1,4-Di-*O*-*tert*-alkyl-L-threitols as Chiral Auxiliaries in the Asymmetric Nucleophilic Addition of Alkyllithiums to Hydrazones†

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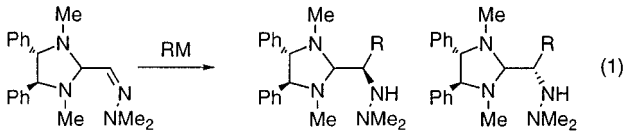
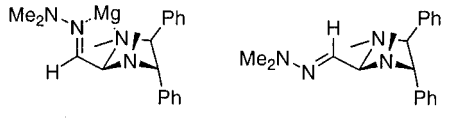
The applications of 1,4-di-*O*-tert-alkyl-L-threitols as chiral auxiliaries in the asymmetric nucleophilic addition of alkyllithiums to hydrazones are investigated. Chiral acetal-hydrazones **9**, obtained from the chiral acetals **8** by ozonolysis followed by treatment with dimethylhydrazine, are allowed to react with organolithium reagents in toluene at − 78 °C to give **15** with excellent diastereoselectivity. The stereochemical assignments were based on the X-ray crystal structure of **17a**. The absolute configuration at C_2 of the major isomer of the adducts **15** was thereby determined to be *S*. The nucleophile thus attacked from the *si* face of the C=N moiety. The effect of solvent on the diastereoselectivity of the reactions of **9** with organolithium reagents is reported. Polar aprotic solvent shows poor diastereoselectivity, and the diastereoselectivity is reversed when the reaction is carried out in THF. Reaction of *dl*-**14** with methyllithium has been studied for comparison purposes and the reaction shows the opposite selectivity. Chelation intermediates **18** and **26** are proposed for these reactions to account for the observed stereoselectivities.

Chiral amines, as a class of compounds, exhibit a variety of biological activities and have served as useful reactive intermediates in organic synthesis.[1] The reductions of ketimines and nucleophilic additions to aldimines in a chiral environment provide a useful entry to the corresponding asymmetric amines.[3] To this end, there has been increasing use of chiral hydrazones as precursors of chiral amines.[4−6] For example, reactions of **1** with Grignard reagents lead to **2** as the major product (eq 1).[5] The chelation intermediate **4** has been suggested to be responsible for the selectivity. In contrast, **3** is obtained predominantly when an organolithium reagent is employed as the alkylating agent. Presumably, the latter reaction proceeds by nucleophilic attack from the *si* face of the nonchelative imine **5**.



1 **2** **3**



4 **5**

We have recently reported a convenient synthesis of tunable chiral C_2-diols **7** derived from L-threitols **6** (eq 2).[11−13] Excellent diastereoselectivities have been found in the Simmons−Smith cyclopropanation[13] and in ring openings of acetals[11a] using these tunable chiral auxiliaries. The alkoxy side chain in **7** may serve either as a

† Dedicated to Professor N. C. Yang on the occasion of his 70th birthday.

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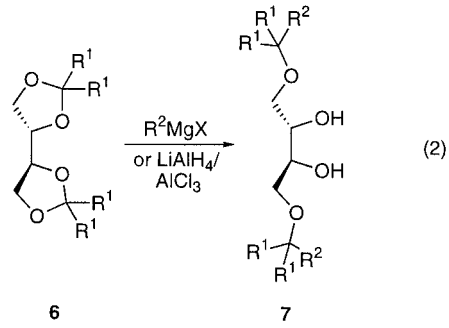
Table 1. Synthesis of Hydrazone 9

R^1	R^2	**8** (%yield)	**9** (%yield)
H	H	**a** (90)	**a** (88)
Me	H	**b** (86)	**b** (92)
i-Pr	H	**c** (83)	**c** (90)
H	Me	**d** (81)	**d** (75)
Me	Me	**e** (85)	**e** (70)
i-Pr	Me	**f** (85)	**f** (88)

bulky substituent or as an additional auxiliary ligand

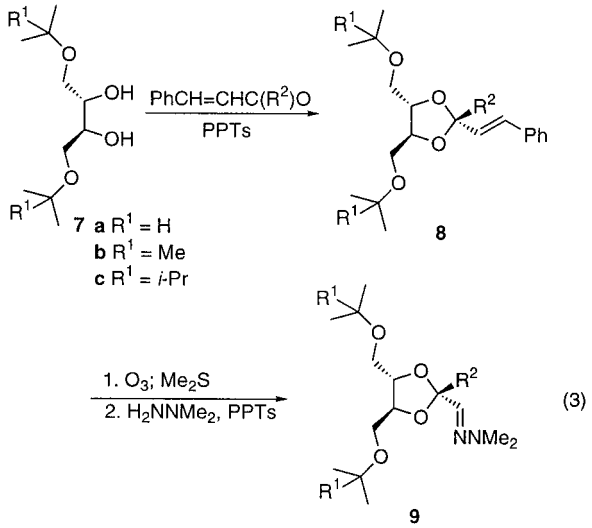


6 7 (2)

during the formation of a chelating complex with a metal catalyst in such a way that the stereoselectivity of these reactions is enhanced. In this paper, we wish to report the details of the use of these chiral diol auxiliaries in the asymmetric nucleophilic addition of organolithium reagents to hydrazones.

Results

Synthesis of 9. Acid-catalyzed reaction of chiral diol **7** with an α,β-unsaturated carbonyl compound (R^2 = H or Me) gave the corresponding acetal **8a** or ketal **8b**.[13] Ozonolysis[15] of **8** followed by treatment with dimethylhydrazine afforded acetal-hydrazones **9** in good yield (eq 3). The results are tabulated in Table 1. Reference



(3)

compounds **12**[4,16] and **14** were prepared following similar

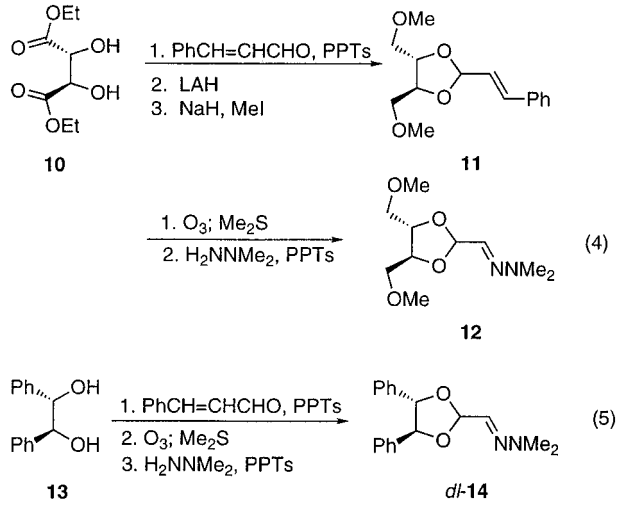
Table 2. Reactions of 9b (R^1 = Me, R^2 = H) with R^3Li under Different Conditions

R^3	temp (reaction time)	2*S*/2*R*
Me	25 °C (12 h)	55/45
	−25 °C (12 h)	76/24
	−78 °C (4 h) then 25 °C (8 h)	88/12
	−78 °C (10 h)	95/5
n-Bu	−15 °C (10 h)	71/29
	−78 °C (10 h)	92/8

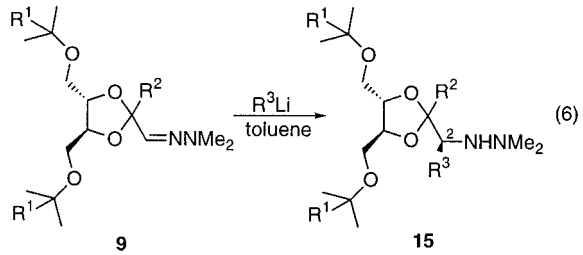
Table 3. Reaction of Organolithium Reagents with 9 in Toluene at −78 °C

entry	**9**	R^1	R^2	R^3	**15** (%yield)	2*S*/2*R*
1	**a**	H	H	Me	**a** (88)	91:9
2	**a**	H	H	*n*-Bu	**b** (75)	89:11
3	**a**	H	H	Ph	**c** (71)	98:2
4	**b**	Me	H	Me	**d** (90)	95:5
5	**b**	Me	H	*n*-Bu	**e** (83)	92:8
6	**b**	Me	H	Ph	**f** (85)	98:2
7	**c**	*i*-Pr	H	Me	**g** (86)	91:9
8	**c**	*i*-Pr	H	*n*-Bu	**h** (73)	92:8
9	**c**	*i*-Pr	H	Ph	**i** (70)	98:2
10	**d**	H	Me	Me	**j** (84)	>99:1
11	**d**	H	Me	*n*-Bu	**k** (68)	98:2
12	**e**	Me	Me	Me	**l** (82)	>99:1
13	**e**	Me	Me	*n*-Bu	**m**(70)	98:2

procedures (eqs 4 and 5).



Nucleophilic Addition to 9. In the beginning of this investigation, we screened the conditions for the nucleophilic addition of alkyllithium to **9** to form **15** (eq 6).



Reaction at low temperature was essential to achieve

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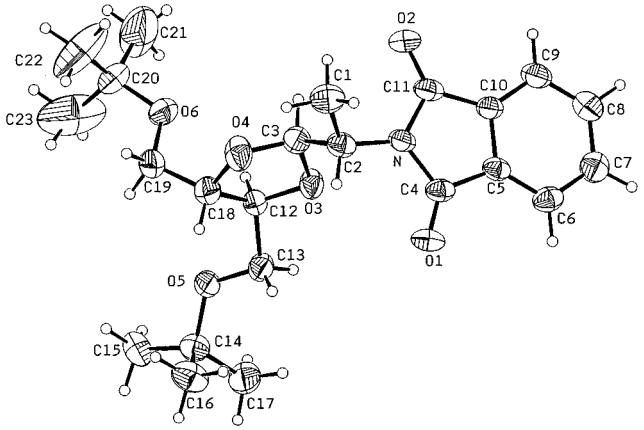
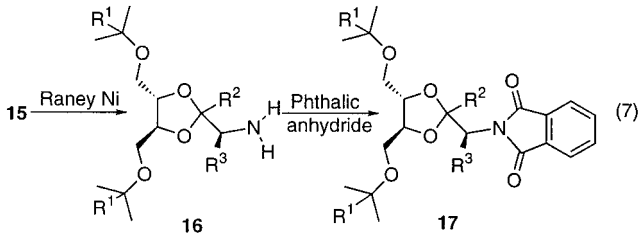


Figure 1. ORTEP of (2*S*)-**17a**. Thermal ellipsoids are shown in 30% probability.

Table 4. Conversion of 15 to Phthalimide 17

16	R^1	R^2	R^3	**17** (%yield)
d	Me	H	Me	**a** (91)
e	Me	H	*n*-Bu	**b** (85)
k	H	Me	*n*-Bu	**c** (93)
l	Me	Me	Me	**d** (82)
m	Me	Me	*n*-Bu	**e** (85)

high diatereoselectivity (Table 2). Table 3 summarizes representative examples of the nucleophilic addition of organolithium reagents to **9**. The diastereomeric ratio was determined by ^{1}H NMR spectroscopy of **15**. The signal for the proton at C_2 of the 2*S*-isomer appeared at a slightly higher field ($\Delta\delta \sim 0.02-0.04$) than that of the corresponding 2*R*-isomer.[17] Treatment of the major stereoisomers (2*S*)-**15** with Raney nickel followed by phthalic anhydride yielded the corresponding phthalimides (2*S*)-**17** (eq 7) The results are outlined in Table 4.



The X-ray structure of (2*S*)-**17a** is shown in Figure 1 and the absolute configuration at C_2 of the major isomer of the adducts **15** was thereby determined.

Discussion

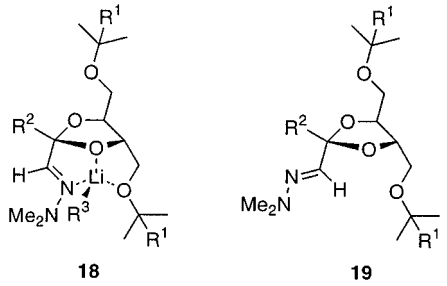
As can be seen from Table 3, good to excellent dastereoselectivities were obtained from the reaction of **9** with organolithium reagents in toluene at −78 °C. Nucleophilic addition occurred preferentially from the *si* face of the hydrazone moiety in **9**. Two possible conformers **18** and **19** are proposed to rationalize the observed stereoselectivity. In **18**, lithium can coordinate to the imino nitrogen atom as well as to the two oxygen atoms to form a chelation complex. Then direct transfer of R^3 anion from lithium may occur stereoselectively from the *si* face of the C=N moiety. Similar intermediate has been suggested in the $CeCl_3$-mediated nucleophilic addition of chiral oximes.[14] Alternatively, conformers **19** and **5**[5] are similar and the nucleophilic attack may thus occur from the less hindered *si* face of the imine moiety. To differentiate these two possibilities, an investigation of the solvent effect on the reaction of **9** with organolithium reagents have been carried out.

(17) For the purpose of simplification, the numbering used throughout text is based on the numbering for the corresponding unprotected 2-aminoalkanals. Hence, the postion of attachment the amino or the hydrazino group in **15** is considered as C_2. The nomenclature for **15** should be 4,5-Bis(alkoxymethyl)-2-[1-(N′,N′-dimethylhydrazino)alkyl]-dioxolane.

Table 5. Solvent Effect on the Diastereoselectivity of the Addition of RLi to 9 at −78 °C

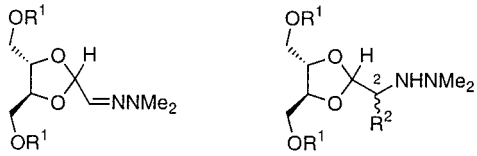
entry	substrate	RLi	solvent	product (2*S*/2*R*)
14	**9a**	n-BuLi	ether	**15b** (76/24)
15		n-BuLi	THF	**15b** (31/69)
16		PhLi	THF	**15c** (33/67)
17	**9b**	n-BuLi	ether	**15e** (83/17)
18		n-BuLi	THF	**15e** (35/65)
19		PhLi	THF	**15f** (37/63)
20	**9c**	n-BuLi	ether	**15h** (60/40)
21		n-BuLi	THF	**15h** (32/68)
22	**20a**	MeLi	ether	**21a** (80/20)[a]
23		n-BuLi	ether	**21b** (55/45)[a]
24	**20b**	n-BuLi	toluene	**21c** (78/22)
25		n-BuLi	THF	**21d** (36/64)

[a] Reference 4.



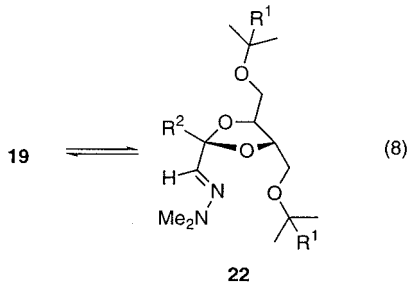
Solvent Effect. Organolithium compounds are known to form complexes with the oxygen donor solvents. Accordingly, the stability of the chelation complex **18** in a nonpolar hydrocarbon solvent and in a polar aprotic solvent would be quite different. In other words, if intermediate **18** is responsible for the formation of **15**, the selectivity might be changed when the reaction is carried out in a polar solvent. Thus, the effect of solvent on the diastereoselectivity of the reactions of **9** with organolithium reagents is summarized in Table 5.

It is interesting to note that the reactions of **20a** with alkyllithium in ether yield **21a** and **21b** with poor selectivity (entries 22 and 23).[4] The reactions of related methoxy derivative **20b** with *n*-BuLi at −78 °C in toluene as well as in THF were also examined (entries 24 and 25). These reactions were much less selective than those with a bulky alkoxy substituent in the chiral auxiliary under the same conditions (entry 24, cf Table 3).

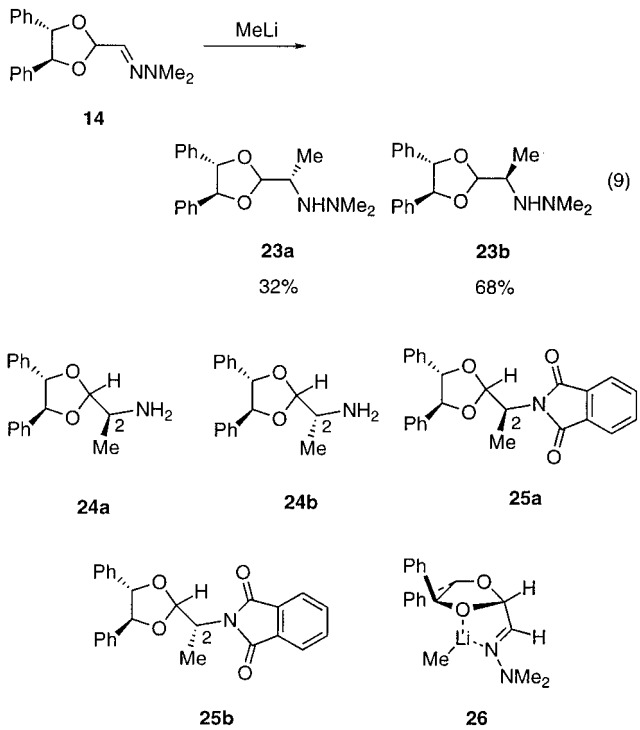


As is evident from Table 5, the diastereoselectivity was reversed when the reaction was carried out in THF as

opposed to diethyl ether. Furthermore, when **9b** was treated with MeLi in toluene in the presence of 2 equiv of TMEDA, a 33/67 (2*S*/2*R*) diastereomeric mixture of **15d** was obtained. Again, this selectivity is opposite to that obtained from the same reaction in the absence of an amine ligand (entry 4, Table 3). Both THF and TMEDA are good donor ligands for organolithium compounds. The oxygen atoms of **9** may be less competitive in the accommodation of lithium to form intermediate **18** when the reaction is carried out in THF or in the presence of such a chelating amine. There might exist a rapid conformational equilibrium between **19** and **22** (eq 8) making the nucleophilic addition less selective.



Reaction of *dl*-14 with MeLi. To show that **18** is involved in the overall asymmetric nucleophilic addition to **9**, we examined the reaction of *dl*-**14** with methyllithium (eq 9). The hydrazines **23** were converted to **25** in a manner similar to that described in eq 7. The X-ray structure of **25b** was determined; hence the relative configuration at C_2 of **23b** is established. The nucleophile may attack preferentially from the *re* face (or *si* face if the other enantiomeric form of **14** is considered) of the carbon−nitrogen double bond of **14**. The chelation intermediate **26** appears to prevail, and the transfer of the alkyl anion may occur from the less hindered face.



It is important to note that the diastereoselectivity shown in eq 9 was opposite to those summarized in Tables 3 and 5. Furthermore, the reaction assisted by stilbene diol moiety **14** was much less selective than those using tunable diols **6** as the chiral auxiliary. By comparing **18** with **26**, it is clear that the alkoxy side chain in **9** plays a pivotal role in directing the diastereoselective addition of organolithium nucleophiles to the hydrazone moiety.

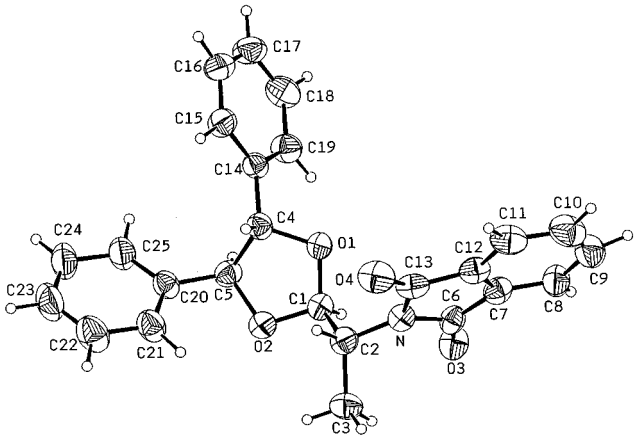


Figure 2. ORTEP of **25b**. Thermal ellipsoids are shown in 30% probability.

Conclusion

In summary, we have demonstrated another useful application of the tunable chiral auxiliary **6** in asymmetric synthesis. Our results show that the bulky alkoxy moiety in **9** may serve as an additional auxiliary ligand to form a chelating complex with the metal catalyst. The stereoselectivity of the nucleophilic addition reactions of alkyllithiums to **9** in aromatic hydrocarbon solvent is enhanced. The present results along with our earlier work[11−13] suggest that the bulky alkoxy group of **8** has a demonstrated role as a chiral auxiliary in asymmetric synthesis. The selectivities in these reactions are higher than those in reactions employing simple methoxy or even benzyloxy auxiliaries **6**. Further applications of **8** are under study.

Experimental Section

General Procedure for the Preparation of 4,5-Bis(alkoxymethyl)-2-(2-phenylethenyl)dioxolane (8). A benzene solution of the α,*β*-unsaturated aldehyde or ketone (1 equiv), **7** (1 equiv), and PPTs (1 mol %) was refluxed overnight, cooled, diluted with ether, washed with saturated $NaHCO_3$ and brine, and dried ($MgSO_4$). The organic solution was evaporated in vacuo to give the residue which was chromatographed on silica gel (5% EtOAc in hexane) to give **8**.

4,5-Bis(isopropoxymethyl)-2-(2-phenylethenyl)dioxolane (8a): 90%: $[\alpha]^{20}_D = +13.3$ (*c* 11.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (d, $J = 6.1$ Hz, 12 H), 3.51−3.70 (m, 6 H), 3.98 (dt, $J = 4.9$, 6.5 Hz, 1 H), 4.05 (dt, $J = 6.4$, 6.5 Hz, 1 H), 5.56 (d, $J = 6.3$ Hz, 1 H), 6.16 (dd, $J = 6.3$, 16.0 Hz, 1 H), 6.74 (d, $J = 16.0$ Hz, 1 H), 7.21−7.34 (m, 3 H), 7.35−7.41 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.9, 22.0, 68.5, 68.8, 72.3, 72.3, 77.4, 78.5, 104.2, 125.4, 126.9, 128.2, 128.5, 135.1, 135.8; HRMS calcd for $C_{19}H_{28}O_4$ 320.1988, found 320.1988.

4,5-Bis(*tert*-butoxymethyl)-2-(2-phenylethenyl)dioxolane (8b): 86%; mp 43−44 °C; $[\alpha]^{27}_D = +15.6$ (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.22 (s, 18 H), 3.46−3.63 (m, 4 H), 3.93 (dt, $J = 5.1$, 6.5 Hz, 1 H), 4.00 (q, $J = 6.5$ Hz, 1 H), 5.55 (d, $J = 6.1$ Hz, 1 H), 6.16 (dd, $J = 6.1$, 16.1 Hz, 1 H), 6.73 (d, $J = 16.1$ Hz, 1 H), 7.18−7.32 (m, 3 H), 7.33−7.40 (m, 2 H);

^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.4, 62.6, 63.0, 73.1, 73.2, 78.4, 79.1, 104.1, 125.6, 126.9, 128.2, 128.4, 134.9, 135.9; HRMS calcd for $C_{21}H_{32}O_4$ 348.2301, found 348.2304.

4,5-Bis(thexyloxymethyl)-2-(2-phenylethenyl)dioxolane (8c): 83%; $[\alpha]^{25}_D$ = +16.8 (*c* 3.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (d, *J* = 6.7 Hz, 3 H), 0.87 (d, *J* = 6.7 Hz, 3 H), 0.88 (d, *J* = 6.7 Hz, 6 H), 1.08 (s, 12 H), 1.78 (septet, *J* = 6.7 Hz, 1 H), 1.79 (septet, *J* = 6.7 Hz, 1 H), 3.41−3.60 (m, 4 H), 3.97 (dt, *J* = 4.6, 6.4 Hz, 1 H), 4.05 (q, *J* = 6.4 Hz, 1 H), 5.55 (d, *J* = 6.2 Hz, 1 H), 6.15 (dd, *J* = 6.2, 15.9 Hz, 1 H), 6.73 (d, *J* = 15.9 Hz, 1 H), 7.21−7.32 (m, 3 H), 7.34−7.40 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.5, 17.5, 22.0, 22.1, 35.7, 35.9, 61.9, 62.3, 77.5, 78.7, 78.9, 104.2, 125.8, 126.9, 128.2, 128.5, 134.9, 136.0; HRMS calcd for $C_{25}H_{40}O_4$ 404.2927, found 404.2922.

4,5-Bis(isopropoxymethyl)-2-methyl-2-(2-phenylethenyl)dioxolane (8d): 81%; $[\alpha]^{24}_D$ = +2.2 (*c* 10.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.13 (d, *J* = 6.1 Hz, 3 H), 1.14 (d, *J* = 6.1 Hz, 3 H), 1.16 (d, *J* = 6.1 Hz, 6 H), 1.56 (s, 3 H), 3.39−3.76 (m, 6 H), 3.90−4.02 (m, 2 H), 6.24 (d, *J* = 16.0 Hz, 1 H), 6.72 (d, *J* = 16.0 Hz, 1 H), 7.15−7.44 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.8, 21.9, 26.3, 68.7, 69.0, 72.0, 72.2, 78.3, 78.4, 108.4, 126.6, 127.7, 128.4, 129.2, 131.3, 136.3; HRMS calcd for $C_{20}H_{30}O_4$ 334.2144, found 334.2147.

4,5-Bis(*tert*-butoxymethyl)-2-methyl-2-(2-phenylethenyl)dioxolane (8e): 85%; $[\alpha]^{27}_D$ = +2.1 (*c* 5.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9 H), 1.18 (s, 9 H), 1.55 (s, 3 H), 3.47−3.58 (m, 4 H), 3.86−3.92 (m, 2 H), 6.25 (d, *J* = 16.1 Hz, 1 H), 6.72 (d, *J* = 16.1, 1 H), 7.18−7.41 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 27.4, 63.0, 63.3, 73.1, 73.2, 78.7, 79.3, 108.4, 126.7, 127.7, 128.5, 129.2, 131.5, 136.4; HRMS calcd for $C_{22}H_{34}O_4$ 362.2457, found 362.2448.

4,5-Bis(thexyloxymethyl)-2-methyl-2-(2-phenylethenyl)-dioxolane (8f): 85%; $[\alpha]^{27}_D$ = +5.7 (*c* 3.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.84 (d, *J* = 6.4 Hz, 6 H), 0.86 (d, *J* = 6.4 Hz, 6 H), 1.06 (s, 6 H), 1.08 (s, 6 H), 1.55 (s, 3 H), 1.77 (septet, *J* = 6.4 Hz, 1 H), 1.78 (septet, *J* = 6.4 Hz, 1 H), 3.37−3.62 (m, 4 H), 3.88−4.01 (m, 2 H), 6.25 (d, *J* = 16.1 Hz, 1 H), 6.73 (d, *J* = 16.1 Hz, 1 H), 7.16−7.44 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.5, 17.5, 21.9, 22.0, 22.0, 22.1, 26.4, 35.3, 35.6, 62.1, 62.4, 78.7, 79.4, 108.2, 126.7, 127.7, 128.5, 129.2, 131.6, 136.5; HRMS calcd for $C_{26}H_{42}O_4$ 418.3083, found 418.3089.

General Procedure for the Preparation of 4,5-Bis(alkoxymethyl)-2-formyldioxolane *N*,*N*-Dimethylhydrazone (9). A methanolic solution (250 mL) of **8** (33 mmol) at −78 °C was bubbled with ozone. The mixture was stirred at −78 °C for 8−12 h and quenched by the dropwise addition of Me_2S (0.10 mol). After the reaction was warmed to room temperature, the solvent was evaporated in vacuo to give the residue to which was added CH_2Cl_2 (50 mL), PPTs (1.0 mmol), and H_2NNMe_2 (70 mmol). The mixture was then stirred at rt for 4−6 h, quenched with K_2CO_3, filtered, evaporated, and purified by chromatography.

4,5-Bis(isopropoxymethyl)-2-formyldioxolane *N*,*N*-Dimethylhydrazone (9a): 88%; $[\alpha]^{27}_D$ = +0.8 (*c* 4.5, $CHCl_3$); IR (neat) ν 1666 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.1 Hz, 6 H), 1.14 (d, *J* = 6.0 Hz, 6 H), 2.81 (s, 6 H), 3.45−3.67 (m, 6 H), 3.90−4.02 (m, 2 H), 5.40 (d, *J* = 6.3 Hz, 1 H), 6.28 (d, *J* = 6.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 21.8, 42.0, 68.3, 68.6, 72.0, 72.1, 77.7, 78.3, 103.6, 128.7; HRMS calcd for $C_{14}H_{28}O_4N_2$ 288.2049, found 288.2049.

4,5-Bis(*tert*-butoxymethyl)-2-formyldioxolane *N*,*N*-Dimethylhydrazone (9b); 95%; $[\alpha]^{27}_D$ = +7.9 (*c* 2.8, $CHCl_3$); IR (neat) ν 1600 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (s, 9 H), 1.16 (s, 9 H), 2.80, (s, 6 H), 3.38−3.57 (m, 4 H), 3.84−3.95 (m, 2 H), 5.39 (d, *J* = 6.0 Hz; 1 H), 6.27 (d, *J* = 6.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.4, 42.2, 62.6, 63.0, 73.1, 73.2, 78.3, 79.0, 103.6, 129.1; HRMS calcd for $C_{16}H_{32}O_4N_2$ 316.2362, found 316.2354.

4,5-Bis(thexyloxymethyl)-2-formyldioxolane *N*,*N*-Dimethylhydrazone (9c): 95%; $[\alpha]^{24}_D$ = +10.9 (*c* 2.9, $CHCl_3$); IR (neat) ν 1601 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.8 Hz, 12 H), 1.03 (s, 6 H), 1.04 (s, 6 H), 1.74 (septet, *J* = 6.8 Hz, 1 H), 1.75 (septet, *J* = 6.8 Hz, 1 H), 2.80 (s, 6 H), 3.37−3.58 (m, 4 H), 3.90−4.02 (m, 2 H), 5.38 (d, *J* = 6.0 Hz, 1 H), 6.27 (d, *J* = 6.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4, 17.5, 21.9, 22.0, 35.7, 35.7, 42.2, 61.7, 62.1, 77.3, 77.4, 78.5, 78.7, 103.6, 129.3; HRMS calcd for $C_{20}H_{40}O_4N_2$ 372.2988, found 372.2995.

4,5-Bis(isopropoxymethyl)-2-formyl-2-methyldioxolane *N*,*N*-Dimethylhydrazone (9d): 75%; $[\alpha]^{27}_D$ = +5.8 (*c* 4.6, $CHCl_3$); IR (neat) ν 1617 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.0 Hz, 12 H), 1.52 (s, 3 H), 2.74 (s, 6 H), 3.46−3.64 (m, 6 H), 3.90−4.01 (m, 2 H), 6.45 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 21.9, 23.7, 42.5, 68.7, 68.8, 72.1, 72.2, 78.3, 78.3, 108.3, 134.5; HRMS calcd for $C_{15}H_{30}O_4N_2$ 302.2206, found 302.2206.

4,5-Bis(*tert*-butoxymethyl)-2-formyl-2-methyldioxolane *N*,*N*-Dimethylhydrazone (9e): 70%; $[\alpha]^{25}_D$ = +9.7 (*c* 0.3, $CHCl_3$); IR (neat) ν 1601 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (s, 18 H), 1.55 (s, 3 H), 2.76, (s, 6 H), 3.42−3.59 (m, 4 H), 3.88−4.00 (m, 2 H), 6.49 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5, 27.3, 42.4, 62.9, 63.1, 72.9, 72.9, 78.5, 78.9, 108.1, 134.6; HRMS calcd for $C_{17}H_{34}O_4N_2$ 330.2519, found 330.2504.

4,5-Bis(thexyloxymethyl)-2-formyl-2-methyldioxolane *N*,*N*-Dimethylhydrazone (9f): 88%; $[\alpha]^{27}_D$ = +7.4 (*c* 2.7, $CHCl_3$); IR (neat) ν 1603 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (d, *J* = 6.8 Hz, 12 H), 1.05 (s, 12 H), 1.53 (s, 3 H), 1.77 (septet, *J* = 6.8 Hz, 2 H), 2.75 (s, 6 H), 3.38−3.57 (m, 4 H), 3.90−4.01 (m, 2 H), 6.47 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.4, 17.5, 21.9, 22.0, 23.7, 35.5, 42.5, 62.0, 62.2, 77.3, 77.4, 78.8, 78.9, 108.1, 135.0; HRMS calcd for $C_{21}H_{42}O_4N_2$ 386.3145, found 386.3145.

***dl*-4,5-Diphenyl-2-formyldioxolane *N*,*N*-Dimethylhydrazone (*dl*-14).** According to the general procedure for the preparation of **9**, a solution of acetal *trans*-4,5-diphenyl-2-(2-phenylethenyl)-1,3-dioxolane[18] (6.56 g, 20 mmol) in MeOH (250 mL) was treated at −78 °C with ozone and was quenched with Me_2S (3.10 g, 0.05 mol) to give the residue, which was allowed to react with H_2NNMe_2 (2.70 g, 45 mmol) in the presence of PPTs (0.25 g, 1.0 mmol) in CH_2Cl_2 (50 mL) to give *dl*-**14** (3.49 g, 59%): mp 94−96 °C; IR (KBr) ν 1595 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.93 (s, 6 H), 4.81 (d, *J* = 7.8 Hz, 1 H), 4.84 (d, *J* = 7.8 Hz, 1 H), 5.89 (d, *J* = 6.2 Hz, 1 H), 6.55 (d, *J* = 6.2 Hz, 1 H), 7.21−7.35 (m, 10 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 42.3, 84.9, 86.5, 104.6, 126.3, 126.8, 128.1, 128.3, 128.4, 128.5, 136.7, 138.2; HRMS calcd for $C_{18}H_{20}O_2N_2$ 296.1525, found 296.1523.

General Procedure for the Addition of Alkyllithium to 9. To a solution of hydrazone (1.0 mmol) in toluene or other solvent (50 mL) at −78 °C was added alkyllithium dropwise via syringe. The reaction mixture was stirred at −78 °C for 4−16 h and quenched with saturated NH_4Cl at −78 °C. The reaction mixture was allowed to warm to rt and filtered through a short column of silica gel. After removal of the solvent in vacuo, the residue was subjected to ^{1}H NMR analysis to determine diastereoselectivity. The crude mixture was then chromatographed on silica gel (10% EtOAc in hexane with 2% Et_3N) to afford purified diastereomeric product **15**.

15a (88%, 2*S*/2*R* = 91/9); (2*S*)-**15a**: $[\alpha]^{24}_D$ = +1.9 (*c* 11.0, $CHCl_3$); IR (neat) ν 3390 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (d, *J* = 6.2 Hz, 3 H), 1.11 (d, *J* = 5.9 Hz, 6 H), 1.13 (d, *J* = 5.9 Hz, 6 H), 1.90−2.10 (br s, 1 H), 2.38 (s, 6 H), 2.95 (dq, *J* = 4.2, 6.2 Hz, 1 H), 3.42−3.65 (m, 6 H), 3.84 (dt, *J* = 5.0, 6.6 Hz, 1 H), 3.95 (dt, *J* = 5.3, 6.6 Hz, 1 H), 4.95 (d, *J* = 4.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 21.9, 22.0, 48.1, 55.2, 68.3, 68.6, 72.1, 72.2, 77.6, 78.6, 105.1; HRMS calcd for $C_{15}H_{32}O_4N_2$ 304.2362, found 304.2355.

15b (75%, 2*S*/2*R* = 89/11); (2*S*)-**15b**: $[\alpha]^{24}_D$ = −11.3 (*c* 5.6, $CHCl_3$); IR (neat) ν 3392 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.7 Hz, 3 H), 1.14 (d, *J* = 5.6 Hz, 6 H), 1.15 (d, *J* = 6.0 Hz, 6 H), 1.25−1.48 (m, 5 H), 1.49−1.64 (m, 1 H), 1.70−1.95 (br s, 1 H), 2.40 (s, 6 H), 2.71−2.86 (m, 1 H), 3.47−3.67 (m, 6 H), 3.86 (dt, *J* = 5.1, 6.5 Hz, 1 H), 3.97 (dt, *J* = 5.2, 6.5 Hz, 1 H), 5.08 (d, *J* = 3.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.9, 22.0, 23.1, 28.2, 28.4, 48.1, 59.6, 68.4, 68.6, 72.2, 72.3, 77.5, 78.6, 104.5; HRMS calcd for $C_{18}H_{38}O_4N_2$ 346.2832, found 346.2858.

(18) Campi, E. M.; Jackson, W. R.; Perlmutter, P.; Tasdelen, E. E. *Aust. J. Chem.* **1993**, *46*, 995.

15c (71%, 2*S*/2*R* = 98/2); (2*S*)-**15c**: $[\alpha]^{26}_D$ = +16.2 (*c* 5.1, $CHCl_3$); IR (neat) ν 3481 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (d, *J* = 6.0 Hz, 6 H), 1.13 (d, *J* = 6.4 Hz, 3 H), 1.14 (d, *J* = 6.4 Hz, 3 H), 1.60−1.95 (br s, 1 H), 2.40 (s, 6 H), 3.36−3.63 (m, 6 H), 3.76 (q, *J* = 5.7 Hz, 1 H), 3.92 (q, *J* = 5.7 Hz, 1 H), 3.98 (d, *J* = 4.4 Hz, 1 H), 5.11 (d, *J* = 4.4 Hz, 1 H), 7.18−7.35 (m, 3 H), 7.36−7.44 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 21.9, 22.0, 47.8, 65.0, 68.1, 68.5, 72.1, 72.2, 77.6, 78.5, 105.3, 127.3, 127.9, 128.5, 139.2; HRMS calcd for $C_{20}H_{34}O_4N_2$ 366.2519, found 366.2508.

15d (90%, 2*S*/2*R* = 95/5); (2*S*)-**15d**: $[\alpha]_D^{20}$ = +0.2 (*c* 11.2, $CHCl_3$); IR (neat) ν 3400 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, *J* = 6.2 Hz, 3 H), 1.16 (s, 9 H), 1.17 (s, 9 H), 2.68−2.90 (br s, 1 H), 2.39 (s, 6 H), 2.96 (dq, *J* = 4.2, 6.2 Hz, 1 H), 3.35−3.56 (m, 4 H), 3.80 (q, *J* = 5.8 Hz, 1 H), 3.90 (q, *J* = 5.8 Hz, 1 H), 4.95 (d, *J* = 4.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 27.4, 48.0, 55.2, 62.5, 63.7, 73.2, 73.2, 78.0, 79.3, 105.0; HRMS calcd for $C_{17}H_{36}O_4N_2$ 332.2675, found 332.2672.

15e (83%, 2*S*/2*R* = 92/8); (2*S*)-**15e**: $[\alpha]^{24}_D$ = −13.4 (*c* 6.5, $CHCl_3$); IR (neat) ν 3481 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.5 Hz, 3 H), 1.14 (s, 9 H), 1.16 (s, 9 H), 1.17−1.62 (m, 6 H), 2.29−2.40 (br s, 1 H), 2.38 (s, 6 H), 2.71−2.80 (m, 1 H), 3.35−3.55 (m, 4 H), 3.79 (dt, *J* = 5.1, 6.5 Hz, 1 H), 3.89 (dt, *J* = 5.3, 6.5 Hz, 1 H), 5.06 (d, *J* = 3.2 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 23.1, 27.4, 27.4, 28.2, 28.4, 48.1, 59.6, 62.6, 62.9, 73.2, 79.1, 81.9, 104.4; HRMS calcd for $C_{20}H_{42}O_4N_2$ 374.3145, found 374.3147. (2*R*)-**15e**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (t, *J* = 6.5 Hz, 3 H), 1.13 (s, 9 H), 1.14 (s, 9 H), 1.15−1.65 (m, 6 H), 2.29−2.39 (br s, 1 H), 2.37 (s, 6 H), 2.71−2.80 (m, 1 H), 3.35−3.52 (m, 4 H), 3.83 (dt, *J* = 5.0, 6.3 Hz, 1 H), 3.88 (dt, *J* = 5.1, 6.3 Hz, 1 H), 5.02 (d, *J* = 3.2 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0, 23.0, 27.4, 27.4, 28.3, 28.7, 48.1, 59.5, 62.6, 62.7, 73.1, 77.9, 78.7, 104.3.

15f (85%, 2*S*/2*R* = 98/2); (2*S*)-**15f**: $[\alpha]^{26}_D$ = +17.0 (*c* 5.4, $CHCl_3$); IR (neat) ν 3478 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 9 H), 1.16 (s, 9 H), 1.55−1.79 (br s, 1 H), 2.40 (s, 6 H), 3.24−3.48 (m, 4 H), 3.71 (q, *J* = 5.7 Hz, 1 H), 3.87 (q, *J* = 5.7 Hz, 1 H), 3.99 (d, *J* = 4.4 Hz, 1 H), 5.10 (d, *J* = 4.4 Hz, 1 H), 7.21−7.45 (m, 5 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.4, 27.5, 47.9, 62.4, 62.9, 65.0, 73.2, 78.0, 79.1, 105.3, 127.4, 127.9, 128.6, 139.4; HRMS calcd for $C_{22}H_{38}O_4N_2$ 394.2832, found 394.2838.

15g (86%, 2*S*/2*R* = 91/9); (2*S*)-**15g**: $[\alpha]^{25}_D$ = −0.8 (*c* 3.8, $CHCl_3$); IR (neat) ν 3443 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (d, *J* = 6.7 Hz, 9 H), 0.84 (d, *J* = 6.7 Hz, 3 H), 1.01−1.07 [(m, 15 H), embodied a singlet at δ 1.04 (s, 6 H), a singlet at δ 1.06 (s, 6 H)], 1.73 (septet, *J* = 6.7 Hz, 1 H), 1.75 (septet, *J* = 6.7 Hz, 1 H), 2.00−2.20 (br s, 1 H), 2.38 (s, 6 H), 2.93 (dq, *J* = 4.2, 6.5 Hz, 1 H), 3.33−3.51 (m, 4 H), 3.83 (q, *J* = 5.7 Hz, 1 H), 3.95 (q, *J* = 5.7 Hz, 1 H), 4.93 (d, *J* = 4.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1, 17.4, 17.5, 17.5, 21.9, 22.0, 22.1, 35.6, 35.8, 48.2, 55.4, 61.7, 62.2, 77.3, 78.1, 79.0, 105.0; HRMS calcd for $C_{21}H_{44}O_4N_2$ 388.3301, found 388.3301.

15h (73%, 2*S*/2*R* = 92/8); (2*S*)-**15h**: $[\alpha]^{24}_D$ = −10.6 (*c* 9.9, $CHCl_3$); IR (neat) ν 3481 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (d, *J* = 6.7 Hz, 12 H), 0.86 (t, *J* = 6.9 Hz, 3 H), 1.03 (s, 6 H), 1.05 (s, 6 H), 1.20−1.61 (m, 7 H), 1.73 (septet, *J* = 6.7 Hz, 1 H), 1.75 (septet, *J* = 6.7 Hz, 1 H), 2.38 (s, 6 H), 2.71−2.79 (m, 1 H), 3.36−3.50 (m, 4 H), 3.83 (q, *J* = 5.7 Hz, 1 H), 3.95 (q, *J* = 5.7 Hz, 1 H), 5.05 (d, *J* = 3.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 17.4, 17.5, 17.5, 21.9, 22.0, 23.1, 28.2, 28.4, 35.6, 35.8, 48.1, 59.7, 61.8, 62.0, 77.3, 77.4, 78.0, 78.7, 104.3; HRMS calcd for $C_{24}H_{50}O_4N_2$ 430.3771, found 430.3772.

15i (70%, 2*S*/2*R* = 98/2); (2*S*)-**15i**: $[\alpha]^{26}_D$ = +5.4 (*c* 5.3, $CHCl_3$); IR (neat) ν 3337 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.79 (d, *J* = 7.0 Hz, 6 H), 0.85 (d, *J* = 7.0 Hz, 3 H), 0.86 (d, *J* = 7.0 Hz, 3 H), 0.99 (s, 6 H), 1.04 (s, 6 H), 1.73 (septet, *J* = 6.7 Hz, 1 H), 1.75 (septet, *J* = 6.7 Hz, 1 H), 1.62−1.80 (br s, 1 H), 2.40 (s, 6 H), 3.26 (dd, *J* = 5.6, 9.3 Hz, 1 H), 3.32 (dd, *J* = 5.2, 9.3 Hz, 1 H), 3.33 (dd, *J* = 5.6, 9.3 Hz, 1 H), 3.39 (dd, *J* = 5.0, 9.3 Hz, 1 H), 3.76 (dt, *J* = 5.0, 5.6 Hz, 1 H), 3.90 (dt, *J* = 5.2, 5.6 Hz, 1 H), 3.96 (d, *J* = 4.7 Hz, 1 H), 5.08 (d, *J* = 4.7 Hz, 1 H), 7.18−7.33 (m, 3 H), 7.37−7.44 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.4, 17.4, 17.5, 21.9, 21.9, 22.0, 22.1, 35.5, 35.8, 47.9, 61.6, 62.1, 65.1, 77.4, 77.4, 78.0, 79.0, 105.3, 127.3, 127.9, 128.5, 139.4; HRMS calcd for $C_{26}H_{46}O_4N_2$ 450.3458, found 450.3463.

15j (84%, 2*S*/2*R* >99/1); (2*S*)-**15j**: $[\alpha]^{25}_D$ = +38.3 (*c* 3.6, $CHCl_3$); IR (neat) ν 3441 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, *J* = 6.4 Hz, 3 H), 1.12 (d, *J* = 6.2 Hz, 6 H), 1.13 (d, *J* = 6.2 Hz, 6 H), 1.30 (s, 3 H), 1.85−2.20 (br s, 1 H), 2.37 (s, 6 H), 2.88 (q, *J* = 6.4 Hz, 1 H), 3.39−3.63 (m, 6 H), 3.86 (dt, *J* = 5.0, 8.1 Hz, 1 H), 3.97 (dt, *J* = 5.0, 8.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 21.1, 21.8, 21.9, 47.9, 59.2, 68.7, 68.7, 72.1, 72.1, 78.2, 111.6; HRMS calcd for $C_{16}H_{34}O_4N_2$ 318.2519, found 318.2524.

15k (68%, 2*S*/2*R* = 98/2); (2*S*)-**15k**: $[\alpha]^{28}_D$ = +8.1 (*c* 9.4, $CHCl_3$); IR (neat) ν 3446 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, *J* = 7.1 Hz, 3 H), 1.11 (d, *J* = 6.3 Hz, 6 H), 1.12 (d, *J* = 5.8 Hz, 6 H), 1.20−1.59 [(m, 9 H), embodied a singlet at δ 1.32 (s, 3 H)], 2.10−2.28 (br s, 1 H), 2.36 (s, 6 H), 2.68 (dd, *J* = 4.5, 6.5 Hz, 1 H), 3.45−3.63 (m, 6 H), 3.83 (dt, *J* = 5.0, 8.2 Hz, 1 H), 3.98 (ddd, *J* = 3.9, 5.2, 8.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.9, 22.0, 22.2, 23.2, 29.4, 30.1, 47.9, 64.1, 68.7, 68.8, 72.1, 72.2, 78.0, 78.2, 112.0; HRMS calcd for $C_{19}H_{40}O_4N_2$ 360.2988, found 360.2979.

15l (82%, 2*S*/2*R* > 99/1); (2*S*)-**15l**: $[\alpha]^{23}_D$ = +29.2 (*c* 18.9, $CHCl_3$); IR (neat) ν 3438 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (d, *J* = 6.3 Hz, 3 H), 1.14 (s, 9 H), 1.15 (s, 9 H), 1.28 (s, 3 H), 2.29−2.35 (br s, 1 H), 2.36 (s, 6 H), 2.86 (q, *J* = 6.3 Hz, 1 H), 3.39−3.56 (m, 4 H), 3.81 (dt, *J* = 5.3, 8.1 Hz, 1 H), 3.91 (dt, *J* = 5.2, 8.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 21.2, 27.3, 27.3, 47.9, 59.2, 62.9, 63.0, 72.9, 78.4, 78.9, 111.4; HRMS calcd for $C_{18}H_{38}O_4N_2$ 346.2832, found 346.2832.

15m (70%, 2*S*/2*R* = 98/2); (2*S*)-**15m**: $[\alpha]^{27}_D$ = +8.9 (*c* 2.2, $CHCl_3$); IR (neat) ν 3435 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.9 Hz, 3 H), 1.13 (s, 9 H), 1.15 (s, 9 H), 1.18−1.60 [(m, 9 H), embodied a singlet at δ 1.32 (s, 3 H)], 2.15−2.30 (br s, 1 H), 2.36 (s, 6 H), 2.68 (dd, *J* = 4.6, 6.5 Hz, 1 H), 3.36−3.58 (m, 4 H), 3.79 (ddd, *J* = 4.8, 5.9, 8.3 Hz, 1 H), 3.93 (ddd, *J* = 4.8, 5.9, 8.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.3, 23.2, 27.4, 27.4, 29.4, 30.1, 47.9, 62.9, 63.1, 64.1, 73.0, 73.1, 78.2, 79.0, 111.9; HRMS calcd for $C_{21}H_{44}O_4N_2$ 388.3301, found 388.3304.

23b (79%, de 56%); ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, *J* = 6.9 Hz, 3 H), 1.34−1.85 (m, 7 H), 2.48 (s, 6 H), 3.02−3.15 (m, 1 H), 4.70 (d, *J* = 8.1 Hz, 1 H), 4.74 (d, *J* = 8.1 Hz, 1 H), 5.51 (d, *J* = 3.9 Hz, 1 H), 7.18−7.35 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 23.1, 28.1, 28.3, 48.2, 60.3, 85.0, 86.9, 105.6, 126.4, 126.8, 128.1, 128.4, 128.5, 139.6.

General Procedure for the Reductive Cleavage of the N−N bond of 15. A mixture of hydrazine (1.0 mmol) and excess W2 Raney nickel in methanol (50 mL) was refluxed for 1−2 h and then filtered through a short column of flash silica gel. The filtrate was evaporated in vacuo, and the residue was chromatographed (25% EtOAc in hexane with 2% Et_3N) to give amine **16**. In certain cases, **16** was used directly for the next transformation into **17**.

(2*S*)-**16a**: 77%; $[\alpha]^{30}_D$ = −4.7 (*c* 4.3, $CHCl_3$); IR (neat) ν 3374 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, *J* = 6.9 Hz, 3 H), 1.15 (s, 18 H), 1.28 (s, 3 H), 1.55−1.69 (br s, 2 H), 2.84 (q, *J* = 6.6 Hz, 1 H), 3.39−3.56 (m, 4 H), 3.87 (dt, *J* = 4.7, 8.2 Hz, 1 H), 3.95 (dt, *J* = 4.5, 8.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8, 21.7, 27.4, 53.6, 62.4, 63.3, 73.1, 78.3, 79.0, 112.1.

(2*S*)-**16b**: 80%; IR (neat) ν 3383 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.83 (t, *J* = 7.0 Hz, 3 H), 0.95−1.59 [(m, 29 H), embodied a singlet at δ 1.12 (s, 18 H), a singlet at δ 1.26 (s, 3 H)], 2.59 (dd, *J* = 2.2, 10.1 Hz, 1 H), 3.40−3.56 (m, 4 H), 3.87 (dt, *J* = 5.0, 8.1 Hz, 1 H), 3.95 (dt, *J* = 4.5, 8.1 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 21.3, 22.7, 27.3, 29.1, 31.5, 58.1, 62.3, 63.1, 72.9, 78.4, 78.6, 112.1; HRMS calcd for $C_{19}H_{40}O_4N$ (M^++1) 346.2957, found 346.2957.

General Procedure for the Synthesis of Phthalimide 17. A mixture of **16** (1.0 mmol) and phthalic anhydride (1.0 mmol) in ether (50 mL) was stirred at rt for 2 h. Solvent was removed in vacuo to give the residue to which were added excess NaOAc (10.0 mmol) and acetic anhydride (60 mL). The mixture was refluxed for 1 h. Water was added and the mixture was extracted with ether (50 mL × 3), dried ($MgSO_4$),

and concentrated to give the residue which was chromatographed on silica gel (25% EtOAc in hexane) to give **17**.

(2*S*)-**17a**: 91%; mp 95−97 °C; $[\alpha]^{24}_D = +4.1$ (*c* 5.4, $CHCl_3$); IR (KBr) ν 1713, 1699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 9 H), 1.17 (s, 9 H), 1.50 (d, $J = 7.2$ Hz, 3 H), 3.34 (dd, $J =$ 5.6, 9.3 Hz, 1 H), 3.39−3.54 (m, 3 H), 3.85 (q, $J = 6.2$ Hz, 1 H), 3.94 (dt, $J = 5.2$, 6.2 Hz, 1 H), 4.24 (quint, $J = 7.2$ Hz, 1 H), 5.58 (d, $J = 7.2$ Hz, 1 H), 7.63−7.83 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 27.3, 27.4, 50.6, 62.4, 63.1, 73.1, 73.2, 78.7, 79.1, 103.1, 123.1, 132.0, 133.7, 168.1; HRMS calcd for $C_{23}H_{33}O_6N$ 419.2308, found 419.2294.

(2*S*)-**17b**: 85%; $[\alpha]^{24}_D = -5.6$ (*c* 7.8, $CHCl_3$); IR (neat) ν 1716 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.81 (t, $J = 6.7$ Hz, 3 H), 1.09 (s, 9 H), 1.10−1.35 [(m, 13 H), embodied a singlet at δ 1.17 (s, 9 H)], 1.69−1.92 (m, 1 H), 2.01−2.30 (m, 1 H), 3.26−3.57 (m, 4 H), 3.77−3.99 (m, 2 H), 4.11 (ddd, $J = 4.1$, 7.3, 11.4 Hz, 1 H), 5.55 (d, $J = 7.3$ Hz, 1 H), 7.63−7.84 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.3, 27.2, 27.3, 27.4, 28.2, 55.6, 62.5, 63.2, 73.1, 78.5, 79.1, 102.8, 123.2, 132.0, 133.8, 168.5; HRMS calcd for $C_{26}H_{39}O_6N$ 461.2777, found 461.2779.

(2*S*)-**17c**: 93%; $[\alpha]^{30}_D = +10.2$ (*c* 1.7, $CHCl_3$); IR (neat) ν 1777, 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, $J = 7.3$ Hz, 3 H), 1.01−1.15 [(m, 15 H), embodied a doublet at δ 1.07 (d, $J = 7.1$ Hz, 3 H), a doublet at δ 1.09 (d, $J = 7.4$ Hz, 3 H), a doublet at δ 1.12 (d, $J = 7.1$ Hz, 6 H)], 1.20−1.35 (m, 1 H), 1.45 (s, 3 H), 1.64−1.89 (m, 1 H), 2.35−2.53 (m, 1 H), 3.40−3.65 (m, 6 H), 3.87 (dt, $J = 4.5$, 8.7 Hz, 1 H), 3.93 (ddd, $J =$ 4.2, 6.3, 8.7 Hz, 1 H), 4.24 (dd, $J = 3.6$, 12.3 Hz, 1 H), 7.63−7.82 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.7, 21.8, 21.9, 22.0, 22.2, 23.2, 25.2, 28.7, 58.6, 68.3, 68.7, 72.0, 72.2, 78.3, 79.1, 110.8, 122.97, 123.1, 131.4, 132.2, 133.6, 133.8, 168.3, 169.0; HRMS calcd for $C_{25}H_{37}O_6N$ 447.2621, found 447.2621.

(2*S*)-**17d**: 82%; $[\alpha]^{24}_D = +19.4$ (*c* 1.2, $CHCl_3$); IR (neat) ν 1775, 1717, 1699 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.13 (s, 9 H), 1.15 (s, 9 H), 1.43 (s, 3 H), 1.59 (d, $J = 7.4$ Hz, 3 H), 3.39−3.60 (m, 4 H), 3.8−3.96 (m, 2 H), 4.44 (q, $J = 7.4$ Hz, 1 H), 7.61−7.82 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.8, 22.9, 27.4, 53.5, 62.7, 62.9, 73.1, 73.2, 79.0, 79.5, 110.9, 123.1, 131.9, 133.7, 168.4; HRMS calcd for $C_{24}H_{36}O_6N$ ($M^+ + 1$) 434.2543, found 434.2538.

(2*S*)-**17e**: 85%; $[\alpha]^{24}_D = +7.6$ (*c* 3.0, $CHCl_3$); IR (neat) ν 1775, 1717, 1699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.81 (t, $J = 7.3$ Hz, 3 H), 1.10−1.39 [(m, 22 H), embodied a singlet at δ 1.13 (s, 9 H), a singlet at δ 1.15 (s, 9 H)], 1.43 (s, 3 H), 1.73−1.89 (m, 1 H), 2.35−2.52 (m, 1 H), 3.41−3.58 (m, 4 H), 3.78−3.93 (m, 2 H), 4.25 (dd, $J = 3.6$, 12.3 Hz, 1 H), 7.63−7.84 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.2, 23.2, 25.1, 27.3, 28.7, 58.6, 62.7, 62.8, 73.0, 73.1, 78.9, 79.3, 110.7, 123.0, 123.1, 131.4, 132.2, 133.6, 133.8, 168.3, 169.0; HRMS calcd for $C_{27}H_{41}O_6N$ 475.2934, found 475.2938.

Phthalimide 25. In a manner similar to that described above, a mixture of *dl*-**14** (0.59 g, 2.0 mmol) and MeLi (6 mL of a 1.6 M solution in ether, 9.6 mmol) in toluene (60 mL) was stirred at −78 °C for 16 h. After usual workup, the crude **23** (dr = 32/68) was taken up into methanol (50 mL) to which was added excess Raney nickel (W2). The mixture was refluxed for 1h and filtered through a short column of flash silica gel to yield crude **24**. Without further purification, a mixture of crude **24**, phthalic anhydride (0.30 g, 2.0 mmol), and NaOAc (1.96 g, 20.0 mmol) in acetic anhydride (60 mL) was refluxed for 1 h. The mixture was worked up to give **25** (0.22 g, 27%). The diastereomeric mixture was separated by flash column chromatography (silica gel, 25% EtOAc in hexane): **25a**: mp 106−108 °C; IR (KBr) ν 1771, 1711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.67 (d, $J = 7.2$ Hz, 3 H), 4.58 (quint, $J = 7.2$ Hz, 1 H), 4.73 (d, $J = 8.3$ Hz, 1 H), 4.79 (d, $J = 8.3$ Hz, 1 H), 6.03 (d, $J = 7.2$ Hz, 1 H), 7.12−7.35 (m, 10 H); 7.65−7.70 (m, 2 H), 7.79−7.83 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 50.5, 84.7, 87.2, 103.6, 123.23, 126.6, 126.7, 128.2, 128.3, 128.4, 128.5, 132.0, 133.9, 136.1, 136.9, 168.3; HRMS calcd for $C_{25}H_{21}O_4N$ 399.1471, found 399.1494. **25b**: IR (KBr) ν 1771, 1711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.65 (d, $J =$ 6.9 Hz, 3 H), 4.58 (quint, $J = 6.9$ Hz, 1 H), 4.70 (d, $J = 8.2$ Hz, 1 H), 4.74 (d, $J = 8.2$ Hz, 1 H), 6.05 (d, $J = 6.9$ Hz, 1 H), 7.12−7.34 (m, 10 H), 7.65−7.70 (m, 2 H), 7.79−7.85 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 50.8, 85.3, 87.0, 103.7, 123.3, 126.6, 126.7, 128.3, 128.4, 128.5, 128.6, 132.0, 133.9, 135.8, 136.7, 168.3; HRMS calcd for $C_{25}H_{21}O_4N$ 399.1471, found 399.1439.

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Supporting Information Available: The experimental procedure and data for X-ray crystallography and ^1H NMR spectra for **8a**−**f**, **9a**−**f**, (2*S*)-**15a**−**m**, (2*R*)-**15e**, (2*S*)-**16a,b**, (2*S*)-**17a**−**e**, and **25a,b** (50 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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