Alkynyliodonium Salts in Organic Synthesis. Dihydrofuran Formation via a Formal Stevens Shift of a Carbon Substituent within a Disubstituted-Carbon Oxonium Ylide

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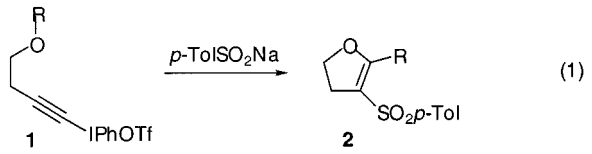
The addition of *p*-toluenesulfinate to the silyl, 1-furanyl, and 1-pyranyl ethers of 1-hydroxybut-3-ynyl(phenyl)iodonium triflate triggers a sequence of reactions that ultimately delivers 2-substituted 3-*p*-toluenesulfonyldihydrofuran products in variable yields. A putative 1,2-group shift within an unsaturated oxonium ylide (Stevens rearrangement) accounts for the oxygen-to-carbon transfer of the ether substituent. Deuterium labeling studies clarify the mechanistic course of this shift by providing evidence consistent with intramolecular substituent transfer and by identifying the primary source of the proton that intercepts the ylide in the major yield-limiting process.

The continuing development of alkynyliodonium salt-derived chemistry for use in heterocycle synthesis has led to efficient sequences for the preparation of indoles, dihydropyrroles, and variously cyclopentannelated dihydropyrroles.[1] The extension of this methodology to dihydrofuran synthesis, **1** → **2** (eq 1), is described herein.



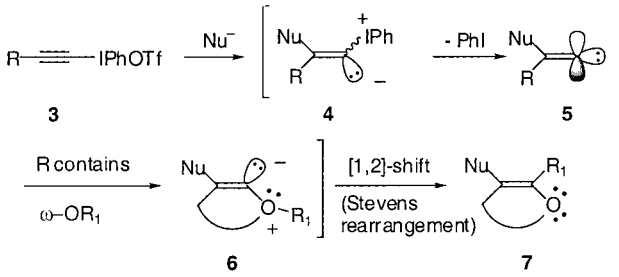
(1)

1 **2**

Work on this transformation was initiated after a chance observation revealed that alkylidene carbenes, derived from alkynyliodonium salts by nucleophile addition (vide infra), had an unexpected propensity for combination with heteroatom lone pairs over the expected 1,5 C−H bond insertion.[2] This dihydrofuran synthesis effectively merges two otherwise unrelated transforms, nucleophilic addition to alkynyliodonium salts and the Stevens rearrangement, in a multistep reaction cascade that affords new C−S, C−O, and C−C bonds at the expense of a C−O ether linkage.

Alkynyl(phenyl)iodonium triflates **3** are potent yet selective electrophiles that combine with many polarizable nucleophiles to furnish singlet alkylidene carbenes **5** following loss of PhI from the intermediate ylide **4** (Scheme 1).[3] As a consequence of the unique reactivity of the iodonium salts **3**, the high energy carbene **5** (ΔH_f ≈ 100 kcal/mol for $H_2C{=}C{:}$)[4] can be accessed under mild conditions that tolerate the presence of a range of electron-rich reaction partners. Much earlier work has delineated the reactivity profile of these unsaturated carbenes, which includes [1,2]-shift to reformulate an alkyne, 1,5- (and occasionally 1,3-) C−H insertion to provide cyclopentene (or cyclopropene)-type products, and alkene cycloaddition to afford methylenecyclopropanes.[5] More recently, alkylidene carbene "insertion" into the lone pair of an appropriately positioned oxygen atom has been proposed, a process that furnishes an intermediate oxonium ylide **6**.[6] The fate of the largely unknown disubstituted-carbon-containing oxonium ylide **6** is not readily predicable, but argument by analogy with related trisubstituted-carbon-containing oxonium ylides **8** (Scheme 2, X = O, R_2 = lone pair) suggested that perhaps a 1,2-migration of R_1 from oxygen to carbon within **6** (formal Stevens rearrangement) might occur to deliver the oxacyclic product **7**.

Scheme 1



The Stevens rearrangement (**8** → **10**, Scheme 2) has been examined for X = N, O, and S, but the bulk of the definitive mechanistic work has been directed toward the ammonium ion series (**8**, X = N, R_1, R_2 = alkyl or aryl).[7] The consensus view, buttressed by a wealth of experimental evidence, cites a bond homolysis/radical recom-

(1) (a) Schildknegt, K.; Bohnstedt, A. C.; Feldman, K. S.; Sambandam, A. *J. Am. Chem. Soc.* **1995**, *117*, 7544, (b) Feldman, K. S.; Bruendl, M. M.; Schildknegt, K. *J. Org. Chem.* **1995**, *60*, 7722, (c) Feldman, K. S.; Bruendl, M. M.; Schildknegt, K.; Bohnstedt, A. C. *J. Org. Chem.* **1996**, *61*, 5440, (d) Feldman, K. S.; Mareska, D. A. *J. Am. Chem. Soc.* **1998**, *120*, 4027, (e) Feldman, K. S.; Mareska, D. A.; *Tetrahedron Lett.* **1998**, *39*, 4781, (f) Feldman, K. S.; Mareska, D. A. *J. Org. Chem.* **1999**, *64*, 5650.

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(4) (a) Ervin, K. M.; Ho, J.; Lineberger, W. C. *J. Phys. Chem.* **1989**, *91*, 5974. (b) Bodor, N.; Dewar, M. J. S.; Wasson, J. S. *J. Am. Chem. Soc.* **1972**, *94*, 9095.

(5) Kirmse, W. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1164.

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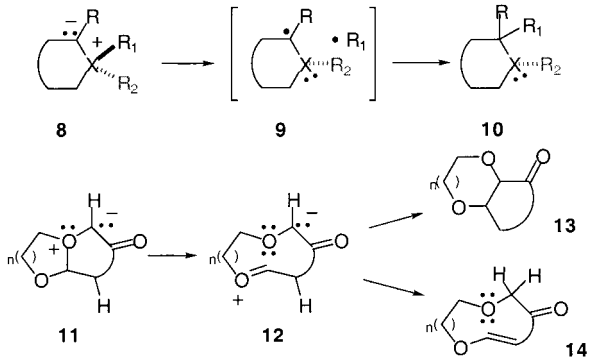
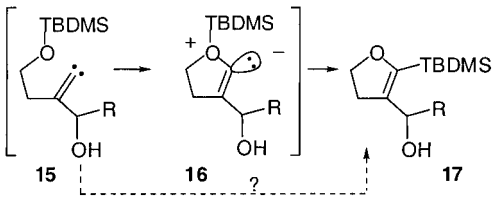
Scheme 2



bination pathway (e.g., **9**) to rationalize the formation of **10**. In the oxonium ylide series, (**8**, X = O, R_2 = lone pair), the detection of radical recombination products (e.g., R_1-R_1) and a migrating aptitude for R_1 that scales with radical stability have been taken as evidence in support of the homolysis/recombination pathway as well.[8] However, the [1,2]-shift for one special case of trisubstituted-carbon oxonium ylide, the ketal-derived species **11**, may deviate from this radical-mediated process. Speculation that an oxygen-assisted heterolysis of the scissile C−O bond in **11** could furnish the nucleophile−electrophile partners in **12** en route to the formal Stevens rearrangement product **13**, or the competitively formed β-H transfer product **14**, has been advanced.[9]

It is difficult to discern which, if any, of these mechanistic options might be applicable to the [1,2]-shift within **6**, given the differences in hybridization and geometry between the anionic carbon in **6** and those in **8** or **11**. A single relevant precedent from Kim's laboratory, which relies on an Eschenmoser-type fragmentation of an epoxy hydrazone to generate the alkylidene carbene **15** (eq 2),



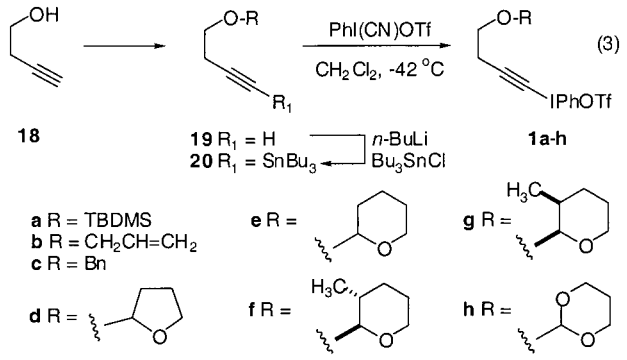
(2)[10]

describes only silicon transfer in a system that failed to furnish [1,2]-shift products with carbon migrating groups (allyl, benzyl) normally proficient in the Stevens rearrangement of trisubstituted-carbon oxonium ylides.[10] Whether the silicon shift proceeds through the ylide **16** or by direct carbene insertion into the O−Si bond remains an open question.

This discouraging precedent suggests that ylides **6** derived from alkynyliodonium salts **3** might not be suitable platforms for the homolysis/radical recombination Stevens sequence. On the other hand, the Kim example does not speak to the heterolysis mechanism proposed for the Stevens-like conversion of ylide **11** into the [1,2]-shift product **13**. Bearing these examples in mind, we undertook exploratory studies of the conversion of butynyliodonium salt ethers **1** into the cyclized Stevens rearrangement products **2**. In particular, a survey of migrating groups R (cf. **1**) in which radical stabilizing ability (as required for **9**) or cation stabilizing ability (as required for **12**) was highlighted, helped delineate the scope of the process.[6] In follow-up studies to these preliminary experiments, select deuterium-labeled substrates were prepared as mechanistic probes to augment the structure/reactivity information. Taken together, these mechanistic investigations help illuminate some of the subtleties that accompany the [1,2]-shift of R from oxygen in **1** to carbon in **2**.

Results and Discussion

The substrates **1a**−**h** examined in this study were all derived from 4-butynol (**18**), eq 3. Ethers **19a**−**e** have



(3)

been described,[11] as have the alkynylstannanes **20a** and **20c**.[12] The remaining ethers **19f**−**h** were prepared by TsOH-catalyzed exchange between **18** and *cis*/*trans* 1-hydroxy-2-methyltetrahydropyran or 2-methoxy-1,3-dioxane, respectively. The derived stannanes **20b,d**−**h** were prepared in good yield (see Experimental Section) by stannylation of the alkyne anions. The alkyne−tin bond of these species was rather labile to hydrolysis, and so purification was best accomplished by flash chromatography on silica gel deactivated by pretreatment with 5% Et_3N in hexane. The alkynyliodonium salts **1a**−**h** were prepared according to the procedure of Stang[13] and used immediately in the next step. Whereas many simple alkynylphenyliodonium salts are stable microcrystalline solids at room temperature, the particular functionalized alkynyliodonium salts used in this investigation typically decomposed when exposed to temperatures much above 0 °C. Therefore, their preparation and manipulation were conducted at low temperatures (−30 to − 42 °C), with final solvent removal performed at <0 °C in vacuo. In

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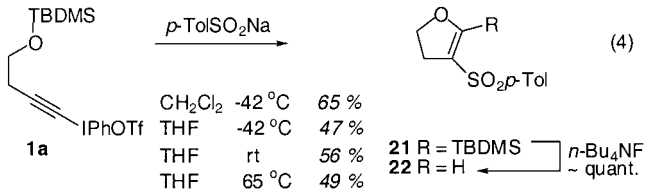
(11) (a) Morimoto, Y.; Yokoe, C.; Kurihara, H.; Kinoshita, T. *Tetrahedron* **1998**, *54*, 12197. (b) Daniel, D.; Middleton, R.; Henry, H. L.; Okamura, W. H. *J. Org. Chem.* **1996**, *61*, 5617. (c) Burns, C. J.; Gill, M.; Saubern, S. *Aust. J. Chem.* **1997**, *50*, 1067. (d) Griffiths, J.; Murphy, J. A. *Tetrahedron* **1992**, *48*, 5543. (e) Berque, I.; Le Menez, P.; Razon, P.; Mahuteau, J.; Férézou, J.-P.; Pancrazi, A.; Ardisson, J.; Brion, J.-D. *J. Org. Chem.* **1999**, *64*, 373.

(12) (a) Kashman, Y.; Groweiss, A.; Lidor, R.; Blasberger, D.; Carmely, S. *Tetrahedron* **1985**, *41*, 1905. (b) Leteux, C.; Veyrières, A. *J. Chem. Soc., Perkin Trans I* **1994**, 2647.

(13) Stang, P. J.; Williamson, B. L.; Zhdankin, V. V. *J. Am. Chem. Soc.*, **1991**, *113*, 5870.

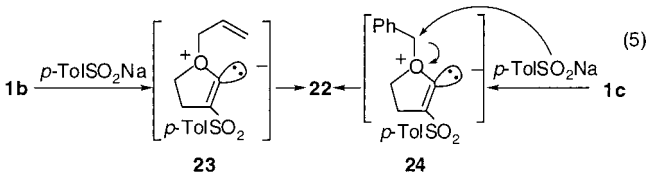
this manner, the white solid or pale yellow oily iodonium salts exhibited no signs of decomposition (darkening, liquefaction). The diastereomeric alkynes **19f** and **19g** were cleanly separated by silica gel chromatography, and the pure isomers were carried forward independently in the next step. Since the alkynyliodonium salts were not isolated, the reported product yields in the cyclization/rearrangement sequence are based on the alkynylstannanes **20a**−**h**.

The silyl ether substrate **1a** was examined first in light of the precedent shown in eq 2. *p*-Toluenesulfinate was chosen as the test case nucleophile as a consequence of its documented success in generating alkylidene carbenes from alkynyliodonium salts[14] and the expectation that the enol ether product would be more stable to hydrolysis if also substituted with a sulfone moiety rather than a N or O group derived, inter alia, from amide or phenoxide nucleophiles. Toward this end, the white solid alkynyliodonium salt **1a** at −42 °C was dissolved in prechilled (−42 °C) CH_2Cl_2 and treated with 1 equiv of sodium *p*-toluenesulfinate. After warming to room temperature, aqueous workup, and chromatographic purification, a single new compound featuring TBDMS and *p*-TolSO_2 groups in a 1:1 ratio (^{1}H NMR) was isolated. Further spectroscopic analysis confirmed that the product was indeed the cyclized/rearranged dihyrofuran species **21** as desired (eq 4). Treatment of this silylalkene with *n*-Bu_4-



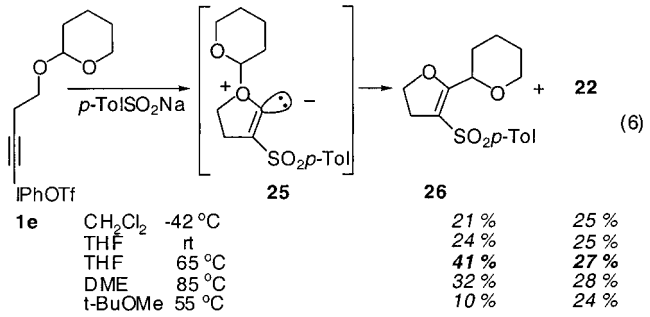
NF in THF cleanly effects desilylation to furnish the dihydrofuran product **22** displaying a characteristic vinyl proton[15] (δ 7.19, t, J = 1.8 Hz) in the ^{1}H NMR spectrum. The good yield and lack of detectable byproducts upon conversion of **1a** into **21** suggested that further optimization might be possible. However, substitution of THF as solvent and exploring a range of temperatures (cf. eq 4) did not improve on the initial run.

Both allyl and benzyl units have high migratory aptitudes in the Stevens rearrangement, although their mechanisms ([2,3]-sigmatropic shift vs homolysis/radical recombination, respectively) may be dissimilar.[8,16] Thus, the substrates **1b** and **1c** were examined as probes for these classical Stevens rearrangement processes. In both cases, treatment of the alkynyliodonium salts in either CH_2Cl_2 or THF with *p*-toluenesulfinate over a range of temperatures (−15 °C (CH_2Cl_2) to 65 °C (THF)) did not afford any detectable 2-substituted dihydrofuran products. Both TLC and ^{1}H NMR analysis of the crude reaction mixture indicated that a multitude of new compounds was formed. The major product isolated in the allyl case was the protonated dihydrofuran **22** (36%), a result suggesting that the desired ylide **23** was formed but did not participate in either [2,3]- or [1,2]-allyl shifts, eq 5. The benzyl ether substrate also afforded the



dihydrofuran **22** (≤10%), along with several alkyne-containing products in small amounts, and significantly, ∼ 5% of *p*-TolSO_2CH_2Ph. Again, it appears the ylide **24** was formed, at least to a small extent, but it decomposed by alternative pathways unrelated to the desired [1,2]-shift (e.g., *p*-TolSO_2 attack on R(R′)$O^{(+)}$−CH_2Ph with expulsion of the good oxonium leaving group to ultimately provide **22**). These results are consistent with the observations of Kim (vide supra), and suggest that C−O bond homolysis within ylides of the type **23**/**24** does not compete with dealkylation and anion protonation. Thus, the goal of observing classic Stevens-type radical chemistry with the disubstituted-carbon ylide series is not likely to be met.

The search for a Stevens-type rearrangement with particularly stable carbocationic migrating groups began with the 1-THP derivative **1e**. The initial experiment run under the best-case conditions with **1a** (CH_2Cl_2, −42 °C → rt) furnished two dihydrofuran-containing products **26** and **22** in similar amounts, eq 6. The formation of the



formal [1,2]-shift product **26** was gratifying, but any mechanistic speculation vis à vis homolysis vs heterolysis of the C−O bond in putative ylide intermediate **25** would be premature at this point. Optimization studies proceeded with **1e** and a survey of solvents and temperatures revealed that, for this substrate, THF at reflux afforded the highest yield of desired product **26**. Variation among other experimental parameters (concentration (0.15 → 0.30 M in **1e**), order of addition, rate of addition) had little effect on yield. Thus, an optimized procedure wherein a −42 °C solution of the alkynyliodonium salt in THF was added rapidly via cannula into a refluxing suspension of 1.3−1.5 equiv of sodium *p*-toluenesulfinate in THF was standardized for subsequent substrates. The structural assignment of **26** was suggested by the spectral data upon comparison to the data for **21** and **22** and secured by HMBC NMR analysis that clearly indicated the carbon connectivity. The 2-bond and 3-bond coupling between the unique methine hydrogen and the alkene carbons,

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(15) The phenylsulfonyl analogue of **22** is known. The key vinyl resonance in the ^{1}H NMR spectrum of this compound occurs at δ 7.25 (t, J = 1.8 Hz). Carretero, J. C.; de Diego, J. E.; Hamdouchi, C. *Tetrahedron* **1999**, *55*, 15159.

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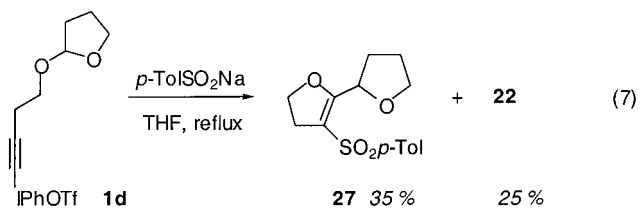
which unambiguously defined the attachment point of the THP and dihydrofuran rings, was particularly diagnostic.

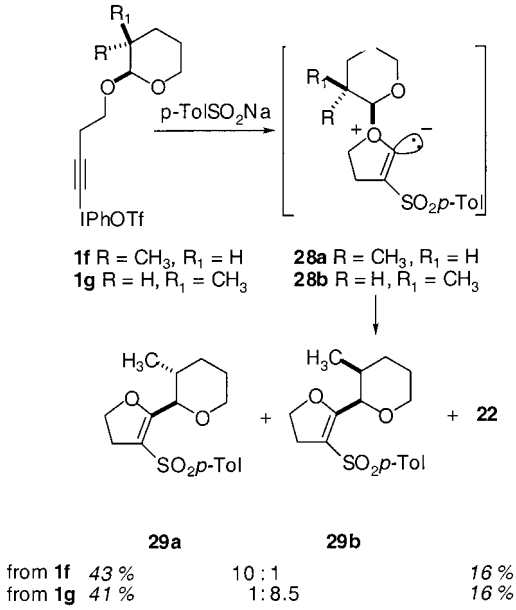
The tetrahydrofuran analogue **1d** performed similarly under the optimized conditions to furnish a modest yield of the cyclization/rearrangement product **27** along with substantial quantities of the proton trapping product **22**, eq 7. The structural identity of **27** rests on a comparison of spectral data with those of **26**.



(7)

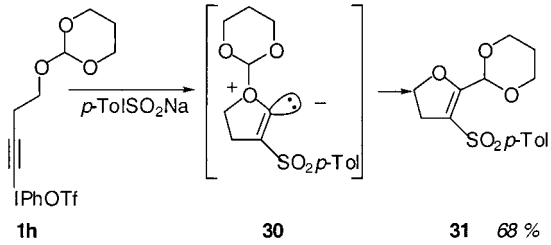
The issue of 1,2-diastereoselectivity was probed with the *trans*- and *cis*-2-methyl-substituted tetrahydropyran ethers **1f** and **1g**, respectively, Scheme 3. At the outset,

Scheme 3



the mechanistic uncertainties surrounding the [1,2] THP shift in **1e** made it difficult to develop an a priori model for diastereoselection with **1f**/**g**, and so these trials were viewed as simple scouting expeditions. Exposure of the isomerically pure trans isomer **1f** to *p*-toluenesulfinate in refluxing THF provided the expected mixture of dihydrofuran-containing products **29a**/**b** and **22** in yields similar to the nor-methyl system **1e**. Interestingly, the formal [1,2]-shift product **29** was produced as a diastereomeric mixture that strongly favored one isomer. The gross structures of **29a**/**b** could be deduced by comparison of spectral data with those of the nor-methyl analogue **26**, and stereochemical assignments were made on the chromatographically purified products **29a** and **29b** on the basis of the observed $J_{1,2}$ values (**29a**, $J_{1,2}$ = 10.0 Hz ⇒ trans; **29b**, $J_{1,2}$ = 3.6 Hz ⇒ cis). An identical experiment with the cis methyl substrate **1g** led to similar results. In this instance, the mixture of [1,2]-shift products favored the cis-configured product **29b**. Thus, the [1,2]-shift of THP within ylide **28a**/**b** appears to proceed largely but not exclusively with retention of stereochemistry. It is noteworthy that the yield of the proton trapping byproduct **22** remained constant with these substrates, but it is less than that observed with the nor-methyl species **1e**.

The final substrate examined, ortho ester **1h**, was selected to explore further the influence of cation stabilization on [1,2]-shift efficiency, eq 8. On the basis of the



(8)

results to this point, the more stable carbocation flanked by two oxygen atoms in intermediate ylide **30** might be expected to facilitate the [1,2]-shift and lead to enhanced yields of the 2-substituted dihydrofuran product **31**. The observed result is in accord with this hypothesis. Treatment of alkynyliodonium salt **1h** with *p*-toluenesulfinate under standard conditions afforded a superior yield of the desired [1,2]-shift product **31**. In addition, not even trace amounts of the proton trapping product **22** could be detected. This latter observation may point to a role for the C(3) hydrogen in the THF or THP rings of **1d**−**g** in forming **22**. On the other hand, it may only reflect an enhanced rate of [1,2]-shift with the dioxygen-substituted ring compared to the process that forms **22**. This issue was addressed by using the C(3) deuterium-labeled THP substrate **33** discussed below.

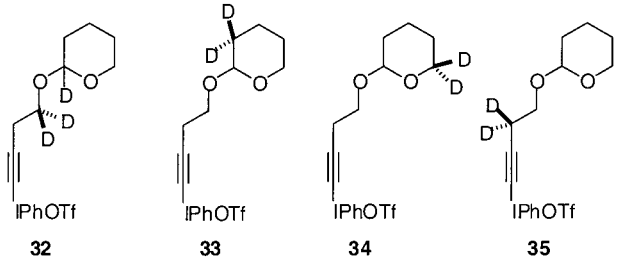
The results obtained with the range of substrates **1a**−**h**, in the aggregate, beg several mechanistic questions:

(1) Do successful [1,2]-shifts occur through C−O homolysis/radical recombination, through C−O heterolysis/dipolar recombination, or via a concerted process?

(2) Is substituent O-to-C migration an inter- or an intramolecular process?

(3) What is the source of the vinylic proton in byproduct **22**?

Insight into these issues might be gleaned from the results of a series of reactions featuring the selectively deuterated substrates **32**−**35**. The THP substituent was chosen as representative of all of the α-oxygenated ether substrates **1d**-**h**, and ultimately caution should be exercised in extrapolating conclusions from the THP series to the THF or 1,3-dioxane species.

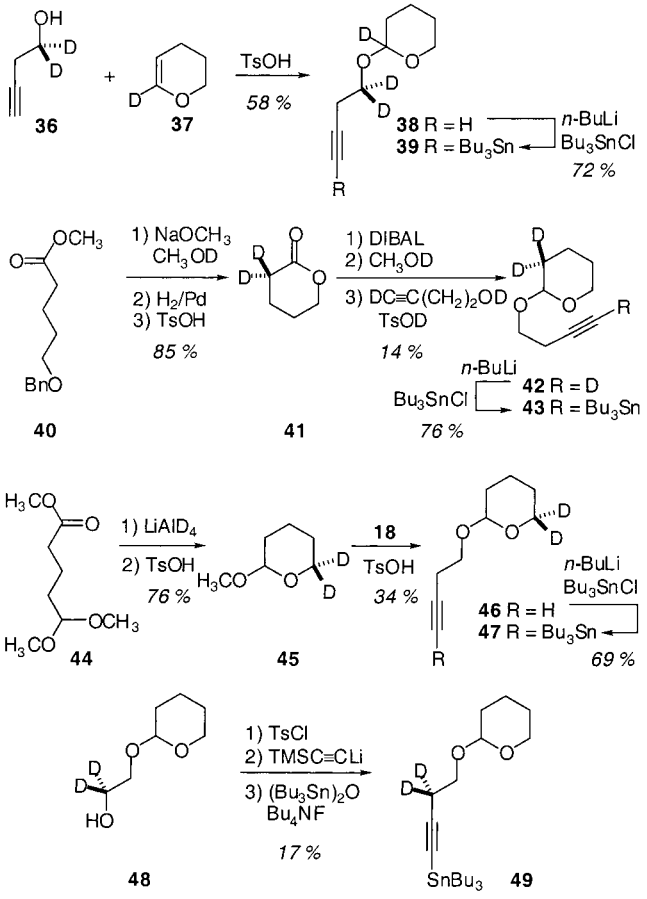


The trideuterated species **32** was designed to address the question of inter- vs intramolecular [1,2]-shift via a crossover experiment. The remaining three dideuterated alkynyliodonium salts **33**−**35** were chosen as probes for the source of the vinyl proton in **22**. The C(3) dideuteriopyran entry **33** seemed like the most plausible candidate

for providing the 2-deutero version of **22** on the basis of the results obtained with **1h** and earlier precedent (**12** → **14**) from Oku's laboratory. However, unexpected difficulties in the synthesis of **33** opened a window of opportunity to explore other more readily prepared alternatives, hence the dideuterated substrates **34** and **35**. The C(6) dideuteriopyran species **34** was prepared to test for the possibility that proton transfer within an intermediate oxonium ylide might be driven by formation of a carbonyl ylide product, a process recently reported by Padwa.[17] Finally, the propargylic dideuterated iodonium salt **35** was synthesized to examine the prospects for intermolecular propargylic deprotonation by ylide **25**, a process that might be facilitated by the strongly electron withdrawing nature of the phenyliodonium group.

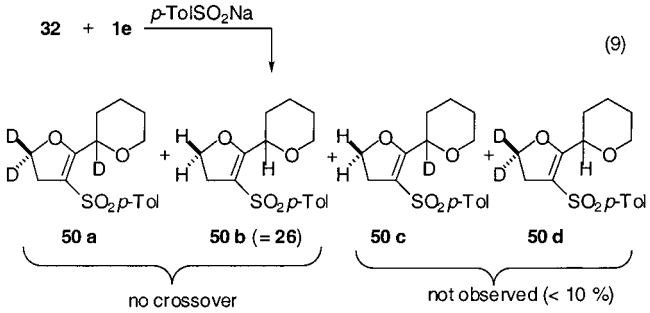
The alkynylstannane precursors to the iodonium salts **32**−**35** were prepared by straightforward syntheses from either known deuterated starting materials (**36**,[18a] **37**,[18b] **48**[18c]) or by highly reliable deuterium incorporation methodology (**40** → **41**, **44** → **45**), Scheme 4. The level of

Scheme 4



residual protium in the stannanes **39**, **47**, and **49** was essentially unmeasurable by ^{1}H NMR and MS techniques. The synthesis and preservation of deuterium content of the C(3)-d_2 species **43** proved to be significantly more challenging. After several false starts, the route shown provided the C(2)-d_2 valarolactone **41** in good yield and with ≥95% deuterium incorporation. However, the lactol derived from **41** by DIBAL reduction tended to lose deuterium upon workup, presumably by enolization of the aldehyde tautomer. This H-for-D exchange was minimized by workup with CH_3OD and, subsequently, by combination of the lactol with butynol-d_2 catalyzed by TsOD. By these procedures, a sample of stannane **43** containing ≥90% deuterium at C(3) of the pyran ring, as judged by MS and ^{13}C NMR measurements, was obtained.

The use of trideuterioalkynyliodonium salt **32** in a crossover experiment to probe for inter- vs intramolecularity in the THP shift is shown in eq 9. Treating a 1.0:



1.0 mixture of **39** and **20e** with PhI(CN)OTf and then sodium *p*-toluenesulfinate as per the standard procedure furnished the 2-THP-containing dihydrofuran product **50** in 40% yield along with undeuterated byproduct **22**. Mass spectral analysis of the purified [1,2]-shift product revealed strong MH^+ signals at *m/e* = 312 and 309 amu corresponding to the trideuterio- and triprotio- versions of **50** (**50a** and **50b**, respectively). Small signals (ca. 10% of the intensity of the *m/e* 309 and 212 signals) at *m/e* 310 and 311 amu, which might correspond to crossover products **50c** and **50d**, can be discounted by comparison to the mass spectrum of **26** (= **50b**) prepared from **1e**. In that spectrum, similar peaks (∼10% of MH^+) appeared as well. So, with at least 90% fidelity, the transfer of THP from oxygen to carbon within ylide **25** proceeds in an intramolecular fashion.

The origin of the vinylic hydrogen in byproduct **22** was first investigated through a series of control experiments designed to eliminate adventitious sources of H. Toward this end, the conversion of alkynylstannane **20e** into the dihydrofuran products **26** and **22** was examined, in independent experiments, with CD_2Cl_2 as solvent for iodonium salt formation, with THF-d_8 for the cyclization sequence, with $C_6D_5SO_2Na$ or with $TolSO_2Na$ recrystallized from D_2O as nucleophiles, and with a D_2O quench upon termination of the reaction. In no instance was any deuterium incorporation detected in the byproduct **22**. Turning to the specifically deuterated substrates, both the C(6)-d_2 species **34** and the propargylic-d_2 analogue **35** were treated, in independent trials, with sodium *p*-toluenesulfinate under standard conditions. Once again, only protium-containing byproduct **22** was formed. The final deuterium-containing substrate synthesized, the C(3)-labeled system **33**, was subjected to sulfinate addition and furnished 42% of the expected C(3)-dideuterated dihydrofuran **26**-d_2. The product of interest, dihydrofuran **22** (25%), was examined by FABMS(+) and ^{1}H NMR spectroscopy to reveal that, indeed, the vinylic position had been partially deuterated. The ^{1}H NMR data indi-

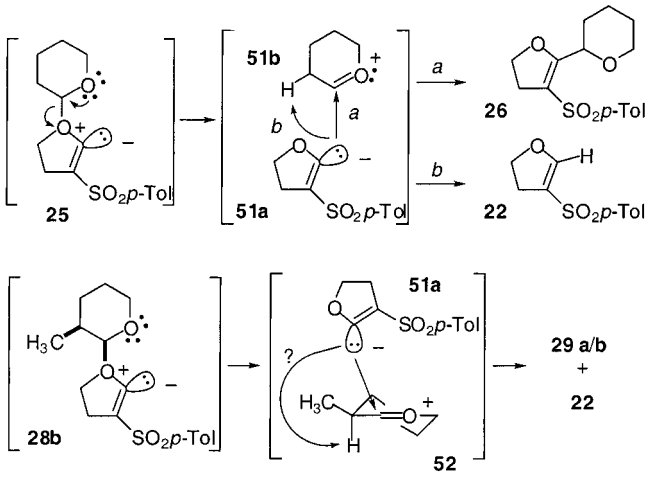
(17) Padwa, A.; Heidelbaugh, T. M.; Kuethe, J. T. *J. Org. Chem.* **1999**, *64*, 2038.

(18) (a) Dua, S.; Bowie, J. H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2097. (b) Oakes, F. T.; Sebastian, J. F. *J. Org. Chem.* **1980**, *45*, 4959. (c) Steiner, R.; Schumann, D.; Hoffmann, H. *Org. Mass Spectrom.* **1983**, *18*, 345.

cated approximately 56% deuterium incorporation, whereas the MS data was more consistent with ~40% deuterium at C(1) of **22**. These results suggest that to a significant extent the vinylic proton in **22** is derived from C(3) of the THP ring. The other source(s) for this proton remains a mystery.

The mechanistic issues raised earlier can now be answered with varying degrees of certainty on the basis of these and prior results. The structure/reactivity profile of the migrating groups R in **1** provides evidence consistent with heterolytic and not homolytic scission of the C−O bond within ylide **6**. An alternative, concerted O-to-C shift with retention of stereochemistry has been considered by Johnson and Roskamp in their seminal studies on trisubstituted-carbon oxonium ylides.[16a] In the case of the disubstituted-carbon oxonium ylide **6**, such a concerted shift would arguably engender a severe energetic penalty as a consequence of unfavorable orbital interactions (a 4-electron/2-orbital interaction for an in-plane shift, poor orbital overlap/strained geometry for an out-of-plane shift). Thus, the weight of evidence supports the heteropolar dissociation/recombination sequence **25** → **51** → **26**/**22** illustrated in Scheme 5 for the prototypical THP case.

Scheme 5



The lack of crossover products with **32** and **1e** and the high levels of diastereoselectivity seen with **1f** and **1g** are consistent with a solvent cage recombination mechanism in which the fragments **51a**/**51b** do not have time to change their relative orientations significantly prior to collapse. Finally, the anion/cation pair **51a**/**51b** apparently partitions between two energetically similar pathways, nucleophile/electrophile capture (path *a*) and proton transfer (path *b*), to furnish the observed products **26** and **22**, respectively. In support of this hypothesis, examination of the crude reaction mixture formed by combining **1e** with *p*-toluenesulfinate in THF-d_8 revealed detectable quantities of dihydropyran. This first-generation mechanistic picture rationalizes the gross features of the conversion of **1e** into **26**/**22**, but one subtle point remains clouded: dissociation of the cis configured ylide **28b** should provide an electrophile/nucleophile pair **52**/**51a**, which is perfectly disposed for recombination but is not at all aligned for C(3) proton abstraction. In this scenario, less byproduct **22** than with the trans isomer **1d** might have been expected. However, the results indicate otherwise. Thus, the details of the molecular reorientations within the solvent cage, which presumably lie at the heart of this anomaly, have yet to be sorted out.

In summary, a new application of alkynyliodonium salts to the synthesis of 2-substituted-3-*p*-toluenesulfonyldihydrofurans has been developed. This transformation features the formation of an intermediate disubstituted-carbon oxonium ylide that suffers [1,2]-shift (formal Stevens rearrangement) en route to dihydrofuran product. Successful reactions appear to require a relatively stable cationic migrating group. Preliminary indications are that moderate levels of 1,2- diastereoselectivity are attainable. Deuterium labeling studies have helped expose some of the mechanistic details of the multistep sequence. The extension of this reaction to more complex substrates is planned.

Experimental Section

General. All moisture- and air-sensitive reactions were performed in flame-dried glassware under a positive pressure of argon with magnetic stirring. Tetrahydrofuan (THF) and diethyl ether (Et_2O) were dried by distillation from sodium/benzophenone under argon. Methylene chloride (CH_2Cl_2), benzene, and triethylamine were distilled from calcium hydride under argon. Anhydrous sodium *p*-toluenesulfinate was purchased from Fluka, ground into a fine powder, and dried under vacuum at ca. 0.2 mmHg at 120 °C for 24 h. Liquid flash chromatography[19] was carried out using 32−63 μm silica gel and the indicated solvent. Deactivated silica gel was prepared by treatment of the silica with 5% triethylamine in hexanes solution prior to use. Hexanes, Et_2O, and EtOAc used in flash chromatography were distilled from calcium hydride prior to use. All melting points are uncorrected. NMR chemical shifts are reported in δ units using tetramethylsilane as an internal standard. Copies of ^{13}C NMR spectra are provided in the Supporting Information to establish purity for those compounds that were not subjected to combustion analysis.

General Procedure A. Stannylation of Terminal Alkynes. A 2.5 M solution of *n*-BuLi in hexane (1 equiv) was added to the alkynyl ether in THF at −78 °C over 5 min. The reaction mixture was allowed to stir at −78 °C for 45 min before the addition of tributyltin chloride (1 equiv). The solution was warmed to ambient temperature and stirred for 2 h. The mixture was treated with saturated NH_4Cl solution and diluted with an equal volume of Et_2O. The organic layer was washed with two portions of H_2O and then brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to afford the crude alkynylstannane. Purification of the crude product by flash chromatography on deactivated silica gel eluting with the indicated solvent afforded the alkynylstannane as a colorless oil

General Procedure B. Iodonium Salt Formation and *p*-Toluenesulfinate Addition. Cyano(phenyl)iodonium triflate[13] (1 equiv) was added to a −42 °C deoxygenated solution of the alkynylstannane in CH_2Cl_2. After 2 h, the solvent was removed in vacuo at <0 °C, and the crude iodonium salt was warmed to ~0 °C and washed with two portions of prechilled (−42 °C) hexanes. The solvent reside was removed in vacuo with $T < 0$ °C to furnish the iodonium salt as a white solid or light yellow oil. This species was used immediately assuming quantitative yield.

The alkynyl(phenyl)iodonium triflate in THF at −42 °C was cannulated rapidly into a refluxing suspension of anhydrous sodium *p*-toluenesulfinate (1.3−1.5 equiv) in THF. The yellow suspension was allowed to reflux for 30 min and then stirred at room temperature for 10 min. The reaction mixture was treated with saturated sodium bicarbonate solution and diluted with an equal volume of Et_2O. The organic layer was washed sequentially with H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to afford the crude

(19) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

dihydrofuran product(s). Purification of this crude material was accomplished by flash chromatography on deactivated silica gel eluting with the indicated solvent.

(4-Allyloxy-but-1-ynyl)tributylstannane (20b). Using General Procedure A, 4-allyloxybut-1-yne (**19b**)[11b] (0.29 g, 2.6 mmol) was converted to 0.65 g of alkynylstannane **20b** (63%) following purification of the crude product with 1% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 5.97−5.84 (m, 1 H), 5.29 (dd, J = 17.0, 1.5 Hz, 1 H), 5.18 (dd, J = 10.6, 1.5 Hz, 1 H), 4.01 (dt, J = 5.7, 1.5 Hz, 2 H), 3.57 (t, J = 7.4 Hz, 2 H), 2.54 (t, J = 7.4 Hz, 2 H), 1.60−1.50 (m, 6 H), 1.39−1.27 (m, 6 H), 0.99−0.88 (m, 15 H); ^{13}C NMR (75 MHz, $CDCl_3$) 134.7, 117.0, 107.7, 83.2, 71.9, 69.0, 28.9 ($J_{C-Sn119}$ = 11.6 Hz), 27.0 ($J_{C-Sn119}$ = 29.8 Hz), 21.6, 13.7, 11.0 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.1 Hz); MS *m/e* (+CI) 343 (Sn^{120}) (M − Bu^+, 100); HRMS (+CI) calcd for $C_{19}H_{35}OSn^{120}$ (M − H^+) 399.1710, found 399.1701.

Tributyl[4-(tetrahydrofuran-2-yloxy)-but-1-ynyl]stannane (20d). Using General Procedure A, 2-but-3-ynyloxytetrahydrofuran (**19d**)[11d] (1.1 g, 7.8 mmol) was converted to 2.0 g of alkynylstannane **20d** (60%) following purification of the crude product with 5% Et_2O/hexanes: IR (film) 2145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 5.16 (t, J = 3.0 Hz, 1 H), 3.91−3.83 (m, 2 H), 3.75 (dt, J = 9.5, 7.5 Hz, 1 H), 3.53 (dt, J = 9.5, 7.5 Hz, 1 H), 2.51 (t, J = 7.5 Hz, 2 H), 2.02−1.78 (m, 4 H), 1.67−1.44 (m, 6 H), 1.38−1.29 (m, 6 H), 0.98−0.88 (m, 15 H); ^{13}C NMR (100 MHz, $CDCl_3$) 108.0, 104.0, 83.0, 67.0, 66.1, 32.5, 29.0 ($J_{C-Sn119}$ = 11.7 Hz), 27.1 ($J_{C-Sn119}$ = 30.1 Hz), 23.5, 21.8, 13.8, 11.1 ($J_{C-Sn119}$ = 191.5 Hz, $J_{C-Sn117}$ = 182.7 Hz); MS *m/e* (+FAB/3NBA) 373 (Sn^{120}) (M − Bu^+, 22); HRMS (+FAB) calcd for $C_{20}H_{38}O_2NaSn^{120}$ 453.1791, found 453.1780.

Tributyl[4-(tetrahydropyran-2-yloxy)but-1-ynyl]stannane (20e). Using General Procedure A, 2-but-3-ynyloxytetrahydropyran (**19e**)[11e] (0.65 g, 4.2 mmol) was converted to 1.7 g of alkynylstannane **20e** (90%) following purification of the crude product with 5% Et_2O/hexanes: IR (film) 2149 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) 4.66 (t, J = 3.2 Hz, 1 H), 3.93−3.79 (m, 2 H), 3.59−3.48 (m, 2 H), 2.56 (t, J = 7.3 Hz, 2 H), 1.88−1.49 (m, 12 H), 1.38−1.28 (m, 6 H), 0.98−0.86 (m, 15 H); ^{13}C NMR (90 MHz, $CDCl_3$) 108.3, 99.1, 83.4, 66.6, 62.5, 31.0, 29.3 ($J_{C-Sn119}$ = 11.7 Hz), 27.4 ($J_{C-Sn119}$ = 29.6 Hz), 25.9, 22.1, 19.8, 14.1, 11.4 ($J_{C-Sn119}$ = 191.2 Hz, $J_{C-Sn117}$ = 183.1 Hz; MS *m/e* (+CI) 387 (Sn^{120}) (M − Bu^+, 22); HRMS (+MALDI) calcd for $C_{21}H_{40}O_2NaSn^{120}$ 467.1948, found 467.1953.

2-But-3-ynyloxy-3-methyltetrahydropyrans (19f and 19g). A 1.0 M solution of DIBAL-H in hexane (42 mL, 42 mmol) was added to a −42 °C solution of 3-methyl-valerolactone[20] (4.3 g, 38 mmol) in 18 mL of THF over 1.5 h. The reaction mixture was warmed to −20 °C after the addition was complete. After 1 h, the reaction mixture was carefully treated with 35 mL of methanol. The white slurry was filtered, and the salts were washed with three 100 mL portions of methanol. The solvent was removed under water aspirator pressure at room temperature, and the residue was distilled to afford 2.5 g (59%) of impure *cis*- and *trans*-3-methylpyran-2-ol.

p-Toluenesulfonic acid monohydrate (21 mg, 0.11 mmol) followed by but-3-ynol (0.80 mL, 0.11 mmol) was added to the mixture of *cis*- and *trans*-3-methylpyran-2-ol (2.7 g, 23 mmol) in 9 mL of benzene. The solution was refluxed for 3 h with Dean−Stark collection of water. Saturated sodium bicarbonate solution (10 mL) was added followed by 50 mL of Et_2O. The phases were separated, and the organic layer was washed sequentially with 20 mL of saturated bicarbonate solution and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to provide a yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with 5% Et_2O/hexanes afforded 1.5 g (89%) of a colorless oil as a mixture of cis and trans ethers **19f**/**19g**. The isomers were separated by flash chromatography on silica gel eluting with 95% benzene/hexanes.

(20) Prepared according to a procedure reported by Takacs, J. M.; Newsome, P. W.; Kuehn, C.; Takusagawa, F. *Tetrahedron* **1990**, *46*, 5507. For characterization data see: Bachi, M. D., Bosch, E. *J. Org. Chem.* **1992**, *57*, 4696.

Data for 19g: IR (film) 3310, 2122 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.57 (d, J = 3.0 Hz, 1 H), 3.84−3.71 (m, 2 H), 3.53 (dt, J = 9.8, 7.2 Hz, 2 H), 2.48 (dt, J = 6.8, 2.6 Hz, 2 H), 1.96 (t, J = 2.6 Hz, 1 H), 1.81−1.46 (m, 5 H), 0.89 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 100.7, 81.8, 69.2, 65.6, 59.8, 35.0, 26.2, 25.7, 20.0, 16.8; MS *m/e* (+CI) 169 (MH^+, 60). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.19; H, 9.77.

Data for 19f: IR (film) 3297, 2122 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.09 (d, J = 6.8 Hz, 1 H), 3.99−3.87 (m, 2 H), 3.60 (dt, J = 9.8, 7.2 Hz, 1 H), 3.49−3.41 (m, 1 H), 2.50 (dt, J = 7.2, 2.6 Hz, 2 H), 1.97 (t, J = 2.6 Hz, 1 H), 1.90−1.81 (m, 1 H), 1.64−1.47 (m, 3 H), 1.27−1.15 (m, 1 H), 0.96 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 105.9, 81.4, 69.2, 66.5, 64.9, 34.9, 29.5, 24.3, 20.0, 16.7; MS *m/e* (+CI) 169 (MH^+, 24). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.43; H, 9.88.

Tributyl[4-(*trans*-3-methyltetrahydropyran-2-yloxy)-but-1-ynyl]stannane (20f). Using General Procedure A, 2-but-3-ynyloxy-*trans*-3-methyltetrahydropyran (**19f**) (88 mg, 0.52 mmol) was converted to 0.20 g of alkynylstannane **20f** (86%) following purification of the crude product with 4% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.10 (d, J = 6.4 Hz, 1 H), 3.99−3.84 (m, 2 H), 3.59 (dt, J = 9.8, 7.5 Hz, 1 H), 3.49−3.41 (m, 1 H), 2.55 (t, J = 7.2 Hz, 2 H), 1.90−1.81 (m, 1 H), 1.60−1.49 (m, 8 H), 1.39−1.27 (m, 8 H), 0.98−0.88 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) 107.9, 105.8, 83.0, 67.2, 64.9, 34.9, 29.5, 28.9 ($J_{C-Sn119}$ = 11.6 Hz), 27.0 ($J_{C-Sn119}$ = 30.5 Hz), 24.4, 21.7, 16.7, 13.7, 10.9 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.8 Hz; MS *m/e* (+APCI) 459 (Sn^{120}) (MH^+, 5); HRMS (+ESI) calcd for $C_{22}H_{43}O_2Sn^{120}$ (MH^+) 459.2285, found 459.2263.

Tributyl[4-(*cis*-3-methyltetrahydropyran-2-yloxy)but-1-ynyl]stannane (20 g). Using General Procedure A, 2-but-3-ynyloxy-*cis*-3-methyltetrahydropyran (**19g**) (0.15 g, 0.89 mmol) was converted to 0.35 g of alkynylstannane **20g** (87%) following purification of the crude product with 4% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.57 (d, J = 3.0 Hz, 1 H), 3.82−3.72 (m, 2 H), 3.54−3.46 (m, 2 H), 2.54 (dt, J = 6.9, 1.9 Hz, 2 H), 1.80−1.43 (m, 11 H), 1.39−1.27 (m, 6 H), 1.07−0.87 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) 108.4, 100.6, 83.0, 66.3, 59.7, 35.1, 29.1 ($J_{C-Sn119}$ = 11.6 Hz), 27.2 ($J_{C-Sn119}$ = 29.8 Hz), 26.3, 25.8, 21.7, 17.0, 13.9, 11.1 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.1 Hz; MS *m/e* (+ESI) 481 (Sn^{119}) (MNa^+, 100); HRMS (+ESI) calcd for $C_{22}H_{42}O_2NaSn^{120}$ 481.2104, found 481.2075.

2-But-3-ynyloxy-[1,3]-dioxane (19h). But-3-ynol (0.80 mL, 0.11 mmol) followed by *p*-toluenesulfonic acid monohydrate (10 mg, 0.055 mmol) was added to 2-methoxy-1,3-dioxane (2.6 g, 22 mmol). The neat mixture was heated to 110−120 °C, and the methanol formed was removed with a short path distillation apparatus. After 15 h, the reaction mixture was cooled to room temperature. Purification of the crude product by flash chromatography on silica gel eluting with 10% Et_2O/hexanes afforded 0.36 g (21%) of **19h** as a colorless oil: IR (film) 3285, 2120 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) 5.30 (s, 1 H), 3.90−3.85 (m, 2 H), 3.56 (t, J = 7.0 Hz, 2 H), 3.35−3.29 (m, 2 H), 2.28 (dt, J = 7.0, 2.5 Hz, 2 H), 1.72 (t, J = 2.5 Hz, 1 H), 1.37−1.27 (m, 1 H), 1.06−0.98 (m, 1 H); ^{13}C NMR (100 MHz, C_6D_6) 109.4, 81.4, 69.8, 63.0, 61.0, 25.1, 20.2; MS *m/e* (+CI) 157 (MH^+, 100). Anal. Calcd for $C_8H_{12}O_3$: C, 61.25; H, 7.74. Found: C, 61.46; H, 7.88.

Tributyl[4-([1,3]-dioxan-2-yloxy)but-1-ynyl]stannane (20h). Using General Procedure A, the ortho ester **19h** (0.12 g, 0.77 mmol) was converted to 0.26 g of alkynylstannane **20h** (75%) following purification of the crude product with 3% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 5.36 (s, 1 H), 3.97−3.89 (m, 2 H), 3.71 (t, J = 7.2 Hz, 2 H), 3.38−3.29 (m, 2 H), 2.56 (t, J = 7.2 Hz, 2 H), 1.76−1.56 (m, 6 H), 1.43−1.31 (m, 7 H), 1.09−0.90 (m, 16 H); ^{13}C NMR (75 MHz, C_6D_6) 109.4, 108.4, 83.1, 63.9, 60.8, 29.4 ($J_{C-Sn119}$ = 11.6 Hz), 27.4 ($J_{C-Sn119}$ = 29.8 Hz), 25.2, 22.2, 13.9, 11.2 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.8 Hz; MS *m/e* (+CI) 447 (Sn^{120}) (MH^+, 14); HRMS (+CI) calcd for $C_{20}H_{39}O_3Sn^{120}$ (M + H^+) 447.1921, found 447.1929.

***tert*-Butyldimethyl[3-(toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]silane (21).** By using a modified version of General

Procedure B (CH_2Cl_2 as solvent, −42 °C → room temperature), alkynylstannane **20a** (0.11 g, 0.23 mmol) was converted into 52 mg (65%) of **21** as a white solid, mp 86−87 °C: IR (KBr) 1558, 1312 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 7.76 (d, J = 8.2 Hz, 2 H), 7.32 (d, J = 7.9 Hz, 2 H), 4.40 (t, J = 10.0 Hz, 2 H), 2.78 (t, J = 10.0 Hz, 2 H), 2.43 (s, 3 H), 0.99 (s, 9 H), 0.36 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 173.7, 143.5, 138.5, 129.6, 127.3, 125.5, 72.1, 31.3, 26.8, 21.5, 17.5, −5.0; MS *m/e* (+CI) 339 (MH^+, 7). Anal. Calcd for $C_{17}H_{26}O_3SSi$: C, 60.31; H, 7.74. Found: C, 60.14; H, 7.69.

4-(Toluene-4-sulfonyl)-2,3-dihydrofuran (22). A 1 M solution of *n*-Bu_4NF in THF (62 μL, 0.062 mmol) was added to the silylalkene **21** (21 mg, 0.062 mmol) in 5 mL of THF. After stirring for 30 min at room temperature, 1 M NH_4Cl solution was added, and the aqueous phase was extracted with Et_2O. The combined organic layers were washed with H_2O and then brine, dried over Na_2SO_4, filtered, and concentrated to obtain 19 mg of a white solid, mp 106−107 °C: IR (film) 1607 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 7.77 (d, J = 8.2 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.19 (t, J = 1.8 Hz, 1 H), 4.59 (t, J = 9.6 Hz, 2 H), 2.78 (dt, J = 9.6, 1.7 Hz, 2 H), 2.43 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$)156.3, 144.0, 137.8,129.7, 127.3, 117.6, 74.0, 28.1, 21.6; MS *m/e* (+FAB/3NBA) 225 (MH^+, 70). Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.91; H, 5.39. Found: C, 58.80; H, 5.54.

3′-(Toluene-4-sulfonyl)-2,3,4,5,4′,5′-hexahydro[2,2′]bifuranyl (27). Using General Procedure B, the alkynylstannane **20d** (0.11 g, 0.26 mmol) was converted into 26 mg of dihydrofuran **27** (35%) as a white solid following chromatographic purification with the gradient 20% Et_2O/hexanes, 25% Et_2O/hexanes, and 30% Et_2O/hexanes, mp 111−112 °C: IR (film) 1628 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.77 (d, J = 8.0 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 5.54 (t, J = 6.0 Hz, 1 H), 4.43 (t, J = 11.0 Hz, 2 H), 3.97−3.87 (m, 2 H), 3.01−2.93 (m, 1 H), 2.78−2.70 (m, 1H), 2.43 (s, 3 H), 2.31−2.25 (m, 1 H), 2.08−1.93 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 167.9, 144.0, 138.5, 129.9, 127.2, 110.7, 71.5, 70.5, 69.8, 30.8, 30.5, 26.5, 21.7; MS *m/e* (+CI) 295 (MH^+, 54). Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.21; H, 6.16. Found: C, 61.20; H, 6.32. In addition, 15 mg (25%)of **22** was isolated as a white solid.

2-[3-(Toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]tetrahydropyran (26). Using General Procedure B, the alkynylstannane **20e** (0.15 g, 0.34 mmol) was converted into 42 mg of dihydrofuran **26** (41%) as a white solid following chromatographic purification with 25% EtOAc/hexanes, mp 98 °C (decomp): IR (film) 1629 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.76 (d, J = 8.5 Hz, 2 H), 7.33 (d, J = 8.0 Hz, 2 H), 5.09−5.06 (m, 1 H), 4.51−4.40 (m, 2 H), 4.08 (dd, J = 11.0, 4.0 Hz, 1 H), 3.60 (dd, J = 11.5, 2.5 Hz, 1 H), 2.99−2.91 (m, 1 H), 2.78−2.70 (m, 1 H), 2.44 (s, 3 H), 1.93−1.89 (m, 1 H), 1.77−1.54 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) 166.2, 143.9, 138.4, 129.7, 127.1, 109.7, 71.5, 70.6, 68.9, 30.3, 29.4, 25.4, 23.0, 21.6; MS *m/e* (+CI) 309 (MH^+, 100). Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.31; H, 6.54. Found: C, 62.46; H, 6.62. In addition,21 mg (27%) of **22** was isolated as a white solid.

***trans*-3-Methyl-2-[3-(toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]tetrahydropyran (29a).** Using General Procedure B, the alkynylstannane **20f** (0.10 g, 0.22 mmol) was converted into 30 mg of dihydrofurans **29a/b** (43%, 10:1 mixture of **29a** to **29b**) as a white solid following chromatographic purification with the solvent gradient 20% EtOAc/hexanes, 25% EtOAc/hexanes, and 30% EtOAc/hexanes. The ratio of isomers was calculated by averaging the integration ratios of the methyl doublets and the C(H)O protons in the ^1H NMR spectrum of the crude product mixture. Partial purification of the individual isomers was achieved through the aforementioned chromatography.

Data for 29a: IR (film) 1622 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) 7.95 (d, J = 8.2 Hz, 2 H), 6.81 (d, J = 8.7 Hz, 2 H), 5.11 (d, J = 10.0 Hz, 1 H), 3.93−3.89 (m, 1 H), 3.68−3.53 (m, 2 H), 3.42−3.35 (m, 1 H), 2.65−2.56 (m, 1 H), 2.34−2.22 (m, 1 H), 2.01−1.87 (m, 1 H), 1.88 (s, 3 H), 1.59−1.49 (m, 2 H), 1.16−1.03 (m, 2 H) 0.92 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (90 MHz, C_6D_6) 165.1, 143.2, 140.1, 129.7, 128.5, 113.6, 76.6, 69.8, 68.6, 32.7, 32.1, 30.8, 26.6, 21.1, 17.8; MS *m/e* (+CI) 323 (MH^+, 100). Anal. Calcd for $C_{17}H_{22}O_4S$: C, 63.33; H, 6.88. Found: C, 63.00; H, 6.94. In addition, 8 mg (16%) of **22** was isolated as a white solid.

***cis*-3-Methyl-2-[3-(toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]tetrahydropyran (29b).** Using General Procedure B, the alkynylstannane **20g** (0.11 g, 0.24 mmol) was converted into 32 mg of dihydrofurans **29a/b** (41%, 8.5:1 mixture of **29b** to **29a**) as a white solid following chromatographic purification with the solvent gradient 20% EtOAc/hexanes, 25% EtOAc/hexanes, and 30% EtOAc/hexanes. The ratio of isomers was calculated by averaging the integration ratios of the methyl doublets and the C(H)O protons in the ^1H NMR spectrum of the crude product mixture. Partial purification of the individual isomers was achieved through the aforementioned chromatography.

Data for 29b: IR (film) 1622 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) 7.89 (d, J = 8.2 Hz, 2 H), 6.79 (d, J = 8.7 Hz, 2 H), 5.65 (d, J = 3.6 Hz, 1 H), 3.87 (dt, J = 11.5, 3.6 Hz, 1 H), 3.69−3.42 (m, 3 H), 2.64−2.54 (m, 1 H), 2.32−2.22 (m, 2 H), 1.88 (s, 3 H), 1.71−1.45 (m, 3 H), 1.10−1.05 (m, 1 H) with overlapping 1.08 (d, J = 7.3 Hz, 3 H); ^{13}C NMR (90 MHz, C_6D_6) 167.8, 143.6, 140.5, 130.1, 127.8, 111.2, 73.9, 70.3, 68.0, 33.3, 30.8, 30.2, 22.7, 21.5, 15.0; MS *m/e* (+CI) 323 (MH^+, 100). Anal. Calcd for $C_{17}H_{22}O_4S$: C, 63.33; H, 6.88. Found: C, 62.86; H, 6.93. In addition,8 mg (16%) of **22** was isolated as a white solid.

2-[3-(Toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]-[1,3]-dioxane (31). Using General Procedure B, the alkynylstannane **20h** (0.12 g, 0.27 mmol) was converted into 56 mg of dihydrofuran **31** (68%) as a white solid following chromatographic purification with the solvent gradient 15% Et_2O/hexanes, 20% Et_2O/hexanes, 25% Et_2O/hexanes, 30% Et_2O/hexanes and 50% EtOAc/hexanes, mp 184−185 °C: IR (film) 1647 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 7.93 (d, J = 8.7 Hz, 2 H), 6.81 (d, J = 7.9 Hz, 2 H), 6.59 (s, 1 H), 3.83 (dd, J = 10.6, 4.9 Hz, 2 H), 3.61−3.51 (m, 4 H), 2.31 (t, J = 10.2 Hz, 2 H), 1.90−1.77 (m, 1 H) with overlapping 1.88 (s, 3 H), 0.57−0.53 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) 161.6, 143.4, 139.7, 129.8, 128.1, 113.0, 94.2, 70.3, 67.2, 30.5, 25.8, 21.1; MS *m/e* (+CI) 311 (MH^+, 100). Anal. Calcd for $C_{15}H_{18}O_5S$: C, 58.05; H, 5.84. Found: C, 58.19; H, 6.03.

2-^2H-2-([1,1-$^2H_2$]-But-3-ynyloxy)tetrahydropyran (38). A 1−2 M hexanes solution of 6-deuteriodihydropyran[18b] (10 mL) and *p*-toluenesulfonic acid monohydrate (68 mg, 0.36 mmol) was added to [1,1-$^2H_2$]-but-3-ynol[18a] (0.26 g, 3.6 mmol) in 5 mL of CH_2Cl_2. After 2 h, the reaction mixture was treated with 5 mL of saturated sodium bicarbonate solution and diluted with 50 mL of Et_2O. The phases were separated, and the organic layer was washed with 10 mL of H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to provide a yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with 5% Et_2O/hexanes afforded 329 mg (58%) of **38** as a colorless oil: IR (film) 3295, 2107 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 3.79−3.71 (m, 1 H), 3.38−3.32 (m, 1 H), 2.30 (s, 2 H), 1.75 (t, J = 2.6 Hz, 1 H) overlapping 1.75−1.70 (m, 1 H), 1.55−1.49 (m, 2 H), 1.33−1.19 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 98.0 (t), 81.7, 69.6, 64.8 (q), 61.4, 30.6, 25.8, 20.1, 19.3; MS *m/e* (+CI) 158 (MH^+, 6); HRMS (+CI) calcd for $C_9H_{12}D_3O_2$ (MH^+)158.1260, found 158.1263.

Tributyl[[4,4-$^2H_2$]-4-([2-^2H]-tetrahydropyran-2-yloxy)-but-1-ynyl]stannane (39). Using General Procedure A, the trideuterated but-3-ynyl ether **38** (0.16 g, 1.0 mmol) was converted to 320 mg of alkynylstannane **39** (72%) following purification of the crude product with 3% Et_2O/hexanes: IR (film) 2154 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 3.83−3.75 (m, 1 H), 3.36 (ddt, J = 15.7, 4.1, 1.5 Hz, 1 H), 2.56 (s, 2 H), 1.79−1.18 (m, 16 H), 1.01 (t, J = 7.9 Hz, 6 H), 0.93 (t, J = 7.2 Hz, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 108.8 ($J_{C-Sn119}$ = 36.3 Hz), 97.8 (t), 82.7, 65.6 (pentet), 61.3, 30.7, 29.3 ($J_{C-Sn119}$ = 11.6 Hz), 27.4 ($J_{C-Sn119}$ = 29.8 Hz), 25.9, 22.0, 19.3, 13.9, 11.2 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.1 Hz; MS *m/e* (+CI) 448 (Sn^{120}) (MH^+, 5); HRMS (+CI) calcd for $C_{21}H_{38}D_3O_2Sn^{120}$ (MH^+) 448.2317, found 448.2305.

[2,2-$^2H_2$]-δ-Valerolactone (41). Sodium methoxide (0.28 g, 5.2 mmol) was added to 5-benzyloxypentanoic acid methyl

ester[21] (2.1 g, 9.4 mmol) in 20 mL of MeOD. After 17 h at reflux, the solution was cooled to room temperature and concentrated in vacuo. The residue was taken up in 100 mL of Et_2O and 50 mL of H_2O. The aqueous layer was extracted with three 20 mL portions of Et_2O, and the combined organic phases were rinsed with 20 mL of brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to afford 1.8 g (85%) of crude methyl 5-benzyloxy-[2,2-$^2H_2$]-pentanoate as a colorless oil with 96% deuterium incorporation: IR (film) 1736 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) 7.29−7.09 (m, 5 H), 4.27 (s, 2 H), 3.32 (s, 3 H), 3.20 (t, J = 6.4 Hz, 2 H), 1.65, J = 7.3 Hz, 2 H), 1.52−1.44 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 173.3, 139.4, 128.5, 127.7, 127.6, 72.9, 69.9, 50.9, 33.2 (pentet), 29.4, 22.0; MS *m/e* (+CI) 225 (MH^+, 100); HRMS (+CI) calcd for $C_{13}H_{17}D_2O_3$ 225.1460, found 225.1453.

10% Pd/C (43 mg, 0.40 mmol) was added to methyl 5-benzyloxy-[2,2-$^2H_2$]pentanoate (1.8 g, 8.0 mmol) in 40 mL of THF. The system was purged with Ar and then with hydrogen. The reaction mixture was stirred under 1 atm of hydrogen for 18 h. The suspension was filtered through a plug of Celite, and the solid was washed with 50 mL of Et_2O. The solution was concentrated in vacuo to afford 1.1 g (100%) of methyl 5-hydroxy-[2,2-$^2H_2$]pentanoate as a colorless oil: IR (film) 3408,1737 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 3.38 (br d, J = 6.0 Hz, 2 H), 3.34 (s, 3 H), 1.59 (t, J = 6.8 Hz, 2 H), 1.40−1.34 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 173.8, 62.0, 51.0, 33.2 (pentet), 32.3, 21.4; MS *m/e* (+CI) 135 (MH^+, 100); HRMS (+CI) calcd for $C_6H_{11}D_2O_3$ 135.0990, found 135.0996.

p-Toluenesulfonic acid monohydrate (14 mg, 0.075 mmol) was added to methyl 5-hydroxy-[2,2-$^2H_2$]-pentanoate(1.0 g, 7.5 mmol) in 75 mL of benzene. After refluxing the solution for 48 h with Dean−Stark removal of water, the reaction mixture was cooled to room temperature. The organic layer was washed once with 10 mL of H_2O and with two 20 mL portions of brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo at 0 °C to provide 0.78 g (100%) of 90−95% pure lactone **41** as a pale yellow oil: IR (film) 1732 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) 3.56 (t, J = 5.8 Hz, 2 H), 0.98−0.88 (dm, 4 H); ^{13}C NMR (100 MHz, C_6D_6)169.7, 68.3, 29.2 (t), 22.1, 18.7. GCMS 102 (M^+, 73); HRMS (+APCI) calcd for $C_5H_7D_2O_2$ (MH^+) 103.0726, found 103.0721.

[3,3-$^2H_2$]-2-([4-^2H]-But-3-ynyloxy)tetrahydropyran (42). A 1.0 M solution of DIBAL-H in hexane (6.7 mL, 6.7 mmol) was added dropwise over 1 h to [2,2-$^2H_2$]-δ-valerolactone (**41**) (0.71 g, 7.0 mmol) in 5 mL of THF at −42 °C. The reaction mixture was warmed to −20 °C and was stirred there for 1 h. MeOD (0.54 mL, 13.4 mmol) was added, and the cloudy solution was warmed to room temperature. The suspension was cooled to 0 °C and filtered, and the salts were washed with five 20 mL portions of Et_2O. The combined organic washes were concentrated in vacuo at 0 °C to afford 0.16 g (22%) of crude [3,3-$^2H_2$]-2-hydroxy-tetrahydropyran as a colorless oil: CIMS *m/e* 103 ($M - H^+$, 26).

MeOD (12 mL) was added to [3,3-$^2H_2$]-2-hydroxy-tetrahydropyran (0.15 g, 1.4 mmol). After 2 h, the solvent was distilled off at atmospheric pressure, and the remaining oil was diluted with 4 mL of benzene. [4-^2H]-But-3-yn-[1-^2H]-ol (0.85 mL, 1.1 mmol) and *p*-toluenesulfonic ^2H-acid·D_2O (2 mg, 0.010 mmol) were added. After 2 h at reflux, the solution was cooled to room temperature. The reaction mixture was treated with 5 mL of saturated sodium bicarbonate solution and diluted with 50 mL of Et_2O. The phases were separated, and the organic layer was washed with 10 mL of brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo at 0 °C to afford a pale yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with 5% Et_2O/hexanes afforded 0.11 g (64%) of **42** as a colorless oil: IR (film) 2590 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) 4.50 (s, 1 H), 3.82−3.71 (m, 2 H), 3.43−3.30 (m, 2 H), 2.30 (t, J = 6.8 Hz, 2 H), 1.75−1.68 (m, 1 H), 1.40−1.17 (dm, 3 H); ^{13}C NMR (90 MHz, C_6D_6) 98.4, 81.3, 69.3 (t), 65.7, 61.5, 30.4 (pentet), 25.8, 19.3, 19.2; MS *m/e* (+CI) 157 (MH^+, 1); HRMS (+CI) calcd for $C_9H_{11}D_3O_2$ 157.1179, found 157.1182.

Tributyl[4-([3,3-$^2H_2$]-tetrahydropyran-2-yloxy)but-1-ynyl]stannane (43). Using General Procedure A, the trideuterated but-3-ynyl ether **42** (78 mg, 0.50 mmol) was converted to 170 mg of alkynylstannane **43** (76%) following purification of the crude product with 4% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 4.58 (s, 1 H), 3.93(dt, J = 9.4, 7.2 Hz, 1 H), 3.88−3.75 (m, 1 H), 3.55 (dt, J = 9.4, 7.2 Hz, 1 H), 3.40−3.34 (m, 1 H), 2.57 (t, J = 7.2 Hz, 2 H), 1.72−1.61 (m, 7 H), 1.44−1.31 (m, 7 H), 1.1 (t, J = 8.3 Hz, 6 H), 0.92 (t, J = 7.2 Hz, 11 H); ^{13}C NMR (75 MHz, C_6D_6) 108.9, 98.3, 82.8, 66.4, 61.4, 30.5 (t), 29.4 ($J_{C-Sn119}$ = 10.9 Hz), 27.4 ($J_{C-Sn119}$ = 29.8 Hz), 25.9, 22.2, 19.2, 13.9, 11.2 ($J_{C-Sn119}$ = 191.8 Hz, $J_{C-Sn117}$ = 183.8 Hz; MS *m/e* (+CI) 447 (Sn^{120}) (MH^+, 100); HRMS (+CI) calcd for $C_{21}H_{37}D_2O_2Sn^{120}$ ($M - H^+$) 445.2097, found 445.2106.

[6,6-$^2H_2$]-2-methoxytetrahydropyran (45). A 5 mL solution of methyl 5-formylpentanoate dimethyl acetal[22] (0.48 g, 2.8 mmol) in Et_2O was cannulated over 10 min into a suspension of $LiAlD_4$ (0.11 g, 2.7 mmol) in 16 mL of Et_2O at 0 °C. After 2 h at 0 °C, the reaction mixture was treated sequentially with 0.11 mL of H_2O, 0.11 mL of 15% NaOH solution, and 0.33 mL of H_2O. After 5 min, the suspension was allowed to warm to room temperature and stirred for 1 h. The salts were filtered and washed with five 30 mL portions of Et_2O. The combined organic washings were dried over Na_2SO_4 and concentrated to afford 0.39 g (96%) of [1,1-$^2H_2$]-5-formylpentanol dimethyl acetal as a colorless oil: IR (film) 3418 cm^{-1}; ^1H NMR (300 MHz, C_6D6) 4.27 (t, J = 5.7 Hz, 1 H), 3.14 (s, 6 H), 1.62−1.55 (m, 2 H), 1.41−1.32 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6) 104.7, 61.8 (pentet), 52.3, 32.7, 32.6, 21.3; MS *m/e* (+APCI/NH_4OAc in MeOH) 168 ($M + NH_4^+$, 2); HRMS (+APCI/NH_4OAc in MeOH) calcd for $C_6H_9D_2O_2$ ($M - H^+$) 117.0885, found 117.0891.

p-Toluenesulfonic acid monohydrate (5 mg, 0.025 mmol) was added to [1,1-$^2H_2$]-5-formylpentanol dimethyl acetal (0.38 g, 2.5 mmol) in 3 mL of CH_2Cl_2 at 0 °C. After 17 h, the solution was concentrated in vacuo to afford 0.24 g (80%) of [6,6-$^2H_2$]-2-methoxytetrahydropyran (**45**) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) 4.44 (t, J = 3.0 Hz, 1 H), 3.27 (s, 3 H), 1.80−1.52 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 99.7, 55.0, 30.5 superimposed on 30.4 (t), 25.2, 19.3; MS *m/e* (+CI) 117 ($M-H^+$, 18); HRMS (+APCI/NH_4OAc in MeOH) calcd for $C_6H_9D_2O_2$ ($M - H^+$) 117.0885, found 117.0891.

2-But-3-ynyloxy-[6,6-$^2H_2$]-tetrahydropyran (46). But-3-ynol (0.29 mL, 3.8 mmol) and *p*-toluenesulfonic acid monohydrate (3.6 mg, 0.019 mmol) were added to [6,6-$^2H_2$]-2-methoxytetrahydropyran (**45**) (0.22 g, 1.9 mmol) in 6 mL of CH_2Cl_2. After 19 h, the reaction mixture was treated with 5 mL of saturated sodium bicarbonate solution and diluted with 50 mL of Et_2O. The phases were separated, and the organic layer was washed with 10 mL of H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo at 0 °C to provide a yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with 5% Et_2O/hexanes afforded 0.10 g (34%) of **46** as a colorless oil: IR (film) 3294, 2122 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) 4.51 (t, J = 3.4 Hz, 1 H), 3.78 (dt, J = 9.4, 7.2 Hz, 1 H), 3.39 (dt, J = 9.4, 6.8 Hz, 1 H), 2.30 (td, J = 7.2, 2.6 Hz, 2 H), 1.74 (t, J = 2.6 Hz, 1 H) superimposed on 1.78−1.64 (m, 1 H), 1.59−1.45 (m, 2 H), 1.37−1.16 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 98.4, 81.7, 69.6, 65.6, 60.7 (t), 30.8, 25.6, 20.3, 19.3.

Tributyl[4-([6,6-$^2H_2$]-tetrahydropyran-2-yloxy)but-1-ynyl]stannane (47). Using General Procedure A, the dideuterated but-3-ynyl ether **46** (90 mg, 0.58 mmol) was converted to 180 mg of alkynylstannane **47** (69%) following purification of the crude product with 5% Et_2O/hexanes: IR (film) 2153 cm^{-1}; ^1H NMR (360 MHz, C_6D_6) 4.59 (t, J = 3.2 Hz, 1 H), 3.39 (dt, J = 9.1, 7.3 Hz, 1 H), 3.56 (dt, J = 9.6, 6.8 Hz, 1 H), 2.58 (t, J = 6.8 Hz, 2 H), 1.77−1.52 (m, 9 H), 1.43−1.21 (m, 9 H),

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1.02 (t, J = 8.2 Hz, 6 H), 0.92 (t, J = 7.3 Hz, 9 H); ^{13}C NMR (90 MHz, C_6D_6) 108.9, 98.4, 82.8, 66.4, 60.7 (pentet), 30.9, 29.4 ($J_{C-Sn119}$ = 11.7 Hz), 27.4 ($J_{C-Sn119}$ = 29.6 Hz), 25.7, 22.2, 19.3, 13.9, 11.2 ($J_{C-Sn119}$ = 192.1 Hz, $J_{C-Sn117}$ = 183.1 Hz).

Tributyl[[3,3-$^2H_2$]-4-(tetrahydropyran-2-yloxy)-but-1-ynyl]stannane (49). Pyridine (3.7 mL, 45.5 mmol) and *p*-toluenesulfonyl chloride (3.2 g, 16.9 mmol) were added to the monotetrahydropyranyl ether of [1,1-$^2H_2$]-ethylene glycol[18c] (2.0 g, 13.0 mmol) in 13 mL of CH_2Cl_2. After 12 h, the reaction mixture was treated with 10 mL of saturated sodium bicarbonate solution and diluted with 50 mL of Et_2O. The phases were separated, and the organic layer was washed with 10 mL of H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo at 0 °C to provide a yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with a gradient of 10% Et_2O/hexanes to 25% Et_2O/hexanes afforded 3.2 g (82%) of 2-(tetrahydropyran-2-yloxy)-[1,1-$^2H_2$]-ethyl tosylate as a colorless oil: IR (film) 1598 cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) 7.75 (d, J = 8.2 Hz, 2 H), 6.69 (d, J = 8.7 Hz, 2 H), 4.36 (t, J = 3.2 Hz, 1 H), 3.65−3.57 (m, 1 H) superimposed by 3.59 (d, J = 11.8 Hz, 1 H), 3.29−3.24 (m, 1 H) superimposed by 3.26 (d, J = 12.3 Hz, 1 H), 1.88 (s, 3 H), 1.63−1.55 (m, 1 H), 1.44−1.40 (m, 2 H), 1.32−1.12 (dm, 3 H); ^{13}C NMR (90 MHz, C_6D_6)144.1, 134.5, 129.8, 129.7, 98.6, 68.8 (pentet), 64.7, 61.5, 30.5, 25.7, 21.1, 19.2; MS *m/e* (+CI) 303 (MH+, 100); HRMS (+CI) calcd for $C_{14}H_{19}D_2O_5S$ (MH^+) 303.1235, found 303.1239.

A 2.5 M solution of *n*-BuLi in hexane (1.7 mL, 4.2 mmol) was added to trimethylsilylacetylene (0.60 mL, 4.3 mmol) in 3 mL of THF at −78 °C. After 1 h, the reaction mixture was warmed to 0 °C, and a 4 mL THF solution of 2-(tetrahydropyran-2-yloxy)-[1,1-$^2H_2$]-ethyl tosylate (1.0 g, 3.3 mmol) and 3 mL of anhydrous DMSO were added. The orange solution was allowed to warm to room temperature and stirred for 12 h. The reaction mixture was treated with 5 mL of H_2O and diluted with 50 mL of Et_2O. The phases were separated and the aqueous layer was extracted with two 20 mL portions of Et_2O. The combined organic layers were washed with 20 mL of H_2O and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to provide 0.46 g of a light yellow oil. Purification of the crude product by flash chromatography on silica gel eluting with 8% Et_2O/hexanes afforded 0.30 g (39%) of [4-([3,3-$^2H_2$]-tetrahydropyran-2-yloxy)but-1-ynyl]trimethylsilane as a colorless oil: IR (film) 2176 cm^{-1}: ^{1}H NMR (360 MHz, C_6D_6) 4.54 (t, J = 3.2 Hz, 1 H), 3.82(d, J = 10.0 Hz, 1 H), 3.78−3.75 (m, 1 H), 3.45 (d, J = 9.6 Hz, 1 H), 3.35 (ddt, J = 10.9, 4.1, 1.4 Hz, 1 H), 1.79−1.69 (m, 1 H), 1.59−1.46 (m, 2 H), 1.40−1.19 (m, 3 H), 0.19 (s, 9 H); ^{13}C NMR (90 MHz, C_6D_6) 104.7, 98.2, 85.4, 65.3, 61.2, 30.6, 25.6, 21.0 (t), 19.1, −0.22; MS *m/e* (+CI) 229 (MH^+, 100); HRMS (+CI) calcd for $C_{12}H_{21}D_2O_2Si$ (MH^+) 229.1593, found 229.1589.

Bis(tributyltin)oxide (0.50 mL, 0.97 mmol) and a 1.0 M solution of tetrabutylammonium fluoride in THF (14 μL, 0.014 mmol) were added to [4-([3,3-$^2H_2$]-tetrahydropyran-2-yloxy)-but-1-ynyl]trimethylsilane (0.21 g, 0.92 mmol) in 11 mL of THF. The reaction mixture was refluxed for 3 h and then cooled to room temperature. The solution was concentrated to afford a light yellow oil. Purification of the crude product by flash chromatography on deactivated silica gel eluting with 5% Et_2O/hexanes afforded 0.22 g (54%) of the stannane **49** as a colorless oil: IR (film) 2153 cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) 4.58 (t, J = 3.6 Hz, 1 H), 3.92(d, J = 9.6 Hz, 1 H), 3.83−3.76 (m, 1 H), 3.55 (d, J = 9.6 Hz, 1 H), 3.39−3.33 (m, 1 H), 1.71−1.52 (m, 7 H), 1.43−1.24 (m, 10 H), 1.03−0.94 (m, 16 H); ^{13}C NMR (100 MHz, C_6D_6)108.8, 98.4, 82.8, 66.3, 61.4, 30.8, 29.3 ($J_{C-Sn119}$ = 10.7 Hz), 27.4 ($J_{C-Sn119}$ = 29.1 Hz), 25.9, 21.6 (pentet), 19.4, 13.9, 11.2 ($J_{C-Sn119}$ = 192.5 Hz, $J_{C-Sn117}$ = 184.0 Hz); MS *m/e* (+CI) 447 (Sn^{120}) (MH^+, 100); HRMS (+CI) calcd for $C_{21}H_{37}D_2O_2Sn^{120}$ ($M - H^+$) 445.2098, found 445.2101.

Crossover Experiment, 32 + 1e. Using General Procedure B, a mixture of the undeuterated alkynylstannane **20e** (78 mg, 0.18 mmol) and the trideuterioalkynylstannane **39** (79 mg, 0.18 mmol) were converted into 44 mg of dihydrofurans **50a** and **26** (40%) as a white solid following chromatographic purification with the solvent gradient 25% Et_2O/hexanes, 35% Et_2O/hexanes and 45% Et_2O/hexanes. Chemical ionization mass spectroscopy indicated no crossover as discussed in the text.

Cyclization of Tributyl[4-([6,6-$^2H_2$]-tetrahydropyran-2-yloxy)but-1-ynyl]stannane (47). Using General Procedure B, the dideuterated alkynylstannane **47** (91 mg, 0.20 mmol) was converted into 44 mg of [6,6-$^2H_2$]-2-[3-(toluene-4-sulfonyl)-4,5-dihydrofuran-2-yl]-tetrahydropyran **26-d_2** (42%) as a white solid following chromatographic purification with a solvent gradient of 20% EtOAc/hexanes, 25% EtOAc/hexanes, and 30% EtOAc/hexanes: IR (film) 1634 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) 7.97 (d, J = 8.1 Hz, 2 H), 6.80 (d, J = 8.1 Hz, 2 H), 5.54 (dd, J = 11.1, 2.3 Hz, 1 H), 3.64−3.51 (m, 2 H), 2.56 (dt, J = 11.1, 2.5 Hz, 1 H), 2.27 (dt, J = 11.4, 3.3 Hz, 1 H), 1.88 (s, 3 H) superimposed on 1.88−1.78 (m, 1 H), 1.68−1.64 (m, 1 H), 1.58−1.33 (m, 1 H), 1.39−1.33 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6)166.7, 143.2, 140.2, 129.9, 111.0, 71.3, 69.9, 68.0 (t), 30.6, 29.0, 25.6, 23.2, 21.1. One aromatic carbon at 127.1 is buried under the benzene signals; MS *m/e* (+CI) 311 (MH^+, 100); HRMS (+CI) calcd for $C_{16}H_{19}D_2O_4S$ (MH^+) 311.1286, found 311.1288. In addition, 9 mg (20%) of the byproduct **22** with no deuterium incorporation into the 2-position was isolated.

Cyclization of Tributyl[[3,3-$^2H_2$]-4-(tetrahydropyran-2-yloxy)-but-1-ynyl]stannane (49). Using General Procedure B, the dideuterated alkynylstannane **49** (0.10 g, 0.22 mmol) was converted into 26 mg of dihydrofuran **26-d_2** (40%) as a white solid following chromatographic purification with a solvent gradient of 25% EtOAc/hexanes, 30% EtOAc/hexanes, and 40% EtOAc/hexanes: IR (film)1631 cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) 7.94 (d, J = 8.7 Hz, 2 H), 6.81 (d, J = 7.8 Hz, 2 H), 5.54 (dd, J = 11.4, 2.3 Hz, 1 H), 3.90 (dt, J = 11.4, 2.3 Hz, 1 H), 3.61 (d, J = 9.1 Hz, 1 H), 3.54 (d, J = 9.1 Hz, 1 H), 3.42 (dt, J = 11.4, 2.3 Hz, 1 H), 1.89 (s, 3 H), 1.88−1.78 (m, 1 H), 1.72−1.52 (m, 2 H), 1.48−1.23 (m, 2 H), 1.09−1.06 (m, 1 H); ^{13}C NMR (90 MHz, C_6D_6)166.7, 143.0, 140.2, 129.8, 110.9, 71.4, 69.8, 68.8, 30.0 (pentet), 29.0, 25.9, 23.3, 21.1. One aromatic carbon at 127.1 is buried under the benzene signals; MS *m/e* (+CI) 311 (MH^+, 100); HRMS (+CI) calcd for $C_{16}H_{19}D_2O_4S$ (MH^+) 311.1286, found 311.1285. In addition, 10 mg (20%) the byproduct **22** with no deuterium incorporation into the 2-position was isolated.

Cyclization of Tributyl[4-([3,3-$^2H_2$]-tetrahydropyran-2-yloxy)but-1-ynyl]stannane (43). Using General Procedure B, the dideuterated alkynylstannane **43** (0.12 g, 0.27 mmol) was converted into 35 mg of dihydrofuran **26-d_2** (42%) as a white solid following chromatographic purification with a solvent gradient of 25% EtOAc/hexanes, 30% EtOAc/hexanes, and 40% EtOAc/hexanes: IR (film) 1633 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) 7.94 (d, J = 8.3 Hz, 2 H), 6.83 (d, J = 7.9 Hz, 2 H), 5.42 (s, 1 H), 3.90 (d, J = 11.3 Hz, 1 H), 3.69−3.52 (m, 2 H), 3.42 (t, J = 9.0 Hz, 1 H), 2.64−2.53 (m, 1 H), 2.34−2.23 (m, 1 H), 1.90 (s, 3 H) superimposed on 1.90−1.81 (m, 1 H), 1.64−1.35 (m, 2 H), 1.08 (br d, J = 11.7 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) 166.6, 143.3, 140.2, 129.8, 111.0, 71.2, 69.9, 68.7, 30.6, 28.5 (pentet), 25.8, 23.0, 21.1. One aromatic carbon at 127.1 is buried under the benzene signals; MS *m/e* (+CI) 311 (MH^+, 100); HRMS (+CI) calcd for $C_{16}H_{19}D_2O_4S$ (MH^+) 311.1286, found 311.1279.

In addition, 15 mg (25%) of the byproduct **22** with some deuterium incorporation into the 2-position was isolated: IR (film)1608 cm^{-1}; ^{1}H NMR (360 MHz, C_6D_6) 7.79 (d, J = 8.2 Hz, 2 H), 6.97 (s, **0.44 H**), 6.79 (d, J = 8.2 Hz, 2 H), 3.62 (t, J = 10.0 Hz, 2 H), 2.23 (t, J = 9.1 Hz, 2 H), 1.89 (s, 3 H); ^{13}C NMR (90 MHz, C_6D_6)156.2, 143.3, 139.5, 129.8, 118.7 (d), 73.5, 28.2, 21.1. One aromatic carbon at 127.3 is buried under the benzene signals; MS *m/e* (+CI) 226 (MH^+, 67); HRMS (+CI) calcd for $C_{11}H_{12}DO_3S$ (MH^+) 226.0648, found 226.0649.

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Supporting Information Available: Copies of ^{13}C NMR spectra for **19f−h**, **20b**, **20d−h**, **38**, **39**, **41−43**, **45−47**, **49**, and the cyclization products from **43**, **47**, and **49**. This material is available free of charge via the Internet at http://pubs.acs.org.

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