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Regioselective Lithium–Iodine Exchange-Initiated Cleavage of 2-Iodomethyl-1,3-dioxanes: A Complex-Induced Proximity Effect

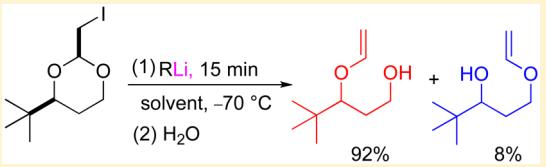
William F. Bailey*,† and Justin D. Fair*,‡

†Department of Chemistry, University of Connecticut, Storrs, Connecticut 06269-3060, United States

‡Department of Chemistry, Indiana University of Pennsylvania, Indiana, Pennsylvania 15705, United States

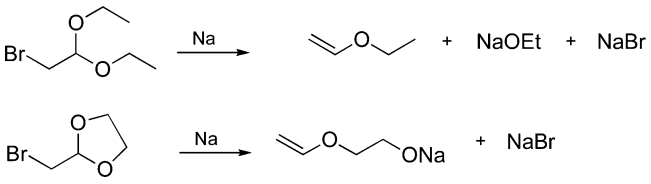
Supporting Information

ABSTRACT: Lithium–iodine exchange-initiated fragmentation of a series of 4-substituted 2-iodomethyl-1,3-dioxanes proceeds rapidly and regioselectively to afford enol ether alcohols by preferential cleavage of the less congested C(2)–O(1) bond. The results demonstrate that a complex-induced proximity effect (CIPE) is likely responsible for the selectivity of the cleavage.



The fragmentation of β-halo acetals upon treatment with sodium metal was discovered by Wislicenus in the late 1870s,[1] and the cleavage of 2-bromomethyl-1,3-dioxolane under similar conditions was reported by Hill and Pidgeon in 1928 (Scheme 1).[2] Swallen and Boord[3] generalized such

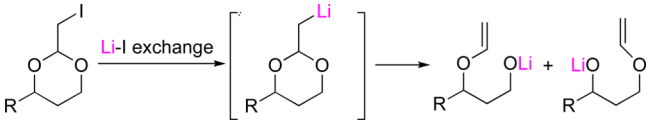
Scheme 1. Boord Fragmentations



reactions using zinc metal to provide olefinic hydrocarbons by the elimination of alkoxide and halogen from β-halo ethers. This reaction, known today as the Boord reaction,[4] can be accomplished with zinc, magnesium, sodium, and lithium as well as a variety of other reagents.[5] This synthesis has the specific advantage of ensuring an exact location of a carbon–carbon double bond. When a β-halo cyclic acetal is symmetrical, as in the example shown in Scheme 1, there is only one possible product of the fragmentation. However, when the Boord reaction is performed on an unsymmetrical β-halo cyclic acetal, there are obviously two possible regioisomeric products.

We were interested in exploring the outcome of the Boord fragmentation of unsymmetrically substituted 2-iodomethyl-1,3-dioxanes initiated by lithium–halogen exchange, as illustrated in Scheme 2. We reasoned that the alkyllithium

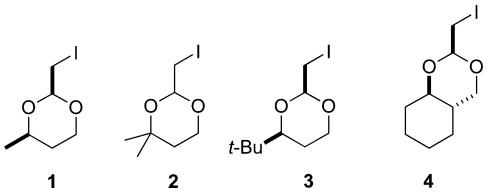
Scheme 2. Fragmentation of Unsymmetrically Substituted 2-Iodomethyl-1,3-dioxanes



used to initiate the cleavage might reasonably be expected to first coordinate with an oxygen atom of the substrate,[6] a phenomenon termed a complex–induced proximity effect (CIPE) by Beak, Meyers, Snieckus, and co-workers.[7] The oxygen atoms in a 1,3-dioxane bearing a substituent (or substituents) at C(4) are sterically distinct, and to the extent that the lithium–iodine exchange is controlled by a CIPE involving complexation of the alkyllithium initiator with the less encumbered oxygen, we reckoned that the fragmentation might result in preferential cleavage of the less congested C–O bond. As demonstrated by the results presented below, this appears to be the case.

The substituted 2-iodomethyl-1,3-dioxanes used in this study, depicted in Chart 1, were prepared in straightforward

Chart 1. 4-Substituted and 4,5-Disubstituted 1,3-Dioxanes



fashion by acid-catalyzed transacetalization between 1,1-diethoxy-2-iodoethane and the appropriate diol; as expected,[8] the thermodynamically more stable *cis* isomers resulted from the condensation reactions. However, although the condensation used to prepare *cis*-2-(iodomethyl)-4-methyl-1,3-dioxane (**1**) resulted in the formation of a preponderance of the *cis* isomer, an approximately 10% yield of the *trans* isomer (bearing an axial 4-methyl group) was also produced. This isomeric mixture was used in the studies described below.

The Boord fragmentations were initiated in separate experiments by addition, under an atmosphere of argon, of *n*-

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BuLi in hexane (1 molar equiv) or *t*-BuLi in pentane (2.2 molar equiv) to 0.05 M solutions of the 2-iodomethyl-1,3-dioxanes (**1**–**4**) in *n*-pentane, diethyl ether, or THF that had been cooled to −70 °C. The resulting solutions were stirred at −70 °C for 15 min, after which water was added and the reaction mixtures were allowed to warm to room temperature. The crude product mixtures were analyzed by both capillary GC and ^{1}H NMR spectroscopy as described below; no effort was made to quantitate the *n*-BuI or isobutylene generated as coproducts of the exchange reactions with *n*-BuLi or *t*-BuLi.

At this juncture it should be noted that the enol ether alcohol products are extremely acid-labile: a catalytic quantity of acid serves to convert both of the products to the corresponding *cis*-2-methyl-4-substituted-1,3-dioxane very rapidly and in quantitative yield. For this reason, it was not possible to separate pure samples of the enol ether alcohol products by column chromatography. Fortunately, this step was not necessary for determination of the regioselectivity of the cleavage. The structures of the two constitutionally isomeric enol ether products were easily established by examination of the OH resonance in the ^{1}H NMR spectrum of the reaction mixture recorded in DMSO-d_6:[9] the primary alcohol products display well-resolved triplets for the hydroxyl proton, while the OH resonance in the secondary alcohol products appears as a doublet. A representative ^{1}H NMR spectrum in DMSO-d_6 of the OH resonances of the cleavage products resulting from the reaction of **4** with *n*-BuLi in pentane (Table 1, entry 20) is shown in Figure 1; the Supporting Information includes

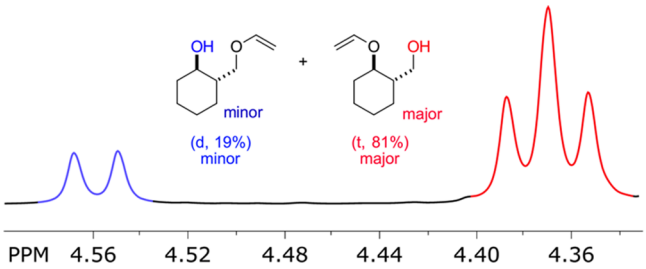


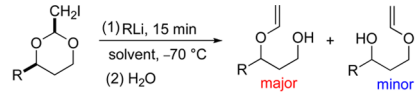
Figure 1. Representative ^{1}H NMR spectrum in DMSO-d_6 of the OH resonances of the cleavage products resulting from reaction of **4** with *n*-BuLi in pentane.

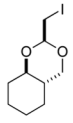
complete NMR spectra in DMSO-d_6, including expansions of the OH region, for all of the cleavage products. Not surprisingly, the extreme acid lability of the products is such that ring closure is observed when samples are prepared in $CDCl_3$ for NMR analysis. Indeed, it was necessary to add a drop of pyridine to such solutions to neutralize any adventitious acid before NMR spectra were recorded in $CDCl_3$.

The relative proportions of the major and minor products formed in the fragmentation reactions were obtained by GC analysis of the product mixtures as well as by integration of the OH resonances in the NMR spectra recorded in DMSO-d_6. The two analysis methods gave identical product ratios within the error of the measurements, and these are summarized in Table 1.

The intramolecular β-elimination ensues very rapidly upon addition of the alkyllithium to solutions of the 2-iodomethyl-dioxanes at −70 °C, and we were unable to detect or trap the putative organolithium intermediate that would be generated by the lithium–iodine exchange. This behavior was not unexpected: the exchange reaction between 2-allyloxyethyl iodide and *t*-BuLi at −78 °C leads quantitatively and essentially instantaneously to ethylene and the lithium salt of allyl alcohol.[10]

Table 1. Lithium–Iodine Exchange-Initiated Cleavage of 2-Iodomethyl-1,3-dioxanes (1–4)



entry	dioxane	RLi	solvent	yield[a],%	major,[b] %	minor.[b] %
1	 **1**	*n*-BuLi	pentane	94	79	21
2			Et_2O	88	84	16
3			THF	89	82	18
4		*t*-BuLi	pentane	91	70	30
5			Et_2O	87	76	24
6			THF	86	56	44
7	 **2**	*n*-BuLi	pentane	96	76	24
8			Et_2O	97	80	20
9			THF	84	74	26
10		*t*-BuLi	pentane	98	66	34
11			Et_2O	94	78	22
12			THF	83	54	46
13	 **3**	*n*-BuLi	pentane	93	92	8
14			Et_2O	92	90	10
15			THF	93	77	23
16		*t*-BuLi	pentane	95	88	12
17			Et_2O	93	88	12
18			THF	92	61	39
19	 **4**	*n*-BuLi	pentane	91	75	25
20			Et_2O	90	81	19
21			THF	84	76	24
22		*t*-BuLi	pentane	86	71	29
23			Et_2O	84	77	23
24			THF	89	56	44

[a]Isolated yields of isomeric mixtures. [b]Proportions of constitutionally isomeric enol alcohols in the product mixtures.

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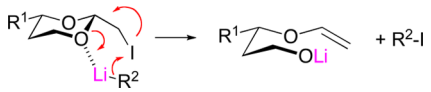
Cursory inspection of the data reveals that the fragmentations proceed in good to excellent yields and that in all cases the major product results from cleavage of the less congested C(2)−O(1) bond of the dioxane. The regioselectivity of the reaction ranges from a high of ∼90/10 to ∼60/40. Both the mode and rapidity of the fragmentations are nicely rationalized if one posits a CIPE involving preferential coordination of the alkyllithium reagent with the less sterically encumbered ring oxygen followed by a concerted, if not entirely synchronous, exchange-initiated cleavage of the C−O bond through a six-membered transition state. This scenario is illustrated in Scheme 3 for the case of a monomeric RLi. Of course, the

Scheme 3. Exchange-Initiated Fragmentation Involving a CIPE



reaction may be (and likely is) more complex than this simple representation suggests: the actual state of aggregation of the organolithium species involved in the fragmentations is, as noted below, not known.

The regioselectivity of the lithium−iodide exchange-initiated fragmentation appears to be related to the initial aggregation state of the organolithium reagent used for the exchange reaction as well as the solvent in which the reaction is conducted. In a given solvent, cleavages initiated using *t*-BuLi are generally slightly less selective than those initiated using *n*-BuLi (Table 1), and in any given solvent *t*-BuLi is less aggregated than is *n*-BuLi.[6] However, it is very likely that the aggregation state of the alkyllithium reagent changes as the reaction proceeds: the cleavage product (a lithium alkoxide) may form a mixed aggregate with any or all of the reagents involved in the process. For this reason, the factors responsible for the range of regioselectivities observed in the fragmentation reactions conducted in various solvents remain somewhat obscure.

The results do demonstrate that complexation between an organolithium aggregate and either O(1) or O(3) of a 4-substituted 1,3-dioxane favors the less sterically hindered oxygen. The fact that having one methyl group and having two methyl groups at C(4) are approximately equally effective in discriminating between complexation at either O(1) and O(3) (cf. dioxanes **1** and **2**; Table 1, entries 1−12) suggests that the steric effect is likely due to the equatorial C(4) substituent. Not surprisingly, the most sterically demanding C(4) substituent, the *tert*-butyl group in dioxane **3**, results in the most selective fragmentation (Table 1, entries 3−18).

In the aggregate, the results presented above demonstrate that a CIPE can influence the outcome of the seemingly simple cleavage of unsymmetrically substituted 2-halomethyl-1,3-dioxanes to give enol ether alcohols. The high regioselectivity observed in these rapid fragmentations reinforces the notion that coordination of a reagent with a substrate prior to reaction may have a profound effect on the outcome of the process.

EXPERIMENTAL SECTION

General Procedures. CAUTION: Organolithium compounds are extremely pyrophoric, and they should be handled only by individuals trained in their proper and safe use.[11] All manipulations of *t*-BuLi were performed in flame-dried glassware under oxygen-free argon using standard cannula and syringe techniques.[11,12] HRMS molecular mass determinations were performed on a TOF mass spectrometer; ionization methods are noted below for individual compounds.

The concentrations of *n*-BuLi in hexane and *t*-BuLi in pentane were determined immediately prior to use by titration with a standard solution of 2-butanol in xylenes using 1,10-phenanthroline as the indicator.[13] Dry diethyl ether and THF were freshly distilled from dark-purple solutions of sodium and benzophenone; dry, alkene-free *n*-pentane was obtained by repetitive washing of technical-grade pentane with concentrated sulfuric acid until the acid layer remained clear, followed by successive washings with water, saturated sodium bicarbonate, and water. The pentane was then dried ($MgSO_4$) and freshly distilled from a dark-purple solution of sodium/benzophenone/tetraglyme.

Literature procedures were followed for the preparation of 4,4-dimethyl-1,3-pentanediol[14] and *trans*-2-(hydroxymethyl)-cyclohexanol;[15] 3-methyl-1,3-butanediol was obtained by methanolysis of 1-acetoxy-3-(acetoxymethoxy)-3-methylbutane.[16]

1,1-Diethoxy-2-iodoethane. A solution of 342 g (1.52 mol) of sodium iodide and 150 g (0.761 mol) of 1,1-diethoxy-2-bromoethane in 1.5 L of acetone was heated at reflux for 5 d. The acetone was removed by rotary evaporation, and the residue was taken up in 250 mL of diethyl ether, washed with 10% aqueous sodium thiosulfate, water, and brine, dried ($MgSO_4$), and concentrated to afford 156 g (84% yield) of 1,1-diethoxy-2-iodoethane as a clear oil: bp 71−73 °C (15 mm) [lit.[17] bp 115 °C (50 mm)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 6H, J = 7.1 Hz), 3.15 (d, 2H, J = 5.5 Hz), 3.54−3.49 (m, 2H), 3.66−3.58 (m, 2H), 4.56 (t, 1H, J = 5.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.7, 15.3, 62.3, 101.9.

***cis*-2-(Iodomethyl)-4-methyl-1,3-dioxane (1).** A solution of 21.4 g (0.237 mol) of 1,3-butanediol and 50.0 g (0.205 mol) of 1,1-diethoxy-2-iodoethane in 90 mL of cyclohexane containing a catalytic quantity of *p*-toluenesulfonic acid was stirred at room temperature for 1 h under an atmosphere of argon. The solution was then distilled until the overhead temperature rose above 65 °C (cyclohexane/ethanol azeotrope; bp = 65 °C). The reaction mixture was allowed to cool, and solid, anhydrous potassium carbonate (ca. 1 g) was added, The mixture was taken up in ether, washed with 10% aqueous sodium thiosulfate, water, and brine, dried ($MgSO_4$), and distilled in the dark from a small quantity (ca. 1 g) of solid sodium thiosulfate to afford 34.4 g (69% yield) of the title compound: bp 68−69 °C (0.6 mm); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (d, 3H, J = 6.2 Hz), 1.42−1.35 (m, 1H), 1.71−1.57 (m, 1H), 3.16 (apparent d, 2H, J = 4.6 Hz), 3.84−3.72 (m, 2H), 4.13−4.08 (m, 1H), 4.53 (apparent t, 1H, J = 4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.3, 21.7, 32.7, 66.9, 73.3, 100.0; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_6H_{12}IO_2$ 242.9882, found 242.9875. Anal. Calcd for $C_6H_{11}IO_2$: C, 29.77; H, 4.58. Found: C, 29.42; H, 4.84.

2-(Iodomethyl)-4,4-dimethyl-1,3-dioxane (2). Following the procedure described above, the reaction of 15.1 g (145 mmol) of 3-methyl-1,3-butanediol with 30.6 g (125 mmol) of 1,1-diethoxy-2-iodoethane in 45 mL of cyclohexane containing a catalytic quantity of *p*-toluenesulfonic acid afforded, after distillation, 21.0 g (66% yield) of the title iodide: bp 74−75 °C (2.6 mm); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34−1.24 {overlapping patterns, 7H, i.e., 1.34−1.24 (m, 1H), 1.26 (s, 3H), 1.29 (s, 3H)}, 1.89−1.82 (m, 1H), 3.13 (d, 2H, J = 4.4 Hz), 4.00−3.86 (m, 2H), 4.71 (t, 1H, J = 4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.6, 21.8, 31.6, 35.6, 63.4, 72.6, 93.9; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_7H_{14}IO_2$ 257.0033, found 257.0043.

***cis*-4-*tert*-Butyl-2-(iodomethyl)-1,3-dioxane (3).** Following the procedure described above, the reaction of 11.61 g (87.8 mmol) of 4,4-dimethyl-1,3-pentanediol with 19.48 g (79.8 mmol) of 1,1-diethoxy-2-iodoethane in 50 mL of cyclohexane containing a catalytic quantity of *p*-toluenesulfonic acid afforded, after distillation, 12.5 g (55% yield) of the title iodide: bp 75−76 °C (0.7 mm); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (s, 9H), 1.32−1.27 (m, 1H), 1.76−1.62 (m, 1H), 3.16 (d, 2H, J = 4.5 Hz), 3.26 (apparent dd, 1H, J = 2.2 Hz, J = 11.3 Hz), 3.77−3.68 (m, 1H), 4.14 (apparent dd, 1H, J = 4.5 Hz, J = 11.3 Hz), 4.48 (t, 1H, J = 4.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.8, 25.3, 25.7, 34.1, 67.1, 84.6, 99.7; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_9H_{18}IO_2$ 285.0351, found 285.0376.

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***t*-2-Iodomethyl-(*r*-4a, *t*-8a)-1,3-dioxadecahydronaphthalene (4).** Following the procedure described above, the reaction of 4.94 g (18.1 mmol) of *trans*-2-(hydroxymethyl)cyclohexanol with 4.02 g (16.5 mmol) of 1,1-diethoxy-2-iodoethane in 30 mL of cyclohexane containing a catalytic quantity of *p*-toluenesulfonic acid afforded, after distillation, 1.5 g (33% yield) of the title iodide: mp 34.1−35.4 °C; bp 100−101 °C (0.5 mm); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89−0.79 (m, 1H), 1.91−1.21 (m, 8H), 3.41−3.16 {overlapping patterns, 4H, i.e., 3.38 (t, 1H, J = 11.0 Hz), 3.30−3.24 (m, 1H), 3.17 (d, 2H, J = 4.5 Hz)}, 3.93 (dd, 1H, J = 4.4 Hz, J = 11.1 Hz), 4.57 (t, 1H, J = 4.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 5.2, 24.7, 25.1, 26.0, 31.5, 40.7, 71.9, 81.7, 100.1; HRMS-ESI (m/z) $[M + H]^+$ calcd for $C_9H_{16}IO_2$ 283.0190, found 283.0197. Anal. Calcd for $C_9H_{15}IO_2$: C, 38.32; H, 5.36. Found: C, 38.71; H, 5.50.

Fragmentation of the Organolithium Derived from *cis*-2-(Iodomethyl)-4-methyl-1,3-dioxane (1). A solution of 0.12 g (0.50 mmol) of **1** in 10 mL of either dry *n*-pentane, diethyl ether, or tetrahydrofuran was cooled to −70 °C under an atmosphere of argon, and either 2.2 molar equiv of *t*-BuLi in pentane or 1.0 molar equiv of *n*-BuLi in hexane was added. The solution was stirred at −70 °C for 15 min, and water was added. The reaction mixture was allowed to warm to room temperature, washed with brine, and dried ($MgSO_4$). GC analysis [5% diphenyl/95% dimethylpolysiloxane, 25 m × 0.20 mm × 0.33 μm; initial temperature of 100 °C for 10 min, 5 °C/min temperature ramp to 240 °C, final time of 15 min] revealed that the reactions produced 4-vinyloxy-2-butanol (short retention time, minor isomer) and 3-vinyloxy-1-butanol[18] (long retention time, major isomer). The product compositions and isolated yields are summarized in Table 1. Structural assignments were made on the basis of the following spectroscopic properties: ^{1}H NMR (300 MHz, DMSO-d_6) [mixture of isomers] δ 1.09 (d, 3H, J = 6.2 Hz, minor isomer), 1.16 (d, 3H, J = 6.2 Hz, major isomer), 1.79−1.51 (m, 2H), 4.37−3.37 (m, 5H), 4.45 (t, 1H, J = 5.0 Hz, OH of major isomer), 4.49 (d, 1H, J = 4.9 Hz, OH of minor isomer), 6.39 (dd, 1H, J = 6.6 Hz, J = 14.1 Hz, =CH−O of major isomer), 6.49 (dd, 1H, J = 6.9 Hz, J = 14.3 Hz, =CH−O of minor isomer). **3-Vinyloxy-1-butanol** (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.25 (d, 3H, J = 6.2 Hz), 1.83−1.73 (m, 2H), 1.93 (br s, 1H) 3.95−3.65 (m, 3H), 4.02 (dd, 1H, J = 1.6 Hz, J = 6.6 Hz), 4.31 (dd, 1H, J = 1.6 Hz, J = 14.3 Hz), 6.31 (dd, 1H, J = 6.6 Hz, J = 14.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 20.1, 39.1, 60.0, 74.3, 88.9, 150.8; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_6H_{12}O_2$ 116.0837, found 116.0833. **4-Vinyloxy-2-butanol** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.22 (d, 3H, J = 6.2 Hz), 1.83−1.76 (m, 2H), 2.07 (apparent br d, 1H, J = 4.0 Hz), 3.92−3.73 (m, 2H), 4.05−3.95 (m, 1H), 4.02 (dd, 1H, J = 2.0 Hz, J = 6.8 Hz), 4.21 (dd, 1H, J = 2.0 Hz, J = 14.3 Hz), 6.46 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 23.8, 38.1, 66.1, 66.4, 87.1, 151.8; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_6H_{12}O_2$ 116.0837, found 116.0826.

Fragmentation of the Organolithium Derived from 2-(Iodomethyl)-4,4-dimethyl-1,3-dioxane (2). A solution of 0.13 g (0.50 mmol) of **2** in 10 mL of either dry *n*-pentane, diethyl ether, or tetrahydrofuran was cooled to −70 °C under an atmosphere of argon, and either 2.2 molar equiv of *t*-BuLi in pentane or 1.0 molar equiv of *n*-BuLi in heptane was added. The solution was stirred at −70 °C for 15 min, and water was added. The reaction mixture was allowed to warm to room temperature, washed with brine, and dried ($MgSO_4$). GC analysis [5% diphenyl/95% dimethylpolysiloxane, 25 m × 0.20 mm × 0.33 μm; initial temperature of 100 °C for 10 min, 5 °C/min temperature ramp to 240 °C, final time of 15 min] revealed that the reactions produced 2-methyl-4-vinyloxy-2-butanol (short retention time, minor isomer) and 3-methyl-3-vinyloxy-1-butanol (long retention time, major isomer). The product compositions and isolated yields are summarized in Table 1. Structural assignments were made on the basis of the following spectroscopic properties: ^{1}H NMR (300 MHz, DMSO-d_6) [mixture of isomers] δ 1.15 (s, 6H, minor isomer), 1.24 (s, 6H, major isomer), 1.78−1.73 (m, 2H), 4.29−3.29 (m, 4H), 4.33 (s, 1H, OH of minor isomer), 4.37 (t, 1H, J = 5.1 Hz, OH of major isomer), 6.51 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz, =CH−O of minor isomer), 6.58 (dd, 1H, J = 6.3 Hz, J = 13.7 Hz, =CH−O of major isomer). **3-Methyl-3-vinyloxy-1-butanol** (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.24 (s, 6H), 1.82−1.69 (m, 2H), 2.43 (br s, 1H), 3.13 (t, 2H, J = 7.0 Hz), 4.02 (dd, 1H, J = 0.8 Hz, J = 6.2 Hz), 4.36 (dd, 1H, J = 0.8 Hz, J = 13.7 Hz), 6.36 (dd, 1H, J = 6.2 Hz, J = 13.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 26.2, 43.4, 59.3, 78.6, 92.1, 145.6; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_7H_{14}O_2$ 130.0994, found 130.0975. **2-Methyl-4-vinyloxy-2-butanol** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.20 (s, 6H), 1.82−1.69 (m, 2H), 2.32 (br s, 1H), 3.82 (t, 2H, J = 6.4 Hz), 3.96 (dd, 1H, J = 2.1 Hz, J = 6.8 Hz), 4.16 (dd, 1H, J = 2.1 Hz, J = 14.3 Hz), 6.43 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 29.7, 41.6, 65.2, 70.4, 87.2, 151.6; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_7H_{14}O_2$ 130.0994, found 130.0999.

Fragmentation of the Organolithium Derived from *cis*-4-*tert*-Butyl-2-(iodomethyl)-1,3-dioxane (3). A solution of 0.14 g (0.50 mmol) of **3** in 10 mL of either dry *n*-pentane, diethyl ether, or tetrahydrofuran was cooled to −70 °C under an atmosphere of argon, and either 2.2 molar equiv of *t*-BuLi in pentane or 1.0 molar equiv of *n*-BuLi in heptane was added. The solution was stirred at −70 °C for 15 min, and water was added. The reaction mixture was allowed to warm to room temperature, washed with brine, and dried ($MgSO_4$). GC analysis [5% diphenyl/95% dimethylpolysiloxane, 25 m × 0.20 mm, 0.33 μm; initial temperature of 40 °C for 30 min, 1.8 °C/min temperature ramp to 240 °C, final time of 15 min] revealed that the reactions produced 4,4-dimethyl-1-vinyloxy-3-pentanol (short retention time, minor isomer) and 4,4-dimethyl-3-vinyloxy-1-pentanol (long retention time, major isomer). The product compositions and isolated yields are summarized in Table 1 Structural assignments were made on the basis of the following spectroscopic properties: ^{1}H NMR (300 MHz, DMSO-d_6) [mixture of isomers] δ 0.83 (s, 9H, minor isomer), 0.86 (s, 9H, major isomer), 1.76−1.42 (m, 2H), 4.20−3.36 (m, 5H), 4.37 (t, 1H, J = 4.8 Hz, OH of major isomer), 4.43 (d, 1H, J = 4.6 Hz, OH of minor isomer), 6.36 (dd, 1H, J = 6.3 Hz, J = 13.8 Hz, =CH−O of major isomer), 6.48 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz, =CH−O of minor isomer). **4,4-Dimethyl-3-vinyloxy-1-pentanol** (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 0.88 (s, 9H), 1.90−1.53 (m, 2H), 2.30 (br s, 1H), 3.51 (m, 1H), 3.77−3.62 (m, 2H), 3.83 (dd, 1H, J = 1.2 Hz, J = 6.3 Hz), 4.26 (dd, 1H, J = 1.2 Hz, J = 13.9 Hz), 6.30 (dd, 1H, J = 6.3 Hz, J = 13.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 25.7, 30.9, 34.9, 59.9, 86.9, 87.0, 151.8; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_9H_{18}O_2$ 158.1307, found 158.1294. **4,4-Dimethyl-1-vinyloxy-3-pentanol** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 0.87 (s, 9H), 1.90−1.53 (m, 2H), 2.20 (br s, 1H), 3.36 (m, 1H), 3.90−3.80 (m, 2H), 3.97 (dd, 1H, J = 1.8 Hz, J = 6.8 Hz), 4.18 (dd, 1H, J = 1.8 Hz, J = 14.3 Hz), 6.42 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 26.2, 33.3, 35.6, 66.9, 77.5, 86.9, 154.6; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_9H_{18}O_2$ 158.1307, found 158.1330.

Fragmentation of the Organolithium Derived from *t*-2-Iodomethyl-(*r*-4a, *t*-8a)-1,3-dioxadecahydronaphthalene (4). A solution of 70 mg (0.25 mmol) of **4** in 5 mL of either dry *n*-pentane, diethyl ether, or tetrahydrofuran was cooled to −70 °C under an atmosphere of argon, and either 2.2 molar equiv of *t*-BuLi in pentane or 1.0 molar equiv of *n*-BuLi in heptane was added. The solution was stirred at −70 °C for 15 min, and water was added. The reaction mixture was allowed to warm to room temperature, washed with brine, dried ($MgSO_4$), and concentrated. NMR analysis in DMSO revealed that the reactions produced a mixture of *trans*-2-vinyloxy-1-hydroxymethylcyclohexane (major isomer) and *trans*-2-(vinyloxymethyl)cyclohexanol (minor isomer). The product compositions and isolated yields are summarized in Table 1. Structural assignments were made on the basis of the following spectroscopic properties: ^{1}H NMR (300 MHz, DMSO-d_6) [mixture of isomers] δ 1.82−1.13 (m, 9H), 4.22−3.26 (m, 5H), 4.37 (t, 1H, J = 5.3 Hz, OH of major isomer), 4.56 (d, 1H, J = 5.5 Hz, OH of minor isomer), 6.39 (dd, 1H, J = 6.5 Hz, J = 14.0 Hz, =CH−O of major isomer), 6.51 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz, =CH−O of minor isomer). ***trans*-2-**

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Vinyloxy-1-hydroxymethylcyclohexane (major isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.80−0.94 (m, 9H), 3.66−3.20 (m, 3H), 3.81 (apparent d, 1H, J = 6.4 Hz), 4.13 (dd, 1H, J = 0.9 Hz, J = 14.0 Hz), 6.15 (dd, 1H, J = 6.4 Hz, J = 14.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 24.1, 24.8, 27.6, 31.3, 44.9, 64.1, 80.1, 88.2, 150.6; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_9H_{16}O_2$ 156.1150, found 156.1126. ***trans*-2-(Vinyloxymethyl)-cyclohexanol** (minor isomer): ^{1}H NMR (300 MHz, $CDCl_3$, 1 drop of pyridine) δ 1.80−0.94 (m, 9H), 3.66−3.20 (m, 3H), 3.84−3.78 (m, 1H), 4.04 (dd, 1H, J = 1.6 Hz, J = 14.3 Hz), 6.29 (dd, 1H, J = 6.8 Hz, J = 14.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, 1 drop of pyridine) δ 24.4, 24.9, 27.8, 35.0, 44.3, 70.7, 71.9, 86.4, 15.6; GC-HRMS-EI (70 eV) (m/z) M^+ calcd for $C_9H_{16}O_2$ 156.1150, found 156.1149.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00496.

NMR spectra of substituted 2-iodomethyl-1,3-dioxanes and fragmentation products (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: William.Bailey@uconn.edu.

*E-mail: J.Fair@iup.edu.

Notes

The authors declare no competing financial interest.

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