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Aldol Reactions with Kinetic Resolution: Scope and Limitations of Ketal- and Dithioketal-Protected β-Ketoaldehydes

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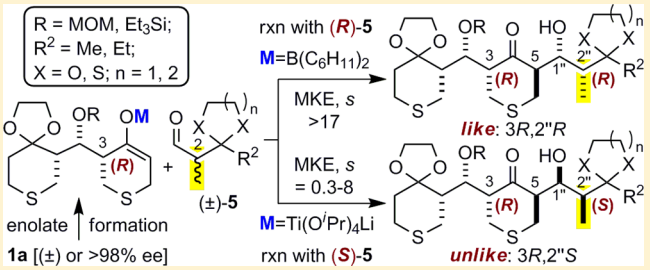
Supporting Information

ABSTRACT: The multiplicativity rule suggests that aldol coupling of chiral reactants will proceed with substantial mutual kinetic enantioselection (MKE) (racemic reactants) or via a highly enantioselective kinetic resolution (KR) (one enantiopure reactant) if the relative topicity is highly selective and the ketone enolate and aldehyde each have high diastereoface selectivity. The scope and limitations of that paradigm were explored by determining the stereoselectivities of aldol reactions of ketone **1a** (known to give 3,5-*trans* aldol adducts with high selectivity) with a series of ketal- and dithioketal-protected β-ketoaldehydes (±)-**5** (predicted to have high Felkin diastereoface selectivity). Using racemic reactants, all reactions of the (*c*-Hex)$_2$B enolates (highly *anti*-selective relative topicity) were remarkably selective and gave the 3,5-*trans*-3,1″-*anti*-1″,2″-*syn* adduct, one of eight possible diastereomers, via a diastereoselective (dr > 20) preferential reaction (MKE > 17) of *like* reactant enantiomers [i.e., (3*R*)-**1a** + (*R*)-**5** and (3*S*)-**1a** + (*S*)-**5**]. Reactions of the corresponding Ti(IV) "ate" enolates (anticipated *syn*-selective relative topicity) were much less selective, and only those of MOM-protected **1a** with dithiolane-protected (±)-**5** (i.e., X = S, *n* = 1) gave high selectivity in favor of the 3,5-*trans*-3,1″-*syn*-1″,2″-*syn* adduct via a diastereoselective (dr > 20) preferential reaction (MKE ≥ 6) of *unlike* reactant enantiomers [i.e., (3*R*)-**1a** + (*S*)-**5** and (3*S*)-**1a** + (*R*)-**5**]. Analogous reactions of the (*c*-Hex)$_2$B and Ti(IV) "ate" enolates of enantiopure (+)-**1a** (R = MOM) with (±)-**5c** (R^2 = Me, X = S, *n* = 1) occurred with KR to give the corresponding enantiopure adducts with the expected stereoselectivity. The adducts have applications in polyproionate synthesis.



INTRODUCTION

In a proof-of-principle study,[1] we previously showed that aldol reactions proceeding with kinetic resolution[2] could be rationally designed. That is, factorizing the kinetically controlled stereoselectivity of aldol couplings of chiral reactants into three stereocontrol elements[3] (relative topicity and diastereoface selectivities of the enolate and aldehyde) and applying the multiplicativity rule[4,5] to those elements suggests that significant kinetic resolution should occur if all three elements are highly biased.[6] That hypothesis was tested in the context of aldol reactions of aldehyde (±)-**2**, known[7] to undergo aldol reactions with very high Felkin diastereoface selectivity, with the four diastereomers of ketone **1**, whose enolates are known[8] to react with aldehydes to give 3,5-*trans* aldol adducts with high diastereoselectivity (Scheme 1). For each diastereomer of **1** (i.e., having a specific configuration at C-1′ and C-6′), aldol reaction with (±)-**2** produces adducts with three new stereocenters (C-5, C-1″, and C-6″), and eight diastereomers are possible (four each from the reactions with (*R*)-**2** and (*S*)-**2**). Using the corresponding enol dicyclohexylborinates (highly *anti*-selective relative topicity),[9] reactions of each of the four enantiopure diastereomers of **1** with (±)-**2** (3 equiv) proceeded with kinetic resolution (preferential reaction with (*R*)-**2**) to give the corresponding adduct **3**[10] (one of eight possible diastereomers) with excellent selectivities. Analogous reactions of (±)-**2** with the Ti(IV) "ate" enolates of **1** (highly *syn*-selective relative topicity)[11] also proceeded with kinetic resolution but with opposite enantioselectivity (preferential reaction with (*S*)-**2**) to give the corresponding adduct **4**[10] with good to excellent selectivities.

The above design paradigm requires both reactants to have high diastereoface selectivity. The near exclusive Felkin diastereoface selectivity observed for aldehyde **2** is attributed to the presence of the dioxolane.[7] The potential inefficient utilization of the racemic reactant (i.e., used in excess with preferential reaction of one enantiomer) is a possible drawback of this strategy for stereoselective coupling of chiral fragments via kinetic resolution. Thus, the benefits of this approach will be maximized in scenarios where the racemic form is obtained much more efficiently than an enantiopure form and/or when the recovered excess can be reused. Racemic **2** satisfies both of the above criteria because: (i) it is easily obtained without chromatography on large scale (20−40 g)[7,12,13] from commodity chemicals, whereas enantiopure **2**[14] is configurationally unstable and considerably more difficult to prepare; and (ii) although **2** was recovered in enantioenriched form (ca. 25−40% ee) from the above aldol reactions with enantiopure **1**,

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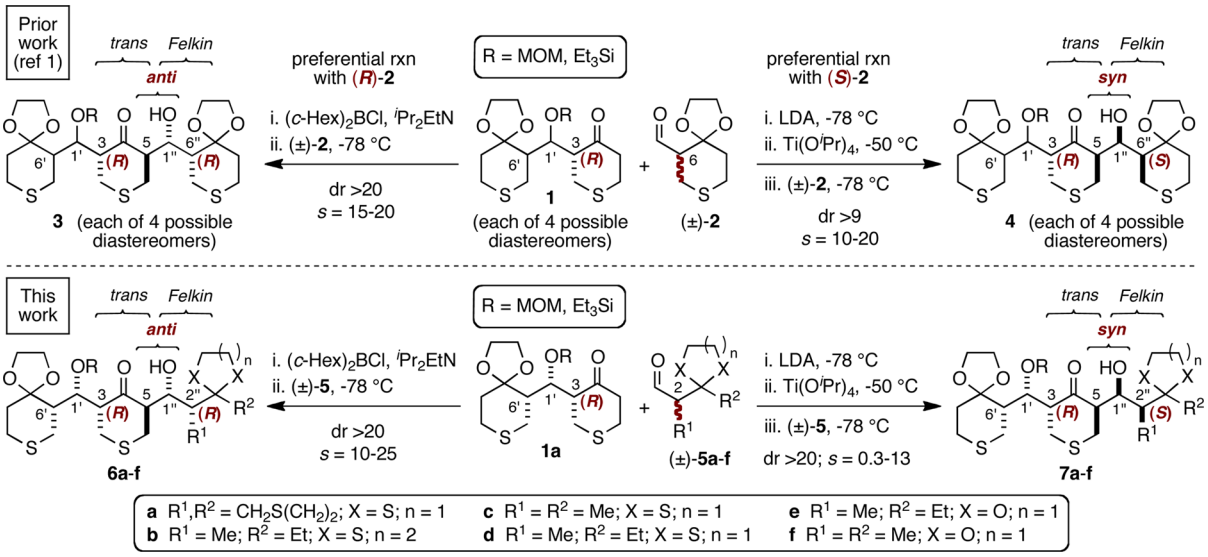
Scheme 1. Rational Design of Aldol Reactions with Kinetic Resolution



it is easily racemized (e.g., in the presence of proline)[15] and can be reused. We speculated that other racemic dithiane-, dithiolane-, or dioxolane-protected enolizable α-substituted-β-ketoaldehydes would also possess high Felkin diastereoface selectivity[16] and undergo aldol reactions via kinetic resolution with advantages similar to those of **2**. To test that hypothesis, we examined aldol reactions of ketone **1a** with aldehydes **5a**–**g** under conditions analogous to those above, and the results are reported herein. In general and under optimized conditions, either adducts **6** (from $(c\text{-Hex})_2$B enolates) or adducts **7** (from Ti(IV) "ate" enolates) were obtained with moderate to excellent selectivities.

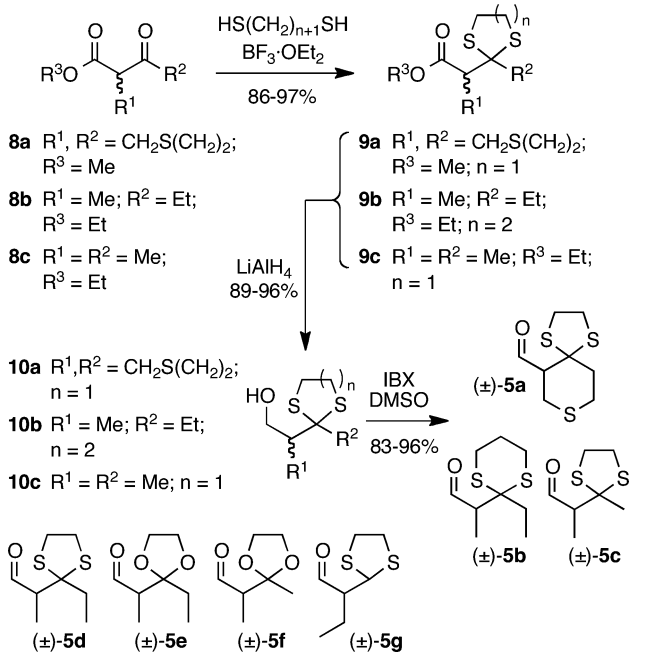
RESULTS AND DISCUSSION

As in previous studies,[1,8] it was convenient to assess the stereoselectivities of the aldol reactions of **1a** with the aldehydes **5** using racemic reactants. In each of these cases, the eight possible diastereomeric aldol adducts are racemic. Analysis of the adduct distribution can reveal both the diastereoselectivities (i.e., double stereodifferentiation)[5] and the relative rates (i.e., mutual kinetic enantioselection, MKE)[17] of the two diastereotopos parallel competitive reactions: (3*R*)-**1a** + (2*R*)-**5** (enantiotopos with (3*S*)-**1a** + (2*S*)-**5**) vs (3*R*)-**1a** + (2*S*)-**5** (enantiotopos with (3*S*)-**1a** + (2*R*)-**5**).[6] Thus, according to Horeau's rule,[18] the ratio of adducts with a 2″,3-*syn* relative configuration (four possible diastereomers) to those with a 2″,3-*anti* relative configuration (four possible diastereomers) is conversion-independent and equal to the MKE. In the absence of nonlinear effects,[19] the MKE determined for a reaction of racemic reactants is equivalent to the selectivity constant (s) in the analogous kinetic resolution where one of the reactants is enantiopure.[6]

Preparation of the Reactants. With the exception of the known (±)-**5g**,[20] all aldehydes **5** were prepared from the corresponding β-ketoesters **8** as reported for (±)-**5d**,[21] (±)-**5e**,[13] and (±)-**5f**[22] and illustrated in Scheme 2 for (±)-**5a**–**c**. Racemic **1a** (R = MOM,[8b] Et_3Si[1]) and (+)-**1a** (R = MOM)[1] were prepared as previously described.

Selective Formation of 6a–f from Aldol Reactions of 5a–f with the $(c\text{-Hex})_2$B Enolate of 1a. The results of reactions of (±)-**5a**–**f** with the enol dicyclohexylborinates

Scheme 2. Synthesis of Aldehydes 5a–c



derived from (±)-**1a** (R = MOM, Et_3Si) are presented in Table 1. For comparison, the results of analogous reactions with aldehyde (±)-**2** are also included (entries 1 and 2).[1] In all cases (entries 3–12), the reactions were remarkably selective and gave the corresponding adduct **6**, one of eight possible diastereomers, as the major or only product with excellent stereoselectivities (dr, >20; MKE, 10 to >20) in good yields (69–79%). The diastereoisomeric adduct **7** was the only minor product detected (i.e., by the presence of diagnostic signals in the ^{1}H NMR spectrum of the crude product), and this diastereomer was isolated in some cases (entries 3, 4, and 8). Although all reactions were highly selective, slightly lower MKE was observed in the reactions with (i) thiopyran aldehydes compared to equivalent "acyclic" aldehydes (cf. entries 1–2 vs 10–11, 3–4 vs 8–9); (ii) dithiolane-protected β-ketoaldehydes compared to equivalent dioxolane-protected β-ketoaldehydes

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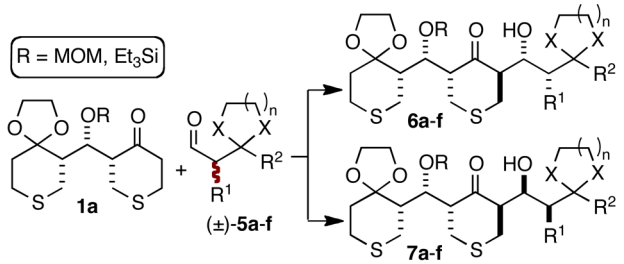
Table 1. Aldol Reactions of the (*c*-Hex)$_2$B Enolate of 1a (R = MOM, Et$_3$Si) with (±)-5[a]



a R^1,R^2 = CH$_2$S(CH$_2$)$_2$; X = S; n = 1 **d** R^1 = Me; R^2 = Et; X = S; n = 1
b R^1 = Me; R^2 = Et; X = S; n = 2 **e** R^1 = Me; R^2 = Et; X = O; n = 1
c R^1 = R^2 = Me; X = S; n = 1 **f** R^1 = R^2 = Me; X = O; n = 1
2 = **5a** with X = O; **3a** = **6a** with X = O; **4a** = **7a** with X = O

entry	ketone	R	aldehyde	aldol adducts (ratio);[b] conversion[b,c] (%)	yield[d] (%)
1[e]	(±)-**1a**	MOM	(±)-**2**	(±)-**3a**, (±)-**4a** (15:1); 92	86
2[e,f]	(±)-**1a**	Et$_3$Si	(±)-**2**	(±)-**3a**, (±)-**4a** (20:1); >95	80
3	(±)-**1a**	MOM	(±)-**5a**	(±)-**6a**, (±)-**7a** (10:1); 92	69
4	(±)-**1a**	Et$_3$Si	(±)-**5a**	(±)-**6a**, (±)-**7a** (11:1); 92	70
5	(±)-**1a**	MOM	(±)-**5b**	(±)-**6b** (dr > 20);[g] >95	89
6	(±)-**1a**	MOM	(±)-**5c**	(±)-**6c** (dr > 20);[g] 90	66
7	(±)-**1a**	Et$_3$Si	(±)-**5c**	(±)-**6c** (dr > 20);[g] >95	75
8	(±)-**1a**	MOM	(±)-**5d**	(±)-**6d**, (±)-**7d** (17:1); 88	79
9	(±)-**1a**	Et$_3$Si	(±)-**5d**	(±)-**6d**, (±)-**7d** (20:1); 90	75
10	(±)-**1a**	MOM	(±)-**5e**	(±)-**6e** (dr > 20);[g] 92	83
11	(±)-**1a**	Et$_3$Si	(±)-**5e**	(±)-**6e** (dr > 20);[g] 92	76
12	(±)-**1a**	MOM	(±)-**5f**	(±)-**6f** (dr > 20);[g] 94	78
13[e]	(−)-*ent*-**1a**[h]	MOM	(±)-**2**	*ent*-**3a**, *ent*-**4a** (9:1); >90	77
14	(+)-**1a**[h]	MOM	(±)-**5c**	(+)-**6c** (dr > 20);[g] 90	81

[a]Enolization with ClB(C$_6$H$_{12}$)$_2$ (2 equiv) and Et$_3$N (2.1 equiv) at −78 °C in CH$_2$Cl$_2$ (ca. 0.1 M in **1a**) for 2 h followed by addition of aldehyde (2 equiv) and 3 h (R = MOM) or 12−16 h (R = Et$_3$Si) reaction time; see Experimental Section for detailed procedures. [b]Determined by ^{1}H NMR of the crude reaction mixture. For entries 1−12, this ratio is a measure of the MKE for the reaction. [c]Estimated from the ratio of adducts to **1a** present in the crude reaction mixture by ^{1}H NMR. [d]Isolated yield of the major adduct. [e]Taken from ref 1. [f]The much lower conversion for this reaction reported in ref 1 presumably resulted from an inadvertent technical error. [g]Only one adduct detected. [h]>98% ee; reaction with 3 equiv of aldehyde.

(cf. entries 1−2 vs 10−11, 3−4 vs 8−9); and (iii) the enolate from (±)-**1a** (R = MOM) compared to that from (±)-**1a** (R = Et$_3$Si) (cf. entries 1 vs 2, 3 vs 4, 8 vs 9). In contrast, reactions of the enol dicyclohexylborinates of (±)-**1a** (R = MOM and Et$_3$Si) with (±)-**5g** gave inseparable mixtures of at least two adducts with low stereoselectivity.

Aldol adducts (±)-**6b−f** arise from *like* combinations[23] of reactant enantiomers [i.e., (3*R*)-**1a** + (*R*)-**5b−f** and (3*S*)-**1a** + (*S*)-**5b−f**].[24] These reactions can produce four possible diastereomers, but adducts (±)-**6b−f** are formed selectively (dr > 20), as expected, because of the biases of the three stereocontrol elements, i.e., Felkin-selective addition of **5** to the boron enolate of **1a** from the face opposite the substituent at C-3 with *anti* relative topicity. In contrast, the diastereomers (±)-**7b−f** must arise from *unlike* combinations[23] of reactant enantiomers [i.e., (3*R*)-**1a** + (*S*)-**5b−f** and (3*S*)-**1a** + (*R*)-**5b−f**].[24] Of the four possible diastereomers that can result from these reactions, only adducts **7** were detected and isolated.[25] It is noteworthy that the formation of **7** requires the same enolate and aldehyde diastereoface selectivities that produce **6** but with *syn* (rather than *anti*) relative topicity. The above discussion also applies to (±)-**6a** and (±)-**7a**; however, because of the change in Cahn−Ingold−Prelog priorities for the stereocenter in **5a** compared to those in **5b−f**, **6a** results from an *unlike* reaction and **7a** results from a *like* reaction.

The highly selective formation of adducts (±)-**6b−f** requires that reactions of the *like* combinations of **1a** and **5b−f** have much higher rate constants than the *unlike* reactions; as noted above, it is the *unlike* reaction of **1a** with **5a** that gives **6a**. We assume that the reactions are kinetically controlled, that they proceed via a "closed" transition state (i.e., with coordination of the aldehyde C═O to the B-enolate), and that coordination of the aldehyde to the enolate is easily reversible and not stereoselective (i.e., no significant preference for coordination of (+)-**1a** with (+)-**5** vs (−)-**5**). Accordingly, the ratio of products **6** and **7** should be dependent on the relative rate constants for reactions of the *like* combinations of **1a** and **5** via chairlike transition states (*anti* relative topicity) to give **6** vs reactions of the *unlike* combinations via twist boat-like transition states (*syn* relative topicity) to give **7** (note: the *like* and *unlike* descriptors are reversed for **6a**/**7a**).[26,27] It is interesting to observe that the structural changes associated with **1a** (R = MOM or Et$_3$Si) and **5a−f** resulted in no detectable changes in the diastereoface selectivities of the derived enolates or aldehydes (i.e., only adducts **6** and **7** detected) and only small changes in the relative preference for *anti* vs *syn* relative topicity (e.g., chairlike vs twist boat-like transition states). These small differences might be due to subtle changes in steric interactions in the relevant transition states but also could be explained by perturbations in the reversibility or stereoselectivity of the aldehyde−enolate coordination step.

As documented in Table 1 (entries 1−12), all reactions of the enol dicyclohexylborinates of (±)-**1a** (R = MOM, Et$_3$Si) with aldehydes (±)-**2** and (±)-**5a−f** showed high levels of MKE (10 to >20), and therefore the analogous reactions of enantiopure **1a** with these aldehydes are expected to occur via kinetic resolution with significant enantioselectivity (*s* = 10 to >20) to give enantiopure **6a−f** with high stereoselectivity. We previously demonstrated a highly selective kinetic resolution in the reaction of (−)-*ent*-**1a** (R = MOM) with (±)-**2** (entry 13).[1,28] To validate that conclusion with an "acyclic" aldehyde, the reaction of (+)-(3*R*)-**1a** (R = MOM) with (±)-**5c** (3 equiv) was conducted under the same conditions to give the adduct (+)-**6c** (from a preferential *like* reaction with (*R*)-**5c**) in good yield with excellent stereoselectivity, as expected (Table 1, entry 14).

Aldol Reactions of 5a−f with the Ti(IV) "ate" Enolate of 1a. Of the several methods investigated in our earlier study of reactions of **1** with (±)-**2**,[1] use of the Ti(IV) "ate" enolates[29] derived by treatment of the LDA-generated Li enolates of (±)-**1** with Ti(O^{i}Pr)$_4$ (2.2 equiv) gave the highest MKE in favor of the 5,1″-*syn* adducts **4** (Scheme 1). The results of analogous reactions of the Ti(IV) "ate" enolates derived from (±)-**1a** (R = MOM, Et$_3$Si) with aldehydes (±)-**5a−f** are

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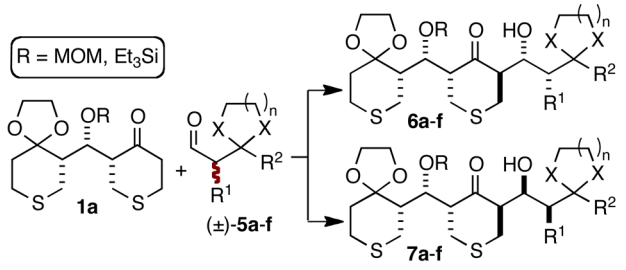
presented in Table 2. For comparison, the results from the reactions with aldehyde (±)-**2** are also included (entries 1 and 2).[1] The reaction of (±)-**5a** with the Ti(IV) "ate" enolate derived from (±)-**1a** (R = MOM) gave a 9:1 mixture of (±)-**7a** (R = MOM) and (±)-**6a** (R = MOM), respectively (entry 3).

Table 2. Aldol Reactions of the Ti(IV) "ate" Enolate of 1a (R = MOM, Et_3Si) with (±)-5[a]



a R^1,R^2 = $CH_2S(CH_2)_2$; X = S; n = 1 **d** R^1 = Me; R^2 = Et; X = S; n = 1
b R^1 = Me; R^2 = Et; X = S; n = 2 **e** R^1 = Me; R^2 = Et; X = O; n = 1
c R^1 = R^2 = Me; X = S; n = 1 **f** R^1 = R^2 = Me; X = O; n = 1
2 = **5a** with X = O; **3a** = **6a** with X = O; **4a** = **7a** with X = O

entry	ketone	R	aldehyde	aldol adducts (ratio);[b] conversion[b,c] (%)	yield[d] (%)
1[e]	(±)-**1a**	MOM	(±)-**2**	(±)-**3a**, (±)-**4a** (1:11); 90	79
2[e]	(±)-**1a**	Et_3Si	(±)-**2**	(±)-**3a**, (±)-**4a**; (1:1.6); 93	31 (20)
3	(±)-**1a**	MOM	(±)-**5a**	(±)-**6a**, (±)-**7a** (1:9); 92	
4[f]	(±)-**1a**	MOM	(±)-**5a**	(±)-**6a**, (±)-**7a** (1:13); >95	73 (6)
5	(±)-**1a**	Et_3Si	(±)-**5a**	(±)-**6a**, (±)-**7a** (1:2); 90	46 (20)
6	(±)-**1a**	MOM	(±)-**5b**	(±)-**6b**, (±)-**7b** (2:1); 94	53 (29)
7	(±)-**1a**	MOM	(±)-**5c**	(±)-**6c**, (±)-**7c** (1:4); 90	
8[f]	(±)-**1a**	MOM	(±)-**5c**	(±)-**6c**, (±)-**7c** (1:6); 92	77[g]
9	(±)-**1a**	Et_3Si	(±)-**5c**	(±)-**6c**, (±)-**7c**; (3:1) 87	52 (20)
10	(±)-**1a**	MOM	(±)-**5d**	(±)-**6d**, (±)-**7d** (1:8 ; 94	69 (6)
11	(±)-**1a**	Et_3Si	(±)-**5d**	(±)-**6d**, (±)-**7d** (1.3:1); 73	29 (24)
12	(±)-**1a**	MOM	(±)-**5e**	(±)-**6e**, (±)-**7e** (1:4); 90	69 (19)
13	(±)-**1a**	Et_3Si	(±)-**5e**	(±)-**6e**, (±)-**7e** (3:1); >95	68 (16)
14	(±)-**1a**	MOM	(±)-**5f**	(±)-**6f**, (±)-**7f** (1:3); 94	53 (18)
15[e]	(−)-*ent*-**1a**[h]	MOM	(±)-**2**	*ent*-**3a**, *ent*-**4a** (1:9); 85	67
16[f]	(+)-**1a**[h]	MOM	(±)-**5c**	(+)-**6c**, (+)-**7c** (1:4); 88	77[g]

[a]Addition of LDA (ca. 0.2 M in THF; 1.1 equiv) to **1** (0.1 M in THF) at −78 °C, after 15 min addition of $Ti(O^iPr)_4$ (2.2 equiv), and then −50 °C for 30 min followed by addition of (±)-**2** at −78 °C and indicated reaction time; see Experimental Section for detailed procedures. [b]Determined by ^1H NMR of the crude reaction mixture. For entries 1−14, this ratio is a measure of the MKE for the reaction. [c]Estimated from the ratio adducts to **1a** present in the crude reaction mixture by ^1H NMR. [d]Isolated yield of the major adduct (minor adduct in parentheses). [e]Taken from ref 1. [f]4.4 equiv of $Ti(O^iPr)_4$. [g]Inseparable mixture of **6c** and **7c** (R = MOM). [h]>98% ee; reaction with 3 equiv of aldehyde.

Consistent with Thornton's observations,[29b] improved stereoselectivity (to 13:1) was obtained by increasing the amount of $Ti(O^iPr)_4$ added to the Li enolate, and (±)-**7a** was isolated in excellent yield (entry 4). Reactions of the Ti(IV) "ate" enolate derived from (±)-**1a** (R = MOM) with the "acyclic" aldehydes (±)-**5b−f** (entries 6−8, 10, 12, and 14) also gave mixtures of the corresponding adducts (±)-**6b−f** and (±)-**7b-f**, two of eight possible diastereomers, but with lower MKE than the reactions with (±)-**5a** or (±)-**2**.[25] Although use of additional $Ti(O^iPr)_4$ resulted in slightly higher selectivity with (±)-**5c** (cf. entries 7 and 8), this modification was not efficacious with the other aldehydes. The reaction with (±)-**5d** (entry 10) was investigated in more detail; however, changing the Ti(IV) source ($Ti(O^iPr)_4$, $TiCl(O^iPr)_3$), the Ti(IV) stoichiometry (2.2, 4.4, 8.8 equiv), the transmetalation reaction time (0.5, 1, 2 h), the aldol reaction time (0.5, 2, 10 h), or the Li enolate ("amine free" vs LDA-generated) had only negligible effects on the observed selectivity. As with (±)-**2**, reactions of (±)-**5a** and (±)-**5c−e** with the Ti(IV) "ate" enolate derived from (±)-**1a** (R = Et_3Si) were much less selective than those from (±)-**1a** (R = MOM) (cf. entries 3 and 5; 7 and 9; 10 and 11; 12 and 13). In all cases, adducts **7** were produced with greater selectivity in reactions with dithiolane-protected *β*-ketoaldehydes compared to those with equivalent dioxolane-protected *β*-ketoaldehydes (cf. entries 1 and 4; 2 and 5; 8 and 14; 10 and 12; 11 and 13).

As noted above, adducts **6** and **7** arise from different reactions: (±)-**6a** and (±)-**7b-f** (R = MOM, Et_3Si) from *unlike* combinations reactant enantiomers [i.e., (3*R*)-**1a** + (*S*)-**5a−f** and (3*S*)-**1a** + (*R*)-**5a−f**], and (±)-**7a** and (±)-**6b−f** (R = MOM, Et_3Si) from *like* combinations reactant enantiomers [i.e., (3*R*)-**1a** + (*R*)-**5a−f** and (3*S*)-**1a** + (*S*)-**5a−f**]. Both of these reactions are highly diastereoselective, as only one adduct was detected from each (dr > 20).[25] Assuming the reactions are kinetically controlled, the ratio of adducts (±)-**6** and (±)-**7** provides a measure of the MKE for the reaction of the racemic reactants and reflects the ratio of rate constants for the competing *like* and *unlike* reactions. However, relating the observed changes in MKE to the structures of the reactants is complicated because the structure and aggregation state of Ti(IV) "ate" enolates are uncertain,[30] and it is not clear whether the competing transition states for the *like* and *unlike* reactions are the same type (e.g., "closed" chair vs twist-boat) or different types (e.g., "closed" vs "open").[26,31] The much higher MKE observed for reactions of the enolate from (±)-**1a** (R = MOM) compared to those from (±)-**1a** (R = Et_3Si) suggests that intramolecular coordination of the C-1′ ether to the Ti enolate is important in favoring the *unlike* reaction (*like* reaction for **7a**). In that case, reaction of the octahedral Ti(IV) "ate" enolate via an "open" transition state could be favored. Alternatively, reaction via a "closed" transition state of a bimetallic enolate, analogous to that proposed by Urpí,[31d] might be favored. Nonetheless, of the new reactions documented in Table 2, only those of (±)-**1a** (R = MOM) with the dithiolane-protected *β*-ketoaldehydes (±)-**5a**, (±)-**5c**, and (±)-**5d** proceeded with a MKE sufficient to expect a reasonably enantioselective kinetic resolution. We previously showed that the reaction of (−)-*ent*-**1a** (R = MOM) with (±)-**2** under these conditions occurred with the expected kinetic resolution to give *ent*-**4a** in good yield (entry 15).[1,28] To test these expectations in a more challenging situation, we conducted the reaction of (+)-**1a** (R = MOM) with (±)-**5c** (expected kinetic resolution selectivity constant, *s* = 6; cf. Table 2 entry 8). Gratifyingly, a 4:1 mixture of (−)-**7c** (R = MOM) and (−)-**6c** (R = MOM), respectively, was

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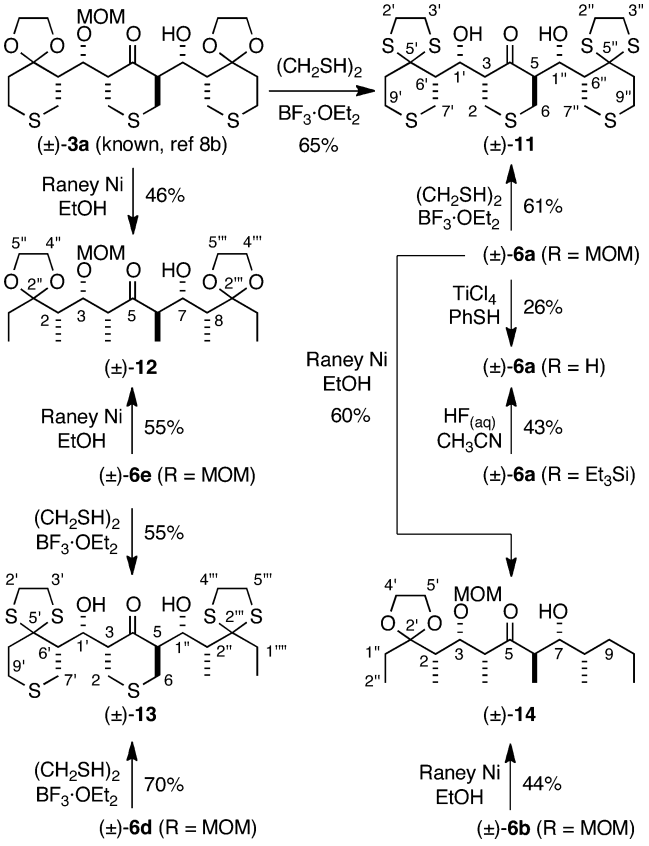
obtained in good yield (entry 16);[28] unfortunately, these diastereomers were inseparable in our hands [note that (−)-**6c** (R = MOM) was obtained in pure form from the boron enolate; cf. Table 1, entry 15].

Determination of the Relative Configurations for 6a–f and 7a–f. The relative configurations for (±)-**6a** (R = MOM), (±)-**6b** (R = MOM), (±)-**6d** (R = MOM), and (±)-**6e** (R = MOM) were correlated to that of the known[8b] (±)-**3a** as illustrated in Scheme 3. Thus, reactions of (±)-**3a**

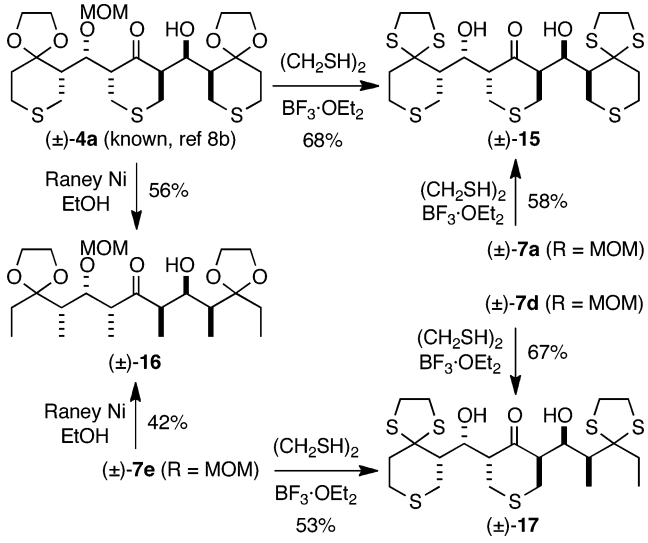
Scheme 3. Correlation of the Relative Configurations of 6a, 6b, 6d, and 6e to 3a[32]



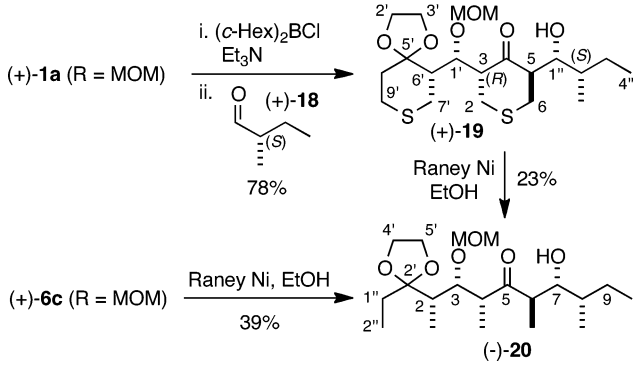
and (±)-**6a** (R = MOM) with $(CH_2SH)_2$ in the presence of $BF_3{\cdot}OEt_2$ gave the same bis-dithioacetal (±)-**11**, and Raney nickel desulfurizations of (±)-**3a** and (±)-**6e** (R = MOM) gave the same hexapropionate derivative (±)-**12a**. Similarly, the relative configurations of (±)-**6e** (R = MOM) and (±)-**6d** (R = MOM) were correlated by their conversions to the same bis-dithioacetal (±)-**13** and those of (±)-**6a** (R = MOM) and (±)-**6b** (R = MOM) by their desulfurizations to the same hexapropionate derivative (±)-**14a**. An identical strategy was used to correlate the relative configurations of (±)-**7a** (R = MOM), (±)-**7d** (R = MOM), and (±)-**7e** (R = MOM) to that of the known[8b] (±)-**4a** (Scheme 4): (±)-**4a** and (±)-**7d** (R = MOM) gave the same bis-dithioacetal (±)-**15**; (±)-**4a** and (±)-**7e** (R = MOM) gave the same hexapropionate derivative (±)-**16**; (±)-**7d** (R = MOM) and (±)-**7e** (R = MOM) gave the same bis-dithioacetal (±)-**17**.

The relative configuration for **6c** (R = MOM) was established as shown in Scheme 5. Aldol reaction of (+)-**18**[33] of known absolute configuration[34] with the enol dicyclohexylborinate of (+)-**1a** (R = MOM) under conditions described

Scheme 4. Correlation of the Relative Configurations of 7a, 7d, and 7e to 4a[32]



Scheme 5. Correlation of the Relative Configuration of 6c (R = MOM) with (+)-19



in Table 1 gave (+)-**19** in good yield. The indicated structure of (+)-**19** is assigned on the basis of the established stereoselectivity for similar aldol reactions of (±)-**1a** (R = MOM) with (±)-**2**, (±)-**5a**, (±)-**5b**, (±)-**5d**, and (±)-**5e**. Reactions of (+)-**6c** (R = MOM) and (+)-**19** with Raney nickel in ethanol gave the same desulfurization product (−)-**20**.[32,35] The structure for (−)-**20** was further corroborated by the very close correspondence of its ^{13}C NMR chemicals shifts (with the exception of those for C8–C10)[36] with those for (±)-**14** (R = MOM).

The relative configuration of (±)-**6a** (R = Et_3Si) was correlated to that of (±)-**6a** (R = MOM) by deprotection of the C-1′ hydroxy group of each to give the same diol product (±)-**6a** (R = H) (Scheme 3). The relative configurations for several of the aldol adducts obtained from (±)-**1a** (R = Et_3Si) were assigned on the basis of the very close correspondence of the ^{13}C NMR chemical shifts of C-5, C-6, C-1″, and C-2″ ($\Delta\delta \leq 0.4$)[36,37] in the Et_3Si-protected adducts with those in the MOM-protected adducts of known relative configuration, i.e., (±)-**6c** (R = MOM vs Et_3Si), (±)-**6d** (R = MOM vs Et_3Si), (±)-**6e** (R = MOM vs Et_3Si), (±)-**7a** (R = MOM vs Et_3Si), (±)-**7c** (R = MOM vs Et_3Si), (±)-**7d** (R = MOM vs Et_3Si), (±)-**7e** (R = MOM vs Et_3Si). The relative configurations for the remaining adducts (±)-**6f** (R = MOM), (±)-**7b** (R = MOM), (±)-**7c** (R = MOM and Et_3Si), and (±)-**7f** (R =

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MOM) are based on the expectation that they are produced in reactions with stereoselectivity consistent with that established above for the aldol reactions of (±)-**1a** (R = MOM) and previously[1] for other diastereomers of **1** (R = MOM, Et_3Si); in all cases, the ^{13}C NMR chemical shifts of C-5, C-6, C-1″, and C-2″ in these adducts are consistent with the assigned relative configuration.

SUMMARY AND CONCLUSIONS

In summary, reactions of the enol dicyclohexylborinates derived from (±)-**1a** (R = MOM, Et_3Si) with (±)-**5a**–**f** showed superb stereoselectivity giving the corresponding 3,5-*trans*-3,1″-*anti*-1″,2″-*syn* adduct (±)-**6a**–**f**, one of eight possible adduct diastereomers, via a highly diastereoselective (dr > 20) preferential reaction (MKE >10) of *like* reactant enantiomers[24] (note: an *unlike* reaction of **1a** with **5a** gives **6a**). The structural diversity among these reactants led to relatively minor changes in stereoselectivity illustrating the generality of this coupling strategy. However, similar reactions with (±)-**5g** were much less selective, perhaps because of lower diastereoface selectivity with this substrate. Analogous reactions of enantiopure **1a** (R = MOM, Et_3Si) with (±)-**5a**–**f** are fully expected to proceed via kinetic resolution with comparable stereoselectivity, and this was demonstrated by the reaction of (+)-(3*R*)-**1a** (R = MOM) with (±)-**5c** to give (+)-**6c** with excellent selectivity.

The Ti(IV) "ate" enolates of (±)-**1a** (R = MOM, Et_3Si) were anticipated to react with *syn*-selective relative topicity (cf. *anti*-selective relative topicity of the boron enolates) and thus favor the reaction of *unlike* reactant enantiomers. Although both the *like* and *unlike* reactions of these enolates with (±)-**5a**–**f** were highly stereoselective (dr > 20), only the reactions of (±)-**1a** (R = MOM) with the dithiolane-protected aldehydes (±)-**5a**, (±)-**5c**, and (±)-**5d** showed significant MKE (i.e., >5) in favor of the 3,2″-*anti* adducts **7**. The potential for kinetic resolution in these "best" cases was demonstrated by the reaction of (+)-(3*R*)-**1a** (R = MOM) with (±)-**5c** to give (+)-**7c** with moderate selectivity, as expected.

The above results suggest that enolizable ketal- and dithioketal-protected α-substituted-β-ketoaldehydes are reliable substrates for stereoselective aldol coupling via kinetic resolution. With **1a** (and presumably other suitable ketones), it is noteworthy that a relatively simple variation in the enolate type, from B to Ti(IV) "ate", changes the relative rate constants for the competing *like* and *unlike* reactions by more than 2 orders of magnitude allowing selective access to either **6** or **7** from the same reactants. In principle, other adduct diastereomers should be available by appropriate manipulation of the diastereoface selectivity of the enolate or aldehyde. These stereochemically rich adducts have applications in polypropionate synthesis,[6] and this strategic coupling of chiral fragments via kinetic resolution provides a useful option in synthetic planning.[38]

EXPERIMENTAL SECTION

General Methods. Anhydrous solvents were distilled under argon atmosphere as follows: tetrahydrofuran (THF) from benzophenone sodium ketyl; CH_2Cl_2 from CaH_2; MeOH from $Mg(OMe)_2$; DMSO from CaH_2 at reduced pressure (stored over 4 Å molecular sieves). All experiments involving air- and/or moisture-sensitive compounds were conducted in an oven-dried round-bottom flask capped with a rubber septum and attached via a needle and connecting tubing to an argon manifold equipped with mercury bubbler (ca. 5 mm positive pressure of argon). Low temperature baths were ice/water (0 °C), $CO_{2(s)}$/CH_3CN (−50 °C), and $CO_{2(s)}$/acetone (−78 °C). Unless otherwise noted, reaction temperatures refer to that of the bath. Concentration refers to removal of volatiles at water aspirator pressure on a rotary evaporator. Preparative TLC (PTLC) was carried out on glass plates (20 × 20 cm) precoated (0.25 mm) with silica gel 60 F_{254}. Materials were detected by visualization under an ultraviolet lamp (254 nm) and/or by treating a 1 cm vertical strip removed from the plate with a solution of phosphomolybdic acid (5%) containing a trace of ceric sulfate in aqueous sulfuric acid (5% v/v) followed by charring on a hot plate. Flash column chromatography (FCC) was performed according to Still et al.[39] with silica gel 60 (40–63 μm). All mixed solvent eluents are reported as v/v solutions. Unless otherwise noted, all reported compounds were homogeneous by thin layer chromatography (TLC) and by ^1H NMR.

Spectral Data. High-resolution mass spectra (HRMS) were obtained on a double focusing high-resolution spectrometer; only partial data are reported. EI ionization was accomplished at 70 eV and CI ionization at 50 eV with ammonia as the reagent gas; only partial data are reported. Alternatively, HRMS were obtained on an LC–MS/MS time-of-flight high-resolution spectrometer with electrospray ionization (ESI) from acetonitrile solution. IR spectra were recorded on a Fourier transform interferometer using a diffuse reflectance cell (DRIFT); only diagnostic and/or intense peaks are reported. Unless otherwise noted, NMR spectra were measured in $CDCl_3$ solution at 500 MHz for ^1H and 125 MHz for ^{13}C. Signals due to the solvent (^{13}C NMR) or residual protonated solvent (^1H NMR) served as the internal standard: $CDCl_3$ (7.26 δ_H, 77.23 δ_C); C_6D_6 (7.16 δ_H, 128.39 δ_C). The ^1H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), ap (apparent); the list of coupling constants (J) corresponds to the order of the multiplicity assignment. Coupling constants (J) are reported to the nearest 0.5 Hz (i.e., ± 0.25 Hz as consistent with the digital resolution ca. 0.2 Hz/pt). The ^1H NMR assignments were made on the basis of chemical shift and multiplicity and were confirmed by homonuclear decoupling and/or two-dimensional correlation experiments (gCOSY, gHSQC, gHMBC).[40] The ^{13}C NMR assignments were made on the basis of chemical shift and multiplicity[41] (as determined by ^{13}C-DEPT or gHSQC) and were confirmed by two-dimensional $^1H/^{13}C$ correlation experiments (gHSQC and/or gHMBC).[40] Specific rotations ($[\alpha]_D$) are the average of 5 determinations at ambient temperature using a 1 mL, 10 dm cell; the units are 10^{-1} deg cm^2 g^{-1}, the concentrations (c) are reported in g/100 mL, and the $[\alpha]_D$ values are rounded to reflect the accuracy of the measured concentrations (the major source of error).

Materials. The following compounds and reagents were prepared as described previously: (±)-**1a** (R = MOM,[8b] Et_3Si[1]); (+)-**1a** (R = MOM)[1] (>98% ee); **5d**;[21] **5e**;[13] **5f**;[22] **8a**;[12] **8b**;[42] W-2 Raney nickel;[43] IBX.[44] $TiCl_4$ and $^iPr_2NH$ were distilled under argon atmosphere from CaH_2. Et_3N was distilled from KOH under argon and stored over KOH. $Ti(O^iPr)_4$ was distilled under argon. All other reagents were commercially available and, unless otherwise noted, were used as received.

1,4,8-Trithiaspiro[4.5]decane-6-carbaldehyde (5a). IBX (4.7 g, 17 mmol) was added to a stirred solution of **10a** (1.90 g, 8.56 mmol) in anhydrous DMSO (15 mL) at room temperature. After 1.5 h (reaction was complete by TLC analysis), the mixture was diluted with ethyl acetate and washed sequentially with saturated aq $NaHCO_3$, water and brine. The organic layer was dried over Na_2SO_4, concentrated, and fractionated by FCC (50% ethyl acetate in hexane) to give the title compound as a pale yellow oil (1.81 g, 96%): IR ν_{max} 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.90 (1H, d, J = 0.7 Hz), 3.37–3.27 (4H, m), 2.97 (1H, ddd, J = 1.5, 3, 14 Hz), 2.91 (1H, dd, J = 3, 9 Hz), 2.86 (1H, ddd, J = 3, 10, 14 Hz), 2.74 (1H, dd, J = 9, 14 Hz), 2.65 (1H, m, J = 1.5, 3, 6, 14 Hz), 2.43 (1H, ddd, J = 3, 6, 14 Hz), 2.30 (1H, ddd, J = 3, 10, 14 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 67.6, 58.4, 44.7, 39.7, 39.1, 29.4, 27.9; LRMS (EI), m/z (relative intensity) 220 ($[M]^+$, 65), 192 (33), 164 (32), 136 (64), 99 (100), 97

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(26), 71 (77); HRMS *m*/*z* calcd. for $C_8H_{12}OS_3$ 220.0050, found 220.0047 (EI).

2-(2-Ethyl-1,3-dithian-2-yl)propanal (5b). Reaction of **10b** (1.52 g, 7.4 mmol) with IBX (3.1 g, 11 mmol) for 2 h according to the above procedure for the synthesis of **10a** gave the title compound as a pale yellow oil (1.24 g, 83%) after fractionation of the crude by FCC (10% ethyl acetate in hexane): IR ν_{max} 1716, 2830, 2733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.96 (1H, d, *J* = 2.5 Hz), 2.86−2.79 (5H, m), 2.12 (1H, dq, *J* = 7.5, 15 Hz), 2.01−1.89 (2H, m), 1.18 (3H, d, *J* = 7 Hz), 1.03 (3H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5 (s), 54.5 (s), 50.8 (d), 29.4 (t), 26.1 (t), 25.5 (t), 24.9 (t), 9.7 (q), 9.4 (q); HRMS *m*/*z* calcd. for $C_9H_{16}OS_2$ 204.0643, found 204.0650 (EI).

2-(2-Methyl-1,3-dithiolan-2-yl)propanal (5c). Reaction of **10c** (583 mg, 3.27 mmol) with IBX (1.8 g, 6.5 mmol) for 1.5 h according to the above procedure for the synthesis of **10a** gave the title compound as a pale yellow oil (520 mg, 90%) after fractionation of the crude by FCC (20% ethyl acetate in hexane): IR ν_{max} 2832, 2726, 1721 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.79 (1H, d, *J* = 2 Hz), 3.40−3.26 (4H, m), 2.76 (1H, dq, *J* = 2, 7 Hz), 1.75 (3H, s), 1.25 (3H, d, *J* = 7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.3 (s), 66.6 (s), 56.8 (d), 40.2 (t), 39.9 (t), 31.6 (q), 13.2 (t); HRMS *m*/*z* calcd. for $C_7H_{12}OS_2$ 176.0330, found 176.0335 (EI).

General Procedure for Aldol Reactions of 1a (R = MOM, Et_3Si) via Its Enol Dicyclohexylborinate. A solution of **1a** in CH_2Cl_2 (0.2 M) was added dropwise via syringe over 5 min to a stirred solution of $(c\text{-Hex})_2BCl$ (1 M in CH_2Cl_2; 2.0 equiv) and Et_3N (2.1 equiv) at −78 °C under Ar. After 2 h, a solution of aldehyde (2−3 equiv) in CH_2Cl_2 (1 M) was added slowly via syringe (ca. 5 min). After the indicated time, the reaction was quenched by sequential addition of phosphate buffer (pH 7; 10 mL/mmol of $(c\text{-Hex})_2BCl$), MeOH (10 mL/mmol of $(c\text{-Hex})_2BCl$), and 30% aq H_2O_2 (5 mL/mmol of $(c\text{-Hex})_2BCl$). The mixture was stirred at 0 °C for 10 min and then was diluted with ice−water and saturated aq Na_2SO_3 (10 mL/mmol of $(c\text{-Hex})_2BCl$) and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to the crude product that was analyzed by ^1H NMR.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(*S*)-(6*S*)-1,4,8-trithiaspiro[4.5]-dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6a (R = MOM)].[36] Reaction of (±)-**5a** (179 mg, 0.81 mmol) with (±)-**1a** (R = MOM) (141 mg, 0.40 mmol) via the boron enolate for 2 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 10:1 mixture of (±)-**6a** (R = MOM) and (±)-**7a** (R = MOM), respectively. Fractionation of the crude FCC (20−40% ethyl acetate in hexane) afforded recovered (±)-**5a** (79 mg, 44%), a 2:1 mixture (by ^1H NMR) of (±)-**1a** (R = MOM) and (±)-**7a** (R = MOM) (35 mg), respectively, and the title compound (156 mg, 69%): IR ν_{max} 3463, 1712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.86 (1H, br dd, *J* = 5, 7 Hz, HC-1″), 4.70 (1H, d, *J* = 6 Hz, OCH_2O), 4.66 (1H, d, *J* = 6 Hz, OCH_2O), 4.46 (1H, dd, *J* = 4.5, 5.5 Hz, HC-1′), 4.1−3.91 (4H, m, H_2C-2′, H_2C-3′), 3.42−3.22 (4H, m, H_2C-2″, H_2C-3″), 3.37 (3H, s, H_3CO), 3.19−3.15 (1H, m, HC-3), 3.03−2.89 (7H, m, HO, H_2C-2, HC-5, HC-6, HC-9″), 2.89−2.69 (6H, m, HC-6, H_2C-7′, H_2C-7″, HC-9′), 2.50−2.46 (3H, m, HC-9′, HC-9″, HC-10″), 2.28 (1H, ddd, *J* = 3, 12, 13.5 Hz, HC-10″), 2.13−2.06 (3H, m, HC-6′, HC-6″, HC-10′), 1.70 (1H, ddd, *J* = 3.5, 13, 13 Hz, HC-10′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.9 (s, C-4), 108.9 (s, C-5′), 98.5 (t, OCH_2O), 73.6 (s, C-5″), 72.3 (d, C-1′), 71.6 (d, C-1″), 64.7 (t, C-2′), 64.6 (t, C-3′), 57.6 (d, C-3), 56.8 (q, CH_3O), 56.1 (d, C-5), 51.6 (d, C-6″), 49.2 (d, C-6′), 47.2 (t, C-10″), 39.7 (t, C-2″), 39.3 (t, C-3″), 36.4 (t, C-10′), 33.4 (t, C-6), 31.9 (t, C-2), 28.9 (t, C-7′), 28.2 (t, C-7″ or C-9″), 28.1 (t, C-7″ or C-9″), 26.7 (t, C-9′); HRMS *m*/*z* calcd. for $C_{23}H_{36}O_6S_5$+Na 591.1007, found 591.0997 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(*S*)-(6*S*)-1,4,8-trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6a (R = Et_3Si)].[36] Reaction of (±)-**5a** (31 mg, 0.14 mmol) with (±)-**1a** (R = Et_3Si) (29 mg, 0.069 mmol) via the boron enolate for 15 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 11:1 mixture of (±)-**6a** (R = Et_3Si) and (±)-**7a** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (10% ethyl acetate in hexane; multiple developments) afforded recovered (±)-**5a** (12 mg, 39%), (±)-**7a** (R = Et_3Si) (3 mg, 7%), and the title compound (31 mg, 70%): IR ν_{max} 3467, 1710 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.06 (1H, br dd, *J* = 3, 8 Hz, HC-1″), 4.65 (1H, dd, *J* = 2, 7.5 Hz, HC-1′), 4.02−3.82 (4H, m, H_2C-2′, H_2C-3′), 3.44−3.24 (4H, m, H_2C-2″,′ H_2C-3″), 3.21−3.18 (1H, m, HC-3), 3.06−2.93 (4H, m, HO, HC-2, HC-6, HC-9″), 2.87−2.68 (8H, m, HC-2, HC-5, HC-6, H_2C-7′, H_2C-7″, HC-9′), 2.56 (1H, br d, *J* = 14 Hz, HC-9″), 2.51−2.46 (2H, m, HC-9′, HC-10″), 2.29 (1H, ddd, *J* = 3, 12, 13.5 Hz, HC-10″), 2.11−1.99 (3H, m, HC-6′, HC-6″. HC-10′), 1.68 (1H, ddd, *J* = 4, 12, 13.5 Hz, HC-10′), 0.93 (9H, t, *J* = 8 Hz, $H_3CCSi \times 3$), 0.67−0.60 (6H, m, $H_2CSi \times 3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.1 (s, C-4), 109.5 (s, C-5′), 73.4 (s, C-5″), 71.2 (d, C-1″), 66.4 (d, C-1′), 64.84 (t, C-2′), 64.82 (t, C-3′), 58.4 (d, C-3), 55.6 (d, C-5), 51.9 (d, C-6″), 49.8 (d, C-6′), 47.3 (t, C-10″), 39.8 (t, C-2″), 39.5 (t, C-3″), 37.1 (t, C-10′), 32.7 (t, C-6), 29.8 (t, C-2), 29.2 (t, C-7′), 28.7 (t, C-7″), 28.3 (t, C-9″), 26.7 (t, C-9′), 7.4 (q × 3, CH_3CSi), 5.4 (t × 3, CH_2Si); HRMS *m*/*z* calcd. for $C_{27}H_{46}O_5SiS_5$+Na 661.1610, found 661.1623 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-ylhydroxymethyl]-5-[(*S*)-(6*S*)-1,4,8-trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6a (R = H)].[36] $TiCl_4$ (29 μL, 49 mg, 0.26 mmol) was added dropwise via syringe to a stirred solution of (±)-**6a** (R = MOM) (29 mg, 0.051 mmol) in CH_2Cl_2 (2.6 mL, 0.02 M) at −78 °C under argon. After 5 min, a fine yellow slurry developed, and thiophenol (52 μL, 56 mg, 0.51 mmol) was added dropwise to the mixture resulting in a red-orange fine slurry. After 2 h, MeOH (2 mL) was added (the mixture became colorless), and the cooling bath was removed. Phosphate buffer (pH = 7; 8 mL) was added, and after 3 min, the mixture was diluted with saturated aq $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, concentrated, and fractionated by FCC (40% ethyl acetate in hexane) to give recovered (±)-**6a** (R = MOM) (17 mg, 59%) and the title compound (7 mg, 26%): IR ν_{max} 3500, 1706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.17 (1H, dd, *J* = 2.5, 9 Hz, HC-1″), 4.59−4.54 (1H, br d, *J* = 8.5 Hz, HC-1′), 4.11−3.94 (4H, m, $H_2CO \times 2$), 3.46−3.20 (6H, m, HC-2, HC-3, $H_2CS \times 2$), 3.3.26 (1H, br s, HOC-1′), 3.08−2.91 (4H, m, HOC-1″, HC-6, HC-7′, HC-9″), 2.87−2.69 (7H, m, HC-2, HC-5, HC-6, HC-7′, H_2C-7″, HC-9′), 2.60−2.46 (3H, m, HC-9′, HC-9″, HC-10″), 2.30 (1H, ddd, *J* = 3,11.5, 14 Hz, HC-10″), 2.21 (1H, ddd, *J* = 2, 3, 10 Hz, HC-6′), 2.15 (1H, ddd, *J* = 2.5, 4.5, 13.5 Hz, HC-10′), 2.04 (1H, ap dd, *J* = 5, 8.5 Hz, HC-6″), 1.75 (1H, ddd, *J* = 3.5, 11, 13.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.3 (s, C-4), 110.3 (s, C-5′), 73.2 (s, C-5″), 70.8 (d, C-1″), 67.5 (d, C-1′), 64.8 (t, C-2′), 64.3 (t, C-3′), 56.5 (d, C-5), 54.6 (d, C-3), 51.7 (d, C-6″), 47.3 (t, C-10″), 45.7 (d, C-6′), 40 (t, C-2″), 39.6 (t, C-2″), 36.0 (t, C-10′), 34.4 (t, C-2), 34.2 (t, C-6), 28.7 (t, C-7″), 28.3 (t, C-9″), 26.7 (t, C-9′), 26.3 (t, C-7′); HRMS *m*/*z* calcd. for $C_{21}H_{32}O_5S_5$+Na 547.0745, found 547.0729 (ESI). A solution of 30% aq HF (0.9 mL) was added to a stirred solution of (±)-**6a** (R = Et_3Si) (9 mg, 0.014 mmol) in CH_3CN (2 mL) at 0 °C. After 5 min, the mixture was diluted with ethyl acetate and washed sequentially with saturated aq $NaHCO_3$ and brine, dried over Na_2SO_4, concentrated, and fractionated by PTLC (30% ethyl acetate in hexane, multiple developments) to give the title compound (3 mg, 43%) whose ^1H NMR data closely matched those above.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*R*)-2-(2-ethyl-1,3-dithian-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6b (R = MOM)].[36] Reaction of (±)-**5b** (29 mg, 0.14 mmol) with (±)-**1a** (R = MOM) (24 mg, 0.069 mmol) via the boron enolate for 3 h gave a crude product whose ^1H NMR spectrum indicated the presence of a (±)-**6b** (R= MOM) as a single adduct (dr > 20). Fractionation of the crude by FCC (30% ethyl acetate in hexane) afforded recovered (±)-**5b** (8 mg, 27%), (±)-**1a** (R = MOM) (2 mg, 8%), and the title compound (34 mg, 89%): IR ν_{max} 3500, 1706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.04 (1H, dd, *J* = 4.5, 9 Hz, HC-1″), 4.69 (1H, d, *J* = 6 Hz, OCH_2O), 4.67 (1H, d, *J* = 6 Hz, OCH_2O), 4.46 (4H, dd, *J* = 5, 5 Hz, HC-1′), 4.06−3.93 (4H, m, H_2C-2′, H_2C-3′), 3.36 (3H, s, H_3CO),

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3.25 (1H, ddd, J = 4.5, 5, 9.5 Hz, HC-3), 3.11−2.64 (12H, m, H_2C-2, H_2C-4‴, HC-5, H_2C-6, H_2C-6‴, H_2C-7′, HC-9′), 2.70 (1H, d, J = 4.5 Hz, HO), 2.50 (1H, br d, J = 13 Hz, HC-9′), 2.29 (1H, dq, J = 7.5, 15 Hz, HC-1‴), 2.11−1.97 (4H, m, HC-1‴, HC-5‴, HC-6′, HC-10′), 1.93−1.85 (2H, m, HC-2″, HC-5‴), 1.68 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.09 (3H, d, J = 7 Hz, H_3C-3″), 0.99 (3H, t, J = 7.5 Hz, H_3C-2‴); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.2 (s, C-4), 108.9 (s, C-5′), 98.6 (t, OCH_2O), 72.7 (d, C-1′), 70.2 (d, C-1″), 64.6 (t, C-2′), 64.6 (t, C-3′), 59.4 (s, C-2‴), 57.4 (d, C-3), 56.8 (q, CH_3O), 55.9 (d, C-5), 49.1 (d, C-6′), 41.3 (d, C-2″), 36.2 (t, C-10′), 32.9 (t, C-6), 31.5 (t, C-2), 29.2 (t, C-1‴), 28.4 (t, C-7′), 26.7 (t, C-9′), 26.1 (t, C-4″), 25.9 (t, C-6″), 25.2 (t, C-5″), 9.6 (q, C-2‴), 7.6 (q, C-3″); HRMS m/z calcd. for $C_{24}H_{40}O_6S_4$+Na 575.1599, found 575.1600 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*R*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6c (R = MOM)].[36] Reaction of (±)-**5c** (46 mg, 0.26 mmol) with (±)-**1a** (R = MOM) (45 mg, 0.13 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of (±)-**6c** (R = MOM) as a single adduct (dr > 20). Fractionation of the crude by FCC (30−50% ethyl acetate in hexane) afforded recovered aldehyde (±)-**5c** (18 mg, 39%) and the title compound (45 mg, 66%): IR ν_{max} 3512, 1704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70−4.63 (3H, m, HC-1″, OCH_2O), 4.49 (1H, dd, J = 5, 5.5 Hz, HC-1′), 4.08−3.91 (4H, m, H_2C-2′, H_2C-3′), 3.38−3.24 (4H, m, H_2C-4‴, H_2C-5‴), 3.36 (3H, s, H_3CO), 3.17 (1H, ddd, J = 4, 5.5, 9 Hz, HC-3), 3.10 (1H, dd, J = 9, 13.5 Hz, HC-2), 3.02−2.94 (1H, m, HC-2, HC-6), 2.92 (1H, d, J = 4 Hz, HO), 2.90−2.65 (5H, m, J = 7 Hz, HC-5, HC-6, H_2C-7′, HC-9′), 2.50 (1H, br d, J = 13.5 Hz, HC-9′), 2.10−2.07 (2H, m, HC-6′, HC-10′), 2.00 (1H, br q, J = 7 Hz, HC-2″), 1.83 (3H, s, H_3C-1‴), 1.67 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.15 (3H, d, J = 7 Hz, H_3C-3″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.1 (s, C-4), 108.9 (s, C-5′), 98.6 (t, OCH_2O), 72.9 (d, C-1′), 72.3 (s, C-2‴), 71.8 (d, C-1″), 64.7 (t, C-2′), 64.6 (t, C-3′), 57.8 (d, C-3), 56.8 (q, CH_3O), 55.4 (d, C-5), 49.0 (d, C-6′), 46.9 (d, C-2″), 40.1 (t, C-5‴), 39.7 (t, C-5‴), 36.2 (t, C-10′), 32.2 (t, C-6), 31.8 (q, C-1‴), 31.2 (t, C-2), 28.3 (t, C-7′), 26.7 (t, C-9′), 11.5 (q, C-3″); HRMS m/z calcd. for $C_{22}H_{36}O_6S_4$+Na 547.1286, found 547.1298 (ESI).

(3*R*,5*R*)-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*R*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(+)-6c (R = MOM)].[36] Reaction of (±)-**5c** (48 mg, 0.27 mmol) with (+)-**1a** (R = MOM) (31 mg, 0.089 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of **6c** (R = MOM) as a single adduct (dr > 20). Fractionation of the crude by FCC (10−50% ethyl acetate in hexane) afforded recovered (±)-**5c** (21 mg, 43%) and the title compound (38 mg, 81%) ($[\alpha]_D$ +120; c 2.5, $CHCl_3$). NMR data were consistent with those obtained from the racemic material above.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*S*,2*R*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6c (R = Et$_3$Si)].[36] Reaction of (±)-**5c** (21 mg, 0.12 mmol) with (±)-**1a** (R = Et_3Si) (25 mg, 0.060 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of (±)-**6c** (R = Et_3Si) as a single adduct (dr > 20). Fractionation of the crude by PTLC (10% ethyl acetate in hexane; multiple developments) afforded recovered (±)-**5c** (9 mg, 43%), (±)-**1a** (R = Et_3Si) (2 mg, 8%), and the title compound (27 mg, 75%): IR ν_{max} 3500, 1706 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.85 (1H, dd, J = 4, 9 Hz, HC-1″), 4.65 (1H, br d, J = 7 Hz, HC-1′), 4.01−3.85 (4H, m, H_2C-2′, H_2C-3′), 3.39−3.27 (4H, m, H_2C-4‴, H_2C-5‴), 3.23 (1H, br dd, J = 3.5, 9 Hz, HC-3), 3.06−2.95 (2H, m, HC-2, HC-6), 2.87 (1H, dd, J = 3.5, 13.5 Hz, HC-2), 2.80 (1H, ddd, J = 2, 12.5, 13.5 Hz, HC-9′), 2.76 (1H, d, J = 4 Hz, HO), 2.75−2.65 (4H, m, HC-5, HC-6, H_2C-7′), 2.48 (1H, br d, J = 13.5 Hz, HC-9), 2.09−1.96 (3H, m, HC-2″, HC-6′, HC-10′), 1.83 (3H, s, H_3C-1‴), 1.66 (1H, ddd, J = 3.5, 12.5, 13.5 Hz, HC-10′), 1.13 (3H, d, J = 7 Hz, H_3C-3″), 0.93 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.66−0.60 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6 (s, C-4), 109.5 (s, C-5′), 72.1 (d, C-1″), 71.8 (s, C-2‴), 66.6 (d, C-1′), 64.8 (t, C-2′), 64.7 (t, C-3′), 58.3 (d, C-3), 55.7 (d, C-5), 49.7 (d, C-6′), 47.0 (d, C-2″), 40.1 (t, C-4‴), 39.9 (t, C-5‴), 36.9 (t, C-10′), 32.4 (q, C-1‴), 31.8 (t, C-6′), 29.3 (t, C-2), 29.1 (t, C-7′), 26.7 (t, C-9′), 11.4 (q, C-3″), 7.3 (q × 3, CH_3CSi), 5.4 (t × 3, CH_2Si); HRMS m/z calcd. for $C_{26}H_{46}O_5SiS_4$+Na 617.1889, found 617.1900 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*R*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6d (R = MOM)].[36] Reaction of (±)-**5d** (91 mg, 0.48 mmol) with (±)-**1a** (R = MOM) (84 mg, 0.24 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 17:1 mixture of (±)-**6d** (R = MOM) and (±)-**7d** (R = MOM), respectively. Fractionation of the crude FCC (30−40% ethyl acetate in hexane) afforded recovered (±)-**5d** (21 mg, 23%), (±)-**1a** (R = MOM), (±)-**7d** (R = MOM) (6 mg, 5%) and the title compound (102 mg 79%): IR ν_{max} 3508, 1707 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80 (1H, dd, J = 3, 9 Hz, HC-1″), 4.67 (1H, d, J = 6 Hz, OCH_2O), 4.65 (1H, d, J = 6 Hz, OCH_2O), 4.42 (1H, dd, J = 5, 5 Hz, C-1′), 4.04−3.90 (4H, m, H_2C-2′, H_2C-3′), 3.35 (3H, s, H_3CO), 3.32−3.20 (5H, m, HC-3, H_2C-4″, H_2C-5″), 3.06−2.92 (4H, m, HO, H_2C-2, HC-6), 2.85−2.73 (4H, m, HC-5, H_2C-7′, HC-9′), 2.67 (1H, dd, J = 5.5, 13.5 Hz, HC-6), 2.48 (1H, br d, J = 13.5 Hz, HC-9′), 2.12−1.95 (5H, m, H_2C-1‴″, HC-2″, HC-6′, HC-10′), 1.69−1.63 (1H, ddd, J = 3.5, 12.5, 13.5 Hz, HC-10′), 1.09 (3H, d, J = 7 Hz, H_3C-3″), 1.06 (3H, t, J = 7 Hz, H_3C-2‴); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.1 (s, C-4), 109.0 (t, C-5′), 98.7 (t, OCH_2O), 77.8 (s, C-2‴), 72.8 (d, C-1′), 71.0 (d, C-1″), 64.6 (t, C-2′), 64.5 (t, C-3′), 57.3 (d, C-3), 56.7 (q, CH_3O), 55.8 (d, C-5), 49.0 (d, C-6′), 44.4 (d, C-2″), 40.4 (t, C-4‴), 39.8 (t, C-5‴), 36.2 (t, C-10′), 35.9 (t, C-1‴), 32.5 (t, C-6), 31.3 (t, C-2), 28.3 (t, C-7′), 26.7 (t, C-9′), 11.3 (q, C-3″), 10.8 (q, C-2‴); HRMS m/z calcd. for $C_{23}H_{38}O_6S_4$+Na 561.1443, found 561.1460 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*S*,2*R*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6d (R = Et$_3$Si)].[36] Reaction of (±)-**5d** (30 mg, 0.16 mmol) with (±)-**1a** (R = Et_3Si) (33 mg, 0.079 mmol) via the boron enolate for 16 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a >20:1 mixture of (±)-**6d** (R = Et_3Si) and (±)-**7d** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (10% ethyl acetate in hexane; 2 developments) afforded recovered (±)-**5d** (10 mg, 33%), (±)-**1a** (R = Et_3Si) (2 mg, 6%), and the title compound (36 mg, 75%): IR ν_{max} 3500, 1708 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.97 (1H, dd, J = 3, 9 Hz, HC-1″), 4.64 (1H, dd, J = 1.5, 7.5 Hz, HC-1′), 3.99−3.82 (4H, m, H_2C-2′, H_2C-3′), 3.38−3.25 (5H, m, HC-3, H_2C-4‴, H_2C-5‴), 3.03 (1H, dd, J = 11.5, 13.5 Hz, HC-2), 2.98 (1H, dd, J = 3, 13.5 Hz, HC-6), 2.93 (2H, m, J = 3 Hz, HO), 2.87 (4H, m, J = 2.5, 4.5, 13.5 Hz, HC-2), 2.81 (1H, ddd, J = 2.5, 12.5, 13.5 Hz, HC-9′), 2.78−2.62 (4H, m, HC-5, HC-6, H_2C-7′), 2.48 (1H, br d, J = 13.5 Hz, HC-9′), 2.09 (1H, ddd, J = 4, 7.5, 11 Hz, HC-6′), 2.08−1.95 (3H, m, H_2C-1‴, HC-2″), 1.67 (1H, ddd, HC-10′), 1.09 (3H, d, J = 7 Hz, HC-3″), 1.08 (3H, t, J = 7 Hz, HC-2‴), 0.94 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.71−0.59 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.7 (s, C-4), 109.5 (s, C-5′), 77.7 (s, C-2‴), 71.1 (d, C-1″), 66.6 (d, C-1′), 64.9 (t, C-2′), 64.7 (t, C-3′), 58.1 (d, C-3), 55.9 (d, C-5), 49.6 (d, C-6′), 44.5 (d, C-2″), 40.5 (t, C-4‴), 39.9 (t, C-5‴), 37.0 (t, C-10′), 36.5 (t, C-1‴), 32.2 (t, C-6), 29.6 (t, C-2), 29.2 (t, C-7′), 26.7 (t, C-9′), 11.4 (q, C-3″), 10.9 (q, C-2‴), 7.3 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd. for $C_{27}H_{48}O_5SiS_4$+Na 631.2046, found 631.2023 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*R*)-2-(2-ethyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6e (R = MOM)].[36] Reaction of (±)-**5e** (122 mg, 0.77 mmol) with (±)-**1a** (R = MOM) (135 mg, 0.387 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of (±)-**6e** (R = MOM) as a single adduct (dr > 20). Fractionation of the crude FCC (15−90% ethyl acetate in hexane) afforded recovered (±)-**5e** (7 mg, 6%), (±)-**1a** (R = MOM) (2 mg, 1%), and the title compound (162 mg, 83%): IR ν_{max} 3521, 1712 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.69 (1H, br d, J = 9.5 Hz, HC-1″), 4.67 (1H, d, J = 6 Hz, OCH_2O), 4.65 (1H, d, J = 6 Hz, OCH_2O), 4.38 (1H, dd, J = 5, 5

Hz, HC-1′), 4.01−3.90 (8H, m, H_2CO × 4), 3.35 (3H, s, H_3CO), 3.31 (1H, ddd, J = 4.5, 5, 10 Hz, HC-3), 3.03−2.94 (1H, m, H_2C-2, HC-6), 2.91 (1H, d, J = 2 Hz, HO), 2.83−2.75 (1H, m, HC-5, H_2C-7′, HC-9′), 2.58 (1H, ddd, J = 2, 5, 14 Hz, HC-6), 2.48−2.45 (1H, m, HC-9′), 2.11 (1H, ddd, J = 4.5, 5, 10 Hz, HC-6′), 2.04 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-10′), 1.91 (1H, br q, J = 7, 14 Hz, HC-2″), 1.80−1.69 (2H, m, H_2C-1‴), 1.66 (1H, ddd, J = 3.5, 12.5. 13.5 Hz, H_3C-10′), 0.93 (3H,, J = 7 Hz, H_3C-3″), 0.89 (3H,, J = 7.5 Hz, H_3C-2‴); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.7 (s, C-4), 114.5 (s, C-2‴), 109.0 (s, C-5′), 98.7 (t, OCH_2O), 72.9 (d, C-1′), 69.3 (d, C-1″), 65.8 (t, CH_2O), 65.1 (t, CH_2O), 64.7 (t, CH_2O), 64.5 (t, CH_2O), 56.8 (d, C-3), 56.6 (q, CH_3O), 54.9 (d, C-5), 49.0 (d, C-6′), 39.3 (d, C-2″), 36.4 (t, C-10′), 32.5 (t, C-6), 31.5 (t, C-2), 28.4 (t, C-1‴ or C-7′), 28.3 (t, C-1‴ or C-7′), 26.7 (t, C-9′), 8.2 (q, C-2‴), 7.0 (q, C-3″); HRMS m/z calcd. for $C_{23}H_{38}O_8S_2$+Na 529.1900, found 529.1898 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*R*,2*R*)-2-(2-ethyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6e (R = Et_3Si)].[36] Reaction of (±)-**5e** (28 mg, 0.18 mmol) with (±)-**1a** (R = Et_3Si) (37 mg, 0.088 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of (±)-**6e** (R = Et_3Si) as a single adduct (dr > 20). Fractionation of the crude by FCC (25% ethyl acetate in hexane) afforded recovered (±)-**5e** (7 mg, 25%) and the title compound (39 mg, 76%): IR ν_{max} 3518, 1711 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80 (1H, br d, J = 10 Hz, C-1″), 4.62 (1H, dd, J = 1.5, 8 Hz, C-1′), 4.03−3.85 (8H, m, H_2CO × 4), 3.37 (1H, ddd, J = 1.5, 5, 11.5 Hz, HC-3), 3.04 (1H, dd, J = 11.5, 13.5 Hz, HC-2), 2.98 (1H, dd, J = 3.5, 14 Hz, HC-6), 2.89 (1H, br s, HO), 2.87 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-2), 2.81 (1H, ddd, J = 3, 13, 13.5 Hz, HC-9′), 2.77−2.63 (3H, m, HC-5, H_2C-7′), 2.61 (1H, ddd, J = 3, 3, 14 Hz, HC-6), 2.48 (1H, br d, J = 13.5 Hz, HC-9′), 2.10 (1H, ddd, J = 4, 8, 11 Hz, HC-6′), 2.04−1.95 (2H, m, HC-2″, HC-10′), 0.96−0.90 (15H, m, H_3C-2‴, H_3C-3″, H_3CCSi × 3), 0.69−0.60 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5 (s, C-4), 114.7 (s, C-2‴), 109.5 (s, C-5′), 69.5 (d, C-1″), 66.6 (d, C-1′), 65.9 (t, CH_2O), 65.2 (t, CH_2O), 65.0 (t, CH_2O), 64.8 (t, CH_2O), 57.2 (d, C-3), 54.9 (d, C-5), 49.7 (d, C-6′), 39.1 (d, C-2″), 37.2 (t, C-10′), 32.2 (t, C-6), 29.8 (t, C-2), 29.2 (t, C-7′), 28.5 (t, C-1‴), 26.6 (t, C-9′), 8.3 (q, C-2‴), 7.3 (q × 3, CH_3CSi), 6.7 (q, C-3″), 5.3 (q × 3, CH_2Si); HRMS m/z calcd. for $C_{27}H_{48}O_7SiS_2$+Na 599.2502, found 599.2485 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*R*)-2-(2-methyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-6f (R = MOM)].[36] Reaction of (±)-**5f** (19 mg, 0.13 mmol) with (±)-**1a** (R = MOM) (23 mg, 0.066 mmol) via the boron enolate for 3 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of (±)-**6f** (R = MOM) as a single adduct (dr > 20). Fractionation of the crude by FCC (30% ethyl acetate in hexane) afforded recovered (±)-**5f** (3 mg, 16%), (±)-**1a** (R = MOM) (2 mg, 9%), and the title compound (25 mg, 78%): IR ν_{max} 3524, 1710 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70−4.64 (3H, m, HC-1″, OCH_2O), 4.43 (1H, dd, J = 5, 5 Hz, HC-1′), 4.05−3.90 (8H, m, H_2CO × 4), 3.36 (3H, s, H_3CO), 3.27 (1H, ddd, J = 4, 5, 9.5 Hz, HC-3), 3.06 (1H, dd, J = 10, 13.5 Hz, HC-2), 2.99−2.94 (2H, m, HC-2, HC-6), 2.87−2.75 (5H, m, HO, HC-5, H_2C-7′, HC-9′), 2.61 (1H, ddd, J = 1.5, 6, 13.5 Hz, HC-6), 2.49 (1H, br d, J = 13.5 Hz, HC-9′), 2.10 (1H, ddd, J = 4, 5, 10.5 Hz, HC-6′), 2.06 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-10′), 1.82 (1H, br q, J = 7 Hz, HC-2″), 1.67 (1H, ddd, J = 3.5, 12.5, 13.5 Hz, HC-10′), 1.37 (3H, s, H_3C-1‴), 0.98 (3H, d, J = 7 Hz, H_3C-3″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.1 (s, C-4), 112.5 (s, C-2‴), 109.0 (s, C-5′), 98.7 (t, OCH_2O), 73 (d, C-1′), 69.4 (d, C-1″), 65.1 (t, CH_2O), 64.7 (t, CH_2O), 64.64 (t, CH_2O), 64.57 (t, CH_2O), 57 (d, C-3), 56.8 (q, CH_3O), 54.8 (d, C-5), 49.1 (d, C-6′), 42.4 (d, C-2″), 36.4 (t, C-10′), 32.3 (t, C-6), 31.3 (t, C-2), 28.4 (t, C-7′), 26.7 (t, C-9′), 22.4 (q, C-1‴), 7.5 (q, C-3″); HRMS m/z calcd. for $C_{22}H_{36}O_8S_2$+Na 515.1743, found 515.1761 (ESI).

General Procedure for Aldol Reactions of 1a (R = MOM, Et_3Si) via Its Ti(IV) "ate" Enolate. A sufficient amount of LDA (0.5 M in THF) was prepared by dropwise addition of *n*-BuLi (1−2 M in hexane, freshly titrated; 1 equiv) to a stirred solution of ^{i}Pr$_2$NH (0.5 M in THF; 1.05 equiv) at 0 °C under argon. After 20 min, the resulting LDA solution (1.1 equiv) was added via syringe to a stirred solution of **1a** in THF (0.1 M) at −78 °C under Ar.[45] After 15 min, Ti(OiPr)$_4$ (2.2 or 4.4 equiv) was added. The reaction mixture was stirred for 10 min at −78 °C, 30 min at −50 °C, and finally 5 min at −78 °C. A solution of aldehyde (2 or 3 equiv) in THF (0.8 M) was added via syringe. After the indicated time, the reaction was quenched by addition of saturated aq NH_4Cl and the mixture was extracted with ethyl acetate. The combined organic layers were filtered through a short column layered with Na_2SO_4, SiO_2, and Na_2SO_4, and the combined filtrate and ethyl acetate washings were concentrated to give the crude product that was analyzed by ^{1}H NMR.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-ylhydroxmethyl]-5-[(*R*)-(6*R*)-1,4,8-trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7a (R = MOM)].[36] Reaction of (±)-**5a** (66 mg, 0.30 mmol) with (±)-**1a** (R = MOM) (51 mg, 0.15 mmol) via the Ti(IV) "ate" enolate (4.4 equiv of Ti(O^{i}Pr)$_4$) for 1 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 1:13 mixture of (±)-**6a** (R = MOM) and (±)-**7a** (R = MOM), respectively. Fractionation of the crude by FCC (20−40% ethyl acetate in hexane) afforded recovered (±)-**5a** (22 mg, 33%), (±)-**1a** (R = MOM) (2 mg, 4%), (±)-**6a** (R = MOM) (5 mg, 6%) and the title compound (62 mg, 73%): IR ν_{max} 3453, 1699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.11 (1H, br dd, J = 2, 9 Hz, HC-1″), 4.69 (1H, d, J = 6 Hz, OCH_2O), 4.63 (1H, d, J = 6 Hz, OCH_2O), 4.59 (1H, dd, J = 3, 6.5 Hz, HC-1′), 4.10−43.92 (4H, m, H_2C-2′, HC-3′), 3.50 (1H, d, J = 2 Hz, HO), 3.39−3.28 (4H, m, H_2C-2″, H_2C-3″), 3.37 (3H, s, H_3CO), 3.18 (1H, br dd, J = 3.5, 13.5 Hz, HC-6), 3.10−2.92 (6H, m, H_2C-2, HC-3, HC-5, HC-6, HC-9″), 2.88 (1H, dd, J = 11.5, 13.5 Hz, HC-7′), 2.82 (1H, ddd, J = 3, 13, 13 Hz, HC-9′), 2.78−2.68 (3H, m, HC-7′, H_2C-7″), 2.58−2.35 (4H, m, HC-9′, HC-9″, H_2C-10″), 2.08 (1H, ddd, J = 4.9, 8.8 Hz, HC-10′), 2.01 (1H, dd, HC-6″), 1.92 (1H, ddd, J = 3, 3.5, 11.5 Hz, HC-6′), 1.77 (1H, ddd, J = 4, 13, 13 Hz, HC-10′); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.5 (s, C-4), 108.9 (s, C-5′), 98.5 (t, OCH_2O), 73.8 (s, C-5″), 71.7 (d, C-1′), 69.5 (d, C-1″), 64.8 (t, C-2′), 64.5 (t, C-3′), 58.3 (d, C-3), 56.8 (q, CH_3O), 55.7 (d, C-5), 50.1 (d, C-6″ or C-6′), 49.9 (d, C-6′ or C-6″), 47.3 (t, C-10″), 39.5 (t, C-2″), 39.4 (t, C-3″), 36.2 (t, C-10′), 33.8 (t, C-6), 32.8 (t, C-2), 28.15 (t, C-7′, C7″ or C-9″), 28.07 (t, C-7′, C7″ or C-9″), 28.05 (t, C-7′, C7″ or C-9″), 26.8 (t, C-9′); HRMS m/z calcd. for $C_{23}H_{36}O_6S_5$+Na 591.1007, found 591.1015 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(*R*)-(6*R*)-1,4,8-trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7a (R = Et_3Si)].[36] Reaction of (±)-**5a** (40 mg, 0.18 mmol) with (±)-**1a** (R = Et_3Si) (37 mg, 0.088 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of Ti(O^{i}Pr)$_4$) for 16 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 1:2 mixture of (±)-**6a** (R = Et_3Si) and (±)-**7a** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (10% ethyl acetate in hexane; multiple developments) afforded recovered (±)-**5a** (10 mg, 25%), (±)-**1a** (R = Et_3Si) (6 mg, 23%), (±)-**6a** (R = Et_3Si) (11 mg, 20%), and the title compound (26 mg, 46%): IR ν_{max} 3448, 1698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (1H, br d, J = 10 Hz, HC-1″), 4.74 (1H, br s, HC-1′), 4.07−3.89 (4H, m, H_2C-2′, H_2C-3′), 3.50 (1H, br s, HO), 3.42−3.23 (4H, m, H_2C-2″, H_2C-3″), 3.12 (1H, br d, J = 13.5 Hz, HC-6), 3.05−2.73 (10H, m, H_2C-2, HC-3, HC-5, HC-6, HC-7′, H_2C-7″, HC-9′, HC-9″), 2.67 (1H, br d, J = 13.5 Hz, HC-7′), 2.55 (1H, br d, J = 14 Hz, HC-9″), 2.49−2.43 (2H, m, HC-9′, HC-10″), 2.31 (1H, ddd, J = 2.5, 12, 13.5 Hz, HC-10″), 2.05−2.00 (2H, m, HC-6′, HC-10′), 1.94 (1H, dd, J = 6.5, 7 Hz, HC-6″), 1.69 (, ddd, J = 3.5, 13, 13.5 Hz, HC-10′), 0.94 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.68−0.57 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9 (s, C-4), 109.6 (s, C-5′), 73.6 (s, C-5″), 69.4 (d, C-1″), 65.4 (d, C-1′), 65.1 (t, C-2′), 64.4 (t, C-3′), 59.9 (d, C-3), 55.9 (d, C-5), 51.0 (d, C-6″), 49.4 (d, C-6′), 47.0 (t, C-10″), 39.7 (t, C-2″), 39.5 (t, C-3″), 36.3 (t, C-10′), 33.0 (t, C-6), 30.7 (t, C-2), 28.8 (t, C-7′), 28.2 (t, C-7″ or C-9″), 28.0 (t, C-7″ or C-9″), 26.6 (t, C-9′), 7.3 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd. for $C_{27}H_{46}O_5SiS_5$+Na 661.1610, found 661.1604 (ESI).

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(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*S*)-2-(2-ethyl-1,3-dithian-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7b (R = MOM)].[36] Reaction of (±)-**5b** (37 mg, 0.18 mmol) with (±)-**1a** (R = MOM) (31 mg, 0.089 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of $Ti(O^iPr)_4$) for 0.5 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 2:1 mixture of (±)-**6b** (R = MOM) and (±)-**7b** (R = MOM), respectively. Fractionation of the crude by FCC (30% ethyl acetate in hexane) afforded recovered (±)-**5b** (8 mg, 22%), (±)-**1a** (R = MOM) (2 mg, 6%), (±)-**6b** (R = MOM) (26 mg, 53%), and the title compound (14 mg, 29%): IR ν_{max} 3500, 1700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.08 (1H, dd, J = 3.5, 9 Hz, HC-1″), 4.68 (1H, d, J = 6 Hz, OCH_2O), 4.63 (1H, d, J = 6 Hz, OCH_2O), 4.57 (1H, dd, J = 3.5, 6 Hz, HC-1′), 4.06−3.92 (4H, m, H_2C-2′, H_2C-3′), 3.35 (3H, s, H_3CO), 3.15−3.11 (2H, m, HC-2, HC-6), 3.03−2.62 (10H, m, HC-2, HC-3, H_2C-4‴, HC-5, H_2C-6‴, H_2C-7′, HC-9′), 2.70 (1H, d, J = 3.5 Hz, HO), 2.49 (1H, br d, J = 13.5 Hz, HC-9′), 2.29 (1H, dq, J = 7.5, 15 Hz, HC-1⁗), 2.08−1.85 (5H, HC-1⁗, H_2C-5‴, HC-6′ HC-10′), 1.79 (1H, br q, J = 7 Hz, HC-2″), 1.62−1.55 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.05 (3H, d, J = 7 Hz, H_3C-3″), 0.96 (3H, t, J = 7.5 Hz, H_3C-2⁗); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.5 (s, C-4), 108.7 (s, C-5′), 98.5 (t, OCH_2O), 72.3 (d, C-1′), 68.4 (d, C-1″), 64.7 (t, C-2′), 64.5 (t, C-3′), 59.6 (s, C-2″), 57.9 (d, C-3), 56.7 (q, CH_3O), 55.9 (d, C-5), 49.3 (d, C-6′), 41.5 (d, C-2″), 36.1 (t, C-10′), 32.8 (t, C-6), 31.8 (t, C-2), 29.6 (t, C-1⁗), 28.1 (t, C-7′), 26.7 (t, C-9′), 26.0 (t, C-4″), 25.9 (t, C-6″), 25.3 (t, C-5‴), 9.7 (q, C-2⁗), 7.4 (q, C-3″); HRMS m/z calcd. for $C_{24}H_{40}O_6S_4$+Na 575.1599, found 575.1614 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*S*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7c (R = MOM)].[36] Reaction of (±)-**5c** (32 mg, 0.18 mmol) with (±)-**1a** (R = MOM) (31 mg, 0.089 mmol) via the Ti(IV) "ate" enolate (4.4 equiv of $Ti(O^iPr)_4$) for 2 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 1:6 mixture of (±)-**6c** (R = MOM) and (±)-**7c** (R = MOM), respectively. Fractionation of the crude by PTLC (5% ethyl ether in CH_2Cl_2) afforded recovered aldehyde (±)-**5c** (16 mg, 50%), (±)-**1a** (R = MOM) (4 mg, 13%), and an inseparable 1:6 mixture of (±)-**6c** (R = MOM) and (±)-**7c** (R = MOM), respectively (36 mg, 77%): IR ν_{max} 3458, 1700 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ for **7c** 5.25 (1H, dd, J = 2, 9 Hz, HC-1″), 4.72−4.69 (2H, m, HC-1′, OCHO), 4.63 (1H, d, J = 6 Hz, OCHO), 3.52−3.424 (4H, m, H_2CO × 2), 3.23−3.12 (2H, m, HC-3, HC-6), 3.16 (3H, s, H_3CO), 3.12−2.83 (6H, m, H_2C-2, HC-5, HC-6, H_2C-7), 2.82−2.64 (6H, m, HO, HC-9′, H_2CS × 2), 2.26−2.21 (1H, m, HC-9′), 2.17 (1H, ddd, J = 4, 4, 10.5 Hz, HC-6′), 2.02 (1H, br q, J = 7 Hz, HC-2″), 1.84 (3H, s, H_3C-1⁗), 1.69 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-10′), 1.55 (1H, ddd, J = 3.5, 12, 15.5 Hz, HC-10′), 1.25 (3H, d, J = 7 Hz, H_3C-3″); ^{13}C NMR (125 MHz, C_6D_6) δ for **7c** 209.6 (s, C-4), 109.2 (s, C-5′), 98.5 (t, OCH_2O), 72.6 (s, C-2″), 72.5 (d, C-1′), 69.7 (t, C-1″), 64.5 (t, C-2′), 64.3 (t, C-3′), 58.1 (d, C-3), 57.0 (d, C-5), 56.2 (q, CH_3O), 50.1 (d, C-6′), 46.5 (d, C-2″), 40.1 (t, C-4′), 39.7 (t, C-5′), 36.5 (t, C-10′), 33.1 (q, C-1⁗), 32.6 (t, C-6), 31.7 (t, C-2), 28.8 (t, C-7′), 26.9 (t, C-9′), 11.5 (q, C-3″); HRMS m/z calcd. for $C_{22}H_{36}O_6S_4$+Na 547.1286, found 547.1272 (ESI).

(3*R*,5*R*)-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*S*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(+)-7c (R = MOM)].[36] Reaction of (±)-**5c** (49 mg, 0.28 mmol) with (+)-**1a** (R = MOM) (32 mg, 0.092 mmol) via the Ti(IV) "ate" enolate (4.4 equiv of $Ti(O^iPr)_4$) for 2 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 1:4 mixture of **6c** (R = MOM) and **7c** (R = MOM), respectively. Fractionation of the crude by PTLC (5% ethyl ether in CH_2Cl_2) afforded recovered (±)-**5c** (16 mg, 33%), (+)-**1a** (R = MOM) (4 mg, 13%), and an inseparable 1:4 mixture of **6c** (R = MOM) and **7c** (R = MOM), respectively (37 mg, 77%) ($[\alpha]_D$ +99; c 2.5, $CHCl_3$). NMR data for the mixture were consistent with those obtained from the racemic material above.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*R*,2*S*)-2-(2-methyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7c (R = Et_3Si)].[36] Reaction of (±)-**5c** (35 mg, 0.2 mmol) with (±)-**1a** (R = Et_3Si) (43 mg, 0.10 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of $Ti(O^iPr)_4$) for 3 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 3:1 mixture of (±)-**6c** (R = Et_3Si) and (±)-**7c** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (10% ethyl acetate in hexane; multiple developments) afforded recovered (±)-**5c** (10 mg, 29%), (±)-**1a** (R = Et_3Si) (6 mg, 14%), (±)-**6c** (R = Et_3Si) (26 mg, 44%), a 3:1 mixture of (±)-**6c** (R = Et_3Si) and the title compound, respectively (8 mg, 14%), and the title compound (10 mg, 17%): IR ν_{max} 3453, 1699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.13 (1H, dd, J = 3, 9.5 Hz, HC-1″), 4.68 (1H, dd, J = 2, 6.5 Hz, HC-1′), 4.05−3.79 (4H, m, H_2C-2′, H_2C-3′), 3.39−3.31 (4H, m, H_2C-4‴, H_2C-5‴), 3.18 (1H, ddd, J = 3, 3.5, 14 Hz, HC-6), 3.12 (1H, d, J = 3 Hz, HO), 3.04 (1H, dd, J = 10.5, 13 Hz, HC-2), 2.99 (1H, dd, J = 3.5, 14 Hz, HC-6), 2.95−2.84 (2H, m, HC-2, HC-3), 2.82−2.68 (2H, m, HC-5, H_2C-7′, HC-9′), 2.49 (1H, ddd, J = 3.5, 3.5, 13.5 Hz, HC-9′), 2.05−1.99 (2H, m, HC-6′, HC-10′), 1.82 (3H, s, H_3C-1⁗), 1.75 (1H, q, J = 6.5 Hz, HC-2″), 1.64 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.15 (3H, d, J = 7 Hz, H_3C-3″), 0.93 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.67−0.57 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1 (s, C-4), 109.6 (s, C-5′), 72.1 (s, C-2‴), 69.3 (d, C-1″), 65.9 (d, C-1′), 64.9 (t, C-2′), 64.5 (t, C-3′), 59.3 (d, C-3), 56.5 (d, C-5), 50.3 (d, C-6′), 45.5 (d, C-2″), 40.5 (t, C-4‴), 40.0 (t, C-5‴), 36.3 (t, C-10′), 33.7 (q, C-1⁗), 32.3 (t, C-6), 30.0 (t, C-2), 29.1 (t, C-7′), 26.7 (t, C-9′), 11.4 (q, C-3″), 7.3 (q × 3, CH_3CSi), 5.4 (t × 3, CH_2Si); HRMS m/z calcd. for $C_{26}H_{46}O_5SiS_4$+Na 617.1889, found 617.1913 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*S*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7d (R = MOM)].[36] Reaction of (±)-**5d** (128 mg, 0.67 mmol) with (±)-**1a** (R = MOM) (117 mg, 0.34 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of $Ti(O^iPr)_4$) for 0.5 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 1:8 mixture of (±)-**6d** (R = MOM) and (±)-**7d** (R = MOM), respectively. Fractionation of the crude by FCC (25−35% ethyl acetate in hexane) afforded recovered (±)-**5d** (50 mg, 59%), (±)-**1a** (R = MOM) (25 mg, 21%), a 4:1 mixture of (±)-**6d** (R = MOM) and the title compound, respectively (15 mg, 8%), and the title compound (124 mg, 69%): IR ν_{max} 3455, 1700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.05 (1H, br d, J = 9.5 Hz, HC-1″), 4.66 (1H, d, J = 6 Hz, OCH_2O), 4.62 (1H, d, J = 6 Hz, OCH_2O), 4.50 (1H, dd, J = 4, 4.5 Hz, HC-1′), 4.07−3.92 (4H, m, H_2C-2′, H_2C-3′), 3.46 (1H, br s, HO), 3.34 (3H, s, H_3CO), 3.33−3.25 (4H, m, H_2C-4‴, H_2C-5‴), 3.12−3.08 (2H, m, H_2C-6), 3.07−2.95 (3H, m, H_2C-2, HC-3), 2.89−2.72 (4H, m, HC-5, H_2C-7′, HC-9′), 2.49 (1H, br d, J = 13.5 Hz, HC-9′), 2.09−1.89 (4H, m, H_2C-1⁗, HC-6′, HC-10′), 1.83 (1H, br q, J = 7 Hz, HC-2″), 1.60 (1H, ddd, J = 3.5, 12.5, 13.5 Hz, HC-10′), 1.05 (3H, d, J = 7 Hz, H_3C-3″), 1.03 (3H, t, J = 7.5 Hz, H_3C-2⁗); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4 (s, C-4), 108.8 (t, C-5′), 98.4 (t, OCH_2O), 78.0 (s, C-2‴), 72.1 (d, C-1′), 69.1 (d, C-1″), 64.7 (t, C-2′), 64.5 (t, C-3′), 57.6 (d, C-3), 56.7 (q, CH_3O), 56.3 (d, C-5), 49.6 (d, C-6′), 42.8 (d, C-2″), 40.3 (t, C-4‴), 39.8 (t, C-5‴), 37.0 (t, C-1⁗), 36.1 (t, C-10′), 33.0 (t, C-6), 32.1 (t, C-2), 28.2 (t, C-7′), 26.7 (t, C-9′), 11.5 (q, C-3″), 10.8 (q, C-2⁗); HRMS m/z calcd. for $C_{23}H_{38}O_6S_4$+Na 561.1443, found 561.1455 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*R*,2*S*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7d (R = Et_3Si)].[36] Reaction of (±)-**5d** (23 mg, 0.12 mmol) with (±)-**1a** (R = Et_3Si) (26 mg, 0.062 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of $Ti(O^iPr)_4$) for 16 h gave a crude product whose ^1H NMR spectrum indicated the presence of a 1.3:1 mixture of (±)-**6d** (R = Et_3Si) and (±)-**7d** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (10% ethyl acetate in hexane; multiple developments) afforded recovered (±)-**5d** (5 mg, 22%), (±)-**1a** (R = Et_3Si) (6 mg, 23%), (±)-**6d** (R = Et_3Si) (11 mg, 29%), and the title compound (9 mg, 24%): IR ν_{max} 3474, 1710 cm^1; ^1H NMR (500 MHz, $CDCl_3$) δ 5.11 (1H, dd, J = 2, 10 Hz, HC-1″), 4.71 (1H, dd, J = 2.5, 6 Hz, HC=1′), 4.05−3.81 (4H, m, H_2C-2′, H_2C-3′), 3.44 (1H, d, J = 2 Hz, HO), 3.36−3.23 (4H, m, H_2C-4‴, H_2C-5‴), 3.16 (1H, ddd, J = 2, 4.5, 13.5

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Hz, HC-6), 3.07−2.96 (2H, m, HC-2, HC-6), 2.94−2.85 (2H, m, HC-2, HC-3), 2.81−2.65 (4H, m, HC-5, H_2C-7′, HC-9′), 2.549 (1H, br d, J = 13.5 Hz, HC-9′), 2.05−1.94 (4H, m, H_2C-1‴, HC-6′, HC-10′), 1.81 (1H, br q, J = 7 Hz, HC-2″), 1.61 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.08 (3H, d, J = 7 Hz, H_3C-3″), 1.04 (3H, t, J = 7 Hz, HC-2⁗), 0.93 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.66−0.58 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1 (s, C-4), 109.4 (s, C-5′), 77.9 (s, C-2‴), 69.0 (d, C-1″), 66.0 (d, C-1′), 64.9 (t, C-2′), 64.5 (t, C-3′), 59.1 (d, C-3), 56.2 (d, C-5), 50.1 (d, C-6′), 42.8 (d, C-2″), 40.5 (t, C-4‴), 40.0 (t, C-5‴), 37.0 (t, C-1‴), 36.5 (t, C-10′), 32.2 (t, C-6), 30.0 (t, C-2), 29.0 (t, C-7′), 26.7 (t, C-9′), 11.6 (q, C-3″), 10.9 (q, C-2⁗), 7.4 (q × 3, CH_3CSi), 5.4 (t × 3, CH_2Si); HRMS m/z calcd. for $C_{27}H_{48}O_5SiS_4$+Na 631.2046, found 631.2066 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*S*)-2-(2-ethyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7e (R = MOM)].[36] Reaction of (±)-**5e** (85 mg, 0.54 mmol) with (±)-**1a** (R = MOM) (95 mg, 0.27 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of Ti(O^iPr)$_4$) for 0.5 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 1:4 mixture of (±)-**6e** (R = MOM) and (±)-**7e** (R = MOM), respectively. Fractionation of the crude by FCC (30−50% ethyl acetate in hexane) afforded recovered (±)-**5e** (20 mg, 24%), (±)-**1a** (R = MOM) (9 mg, 9%), (±)-**6e** (R = MOM) (26 mg, 19%), and the title compound (95 mg. 69%): IR ν_{max} 3515, 1700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.66 (1H, d, J = 6 Hz, OCH_2O), 4.63 (1H, d, J = 6 Hz, OCH_2O), 4.55 (1H, br d, J = 9.5 Hz, HC-1″), 4.53 (1H, dd, J = 4.5, 5.5 Hz, HC-1′), 4.04−3.90 (8H, m, H_2CO × 4), 3.35 (3H, s, H_3CO), 3.16−3.06 (2H, m, HC-2, HC-6), 3.12 (1H, br d, HO), 3.03−2.88 (4H, m, HC-2, HC-3, HC-5, HC-6), 2.84 (1H, dd, J = 11, 14 Hz, HC-7′), 2.82−2.70 (2H, v, HC-7′, HC-9′), 2.49 (1H, br d, J = 13.5 Hz, HC-9′), 2.05 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-10′), 1.91 (1H, ddd, J = 3.5, 4, 11 Hz, HC-6′), 1.82 (1H, dq, J = 1, 7 Hz, HC-2″), 1.73−1.65 (2H, m, H_2C-1‴), 1.60 (1H, ddd, J = 3.5,12, 13.5 Hz, HC-10′), 0.96 (3H, d, J = 7 Hz, H_3C-3″), 0.89 (3H, T, J = 7.5 Hz, H_3C-2⁗); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6 (s, C-4), 114.9 (s, C-2‴), 108.8 (s, C-5′), 98.6 (t, OCH_2O), 72.3 (d, C-1′), 67.8 (d, C-1″), 65.6 (t, CH_2O), 65.2 (t, CH_2O), 64.61 (t, CH_2O), 64.55 (t, CH_2O), 56.8 (q, CH_3O), 56.7 (d, C-3), 55.1 (d, C-5), 49.2 (d, C-6′), 39.8 (d, C-2″), 36.1 (t, C-10′), 32.8 (t, C-2 or C-6), 31.8 (t, C-6 or C-2), 28.2 (t, C-1‴ or C-7′), 28.1 (t, C-1‴ or C-7′), 26.7 (t, C-9′), 8.2 (q, C-2⁗), 7.6 (q, C-3″); HRMS m/z calcd. for $C_{23}H_{38}O_8S_2$+Na 529.1900, found 529.1912 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(triethylsilyloxy)methyl]-5-[(1*S*,2*S*)-2-(2-ethyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7e (R = Et_3Si)].[36] Reaction of (±)-**5e** (17 mg, 0.11 mmol) with (±)-**1a** (R = Et_3Si) (22 mg, 0.053 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of Ti(O^iPr)$_4$) for 15 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 3:1 mixture of (±)-**6e** (R = Et_3Si) and (±)-**7e** (R = Et_3Si), respectively. Fractionation of the crude by PTLC (25% ethyl acetate in hexane) afforded recovered (±)-**5e** (2 mg, 12%), (±)-**1a** (R = Et_3Si) (3 mg, 14%), (±)-**6e** (R = Et_3Si) (21 mg, 68%), and the title compound (5 mg, 16%): IR ν_{max} 3515, 1700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.71−4.66 (2H, m, HC-1′, HC-1″), 4.08−3.79 (8H, m, H_2CO × 4), 3.18 (1H, br s, HO), 3.13 (1H, ddd, J = 2, 4.5, 3.5 Hz, HC-6), 3.08−2.98 (2H, m, HC-2, HC-6), 2.88−2.74 (4H, m, HC-2, HC-3, HC-5, HC-9′), 2.73−2.68 (2H, m, H_2C-7′), 2.52−2.47 (1H, ddd, J = 3.5, 4, 13.5 Hz, HC-9′), 2.03−1.97 (2H, m, HC-6′, HC-10′), 1.79−1.66 (3H, m, HC-2″, H_2C-1‴), 1.61 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 0.98 (3H, d, J = 7 Hz, H_3C-3″), 0.94 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.88 (3H, t, J = 7.5 Hz, H_3C-2⁗), 0.69−0.57 (6H, m, H_2CSi × 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.0 (s, C-4), 114.9 (s, C-2‴), 109.4 (s, C-5′), 67.5 (d, C-1″), 66.1 (d, C-1′), 65.9 (t, CH_2O), 65.3 (t, CH_2O), 64.6 (t, CH_2O), 64.5 (t, CH_2O), 59.2 (d, C-3), 55.4 (d, C-5), 49.7 (d, C-6′), 40.1 (d, C-2″), 36.4 (t), 32.0 (t, C-6), 29.8 (t, C-2), 29.0 (t, C-7′), 28.5 (t, C-1‴), 26.7 (t, C-9′), 8.3 (q, C-2⁗), 7.45 (q, C-3″), 7.34 (q × 3, CH_3CSi), 5.4 (q × 3, CH_2Si); (ESI), m/z (relative intensity); HRMS m/z calcd. for $C_{27}H_{48}O_7SiS_2$+Na 599.2502, found 599.2525 (ESI).

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*S*,2*S*)-2-(2-methyl-1,3-dioxolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-7f (R = MOM)].[36] Reaction of (±)-**5f** (20 mg, 0.14 mmol) with (±)-**1a** (R = MOM) (24 mg, 0.069 mmol) via the Ti(IV) "ate" enolate (2.2 equiv of Ti(O^iPr)$_4$) for 1 h gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 1:3 mixture of (±)-**6f** (R = MOM) and (±)-**7f** (R = MOM), respectively. Fractionation of the crude by FCC (30% ethyl acetate in hexane) afforded recovered (±)-**5f** (3 mg, 15%), (±)-**1a** (R = MOM) (1 mg, 4%), (±)-**6f** (R = MOM) (6 mg, 18%), and the title compound (18 mg, 53%): IR ν_{max} 3513, 1701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70−4.62 (3H, m, HC-1″, OCH_2O), 4.47 (1H, dd, J = 4, 5 Hz, HC-1′), 4.07−3.92 (8H, m, H_2CO × 4), 3.35 (3H, s, H_3CO), 3.15 (1H, dd, J = 4, 13.5 Hz, HC-6), 3.08−3.01 (3H, m, HO, HC-2, HC-6), 2.99−2.89 (3H, m, HC-2, HC-3, HC-6), 2.87−2.72 (3H, m, H_2C-7′, HC-9′), 2.49 (1H, br d, J = 13.5 Hz, HC-9′), 2.07 (1H, ddd, J = 3, 4, 14 Hz, HC-10′), 1.95 (1H, ddd, J = 3.5, 4, 10.5 Hz, HC-6′), 1.69 (1H, br q, J = 7 Hz, HC-2″), 1.63 (1H, ddd, J = 3.5, 13, 14 Hz, HC-10′), 1.34 (3H, s, H_3C-1‴), 0.99 (3H, d, J = 7 Hz, H_3C-3″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.9 (s, C-4), 112.7 (s, C-2‴), 108.9 (s, C-5′), 98.6 (t, OCH_2O), 72.4 (d, C-1′), 67.8 (d, C-1″), 65.1 (t, CH_2O), 64.65 (t, CH_2O), 64.60 (t, CH_2O), 64.5 (t, CH_2O), 57.8 (d, C-3), 56.7 (q, CH_3O), 55.4 (d, C-5), 49.4 (d, C-6′), 42.7 (d, C-2″), 36.1 (t, C-10′), 32.8 (t, C-6), 32.1 (t, C-2), 28.2 (t, C-7′), 26.8 (t, C-9′), 22.3 (q, C-1⁗), 7.8 (q, C-3″); HRMS m/z calcd. for $C_{22}H_{36}O_8S_2$+Na 515.1743, found 515.1763 (ESI).

Methyl 1,4,8-Trithiaspiro[4.5]decane-6-carboxylate (9a). A solution of **8a** (7.3 g, 42 mmol), 1,2-ethanedithiol (4.2 mL, 4.7 g, 50 mmol), and p-TsOH·H_2O (1.6 g, 8.4 mmol) in benzene (50 mL) was heated under reflux with continuous removal of water (0.8 mL) via a Dean−Stark trap. After 20 h (reaction was complete by TLC analysis), the cooled mixture was diluted with ether and washed sequentially with saturated aq $NaHCO_3$, water and brine, dried over Na_2SO_4, concentrated, and fractionated by FCC (50% ether in hexane) to give the title compound (9.4 g, 90%): IR ν_{max} 1730 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (3H, s), 3.30−3.15 (6H, m), 3.02 (1H, ap ddd, J = 1.5, 4.5, 14 Hz), 2.91−2.84 (2H, m), 2.65−2.59 (1H, m), 2.21−2.16 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7 (s), 68.2 (s), 54.3 (d), 52.1 (q), 40.4 (t), 39.4 (t), 38.6 (t), 31.7 (t), 28.4 (t); HRMS m/z calcd. for $C_9H_{14}O_2S_3$ 250.0156, found 250.0149 (EI).

Ethyl 2-(2-Ethyl-1,3-dithian-2-yl)propanoate (9b). BF_3·OEt_2 (1.1 equiv) was added to a stirred solution of **8b** (7.0 g, 45 mmol) and 1,3-propanedithiol (4.8 mL, 5.4 g, 47 mmol) in CH_2Cl_2 (64 mL) at room temperature under Ar. After 30 min, the mixture was diluted with diethyl ether and saturated aq $NaHCO_3$ was added with vigorous stirring (***Caution!*** *Effervescence*). After 30 min, the organic layer was washed sequentially with water and brine, dried over Na_2SO_4, concentrated, and fractioned by FCC (15% ethyl acetate in hexane) to give the title compound as a pale yellow oil (9.5 g, 86%): IR ν_{max} 1734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.22−4.09 (2H, m), 3.40 (1H, q, J = 7 Hz), 3.12 (1H, ddd, J = 3, 11.5, 14.5 Hz), 2.93 (1H, ddd, J = 3, 11.5, 14.5 Hz), 2.71−2.66 (2H, m), 2.19 (1H, dq, J = 7.5, 15 Hz), 2.05−1.99 (1H, m), 1.89−1.78 (2H, m), 1.31 (3H, d, J = 7 Hz), 1.27 (3H, t, J = 7 Hz), 1.10 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5 (s), 60.6 (t), 55.6 (s), 46.3 (d), 27.9 (t), 26.2 (t), 26.1 (t), 24.8 (t), 14.4 (q), 13.7 (q), 9.4 (q); HRMS m/z calcd. for $C_{11}H_{20}O_2S_2$ 248.0905, found 248.0904 (EI).

Ethyl 2-(2-Methyl-1,3-dithiolan-2-yl)propanoate (9c). Reaction of **8c** (**2.10** g, 14.6 mmol) with 1,2-ethaneanedithiol and BF_3·OEt_2 according to the above procedure for the synthesis of **9b** gave the title compound as a pale yellow oil (3.1 g, 97%) after fractionation of the crude by FCC (15% ethyl acetate in hexane): IR ν_{max} 1731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.15 (2H, ap q, J = 7 Hz), 3.34−3.22 (4H, m), 2.97 (1H, q, J = 7 Hz), 1.85 (3H, s), 1.38 (3H, d, J = 7 Hz), 1.26 (3H, t, J = 7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1 (s), 68.0 (s), 60.7 (t), 52.5 (d), 40.1 (t), 39.9 (t), 29.5 (q), 16.1 (q), 14.4 (q); HRMS m/z calcd. for $C_9H_{16}O_2S_2$ 220.0592, found 220.0595 (EI).

1,4,8-Trithiaspiro[4.5]decan-6-ylmethanol (10a). A solution of **9a** (3.03 g, 12.1 mmol) in THF (6 mL plus 2× 2 mL rinses) was

added via syringe to a stirred suspension of $LiAlH_4$ (0.35 g, 9.1 mmol) in THF (10 mL) at 0 °C under Ar. The ice bath was removed, and after 4 h, the reaction was complete by TLC. The mixture was cooled to 0 °C, and water (0.4 mL) (***Caution!*** *H_2 evolution*), 15% (w/v) aq NaOH (0.4 mL), and water (1.2 mL) were added sequentially with vigorous stirring. The ice bath was removed, and the grayish suspension turned white during 1 h. The mixture was filtered through a short pad of Na_2SO_4 and Celite, washing with ethyl acetate. The combined filtrate and washings were concentrated to give the crude compound that was fractionated by FCC (20% ethyl acetate in hexane) to give the title compound as a pale yellow oil (2.5 g, 93%): IR ν_{max} 3396 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.08 (1H, dd, J = 4.5, 11.5 Hz), 3.86 (1H, dd, J = 6, 11.5 Hz), 3.33−3.23 (4H, m), 2.93 (1H, br d, J = 14 Hz), 2.84 (1H, ddd, J = 2.5, 9.5, 13.5 Hz), 2.70−2.64 (2H, m), 2.38 (1H, ddd, J = 3, 6.5, 14 Hz), 2.29−2.22 (2H, m), 2.22 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 71.4 (s), 64.9 (t), 50.9 (d), 44.9 (br t), 39.39 (t), 39.10 (t), 31.2 (t), 28.0 (t); HRMS m/z calcd. for $C_8H_{14}OS_3$ 222.0207, found 222.0207 (EI).

2-(2-Ethyl-1,3-dithian-2-yl)propan-1-ol (10b). Reaction of **9b** (5.5 g, 22 mmol) with $LiAlH_4$ (1.5 g, 38.5 mmol) for 9 h according to the above procedure for the synthesis of **10a** gave the title compound as a pale yellow oil (4.0 g, 89%) after fractionation of the crude by FCC (20% ethyl acetate in hexane): IR ν_{max} 3419 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.96 (1H, ddd, J = 5.5, 6,11.5 Hz), 3.73 (1H, ddd, J = 5.5, 6.5,11.5 Hz), 2.89−2.72 (4H, m), 2.40 (1H, dd, J = 6, 6.5 Hz), 2.25−2.17 (1H, m), 2.11 (1H, dq, J = 7.5, 15 Hz), 1.97−1.87 (3H, m), 1.11 (3H, d, J = 7 Hz), 1.03 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 65.5 (t), 57.8 (s), 41.1 (d), 28.8 (t), 25.9 (t), 25.8 (t), 25.3 (t), 12.8 (q), 9.4 (q); HRMS m/z calcd. for $C_9H_{18}OS_2$ 206.0790, found 206.0792 (EI).

2-(2-Methyl-1,3-dithiolan-2-yl)propan-1-ol (10c). Reaction of **9c** (2.90 g, 13.2 mmol) with $LiAlH_4$ (0.55 g, 14 mmol) for 1.5 h according to the above procedure for the synthesis for **10a** give the title compound as a pale yellow oil (2.25 g, 96%) after fractionation of the crude by FCC (20% ethyl acetate in hexane): IR ν_{max} 3389 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.87 (1H, dd, J = 5.5, 11 Hz), 3.62 (1H, dd, J = 5.5, 11 Hz), 3.35−3.26 (4H, m), 2.33 (1H, br s), 2.14 (1H, ddq, J = 5.5, 5.5, 7 Hz), 1.73 (3H, s), 1.15 (3H, d, J = 7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 70.4 (s), 66.7 (t), 47.7 (d), 39.8 (t), 39.6 (t), 31.0 (q), 16.0 (q); HRMS m/z calcd. for $C_7H_{14}OS_2$ 178.0486, found 178.0481 (EI).

General Procedure for Conversion of Dioxolanes to Dithiolanes. $BF_3{\cdot}OEt_2$ (0.25 equiv) was added to a solution of the aldol adduct and 1,2-ethanedithiol (4 equiv) in CH_2Cl_2 (ca. 0.1 M in adduct) at room temperature under Ar. The reaction was monitored by TLC, and when complete, the mixture was diluted with CH_2Cl_2, and aq NaOH (10% w/v) was added with vigorous stirring. After 30 min, the organic layer was washed with water, dried over Na_2SO_4, and concentrated to give the crude product.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*R*)-1,4,8-Trithiaspiro[4.5]dec-6-ylhydroxymethyl]-5-[(*S*)-(6*S*)-1,4,8-trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-11].[36] Reaction of (±)-**3a** (R = MOM) (16 mg, 0.030 mmol) with 1,2-ethanedithiol/$BF_3{\cdot}OEt_2$ according to the general procedure for 1 h and fractionation of the crude by FCC (40% ethyl acetate in hexane) gave the title compound (11 mg, 65%): IR ν_{max} 3454, 1705 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.09 (1H, br dd, J = 3, 9 Hz, HC-1″), 4.09 (1H, br d, J = 2, 9.5 Hz, HC-1′), 3.48 (1H, d, J = 3 Hz, HOC-1′), 3.47−3.22 (9H, m, HC-2, H_2CS × 4), 3.18 (1H, ddd, J = 4, 9, 9.5 Hz, HC-3), 3.07−2.87 (6H, m, HC-2, HC-5, HC-6, HC-9′, HC-9″), 3.01 (1H, d, HOC-1″), 2.84−2.66 (5H, m, HC-6, H_2C-7′, H_2C-7″), 2.61−2.52 (2H, m, HC-9′, HC-9″), 2.52−2.44 (2H, m, HC-10′, HC-10″), 2.38−2.27 (2H, m, HC-10′, HC-10″), 2.23 (1H, br dd, J = 3, 10 Hz, HC-6′), 2.09−2.03 (1H, m, HC-6″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.4 (s, C-4), 73.6 (s, C-5′), 73.3 (s, C-5″), 70.8 (d, C-1″), 69.9 (d, C-1′), 56.6 (d, C-5), 55.8 (d, C-3), 51.5 (d, C-6″), 49.1 (d, C-6′), 47.4 (t, C-10′ or C-10″), 46.8 (t, C-10′ or C-10″), 39.9 (t, CH_2S), 39.6 (t, CH_2S), 39.3 (t, CH_2S), 39.2 (t, CH_2S), 34.6 (t, C-2), 34.3 (t, C-6), 28.8 (t, C-7″), 28.3 (t × 2, C-7′, C-9′ or C-9″), 28.1 (t, C-9′ or C-9″); HRMS m/z calcd. for $C_{21}H_{32}O_3S_7$+Na 579.0288, found 579.0301 (ESI). Similar reaction of (±)-**6a** (R = MOM) (19 mg, 0.033 mmol) for 1 h also gave the title compound (11 mg, 61%) whose ^1H NMR data closely matched those above.

General Procedure for Raney Nickel Desulfurization. A suspension of Raney Ni (W-2) (ca. 1 mL settled volume/50 mg of substrate) in ethanol was added in one portion to a stirred solution of substrate in ethanol (0.01 M), and the reaction mixture was heated under reflux. The reaction was monitored by TLC, and when complete, the mixture was decanted and the solid was suspended in ethanol and heated under reflux with vigorous stirring for several min. The above washing procedure was repeated with ethyl acetate and with acetone. The supernatants were filtered through a pad of Celite, and the combined filtrates were concentrated to give the crude product.

(2*S*,3*R*,4*R*,6*R*,7*S*,8*R*)-*rel*-2,8-Bis(2-ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-methoxymethoxy-4,6-dimethylnonan-5-one [(±)-12].[36] Desulfurization of (±)-**6e** (50 mg, 0.099 mmol) with Raney Ni (0.5 mL settled volume) according to the general procedure for 1 h followed by fractionation of the crude by PTLC (30% ethyl acetate in hexane) gave the title compound (24 mg, 55%): IR ν_{max} 3519, 1710 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.70 (1H, d, J = 6.5 Hz, OCH_2O), 4.59 (1H, d, J = 6.5 Hz, OCH_2O), 4.03 (1H, dd, J = 3.5, 4 Hz, HC-3), 4.01−3.93 (9H, m, HC-7, H_2CO × 4), 3.35 (3H, s, H_3CO), 3.12−3.06 (2H, m, HO, HC-4), 2.97 (1H, dq, J = 7, 9.5 Hz, HC-6), 2.05−1.98 (2H, m, HC-2, HC-8), 1.72 (2H, ap q, J = 7.5 Hz, H_2CC-2″), 1.69 (2H, ap q, J = 7.5 Hz, H_2CC-2‴), 1.10 (3H, d, J = 7 Hz, H_3CC-4), 0.97 (3H, d, J = 7 Hz, H_3C-9), 0.95 (3H, d, J = 7 Hz, H_3C-1 or H_3C-6), 0.94 (3H, d, J = 7 Hz, H_3C-1 or H_3C-6), 0.88 (6H, ap t, J = 7.5 Hz, H_3CCH_2 × 2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.3 (s, C-5), 114.9 (s, C-2‴), 113.8 (s, C-2″), 97.0 (t, OCH_2O), 76.4 (d, C-3), 74.3 (d, C-7), 65.7 (t, CH_2O), 65.28 (t, CH_2O), 65.26 (t, CH_2O), 64.9 (t, CH_2O), 56.4 (q, CH_3O), 53.2 (d, C-4), 48.2 (d, C-6), 42.2 (d, C-2), 38.4 (q, C-8), 28.3 (t, CH_2C-2‴), 26.9 (t, CH_2C-2″), 13.2 (q, CH_3C-6), 11.3 (q, CH_3C-4), 10.7 (q, C-1), 8.4 (q, CH_3CH_2C-2‴), 7.7 (q, CH_3CH_2C-2″), 6.6 (q, C-9); HRMS m/z calcd. for $C_{23}H_{42}O_8$+Na 469.2771, found 469.2769 (ESI). Similar desulfurization of (±)-**3a** (16 mg, 0.030 mmol) with Raney Ni as described above also gave the title compound (6 mg, ca. 90% pure) whose ^1H NMR data closely matched those above.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*R*)-1,4,8-Trithiaspiro[4.5]dec-6-yl-(hydroxy)methyl]-5-[(1*S*,2*R*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-13].[36] Reaction of (±)-**6d** (R = MOM) (16 mg, 0.030 mmol) with 1,2-ethanedithiol/$BF_3{\cdot}OEt_2$ according to the general procedure for 1 h and fractionation of the crude by FCC (30% ethyl acetate in hexane) gave the title compound (11 mg, 70%): IR ν_{max} 3454, 1704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.02 (1H, br dd, J = 3, 9 Hz, HC-1′), 4.97 (1H, br dd, J = 2.5, 9.5 Hz, HC-1″), 3.52 (1H, d, J = 3 Hz, HOC-1′), 3.40−3.19 (10H, m, HC-2, HC-3, H_2CS × 4), 3.04 (1H, d, J = 2.5 Hz, HOC-1″), 3.00 (1H, dd, J = 4, 13.5 Hz, HC-6), 2.78−2.89 (2H, m, HC-2, HC-9′), 2.86 (1H, ddd, J = 4.5, 5, 9.5 Hz, HC-5), 2.80−2.67 (3H, m, HC-6, H_2C-7′), 2.56 (1H, br d, J = 13.5 Hz, HC-9′), 2.49 (1H, ddd, J = 2.5, 5, 14 Hz, HC-10′), 2.33 (2H, ddd, J = 3, 11, 14 Hz, hC-10′), 2.22 (1H, dd, J = 4, 9.5 Hz, HC-6′), 2.10−1.99 (2H, m, H_2C-1‴), 1.96 (1H, q, J = 7 Hz, HC-2″), 1.11 (3H, d, J = 7 Hz, H_3C-3″), 1.07 (3H, t, J = 7 Hz, H_3C-2‴); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.1 (s, C-4), 77.7 (s, C-2‴), 73.6 (s, C-5′), 70.9 (d, C-1″), 70.0 (d, C-1′), 56.9 (d, C-5), 55.8 (d, C-3), 49.0 (d, C-6′), 46.6 (t, C-10′), 44.1 (d, C-2″), 40.5 (t, CH_2S), 40.0 (t, CH_2S), 39.4 (t, CH_2S), 39.2 (t, CH_2S), 36.4 (t, C-1‴), 34.7 (t, C-2), 34.1 (t, C-6), 28.2 (t, C-7′), 28.1 (t, C-9′), 11.7 (q, C-3″), 10.9 (q, C-2‴); HRMS m/z calcd. for $C_{21}H_{34}O_3S_6$+Na 549.0724, found 549.0720 (ESI). Similar reaction of (±)-**6e** (21 mg, 0.041 mmol) for 1 h also gave the title compound (12 mg, 55%) whose ^1H NMR data closely matched those above.

(2*S*,3*R*,4*R*,6*R*,7*R*,8*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-methoxymethoxy-4,6,8-trimethylundecan-5-one [(±)-14].[36] Desulfurization of(±)-**6a** (51 mg, 0.090 mmol) with Raney Ni (0.5 mL settled volume) according to the general procedure for 2 h followed by fractionation of the crude by PTLC (30% ethyl acetate in hexane) gave the title compound (21 mg, 60%): IR ν_{max}

3504, 1707 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.70 (1H, d, J = 6.5 Hz, OCH_2O), 4.59 (1H, d, J = 6.5 Hz, OCH_2O), 4.06 (1H, ddd, J = 3, 5.5 Hz, HC-3), 3.96 (4H, br s, H_2C-4′, H_2C-5′), 3.63 (1H, ddd, J = 3, 5.5, 8.5 Hz, HC-7), 3.36 (3H, s, H_3CO), 3.03 (2H, dq, J = 6, 7 Hz, HC-4), 2.97 (1H, dq, J = 8.5, 7 Hz, HC-6), 2.15 (1H, d, J = 5.5 Hz, HO), 1.94 (1H, dq, J = 3, 7 Hz, HC-2), 1.76−1.65 (2H, m, H_2C-1″), 1.60−1.50 (1H, m, HC-8), 1.40−1.20 (4H, m, H_2C-9, H_2C-10), 1.13 (3H, d, J = 7 Hz, H_3CC-4), 1.04 (3H, d, J = 7 Hz, H_3CC-6), 0.95 (3H, d, J = 7 Hz, H_3C-1), 0.89 (3H, t, J = 7 Hz, H_3C-11), 0.87 (3H, d, J = 7 Hz, H_3CC-8), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.3 (s, C-5), 113.6 (s, C-2′), 97.5 (t, OCH_2O), 76.7 (d, C-3 or C-7), 76.6 (d, C-3 or C-7), 65.3 (t, C-4′), 65.2 (t, C-5′), 56.5 (q, CH_3O), 52.0 (d, C-4), 48.4 (d, C-6), 42.3 (d, C-2), 36.6 (t, C-9), 34.5 (d, C-8), 27.1 (t, C-1″), 20.6 (t, C-10), 14.5 (q, C-11), 13.8 (q, CH_3C-6), 12.7 (q, CH_3C-6), 12.4 (q, CH_3C-4), 10.4 (q, C-1), 7.7 (q, C-2″); HRMS m/z calcd. for $C_{21}H_{40}O_6$+Na 411.2722, found 411.2714 (ESI). Similar desulfurization of (±)-**6b** (R = MOM) (22 mg, 0.040 mmol) with Raney Ni as described above also gave the title compound (21 mg, 60%) whose ^1H NMR data closely matched those above.

(3*R*,5*R*)-*rel*-3,5-bis[(*R*)-(6*R*)-1,4,8-Trithiaspiro[4.5]dec-6-ylhydroxymethyl]tetrahydro-4*H*-thiopyran-4-one [(±)-15].[36] Reaction of (±)-**4a** (R = MOM) (51 mg, 0.095 mmol) with 1,2-ethanedithiol/BF_3·OEt_2 according to the general procedure for 1 h and fractionation of the crude by FCC (40% ethyl acetate in hexane) gave the title compound (36 mg, 68%): IR ν_{max} 3447, 1696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.12 (2H, br dd, J = 2, 9 Hz, HC-1′, HC-1″), 3.43 (2H, d, J = 2 Hz, HO × 2), 3.42−3.24 (5H, m, H_2CS × 4), 3.21−3.15 (1H, m, HC-2, HC-6), 3.07−2.94 (7H, m, HC-2, HC-3, HC-5, HC-6, HC-9′, HC-9″), 2.80−2.70 (4H, m, H_2C-7′, H_2C-7″), 2.59−2.53 (2H, m, HC-9′ HC-9″), 2.46−2.40 (4H, m, H_2C-10′, H_2C-10″), 1.94 (2H, ap dd, J = 4.5, 9.5 Hz, HC-6′, HC-6″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.2 (s, C-4), 73.7 (s × 2, C-5′, C-5″), 69.0 (d × 2, C-1′, C-1″), 56.6 (d × 2, C-3, C-5), 50.9 (d × 2, C-6′, C-6″), 47.4 (t × 2, C-10′, C-10″), 39.6 (t × 2, C-2′, C-2″), 39.5 (t × 2, C-3′, C-3″), 34.4 (t × 2, C-2, C-6), 28.4 (t × 2, C-7′, C-7″), 28.3 (t × 2, C-9′, C-9″); HRMS m/z calcd. for $C_{21}H_{32}O_3S_7$+Na 579.0288, found 579.0304 (ESI). Similar reaction of (±)-**7a** (R = MOM) (19 mg, 0.033 mmol) as above also gave the title compound (7 mg, 58%) whose ^1H NMR data closely matched those above.

(2*S*,3*R*,4*R*,6*R*,7*R*,8*S*)-*rel*-2,8-Bis(2-ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-methoxymethoxy-4,6-dimethylnonan-5-one [(±)-16].[36] Desulfurization of (±)-**4a** (52 mg, 0.097 mmol) with Raney Ni (0.5 mL settled volume) according to the general procedure for 1 h followed by fractionation of the crude by PTLC (30% ethyl acetate in hexane) gave the title compound (24 mg; ca. 85% purity): IR ν_{max} 3526, 1704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.69 (1H, d, J = 6.5 Hz, OCH_2O), 4.59 (1H, d, J = 6.5 Hz, OCH_2O), 4.06−4.03 (2H, m, HC-3, HC-7), 4.01−3.93 (8H, m, H_2CO × 4), 3.35 (3H, s, H_3CO), 3.05 (1H, br s, HO), 3.01−2.93 (2H, m, HC-4, HC-6), 1.91 (1H, dq, J = 3, 7 Hz, HC-2), 1.80 (1H, dq, J = 1.5, 7 Hz, HC-8), 1.75−1.64 (4H, m, H_2C × 2), 1.21 (3H, d, J = 7 Hz, H_3CC-6), 1.10 (3H, d, J = 7 Hz, H_3CC-4), 0.96 (3H, d, J = 7 Hz, H_3CC-8), 0.94 (3H, d, J = 7 Hz, H_3CC-2), 0.86 (3H, t, J = 7.5 Hz, H_3CCH_2), 0.85 (3H, t, J = 7.5 Hz, H_3CCH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.1 (s, C-5), 114.7 (s, C-2″), 113.6 (s, C-2‴), 97.6 (t, OCH_2O), 76.4 (d, C-3), 72.0 (d, C-7), 65.7 (t, CH_2O), 65.3 (t, CH_2O), 65.2 (t, CH_2O), 65.0 (t, CH_2O), 56.5 (q, CH_3O), 51.9 (d, C-4), 49.4 (d, C-6), 42.5 (d, C-2), 39.8 (d, C-8), 28.1 (t, CH_2C-2″ or CH_2C-2‴), 27.1 (t, CH_2C-2″ or CH_2C-2‴), 14.1 (q, CH_3C-6), 12.3 (q, CH_3C-4), 10.4 (q, C-1), 8.1 (q, CH_3CH_2), 7.7 (q, C-9), 7.6 (q, CH_3CH_2); HRMS m/z calcd. for $C_{23}H_{42}O_8$+Na 469.2771, found 469.2792 (ESI). Similar desulfurization of (±)-**7e** (30 mg, 0.059 mmol) as described above also gave the title compound (11 mg, 42%) whose ^1H and ^{13}C NMR data closely matched those above.

(3*R*,5*R*)-*rel*-3-[(*R*)-(6*R*)-1,4,8-Trithiaspiro[4.5]dec-6-yl-(hydroxy)methyl]-5-[(1*R*,2*S*)-2-(2-ethyl-1,3-dithiolan-2-yl)-1-hydroxypropyl]tetrahydro-4*H*-thiopyran-4-one [(±)-17].[36] Reaction of (±)-**7d** (R = MOM) (12 mg, 0.022 mmol) with 1,2-ethanedithiol/BF_3·OEt_2 according to the general procedure for 0.5 h and fractionation of the crude by FCC (25% ethyl acetate in hexane) gave the title compound (8 mg, 67%): IR ν_{max} 3450, 1696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.11 (1H, br d, J = 9.5 Hz, HC-1″), 5.04 (1H, dd, J = 2, 9 Hz, HC-1′), 3.55 (1H, d, J = 2 Hz, HOC-1″), 3.41−3.26 (9H, m, HOC-1′, H_2CS × 4), 3.22 (1H, dd, J = 4, 13.5 Hz, HC-2), 3.13 (2H, ap d, J = 5 Hz, H_2C-6), 3.10−3.05 (1H, ddd, J = 4.5, 8.5, 9 Hz, HC-3), 3.0−2.92 (3H, m, HC-2, HC-5, HC-9′), 2.78−2.70 (2H, m, H_2C-7′), 2.54 (1H, br d, J = 14 Hz, HC-9′), 2.46 (1H, ddd, J = 2.5, 4, 14 Hz, HC-10′), 2.27 (1H, ddd, J = 3, 12, 14 Hz, HC-10′), 2.08−1.96 (3H, m, H_2C-1‴, HC-6′), 1.78 (1H, q, J = 7 Hz, HC-2″), 1.082 (3H, d, J = 7 Hz, H_3C-3″), 1.079 (3H, t, J = 7 Hz, H_3C-2‴); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.8 (s, C-4), 78.2 (s, C-2‴), 73.7 (s, C-5′), 69.4 (d, C-1′), 69.1 (d, C-1″), 57.4 (d, C-5), 56.4 (d, C-3), 50.6 (d, C-6′), 47.6 (t, C-10′), 43.6 (d, C-2″), 40.5 (t, CH_2S), 40.1 (t, CH_2S), 39.4 (t, CH_2S), 39.3 (t, CH_2S), 37.0 (t, C-1‴), 34.4 (t, C-2 or C-6), 34.3 (t, C-2 or C-6), 28.6 (t, C-7′), 28.1 (t, C-9′), 11.8 (q, C-3″), 10.9 (q, C-2‴); HRMS m/z calcd. for $C_{21}H_{34}O_3S_6$+Na 549.0724, found 549.0741 (ESI). Similar reaction of (±)-**7e** (R = MOM) (14 mg, 0.028 mmol) also gave the title compound (8 mg, 53%) whose ^1H NMR data closely matched with those above.

(3*R*,5*R*)-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl-(methoxymethoxy)methyl]-5-[(1*R*,2*S*)-1-hydroxy-2-methylbutyl]tetrahydro-4*H*-thiopyran-4-one [(+)-19].[36] Reaction of (+)-**18** (15 mg, 0.17 mmol) with (+)-**1a** (R = MOM) (29 mg, 0.083 mmol) via the boron enolate for 23 h gave a crude product whose ^1H NMR spectrum indicated the presence of 14:1 mixture of **19** and an unidentified product, respectively. Fractionation of the crude by FCC (20−30% ethyl acetate in hexane) afforded recovered (+)-**1a** (R = MOM) (2 mg, 7%) and the title compound (28 mg, 78%) ($[\alpha]_D$ +82 ; c 1.1, $CHCl_3$): IR ν_{max} 3526, 1704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.70 (1H, d, J = 6 Hz, OCH_2O), 4.61 (1H, d, J = 6 Hz, OCH_2O), 4.56 (1H, dd, J = 4.5, 6.5 Hz, HC-1′), 4.10−3.91 (4H, m, H_2CO × 2), 4.03−3.90 (1H, ddd, J = 3, 5.5, 8 Hz, HC-1″), 3.36 (3H, s, H_3CO), 3.19 (1H, ddd, J = 1, 7.5, 13.5 Hz, HC-2), 3.06−3.01 (1H, m, J = 4.5, 7, 7 Hz, HC-3), 2.98−2.89 (3H, m, HC-2, HC-5, HC-6), 2.84−2.64 (4H, m, HC-6, H_2C-7′, HC-9′), 2.59 (1H, d, J = 5.5 Hz, HO), 2.50 (1H, br d, J = 13.5 Hz, HC-9′), 2.07 (1H, ddd, J = 3, 4.5, 13.5 Hz, HC-10′), 2.03 (1H, ddd, J = 4, 4, 10.5 Hz, HC-6′), 1.65 (1H, ddd, J = 3.5, 12, 13.5 Hz, HC-10′), 1.57−1.40 (2H, m, HC-2″, HC-3″), 1.38−1.29 (1H, m, HC-3″), 0.92 (3H, t, J = 7 Hz, H_3C-4″), 0.88 (3H, d, J = 6.5 Hz, H_3CC-2″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.3 (s, C-4), 108.9 (s, C-5′), 98.5 (t, OCH_2O), 72.95 (t, C-1′ or C-1″), 72.93 (d, C-1′ or C-1″), 64.7 (t, C-2′), 64.5 (t, C-3′), 58.3 (d, C-3), 56.8 (q, CH_3O), 53.8 (d, C-5), 49.0 (d, C-6′), 36.3 (d, C-2″), 36.1 (t, C-10′), 31.4 (q, C-6), 30.3 (t, C-2), 28.2 (t, C-7′), 27.0 (t, C-3″), 26.7 (t, C-9′), 12.4 (q, CH_3C-2″), 12.1 (q, C-4″); HRMS m/z calcd. for $C_{20}H_{34}O_6S_2$+Na 457.1689, found 457.1697 (ESI).

(2*S*,3*R*,4*R*,6*R*,7*R*,8*S*)-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-methoxymethoxy-4,6,8-trimethyldecan-5-one [(−)-20].[36] Desulfurization of (+)-**6c** (R = MOM) (32 mg, 0.061 mmol) with Raney Ni (0.5 mL settled volume) according to the general procedure for 2 h followed by fractionation of the crude by PTLC (25% ethyl acetate in hexane) gave the title compound (9 mg, 39%) ($[\alpha]_D$ −5; c 0.9, $CHCl_3$): IR ν_{max} 3503, 1706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.71 (1H, d, J = 6.5 Hz, OCH_2O), 4.59 (1H, d, J = 6.5 Hz, OCH_2O), 4.07 (1H, dd, J = 3, 5.5 Hz, HC-3), 3.96 (4H, ap s, H_2CO × 2), 3.69−3.63 (1H, m, HC-7), 3.37 (3H, s, H_3CO), 3.02 (1H, dq, J = 5.5, 7 Hz, HC-4), 2.97 (1H, dq, J = 8.5, 7 Hz, HC-6), 2.14 (1H, d, J = 5.5 Hz, HO), 1.96 (1H, dq, J = 3, 7 Hz, HC-2), 1.76−1.65 (2H, m, H_2C-1″), 1.49−1.38 (2H, m, HC-8, HC-9), 1.33−1.24 (1H, m, HC-9), 1.14 (3H, d, J = 7 Hz, H_3CC-4), 1.04 (3H, d, J = 7 Hz, H_3CC-6), 0.96 (3H, d, J = 7 Hz, H_3CC-2), 0.92 (3H, t, J = 7.5 Hz, H_3C-10), 0.88 (3H, d, J = 7 Hz, H_3CC-8), 0.87 (3H, t, J = 7 Hz, H_3C-2″); ^{13}C NMR (125 MHz, $CDCl_3$) δ 218.3 (s, C-5), 113.6 (s, C-2′), 97.6 (t, OCH_2O), 76.6 (t, C-3), 76.4 (d, C-7), 65.3 (t, C-4′ or C-5′), 65.2 (t, C-4′ or C-5′), 56.5 (q, CH_3O), 52.0 (d, C-4), 48.5 (d, C-6), 42.3 (d, C-2), 36.7 (q, C-8), 27.1 (t × 2, C-1″ and C-9), 13.8 (q, CH_3C-6), 12.5 (q, CH_3C-4 or CH_3C-8), 12.4 (q, CH_3C-4 or CH_3C-8), 12.1 (q, C-10), 10.4 (q, C-2), 7.7 (q, C-2″); HRMS m/z calcd. for $C_{20}H_{38}O_6$+Na 397.2560, found 397.2567 (ESI). Similar desulfurization of (+)-**19** (25 mg, 0.058 mmol) with Raney Ni as described above also gave the title compound (5 mg, 23%) whose ^1H NMR data closely matched with those above.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(25) Adducts **6** and **7** are reliably detected in the ^{1}H NMR spectrum of the crude product because of the availability of authentic samples. While not evident by ^{1}H NMR, we cannot rule out the presence of small amounts (<5%) of other diastereomers.

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