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Synthesis of Furanosyl *C*-1 Glycals through Palladium-Catalyzed Reactions of a Furanosyl 2,3-Anhydro-*exo*-glycal

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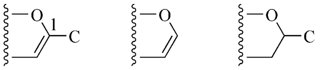
Keywords: Glycals / Carbohydrates / Electrophilic substitution / Nucleophilic substitution / Palladium / Umpolung

A furanose-derived 2,3-anhydro-*exo*-glycal, readily available from D-mannose in four steps, has proven to be a useful substrate in the preparation of a variety of highly functionalized C-1 glycals. Upon treatment with Pd^0 it affords a π-allyl palladium complex that can react with nucleophiles such as amines, ethyl malonate, or vinylstannanes. On the other hand, umpolung of the π-allyl palladium complex with Et_2Zn facilitates its reaction with electrophilic aldehydes and ketones.

Introduction

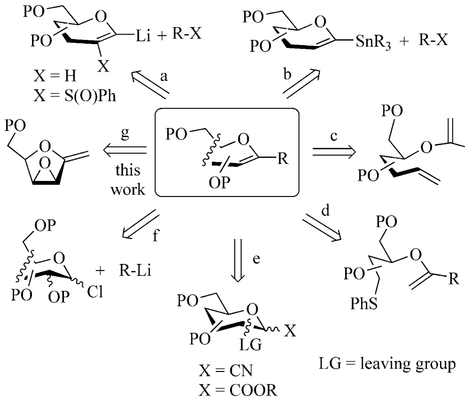
C-1-Substituted glycals (e.g., **1**) are well-recognized intermediates in a variety of synthetic protocols leading either to carbohydrate mimetics or to complex molecules.[1,2] In comparison with glycals (e.g., **2**),[3] they present an additional carbon substituent at the anomeric position (C-1) while maintaining their enol ether functionality. The former facilitates an easy retrosynthetic correlation with biologically relevant *C*-glycosides (e.g., **3**),[4,5] whereas the enol ether moiety permits the incorporation of additional functionality in the carbohydrate entity (Figure 1).[6]



1 **2** **3**

Figure 1. C-1 glycal (**1**), glycal (**2**), and C-glycoside (**3**).

The initial synthetic strategies directed towards *C*-1 glycals were addressed by *C*-1 deprotonation of substituted glycal derivatives.[7–9] It was thus shown that *C*-1-lithiated glycals, generated either by direct proton abstraction or by transmetallation of *C*-1 tributylstannyl glycals, could react with diverse electrophiles (such as alkyl halides, aldehydes, ketones, oxiranes, quinines, or hexacarbonyl chromium)[7–14] to generate *C*-1-substituted glycals (Scheme 1, a, X = H). Despite the straightforward nature of this approach, however, the preparation and handling of these lithio reagents has been sometimes found to be troublesome.[15,16] In this context, Schmidt and co-workers described the direct 1-*C*-lithiation of 2-phenylsulfinyl-D-glycals [Scheme 1, a, X = S(O)Ph].[17,18] On the other hand, *C*-1-stannyl[19,20] or *C*-1-iodo glycals have been successfully used in palladium-mediated coupling reactions[21–23] with activated substrates (Scheme 1, b). This approach was also applied to furanoid glycals.[24] These methods generally lead to good yields of *C*-1 glycals, but they still need an initial metallation step for the preparation of the required *C*-1 stannyl (or iodo) glycal.



Scheme 1. Strategies for the synthesis of *C*-1 glycals.

Approaches to *C*-1 alkyl glycals, based on open-chain derivatives, have been described recently (Scheme 1, c,d).[25] In this context, Postema and co-workers designed an approach based on an enol ether–olefin ring-closing metathesis protocol (Scheme 1, c),[25–29] whereas Mootoo and co-workers employed an intramolecular oxocarbenium ion–alkene cyclization on an acetal-enol ether precursor as the key step in the ring-forming reaction (Scheme 1, d).[30]

Base-induced elimination of 1-CN glycosides has been used in the preparation of 1-cyanoglycals (Scheme 1, e), which are useful precursors of heterocyclic *C*-1 glycals.[31,32]

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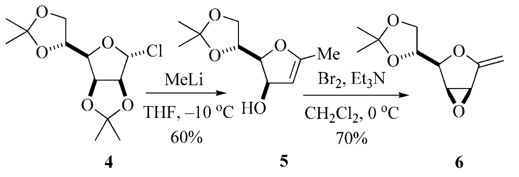
2,3-Dehydroneuraminic acid derivatives, which can be regarded as C-1-substituted glycals, have been obtained mainly by elimination procedures on peracetylated neuraminic ester derivatives (Scheme 1, e, X = COOR).[33] These biologically relevant compounds, related to neuraminidase inhibitors,[34,35] can be used in the preparation of sialic acid derivatives functionalized at C-3.[36] Other methods have also been used in the preparation of C-1-substituted glycals.[37]

We have reported a method for the preparation of furanosyl and pyranosyl *C*-1 glycals based on treatment of glycosyl chlorides with organolithium reagents (Scheme 1, f).[38–40] More recently, we have become interested in the preparation and chemistry of furanose-derived 2,3-anhydro *exo*-glycals,[41] and found that they could be used in the synthesis of *C*-1 glycals (Scheme 1, g).[42] Here we present a detailed report on our studies on the versatility of 2,3-anhydro-*exo*-glycals in the synthesis of *C*-1 glycals.

Results and Discussion

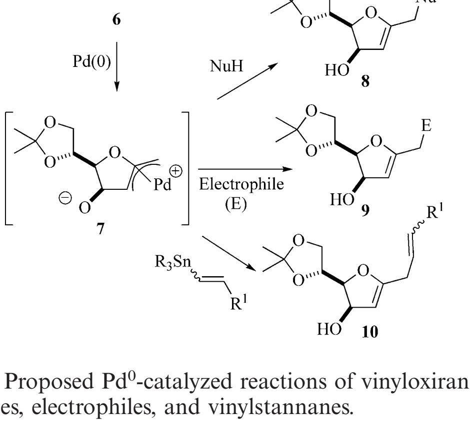
Synthesis

The key intermediate for these studies was the 2,3-anhydro *exo*-glycal **6** (Scheme 2). This compound can be efficiently prepared in four steps from commercially available D-mannose via the glycosyl chloride **4**.[39]



Scheme 2. Preparation of the 2,3-anhydro *exo*-glycal **6**.

Compound **6** is a valuable synthon for organic synthesis, owing to its rich functionality. Of special interest to us was the vinyloxirane moiety, because it was known that Pd^0-catalyzed reactions of vinyl epoxides could lead to π-allylpalladium intermediates such as **7** (Scheme 3).[43,44] Accordingly, we set out to explore the behavior of **7** with pronucleophiles (NuH), electrophiles, and vinylstannanes (vide infra), to gain access to compounds of type **8**, **9**, and **10**, respectively.



Scheme 3. Proposed Pd^0-catalyzed reactions of vinyloxirane **6** with nucleophiles, electrophiles, and vinylstannanes.

Reaction with Nucleophiles

π-Allylpalladium intermediates such as **7** are known to react with soft carbon nucleophiles and amines to give substituted allylic alcohols such as **8**. In order to test this transformation, we first treated vinyloxirane **6** with Pd(OAc)$_2$ and PPh$_3$ in THF overnight at room temp. in the presence of methyl malonate. We were able to isolate compound **11**, which displayed a signal at δ = 100.6 ppm (^{13}C NMR), and a doublet at δ = 4.92 ppm (J = 2.9 Hz, ^{1}H NMR), corresponding to C-2 and H-2, respectively. From this, compound **11** was the result of a 1,4-addition to the vinyloxirane system. Similar results were obtained when the same procedure was carried out with diverse primary and secondary amines to yield allylic derivatives **12**–**16** (Figure 2).

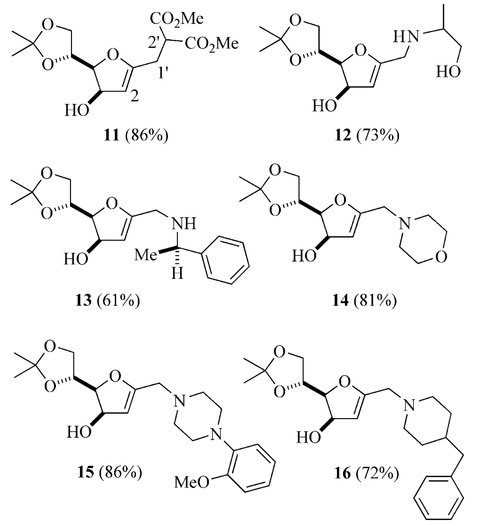
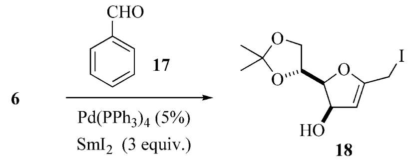


Figure 2. Allylic alcohols resulting from Pd^0-catalyzed reactions between vinyloxirane **6** and methyl malonate or primary or secondary amines [Pd(OAc)$_2$, PPh$_3$, THF, room temp., overnight].

Reactions with Electrophiles

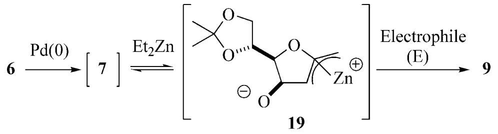
The reactions of electrophilic π-allylpalladium complexes can only be applied to soft carbon nucleophiles.[45] Because that limited reactivity implied a restraint to our methodology, we turned our attention to π-allyl species that could function as nucleophiles, rather than electrophiles, and therefore react with carbon electrophiles. Several examples of polarity inversion in π-allylpalladium species by transmetallation with low-valency metals had been described. These included treatment with chromium,[46] tin,[47] samarium,[48] and indium.[49] More recently, Et$_3$B and Et$_2$Zn have also been used in the Pd-catalyzed generation of nucleophilic allyl species from allyl esters and ethers.[50] In this context, we decided to study the umpolung of the π-allylpalladium species **7** with SmI$_2$ and Et$_2$Zn.

We first examined the reaction between vinyloxirane **6** and benzaldehyde (**17**) in the presence of $Pd(PPh_3)_4$ and SmI_2[51] (Scheme 4). However, no coupling products were observed, and only the allylic iodide **18** could be isolated. The same compound was also obtained when benzaldehyde was omitted from the reaction media. The formation of **18** could be explained in terms of a 1,4 addition of SmI_3 to the vinyloxirane.[52]



Scheme 4. Reaction of vinyloxirane **6** with Pd^0/SmI_2.

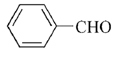
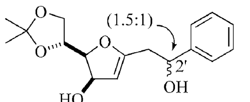
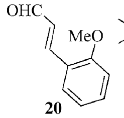
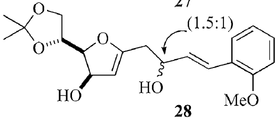
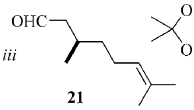
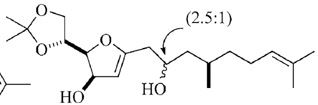
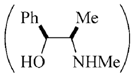
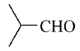
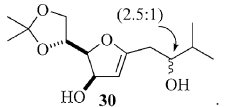
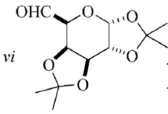
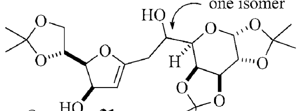
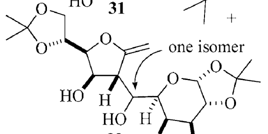
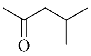
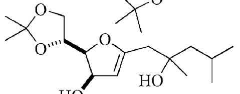
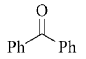
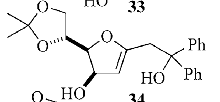
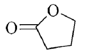
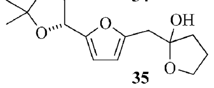
We next turned our attention to the preparation of allylzinc derivatives capable of reacting with electrophiles.[53] To the best of our knowledge, at the onset of this work there were no examples of the preparation of allylzinc derivatives from vinyl epoxides.[54] The proposed reaction pathway for this transformation[55] would involve ligand transfer of the π-allylpalladium intermediate **7** to Et_2Zn to generate the reactive allylic zinc species (e.g., **19**), which could react with the electrophile (E) to generate the coupled derivative **9** (Scheme 5).



Scheme 5. Proposed reaction pathway for Pd^0/Et_2Zn-catalyzed reactions between vinyloxirane **6** and electrophiles.

Solutions containing the vinyl epoxide **6**, $Pd(PPh_3)_4$, and the corresponding electrophile in THF were thus treated at room temperature with Et_2Zn. As electrophiles we selected aldehydes **17**, **20**–**23**, ketones **24**, **25**, and lactone **26**, and our results are displayed in Table 1.

Table 1. Reactions between the vinyloxirane **6** and electrophiles (aldehydes, ketones, and lactones) mediated by Pd^0/Et_2Zn in THF.

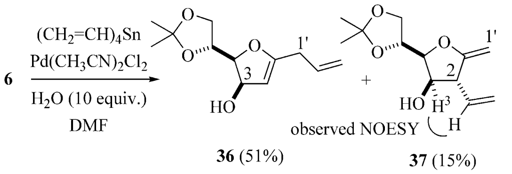
Entry	Electrophile	Product(s)	Yield (%)
i	 **17**	 **27**	83
ii	 **20**	 **28**	70
iii	 **21**	 **29**	72
iv	**21**	 **29** (3:1 ratio at C-2')	63
v	 **22**	 **30**	63
vi	 **23**	 **31** +  **32**	43 14
vii	 **24**	 **33**	48
viii	 **25**	 **34**	68
ix	 **26**	 **35**	23

The reactions took place smoothly, with disappearance of the starting material normally occurring within 1–3 h. The reactions between compound **6** and aldehydes gave good yields of coupled products, with excellent 1,4-regioselectivities (Table 1, Entries *i*–*vi*). Benzaldehyde (**17**) yielded a 1.5:1 diastereomeric mixture of allylic alcohols **27**, and *o*-methoxycinnamaldehyde similarly yielded the mixture **20** (Table 1, Entries *i* and *ii*, respectively). Slightly higher diastereomeric ratios (2.5:1) were observed in the reactions of **6** with citronellal (**21**) and isobutyraldehyde (**22**) (Table 1, Entries *iii* and *v*, respectively). In view of some literature precedents on the effect of chiral ligands on the enantioselective alkylation of aldehydes with Et_2Zn,[56,57] we decided to evaluate the effect of the addition of (1*S*,2*R*)-ephedrine as a chiral additive in the reaction between citronellal (**21**) and the vinyloxirane **6**. However, only a negligible increase in the diastereomeric ratio of **29** was observed (Table 1, Entry *iv*). The reaction between **6** and the galactose-derived aldehyde **23** yielded two single derivatives, **31** and **32**, arising from regioisomeric attacks on the π-allylzinc derivative, rather than from facial differentiation on the carbonyl group (Table 1, Entry *vi*). Ketones **24** and **25** gave moderate yields of the tertiary hydroxy derivatives **33** and **34** (Table 1, Entries *vii* and *viii*, respectively). γ-Butyrolactone (**26**), a poorer electrophile, yielded furan **35** in a reduced 23% yield.[58,59]

Reactions with Stannanes

In order to extend the usefulness of the π-allyl derivatives generated from vinyloxirane **6** upon treatment with Pd^0, we turned our attention to the significant work of Stille's[60] and Echavarren's[61] groups on the use of stannanes as mild nucleophiles in palladium-catalyzed couplings with vinyl epoxides.

We first explored the reaction between **6** and the commercially available tetravinyltin under the conditions recommended by Stille and co-workers (Scheme 6).[60b] The reaction took place smoothly to give a mixture of the regioisomeric derivatives **36** and **37**, resulting from 1,4- and 1,2-addition, respectively, to the allylic system. In keeping with literature precedents, compound **37**, generated by 1,2-addition, was obtained as the minor isomer. The structural assignments were based on study of the compounds' ^{1}H and ^{13}C NMR spectra. Thus, with regard to regiochemistry, in the case of **36** we were able to identify a signal at δ = 32.7 ppm corresponding to C-1′ (^{13}C NMR), whereas a signal at δ = 83.5 ppm, corresponding to C-1′, was observed in the ^{13}C NMR spectrum of **37**. Additionally, the observed coupling patterns for the non-terminal vinylic proton in compounds **36** and **37** were also indicative. The –CH= proton in compound **37** thus appeared, as expected, at δ = 5.78 ppm as a ddd (17.1, 10.0, and 6.8 Hz), whereas a poorly resolved multiplet was observed at δ = 5.84 ppm for the –CH= proton in compound **36**.



Scheme 6. $Pd(CH_3CN)_2Cl_2$-catalyzed reaction between vinyloxirane **6** and tetravinyltin.

The configuration at C-2 in compound **37**, inferred on mechanistic grounds, was confirmed by a NOESY experiment that showed the correlation of H-3 with the non-terminal vinylic proton.

We next decided to broaden this approach through the use of more complex vinylstannanes. These are readily available by Et_3B-catalyzed radical addition of Bu_3SnH to terminal alkynes by a protocol described by Oshima and co-workers.[62,63] Accordingly, we prepared the alkenylstannanes **38**–**41** (Figure 3) from the corresponding alkynes. The precursor for stannane **38** was commercially available phenylacetylene, whereas the rest of the stannanes **39**–**41** were readily obtained by propargylation (propargyl bromide, NaH) followed by Et_3B-catalyzed stannylation.

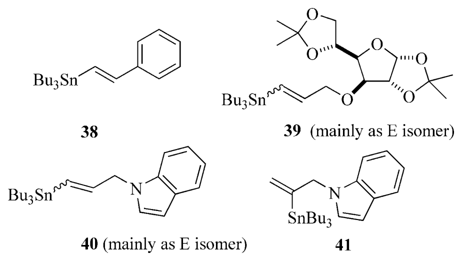
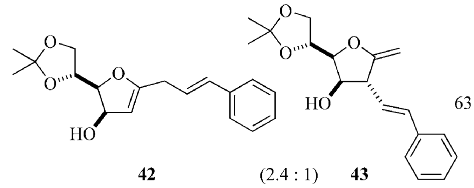
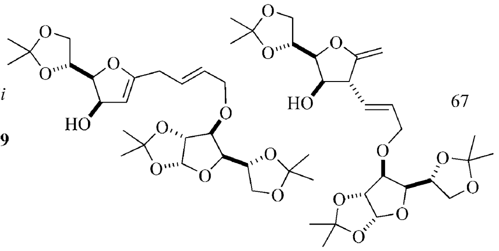
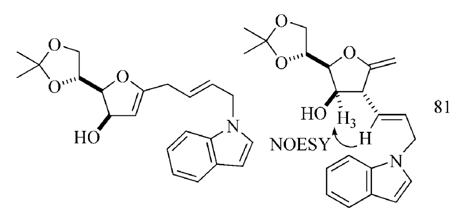
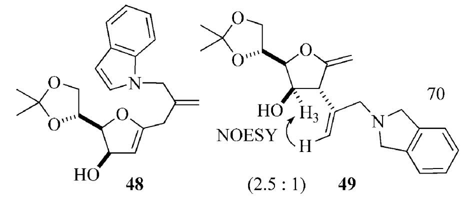


Figure 3. Vinylstannanes **38**–**41**, prepared by Et_3B-catalyzed radical addition of Bu_3SnH to terminal alkynes.

We applied Stille reaction conditions[60b] to the vinyloxirane **6** and the vinylstannanes **38**–**41**, and our results are outlined in Table 2. In each case a mixture of 1,4- and 1,2-regioisomers was obtained (Table 2, Entries *i*–*v*). These results are consistent with Stille's previous findings. The C-1 glycal derivatives (1,4-isomers) were always obtained as the major isomers and proved to be very sensitive to acid, affording furan derivatives. Accordingly, Et_3N (3%) was used in all column chromatography purifications. The stereochemistry at C-2 was unambiguously assigned, on the basis of NOESY experiments (see Table 2), for compounds **47** and **49**, and was assumed in derivatives **43** and **45**.

Table 2. Reactions between vinyloxirane **6** and vinylstannanes **38**–**41**.

Entry Stannane	Products (ratio)	Yield (%)
i **38**	 **42** (2.4 : 1) **43**	63
ii **39**	 **44** (4.6 : 1) **45**	67
iii **40**	 **46** (3 : 1) **47**	81
iv **41**	 **48** (2.5 : 1) **49**	70

Conclusions

The furanose-derived 2,3-anhydro-*exo*-glycal **6** has revealed itself to be a valuable substrate in the preparation of a variety of highly functionalized C-1 glycals. Upon treatment with Pd^0, compound **6** is smoothly transformed into a π-allyl palladium species such as **7**, which can react with primary or secondary amines or with ethyl malonate to give C-1 glycals resulting from 1,4-addition to the allylic system. However, the π-allyl palladium species **7** also reacts with stannanes to give mixtures of C-1 glycals (resulting from

1,4-addition) and C-2 branched furanose *exo*-glycals (from 1,2-addition), with the former prevailing. Finally, umpolung of **7** could be effected by treatment with Et_2Zn, which permits its coupling with electrophiles. Thus, aldehydes and ketones gave moderate to good yields of allylic alcohols resulting from 1,4-addition. The observed diastereomeric excesses varied from 2.5:1 to 3.5:1, and in the case of citronellal (**21**) the diastereomeric excess was not noticeably affected by the addition of a chiral ligand. On the other hand, the reaction between **6** and the galactose diacetonide aldehyde **23** was completely stereoselective, but still gave a mixture of 1,2- and 1,4-regioisomers.

Experimental Section

General Remarks: All reactions were performed in dry flasks fitted with glass stoppers or rubber septa under positive pressure of Ar, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Optical rotations were determined for solutions in chloroform. Flash column chromatography was performed with 230–400 mesh silica gel. Thin-layer chromatography (TLC) was conducted on Kieselgel 60 F254 (Merck). Spots were observed first under UV irradiation (254 nm) and then by charring with a solution of aqueous H_2SO_4 (20%, 200 mL) in AcOH (800 mL). Anhydrous $MgSO_4$ or Na_2SO_4 were used to dry organic solutions during workup, and evaporation of the solvents was performed under vacuum with a rotary evaporator. Solvents were dried and purified by standard methods. Unless otherwise noted, ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 50 MHz, respectively. Chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ = 7.25 ppm). API-ES stands for atmospheric pressure-positive electrospray ionization.

1,4-Anhydro-5,6-*O*-isopropylidene-2-deoxy-1-*C*-methyl-D-*arabino*-hex-1-enitol (5): A solution of the glycosyl chloride **4**[39] (2.5 g, 8.9 mmol) in dry THF (25 mL) was cooled to 0 °C and then treated with MeLi (16.7 mL, 1.6 M in Et_2O, 26.7 mmol, 3 equiv.). After stirring for 2 h, once TLC analyses showed total disappearance of the starting material, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl. After partitioning between water and diethyl ether, the organic layer was dried with $MgSO_4$ and concentrated. The residue was purified by flash chromatography (hexane/EtOAc, 90:10) to give the C-1 glycal **5** (1.0 g, 60%): $[\alpha]_D^{25}$ = –4.5 (*c* = 0.42, in $CHCl_3$). ^1H NMR: δ = 6.1 (7.4 Hz, 1 H, 4-H), 4.53 (dt, *J* = 7.4, 6.0 Hz, 1 H, 5-H), 4.68 (m, 1 H, 3-H), 4.69 (br. s, 1 H, 2-H) ppm. ^{13}C NMR: δ = 25. 3, 25.8, 27.4, 67.5, 74.0, 74.6, 86.3, 100.6, 105.9, 169.0 ppm. MS: *m*/*z* = 201.0 $[M + 1]^+$, 200.0 $[M]^+$.

2,5:3,4-Dianhydro-1-deoxy-D-*manno*-hept-1-enitol (6): A solution of Br_2 (1.4 mL, 27.5 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a cooled (0 °C) solution of C-1 methyl glycal **5** (5.0 g, 25 mmol) in CH_2Cl_2 (250 mL) containing Et_3N (50 mL). The mixture was stirred at room temperature overnight, after which the reaction mixture was diluted with CH_2Cl_2 (300 mL) and washed with aqueous sodium thiosulfate (10%) and water. The organic layer was then dried and concentrated and the residue was purified by flash chromatography (hexane/EtOAc, 95:5) to give oxirane **6** (3.5 g, 70%); m.p. 41–42 °C. $[\alpha]_D^{25}$ = + 56.2 (*c* =1.0, $CHCl_3$). ^1H NMR: δ = 1.32 (s, 3 H, Me), 1.40 (s, 3 H, Me), 3.87–4.16 (m, 6 H), 4.32 (d, *J* = 2.0 Hz, 1 H, 1-H), 4.44 (d, *J* = 2.0 Hz, 1 H, 1′-H) ppm. ^{13}C NMR: δ = 25.0, 26.6, 55.2, 57.1, 66.9, 72.9, 79.9, 87.3, 109.3, 157.2 ppm. MS (API-ES positive): *m*/*z* = 199.1 $[M + 1]^+$. $C_{10}H_{14}O_4$ (198.09): calcd. C 60.59, H 7.12; found C 60.37, H 7.03.

General Procedure for Pd^0-Catalyzed Reactions between Epoxide 6 and Nucleophiles: A solution of epoxide **6** in dry THF (6 mL mmol^{-1}) was treated under argon with Ph_3P (1 equiv.), $Pd(OAc)_2$ (0.2 equiv.), and the corresponding nucleophile (1.3 equiv.). The resulting suspension was stirred at room temperature under argon. After the starting materials had been consumed (TLC), the mixture was diluted with EtOAc and washed with brine. The organic layer was dried, concentrated, and subjected to silica gel column chromatography.

Compound 11: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and dimethyl malonate (112 µL, 0.97 mmol) were treated according to the General Procedure. After purification (hexane/EtOAc, 40:60), compound **11** (213 mg, 86%) was obtained as a colorless oil: $[\alpha]_D^{25}$ = –20.0 (*c* = 3.0, $CHCl_3$). ^1H NMR (C_6D_6): δ = 1.32 (s, 3 H, Me), 1.39 (s, 3 H, Me), 2.75 (d, *J* = 7.0 Hz, 2 H, CH_2–CH), 3.62 (t, *J* = 7.5 Hz, 1 H, *CH*–CH_2), 3.69 (s, 6 H, OMe), 3.92 (dd, *J* = 5.4, 8.4 Hz, 1 H, 6-H), 4.01 (dd, *J* = 6.3, 8.5 Hz, 6′-H), 4.13 (t, *J* = 6.8 Hz, 1 H, 4-H), 4.39–4.45 (m, 1 H, 5-H), 4.79–4.82 (br. m, 1 H, 3-H), 4.92 (d, *J* = 2.9 Hz,1 H, 2-H) ppm. ^{13}C NMR: δ = 25.0, 26.6, 27.3, 49.0, 52.6, 66.4, 72.7, 73.3, 85.0, 100.6, 109.0, 159.4, 168.6, 168.7 ppm. MS (API-ES positive): *m*/*z* = 330.2 $[M]^+$, 331.1 $[M + 1]^+$. $C_{15}H_{22}O_8$ (330.13): calcd. C 54.54, H 6.71; found C 54.33, H 6.61.

Compound 12: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and L-alaninol (75 µL, 0.97 mmol) were treated according to the General Procedure. After purification (MeOH/EtOAc, 10:90), compound **12** was obtained as an oil (149 mg, 73%). $[\alpha]_D^{25}$ = –6.3 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 1.04 (d, *J* = 6.4 Hz, 3 H, CH_3–CH), 1.37 (s, 3 H, Me), 1.46 (s, 3 H, Me), 2.83 (m, 1 H, *CH*–CH_3), 3.25–3.61 (m, 4 H, CH_2–OH, CH_2–N), 4.0 (dd, *J* = 5.0, 8.7 Hz, 1 H, 6-H), 4.16 (dd, *J* = 6.3, 8.6 Hz, 1 H, 6′-H), 4.23 (dd, *J* = 6.4, 7.3 Hz, 1 H, 4-H), 4.47–4.53 (m, 1 H, 5-H), 4.89 (dd, *J* = 2.6, 6.3 Hz, 1 H, 3-H), 5.12 (d, *J* = 2.5 Hz, 1 H, 2-H) ppm. ^{13}C NMR: δ = 16.8, 25.0, 26.7, 43.6, 53.7, 65.4, 66.7, 72.9, 73.4, 85.2, 100.5, 109.2, 161.3 ppm. MS (API-ES positive): *m*/*z* = 274.0 $[M + 1]^+$. $C_{13}H_{23}NO_5$ (273.17): calcd. C 57.13, H 8.48, N 5.12; found C 56.99, H 8.54, N 5.19.

Compound 13: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and (*R*)-(+)-α-methylbenzylamine (124 µL, 0.97 mmol) were treated according to the General Procedure. After purification (hexane/EtOAc, 10:90), compound **13** (149 mg, 73%) was obtained as an oil. $[\alpha]_D^{25}$ = +11.3 (*c* = 1.5, $CHCl_3$). ^1H NMR: δ = 1.35 (d, *J* = 6.6 Hz, 3 H, CH_3–), 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 3.19 (s, 2 H, C*H*$_2$N), 3.80 (q, *J* = 6.6 Hz, 1 H, *CH*–NH), 3.99 (dd, *J* = 5.3, 8.5 Hz, 1 H, 6-H), 4.13 (m, 2 H, 4-H, 6′-H), 4.48 (m, 1 H, 5-H), 4.87 (dd, *J* = 2.6, 6.5 Hz, 1 H, 3-H), 5.05 (d, *J* = 2.6 Hz, 1 H, 2-H), 7–32 (m, 5 H, H_{arom}) ppm. MS (API-ES positive): *m*/*z* = 320.0 $[M + 1]^+$. $C_{18}H_{25}NO_4$ (319.39): calcd. C 67.69, H 7.89, N 4.39; found C 67.51, H 7.67, N 4.23.

Compound 14: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and morpholine (85 µL, 0.97 mmol) were treated according to the General Procedure. After purification by flash chromatography (hexane/EtOAc, 30:70), compound **14** was obtained as a colorless oil (173 mg, 81%): $[\alpha]_D^{25}$ = –30.5 (*c* = 1.0, $CHCl_3$). ^1H NMR: δ = 1.37 (s, 3 H, Me), 1.45 (s, 3 H, Me), 2.49 (t, *J* = 4.6 Hz, 4 H, 2×C*H*$_2$N), 3.10 (m, 2 H, C*H*$_2$N), 3.71 (t, *J* = 4.6 Hz, 4 H, 2×CH_2O), 4.05 (dd, *J* = 4.8, 8.6 Hz, 1 H, 6-H), 4.14–4.22 (m, 2 H, 4-H, 6′-H), 4.45–4.52

(m, 1 H, 5-H), 4.92 (dd, *J* = 2.6, 6.3 Hz, 1 H, 3-H), 5.14 (d, *J* = 2.8 Hz, 1 H, 2-H) ppm. ^{13}C NMR: δ = 25.1, 26.8, 53.5 (×2), 55.4, 66.7 (×2), 67.1, 72.9, 73.4, 85.1, 102.4, 109.2, 159.3 ppm. MS (API-ES positive): *m*/*z* = 286.4 [M + 1]$^+$. $C_{14}H_{23}NO_5$ (285,33): calcd. C 58.93, H 8.12, N 4.91; found C 58.79, H 7.97, N 4.81.

Compound 15: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and 1-(4-methoxyphenyl)piperazine (186 mg, 0.97 mmol) were treated according to the General Procedure. After purification by flash chromatography (hexane/EtOAc, 30:70), compound **15** was obtained as a colorless oil (251 mg, 86%): $[\alpha]_D^{25}$ = –30.7 (*c* = 2.7, $CHCl_3$). ^{1}H NMR: δ = 1.38 (br. s, 3 H, Me), 1.46 (s, 3 H, Me), 2.71 (br. s, 4 H, CH_2–CH_2), 3.10 (s, 4 H, CH_2–CH_2), 3.18 (d, *J* = 3.5 Hz, 2 H, CH_2N), 3.85 (s, 3 H, OMe), 4.0 (dd, *J* = 4.7, 8.6 Hz, 1 H, 6-H), 4.21 (dd, *J* = 6.1, 8.5 Hz, 1 H, 6′-H), 4.22 (dd, *J* = 6.4, 9.5 Hz, 1 H, 4-H), 4.47–4.54 (m, 1 H, 5-H), 4.93 (dd, *J* = 2.6, 6.4 Hz, 1 H, 3-H), 5.16 (d, *J* = 2.6 Hz, 1 H, 2-H), 6.8–7.02 (m, 4 H, H_{arom}) ppm. ^{13}C NMR: δ = 25.6, 27.3, 50.7, 53.8, 55.6, 67.5, 73.4, 73.9, 85.5, 102.7, 109.6, 111.5, 118.6, 121.3, 123.3, 141.1, 125.6, 160.2 ppm. MS (API-ES positive): *m*/*z* = 391.2 [M + 1]$^+$. $C_{21}H_{30}N_2O_5$ (390.21): calcd. C 64.59, H 7.74, N 7.17; found C 64.49, H 7.80, N 6.98.

Compound 16: Oxirane **6** (150 mg, 0.75 mmol), Ph_3P (198 mg, 0.75 mmol), $Pd(OAc)_2$ (16 mg, 0.07 mmol), and 4-benzylpiperidine (170 µL, 0.97 mmol) were treated according to the General Procedure. After purification by flash chromatography (hexane/EtOAc, 30:70), compound **16** was obtained as a colorless oil (251 mg, 81%): $[\alpha]_D^{25}$ = –29.9 (*c* = 0.6, $CHCl_3$). ^{1}H NMR: δ = 1.33 (m, 2 H, CH_2–), 1.38 (s, 3 H, Me), 1.45 (s, 3 H, Me), 1.55 (m, 3 H, CH– and CH_2–), 2.0 (m, 2 H, *CH_2*–), 2.52 (d, *J* = 6.8 Hz, 2 H, CH_2N), 2.88 (m, 2 H, CH_2–N), 3.07 (m, 2 H, CH_2N), 4.04 (dd, *J* = 4.9, 8.7 Hz, 1 H, 6-H), 4.16 (dd, *J* = 6.1, 8.5 Hz, 1 H, 6′-H), 4.20 (dd, *J* = 6.3, 8.3 Hz, 1 H, 4-H), 4.48 (ddd, *J* = 5.0, 6.1, 8.3 Hz, 1 H, 5-H), 4.90 (dd, *J* = 2.5, 6.3 Hz, 1 H, 3-H), 5.10 (d, *J* = 2.5 Hz, 1 H, 2-H), 7.26 (m, 5 H, H_{arom}) ppm. ^{13}C NMR: δ = 25.2, 26.8, 31.9 (×2), 37.6, 43.1, 53.7, 54.0, 55.4, 67.1, 72.9, 73.5, 85.1, 101.9, 109.2, 125.7, 128.1, 129.1, 140.6, 160.2 ppm. MS (API-ES positive): *m*/*z* = 374.0 [M + 1]$^+$. $C_{22}H_{31}NO_4$ (373,48): calcd. C 70.75, H 8.37, N 3.75; found C 70.69, H 8.28, N 3.91.

Compound 18: A solution of the oxirane **6** (150 mg, 0.75 mmol) in dry THF (5 mL) was cooled to –78 °C and then treated with $Pd(PPh_3)_4$ (30 mg, 0.02 mmol) and SmI_2 (22.5 mL, 0.1 M in THF, 2.25 mmol, 3 equiv.). After stirring for 2 h, as soon as TLC analyses showed total disappearance of the starting material, the reaction mixture was quenched with aqueous K_2CO_3. After partitioning between water and diethyl ether, the organic layer was dried with $MgSO_4$ and concentrated. The residue was purified by flash chromatography (hexane/EtOAc/Et_3N, 35:60:5) to give the highly unstable compound **18** (97.8 mg, 40%). ^{1}H NMR: δ = 5.20 (m, 1 H, 2-H), 4.85 (dd, *J* = 6.0, 2.9 Hz, 1 H, 3-H), 4.40 (m, 1 H, 4-H), 4.19 (dd, *J* = 8.3, 6.4 Hz, 1 H, 6′-H), 4.09 (m, 1 H, 5-H), 3.97 (dd, *J* = 8.2, 4.9 Hz, 1 H, 6-H), 3.72 (s, 2 H, CH_2I), 1.52 (s, 3 H, Me), 1.46 (s, 3 H, Me) ppm. ^{13}C NMR: δ = 159.4, 109.4, 101.3, 85.6, 74.0, 72.8, 66.9, 26.8, 25.2, 6.0 ppm.

General Procedure for Pd^0/Et_2Zn-Catalyzed Reactions between Epoxide 6 and Electrophiles: A solution of epoxide **6** in dry THF (6 mL mmol^{-1}) under argon was treated with $Pd(PPh_3)_4$ (0.2 equiv.), the corresponding electrophile (1.3 equiv.), and Et_2Zn. The resulting mixture was stirred at room temperature under argon. After the starting materials had been consumed (TLC), the mixture was diluted with EtOAc and washed with aqueous $NaHCO_3$ and brine. The organic layer was dried, concentrated, and subjected to silica gel column chromatography.

Compound 27: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), benzaldehyde (**17**) (68 µL, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 35:60:5) to yield compound **27** as an inseparable 1.5:1 mixture of diastereomers (118 mg, 83%). ^{1}H NMR (selected peaks for the major isomer): δ = 7.32 (m, 5 H), 5.00 (d, *J* = 2.9 Hz, 1 H, 2-H), 4.92 (m, 1 H), 4.81 (m, 1 H), 4.47 (m, 1 H), 4.20 (t, *J* = 7.0 Hz, 1 H), 4.12 (dd, *J* = 8.5, 6.4 Hz, 1 H), 3.99 (dd, *J* = 8.7, 5.1 Hz, 1 H), 2.56 (m, 2 H), 1.42 (s, 3 H), 1.34 (s, 3 H) ppm. ^{13}C NMR (selected peaks for the major isomer): δ = 158.9, 131.0, 127.2, 126.3, 124.3, 107.8, 100.1, 83.8, 72.3, 71.7, 70.0, 65.3, 36.9, 25.4, 23.8 ppm. MS (API-ES positive): *m*/*z* = 307.3 [M + 1]$^+$. $C_{17}H_{22}O_5$ (306,35): calcd. C 66.65, H 7.24; found C 66.52, H 7.17.

Compound 28: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), 2-methoxycinnamaldehyde (**20**, 109 mg, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 25:70:5) to yield compound **28** as an inseparable 1.5:1 mixture of diastereomers (114 mg, 70%). ^{1}H NMR (selected peaks for the major isomer): δ = 7.40 (m, 1 H), 7.12 (d, *J* = 7.5 Hz, 1 H), 6.88 (m, 3 H), 6.20 (dd, *J* = 6.8, 6.6 Hz, 1 H), 5.06 (s, 1 H), 4.86 (m, 1 H), 4.56 (m, 1 H), 4.25 (m, 1 H), 4.15 (m, 1 H), 4.04 (m, 1 H), 3.82 (s, 3 H), 2.50 (t, *J* = 6.0 Hz, 2 H), 1.45 (s, 3 H), 1.37 (s, 3 H) ppm. ^{13}C NMR (selected peaks for the major isomer): δ = 160.6, 157.1, 132.1, 131.9, 129.2, 127.4, 125.9, 121.1, 111.2, 109.5, 101.9, 85.6, 74.1, 73.5, 71.0, 67.1, 55.8, 36.8, 27.2, 25.5 ppm. MS (API-ES positive): *m*/*z* = 363.4 [M + 1]$^+$. $C_{20}H_{26}O_6$ (362,41): calcd. C 66.28, H 7.23; found C 66.31, H 7.09.

Compound 32: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), (*R*)-citronellal (**21**, 102 µL, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 15:80:5) to yield compound **32** as separable mixture of diastereomers (3:1, 114 mg, 70%).

Major Isomer: M.p. 54–55 °C. $[\alpha]_D^{25}$ = –268.0 (*c* = 0.9, $CHCl_3$). ^{1}H NMR: δ = 5.09 (m, 1 H), 5.02 (d, *J* = 2.6 Hz, 1 H), 4.50 (ddd, *J* = 7.0, 6.3, 5.1 Hz, 1 H), 4.23 (t, *J* = 7.0 Hz, 1 H), 4.16 (dd, *J* = 8.6, 6.3 Hz, 1 H), 4.02 (dd, *J* = 8.6, 5.1 Hz, 1 H), 3.90 (m, 1 H), 2.35 (dd, *J* = 14.8, 3.2 Hz, 1 H), 2.22 (dd, *J* = 14.8, 8.5 Hz, 1 H), 1.92 (m, 3 H), 1.68 (s, 3 H), 1.59 (s, 3 H), 1.45 (s, 3 H), 1.37 (s, 3 H), 1.36 (m, 2 H), 1.22 (m, 4 H), 0.91 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR: δ = 161.1, 131.4, 124.7, 109.2, 101.1, 85.2, 73.7, 73.1, 67.3, 66.8, 44.6, 36.7, 36.5, 29.3, 26.8, 25.7, 25.3, 25.2, 20.1, 17.7 ppm. MS (API-ES positive): *m*/*z* = 353.2 [M + 1]$^+$. $C_{20}H_{34}O_5$ (352,24): calcd. C 67.76, H 9.76; found C 67.58, H 9.83.

Minor Isomer: $[\alpha]_D^{25}$ = –55.0 (*c* = 0.5, $CHCl_3$). ^{1}H NMR: δ = 5.10 (m, 1 H), 5.02 (d, *J* = 2.7 Hz, 1 H), 4.92 (dd, *J* = 6.8, 2.7 Hz, 1 H), 4.49 (ddd, *J* = 4.9, *J* = 7.7, 6.3 Hz, 1 H), 4.23 (dd, *J* = 7.7, 6.5 Hz, 1 H), 4.16 (dd, *J* = 8.5, 6.3 Hz, 1 H), 4.02 (dd, *J* = 8.5, 4.9 Hz, 1 H), 3.90 (m, 1 H), 2.36 (dd, *J* = 15.0, 4.0 Hz, 1 H), 2.28 (dd, *J* = 15.0, 8.2 Hz, 1 H), 1.92 (m, 3 H), 1.67 (s, 3 H), 1.60 (s, 3 H), 1.46 (s, 3 H), 1.38 (s, 3 H), 1.22 (m, 4 H), 0.91 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR: δ = 161.1, 131.4, 124.7, 109.3, 101.0, 85.2, 73.7, 73.1, 67.1, 66.9, 44.4, 37.8, 36.9, 28.9, 26.8, 25.7, 25.4, 25.2, 19.1, 17.6 ppm. MS (API-ES positive): *m*/*z* = 353.2 [M + 1]$^+$. $C_{20}H_{34}O_5$ (352,24): calcd. C 67.76, H 9.76; found C 67.59, H 9.51.

Compound 30: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), isobutyraldehyde (**22**, 62 µL, 0.67 mmol), and Et_2Zn (1.1 mL, solution 1.0 M in hexanes, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 25:70:5) to yield compound **30** as an inseparable mixture of diastereomers (2.5:1, 77 mg, 63%). ^1H NMR (selected peaks for the major isomer): δ = 5.01 (d, *J* = 2.4 Hz, 1 H), 4.85 (m, 1 H), 4.50 (dt, *J* = 11.6, 6.2 Hz, 1 H), 4.23 (dd, *J* = 13.6, 6.6 Hz, 1 H), 4.11 (dd, *J* = 8.7, 6.4 Hz, 1 H), 4.01 (ddd, *J* = 6.4, 5.1, 3.4 Hz, 1 H), 3.59 (m, 1 H), 2.29 (m, 2 H), 1.67 (m, 1 H), 1.45 (s, 3 H), 1.37 (s, 3 H), 0.92 (s, 6 H) ppm. ^{13}C NMR (selected peaks for the major isomer): δ = 161.8, 109.5, 101.3, 85.5, 74.2, 74.0, 73.4, 67.1, 33.8, 33.5, 27.1, 25.5, 18.9, 17.8 ppm. MS (API-ES positive): *m*/*z* = 273.2 $[M + 1]^+$. $C_{14}H_{24}O_5$ (272.16): calcd. C 61.74, H 8.88; found C 61.59, H 8.67.

Compounds 31 and 32: Oxirane **9** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), aldehyde **26**[64] (174 mg, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 25:70:5) to yield compound **32** (29 mg, 14%), followed by compound **31** (88 mg, 43%).

Compound 31: ^1H NMR: δ = 5.53 (d, *J* = 4.9 Hz, 1 H), 5.08 (d, *J* = 2.6 Hz, 1 H), 4.89 (dd, *J* = 6.2, 2.6 Hz, 1 H), 4.62 (dd, *J* = 8.1, 2.3 Hz, 1 H), 4.48 (m, 2 H), 4.31 (dd, *J* = 5.1, 2.3 Hz, 1 H), 4.23 (t, *J* = 6.5 Hz, 1 H), 4.14 (dd, *J* = 8.5, 6.2 Hz, 1 H), 3.99 (m, 2 H), 3.58 (dd, *J* = 8.2, 1.6 Hz, 1 H), 2.76 (dd, *J* = 15.2, 2.6 Hz, 1 H), 2.30 (dd, *J* = 15.2, 9.2 Hz, 1 H), 1.51 (s, 3 H), 1.46 (s, 3 H), 1.44 (s, 3 H), 1.37 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H) ppm. ^{13}C NMR: δ = 161.1, 109.3, 108.6, 101.1, 96.5, 85.3, 73.7, 73.1, 70.8, 70.7 (×3), 69.7, 68.4, 66.9, 33.0, 26.9, 26.1, 26.0, 25.3, 25.0, 24.4 ppm. MS (API-ES positive): *m*/*z* = 459.2 $[M + 1]^+$. $C_{22}H_{34}O_{10}$ (458.21): calcd. C 57.63, H 7.47; found C 57.52, H 7.67.

Compound 32: ^1H NMR: δ = 5.55 (d, *J* = 5.4 Hz, 1 H), 4.64 (dd, *J* = 8.0, 2.2 Hz, 1 H), 4.49 (m, 2 H), 4.41 (dd, *J* = 8.0, 2.2 Hz, 1 H), 4.33 (m, 3 H), 4.26 (br. s, 1 H), 4.10 (m, 2 H), 3.99 (m, 2 H), 3.82 (dd, *J* = 9.0, 2.2 Hz, 1 H), 1.53 (s, 3 H), 1.45 (s, 3 H), 1.42 (s, 3 H), 1.36 (s, 6 H), 1.32 (s, 3 H) ppm. ^{13}C NMR: δ = 160.2, 110.5, 109.2, 108.5, 96.4, 84.6 (×2), 76.0, 73.4, 70.7 (×3), 70.0, 68.3, 67.6, 52.5, 26.7, 25.9, 25.5, 25.1, 24.7, 24.5 ppm. MS (API-ES positive): *m*/*z* = 459.2 $[M + 1]^+$. $C_{22}H_{34}O_{10}$ (458.21): calcd. C 57.63, H 7.47; found C 57.45, H 7.31.

Compound 33: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), isobutyl methyl ketone (**24**, 1.5 equiv., 110 µL, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 25:70:5) to yield compound **33** as an inseparable mixture of diastereomers (2.5:1) (65 mg, 48%). ^1H NMR (selected peaks for the major isomer): δ = 5.00 (d, *J* = 2.7 Hz, 1 H), 4.88 (m, 1 H), 4.47 (ddd, *J* = 7.6, 6.4, 5.0 Hz, 1 H), 4.20 (m, 1 H), 4.14 (dd, *J* = 8.6, 6.4 Hz, 1 H), 3.99 (dd, *J* = 8.6, 5.0 Hz, 1 H), 2.34 (m, 2 H), 2.06 (br. s, 1 H), 2.05 (br. s, 1 H), 1.78 (m, 1 H), 1.45 (s, 3 H), 1.41–1.37 (m, 2 H), 1.37 (s, 3 H), 1.21 (s, 3 H), 0.94 (m, 6 H) ppm. ^{13}C NMR (selected peaks for the major isomer): δ = 160.7, 109.3, 102.4, 85.3, 73.4, 73.0, 72.3, 66.8, 50.3, 41.1, 27.1, 26.8, 25.1, 24.8, 24.5, 24.2 ppm. MS (API-ES positive): *m*/*z* = 323.3 $[M + Na]^+$. $C_{16}H_{28}O_5$ (300.19): calcd. C 63.97, H 9.40; found C 63.81, H 9.43.

Compound 34: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), benzophenone (**25**, 1.5 equiv., 123 mg, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 30:65:5) to yield compound **34** (117 mg, 68%). ^1H NMR: δ = 7.32 (m, 10 H), 5.02 (d, *J* = 2.9 Hz, 1 H), 4.92 (m, 1 H), 4.81 (m, 1 H), 4.47 (m, 1 H), 4.20 (t, *J* = 7.0 Hz, 1 H), 4.12 (dd, *J* = 8.5, 6.4 Hz, 1 H), 3.99 (dd, *J* = 8.7, 5.1 Hz, 1 H), 2.56 (m, 2 H), 1.42 (s, 3 H), 1.34 (s, 3 H) ppm. ^{13}C NMR: δ = 158.9, 131.0, 127.2, 126.3, 124.3, 107.8, 100.1, 83.8, 72.3, 71.7, 70.0, 65.3, 36.9, 25.4, 23.8 ppm. MS (API-ES positive): *m*/*z* = 383.2 $[M + H]^+$. $C_{23}H_{26}O_5$ (382.17): calcd. C 72.23, H 6.85; found C 71.98, H 6.69.

Compound 35: Oxirane **6** (90 mg, 0.45 mmol), $Pd(PPh_3)_4$ (26 mg, 0.02 mmol), γ-butyrolactone (**26**) (1.5 equiv., 110 µL mg, 0.67 mmol), and Et_2Zn (1.0 M solution in hexanes, 1.1 mL, 1.12 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compound **35** (28 mg, 23%). ^1H NMR: δ = 6.26 (d, *J* = 3.2 Hz, 1 H), 6.04 (d, *J* = 3.2 Hz, 1 H), 5.04 (t, *J* = 7.6 Hz, 1 H), 4.20 (dd, *J* = 8.3, 6.4, Hz, 1 H), 4.08 (m, 3 H), 3.74 (ddd, *J* = 15.1, 8.3, 6.6 Hz, 1 H), 3.73 (ddd, *J* = 15.1, 8.3, 7.1 Hz, 1 H), 2.90 (dd, *J* = 14.9, 6.6 Hz, 1 H), 2.76 (dd, *J* = 14.9, 6.6 Hz, 1 H), 2.00 (m, 1 H), 2.05 (br. s, 1 H), 1.78 (m, 1 H), 1.45 (s, 3 H), 1.87 (s, 3 H), 1.49 (s, 3 H), 1.44 (m, 3 H) ppm. ^{13}C NMR: δ = 153.8 (×2), 109.7, 109.4, 107.2 (×2), 71.4, 68.0, 67.8, 34.4, 31.1, 26.4, 26.0, 25.6 ppm. MS (API-ES positive): *m*/*z* = 282.3 $[M + Na]^+$. $C_{14}H_{20}O_5$ (268.30): calcd. C 62.67, H 7.51; found C 62.47, H 7.69.

General Procedure for the Preparation of Alkenylstannanes 39 and 40: Triethylborane (0.1 mol equiv. of a hexane solution) was added under argon at 0 °C to a stirred solution of the corresponding terminal alkyne (1.0 mol equiv.) and tributyltin hydride (1.1 mol equiv.) in toluene (10 mL mmol^{-1}). The reaction mixture was stirred for 24 h and was then concentrated under reduced pressure. The residue was purified by flash chromatography.

Compound 39:[65] This compound was prepared from 1,2:5,6-di-*O*-isopropylidene-3-*O*-propargyl-α-D-*gluco*-furanose[66] (700 mg, 2.34 mmol). Workup entailed concentration of the mixture and subjection to chromatography (hexane/EtOAc, 98:2) to give **39** (mainly as the *E* isomer, 1.3 g, 95%). ^1H NMR (200 MHz): δ = 6.26 (dt, *J* = 1.2, *J* = 19.0 Hz, 1 H), 6.02 (dt, *J* = 5.0, *J* = 19.0 Hz, 1 H), 5.90 (d, *J* = 3.8 Hz, 1 H), 4.56 (d, *J* = 3.8 Hz, 1 H), 4.34 (m, 1 H), 4.05 (m, 6 H), 1.51 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.29 (m, 6 H), 0.92 (m, 6 H), 0.90 (t, *J* = 7.2 Hz, 9 H) ppm. ^{13}C NMR: δ = 144.0, 131.8, 111.8, 109.9, 105.3, 82.8, 81.3, 74.0, 72.6, 67.3, 29.15 (×3), 27.3 (×3), 26.9, 26.3, 25.5, 13.8 (×3), 9.5 (×3) ppm.

Compound 40: This compound was prepared from *N*-propargylindole[67] (600 mg, 3.86 mmol). Purification was carried out by flash chromatography (hexane) to yield the alkenylstannane **39** (1.32 g, 76%, along with the *Z* isomer, 320 mg, 19%). ^1H NMR: δ = 7.72 (d, *J* = 7.8 Hz, 1 H), 7.40 (d, *J* = 8.1 Hz, 1 H), 7.27 (dd, *J* = 8.1, 6.9 Hz, 1 H), 7.19 (dd, *J* = 7.8, 6.9 Hz, 1 H), 7.16 (d, *J* = 3.0 Hz, 1 H), 6.60 (d, *J* = 3.0 Hz, 1 H), 4.83 (d, *J* = 1.8 Hz, 2 H), 6.17 (m, 2 H), 1.54 (m, 6 H), 1.37 (m, 6 H), 0.96 (m, 15 H) ppm. ^{13}C NMR: δ = 142.5, 136.1, 131.6, 128.6, 127.9, 121.3, 120.8, 119.2, 109.8, 101.1, 52.0, 29.0 (×3), 27.2 (×3), 13.7 (×3), 9.4 (×3) ppm.

Compound 41: A solution of *N*-propargylindole (600 mg, 3.86 mmol) in dry toluene (60 mL) was cooled to 0 °C and treated under argon with $Pd_2(dba)_2$ (80 mg, 0.015 mmol), PPh_3 (102 mg, 0.36 mmol), and $HSnBu_3$ (2 mL, 7.8 mmol). The resulting mixture was stirred for 12 h. Workup involved concentration of the mixture and subjection to chromatography (hexane/EtOAc, 98:2) to give **41** (863 mg, 50%), along with terminal stannane **40** (690 mg, 40%). For **41**: ^1H NMR: δ = 7.66 (d, *J* = 7.8 Hz, 1 H), 7.32 (d, *J* = 7.8 Hz, 1 H), 7.21 (m, 1 H), 7.13 (m, 1 H), 7.08 (d, *J* = 3.3 Hz, 1 H), 6.55 (d, *J* = 3.3 Hz, 1 H), 5.67 (q, *J* = 1.8 Hz, 1 H), 5.35 (q, *J* = 1.8 Hz, 1 H), 4.89 (t, *J* = 1.8 Hz, 2 H), 1.42 (m, 6 H), 1.29 (m, 6 H), 0.90 (t, *J* = 7.5 Hz, 9 H), 0.81 (t, *J* = 8.1 Hz, 6 H) ppm.

General Procedure for Reactions between the Vinyloxirane and Alkenylstannanes: A solution of epoxide **6** in DMF (5 mL mmol^{-1}) was cooled to 0 °C and treated under argon with H_2O (10 equiv.), the corresponding vinylstannane (1.5 equiv.), and $Pd(CH_3CN)_2Cl_2$ (0.05 equiv.). The resulting mixture was stirred at room temperature under argon. After the starting materials had been consumed (TLC), the mixture was diluted with EtOAc and washed with brine. The organic layer was dried, concentrated, and subjected to silica gel column chromatography.

Compounds 36 and 37: Oxirane **6** (50 mg, 0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (3 mg, 0.01 mmol), and tetravinyltin (68 µL, 0.37 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compounds **36** (29 mg, 51%) and **37** (9 mg, 15%).

Compound 36: ^1H NMR: δ = 5.84 (m, 1 H), 5.13 (m, 2 H), 4.95 (s, 1 H), 4.90 (br. s, 1 H), 4.49 (ddd, J = 8.1, 6.3, 5.1 Hz, 1 H), 4.17 (m, 2 H), 4.02 (dd, J = 8.4, 5.1 Hz, 1 H), 2.91 (m, 2 H), 1.82 (s, 1 H), 1.46 (s, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR: δ = 162.5, 132.4, 117.7, 109.2, 99.2, 85.1, 73.8, 73.0, 67.0, 32.7, 26.8, 25.2 ppm. MS (API-ES positive): m/z = 227.0 $[M + H]^+$. $C_{12}H_{18}O_4$ (226.12): calcd. C 63.70, H 8.02; found C 63.59, H 8.15.

Compound 37: ^1H NMR: δ = 5.78 (ddd, J = 17.1, 10.0, 6.8 Hz, 1 H), 5.27 (dd, J = 17.1, 1.5 Hz, 1 H), 5.20 (dd, J = 10.0, 1.2 Hz, 1 H), 4.40 (s, 1 H), 4.34 (ddd, J = 8.8, 6.1, 4.9 Hz, 1 H), 4.26 (dd, J = 6.8, 3.4 Hz, 1 H), 4.19 (dd, J = 8.8, 6.1 Hz, 1 H), 4.09 (dd, J = 8.6, 4.1 Hz, 1 H), 4.02 (dd, J = 8.8, 4.9 Hz, 1 H), 3.94 (s, 1 H), 3.36 (m, 1 H), 1.57 (s, 1 H), 1.44 (s, 3 H), 1.37 (s, 3 H) ppm. ^{13}C NMR: δ = 161.8, 134.7, 117.6, 109.7, 83.5, 82.6, 75.8, 73.4, 67.6, 54.1, 26.8, 25.2 ppm. MS (API-ES positive): m/z = 249.0 $[M + H]^+$, 227.0 $[M + H]^+$. $C_{12}H_{18}O_4$ (226.12): calcd. C 63.70, H 8.02; found C 63.81, H 8.03.

Compounds 42 and 43: Oxirane **6** (50 mg, 0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (3 mg, 0.01 mmol), and tributyl[(*E*)-styryl]tin **38** (145 mg, 0.37 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compounds **42** (33 mg, 44%) and **43** (14 mg, 19%).

Compound 42: ^1H NMR: δ = 7.26–7.43 (m, 5 H), 6.15 (d, J = 15.8 Hz, 1 H), 6.14 (dd, J = 15.8, 7.0 Hz, 1 H), 5.00 (s, 1 H), 4.93 (br. s, 1 H), 4.43–4.32 (m, 1 H), 4.13–4.25 (m, 2 H), 4.04 (dd, J = 8.6, 5.1 Hz, 1 H), 3.08 (d, J = 7.0 Hz, 2 H), 2.58 (d, J = 3.8 Hz, 1 H), 1.48 (s, 3 H), 1.40 (s, 3 H) ppm. ^{13}C NMR: δ = ($CDCl_3$, 75 MHz) 162.5, 132.7, 128.5 (×2), 128.2, 127.7, 127.3, 126.3, 109.7, 109.2, 99.3, 85.2, 73.8, 73.0, 67.5, 31.8, 26.8, 25.2 ppm. MS (API-ES positive): m/z = 325.3 $[M + Na]^+$. $C_{18}H_{22}O_4$ (302.15): calcd. C 71.50, H 7.33; found C 71.37, H 7.23.

Compound 43: ^1H NMR: δ = 7.25–7.42 (m, 5H), 5.78 (ddd, J = 17.1, 10.0, 6.8 Hz, 1 H), 5.27 (dd, J = 17.1, 1.5 Hz, 1 H), 5.20 (dd, J = 10.0, 1.2 Hz, 1 H), 4.40 (s, 1 H), 4.34 (ddd, J = 8.8, 6.1, 4.1 Hz, 1 H), 4.26 (dd, J = 6.8, 3.4 Hz, 1 H), 4.19 (dd, J = 8.6, 6.1 Hz, 1 H), 4.09 (dd, J = 8.6, 4.1 Hz, 1 H), 4.02 (dd, J = 8.8, 4.9 Hz, 1 H), 3.94 (s, 1 H), 3.36 (m, 1 H), 1.57 (s, 1 H), 1.44 (s, 3 H), 1.37 (s, 3 H) ppm. ^{13}C NMR: δ = 163.2, 136.3, 132.0, 128.7 (×2), 128.6 (×2), 128.4, 127.4, 109.9, 83.2, 82.2, 77.0, 73.6, 67.6, 48.8, 26.8, 25.2 ppm. MS (API-ES positive): m/z = 325.3 $[M + Na]^+$. $C_{18}H_{22}O_4$ (302.15): calcd. C 71.50, H 7.33; found C 71.44, H 7.03.

Compounds 44 and 45: Oxirane **6** (50 mg, 0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (3 mg, 0.01 mmol), and the alkenylstannane **39** (221 mg, 0.37 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compounds **44** (68 mg, 55%) and **45** (15 mg, 12%).

Compound 44: ^1H NMR: δ = 5.89 (d, J = 3.7 Hz, 1 H), 5.71 (m, 2 H), 4.95 (s, 1 H), 4.90 (br. s, 1 H), 4.54 (d, J = 3.7 Hz, 1 H), 4.48 (m, 1 H), 4.40–3.92 (m, 10 H), 2.93 (d, J = 3.0 Hz, 2 H), 1.86 (d, J = 4.6 Hz, 1 H), 1.51 (s, 3 H), 1.44 (s, 6 H), 1.37 (s, 6 H), 1.33 (s, 3 H) ppm. ^{13}C NMR (75 MHz): δ = 162.2, 129.0, 127.8, 111.7, 109.2, 108.9, 105.2, 99.2, 85.1, 82.8, 81.1, 73.7, 72.9, 72.4, 70.6, 67.2, 66.9, 31.2, 27.8, 26.8 (×3), 26.2, 25.4, 25.2 ppm. MS (API-ES positive): m/z = 498.1 $[M]^+$. $C_{25}H_{38}O_{10}$ (498.25): calcd. C 60.23, H 7.62; found C 60.29, H 7.47.

Compound 45: ^1H NMR: δ = 5.89 (d, J = 3.7 Hz, 1 H), 5.76 (d, J = 8.3 Hz, 1 H), 5.72 (d, J = 8.3 Hz, 1 H), 4.55 (d, J = 3.7 Hz, 1 H), 4.40–3.93 (m, 14 H), 3.38 (br. s, 1 H), 2.52 (d, J = 4.0 Hz, 1 H), 1.51 (s, 3 H), 1.45 (s, 3 H), 1.44 (s, 3 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H) ppm. ^{13}C NMR (75 MHz): δ = 161.9, 129.6, 129.2, 111.8, 109.7, 109.0, 105.2, 82.8, 82.5, 81.5, 81.1, 77.1, 75.9, 73.4, 72.3, 70.3, 67.5, 67.4, 52.9, 26.8 (×3), 26.2, 25.4, 25.1 ppm. MS (API-ES positive): m/z = 498.1 $[M]^+$. $C_{25}H_{38}O_{10}$ (498.25): calcd. C 60.23, H 7.62; found C 60.17, H 7.51.

Compounds 46 and 47: Oxirane **6** (50 mg, 0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (3 mg, 0.01 mmol), and the alkenylstannane **40** (167 mg, 0.37 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compounds **46** (54 mg, 61%) and **47** (17 mg, 20%).

Compound 46: ^1H NMR: δ = 7.64 (d, J = 8.1 Hz, 1 H), 7.33 (d, J = 7.9 Hz, 1 H), 7.21 (t, J = 8.1 Hz, 1 H), 7.13 (d, J = 8.1 Hz, 1 H), 7.10 (d, J = 2.7 Hz, 1 H), 6.52 (d, J = 2.7 Hz, 1 H), 5.79–5.54 (m, 2 H), 4.75–4.69 (s, 1 H), 4.88 (s, 1 H), 4.71 (d, J = 5.7 Hz, 2 H), 4.46 (ddd, J = 8.1, 6.3, 5.1 Hz, 1 H), 4.20–4.08 (m, 1 H), 4.15 (dd, J = 8.7, 6.3 Hz, 1 H), 3.99 (dd, J = 8.7, 5.1 Hz, 1 H), 2.89 (d, J = 6.3 Hz, 2 H), 2.59 (d, J = 6.3 Hz, 1 H), 1.47 (s, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR: δ = 162.0, 133.0, 128.5, 127.6 (×2), 127.3, 121.4, 120.9, 119.4, 109.5, 109.2, 101.3, 99.3, 85.1, 73.7, 72.9, 66.9, 47.9, 31.0, 26.8, 25.2 ppm. MS (API-ES positive): m/z = 356.0 $[M + H]^+$. $C_{21}H_{25}NO_4$ (355.42): calcd. C 70.96, H 7.09, N 3.94; found C 71.03, H 7.15, N 3.89.

Compound 47: ^1H NMR: δ = 7.65 (d, J = 8.0 Hz, 1 H), 7.31 (d, J = 8.0 Hz, 1 H), 7.21 (dd, J = 6.9, 1.2 Hz, 1 H), 7.15 (dd, J = 10.3, 1.2 Hz, 1 H), 7.09 (d, J = 3.2 Hz, 1 H), 6.52 (d, J = 3.2 Hz, 1 H), 5.87 (ddt, J = 15.3, 5.7, 1.2 Hz, 1 H), 5.47 (ddt, J = 15.3, 6.9, 1.5 Hz, 1 H), 4.74 (d, J = 3.6 Hz, 1 H), 4.38 (s, 1 H), 4.31 (ddd, J = 8.4, 6.0, 5.1 Hz, 1 H), 4.19–4.14 (m, 1 H), 4.03 (dd, J = 8.4, 4.2 Hz, 1 H), 3.99 (dd, J = 8.7, 4.8 Hz, 1 H), 3.89 (t, J = 1.5 Hz, 1 H), 3.32 (br. d, J = 5.4 Hz, 1 H), 2.55 (d, J = 3.9 Hz, 1 H), 1.43 (s, 3 H), 1.36 (s, 3 H) ppm. ^{13}C NMR: δ = 161.6, 135.9, 129.4, 128.6, 128.5, 127.6, 121.5, 120.9, 119.4, 109.7, 109.5, 101.5, 83.7, 82.4, 75.7, 73.2, 67.4, 52.7, 47.8, 26.8, 25.1 ppm. MS (API-ES positive): m/z = 356.0 $[M + H]^+$. $C_{21}H_{25}NO_4$ (355.42): calcd. C 70.96, H 7.09, N 3.94; found C 70.87, H 7.01, N 3.79.

Compounds 48 and 49: Oxirane **6** (50 mg, 0.25 mmol), $Pd(CH_3CN)_2Cl_2$ (3 mg, 0.01 mmol), and the alkenylstannane **41** (167 mg, 0.37 mmol) were treated according to the General Procedure. Purification was carried out by flash chromatography (hexane/EtOAc/Et_3N, 70:25:5) to yield compounds **48** (44 mg, 50%) and **49** (16 mg, 20%).

Compound 48: ^1H NMR: δ = 7.64 (d, J = 7.8 Hz, 1 H), 7.31 (d, J = 8.3 Hz, 1 H), 7.21 (m, 1 H), 7.11 (m, 1 H), 7.09 (d, J = 3.0 Hz, 1 H), 6.52 (d, J = 3.2 Hz, 1 H), 5.07 (s, 1 H), 4.92 (s, 1 H), 4.85 (br. s, 1 H), 4.81 (m, 1 H), 4.72 (s, 2 H), 4.41 (ddd, J = 7.8, 6.4, 5.4 Hz, 1 H), 4.17–4.08 (m, 2 H), 3.96 (dd, *J* = 8.6, 5.4 Hz, 1 H), 2.86 (s, 2 H), 2.36 (s, 1 H), 1.46 (s, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR (75 MHz): δ = 160.7, 140.0, 136.2, 129.0, 128.3, 121.5, 120.9, 119.4, 115.6, 109.7, 109.1, 101.3, 100.3, 85.2, 73.5, 72.9, 66.7, 60.3, 51.1, 26.8, 25.2 ppm. MS (API-ES positive): *m*/*z* = 378.0 [M + Na]$^+$. $C_{21}H_{25}NO_4$ (355.42): calcd. C 70.96, H 7.09, N 3.94; found C 70.85, H 7.03, N 3.90.

Compound 49: ^{1}H NMR: δ = 7.64 (d, *J* = 7.8 Hz, 1 H), 7.30 (d, *J* = 8.3 Hz, 1 H), 7.20 (m, 1 H), 7.11 (m, 1 H), 6.55 (d, *J* = 3.2 Hz, 1 H), 5.14 (s, 1 H), 4.93 (s, 1 H), 4.82 (d, *J* = 3.2 Hz, 2 H), 4.44 (s, 1 H), 4.29 (ddd, *J* = 8.3, 6.1, 4.9 Hz, 1 H), 4.14 (dd, *J* = 8.8, 6.1 Hz, 1 H), 4.08 (m, 1 H), 3.99–3.95 (m, 2 H), 3.90 (s, 1 H), 3. 24 (s, 1 H), 2.29 (d, *J* = 3.7 Hz, 1 H), 1.38 (s, 3 H), 1.34 (s, 3 H) ppm. ^{13}C NMR: δ = 161.8, 142.3, 136.0, 128.5, 128.1, 121.8, 121.1, 119.7, 115.4, 109.6, 109.5, 101.9, 83.9, 82.9, 74.9, 73.2, 67.4, 54.6, 50.5, 26.8, 25.1 ppm. MS (API-ES positive): *m*/*z* = 378.0 [M + Na]$^+$, 356.0 [M + 1]$^+$. $C_{21}H_{25}NO_4$ (355.42): calcd. C 70.96, H 7.09, N 3.94; found C 70.79, H 7.03, N 3.81.

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