establish whether any selectivity resulted from this modification. Fluorescence polarization assays have revealed geldanamycin to exhibit a high affinity towards three of the four isoforms (Hsp90 α , Hsp90 β , Grp94), as compared to the mitochondrial localized isoform, TRAP1.¹⁵ Therefore, the affinity of these molecules for Hsp90 α , Hsp90 β , and Grp94 was determined using a fluorescence polarization assay. The results are summarized in Table 1.

Table 1. Epoxy Analogues Apparent Affinity Data

CMPD	K _D (μ M)		
	Hsp90 α	Hsp90 β	Grp94
A	3.41 ± 0.60	1.08 ± 0.073	2.55 ± 0.46
B	0.083 ± 0.029	0.054 ± 0.0001	0.13 ± 0.07
C	0.76 ± 0.26	0.395 ± 0.053	1.10 ± 0.49
D	0.32 ± 0.09	0.24 ± 0.04	0.54 ± 0.09
17-A	>10	>10	>10
17-B	0.90 ± 0.38	0.81 ± 0.09	1.13 ± 0.02

Consistent with the anti-proliferative data, compound **B** displayed a high affinity for all three Hsp90 isoforms. Compared to diastereomer **A**, compound **B** manifested ~ 20 x's higher affinity. Intriguingly, compounds **C** and **D** exhibited no anti-proliferative activity, but retained sub-micromolar affinity towards Hsp90.

In order to validate that compound **B** manifests its anti-proliferative activity via Hsp90 inhibition, the ability of compound **B** to induce client protein degradation was investigated. Client protein degradation occurs as a result of Hsp90 inhibition, because the protein substrate is unable to reach conformation maturation and instead, is degraded via the ubiquitin-proteasome pathway. Therefore, SKBr-3 cells were treated with increasing concentrations of compound **B** and select Hsp90-dependent client proteins were evaluated via Western-blot analysis (Figure 7). Consistent with Hsp90 inhibition, the EGF receptor and HER2 levels were reduced in a dose-dependent manner. In addition, treatment of cells with geldanamycin is known to induce the heat shock response, which results in the increased expression of Hsp70 and/or Hsp90.¹⁶ As shown in Figure 7, compound **B** induced a dose-dependent increase in the expression of Hsp70 and Hsp90, consistent with Hsp90 inhibition in the cellular environment.

Figure 7. Compound B Client Protein Degradation Assay

Historically, strategies to diversify geldanamycin have focused on the quinone moiety. However, these results suggest that it may be advantageous to develop analogues of geldanamycin through innovative chemical diversity methods such as that described herein, which provided access to analogues that were otherwise unobtainable.

CONCLUSIONS

These studies provide significant evidence that peptide modified catalytic functionalities can deliver dramatic reversals of stereo-, site- and functional group selectivity in complex molecular settings. Complementary to studies of site-selective natural product diversification in settings where explicit targeting strategies may be derived, for example the glycopeptide antibiotics,³⁶⁻³⁹ this report shows the generality of these ideas for application to both a new natural product scaffold (geldanamycin), and to a reaction class that might have seemed recalcitrant to the approach (functional group-selective epoxidation). Unique chemical discoveries emerged that highlight a potentially fertile intersection for discovery when the domains of complex catalysts and complex substrates are compelled to interact. Certainly in this case, the new products formed, and possibly the selective formation of previously unassigned geldanamycin oxides, would have been elusive absent the diversification of the geldanamycin scaffold with catalysts targeting outer sphere interactions.

Selective access to samples of **A**, **B**, **C** and **D** also delivered new information about the biological potential resident in these new derivatives, and present an enigma worthy of further study – that the quinone analogs **C** and **D** maintain Hsp90 affinity, while losing anti-proliferative effects.⁴⁰ Accordingly, to the extent that these chemical studies unveiled previously unknown, and resolved previously unassigned, geldanamycin analogs, perhaps these studies have also added incentive to search for additional presently cryptic catalyst-enabled structures, creating opportunities for resolving additional cryptic biological ambiguities.

ASSOCIATED CONTENT

Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website at DOI:

AUTHOR INFORMATION

Corresponding Author

*E-mail: scott.miller@yale.edu

ORCID

Scott J. Miller: 0000-0001-7817-1318
Margaret J. Hilton: 0000-0003-1843-2322
Brian S. J. Blagg: 0000-0002-6200-3480

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

S.J.M. is grateful to the National Institute of General Medical Sciences (NIGMS) of the NIH R35 GM132092). M.J.H. would like to thank the NIGMS of the NIH for support (F32GM125119). We thank Dr. Yu Tang and Dr. Sheng-Ying Hsieh for sharing peptide catalysts (Yale). B.S.J.B. is grateful to the NIH for financial support (CA213566).

REFERENCES

- (1) Wolfenden, R.; Snider, M. J. The Depth of Chemical Time and the Power of Enzymes as Catalysts. *Acc. Chem. Res.* **2001**, *34*, 938.
- (2) Benkovic, S. J.; Hammes-Schiffer, S. A Perspective on Enzyme Catalysis. *Science* **2003**, *301*, 1196.
- (3) Trost, B. M. Asymmetric catalysis: An enabling science. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5348.
- (4) Shugrue, C. R.; Miller, S. J. Applications of Nonenzymatic Catalysts to the Alteration of Natural Products. *Chem. Rev.* **2017**, *117*, 11894.
- (5) Robles, O.; Romo, D. Chemo- and site-selective derivatizations of natural products enabling biological studies. *Nat. Prod. Rep.* **2014**, *31*, 318.
- (6) Peris, G.; Jakobsche, C. E.; Miller, S. J. Aspartate-Catalyzed Asymmetric Epoxidation Reactions. *J. Am. Chem. Soc.* **2007**, *129*, 8710.
- (7) Lichtor, P. A.; Miller, S. J. Combinatorial evolution of site- and enantioselective catalysts for polyene epoxidation. *Nat. Chem.* **2012**, *4*, 990.
- (8) Romney, D. K.; Colvin, S. M.; Miller, S. J. Catalyst Control over Regio- and Enantioselectivity in Baeyer–Villiger Oxidations of Functionalized Ketones. *J. Am. Chem. Soc.* **2014**, *136*, 14019.
- (9) Alford, J. S.; Abascal, N. C.; Shugrue, C. R.; Colvin, S. M.; Romney, D. K.; Miller, S. J. Aspartyl Oxidation Catalysts That Dial In Functional Group Selectivity, along with Regio- and Stereoselectivity. *ACS Cent. Sci.* **2016**, *2*, 733.
- (10) Whitesell, L.; Minnaugh, E. G.; De Costa, B.; Myers, C. E.; Neckers, L. M. Inhibition of heat shock protein HSP90-pp60v-src heteroprotein complex formation by benzoquinone ansamycins: essential role for stress proteins in oncogenic transformation. *Proc. Natl. Acad. Sci. U. S. A.* **1994**, *91*, 8324.
- (11) Prodromou, C.; Roe, S. M.; O'Brien, R.; Ladbury, J. E.; Piper, P. W.; Pearl, L. H. Identification and Structural Characterization of the ATP/ADP-Binding Site in the Hsp90 Molecular Chaperone. *Cell* **1997**, *90*, 65.
- (12) Li, L.; Wang, L.; You, Q.-D.; Xu, X.-L. Heat Shock Protein 90 Inhibitors: An Update on Achievements, Challenges, and Future Directions. *J. Med. Chem.* **2019**, DOI: 10.1021/acs.jmedchem.9b00940.
- (13) Taldone, T.; Sun, W.; Chiosis, G. Discovery and development of heat shock protein 90 inhibitors. *Bioorg. Med. Chem.* **2009**, *17*, 2225.
- (14) Franke, J.; Eichner, S.; Zeilinger, C.; Kirschning, A. Targeting heat-shock-protein 90 (Hsp90) by natural products: geldanamycin, a show case in cancer therapy. *Nat. Prod. Rep.* **2013**, *30*, 1299.
- (15) Chaudhury, S.; Welch, T. R.; Blagg, B. S. J. Hsp90 as a Target for Drug Development. *ChemMedChem* **2006**, *1*, 1331.
- (16) J. G. Supko, R. L. H., M. R. Grever, L. Malspeis. Preclinical pharmacologic evaluation of geldanamycin as an antitumor agent. *Cancer Chemother. Pharmacol.* **1995**, *36*, 305.
- (17) For total syntheses of geldanamycin, see: a) Qin, H.-L.; Panek, J. S. Total Synthesis of the Hsp90 Inhibitor Geldanamycin. *Org. Lett.* **2008**, *10*, 2477; b) Andrus, M. B.; Meredith, E. L.; Hicken, E. J.; Simmons, B. L.; Glancey, R. R.; Ma, W. Total Synthesis of (+)-Geldanamycin and (–)-o-Quinogeldanamycin: Asymmetric Glycolate Aldol Reactions and Biological Evaluation. *J. Org. Chem.* **2003**, *68*, 8162.
- (18) For a recent contribution describing total synthesis-based analog syntheses with an extensive bibliography, see: Jin, L.; Zhang, R.; Zhang, Z.; Bian, C.; Yu, X. Total synthesis based modification of benzoquinone ansamycin antibiotics: C8 diversification of C5-C15 fragments. *Tet. Lett.* **2019**, *60*, 547.
- (19) For examples of biosynthetic analogs of geldanamycin, see: a) Patel, K.; Piagentini, M.; Rascher, A.; Tian, Z.-Q.; Buchanan, G. O.; Regentin, R.; Hu, Z.; Hutchinson, C. R.; McDaniel, R. Engineered Biosynthesis of Geldanamycin Analogs for Hsp90 Inhibition. *Chem. Biol.* **2004**, *11*, 1625; b) Buchanan, G. O.; Regentin, R.; Piagentini, M.; Rascher, A.; McDaniel, R.; Galazzo, J. L.; Licari, P. J. Production of 8-Demethylgeldanamycin and 4,5-Epoxy-8-demethylgeldanamycin from a Recombinant Strain of *Streptomyces hygroscopicus*. *J. Nat. Prod.* **2005**, *68*, 607.
- (20) Khandelwal, A.; Crowley, V. M.; Blagg, B. S. J. Natural Product Inspired N-Terminal Hsp90 Inhibitors: From Bench to Bedside? *Med. Res. Rev.* **2016**, *36*, 92.
- (21) Kitson, R. R. A.; Moody, C. J. Learning from Nature: Advances in Geldanamycin- and Radicol-Based Inhibitors of Hsp90. *J. Org. Chem.* **2013**, *78*, 5117.
- (22) Yñíguez-Gutiérrez, A. E.; Bachmann, B. O. Fixing the Unfixable: The Art of Optimizing Natural Products for Human Medicine. *J. Med. Chem.* **2019**, *62*, 8412.
- (23) Schulte, T. W.; Neckers, L. M. The benzoquinone ansamycin 17-allylamino-17-demethoxygeldanamycin binds to HSP90 and shares important biologic activities with geldanamycin. *Cancer Chemother. Pharmacol.* **1998**, *42*, 273.
- (24) Biamonte, M. A.; Van de Water, R.; Arndt, J. W.; Scannevin, R. H.; Perret, D.; Lee, W.-C. Heat Shock Protein 90: Inhibitors in Clinical Trials. *J. Med. Chem.* **2010**, *53*, 3.
- (25) Henbest, H. B.; Wilson, R. A. L. 376. Aspects of stereochemistry. Part I. Stereospecificity in formation of epoxides from cyclic allylic alcohols. *J. Chem. Soc.* **1957**, 1958.
- (26) Haque, T. S.; Little, J. C.; Gellman, S. H. Stereochemical Requirements for β -Hairpin Formation: Model Studies with Four-Residue Peptides and Depsipeptides. *J. Am. Chem. Soc.* **1996**, *118*, 6975.
- (27) Gunasekaran, K.; Gomathi, L.; Ramakrishnan, C.; Chandrasekhar, J.; Balaram, P. Conformational interconversions in peptide β -turns: analysis of turns in proteins and computational estimates of barriers. *J. Mol. Biol.* **1998**, *284*, 1505.
- (28) Wilmut, C. M.; Thornton, J. M. Analysis and prediction of the different types of β -turn in proteins. *J. Mol. Biol.* **1988**, *203*, 221.
- (29) Abascal, N. C.; Miller, S. J. Solution Structures and Molecular Associations of a Peptide-Based Catalyst for the Stereoselective Baeyer–Villiger Oxidation. *Org. Lett.* **2016**, *18*, 4646.
- (30) Rigling, C.; Kisunzu, J. K.; Duschmalé, J.; Häussinger, D.; Wiesner, M.; Ebert, M.-O.; Wennemers, H. Conformational Properties of a Peptidic Catalyst: Insights from NMR Spectroscopic Studies. *J. Am. Chem. Soc.* **2018**, *140*, 10829.
- (31) Yan, X. C.; Metrano, A. J.; Robertson, M. J.; Abascal, N. C.; Tirado-Rives, J.; Miller, S. J.; Jorgensen, W. L. Molecular Dynamics Simulations of a Conformationally Mobile Peptide-Based Catalyst for Atroposelective Bromination. *ACS Catal.* **2018**, *8*, 9968.
- (32) Thiel, W. Computational Catalysis—Past, Present, and Future. *Angew. Chem. Int. Ed.* **2014**, *53*, 8605.
- (33) Lam, Y.-H.; Grayson, M. N.; Holland, M. C.; Simon, A.; Houk, K. N. Theory and Modeling of Asymmetric Catalytic Reactions. *Acc. Chem. Res.* **2016**, *49*, 750.
- (34) Mellatyar, H.; Talaie, S.; Pilehvar-Soltanahmadi, Y.;

- Barzegar, A.; Akbarzadeh, A.; Shahabi, A.; Barekati-Mowahed, M.; Zarghami, N. Targeted cancer therapy through 17-DMAG as an Hsp90 inhibitor: Overview and current state of the art. *Biomed. Pharmacother.* **2018**, *102*, 608.
- (35) Tian, Z.-Q.; Liu, Y.; Zhang, D.; Wang, Z.; Dong, S. D.; Carreras, C. W.; Zhou, Y.; Rastelli, G.; Santi, D. V.; Myles, D. C. Synthesis and biological activities of novel 17-aminogeldanamycin derivatives. *Bioorg. Med. Chem.* **2004**, *12*, 5317.
- (36) Han, S.; Miller, S. J. Asymmetric Catalysis at a Distance: Catalytic, Site-Selective Phosphorylation of Teicoplanin. *J. Am. Chem. Soc.* **2013**, *135*, 12414.
- (37) Pathak, T. P.; Miller, S. J. Site-Selective Bromination of Vancomycin. *J. Am. Chem. Soc.* **2012**, *134*, 6120.
- (38) Fowler, B. S.; Laemmerhold, K. M.; Miller, S. J. Catalytic Site-Selective Thiocarbonylations and Deoxygenations of Vancomycin Reveal Hydroxyl-Dependent Conformational Effects. *J. Am. Chem. Soc.* **2012**, *134*, 9755.
- (39) Pathak, T. P.; Miller, S. J. Chemical Tailoring of Teicoplanin with Site-Selective Reactions. *J. Am. Chem. Soc.* **2013**, *135*, 8415.
- (40) Chiosis, G.; Neckers, L. Tumor Selectivity of Hsp90 Inhibitors: The Explanation Remains Elusive. *ACS Chem. Biol.* **2006**, *1*, 279.

Insert Table of Contents artwork here

(b)-Manuscript.pdf (1.08 MiB)

[view on ChemRxiv](#) • [download file](#)

Catalysis-Enabled Access to Cryptic Geldanamycin Oxides

Margaret J. Hilton,[†] Christopher M. Brackett,[‡] Brandon Q. Mercado,[†] Brian S. J. Blagg,[‡] Scott J. Miller^{†*}

[†]Department of Chemistry, Yale University, New Haven, Connecticut 06520, United States

[‡]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States

Supporting Information

Table of Contents

I.	General Information	2
II.	Peptide Synthesis	3
III.	Peptide Screening Conditions and Results	8
IV.	Large Scale Reaction Conditions	10
V.	Liquid Chromatography Chromatograms	12
VI.	Model Quinone Synthesis and Reactions	18
VII.	Biological Testing	19
VIII.	NMR Spectra	20
IX.	X-Ray Crystallography Data	26
X.	References	105

I. General Information

All reactions were carried out under benchtop conditions, without exclusion of air or moisture, unless otherwise stated. Room temperature is considered 20–23 °C. All reagents were obtained from commercial suppliers and used as received, without further purification, unless otherwise stated. Geldanamycin and 17-AAG were purchased from Alfa Aesar and used as received. THF, CH₂Cl₂, DMF, and PhMe were dried over alumina and dispensed under argon from a Seca Solvent purification system by GlassContour. Triethylamine (Et₃N), N,N'-diisopropyl ethylamine (i-Pr₂NEt), and N,N'-diisopropylamine (i-Pr₂NH) were distilled over CaH under a nitrogen atmosphere prior to use. Deionized water was used for reactions, extractions, and RP chromatography. HPLC grade solvents were used for all other chromatography.

Unless otherwise stated, all NMR data were acquired at ambient temperature. NMR solvents, were purchased from Cambridge Isotopes and used as received. NMR spectra were processed with MestReNova x64-12.0.1-20560 software using the baseline and phasing correction features. Multiplicities and coupling constants were calculated using the multiplet analysis feature with manual intervention as necessary. ¹H NMR spectra were obtained on Agilent 400 MHz, 500 MHz or 600 MHz spectrometers. Proton chemical shifts (δ) are reported in ppm and referenced to residual solvent peaks for CDCl₃ (δ 7.26 ppm). Proton data are reported as chemical shift, (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), heptet (hept), multiplet (m), broad singlet (bs), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of doublet of triplets (ddt), doublet of triplets (dt), doublet of triplet of triplets (dtt), etc. and apparent (app)] coupling constants [Hz], and integrations). ¹³C NMR spectra were obtained on Agilent 500 (125 MHz) MHz or 600 (150 MHz) MHz spectrometers with full proton decoupling. Carbon chemical shifts (δ) are reported in ppm and referenced to residual solvent peaks for CDCl₃ (δ 77.2 ppm). Analytical thin-layer chromatography (TLC) was performed using EMD Millipore silica gel 60 F254 precoated plates (0.25 mm thickness) and developed plates were visualized using a UV lamp and/or potassium permanganate (KMnO₄) stain. TLC R_f values are reported.

Normal-phase flash-column chromatography was performed using an automated Biotage Isolera One flash purification system equipped with a 10, 25, or 50 g SNAP Ultra (HP Sphere, 25 μm silica) cartridge. Reversed-phase flash-column chromatography was performed using an automated Biotage Isolera One flash purification system equipped with a 12, 30, 60 or 120 g SNAP C-18 (HS 50 μm silica) or SNAP Ultra C-18 (HP Sphere, 25 μm silica) cartridge. Preparative reverse phase HPLC was performed using a Shimadzu Prominence system equipped with LC-20AP pumps, CBM-20A Communications BUS module, SPD-20A UV/vis detector, SIL-10AP autosampler, and FRC-10A fractions collector. Ultra-high performance liquid chromatography-mass spectrometry (UPLC/MS) was performed on a Waters Acquity SQD2 instrument equipped with an CORTECS C18 column (1.6 μm particle size, 3.0 x 50 mm) and an Ultra BEH C-18 column (1.7 μm particle size, 2.1 x 50 mm), a dual atmospheric pressure chemical ionization (API)/electrospray ionization (ESI) mass spectrometry detector, and a photodiode array detector. High-resolution mass spectrometry (HRMS) was conducted by the service of Chemical and Biophysical Instrumentation Center in the chemistry department at Yale University on a Waters Xevo Q-TOF high-resolution Mass Spectrometry using ESI. Infrared spectra were recorded on a Nicolet 6700 ATR/FT-ATR spectrometer, and ν_{max} are partially reported in cm⁻¹. Optical rotations were recorded on a Autopol VI Automatic Polarimeter at the sodium D-line (589 nm) using a Type 40T TempTrol™ cell of 0.50 dm path length at 20 °C and reported as follows: [α]_d^{temp}, concentration (c in g/100 mL), and solvent.

Abbreviations:

Ac = acetyl; Acpc = 1-aminocyclopropane-1-carboxylic acid; Aib = α -aminoisobutyric acid; Aic = 2-aminoindane-2-carboxylic acid; Boc = tert-butoxycarbonyl; Bn = benzyl; Bz = benzoyl; Cbz = carboxybenzyl; Dap = 2,3-diaminopropionic acid; DIC = *N,N*-diisopropylcarbodiimide; DMAP = 4-dimethylaminopyridine; DMF = *N,N*-dimethylformamide; EDC•HCl = *N*-(3-Dimethylaminopropyl)-*N*-ethylcarbodiimide hydrochloride; ESI = electrospray ionization; EtOAc = ethyl acetate; Fmoc = 9-fluorenylmethoxycarbonyl; HATU = O-(7-azabenzotriazol-1-yl)-*N,N,N,N*-tetramethyluronium hexafluorophosphate; HBTU = O-(Benzotriazol-1-yl)-*N,N,N,N*-tetramethyluronium hexafluorophosphate; HCTU = 2-(6-chloro-1-*H*-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate; HOBt = 1-hydroxybenzotriazole; HPLC = high-performance liquid chromatography; HRMS = high-resolution mass spectrometry; IR = infrared; UPLC-MS = ultraperformance liquid chromatography mass spectrometry; NMM = 4-methylmorpholine; NMR = nuclear magnetic resonance; RP = reversed-phase; rt = room temperature; TFA = trifluoroacetic acid; THF = tetrahydrofuran; TLC = thin-layer chromatography; TOF = time-of-flight.

II. Peptide Synthesis

1. General Procedure A: Solid Phase Peptide Synthesis

Coupling and Fmoc-Deprotection

First, 2-chlorotrityl resins (H-Xaa-2-ClTrt-Resin, 1 equiv) were swelled in CH_2Cl_2 for 20 min. Then, the appropriate amino acid monomers (Fmoc-Yaa-OH, 3 equiv) were coupled using Cl-HOBt (3 equiv), HCTU (3 equiv), and *N*-methylmorpholine (6 equiv) in *N*-methyl-2-pyrrolidone (NMP). The amino acid, coupling reagents, and base were premixed before adding to the solid support. Couplings generally proceeded for 3 to 5 h. Deprotections were achieved with 20% (v/v) piperidine in DMF for approximately 20 min. The solid phase was rinsed thoroughly with CH_2Cl_2 and DMF between each coupling and deprotection step. Coupling and deprotections steps proceeded until the desired *N*-terminal residue is reached (in most cases, Boc-Asp(OBzl)-OH, 3 equiv).

Cleavage

The peptide was cleaved from the resin with 20% (v/v) hexafluoroisopropanol (HFIP) in CH₂Cl₂ for about 30 min, causing the resin to turn a deep red color. The liquid was collected into a flask, and the resin was rinsed with CH₂Cl₂. This procedure was repeated to ensure complete cleavage. The crude material was purified using Biotage reversed phase chromatography, eluting with a gradient of 30% MeOH in H₂O to 100% MeOH. Purity was confirmed by UPLC/MS, and the peptide was carried forward upon concentration and drying.

C-terminal Methylation

The peptide was dissolved in MeOH (~5 mL, ~0.6 M) and cooled in an ice bath. Dropwise addition of (trimethylsilyl)diazomethane solution (2 M, ~4 equiv) proceeded until the reaction mixture retained a light yellow color. The reaction was monitored by UPLC/MS to ensure complete conversion. The reaction was stirred at ambient temperature for ~5 min, after which excess (trimethylsilyl)diazomethane was quenched with AcOH (drops). The reaction mixture was concentrated under reduced pressure and carried forward to the next step.

N-terminal Benzyl Deprotection

The peptide was placed under an inert atmosphere, to which Pd/C (10 mol%) was added. MeOH (~5 mL, ~0.6 M) was added. The reaction flask was evacuated and refilled with H₂ (3x) and was subsequently allowed to stir under ambient temperature for ~1 h. The reaction mixture was filtered using a syringe filter and MeOH to remove Pd/C and then concentrated under reduced pressure. The purity was checked by UPLC/MS. If needed, the peptide was purified using Biotage reversed phase chromatography, eluting with a gradient of 30% MeOH in H₂O to 100% MeOH.

2. General Procedure B: Solution-Phase Peptide Synthesis

Coupling

Beginning with the desired C-terminal amino acid methyl ester (H-Xaa-OMe, 1 equiv), peptide couplings proceeded in CH₂Cl₂ (1 M) using the appropriate Boc-protected amino acid (Boc-Yaa-OH, 1.2 equiv), HATU (1.2 equiv) and DIPEA (2.4 equiv). The reaction was allowed to stir at ambient temperature for ~30 min to 1 h. The reaction was monitored by UPLC/MS to ensure complete conversion. Upon completion, the reaction was washed using aqueous citric acid (10% w/v, 15 mL), saturated NaHCO₃ solution (15 mL), and brine (15 mL). The aqueous layers were extracted with CH₂Cl₂ (15 mL). The combined organic layers were dried using Na₂SO₄ and concentrated under reduced pressure. Coupling and deprotection steps proceeded in sequence until the desired N-terminal residue is reached (in most cases, Boc-Asp(OBzl)-OH, 1.2 equiv). The peptide underwent benzyl deprotection using Pd/C and H₂ as described in the above procedure to reveal the free acid.

Boc-Deprotection

Boc-protected amino acids were subjected to 4 M HCl/dioxane (~3 mL, ~1 M), stirring at ambient temperature for ~1 h. The reaction was monitored by UPLC/MS to ensure complete conversion. Upon concentration under reduced pressure, CH₂Cl₂ was added to the flask, which was concentrated under reduced pressure again to provide white solids, in most cases. Before carrying forward to the next coupling step, the peptide was dried under high vacuum for ~1 h.

3. Peptide Characterization Data

Boc-Asp-Pro-D-Lys(*Z*)-D-Pro-Tyr(*t*-Bu)-OMe (P1)

P1 was synthesized according to **General Procedure A**, and its spectroscopic data matched that in a previous report.¹

Boc-Asp-Pro-Asn(*trt*)-D-Phe-Pro-Asn(*trt*)-OMe (P2)

P2 was synthesized according to **General Procedure A**, and its spectroscopic data matched that in a previous report.²

Peptides P4-P9, P20, and S1-S5 were synthesized according to **General Procedure A**, and their spectroscopic data matched that in a previous report.³

(S1: Boc-D-Asp-D-Pro-Acpc-Phe-OMe, S2: Boc-D-Asp-Pro-Acpc-Phe-OMe, S3: Boc-Asp-Pro-D-Val-Leu-NHⁱPr, S4: CBz-D-Asp-D-Hyp(Bn)-Val-(*R*)-MBA, S5: Boc-Asp-D-Ser(Bn)-D-Pro-Dap(Boc)-OMe)

Boc-Asp-Acpc-D-Asp(*t*-Bu)-Val-OMe (P10)

P10 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.85 mmol), providing a white solid (371 mg, 73% yield); *R*_f 0.19 (5% MeOH, CH₂Cl₂); [*α*]_D²⁰ +19.5 (*c* 0.50, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.64 (d, *J* = 8.9 Hz, 1H), 7.24 (br s, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 5.70 (d, *J* = 9.6 Hz, 1H), 4.90 (td, *J* = 8.2, 5.7 Hz, 1H), 4.52 (s, 1H), 4.20 (t, *J* = 7.1 Hz, 1H), 3.74 (s, 3H), 3.22 (d, *J* = 17.5 Hz, 1H), 2.86 (dd, *J* = 16.0, 5.7 Hz, 1H), 2.69 (dd, *J* = 17.6, 4.2 Hz, 2H), 2.23 – 2.08 (m, *J* = 6.8 Hz, 1H), 1.77 – 1.64 (m, 1H), 1.53 – 1.48 (m, 1H), 1.46 (s, 9H), 1.42 (s, 9H), 1.11 – 1.03 (m, 2H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 174.8, 173.8, 173.1, 171.31, 171.25, 170.8, 155.6, 81.6, 81.2, 58.7, 52.4, 51.1, 50.3, 37.2, 36.7, 34.8, 30.3, 28.3, 28.0, 19.0, 18.4, 17.9, 16.8; IR (*neat*) 3320, 2977, 1718, 1660, 1523, 1368, 1276, 1251, 1211, 1152, 1045, 1025, 915, 848, 730, 647 cm⁻¹; HRMS (ESI) *m/z* calc'd for C₂₇H₄₅N₄O₁₁ [M+H⁺] 601.3085, found 601.3102.

Boc-Asp-D-Phe-D-Asp(*t*-Bu)-Val-OMe (P11)

P11 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (50 mg, 26% yield); HRMS (ESI) *m/z* calc'd for C₃₂H₄₉N₄O₁₁ [M+H⁺] 665.3398, found 665.3413.

Boc-Asp-D-Val-D-Asp(*t*-Bu)-Val-OMe (P12)

P12 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (97 mg, 55% yield); HRMS (ESI) *m/z* calc'd for C₂₈H₄₉N₄O₁₁ [M+H⁺] 617.3398, found 617.3398.

Boc-Asp-Phe-D-Asp(*t*-Bu)-Val-OMe (P13)

P13 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (122 mg, 64% yield); **HRMS** (ESI) m/z calc'd for C₃₂H₄₉N₄O₁₁ [M+H⁺] 665.3398, found 665.3390.

Boc-Asp-Val-D-Asp(*t*-Bu)-Val-OMe (P14)

P14 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (96 mg, 55% yield); **HRMS** (ESI) m/z calc'd for C₂₈H₄₉N₄O₁₁ [M+H⁺] 617.3398, found 617.3398.

Boc-Asp-Pro-D-Asp(*t*-Bu)-Val-OMe (P15)

P15 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (101 mg, 57% yield) **HRMS** (ESI) m/z calc'd for C₂₈H₄₇N₄O₁₁ [M+H⁺] 615.3242, found 615.3262.

Boc-Asp-Aic-D-Asn(trt)-Val-OMe (P16)

P16 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (87 mg, 35% yield) **HRMS** (ESI) m/z: [M+H⁺] calcd for C₄₈H₅₆N₅O₁₀ 862.4027, found 862.3950.

Boc-Asp-Aic-D-Leu-Val-OMe (P17)

P17 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.29 mmol), providing a white solid (96 mg, 54% yield); **HRMS** (ESI) m/z: [M+H⁺] calcd for C₃₁H₄₇N₄O₉ 619.3343, found 619.3330.

Boc-Asp-Aic-D-Asp(*t*-Bu)-Gly-OMe (P18)

P18 was synthesized according to **General Procedure A** using H-Gly-2-Cl-Trt resin (0.25 mmol), providing a white solid (31 mg, 19% yield); **HRMS** (ESI) m/z calc'd for C₃₀H₄₃N₄O₁₁ [M+H⁺] 635.2928, found 635.2927.

Boc-Asp-Aic-D-Asp(*t*-Bu)-Tyr(*t*-Bu)-OMe (P19)

P19 was synthesized according to **General Procedure A** using H-Val-2-Cl-Trt resin (0.21 mmol), providing a white solid (18 mg, 7% yield); **HRMS** (ESI) m/z calc'd for C₄₁H₅₇N₄O₁₂ [M+H⁺] 797.3973, found 797.3958.

Boc-Asp-Acpc-D-Asp(OMe)-OMe was synthesized using **General Procedure B** starting from Boc-D-Asp(OH)-OMe (100 mg, 0.4 mmol, 1 equiv), which was first methylated using (trimethylsilyl)diazomethane as described in the methylation protocol in **General Procedure A** to provide Boc-D-Asp(OMe)-OMe. Then, Boc-group deprotections and peptide couplings proceeded in sequence with Boc-Acpc-OH, followed by Boc-Asp(OBzl)-OH. Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white solid was obtained (111 mg, 60% yield); **HRMS** (ESI) m/z calc'd for C₁₉H₃₀N₃O₁₀ [M+H⁺] 460.1931, found 460.1927.

Boc-Asp-Acpc-OMe was synthesized using **General Procedure B** starting from Boc-Acpc-OH (100 mg, 0.5 mmol, 1 equiv), which was first methylated using (trimethylsilyl)diazomethane as

described in the methylation protocol in **General Procedure A** to provide Boc-Acpc-OMe. Then, Boc-group deprotection and peptide coupling proceeded with Boc-Asp(OBzl)-OH. Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (42 mg, 25% yield); **HRMS** (ESI) m/z calc'd for $C_{14}H_{23}N_2O_7$ $[M+H^+]$ 331.1505, found 331.1486.

Boc-Asp-Pro-D-Lys(Z)-D-Pro-OMe was synthesized using **General Procedure B** starting H-D-Pro-OMe.HCl. Then, Boc-group deprotections and peptide couplings proceeded in sequence with Boc-D-Lys(Z)-OH, Boc-Pro-OH, and Boc-Asp(OBzl)-OH. Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (203 mg, 29% yield); **HRMS** (ESI) m/z calc'd for $C_{34}H_{50}N_5O_{11}$ $[M+H^+]$ 704.3507, found 704.3506.

Boc-Asp-Pro-D-Lys(Z)-OMe was synthesized using **General Procedure B** starting from H-D-Lys(Z)-OMe.HCl (331 mg, 1 mmol, 1 equiv). Then, Boc-group deprotections and peptide couplings proceeded in sequence with Boc-Pro-OH and Boc-Asp(OBzl)-OH. Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (45 mg, 7% yield); **HRMS** (ESI) m/z calc'd for $C_{29}H_{43}N_4O_{10}$ $[M+H^+]$ 607.2979, found 607.2968.

Boc-Asp-Pro-OMe was synthesized using **General Procedure B** starting from H-Pro-OMe.HCl (166 mg, 1 mmol, 1 equiv). Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (94 mg, 27% yield); **HRMS** (ESI) m/z calc'd for $C_{15}H_{25}N_2O_7$ $[M+H^+]$ 345.1662, found 345.1642.

Boc-Asp-D-Pro-OMe was synthesized using **General Procedure B** starting from H-D-Pro-OMe.HCl (99 mg, 0.6 mmol, 1 equiv). Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (108 mg, 63% yield); **HRMS** (ESI) m/z calc'd for $C_{15}H_{25}N_2O_7$ $[M+H^+]$ 345.1662, found 345.1661.

Boc-D-Asp-Pro-OMe was synthesized using **General Procedure B** starting from H-Pro-OMe.HCl (99 mg, 0.6 mmol, 1 equiv). Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (88 mg, 51% yield); **HRMS** (ESI) m/z calc'd for $C_{15}H_{25}N_2O_7$ $[M+H^+]$ 345.1662, found 345.1656.

Boc-D-Asp-D-Pro-OMe was synthesized using **General Procedure B** starting from H-D-Pro-OMe.HCl (99 mg, 0.6 mmol, 1 equiv). Benzyl deprotection was performed as outlined in **General Procedure A**. Upon reversed-phase column purification, a white semi-solid was obtained (75 mg, 44% yield); **HRMS** (ESI) m/z calc'd for $C_{15}H_{25}N_2O_7$ $[M+H^+]$ 345.1662, found 345.1660.

III. Peptide Screening Conditions and Results

General Procedure C: Small Scale Peptide Screening

Several reactions were performed simultaneously. The appropriate peptides (50 mol%) were added to individual 1 dram vials equipped with stir bars. Standard solutions of i) geldanamycin (2.8 mg or 5 μ mol per reaction, 1 equiv), including benzyl benzoate (1.5 μ L per reaction) as an internal standard, and ii) DMAP (0.3 mg or 2.5 μ mol per reaction, 50 mol%) were prepared in CHCl_3 , so that the final volume totaled 0.5 mL CHCl_3 (10 mM) per reaction. The appropriate amount of each standard solution was added to the reaction vials, to which were added H_2O_2 (30% aq, 2.5 μ L, 25 μ mol, 5 equiv), followed by DIC (3.9 μ L, 25 μ mol, 5 equiv). The reactions were stirred vigorously at ambient temperature for 24 h, after which they were filtered through a short plug of SiO_2 and Na_2SO_4 with 10% MeOH/ CH_2Cl_2 and concentrated under reduced pressure. The reactions were prepared for analysis by UPLC/MS.

General Procedure D: Reactions with *m*-CPBA

A standard solution of geldanamycin (2.8 mg or 5 μ mol per reaction, 1 equiv), including benzyl benzoate (1.5 μ L per reaction) as an internal standard, in CH_2Cl_2 was prepared so that the final reaction volume totaled 0.5 mL CH_2Cl_2 (10 mM). To this solution in a vial equipped with stir bar was added *m*-CPBA (2 equiv). The reactions were stirred at ambient temperature for 24 h, after which they were filtered through a short plug of SiO_2 and Na_2SO_4 with 10% MeOH/ CH_2Cl_2 and concentrated under reduced pressure. The reactions were prepared for analysis by UPLC/MS.

Table S1. Results from Peptide Screening (Figures 1 and 2)^a

Entry	Peptide	% A ^{b,c}	% B ^{b,c}	% C ^{b,c}	% D ^{b,c}	% Yield ^d
1.2	Boc-Asp-OMe	7.0	14.3	7.3	0	28.6
1.3	P4	11.3	6.7	6.2	0	24.2
1.4	P5	10.8	11.7	19.0	2.5	43.9
1.5	P6	5.4	9.4	3.6	0.0	18.4
1.6	P7	6.1	8.4	4.4	6.9	25.8
1.7	P2	1.4	2.5	3.9	0.5	8.5
1.8	P8	59.1	22.2	4.8	1.0	87.1
1.9	P9	45.5	19.3	2.8	0.3	67.9
1.10	P1	0.3	0.6	26.6	7.5	35.0
2.1	P10	19.0	6.1	4.2	1.6	30.9
2.2	P11	25.3	11.2	3.1	4.5	44.1
2.3	P12	29.8	12.3	5.6	2.9	50.7
2.4	P13	23.4	10.5	6.3	4.7	45.0
2.5	P14	13.3	10.5	7.7	0.6	32.0
2.6	P15	6.7	6.8	5.7	0	19.2
2.7	P16	12.0	17.4	3.3	1.5	34.2
2.8	P17	14.2	6.3	4.9	4.9	30.3
2.9	P18	31.5	24.1	3.9	1.9	61.4
2.10	P19	41.3	18.6	4.2	3.6	67.7
2.11	P20	24.1	13.9	20.4	2.4	60.9
	S1	8.7	5.5	5.6	0	19.8
	S2	11.4	17.5	12.5	1.2	42.6
	S3	5.9	8.0	7.8	6.0	27.8
	S4	8.2	8.3	7.6	0.7	24.7
	S5	26.3	15.8	1.9	0.1	44.1

^aAll data is an average of at least two trials using **General Procedure C**. ^bDetermined using UPLC with an internal standard and calibration curve. ^cProduct distributions shown in main text are adjusted to total 100%. For example % A = A/(A+B+C+D) x 100. ^dSummed yields of A+B+C+D.

Table S2. Results from Peptide Truncations and Diastereomers (Figure 3)^a

Entry	Peptide	% A ^{b,c}	% B ^{b,c}	% C ^{b,c}	% D ^{b,c}	% Yield ^d
3.1	Boc-Asp-Acpc-D-Asp(OMe)-OMe	18.8	9.9	5.0	0.2	33.9
3.2	Boc-Asp-Acpc-OMe	9.7	11.7	6.9	0.6	29.0
3.3	Boc-Asp-Pro-D-Lys(Z)-D-Pro-OMe	0.6	0.7	4.8	0.4	6.4
3.4	Boc-Asp-Pro-D-Lys(Z)-OMe	0.9	1.1	4.6	0.3	7.0
3.5	Boc-Asp-Pro-OMe	0.3	1.5	36.0	14.3	52.0
3.6	Boc-Asp-D-Pro-OMe	6.7	14.2	7.7	0.3	28.8
3.7	Boc-D-Asp-Pro-OMe	7.3	14.5	5.9	0.3	28.1
3.8	Boc-D-Asp-D-Pro-OMe	9.7	14.7	6.0	0.3	30.6

^aAll data is an average of at least two trials using **General Procedure C**. ^bDetermined using UPLC with an internal standard and calibration curve. ^cProduct distributions shown in main text are adjusted to total 100%. For example, % A = A/(A+B+C+D) x 100. ^dSummed yields of A+B+C+D.

IV. Large Scale Reaction Conditions

Geldanamycin (14 mg, 25 μ mol, 1.0 equiv), Boc-Asp-Acpc- D Asp(*t*-Bu)-Val-OMe (3.8 mg, 6.3 μ mol, 25 mol%), and DMAP (0.80 mg, 6.3 μ mol, 25 mol%) are added to a 10 mL round bottom flask, equipped with a stir bar. Chloroform (2.5 mL) is added to the flask, followed by H₂O₂ (30% aq. soln, 25 μ L, 250 μ mol, 10 equiv) and DIC (39 μ L, 250 μ mol, 10 equiv). The reaction is stirred vigorously for 24 h at ambient temperature. The reaction is filtered through a short plug of Na₂SO₄ and silica using MeOH/CH₂Cl₂ (10% v/v). An internal standard is added (benzyl benzoate), and the reaction is analyzed using UPLC. The reaction mixture is purified using reversed phase preparatory HPLC, followed by extraction with CH₂Cl₂, to provide **A** as a yellow solid (5.6 mg, 38% yield): *R*_f 0.46 (10% MeOH in CH₂Cl₂); [α]_D²⁰ +125.6 (c 0.20, 10% MeOH/CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.84 (s, 1H), 7.22 (s, 1H), 6.94 (s, 1H), 6.53 (t, *J* = 11.4 Hz, 1H), 5.89 – 5.75 (m, 1H), 4.95 (s, 1H), 4.77 (br s, 2H), 4.53 (s, 1H), 4.12 (s, 3H), 3.81 (dd, *J* = 7.5, 2.2 Hz, 1H), 3.45 – 3.40 (m, 1H), 3.40 (s, 3H), 3.33 (s, 3H), 2.96 (br s, 1H), 2.51 – 2.37 (m, 2H), 2.01 (s, 3H), 1.90 – 1.81 (m, 1H), 1.79 – 1.72 (m, 1H), 1.70 – 1.64 (m, 3H), 1.42 (s, 3H), 1.30 – 1.22 (m, 2H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (126 MHz, 10% MeOD-*d*₄/CDCl₃) δ 184.3, 184.2, 169.0, 157.1, 156.8, 138.2, 135.3, 128.0, 127.6, 126.1, 111.2, 111.2, 81.2, 76.5, 70.8, 62.8, 61.8, 61.5, 57.1, 56.9, 34.0, 32.8, 31.7, 29.6, 29.2, 22.2, 14.4, 12.2, 10.3; IR (neat) 3435, 2924, 2853, 1739, 1708, 1697, 1653, 1612, 1514, 1458, 1378, 1359, 1201, 1107, 1064, 1043 cm⁻¹; HRMS (ESI) *m/z* calc'd for C₂₉H₄₁N₂O₁₀ [M+H⁺] 577.2761, found 577.2785.

In the same reaction as above, **B** was isolated as a yellow semisolid (1.4 mg, 10% yield): *R*_f 0.25 (5% MeOH in CH₂Cl₂); [α]_D²⁰ +33.3 (c 0.04, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.70 (s, 1H), 7.23 (s, 1H), 6.97 (d, *J* = 11.4 Hz, 1H), 6.49 (t, *J* = 11.3 Hz, 1H), 5.85 (t, *J* = 10.0 Hz, 1H), 4.86 (br s, 2H), 4.65 (d, *J* = 8.9 Hz, 1H), 4.14 – 4.09 (m, 1H), 4.09 (s, 3H), 4.01 – 3.95 (m, 1H), 3.72 – 3.64 (m, 1H), 3.37 (s, 3H), 3.33 (s, 3H), 3.06 (d, *J* = 8.8 Hz, 1H), 2.62 (d, *J* = 12.5 Hz, 1H), 2.38 – 2.23 (m, 1H), 2.00 (s, 3H), 1.72 – 1.47 (m, 6H), 1.39 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 184.3, 184.1, 168.7, 163.1, 156.7, 156.1, 138.5, 136.7, 135.2, 128.5, 127.5, 126.2, 116.4, 111.5, 81.7, 81.3, 75.8, 72.6, 61.5, 60.4, 57.1, 56.2, 36.5, 34.7, 29.7, 22.1, 12.5, 12.3, 11.3; IR (neat) 2953, 2925, 2854, 2181, 2160, 2154, 2044, 2027, 1723, 1652, 1605, 1501, 1376, 1193, 1135, 1072 cm⁻¹; HRMS (ESI) *m/z* calc'd for C₂₉H₄₁N₂O₁₀ [M+H⁺] 577.2761, found 577.2740.

Geldanamycin (14 mg, 25 μ mol, 1.0 equiv), Boc-Asp-Pro- D Lys(Z)- D Pro-Tyr(*t*-Bu)-OMe (3.8 mg, 6.3 μ mol, 25 mol%), and DMAP (3.2 mg, 25 μ mol, 1 equiv) are added to a 10 mL round bottom flask, equipped with a stir bar. Chloroform (2.5 mL) is added to the flask, followed by H₂O₂ (30% aq. soln, 50 μ L, 5 mmol, 20 equiv) and DIC (78 μ L, 5 mmol, 20 equiv). The reaction is stirred vigorously for 24 h at ambient temperature. The reaction is filtered through a short plug of Na₂SO₄ and silica using MeOH/CH₂Cl₂ (10% v/v). An internal standard is added (benzyl benzoate), and the reaction is analyzed using UPLC. The reaction mixture is purified using reversed phase preparatory HPLC, followed by extraction with CH₂Cl₂, to provide **C** as an off-white solid (4.7 mg,

33% yield): **R_f** 0.45 (10% MeOH in CH₂Cl₂); [α]_D²⁰ +143.3 (c 0.24, 10% MeOH/CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.42 (s, 1H), 7.51 (s, 1H), 6.91 (d, *J* = 10.5 Hz, 1H), 6.54 (t, *J* = 11.8 Hz, 1H), 5.89 (t, *J* = 10.2 Hz, 1H), 5.69 (d, *J* = 9.5 Hz, 1H), 5.24 (s, 1H), 4.73 (br s, 2H), 4.33 (d, *J* = 8.6 Hz, 1H), 3.78 (s, 3H), 3.52 (dd, *J* = 8.1, 3.6 Hz, 1H), 3.41 – 3.38 (m, 1H), 3.37 (s, 3H), 3.32 (s, 3H), 2.76 (tt, *J* = 10.1, 6.8 Hz, 1H), 2.37 (dd, *J* = 14.0, 4.3 Hz, 1H), 2.01 (s, 3H), 1.96 – 1.88 (m, 1H), 1.84 – 1.74 (m, 4H), 1.77 (s, 3H), 1.00 (t, *J* = 6.4 Hz, 6H); ¹³C NMR (126 MHz, 10% MeOD-d₄/CDCl₃) δ 190.5, 189.2, 168.9, 156.8, 139.6, 136.7, 134.4, 132.8, 132.1, 128.2, 126.2, 114.1, 84.1, 81.4, 80.9, 80.7, 73.2, 67.3, 57.4, 57.2, 56.7, 34.8, 33.2, 32.8, 25.7, 23.0, 13.3, 13.2, 12.4; **IR** (neat) 3436, 2925, 2854, 1735, 1684, 1616, 1514, 1379, 1349, 1328, 1132, 1109, 1049 cm⁻¹; **HRMS** (ESI) *m/z* calc'd for C₂₉H₄₁N₂O₁₀ [M+H⁺] 577.2761, found 577.2736.

In the same reaction as above, **D** was isolated as an off-white solid (2.0 mg, 14% yield): **R_f** 0.56 (10% MeOH in CH₂Cl₂); [α]_D²⁰ + 13.9 (c 0.18, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.41 (s, 1H), 7.43 (s, 1H), 6.86 (d, *J* = 11.7 Hz, 1H), 6.52 (t, *J* = 11.3 Hz, 1H), 5.95 (t, *J* = 9.0 Hz, 1H), 5.54 (d, *J* = 9.8 Hz, 1H), 5.01 (s, 1H), 4.87 (s, 2H), 4.30 (d, *J* = 8.1 Hz, 1H), 3.78 (s, 3H), 3.39 (s, 3H), 3.34 (s, 3H), 3.31 (d, *J* = 10.3 Hz, 1H), 3.24 (d, *J* = 9.1 Hz, 1H), 2.90 – 2.76 (m, 1H), 2.24 – 2.10 (m, 2H), 2.00 (s, 3H), 1.90 – 1.82 (m, 1H), 1.77 (s, 3H), 1.71 – 1.62 (m, 2H), 1.36 – 1.28 (m, 1H), 1.10 (d, *J* = 6.1 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 190.4, 188.7, 168.2, 156.0, 139.3, 138.4, 134.5, 134.0, 131.9, 127.8, 125.8, 113.8, 84.5, 82.6, 82.5, 80.5, 73.0, 67.1, 57.9, 57.2, 56.8, 33.0, 31.9, 31.7, 29.7, 24.3, 12.6, 12.4, 12.0; **IR** (neat); 3454, 2926, 2855, 1717, 1682, 1502, 1456, 1376, 1325, 1198, 1129, 1097, 1058 cm⁻¹; **HRMS** (ESI) *m/z* calc'd for C₂₉H₄₁N₂O₁₀ [M+H⁺] 577.2761, found 577.2770.

17-AAG (14.6 mg, 25 μ mol, 1.0 equiv), Boc-Asp-Acp-^DAsp(*t*-Bu)-Val-OMe (3.8 mg, 6.3 μ mol, 25 mol%), and DMAP (0.80 mg, 6.3 μ mol, 25 mol%) are added to a 10 mL round bottom flask, equipped with a stir bar. Chloroform (2.5 mL) is added to the flask, followed by H₂O₂ (30% aq. soln, 25 μ L, 250 μ mol, 10 equiv) and DIC (39 μ L, 250 μ mol, 10 equiv). The reaction is stirred vigorously for 24 h at ambient temperature. The reaction is filtered through a short plug of Na₂SO₄ and silica using MeOH/CH₂Cl₂ (10% v/v). An internal standard is added (benzyl benzoate), and the reaction is analyzed using UPLC. The reaction mixture is purified using reversed phase preparatory HPLC, followed by extraction with CH₂Cl₂, to provide **17-A** as a purple solid (4.9 mg, 32% yield): **R_f** 0.43 (5% MeOH/CH₂Cl₂); [α]_D²⁰ -73.2 (c 0.06, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.32 (s, 1H), 7.23 (s, 1H), 6.98 (br d, *J* = 11.3 Hz, 1H), 6.58 (t, *J* = 11.4 Hz, 1H), 6.43 (t, *J* = 6.0 Hz, 1H), 5.92 (ddt, *J* = 16.0, 10.5, 5.3 Hz, 1H), 5.80 (t, *J* = 9.9 Hz, 1H), 5.37 – 5.21 (m, 2H), 5.16 – 4.79 (br s, 2H), 4.74 (s, 1H), 4.49 (br d, *J* = 9.8 Hz, 1H), 4.15 (t, *J* = 5.9 Hz, 2H), 3.76 (dd, *J* = 7.8, 2.6 Hz, 1H), 3.45 (dt, *J* = 7.5, 3.7 Hz, 1H), 3.34 (s, 3H), 3.33 (s, 3H), 3.07 (s, 1H), 2.66 (d, *J* = 13.9 Hz, 1H), 2.33 (dd, *J* = 14.0, 10.2 Hz, 1H), 2.02 (s, 3H), 1.90 – 1.76 (m, 3H), 1.70 (t, *J* = 4.4 Hz, 2H), 1.45 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (126 MHz, 10% MeOD-d₄/CDCl₃) 183.9, 180.4, 168.8, 156.8, 145.0, 141.2, 134.3, 132.6, 127.8,

126.5, 118.1, 108.1, 108.1, 81.7, 75.9, 71.1, 63.6, 62.2, 56.7, 56.7, 47.5, 34.5, 33.3, 32.9, 29.5, 28.1, 27.7, 22.2, 14.2, 12.1, 10.4; **IR** (neat) 3425, 3362, 2918, 2850, 1737, 1707, 1694, 1587, 1500, 1377, 1106, 1063, 1041 cm^{-1} ; **HRMS** (ESI) m/z calc'd for $\text{C}_{31}\text{H}_{44}\text{N}_3\text{O}_9$ $[\text{M}+\text{H}^+]$ 602.3077, found 602.3073.

In the same reaction as above, **17-B** was isolated as a purple solid (0.5 mg, 3% yield): **HRMS** (ESI) m/z calc'd for $\text{C}_{31}\text{H}_{44}\text{N}_3\text{O}_9$ $[\text{M}+\text{H}^+]$ 602.3077, found 602.3087.

V. Liquid Chromatography Chromatograms

UPLC chromatograms

UPLC method: Gradient 10% MeCN (0.1% formic acid) in H_2O (0.1% formic acid) to 98% MeCN (0.1% formic acid) in H_2O (0.1% formic acid) over 4 min at 0.8 mL/min.

Column: CORTECS C18 (1.6 μm particle size, 3.0 x 50 mm)

All UPLC data was processed with MestReNova x64 using PDA total absorbance chromatograms and the default settings for "trace baseline correction". Manual integration intervention was applied when necessary.

Crude reaction mixture using **P10**:

Purified **A***:

Purified **B**:

*Small amount of **B** remains upon column purification of **A**. Compound **A** can be further purified through crystallization. Via vapor diffusion, **A** was dissolved in a minimal amount of 10% MeOH in CH_2Cl_2 in a 1 dram vial, and pentane was used as the anti-solvent in a 20 mL scintillation vial. The crystallization chamber was placed in a refrigerator at 4 °C. Yellow needles form within several days. The crystal structure of **A** was obtained from a crystal formed using this procedure (see X-ray section below).

Crude reaction mixture using **P1**:

Purified **C**:

Purified **D**:

Crude reaction mixture using **17-AAG** & **P10**:

Purified major (**17-A**):

Purified minor (**17-B**):

Crude reaction mixture using **17-AAG** and **m-CPBA** (30% conversion):

Crude reaction mixture using **17-AAG** and **P1** (10% conversion):

Preparatory HPLC Purification Conditions

Method: Gradient using MeCN (0.1% formic acid) in H₂O (0.1% formic acid) over 35 min at 15 mL/min (see table below for gradients).

Time (min)	% MeCN in H ₂ O
0-4	0-10
4-10	10-30
10-25	30-55
25-35	55-95

Column: SymmetryPrep C8 (7 µm particle size, 19 x 300 mm)

Example Chromatograms from Prep HPLC

Structural Assignment of Product B – Comparison to Geldanamycin and Product A

Product **B** has three alkenyl protons, which correlate to one another in a similar pattern as in **A** (see COSY spectra below). Thus, **B** was concluded to be an 8,9-epoxide yet opposite diastereomer to **A**.

COSY – A

COSY – B

VI. Model Quinone Synthesis and Reactions

2-methoxy-1,4-benzoquinone was synthesized according to a reported procedure, and the spectra matched that of the previously reported.⁴

2-(N-benzamide)-1,4-benzoquinone was synthesized according to a reported procedure, and the spectra matched that of the previously reported.⁵

2-(N-benzamide)-5-methoxy-1,4-benzoquinone was synthesized according to a reported procedure.⁵

Using **General Procedure C** with **P1** resulted in decomposition of each of the quinones. Using **General Procedure D** (*m*-CPBA) resulted in no reaction of the quinones. **General Procedure E** (see below, with the respective quinone in place of geldanamycin) resulted in decomposition of each of the quinones.

General Procedure E: Nucleophilic Epoxidation Reactions

A standard solution of geldanamycin (2.8 mg or 5 μ mol per reaction, 1 equiv), including benzyl benzoate (1.5 μ L per reaction) as an internal standard, in CH_2Cl_2 was prepared so that the final reaction volume totaled 0.5 mL CH_2Cl_2 (10 mM). To this solution in a 1 dram vial equipped with stir bar was added *t*-BuOOH (5 M in decane, 1 μ L, 1 equiv), followed by DBU (0.5 equiv, delivered from a standard solution in CH_2Cl_2). The reactions were stirred at ambient temperature for 24 h, after which they were filtered through a short plug of SiO_2 and Na_2SO_4 with 10% MeOH/ CH_2Cl_2 and concentrated under reduced pressure. The reactions were prepared for analysis by UPLC/MS.

Using the above procedure, 77% conversion of geldanamycin afforded 61% **C** and 3% **D**. Compounds **A** and **B** were not observed. An additional product that is likely from hydrolysis of the 17-OMe group (*m/z* matches loss of OMe, plus OH) was also observed in 12%.

VII. Biological Testing

Fluorescence Polarization

Assay was performed in 96-well format in black, flat-bottom plates (Santa Cruz Biotechnology) with a final volume of 100 μ L. Twenty-five microliters of assay buffer (20 mM HEPES, pH 7.3, 50 mM KCl, 5 mM $MgCl_2$, 20 mM Na_2MoO_4 , 2 mM DTT, 0.1 mg/mL BGG, and 0.01% NP-40) containing 6 nM FITC-GDA (fluorescent tracer, stock in DMSO and diluted in assay buffer) and 50 μ L of assay buffer containing 10 nM of either Grp94, Hsp90 α , or Hsp90 β were added to each well. Compounds were tested in triplicate wells (1% DMSO final concentration). For each plate, wells containing buffer only (background), tracer in buffer only (low polarization control), and protein and tracer in buffer with 1% DMSO (high polarization control) were included. Plates were incubated at 4 °C with rocking for 24 h. Polarization values (in mP units) were measured at 37 °C with an excitation filter at 485 nm and an emission filter at 528 nm. Polarization values were correlated to % tracer bound and compound concentrations. The concentration at which the tracer was 50% displaced by the inhibitor was determined using Graphpad Prism.

Anti-proliferative assay for MCF-7 and SkBr3 cells

Cells were grown to confluence and seeded at 2000 cells/well/0.1 mL in a 96-well plate and placed back in the incubator for 24 h. Compounds or vehicle were administered at the desired concentrations (1% DMSO final concentration) and incubated for 72 h. The percentage of viable cells was determined using the MTS/PMS cell proliferation kit (Promega) per the manufacturer's instructions. Cells treated with vehicle were normalized to 100% proliferation and values adjusted accordingly.

Western blot for SkBr-3 cells

SkBr-3 cells were seeded into 10 cm dishes and grown to 70% confluence. Compound (administered as a solution in DMSO) or vehicle was diluted into 5 mL fresh media (assay concentration of 1% DMSO) and added to the dishes, which were returned to the incubator for 24 h. Cells were harvested in cold PBS and lysed using MPER (Thermo Scientific) supplemented with protease and phosphatase inhibitors (Roche) per manufacturer's directions. Lysates were clarified at 14 000 g for 15 m at 4 °C. Protein concentrations were determined using the Pierce BCA protein assay kit per the manufacturer's instructions. Equal amounts of protein (10 μ g) were electrophoresed under reducing conditions (10% tris-glycine gels), transferred to PVDF (Millipore ImmobilonP), and immunoblotted with the corresponding primary antibody. Membranes were incubated with an appropriate horseradish peroxidase-labeled secondary antibody, developed with a chemiluminescent substrate (Bio-Rad Clarity), and visualized with autoradiography film (Midsco).

VIII. NMR Spectra

IX. X-Ray Crystallography Data

Low-temperature diffraction data (ω -scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Saturn994+ CCD detector with Cu K α (λ = 1.54178 Å) for the structures **A**, **C**, **D**, and **17-A**. All diffraction images were processed and scaled using Rigaku Oxford Diffraction software.⁶ The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL.⁷ All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. Unless stated otherwise, the isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups).

The full numbering scheme of all compounds can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC numbers: 1964613 (Compound **A**), 1964602 (Compound **C**), 1964609 (Compound **D**), and 1964610 (Compound **17-A**). These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Table S3. Details of Crystal Structures

Compound	A	C	D	17-A
Data Code	007b-19042	007a-19010	007b-19137	007b-19118
CCDC Number	1964613	1964602	1964609	1960610
Empirical Formula	C ₂₉ H ₄₀ N ₂ O ₁₀	C ₂₉ H ₄₀ N ₂ O ₁₀	C ₂₉ H ₄₀ N ₂ O ₁₀	C ₃₁ H ₄₃ N ₃ O ₉
Temperature (K)	93(2)	93(2)	93(2)	93(2)
Wavelength (Å)	1.54184	1.54184	1.54184	1.54184
Crystal System	Monoclinic	Monoclinic	Orthorhombic	Monoclinic
Space Group	<i>P</i> 2 ₁	<i>P</i> 2 ₁	<i>P</i> 2 ₁ 2 ₁ 2 ₁	<i>P</i> 2 ₁
<i>a</i> (Å)	16.1463(3)	12.5726(4)	8.1886(2)	15.2434(7)
<i>b</i> (Å)	7.84730(10)	7.5849(2)	18.7570(3)	7.8592(2)
<i>c</i> (Å)	30.1019(5)	16.0036(4)	20.4466(4)	15.5165(9)
α (°)	90	90	90	90
β (°)	103.866(2)	99.298(3)	90	105.045(5)
γ (°)	90	90	90	90
<i>V</i> (Å ³)	3702.91(11)	1506.08(7)	3140.47	1795.17(15)
<i>Z</i>	4	2	4	2
Density (g/cm ³)	1.034	1.272	1.220	1.113
Absorption coefficient (mm ⁻¹)	0.650	0.799	0.767	0.676
Completeness	99.9%	99.9%	99.5%	99.5%
Data / restraints / parameters	12841 / 83 / 833	5277 / 1 / 378	5520 / 0 / 393	5277 / 1 / 378
<i>R</i> 1, <i>wR</i> 2 (<i>I</i> > 2 σ (<i>I</i>))	0.0372, 0.1054	0.0596, 0.1511	0.0365, 0.0941	0.0910, 0.2251
<i>R</i> 1, <i>wR</i> 2 (all data)	0.0383, 0.1064	0.0651, 0.1558	0.0410, 0.0968	0.1318, 0.2609
GOF	1.056	1.064	1.037	1.048
Absolute structure parameter	1.25(6)	0.05(10)	-0.03(6)	-0.5(3)
Largest Diff. Peak, Hole (e/Å ³)	0.228, -0.159	0.321, -0.260	0.168, -0.196	0.886, -0.314

Refinement details for **A**:

The quinone and methoxy groups in both models are disordered over two positions. The site occupancies were freely refined for both models. All chemically similar bonds were restrained to have similar distances. The quinone groups were restrained to behave as rigid bodies. C14 and C14B are very close in proximity and required the minor occupancy atom, C14B, be constrained to the same atomic displacement parameter as the major, C14. The program SQUEEZE⁸ was used to compensate for the contribution of disordered solvents contained in voids within the crystal lattice from the diffraction intensities. This procedure was applied to the data file and the submitted model is based on the solvent removed data. Based on the total electron density found in the voids (305 e/Å³), it is likely that ~2 dichloromethane molecules are present in the unit cell. See "_platon_squeeze_details" in the .cif for more information.

Figure S1. The complete numbering scheme of **A** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S4. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **A**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	10060(1)	4525(2)	7219(1)	36(1)
O(2)	10906(1)	2328(2)	6103(1)	33(1)
O(3)	12915(1)	2450(3)	6963(1)	42(1)
O(4)	10765(1)	-1894(3)	5830(1)	37(1)
O(5)	12857(8)	-390(17)	5070(5)	43(2)
O(5B)	12791(8)	-880(20)	4967(5)	50(2)
O(6)	11508(4)	662(17)	4360(3)	54(2)
O(6B)	11425(5)	-210(20)	4235(3)	59(3)
O(7)	8562(1)	-415(3)	4499(1)	37(1)
O(8)	9007(1)	-628(2)	6876(1)	34(1)
O(9)	8507(1)	2138(2)	7281(1)	34(1)
O(10)	8017(1)	4859(3)	7207(1)	44(1)
N(1)	7931(2)	3207(3)	7815(1)	43(1)
N(2)	9476(1)	-948(3)	5187(1)	33(1)
C(1)	9883(2)	2729(3)	7126(1)	30(1)
C(2)	10312(2)	3739(3)	6834(1)	29(1)
C(3)	11254(2)	3744(3)	6855(1)	33(1)
C(4)	11482(2)	2353(3)	6547(1)	30(1)
C(5)	12407(2)	2521(3)	6506(1)	34(1)
C(6)	12668(2)	1230(4)	6183(1)	36(1)
C(7)	12596(2)	-660(4)	6295(1)	36(1)
C(8)	12537(2)	-1775(4)	5860(1)	38(1)
C(9)	11854(2)	-1268(3)	5449(1)	35(1)
C(10)	10968(2)	-1379(3)	5484(1)	32(1)
C(11)	10259(2)	-851(3)	5080(1)	31(1)
C(12)	10431(2)	-363(4)	4684(1)	36(1)
C(13)	11328(7)	-70(20)	4680(4)	39(3)
C(13B)	11297(7)	-480(20)	4613(4)	39(3)
C(14)	12037(9)	-530(20)	5077(4)	29(2)
C(14B)	11993(9)	-950(20)	5023(4)	29(2)
C(15)	8685(2)	-580(3)	4914(1)	31(1)

C(16)	7988(2)	-372(3)	5158(1)	32(1)
C(17)	8188(2)	148(4)	5593(1)	34(1)
C(18)	7610(2)	421(4)	5889(1)	38(1)
C(19)	7873(2)	758(4)	6338(1)	36(1)
C(20)	8780(2)	867(3)	6605(1)	30(1)
C(21)	8945(2)	2412(3)	6921(1)	29(1)
C(22)	10347(2)	1537(4)	7489(1)	40(1)
C(23)	11498(2)	5550(4)	6744(1)	39(1)
C(24)	13741(2)	3148(5)	7018(1)	54(1)
C(25)	13355(2)	-1278(4)	6669(1)	49(1)
C(26)	13113(3)	-279(9)	4632(2)	99(2)
C(27)	7106(2)	-695(5)	4873(1)	46(1)
C(28)	9150(2)	-2090(4)	6618(1)	45(1)
C(29)	8138(2)	3532(3)	7424(1)	35(1)
O(11)	16086(1)	-376(2)	7942(1)	41(1)
O(12)	14670(1)	-2229(3)	8861(1)	36(1)
O(13)	12977(1)	-1993(3)	7822(1)	42(1)
O(13B)	12059(6)	-5798(12)	9622(4)	35(2)
O(14)	12118(4)	-5109(16)	9518(3)	63(2)
O(14B)	13058(8)	-5053(11)	10472(4)	39(2)
O(15)	13108(5)	-4390(20)	10400(3)	92(4)
O(16)	14652(1)	-6504(3)	9151(1)	36(1)
O(17)	16218(1)	-4988(2)	10667(1)	35(1)
O(18)	16981(1)	-5526(2)	8454(1)	36(1)
O(19)	17631(1)	-2855(2)	8119(1)	37(1)
O(20)	18133(1)	-136(3)	8213(1)	44(1)
N(3)	18293(2)	-1809(3)	7617(1)	45(1)
N(4)	15624(1)	-5557(3)	9918(1)	34(1)
C(30)	16166(2)	-2160(3)	8087(1)	35(1)
C(31)	15626(2)	-964(3)	8272(1)	34(1)
C(32)	14666(2)	-855(4)	8128(1)	37(1)
C(33)	14270(2)	-2204(3)	8381(1)	33(1)
C(34)	13302(2)	-1992(4)	8310(1)	34(1)
C(35)	12893(2)	-3307(3)	8564(1)	35(1)
C(36)	13048(2)	-5185(3)	8470(1)	35(1)
C(37)	12848(2)	-6351(4)	8842(1)	38(1)

C(38)	13327(2)	-5917(3)	9322(1)	35(1)
C(39)	14257(2)	-6018(3)	9431(1)	30(1)
C(40)	14763(2)	-5503(3)	9897(1)	29(1)
C(41)	14373(2)	-5051(3)	10226(1)	34(1)
C(42)	13464(7)	-4890(20)	10107(4)	54(5)
C(42B)	13422(8)	-5210(30)	10152(5)	29(3)
C(43)	12959(7)	-5269(19)	9638(4)	39(3)
C(43B)	12925(10)	-5690(30)	9678(5)	26(3)
C(44)	16301(2)	-5153(3)	10276(1)	30(1)
C(45)	17138(2)	-4929(3)	10158(1)	34(1)
C(46)	17153(2)	-4508(3)	9727(1)	34(1)
C(47)	17894(2)	-4250(4)	9541(1)	37(1)
C(48)	17847(2)	-4023(4)	9094(1)	37(1)
C(49)	17050(2)	-4007(3)	8717(1)	31(1)
C(50)	17027(2)	-2498(3)	8395(1)	33(1)
C(51)	15806(2)	-3419(4)	7715(1)	47(1)
C(52)	14405(2)	979(4)	8203(1)	44(1)
C(53)	12162(2)	-1234(4)	7682(1)	49(1)
C(54)	12501(2)	-5751(4)	8001(1)	44(1)
C(55)	11608(4)	-4883(16)	9844(4)	75(3)
C(55B)	11561(8)	-4262(18)	9611(8)	71(5)
C(56)	17908(2)	-5120(5)	10549(1)	50(1)
C(57)	16768(2)	-6995(4)	8684(1)	44(1)
C(58)	18030(2)	-1451(3)	7992(1)	36(1)

Table S5. Bond lengths [Å] and angles [°] for **A**.

O(1)-C(1)	1.452(3)
O(1)-C(2)	1.454(3)
O(2)-C(4)	1.433(3)
O(2)-H(2)	0.8400
O(3)-C(24)	1.413(4)
O(3)-C(5)	1.425(3)
O(4)-C(10)	1.232(3)

O(5)-C(14)	1.335(12)
O(5)-C(26)	1.475(15)
O(5B)-C(26)	1.327(16)
O(5B)-C(14B)	1.340(12)
O(6)-C(13)	1.214(12)
O(6B)-C(13B)	1.225(11)
O(7)-C(15)	1.222(3)
O(8)-C(20)	1.425(3)
O(8)-C(28)	1.434(3)
O(9)-C(29)	1.364(3)
O(9)-C(21)	1.444(3)
O(10)-C(29)	1.220(3)
N(1)-C(29)	1.323(3)
N(1)-H(1A)	0.8800
N(1)-H(1B)	0.8800
N(2)-C(15)	1.373(3)
N(2)-C(11)	1.379(3)
N(2)-H(2A)	0.8800
C(1)-C(2)	1.474(3)
C(1)-C(22)	1.496(4)
C(1)-C(21)	1.511(4)
C(2)-C(3)	1.506(4)
C(2)-H(2B)	1.0000
C(3)-C(23)	1.529(4)
C(3)-C(4)	1.533(4)
C(3)-H(3)	1.0000
C(4)-C(5)	1.532(3)
C(4)-H(4A)	1.0000
C(5)-C(6)	1.532(4)
C(5)-H(5)	1.0000
C(6)-C(7)	1.531(4)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(25)	1.530(4)
C(7)-C(8)	1.559(4)
C(7)-H(7)	1.0000

C(8)-C(9)	1.500(4)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(14)	1.352(12)
C(9)-C(14B)	1.376(11)
C(9)-C(10)	1.461(3)
C(10)-C(11)	1.515(3)
C(11)-C(12)	1.343(3)
C(12)-C(13B)	1.467(11)
C(12)-C(13)	1.470(12)
C(12)-H(12B)	0.9500
C(12)-H(12A)	0.9500
C(13)-C(14)	1.490(17)
C(13B)-C(14B)	1.503(16)
C(15)-C(16)	1.494(3)
C(16)-C(17)	1.337(4)
C(16)-C(27)	1.496(4)
C(17)-C(18)	1.450(3)
C(17)-H(17)	0.9500
C(18)-C(19)	1.343(4)
C(18)-H(18)	0.9500
C(19)-C(20)	1.495(4)
C(19)-H(19)	0.9500
C(20)-C(21)	1.525(3)
C(20)-H(20)	1.0000
C(21)-H(21)	1.0000
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9800

C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(26)-H(26D)	0.9800
C(26)-H(26E)	0.9800
C(26)-H(26F)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
O(11)-C(31)	1.452(3)
O(11)-C(30)	1.463(3)
O(12)-C(33)	1.435(3)
O(12)-H(12)	0.8400
O(13)-C(53)	1.414(4)
O(13)-C(34)	1.435(3)
O(13B)-C(43B)	1.369(15)
O(13B)-C(55B)	1.445(14)
O(14)-C(43)	1.324(11)
O(14)-C(55)	1.437(11)
O(14B)-C(42B)	1.248(14)
O(15)-C(42)	1.229(10)
O(16)-C(39)	1.232(3)
O(17)-C(44)	1.222(3)
O(18)-C(49)	1.421(3)
O(18)-C(57)	1.428(3)
O(19)-C(58)	1.375(3)
O(19)-C(50)	1.451(3)
O(20)-C(58)	1.217(3)
N(3)-C(58)	1.329(3)
N(3)-H(3A)	0.8800
N(3)-H(3B)	0.8800

N(4)-C(44)	1.376(3)
N(4)-C(40)	1.378(3)
N(4)-H(4)	0.8800
C(30)-C(31)	1.478(3)
C(30)-C(50)	1.498(4)
C(30)-C(51)	1.501(4)
C(31)-C(32)	1.509(4)
C(31)-H(31)	1.0000
C(32)-C(52)	1.531(4)
C(32)-C(33)	1.531(4)
C(32)-H(32)	1.0000
C(33)-C(34)	1.534(4)
C(33)-H(33)	1.0000
C(34)-C(35)	1.525(4)
C(34)-H(34)	1.0000
C(35)-C(36)	1.533(4)
C(35)-H(35A)	0.9900
C(35)-H(35B)	0.9900
C(36)-C(37)	1.537(4)
C(36)-C(54)	1.542(3)
C(36)-H(36)	1.0000
C(37)-C(38)	1.505(3)
C(37)-H(37A)	0.9900
C(37)-H(37B)	0.9900
C(38)-C(43)	1.337(11)
C(38)-C(43B)	1.392(14)
C(38)-C(39)	1.462(3)
C(39)-C(40)	1.501(3)
C(40)-C(41)	1.342(3)
C(41)-C(42)	1.430(11)
C(41)-C(42B)	1.503(13)
C(41)-H(41A)	0.9500
C(41)-H(41)	0.9500
C(42)-C(43)	1.482(15)
C(42B)-C(43B)	1.508(19)
C(44)-C(45)	1.489(3)

C(45)-C(46)	1.344(4)
C(45)-C(56)	1.501(4)
C(46)-C(47)	1.452(4)
C(46)-H(46)	0.9500
C(47)-C(48)	1.341(4)
C(47)-H(47)	0.9500
C(48)-C(49)	1.498(4)
C(48)-H(48)	0.9500
C(49)-C(50)	1.526(3)
C(49)-H(49)	1.0000
C(50)-H(50)	1.0000
C(51)-H(51A)	0.9800
C(51)-H(51B)	0.9800
C(51)-H(51C)	0.9800
C(52)-H(52A)	0.9800
C(52)-H(52B)	0.9800
C(52)-H(52C)	0.9800
C(53)-H(53A)	0.9800
C(53)-H(53B)	0.9800
C(53)-H(53C)	0.9800
C(54)-H(54A)	0.9800
C(54)-H(54B)	0.9800
C(54)-H(54C)	0.9800
C(55)-H(55A)	0.9800
C(55)-H(55B)	0.9800
C(55)-H(55C)	0.9800
C(55B)-H(55D)	0.9800
C(55B)-H(55E)	0.9800
C(55B)-H(55F)	0.9800
C(56)-H(56A)	0.9800
C(56)-H(56B)	0.9800
C(56)-H(56C)	0.9800
C(57)-H(57A)	0.9800
C(57)-H(57B)	0.9800
C(57)-H(57C)	0.9800

C(1)-O(1)-C(2)	60.95(15)
C(4)-O(2)-H(2)	109.5
C(24)-O(3)-C(5)	114.0(2)
C(14)-O(5)-C(26)	120.7(11)
C(26)-O(5B)-C(14B)	132.3(14)
C(20)-O(8)-C(28)	113.71(18)
C(29)-O(9)-C(21)	116.52(19)
C(29)-N(1)-H(1A)	120.0
C(29)-N(1)-H(1B)	120.0
H(1A)-N(1)-H(1B)	120.0
C(15)-N(2)-C(11)	128.4(2)
C(15)-N(2)-H(2A)	115.8
C(11)-N(2)-H(2A)	115.8
O(1)-C(1)-C(2)	59.60(15)
O(1)-C(1)-C(22)	115.1(2)
C(2)-C(1)-C(22)	123.1(2)
O(1)-C(1)-C(21)	111.8(2)
C(2)-C(1)-C(21)	114.5(2)
C(22)-C(1)-C(21)	118.1(2)
O(1)-C(2)-C(1)	59.45(15)
O(1)-C(2)-C(3)	115.99(19)
C(1)-C(2)-C(3)	126.2(2)
O(1)-C(2)-H(2B)	114.4
C(1)-C(2)-H(2B)	114.4
C(3)-C(2)-H(2B)	114.4
C(2)-C(3)-C(23)	107.7(2)
C(2)-C(3)-C(4)	111.1(2)
C(23)-C(3)-C(4)	114.6(2)
C(2)-C(3)-H(3)	107.7
C(23)-C(3)-H(3)	107.7
C(4)-C(3)-H(3)	107.7
O(2)-C(4)-C(5)	110.76(18)
O(2)-C(4)-C(3)	112.1(2)
C(5)-C(4)-C(3)	111.6(2)
O(2)-C(4)-H(4A)	107.4
C(5)-C(4)-H(4A)	107.4

C(3)-C(4)-H(4A)	107.4
O(3)-C(5)-C(4)	105.46(19)
O(3)-C(5)-C(6)	113.9(2)
C(4)-C(5)-C(6)	114.6(2)
O(3)-C(5)-H(5)	107.5
C(4)-C(5)-H(5)	107.5
C(6)-C(5)-H(5)	107.5
C(7)-C(6)-C(5)	116.9(2)
C(7)-C(6)-H(6A)	108.1
C(5)-C(6)-H(6A)	108.1
C(7)-C(6)-H(6B)	108.1
C(5)-C(6)-H(6B)	108.1
H(6A)-C(6)-H(6B)	107.3
C(25)-C(7)-C(6)	112.3(2)
C(25)-C(7)-C(8)	108.5(2)
C(6)-C(7)-C(8)	110.5(2)
C(25)-C(7)-H(7)	108.5
C(6)-C(7)-H(7)	108.5
C(8)-C(7)-H(7)	108.5
C(9)-C(8)-C(7)	115.4(2)
C(9)-C(8)-H(8A)	108.4
C(7)-C(8)-H(8A)	108.4
C(9)-C(8)-H(8B)	108.4
C(7)-C(8)-H(8B)	108.4
H(8A)-C(8)-H(8B)	107.5
C(14)-C(9)-C(10)	119.7(6)
C(14B)-C(9)-C(10)	117.3(6)
C(14)-C(9)-C(8)	122.2(6)
C(14B)-C(9)-C(8)	124.4(6)
C(10)-C(9)-C(8)	117.6(2)
O(4)-C(10)-C(9)	122.9(2)
O(4)-C(10)-C(11)	117.7(2)
C(9)-C(10)-C(11)	119.4(2)
C(12)-C(11)-N(2)	128.3(2)
C(12)-C(11)-C(10)	120.8(2)
N(2)-C(11)-C(10)	110.9(2)

C(11)-C(12)-C(13B)	121.2(5)
C(11)-C(12)-C(13)	117.8(5)
C(11)-C(12)-H(12B)	119.4
C(13B)-C(12)-H(12B)	119.4
C(11)-C(12)-H(12A)	121.1
C(13)-C(12)-H(12A)	121.1
O(6)-C(13)-C(12)	120.4(9)
O(6)-C(13)-C(14)	118.0(10)
C(12)-C(13)-C(14)	121.5(9)
O(6B)-C(13B)-C(12)	120.3(9)
O(6B)-C(13B)-C(14B)	123.2(10)
C(12)-C(13B)-C(14B)	116.6(9)
O(5)-C(14)-C(9)	117.6(12)
O(5)-C(14)-C(13)	122.7(11)
C(9)-C(14)-C(13)	119.5(11)
O(5B)-C(14B)-C(9)	120.1(11)
O(5B)-C(14B)-C(13B)	116.0(11)
C(9)-C(14B)-C(13B)	123.6(10)
O(7)-C(15)-N(2)	122.3(2)
O(7)-C(15)-C(16)	122.2(2)
N(2)-C(15)-C(16)	115.5(2)
C(17)-C(16)-C(15)	118.8(2)
C(17)-C(16)-C(27)	125.9(2)
C(15)-C(16)-C(27)	115.3(2)
C(16)-C(17)-C(18)	127.4(2)
C(16)-C(17)-H(17)	116.3
C(18)-C(17)-H(17)	116.3
C(19)-C(18)-C(17)	123.6(2)
C(19)-C(18)-H(18)	118.2
C(17)-C(18)-H(18)	118.2
C(18)-C(19)-C(20)	125.8(2)
C(18)-C(19)-H(19)	117.1
C(20)-C(19)-H(19)	117.1
O(8)-C(20)-C(19)	110.2(2)
O(8)-C(20)-C(21)	108.30(18)
C(19)-C(20)-C(21)	112.5(2)

O(8)-C(20)-H(20)	108.6
C(19)-C(20)-H(20)	108.6
C(21)-C(20)-H(20)	108.6
O(9)-C(21)-C(1)	110.05(19)
O(9)-C(21)-C(20)	107.84(19)
C(1)-C(21)-C(20)	113.2(2)
O(9)-C(21)-H(21)	108.6
C(1)-C(21)-H(21)	108.6
C(20)-C(21)-H(21)	108.6
C(1)-C(22)-H(22A)	109.5
C(1)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(1)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(3)-C(23)-H(23A)	109.5
C(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(3)-C(24)-H(24A)	109.5
O(3)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
O(3)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(7)-C(25)-H(25A)	109.5
C(7)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(7)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
O(5)-C(26)-H(26A)	109.5
O(5)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5

O(5)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
O(5B)-C(26)-H(26D)	109.5
O(5B)-C(26)-H(26E)	109.5
H(26D)-C(26)-H(26E)	109.5
O(5B)-C(26)-H(26F)	109.5
H(26D)-C(26)-H(26F)	109.5
H(26E)-C(26)-H(26F)	109.5
C(16)-C(27)-H(27A)	109.5
C(16)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(16)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(8)-C(28)-H(28A)	109.5
O(8)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(8)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(10)-C(29)-N(1)	126.8(2)
O(10)-C(29)-O(9)	122.8(2)
N(1)-C(29)-O(9)	110.4(2)
C(31)-O(11)-C(30)	60.93(16)
C(33)-O(12)-H(12)	109.5
C(53)-O(13)-C(34)	113.1(2)
C(43B)-O(13B)-C(55B)	119.7(13)
C(43)-O(14)-C(55)	122.8(8)
C(49)-O(18)-C(57)	113.76(18)
C(58)-O(19)-C(50)	115.30(19)
C(58)-N(3)-H(3A)	120.0
C(58)-N(3)-H(3B)	120.0
H(3A)-N(3)-H(3B)	120.0
C(44)-N(4)-C(40)	129.2(2)
C(44)-N(4)-H(4)	115.4

C(40)-N(4)-H(4)	115.4
O(11)-C(30)-C(31)	59.15(16)
O(11)-C(30)-C(50)	110.9(2)
C(31)-C(30)-C(50)	115.1(2)
O(11)-C(30)-C(51)	114.6(2)
C(31)-C(30)-C(51)	122.7(3)
C(50)-C(30)-C(51)	118.7(2)
O(11)-C(31)-C(30)	59.92(15)
O(11)-C(31)-C(32)	116.3(2)
C(30)-C(31)-C(32)	125.9(2)
O(11)-C(31)-H(31)	114.4
C(30)-C(31)-H(31)	114.4
C(32)-C(31)-H(31)	114.4
C(31)-C(32)-C(52)	108.1(2)
C(31)-C(32)-C(33)	109.9(2)
C(52)-C(32)-C(33)	114.5(2)
C(31)-C(32)-H(32)	108.1
C(52)-C(32)-H(32)	108.1
C(33)-C(32)-H(32)	108.1
O(12)-C(33)-C(32)	111.7(2)
O(12)-C(33)-C(34)	109.81(19)
C(32)-C(33)-C(34)	112.9(2)
O(12)-C(33)-H(33)	107.4
C(32)-C(33)-H(33)	107.4
C(34)-C(33)-H(33)	107.4
O(13)-C(34)-C(35)	114.6(2)
O(13)-C(34)-C(33)	104.6(2)
C(35)-C(34)-C(33)	114.0(2)
O(13)-C(34)-H(34)	107.8
C(35)-C(34)-H(34)	107.8
C(33)-C(34)-H(34)	107.8
C(34)-C(35)-C(36)	116.7(2)
C(34)-C(35)-H(35A)	108.1
C(36)-C(35)-H(35A)	108.1
C(34)-C(35)-H(35B)	108.1
C(36)-C(35)-H(35B)	108.1

H(35A)-C(35)-H(35B)	107.3
C(35)-C(36)-C(37)	111.5(2)
C(35)-C(36)-C(54)	111.2(2)
C(37)-C(36)-C(54)	108.7(2)
C(35)-C(36)-H(36)	108.4
C(37)-C(36)-H(36)	108.4
C(54)-C(36)-H(36)	108.4
C(38)-C(37)-C(36)	114.4(2)
C(38)-C(37)-H(37A)	108.6
C(36)-C(37)-H(37A)	108.6
C(38)-C(37)-H(37B)	108.6
C(36)-C(37)-H(37B)	108.6
H(37A)-C(37)-H(37B)	107.6
C(43)-C(38)-C(39)	118.0(5)
C(43B)-C(38)-C(39)	118.6(7)
C(43)-C(38)-C(37)	123.7(5)
C(43B)-C(38)-C(37)	122.8(7)
C(39)-C(38)-C(37)	117.9(2)
O(16)-C(39)-C(38)	122.4(2)
O(16)-C(39)-C(40)	118.0(2)
C(38)-C(39)-C(40)	119.6(2)
C(41)-C(40)-N(4)	128.5(2)
C(41)-C(40)-C(39)	121.0(2)
N(4)-C(40)-C(39)	110.48(19)
C(40)-C(41)-C(42)	118.2(4)
C(40)-C(41)-C(42B)	120.8(6)
C(40)-C(41)-H(41A)	119.6
C(42B)-C(41)-H(41A)	119.6
C(40)-C(41)-H(41)	120.9
C(42)-C(41)-H(41)	120.9
O(15)-C(42)-C(41)	118.5(8)
O(15)-C(42)-C(43)	120.3(10)
C(41)-C(42)-C(43)	121.2(8)
O(14B)-C(42B)-C(41)	122.1(12)
O(14B)-C(42B)-C(43B)	120.8(13)
C(41)-C(42B)-C(43B)	117.0(11)

O(14)-C(43)-C(38)	116.3(9)
O(14)-C(43)-C(42)	122.4(9)
C(38)-C(43)-C(42)	121.2(9)
O(13B)-C(43B)-C(38)	123.2(12)
O(13B)-C(43B)-C(42B)	115.3(12)
C(38)-C(43B)-C(42B)	121.4(12)
O(17)-C(44)-N(4)	121.9(2)
O(17)-C(44)-C(45)	122.2(2)
N(4)-C(44)-C(45)	115.8(2)
C(46)-C(45)-C(44)	119.1(2)
C(46)-C(45)-C(56)	125.4(2)
C(44)-C(45)-C(56)	115.4(2)
C(45)-C(46)-C(47)	127.8(2)
C(45)-C(46)-H(46)	116.1
C(47)-C(46)-H(46)	116.1
C(48)-C(47)-C(46)	123.5(3)
C(48)-C(47)-H(47)	118.3
C(46)-C(47)-H(47)	118.3
C(47)-C(48)-C(49)	126.3(2)
C(47)-C(48)-H(48)	116.8
C(49)-C(48)-H(48)	116.8
O(18)-C(49)-C(48)	110.7(2)
O(18)-C(49)-C(50)	108.03(18)
C(48)-C(49)-C(50)	111.9(2)
O(18)-C(49)-H(49)	108.7
C(48)-C(49)-H(49)	108.7
C(50)-C(49)-H(49)	108.7
O(19)-C(50)-C(30)	109.4(2)
O(19)-C(50)-C(49)	107.29(19)
C(30)-C(50)-C(49)	114.1(2)
O(19)-C(50)-H(50)	108.6
C(30)-C(50)-H(50)	108.6
C(49)-C(50)-H(50)	108.6
C(30)-C(51)-H(51A)	109.5
C(30)-C(51)-H(51B)	109.5
H(51A)-C(51)-H(51B)	109.5

C(30)-C(51)-H(51C)	109.5
H(51A)-C(51)-H(51C)	109.5
H(51B)-C(51)-H(51C)	109.5
C(32)-C(52)-H(52A)	109.5
C(32)-C(52)-H(52B)	109.5
H(52A)-C(52)-H(52B)	109.5
C(32)-C(52)-H(52C)	109.5
H(52A)-C(52)-H(52C)	109.5
H(52B)-C(52)-H(52C)	109.5
O(13)-C(53)-H(53A)	109.5
O(13)-C(53)-H(53B)	109.5
H(53A)-C(53)-H(53B)	109.5
O(13)-C(53)-H(53C)	109.5
H(53A)-C(53)-H(53C)	109.5
H(53B)-C(53)-H(53C)	109.5
C(36)-C(54)-H(54A)	109.5
C(36)-C(54)-H(54B)	109.5
H(54A)-C(54)-H(54B)	109.5
C(36)-C(54)-H(54C)	109.5
H(54A)-C(54)-H(54C)	109.5
H(54B)-C(54)-H(54C)	109.5
O(14)-C(55)-H(55A)	109.5
O(14)-C(55)-H(55B)	109.5
H(55A)-C(55)-H(55B)	109.5
O(14)-C(55)-H(55C)	109.5
H(55A)-C(55)-H(55C)	109.5
H(55B)-C(55)-H(55C)	109.5
O(13B)-C(55B)-H(55D)	109.5
O(13B)-C(55B)-H(55E)	109.5
H(55D)-C(55B)-H(55E)	109.5
O(13B)-C(55B)-H(55F)	109.5
H(55D)-C(55B)-H(55F)	109.5
H(55E)-C(55B)-H(55F)	109.5
C(45)-C(56)-H(56A)	109.5
C(45)-C(56)-H(56B)	109.5
H(56A)-C(56)-H(56B)	109.5

C(45)-C(56)-H(56C)	109.5
H(56A)-C(56)-H(56C)	109.5
H(56B)-C(56)-H(56C)	109.5
O(18)-C(57)-H(57A)	109.5
O(18)-C(57)-H(57B)	109.5
H(57A)-C(57)-H(57B)	109.5
O(18)-C(57)-H(57C)	109.5
H(57A)-C(57)-H(57C)	109.5
H(57B)-C(57)-H(57C)	109.5
O(20)-C(58)-N(3)	127.8(2)
O(20)-C(58)-O(19)	122.7(2)
N(3)-C(58)-O(19)	109.5(2)

Symmetry transformations used to generate equivalent atoms:

Table S6. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **A**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
O(1)	53(1)	26(1)	31(1)	-3(1)	16(1)	-1(1)
O(2)	35(1)	36(1)	27(1)	-1(1)	5(1)	-3(1)
O(3)	38(1)	47(1)	36(1)	8(1)	2(1)	-5(1)
O(4)	37(1)	40(1)	34(1)	7(1)	12(1)	2(1)
O(5)	36(3)	45(6)	54(6)	0(3)	23(3)	-6(3)
O(5B)	37(3)	61(8)	56(6)	0(4)	19(3)	-6(4)
O(6)	62(3)	58(5)	52(4)	13(4)	34(3)	-7(3)
O(6B)	62(3)	79(7)	45(3)	14(4)	29(2)	0(4)
O(7)	43(1)	44(1)	25(1)	-2(1)	7(1)	6(1)
O(8)	52(1)	24(1)	32(1)	1(1)	22(1)	3(1)
O(9)	48(1)	26(1)	35(1)	1(1)	26(1)	4(1)
O(10)	66(1)	29(1)	45(1)	5(1)	28(1)	13(1)
N(1)	65(2)	31(1)	45(1)	2(1)	36(1)	13(1)
N(2)	34(1)	42(1)	24(1)	1(1)	10(1)	3(1)
C(1)	43(1)	23(1)	27(1)	1(1)	13(1)	2(1)

C(2)	41(1)	23(1)	24(1)	1(1)	10(1)	1(1)
C(3)	40(1)	31(1)	26(1)	0(1)	7(1)	-5(1)
C(4)	34(1)	30(1)	25(1)	5(1)	7(1)	-3(1)
C(5)	36(1)	33(1)	32(1)	6(1)	6(1)	-2(1)
C(6)	34(1)	34(2)	41(1)	7(1)	14(1)	0(1)
C(7)	32(1)	32(1)	44(1)	7(1)	7(1)	2(1)
C(8)	30(1)	34(2)	54(2)	2(1)	14(1)	2(1)
C(9)	35(1)	27(1)	46(1)	-3(1)	14(1)	-1(1)
C(10)	36(1)	25(1)	36(1)	0(1)	13(1)	2(1)
C(11)	38(1)	25(1)	31(1)	-3(1)	12(1)	-1(1)
C(12)	41(1)	36(2)	34(1)	2(1)	13(1)	0(1)
C(13)	53(4)	30(8)	41(4)	1(5)	26(3)	2(3)
C(13B)	47(4)	30(8)	47(5)	0(5)	23(3)	-5(3)
C(14)	36(2)	6(6)	49(3)	-11(3)	18(2)	-8(3)
C(14B)	36(2)	6(6)	49(3)	-11(3)	18(2)	-8(3)
C(15)	35(1)	27(1)	32(1)	-1(1)	9(1)	1(1)
C(16)	33(1)	30(1)	34(1)	-1(1)	9(1)	1(1)
C(17)	33(1)	36(1)	35(1)	0(1)	12(1)	0(1)
C(18)	33(1)	42(2)	41(1)	-4(1)	15(1)	1(1)
C(19)	35(1)	35(1)	42(1)	-4(1)	21(1)	0(1)
C(20)	39(1)	26(1)	29(1)	0(1)	20(1)	1(1)
C(21)	40(1)	24(1)	28(1)	4(1)	18(1)	3(1)
C(22)	48(2)	37(2)	35(1)	11(1)	10(1)	1(1)
C(23)	45(1)	31(1)	43(1)	-3(1)	14(1)	-9(1)
C(24)	37(1)	58(2)	59(2)	2(2)	-3(1)	-7(1)
C(25)	36(1)	42(2)	61(2)	12(1)	-2(1)	-1(1)
C(26)	68(2)	145(5)	99(3)	-38(4)	51(2)	-24(3)
C(27)	35(1)	62(2)	41(1)	-9(1)	8(1)	1(1)
C(28)	71(2)	28(1)	43(1)	-1(1)	27(1)	8(1)
C(29)	44(1)	27(1)	36(1)	-4(1)	18(1)	4(1)
O(11)	61(1)	29(1)	38(1)	8(1)	23(1)	5(1)
O(12)	41(1)	38(1)	28(1)	-2(1)	5(1)	6(1)
O(13)	50(1)	38(1)	31(1)	-2(1)	-3(1)	8(1)
O(13B)	28(3)	37(5)	41(4)	6(3)	12(2)	10(3)
O(14)	37(2)	87(6)	63(4)	-15(4)	9(2)	15(3)
O(14B)	52(4)	33(4)	43(3)	1(3)	29(3)	-6(3)

O(15)	44(3)	160(10)	75(5)	-65(6)	20(3)	13(5)
O(16)	37(1)	42(1)	30(1)	-4(1)	9(1)	0(1)
O(17)	39(1)	40(1)	26(1)	1(1)	9(1)	-4(1)
O(18)	54(1)	23(1)	40(1)	0(1)	30(1)	-1(1)
O(19)	54(1)	24(1)	45(1)	2(1)	35(1)	-1(1)
O(20)	64(1)	30(1)	46(1)	0(1)	27(1)	-7(1)
N(3)	65(2)	33(1)	47(1)	3(1)	37(1)	-9(1)
N(4)	37(1)	45(1)	23(1)	-2(1)	11(1)	-4(1)
C(30)	55(2)	26(1)	31(1)	2(1)	20(1)	4(1)
C(31)	48(1)	28(1)	30(1)	1(1)	16(1)	4(1)
C(32)	50(1)	31(1)	29(1)	-4(1)	9(1)	3(1)
C(33)	43(1)	27(1)	27(1)	-5(1)	5(1)	6(1)
C(34)	41(1)	30(1)	30(1)	-6(1)	3(1)	5(1)
C(35)	35(1)	31(1)	36(1)	-6(1)	4(1)	6(1)
C(36)	38(1)	30(1)	32(1)	-7(1)	-1(1)	3(1)
C(37)	35(1)	34(1)	40(1)	-2(1)	2(1)	2(1)
C(38)	36(1)	30(1)	37(1)	-2(1)	6(1)	3(1)
C(39)	36(1)	27(1)	28(1)	1(1)	9(1)	1(1)
C(40)	35(1)	26(1)	28(1)	1(1)	9(1)	-4(1)
C(41)	38(1)	33(1)	31(1)	-1(1)	10(1)	4(1)
C(42)	55(5)	61(10)	51(5)	-24(6)	21(4)	-3(4)
C(42B)	28(5)	27(6)	36(5)	7(4)	13(4)	9(4)
C(43)	39(4)	26(7)	53(5)	1(4)	10(3)	4(3)
C(43B)	31(5)	13(8)	34(5)	10(4)	12(3)	0(4)
C(44)	35(1)	26(1)	28(1)	3(1)	8(1)	-1(1)
C(45)	37(1)	32(1)	31(1)	-1(1)	8(1)	-1(1)
C(46)	35(1)	35(1)	33(1)	2(1)	11(1)	0(1)
C(47)	36(1)	36(2)	42(1)	2(1)	14(1)	0(1)
C(48)	40(1)	31(1)	47(1)	3(1)	25(1)	0(1)
C(49)	42(1)	24(1)	35(1)	0(1)	23(1)	0(1)
C(50)	49(1)	24(1)	33(1)	-2(1)	26(1)	0(1)
C(51)	66(2)	41(2)	36(1)	-11(1)	17(1)	5(1)
C(52)	52(2)	31(2)	47(2)	5(1)	10(1)	7(1)
C(53)	53(2)	38(2)	45(2)	-2(1)	-7(1)	9(1)
C(54)	55(2)	33(2)	37(1)	-8(1)	-6(1)	3(1)
C(55)	37(3)	100(7)	91(6)	21(5)	24(3)	10(3)

C(55B)	56(6)	58(8)	105(12)	-6(7)	29(7)	16(5)
C(56)	35(1)	77(2)	37(1)	12(2)	5(1)	6(1)
C(57)	64(2)	30(1)	48(2)	3(1)	32(1)	-8(1)
C(58)	50(2)	26(1)	40(1)	4(1)	22(1)	-2(1)

Table S7. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **A**.

	x	y	z	U(eq)
H(2)	11073	3022	5931	49
H(1A)	7679	3995	7944	52
H(1B)	8046	2204	7946	52
H(2A)	9484	-1291	5466	40
H(2B)	9941	4042	6528	35
H(3)	11563	3485	7177	39
H(4A)	11430	1230	6695	36
H(5)	12474	3685	6384	41
H(6A)	12313	1435	5870	43
H(6B)	13267	1464	6176	43
H(7)	12064	-828	6404	44
H(8A)	13094	-1733	5777	46
H(8B)	12437	-2972	5937	46
H(12B)	9984	68	4446	44
H(12A)	9988	-216	4415	44
H(17)	8775	363	5724	41
H(18)	7014	359	5757	45
H(19)	7444	944	6500	43
H(20)	9155	950	6385	35
H(21)	8697	3441	6743	35
H(22A)	10923	1974	7618	60
H(22B)	10384	410	7355	60
H(22C)	10038	1447	7731	60
H(23A)	11318	5741	6413	58

H(23B)	12117	5691	6846	58
H(23C)	11215	6377	6902	58
H(24A)	14081	2405	6869	81
H(24B)	14016	3240	7344	81
H(24C)	13697	4281	6877	81
H(25A)	13886	-1045	6577	73
H(25B)	13303	-2506	6714	73
H(25C)	13362	-678	6955	73
H(26A)	13735	-180	4692	148
H(26B)	12926	-1308	4451	148
H(26C)	12847	723	4462	148
H(26D)	13732	-448	4710	148
H(26E)	12858	-886	4348	148
H(26F)	12985	940	4591	148
H(27A)	6942	223	4649	69
H(27B)	6705	-732	5071	69
H(27C)	7094	-1786	4714	69
H(28A)	8625	-2363	6388	67
H(28B)	9313	-3062	6825	67
H(28C)	9608	-1844	6465	67
H(12)	14404	-1579	9000	54
H(3A)	18579	-1044	7501	53
H(3B)	18181	-2810	7485	53
H(4)	15761	-5898	9666	41
H(31)	15878	-586	8594	41
H(32)	14485	-1105	7793	44
H(33)	14371	-3340	8253	40
H(34)	13195	-838	8426	41
H(35A)	12269	-3106	8486	42
H(35B)	13104	-3100	8896	42
H(36)	13663	-5330	8470	42
H(37A)	12228	-6291	8824	45
H(37B)	12982	-7541	8775	45
H(41A)	14702	-4625	10509	41
H(41)	14692	-4844	10530	41
H(46)	16613	-4361	9519	41

H(47)	18442	-4242	9747	44
H(48)	18370	-3857	9008	44
H(49)	16547	-3929	8856	37
H(50)	17219	-1455	8582	39
H(51A)	15263	-2990	7530	71
H(51B)	15712	-4512	7853	71
H(51C)	16209	-3576	7521	71
H(52A)	13803	1146	8050	66
H(52B)	14757	1771	8076	66
H(52C)	14489	1192	8531	66
H(53A)	12005	-1138	7347	73
H(53B)	12175	-96	7818	73
H(53C)	11741	-1941	7783	73
H(54A)	12579	-6975	7961	67
H(54B)	12678	-5121	7758	67
H(54C)	11899	-5516	7985	67
H(55A)	11005	-4799	9683	112
H(55B)	11783	-3837	10020	112
H(55C)	11688	-5860	10053	112
H(55D)	11432	-3781	9301	107
H(55E)	11885	-3431	9827	107
H(55F)	11027	-4532	9696	107
H(56A)	17933	-4167	10762	76
H(56B)	18424	-5124	10432	76
H(56C)	17870	-6195	10709	76
H(57A)	16759	-8002	8491	66
H(57B)	16204	-6838	8746	66
H(57C)	17194	-7153	8974	66

Table S8. Torsion angles [°] for **A**.

C(2)-O(1)-C(1)-C(22)	115.1(2)
C(2)-O(1)-C(1)-C(21)	-106.5(2)
C(1)-O(1)-C(2)-C(3)	-118.4(2)

C(22)-C(1)-C(2)-O(1)	-101.8(3)
C(21)-C(1)-C(2)-O(1)	101.9(2)
O(1)-C(1)-C(2)-C(3)	101.4(3)
C(22)-C(1)-C(2)-C(3)	-0.4(4)
C(21)-C(1)-C(2)-C(3)	-156.7(2)
O(1)-C(2)-C(3)-C(23)	-75.3(3)
C(1)-C(2)-C(3)-C(23)	-145.2(2)
O(1)-C(2)-C(3)-C(4)	158.4(2)
C(1)-C(2)-C(3)-C(4)	88.5(3)
C(2)-C(3)-C(4)-O(2)	46.3(3)
C(23)-C(3)-C(4)-O(2)	-76.1(3)
C(2)-C(3)-C(4)-C(5)	171.1(2)
C(23)-C(3)-C(4)-C(5)	48.8(3)
C(24)-O(3)-C(5)-C(4)	-159.6(2)
C(24)-O(3)-C(5)-C(6)	74.0(3)
O(2)-C(4)-C(5)-O(3)	-177.4(2)
C(3)-C(4)-C(5)-O(3)	57.0(3)
O(2)-C(4)-C(5)-C(6)	-51.3(3)
C(3)-C(4)-C(5)-C(6)	-176.9(2)
O(3)-C(5)-C(6)-C(7)	62.4(3)
C(4)-C(5)-C(6)-C(7)	-59.1(3)
C(5)-C(6)-C(7)-C(25)	-80.5(3)
C(5)-C(6)-C(7)-C(8)	158.1(2)
C(25)-C(7)-C(8)-C(9)	-176.5(2)
C(6)-C(7)-C(8)-C(9)	-52.9(3)
C(7)-C(8)-C(9)-C(14)	108.8(9)
C(7)-C(8)-C(9)-C(14B)	126.8(9)
C(7)-C(8)-C(9)-C(10)	-63.2(3)
C(14)-C(9)-C(10)-O(4)	-173.5(8)
C(14B)-C(9)-C(10)-O(4)	169.4(8)
C(8)-C(9)-C(10)-O(4)	-1.3(4)
C(14)-C(9)-C(10)-C(11)	6.8(9)
C(14B)-C(9)-C(10)-C(11)	-10.3(8)
C(8)-C(9)-C(10)-C(11)	179.0(2)
C(15)-N(2)-C(11)-C(12)	0.4(5)
C(15)-N(2)-C(11)-C(10)	-179.9(2)

O(4)-C(10)-C(11)-C(12)	-176.5(3)
C(9)-C(10)-C(11)-C(12)	3.3(4)
O(4)-C(10)-C(11)-N(2)	3.8(3)
C(9)-C(10)-C(11)-N(2)	-176.4(2)
N(2)-C(11)-C(12)-C(13B)	-174.3(9)
C(10)-C(11)-C(12)-C(13B)	6.1(9)
N(2)-C(11)-C(12)-C(13)	169.0(9)
C(10)-C(11)-C(12)-C(13)	-10.7(9)
C(11)-C(12)-C(13)-O(6)	-166.8(11)
C(11)-C(12)-C(13)-C(14)	9.1(17)
C(11)-C(12)-C(13B)-O(6B)	172.0(11)
C(11)-C(12)-C(13B)-C(14B)	-8.0(16)
C(26)-O(5)-C(14)-C(9)	155.1(13)
C(26)-O(5)-C(14)-C(13)	-19.4(19)
C(10)-C(9)-C(14)-O(5)	177.0(8)
C(8)-C(9)-C(14)-O(5)	5.1(15)
C(10)-C(9)-C(14)-C(13)	-8.3(16)
C(8)-C(9)-C(14)-C(13)	179.9(9)
O(6)-C(13)-C(14)-O(5)	-9(2)
C(12)-C(13)-C(14)-O(5)	175.1(12)
O(6)-C(13)-C(14)-C(9)	176.7(12)
C(12)-C(13)-C(14)-C(9)	1(2)
C(26)-O(5B)-C(14B)-C(9)	-164.4(15)
C(26)-O(5B)-C(14B)-C(13B)	9(2)
C(10)-C(9)-C(14B)-O(5B)	-178.1(9)
C(8)-C(9)-C(14B)-O(5B)	-8.1(15)
C(10)-C(9)-C(14B)-C(13B)	8.4(16)
C(8)-C(9)-C(14B)-C(13B)	178.4(10)
O(6B)-C(13B)-C(14B)-O(5B)	7(2)
C(12)-C(13B)-C(14B)-O(5B)	-173.2(11)
O(6B)-C(13B)-C(14B)-C(9)	-179.6(12)
C(12)-C(13B)-C(14B)-C(9)	0.5(19)
C(11)-N(2)-C(15)-O(7)	14.5(4)
C(11)-N(2)-C(15)-C(16)	-164.7(2)
O(7)-C(15)-C(16)-C(17)	-151.9(3)
N(2)-C(15)-C(16)-C(17)	27.3(4)

O(7)-C(15)-C(16)-C(27)	25.1(4)
N(2)-C(15)-C(16)-C(27)	-155.6(3)
C(15)-C(16)-C(17)-C(18)	-179.8(3)
C(27)-C(16)-C(17)-C(18)	3.5(5)
C(16)-C(17)-C(18)-C(19)	172.1(3)
C(17)-C(18)-C(19)-C(20)	-1.4(5)
C(28)-O(8)-C(20)-C(19)	75.8(3)
C(28)-O(8)-C(20)-C(21)	-160.8(2)
C(18)-C(19)-C(20)-O(8)	-104.3(3)
C(18)-C(19)-C(20)-C(21)	134.7(3)
C(29)-O(9)-C(21)-C(1)	93.9(2)
C(29)-O(9)-C(21)-C(20)	-142.2(2)
O(1)-C(1)-C(21)-O(9)	-88.8(2)
C(2)-C(1)-C(21)-O(9)	-154.2(2)
C(22)-C(1)-C(21)-O(9)	48.2(3)
O(1)-C(1)-C(21)-C(20)	150.47(19)
C(2)-C(1)-C(21)-C(20)	85.1(3)
C(22)-C(1)-C(21)-C(20)	-72.5(3)
O(8)-C(20)-C(21)-O(9)	-53.1(2)
C(19)-C(20)-C(21)-O(9)	68.9(2)
O(8)-C(20)-C(21)-C(1)	68.8(2)
C(19)-C(20)-C(21)-C(1)	-169.1(2)
C(21)-O(9)-C(29)-O(10)	15.1(4)
C(21)-O(9)-C(29)-N(1)	-165.9(2)
C(31)-O(11)-C(30)-C(50)	-107.5(2)
C(31)-O(11)-C(30)-C(51)	114.8(3)
C(30)-O(11)-C(31)-C(32)	-118.0(3)
C(50)-C(30)-C(31)-O(11)	100.4(2)
C(51)-C(30)-C(31)-O(11)	-101.0(3)
O(11)-C(30)-C(31)-C(32)	102.3(3)
C(50)-C(30)-C(31)-C(32)	-157.3(2)
C(51)-C(30)-C(31)-C(32)	1.3(4)
O(11)-C(31)-C(32)-C(52)	-81.1(3)
C(30)-C(31)-C(32)-C(52)	-151.7(2)
O(11)-C(31)-C(32)-C(33)	153.3(2)
C(30)-C(31)-C(32)-C(33)	82.7(3)

C(31)-C(32)-C(33)-O(12)	46.6(3)
C(52)-C(32)-C(33)-O(12)	-75.2(3)
C(31)-C(32)-C(33)-C(34)	170.9(2)
C(52)-C(32)-C(33)-C(34)	49.1(3)
C(53)-O(13)-C(34)-C(35)	75.3(3)
C(53)-O(13)-C(34)-C(33)	-159.2(2)
O(12)-C(33)-C(34)-O(13)	-179.7(2)
C(32)-C(33)-C(34)-O(13)	54.9(3)
O(12)-C(33)-C(34)-C(35)	-53.8(3)
C(32)-C(33)-C(34)-C(35)	-179.2(2)
O(13)-C(34)-C(35)-C(36)	65.3(3)
C(33)-C(34)-C(35)-C(36)	-55.1(3)
C(34)-C(35)-C(36)-C(37)	162.7(2)
C(34)-C(35)-C(36)-C(54)	-75.7(3)
C(35)-C(36)-C(37)-C(38)	-55.8(3)
C(54)-C(36)-C(37)-C(38)	-178.8(2)
C(36)-C(37)-C(38)-C(43)	110.8(8)
C(36)-C(37)-C(38)-C(43B)	128.5(11)
C(36)-C(37)-C(38)-C(39)	-61.6(3)
C(43)-C(38)-C(39)-O(16)	-175.7(8)
C(43B)-C(38)-C(39)-O(16)	167.4(11)
C(37)-C(38)-C(39)-O(16)	-2.9(4)
C(43)-C(38)-C(39)-C(40)	3.8(8)
C(43B)-C(38)-C(39)-C(40)	-13.1(11)
C(37)-C(38)-C(39)-C(40)	176.6(2)
C(44)-N(4)-C(40)-C(41)	-0.5(5)
C(44)-N(4)-C(40)-C(39)	178.6(2)
O(16)-C(39)-C(40)-C(41)	-176.3(2)
C(38)-C(39)-C(40)-C(41)	4.2(4)
O(16)-C(39)-C(40)-N(4)	4.5(3)
C(38)-C(39)-C(40)-N(4)	-175.0(2)
N(4)-C(40)-C(41)-C(42)	172.3(10)
C(39)-C(40)-C(41)-C(42)	-6.8(10)
N(4)-C(40)-C(41)-C(42B)	-174.9(12)
C(39)-C(40)-C(41)-C(42B)	6.0(13)
C(40)-C(41)-C(42)-O(15)	-176.1(12)

C(40)-C(41)-C(42)-C(43)	2.2(19)
C(40)-C(41)-C(42B)-O(14B)	168.7(16)
C(40)-C(41)-C(42B)-C(43B)	-7(2)
C(55)-O(14)-C(43)-C(38)	162.7(15)
C(55)-O(14)-C(43)-C(42)	-13(2)
C(39)-C(38)-C(43)-O(14)	176.3(8)
C(37)-C(38)-C(43)-O(14)	3.9(14)
C(39)-C(38)-C(43)-C(42)	-8.4(16)
C(37)-C(38)-C(43)-C(42)	179.2(10)
O(15)-C(42)-C(43)-O(14)	-1(2)
C(41)-C(42)-C(43)-O(14)	-179.1(12)
O(15)-C(42)-C(43)-C(38)	-175.8(13)
C(41)-C(42)-C(43)-C(38)	6(2)
C(55B)-O(13B)-C(43B)-C(38)	-104(2)
C(55B)-O(13B)-C(43B)-C(42B)	73(2)
C(39)-C(38)-C(43B)-O(13B)	-171.1(13)
C(37)-C(38)-C(43B)-O(13B)	-1(2)
C(39)-C(38)-C(43B)-C(42B)	12(2)
C(37)-C(38)-C(43B)-C(42B)	-178.5(15)
O(14B)-C(42B)-C(43B)-O(13B)	5(3)
C(41)-C(42B)-C(43B)-O(13B)	-179.3(16)
O(14B)-C(42B)-C(43B)-C(38)	-177.9(19)
C(41)-C(42B)-C(43B)-C(38)	-2(3)
C(40)-N(4)-C(44)-O(17)	14.6(4)
C(40)-N(4)-C(44)-C(45)	-165.3(3)
O(17)-C(44)-C(45)-C(46)	-155.8(3)
N(4)-C(44)-C(45)-C(46)	24.1(4)
O(17)-C(44)-C(45)-C(56)	21.3(4)
N(4)-C(44)-C(45)-C(56)	-158.8(3)
C(44)-C(45)-C(46)-C(47)	-179.2(3)
C(56)-C(45)-C(46)-C(47)	3.9(5)
C(45)-C(46)-C(47)-C(48)	172.0(3)
C(46)-C(47)-C(48)-C(49)	-0.5(5)
C(57)-O(18)-C(49)-C(48)	72.8(3)
C(57)-O(18)-C(49)-C(50)	-164.3(2)
C(47)-C(48)-C(49)-O(18)	-106.7(3)

C(47)-C(48)-C(49)-C(50)	132.7(3)
C(58)-O(19)-C(50)-C(30)	88.0(3)
C(58)-O(19)-C(50)-C(49)	-147.7(2)
O(11)-C(30)-C(50)-O(19)	-84.7(2)
C(31)-C(30)-C(50)-O(19)	-149.4(2)
C(51)-C(30)-C(50)-O(19)	51.1(3)
O(11)-C(30)-C(50)-C(49)	155.14(19)
C(31)-C(30)-C(50)-C(49)	90.4(3)
C(51)-C(30)-C(50)-C(49)	-69.1(3)
O(18)-C(49)-C(50)-O(19)	-48.7(3)
C(48)-C(49)-C(50)-O(19)	73.4(3)
O(18)-C(49)-C(50)-C(30)	72.6(2)
C(48)-C(49)-C(50)-C(30)	-165.3(2)
C(50)-O(19)-C(58)-O(20)	26.2(4)
C(50)-O(19)-C(58)-N(3)	-156.2(2)

Symmetry transformations used to generate equivalent atoms:

Refinement details for **C**

Figure S2. The complete numbering scheme of **C** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S9. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **C**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2600(3)	5687(5)	5232(2)	43(1)
O(2)	4290(3)	4232(5)	7004(2)	45(1)
O(3)	2787(3)	4933(6)	8708(2)	57(1)
O(4)	4495(3)	8288(5)	6476(2)	44(1)
O(5)	1306(3)	7646(5)	4465(2)	45(1)
O(6)	2686(3)	7459(6)	3284(2)	55(1)
O(7)	6524(3)	6744(5)	4256(2)	43(1)
O(8)	7696(3)	7336(5)	8817(2)	46(1)
O(9)	8648(3)	4284(5)	9449(2)	44(1)
O(10)	9292(3)	1643(5)	9089(3)	58(1)
N(1)	5794(3)	7421(6)	5419(3)	40(1)
N(2)	10084(4)	3163(6)	10255(3)	46(1)
C(1)	6699(5)	3884(7)	9016(3)	42(1)
C(2)	5918(4)	3243(7)	8419(3)	43(1)
C(3)	4746(4)	3005(7)	8442(3)	43(1)
C(4)	4090(4)	4361(7)	7848(3)	42(1)
C(5)	2875(4)	4310(8)	7886(3)	44(1)
C(6)	2181(4)	5339(7)	7177(3)	43(1)
C(7)	2404(4)	7331(8)	7154(3)	43(1)
C(8)	2175(4)	8073(7)	6248(3)	42(1)
C(9)	2847(4)	7437(7)	5612(3)	40(1)
C(10)	4045(4)	7748(6)	5786(3)	40(1)
C(11)	4694(4)	7406(7)	5107(3)	39(1)
C(12)	4247(4)	7196(7)	4291(3)	44(1)
C(13)	3071(4)	7297(7)	4033(3)	44(1)
C(14)	2367(4)	7211(7)	4697(3)	41(1)
C(15)	6643(4)	7036(7)	5018(3)	38(1)
C(16)	7722(4)	6923(6)	5565(3)	38(1)
C(17)	7791(4)	6621(7)	6390(4)	44(1)
C(18)	8761(4)	6419(8)	7009(3)	44(1)
C(19)	8764(4)	6125(7)	7835(3)	44(1)

C(20)	7785(4)	5905(7)	8249(3)	43(1)
C(21)	7771(4)	4183(7)	8728(3)	42(1)
C(22)	6557(5)	4424(11)	9884(4)	62(2)
C(23)	4421(5)	1084(8)	8212(4)	49(1)
C(24)	1887(6)	4314(12)	9042(4)	72(2)
C(25)	1736(5)	8360(8)	7703(4)	49(1)
C(26)	701(5)	6520(9)	3828(4)	53(2)
C(27)	8665(4)	7019(7)	5107(3)	45(1)
C(28)	7277(6)	8898(8)	8392(4)	60(2)
C(29)	9353(5)	2907(7)	9560(3)	45(1)

Table S10. Bond lengths [Å] and angles [°] for **C**.

O(1)-C(14)	1.440(6)
O(1)-C(9)	1.471(6)
O(2)-C(4)	1.416(6)
O(2)-H(2)	0.8400
O(3)-C(24)	1.408(8)
O(3)-C(5)	1.418(7)
O(4)-C(10)	1.227(6)
O(5)-C(14)	1.366(6)
O(5)-C(26)	1.449(7)
O(6)-C(13)	1.224(6)
O(7)-C(15)	1.223(6)
O(8)-C(28)	1.424(7)
O(8)-C(20)	1.432(6)
O(9)-C(29)	1.363(7)
O(9)-C(21)	1.463(6)
O(10)-C(29)	1.214(7)
N(1)-C(15)	1.363(7)
N(1)-C(11)	1.392(6)
N(1)-H(1)	0.8800
N(2)-C(29)	1.338(7)
N(2)-H(2A)	0.8800

N(2)-H(2B)	0.8800
C(1)-C(2)	1.346(7)
C(1)-C(22)	1.487(8)
C(1)-C(21)	1.510(8)
C(2)-C(3)	1.491(8)
C(2)-H(2C)	0.9500
C(3)-C(23)	1.542(8)
C(3)-C(4)	1.545(7)
C(3)-H(3)	1.0000
C(4)-C(5)	1.540(8)
C(4)-H(4)	1.0000
C(5)-C(6)	1.529(8)
C(5)-H(5)	1.0000
C(6)-C(7)	1.538(8)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(25)	1.524(8)
C(7)-C(8)	1.539(7)
C(7)-H(7)	1.0000
C(8)-C(9)	1.504(7)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(14)	1.501(7)
C(9)-C(10)	1.505(7)
C(10)-C(11)	1.484(8)
C(11)-C(12)	1.346(7)
C(12)-C(13)	1.472(7)
C(12)-H(12)	0.9500
C(13)-C(14)	1.490(8)
C(15)-C(16)	1.493(7)
C(16)-C(17)	1.329(7)
C(16)-C(27)	1.494(8)
C(17)-C(18)	1.450(7)
C(17)-H(17)	0.9500
C(18)-C(19)	1.339(7)
C(18)-H(18)	0.9500

C(19)-C(20)	1.499(8)
C(19)-H(19)	0.9500
C(20)-C(21)	1.516(8)
C(20)-H(20)	1.0000
C(21)-H(21)	1.0000
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800

C(14)-O(1)-C(9)	62.0(3)
C(4)-O(2)-H(2)	109.5
C(24)-O(3)-C(5)	115.4(5)
C(14)-O(5)-C(26)	115.3(4)
C(28)-O(8)-C(20)	112.8(4)
C(29)-O(9)-C(21)	117.0(4)
C(15)-N(1)-C(11)	129.6(4)
C(15)-N(1)-H(1)	115.2
C(11)-N(1)-H(1)	115.2

C(29)-N(2)-H(2A)	120.0
C(29)-N(2)-H(2B)	120.0
H(2A)-N(2)-H(2B)	120.0
C(2)-C(1)-C(22)	125.4(6)
C(2)-C(1)-C(21)	115.0(5)
C(22)-C(1)-C(21)	119.4(5)
C(1)-C(2)-C(3)	129.6(5)
C(1)-C(2)-H(2C)	115.2
C(3)-C(2)-H(2C)	115.2
C(2)-C(3)-C(23)	109.5(5)
C(2)-C(3)-C(4)	109.6(4)
C(23)-C(3)-C(4)	112.8(4)
C(2)-C(3)-H(3)	108.3
C(23)-C(3)-H(3)	108.3
C(4)-C(3)-H(3)	108.3
O(2)-C(4)-C(5)	111.5(4)
O(2)-C(4)-C(3)	112.4(4)
C(5)-C(4)-C(3)	113.2(4)
O(2)-C(4)-H(4)	106.4
C(5)-C(4)-H(4)	106.4
C(3)-C(4)-H(4)	106.4
O(3)-C(5)-C(6)	113.4(5)
O(3)-C(5)-C(4)	104.8(4)
C(6)-C(5)-C(4)	114.1(4)
O(3)-C(5)-H(5)	108.1
C(6)-C(5)-H(5)	108.1
C(4)-C(5)-H(5)	108.1
C(5)-C(6)-C(7)	115.7(4)
C(5)-C(6)-H(6A)	108.3
C(7)-C(6)-H(6A)	108.3
C(5)-C(6)-H(6B)	108.3
C(7)-C(6)-H(6B)	108.3
H(6A)-C(6)-H(6B)	107.4
C(25)-C(7)-C(6)	111.7(5)
C(25)-C(7)-C(8)	108.6(5)
C(6)-C(7)-C(8)	112.0(4)

C(25)-C(7)-H(7)	108.1
C(6)-C(7)-H(7)	108.1
C(8)-C(7)-H(7)	108.1
C(9)-C(8)-C(7)	118.7(5)
C(9)-C(8)-H(8A)	107.6
C(7)-C(8)-H(8A)	107.6
C(9)-C(8)-H(8B)	107.6
C(7)-C(8)-H(8B)	107.6
H(8A)-C(8)-H(8B)	107.1
O(1)-C(9)-C(14)	58.0(3)
O(1)-C(9)-C(8)	117.7(4)
C(14)-C(9)-C(8)	121.0(5)
O(1)-C(9)-C(10)	110.8(4)
C(14)-C(9)-C(10)	115.6(4)
C(8)-C(9)-C(10)	118.6(4)
O(4)-C(10)-C(11)	119.2(5)
O(4)-C(10)-C(9)	121.5(5)
C(11)-C(10)-C(9)	119.3(4)
C(12)-C(11)-N(1)	125.7(5)
C(12)-C(11)-C(10)	122.6(5)
N(1)-C(11)-C(10)	111.6(4)
C(11)-C(12)-C(13)	120.6(5)
C(11)-C(12)-H(12)	119.7
C(13)-C(12)-H(12)	119.7
O(6)-C(13)-C(12)	120.0(5)
O(6)-C(13)-C(14)	121.1(5)
C(12)-C(13)-C(14)	118.9(4)
O(5)-C(14)-O(1)	116.8(4)
O(5)-C(14)-C(13)	117.5(4)
O(1)-C(14)-C(13)	111.8(4)
O(5)-C(14)-C(9)	117.3(4)
O(1)-C(14)-C(9)	60.0(3)
C(13)-C(14)-C(9)	119.9(4)
O(7)-C(15)-N(1)	121.9(4)
O(7)-C(15)-C(16)	121.8(5)
N(1)-C(15)-C(16)	116.3(4)

C(17)-C(16)-C(15)	120.0(5)
C(17)-C(16)-C(27)	124.5(5)
C(15)-C(16)-C(27)	115.3(4)
C(16)-C(17)-C(18)	127.6(5)
C(16)-C(17)-H(17)	116.2
C(18)-C(17)-H(17)	116.2
C(19)-C(18)-C(17)	124.1(5)
C(19)-C(18)-H(18)	118.0
C(17)-C(18)-H(18)	118.0
C(18)-C(19)-C(20)	125.7(5)
C(18)-C(19)-H(19)	117.2
C(20)-C(19)-H(19)	117.2
O(8)-C(20)-C(19)	110.6(4)
O(8)-C(20)-C(21)	108.8(4)
C(19)-C(20)-C(21)	113.3(4)
O(8)-C(20)-H(20)	108.0
C(19)-C(20)-H(20)	108.0
C(21)-C(20)-H(20)	108.0
O(9)-C(21)-C(1)	111.3(4)
O(9)-C(21)-C(20)	106.6(4)
C(1)-C(21)-C(20)	111.5(4)
O(9)-C(21)-H(21)	109.1
C(1)-C(21)-H(21)	109.1
C(20)-C(21)-H(21)	109.1
C(1)-C(22)-H(22A)	109.5
C(1)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(1)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(3)-C(23)-H(23A)	109.5
C(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5

O(3)-C(24)-H(24A)	109.5
O(3)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
O(3)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(7)-C(25)-H(25A)	109.5
C(7)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(7)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
O(5)-C(26)-H(26A)	109.5
O(5)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
O(5)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(16)-C(27)-H(27A)	109.5
C(16)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(16)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(8)-C(28)-H(28A)	109.5
O(8)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(8)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(10)-C(29)-N(2)	126.6(5)
O(10)-C(29)-O(9)	123.3(5)
N(2)-C(29)-O(9)	110.0(5)

Symmetry transformations used to generate equivalent atoms:

Table S11. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **C**. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
O(1)	46(2)	37(2)	42(2)	0(2)	-2(2)	-2(2)
O(2)	47(2)	47(2)	41(2)	-1(2)	5(2)	-2(2)
O(3)	51(2)	83(3)	37(2)	5(2)	7(2)	8(2)
O(4)	42(2)	46(2)	44(2)	-4(2)	1(2)	-1(2)
O(5)	38(2)	52(2)	43(2)	-1(2)	-3(2)	0(2)
O(6)	47(2)	73(3)	42(2)	7(2)	-4(2)	-2(2)
O(7)	39(2)	47(2)	39(2)	-2(2)	-1(2)	5(2)
O(8)	47(2)	37(2)	48(2)	0(2)	-8(2)	2(2)
O(9)	47(2)	36(2)	42(2)	0(2)	-13(2)	2(2)
O(10)	62(3)	44(2)	60(2)	-5(2)	-18(2)	10(2)
N(1)	36(2)	46(2)	36(2)	0(2)	-3(2)	-2(2)
N(2)	44(3)	43(2)	46(3)	7(2)	-9(2)	2(2)
C(1)	52(3)	33(3)	38(3)	6(2)	-5(2)	2(2)
C(2)	51(3)	41(3)	35(3)	-2(2)	-2(2)	1(3)
C(3)	43(3)	46(3)	36(3)	1(2)	-2(2)	-1(2)
C(4)	45(3)	38(3)	41(3)	1(2)	2(2)	-2(2)
C(5)	47(3)	41(3)	41(3)	3(2)	-1(2)	-3(2)
C(6)	41(3)	45(3)	42(3)	0(2)	-3(2)	-7(2)
C(7)	31(3)	53(3)	43(3)	-1(3)	-1(2)	-6(2)
C(8)	41(3)	40(3)	42(3)	1(2)	0(2)	-1(2)
C(9)	43(3)	35(3)	40(3)	5(2)	3(2)	0(2)
C(10)	47(3)	27(2)	42(3)	3(2)	-6(2)	3(2)
C(11)	39(3)	33(3)	43(3)	6(2)	-1(2)	2(2)
C(12)	45(3)	42(3)	43(3)	2(2)	5(2)	0(2)
C(13)	48(3)	36(3)	42(3)	1(2)	-4(2)	-1(2)
C(14)	43(3)	32(3)	45(3)	-1(2)	-6(2)	-1(2)
C(15)	37(3)	31(3)	45(3)	4(2)	-1(2)	0(2)
C(16)	39(3)	31(3)	43(3)	-3(2)	-2(2)	2(2)
C(17)	36(3)	41(3)	52(3)	-1(2)	1(2)	3(2)
C(18)	34(3)	45(3)	51(3)	3(2)	0(2)	3(2)
C(19)	38(3)	44(3)	44(3)	1(2)	-8(2)	5(2)

C(20)	45(3)	39(3)	39(3)	-2(2)	-11(2)	3(2)
C(21)	42(3)	41(3)	36(3)	0(2)	-10(2)	5(2)
C(22)	58(4)	88(5)	40(3)	-7(3)	3(3)	-15(4)
C(23)	42(3)	46(3)	58(3)	2(3)	1(3)	-3(3)
C(24)	61(4)	102(6)	55(4)	24(4)	22(3)	24(4)
C(25)	49(3)	53(3)	45(3)	-4(3)	4(2)	-4(3)
C(26)	46(3)	58(4)	51(3)	-8(3)	-6(3)	-4(3)
C(27)	49(3)	40(3)	43(3)	0(2)	-3(2)	1(2)
C(28)	66(4)	37(3)	71(4)	3(3)	-11(3)	7(3)
C(29)	48(3)	38(3)	45(3)	7(2)	-7(2)	-5(2)

Table S12. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **C**.

	x	y	z	U(eq)
H(2)	4068	3253	6800	68
H(1)	5967	7724	5954	48
H(2A)	10586	2366	10410	55
H(2B)	10063	4127	10557	55
H(2C)	6147	2889	7907	52
H(3)	4617	3236	9033	51
H(4)	4351	5552	8057	50
H(5)	2636	3051	7846	53
H(6A)	1414	5168	7231	52
H(6B)	2287	4825	6628	52
H(7)	3183	7530	7382	52
H(8A)	1411	7820	6017	50
H(8B)	2250	9371	6286	50
H(12)	4695	6980	3877	52
H(17)	7127	6526	6598	53
H(18)	9436	6500	6817	53
H(19)	9446	6048	8188	52

H(20)	7136	5930	7796	52
H(21)	7915	3189	8352	50
H(22A)	5790	4381	9933	94
H(22B)	6827	5627	9994	94
H(22C)	6959	3618	10298	94
H(23A)	4498	855	7622	74
H(23B)	3669	896	8284	74
H(23C)	4888	280	8585	74
H(24A)	1224	4718	8684	107
H(24B)	1911	4772	9617	107
H(24C)	1897	3023	9056	107
H(25A)	968	8196	7486	74
H(25B)	1916	9616	7689	74
H(25C)	1895	7931	8287	74
H(26A)	971	6668	3291	80
H(26B)	-63	6843	3751	80
H(26C)	787	5287	4010	80
H(27A)	8913	5823	5007	68
H(27B)	9250	7678	5449	68
H(27C)	8451	7617	4563	68
H(28A)	7757	9281	8002	91
H(28B)	7229	9828	8809	91
H(28C)	6559	8659	8074	91

Table S13. Torsion angles [°] for **C**.

C(22)-C(1)-C(2)-C(3)	3.8(10)
C(21)-C(1)-C(2)-C(3)	-171.4(5)
C(1)-C(2)-C(3)-C(23)	-126.6(6)
C(1)-C(2)-C(3)-C(4)	109.1(6)
C(2)-C(3)-C(4)-O(2)	57.2(6)
C(23)-C(3)-C(4)-O(2)	-65.0(6)
C(2)-C(3)-C(4)-C(5)	-175.4(4)
C(23)-C(3)-C(4)-C(5)	62.3(6)

C(24)-O(3)-C(5)-C(6)	82.0(6)
C(24)-O(3)-C(5)-C(4)	-152.9(5)
O(2)-C(4)-C(5)-O(3)	-164.3(4)
C(3)-C(4)-C(5)-O(3)	67.9(6)
O(2)-C(4)-C(5)-C(6)	-39.6(6)
C(3)-C(4)-C(5)-C(6)	-167.5(4)
O(3)-C(5)-C(6)-C(7)	58.2(6)
C(4)-C(5)-C(6)-C(7)	-61.7(7)
C(5)-C(6)-C(7)-C(25)	-88.2(6)
C(5)-C(6)-C(7)-C(8)	149.7(5)
C(25)-C(7)-C(8)-C(9)	172.0(5)
C(6)-C(7)-C(8)-C(9)	-64.2(6)
C(14)-O(1)-C(9)-C(8)	111.0(5)
C(14)-O(1)-C(9)-C(10)	-107.9(4)
C(7)-C(8)-C(9)-O(1)	77.4(6)
C(7)-C(8)-C(9)-C(14)	144.9(5)
C(7)-C(8)-C(9)-C(10)	-60.7(7)
O(1)-C(9)-C(10)-O(4)	-131.0(5)
C(14)-C(9)-C(10)-O(4)	165.6(5)
C(8)-C(9)-C(10)-O(4)	9.7(7)
O(1)-C(9)-C(10)-C(11)	49.5(6)
C(14)-C(9)-C(10)-C(11)	-14.0(7)
C(8)-C(9)-C(10)-C(11)	-169.8(5)
C(15)-N(1)-C(11)-C(12)	-8.5(9)
C(15)-N(1)-C(11)-C(10)	174.4(5)
O(4)-C(10)-C(11)-C(12)	-164.9(5)
C(9)-C(10)-C(11)-C(12)	14.7(7)
O(4)-C(10)-C(11)-N(1)	12.3(7)
C(9)-C(10)-C(11)-N(1)	-168.2(4)
N(1)-C(11)-C(12)-C(13)	-176.8(5)
C(10)-C(11)-C(12)-C(13)	0.0(8)
C(11)-C(12)-C(13)-O(6)	165.4(5)
C(11)-C(12)-C(13)-C(14)	-14.2(8)
C(26)-O(5)-C(14)-O(1)	-74.7(6)
C(26)-O(5)-C(14)-C(13)	62.6(6)
C(26)-O(5)-C(14)-C(9)	-143.0(5)

C(9)-O(1)-C(14)-O(5)	-107.5(5)
C(9)-O(1)-C(14)-C(13)	112.9(5)
O(6)-C(13)-C(14)-O(5)	-12.0(8)
C(12)-C(13)-C(14)-O(5)	167.6(5)
O(6)-C(13)-C(14)-O(1)	127.3(5)
C(12)-C(13)-C(14)-O(1)	-53.1(6)
O(6)-C(13)-C(14)-C(9)	-165.8(5)
C(12)-C(13)-C(14)-C(9)	13.8(7)
O(1)-C(9)-C(14)-O(5)	106.8(5)
C(8)-C(9)-C(14)-O(5)	1.5(7)
C(10)-C(9)-C(14)-O(5)	-153.7(4)
C(8)-C(9)-C(14)-O(1)	-105.3(5)
C(10)-C(9)-C(14)-O(1)	99.5(5)
O(1)-C(9)-C(14)-C(13)	-99.4(5)
C(8)-C(9)-C(14)-C(13)	155.4(5)
C(10)-C(9)-C(14)-C(13)	0.2(7)
C(11)-N(1)-C(15)-O(7)	6.4(9)
C(11)-N(1)-C(15)-C(16)	-171.4(5)
O(7)-C(15)-C(16)-C(17)	-156.0(5)
N(1)-C(15)-C(16)-C(17)	21.8(7)
O(7)-C(15)-C(16)-C(27)	19.0(7)
N(1)-C(15)-C(16)-C(27)	-163.2(4)
C(15)-C(16)-C(17)-C(18)	178.0(5)
C(27)-C(16)-C(17)-C(18)	3.5(9)
C(16)-C(17)-C(18)-C(19)	179.6(6)
C(17)-C(18)-C(19)-C(20)	1.9(9)
C(28)-O(8)-C(20)-C(19)	78.4(6)
C(28)-O(8)-C(20)-C(21)	-156.5(5)
C(18)-C(19)-C(20)-O(8)	-113.9(6)
C(18)-C(19)-C(20)-C(21)	123.6(6)
C(29)-O(9)-C(21)-C(1)	109.3(5)
C(29)-O(9)-C(21)-C(20)	-128.9(5)
C(2)-C(1)-C(21)-O(9)	-160.4(5)
C(22)-C(1)-C(21)-O(9)	24.1(7)
C(2)-C(1)-C(21)-C(20)	80.7(6)
C(22)-C(1)-C(21)-C(20)	-94.8(6)

O(8)-C(20)-C(21)-O(9)	-56.1(5)
C(19)-C(20)-C(21)-O(9)	67.4(5)
O(8)-C(20)-C(21)-C(1)	65.6(5)
C(19)-C(20)-C(21)-C(1)	-170.9(4)
C(21)-O(9)-C(29)-O(10)	1.0(8)
C(21)-O(9)-C(29)-N(2)	-178.1(4)

Symmetry transformations used to generate equivalent atoms:

Table S14. Hydrogen bonds for **C** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2)...O(7)#1	0.84	2.08	2.830(5)	148.9
N(2)-H(2A)...O(8)#2	0.88	2.31	3.008(6)	136.4
N(2)-H(2A)...O(9)#2	0.88	2.52	3.343(6)	155.1
N(2)-H(2B)...O(10)#3	0.88	2.11	2.902(6)	148.5

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1 #2 -x+2,y-1/2,-z+2 #3 -x+2,y+1/2,-z+2

Refinement details for **D**:

The model of atoms H1, H2A, and H2B were placed based on the Fourier difference map and freely refined.

Figure S3. The complete numbering scheme of **D** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S15. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **D**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	625(2)	8408(1)	3935(1)	44(1)
O(2)	5189(3)	6500(1)	3867(1)	38(1)

O(3)	5140(2)	6125(1)	2120(1)	36(1)
O(4)	1202(2)	6632(1)	4066(1)	39(1)
O(5)	2858(3)	8955(1)	3376(1)	47(1)
O(6)	3984(3)	9133(1)	4643(1)	49(1)
O(7)	2452(3)	7361(1)	6281(1)	40(1)
O(8)	2421(2)	4073(1)	4456(1)	37(1)
O(9)	5162(2)	3362(1)	4768(1)	32(1)
O(10)	7855(2)	3300(1)	5019(1)	42(1)
N(1)	1972(3)	6855(1)	5286(1)	36(1)
N(2)	6197(3)	2320(1)	5051(1)	40(1)
C(1)	5719(3)	4358(1)	3999(1)	31(1)
C(2)	6117(3)	5041(1)	3918(1)	35(1)
C(3)	6365(3)	5456(1)	3295(1)	34(1)
C(4)	5125(3)	6082(1)	3282(1)	33(1)
C(5)	5299(3)	6576(1)	2684(1)	33(1)
C(6)	4099(3)	7204(1)	2692(1)	35(1)
C(7)	2279(4)	7023(1)	2679(1)	35(1)
C(8)	1234(4)	7617(1)	2985(1)	38(1)
C(9)	1616(3)	7819(1)	3681(1)	35(1)
C(10)	1667(3)	7238(1)	4184(1)	35(1)
C(11)	2213(3)	7422(1)	4866(1)	34(1)
C(12)	2898(4)	8053(1)	5016(1)	37(1)
C(13)	3149(3)	8604(1)	4526(2)	39(1)
C(14)	2342(4)	8512(1)	3863(1)	38(1)
C(15)	2247(4)	6823(1)	5949(1)	36(1)
C(16)	2249(4)	6092(1)	6238(1)	37(1)
C(17)	2636(4)	5543(1)	5846(1)	39(1)
C(18)	2735(4)	4795(1)	6009(1)	42(1)
C(19)	3159(4)	4292(1)	5580(1)	42(1)
C(20)	3586(4)	4411(1)	4874(1)	35(1)
C(21)	5279(3)	4129(1)	4689(1)	32(1)
C(22)	5570(4)	3813(1)	3470(1)	43(1)
C(23)	8153(4)	5702(2)	3235(2)	41(1)
C(24)	5809(4)	6434(2)	1542(1)	45(1)
C(25)	1653(4)	6892(2)	1987(1)	46(1)
C(26)	2226(5)	9674(2)	3430(2)	56(1)

C(27)	1959(4)	6054(2)	6960(1)	46(1)
C(28)	917(4)	4457(2)	4420(2)	53(1)
C(29)	6534(3)	3008(1)	4957(1)	32(1)

Table S16. Bond lengths [Å] and angles [°] for **D**.

O(1)-C(14)	1.427(4)
O(1)-C(9)	1.466(3)
O(2)-C(4)	1.431(3)
O(2)-H(2)	0.96(4)
O(3)-C(24)	1.425(3)
O(3)-C(5)	1.436(3)
O(4)-C(10)	1.222(3)
O(5)-C(14)	1.363(3)
O(5)-C(26)	1.450(3)
O(6)-C(13)	1.228(3)
O(7)-C(15)	1.228(3)
O(8)-C(20)	1.428(3)
O(8)-C(28)	1.429(3)
O(9)-C(29)	1.362(3)
O(9)-C(21)	1.451(3)
O(10)-C(29)	1.220(3)
N(1)-C(15)	1.377(4)
N(1)-C(11)	1.379(3)
N(1)-H(1)	0.90(4)
N(2)-C(29)	1.333(4)
N(2)-H(2A)	0.93(4)
N(2)-H(2B)	0.89(4)
C(1)-C(2)	1.333(4)
C(1)-C(22)	1.493(4)
C(1)-C(21)	1.519(4)
C(2)-C(3)	1.506(4)
C(2)-H(2C)	0.9500
C(3)-C(23)	1.540(4)

C(3)-C(4)	1.553(4)
C(3)-H(3)	1.0000
C(4)-C(5)	1.540(4)
C(4)-H(4)	1.0000
C(5)-C(6)	1.533(4)
C(5)-H(5)	1.0000
C(6)-C(7)	1.529(4)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(25)	1.524(4)
C(7)-C(8)	1.538(4)
C(7)-H(7)	1.0000
C(8)-C(9)	1.507(4)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(14)	1.478(4)
C(9)-C(10)	1.499(4)
C(10)-C(11)	1.505(4)
C(11)-C(12)	1.346(4)
C(12)-C(13)	1.454(4)
C(12)-H(12)	0.9500
C(13)-C(14)	1.518(4)
C(15)-C(16)	1.492(4)
C(16)-C(17)	1.345(4)
C(16)-C(27)	1.497(4)
C(17)-C(18)	1.444(4)
C(17)-H(17)	0.9500
C(18)-C(19)	1.334(4)
C(18)-H(18)	0.9500
C(19)-C(20)	1.502(4)
C(19)-H(19)	0.9500
C(20)-C(21)	1.531(4)
C(20)-H(20)	1.0000
C(21)-H(21)	1.0000
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800

C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800
C(26)-H(26C)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800

C(14)-O(1)-C(9)	61.41(17)
C(4)-O(2)-H(2)	105(2)
C(24)-O(3)-C(5)	113.0(2)
C(14)-O(5)-C(26)	113.6(2)
C(20)-O(8)-C(28)	112.5(2)
C(29)-O(9)-C(21)	117.5(2)
C(15)-N(1)-C(11)	128.6(2)
C(15)-N(1)-H(1)	119(2)
C(11)-N(1)-H(1)	112(2)
C(29)-N(2)-H(2A)	121(2)
C(29)-N(2)-H(2B)	116(3)
H(2A)-N(2)-H(2B)	123(3)
C(2)-C(1)-C(22)	126.0(2)
C(2)-C(1)-C(21)	116.5(2)
C(22)-C(1)-C(21)	117.4(2)
C(1)-C(2)-C(3)	129.4(2)

C(1)-C(2)-H(2C)	115.3
C(3)-C(2)-H(2C)	115.3
C(2)-C(3)-C(23)	110.5(2)
C(2)-C(3)-C(4)	108.5(2)
C(23)-C(3)-C(4)	113.2(2)
C(2)-C(3)-H(3)	108.2
C(23)-C(3)-H(3)	108.2
C(4)-C(3)-H(3)	108.2
O(2)-C(4)-C(5)	109.29(19)
O(2)-C(4)-C(3)	112.1(2)
C(5)-C(4)-C(3)	114.1(2)
O(2)-C(4)-H(4)	107.0
C(5)-C(4)-H(4)	107.0
C(3)-C(4)-H(4)	107.0
O(3)-C(5)-C(6)	113.8(2)
O(3)-C(5)-C(4)	105.91(19)
C(6)-C(5)-C(4)	113.2(2)
O(3)-C(5)-H(5)	107.9
C(6)-C(5)-H(5)	107.9
C(4)-C(5)-H(5)	107.9
C(7)-C(6)-C(5)	117.0(2)
C(7)-C(6)-H(6A)	108.0
C(5)-C(6)-H(6A)	108.0
C(7)-C(6)-H(6B)	108.0
C(5)-C(6)-H(6B)	108.0
H(6A)-C(6)-H(6B)	107.3
C(25)-C(7)-C(6)	112.4(2)
C(25)-C(7)-C(8)	107.9(2)
C(6)-C(7)-C(8)	112.0(2)
C(25)-C(7)-H(7)	108.1
C(6)-C(7)-H(7)	108.1
C(8)-C(7)-H(7)	108.1
C(9)-C(8)-C(7)	116.8(2)
C(9)-C(8)-H(8A)	108.1
C(7)-C(8)-H(8A)	108.1
C(9)-C(8)-H(8B)	108.1

C(7)-C(8)-H(8B)	108.1
H(8A)-C(8)-H(8B)	107.3
O(1)-C(9)-C(14)	58.00(17)
O(1)-C(9)-C(10)	108.7(2)
C(14)-C(9)-C(10)	117.2(2)
O(1)-C(9)-C(8)	114.2(2)
C(14)-C(9)-C(8)	122.9(2)
C(10)-C(9)-C(8)	118.1(2)
O(4)-C(10)-C(9)	122.2(2)
O(4)-C(10)-C(11)	119.2(2)
C(9)-C(10)-C(11)	118.5(2)
C(12)-C(11)-N(1)	126.6(2)
C(12)-C(11)-C(10)	122.4(2)
N(1)-C(11)-C(10)	110.9(2)
C(11)-C(12)-C(13)	121.9(2)
C(11)-C(12)-H(12)	119.0
C(13)-C(12)-H(12)	119.0
O(6)-C(13)-C(12)	121.3(3)
O(6)-C(13)-C(14)	120.5(3)
C(12)-C(13)-C(14)	118.2(2)
O(5)-C(14)-O(1)	117.6(2)
O(5)-C(14)-C(9)	118.5(2)
O(1)-C(14)-C(9)	60.59(17)
O(5)-C(14)-C(13)	116.6(2)
O(1)-C(14)-C(13)	110.6(2)
C(9)-C(14)-C(13)	120.0(2)
O(7)-C(15)-N(1)	122.0(2)
O(7)-C(15)-C(16)	122.5(2)
N(1)-C(15)-C(16)	115.5(2)
C(17)-C(16)-C(15)	117.9(2)
C(17)-C(16)-C(27)	126.1(2)
C(15)-C(16)-C(27)	115.8(2)
C(16)-C(17)-C(18)	128.3(3)
C(16)-C(17)-H(17)	115.8
C(18)-C(17)-H(17)	115.8
C(19)-C(18)-C(17)	123.3(3)

C(19)-C(18)-H(18)	118.4
C(17)-C(18)-H(18)	118.4
C(18)-C(19)-C(20)	126.0(2)
C(18)-C(19)-H(19)	117.0
C(20)-C(19)-H(19)	117.0
O(8)-C(20)-C(19)	110.7(2)
O(8)-C(20)-C(21)	107.7(2)
C(19)-C(20)-C(21)	113.3(2)
O(8)-C(20)-H(20)	108.3
C(19)-C(20)-H(20)	108.3
C(21)-C(20)-H(20)	108.3
O(9)-C(21)-C(1)	113.5(2)
O(9)-C(21)-C(20)	104.8(2)
C(1)-C(21)-C(20)	110.2(2)
O(9)-C(21)-H(21)	109.4
C(1)-C(21)-H(21)	109.4
C(20)-C(21)-H(21)	109.4
C(1)-C(22)-H(22A)	109.5
C(1)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(1)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(3)-C(23)-H(23A)	109.5
C(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(3)-C(24)-H(24A)	109.5
O(3)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
O(3)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(7)-C(25)-H(25A)	109.5

C(7)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(7)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
O(5)-C(26)-H(26A)	109.5
O(5)-C(26)-H(26B)	109.5
H(26A)-C(26)-H(26B)	109.5
O(5)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5
C(16)-C(27)-H(27A)	109.5
C(16)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(16)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(8)-C(28)-H(28A)	109.5
O(8)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(8)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(10)-C(29)-N(2)	127.2(3)
O(10)-C(29)-O(9)	122.8(2)
N(2)-C(29)-O(9)	110.1(2)

Symmetry transformations used to generate equivalent atoms:

Table S17. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **D**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
O(1)	45(1)	32(1)	54(1)	-3(1)	6(1)	3(1)

O(2)	50(1)	28(1)	36(1)	-1(1)	4(1)	-1(1)
O(3)	49(1)	27(1)	32(1)	-1(1)	3(1)	1(1)
O(4)	50(1)	27(1)	40(1)	-3(1)	3(1)	-5(1)
O(5)	64(1)	29(1)	48(1)	3(1)	14(1)	-2(1)
O(6)	54(1)	33(1)	60(1)	-2(1)	0(1)	-9(1)
O(7)	52(1)	26(1)	42(1)	-5(1)	-1(1)	4(1)
O(8)	38(1)	24(1)	49(1)	4(1)	2(1)	4(1)
O(9)	39(1)	15(1)	43(1)	3(1)	-2(1)	0(1)
O(10)	40(1)	26(1)	59(1)	3(1)	-7(1)	-2(1)
N(1)	50(1)	21(1)	37(1)	-3(1)	-1(1)	-1(1)
N(2)	40(2)	22(1)	58(2)	4(1)	-5(1)	4(1)
C(1)	33(1)	23(1)	36(1)	-2(1)	-1(1)	3(1)
C(2)	43(2)	25(1)	37(1)	-1(1)	-4(1)	-1(1)
C(3)	42(2)	24(1)	37(1)	-1(1)	-1(1)	-4(1)
C(4)	41(2)	24(1)	34(1)	1(1)	0(1)	-4(1)
C(5)	40(2)	24(1)	34(1)	-1(1)	0(1)	-2(1)
C(6)	47(2)	22(1)	35(1)	1(1)	1(1)	-1(1)
C(7)	44(2)	24(1)	37(1)	-1(1)	0(1)	1(1)
C(8)	45(2)	30(1)	38(1)	1(1)	0(1)	4(1)
C(9)	41(2)	25(1)	40(1)	-2(1)	4(1)	4(1)
C(10)	38(1)	29(1)	39(1)	-3(1)	5(1)	1(1)
C(11)	41(2)	26(1)	36(1)	-2(1)	3(1)	1(1)
C(12)	45(2)	28(1)	37(1)	-4(1)	1(1)	0(1)
C(13)	40(2)	27(1)	51(2)	-4(1)	6(1)	-3(1)
C(14)	44(2)	27(1)	44(2)	0(1)	9(1)	0(1)
C(15)	40(1)	26(1)	42(1)	-4(1)	3(1)	3(1)
C(16)	43(2)	26(1)	42(1)	-1(1)	3(1)	2(1)
C(17)	49(2)	28(1)	40(1)	1(1)	5(1)	2(1)
C(18)	57(2)	29(1)	40(1)	2(1)	9(1)	3(1)
C(19)	62(2)	22(1)	42(1)	5(1)	9(1)	4(1)
C(20)	48(2)	16(1)	40(1)	2(1)	7(1)	2(1)
C(21)	44(2)	14(1)	38(1)	1(1)	-2(1)	-2(1)
C(22)	65(2)	25(1)	39(1)	-4(1)	2(1)	-4(1)
C(23)	43(2)	31(1)	48(2)	3(1)	3(1)	0(1)
C(24)	59(2)	42(2)	36(2)	3(1)	5(1)	3(1)
C(25)	54(2)	44(2)	41(2)	-9(1)	-5(1)	4(1)

C(26)	80(2)	26(2)	61(2)	6(1)	11(2)	2(2)
C(27)	66(2)	31(2)	42(2)	1(1)	5(1)	8(1)
C(28)	45(2)	40(2)	75(2)	9(2)	1(2)	14(1)
C(29)	38(2)	23(1)	36(1)	0(1)	-1(1)	4(1)

Table S18. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **D**.

	x	y	z	U(eq)
H(2)	6190(50)	6770(20)	3834(18)	64(11)
H(1)	1630(40)	6464(19)	5073(17)	54(10)
H(2A)	5140(50)	2145(18)	4996(16)	47(9)
H(2B)	7020(50)	2060(20)	5202(19)	66(11)
H(2C)	6267	5305	4310	42
H(3)	6118	5134	2919	41
H(4)	4009	5867	3260	39
H(5)	6432	6775	2686	40
H(6A)	4316	7489	3090	42
H(6B)	4342	7511	2311	42
H(7)	2109	6578	2938	42
H(8A)	1346	8049	2710	45
H(8B)	75	7467	2964	45
H(12)	3226	8141	5454	44
H(17)	2875	5661	5404	47
H(18)	2486	4654	6444	51
H(19)	3195	3815	5735	50
H(20)	3559	4935	4785	42
H(21)	6107	4322	5003	39
H(22A)	6275	3406	3571	65
H(22B)	5905	4024	3052	65
H(22C)	4434	3653	3439	65
H(23A)	8420	6020	3600	61

H(23B)	8301	5957	2821	61
H(23C)	8876	5286	3245	61
H(24A)	5735	6091	1182	68
H(24B)	6956	6557	1618	68
H(24C)	5196	6865	1430	68
H(25A)	1769	7329	1728	69
H(25B)	499	6755	2004	69
H(25C)	2288	6509	1783	69
H(26A)	2838	9990	3137	83
H(26B)	2344	9841	3882	83
H(26C)	1069	9679	3308	83
H(27A)	2820	6316	7190	69
H(27B)	1971	5554	7101	69
H(27C)	895	6265	7063	69
H(28A)	161	4206	4129	80
H(28B)	1123	4937	4250	80
H(28C)	435	4491	4858	80

Table S19. Torsion angles [°] for **D**.

C(22)-C(1)-C(2)-C(3)	6.2(5)
C(21)-C(1)-C(2)-C(3)	-169.9(3)
C(1)-C(2)-C(3)-C(23)	-115.2(3)
C(1)-C(2)-C(3)-C(4)	120.1(3)
C(2)-C(3)-C(4)-O(2)	52.2(3)
C(23)-C(3)-C(4)-O(2)	-70.8(3)
C(2)-C(3)-C(4)-C(5)	177.1(2)
C(23)-C(3)-C(4)-C(5)	54.0(3)
C(24)-O(3)-C(5)-C(6)	75.3(3)
C(24)-O(3)-C(5)-C(4)	-159.8(2)
O(2)-C(4)-C(5)-O(3)	-177.1(2)
C(3)-C(4)-C(5)-O(3)	56.5(3)
O(2)-C(4)-C(5)-C(6)	-51.8(3)
C(3)-C(4)-C(5)-C(6)	-178.2(2)

O(3)-C(5)-C(6)-C(7)	59.2(3)
C(4)-C(5)-C(6)-C(7)	-61.7(3)
C(5)-C(6)-C(7)-C(25)	-83.7(3)
C(5)-C(6)-C(7)-C(8)	154.7(2)
C(25)-C(7)-C(8)-C(9)	178.3(2)
C(6)-C(7)-C(8)-C(9)	-57.5(3)
C(14)-O(1)-C(9)-C(10)	110.9(3)
C(14)-O(1)-C(9)-C(8)	-114.9(3)
C(7)-C(8)-C(9)-O(1)	177.5(2)
C(7)-C(8)-C(9)-C(14)	111.2(3)
C(7)-C(8)-C(9)-C(10)	-52.8(3)
O(1)-C(9)-C(10)-O(4)	122.2(3)
C(14)-C(9)-C(10)-O(4)	-174.9(3)
C(8)-C(9)-C(10)-O(4)	-10.0(4)
O(1)-C(9)-C(10)-C(11)	-53.9(3)
C(14)-C(9)-C(10)-C(11)	9.0(4)
C(8)-C(9)-C(10)-C(11)	173.9(2)
C(15)-N(1)-C(11)-C(12)	5.6(5)
C(15)-N(1)-C(11)-C(10)	-177.0(3)
O(4)-C(10)-C(11)-C(12)	172.9(3)
C(9)-C(10)-C(11)-C(12)	-10.9(4)
O(4)-C(10)-C(11)-N(1)	-4.7(4)
C(9)-C(10)-C(11)-N(1)	171.5(2)
N(1)-C(11)-C(12)-C(13)	177.6(3)
C(10)-C(11)-C(12)-C(13)	0.3(4)
C(11)-C(12)-C(13)-O(6)	-169.2(3)
C(11)-C(12)-C(13)-C(14)	11.1(4)
C(26)-O(5)-C(14)-O(1)	59.0(3)
C(26)-O(5)-C(14)-C(9)	128.7(3)
C(26)-O(5)-C(14)-C(13)	-76.0(3)
C(9)-O(1)-C(14)-O(5)	108.8(3)
C(9)-O(1)-C(14)-C(13)	-113.7(2)
O(1)-C(9)-C(14)-O(5)	-107.5(3)
C(10)-C(9)-C(14)-O(5)	156.5(2)
C(8)-C(9)-C(14)-O(5)	-7.6(4)
C(10)-C(9)-C(14)-O(1)	-96.0(3)

C(8)-C(9)-C(14)-O(1)	99.9(3)
O(1)-C(9)-C(14)-C(13)	98.1(3)
C(10)-C(9)-C(14)-C(13)	2.1(4)
C(8)-C(9)-C(14)-C(13)	-162.0(3)
O(6)-C(13)-C(14)-O(5)	13.2(4)
C(12)-C(13)-C(14)-O(5)	-167.1(2)
O(6)-C(13)-C(14)-O(1)	-124.8(3)
C(12)-C(13)-C(14)-O(1)	54.9(3)
O(6)-C(13)-C(14)-C(9)	168.1(3)
C(12)-C(13)-C(14)-C(9)	-12.2(4)
C(11)-N(1)-C(15)-O(7)	15.1(5)
C(11)-N(1)-C(15)-C(16)	-165.9(3)
O(7)-C(15)-C(16)-C(17)	-155.2(3)
N(1)-C(15)-C(16)-C(17)	25.9(4)
O(7)-C(15)-C(16)-C(27)	19.5(4)
N(1)-C(15)-C(16)-C(27)	-159.4(3)
C(15)-C(16)-C(17)-C(18)	179.5(3)
C(27)-C(16)-C(17)-C(18)	5.3(6)
C(16)-C(17)-C(18)-C(19)	-178.9(3)
C(17)-C(18)-C(19)-C(20)	-0.3(5)
C(28)-O(8)-C(20)-C(19)	75.8(3)
C(28)-O(8)-C(20)-C(21)	-159.8(2)
C(18)-C(19)-C(20)-O(8)	-115.5(3)
C(18)-C(19)-C(20)-C(21)	123.4(3)
C(29)-O(9)-C(21)-C(1)	91.6(3)
C(29)-O(9)-C(21)-C(20)	-148.1(2)
C(2)-C(1)-C(21)-O(9)	-168.9(2)
C(22)-C(1)-C(21)-O(9)	14.6(3)
C(2)-C(1)-C(21)-C(20)	73.9(3)
C(22)-C(1)-C(21)-C(20)	-102.6(3)
O(8)-C(20)-C(21)-O(9)	-57.4(2)
C(19)-C(20)-C(21)-O(9)	65.4(3)
O(8)-C(20)-C(21)-C(1)	65.1(2)
C(19)-C(20)-C(21)-C(1)	-172.1(2)
C(21)-O(9)-C(29)-O(10)	-4.9(4)
C(21)-O(9)-C(29)-N(2)	175.6(2)

Symmetry transformations used to generate equivalent atoms:

Table S20. Hydrogen bonds for **D** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2)...O(7)#1	0.96(4)	1.95(4)	2.844(3)	154(3)
N(1)-H(1)...O(4)	0.90(4)	2.11(3)	2.606(3)	114(3)
N(1)-H(1)...O(6)#2	0.90(4)	2.51(4)	3.073(3)	122(3)
N(2)-H(2A)...O(10)#3	0.93(4)	2.05(4)	2.977(3)	173(3)
N(2)-H(2B)...O(8)#4	0.89(4)	2.25(4)	2.974(3)	138(3)

Symmetry transformations used to generate equivalent atoms:

#1 $x+1/2, -y+3/2, -z+1$ #2 $x-1/2, -y+3/2, -z+1$ #3 $x-1/2, -y+1/2, -z+1$

#4 $x+1/2, -y+1/2, -z+1$

Refinement details for **17-A**:

The methylene alkene group is disordered over three positions. The site occupancies were constrained to be identical, and all chemically identical C-C bonds were restrained to be similar. The thermal parameters were restrained to behave as a rigid, isotropic group with similar values to those in the same disordered group. The program SQUEEZE⁸ was used to compensate for the contribution of disordered solvents contained in voids within the crystal lattice from the diffraction intensities. This procedure was applied to the data file and the submitted model is based on the solvent removed data. Based on the total electron density found in the voids ($85 \text{ e}/\text{\AA}^3$), it is likely that 2 dichloromethane solvent molecules are present in the unit cell. See "_platon_squeeze_details" in the .cif for more information.

Figure S4. The complete numbering scheme of **17-A** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S21. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **17-A**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	9252(4)	7722(7)	7745(4)	55(2)
O(2)	7270(3)	5638(7)	5541(4)	50(1)
O(3)	9177(4)	5951(7)	4544(4)	55(2)
O(4)	3850(5)	3193(9)	2576(5)	77(2)
O(5)	6648(4)	1432(7)	5222(4)	54(1)
O(6)	3787(4)	2870(7)	5752(4)	58(2)
O(7)	8331(4)	2539(6)	8250(4)	55(2)
O(8)	9075(4)	5169(6)	9277(4)	51(2)
O(9)	9007(4)	7894(7)	9724(4)	64(2)
N(1)	5238(4)	2434(8)	5681(5)	53(2)
N(2)	10126(6)	6113(9)	10434(5)	73(3)
N(26)	5437(7)	2816(13)	2156(6)	87(3)
C(1)	9020(5)	5907(9)	7746(6)	48(2)
C(2)	8557(5)	7025(9)	6977(6)	49(2)
C(3)	8733(5)	7084(9)	6097(6)	45(2)
C(4)	8186(5)	5708(9)	5466(6)	47(2)
C(5)	8224(5)	5926(10)	4516(6)	53(2)
C(6)	7669(6)	4629(10)	3875(6)	51(2)
C(7)	7864(5)	2734(9)	4082(6)	49(2)
C(8)	7079(6)	1591(11)	3602(7)	58(2)
C(9)	6150(6)	2059(9)	3692(6)	51(2)
C(10)	5429(7)	2601(12)	3016(6)	63(2)
C(11)	4512(6)	2941(11)	3210(7)	63(2)
C(12)	4430(5)	2916(10)	4107(6)	53(2)
C(13)	5172(5)	2487(9)	4782(6)	49(2)
C(14)	6043(5)	1929(9)	4571(6)	47(2)
C(15)	4582(5)	2771(9)	6118(6)	46(2)
C(16)	4921(5)	2991(10)	7113(6)	50(2)
C(17)	5785(6)	3457(10)	7453(6)	52(2)
C(18)	6248(6)	3709(11)	8376(6)	56(2)
C(19)	7141(6)	3998(10)	8690(6)	53(2)

C(20)	7813(5)	4076(8)	8158(6)	47(2)
C(21)	8479(5)	5563(8)	8403(5)	47(2)
C(22)	9742(6)	4697(11)	7663(7)	62(2)
C(23)	8551(6)	8917(10)	5722(7)	61(2)
C(24)	9379(7)	6728(12)	3791(7)	65(2)
C(25)	8743(6)	2182(11)	3868(7)	66(2)
C(27)	4260(6)	2719(15)	7624(7)	70(3)
C(28)	7842(7)	1112(10)	7794(7)	68(3)
C(29)	9381(6)	6509(10)	9819(6)	55(2)
C(30)	6142(17)	2950(40)	1621(17)	194(9)
C(31)	7000(50)	3810(150)	1380(80)	206(19)
C(32)	7840(30)	3420(80)	1350(40)	115(15)
C(33)	7060(30)	3070(90)	1330(40)	132(15)
C(34)	7750(40)	4470(150)	1310(70)	210(30)
C(35)	6850(60)	2230(140)	1130(70)	200(20)
C(36)	7560(40)	1640(100)	980(50)	190(30)

Table 22. Bond lengths [Å] and angles [°] for **17-A**.

O(1)-C(1)	1.470(9)
O(1)-C(2)	1.479(9)
O(2)-C(4)	1.432(10)
O(2)-H(2)	0.8400
O(3)-C(24)	1.421(11)
O(3)-C(5)	1.443(10)
O(4)-C(11)	1.228(11)
O(5)-C(14)	1.241(9)
O(6)-C(15)	1.200(8)
O(7)-C(28)	1.429(9)
O(7)-C(20)	1.430(8)
O(8)-C(29)	1.353(9)
O(8)-C(21)	1.456(9)
O(9)-C(29)	1.220(10)
N(1)-C(15)	1.371(11)

N(1)-C(13)	1.373(11)
N(1)-H(1)	0.8800
N(2)-C(29)	1.317(11)
N(2)-H(2A)	0.8800
N(2)-H(2B)	0.8800
N(26)-C(10)	1.349(13)
N(26)-C(30)	1.52(2)
N(26)-H(26)	0.8800
C(1)-C(22)	1.485(12)
C(1)-C(21)	1.492(13)
C(1)-C(2)	1.501(11)
C(2)-C(3)	1.459(12)
C(2)-H(2C)	1.0000
C(3)-C(4)	1.550(11)
C(3)-C(23)	1.552(11)
C(3)-H(3)	1.0000
C(4)-C(5)	1.498(13)
C(4)-H(4)	1.0000
C(5)-C(6)	1.519(12)
C(5)-H(5)	1.0000
C(6)-C(7)	1.536(10)
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(25)	1.525(12)
C(7)-C(8)	1.527(12)
C(7)-H(7)	1.0000
C(8)-C(9)	1.504(13)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.376(12)
C(9)-C(14)	1.418(12)
C(10)-C(11)	1.527(14)
C(11)-C(12)	1.430(13)
C(12)-C(13)	1.370(11)
C(12)-H(12)	0.9500
C(13)-C(14)	1.512(12)

C(15)-C(16)	1.506(12)
C(16)-C(17)	1.336(11)
C(16)-C(27)	1.451(13)
C(17)-C(18)	1.436(13)
C(17)-H(17)	0.9500
C(18)-C(19)	1.340(12)
C(18)-H(18)	0.9500
C(19)-C(20)	1.475(13)
C(19)-H(19)	0.9500
C(20)-C(21)	1.530(10)
C(20)-H(20)	1.0000
C(21)-H(21)	1.0000
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(30)-C(33)	1.58(2)
C(30)-C(35)	1.58(2)
C(30)-C(31)	1.59(2)
C(30)-H(30A)	0.9900
C(30)-H(30B)	0.9900
C(30)-H(30E)	0.9900

C(30)-H(30F)	0.9900
C(30)-H(30C)	0.9900
C(30)-H(30D)	0.9900
C(31)-C(32)	1.33(9)
C(31)-H(31)	0.9500
C(32)-H(32A)	0.9500
C(32)-H(32B)	0.9500
C(33)-C(34)	1.52(8)
C(33)-H(33)	0.9500
C(34)-H(34A)	0.9500
C(34)-H(34B)	0.9500
C(35)-C(36)	1.26(3)
C(35)-H(35)	0.9500
C(36)-H(36A)	0.9500
C(36)-H(36B)	0.9500

C(1)-O(1)-C(2)	61.2(5)
C(4)-O(2)-H(2)	109.5
C(24)-O(3)-C(5)	114.5(6)
C(28)-O(7)-C(20)	114.2(6)
C(29)-O(8)-C(21)	116.4(6)
C(15)-N(1)-C(13)	128.8(7)
C(15)-N(1)-H(1)	115.6
C(13)-N(1)-H(1)	115.6
C(29)-N(2)-H(2A)	120.0
C(29)-N(2)-H(2B)	120.0
H(2A)-N(2)-H(2B)	120.0
C(10)-N(26)-C(30)	137.5(13)
C(10)-N(26)-H(26)	111.2
C(30)-N(26)-H(26)	111.2
O(1)-C(1)-C(22)	115.9(7)
O(1)-C(1)-C(21)	110.6(6)
C(22)-C(1)-C(21)	119.7(7)
O(1)-C(1)-C(2)	59.7(5)
C(22)-C(1)-C(2)	120.8(8)
C(21)-C(1)-C(2)	114.8(7)

C(3)-C(2)-O(1)	118.3(6)
C(3)-C(2)-C(1)	126.8(7)
O(1)-C(2)-C(1)	59.1(5)
C(3)-C(2)-H(2C)	113.7
O(1)-C(2)-H(2C)	113.7
C(1)-C(2)-H(2C)	113.7
C(2)-C(3)-C(4)	111.7(6)
C(2)-C(3)-C(23)	108.8(7)
C(4)-C(3)-C(23)	113.4(7)
C(2)-C(3)-H(3)	107.6
C(4)-C(3)-H(3)	107.6
C(23)-C(3)-H(3)	107.6
O(2)-C(4)-C(5)	111.8(6)
O(2)-C(4)-C(3)	110.6(6)
C(5)-C(4)-C(3)	113.0(7)
O(2)-C(4)-H(4)	107.0
C(5)-C(4)-H(4)	107.0
C(3)-C(4)-H(4)	107.0
O(3)-C(5)-C(4)	105.5(6)
O(3)-C(5)-C(6)	114.4(7)
C(4)-C(5)-C(6)	114.2(7)
O(3)-C(5)-H(5)	107.4
C(4)-C(5)-H(5)	107.4
C(6)-C(5)-H(5)	107.4
C(5)-C(6)-C(7)	118.0(7)
C(5)-C(6)-H(6A)	107.8
C(7)-C(6)-H(6A)	107.8
C(5)-C(6)-H(6B)	107.8
C(7)-C(6)-H(6B)	107.8
H(6A)-C(6)-H(6B)	107.1
C(25)-C(7)-C(8)	110.4(7)
C(25)-C(7)-C(6)	111.3(7)
C(8)-C(7)-C(6)	112.6(7)
C(25)-C(7)-H(7)	107.5
C(8)-C(7)-H(7)	107.5
C(6)-C(7)-H(7)	107.5

C(9)-C(8)-C(7)	116.6(7)
C(9)-C(8)-H(8A)	108.1
C(7)-C(8)-H(8A)	108.1
C(9)-C(8)-H(8B)	108.1
C(7)-C(8)-H(8B)	108.1
H(8A)-C(8)-H(8B)	107.3
C(10)-C(9)-C(14)	119.1(8)
C(10)-C(9)-C(8)	126.2(9)
C(14)-C(9)-C(8)	114.8(7)
N(26)-C(10)-C(9)	125.6(10)
N(26)-C(10)-C(11)	114.6(8)
C(9)-C(10)-C(11)	119.7(9)
O(4)-C(11)-C(12)	121.3(9)
O(4)-C(11)-C(10)	118.3(9)
C(12)-C(11)-C(10)	120.3(8)
C(13)-C(12)-C(11)	119.0(8)
C(13)-C(12)-H(12)	120.5
C(11)-C(12)-H(12)	120.5
C(12)-C(13)-N(1)	127.8(8)
C(12)-C(13)-C(14)	120.2(8)
N(1)-C(13)-C(14)	112.0(7)
O(5)-C(14)-C(9)	123.9(8)
O(5)-C(14)-C(13)	115.1(8)
C(9)-C(14)-C(13)	121.0(7)
O(6)-C(15)-N(1)	123.7(8)
O(6)-C(15)-C(16)	120.9(7)
N(1)-C(15)-C(16)	115.4(6)
C(17)-C(16)-C(27)	125.3(8)
C(17)-C(16)-C(15)	118.5(8)
C(27)-C(16)-C(15)	116.2(7)
C(16)-C(17)-C(18)	127.6(9)
C(16)-C(17)-H(17)	116.2
C(18)-C(17)-H(17)	116.2
C(19)-C(18)-C(17)	125.1(9)
C(19)-C(18)-H(18)	117.4
C(17)-C(18)-H(18)	117.4

C(18)-C(19)-C(20)	126.2(9)
C(18)-C(19)-H(19)	116.9
C(20)-C(19)-H(19)	116.9
O(7)-C(20)-C(19)	110.8(6)
O(7)-C(20)-C(21)	107.9(6)
C(19)-C(20)-C(21)	113.9(7)
O(7)-C(20)-H(20)	108.0
C(19)-C(20)-H(20)	108.0
C(21)-C(20)-H(20)	108.0
O(8)-C(21)-C(1)	110.7(6)
O(8)-C(21)-C(20)	106.4(6)
C(1)-C(21)-C(20)	114.6(7)
O(8)-C(21)-H(21)	108.3
C(1)-C(21)-H(21)	108.3
C(20)-C(21)-H(21)	108.3
C(1)-C(22)-H(22A)	109.5
C(1)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(1)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(3)-C(23)-H(23A)	109.5
C(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
O(3)-C(24)-H(24A)	109.5
O(3)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
O(3)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(7)-C(25)-H(25A)	109.5
C(7)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5

C(7)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
C(16)-C(27)-H(27A)	109.5
C(16)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(16)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(7)-C(28)-H(28A)	109.5
O(7)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(7)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5
H(28B)-C(28)-H(28C)	109.5
O(9)-C(29)-N(2)	125.9(7)
O(9)-C(29)-O(8)	123.0(7)
N(2)-C(29)-O(8)	111.1(7)
N(26)-C(30)-C(33)	164(3)
N(26)-C(30)-C(35)	155(5)
N(26)-C(30)-C(31)	153(5)
N(26)-C(30)-H(30A)	94.9
C(33)-C(30)-H(30A)	94.9
N(26)-C(30)-H(30B)	94.9
C(33)-C(30)-H(30B)	94.9
H(30A)-C(30)-H(30B)	103.2
N(26)-C(30)-H(30E)	97.7
C(35)-C(30)-H(30E)	97.7
N(26)-C(30)-H(30F)	97.7
C(35)-C(30)-H(30F)	97.7
H(30E)-C(30)-H(30F)	103.7
N(26)-C(30)-H(30C)	98.2
C(31)-C(30)-H(30C)	98.2
N(26)-C(30)-H(30D)	98.2
C(31)-C(30)-H(30D)	98.2
H(30C)-C(30)-H(30D)	103.7

C(32)-C(31)-C(30)	140(9)
C(32)-C(31)-H(31)	110.0
C(30)-C(31)-H(31)	110.0
C(31)-C(32)-H(32A)	120.0
C(31)-C(32)-H(32B)	120.0
H(32A)-C(32)-H(32B)	120.0
C(34)-C(33)-C(30)	136(6)
C(34)-C(33)-H(33)	112.1
C(30)-C(33)-H(33)	112.1
C(33)-C(34)-H(34A)	120.0
C(33)-C(34)-H(34B)	120.0
H(34A)-C(34)-H(34B)	120.0
C(36)-C(35)-C(30)	162(10)
C(36)-C(35)-H(35)	99.2
C(30)-C(35)-H(35)	99.2
C(35)-C(36)-H(36A)	120.0
C(35)-C(36)-H(36B)	120.0
H(36A)-C(36)-H(36B)	120.0

Symmetry transformations used to generate equivalent atoms:

Table S23. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **17-A**. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
O(1)	59(3)	28(3)	72(4)	3(3)	3(3)	-7(2)
O(2)	48(3)	32(3)	68(4)	2(2)	11(3)	-1(2)
O(3)	49(3)	40(3)	79(4)	13(3)	21(3)	2(2)
O(4)	68(4)	65(4)	83(5)	9(4)	-7(4)	12(3)
O(5)	59(3)	36(3)	64(4)	3(3)	11(3)	4(2)
O(6)	51(3)	39(3)	81(4)	-8(3)	9(3)	-3(3)
O(7)	62(3)	16(2)	73(4)	-3(2)	-9(3)	5(2)
O(8)	52(3)	23(2)	68(4)	-4(2)	-3(3)	-1(2)
O(9)	61(3)	28(3)	92(4)	-14(3)	0(3)	1(3)

N(1)	48(4)	40(4)	64(5)	-5(3)	4(3)	3(3)
N(2)	87(6)	26(3)	83(6)	-11(3)	-21(5)	5(3)
N(26)	92(6)	80(6)	78(6)	24(5)	4(5)	9(5)
C(1)	48(4)	21(3)	72(5)	4(3)	8(4)	-3(3)
C(2)	41(4)	29(4)	73(6)	3(4)	8(4)	4(3)
C(3)	42(4)	29(4)	61(5)	8(3)	9(3)	0(3)
C(4)	48(4)	27(4)	61(5)	8(3)	5(4)	6(3)
C(5)	51(5)	29(4)	74(6)	8(4)	8(4)	7(3)
C(6)	62(5)	30(4)	59(5)	4(4)	14(4)	3(4)
C(7)	59(5)	25(3)	63(5)	9(4)	17(4)	6(3)
C(8)	64(5)	39(4)	70(6)	1(4)	16(4)	3(4)
C(9)	58(5)	25(4)	65(6)	-1(3)	8(4)	-7(3)
C(10)	74(6)	45(5)	63(6)	16(4)	4(4)	-2(4)
C(11)	67(5)	30(4)	84(7)	1(4)	6(5)	-6(4)
C(12)	52(4)	35(4)	69(6)	-7(4)	12(4)	0(4)
C(13)	46(4)	24(4)	74(6)	2(3)	10(4)	-1(3)
C(14)	46(4)	28(4)	61(5)	-3(3)	3(4)	-3(3)
C(15)	37(4)	23(3)	73(5)	-4(4)	8(4)	-2(3)
C(16)	51(4)	32(4)	66(5)	-4(4)	11(4)	-3(3)
C(17)	58(5)	35(4)	60(5)	3(4)	9(4)	-7(3)
C(18)	57(5)	45(5)	65(6)	-4(4)	14(4)	-9(4)
C(19)	58(5)	34(4)	64(5)	1(4)	11(4)	-6(4)
C(20)	50(4)	15(3)	67(5)	-2(3)	-4(4)	-2(3)
C(21)	52(4)	17(3)	62(5)	-1(3)	-3(4)	0(3)
C(22)	60(5)	37(4)	85(7)	10(4)	13(5)	12(4)
C(23)	64(5)	33(4)	83(7)	10(4)	12(5)	-11(4)
C(24)	68(6)	44(5)	88(7)	12(5)	25(5)	2(4)
C(25)	69(6)	40(5)	92(7)	7(4)	28(5)	9(4)
C(27)	54(5)	71(6)	82(6)	-15(6)	13(5)	-11(5)
C(28)	72(6)	27(4)	88(7)	-15(4)	-10(5)	-9(4)
C(29)	52(5)	34(4)	72(6)	-16(4)	3(4)	-8(4)
C(30)	219(17)	184(19)	197(18)	6(17)	87(13)	36(15)
C(31)	206(19)	206(19)	205(19)	0(3)	54(6)	0(3)
C(32)	116(15)	115(16)	114(15)	-1(6)	28(7)	1(6)
C(33)	190(20)	150(40)	60(20)	20(30)	40(18)	40(20)
C(34)	210(30)	210(30)	210(30)	0(6)	55(10)	1(6)

C(35)	240(30)	210(50)	190(40)	20(40)	100(30)	60(30)
C(36)	230(40)	170(60)	190(50)	-10(50)	90(40)	30(40)

Table S24. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **17-A**.

	x	y	z	U(eq)
H(2)	6928	6159	5110	75
H(1)	5773	2145	6023	63
H(2A)	10398	6883	10824	88
H(2B)	10352	5078	10455	88
H(26)	4882	2899	1808	104
H(2C)	7921	7339	6975	59
H(3)	9393	6838	6177	54
H(4)	8473	4586	5674	57
H(5)	7971	7077	4316	63
H(6A)	7758	4857	3276	61
H(6B)	7020	4834	3839	61
H(7)	7947	2575	4738	59
H(8A)	7058	1584	2959	70
H(8B)	7215	416	3826	70
H(12)	3869	3193	4232	63
H(17)	6134	3643	7036	63
H(18)	5894	3667	8797	68
H(19)	7361	4170	9315	64
H(20)	7476	4200	7516	57
H(21)	8127	6612	8458	56
H(22A)	10033	5110	7209	92
H(22B)	9473	3576	7488	92
H(22C)	10197	4607	8238	92
H(23A)	7895	9130	5546	92
H(23B)	8797	9043	5202	92

H(23C)	8846	9737	6183	92
H(24A)	9331	5880	3318	98
H(24B)	9999	7185	3963	98
H(24C)	8949	7654	3573	98
H(25A)	8714	2460	3246	98
H(25B)	8823	952	3959	98
H(25C)	9257	2779	4263	98
H(27A)	3741	3481	7405	105
H(27B)	4540	2956	8255	105
H(27C)	4051	1535	7556	105
H(28A)	7668	1334	7151	102
H(28B)	7294	926	8002	102
H(28C)	8227	96	7917	102
H(30A)	5865	3968	1279	232
H(30B)	5894	1999	1215	232
H(30E)	6551	3780	2011	232
H(30F)	5783	3663	1128	232
H(30C)	5722	2956	1016	232
H(30D)	6370	1769	1699	232
H(31)	6860	4951	1195	247
H(32A)	8075	2317	1513	138
H(32B)	8204	4255	1164	138
H(33)	7221	2017	1120	158
H(34A)	7658	5584	1503	256
H(34B)	8265	4218	1097	256
H(35)	6476	2261	530	245
H(36A)	8082	1458	1465	226
H(36B)	7584	1385	390	226

Table S25. Torsion angles [°] for **17-A**

C(2)-O(1)-C(1)-C(22)	112.1(9)
C(2)-O(1)-C(1)-C(21)	-107.4(7)
C(1)-O(1)-C(2)-C(3)	-118.1(8)

O(1)-C(1)-C(2)-C(3)	104.1(8)
C(22)-C(1)-C(2)-C(3)	0.1(12)
C(21)-C(1)-C(2)-C(3)	-155.7(7)
C(22)-C(1)-C(2)-O(1)	-103.9(8)
C(21)-C(1)-C(2)-O(1)	100.3(7)
O(1)-C(2)-C(3)-C(4)	156.2(6)
C(1)-C(2)-C(3)-C(4)	85.1(9)
O(1)-C(2)-C(3)-C(23)	-77.9(8)
C(1)-C(2)-C(3)-C(23)	-149.0(7)
C(2)-C(3)-C(4)-O(2)	43.8(8)
C(23)-C(3)-C(4)-O(2)	-79.5(8)
C(2)-C(3)-C(4)-C(5)	169.9(6)
C(23)-C(3)-C(4)-C(5)	46.6(9)
C(24)-O(3)-C(5)-C(4)	-158.8(7)
C(24)-O(3)-C(5)-C(6)	74.7(9)
O(2)-C(4)-C(5)-O(3)	-179.2(6)
C(3)-C(4)-C(5)-O(3)	55.3(8)
O(2)-C(4)-C(5)-C(6)	-52.7(8)
C(3)-C(4)-C(5)-C(6)	-178.2(6)
O(3)-C(5)-C(6)-C(7)	66.2(10)
C(4)-C(5)-C(6)-C(7)	-55.6(10)
C(5)-C(6)-C(7)-C(25)	-75.4(10)
C(5)-C(6)-C(7)-C(8)	160.1(8)
C(25)-C(7)-C(8)-C(9)	-175.5(7)
C(6)-C(7)-C(8)-C(9)	-50.5(10)
C(7)-C(8)-C(9)-C(10)	114.2(10)
C(7)-C(8)-C(9)-C(14)	-65.0(10)
C(30)-N(26)-C(10)-C(9)	-15(3)
C(30)-N(26)-C(10)-C(11)	167(2)
C(14)-C(9)-C(10)-N(26)	178.7(9)
C(8)-C(9)-C(10)-N(26)	-0.5(14)
C(14)-C(9)-C(10)-C(11)	-3.9(12)
C(8)-C(9)-C(10)-C(11)	176.9(8)
N(26)-C(10)-C(11)-O(4)	7.6(12)
C(9)-C(10)-C(11)-O(4)	-170.1(8)
N(26)-C(10)-C(11)-C(12)	-174.1(8)

C(9)-C(10)-C(11)-C(12)	8.2(12)
O(4)-C(11)-C(12)-C(13)	174.5(8)
C(10)-C(11)-C(12)-C(13)	-3.7(12)
C(11)-C(12)-C(13)-N(1)	178.1(7)
C(11)-C(12)-C(13)-C(14)	-4.3(11)
C(15)-N(1)-C(13)-C(12)	0.9(13)
C(15)-N(1)-C(13)-C(14)	-176.8(7)
C(10)-C(9)-C(14)-O(5)	179.0(8)
C(8)-C(9)-C(14)-O(5)	-1.7(10)
C(10)-C(9)-C(14)-C(13)	-4.1(11)
C(8)-C(9)-C(14)-C(13)	175.2(6)
C(12)-C(13)-C(14)-O(5)	-174.2(7)
N(1)-C(13)-C(14)-O(5)	3.8(9)
C(12)-C(13)-C(14)-C(9)	8.7(10)
N(1)-C(13)-C(14)-C(9)	-173.4(7)
C(13)-N(1)-C(15)-O(6)	14.4(12)
C(13)-N(1)-C(15)-C(16)	-166.5(7)
O(6)-C(15)-C(16)-C(17)	-157.1(8)
N(1)-C(15)-C(16)-C(17)	23.7(10)
O(6)-C(15)-C(16)-C(27)	21.2(11)
N(1)-C(15)-C(16)-C(27)	-157.9(8)
C(27)-C(16)-C(17)-C(18)	3.0(14)
C(15)-C(16)-C(17)-C(18)	-178.9(8)
C(16)-C(17)-C(18)-C(19)	172.4(9)
C(17)-C(18)-C(19)-C(20)	-1.4(14)
C(28)-O(7)-C(20)-C(19)	73.0(10)
C(28)-O(7)-C(20)-C(21)	-161.7(8)
C(18)-C(19)-C(20)-O(7)	-102.7(9)
C(18)-C(19)-C(20)-C(21)	135.5(8)
C(29)-O(8)-C(21)-C(1)	87.5(8)
C(29)-O(8)-C(21)-C(20)	-147.3(7)
O(1)-C(1)-C(21)-O(8)	-89.4(7)
C(22)-C(1)-C(21)-O(8)	49.4(9)
C(2)-C(1)-C(21)-O(8)	-154.5(6)
O(1)-C(1)-C(21)-C(20)	150.3(6)
C(22)-C(1)-C(21)-C(20)	-70.9(9)

C(2)-C(1)-C(21)-C(20)	85.1(8)
O(7)-C(20)-C(21)-O(8)	-52.6(9)
C(19)-C(20)-C(21)-O(8)	70.8(8)
O(7)-C(20)-C(21)-C(1)	70.1(8)
C(19)-C(20)-C(21)-C(1)	-166.5(7)
C(21)-O(8)-C(29)-O(9)	20.7(13)
C(21)-O(8)-C(29)-N(2)	-158.4(8)
C(10)-N(26)-C(30)-C(33)	-5(14)
C(10)-N(26)-C(30)-C(35)	80(11)
C(10)-N(26)-C(30)-C(31)	-59(11)
N(26)-C(30)-C(31)-C(32)	119(13)
N(26)-C(30)-C(33)-C(34)	-79(15)
N(26)-C(30)-C(35)-C(36)	-81(37)

Symmetry transformations used to generate equivalent atoms:

Table S26. Hydrogen bonds for **17-A** [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2)...O(6)#1	0.84	2.01	2.832(8)	167.0
N(2)-H(2A)...O(7)#2	0.88	2.15	2.909(9)	143.7
N(2)-H(2B)...O(9)#3	0.88	2.03	2.894(10)	166.8

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1 #2 -x+2,y+1/2,-z+2 #3 -x+2,y-1/2,-z+2

X. References

1. Romney, D. K.; Colvin, S. M.; Miller, S. J., Catalyst Control over Regio- and Enantioselectivity in Baeyer–Villiger Oxidations of Functionalized Ketones. *J. Am. Chem. Soc.* **2014**, *136*, 14019-14022.
2. Lichtor, P. A.; Miller, S. J., Combinatorial evolution of site- and enantioselective catalysts for polyene epoxidation. *Nat Chem* **2012**, *4*, 990-995.
3. Hsieh, S.-Y.; Tang, Y. U.; Crotti, S.; Stone, E.; Miller, S. J., Catalytic Enantioselective Pyridine N-Oxidation. *J. Am. Chem. Soc.* **2019**, *141*, 18624-18629.
4. Storch, G.; Kim, B.; Mercado, B. Q.; Miller, S. J., A Stereodynamic Redox-Interconversion Network of Vicinal Tertiary and Quaternary Carbon Stereocenters in Hydroquinone–Quinone Hybrid Dihydrobenzofurans. *Angew. Chem. Int. Ed.* **2018**, *57*, 15107-15111.
5. Nawrat, C. C.; Lewis, W.; Moody, C. J., Synthesis of Amino-1,4-benzoquinones and Their Use in Diels–Alder Approaches to the Aminonaphthoquinone Antibiotics. *J. Org. Chem.* **2011**, *76*, 7872-7881.
6. CrysAlisPro, R. O., The Woodlands, TX, **2015**.
7. Sheldrick, G. M., A Short History of SHELX. *Acta Crystallogr A.* **2008**, *A64*, 112-122.
8. Spek, A. L., PLATON SQUEEZE: a tool for the calculation of the disordered solvent contribution to the calculated structure factors. *Acta Cryst* **2015**, (C71), 9-18.

(c)-SI.pdf (2.66 MiB)

[view on ChemRxiv](#) • [download file](#)