Regioselective and Divergent Opening of Vinyl Epoxides with Alkyne Nucleophiles

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A divergent procedure for nucleophilic ring-opening of vinyl epoxides with alkynes has been developed. The combination of lithium acetylides and $BF_3{\cdot}OEt_2$ afforded the S_N2 products, whereas alkynylalanes gave S_N2' addition. The regioselectivity of these processes is affected by the alkyne substituent. Ethoxyacetylene added with complete regiocontrol under both S_N2 and S_N2' conditions, and the S_N2 isomeric adducts could be rearranged into γ-butyrolactones. The synthetic utility of the process is demonstrated by a short synthesis of γ-butyrolactone **24**, a key intermediate in the synthesis of prostaglandin $PGF_{2\alpha}$.

Introduction

Vinyl epoxides are commonly used as starting materials in organic synthesis[1] and belong to the class of allylic electrophiles, which can undergo nucleophilic addition reactions in either S_N2 or S_N2' fashion (Figure 1). Consequently, the ability to control the regiochemical outcomes of nucleophilic additions to these substrates is critical and considerable effort has been devoted to the development of processes that proceed regioselectively.

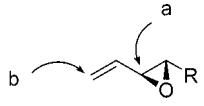

Figure 1. Nucleophilic attack on a vinyl epoxide according to the a) S_N2, or b) S_N2' mechanisms.

Conjugate additions of carbon nucleophiles to vinyl epoxides have been extensively studied and can be accomplished by Pd-catalyzed allylic alkylations with soft, stabilized nucleophiles,[2] organocopper reagents,[3] or copper-catalyzed additions of organomagnesium[4] or organozinc compounds.[5,6] On the other hand, regioselective S_N2 displacements can be achieved through the use of alkyllithiums in the presence of $BF_3{\cdot}OEt_2$,[7] Grignard reagents,[8] or trialkylzincates and aluminates,[9] although regioisomeric mixtures are usually obtained. A drawback with these methods is that different techniques have to be used for regioselective S_N2 and S_N2' additions. A divergent strategy that would allow selective nucleophilic additions both to the S_N2 and to the S_N2' positions, depending on the reaction conditions, would be a major improvement. A few examples of regiodivergent additions of carbon nucleophiles to vinyl epoxides have been reported: $AlMe_3$, for instance, predominately afforded the S_N2 product in addition to 4,5-epoxy-2-hexenoate, whereas LiMeCuCN afforded predominately the S_N2' adduct, albeit with low regioselectivity.[10] A divergent approach using lithiated dithianes, in which the regiochemical outcome was controlled by steric factors, was recently developed. In this procedure, sterically unencumbered dithianes add to the activated allylic position (S_N2), whereas sterically hindered dithianes add to the more accessible terminal position (S_N2').[11] Both the S_N2 and the S_N2' processes proceed with excellent regioselectivity. We have previously reported that the regiochemistry in additions of ethoxyacetylide to vinyl epoxides can be controlled by varying the counterion.[12] The combination of lithium ethoxyacetylide and $BF_3{\cdot}OEt_2$ afforded the S_N2 adduct, while the corresponding alkynylalane gave S_N2' addition, both processes proceeding with complete regioselectivity. Here we report our detailed results obtained by use of different alkyne nucleophiles in regioselective openings of vinyl epoxides.

Results and Discussion

We envisaged that the regioselectivity in opening of vinyl epoxides might be controllable through careful tuning of the hard and soft properties of the nucleophiles. Hard nucleophiles should mainly be influenced by coulombic attractions with the substrate and react under charge control (S_N2), whereas softer nucleophiles should react through HOMO–LUMO interactions, resulting in an orbital-controlled reaction (S_N2').[13] The initial focus was directed

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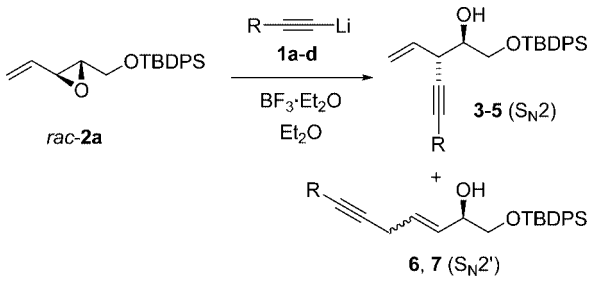
Table 1. Addition of acetylides **1a**–**d** to vinyl epoxide **2a**.[a]



Entry	**1** (R =)	*T* (°C)/*t* (h)	Conversion (%)[b]	S_N2/S_N2'[b]	Product
1	**a** (Ph)	–20/18	66	51:49	**3**, **6**
2	**b** (4-MeOPh)	–20/18	67	76:24	**4**, **7**
3	**c** (TMS)	–20/18	0	N/A	N/A
4	**d** (OEt)	–78/1	100	> 98:2	**5**

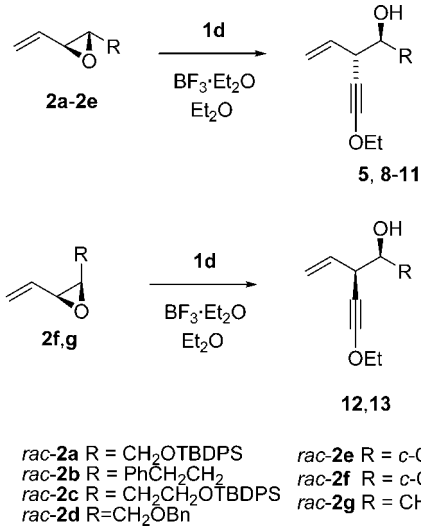
[a] Reaction conditions: **1** (2.5 equiv.), **2a** (1 equiv.) and $BF_3{\cdot}OEt_2$ (2.5 equiv.) in Et_2O. [b] Determined by ^1H NMR analysis of the crude product.

towards investigating how the electronic properties of the alkyne substituent affected the regioselectivity under charge control (i.e., an S_N2 process). For initial screening, four alkynyl anions with different electronic properties were chosen as representative nucleophiles (Table 1). The reactions between **2a**[14] and lithium acetylides **1a** and **1b** proceeded with moderate levels of conversion and regioselectivity in Et_2O at –20 °C (Entries 1, 2). Attempts to optimize the process by changing solvent met with no success: no reaction was observed in THF, whereas vinyl epoxide **2a** decomposed in PhMe. Lithium acetylide **1c** gave no addition product at –20 °C, and higher reaction temperatures again resulted in decomposition. A substantial improvement was observed with ethoxyacetylide **1d**, which gave full conversion and complete S_N2 regioselectivity at –78 °C. Apparently, electron-donating substituents increase the reactivity of the lithium acetylide and, more importantly, the S_N2 regioselectivity.

Subsequently, the influence of the vinyl epoxide structure was investigated, by employment of substrates **2b**–**f** (Table 2).[14] Gratifyingly, ring-opening with **1d** exclusively afforded homoallylic alcohols **8**–**13** in good yields and with complete S_N2 regioselectivity.[15] Furthermore, the reaction proceeded with comparable yields irrespective of the electronic and steric properties of the R group (Entries 1–5) or epoxide configuration (Entries 6, 7), thus broadening the scope of the transformation.

To probe the stereochemical outcome of the alkynylation, alcohol **5** was transformed into *cis*-γ-butyrolactone **14** through a retro-ene reaction, followed by intramolecular trapping of the ketene (Scheme 1).[16] The relative stereochemistry of lactone **14** was established by chemical correlation[17] and revealed that the addition had indeed taken place with inversion. Consequently, the relative stereochemistry of the formed homoallylic alcohols is directly related to the *cis*- or *trans*-stereochemistry of the starting vinyl epoxides, thus giving ready access to *cis*- or *trans*-β,γ-disubstituted γ-butyrolactones, respectively.

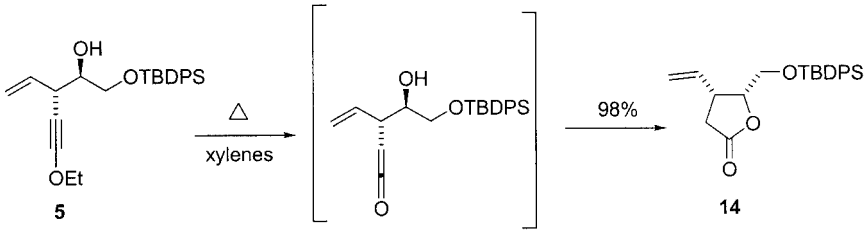
Table 2. Regioselective S_N2 opening of *rac*-vinyl epoxides **2a**–**g** with ethoxyacetylide **1d**.[a]



Entry	**2**	R	Yield[b](%)	S_N2/S_N2'[c]	Product
1	**2a**	$CH_2OTBDPS$	64	>98:2	**5**
2	**2b**	$PhCH_2CH_2$	61	>98:2	**8**
3	**2c**	$CH_2CH_2OTBDPS$	62	>98:2	**9**
4	**2d**	CH_2OBn	52	>98:2	**10**
5	**2e**	*c*-C_6H_{11}	61	>98:2	**11**
6	**2f**	*c*-C_6H_{11}	63	>98:2	**12**
7	**2g**	$CH_2OTBDPS$	65	>98:2	**13**

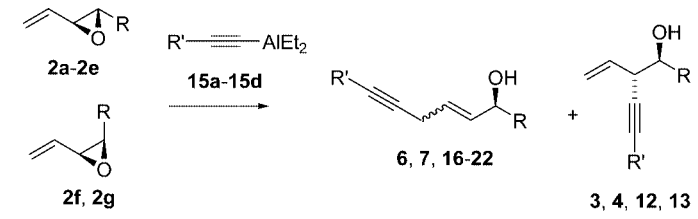
[a] Reaction conditions: **1d** (2.5 equiv.), **2** (1 equiv.) and $BF_3{\cdot}OEt_2$ (2.5 equiv.). [b] Isolated yield. [c] Determined by ^1H NMR analysis of the crude product.

Alkynylalanes have previously been used for ring-opening of oxiranes[18–20] and the soft character of these reagents has enabled Michael additions to enones.[21] Somewhat surprisingly, these reagents had not previously been exploited in S_N2' opening of vinyl epoxides.[12] As alkynylalanes are readily prepared from the corresponding lithium ace-



Scheme 1. Transformation of **5** into γ-butyrolactone **14**.

Table 3. Conjugate additions of alkynylalanes **15** to *rac*-vinyl epoxides **2a**–**g**.[a]



rac-**2a** R = $CH_2OTBDPS$
rac-**2b** R = $PhCH_2CH_2$
rac-**2c** R = $CH_2CH_2OTBDPS$
rac-**2d** R = CH_2OBn
rac-**2e** R = *c*-C_6H_{11}
rac-**2f** R = *c*-C_6H_{11}
rac-**2g** R = $CH_2OTBDPS$

Entry	**2**	**15** (R′ =)	S_N2/S_N2'[b]	*E*/*Z*[b]	Product	Yield[c] (%)
1	**2a**	**a** (Ph)	29:71	70:30	**3**, **6**	84
2	**2a**	**b** (4-MeOPh)	30:70	70:30	**4**, **7**	90
3	**2a**	**c** (TMS)	<2:98	84:16[d]	**16**	76
4	**2a**	**d** (OEt)	<2:98	22:78	**17**	65
5	**2b**	**d** (OEt)	<2:98	70:30	**18**[e]	59[f]
6	**2c**	**d** (OEt)	<2:98	70:30[g]	**19**	55
7	**2d**	**d** (OEt)	>98:2	N/A	**10**	62
8	**2e**	**d** (OEt)	<2: 98	22: 68	**20**	65
9	**2f**	**d** (OEt)	34:66	>98:2	**21**, **12**	55
10	**2g**	**d** (OEt)	62:38	>98:2	**22**, **13**	65

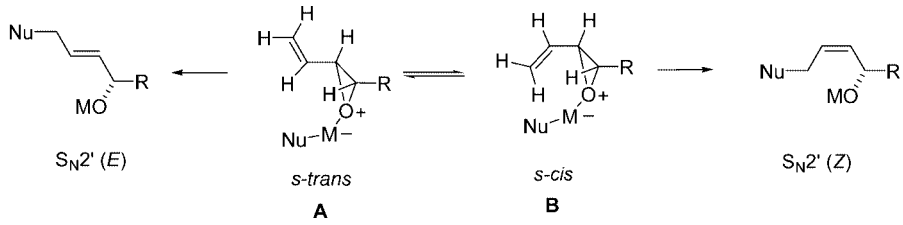
[a] Reaction conditions: **2** (1 equiv.) and **15** (2 equiv.) in PhMe for 12 h at 25 °C. [b] Determined by ^1H NMR analysis of the crude product. [c] Isolated yield. [d] *E*:*Z* isomers could be separated by flash chromatography. [e] Compound **23** formed as by-product, see text. [f] Combined yield of **18** and **23**. [g] Ratio of stereoisomers; *E*:*Z* assignment not possible.

tylides,[22] they were ideal candidates for conjugate additions in our divergent strategy. As shown in Table 3, the alkynylation of vinyl epoxide **2a** with alkynylalanes **15a** and **15b** proceeded in excellent yields to give regioisomeric mixtures of the S_N2 and S_N2' adducts (Entries 1, 2). In contrast with the S_N2 addition reactions, the chemoselectivity is not influenced by the electronic properties of the aromatic substituent. Nevertheless, to our delight, addition of alanes **15c** and **15d** proceeded with complete S_N2' regioselectivity (Entries 3–6, 8).

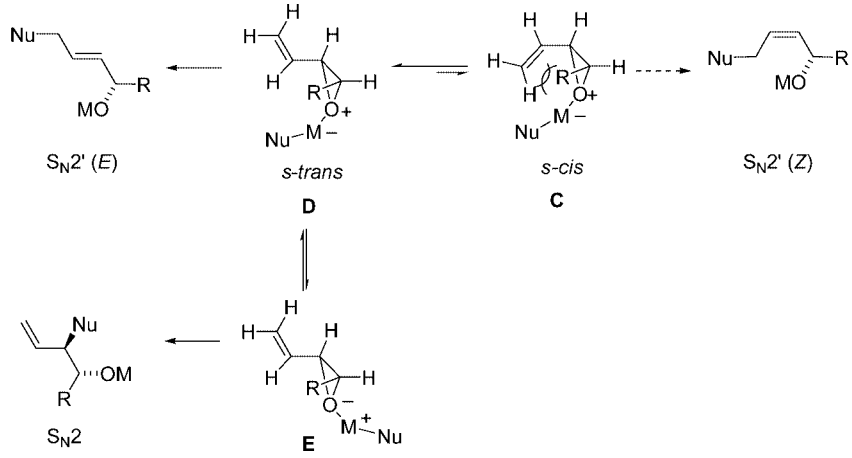
Unfortunately, no general trend could be observed in the *E*:*Z* selectivity of the conjugate additions to *trans*-vinyl epoxides **2a**–**e** (Entries 1–6, 8). We propose that the reaction proceeds by precomplexation of the alkynylalane to the epoxide, followed by intramolecular delivery of the alkyne nucleophile (Scheme 2).[21] In the case of *trans*-vinyl epoxides, reaction through both the s-*trans* (**A**) or the s-*cis* conformer (**B**) is viable, and the S_N2' alkynylations consequently proceed through additions to both conformers, resulting in *E*:*Z* isomeric mixtures.

In contrast, the *cis*-vinyl epoxides **2f** and **2g** gave a diminished S_N2' regioselectivity but complete *E* stereoselectivity (Entries 9–10). The complete *E* selectivity could be explained by severe steric interactions in the s-*cis* conformer (**C**), and consequently the *cis*-vinyl epoxides react exclusively through the s-*trans* conformer (**D**), resulting in a complete S_N2' *E* selectivity (Scheme 3). Previous studies have shown that conjugate additions to enones can only proceed when the substrate–alane complex can adopt a conformation in which the reacting moieties are in close proximity in space.[21] For steric reasons, complexation of the alane to *cis*-vinyl epoxides **2f** and **2g** is likely to occur *trans* to the vinyl moiety (**E**), resulting in an inefficient orbital overlap between the alkynylalane and the olefin. This is likely to retard the S_N2' variant and to make the S_N2 pathway more preferred, which could explain the diminished S_N2' regioselectivity observed in the additions to *cis*-vinyl epoxides **2f** and **2g**.

The conjugate additions of alane **15d** to *trans*-vinyl epoxides **2a**–**e** (Entries 4–8) gave the S_N2' adducts as the only

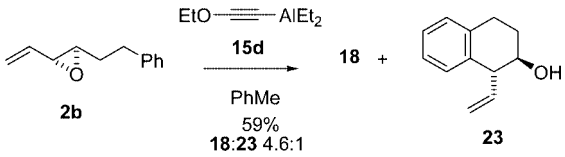


Scheme 2. *E:Z* selectively in the S_N2' alkynylations of *trans*-vinyl epoxides **2a**–**e**.



Scheme 3. *E:Z* selectivity in the S_N2' alkynylations of *cis*-vinyl epoxides **2f** and **2g**.

detectable products, with two exceptions (Entries 5, 7). The S_N2' addition to **2b** afforded alcohol **23** along with the expected product **18** (Scheme 4). Compound **23** is most probably the result of a Friedel–Crafts type of intramolecular ring-opening of vinyl epoxide **2b**, and similar transformations have been described.[23] Vinyl epoxide **2d** afforded only the S_N2 adduct **10** when treated with **15d**, most probably due to complexation of the alane to the benzyloxy moiety, thereby directing the nucleophilic attack (Entry 7). Similar results have been reported in regioselective C3- opening of 2,3-epoxy alcohols with organoaluminium reagents.[24,18] This undesired complexation could be suppressed by protection of the alcohol with the sterically demanding TBDPS group (**2a**, Entry 4).

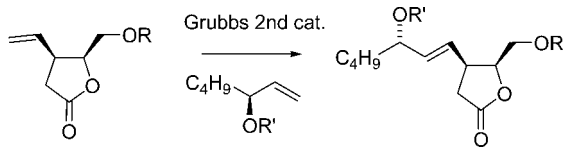


Scheme 4. S_N2' alkynylation of vinyl epoxide **2b** with alane **15d**.

The γ-butyrolactone subunit is a common structural feature in many naturally occurring compounds.[25] Furthermore, these compounds have frequently been used as intermediates in the synthesis of more complex target molecules. One interesting example concerns the pioneering syntheses of prostaglandin $PGF_{2\alpha}$ from D-glucose by Stork and coworkers,[26] which employed lactone **24** as a key intermediate. The potential of our novel regioselective S_N2-opening of vinyl epoxides (vide supra), was demonstrated by the preparation of compound **24** in two steps from γ-butyrolactone (*S*,*S*)-**14**[27] by a cross-metathesis (CM) approach. CM has recently become a powerful method for creating C–C bonds, triggered by the rapid development of more efficient metathesis catalysts with high functional group tolerance.[28,29] Attempts to couple enantiomerically pure lactone (*S*,*S*)-**14** with (*S*)-oct-1-en-3-ol (**25a**)[30] in a CM reaction resulted in low yield of **26**, even after prolonged stirring at room temp. (Table 4, Entry 1). Disappointingly, conduction of the reaction at elevated temperature in CH_2Cl_2 or PhMe resulted in rapid decomposition of the starting material (Entries 2, 3). Protection of the allylic alcohol as the TBDPS ether **25b**[31] also met with no success (Entries 4, 5). Interestingly, desilylation of γ-butyrolactone **14** to yield the corresponding alcohol **27**[17] and subsequent CM gave complete conversion after 2 h at room temp., affording lactone **24** in 57% isolated yield (Entry 6). This type of long-range steric hindrance is unexpected and to the best of our knowledge has not been reported previously.

In conclusion, we have developed a divergent procedure for regioselective alkynylations of vinyl epoxides. Combinations of lithium acetylides and $BF_3{\cdot}OEt_2$ predominantly gave S_N2 displacement, whereas alkynylalanes afforded the S_N2' adducts as the major products. The chemoselectivity in both reactions was shown to be influenced by the alkyne substituent. Ethoxyacetylene added with complete selectivity under both S_N2 and S_N2' conditions and the S_N2 isomeric adducts could by rearranged to γ-butyrolactones. The synthetic utility of the process was demonstrated by a short synthesis of γ-butyrolactone **24**, an advanced intermediate in the synthesis of prostaglandin $PGF_{2\alpha}$.

Table 4. Optimization of the CM reaction.[a]



14 R = TBDPS, **27** R = H — **25a** R' = H, **25b** R' = TBDPS — **24** R = H, R' = H, **26** R = TBDPS, R' = H

Entry	Substrate	**25**	*T* (°C)	*T* (h)	Yield (%)
1	**14**	**a**	r.t.	60	26[b] (**26**)
2	**14**	**a**	40	15	–[c]
3[d]	**14**	**a**	80	3	–[c]
4	**14**	**b**	rt	3	–[e]
5	**14**	**b**	40	6	–[c]
6	**27**	**a**	r.t.	2.5	57 (**24**)

[a] Reaction conditions: Grubbs 2nd generation cat. (10 mol%), **14**/**27** (1 equiv.) and **25** (2 equiv.) in CH_2Cl_2 at the indicated temperature and reaction time. [b] Conversion according to ^{1}H NMR analysis. Product **26** not isolated from the crude mixture and characterized. [c] Starting material decomposed. [d] PhMe was used as solvent. [e] No reaction, starting material was recovered. [d] Compound **25a** was added over 1.5 h.

Experimental Section

Representative Experimental Procedure – S_N2 Alkynylation of Vinyl Epoxide 2a with Lithium Ethoxyacetylide – (2*S,3*R**)-1-*tert*-Butyldiphenylsilyloxy-3-(ethoxyethynyl)pent-4-en-2-ol (5):** BuLi (265 μL, 0.5 mmol, 1.9 M in hexanes) was added at –78 °C to a stirred solution of ethoxyacetylene (145 μL, 0.6 mmol, 40% in hexanes) in dry Et_2O (1.5 mL) and the solution was stirred for 20 min prior to addition of $BF_3{\cdot}OEt_2$ (65 μL, 0.5 mmol) and vinyl epoxide **2a** (68 mg, 0.2 mmol) in Et_2O (1 mL). The resulting mixture was stirred at –78 °C for 1 h and was then quenched with sat. $NaHCO_3$ (5 mL), allowed to warm to room temp., and extracted with Et_2O (2 × 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and evaporated to give a brownish oil. Flash chromatography (pentane/EtOAc 15:1) of the residue yielded **5** (52 mg, 64%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (m, 4 H), 7.43 (m, 6 H), 5.92 (ddd, *J* = 17.0, 10.0, 6.1 Hz, 1 H), 5.36 (dt, *J* = 17.0, 1.6 Hz, 1 H), 5.16 (dt, *J* = 10.0, 1.6 Hz, 1 H), 3.95 (q, *J* = 7.1 Hz, 2 H), 3.82 (m, 2 H), 3.63 (m, 1 H), 3.28 (m, 1 H), 2.54 (d, *J* = 5.1 Hz, 1 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 1.07 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 135.59, 135.55, 133.2, 133.1, 129.8, 127.7, 120.0, 116.4, 93.7, 74.4, 74.2, 65.8, 38.0, 34.7, 26.8, 19.3, 14.3 ppm. IR (neat): $\tilde{\nu}$ = 2930, 2270, 1110 cm^{-1}. HRMS (FAB+) calcd. for $C_{25}H_{33}O_3Si$ [*M* + H]$^+$: 409.2199, found: 409.2203.

Representative Experimental Procedure – S_N2' Alkynylation of Vinyl Epoxide 2a with Aluminium Ethoxyacetylide – 1-*tert*-Butyldiphenylsilyloxy-7-ethoxyhept-3-en-6-yn-2-ol (17): BuLi (195 μL, 0.5 mmol, 2.5 M in hexanes) was added at 0 °C to a stirred solution of ethoxyacetylene (175 μL, 0.75 mmol) in dry toluene (1.5 mL), and the solution was stirred for 10 min, after which $AlClEt_2$ (485 μL, 0.5 mmol, 1 M in hexanes) was added. After 30 min, **2a** in PhMe (1 mL) was added, and the resulting mixture was stirred at room temp. overnight. The reaction was quenched with H_2O (5 mL) and extracted with Et_2O (2 × 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and evaporated to give a brownish oil. Flash chromatography (pentane/EtOAc 15:1) of the residue yielded the desired S_N2' adduct **17** (64 mg, 65%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, peaks assigned from an *E:Z* isomeric mixture): δ = 7.71 (m, 4 H_{maj}, 4 H_{min}), 7.43 (m, 6 H_{maj}, 6 H_{min}), 5.71 (m, 2 H_{min}), 5.57 (ddt, *J* = 10.9, 7.1, 1.2 Hz, 1 H_{maj}), 5.37 (m, 1 H_{maj}), 4.59 (m, 1 H_{maj}), 4.29 (m, 1 H_{min}), 4.03 (q, *J* = 7.1 Hz, 2 H_{min}), 3.97 (q, *J* = 7.1 Hz, 2 H_{maj}), 3.62 (m, 2 H_{maj}, 2 H_{min}), 2.83 (m, 2 H_{maj}, 2 H_{min}), 2.63 (d, *J* = 3.4 Hz, 1 H_{min}), 2.61 (d, *J* = 2.8 Hz, 1 H_{maj}), 1.36 (t, *J* = 7.1 Hz, 3 H_{min}), 1.33 (t, *J* = 7.1 Hz, 3 H_{maj}), 1.09 (s, 9 H_{maj}, 9 H_{min}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, peaks assigned from an *E:Z* isomeric mixture): δ = 135.6, 135.5, 133.2, 133.11, 133.08, 133.0, 130.4, 129.9, 129.8, 129.1, 128.9, 128.4, 127.79, 129.77, 91.4, 89.4, 74.0, 73.9, 72.5, 71.7, 68.4, 67.9, 67.4, 35.2, 34.0, 26.8, 20.4, 19.2, 16.2, 14.4, 14.3 ppm. IR (neat): $\tilde{\nu}$ = 2930, 2270, 1110 cm^{-1}. HRMS (FAB+) calcd. for $C_{25}H_{33}O_3Si$ [*M* + H]$^+$: 409.2199, found: 409.2195.

(4*S,5*S**)-5-*tert*-Butyldiphenylsilyloxymethyl-4-vinyldihydrofuran-2-one (14):** A stirred solution of **5** (18 mg, 44 μmol) in freshly distilled xylenes (1.5 mL) was heated to reflux for 2 h. The mixture was cooled to room temperature and the solvents were removed. Flash chromatography (pentane/EtOAc 15:1) of the residue yielded the desired lactone **14** (16 mg, 98%) as a white solid. m.p. 111.5–113.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (m, 4 H), 7.44 (m, 6 H), 5.99 (m, 1 H), 5.24 (d, *J* = 13.2 Hz, 1 H), 5.20 (d, *J* = 6.2 Hz, 1 H), 4.51 (dt, *J* = 8.2, 2.5 Hz, 1 H), 3.87 (dd, *J* = 11.7, 3.0 Hz, 1 H), 3.75 (dd, *J* = 11.7, 2.2 Hz), 3.36 (m, 1 H), 2.81 (dd, *J* = 17.2, 10.5 Hz, 1 H), 2.62 (dd, *J* = 17.2, 9.3 Hz, 1 H), 1.07 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.4, 135.7, 135.5, 134.5, 132.7, 132.0, 129.9, 127.8, 118.9, 82.0, 63.3, 42.7, 34.8, 26.7, 19.0 ppm. IR (neat): $\tilde{\nu}$ = 2930, 1780 cm^{-1}. HRMS (FAB+) calcd. for $C_{23}H_{29}O_3Si$ [*M* + H]$^+$: 381.1886, found: 381.1885.

(4*S*,5*S*)-5-Hydroxymethyl-4-vinyldihydrofuran-2-one (27): Bu_4NF (70 mg, 0.22 mmol) was added to a stirred solution of γ-butyrolactone (*S*,*S*)-**14** (70 mg, 0.18 mmol) in THF (3 mL). After 2 h, H_2O (5 mL) was added and the solution was extracted with Et_2O (3 × 5 mL). The combined organic phases were dried ($MgSO_4$) and filtered, and the solvents were evaporated. Flash chromatography (pentane/EtOAc 1:1) of the residue yielded the pure title compound **27** (25.1 mg, 97%) as a colorless oil. $[\alpha]_D^{20}$ + 57.2 (*c* = 0.52, $CHCl_3$) [ref.[1] $[\alpha]_D^{23}$ + 59.8 (*c* = 2.6, $CHCl_3$)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.90 (ddd, *J* = 17.1, 10.1, 8.8 Hz, 1 H), 5.23 (d, *J* = 17.1 Hz, 1 H), 5.21 (d, *J* = 10.1 Hz, 1 H), 4.58 (m, 1 H), 3.80 (m, 2 H), 3.34 (m, 1 H), 2.64 (d, *J* = 8.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 134.0, 118.9, 82.2, 62.3, 42.1, 34.4 ppm.

(4*S*,5*S*)-(*E*)-4-(3-Hydroxyhept-1-enyl)-5-hydroxymethyldihydrofuran-2-one (24): Grubbs 2nd generation cat. (6.0 mg, 7 μmol) was added to a stirred solution of **26** (10 mg, 70 μmol) and (*S*)-oct-1-en-3-ol **25a** (19 mg, 0.15 mmol) in CH_2Cl_2 (1 mL), and the resulting mixture was stirred at room temp. for 2.5 h, followed by evaporation of the solvents. Flash chromatography (pentane/EtOAc 1:2) of the residue yielded lactone **24** (9.6 mg, 57%) as a colorless oil. $[\alpha]_D^{20}$ +39.8 (*c* = 0.65, MeOH) {ref.[2] $[\alpha]_D^{25}$ + 42.6 (*c* = 1.55, MeOH)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.76 (dd, *J* = 15.5, 8.3 Hz, 1 H), 5.69 (dd, *J* = 15.5, 5.9 Hz, 1 H), 4.58 (m, 1 H), 4.14 (m, 1 H), 3.84 (m, 2 H), 3.34 (m, 1 H), 2.62 (d, *J* = 8.9 Hz, 1 H), 2.19 (m, 1 H), 1.74–1.30 (m, 9 H), 0.90 (t, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9, 137.44, 126.2, 83.5, 72.1, 62.1, 40.8, 37.2, 34.9, 31.6, 25.0, 22.6, 14.0 ppm.

Supporting Information: (see footnote on the first page of this article): Experimental and/or spectroscopic data for compounds **3**–**4**, **6**–**13**, **16**, and **18**–**22**, and ^{1}H and ^{13}C NMR spectra for compounds **3**–**14** and **16**–**22**.

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