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Diastereoselective carbonyl addition reactions promoted by ytterbium(III) triflate[†]

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Summary — The addition of organolithium and organomagnesium reagents to diverse classes of chiral aldehydes and ketones generally proceeds in high yields and often with excellent diastereoselectivities when the reactions are mediated by ytterbium(III) trifluoromethanesulfonate [ytterbium triflate, $Yb(OTf)_3$]. A variety of functionalized organolithiums and organomagnesiums were examined in conjunction with a similarly diverse series of carbonyl substrates. The results of the $Yb(OTf)_3$-promoted reactions were compared with those obtained without this additive. Although in some cases the advantages of $Yb(OTf)_3$ were evident, in other cases comparable or even better results were obtained with the parent organometallic itself. The $Yb(OTf)_3$-promoted reactions appear particularly effective in achieving non-chelation controlled (Felkin–Anh) addition to alkoxy-substituted aldehydes and ketones.

carbonyl addition / asymmetric induction / organolanthanide

Résumé — Réactions diastéréosélectives d'addition sur les composés carbonyles via le triflate d'ytterbium(III). L'addition de réactifs organolithiés ou organomagnésiés sur diverses classes d'aldéhydes et cétones chirales a lieu en général avec des rendements élevés et souvent avec d'excellentes diastéréosélectivités quand les réactions sont réalisées en présence de trifluorométhanesulfonate d'ytterbium(III) [$Yb(OTf)_3$]. Une variété d'organolithiens et organomagnésiens fonctionnalisés ainsi qu'une variété de dérivés carbonylés ont été examinées. Les résultats des réactions induites avec $Yb(OTf)_3$ ont été comparés à ceux obtenus sans utilisation de $Yb(OTf)_3$. Ainsi dans certains cas les avantages de $Yb(OTf)_3$ paraissent évidents, dans d'autres cas, comparables à ceux obtenus avec l'organométallique apparenté. Les réactions induites par $Yb(OTf)_3$ s'avèrent particulièrement efficaces dans l'addition, sans contrôle chélatant (Felkin–Anh), sur les aldéhydes et les cétones alcoxy substitués.

induction asymétrique / organolanthanide / addition sur les composés carbonyles

Introduction

Carbonyl addition reactions represent perhaps the most fundamental means by which synthetic chemists construct organic molecules. Although in many instances organolithium or organomagnesium reagents are perfectly adequate for the purpose, these nucleophiles often exhibit shortcomings when they are utilized in conjunction with chiral carbonyl substrates, where high diastereoselectivities are required. To remedy this situation a variety of strategies has been employed, including the modification of ligands on organomagnesium reagents [1], the alteration of substituents on directing groups proximate to the carbonyl functionality [1c], and the use of Lewis acids that modify the approach of the nucleophile to the carbonyl [2]. By far the most common approach to achieving high diastereoselectivity, however, is to alter the nature of the organometallic itself [3]. Thus, a variety of diverse organometallics has been utilized to achieve both high yields and high diastereoselectivities in reactions with chiral aldehydes and ketones, most notably organotitaniums and various organolanthanides.

Some time ago we communicated our initial results on the utilization of ytterbium trifluoromethanesulfonate [ytterbium triflate, $Yb(OTf)_3$] as an additive to organolithiums and organomagnesiums to enhance diastereoselectivity in reactions of these organometallics to methyl cyclohexanones, 4-*tert*-butylcyclohexanone, and 2-phenylpropanal [3a]. In this contribution, we describe the use of this protocol in more diverse systems, and compare the efficiency of these reagents with the parent organometallics.

Results and discussion

It is customary to utilize 2-methylcyclohexanone as a platform on which to examine diastereoselectivity, but most often relatively common nucleophilic components

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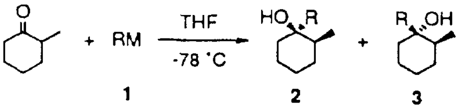
[†] Dedicated with great warmth and respect to Professeur Henri Kagan, whose kindness, creativity, and tranquil leadership in so many areas of chemistry have made him one of his generation's most revered chemists.

* Correspondence and reprints

(methyl, ethyl, and phenyl groups, for example) are utilized in these model systems. Having already performed these standard experiments using the Yb(OTf)$_3$ protocol, we were eager to expand the range of nucleophiles to determine whether or not dramatic improvements could be observed in more diverse systems. Consequently, a variety of oxygenated organolithiums were chosen and their reaction with 2-methylcyclohexanone were examined both in the presence and absence of Yb(OTf)$_3$ (eq 1).


(1)

RM = **1a**: $LiCH_2OCH_3$
1b: $LiCH_2OCH_2Ph$
1c: $LiCH_2OCH_2OCH_3$
1d: 2-furyllithium
1e: 1-ethoxyethenyllithium

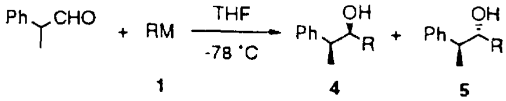
To make a direct comparison between the two protocols, all of the reactions were performed under a standard set of conditions (THF, −78 °C) that we expected to be nearly optimal. Consequently, little effort was made to optimize each individual reaction. Furthermore, the reactions were performed only once or twice for each combination of reagent and substrates, and thus some range or variability in the data was expected (table I).

Table I. Reaction of oxygenated nucleophiles with 2-methylcyclohexanone.

Entry	*Nucleophile (RM)*	*Isolated yield (%)*	*Diastereoselectivity (**2**:**3**)*
1	**1a**	50	95:5
2	**1a**/Yb(OTf)$_3$	39	87:13
3	**1b**	88	98:2
4	**1b**/Yb(OTf)$_3$	70	98:2
5	**1c**	57	96:4
6	**1c**/Yb(OTf)$_3$	60	97:3
7	**1d**	82	74:26
8	**1d**/Yb(OTf)$_3$	90	> 99:< 1
9	**1e**	61	96:4
10	**1e**/Yb(OTf)$_3$	68	97:3

Perhaps surpringly, in most cases both the yields and the diastereoselectivities in these particular reactions were remarkably similar regardless of whether or not Yb(OTf)$_3$ was utilized as an additive. Even in the two cases where distinct differences were detected (entries 2 and 7), one could argue as to whether complete optimization of the reaction would bring about better and perhaps more consistent results between the two protocols.

Similar results were observed in the reaction of the same organometallic nucleophiles with 2-phenylpropanal (eq 2).


(2)

RM = **1a**: $LiCH_2OCH_3$
1b: $LiCH_2OCH_2Ph$
1c: $LiCH_2OCH_2OCH_3$
1d: 2-furyllithium
1e: 1-ethoxyethenyllithium

As outlined in table II, the reactions utilizing the organolithium reagents themselves were typically better in terms of diastereoselectivity than the systems with Yb(OTf)$_3$ as an additive. Reetz and coworkers have noted a similar phenomenon recently in a reexamination of the reaction of organolithiums and organomagnesiums with 2-phenylpropanal [4]. As pointed out in that contribution, because of the high levels of asymmetric induction that can be achieved with organolithiums themselves with 2-phenylpropanal, only diastereoselectivities ⩾ 97:3 with other systems may warrant serious attention.

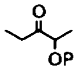
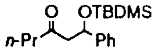
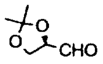
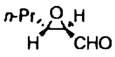
Table II. Reaction of oxygenated nucleophiles with 2-methylpropanal.

Entry	*Nucleophile (RM)*	*Isolated yield (%)*	*Diastereoselectivity (**4**:**5**)*
1	**1a**	72	89:11
2	**1a**/Yb(OTf)$_3$	62	77:23
3	**1b**	87	90:10
4	**1b**/Yb(OTf)$_3$	76	70:30
5	**1c**	40	87:13
6	**1c**/Yb(OTf)$_3$	61	99:1
7	**1d**	80	83:17
8	**1d**/Yb(OTf)$_3$	97	87:13
9	**1e**	85	98:2
10	**1e**/Yb(OTf)$_3$	52	89:11

An examination of the diastereoselectivities achieved in reactions of simple organometallic nucleophiles with oxygenated carbonyl substrates was undertaken in the final aspect of the current study (table III). Here, substantial differences can be noted between reactions performed with and without Yb(OTf)$_3$. In particular, Yb(OTf)$_3$ reverses the diastereoselectivity observed in reactions of α-benzyloxy-substituted ketones (entries 1–4). Whereas methyllithium itself provides modest selectivity for the chelation-controlled carbonyl addition [5], the addition of Yb(OTf)$_3$ affords modest levels of diastereoselectivity for the Felkin–Anh addition product. For substrates that are expected to favor Felkin–Anh addition (eg, **6**, P = TBDMS), the levels of diastereoselectivity that can be attained using Yb(OTf)$_3$ as an additive are quite impressive (entries 5–10). This selectivity carries over to β-substituted ketones as well [6]. Thus, the effect of Yb(OTf)$_3$ appears substantial, as both yields and diastereoselectivities can be improved with this additive (entries 11–14).

Diastereoselectivities in the addition of organometallics to (+)-2,3-*O*-isopropylidene-D-glyceraldehyde have been well studied, although there remains perhaps some controversy concerning the nature and source of the selectivity [7]. For the purposes of this discussion, this makes little difference as the results achieved by

Table III. Reaction of nucleophiles with oxygenated carbonyl substrates.

Entry	*Substrate*	*Nucleophile (RM)*	*Products* *% Isolated yield* *(diastereoselectivity)*
	 **6**		 **7** + **8**
1	P = Bn	MeLi	a 84 (70:30)
2		MeLi/Yb(OTf)$_3$	96 (27:73)
3		BuLi	b 83 (76:24)
4		BuLi/Yb(OTf)$_3$	85 (22:78)
5	P = TBDMS	MeLi	c 75 (11:89)
6		MeLi/Yb(OTf)$_3$	86 (3:97)
7		BuLi	d 83 (4:96)
8		BuLi/Yb(OTf)$_3$	87 (< 1:> 99)
9		vinylmagnesium bromide	e 39 (20:80)
10		vinylmagnesium bromide/Yb(OTf)$_3$	31 (< 1:> 99)
	 **9**		 **10** + **11**
11		MeLi	a 78 (86:14)
12		MeLi/Yb(OTf)$_3$	92 (94:6)
13		BuLi	b 75 (> 99:< 1)
14		BuLi/Yb(OTf)$_3$	85 (> 99:< 1)
	 **12**		 **13** + **14**
15		MeLi	a 60 (68:32)
16		MeLi/Yb(OTf)$_3$	65 (67:33)
17		BuLi	b 76 (79:21)
18		BuLi/Yb(OTf)$_3$	71 (59:41)
19		vinylmagnesium bromide	c 34 (56:44)
20		vinylmagnesium bromide/Yb(OTf)$_3$	36 (54:46)
	 **15**		 **16** + **17**
21		MeLi	a 80 (59:41)
22		MeLi/Yb(OTf)$_3$	82 (74:26)
23		BuLi	b 70 (80:20)
24		BuLi/Yb(OTf)$_3$	85 (65:35)

adding various organometallics to this substrate in the presence and absence of Yb(OTf)$_3$ are nearly indistinguishable. The same may be said for the addition to the epoxy aldehyde **15** [8], wherein quite mixed results were achieved.

Conclusion

The utilization of Yb(OTf)$_3$ as an additive in the diastereoselective addition of organolithiums and organomagnesiums to chiral aldehydes and ketones has been examined. Although in some cases no apparent advantage is gained through its use, there are some classes of substrates for which this protocol appears to be highly beneficial. The present study has revealed, for example, that enhanced selectivities for the Felkin–Anh addition to alkoxy-substituted carbonyl substrates can be achieved utilizing Yb(OTf)$_3$-promoted reactions. This, combined with the fact that diverse nucleophiles can be utilized in the reaction and that enolization is minimized [3a] provides an incentive to test the protocol in other systems where organolithiums and organomagnesiums fail to provide satisfactory results. As reported previously [4], however, it is noted that complete optimization of each individual system may be required to extract meaningful results from such studies.

Experimental section

General procedure

To a stirred solution of Yb(OTf)$_3$ (1.00–1.80 equiv) in THF (10 mL/mmol) under Ar at −78 °C was added the corresponding organolithium compound (1.15–2.00 equiv). After the mixture was stirred for 0.5 h at −78 °C, the desired carbonyl substrate (1.00 equiv) dissolved as a minimum of THF was added dropwise. The solution changed color from purple-red or orange to colorless or pale yellow in almost all cases. After 2.5 h at -78 °C the reaction was hydrolyzed with saturated aqueous NaHCO$_3$ and warmed to room temperature. The organic phase was separated, and the aqueous phase was extracted with Et$_2$O. The combined organic extracts were washed with brine and dried over MgSO$_4$. After removal of solvent the residue was purified by flash chromatography.

• *1-(Methoxymethyl)-2-methylcyclohexanol* ***2a, 3a***

Following the general procedure described above, 2-methylcyclohexanone (0.112 g, 1.00 mmol) was added to a solution of methoxymethyllithium (1.11 equiv) and Yb(OTf)$_3$ (1.11 equiv) in THF. The color of the solution changed from brown to pale orange. Capillary gas chromatographic analysis revealed that the product was generated as an 86.5:13.5 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.8:0.2, hexanes/EtOAc) to provide 0.0546 g (38.5%) of 1-(methoxymethyl)-2-methylcyclohexanol.

IR (neat): 3 495.5, 2 930.1, 2 855.2, 2 357.1, 2 332.3, 1 732.7, 1 650.1, 1 455.3, 1 397.3, 1 273.0, 1 210.8, 1 135.7, 1 115.2, 1 040.5, 990.2, 952.5, 917.1, 663.7 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 3.35 (s, 3H), 3.30 (d, J = 9.0 Hz, 1H), 3.20 (d, J = 9.0 Hz, 1H), 1.87 (s, 1H), 1.22–1.80 (m, 9H), 0.87 (d, J = 6.3 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 79.36, 72.30, 59.24, 36.47, 34.92, 31.85, 30.34, 25.35, 21.40, 15.17.

HRMS calc for C$_9$H$_{18}$O$_2$: 158.1299. Found 158.1292.

LRMS (EI) m/z 158 (3), 137 (10), 113 (100).

• *1-[(Benzyloxy)methyl]-2-methylcyclohexanol* ***2b, 3b***

Following the general procedure described above, 2-methylcyclohexanone (0.112 g, 1.00 mmol) was added to a solution of (benzyloxy)methyllithium (1.30 equiv) and Yb(OTf)$_3$ (1.00 equiv) in THF. The solution changed color from orange to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 97.7:2.3 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.164 g (70%) of 1-[(benzyloxy)methyl]-2-methylcyclohexanol.

IR (neat): 3 478.0, 3 087.5, 3 063.5, 3 029.6, 1 948.5, 1 870.1, 1 807.4, 1 604.0, 1 586.2, 1 496.2, 1 374.5, 1 298.7, 1 273.1, 1 250.6, 1 159.7, 1 028.1, 910.2, 862.0 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.33 (s, 5H), 4.60 (d, J = 12 Hz, 1H), 4.52 (d, J = 12 Hz, 1H), 3.43 (d, J = 8.7 Hz, 1H), 3.33 (d, J = 8.7 Hz, 1H), 1.89 (s, 1H), 1.20–1.90 (m, 9H), 1.03 (d, J = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 138.44, 128.41, 127.58, 127.64, 76.81, 73.44, 72.50, 36.49, 35.14, 30.40, 25.46, 21.48, 15.30.

HRMS calc for C$_{15}$H$_{22}$O$_2$: 234.1744. Found 234.1749.

LRMS (EI) m/z 234 (1.5), 203 (5), 143 (2), 113 (100), 91 (50).

• *1-[(Methoxymethoxy)methyl]-2-methylcyclohexanol* ***2c, 3c***

Following the general procedure described above, 2-methylcyclohexanone (0.0896 g, 0.80 mmol) was added to a solution of (methoxymethoxy)methyllithium (2.00 equiv) and Yb(OTf)$_3$ (1.60 equiv) in THF. The solution changed color from purple-red to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 97:3 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.090 g (60%) of 1-[(methoxymethoxy)methyl]-2-methylcyclohexanol.

IR (neat): 3 493.5, 2 932.2, 2 858.9, 2 854.3, 2 363.1, 2 338.0, 1 734.2, 1 653.2, 1 458.4, 1 398.6, 1 275.1, 1 147.8, 1 111.1, 1 043.6, 993.5, 918.0 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 4.63 (s, 2H), 3.47 (d, J = 11.3 Hz, 1H), 3.40 (d, J = 11.3 Hz, 1H), 3.36 (s, 3H), 1.93 (s, 1H), 1.20–1.80 (m, 9H), 0.89 (d, J = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 97.02, 74.86, 72.18, 55.28, 36.41, 34.81, 30.32, 25.32, 21.39, 15.12.

HRMS calc for C$_{10}$H$_{20}$O$_3$: 188.1412. Found 188.1423.

LRMS (EI) m/z 188 (7), 171 (3.5), 167 (10), 156 (10), 113 (100), 95 (40), 69 (15).

• *1-(2-Furyl)-2-methylcyclohexanol* ***2d, 3d***

Following the general procedure described above, 2-methylcyclohexanone (0.124 g, 1.10 mmol) was added to a solution of 2-furyllithium (1.36 equiv) and Yb(OTf)$_3$ (1.18 equiv) in THF. The solution changed color from bright yellow to pale yellow. Capillary gas chromatographic analysis revealed that only one diastereomer was generated. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.163 g (90%) of 1-(2-furyl)-2-methylcyclohexanol.

IR (neat): 3 482.7, 3 116.9, 2 932.9, 2 858.0, 1 724.5, 1 584.0, 1 545.9, 1 501.5, 1 222.6, 924.6, 860.0 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ 7.30 (s, 1H), 6.31 (d, J = 3.0 Hz, 1H), 6.19 (d, J = 3.0 Hz, 1H), 1.20–2.00 (m, 10H), 0.75 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$): δ 160.89, 140.88, 110.02, 104.02, 73.70, 38.35, 38.55, 29.80, 25.58, 21.31, 15.74.

HRMS calc for C$_{11}$H$_{16}$O$_2$: 180.1150. Found 180.1142.

LRMS (EI) m/z 180 (20), 163 (2), 151 (10), 137 (14), 123 (100), 95 (35), 68 (10).

• *1-(1-Ethoxyethenyl)-2-methylcyclohexanol* ***2e, 3e***

Following the general procedure described above, 2-methylcyclohexanone (0.112 g, 1.00 mmol) was added to a solution of 1-ethoxyethenyllithium (2.00 equiv) and Yb(OTf)$_3$ (1.80 equiv) in THF. The solution changed color from bright yellow to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 97:3 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) to provide 0.1249 g (68%) of 1-(1-ethoxyethenyl)-2-methylcyclohexanol.

IR (neat): 3 475.0, 3 062.0, 3 027.7, 2 961.0, 2 929.0, 2 873.7, 2 356.3, 2 338.9, 1 947.7, 1 716.2, 1 601.9, 1 381.5, 1 494.0, 1 359.0, 1 188.0, 1 019.3 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 4.23 (d, J = 2.1 Hz, 1H), 3.92 (d, J = 2.1 Hz, 1H), 3.71 (m, 2H), 2.15 (s, 1H), 1.20–1.90 (m, 12H), 0.73 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 167.40, 78.82, 75.17, 62.94, 37.39, 36.46, 29.80, 25.94, 21.40, 15.44, 14.38.

HRMS calc for C$_{11}$H$_{20}$O$_2$: 184.1495. Found 184.1490.

LRMS (EI) m/z 184 (50), 155 (15), 137 (20), 113 (90), 95 (100), 81 (20), 69 (40).

- *1-Methoxy-3-phenyl-2-butanol* **4a, 5a**

Following the general procedure described above, 2-phenylpropanal (0.121 g, 0.90 mmol) was added to a solution of methoxymethyllithium (1.11 equiv) and Yb(OTf)$_3$ (1.11 equiv) in THF. The solution changed color from brown to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 76.9:23.1 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.8:0.2, hexanes/EtOAc) to provide 0.1005 g (62%) of 1-methoxy-3-phenyl-2-butanol.

IR (neat): 3 500.0, 3 070.5, 3 028.6, 2 940.4, 2 882.3, 1 950.1, 1 723.0, 1 602.3, 1 582.6, 1 490.2, 1 403.7, 1 378.2, 1 290.3, 1 030.5 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.19–7.31 (m, 5H), 3.82 (m, 1H), 3.30 (s, 3H), 3.16 (m, 2H), 2.80 (m, 1H), 2.45 (s, 1H), 1.38 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 144.03, 128.54, 127.63, 126.55, 75.18, 74.72, 58.88, 43.01, 17.62.

HRMS calc for C$_{11}$H$_{17}$O$_2$: 181.1278. Found 181.1276.

LRMS (EI) m/z 181 (M + 1, 2.5), 135 (10), 117 (10), 106 (100).

- *1-(Benzyloxy)-3-phenyl-2-butanol* **4b, 5b**

Following the general procedure described above, 2-phenylpropanal (0.0537 g, 0.4 mmol) was added to a solution of (benzyloxy)methyllithium (1.25 equiv) and Yb(OTf)$_3$ (0.4 equiv) in THF. The solution changed color from orange to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 70:30 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.778 g (76%) of 1-(benzyloxy)-3-phenyl-2-butanol.

IR (neat): 3 448.2, 3 083.7, 3 061.2, 3 027.8, 2 963.7, 2 906.0, 2 869.6, 2 362.0, 1 948.6, 1 876.2, 1 809.3, 1 733.6, 1 601.7, 1 583.1, 1 542.0, 1 307.9, 1 205.6, 913.2 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.20–7.39 (m, 10H), 4.50 (d, J = 13.2 Hz, 1H), 4.43 (d, J = 13.2 Hz, 1H), 3.88 (m, 1H), 3.32 (m, 2H), 2.87 (m, 1H), 2.60 (s, 1H), 1.41 (d, J = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 144.11, 138.02, 128.56, 128.47, 128.17, 127.79, 74.92, 73.29, 72.86, 43.00, 17.69.

HRMS calc for C$_{17}$H$_{20}$O$_2$: 256.1651. Found 256.1645.

LRMS (EI) m/z 256 (2), 151 (5), 135 (10), 105 (100), 91 (90), 77 (15).

- *1-(Methoxymethoxy)-3-phenyl-2-butanol* **4c, 5c**

Following the general procedure described above, 2-phenylpropanal (0.134 g, 1.00 mmol) was added to a solution of (methoxymethoxy)methyllithium (1.15 equiv) and Yb(OTf)$_3$ (1.00 equiv) in THF. The solution changed color from purple-red to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as a 98.6:1.4 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.1518 g (61%) of 1-(methoxymethoxy)-3-phenyl-2-butanol.

IR (neat): 3 456.0, 3 083.0, 3 060.0, 3 027.0, 2 930.0, 2 883.0, 1 951.0, 1 725.0, 1 601.6, 1 582.3, 1 493.9, 1 294.2, 1 377.5, 1 403.8, 1 036.8 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.20–7.33 (m, 5H), 4.59 (s, 2H), 3.83 (m, 1H), 3.41 (m, 2H), 3.34 (s, 3H), 1.57 (s, 1H), 2.82 (m, 1H), 1.39 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 144.01, 129.11, 128.57, 128.09, 97.05, 74.99, 71.45, 55.38, 42.99, 17.62.

HRMS calc for C$_{12}$H$_{19}$O$_3$: 211.1334. Found 211.1317.

LRMS (EI) m/z 211 (M + 1, 0.5), 192 (1), 150 (7), 135 (10), 118 (10), 105 (100), 91 (20), 73 (25).

- *1-(2-Furyl)-2-phenyl-1-propanol* **4d, 5d**

Following the general procedure described above, 2-phenylpropanal (0.134 g, 1.00 mmol) was added to a solution of 2-furyllithium (1.50 equiv) and Yb(OTf)$_3$ (1.30 equiv) in THF. The solution changed color from bright yellow to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as an 87:13 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.196 g (97%) of 1-(2-furyl)-2-phenyl-1-propanol.

IR (neat): 3 412.5, 3 063.3, 3 030.5, 2 878.2, 2 968.8, 2 934.0, 1 603.0, 1 495.0, 1 452.6, 1 377.3, 1 230.7, 1 147.8, 1 072.6, 1 008.9, 883.0 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.21–7.35 (m, 6H), 6.28 (d, J = 2.7 Hz, 1H), 6.09 (d, J = 2.7 Hz, 1H), 4.79 (d, J = 6.6 Hz, 1H), 3.32 (dt, J = 6.6, 6.9 Hz, 1H), 2.44 (s, 1H), 1.43 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 155.52, 143.36, 141.51, 128.30, 127.88, 126.58, 110.12, 106.69, 78.87, 44.89, 16.05.

HRMS calc for C$_{13}$H$_{14}$O$_2$: 202.0994. Found 202.0990.

LRMS (EI) m/z 202 (3), 185 (30), 97 (100), 77 (10).

- *1-Ethoxy-4-phenyl-1-penten-3-ol* **4e, 5e**

Following the general procedure described above, 2-phenylpropanal (0.134 g, 1.00 mmol) was added to a solution of 1-ethoxyethenyllithium (2.00 equiv) and Yb(OTf)$_3$ (1.80 equiv) in THF. The solution changed color from bright yellow to pale yellow. Capillary gas chromatographic analysis revealed that the product was generated as an 89:11 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) to provide 0.107 g (52%) of 1-ethoxy-4-phenyl-1-penten-3-ol.

IR (neat): 3 473.0, 3 061.5, 3 027.3, 2 974.0, 2 929.0, 1 947.0, 1 711.0, 1 602.0, 1 494.0, 1 453.0, 1 375.0, 1 360.0, 1 240.0, 1 186.9, 1 119.8, 1 060.6, 1 018.6, 997.0, 964.8 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.22–7.34 (m, 5H), 4.09 (dd, J = 1.8, 6.6 Hz, 1H), 3.99 (d, J = 1.8 Hz, 1H), 3.89 (d, J = 2.4 Hz, 1H), 3.67 (m, 2H), 3.12 (dt, J = 7.2, 6.6 Hz, 1H), 2.18 (d, J = 6.3 Hz, 1H), 1.37 (d, J = 7.2 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 161.69, 144.14, 128.15, 127.95, 126.32, 82.52, 77.80, 62.74, 43.71, 15.70, 14.30.

HRMS calc for C$_{13}$H$_{18}$O$_2$: 206.1402. Found 206.1408.

LRMS (EI) m/z 206 (20), 105 (100), 91 (40), 73 (45).

- *2-Benzyloxy-3-methyl-3-pentanol* **7a, 8a**

Following the general procedure described above, 2-benzyloxy-3-pentanone (0.307 g, 1.60 mmol) was added to a solution of methyllithium (1.13 equiv) and Yb(OTf)$_3$ (1.06 equiv) in THF. The solution remained purple-red in color. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) followed by Kugelrohr distillation to provide 0.3205 g (96.3%) of 2-benzyloxy-3-methyl-3-pentanol. ^{13}C NMR analysis revealed that the product was generated as a 73:27 mixture of diastereomers.

IR (neat): 3 553.9, 3 139.9, 3 051.0, 3 014.9, 2 952.3, 2 903.9, 2 051.5, 1 555.7, 1 485.5, 1 426.0, 1 351.7, 1 233.9, 1 190.5, 1 157.6, 1 070.3, 1 034.3, 1 011.5, 948.2, 883.0, 796.4 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.20–7.40 (m, 5H), 4.68 (d, J = 11.7 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 3.41 (q, J = 6.3 Hz, 1H), 2.30 (s, 1H), 1.25–1.65 (m, 1H), 1.19 (d, $J = 6.3$ Hz, 3H), 1.15 (s, 3H), 0.92 (t, $J = 7.5$ Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 138.70, 128.40, 127.66, 127.61, 81.48, 74.76, 71.37, 28.97, 22.62, 13.46, 7.58.

LRMS (EI) m/z 208 (0.1), 191 (100), 179 (10), 167 (10), 135 (25), 117 (70).

Anal calc for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.88; H, 9.59.

• *2-Benzyloxy-3-ethyl-3-heptanol* **7b, 8b**

Following the general procedure described above, 2-benzyloxy-3-pentanone (0.307 g, 1.60 mmol) was added to a solution of *n*-butyllithium (1.13 equiv) and Yb(OTf)$_3$ (1.06 equiv) in THF. The solution changed color from purple-red to colorless. The product was purified by flash chromatography (silica gel, 7:3, hexanes/dichloromethane) followed by Kugelrohr distillation to provide 0.340 g (85%) of 2-benzyloxy-3-ethyl-3-heptanol. ^{13}C NMR analysis revealed that the product was generated as a 77.5:22.5 mixture of diastereomers.

IR (neat): 3 470.0, 2 956.5, 2 872.1, 2 358.5, 1 725.8, 1 710.4, 1 691.7, 1 658.4, 1 586.2, 1 548.2, 1 529.8, 1 512.7, 1 494.3, 1 453.4, 1 377.4, 1 113.3, 960.2 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 7.30–7.40 (m, 5H), 4.68 (d, $J = 11.4$ Hz, 1H), 4.42 (d, $J = 11.7$ Hz, 1H), 3.48 (q, $J = 6.0$ Hz, 1H), 2.20 (s, 1H), 1.22–1.65 (m, 8H), 1.19 (d, $J = 6.3$ Hz, 3H), 0.80–1.00 (m, 6H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 138.75, 128.37, 127.71, 127.58, 79.12, 75.93, 71.31, 35.03, 26.91, 25.51, 23.48, 14.11, 13.08, 7.53.

LRMS (EI) m/z 250 (0.1), 133 (20), 181 (10), 143 (70), 115 (100).

Anal calc for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 77.14; H, 10.58.

• *2-[(tert-Butyldimethylsilyl)oxy]-3-methyl-3-pentanol* **7c, 8c**

Following the general procedure described above, 2-[(*tert*-butyldimethylsilyl)oxy]-3-pentanone (0.216 g, 1.00 mmol) was added to a solution of methyllithium (1.20 equiv) and Yb(OTf)$_3$ (1.10 equiv) in THF. The solution changed color from purple-red to colorless. Capillary gas chromatographic analysis revealed that the product was generated as a 97.3:2.7 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) followed by Kugelrohr distillation to provide 0.1993 g (85.8%) of 2-[(*tert*-butyldimethylsilyl)oxy]-3-methyl-3-pentanol.

IR (neat): 3 573.7, 2 956.6, 2 935.4, 2 887.0, 2 360.6, 1 464.0, 1 375.3, 1 314.9, 1 254.8, 1 169.6, 1 102.3, 1 057.2, 1 005.7, 963.1, 913.2, 834.2, 666.8 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$) (major diastereomer): δ 3.65 (q, $J = 6.3$ Hz, 1H), 2.26 (s, 1H), 1.40–1.51 (m, 2H), 1.09 (d, $J = 6.0$ Hz, 3H), 1.03 (s, 3H), 0.91 (t, $J = 7.2$ Hz, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) (major diastereomer): δ 74.50, 73.60, 31.10, 25.74, 20.22, 18.02, 17.90, 7.80, −4.13, −5.07.

LRMS (EI) m/z 231 (0.1), 217 (0.3), 201 (0.4), 187 (10), 175 (50), 159 (30), 119 (20), 103 (20), 75 (100).

Anal calc for $C_{12}H_{28}O_2Si$: C, 62.01; H, 12.14. Found: C, 61.97; H, 11.88.

• *2-[(tert-Butyldimethylsilyl)oxy]-3-ethyl-3-heptanol* **7d, 8d**

Following the general procedure described above, 2-[(*tert*-butyldimethylsilyl)oxy]-3-pentanone (0.216 g, 1.00 mmol) was added to a solution of *n*-butyllithium (1.20 equiv) and Yb(OTf)$_3$ (1.10 equiv) in THF. The solution changed color from purple-red to colorless. Capillary gas chromatographic analysis revealed that only one diastereomer was generated. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) followed by Kugelrohr distillation to provide 0.2375 g (86.7%) of 2-[(*tert*-butyldimethylsilyl)oxy]-3-ethyl-3-heptanol.

IR (neat): 3 569.1, 2 861.4, 2 737.7, 2 361.6, 1 920.4, 1 719.9, 1 463.8, 1 377.7, 1 333.4, 1 254.5, 1 217.5, 1 169.0, 1 095.6, 998.5, 952.6, 834.4, 775.9, 669.4 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ 3.69 (q, $J = 6.3$ Hz, 1H), 2.13 (s, 1H), 1.40–1.55 (m, 2H), 1.20–1.38 (m, 4H), 1.08 (d, $J = 6.3$ Hz, 3H), 0.80–0.95 (m, 17H), 0.07 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (75 MHz, CDCl$_3$): δ 75.70, 72.36, 33.05, 28.36, 25.76, 25.38, 23.48, 17.90, 17.51, 13.99, 7.78, −4.11, −5.08.

LRMS (EI) m/z 273 (M − 1, 0.1), 217 (60), 201 (20), 159 (30), 133 (15), 115 (50), 75 (100).

Anal calc for $C_{15}H_{34}O_2Si$: C, 65.63; H, 12.48. Found: C, 65.67; H, 12.14.

• *4-[(tert-Butyldimethylsilyl)oxy]-3-ethyl-1-penten-3-ol* **7e, 8e**

Following the general procedure described above, 2-[(*tert*-butyldimethylsilyl)oxy]-3-pentanone (0.216 g, 1.00 mmol) was added to a solution of vinylmagnesium bromide (1.20 equiv) and Yb(OTf)$_3$ (1.10 equiv) in THF. The solution changed color from purple-red to colorless. Capillary gas chromatographic analysis revealed that only one diastereomer was generated. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) to provide 0.754 g (30.9%) of 2-[(*tert*-butyldimethylsilyl)oxy]-3-ethyl-1-penten-3-ol.

IR (neat): 3 768.4, 3 131.1, 2 907.1, 1 807.2, 1 550.0, 1 430.5, 1 398.6, 1 320.3, 1 221.9, 1 025.9, 950.8, 889.0, 795.7, 729.4, 651.6 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ 5.66 (dd, $J = 10.8$, 17.4 Hz, 1H), 5.26 (dd, $J = 1.8$, 17.4 Hz, 1H), 5.16 (dd, $J = 1.8$, 10.8 Hz, 1H), 3.68 (q, $J = 6.3$ Hz, 1H), 2.28 (s, 1H), 1.48–1.69 (m, 2H), 1.08 (d, $J = 6.3$ Hz, 3H), 0.88 (s, 9H), 0.85 (t, $J = 7.5$ Hz, 3H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (75 MHz, CDCl$_3$): δ 139.22, 114.34, 73.65, 29.81, 25.78, 18.28, 7.58, −4.08, −5.01.

HRMS calc for $C_{13}H_{29}O_2Si$: 245.2860. Found 245.2856.

LRMS (EI) m/z 245 (M + 1, 0.5), 227 (10), 187 (40), 159 (90), 145 (15), 115 (30), 95 (25), 75 (100).

• *1-[(tert-Butyldimethylsilyl)oxy]-3-methyl-1-phenyl-3-hexanol* **10a, 11a**

Following the general procedure described above, 1-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]-3-hexanone (0.306 g, 1.00 mmol) was added to a solution of methyllithium (1.20 equiv) and Yb(OTf)$_3$ (1.10 equiv) in THF. The solution changed color from purple-red to orange. Capillary gas chromatographic analysis revealed that the product was generated as a 93.8:6.2 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) followed by Kugelrohr distillation to provide 0.296 g (91.8%) of 1-[(*tert*-butyldimethylsilyl)oxy]-3-methyl-1-phenyl-3-hexanol.

IR (neat): 3 241.0, 3 049.6, 3 013.5, 2 008.0, 1 484.0, 1 425.8, 1 301.2, 1 222.3, 1 169.7. 1 113.9, 1 016.9, 964.4, 900.5 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 7.20–7.30 (m, 5H), 5.03 (dd, *J* = 2.4, 11.1 Hz, 1H), 4.34 (s, 1H), 2.01 (m, 1H), 1.56 (dd, *J* = 2.4, 14.4 Hz, 1H), 1.39 (m, 2H), 1.33 (s, 3H), 0.88 (br s, 14H), 0.08 (s, 3H), −0.39 (s, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 144.84, 128.36, 127.68, 126.32, 74.72, 72.25, 49.74, 46.48, 25.76, 25.66, 17.76, 16.76, 14.61, −4.19, −5.08.

LRMS (EI) *m/z* 322 (0.5), 221 (50), 181 (100), 161 (30), 147 (30), 131 (30).

Anal calc for $\mathrm{C_{19}H_{34}O_2Si}$: C, 70.75; H, 10.62. Found: C, 70.44; H, 10.56.

- *4-{2-[(tert-Butyldimethylsilyl)oxy]-2-phenylethyl}-4-octanol* **10b, 11b**

Following the general procedure described above, 1-phenyl-1-[(*tert*-butyldimethylsilyl)oxy]-3-hexanone (0.306 g, 1.00 mmol) was added to a solution of *n*-butyllithium (1.20 equiv) and $\mathrm{Yb(OTf)_3}$ (1.10 equiv) in THF. The solution changed color from purple-red to colorless. Capillary gas chromatographic analysis revealed that only one diastereomer was generated. The product was purified by flash chromatography (silica gel, 9.5:0.5, hexanes/EtOAc) followed by Kugelrohr distillation to provide 0.3094 g (85%) of 4-{2-[(*tert*-butyldimethylsilyl)oxy]-2-phenylethyl}-4-octanol.

IR (neat): 3 521.4, 3 064.2, 3 028.4, 2 361.5, 1 715.7, 1 603.7, 1 493.8, 1 405.9, 1 390.5, 1 362.1, 1 198.9, 1 139.8, 1 026.2, 1 004.3, 970.8, 755.1, 666.0, 638.6 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): δ 7.20–7.30 (m, 5H), 4.99 (dd, *J* = 2.4, 11.1 Hz, 1H), 4.19 (s, 1H), 1.98 (m, 1H), 1.50–1.80 (m, 3H), 1.20–1.50 (m, 6H), 0.97 (t, *J* = 6.6 Hz, 3H), 0.88 (br s, 14H), 0.08 (s, 3H), −0.38 (s, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): δ 144.97, 128.36, 127.67, 126.26, 74.40, 74.16, 48.03, 42.48, 37.78, 26.44, 23.44, 17.77, 16.36, 14.62, 14.13, −4.18, −5.06.

LRMS (EI) *m/z* 364 (0.2), 307 (20), 249 (50), 221 (100), 203 (90), 182 (95), 163 (60), 145 (70), 129 (95).

Anal calc for $\mathrm{C_{22}H_{39}O_2Si}$: C, 72.67; H, 10.81. Found: C, 72.75; H, 11.02.

- *2,3-O-Isopropylidene-1-methylglycerol* **13a, 14a**

Following the general procedure described above, (+)-2,3-*O*-isopropylidene-D-glyceraldehyde (0.246 g, 1.28 mmol) was added to a solution of methyllithium (1.11 equiv) and $\mathrm{Yb(OTf)_3}$ (1.05 equiv) in THF. The solution remained purple-red in color. Capillary gas chromatographic analysis revealed that the product was generated as a 66.6:33.4 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 1:1, hexanes/EtOAc) to provide 0.1803 g (65%) of 2,3-*O*-isopropylidene-1-methylglycerol.

IR (neat): 3 400.0, 3 067.5, 2 958.8, 2 436.7, 1 816.8, 1 542.1, 1 413.4, 1 321.8, 1 237.5, 1 184.2, 1 129.7, 902.6, 773.1 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 3.75–4.00 (m, 3H), 3.62 (m, 1H), 2.54 (s, 1H), 1.37 (s, 3H), 1.30 (s, 3H), 1.10 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 109.08, 79.43, 66.87, 64.73, 26.35, 25.08, 18.36.

HRMS calc for $\mathrm{C_7H_{15}O_3}$: 147.0909. Found 147.0911.

LRMS (CI) *m/z* 147 (M + 1, 10), 131 (5), 101 (2), 89 (6), 57 (100).

- *2,3-O-Isopropylidene-1-butylglycerol* **13b, 14b**

Following the general procedure described above, (+)-2,3-*O*-isopropylidene-D-glyceraldehyde (0.166 g, 1.28 mmol) was added to a solution of *n*-butyllithium (1.17 equiv) and $\mathrm{Yb(OTf)_3}$ (1.09 equiv) in THF. The solution changed color from purple-red to colorless. Capillary gas chromatographic analysis revealed that the product was generated as a 59.2:40.8 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 1:1, hexanes/EtOAc) to provide 0.1711 g (71.3%) of 2,3-*O*-isopropylidene-1-butylglycerol.

IR (neat): 3 455.8, 2 984.0, 2 932.7, 2 872.6, 2 359.4, 1 645.8, 1 460.3, 1 375.6, 1 252.5, 1 215.4, 1 157.3, 1 066.4, 913.1, 854.7, 794.2, 731.7 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 3.80–4.00 (m, 3H), 3.60–3.70 (m, 1H), 2.42 (s, 1H), 1.36 (s, 3H), 1.30 (s, 3H), 1.20–1.50 (m, 6H), 0.84 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 108.86, 78.68, 70.63, 64.63, 32.35, 27.80, 26.36, 25.19, 22.54, 13.86.

HRMS calc for $\mathrm{C_{10}O_3H_{21}}$: 189.1412. Found 189.1490.

LRMS (CI) *m/z* 189 (M + 1, 0.4), 173 (40), 131 (10), 113 (15), 101 (100), 85 (10), 73 (20).

- *2,3-O-Isopropylidene-1-ethenylglycerol* **13c, 14c**

Following the general procedure above, (+)-2,3-*O*-isopropylidene-D-glyceraldehyde (0.208 g, 1.60 mmol) was added to a solution of vinylmagnesium bromide (1.13 equiv) and $\mathrm{Yb(OTf)_3}$ (1.06 equiv) in THF. The solution changed color from purple-red to pale yellow. The product was purified by flash chromatography (silica gel, 1:1, hexanes/EtOAc) to provide 0.091 g (36%) of 2,3-*O*-isopropylidene-1-ethenylglycerol. ^{13}C NMR analysis revealed that the product was generated as a 54:46 mixture of diastereomers.

IR (neat): 3 450.0, 3 052.0, 2 959.7, 2 916.4, 2 763.4, 1 664.6, 1 589.5, 1 497.5, 1 443.0, 1 347.8, 1 181.7, 1 118.4, 1 011.2, 956.6, 893.3, 810.8, 766.6 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 5.70–5.88 (m, 1H), 5.36 (dd, *J* = 1.2, 17.4 Hz, 1H), 5.22 (dd, *J* = 1.5, 10.5 Hz, 1H), 3.70–4.30 (m, 4H), 2.50 (s, 1H), 1.42 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 135.87, 116.93, 109.43, 78.05, 71.87, 64.78, 26.34, 25.04.

HRMS calc for $\mathrm{C_8H_{14}O_3}$: 158.0943. Found 158.0936.

LRMS (CI) *m/z* 159 (M + 1, 30), 131 (40), 101 (100).

- *trans-3,4-Epoxy-2-heptanol* **16a, 17a**

Following the general procedure described above, *trans*-2,3-epoxyhexanal (0.098 g, 1.00 mmol) was added to a solution of methyllithium (1.20 equiv) and $\mathrm{Yb(OTf)_3}$ (1.10 equiv) in THF. The solution changed color from purple-red to orange. Capillary gas chromatographic analysis revealed that the product was generated as a 73.5:26.3 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 8:2, hexanes/EtOAc) to provide 0.1066 g (82%) of *trans*-3,4-epoxy-2-heptanol.

IR (neat): 3 700.0, 3 420.0, 2 963.9, 2 932.9, 2 874.1, 2 358.5, 1 723.5, 1 460.3, 1 378.5, 1 281.5, 1 147.9, 1 101.6, 1 069.2, 1 009.0, 944.6, 906.7, 879.2, 766.3 cm^{-1}.

^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 3.55–3.90 (m, 1H), 3.50–3.60 (m, 1H), 2.64–2.71 (tdd, *J* = 2.7, 2.1, 5.1 Hz, 1H), 2.18 (s, 1H), 1.30–1.60 (m, 4H), 1.18 (d, *J* = 6.3 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$) (major diastereomer): δ 67.17, 61.16, 54.35, 33.06, 18.74, 18.19, 13.29.

HRMS calc for $\mathrm{C_7H_{15}O_2}$: 131.1072. Found 131.1084.

LRMS (EI) *m/z* 131 (M + 1, 10), 113 (100), 95 (30), 87 (15), 75 (20).

- *trans-6,7-Epoxy-5-decanol* **16b, 17b**

Following the general procedure described above, *trans*-2,3-epoxyhexanal (0.074 g, 0.75 mmol) was added to a solution of *n*-butyllithium (1.20 equiv) and $\mathrm{Yb(OTf)_3}$

(1.11 equiv) in THF. The solution changed color from purple-red to orange. Capillary gas chromatographic analysis revealed that the product was generated as a 65.3:34.7 mixture of diastereomers. The product was purified by flash chromatography (silica gel, 9:1, hexanes/EtOAc) to provide 0.1095 g (84.9%) of *trans*-6,7-epoxy-5-decanol.

IR (neat): 3 734.2, 3 436.0, 2 959.0, 2 932.3, 2 872.9, 2 360.2, 1 716.1, 1 683.9, 1 653.2, 1 636.0, 1 558.1, 1 540.3, 1 507.3, 1 465.8, 1 379.5, 1 270.6, 1 034.3, 908.7, 796.8, 731.8 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (major diastereomer): δ 3.68–3.78 (m, 1H), 3.32–3.42 (m, 1H), 2.66–2.72 (tdd, $J = 2.7$, 2.1, 5.1 Hz, 1H), 2.10 (s, 1H), 1.20–1.60 (m, 10H), 0.75–1.00 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) (major diastereomer): δ 68.02, 60.45, 54.30, 33.09, 32.68, 26.88, 22.14, 18.74, 13.38, 13.30.

HRMS calc for $C_{10}H_{21}O_2$: 173.1542. Found 173.1530.

LRMS (EI) m/z 173 (M + 1, 10), 155 (100), 137 (20), 117 (10), 99 (20), 85 (50), 69 (20), 57 (30).

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