JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

Synthesis of AD-Dihydrodipyrrins Equipped with Latent Substituents of Native Chlorophylls and Bacteriochlorophylls

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Cite This: https://doi.org/10.1021/acs.joc.1c01239 Read Online

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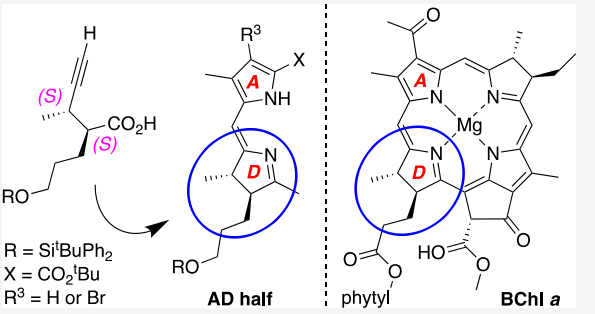
ABSTRACT: Native chlorophylls and bacteriochlorophylls share a common *trans*-substituted pyrroline ring D (17-propionic acid, 18-methyl), whereas diversity occurs in ring A particularly at the 3-position. Two dihydrodipyrrins equipped with native-like D-ring substituents and tailorable A-ring substituents have been synthesized. The synthesis relies on a Schreiber-modified Nicholas reaction to construct the stereochemically defined precursor to ring D, a dialkyl-substituted pent-4-ynoic acid. The carboxylic acid group of the intact propionic acid proved unworkable, whereupon protected propionate ($-CO_2{}^tBu$) and several latent propyl ethers were examined. The *tert*-butyldiphenylsilyl-protected propanol substituent proved satisfactory for reaction of the chiral *N*-acylated oxazolidinone, affording (2*S*,3*S*)-2-(3-((*tert*-butyldiphenylsilyl)-oxy)propyl)-3-methylpent-4-ynoic acid in ~30% yield over 8 steps. Two variants for ring A, 2-*tert*-butoxycarbonyl-3-Br/H-5-iodo-4-methylpyrrole, were prepared via the Barton−Zard route. Dihydrodipyrrin formation from the pyrrole and pentynoic acid entailed Jacobi Pd-mediated lactone formation, Petasis methenylation, and Paal−Knorr-type pyrroline formation. The two AD-dihydrodipyrrins bear the D-ring methyl and protected propanol groups with a stereochemical configuration identical to that of native (bacterio)chlorophylls, and a bromine or no substitution in ring A corresponding to the 3-position of (bacterio)chlorophylls. The analogous β-position of a lactone−pyrrole intermediate on the path to the dihydrodipyrrin also was successfully brominated, opening opportunities for late-stage diversification in the synthesis of (bacterio)chlorophylls.



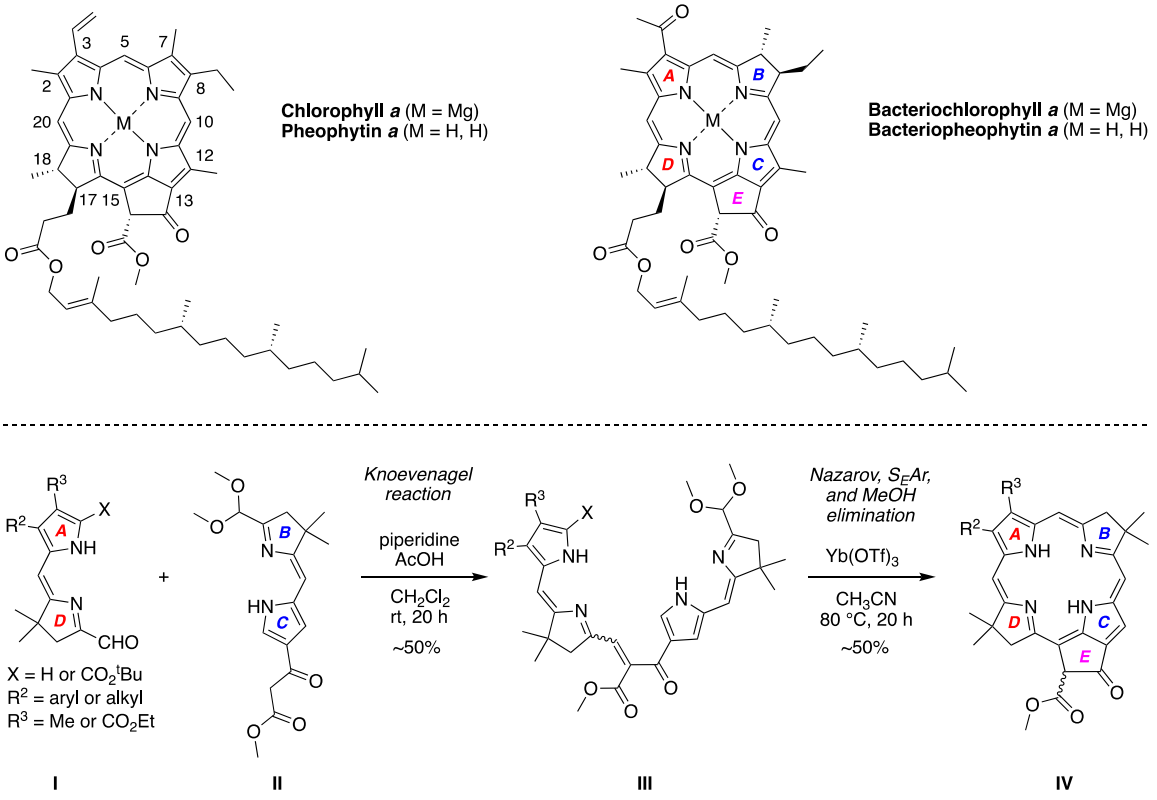
INTRODUCTION

Chlorophyll *a* and bacteriochlorophyll *a* are the chief light absorbers for oxygenic and anoxygenic photosynthesis, respectively (Scheme 1).[1] Members of the family of chlorophylls and bacteriochlorophylls differ in a number of peripheral substituents but typically have two common structural features: the substituents of pyrrole ring C and pyrroline ring D. Pyrrole ring C contains a 12-methyl group as well as a 13-keto group that is part of the annulated ring E. Pyrroline ring D contains a 17-propionic acid and an 18-methyl group in a *trans* configuration. The propionic acid group is invariably esterified with phytol or other hydrocarbon such as farnesol or geranylgeraniol. We note that there are members of the photosynthetic tetrapyrroles (chlorophylls c_1, c_2, c_3) that contain an unesterified, acrylic acid group at the 17-position in lieu of the propionic acid group, but such chlorophylls also contain the phytoporphyrin chromophore (unsaturated ring D), are found in brown algae, and are less common.[2]

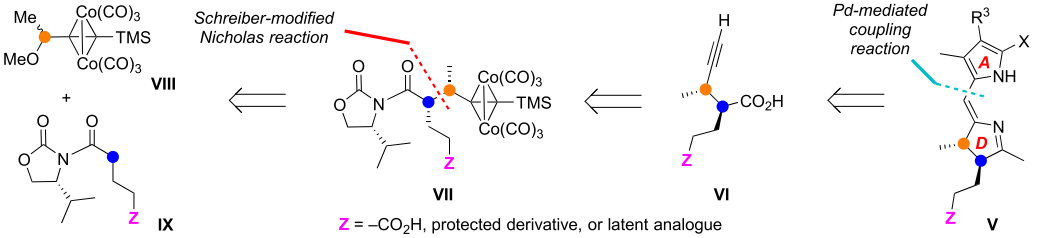
We are working toward the *de novo* synthesis of native (bacterio)chlorophylls, which would complement the present methods of semisynthesis[3−6] and afford full control over the composition and patterns of the macrocycle substituents. A general strategy toward bacteriochlorophylls is shown in Scheme 1 as first demonstrated for use with *gem*-dimethyl-substituted pyrroline rings (B, D).[7] The route relies on the selective joining via Knoevenagel condensation of an AD half and a BC half, where each half contains the saturated ring that gives rise to the corresponding pyrroline unit of rings B and D, followed by double-ring closure via Nazarov cyclization, electrophilic aromatic substitution (S_EAr), and elimination of methanol. A current objective is to adapt the general synthesis to accommodate the substituents characteristic of the native macrocycles. To date, we have synthesized the ring C pyrrole,[8] shown that stereodefined model substituents (17-methyl, 18-ethyl) in ring D can be incorporated at an early stage of the synthesis and carried through Knoevenagel and double-ring closure processes to form the macrocycle without loss of stereochemical integrity,[9] refined the conditions for the double-ring closure,[10] and explored the direct synthesis of bacteriochlorophyll model

Received: May 27, 2021

Scheme 1. Native Pigments (Top) and Route to Model Bacteriochlorins (Bottom)



Scheme 2. Retrosynthetic Analysis of the AD Half



compounds containing a 3-acetyl as well as other substituents.[11]

The prior incorporation of an acetyl[11] or carboethoxy[9,10] group at the 3-position in each case required independent synthesis beginning with the corresponding substituted pyrrole. Bacteriochlorophyll *a* contains a 3-acetyl group. Hence the direct synthesis was enticing, but several reaction steps encountered poor yields due to the acetyl group.[11] While access to the authentic native structures is *sine qua non* for a natural products total synthesis, the 3-position also is a site where the installation of auxochromes can impart significant tuning of the long-wavelength absorption band.[12,13] Accordingly, the ability to install a variety of groups, including an acetyl, at this site is highly desirable.

The acetyl group and many other auxochromes have been installed via Pd-mediated coupling of synthetic 3-bromobacteriochlorins,[13] which were equipped with a *gem*-dimethyl substituent in each pyrroline ring and did not include ring E. The corresponding *gem*-dimethyl-substituted dihydrodipyrrin precursors were prepared via a route that did not entail any Pd-mediated coupling steps. The *trans*-dialkyl-substituted dihydrodipyrrins, by contrast, are constructed via Pd-mediated joining of a 2-iodopyrrole and a *trans*-dialkyl-substituted pentynoic acid.[9,11] While the opportunity for late-stage diversification of bacteriochlorophyll macrocycles afforded by the presence of a 3-bromine atom is tantalizing, we anticipated challenges in accommodating the bromine in the route to *trans*-dialkyl-substituted dihydrodipyrrins.

In the results described herein, the first focus concerns the methodology for installation of the desired propionic acid substituent in the AD-dihydrodipyrrin. While ostensibly a small change from the established route that accommodates an ethyl group at the same site, considerable experimentation was required to achieve access for this essential substituent. The second focus concerns installation of a bromine atom in appropriate precursors to the AD-dihydrodipyrrin. Two routes were explored, the use of a 4-bromo-2-iodopyrrole where the 4-bromo atom is carried through the Pd-mediated coupling at the 2-iodo site with a *trans*-dialkyl-substituted pentynoic acid, and the bromination of a lactone–pyrrole intermediate following the Pd-mediated joining process. The studies provide a deeper understanding of the ability to install both essential and desired substituents in key precursors to native bacteriochlorophylls.

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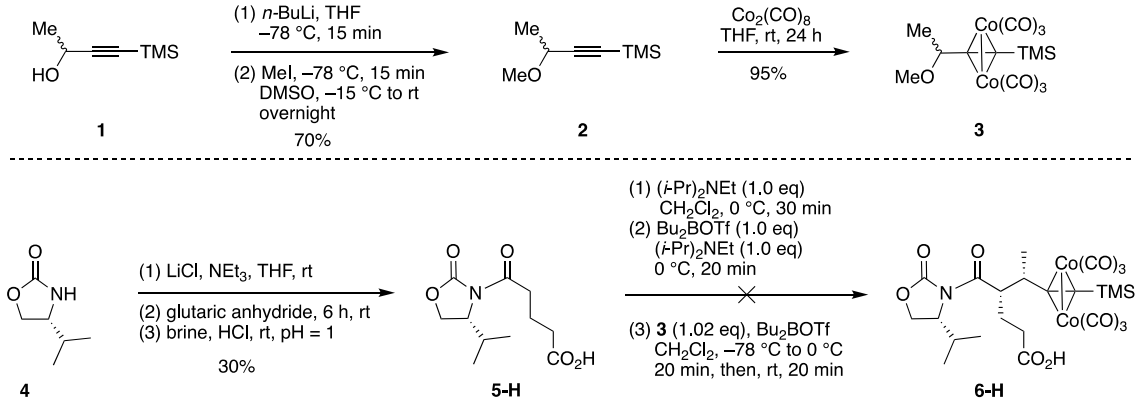
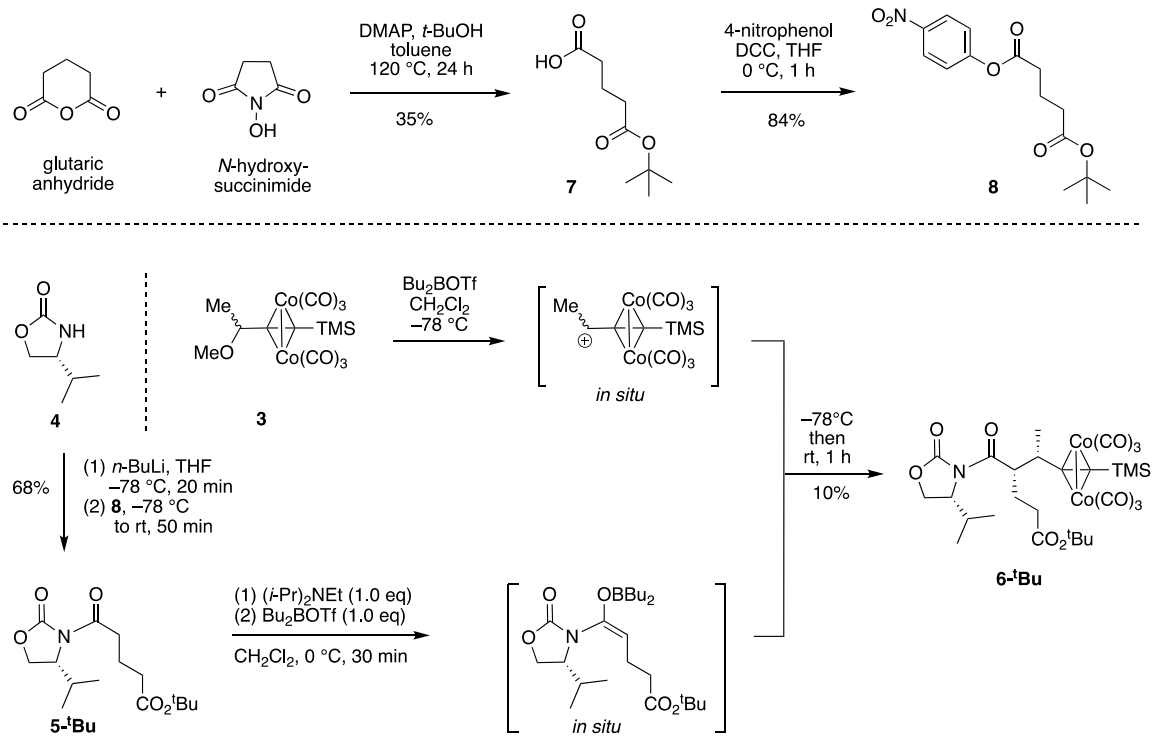
Scheme 3. Attempted Synthesis with an Unprotected Propionic Acid



Scheme 4. Attempted Synthesis with a *tert*-Butyl Propionate



RESULTS AND DISCUSSION

The target AD half (**V**) presents several distinct features: (1) stereodefined substituents at the vicinal β-positions of the pyrroline ring; (2) a methyl group at one β-position of the pyrrole, which typically potentiates reactivity (by ~10−30 fold,[14] or 8−170-fold[15]) toward electrophiles; (3) susceptibility to tautomerization to give the dipyrromethane; and (4) susceptibility to oxidation to give the dipyrrin. The retrosynthesis is shown in Scheme 2. A simple and very desirable scenario is to employ the unprotected propionic acid substituent (Z = CO_2H) throughout the synthesis and then attach the phytol group after the macrocycle is formed. Our initial approach focused on early installation of the vicinal methyl and propionic acid substituents (in **VI** and **VII**) via a Schreiber-modified Nicholas reaction,[16−20] where the requisite stereochemistry is achieved with $Co_2(CO)_6$-protected propargyl substrate **VIII** and chiral 2-oxooxazolidine **IX**.

Synthesis of a D Ring Precursor. Treatment of **1** with *n*-BuLi at −78 °C, followed by MeI, afforded **2** (70% yield), which, upon addition into a solution of $Co_2(CO)_8$ in distilled THF, afforded **3** in 95% yield. The procedure complements a prior route where reaction of 3-methoxybut-1-yne[21] in the presence of *n*-BuLi and TMSCl gave **2**, which was treated with of $Co_2(CO)_8$ in CH_2Cl_2 to give **3**.[19] The formation of **3** is readily observed by the characteristic absorption spectrum (peak at 351 nm; see Supporting Information). *N*-Acylation of chiral auxiliary (*R*)-4-isopropyl-2-oxazolidinone (**4**)[22] with glutaric anhydride in the presence of LiCl and NEt_3 afforded **5-H** in 30% yield. The standard Schreiber-modified Nicholas reaction of **3** and **5-H** did not afford the desired product, however, even though all of the starting material was consumed (Scheme 3). One interpretation is that the remote carboxylic acid serves as a competing nucleophile in reaction with the dicobalt hexacarbonyl propargyl cation derived from **3**.

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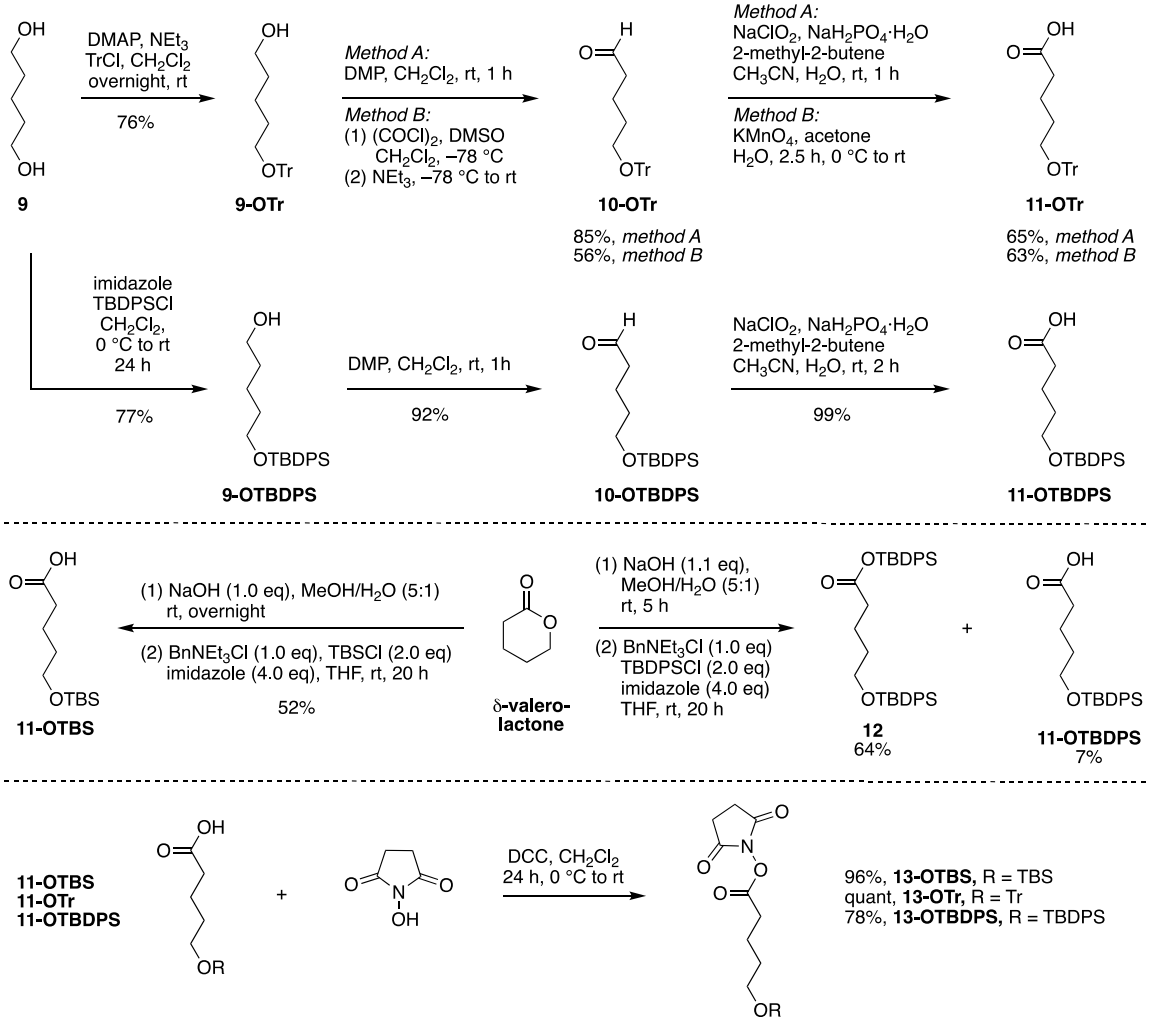
Scheme 5. Preparation of Active Esters of 5-Substituted Pentanoic Acids



To prepare esters as masked propionic acid groups for the Nicholas reaction, glutaric anhydride and *N*-hydroxysuccinimide were heated at 120 °C in the presence of DMAP to give **7**[23] in 35% yield. DCC-mediated coupling of **7** and 4-nitrophenol gave the active ester **8** in 84% yield. *N*-Acylation of chiral oxazolidinone **4** with active ester **8** gave *tert*-butyl protected carboxylic acid **5-^{t}Bu** in 68% yield, but the subsequent condensation of **5-^{t}Bu** and **3** afforded **6-^{t}Bu** in only 10% yield (Scheme 4). Investigations to increase the yield, such as using THF, prolonging the reaction time, and raising the reaction temperature, were not successful. Thus, the propionic acid substituent and its *tert*-butyl ester derivative proved to be poor substrates for the Nicholas reaction.

We turned to prepare several protected alcohols as candidates to generate the Nicholas adduct. The bulky trityl (Tr), *tert*-butyldimethylsilyl (TBS), and *tert*-butyldiphenylsilyl (TBDPS) ethers were sought. Compounds **11-OTBS**,[24] **11-OTr**,[25] and **11-OTBDPS**[26] are known but were prepared in new routes. The inexpensive starting material pentane-1,5-diol (**9**) was treated with TrCl or TBDPSCl to give mono-protected **9-OTr**[27] or **9-OTBDPS**,[28] which, upon oxidation with Dess–Martin periodinane (DMP),[29] gave the corresponding aldehyde **10-OTr**[30]**/-OTBDPS**;[31] subsequent Pinnick oxidation[32] gave the corresponding carboxylic acid **11-OTr/-OTBDPS**. Base-catalyzed ring opening of *δ*-valerolactone, followed by TBSCl protection, afforded pentanoic acid **11-OTBS** in 52% yield. Phase-transfer catalysis with $BnNEt_3Cl$ was found to be necessary to improve the yield from 12% (without $BnNEt_3Cl$) to 52%. Application of the same condition to prepare **11-OTBDPS**, however, was not successful, affording instead the bis(TBDPS)-protected compound **12** in 64% yield along with the **11-OTBDPS** in 7% yield. DCC coupling of each carboxylic acid **11-OTBS/-OTr/-OTBDPS** with *N*-hydroxysuccinimide gave the corresponding active ester **13-OTBS/-OTr/-OTBDPS** in high yield (Scheme 5).

The *N*-acylation of chiral auxiliary **4** with an active ester afforded the desired Nicholas substrates **14-OTBS/-OTr/-OTBDPS** in high yields (Scheme 6). We also sought to prepare **14-OTBS** by coupling of **4** and **11-OTBS** using DCC or 1-ethyl-3-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC·HCl) or by base-catalyzed ring opening of *δ*-valerolactone, followed by acylation of **4**, but these attempts turned out to be unsuccessful (see Supporting Information). The TBS- and Tr-protected compounds **14-OTBS** and **14-OTr** did not give the corresponding Nicholas adducts (**15-OTBS** and **-OTr**), as ^{1}H NMR analysis showed peaks only from the chiral auxiliary, TMS group, and pendant group, indicating loss of the alcohol protective group.

https://doi.org/10.1021/acs.joc.1c01239
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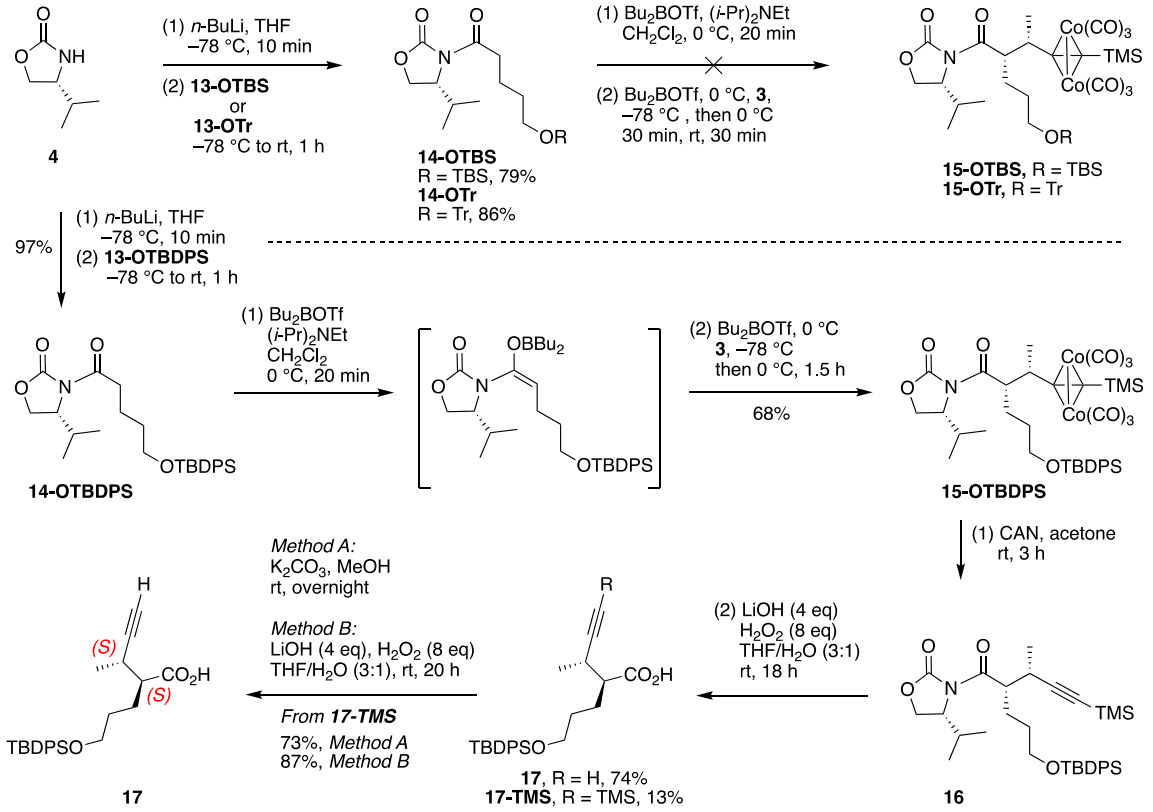
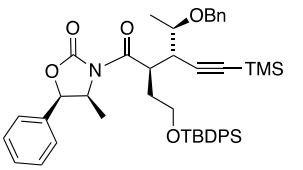
Scheme 6. Synthesis of a Protected, *trans*-Dialkyl-Substituted Precursor to Ring D



Reactions carried out at lower temperature (quenching the reaction at −78 °C), lower concentration, different solvents (THF and CH_2Cl_2), or shorter time (1−2 h to 20 min) gave no better results with these two substrates.

On the other hand, the TBDPS-protected alcohol substrate **14-OTBDPS** afforded the desired Nicholas adduct **15-OTBDPS** in 43% yield upon reaction at a 0.50 mmol scale, and the yield increased to 68% when a large-scale reaction mixture (29.2 mmol) was quenched at 0 °C; other diastereomers were not observed (Scheme 6). **15-OTBDPS** was directly used in the next two steps: (1) demetalation by CAN to afford the crude intermediate **16**, and (2) cleavage of the chiral auxiliary by 4.0 equiv of LiOH and 8.0 equiv of H_2O_2 in THF/water (3:1).[33] Purification by chromatography afforded the desired **17** (74% yield) along with **17-TMS** (13% yield). The TMS moiety of **17-TMS** could be removed by treatment with K_2CO_3 in methanol (method A) or with $LiOH/H_2O_2$ (method B). In short, **17** could be obtained in ∼30% yield over 8 steps beginning with **3** and **9**.

Jacobi and Zheng carried out a Nicholas reaction to prepare a compound (**18**)[34,35] that presents some structural features similar to that of **16**. Application of the standard hydrolysis conditions ($LiOH/H_2O_2$)[33] to **18** afforded a mixture of unwanted products.[32,33] The absence of the desired product was attributed to intramolecular coordination of the lithium ion with the TBDPS ether oxygen atom and the *exo*-carbonyl oxygen atom, resulting in *endo*-ring opening rather than hydrolysis by attack at the *exo*-carbonyl site. Ultimately, the desired product was obtained upon use of modified hydrolysis conditions.[34,35] By contrast, the smooth hydrolysis in our case leading to **17** likely stems from the additional methylene in the chain (propyl-OTBDPS versus ethyl-OTBDPS in **18**), rendering such intramolecular coordination less likely.



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Synthesis of the Ring A Pyrrole. Ring A of chlorophyll *a* contains 2-methyl-3-vinyl substituents, whereas that of bacteriochlorophyll *a* contains 2-methyl-3-acetyl substituents. One synthetic strategy is to prepare the 2-methyl-3-bromo-(bacterio)chlorophyll macrocycle or analogue for Pd-mediated late-stage diversification to install the 3-vinyl or 3-acetyl groups. In this strategy, the 3-bromo substituent could be introduced by bromination of the intact macrocycle, bromination of an intermediate on the path to the macrocycle, or by use of the corresponding bromopyrrole at the outset of the synthesis.

Regardless of the strategy, the ring A pyrrole requires the presence of a deactivating group to impart stability. The *α*-*tert*-butoxycarbonyl group was chosen for the pyrrole (2-position) to serve the additional following roles: (1) directing substituent for the *α*′-iodination of the pyrrole (5-position); (2) blocking moiety for installing the bromine atom at the *β*-position on both the pyrrole (3-position) and the corresponding lactone−pyrrole; and (3) an *α*-pyrrole protecting group that is expected to be easily removed in the final double-ring (Nazarov-S_EAr) closure process.[7]

The ring A pyrrole, with or without the corresponding bromine atom, was prepared beginning with the Barton−Zard[36,37] route. Treatment of 2-nitro-1-propanol with acetic anhydride and DMAP afforded **19** in 81% yield. Compounds

https://doi.org/10.1021/acs.joc.1c01239
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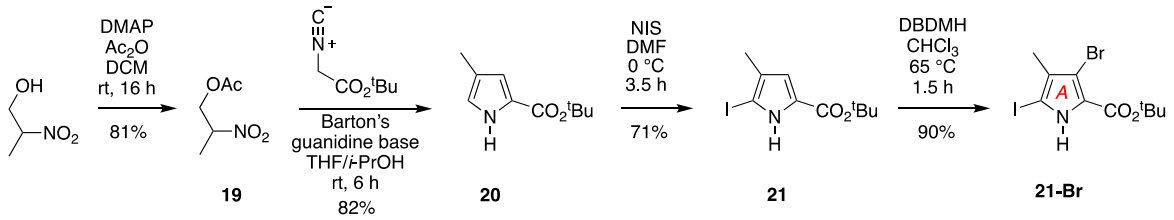
Table 1. Investigation of the Bromination of Iodopyrrole 21[a]

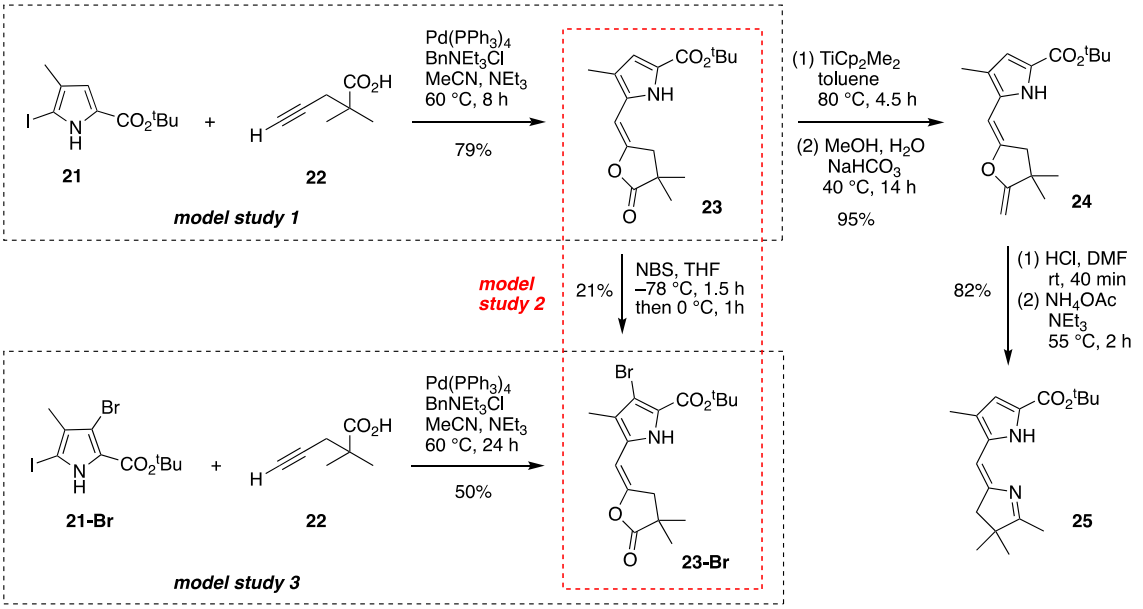
entry	bromination reagent	solvent	temperature	isolated yield: recov. SM	isolated yield: **21-Br**
1	NBS (1.0 equiv)	THF	−78 to 0 °C	20%	trace
2	fresh NBS (1.5 equiv)	DMF	0 °C to rt	13%	trace
3	fresh NBS (2.0 equiv)	DMF	rt to 65 °C	0	0
4	DBDMH (0.5 equiv)	DMF	rt to 65 °C	0	0
5	DBDMH (1.0 equiv)	$CHCl_3$	60 °C	0	48%
6[b]	DBDMH (1.0 equiv)	$CHCl_3$	65 °C	0	90%

[a]Each reaction was performed with 25 mg of pyrrole **21** (0.08 mmol, 6.2 mM) unless noted otherwise. Freshly distilled THF and anhydrous DMF and $CHCl_3$ were used. Fresh NBS was prepared by recrystallization (water) of commercial NBS. [b]5.0 mmol of **21** in 100 mL of $CHCl_3$.

Scheme 7. Synthesis of Pyrroles for Use as Ring A



Scheme 8. Model Studies Concerning (Bromo)Pyrrole−Lactone Formation



19 and *tert*-butyl isocyanoacetate in the presence of Barton's guanidine base [2-(*tert*-butyl)-1,1,3,3-tetramethylguanidine] afforded pyrrole **20**[36] in a larger scale (28-fold) and increased yield (from 70% to 82%) versus an earlier report.[37] Addition of *N*-iodosuccinimide (NIS) in four batches over 2 h gave 5-iodopyrrole **21** in 71% yield. Attempted electrophilic bromination at the 3-position resulted in unexpected troubles; however, upon treatment of **21** with NBS, TLC analysis indicated very little product formation, corroborated by analysis by HPLC-MS and ^{1}H NMR spectroscopy. The low yield could come from the deactivating effect of the *tert*-butoxycarbonyl group toward electrophilic substitution of pyrroles.[38] A more reactive brominating reagent, 1,3-dibromo-5,5-dimethylhydantoin (DBDMH),[39] was found to afford the 3-bromopyrrole **21-Br** in 48% yield (Table 1, entry 5). Reaction of **21** at a larger scale than in the screening study of Table 1 (from 0.08 to 5.0 mmol) and increased concentration (from 6.2 mM to 50 mM) at 65 °C increased the yield to 90% (Scheme 7 and Table 1, entry 6). The single-crystal X-ray structure of both **21** and **21-Br** (Supporting Information) confirmed the pyrrole substituent positions.

Synthesis of a Model AD Half. The formation of the AD half relies on the 2-halo-pyrrole plus 5-pentynoic acid coupling strategy that has been used previously.[9−11,38,40−46] Before embarking on the use of the valuable compound **17**, we carried out three short model studies (Scheme 8). The objectives of the model studies were to identify suitable Pd-mediated coupling conditions and also to explore how to gain access to (bacterio)chlorophylls bearing 3-substituents.

Model Study 1. Pd-catalyzed lactone−pyrrole formation typically has been carried out with the alkyne in excess at elevated temperature (80 or 130 °C) for 24 h.[38] To find milder conditions, we investigated the use of a simple

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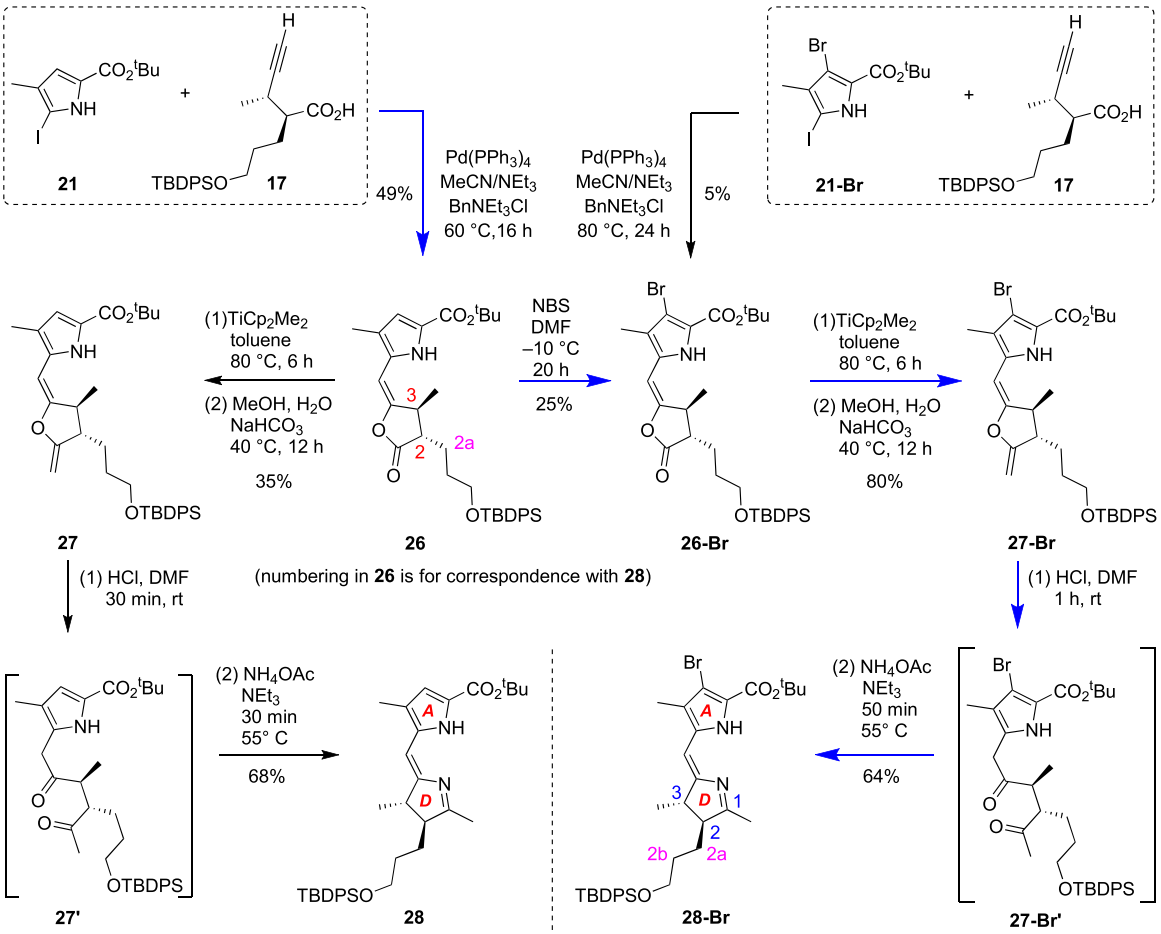
Table 2. Investigation of Halogenation of Lactone−Pyrrole 23[a]

entry	halogenation reagent	additive	solvent	temperature	results
1	NBS (1.0 equiv)		THF	−78 °C to rt	trace
2	PPh_3Br_2 (1.0 equiv)		DCM	0 °C to rt	recov. *Z*-**23**
3[b]	NBS	2,6-DTBP	DMF	0 °C	**23-Br** 15%[c]
4	NBS	K_2CO_3	CH_3CN	rt	decomposition
5	NIS (1.0 equiv)		DMF	0 °C	trace
6	TBCO	TBP, K_2CO_3	CH_3CN	0 °C to rt	trace
7	DBDMH (1.0 equiv)	2,6-DTBP	$CHCl_3$	60 °C	decomposition
8[b]	NBS		THF	−78 to 0 °C	**23-Br** 21%[c]
9[b]	NBS		$CHCl_3$	0 °C	**23-Br** 18%[c]

[a]The reaction was performed with 0.033 mmol of **23** in 330 μL of solvent unless noted otherwise. [b]The reaction was performed with 0.10 mmol of **23** in 1.0 mL of solvent. [c]The isolated yield was determined following TLC separation.

Scheme 9. Synthesis of Two AD-Dihydrodipyrrins



alkynoic acid lacking *trans*-dialkyl substituents (**22**) with 5-iodopyrrole **21** at various concentrations, temperatures (24, 40, 60, and 80 °C), and duration in small-scale reactions (see Supporting Information). Concentrations lower than 0.1 M proved deleterious, whereas lower temperatures remained satisfactory; indeed, the reaction afforded an excellent yield at room temperature (24 °C) over 24 h or at 60 °C for 5 h. The best conditions identified upon implementation at a 200-fold larger scale (10 mmol) gave **23** in 79% isolated yield (Scheme 8). Treatment of **23** with the Petasis methenylation reagent[47] afforded ene−lactone−pyrrole **24** in 95% yield. The subsequent Paal−Knorr[48,49] pyrroline formation[38] of **24** in the presence of NH_4OAc/NEt_3 produced dihydrodipyrrin **25** in 82% yield.

Model Study 2. The introduction of a bromine atom at the site in a precursor destined to be the macrocycle 3-position was examined using lactone−pyrrole **23**. Treatment of **23** with NBS at −78 °C for 1 h and then at room temperature for 1 h gave many unknown spots on TLC and a great loss of product (Table 2, entry 1). With PPh_3Br_2[50] at 0 °C for 1 h and then 8 h at room temperature, TLC analysis showed a new spot with no starting material remaining (entry 2). However, the *E*-lactone−pyrrole **23** was seemingly converted to the *Z*-lactone−pyrrole, as the N−H proton peak of the new product appeared at 9.40 ppm instead of 8.40 ppm of **23**, which may result from a trace of acid (HBr) produced in the reaction. (While dihydrodipyrrins are more stable as the *Z*-isomer due to intramolecular hydrogen-

https://doi.org/10.1021/acs.joc.1c01239
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bonding,[38,41] and exhibit a larger downfield shift of the N−H proton,[38,41] studies of the relative stabilities of lactone−pyrroles have apparently not been carried out.) When the proton scavenger 2,6-di-*tert*-butylpyridine (2,6-DTBP)[51,52] was added to the reaction mixture, the desired product was obtained in 15% yield (entry 3), whereas treatment with K_2CO_3 in acetonitrile caused decomposition of **23** (entry 4). NIS and 2,4,4,6-tetrabromo-2,5-cyclohexadienone (TBCO)[46,53] were also examined (entries 5 and 6), but only a trace of product was detected on TLC. Treatment with DBDMH at 60 °C caused decomposition of **23** (entry 7). Bromination with NBS at −78 °C for 1.5 h and then in an ice bath for 1 h afforded **23-Br** in 21% yield upon TLC separation (entry 8). The reaction at 0 °C for 1−2 h afforded **23-Br** in 18% yield (entry 9).

Model Study 3. The chemoselectivity of Pd-mediated coupling was examined with 5-iodo-3-bromopyrrole (**21-Br**). The Pd-mediated coupling of **21-Br** and **22** under standard conditions[38] afforded the corresponding lactone−pyrrole **23-Br** in 50% yield. Variation of the conditions, including the ratio of pyrrole **21-Br** and **22** (0.98 equiv or 2.0 equiv) in CH_3CN with $Pd(PPh_3)_4$, $BnNEt_3Cl$, and NEt_3 at 80 °C, did not alter the ∼50% yield of **23-Br**. Lowering the temperature to 60 °C for 24 h also afforded **23-Br** in ∼50% yield. Use of 2.0 equiv of alkynoic acid **22** versus **21-Br** still gave **23-Br** in 50% yield. While yields of >50% were not obtained, the 3-bromo site appeared to be relatively unreactive, which may stem in part from the steric hindrance provided by the 5-*tert*-butoxycarbonyl moiety.

In conclusion, from the three model studies, the bromine atom destined for the (bacterio)chlorophyll 3-position can be installed early (bromination of the pyrrole) or at an intermediate stage (bromination of the lactone−pyrrole). Early installation relies on chemoselective Pd-mediated ethynylation of a 5-iodo-3-bromopyrrole (**21-Br**) to give the lactone−pyrrole−bromide **23-Br** (90% bromination, 50% ethynylation), whereas installation of the bromine after ethynylation to form the lactone−pyrrole **23** also affords **23-Br** (79% ethynylation, 21% bromination), albeit in overall lower yield. The model studies revealed fundamental reactivity, albeit safeguarded from epimerization, tautomerization, and oxidation by the presence of the stabilizing *gem*-dimethyl group in the substrates examined (**22**−**25**, **23-Br**).

Synthesis of AD Halves Equipped with Latent Substituents of the Native Macrocycles. The three model routes were extended to the preparation of AD halves that incorporate the stereodefined substituents of **17**; in this synthetic route, three deleterious processes (epimerization, tautomerization, and oxidation) are possible and must be avoided to gain access to the AD halves (Scheme 9). The reaction of 5-iodo-3-bromopyrrole **21-Br** with TBDPS-protected pentynoic acid **17** gave the target **26-Br** in 5% yield, accompanied by a mixture of dehalogenated pyrroles. Many attempts such as tuning the temperature (60, 80, and 100 °C), concentration (0.1−0.5 M), and the amount of **17** (0.98, 1.0, and 1.2 equiv) did not afford improved yields. Thus, the early installation of the bromine atom was not attractive in this case despite the success of the model study.

We turned to the reaction of the 5-iodopyrrole lacking the 3-bromine atom (**21**). Treatment of pyrrole **21** and **17** with $BnNEt_3Cl$ and $Pd(PPh_3)_4$ at either 24 °C for 24 h or 60 °C for 16 h afforded the target **26** in 49% yield (Scheme 9). Treatment of **26** with NBS in DMF at −10 °C afforded **26-Br** in 25% yield. Many attempts using different solvents (THF or hexafluoroisopropanol[54]) or adding K_2CO_3 did not improve the yield. Subsequent Petasis methylenation[38,41,47] with $TiCp_2Me_2$ in toluene afforded the ene−lactone−pyrrole **27-Br** in 80% yield. Acid-catalyzed ring opening of **27-Br** by addition of HCl was monitored by UV−vis absorption spectroscopy. The ene−lactone−pyrrole **27-Br** exhibits a long-wavelength absorption peak at 299 nm. After 10 min, the absorption at 299 nm declined and reached minimal intensity after ∼60 min (Figure 1, panel A). The change in spectral features was consistent with formation of the pyrrole−diketone intermediate **27-Br′**. The Paal−Knorr[48,49] reaction of the pyrrole−diketone **27-Br′** leading to the dihydrodipyrrin in the presence of NH_4OAc and NEt_3 was similarly monitored, where the absorption of the crude dihydrodipyrrin **28-Br** at 344 nm increased and reached maximum intensity after ∼40 min (Figure 1, panel B). In this manner, AD-dihydrodipyrrin **28-Br** was obtained in 64% yield. The formation of dihydrodipyrrin **28-Br** is quite similar to that of **25**, with one critical distinction: the *gem*-dimethyl group in **25** precludes tautomerization or oxidation to form the dipyrromethane or dipyrrin, respectively,[9] whereas both processes as well as epimerization can accrue in the formation of the *trans*-dialkyl-substituted **28-Br**.

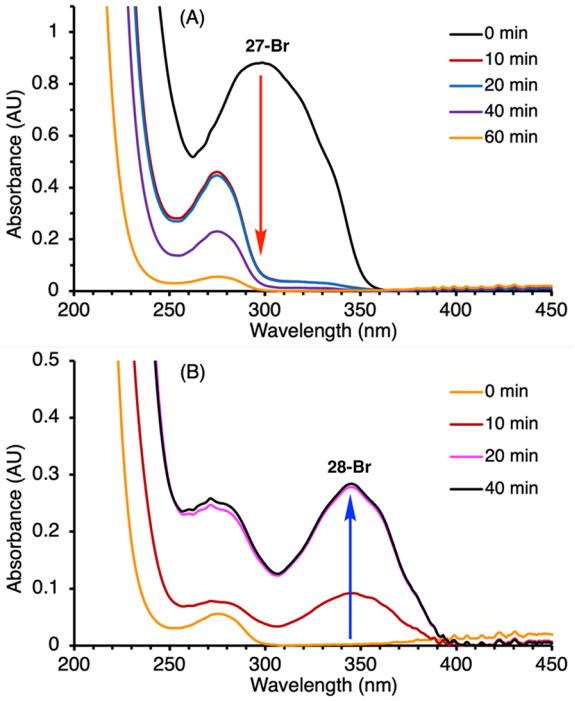

Figure 1. Absorption spectra in acetonitrile at room temperature. (A) Ring opening of ene−lactone−pyrrole **27-Br** (black line) to form diketone−pyrrole intermediate **27-Br′** (orange line), causing loss of absorption at ∼300 nm (red arrow). (B) Ring closure of diketone−pyrrole **27-Br′** (orange line) to give dihydrodipyrrin **28-Br** (black line), with growth of absorption at ∼340 nm (blue arrow).

The lactone−pyrrole **26** was also subjected to Petasis methenylation[38,41,47] to give **27**, which, upon acid-catalyzed ring opening and Paal−Knorr[48,49] reaction, afforded AD-dihydrodipyrrin **28**. The yields of formation of the unbrominated **27** and **28** were 35% and 68%, to be compared with the brominated counterparts **27-Br** and **28-**

https://doi.org/10.1021/acs.joc.1c01239
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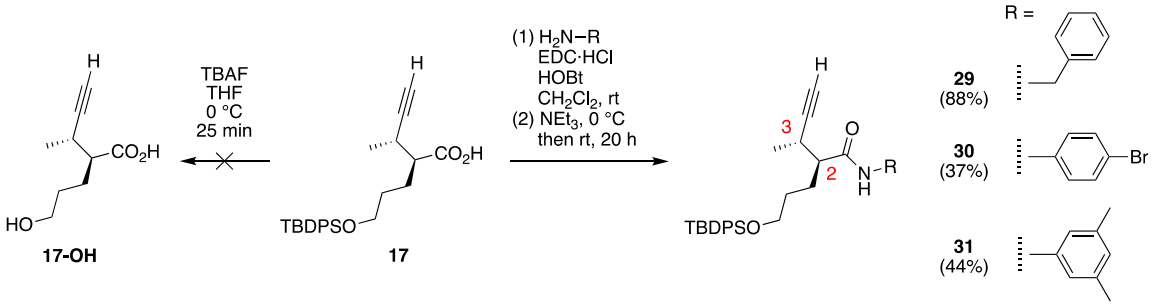
Scheme 10. Derivatization of 17 for Single-Crystal X-ray Examination



Br in 80% and 64%, respectively. The target dihydrodipyrrins **28** and **28-Br** were obtained as yellow oils and were stable upon storage under argon at −20 °C for at least several months. In summary, the TBDPS-protected (2*S*,3*S*)-2-(3-hydroxypropyl)-3-methylpent-4-ynoic acid (**17**) was converted with stereochemical fidelity via lactone−pyrrole **26** to the corresponding *trans*-dialkyl-substituted dihydrodipyrrin (3*S*,4*S*)-2-(3-methyl-4-((*tert*-butyldiphenylsilyl)propyl)-dipyrrin (**28**). The preferred path to **28-Br** (blue arrows, Scheme 9) relies on bromination of the lactone−pyrrole **26** rather than beginning with the *β*-bromopyrrole **21-Br**.

Structure Determination. The intermediates and target compounds were characterized by the standard battery of analytical methods. The stereochemistry of the pyrroline substituents in the lactone−pyrrole **26** and the dihydrodipyrrins **28** and **28-Br** was probed by examination of the vicinal coupling constant $J_{H^2-H^3}$. The value of $J_{H^2-H^3}$ was 3.4 Hz (**26**) and 3.8 Hz (**28** and **28-Br**). The coupling constant values are consistent with the *trans* configuration of the vicinal protons.[9,11,55] Moreover, 2D NOESY spectroscopy of **26** showed a correlation between the 3-proton and the 2a-protons (first methylene of the propanol substituent), and the 3-methyl and the 2-proton without observing a correlation between the 2- and the 3-protons (see Scheme 9 for numbering). For **28-Br**, a correlation was observed between the 3- and 2a-/2b-protons (first/second methylenes of the propanol substituent), but not between the 2- and 3-protons of **28-Br** (Supporting Information). The results are consistent with the expected *trans* stereochemistry of the lactone−pyrroles and dihydrodipyrrins.

To establish the absolute stereochemistry, we sought single-crystal X-ray determination of one or more compounds along the series **15-OTBDPS** to **28** or **28-Br**. Compounds **15-OTBDPS**, **16**, **17**, **17-TMS**, **26**, **26-Br**, **27**, **27-Br**, **28**, and **28-Br** were obtained as oils at room temperature. We focused on preparing derivatives of **17** that afforded crystals at room temperature. Attempts to remove the TBDPS group in the presence of TBAF did not afford the corresponding alcohol **17-OH**, and treatment with NaOH to give the sodium carboxylate failed to provide a solid product. Treatment of the carboxylic acid with an amine (benzylamine, *p*-bromoaniline, or 3,5-dimethylaniline) in the presence of EDC·HCl, 1-hydroxybenzotriazole (HOBt), and NEt_3 in CH_2Cl_2 produced the corresponding amide (Scheme 10). Amides **29** and **30** were oils, but **31** was a solid at room temperature. Single-crystal X-ray analysis of **31** confirmed the (2*S*,3*S*)-configuration (see Supporting Information). The same absolute configuration is inferred for the synthetic series leading to the target dihydrodipyrrins **28** and **28-Br**.

OUTLOOK

A general feature of the proposed *de novo* synthesis of native (bacterio)chlorophylls is introduction of peripheral functional groups, or latent analogues thereof, early in the synthetic plan, thereby limiting required transformations of the intact macrocycles. The Schreiber-modified Nicholas reaction provides an effective means for constructing stereodefined disubstituted pentynoic acids, but the propionic acid substituent as required for the authentic pyrroline ring D proved incompatible. Ultimately, the TBDPS-protected propanol was found to be a suitable latent substituent and was prepared in a 5 g quantity in an 8-step process. The corresponding lactone−pyrrole and dihydrodipyrrin therefrom were obtained bearing (1) the methyl and protected propanol substituents in *trans* configuration in pyrroline ring D, and (2) the presence or absence of a bromine atom in ring A. The bromine atom was best introduced by direct bromination of the lactone−pyrrole rather than via the bromopyrrole precursor. The bromine in ring A is at the site corresponding to the 3-position of the (bacterio)chlorophyll macrocycle. The ability to install diverse substituents at the 3-position is an essential objective given the effect of auxochromes at this site in tuning the long-wavelength absorption band of bacteriochlorophylls. The next step is to utilize the advances reported herein to gain synthetic access to the native photosynthetic tetrapyrrole macrocycles.

EXPERIMENTAL SECTION

General Methods. ^1H NMR and ^{13}C NMR spectra were collected at room temperature in $CDCl_3$ unless noted otherwise. Electrospray ionization mass spectrometry (ESI-MS) data are reported for the molecular ion or protonated molecular ion. Anhydrous THF used in all reactions was freshly distilled from Na/benzophenone ketyl unless noted otherwise. THF (ACS grade) was used as received. Anhydrous $CHCl_3$ was stabilized with amylenes and used as received. Anhydrous CH_2Cl_2 was stabilized with 40−150 ppm amylenes and used as received. Anhydrous acetonitrile was used as received. NBS was used as received unless noted otherwise. All commercially available compounds were used as received. (*R*)-4-Isopropyl-2-oxazolidinone (**4**)[22] was obtained commercially and exhibited 99% purity (GC) and 99% ee (chiral GC). Noncommercial compounds **7**,[23] **9-OTr**,[27] **9-OTBDPS**,[28] **10-OTr**,[30] **10-OTBDPS**,[31] **11-OTBS**,[24] **11-OTr**,[25] **11-OTBDPS**,[26] **19**,[36,37] and **20**[36,37] are known, but were prepared here via alternative methods.

(3-Methoxybut-1-yn-1-yl)trimethylsilane (2). A solution of **1** (11.7 g, 80 mmol) in anhydrous THF (280 mL) at −78 °C was treated dropwise with *n*-BuLi (50 mL, 80 mmol, 1.6 M in hexanes) over 10 min. After the addition, the mixture was treated with MeI (39.8 mL, 640. mmol), and then the flask was allowed to warm to −15 °C in an ethylene glycol/dry ice bath over 30 min. DMSO (11.8 mL, ACS grade) was added to the reaction mixture at −15

https://doi.org/10.1021/acs.joc.1c01239
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°C, giving rise to a yellow precipitate. The resulting suspension was stirred for 1 h at −15 °C and then 21 h at room temperature. The reaction mixture was poured into a beaker containing saturated aqueous NH_4Cl and ice. The organic layer was separated, dried (Na_2SO_4), and purified by atmospheric distillation (Vigreux column, 14/20, 200 mm height) with heating in a sand bath to collect a colorless oil (8.82 g, 70%): bp 135−143 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.90 (q, J = 6.6 Hz, 1H), 3.24 (s, 3H), 1.25 (d, J = 6.7 Hz, 3H), 0.02 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 105.5, 89.7, 67.3, 56.3, 22.0, 0.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_8H_{17}OSi$ 157.1043; found 157.1038.

***d,l*-1-(Trimethylsilyl)-3-methoxy-1-butyne, hexacarbonyldicobaltate Complex (3).** Following a reported procedure[20] with some modification, a solution of $Co_2(CO)_8$ (5.10 g, 14.9 mmol) in anhydrous THF (77 mL) was treated with **2** (2.00 g, 14.2 mmol) in anhydrous THF (12.8 mL + 4 mL rinse) under argon. The bright-brown mixture was stirred for 24 h at room temperature. The solvent was removed and the residue was chromatographed [silica, hexanes then hexanes/ethyl acetate (20:1), 6 cm × 30 cm; TLC R_f = 0.90 in hexanes/ethyl acetate (20:1)] to afford a bright-orange gum (5.40 g, 95%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.47 (q, J = 6.2 Hz, 1H), 3.48 (s, 3H), 1.48 (d, J = 6.3 Hz, 3H), 0.31 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 200.4, 113.3, 77.8, 57.2, 22.8, 0.8; HRMS (ESI-TOF) m/z: $[(M - OCH_3) + H]^+$ calcd for $C_{13}H_{14}Co_2O_6Si$ 410.9140; found 410.9126.

(*R*)-5-(4-Isopropyl-2-oxooxazolidin-3-yl)-5-oxopentanoic Acid (5-H). A solution of **4** (1.29 g, 10.1 mmol) in anhydrous THF (15 mL) was treated with LiCl (466 mg, 11.1 mmol) and NEt_3 (1.81 mL, 13.0 mmol) under argon. The mixture was stirred for 5 min at room temperature, and then glutaric anhydride (1.34 g, 11.7 mmol) was added in one batch. The reaction mixture was stirred vigorously at room temperature for 6 h before the addition of brine. Then, the mixture was acidified by the addition of 2 M HCl (7.0 mL) to pH = 1 and extracted with CH_2Cl_2. The organic layer was separated, dried (Na_2SO_4), and concentrated to a pale-yellow oil. The oil was chromatographed [silica, hexanes/ethyl acetate (1:1)] to afford a white solid (729 mg, 30%): mp 71−73 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.15 (br s, 1H), 4.44 (m, 1H), 4.29 (t, J = 8.8 Hz, 1H), 4.22 (dd, J_1 = 9.1 Hz, J_2 = 3.0 Hz, 1H), 3.01 (m, 2H), 2.46 (t, J = 7.4 Hz, 2H), 2.37 (m, 1H), 2.00 (m, 2H), 0.92 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 179.0, 172.4, 154.1, 63.5, 58.4, 34.5, 32.9, 28.4, 19.1, 17.9, 14.6; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{11}H_{17}NO_5Na$ 266.0999; found 266.0993.

***tert*-Butyl (*R*)-5-(4-Isopropyl-2-oxooxazolidin-3-yl)-5-oxopentanoate (5-^{t}Bu).** A solution of **4** (646 mg, 5.00 mmol) in anhydrous THF (80 mL) at −78 °C was treated dropwise with *n*-BuLi (3.2 mL, 1.6 M in hexanes, 5.1 mmol). The reaction mixture was stirred for 20 min at −78 °C. Then, the resulting mixture was treated with **8** (1.63 g, 5.25 mmol) in one batch. The reaction mixture was stirred for 30 min at −78 °C and then for 20 min at room temperature. TLC analysis [silica, hexanes/ethyl acetate (2:1), R_f = 0.53] indicated that **4** was consumed. The reaction mixture was poured into a beaker containing saturated aqueous NH_4Cl and diethyl ether. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting residue was dissolved in CH_2Cl_2 and treated with excess saturated aqueous $NaHCO_3$. The resulting mixture was stirred vigorously at room temperature for 1 h and then extracted with CH_2Cl_2. The organic extract was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. The resulting residue was chromatographed [silica, hexanes/ethyl acetate (2:1), 3 cm × 15 cm] to afford an orange oil (1.01 g, 68%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.43 (m, 1H), 4.28 (t, J = 8.7 Hz, 1H), 4.21 (dd, J_1 = 9.1 Hz, J_2 = 3.0 Hz, 1H), 3.04−2.91 (m, 2H), 2.37 (m, 1H), 2.31 (t, J = 7.4 Hz, 2H), 2.00−1.90 (m, 2H), 1.45 (s, 9H), 0.92 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 172.5, 172.3, 154.0, 80.3, 63.4, 58.4, 34.6, 34.5, 28.4, 28.1, 19.7, 17.9, 14.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{25}NO_5Na$ 322.1625; found 322.1623.

(*R*)-3-((2*S*,3*S*)-2-(3-(*tert*-Butyloxy)-3-oxopropyl)-3-methyl-5-(trimethylsilyl)pent-4-ynoyl)-4-isopropyloxazolidin-2-one, Hexacarbonyldicobalt Complex (6-^{t}Bu). A solution of **5-^{t}Bu** (220 mg, 0.73 mmol) in anhydrous CH_2Cl_2 (1.0 mL) at 0 °C under argon was treated with distilled $(i\text{-Pr})_2NEt$ (128 μL, 0.73 mmol) and Bu_2BOTf (730 μL, 0.73 mmol) in a first flask. In a second flask, a solution of **3** (110 mg, 0.25 mmol) in anhydrous CH_2Cl_2 (1.0 mL) at −78 °C under argon was treated with Bu_2BOTf (730 μL, 0.73 mmol), and the reaction mixture was stirred for 10 min. The first flask was cooled to −78 °C, and then the contents of the second flask (dicobalt octacarbonyl propargylic cation) were transferred into the first flask via syringe over 10 min. The reaction mixture was allowed to warm to 0 °C (over 30 min) and then to room temperature (over 30 min). The reaction mixture was treated with aqueous sodium phosphate buffer (pH 7, 0.1 M, 3 mL). The organic layer was then separated, dried (Na_2SO_4), and concentrated to a dark oil. The dark oil was chromatographed [silica, hexanes/ethyl acetate (6:1); TLC R_f = 0.64 in hexanes/ethyl acetate (3:1)] to afford a bright-red oil (51 mg, 10%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.53 (dt, J_1 = 8.0 Hz, J_2 = 3.5 Hz, 1H), 4.30 (t, J = 8.7 Hz, 1H), 4.21 (dd, J_1 = 9.1 Hz, J_2 = 3.1 Hz, 1H), 4.04 (dd, J_1 = 12.2 Hz, J_2 = 2.7 Hz, 1H), 3.45 (dd, J_1 = 7.1 Hz, J_2 = 2.4 Hz, 1H), 2.33−2.29 (m, 1H), 2.29−2.21 (m, 1H), 2.19 (dd, J_1 = 15.4 Hz, J_2 = 4.2 Hz, 1H), 2.12−2.04 (m, 1H), 1.86−1.81 (m, 1H), 1.42 (s, 9H), 1.24 (d, J = 7.2 Hz, 3H), 0.93 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.35 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 200.3, 173.3, 171.8, 153.3, 114.6, 80.3, 63.3, 58.2, 48.6, 41.6, 33.8, 28.6, 28.1, 19.9, 18.4, 17.9, 14.6, 1.31, 1.13; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{38}Co_2NO_{11}Si$ 710.0873; found 710.0863.

5-*tert*-Butoxy-5-oxopentanoic Acid (7). A solution of glutaric anhydride (22.8 g, 200. mmol) and *N*-hydroxysuccinimide (11.5 g, 100. mmol) in anhydrous toluene (120 mL) under argon was treated with DMAP (4.88 g, 40.0 mmol) and anhydrous *tert*-butanol (57.4 mL, 600. mmol). The resulting mixture was heated in an oil bath at 120 °C and stirred for 24 h and then was allowed to cool to room temperature. The reaction mixture was washed (10% aqueous $NaHSO_4$ solution, water, and brine) and extracted with ethyl acetate. The organic extract was dried (Na_2SO_4) and concentrated to a yellow oil. Chromatography [silica, hexanes/ethyl acetate (3:1) to ethyl acetate] afforded a colorless oil (13.2 g, 35%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.29 (br s, 1H), 2.42 (t, J = 7.4 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 1.92 (quintet, J = 7.4 Hz, 2H), 1.45 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 179.3, 172.3, 80.5, 34.4, 33.1, 28.1, 20.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_9H_{16}O_4Na$ 211.0941; found 211.0938.

***tert*-Butyl (4-Nitrophenyl)glutarate (8).** A solution of **7** (8.46 g, 45.0 mmol) in anhydrous THF (135 mL) was treated with 4-nitrophenol (6.88 g, 49.5 mmol) and DCC (13.9 g, 67.5 mmol) under argon at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, at which point TLC analysis [silica, R_f = 0.50 in hexanes/ethyl acetate (3:1)] indicated that the reaction was completed. The reaction mixture was filtered under vacuum, and the filtered material was washed with diethyl ether. The filtrate was concentrated, dissolved in CH_2Cl_2, and treated with excess hexanes. The resulting suspension was stored overnight at −20 °C. The resulting white precipitate was removed by vacuum filtration. The filtrate was dissolved in CH_2Cl_2 and treated with excess saturated aqueous $NaHCO_3$. The resulting mixture was stirred vigorously at room temperature for 1 h and then extracted with CH_2Cl_2. TLC analysis [silica, hexanes/ethyl acetate (3:1)] indicated the excess 4-nitrophenol was removed. The organic layer was separated, dried (Na_2SO_4), and concentrated to a yellow oil. The resulting oil was chromatographed [silica, hexanes/ethyl acetate (3:1), 6 cm × 15 cm] to afford a pale-yellow solid (11.7 g, 84%): mp 49−50 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, J = 9.2 Hz, 2H), 7.29 (d, J = 9.1 Hz, 2H), 2.68 (t, J = 7.4 Hz, 2H), 2.38 (t, J = 7.2 Hz, 2H), 2.04 (p, J = 7.3 Hz, 2H), 1.47 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 172.0, 170.6, 155.4, 145.3, 125.2, 122.4, 80.7, 34.2, 33.3, 28.1, 20.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{19}NO_6Na$ 332.1105; found 332.1106.

https://doi.org/10.1021/acs.joc.1c01239
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5-(Trityloxy)pentan-1-ol (9-OTr). A solution of **9** (21.87 g, 210.0 mmol) in anhydrous CH_2Cl_2 (180 mL) was treated with DMAP (730 mg, 6.0 mmol) and NEt_3 (16.6 mL, 120 mmol) under argon. The reaction mixture was stirred for 10 min at room temperature, followed by addition of TrCl (16.72 g, 60.00 mmol). The reaction mixture was stirred overnight before adding water (100 mL). The organic layer was washed with HCl (2 M, 50 mL × 3), washed with saturated aqueous $NaHCO_3$ (100 mL × 3), dried (Na_2SO_4), and concentrated to a thick yellow oil. Chromatography [silica, hexanes/ethyl acetate (2:1); TLC R_f = 0.60 in hexanes/ethyl acetate (3:1)] afforded a yellow oil (15.80 g, 76%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (dd, J_1 = 8.5 Hz, J_2 = 1.4 Hz, 6H), 7.26 (dd, J_1 = 8.7 Hz, J_2 = 7.0 Hz, 6H), 7.22−7.18 (m, 3H), 3.55 (t, J = 6.6 Hz, 2H), 3.06 (t, J = 6.6 Hz, 2H), 1.76 (br s, 1H), 1.63 (p, J = 6.8 Hz, 2H), 1.49 (m, 2H), 1.41 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 144.5, 128.8, 127.8, 126.9, 86.4, 63.6, 62.9, 32.6, 29.9, 22.6; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{26}O_2Na$ 369.1825; found 369.1820.

5-(Trityloxy)pentanal (10-OTr). *Method A.* A solution of **9-OTr** (9.64 g, 27.8 mmol) in anhydrous CH_2Cl_2 (278 mL) under argon was treated with DMP (15.4 g, 36.3 mmol, 1.3 equiv). The reaction mixture was stirred at room temperature for 1 h, and TLC analysis [silica, hexanes/ethyl acetate (2:1)] indicated that the reaction was completed. A 10% aqueous $Na_2S_2O_3$ solution (550 mL) was added to the reaction mixture, and the resulting mixture was stirred for 20 min at room temperature. The organic layer was separated, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was passed through a silica pad [hexanes/ethyl acetate (2:1)], which removed an insoluble white solid and afforded a colorless oil (8.17 g, 85%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.70 (s, 1H), 7.43 (d, J = 7.7 Hz, 6H), 7.28 (t, J = 7.6 Hz, 6H), 7.22 (d, J = 7.3 Hz, 3H), 3.08 (t, J = 6.2 Hz, 2H), 2.36 (td, J_1 = 7.3 Hz, J_2 = 1.7 Hz, 2H), 1.75−1.68 (m, 2H), 1.66−1.60 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 202.6, 144.4, 128.7, 127.8, 126.9, 86.5, 62.9, 43.6, 29.5, 19.1; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{24}O_2Na$ 367.1669; found 367.1669.

Method B. A solution of $(COCl)_2$ (920 μL, 10.6 mmol) in anhydrous CH_2Cl_2 (18 mL) was treated dropwise with a solution of DMSO (1.2 mL) in anhydrous CH_2Cl_2 (3.3 mL) under argon at −78 °C over 10 min. The reaction mixture was stirred for 20 min; then **9-OTr** (2.83 g, 8.17 mmol) in anhydrous CH_2Cl_2 (5.3 mL) was added over 10 min. After 1 h, freshly distilled NEt_3 (2.30 mL) was added at −78 °C, and then the reaction mixture was allowed to warm to room temperature over 1 h. Saturated aqueous NH_4Cl was added, and the organic layer was separated, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, hexanes/ethyl acetate (3:1)] to afford a colorless oil (1.64 g, 56%), which was characterized by ^{1}H NMR spectroscopy and found to afford data in accord with those from Method A.

5-(Trityloxy)pentanoic Acid (11-OTr). *Method A.* A solution of **10-OTr** (3.60 g, 10.0 mmol) and 2-methyl-2-butene (4.24 mL, 40.0 mmol) in CH_3CN (30 mL) was treated with a solution of $NaClO_2$ (1.36 g, 15.0 mmol) and $NaH_2PO_4{\cdot}H_2O$ (276 mg, 2.0 mmol) in water (15 mL) at room temperature. The reaction mixture was stirred for 2 h, and then 2 M HCl (15 mL) and ethyl acetate (100 mL) were added. The organic layer was dried (Na_2SO_4) and concentrated. Recrystallization (CH_2Cl_2/hexanes) afforded a pale-yellow solid (2.24 g, 65%): mp 142−145 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 7.7 Hz, 6H), 7.29 (t, J = 7.6 Hz, 6H), 7.22 (t, J = 7.0 Hz, 3H), 3.08 (t, J = 6.2 Hz, 2H), 2.33 (t, J = 7.4 Hz, 2H), 1.74 (t, J = 7.7 Hz, 2H), 1.66 (t, J = 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 179.3, 144.3, 128.7, 127.7, 126.9, 86.4, 62.9, 33.7, 29.4, 21.6; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{24}H_{24}O_3Na$ 383.1618; found 383.1610.

Method B. A solution of **10-OTr** (384 mg, 1.12 mmol) in acetone/H_2O (6 mL, v/v, 3:1) was treated with $KMnO_4$ (177 mg, 1.12 mmol) in batches at 0 °C over 20 min. The reaction mixture was stirred vigorously at room temperature for 2 h. A solution of 30% $NaHSO_3$ was added dropwise over 30 min. The resulting mixture was acidified by addition of 2 M HCl until the mixture became colorless. The mixture was then extracted with ethyl acetate, dried (Na_2SO_4), and concentrated. Recrystallization (CH_2Cl_2/hexanes) overnight at −20 °C afforded a white solid (255 mg, 63%), which was characterized by ^{1}H NMR spectroscopy and found to afford data in accord with those from Method A.

5-((*tert*-Butyldiphenylsilyl)oxy)pentan-1-ol (9-OTBDPS). A mixture of **9** (63.75 g, 612.1 mmol) and imidazole (91.8 mmol, 6.25 g) in anhydrous CH_2Cl_2 (500 mL) at 0 °C under argon was treated dropwise with a solution of TBDPSCl (21.1 g, 76.5 mmol) in anhydrous CH_2Cl_2 (150 mL) over 1 h. Then, the reaction mixture was stirred for 24 h at room temperature. The mixture was washed with water and saturated aqueous NH_4Cl. The organic layer was separated, dried (Na_2SO_4), and concentrated to an oil. Chromatography [silica, hexanes/ethyl acetate (4:1), then ethyl acetate; TLC R_f = 0.13 in hexanes/ethyl acetate (3:1)] afforded a colorless oil (20.3 g, 77%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69−7.65 (m, 4H), 7.41−7.33 (m, 6H), 3.67 (t, J = 6.5 Hz, 2H), 3.57 (t, J = 6.7 Hz, 2H), 1.97 (s, 1H), 1.61−1.56 (m, 2H), 1.52 (dt, J_1 = 15.0 Hz, J_2 = 6.7 Hz, 2H), 1.44−1.38 (m, 2H), 1.06 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 135.6, 134.1, 129.6, 127.7, 63.9, 62.8, 32.5, 32.4, 27.0, 22.1, 19.3; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{31}O_2Si$ 343.2088; found 343.2087.

5-((*tert*-Butyldiphenylsilyl)oxy)pentanal (10-OTBDPS). A solution of **9-OTBDPS** (20.13 g, 58.77 mmol) in anhydrous CH_2Cl_2 (588 mL) at room temperature under argon was treated with DMP (29.9 g, 70.6 mmol). The reaction mixture was stirred for 1 h, at which point TLC analysis [silica, R_f = 0.88 in hexanes/ethyl acetate (3:1)] indicated the reaction was completed. A solution of 20% $Na_2S_2O_3$ (600 mL) was added. The organic layer was separated, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was passed through a silica pad [silica, hexanes/ethyl acetate (3:1)] to afford a colorless oil (18.33 g, 92%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (d, J = 1.9 Hz, 1H), 7.69−7.64 (m, 4H), 7.38 (dt, J_1 = 14.2 Hz, J_2 = 7.0 Hz, 6H), 3.67 (t, J = 6.2 Hz, 2H), 2.38 (td, J_1 = 7.4 Hz, J_2 = 1.8 Hz, 2H), 1.72 (p, J = 7.4 Hz, 2H), 1.59 (dt, J_1 = 9.1 Hz, J_2 = 6.3 Hz, 2H), 1.06 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 202.5, 135.5, 133.8, 129.6, 127.6, 63.2, 43.5, 31.8, 26.9, 19.2, 18.5; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{29}O_2Si$ 341.1931; found 341.1929.

5-((*tert*-Butyldiphenylsilyl)oxy)pentanoic Acid (11-OTBDPS). A solution of **10-OTBDPS** (18.33 g, 53.83 mmol) and 2-methyl-2-butene (22.8 mL, 215 mmol) in CH_3CN (180 mL) was treated with a solution of $NaClO_2$ (7.30 g, 80.7 mmol) and $NaH_2PO_4{\cdot}H_2O$ (1.48 g, 10.8 mmol) in water (90 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h, at which point TLC analysis [silica, R_f = 0.57 in hexanes/ethyl acetate (3:1)] indicated that the reaction was completed. Then, the reaction mixture was treated with 2 M HCl (80 mL) and extracted with ethyl acetate. The organic layer was separated, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, hexanes/ethyl acetate (2:1)] to afford a colorless oil (18.94 g, 99%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.74 (s, 1H), 7.68−7.64 (m, 4H), 7.43−7.35 (m, 6H), 3.67 (t, J = 6.2 Hz, 2H), 2.36 (t, J = 7.5 Hz, 2H), 1.74 (p, J = 7,5 Hz, 2H), 1.64−1.58 (m, 2H), 1.05 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 180.0, 135.6, 133.9, 129.6, 127.7, 63.3, 33.8, 31.8, 26.9, 21.2, 19.2; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{29}O_3Si$ 357.1881; found 357.1880.

5-((*tert*-Butyldimethylsilyl)oxy)pentanoic Acid (11-OTBS). A solutionof δ-valerolactone (2.00 g, 20.0 mmol) in methanol/H_2O (24 mL, v/v, 5:1) was treated with NaOH (mesh, 800 mg, 20.0 mmol) at room temperature. The reaction mixture was stirred overnight at room temperature. The solvent was removed, and the residue was further dried under high vacuum for 2 h to afford the corresponding sodium carboxylate as a white solid. The suspension of the sodium carboxylate in anhydrous THF (180 mL) was treated with $BnNEt_3Cl$ (4.56 g, 20.0 mmol), imidazole (5.45 g, 80.0 mmol), and TBSCl (6.03 g, 40.0 mmol) under argon at room temperature. The reaction mixture was stirred vigorously for 20 h at room

https://doi.org/10.1021/acs.joc.1c01239
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temperature. Water (60 mL) was added, followed by the addition of 2 M HCl (35 mL). The mixture was extracted with diethyl ether. The organic layer was separated, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, hexanes/ethyl acetate (6:1); TLC R_f = 0.46 in hexanes/ethyl acetate (6:1)] to afford a colorless oil (2.40 g, 52%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.54 (s, 1H), 3.59 (t, J = 6.3 Hz, 2H), 2.33 (t, J = 7.5 Hz, 2H), 1.65 (p, J = 7.5 Hz, 2H), 1.52 (dq, J_1 = 9.8 Hz, J_2 = 6.4 Hz, 2H), 0.84 (s, 9H), 0.00 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 180.1, 62.6, 33.8, 32.0, 25.9, 21.2, 18.3, −5.4; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{25}O_3Si$ 233.1568; found 233.1567.

***tert*-Butyldiphenylsilyl 5-((*tert*-Butyldiphenylsilyl)oxy)-pentanoate (12).** Under the general procedure for **11-OTBS**, δ-valerolactone (2.00 g, 20.0 mmol) in methanol/H_2O (24 mL, v/v, 5:1) was treated with NaOH (powder, 880 mg, 22.0 mmol). A mixture of the corresponding crude sodium carboxylate, $BnNEt_3Cl$ (4.56 g, 20.0 mmol), imidazole (5.45 g, 80.0 mmol), and TBDPSCl (10.99 g, 40.0 mmol) in anhydrous THF (100 mL) was stirred for 20 h. Chromatography [silica, hexanes/ethyl acetate (20:1), 1% acetic acid; TLC R_f = 0.70 in hexanes/ethyl acetate (6:1)] afforded first the title compound as a colorless oil (7.60 g, 64%) and second **11-OTBDPS** as a colorless oil (485 mg, 7% yield). Data for the title compound: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69−7.65 (m, 8H), 7.40 (dd, J_1 = 7.9 Hz, J_2 = 5.8 Hz, 4H), 7.38−7.33 (m, 8H), 3.68 (t, J = 6.2 Hz, 2H), 2.47 (t, J = 7.6 Hz, 2H), 1.81 (p, J = 7.6 Hz, 2H), 1.65−1.60 (m, 2H), 1.11 (s, 9H), 1.05 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 172.9, 135.6, 135.4, 134.0, 132.1, 130.1, 129.6, 127.8, 127.7, 63.5, 36.0, 32.0, 27.0, 27.0, 21.8, 19.3, 19.2; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{37}H_{46}O_3Si_2Na$ 617.2878; found 617.2871.

General Procedure I, DCC Coupling Reaction to Afford NHS-Active Esters. A solution of carboxylic acid (1.0 equiv) and *N*-hydroxysuccinimide (1.5 equiv) in anhydrous CH_2Cl_2 at 0 °C under argon was treated with DCC (1.5 equiv). The reaction mixture was stirred at 0 °C for 1 h and then 23 h at room temperature. The solvent was removed, and the residue was diluted with diethyl ether. The resulting suspension was passed through a silica pad, eluting with diethyl ether. The filtrate was concentrated and chromatographed to afford the corresponding NHS-active ester.

*2,5-Dioxopyrrolidin-1-yl-5-((tert-butyldimethylsilyl)oxy)pentanoate (**13-OTBS**).* Following general procedure I, a solution of **11-OTBS** (1.86 g, 8.00 mmol) and *N*-hydroxysuccinimide (1.38 g, 12.0 mmol) in anhydrous CH_2Cl_2 (40 mL) was treated with DCC (2.48 g, 12.0 mmol). Chromatography [silica, hexanes/ethyl acetate (2:1); TLC R_f = 0.48 in hexanes/ethyl acetate (3:1)] afforded a colorless oil (2.53 g, 96%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.65 (t, J = 6.2 Hz, 2H), 2.83 (d, J = 6.6 Hz, 4H), 2.65 (t, J = 7.5 Hz, 2H), 1.82 (p, J = 7.5 Hz, 2H), 1.66−1.60 (m, 2H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.2, 168.6, 62.3, 31.7, 30.7, 25.9, 25.6, 21.3, 18.3, −5.4; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{15}H_{28}NO_5Si$ 330.1731; found 330.1732.

*2,5-Dioxopyrrolidin-1-yl-5-(trityloxy)pentanoate (**13-OTr**).* Following general procedure I, a solution of **11-OTr** (2.70 g, 7.85 mmol) and *N*-hydroxysuccinimide (1.36 g, 11.8 mmol) in anhydrous CH_2Cl_2 (80 mL) was treated with DCC (2.43 g, 12.0 mmol). Silica pad filtration [eluting with diethyl ether, R_f = 0.25 in hexanes/ethyl acetate (2:1)] afforded a white solid (3.59 g, quantitative): mp 126−129 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 6H), 7.29 (t, J = 7.6 Hz, 6H), 7.23 (t, J = 7.1 Hz, 3H), 3.10 (t, J = 6.2 Hz, 2H), 2.81 (s, 4H), 2.58 (t, J = 7.4 Hz, 2H), 1.86 (p, J = 7.5 Hz, 2H), 1.72 (dt, J_1 = 9.1 Hz, J_2 = 6.2 Hz, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.1, 168.5, 144.3, 128.6, 127.8, 126.9, 86.5, 62.6, 30.7, 29.1, 25.6, 21.6; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{28}H_{27}NO_5Na$480.1781; found 480.1778.

*2,5-Dioxopyrrolidin-1-yl-5-((tert-butyldiphenylsilyl)oxy)pentanoate (**13-OTBDPS**).* Following general procedure I, a solution of **11-OTBDPS** (19.18 g, 53.79 mmol) and *N*-hydroxysuccinimide (9.29 g, 80.7 mmol) in anhydrous CH_2Cl_2 (270 mL) was treated with DCC (16.7 g, 80.7 mmol). Chromatography [silica, hexanes/ethyl acetate (3:1); TLC R_f = 0.30 in hexanes/ethyl acetate (3:1)] afforded a colorless oil (18.94 g, 78%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68−7.64 (m, 4H), 7.43−7.40 (m, 2H), 7.38 (dd, J_1 = 7.8 Hz, J_2 = 6.2 Hz, 4H), 3.69 (t, J = 6.1 Hz, 2H), 2.84−2.74 (m, 4H), 2.61 (t, J = 7.5 Hz, 2H), 1.86 (p, J = 7.5 Hz, 2H), 1.70−1.63 (m, 2H), 1.05 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 169.2, 168.6, 135.6, 133.8, 129.7, 127.7, 63.1, 31.5, 30.7, 26.9, 25.6, 21.3, 19.2; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{25}H_{31}NO_5SiNa$ 476.1864; found 476.1859.

General Procedure II, Acylation of the Chiral Auxiliary 4 with an Active Ester. A solution of **4** (1.0 equiv) in anhydrous THF at −78 °C under argon was treated with *n*-BuLi (1.0 equiv). The reaction mixture was stirred for 10−15 min at −78 °C, followed by addition of the active ester (1.05−1.1 equiv). The reaction mixture was stirred for 10−15 min at −78 °C and then was allowed to warm to room temperature over 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic extract was separated, dried (Na_2SO_4), and concentrated. Chromatography afford the corresponding product.

*(R)-3-(5-((tert-Butyldimethylsilyl)oxy)pentanoyl)-4-isopropyloxazolidin-2-one (**14-OTBS**).* Following general procedure II, a solution of **4** (258 mg, 2.00 mmol) in anhydrous THF (27 mL) was treated with *n*-BuLi (1.25 mL, 1.6 M in hexanes, 2.0 mmol), followed by a solution of **13-OTBS** (691 mg, 2.1 mmol) in anhydrous THF (5.0 mL). Chromatography [silica, hexanes/ethyl acetate (6:1) to (1:1); TLC R_f = 0.73 in hexanes/ethyl acetate (2:1)] afforded a yellow oil (539 mg, 79%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.43 (dt, J_1 = 8.3 Hz, J_2 = 3.4 Hz, 1H), 4.26 (t, J = 8.7 Hz, 1H), 4.20 (dd, J_1 = 9.1 Hz, J_2 = 2.9 Hz, 1H), 3.64 (t, J = 6.4 Hz, 2H), 3.01 (ddd, J_1 = 16.8 Hz, J_2 = 8.3 Hz, J_3 = 6.5 Hz, 1H), 2.89 (ddd, J_1 = 16.8 Hz, J_2 = 8.2 Hz, J_3 = 6.8 Hz, 1H), 2.37 (doublet of quintets, J_1 = 7.0 Hz, J_2 = 3.9 Hz, 1H), 1.77−1.67 (m, 2H), 1.62−1.55 (m, 2H), 0.92 (d, J = 7.0 Hz, 3H), 0.89 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H), 0.05 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 173.2, 154.0, 63.3, 62.8, 58.4, 35.3, 32.2, 28.4, 26.0, 20.1, 18.3, 18.0, 14.7, −5.3; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{34}NO_4Si$ 344.2252; found 344.2260.

*(R)-4-Isopropyl-3-(5-(trityloxy)pentanoyl)oxazolidin-2-one (**14-OTr**).* Following general procedure II, a solution of **4** (646 mg, 5.00 mmol) in anhydrous THF (50 mL) was treated with *n*-BuLi (3.20 mL, 1.6 M in hexanes, 5.0 mmol), followed by **13-OTr** (2.52 g, 5.51 mmol). Chromatography [silica, hexanes/ethyl acetate (4:1); TLC R_f = 0.54 in hexanes/ethyl acetate (2:1)] afforded a white solid (2.02 g, 86%): mp 127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (d, J = 7.8 Hz, 6H), 7.28 (t, J = 7.6 Hz, 6H), 7.21 (t, J = 7.3 Hz, 3H), 4.40 (dt, J_1 = 7.7 Hz, J_2 = 3.5 Hz, 1H), 4.21 (t, J = 8.7 Hz, 1H), 4.16 (dd, J_1 = 9.1 Hz, J_2 = 3.1 Hz, 1H), 3.09 (t, J = 6.3 Hz, 2H), 2.97 (dt, J_1 = 16.9 Hz, J_2 = 7.2 Hz, 1H), 2.86 (dt, J_1 = 16.8 Hz, J_2 = 7.3 Hz, 1H), 2.35 (doublet of quintets, J_1 = 7.0 Hz, J_2 = 3.8 Hz, 1H), 1.79−1.73 (m, 2H), 1.68 (p, J = 6.7 Hz, 2H), 0.89 (d, J = 7.1 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 173.1, 154.0, 144.4, 128.7, 127.7, 126.8, 86.4, 63.3, 63.2, 58.3, 35.4, 29.5, 28.4, 21.3, 18.0, 14.7; HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{30}H_{33}NO_4Na$ 494.2302; found 494.2306.

*(R)-3-(5-((tert-Butyldimethylsilyl)oxy)pentanoyl)-4-isopropyloxazolidin-2-one (**14-OTBDPS**).* Following general procedure II, a solution of **4** (3.87 g, 30.0 mmol) in anhydrous THF (300 mL) was treated with *n*-BuLi (18.75 mL, 1.6 M in hexanes, 30. mmol), followed by **13-OTBDPS** (15.0 g, 33.0 mmol). Chromatography [silica, hexanes/ethyl acetate (6:1 to 3:1); TLC R_f = 0.50 in hexanes/ethyl acetate (3:1)] afforded a colorless oil (13.68 g, 97%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68−7.64 (m, 4H), 7.38 (dt, J_1 = 14.2 Hz, J_2 = 7.0 Hz, 6H), 4.42 (dt, J_1 = 7.7 Hz, J_2 = 3.4 Hz, 1H), 4.23 (t, J = 8.7 Hz, 1H), 4.18 (dd, J_1 = 9.1 Hz, J_2 = 3.0 Hz, 1H), 3.69 (t, J = 6.3 Hz, 2H), 3.03−2.96 (m, 1H), 2.87 (dt, J_1 = 16.6 Hz, J_2 = 7.5 Hz, 1H), 2.36 (doublet of quintets, J_1 = 7.0 Hz, J_2 = 3.9 Hz, 1H), 1.76 (ddt, J_1 = 11.5 Hz, J_2 = 7.1 Hz, J_3 = 4.1 Hz, 2H), 1.63 (p, J = 6.7 Hz, 2H), 1.05 (s, 9H), 0.90 (d, J = 7.1 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 173.2, 154.1,

https://doi.org/10.1021/acs.joc.1c01239
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135.6, 134.0, 130.0, 127.6, 63.5, 63.3, 58.4, 35.3, 32.0, 28.4, 26.9, 20.9, 19.2, 18.0, 14.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{27}H_{37}NO_4SiNa$ 490.2384; found 490.2389.

(*R*)-3-((2*S*,3*S*)-2-(3-((*tert*-Butyldiphenylsilyl)oxy)propyl)-3-methyl-5-(trimethylsilyl)pent-4-ynoyl)-4-isopropyloxazolidin-2-one, Hexacarbonyldicobalt Complex (15-OTBDPS). A solution of **14-OTBDPS** (13.7 g, 29.2 mmol) in anhydrous CH_2Cl_2 (75 mL) at 0 °C under argon was treated with distilled $(i\text{-Pr})_2NEt$ (5.09 mL, 29.2 mmol). After 5 min, Bu_2BOTf (29.2 mL, 29.2 mmol) was added. The reaction mixture was stirred for 10 min at 0 °C and then treated with Bu_2BOTf (29.2 mL, 29.2 mmol) via an addition funnel. When the addition was completed, the resulting mixture was cooled to −78 °C and treated dropwise with a solution of **3** (12.9 g, 29.2 mmol) in anhydrous CH_2Cl_2 (75 mL) over 15 min. After the addition was completed, the reaction mixture was allowed to warm to 0 °C over 1.5 h, whereupon TLC analysis [silica, hexanes/ethyl acetate (20:1)] indicated that **3** was consumed. The reaction mixture was treated with sodium phosphate buffer (pH 7, 0.1 M) at 0 °C, and the organic layer was then separated, dried (Na_2SO_4), and concentrated to a dark oil. The dark oil was chromatographed [silica, hexanes to hexanes/ethyl acetate (20:1)] to give a dark band [R_f = 0.59 in hexanes/ethyl acetate (6:1)], which afforded a bright-red oil (17.5 g, 68%): ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.36 (td, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 4H), 7.14−7.05 (m, 6H), 4.23−4.19 (m, 1H), 3.95 (t, J = 8.8 Hz, 1H), 3.90 (dd, J_1 = 9.1 Hz, J_2 = 3.2 Hz, 1H), 3.80 (dt, J_1 = 11.9 Hz, J_2 = 2.2 Hz, 1H), 3.36−3.32 (m, 2H), 3.12 (dd, J_1 = 7.1 Hz, J_2 = 2.4 Hz, 1H), 2.02 (tt, J_1 = 6.9 Hz, J_2 = 3.4 Hz, 1H), 1.79−1.72 (m, 1H), 1.30−1.17 (m, 3H), 0.92 (d, J = 7.1 Hz, 3H), 0.75 (s, 9H), 0.64 (d, J = 7.1 Hz, 3H), 0.58 (d, J = 6.9 Hz, 3H), 0.00 (s, 9H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$): δ 200.3, 173.7, 153.3, 135.5, 134.8, 134.0, 133.9, 129.5, 127.6, 115.1, 64.1, 63.1, 58.2, 49.2, 41.4, 31.1, 28.6, 26.9, 20.8, 19.2, 18.3, 18.0, 14.5, 1.14; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{40}H_{49}Co_2NO_{10}Si_2Na$ 900.1451; found 900.1462.

(2*S*,3*S*)-2-(3-((*tert*-Butyldiphenylsilyl)oxy)propyl)-3-methylpent-4-ynoic Acid (17). From **15-OTBDPS**: a solution of **15-OTBDPS** (16.1 g, 18.3 mmol) in acetone (330 mL) was treated with CAN (beginning with 1 equiv and adding additional aliquots until the reaction completed) at room temperature until the characteristic dark-red spot due to the starting material no longer appeared upon TLC analysis [silica, hexanes/ethyl acetate (10:1)]. The additional aliquots of CAN typically consisted of 0.5 equiv every 20 min for the first hour and then 0.5 equiv every 30 min until the reaction was completed, typically a total duration of ∼3 h. Then, the solvent was removed. The resulting residue was washed with diethyl ether and water. The organic layer was separated, dried (Na_2SO_4), and concentrated to a yellow oil. The yellow oil was passed through a silica pad [hexanes/ethyl acetate (6:1); TLC R_f = 0.50 in hexanes/ethyl acetate (6:1)], and the filtrate was collected and concentrated to give **16** as a colorless oil (10.3 g). The intermediate **16** was not characterized but was subjected to the next reaction using the standard hydrolysis conditions[33] for the *N*-acylated oxazolidinone. Thus, the oil in its entirety (10.3 g, ∼17.4 mmol) was dissolved in a mixture of THF (195 mL, ACS grade) and H_2O (65 mL) and then was treated with 30% H_2O_2 (15.8 g, 139 mmol) and LiOH (1.67 g, 69.6 mmol) at room temperature. The resulting mixture was stirred for 18 h at room temperature before addition of 1.5 N Na_2SO_3 solution. The resulting mixture was stirred for 1 h and then treated with a saturated aqueous $NaHCO_3$ solution. The THF was removed by rotary evaporation, and the remaining aqueous solution was washed with CH_2Cl_2 and acidified by 2 M HCl to pH 1. The organic layer was separated, and the aqueous layer was further extracted with ethyl acetate. The combined organic extract was dried (Na_2SO_4) and concentrated to a colorless oil. Chromatography [silica, hexanes/ethyl acetate (2:1) with 1% acetic acid] afforded first **17-TMS** (minor product, data are provided below; silica TLC R_f = 0.62 in hexanes/ethyl acetate (6:1) with 1% acetic acid) as a colorless oil (1.16 g, 13%), followed by the title compound (major product; silica TLC R_f = 0.30 in hexanes/ethyl acetate (3:1) with 1% acetic acid) as a yellow oil (5.55 g, 74%): ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68−7.63 (m, 4H), 7.44−7.35 (m, 6H), 3.67 (hept, J_1 = 6.0 Hz, J_2 = 5.2 Hz, 2H), 2.81 (doublet of quintets, J_1 = 6.9 Hz, J_2 = 2.3 Hz, 1H), 2.49 (p, J = 5.2 Hz, 1H), 2.09 (d, J = 2.4 Hz, 1H), 1.84−1.71 (m, 2H), 1.68−1.53 (m, 2H), 1.23 (d, J = 7.0 Hz, 3H), 1.04 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 179.5, 135.6, 133.9, 129.6, 127.6, 85.9, 69.9, 63.4, 50.0, 30.3, 27.9, 26.9, 25.3, 19.2, 17.9; HRMS (ESI-TOF) m/z: $[M - H]^-$ calcd for $C_{25}H_{31}O_3Si$ 407.2048; found 407.2042.

Data for (2*S*,3*S*)-2-(3-((*tert*-Butyldiphenylsilyl)oxy)propyl)-3-methyl-5-(trimethylsilyl)pent-4-ynoic Acid (17-TMS). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55 (d, J = 7.2 Hz, 4H), 7.32−7.23 (m, 6H), 3.56 (td, J_1 = 6.0 Hz, J_2 = 3.6 Hz, 2H), 2.69 (q, J = 6.9 Hz, 1H), 2.35 (dt, J_1 = 9.3 Hz, J_2 = 5.6 Hz, 1H), 1.65−1.61 (m, 2H), 1.58−1.42 (m, 2H), 1.09 (d, J = 7.0 Hz, 3H), 0.94 (s, 9H), 0.00 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 180.1, 135.5, 133.8, 133.8, 129.5, 127.6, 108.5, 86.1, 63.5, 50.4, 30.4, 29.1, 26.8, 25.2, 19.1, 17.7, 0.00; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{41}O_3Si_2$ 481.2589; found 481.2586.

Conversion from 17-TMS to 17. *Method A.* A solution of **17-TMS** (240. mg, 0.500 mmol) in methanol (20 mL) was treated with potassium carbonate (208 mg, 1.50 mmol) at room temperature. The resulting mixture was stirred overnight before addition of 2 M HCl. The resulting mixture was extracted with ethyl acetate. The organic extract was dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (6:1)] to afford a colorless oil (149 mg, 73%), which exhibited ^{1}H NMR and ^{13}C NMR spectra consistent with those of **17**.

Method B. A solution of **17-TMS** (240. mg, 0.500 mmol) in a mixture of THF and water (8.0 mL, 3:1, v/v) at room temperature was treated with 30% H_2O_2 (136 mg, 4.00 mmol) and LiOH (48 mg, 2.0 mmol). The reaction mixture was stirred for 20 h at room temperature and then was cooled to 0 °C and treated with 1.5 N Na_2SO_3 solution. The resulting mixture was stirred for 1 h at 0 °C and then was treated with a saturated aqueous $NaHCO_3$ solution. The resulting mixture was extracted with dichloromethane and acidified by addition of 2 M HCl to pH ∼ 1. The aqueous layer was then further extracted with ethyl acetate. The organic extracts were combined, dried (Na_2SO_4), and concentrated to a yellow oil. The yellow oil was chromatographed [silica, hexanes/ethyl acetate (6:1)] to afford a colorless oil (178 mg, 87%), which exhibited ^{1}H NMR and ^{13}C NMR spectra consistent with those of **17**.

2-*tert*-Butoxycarbonyl-4-methylpyrrole (20). Following a reported procedure[36,37] with some modification, a mixture of acetic anhydride (33.0 g, 0.323 mol) and DMAP (800. mg, 6.55 mmol) in CH_2Cl_2 (100 mL) at room temperature was stirred for 10 min. Then, a sample of 2-nitro-1-propanol (20.0 g, 0.190 mol) was added slowly with ensuing reflux. The reaction mixture was stirred for 16 h at room temperature. Methanol (20 mL) was added, and the mixture was stirred for 1 h. The mixture was washed with aqueous saturated $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting residue was passed through a silica column (CH_2Cl_2) to afford a clear blue liquid, which constituted the stock starting material **19** (22.8 g, 81%). A mixture of *tert*-butyl isocyanoacetate (4.43 g, 31.3 mmol) and 2-(*tert*-butyl)-1,1,3,3-tetramethylguanidine (11.2 g, 65.4 mmol) in a mixture of THF (ACS grade) and isopropanol (28 mL, 1:1, v/v) was added dropwise to a solution of **19** (5.98 g, 40.7 mmol) in a mixture of THF (ACS grade) and isopropanol (81 mL, 1:1, v/v) via an addition funnel over 1 h. Then the reaction mixture was stirred at room temperature for 5 h before concentration *in vacuo* and chromatography (silica, CH_2Cl_2, 5 cm × 15 cm; TLC R_f = 0.76 in CH_2Cl_2) to afford a white solid (4.65 g, 82%): mp 109−113 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.27 (br s, 1H), 6.69−6.63 (m, 2H), 2.09 (s, 3H), 1.55 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 161.0, 123.9, 120.7, 120.6, 115.4, 80.6, 28.4, 11.7; HRMS (ESI-TOF) m/z: $[M - H]^-$ calcd for $C_{10}H_{14}NO_2$180.1030; found 180.1030.

2-*tert*-Butoxycarbonyl-5-iodo-4-methylpyrrole (21). A solution of **20** (2.56 g, 14.1 mmol) in anhydrous DMF (300 mL) at 0 °C under argon was treated with NIS (793 mg) in one batch. After

https://doi.org/10.1021/acs.joc.1c01239
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30 min, a second batch of NIS (793 mg) was added. After 30 min, a third batch of NIS (793 mg) was added. After 30 min, a fourth batch of NIS (793 mg, a total of 3.17 g, 14.1 mmol) was added, whereupon the flask was allowed to warm to room temperature for 2 h. TLC analysis [silica, ethyl acetate/hexanes (1:8), R_f = 0.60] indicated the reaction was completed. The reaction mixture was poured into a beaker containing a mixture of ethyl acetate and water. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, hexanes, and then hexanes/diethyl ether (9:1) or hexanes/ethyl acetate (15:1), 3 cm × 15 cm] to afford a white solid (3.07 g, 71%): mp 132−133 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.07 (br s, 1H), 6.62 (d, J = 2.7 Hz, 1H), 2.03 (s, 3H), 1.55 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.5, 128.2, 126.6, 115.5, 81.1, 72.5, 28.4, 13.7; HRMS (ESI-TOF) m/z: $[M - H]^-$ calcd for $C_{10}H_{13}INO_2$ 305.9996; found 305.9993.

2-*tert*-Butoxycarbonyl-3-bromo-5-iodo-4-methylpyrrole (21-Br). An oven-dried 200 mL flask equipped with a stir bar was allowed to cool to room temperature under argon. A sample of **21** (1.54 g, 5.00 mmol) was added, followed by anhydrous $CHCl_3$ (100 mL, stabilized with amylenes) via syringe. Then, DBDMH (1.43 g, 5.00 mmol) was added, and the flask was heated in an oil bath at 65 °C. The reaction progress was monitored by TLC; after 1.5 h, the starting material was consumed [product, R_f = 0.20; starting material, R_f = 0.19 in hexanes/CH_2Cl_2 (3:1), silica]. Then the flask was allowed to cool to room temperature, whereupon the mixture was washed with 20% aqueous sodium thiosulfate, brine, and water. The organic phase was dried (Na_2SO_4) and concentrated. The residue was chromatographed [silica, hexanes/CH_2Cl_2(2:1), then CH_2Cl_2, R_f = 0.61 in CH_2Cl_2] to afford a white solid (1.72 g, 90%): mp 154−157 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.13 (br s, 1H), 2.04 (s, 3H), 1.58 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 158.4, 127.2, 125.7, 103.7, 82.2, 71.3, 28.4, 13.3; HRMS (ESI-TOF) m/z: $[M - H]^-$ calcd for $C_{10}H_{12}BrINO_2$ 383.9102; found 383.9102.

5-*tert*-Butoxycarbonyl-3-methyl-2-[(*E*)-(4,4-dimethyl-5-oxodihydrofuran-2(3*H*)-ylidene)methyl]pyrrole (23). Following a reported procedure[38] with some modification, anhydrous acetonitrile was deaerated by bubbling with argon for 30 min in an oven-dried flask containing powdered molecular sieves (3 Å). A sample of NEt_3 was deaerated likewise. Samples of **21** (3.07 g, 10.0 mmol), **22** (1.26 g, 10.0 mmol), and $BnNEt_3Cl$ (2.28 g, 10.0 mmol) were placed in a 200 mL Schlenk flask charged with argon. Then deaerated acetonitrile (100 mL) and NEt_3 (11.1 mL) were added, and the mixture was degassed by three freeze−pump−thaw cycles. Pd(PPh_3)$_4$ (578 mg, 0.500 mmol) was added under argon, and the flask was sealed immediately. The reaction mixture was stirred in an oil bath at 60 °C for 8 h. The flask was allowed to cool to room temperature, and then a mixture of ethyl acetate and water was added. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, ethyl acetate/hexanes (5:1)] to afford a yellow solid (2.42 g, 79%): mp 167−171 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (br s, 1H), 6.63 (d, J = 2.5 Hz, 1H), 6.20 (s, 1H), 2.93 (d, J = 2.1 Hz, 2H), 2.04 (s, 3H), 1.55 (s, 9H), 1.38 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 179.1, 160.8, 147.7, 127.3, 123.4, 120.3, 116.3, 97.0, 80.9, 40.3, 40.1, 28.4, 25.1, 11.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}NO_4$ 306.1700; found 306.1696.

5-*tert*-Butoxycarbonyl-4-bromo-3-methyl-2-[(*E*)-(4,4-dimethyl-5-oxodihydrofuran-2(3*H*)-ylidene)methyl]pyrrole (23-Br). *From Lactone−Pyrrole **23**.* A sample of **23** (30 mg, 98.3 μmol) in an oven-dried 5 mL vial was dissolved in anhydrous THF (1.0 mL) under argon. The solution was cooled to −78 °C and treated with NBS (17.5 mg, 98.3 μmol) in one batch. The reaction mixture was stirred at −78 °C for 1.5 h and then moved to an ice bath and stirred for 1 h. Water and CH_2Cl_2 were added. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by use of an analytical-scale TLC plate [200 μm thick silica, 20 cm × 20 cm plate, hexanes/ethyl acetate (6:1)], from which the title compound was obtained by removal of the silica from the plate and elution by ethyl acetate to afford a pale yellow solid (8.0 mg, 21%): mp 176−179 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.69 (br s, 1H), 6.18 (s, 1H), 2.92−2.89 (m, 2H), 2.01 (s, 3H), 1.59 (s, 9H), 1.35 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 178.9, 159.8, 149.1, 126.5, 121.1, 120.7, 106.0, 96.6, 82.1, 40.3, 40.1, 28.4, 25.1, 10.6; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{22}BrNO_4Na$ 406.0624; found 406.0623.

*From 5-Iodo-3-bromopyrrole **21-Br**.* Following a reported procedure[38] with some modification, anhydrous acetonitrile and NEt_3 were separately deaerated by bubbling with argon for 30 min in an oven-dried flask equipped with powdered molecular sieves (3 Å). A sample of NEt_3 was treated likewise. Samples of **21-Br** (386 mg, 1.00 mmol), **22** (126 mg, 1.00 mmol), and $BnNEt_3Cl$ (341 mg, 1.50 mmol) were placed in a Schlenk flask charged with argon. Then deaerated acetonitrile (10 mL) and NEt_3 (1.68 mL) were added, and the mixture was degassed by three freeze−pump−thaw cycles. Pd(PPh_3)$_4$ (58 mg, 0.050 mmol) was added under argon, and the flask was sealed immediately. The reaction mixture was stirred in an oil bath at 60 °C for 24 h. The flask was allowed to cool to room temperature, and then a mixture of CH_2Cl_2 and water was added. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed [silica, ethyl acetate/hexanes (6:1)] to afford a yellow solid (191 mg, 50%): mp 176−179 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (br s, 1H), 6.18 (d, J = 2.2 Hz, 2H), 2.90 (d, J = 2.1 Hz, 2H), 2.01 (s, 1H), 1.59 (s, 9H), 1.35 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 178.9, 159.9, 149.2, 126.5, 121.1, 120.7, 106.0, 96.7, 82.1, 40.3, 40.1, 28.4, 25.1, 10.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{22}BrNO_4$ 382.0659; found 382.0664.

5-*tert*-Butoxycarbonyl)-3-methyl-2-[(*E*)-(4,4-dimethyl-5-methylenedihydrofuran-2(3*H*)-ylidene)methyl]pyrrole (24). Following a reported procedure[38] with some modification, a solution of $TiCp_2Cl_2$ (11.7 g, 47.0 mmol) in anhydrous toluene (127 mL) was treated with LiMe (1.6 M, 64.4 mL in Et_2O, 100 mmol) at 0 °C under argon. Then the reaction mixture was stirred at 0 °C for 1.5 h in the dark and quenched by the addition of a saturated aqueous NH_4Cl solution. The resulting organic layer was washed with brine and water, dried (Na_2SO_4), and filtered. The (orange) filtrate (~117 mL), which contains the Petasis reagent, was added into a 250 mL flask containing **23** (2.42 g, 7.92 mmol) under argon. The resulting reaction mixture under argon in the dark was stirred in an oil bath at 80 °C for 4.5 h before allowing to cool to room temperature. Then, MeOH (9.38 mL), $NaHCO_3$ (396 mg), and water (95 μL) were added, and the resulting reaction mixture was stirred in an oil bath at 40 °C in the dark for 14 h and then filtered through a Celite pad. The filtrate was collected and concentrated to an orange oil. A silica column was prewashed with 5% NEt_3 in hexanes, followed by CH_2Cl_2 and then hexanes given the sensitivity of the ene−lactone−pyrrole title compound. The column was then used to chromatograph the orange oil [hexanes/ethyl acetate (10:1)] to afford a yellow oil (2.27 g, 95%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 6.62 (d, J = 2.5 Hz, 1H), 5.92 (d, J = 2.0 Hz, 1H), 4.41 (d, J = 2.5 Hz, 1H), 4.02 (d, J = 2.5 Hz, 1H), 2.69 (d, J = 2.0 Hz, 2H), 2.02 (s, 3H), 1.55 (s, 9H), 1.27 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 168.9, 160.9, 153.8, 129.5, 122.3, 118.8, 116.3, 91.8, 80.9, 80.5, 42.2, 40.4, 28.4, 27.7, 11.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{25}NO_3$ 304.1907; found 304.1908.

9-*tert*-Butoxycarbonyl-2,3-dihydro-1,2,2,7-tetramethyldipyrrin (25). Following a reported procedure[38] with some modification, a solution of **24** (412 mg, 1.36 mmol) in DMF (15 mL) was treated with 1 M HCl (350 μL, 0.35 mmol). The reaction mixture was stirred at room temperature for 40 min, whereupon TLC analysis indicated the presence of the diketone intermediate [silica, R_f = 0.29, hexanes/ethyl acetate (6:1)] and the absence of the starting material. Then NH_4OAc (2.09 g, 27.3 mmol) and NEt_3 (3.73 mL, 27.3 mmol) were added, and the resulting mixture was stirred in an oil bath at 55 °C. After 2 h, TLC analysis indicated the presence of product [silica, R_f = 0.75, hexanes/ethyl acetate (6:1)] and the absence of the diketone intermediate. The reaction mixture was allowed to cool to room temperature and then quenched by the

https://doi.org/10.1021/acs.joc.1c01239
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slow addition of a saturated aqueous KH_2PO_4 solution, followed by ethyl acetate. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The resulting mixture was purified by chromatography [silica, hexanes/ethyl acetate (20:1)] to afford a yellow solid (337 mg, 82%): mp 91−96 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.21 (br s, 1H), 6.60 (d, J = 2.8 Hz, 1H), 5.83 (d, J = 1.9 Hz, 1H), 2.58 (d, J = 1.9 Hz, 2H), 2.14 (s, 3H), 2.08 (s, 3H), 1.56 (s, 9H), 1.18 (s, 6H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 188.1, 160.6, 151.2, 131.8, 122.7, 118.3, 115.8, 103.3, 79.9, 48.4, 44.4, 28.4, 25.6, 15.8, 10.8; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{26}N_2O_2$ 303.2067; found 303.2070.

5-*tert*-Butyloxycarbonyl-3-methyl-2-[(*E*)-((3*S*,4*S*)-4-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methyl-5-oxodihydrofuran-2(3*H*)-ylidene)methyl)]pyrrole (26). Following a reported procedure[38] with modification, a solution of **21** (1.58 g, 5.14 mmol), **17** (2.10 g, 5.14 mmol), and $BnNEt_3Cl$ (1.17 g, 5.14 mmol) in anhydrous acetonitrile (103 mL) in a 200 mL Schlenk flask under argon was treated with NEt_3 (5.73 mL). The resulting mixture was deaerated by three freeze−pump−thaw cycles. A sample of $Pd(PPh_3)_4$ (297 mg, 0.257 mmol) was added in one batch under argon. Then, the flask was sealed immediately, heated in an oil bath at 60 °C for 16 h, and then allowed to cool to room temperature. Ethyl acetate and water were added. The organic layer was separated, dried (Na_2SO_4), and concentrated to a yellow oil, which was chromatographed [silica, hexanes to hexanes/ethyl acetate (10:1); TLC R_f = 0.17 in hexanes/ethyl acetate (10:1)] to afford a yellow foam (1.47 g, 49%): ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.70 (br s, 1H), 7.66−7.62 (m, 4H), 7.43−7.35 (m, 6H), 6.64 (d, J = 2.5 Hz, 1H), 6.12 (d, J = 1.6 Hz, 1H), 3.72−3.65 (m, 2H), 2.99 (ddd, J_1 = 7.1 Hz, J_2 = 3.5 Hz, J_3 = 1.7 Hz, 1H), 2.41 (dt, J_1 = 7.4 Hz, J_2 = 3.7 Hz, 1H), 2.03 (s, 3H), 1.86−1.71 (m, 2H), 1.70−1.66 (m, 2H), 1.56 (s, 9H), 1.23 (d, J = 7.1 Hz, 3H), 1.04 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 175.7, 160.7, 154.9, 135.6, 133.7, 133.6, 129.7, 127.7, 126.6, 123.5, 120.6, 116.3, 96.3, 80.9, 63.0, 48.3, 29.5, 28.4, 27.9, 26.9, 19.2, 11.2; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{35}H_{46}NO_5Si$ 588.3140; found 588.3142.

***5*-*tert*-Butyloxycarbonyl-3-methyl-2-[(*E*)-((3*S*,4*S*)-4-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methyl-5-methylenedihydrofuran-2(3*H*)-ylidene)methyl]pyrrole (27).** Following a reported procedure[38] with modification, a solution of $TiCp_2Cl_2$ (2.36 g, 9.48 mmol) in anhydrous toluene (25.2 mL) at 0 °C under argon was treated dropwise with LiMe solution (1.6 M, 12.9 mL in diethyl ether). The resulting reaction mixture was stirred for 1.5 h at 0 °C in the dark, followed by the addition of a saturated aqueous NH_4Cl solution. The organic layer was separated, washed with water and brine, and filtered through cotton to remove dark orange materials, which afforded an orange filtrate (~35 mL) containing the Petasis reagent. A sample of 20 mL of the freshly prepared Petasis reagent was added into a 100 mL flask containing **26** (587 mg, 1.00 mmol) under argon. The resulting mixture was treated with additional $TiCp_2Cl_2$ (53 mg, 0.21 mmol) under argon and heated in an oil bath at 80 °C in the dark for 6 h. Afterward, the resulting mixture was allowed to cool to room temperature, whereupon MeOH (1.18 mL), $NaHCO_3$ (50 mg) and water (12 μL) were added. The reaction mixture was stirred in an oil bath at 40 °C for 12 h and then filtered through a Celite pad to afford a yellow filtrate. A silica column was prewashed with 5% NEt_3 in hexanes, followed by CH_2Cl_2 and then hexanes given the sensitivity of the ene−lactone−pyrrole title compound. The column was then used to chromatograph the yellow product [hexanes/ethyl acetate (10:1); TLC R_f = 0.71 in hexanes/ethyl acetate (10:1)] to afford a yellow foam (207 mg, 35%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (br s, 1H), 7.69−7.62 (m, 4H), 7.43−7.33 (m, 6H), 6.63 (d, J = 2.5 Hz, 1H), 5.84 (s, 1H), 4.51 (d, J = 2.1 Hz, 1H), 4.05 (d, J = 2.1 Hz, 1H), 3.65 (td, J_1 = 6.0, J_2 = 3.4 Hz, 2H), 2.79 (q, J = 7.1 Hz, 1H), 2.47−2.41 (m, 1H), 2.02 (s, 3H), 1.62 (ddd, J_1 = 9.8, J_2 = 6.9, J_3 = 4.6 Hz, 2H), 1.55 (s, 9H), 1.54−1.49 (m, 2H), 1.21 (d, J = 7.1 Hz, 3H), 1.04 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.4, 160.7, 160.3, 135.6, 133.9, 129.6, 128.8, 127.7, 122.4, 119.1, 116.4, 91.2, 84.7, 80.5, 63.5, 48.8, 40.3, 30.9, 29.6, 28.6, 28.5, 26.9, 19.2, 18.9, 11.2; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{36}H_{48}NO_4Si$ 586.3347; found 586.3349.

(2*S*,3*S*)-9-*tert*-Butoxycarbonyl-2-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-2,3-dihydro-1,3,7-trimethyldipyrrin (28). Following a reported procedure[38] with modification, a solution of **27** (29 mg, 0.049 mmol) in anhydrous DMF (500 μL) was treated with 1 M HCl (25 μL) under argon. The reaction progress was monitored by absorption spectroscopy and TLC. After 30 min, absorption spectroscopy (loss of absorption at ~300 nm) and TLC analysis [silica, R_f = 0.15, hexanes/ethyl acetate (10:1)] indicated formation of the diketone intermediate **27′**. Samples of NH_4OAc (77 mg, 1.0 mmol) and NEt_3 (139 μL) were added. The reaction mixture was stirred in an oil bath at 55 °C, and the reaction was monitored by absorption spectroscopy and TLC. After 30 min, absorption spectroscopy (growth in absorption at ~350 nm) and TLC analysis [silica, R_f = 0.46, hexanes/ethyl acetate (10:1)] indicated formation of the dihydrodipyrrin. The reaction mixture was allowed to cool to room temperature, quenched by the addition of saturated aqueous KH_2PO_4 solution, and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated. The resulting crude mixture was chromatographed [silica, hexanes/ethyl acetate (10:1)] to afford a yellow film (20 mg, 68%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.27 (br s, 1H), 7.68 (dt, J_1 = 8.0, J_2 = 1.8 Hz, 4H), 7.49−7.38 (m, 6H), 6.64 (d, J = 2.8 Hz, 1H), 5.77 (d, J = 1.7 Hz, 1H), 3.75−3.68 (m, 2H), 2.62 (ddd, J_1 = 7.2, J_2 = 3.8, J_3 = 1.7 Hz, 1H), 2.39 (dd, J_1 = 8.6, J_2 = 4.1 Hz, 1H), 2.20 (s, 3H), 2.13 (s, 2H), 2.11−2.03 (m, 1H), 1.84 (ddd, J_1 = 12.3, J_2 = 4.7, J_3 = 3.1 Hz, 1H), 1.68−1.61 (m,1H), 1.59 (s, 9H), 1.56−1.55 (m, 1H), 1.47 (ddd, J_1 = 13.0, J_2 = 10.0, J_3 = 6.9 Hz, 1H), 1.20 (d, J = 7.1 Hz, 3H), 1.08 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 182.9, 160.6, 158.5, 135.6, 133.8, 131.9, 129.7, 127.7, 122.8, 118.5, 115.9, 102.6, 79.9, 63.5, 57.8, 41.3, 29.7, 28.4, 27.8, 26.9, 21.0, 19.2, 19.0, 10.9; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{36}H_{49}N_2O_3Si$ 585.3507; found 585.3503; λ_{abs} 350 nm (CH_3CN).

4-Bromo-5-*tert*-butyloxycarbonyl-3-methyl-2-[(*E*)-((3*S*,4*S*)-4-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methyl-5-oxodihydrofuran-2(3*H*)-ylidene)methyl)]pyrrole (26-Br). A solution of **26** (509 mg, 0.866 mmol) in anhydrous DMF (18 mL) under argon in a salt−ice bath at −10 °C was treated with NBS (172 mg, 0.966 mmol) in one batch. The reaction mixture was stirred at −10 °C for 1 h, and then at room temperature for 19 h. The reaction mixture was treated dropwise with a 20% aqueous $Na_2S_2O_3$ solution. The organic layer was separated, washed with water, dried (Na_2SO_4), and concentrated to a yellow oil. Chromatography [silica, hexanes/ethyl acetate (10:1 to 6:1)] afforded a transparent oil (142 mg, 25%): ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.69 (br s, 1H), 7.67−7.63 (m, 4H), 7.43−7.36 (m, 6H), 6.05 (s, 1H), 3.73 (dt, J_1 = 10.6 Hz, J_2 = 5.3 Hz, 1H), 3.71−3.65 (m, 1H), 3.31 (p, J = 7.4 Hz, 1H), 2.83 (td, J_1 = 8.5 Hz, J_2 = 5.3 Hz, 1H), 2.02 (s, 3H), 1.91 (ddd, J_1 = 13.3 Hz, J_2 = 7.0 Hz, J_3 = 3.4 Hz, 1H), 1.67 (dq, J_1 = 10.7 Hz, J_2 = 5.0 Hz, 3H), 1.60 (s, 9H), 1.16 (d, J = 7.2 Hz, 3H), 1.04 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 174.8, 159.6, 155.6, 135.6, 133.6, 129.7, 127.7, 125.9, 121.5, 120.7, 105.9, 95.6, 82.0, 63.2, 43.9, 35.4, 30.2, 28.4, 26.9, 21.2, 19.2, 14.3, 10.5; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{35}H_{45}BrNO_5Si$ 666.2245; found 666.2236.

4-Bromo-5-*tert*-butyloxycarbonyl-3-methyl-2-[(*E*)-((3*S*,4*S*)-4-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methyl-5-methylenedihydrofuran-2(3*H*)-ylidene)methyl]pyrrole (27-Br). Following a reported procedure[38] with modification, a solution of $TiCp_2Cl_2$ (1.40 g, 5.64 mmol) in anhydrous toluene (15.2 mL) at 0 °C under argon was treated dropwise with LiMe solution (1.6 M, 7.80 mL in diethyl ether). The resulting reaction mixture was stirred for 1.5 h at 0 °C in the dark, followed by the addition of a saturated aqueous NH_4Cl solution. The organic layer was separated, washed with water and brine, and filtered through cotton to remove dark orange materials, which afforded an orange filtrate (17−20 mL) containing the Petasis reagent. A sample of 10.5 mL of the freshly prepared Petasis reagent was added into a 25 mL vial containing **26-Br** (400. mg, 0.600 mmol) under argon. The resulting mixture was

https://doi.org/10.1021/acs.joc.1c01239
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treated with additional $TiCp_2Cl_2$ (9.0 mg, 0.036 mmol) under argon and heated in an oil bath at 80 °C in the dark for 6 h. Afterward, the resulting mixture was allowed to cool to room temperature, whereupon MeOH (713 μL), $NaHCO_3$ (30 mg), and water (7.1 μL) were added. The reaction mixture was stirred in an oil bath at 40 °C for 12 h and then filtered through a Celite pad to afford a yellow filtrate. A silica column was prewashed with 5% NEt_3 in hexanes, followed by CH_2Cl_2 and then hexanes given the sensitivity of the ene−lactone−pyrrole title compound. The column was then used to chromatograph the yellow product [hexanes/ethyl acetate (20:1); TLC R_f = 0.38 in hexanes/ethyl acetate (10:1)] to afford a yellow foam (319 mg, 80%): ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.63 (br s, 1H), 7.65−7.63 (m, 4H), 7.43−7.35 (m, 6H), 5.81 (s, 1H), 4.53 (d, J = 2.2 Hz, 1H), 4.07 (dd, J_1 = 2.2, J_2 = 0.9 Hz, 1H), 3.65 (ddt, J_1 = 10.2, J_2 = 6.2, J_3 = 4.2 Hz, 1H), 2.79−2.74 (m, 1H), 2.47−2.41 (m, 1H), 1.99 (s, 3H), 1.64−1.60 (m, 2H), 1.59 (s, 9H), 1.56−1.51 (m, 2H), 1.18 (d, J = 7.1 Hz, 3H), 1.03 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 162.2, 161.8, 159.6, 135.6, 133.8, 129.6, 128.0, 127.6, 119.9, 119.5, 106.0, 90.7, 85.0, 81.5, 63.4, 48.6, 40.4, 30.8, 29.6, 28.4, 26.9, 19.2, 18.9, 10.5; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{36}H_{47}BrNO_4Si$ 664.2452; found 664.2443.

(2*S*,3*S*)-8-Bromo-9-*tert*-butoxycarbonyl-2-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-2,3-dihydro-1,3,7-trimethyldipyrrin (28-Br). Following a reported procedure[38] with modification, a solution of **27-Br** (66 mg, 0.10 mmol) in anhydrous DMF (1.0 mL) was treated with 1 M HCl (50. μL) under argon. The reaction progress was monitored by UV−vis absorption spectroscopy and TLC. After 40 min, another aliquot of 1 M HCl (50. μL) was added. After another 20 min, absorption spectroscopy (loss of absorption at ∼300 nm) and TLC analysis [silica, R_f = 0.2, hexanes/ethyl acetate (10:1)] indicated formation of the diketone intermediate **27-Br′**. Samples of NH_4OAc (154 mg, 2.00 mmol) and NEt_3 (278 μL) were added. The reaction mixture was stirred in an oil bath at 55 °C, and the reaction was monitored by absorption spectroscopy (growth in absorption at ∼350 nm) and TLC. After 40 min, absorption spectroscopy and TLC analysis [silica, R_f = 0.5, hexanes/ethyl acetate (10:1)] indicated dihydrodipyrrin formation. The reaction mixture was allowed to cool to room temperature, quenched with a saturated aqueous KH_2PO_4 solution, and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated. The resulting crude mixture was chromatographed [silica, hexanes/ethyl acetate (10:1)] to afford a yellow film (42 mg, 64%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.51 (br s, 1H), 7.65 (dt, J_1 = 8.0, J_2 = 1.7 Hz, 4H), 7.48−7.34 (m, 6H), 5.72 (d, J = 1.7 Hz, 1H), 3.68 (td, J_1 = 6.1, J_2 = 2.6 Hz, 2H), 2.60 (ddd, J_1 = 7.3, J_2 = 3.8, J_3 = 1.7 Hz, 1H), 2.38 (dt, J_1 = 8.7, J_2 = 4.1 Hz, 1H), 2.19 (s, 3H), 2.07 (s, 3H), 1.86−1.79 (m, 1H), 1.60 (s, 9H), 1.57−1.52 (m, 2H), 1.49−1.41 (m, 1H), 1.17 (d, J = 7.1 Hz, 3H), 1.06 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.0, 159.8, 159.3, 135.6, 133.8, 130.9, 129.7, 127.7, 119.4, 119.0, 105.6, 102.2, 80.7, 63.4, 57.7, 41.4, 29.7, 28.5, 27.7, 26.9, 20.9, 19.2, 19.1, 10.0; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{36}H_{46}BrN_2O_3Si$ 661.2456; found 661.2449, which is consistent with $2e^-/2H^+$ dehydrogenation for the ^{79}Br isotopic species; λ_{abs} 344 nm (CH_3CN).

General Procedure III, EDC Coupling Reaction to Afford Amides. A solution of carboxylic acid **17** (1.0 equiv), EDC·HCl (1.5 equiv), and HOBt (1.5 equiv) in anhydrous CH_2Cl_2 (0.5−1.5 mL) at room temperature under argon was treated with an amine (1.5 equiv). The reaction mixture was stirred at room temperature for 5 min and then cooled to 0 °C and treated dropwise with NEt_3 (1.5 equiv). The reaction mixture was stirred for 20 h at room temperature and diluted with CH_2Cl_2. The resulting mixture was treated with 2 M HCl, followed by the slow addition of saturated aqueous $NaHCO_3$ solution. The resulting organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed to afford the target amide.

(2*S*,3*S*)-*N*-Benzyl-2-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methylpent-4-ynamide (29). Following general procedure III, a solution of **17** (41 mg, 0.10 mmol), EDC·HCl (29 mg, 0.15 mmol), and HOBt (23 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (500 μL) was treated with benzylamine (16 μL, 0.15 mmol), followed by NEt_3 (21 μL, 0.15 mmol). Chromatography [silica, CH_2Cl_2] afforded a colorless oil (44 mg, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59−7.53 (m, 4H), 7.35−7.25 (m, 6H), 7.24−7.15 (m, 5H), 5.99 (t, J = 5.6 Hz, 1H), 4.42−4.31 (m, 2H), 3.58 (td, J_1 = 6.1 Hz, J_2 = 1.5 Hz, 2H), 2.64 (doublet of quintets, J_1 = 7.0 Hz, J_2 = 2.3 Hz, 1H), 2.10 (dt, J_1 = 8.9 Hz, J_2 = 6.8 Hz, 1H), 2.00 (d, J = 2.4 Hz, 1H), 1.65 (dtt, J_1 = 8.0 Hz, J_2 = 6.5 Hz, J_3 = 2.8 Hz, 2H), 1.56−1.42 (m, 2H), 1.14 (d, J = 7.0 Hz, 3H), 0.96 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 173.3, 138.4, 135.6, 133.9, 133.8, 129.6, 128.7, 128.6, 127.9, 127.7, 127.4, 86.6, 70.7, 63.6, 52.2, 43.5, 30.2, 28.2, 27.0, 26.9, 19.2, 18.5; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{32}H_{40}NO_2Si$ 498.2823; found 498.2824.

(2*S*,3*S*)-*N*-(4-Bromophenyl)-2-(3-((*tert*-butyldiphenylsilyl)oxy)propyl)-3-methylpent-4-ynamide (30). Following general procedure III, a solution of **17** (102 mg, 0.250 mmol), EDC·HCl (72 mg, 0.38 mmol), and HOBt (57 mg, 0.38 mmol) in anhydrous CH_2Cl_2 (1.2 mL) was treated with *p*-bromoaniline (65 mg, 0.38 mmol), followed by NEt_3 (53 μL, 0.38 mmol). Chromatography [silica, hexanes/ethyl acetate (5:1)] afforded a colorless oil (52 mg, 37%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1H), 7.68 (dt, J_1 = 8.1 Hz, J_2 = 1.8 Hz, 4H), 7.64−7.49 (m, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.44−7.34 (m, 7H), 3.78 (hept, J_1 = 5.7 Hz, J_2 = 5.2 Hz, 2H), 2.98 (dtt, J_1 = 14.2 Hz, J_2 = 7.4 Hz, J_3 = 3.5 Hz, 2H), 2.30 (d, J = 2.2 Hz, 1H), 2.11−1.96 (m, 2H), 1.88−1.74 (m, 2H), 1.61 (s, 1H), 1.42 (d, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.02 (s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 170.0, 143.5, 135.6, 133.7, 133.7, 129.7, 128.7, 128.6, 127.7, 124.8, 120.5, 108.5, 71.3, 63.1, 48.8, 30.0, 28.3, 26.9, 26.4, 19.3, 18.5; HRMS (ESI-TOF) m/z: [M − H]$^-$ calcd for $C_{31}H_{35}BrNO_2Si$ 560.1626; found 560.1631.

(2*S*,3*S*)-2-(3-((*tert*-Butyldiphenylsilyl)oxy)propyl)-*N*-(3,5-dimethylphenyl)-3-methylpent-4-ynamide (31). Following general procedure III, a solution of **17** (149 mg, 0.365 mmol), EDC·HCl (105 mg, 0.548 mmol), and HOBt (84 mg, 0.55 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was treated with 3,5-dimethylaniline (67 mg, 0.55 mmol), followed by NEt_3 (77 μL, 0.55 mmol). Chromatography [silica, hexanes/ethyl acetate (8:1)] afforded a white solid (82 mg, 44%): mp 123−127 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (ddt, J_1 = 5.6 Hz, J_2 = 4.0 Hz, J_3 = 1.6 Hz, 4H), 7.42 (s, 1H), 7.28−7.23 (m, 2H), 7.20 (dt, J_1 = 8.2 Hz, J_2 = 6.2 Hz, 4H), 6.95 (s, 2H), 6.58 (s, 1H), 3.55 (td, J_1 = 5.9 Hz, J_2 = 3.6 Hz, 2H), 2.62 (td, J_1 = 7.0 Hz, J_2 = 2.5 Hz, 1H), 2.18 (ddd, J_1 = 9.9 Hz, J_2 = 6.7 Hz, J_3 = 5.4 Hz, 1H), 2.12 (s, 6H), 2.09 (d, J = 2.4 Hz, 1H), 1.75−1.59 (m, 2H), 1.51−1.47 (m, 1H), 1.46 (s, 1H), 1.12 (d, J = 7.0 Hz, 3H), 0.90 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 171.7, 138.7, 137.7, 135.6, 134.0, 133.8, 129.7, 129.7, 127.7, 127.7, 126.0, 117.7, 86.4, 71.3, 63.7, 53.0, 30.1, 28.3, 27.6, 27.0, 21.4, 19.3, 18.6; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{33}H_{42}NO_2Si$ 512.2979; found 512.2981. Slow evaporation of an ethyl acetate/cyclohexane solution of the title compound afforded a crystal suitable for X-ray structure determination.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01239.

^{1}H NMR and ^{13}C{^{1}H} NMR data for all new compounds; single-crystal X-ray data for **21**, **21-Br**, and **31**; and additional information concerning exploratory studies (PDF)

Accession Codes

CCDC 2086065−2086067 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre,

https://doi.org/10.1021/acs.joc.1c01239
J. Org. Chem. XXXX, XXX, XXX−XXX

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the NSF (CHE-1760839). Mass spectrometry, NMR, and X-ray structural data were obtained in the Molecular Education, Technology, and Research Innovation Center (METRIC) at NC State University. We thank NC Biotechnology Center for partial funding for the D8Venture X-ray instrument (2019-IDG-1010).

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https://doi.org/10.1021/acs.joc.1c01239
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