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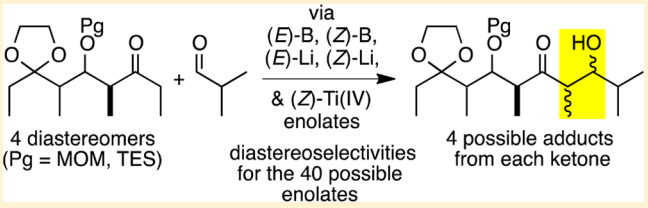
A Systematic Study of the Effects of Relative Configuration, Protecting Group, and Enolate Type on the Diastereoselectivities of Aldol Reactions of a Chiral Ethyl Ketone with 2-Methylpropanal

Dale E. Ward,* Diptarghya Kundu, Mojtaba Biniaz, and Sushital Jana

Department of Chemistry, University of Saskatchewan, 110 Science Place, Saskatoon, Saskatchewan S7N 5C9, Canada

Supporting Information

ABSTRACT: The diastereoselectivities of aldol reactions of 2-methylpropanal with various enolates of 5-*O*-methoxymethyl and 5-*O*-triethylsilyl derivatives of the four racemic diastereomers of 6-(2-ethyl-1,3-dioxolan-2-yl)-5-hydroxy-4-methylheptan-3-one are reported. Reactions of the (*E*)-enol dicyclohexylborinates, (*Z*)-enol 9-BBN borinates (i.e., 9-((*Z*)-enoxy)-9-borabicyclo[3.3.1]nonanes), Li (*E*)-enolates, Li (*Z*)-enolates, and Ti(IV) (*Z*)-enolates were examined. Boron and Li enolates were prepared by standard methods, but Ti(IV) enolates were obtained via transmetalation of the Li (*Z*)-enolates by reaction with $TiCl_n(Oi\text{-}Pr)_{4-n}$ (n = 0−2). Aldol relative topicity (simple diastereoselectivity) was strongly correlated to the enolate geometry: *anti* aldols from (*E*)-enolates and *syn* aldols from (*Z*)-enolates. However, for each enolate type, the diastereoface selectivities varied widely (by factors of 5−400) with the relative configuration and nature of the C5 protecting group in the 8 starting ketones. Plausible transition state models are postulated to rationalize some of these observations. The relative configurations for the complete set of 16 diastereomeric 2-(2-ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one aldol adducts were confirmed by NMR analysis of 12 acetonide derivatives prepared from the corresponding 5,7-*syn* diols. Examination of the NMR data for the above set of aldol adducts revealed consistent trends that were exploited to assign the relative configurations of 13 diastereomeric 2-(2-ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one aldol adducts.



INTRODUCTION

Stereoselective aldol reactions have been intensively investigated for more than four decades, and the basic principles are well established.[1] It is generally recognized that the stereoselectivity of a kinetically controlled aldol reaction of chiral reactants can be *qualitatively* rationalized (and predicted) by application of the multiplicativity rule.[2,3] Accordingly, the stereoselectivity is factorized into three stereocontrol elements:[4] the relative propensity for addition to one or the other face of the ketone enol(ate) (i.e., diastereoface selectivity), the relative propensity for addition to one or the other face of the aldehyde (i.e., diastereoface selectivity), and the relative propensity for reaction via addition of *like* (i.e., *re-re*, *si-si*) vs *unlike* (i.e., *re-si*, *si-re*) faces (i.e., relative topicity). The magnitudes of the diastereoface selectivities for specific reactants and of the relative topicity preference can be evaluated from the results of simpler model reactions (e.g., where one reactant is achiral). Obviously, the diastereoface selectivities for a specific pair of chiral reactants will either reinforce or oppose the preferred relative topicity depending on the enantiomers considered. The former case is said to be "matched" and enhanced diastereoselectivity is expected (double stereodiffentiation), whereas the latter is "mismatched", resulting in diminished diastereoselectivity.[2] It is worth noting that the diastereoselectivities for the "matched" and "mismatched" reactions should become identical as the least biased stereocontrol element becomes unselective; however, high diastereoselectivity is still possible if the remaining stereocontrol elements are highly biased.[5]

Among the most powerful methods for stereoselective C−C coupling of chiral fragments is the "directed" aldol reaction[6] of preformed enol(ate) derivatives with aldehydes. Numerous applications of this approach can be found in syntheses of natural products, particularly of polyketide targets.[7] From the perspective of retrosynthetic analysis of a polypropionate motif (e.g., **1**), identifying a strategic bond for disconnection via an aldol transform relies on accurate prediction of which potential enolate/aldehyde fragment pairs (i.e., **2** and **3**) are likely to undergo aldol coupling with high stereoselectivity (Scheme 1). Even with specific R and R′ groups, a very large number of permutations can be contemplated considering the number of possible reactant stereoisomers (16 diastereomeric combinations of **2** and **3**), enolate types available (e.g., M = B, Li, Si, Sn(II), Ti(IV), etc.), and protecting group variations (i.e., the product of the numbers of possible groups at C-4 in **2** and C-3 in **3**). Despite the extensive investigation of aldol reactions, only a small fraction of those possibilities has been explored, and there are examples of stereoselective syntheses of less than half of the 32 possible diastereomers of **1**.[3] Knowledge of the

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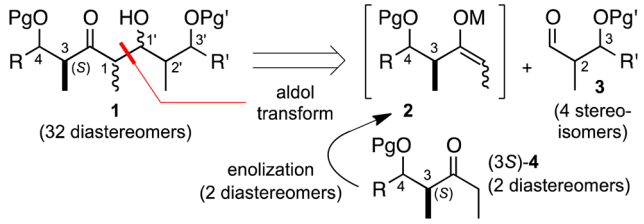
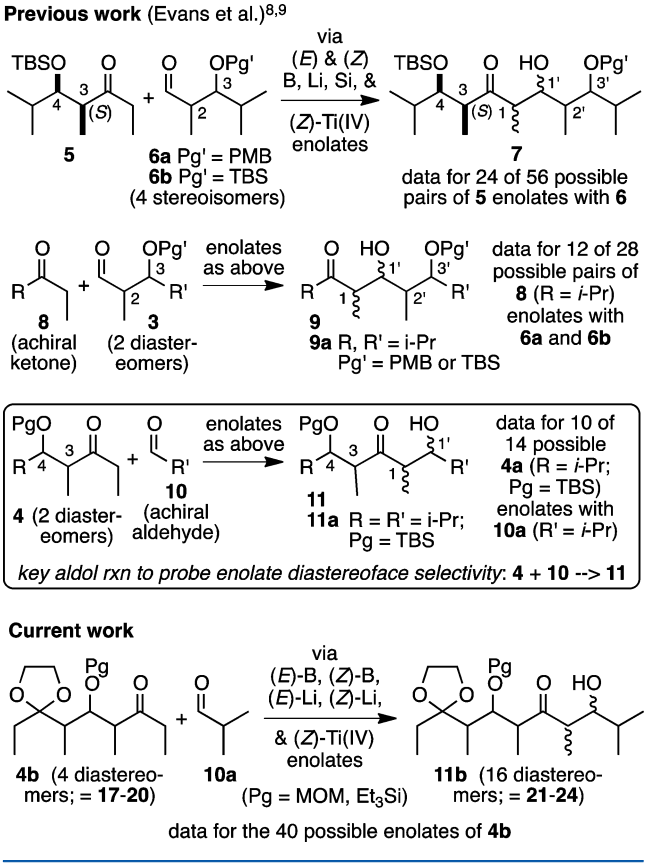
Scheme 1. Retrosynthesis of a Polypropionate Motif via an Aldol Transform Producing Chiral Reactants



structure-selectivity relationships that apply to the stereocontrol elements can help to address these deficiencies and is essential for synthetic planning.

In an important and influential series of papers, the Evans group reported on the stereoselectivities of aldol reactions of B, Li, Si, and Ti(IV) enolates of **5** with aldehydes **6a** and **6b** to give **7** (Pg′ = TBS or PMB) (Scheme 2).[8] The diastereoface

Scheme 2



selectivities of aldehydes **6a** and **6b** were evaluated by reactions with the analogous enolates of **8** (R = *i*-Pr) to give **9a**.[8b−d] Similarly, the diastereoface selectivities of various enolates of **4a** (R = *i*-Pr; Pg = TBS) were evaluated by reactions with **10a** (R′ = *i*-Pr) to give **11a**.[8,9] Others have investigated aldol couplings and diastereoface selectivities of some related substrates,[10,11] and these examples together with Evans' results provide a database that demonstrates observed stereoselectivities can be *qualitatively* predicted according to the principles of the multiplicativity rule.[3] With respect to the three stereocontrol elements, the summary conclusions from these and related[12] studies are as follows:[3,13,14]

- Preferred relative topicities are highly selective and strongly correlated with the enolate geometry (i.e., 1,1′-*anti* adducts from (*E*)-enolates and 1,1′-*syn* adducts from (*Z*)-enolates) with the exception of the enoxysilanes,[8c] where both (*E*)- and (*Z*)-isomers give 1,1′-*syn* adducts with low to excellent selectivity.
- Aldehyde diastereoface selectivity primarily depends on the configuration of the α-methyl group. Reactions with enoxysilanes and (*E*)-enolates give 1′,2′-*syn* adducts with good to excellent selectivity, and reactions with (*Z*)-enolates give 1′,2′-*anti* adducts with moderate to good selectivity modulated by both the Pg′ group and relative configuration of **3**.
- Enolate diastereoface selectivity primarily depends on the configuration of the α-methyl group. Reactions of (*E*)-enoxysilanes, (*E*)-enolates, and certain (*Z*)-enolates [e.g., B, Ti(IV), and Sn(II)] give 1,3-*syn* adducts with good to excellent selectivity, whereas Li (*Z*)-enolates and (*Z*)-enoxysilanes give 1,3-*anti* adducts with moderate to good selectivity.

Although numerous researchers have successfully applied the above considerations to exploit strategic aldol couplings of chiral fragments in the synthesis of natural products,[7,15] this practice has also yielded examples where observed stereoselectivities were surprisingly low[16] or even incongruent[16c] with predictions. Despite the many successes of this approach, the available database[3] has significant gaps in its coverage that limit its application.[17] Scattered reports in the literature suggest that the stereoselectivities of reactions of **2** with **3** can be significantly modulated by the nature of the protecting groups (i.e., Pg and Pg′) and the presence of additional stereocenters (e.g., at C-5 of **2** and C-4 of **3**);[18] however, there have been no systematic studies of the effects of these features. In this paper we report the results of our study on the effects of the relative configuration, protecting group, and enolate type on the diastereoselectivities of aldol reactions of **4b** with **10a** (Scheme 2).

RESULTS AND DISCUSSION

We previously established that aldol reactions proceeding with useful levels of kinetic resolution can be rationally designed using substrates and reaction conditions carefully selected so that the three stereocontrol elements are highly biased.[2d,19] Extending the scope of this strategy depends on identifying appropriate substrates. Toward that end, we sought to find enolates of **4b** that either were sufficiently diastereoface-selective to expect kinetic resolution[2d] in aldol reactions with suitable[19] aldehydes or had low diastereoface selectivity and could be exploited[3,5] for diastereoselective reactions with "mismatched" aldehydes. As noted above, the existing database of aldol diastereoselectivities of various enolates **2** was insufficient to identify suitable candidates in advance.[17]

Preparation of the Reactants. The required substrates **17**−**20** (= **4b**) were prepared from 3-pentanone (**12**) and the known[20] aldehyde **16** as illustrated in Scheme 3. An improved synthesis of **16** starts from **15**, apparently commerically available[21] and readily obtained via Claisen self-condensation of **14**. Most of the known procedures provide **15** in 40−70% yield after distillation and require a large excess of **14**.[22] An exception is Brown's protocol[22c] that uses KH to drive the reaction to completion by deprotonation of both products (i.e., **15** and EtOH); however, the high cost of KH ($200−300/mol) and unfavorable stoichiometry (1 mol of **15** requires 2 mol of KH) together with safety issues makes this method unsuitable for scale-up. We reasoned that an inexpensive base capable of

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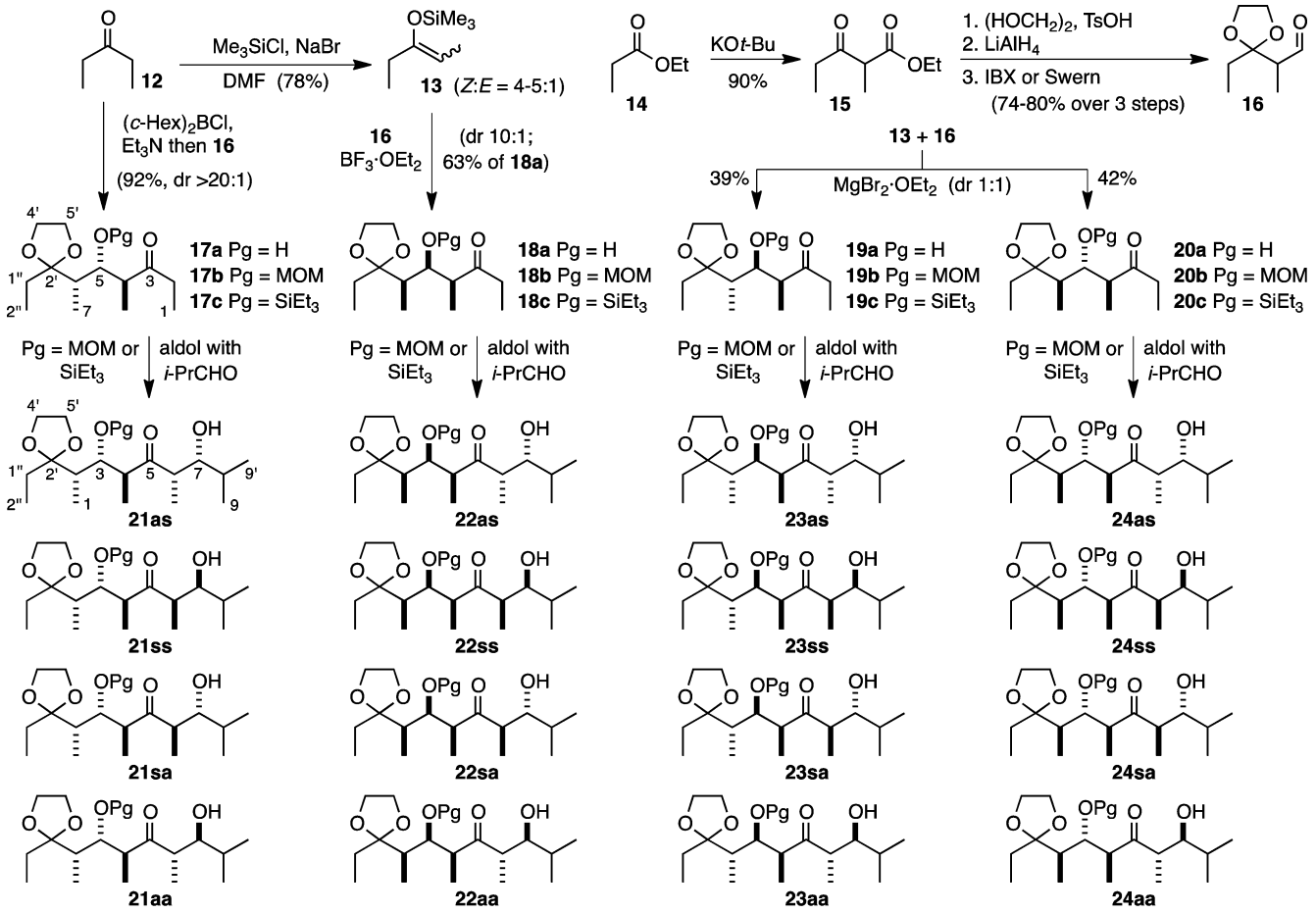
Scheme 3



deprotonating EtOH might be efficacious and were delighted to find that reaction of commercially available **14** ($7−10/mol) and KO*t*-Bu ($20−30/mol; 0.8 equiv) in THF (cf. ref 22e) at ambient temperature overnight gave **15** in 90% yield (75% based on **14**; 50 g scale) with excellent purity after a simple workup (without distillation). Conversion of **15** to **16** was achieved in analogy to previous reports.[20,23]

Reaction of **16** with the (*E*)-enol dicyclohexylborinate derived from **12** at −78 °C gave the 4,5-*anti*-5,6-*syn* Felkin adduct **17a** with excellent stereoselectivity (Scheme 3). The remaining diastereomers were obtained by Mukaiyama aldol reactions of **16** with **13** [*Z*:*E*, 4−5:1], prepared by adapting the method of Iqbal et al.[24] Using $BF_3{\cdot}OEt_2$ as the promoter at −78 °C gave a 10:1 mixture of **18a** and **17a**, respectively, from which **18a** was obtained in good yield by careful fractionation over silica gel. Both **17a** and **18a** arise from the expected[19,20] Felkin addition to aldehyde **16**. In contrast, the reaction mediated by $MgBr_2{\cdot}OEt_2$ at 0 °C gave a separable 1:1 mixture of the 5,6-*anti* adducts (i.e., non-Felkin, chelation control) **19a** and **20a** along with a small amount of **17a** (<5%). This exquisite control over Felkin vs chelation-controlled addition to **16** is noteworthy and perhaps a general feature of this type of aldehyde.[25] Aldol adducts **17a−20a** were converted into their corresponding methoxymethyl (MOM) ethers **17b−20b** (MOM-Cl, *i*-Pr_2EtN, CH_2Cl_2) and triethylsilyl ethers **17c−20c** (Et_3Si-Cl, imidazole, DMF) in good to excellent yields using standard protocols. Each aldol reaction of **4b** (i.e., **17b,c−20b,c**) with *i*-PrCHO (**10a**) can generate up to four adducts (i.e., 32 possible adducts **21−24**),[26] and the results are presented below according to the enolate used. All reactions were conducted at −78 °C, and we presume that adducts are formed with kinetic control under these conditions.[27]

Reactions via (*E*)-Enol Borinates. The results of aldol reactions of *i*-PrCHO (**10a**) with ketones **17−20** via the corresponding (*E*)-enol dicyclohexylborinates are presented in Table 1. Considerable variation in the facility of formation of the enolates was noted. Whereas enolization of some ketones occurred readily at −78 °C (entries 5 and 7), others required warming to −50 °C (entries 1, 2, and 6) or even 0 °C (entries 3, 4, and 8) to achieve high conversions within a reasonable time. Enolizations at 0 °C required optimization as prolonged reaction times often led to lower conversions, presumably due to decomposition of the enolate. In all cases, only 6,7-*anti* aldol adducts were detected by ^1H NMR analysis of the crude reaction mixtures (obtained after oxidative workup) with the 4,6-*syn* adduct being the major or exclusive product.[28] However, the predominance of the 4,6-*syn*-6,7-*anti* adduct (**sa**) over the 4,6-*anti*-6,7-*anti* adduct (**aa**) varied widely among the eight substrates (2−19:1). Very good to excellent selectivity was observed in the majority of cases (entries 2, 3, 5, 6, and 8) including at least one example for each of the four possible diastereomers **17−20**; however, in three cases the selectivity was considerably lower (entries 1, 4, and 7). The isolated yields of adducts were generally similar to the observed conversions except where separation of diastereomers was particularly challenging (e.g., entries 3 and 4).

Literature reports on reactions of achiral aldehydes **10** with (*E*)-enol dicyclohexylborinates derived from **4** (Pg = TBS; R =

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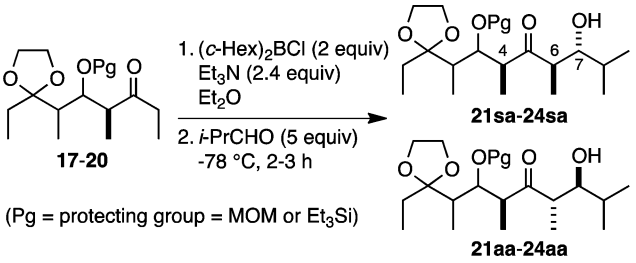
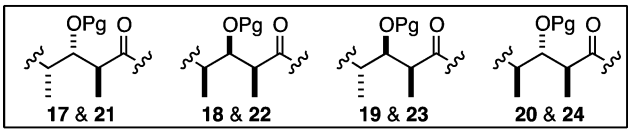
Table 1. Aldol Reactions[26] of *i*-PrCHO with 17−20 (Pg = MOM, Et_3Si) via the (*E*)-Enol Borinate[a]





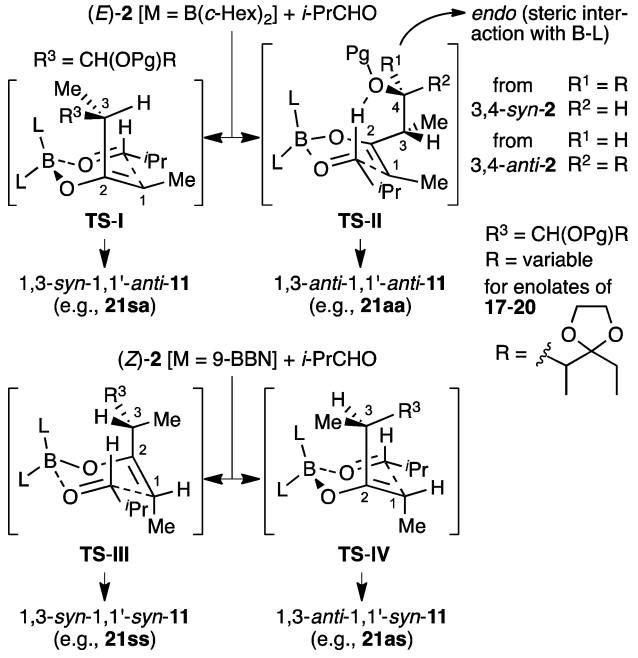
entry	ketone	Pg	enolization temp, time	aldol adducts (ratio);[b] convn[b,c]	yield[d] (%)
1	**17b**	MOM	−50 °C, 2 h	**21sa**, **21aa** (2:1); 95%	62 (26)
2	**17c**	Et_3Si	−50 °C, 1.5 h	**21sa** (dr >19:1);[e] 85%	80
3	**18b**	MOM	0 °C, 2 h	**22sa** (dr >19:1);[e] 95%	64[f]
4	**18c**	Et_3Si	0 °C, 0.5 h	**22sa**, **22aa** (3.5:1); 95%	60[f,g]
5	**19b**	MOM	−78 °C, 1 h	**23sa** (dr >19:1);[e] 95%	87
6	**19c**	Et_3Si	−50 °C, 2.5 h	**23sa**, **23aa**[h] (17:1); 85%	83
7	**20b**	MOM	−78 °C, 2.5 h	**24sa**, **24aa** (6:1); 90%	70 (6)
8	**20c**	Et_3Si	0 °C, 20 min	**24sa** (dr >19:1);[e] 70%	62

[a]Enolization by addition of reagents to a solution of ketone (0.1−0.3 mmol) in Et_2O (0.15−0.20 M) at the indicated temperature and time followed by addition of *i*-PrCHO at −78 °C and workup after 2−3 h; see Experimental Section for detailed procedures. [b]Determined by ^1H NMR of the crude reaction mixture. [c]Estimated from the ratio of adducts to starting ketone present in the crude reaction mixture by ^1H NMR. [d]Isolated yield of the major adduct (isolated yield of minor adduct in parentheses). [e]Only one adduct detected. [f]Lower yield due to difficult fractionation. [g]Plus 31% of a 2:1 mixture of **22aa** and **22sa**, respectively. [h]Tentatively identified.

achiral) indicate that both the 3,4-*syn*[9b,12h,29] and 3,4-*anti*[9b,12h] diastereomers give the corresponding 1,3-*syn*-1,1′-*anti*-**11** adducts selectively (dr >15:1) with few exceptions[12d] (e.g., dr ∼4:1 for 3,4-*syn*-**4** with **10**; R = R′ = 2-propenyl) (Scheme 2). There is a dearth of examples where **4** incorporates an alkyl ether or ester protecting group at C-4, and all include a chiral R group. Although the reported reactions are highly selective, the two 3,4-*syn*-**4** examples[12j,k] gave 1,3-*syn*-1,1′-*anti*-**11** adducts, whereas the two 3,4-*anti*-**4** examples[16c] gave 1,3-*anti*-1,1′-*anti*-**11** adducts. The unusual selectivity observed in the latter examples might be attributed to the presence of a structural feature where the C-4 oxygen is linked to the R group, forming a six-membered ring (e.g., a lactone or 1,3-dioxane); similar selectivity has been observed in analogous reactions of related ketones with chiral aldehydes.[16c,18g]

The results documented in the literature and in Table 1 can be accommodated *qualitatively* by assuming transition states (TSs) with the C1−C2−C3−H torsion angle near the expected[30] 0° thereby orienting the C3-Me and C-4 on opposite faces of the enolate. The 1,3-*syn*-1,1′-*anti*-**11** adducts (**sa**)[26] arise from addition of the aldehyde to the least hindered "Me face" of the enolate via a chairlike TS (**TS-I**)[30] and the 1,3-*anti*-1,1′-*anti*-**11** adducts (**aa**)[26] are formed by addition of the aldehyde to the opposite face of the enolate in a boat-like TS with a favorable formyl H-bond to the C-4 oxygen (**TS-II**)[31] (Scheme 4). The experimentally and computationally observed lower tendency of $OSiR_3$ vs OCH_2R ethers to form this formyl H-bond was attributed to both steric and electronic effects.[31] Thus, **TS-II** should be less important for enolates from R_3Si-protected derivatives of **4**. For 3,4-*syn*-**4** diastereomers (e.g., **18** and **19**), **TS-II** should be particularly disfavored because the R group has the more hindered *endo* orientation in the pseudo bicyclo[4.3.1] framework (steric interaction with B-L). Regardless of the protecting group at C-4 or the R group (chiral or achiral), reactions of all 3,4-*syn*-**4** examples (literature cited above and Table 1, entries 3−6) with **10** gave the 1,3-*syn*-1,1′-*anti*-**11** adduct (**sa**),[26] presumably via **TS-I**, usually with

Scheme 4. Plausible Transition States for Aldol Reactions of 2 (M = BL_2)



excellent stereoselectivity (dr >15:1). The few cases where the selectivity was moderate (dr 3−5:1) can be attributed to sterically undemanding R and R′ groups (i.e., 2-propenyl)[12d] or, in the case of **18c** (Table 1, entry 4), to unspecified conformational contributions of the R group that destabilize **TS-I**.[32] In analogous reactions of 3,4-*anti*-**4**, excellent selectivity in favor of the 1,3-*syn*-1,1′-*anti*-**11** adduct (**sa**)[26] was observed in cases with Pg = R_3Si (literature cited above and Table 1, entries 2 and 8); however, the selectivity was markedly lower with Pg = MOM (Table 1, entries 1 and 7). We attribute the reduced selectivity for **17b** and **20b** (entries 1 and 7) to an

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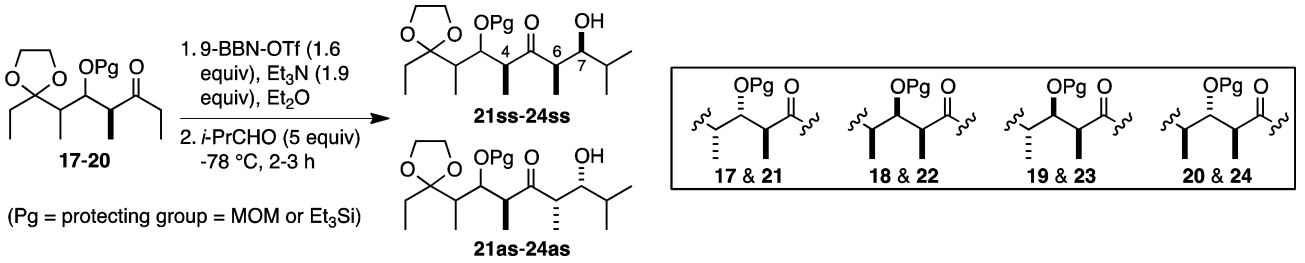
Table 2. Aldol Reactions[26] of *i*-PrCHO with 17−20 (Pg = MOM, Et_3Si) via the (*Z*)-Enol Borinate[a]



entry	ketone	Pg	enolization temp, time	aldol adducts (ratio);[b] convn[b,c]	yield[d] (%)
1	**17b**	MOM	−78 °C, 2 h	**21ss, 21as** (4:1); 70%	53 (13)
2	**17c**	Et_3Si	−50 °C, 2 h	**21ss, 21as** (9:1); 75%	62 (7)
3	**18b**	MOM	−78 °C, 2 h	**22ss** (dr >19:1);[e] 90%	77
4	**18c**	Et_3Si	−78 °C, 4 h	**22ss** (dr >19:1);[e] 80%	67
5	**19b**	MOM	−78 °C, 2.5 h	**23ss** (dr >19:1); 95%	86[f]
6	**19c**	Et_3Si	−50 °C, 4 h[g]	**23ss, 23as** (1.7:1); 75%	41 (22)[h]
7	**20b**	MOM	−78 °C, 2.5 h	**24ss** (dr >19:1); 95%	77[i]
8	**20c**	Et_3Si	−50 °C, 4 h[g]	**24ss, 24as** (2:1); 70%	38 (17)[j]

[a]Enolization by addition of reagents to a solution of ketone (0.1−0.3 mmol) in ether (ca. 0.20 M) at the indicated temperature and time followed by addition of *i*-PrCHO at −78 °C and workup after 2−3 h; see Experimental Section for detailed procedures. [b]Determined by ^{1}H NMR of the crude reaction mixture. [c]Estimated from the ratio of adducts to starting ketone present in the crude reaction mixture by ^{1}H NMR. [d]Isolated yield of the major adduct (isolated yield of minor adduct in parentheses). [e]Only one adduct detected. [f]**23sa** (Pg = MOM) (8%), presumably resulting from the (*E*)-enolate, was also isolated. [g]Ketone solution was 0.35 M. [h]**23sa** (Pg = Et_3Si) (6%), presumably resulting from the (*E*)-enolate, was also isolated. [i]**24sa** (Pg = MOM) (9%), presumably resulting from the (*E*)-enolate, was also isolated. [j]**24sa** (Pg = Et_3Si) (5%), presumably resulting from the (*E*)-enolate, was also isolated.

increased contribution from **TS-II** (i.e., due to the more favorable Pg for formyl H-bond formation and the *exo* orientation of the R group) that is modulated by the conformational effects of R groups with different relative configurations. At least for some 3,4-*anti*-**4** examples where the C-4 oxygen and R group form a six-membered ring, **TS-II** is strongly favored resulting in highly selective formation of the 1,3-*anti*-1,1′-*anti*-**11** adducts.[16c,18g]

Reactions via (*Z*)-Enol Borinates. Table 2 presents the results of aldol reactions of *i*-PrCHO (**10a**) with (*Z*)-enol borinates prepared by treatment of ketones **17−20** with 9-BBN-OTf and Et_3N (i.e., 9-((*Z*)-enoxy)-9-borabicyclo[3.3.1]-nonanes). We observed considerable variation in the reaction conditions required for formation of the enolates. Compared to the MOM-protected ketones **17b−20b**, the Et_3Si-protected analogues **17c−20c** generally required a higher temperature, longer reaction time, and(or) higher concentration, and even with those modifications, only moderate conversions were obtained (70−80%). Isolated yields of aldol adducts were commensurate with the conversions estimated from ^{1}H NMR analysis of the crude reaction product. In all cases, the major aldol adduct had the 4,6-*syn*-6,7-*syn* (**ss**) relative configuration and was produced with low (entries 1, 6, and 8) to excellent selectivity (entries 3−5 and 7) over the 4,6-*anti*-6,7-*syn* adduct (**as**).[28] Small amounts of the 4,6-*syn*-6,7-*anti* aldol adducts (**sa**) were also detected (by ^{1}H NMR) and isolated from several of the crude reaction mixtures (entries 5−8), and we assume these adducts arise from the corresponding (*E*)-enolates.[9c,12c]

Reported examples of reactions of **10** with (*Z*)-enol borinates derived from **4** (Pg = TBS; R = achiral) gave the corresponding 1,3-*syn*-1,1′-*syn*-**11** adducts, generally in moderate yields (60−70%), with high selectivities (dr >12:1) from both 3,4-*anti*[9c,12h] and 3,4-*syn*[9c,12c,d,h] diastereomers of **4**. Reaction of propanal with **18c** via the (*Z*)-enol borinate also gave the corresponding 1,3-*syn*-1,1′-*syn*-**11b** adduct with excellent selectivity.[12k] In the only example with an alkyl ether protecting group at C-4, analogous reaction of a 3,4-*syn*-**4** (Pg = −CH(Me)Ph; R = chiral) with **10a** was reported to give the corresponding 1,3-*syn*-1,1′-*syn*-**11** adduct in 90% yield.[11b] In contrast to the consistently high selectivity shown in the above examples (with limited structural diversity), the results in Table 2 clearly suggest that both the nature of the protecting group and the relative configuration of **17−20** can substantially influence the observed diastereoselectivity in aldol reactions via the (*Z*)-enol borinates. The selective formation of the 1,3-*syn*-1,1′-*syn*-**11** adducts (**ss**)[26] is postulated to arise from **TS-III** (Scheme 4).[12c,30] This arrangement (C1−C2−C3−H torsion angle ca. −150°) presents the best compromise for minimizing both the $A^{1,3}$-strain and steric interactions with the boron ligands (L). The alternative **TS-IV** (C1−C2−C3−H torsion angle ca. 150°) leading to 1,3-*anti*-1,1′-*syn*-**11** adducts (**as**)[26] is disfavored due to the increased $A^{1,3}$-strain relative to **TS-III** (cf. C1−H/R^3 vs C1−H/Me steric interactions).[33] We presume that the variations in diastereoselectivities documented in Table 2 result from changes in the conformational preferences of the different R^3 groups (i.e., different protecting groups and(or) relative configurations) that modulate the relative energies of the competing transition states (e.g., by increasing the R^3/B-L steric interaction in **TS-III**). The expected correlation was not revealed by ground state conformational analysis (molecular mechanics, MMFF) of simple enolate models [(*Z*)-**2** with M = *t*-Bu, Pg = Me or Me_3Si]; however, transition state analysis at an appropriate level of theory may provide a deeper understanding of the origins of the lower diastereoselectivities observed for some enolates.

Reactions via Li (*E*)-Enolates. We could find only a single literature example of a reaction of (*E*)-**2** (M = Li) with an achiral aldehyde:[8d] reaction of 3,4-*syn*-**4a** with **10a** gave a 3.2:1 mixture of 3,1-*syn*-1,1′-*anti*-**11a** and 3,1-*anti*-1,1′-*anti*-**11a**, respectively (84%), along with some 1,1′-*syn* adducts (16%).

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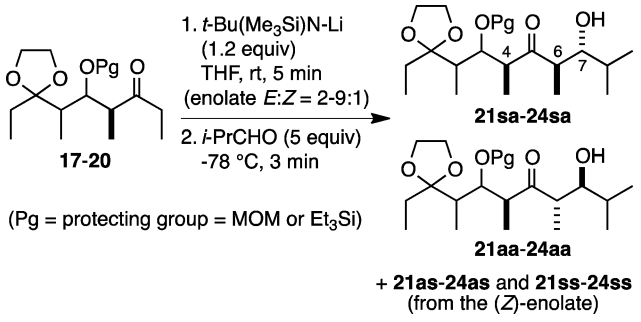
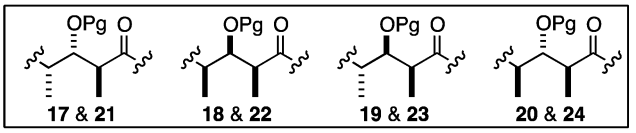
Table 3. Aldol Reactions[26] of *i*-PrCHO with 17−20 (Pg = MOM, Et_3Si) via the Li (*E*)-Enolates[a]





entry	ketone	Pg	enolate (*E*:*Z*)[b]	aldol adducts (ratio);[c] convn[c,d]	adducts *anti*:*syn*[e]	adducts **aa**:**sa**	yield[f] (%)
1	**17b**	MOM	9:1	**21aa**, **21ss**, **21as** (16:1.2:1); 95%	7.6:1	>19:1[g]	79
2	**17c**	Et_3Si	9:1	**21sa**, **21ss** (9.5:1); 95%	9.5:1	<1:19[g]	85
3	**18b**	MOM	3.4:1	**22aa**, **22sa**, **22as**, **22ss** (12:5:3:2); 90%	3.4:1	2.4:1	21[h] (21)
4	**18c**	Et_3Si	2.8:1	**22aa**, **22sa**, **22as**, **22ss** (5:4:2:1); 90%	3:1	1.2:1	14[h] (17)
5	**19b**	MOM	7:1	**23aa**, **23sa**, **23as**, **23ss** (8:4:1:1); 90%	6:1	2:1	41[i] (25)
6	**19c**	Et_3Si	2:1	**23sa**, **23ss**, **23as** (5:1.3:1); 95%	2.2:1	<1:10[g]	59
7	**20b**	MOM	3.5:1	**24sa**, **24as** (3.5:1); 95%	3.5:1	<1:15[g]	70
8	**20c**	Et_3Si	3.3:1	**24sa**, **24aa**,[j] **24as**, **24ss** (20:1:3.3:3); 90%	3.2:1	1:20	63

[a]Enolization by addition of ketone (ca. 0.3 M in THF; 0.1−0.3 mmol) to a solution of *t*-Bu(Me_3Si)N−Li (ca. 0.3 M in THF; 1.2 equiv) at ambient temperature and, after 5 min, addition of *i*-PrCHO at −78 °C followed by quench and workup after 3 min; see Experimental Section for detailed procedures. [b]Determined by ^{1}H NMR of the crude enol ethers obtained by addition of Me_3SiCl/Et_3N to the enolate at −78 °C. [c]Determined by ^{1}H NMR of the crude reaction mixture. [d]Estimated from the ratio of adducts to starting ketone present in the crude reaction mixture by ^{1}H NMR. [e]The ratio of 6,7-*anti*:6,7-*syn* adducts (i.e., [**aa** + **sa**]:[**as** + **ss**]); cf. the enolate *E*:*Z* ratio. [f]Isolated yield of the major 6,7-*anti* adduct (isolated yield of minor 6,7-*anti* adduct in parentheses). [g]Only one 6,7-*anti* adduct detected. [h]Lower yield due to difficult fractionation. [i]An inseparable 10:1 mixture of **23aa** and **23ss**, respectively. [j]Tentatively identified.

We prepared the Li (*E*)-enolates of ketones **17**−**20** according to the procedure of Xie et al.[34] The enolate *E*:*Z* ratios were determined by addition of Me_3SiCl to the enolate at −78 °C and varied widely (2−9:1) with the ketone used; no efforts were made to optimize the selectivities. The results of aldol reactions of these enolates with **10a** are presented in Table 3. Conversions were uniformly high, but the isolated yields of adducts were often lower due to difficulties in purification. Although mixtures of up to four adducts were observed in the crude reaction products (by ^{1}H NMR),[28] the ratios of 6,7-*anti* (i.e., **aa** + **sa**) and 6,7-*syn* (i.e., **as** + **ss**) adducts corresponded closely to the enolate *E*:*Z* ratios. Consequently, we interpret the ratio of **aa** and **sa** adducts to be a reasonable approximation of the diastereoface selectivity of the Li (*E*)-enolate.

The mechanism of aldol reactions of Li enolates is complicated by complex aggregation and solvation phenomena.[35] Several enolates have been shown to be tetrameric in THF solution, but those with sterically demanding substituents can be dimers.[36] Although each Li atom is generally considered to be sufficiently solvated (e.g., by THF) to be tetracoordinate, tricoordinate Li is also common.[37] Because of these issues, the plausible transition states depicted in Scheme 5 do not specify aggregation or solvation (i.e., L represents solvent and(or) another enolate). In half of the examples in Table 3 (entries 2 and 6−8), the 4,6-*syn*-6,7-*anti* adduct (**sa**) was produced with high selectivity comparable to that observed from the corresponding (*E*)-enol borinate and **TS-V**, the Li analogue of **TS-I** postulated above, is a plausible TS for formation of these adducts (Scheme 5). Low to excellent selectivity in favor of the 4,6-*anti*-6,7-*anti* adduct (**aa**) was observed in the remaining examples (entries 1 and 3−5). Although the Li analogue of **TS-II** might account for the **aa** adducts, the Li-chelated **TS-VI** (Scheme 5) seems to better accommodate the

Scheme 5. Plausible Transition States for Aldol Reactions of 2 (M = Li; L_n Implies Unspecified Aggregation/Solvation)

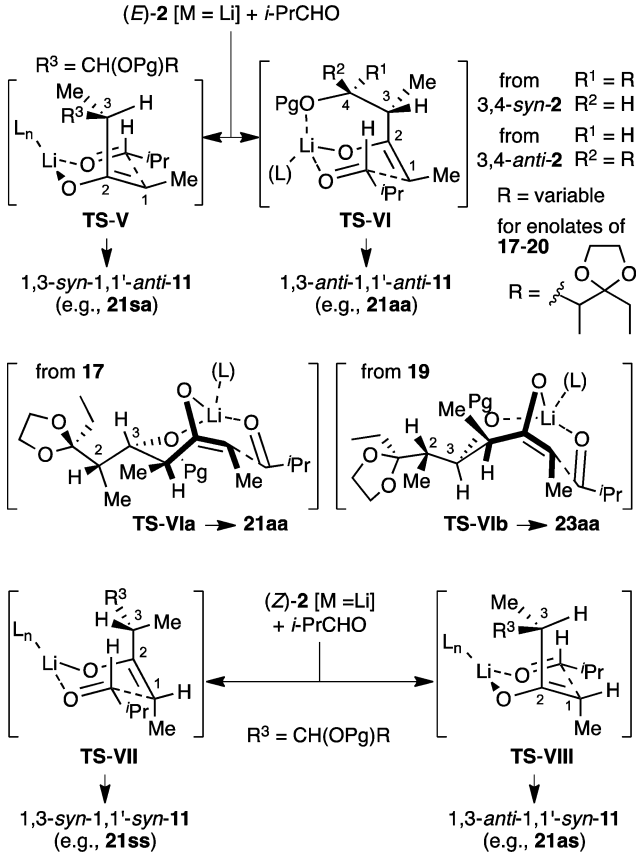


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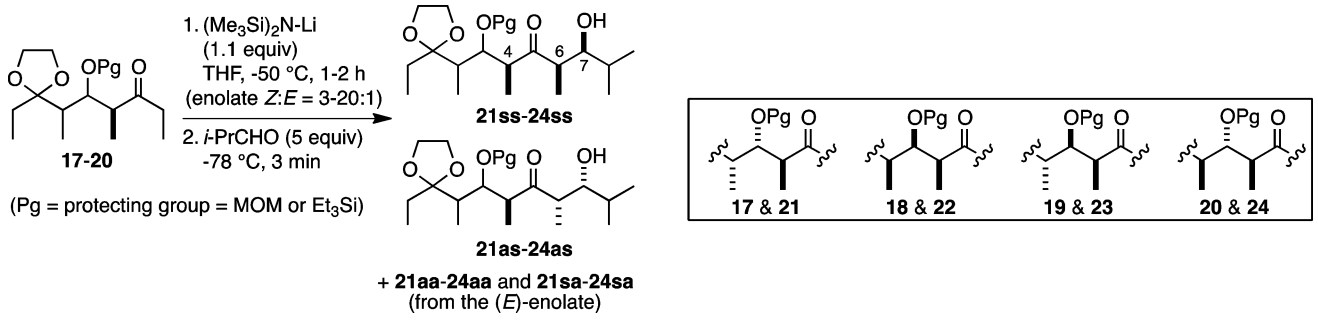
Table 4. Aldol Reactions[26] of *i*-PrCHO with 17−20 (Pg = MOM, Et_3Si) via the Li (*Z*)-Enolates[a]



entry	ketone	Pg	enolate (*Z*:*E*)[b]	aldol adducts (ratio);[c] convn[c,d]	adducts *syn*:*anti*[e]	adducts **as**:**ss**	yield[f] (%)
1	**17b**	MOM	15:1	**21as**, **21ss** (1:3.5); 95%	*g*	1:3.5	70 (20)
2	**17c**	Et_3Si	3:1	**21as**, **21ss**, **21sa** (15:1:6); 90%	2.7:1	15:1	55 (5)
3	**18b**	MOM	10:1	**22as**, **22ss**, **22aa** (9:6:1); 95%	15:1	1.5:1	44 (24)
4	**18c**	Et_3Si	10:1	**22as**, **22ss**, **22aa** (8:4:1); 95%	12:1	2:1	42[h]
5	**19b**	MOM	20:1	**23as**, **23ss** (1.5:1); 95%	*g*	1.5:1	53 (33)
6	**19c**	Et_3Si	15:1	**23as**, **23ss**, **23sa** (8:5:1); 95%	13:1	1.6:1	49 (28)
7	**20b**	MOM	20:1	**24as**, **24ss** (8:1); 95%	*g*	8:1	77 (6)
8[i]	**20c**	Et_3Si	20:1	**24as**, **24ss** (2.7:1); 90%	*g*	2.7:1	61 (18)

[a]Enolization by addition of $(Me_3Si)_2N$−Li (ca. 0.7 M in THF/hexane; 1.1 equiv) to a solution of ketone (ca. 0.15 M in THF; 0.1−0.3 mmol) at −50 °C and, after 1−2 h, addition of *i*-PrCHO at −78 °C and then quench and workup after 3 min; see Experimental Section for detailed procedures. [b]Determined by ^{1}H NMR of the crude enol ethers obtained by addition of Me_3SiCl/Et_3N to the enolate at −78 °C. [c]Determined by ^{1}H NMR of the crude reaction mixture. [d]Estimated from the ratio of adducts to starting ketone present in the crude reaction mixture by ^{1}H NMR. [e]The ratio of 6,7-*syn*:6,7-*anti* adducts (i.e., [**as** + **ss**]:[**aa** + **sa**]); cf. the enolate *Z*:*E* ratio. [f]Isolated yield of the major 6,7-*syn* adduct (isolated yield of minor 6,7-*syn* adduct in parentheses). [g]6,7-*anti* adducts not detected (estimated to be <5%). [h]Lower yield due to difficult fractionation. [i]Enolate formed with 1.4 equiv of LiHMDS at −78 °C for 2 h.

observed results. For both steric and electronic reasons, a lesser contribution from **TS-VI** is expected for enolates with *O*-silyl compared to *O*-alkyl protecting groups, and for each diastereomer **17**−**20**, the relative amount of the **aa** adduct observed is consistently lower with Pg = Et_3Si compared to Pg = MOM. In keeping with the other proposed transition states for (*E*)-enolates, the C1−C2−C3−H torsion angle in **TS-VI** is ca. 0° to minimize $A^{1,3}$-strain. In contrast to **TS-II**, both 3,4-*syn* and 3,4-*anti* diastereomers of (*E*)-**2** (M = Li) can be accommodated with chair- and boat-like conformers of the six-membered Li−O−C5−C4−C3−O(Pg) ring as illustrated for the enolates from **17** (**TS-VIa**) and **19** (**TS-VIb**). A possible explanation for the markedly different stereoselectivity observed for **17b** (entry 1) compared to **20b** (entry 7) arises from the probable conformation of the C3 substituent. Thus, setting the C2−C3 torsion to minimize *syn*-pentane interactions as shown in **TS-VIa** places the largest group in the sterically least congested orientation; inverting the configuration at C-2 (i.e., in **20**) would lead to significantly increased steric interactions. The same analysis applied to **TS-VIb** suggests that the steric interactions for **18b** and **19b** (cf. **TS-VIb** and 2-*epi*-**TS-VIb**) would be less differentiated (note the likely equatorial orientation of Pg). The low diastereoselectivity observed for **18c** (entry 4) in comparison to the other Et_3Si-protected ketones (entries 2, 6, and 8) is a significant anomaly that we are unable to rationalize at present. As with the corresponding (*E*)-enol borinate from **18c**, we presume that conformational effects of the R^3 group somehow sufficiently destabilize **TS-V** (from **18c**) to allow an alternative TS leading to **22aa** (Pg = Et_3Si) to compete effectively.

Reactions via Li (*Z*)-Enolates. Table 4 presents the results of aldol reactions of *i*-PrCHO (**10a**) with Li (*Z*)-enolates prepared by reactions of ketones **17**−**20** with LiHMDS at −50 °C.[38] The enolate *Z*:*E* ratios were determined by addition of Me_3SiCl to the enolate at −78 °C and, with the exception of **17c** (entry 2), were generally high. Reactions of those enolates with **10a** produced aldol adducts with excellent conversions and good isolated yields. The 6,7-*syn* adducts (i.e., **as** + **ss**) were consistently the predominant products. In several cases (entries 2−4 and 6), 6,7-*anti* adducts were also detected in the crude reaction product and occasionally isolated.[28] However, the ratios of 6,7-*syn* (i.e., **as** + **ss**) and 6,7-*anti* (i.e., **aa** + **sa**) adducts corresponded closely to the measured enolate *Z*:*E* ratios. Consequently, we assume the 6,7-*anti* adducts arise from the (*E*)-enolate and interpret the ratio of the 6,7-*syn* adducts (**as** and **ss**) to be a reasonable approximation of the diastereoface selectivity of the Li (*Z*)-enolate. With the exception of **17b** (entry 1), reactions of the Li (*Z*)-enolates of all ketones with **10a** gave the 4,6-*anti*-6,7-*syn* adduct (**as**) as the major product. Diastereoselectivities were generally low (<3:1 for entries 3−6 and 8); however, good to excellent selectivity was observed with the enolates from **17c** (entry 2; 15:1) and **20b** (entry 7; 8:1). Moderate selectivity in favor of the 4,6-*syn*-6,7-*syn* adduct (**ss**) was obtained from **17b** (entry 1; 3.5:1).

McCarthy and Kageyama studied the reactions of **10a** with the Li (*Z*)-enolates of 3,4-*syn*-**4** (R = *i*-Pr) with a variety of protecting groups.[12b] Mixtures of corresponding adducts 3,4-*syn*-**11** (R = R′ = *i*-Pr) were obtained with the 3,1-*anti*-1,1′-*syn* diastereomer consistently predominating over the 3,1-*syn*-1,1′-*syn* diastereomer. Low selectivity (1.1−2:1) was observed from 3,4-*syn*-**4** (R = *i*-Pr) substrates with alkyl ether protecting groups (Pg = Bn, MEM, BOM) and moderate selectivity (4.5−6.4:1) from those with silyl ethers (Pg = TMS, TES, TBS). These results suggest that chelation of the Li by the C-4 oxygen in 3,4-*syn*-**4** (R = *i*-Pr) is not a significant factor for these enolates. Analogous selectivities were observed in similar

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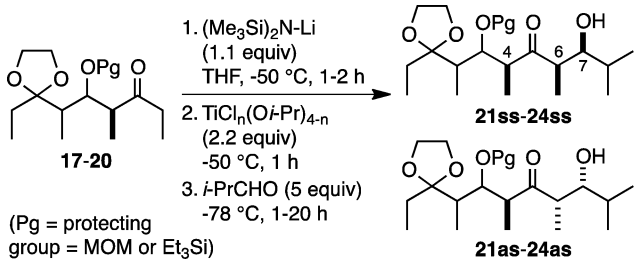
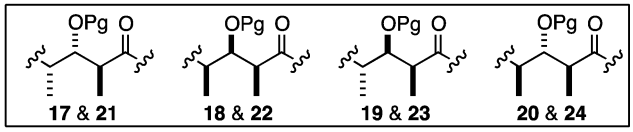
Table 5. Aldol Reactions[26] of *i*-PrCHO with 17−20 (Pg = MOM, Et_3Si) via the Ti(IV) (*Z*)-Enolates[a]





entry	ketone	Pg	Ti(IV) reagent	aldol adducts (ratio);[b] rxn time, convn[b,c]	yield[d] (%)
1	**17b**	MOM	$Ti(Oi\text{-}Pr)_4$	**21ss**, **21as** (10:1); 17 h, 90%	78 (8)
2	**17b**	MOM	$TiCl(Oi\text{-}Pr)_3$	**21ss**, **21as** (13:1); 1.5 h, >95%	87 (7)
3	**17c**	Et_3Si	$Ti(Oi\text{-}Pr)_4$	**21ss** (dr >19:1);[e] 17 h, 70%	63
4	**17c**	Et_3Si	$TiCl(Oi\text{-}Pr)_3$	**21ss** (dr >19:1);[e] 1 h, 95%	86
5	**18b**	MOM	$Ti(Oi\text{-}Pr)_4$	**22ss**, **22as** (6:1); 16 h, 90%	70 (12)
6	**18b**	MOM	$TiCl(Oi\text{-}Pr)_3$	**22ss**, **22as** (12:1); 2 h, 90%	76 (5)
7	**18c**	Et_3Si	$Ti(Oi\text{-}Pr)_4$	**22ss**, **22as** (15:1); 18 h, 85%	73 (5)
8	**18c**	Et_3Si	$TiCl(Oi\text{-}Pr)_3$	**22ss**, **22as** (15:1); 3 h, 85%	71 (4)
9	**19b**	MOM	$Ti(Oi\text{-}Pr)_4$	**23ss**, **23as** (12:1); 20 h, 85%	71 (5)
10	**19b**	MOM	$TiCl(Oi\text{-}Pr)_3$	**23ss**, **23as** (15:1); 5 h, 90%	78 (5)
11	**19c**	Et_3Si	$Ti(Oi\text{-}Pr)_4$	**23ss**, **23as** (10:1); 18 h, 84%	69 (6)
12	**19c**	Et_3Si	$TiCl(Oi\text{-}Pr)_3$	**23ss**, **23as** (13:1); 4 h, 95%	81 (5)
13	**20b**	MOM	$Ti(Oi\text{-}Pr)_4$	**24ss**, **24as** (10:1); 18 h, 85%	69 (6)
14	**20b**	MOM	$TiCl(Oi\text{-}Pr)_3$	**24ss**, **24as** (13:1); 4 h, 90%	76 (5)
15[f]	**20c**	Et_3Si	$Ti(Oi\text{-}Pr)_4$	**24ss**, **24as**, **24sa** (3.6:1:0.5); 18 h, 80%	53 (11)[g]
16[f]	**20c**	Et_3Si	$TiCl(Oi\text{-}Pr)_3$	**24ss**, **24as**, **24sa** (4:1:0.7); 3 h, 90%	62 (14)[g]
17[f]	**20c**	Et_3Si	$TiCl_2(Oi\text{-}Pr)_2$[h]	**24ss**, **24as** (3.7:1);[i] 1.5 h, 90%	ND[j]
18[f,k]	**20c**	Et_3Si	$TiCl_2(Oi\text{-}Pr)_2$[h]	**24ss**, **24as** (9.2:1); 3 h, 65%	55 (5)

[a]Enolization by addition of $(Me_3Si)_2N$−Li (ca. 0.7 M in THF/hexane) to a solution of ketone (ca. 0.15 M in THF; 0.1−0.3 mmol) at −50 °C and, after 1−2 h, addition of the indicated Ti(IV) reagent and transmetalation for 1 h followed by addtition of *i*-PrCHO at −78 °C and workup after the indicated reaction time; see Experimental Section for detailed procedures. [b]Determined by ^{1}H NMR of the crude reaction mixture. [c]Estimated from the ratio of adducts to starting ketone present in the crude reaction mixture by ^{1}H NMR. [d]Isolated yield of the major adduct (isolated yield of minor adduct in parentheses). [e]Only one adduct detected. [f]Enolate formed with 1.4 equiv of LiHMDS at −78 °C for 2 h. [g]**24sa** (Pg = Et_3Si) (5−6%), presumably resulting from the (*E*)-enolate, was also isolated. [h]Transmetalation at −78 °C for 2 h. [i]Ketal deprotected analogues (ca. 10%) were detected by ^{1}H NMR. [j]Not determined. [k]Enolization in the presence of 1 equiv of $(Me_3Si)_2NH$.

reactions with 3,4-*syn*-**4** (Pg = TBS, R = *i*-Pr or 3-propenyl; dr, 3.1−3.3:1)[8d,39] and 3,4-*syn*-**4** (Pg = Bn, R = chiral; dr, 5.4:1).[10a] The sole example of a 3,4-*anti*-**4** (Pg = Bz, R = chiral; dr, 1.7:1) also showed low selectivity in favor of the 3,1-*anti*-1,1′-*syn*-**11** adduct.[12i]

The results in Tables 2 and 4 together with related literature data clearly show that the diastereoface selectivities of aldol reactions of (*Z*)-enol borinates of ethyl ketones **4** are distinctly different from those of the analogous Li (*Z*)-enolates; however, the origin of this difference has not been established. Notwithstanding the complexities of Li enolates alluded to above, **TS-VII** (Scheme 5) is a reasonable model to account for the formation of 3,1-*syn*-1,1′-*syn*-**11** adducts (e.g., **21ss**). As with **TS-III**, the C1−C2−C3−-H torsion angle of ca. −150° reduces the $A^{1,3}$-strain while presenting an unencumbered enolate face and minimal steric interactions with any ligands on Li. We postulate that **TS-VIII** is a plausible model to account for the formation the of 3,1-*anti*-1,1′-*syn*-**11** adducts (e.g., **21as**). In **TS-VIII** the C1−C2−C3−H torsion angle is near 0° thereby minimizing the $A^{1,3}$-strain and orienting the C3-Me and C-4 on opposite faces of the enolate. The steric interactions of the C3-Me with Li ligands would be minimal with either a tricoordinate (no axial ligand) or tetracoordinate Li (an axially oriented solvent molecule). In contrast, the boron analogue of **TS-VIII** is not competitive because of steric interactions between the C3-Me and the large ligands on boron.[30] The relative energies of **TS-VII** and **TS-VIII** reflect the opposing influences of $A^{1,3}$-strain (cf. C1-H/C3-Me vs C1-H/C3-H steric interactions) and steric hindrance of aldehyde approach to the enolate face (cf. C3-H/HC═O vs C3-Me/HC═O interactions) and would be modulated by the conformational preferences of the various R^3 groups.

Reactions via Ti(IV) (*Z*)-Enolates. The results of aldol reactions of **10a** with Ti(IV) (*Z*)-enolates of **17**−**20** are presented in Table 5. Attempts to generate the Ti(IV) enolates using standard "soft enolization" protocols ($TiCl_4$ or $TiCl_3(Oi\text{-}Pr)$ and $i\text{-}Pr_2EtN$)[9a,40] were thwarted due to competing aldol cyclization, elimination, or deprotection of the starting ketones. However, the desired enolates were obtained by transmetalation[41] of the Li (*Z*)-enolates of **17**−**20** (prepared as described in Table 4) with $Ti(Oi\text{-}Pr)_4$ or $TiCl(Oi\text{-}Pr)_3$ under conditions similar to those used in our previous work.[2d,19] The reactions of **17b** and **17c** were optimized with respect to the stoichiometry of the Ti(IV) reagent and transmetalation conditions. Because the Li and Ti(IV) (*Z*)-enolates of **17c** give different aldol adducts on reaction with **10a** (cf. entry 2 in Tables 4 and 5), the extent of Li to Ti transmetalation could be monitored by the ratio of **21as** and **21ss** adducts. Transmetalation was complete (no detectable **21as**) within 1 h at −50 °C but was much slower at −78 °C. Reducing the amount

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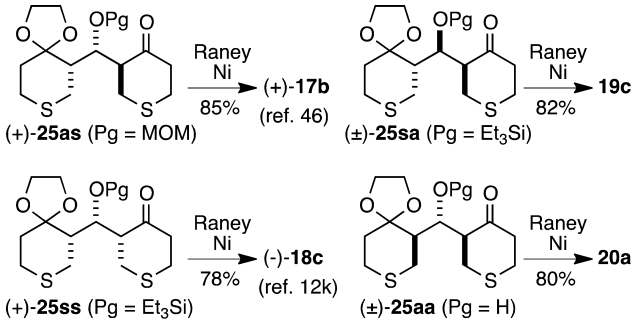
of Ti(IV) reagent to <1.5 equiv resulted in lower selectivities, but use of 4.4 equiv did not improve the selectivity relative to 2.2 equiv. The enolates prepared using $Ti(Oi\text{-}Pr)_4$ were much less reactive than those using $TiCl(Oi\text{-}Pr)_3$ as judged by the aldol reaction times required to reach high conversions (16−20 h vs 1−5 h). To maintain consistency with the results from the other enolates, we did not explore the use of higher temperatures in the aldol reaction. In all cases, the 4,6-*syn*-6,7-*syn* (**ss**) diastereomer was the major adduct, generally produced with good selectivity (≥10:1) that was slightly higher with the enolates prepared with $TiCl(Oi\text{-}Pr)_3$ (entries 1−14).[28] In contrast, only moderate selectivity was observed with enolates of **20c** (entries 15 and 16), and these were the only examples where a 6,7-*anti* adduct was detected (**24sa**). The amount of **24sa** (Pg = Et_3Si) increased with increased transmetalation time (not shown), and we suspected that it was a product of the (*E*)-enolate formed by isomerization of the (*Z*)-enolate. Although **24sa** (Pg = Et_3Si) was not detected in an analogous reaction where transmetalation of the Li (*Z*)-enolate of **20c** (dr 20:1; cf. Table 4, entry 8) was conducted with $TiCl_2(Oi\text{-}Pr)_2$ at −78° for 2 h prior to addition of *i*-PrCHO, those conditions led to an inseparable mixture of adducts **24ss** (Pg = Et_3Si) and **24as** (Pg = Et_3Si) along with their corresponding ketal-deprotected analogues (entry 17). Addition of $(Me_3Si)_2NH$ (1 equiv) prior to enolate formation not only suppressed ketal deprotection but resulted in markedly higher selectivity in favor of **24ss** (Pg = Et_3Si) (entry 18). This result suggests that additives can modify the stereoselectivity of these Ti(IV) enolates, and we are actively investigating the scope of that hypothesis.[42]

Reported examples of reactions of **10** with Ti(IV) (*Z*)-enolates derived from 3,4-*anti*-**4** and 3,4-*syn*-**4** (Pg = TBS; R = achiral) gave the corresponding 1,3-*syn*-1,1′-*syn*-**11** adducts, generally in good yields (82−95%), with high selectivities (dr >15:1).[8b,12h] Comparable selectivities were observed in analogous reactions of a 3,4-*syn*-**4** (Pg = Bn, R = chiral)[10a] and a 3,4-*anti*-**4** (Pg = TBS, R = chiral).[16d] In all of the above examples the enolate was prepared by "soft enolization" ($TiCl_4$, $i\text{-}Pr_2EtN$).[9a] Related examples where transmetalation of a Li enolate was used to prepare the Ti(IV) enolate involve reactions with enantiopure aldehydes, and the corresponding 1,3-*syn*-1,1′-*syn*-**11** adducts were formed with varying selectivity depending on whether the reaction was "matched" (dr 20:1) or "mismatched" (dr 1−9:1).[18a,43] The diastereoselectivities in Table 5 are consistent with the above literature examples. In contrast to the other enolates studied (Tables 1−4), consistently high selectivity (dr ≥9:1) was observed with the Ti(IV) enolates regardless of the relative configuration or protecting group in the starting ketone. Reactions of related Ti(IV) and boron (*Z*)-enolates of **17**−**20** with **10a** give the same 4,6-*syn*-6,7-*syn* (**ss**) adduct predominantly, but the diastereoselectivities of the Ti(IV) enolates show much less variation than the boron enolates (cf. Tables 2 and 5). However, speculating on the origin of that observation is complicated because the structure and aggregation state of Ti(IV) enolates are uncertain.[44,45] This is particularly true for enolates prepared by transmetalation[19,41b] of Li enolates where the presence of the conjugate acid of the Li amide base may play an influential role. Several authors have proposed chelated structures for Ti(IV) (*Z*)-enolates of ketones with a β-alkoxy group, usually evidenced by lower stereoselectivity with a silyl ether vs an alkyl ether protecting group.[45] Although our results (Table 5) do not show this expected relationship of the diastereoselectivity with the protecting group (cf. ref 19), a chelated enolate structure cannot be ruled out. The requirement of 2.2 equiv of Ti(IV) to achieve high selectivity could implicate a bridged bimetallic enolate structure related to those proposed by Urpí.[45b,c] Regardless of the underlying mechanistic details, aldol reactions of the Ti(IV) (*Z*)-enolates of **17**−**20** give reliable stereoselectivity that complements that of the (*Z*)-enol borinates and offers several avenues for optimization (e.g., Li amide base, Ti(IV) reagent, stoichiometry, transmetalation conditions, additives).

Structure Determinations. The relative configurations for **17**−**20** were established by correlations to the known[25] diastereomers of **25** via desulfurization. The ketones (+)-(4*S*)-**17b**,[46] (−)-(4*R*)-**17c**,[15m] and (−)-(4*R*)-**18c**[12k] were previously prepared by desulfurizations of the corresponding derivatives of **25**, and the spectral data for (±)-**17b**, (±)-**17c** and (±)-**18c** obtained from (±)-**16** (Scheme 3) were consistent with those for the corresponding enantiomers above (Scheme 6). Similarly, Raney nickel desulfurizations of (±)-**25sa** (Pg = Et_3Si) and (±)-**25aa** (Pg = H) gave (±)-**19c** and (±)-**20a**, respectively.

Scheme 6. Correlations of 17−20 to Known Diastereomers of 25



Twenty-nine of the 32 possible aldol adducts **11b** were isolated and characterized (i.e., **21**−**24**, Scheme 3).[47] Because all four possible aldol adducts were obtained from each of the four diastereomers **17b**−**20b**, we can confidently assert that the relative configuration of these starting ketones is retained in the corresponding aldol adducts, and we assume the same relationship for adducts obtained from **17c**−**20c**. Consequently, knowledge of the starting ketone and determination of the relative configuration at C4, C6, and C7 in the resulting adduct is sufficient to secure the overall structure. Assignments of the C6, C7 relative configurations for adducts **21**−**24** were based on NMR analysis (Table 6). Thus, the $^3J_{H6-H7}$ coupling constants[48] (J = 6−9 Hz, average = 7.7 Hz) and ^{13}C chemical shifts of the C6-Me groups[49] (δ_C = 13.5−14.9, average = 14.1 ppm) in the 13 6,7-*anti* diastereomers were substantially larger than those in the 16 6,7-*syn* diastereomers ($^3J_{H6-H7}$ = 1−2.5 Hz, average = 1.7 Hz; C6-Me δ_C = 8.1−9.3, average = 8.6 ppm).[50,51] In 13 cases, these assignments were confirmed via the corresponding acetonide derivative **26** prepared in 15−90% yield by DIBAL (dr 5−20:1), $Et_2BOMe/NaBH_4$ (dr >10:1), or $LiAlH_4$ (dr 0.25−5:1) reduction of the aldol adduct followed by treatment of the purified 1,3-*syn* diol product with $Me_2C(OMe)_2$ and *p*-TsOH·H_2O in acetone (Scheme 7).[52]

We are unaware of any direct methods to determine the C4,C6 relative configuration in aldol adducts such as **21**−**24**, and this problem is further complicated with racemic adducts.[53]

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Table 6. Selected NMR Data for Aldol Adducts 21−24

entry	aldol adduct	Pg	$^3J_{H6-H7}$ (Hz)	$^3J_{H7-H8}$ (Hz)	δ_C CH_3C-6	$\Delta\delta_C$ (C7/CH_3C-6)[a]	$\Delta\delta_C$ (C6/C8)[b]	$\Delta\delta_C$ (C9/C9′)[c]
1	**21as**	MOM	2	9	7.9	69.1	17.7	0.6
2	**21ss**	MOM	1.5	9.5	7.9	67.5	18.4	1.2
3	**21sa**	MOM	8.5	3.5	13.5	63.8	21.7	5.9
4	**21aa**	MOM	7.5	4.5	13.4	64.9	19.8	4.8
5	**22as**	MOM	2.5	8.5	8.7	68.1	15.8	0.4
6	**22ss**	MOM	1.5	9.5	9.3	66.8	16.0	1.0
7	**22sa**	MOM	8.5	3	14.6	61.6	20.8	5.9
8	**22aa**	MOM	7	4.5	14.2	64.7	17.7	4.5
9	**23as**	MOM	2	9	9.3	67.4	14.2	0.5
10	**23ss**	MOM	1.5	9	9.3	67.0	15.1	0.9
11	**23sa**	MOM	8.5	3.5	14.8	62.2	18.9	5.6
12	**23aa**	MOM	7	5	14.9	63.9	15.9	4.3
13	**24as**	MOM	2	9	8.1	68.6	17.4	0.6
14	**24ss**	MOM	1	9.5	7.9	67.8	18.6	1.0
15	**24sa**	MOM	8	4	14.0	64.4	21.1	5.1
16	**24aa**	MOM	6	*d*	13.5	64.4	19.7	4.7
17	**21as−24as**	MOM	2−2.5	8.5−9	7.9−9.3	67.4−69.1	14.2−17.7	0.4−0.6
18	**21ss−24ss**	MOM	1−1.5	9−9.5	7.9−9.3	66.8−67.8	15.1−18.6	0.9−1.2
19	**21sa−24sa**	MOM	8−8.5	3−4	13.5−14.8	61.6−64.4	18.9−21.7	5.1−5.9
20	**21aa−24aa**	MOM	6−7.5	4.5−5	13.4−14.2	63.9−64.9	15.9−19.8	4.3−4.7
21	**21as**	Et_3Si	2	9	8.0	69.0	16.6	0.6
22	**21ss**	Et_3Si	1	9.5	9.0	66.7	16.8	1.3
23	**21sa**	Et_3Si	8.5	3	14.2	62.2	21.6	6.0
24	**22as**	Et_3Si	2	8	8.8	67.7	15.8	0.6
25	**22ss**	Et_3Si	1.5	9.5	9.3	67.0	16.9	1.0
26	**22sa**	Et_3Si	7	4.5	14.6	63.8	18.6	4.3
27	**22aa**	Et_3Si	7	5	14.3	64.6	17.8	4.2
28	**23as**	Et_3Si	2	9	9.3	67.4	14.1	0.7
29	**23ss**	Et_3Si	2	9	9.2	67.1	15.3	0.9
30	**23sa**	Et_3Si	7	4.5	14.8	63.7	17.2	4.7
31	**24as**	Et_3Si	1.5	9	8.0	68.7	16.8	0.4
32	**24ss**	Et_3Si	1	9.5	8.3	67.5	17.7	1.7
33	**24sa**	Et_3Si	9	3.5	13.6	64.5	21.2	6.2

[a]Equal to (δ_C C7) − (δ_C CH_3C6). [b]Equal to (δ_C C6) − (δ_C C8). [c]Equal to (δ_C C9) − (δ_C C9′). [d]Not determined due to spectral congestion.

Our strategy to establish this relative configuration (and confirm the above assignments) based on NMR analysis of acetonides **26** prepared from *syn* diol derivatives of aldol adducts **21−24** is illustrated in Scheme 7. Such 1,3-*syn* diol acetonides are expected to adopt a single chair conformation, and this property is essential to the analysis. Acetonides of 1,3-*syn* diols are readily distinguished from those of 1,3-*anti* diols by the ^{13}C NMR chemical shifts of C2 and (more reliably) the two C2-Me groups, and these data were used to confirm that **26** were 1,3-*syn* diol acetonides.[54] There are four possible diastereomers to consider (i.e., **27−30**) depending on the relative configuration at C4, C6, C7 in the starting aldol adducts **21−24**. The 6,7-*syn* adducts produce the 4,5-*syn*-5,6-*syn* diastereomers **27** and **28** and the 6,7-*anti* adducts give the 4,5-*anti*-5,6-*anti* diastereomers **29** and **30**. The relative configurations at C4, C5, and C6 in the acetonide derivatives **26** are easily assigned by ^1H NMR on the basis of the magnitudes of the $^3J_{H4-H5}$ and $^3J_{H5-H6}$ coupling constants (Scheme 7), and in each case, these assignments were consistent with the direct NMR-based determinations of the relative configurations at C6 and C7 in the starting aldol adducts **21−24**. Assignment of the relative configuration at C4 in **26** is based on the expectation that the predominant torsion angle of the C2′−C4 bond can be reliably predicted on the basis of minimization of *syn*-pentane steric interactions thereby orienting H_3C-1′ and HC-3′ in distinct environments that can be probed by NOE correlations to groups on the "rigid" acetonide ring (i.e., HC-4, HC-5, H_3CC-5).

The above approach was tested by transforming the MOM-protected aldol adducts **23as**, **23ss**, **23sa**, and **23aa** (the four possible aldol adducts derived from **19b**) into the acetonides **27c**, **28c**, **29c**, and **30c**, respectively (Scheme 7). The two 4,5-*syn*-5,6-*syn* diastereomers **27c** and **28c** had $^3J_{H2'-H4}$ = 9.5−10 Hz and showed a HC-2′↔H_3CC-5 NOE correlation consistent with a H−C2′−C4−H torsion angle of ca. 180°, as expected. The 2′,5-*syn* relative configuration for **28c** was assigned based on HC-5↔HC-3′ and HC-4↔H_3C-1′ NOE correlations and establishes the 4,6-*syn*-6,7-*syn* relative configuration for **23ss** (Pg = MOM). Therefore, diastereomer **27c** must have the 2′,5-*anti* relative configuration, and this was confirmed by the observation of an HC-5↔H_3C-1′ NOE correlation (complementary to that in **28c**) thereby establishing the 4,6-*anti*-6,7-*syn* relative configuration for **23as** (Pg = MOM). The two 4,5-*anti*-5,6-*anti* diastereomers **29c** and **30c** had $^3J_{H2'-H4} \leq$ 3.5 Hz suggesting a H−C2′−C4−H torsion angle near (±) 60° and showed the expected HC-2′↔H_3CC-5 NOE correlation. The 2′,5-*syn* relative configuration for **29c** was assigned on the basis of HC-4↔H_3C-1′ and HC-5↔HC-3′ NOE correlations and establishes the 4,6-*syn*-6,7-*anti* relative configuration for **23sa** (Pg = MOM). Consequently, **29aa** (Pg = MOM) and **30c** must

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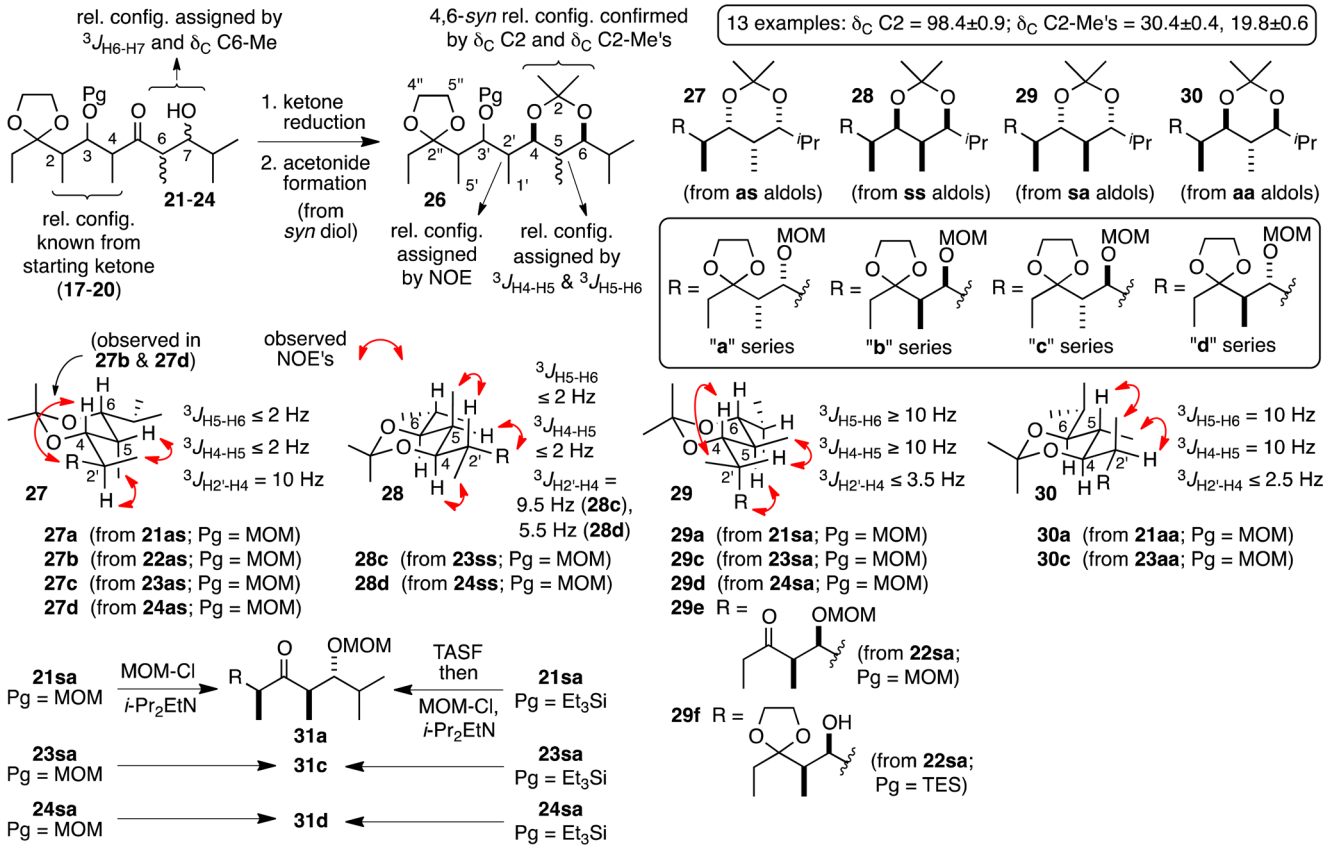
Scheme 7. Determination of the C4, C6 Relative Configuration in Adducts 21−24



have the 4,6-*anti*-6,7-*anti* and 2′,5-*anti* relative configurations, respectively, and the latter was confirmed by observation of a HC-5↔H_3C-1′ NOE correlation in **30c**.

The 6,7-*syn* aldol adducts (i.e., **as** and **ss**)[26] from **17b**, **18b**, and **20b** were assigned as follows. The C2′ relative configurations for the two 4,5-*syn*-5,6-*syn* diastereomers **27d** and **28d** prepared from **24as** and **24ss** (the two 6,7-*syn* adducts from **20b**), respectively, were assigned on the basis of the indicated NOE correlations (Scheme 7) as described above. Although the smaller than expected $^3J_{H2'-H4}$ coupling constant for **28d** (5.5 Hz) suggested a mixture of conformers with different C2′−C4 torsion angles, the anticipated HC-2′↔H_3CC-5, HC-5↔HC-3′, and HC-4↔H_3C-1′ NOE correlations were observed. Moreover, **24as** and **24ss** are the only possible 6,7-*syn* aldol adducts that can arise from **20b**, and assignment of the C4 relative configuration in one of the diastereomers infers the C4 relative configuration in the other. Because the observed NOE correlations in **27d** establish the 2′,5-*anti* relative configuration, the precursor **24as** must be 4,6-*anti*-6,7-*syn*; consequently, **24ss** must be 4,6-*syn*-6,7-*syn*. Using this logic, 4,5-*syn*-5,6-*syn* acetonides **27a** and **27b** were prepared from **21as** and **22as**, respectively (i.e., one of the two possible 6,7-*syn* aldol adducts from each of **17b** and **18b**), and both were assigned the 2′,5-*anti* relative configuration on the basis of the observed NOE correlations indicated in Scheme 7. Thus, the precursors **21as** and **22as** must have the 4,6-*anti*-6,7-*syn* relative configuration, and the alternative 6,7-*syn* adducts **21ss** and **22ss** must have the 4,6-*syn*-6,7-*syn* relative configuration.

The 6,7-*anti* aldol adducts (i.e., **aa** and **sa**)[26] from **17b**, **18b**, and **20b** were assigned in an analogous manner (Scheme 7). The 4,5-*anti*-5,6-*anti* acetonides **29a** and **30a** were prepared from **21sa** and **21aa** (the two 6,7-*anti* adducts from **17b**), respectively. As with **29c**, three relevant NOE correlations were observed in **29a** allowing confident assignment of the 2′,-5-*syn* relative configuration and hence the 4,6-*syn*-6,7-*anti* relative configuration for **21sa**. Consequently, **21aa** must have the 4,6-*anti*-6,7-*anti* relative configuration, and this assignment is confirmed by the complementary HC-5↔H_3C-1′ NOE correlation observed in **30a**. The relative configurations for adducts **22sa** and **24sa** were determined by conversion to acetonides **29e** and **29d**, respectively. Attempted formation of **29b** led to an inseparable mixture of **29b** and **29e** that was converted to **29e** on prolonged reaction time (i.e., by transacetalization with acetone). Both **29b** and **29e** showed the same three characteristic NOE correlations as observed for **29a** and **29c**, thereby allowing assignment of the 2′,-5-*syn* relative configuration and the 4,6-*syn*-6,7-*anti* relative configuration for the precursors **22sa** and **24sa**. Hence, the alternative 6,7-*anti* adducts **22aa** and **24aa** must have the 4,6-*anti*-6,7-*anti* relative configuration.

With the relative configurations for the complete set of 16 diastereomers of **21**−**24** (Pg = MOM) firmly established, we carefully examined the NMR data in search of trends that might allow a direct assignment of the relative configurations of the 13 isolated diastereomers of **21**−**24** (Pg = Et_3Si) (Table 6). In addition to the known criteria (i.e., $^3J_{H6-H7}$ coupling constant[48] and ^{13}C chemical shift[49] of the C6-Me group), both the $^3J_{H7-H8}$ coupling constant and the difference in the ^{13}C chemical shifts of the diastereotopic isopropyl methyl groups [$\Delta\delta_C$(C9/C9′)] also provide clear differentiation of 6,7-*syn* and 6,7-*anti* diastereomers (Table 6, entries 17−20). Distinguishing between the two 6,7-*syn* isomers (**as** and **ss**) and between the

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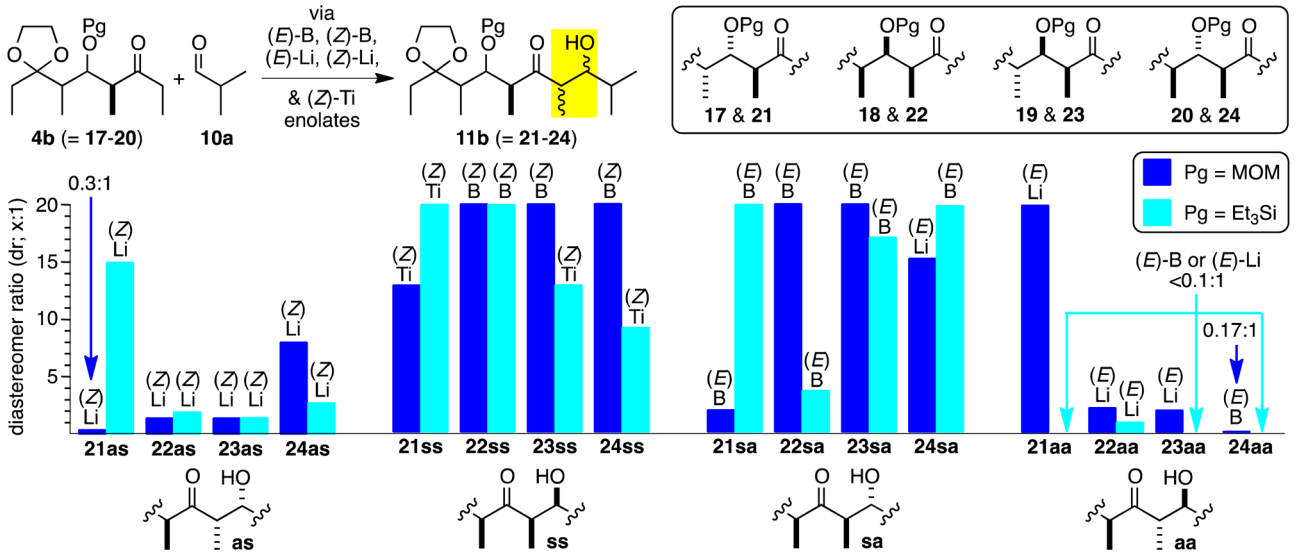

Figure 1. Enolate type producing the highest diastereoselectivity for each of the 32 possible aldol adducts **11b** (= **21**−**24**) arising from aldol reaction of **4b** (= **17**−**20**) with **10a**.

two 6,7-*anti* isomers (**sa** and **aa**) is also possible by the small but consistent differences in both the $^3J_{H6-H7}$ and $^3J_{H7-H8}$ coupling constants and in the $\Delta\delta_C$(C9/C9′) values (entries 17−20).[26] Because $\Delta\delta_C$(C9/C9′) appeared to be sensitive to small conformational changes (e.g., as reflected by the small changes in $^3J_{H6-H7}$ and $^3J_{H7-H8}$), we computed $\Delta\delta_C$'s for other geminal pairs of carbons (C6/C8 and C7/CH_3C6). Although neither of these $\Delta\delta_C$'s produced unique values for each of the four diastereomers (entries 17−20), clear trends emerged when comparing the two 6,7-*syn* isomers (**as** and **ss**) or the two 6,7-*anti* isomers (**sa** and **aa**). That is, the 4,6-*anti*-6,7-*syn* (**as**) and 4,6-*anti*-6,7-*anti* (**aa**) diastereomers consistently had lower $\Delta\delta_C$(C6/C8) and higher $\Delta\delta_C$(C-7/CH_3C6) values compared to the 4,6-*syn*-6,7-*syn* (**ss**) and the 4,6-*syn*-6,7-*anti* (**sa**) diastereomers, respectively.

The relative configurations of the 13 isolated diastereomers of **21**−**24** (Pg = Et_3Si) were assigned using the correlations between the NMR data and the C4, C6, C7 relative configuration of **21**−**24** (Pg = MOM) established above. The C6, C7 relative configurations were readily assigned according to the diagnostic $^3J_{H6-H7}$, $^3J_{H7-H8}$, δ_C(C6-Me), and $\Delta\delta_C$(C9/C9′) values (Table 6, entries 21−33). The pairs of 6,7-*syn* isomers (**as** and **ss**), one from each of **17c**−**20c** (Pg = Et_3Si), were distinguished by comparing both magnitudes and orders of the observed values for $^3J_{H6-H7}$, $^3J_{H7-H8}$, $\Delta\delta_C$(C7/CH_3C6), $\Delta\delta_C$(C6/C8), and $\Delta\delta_C$(C9/C9′) with those expected (entries 17 and 19). Within each pair, all comparisons suggested the same assignment.[55] Among the 6,7-*anti* isomers, only one pair was available (**22sa** and **22aa**; Pg = Et_3Si). Although comparing the orders of the $^3J_{H7-H8}$, $\Delta\delta_C$(C7/CH_3C6), $\Delta\delta_C$(C6/C8), and $\Delta\delta_C$(C9/C9′) values for **22sa** and **22aa** with those expected (entries 18 and 20) permits assignment, the actual values for both isomers match well with those expected for a 4,6-*anti*-6,7-*anti* isomer (cf. entries 26 and 27 with entry 20). To clarify this discrepancy, **22sa** (Pg = Et_3Si) was converted to acetonide **29f** that was shown to have the 2′,5-*syn* relative configuration by NOE (Scheme 7), thereby establishing the 4,6-*syn*-6,7-*anti* relative configuration for **22sa**. Thus, **22aa** must have the 4,6-*anti*-6,7-*anti* relative configuration. Diastereomers **21sa** (Pg = Et_3Si) and **24sa** (Pg = Et_3Si) were assigned on the basis of the perfect match of the observed magnitudes of their $^3J_{H6-H7}$, $^3J_{H7-H8}$, $\Delta\delta_C$(C7/CH_3C6), $\Delta\delta_C$(C6/C8), and $\Delta\delta_C$(C9/C9′) values with those expected for the 4,6-*syn*-6,7-*anti* relative configuration (cf. entries 23 and 33 with entry 19). Similar comparison of the corresponding observed and expected values for **23sa**, with the exception of $\Delta\delta_C$(C7/CH_3C6), suggested the 4,6-*anti*-6,7-*anti* (**aa**) relative configuration (cf. entries 28 and 20). However, the close correspondence of the $^3J_{H6-H7}$ (7 Hz), $^3J_{H7-H8}$ (4.5 Hz), and $\Delta\delta_C$(C7/CH_3C6) (63.8, 63.7) values for **23sa** and **22sa** and the unlikely possibility of selectively obtaining **23aa** from both the (*E*)-enol borinate (Table 1, entry 6) and Li (*E*)-enolate of **19c** (Table 3, entry 6) made the **aa** assignment questionable. Thus, the relative configuration for **23sa** (Pg = Et_3Si) was confirmed by chemical correlation to **23sa** (Pg = MOM) via the derivative **31c** (Scheme 7). For completeness, the assignments for **21sa** (Pg = Et_3Si) and **24sa** (Pg = Et_3Si) were similarly confirmed by correlations to **21sa** (Pg = MOM) and **24sa** (Pg = MOM), respectively (i.e., via **31a** and **31d**; Scheme 7).

SUMMARY AND CONCLUSIONS

Our study on the aldol reactions of *i*-PrCHO (**10a**) with **4b** (4 diastereomers × 2 protecting groups × 5 enolate types = 40 examples) is the most comprehensive to date and clearly demonstrates that the diastereoselectivities are significantly influenced by the relative configuration, protecting group, and enolate type. Consistent with previous reports, the aldol relative topicity (simple diastereoselectivity) was found to be highly selective and very strongly correlated to the enolate geometry: *anti* aldols from (*E*)-enolates and *syn* aldols from (*Z*)-enolates. Although 35 of the 40 examples showed enolate diastereoface selectivity that followed the established trends [i.e., (*E*)-enolates (B and Li) and (*Z*)-enolates (B and Ti(IV)) give 1,3-*syn*-**11b** adducts, whereas Li (*Z*)-enolates give 1,3-*anti*-**11b** adducts with moderate to good selectivity], the diastereoselectivities for six were ≤2:1. Moreover, for each of the enolate types studied, the diastereoface selectivities varied over a wide range (factors of 5−400) with the relative configuration and nature of the C5 protecting group in the 8 starting ketones **4b**. The Ti(IV) enolates (Table 5) were the most reliable, and

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under optimized conditions, diastereoselectivities of ≥9:1 in favor of the **ss** adducts[26] were achieved with all ketones. Although the (*Z*)-enol borinates (Table 2) also gave the **ss** adducts consistently and often with high diastereoselectivity (i.e., ≥9:1), several cases were much less selective. The (*E*)-enol borinates (Table 1) consistently gave the **sa** adducts predominantly, but the selectivity was markedly lower with enolates from the MOM-protected 3,4-*anti*-**4b** ketones **17b** and **19b**. The Li enolates (Tables 3 and 4) were the most capricious with only 11/16 giving the "expected" enolate diastereoface selectivity including four with diastereoselectivities of ≤2:1. Although plausible transition state models are postulated to rationalize some of the observations, such simple models can never capture the complexities of these reactions (e.g., the aggregation and solvation state of the enolate−aldehyde complex). It is interesting to note that of the 32 possible adducts **11b**, only 17 were formed with reasonably high selectivity (≥8:1), 6 with moderate selectivity (2−3:1), and another 4 with poor selectivity (1−2:1) (Figure 1). Even considering the 16 possible adducts after deprotection (i.e., **11b** with Pg = H), only 11 were produced with good stereoselectively (**sa**, 4 of 4; **ss**, 4 of 4; **as**, 2 of 4; **aa**, 1 of 4).[26] Clearly, many challenges remain to be solved to achieve true stereochemical diversity in these reactions. Notwithstanding the above deficiencies, many of the enolates exhibited high diastereoface selectivity (e.g., a single adduct detected) and thus have excellent potential to be exploited in reactions that proceed with kinetic resolution. We are currently exploring that possibility.

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 cm × 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.[56] with silica gel 60 (40−63 μm). All mixed solvent eluents are reported as vol/vol solutions. Unless otherwise noted, all reported compounds were homogeneous by thin layer chromatography (TLC) and by ^{1}H NMR.

Spectral Data. High-resolution mass spectra (HRMS) were obtained on a double focusing high-resolution spectrometer; EI ionization was accomplished at 70 eV and CI ionization at 50 eV with ammonia as the reagent gas. 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 ^{1}H and 125 MHz for ^{13}C. For ^{1}H NMR, 32 K FIDs with a 6000 Hz spectral width (−5−14.5 ppm) were acquired (2.8−3.0 s, 1.0 s relaxation delay, 30° pulse angle), and after zero-filling to 64 K and applying a 0.1 Hz line broadening function, Fourier transformation gave 32 K spectra. For ^{13}C NMR, 64 K FIDs with a 30300 Hz spectral width (−10−230 ppm) were acquired (1.0 s, 2.0 s relaxation delay, 30° pulse angle; 1 s, no relation delay, 20° pulse angle) and after applying a 1 Hz line broadening function gave 32 K spectra (64 K spectra if FID zero-filled to 128 K) after Fourier transformation. Signals due to the solvent (^{13}C NMR) or residual protonated solvent (^{1}H 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 ^{1}H 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 couplings 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 of ca. 0.2 Hz/pt). The ^{1}H 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).[57] Nuclear Overhauser enhancements (NOE) were measured via the 1D DPFGSE-NOE method.[58] The ^{13}C NMR assignments were made on the basis of chemical shift and multiplicity[59] (as determined by ^{13}C-DEPT or gHSQC) and were confirmed by two-dimensional ^{1}H/^{13}C correlation experiments (gHSQC and/or gHMBC).[57]

Materials. The following compounds and reagents were prepared as described previously: **25sa** (Pg = Et_3Si);[2d] **25aa** (Pg = H);[25] MOM-Cl;[60] $(c\text{-Hex})_2BCl$;[61] IBX;[62] W-2 Raney nickel.[63] $TiCl_4$ was distilled under argon atmosphere from CaH_2. Et_3N and *i*-Pr_2EtN were distilled from KOH under argon and stored over KOH. $Ti(Oi\text{-}Pr)_4$ was distilled under argon. Solutions of $TiCl(Oi\text{-}Pr)_3$ and $TiCl_2(Oi\text{-}Pr)_2$ (ca. 0.55 M in THF) were freshly prepared according to Urpí.[45a] All other reagents were commercially available and unless otherwise noted were used as received.

General Procedure for the Preparation of MOM Ethers. *i*-Pr_2EtN (3.5 equiv) and MOM-Cl (3 equiv) were added to a stirred solution of alcohol (0.4−0.8 M in CH_2Cl_2) at 0 °C. The mixture was allowed to warm to ambient temperature, and reaction progress was monitored by TLC. When complete, the reaction mixture was diluted with 4% aq HCl and extracted with CH_2Cl_2. The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated to give the crude product that was fractionated by FCC.

General Procedure for the Preparation of Et_3Si Ethers. Imidazole (1.4 equiv) or Et_3N (1.4 equiv) and Et_3SiCl (1.2 equiv) were sequentially added to a stirred solution of alcohol (0.4−0.8 M in DMF) at room temperature. Reaction progress was monitored by TLC and when complete, the mixture was diluted with ethyl acetate, washed sequentially with 0.2 M aq citric acid (reactions with imidazole) or saturated aq NH_4Cl (reactions with Et_3N) and brine, dried over Na_2SO_4, and concentrated to give the crude product that was fractionated by FCC.

General Procedure for Aldol Reactions via the (*E*)-Enol Borinate (Table 1). $(c\text{-Hex})_2BCl$ (1−2 M in hexane; 1.5−2.5 equiv) and Et_3N [1.2 equiv with respect to $(c\text{-Hex})_2BCl$] were sequentially added to a stirred solution of ketone (ca. 30−100 mg, 0.1−0.3 mmol, 1 equiv) in ether (ca. 0.15−0.20 M) at the indicated temperature under Ar. After the indicated enolization time, the reaction mixture was cooled to −78 °C (if necessary), and *i*-PrCHO (3−5 equiv) was added via syringe. After 2−3 h, the reaction was quenched by sequential addition of phosphate buffer (pH 7; 10 mL/mmol of boron), MeOH (10 mL/mmol of boron), and 30% aq H_2O_2 (5 mL/mmol of boron) with vigorous stirring. The reaction vessel was transferred to an ice bath, and after vigorous stirring for 15 min, the mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product that was analyzed by ^{1}H NMR and then fractionated.

General Procedure for Aldol Reactions via the (*Z*)-Enol Borinate (Table 2). Et_3N (1.2 equiv with respect to 9-BBN-OTf) and 9-BBN-OTf (0.5 M in hexane; 1.5−1.6 equiv) were sequentially added via syringe to a stirred solution of ketone (ca. 30−100 mg, 0.1−0.3 mmol, 1 equiv) in ether (ca. 0.15−0.20 M) at −78 °C under argon.

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After the indicated enolization time, *i*-PrCHO (3−5 equiv) was added via syringe. After 2−3 h, the reaction was quenched by sequential addition of phosphate buffer (pH 7; 10 mL/mmol of boron), MeOH (10 mL/mmol of boron), and 30% aq H_2O_2 (5 mL/mmol of boron) with vigorous stirring. The reaction vessel was transferred to an ice bath, and after vigorous stirring for 15 min, the mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product that was analyzed by ^{1}H NMR and then fractionated.

General Procedure for Aldol Reactions via the Li (*E*)-Enolate (Table 3).[34] *n*-BuLi (1.5−3.0 M in hexanes; 1.2 equiv) was added dropwise to a stirred solution of *tert*-butyl(trimethylsilyl)amine (0.3 M in THF; 1.3 equiv) at 0 °C. The ice bath was removed, and after 15 min, a solution of ketone (0.3 M in THF; ca. 30−100 mg, 0.1−0.3 mmol, 1 equiv) was added dropwise via syringe. After 5 min, the mixture was cooled to −78 °C (quenching the reaction with Me_3SiCl at this stage gave the (*E*)-enol trimethylsilyl ether predominantly; >90%, dr 2−10:1), and *i*-PrCHO (4−5 equiv) was added. After 3 min, the reaction was quenched by addition of saturated aq NH_4Cl, and the mixture was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product that was analyzed by ^{1}H NMR and then fractionated.

General Procedure for Aldol Reactions via the Li (*Z*)-Enolate (Table 4). A solution of LiHMDS (0.6−0.8 M) was prepared by addition of *n*-BuLi (1.5−3 M in hexane; 1.1 equiv) to a stirred solution of $(Me_3Si)_2NH$ (1.2 equiv) in THF (ca. 1 M) at 0 °C under argon. An aliquot of the above solution (1.1 equiv of LiHMDS) was added via syringe to a stirred solution of ketone (ca. 0.1−0.2 M in THF; ca. 30−100 mg, 0.1−0.3 mmol, 1 equiv) at −50 °C under argon (note: in some cases enolization at −78 °C was very slow).[64] After 1 h, the solution was cooled to −78 °C (quenching the reaction with Me_3SiCl at this stage gave the (*Z*)-enol trimethylsilyl ether predominantly; >90%, dr >9:1), and *i*-PrCHO (5 equiv) was added via syringe. After 3 min, the reaction was quenched by addition of saturated aq NH_4Cl, and the mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product that was analyzed by ^{1}H NMR and then fractionated.

General Procedure for Aldol Reactions via the Ti(IV) (*Z*)-Enolate (Table 5). After preparation of the lithium (*Z*)-enolate as described above, the solution was cooled to −78 °C, and $Ti(Oi\text{-}Pr)_4$ or $TiCl_n(Oi\text{-}Pr)_{4-n}$ (n = 1, 2)[45a] (0.55 M in THF; 2.2 equiv) was added via syringe. After the indicated transmetalation time and temperature, the mixture was cooled to −78 °C, and *i*-PrCHO (5 equiv) was added via syringe. After the indicated aldol reaction time, the reaction was quenched by addition of saturated aq NH_4Cl. The mixture was extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product that was analyzed by ^{1}H NMR and then fractionated.

Trimethyl(pent-2-en-3-yloxy)silane (13). Adapting the procedure of Iqbal,[24] anhydrous DMF (400 mL) was added to a flask containing dry NaBr (38.7 g, 0.376 mol) under Ar. After 30 min of stirring, the solid had dissolved, and freshly distilled Me_3SiCl (48 mL, 41 g, 0.37 mol) was added. After 30 min (the mixture had become milky white), 3-pentanone (25 mL, 20 g, 0.24 mol) and Et_3N (53 mL, 38 g, 0.38 mol) were sequentially added. The reaction was monitored by ^{1}H NMR of small aliquots and, after 72 h, had reached 90% conversion (cf. 4−6 h in ref 24). The mixture was extracted with pentane, and the combined extracts were washed sequentially with saturated aq $NaHCO_3$, water, and brine. The organic layer was dried over Na_2SO_4 and subjected to fractional distillation. After the pentane was removed, a small fraction (6.7 g) was obtained at 90−105 °C that was a ca. 2.5:1 mixture of **13** and Et_3N, respectively (by ^{1}H NMR). The remaining yellow oil was **13** as a 5:1 mixture of *Z*:*E* diastereomers (29.1 g, 78%) (cf. a 95:5 mixture (83%) in ref 24).

Ethyl 2-Methyl-3-oxopentanoate (15). Ethyl propionate (57.0 mL, 50.7 g, 0.496 mol) was added dropwise via syringe over 30 min to a stirred solution of KO*t*-Bu (45.5 g, 0.405 mmol) in dry THF (100 mL) at 0 °C. After 1.5 h, the ice bath was removed, and the reaction mixture was allowed to warm to ambient temperature with stirring. After 24 h, the mixture was cooled to 0 °C, and the reaction was quenched by dropwise addition of glacial AcOH (30 mL, 31.5 g, 0.524 mol). The mixture was diluted with toluene (150 mL) and concentrated to give a light yellow solid that was suspended in 1:1 Et_2O/hexane. The mixture was filtered through Celite washing with 1:1 Et_2O/hexane. The combined filtrate and washings were concentrated to give the title compound as a light yellow oil (28.8 g, 90% with respect to KO*t*-Bu).

2-(2-Ethyl-1,3-dioxolan-2-yl)propanal (16). Ethylene glycol (12.7 mL, 14.1 g, 0.226 mol) and *p*-TsOH·H_2O (1.66 g, 8.71 mmol) were added to a stirred solution of **15** (27.6 g, 0.175 mol) in benzene (200 mL), and the mixture was heated under reflux with removal of water via a Dean−Stark trap. After 24 h, the mixture was diluted with ethyl acetate, washed sequentially with saturated aq $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated to give the known[23] crude ketal-ester as a light yellow oil (34.2 g, ca. 95% pure). A solution of the crude ketal (10.0 g) in THF (50 mL) was added via syringe to a stirred suspension of $LiAlH_4$ (1.87 g, 49.4 mmol) in dry THF (100 mL) at 0 °C. The resulting gray suspension was allowed to warm to room temperature. After 2.5 h, water (1.9 mL) was slowly added [**Caution**: H_2 evolution]. The reaction mixture was concentrated to give a gray solid that was taken up in Et_2O (150 mL). 15% aq NaOH (1.9 mL) and water (5.7 mL) were sequentially added dropwise to the vigorously stirred mixture. The initially gray suspension was stirred until a fine white solid formed. The mixture was filtered through Celite washing with ethyl acetate. The combined filtrate and washings were dried over Na_2SO_4 and concentrated to yield the known[20,23] ketal-alcohol as a colorless liquid (7.6 g, ca. 95% pure). Adapting the procedure of More and Finney,[65] IBX (16.8 g, 59.9 mmol) was added to a stirred solution of the crude ketal-alcohol (8.01 g) in acetonitrile (180 mL), and the resulting white suspension was heated to 80 °C. After 2 h, the mixture was cooled in an ice bath and after 1 h was filtered through a medium porosity sintered glass funnel washing with ethyl acetate (3 × 100 mL). The recovered solid (14.5 g) was mainly 2-iodosobenzoic acid that can be reoxidized to IBX with oxone in excellent yield.[20] The combined filtrate and washings were passed through a short column of basic alumina (Brockmann grade 1, 120 g; column diameter, 5.5 cm) eluting with ethyl acetate (100 mL). Concentration of the eluate gave the known[20] crude aldehyde **16** as a colorless liquid (6.55 g, ca. 95% pure; ca. 73% from **15**) that was suitable for use in the preparation of **17a−20a**. Similar results were obtained using Swern oxidation (in place of IBX) as previously described.[20] The aldehyde **16** is susceptible to air oxidation as well as rearrangement to the ketone-acetal (i.e., by transacetalization) but remains unchanged for several months if stored in a freezer (ca. −15 °C) as a frozen solution in degassed (freeze/thaw) benzene (ca. 0.6 M). As required, aliquots from the stock solution are concentrated and used. Fractionation of the above crude **16** (620 mg) by FCC (20% ethyl acetate in hexanes) gave the title compound (596 mg, 74% from **15**).

(4*S*,5*R*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-hydroxy-4-methylheptan-3-one (17a). (*c*-Hex)$_2$BCl (1 M in hexane; 6.2 mL, 6.2 mmol) and Et_3N (1.3 mL, 0.94 g, 9.3 mmol) were sequentially added via syringe to a stirred solution of 3-pentanone (0.85 mL, 0.69 g, 8.1 mmol) in dry Et_2O (45 mL) at 0 °C under argon. After 1 h, the mixture was cooled to −78 °C, and a solution of **16** (0.75 g, 4.7 mmol) in dry Et_2O (2 mL) was added dropwise via syringe. After 17 h, the reaction was quenched by sequential addition of phosphate buffer (pH 7; 12 mL), 30% aq H_2O_2 (7.8 mL), and MeOH (4.8 mL) with vigorous stirring. The reaction vessel was transferred to an ice bath, and after vigorous stirring for 30 min, the mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, concentrated, and reconcentrated from toluene (×3; to remove cyclohexanol) to give the title compound (1.07 g, 92%): dark yellow oil, TLC R_f = 0.3 (30% ethyl acetate in hexane); IR ν_{max} 3525, 1716 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.07 (1H, br d, J = 9.5 Hz, HC-5), 4.02−3.93 (4H, m, H_2C-4′, H_2C-5′), 3.13 (1H, d, J = 1.5 Hz, HO), 2.73 (1H, dq, J = 9.5, 7 Hz, HC-4), 2.63−2.49 (1H, m, H_2C-2), 1.98 (HC-6, br q, J = 7 Hz, HC-6), 1.70 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.05 (3H, t, J = 7.5 Hz, H_3C-1), 0.95 (3H, d, J = 7 Hz, H_3C-7), 0.94 (3H, d, J = 7 Hz, H_3CC-4), 0.88 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C

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NMR ($CDCl_3$) δ 215.6 (s, C-3), 114.8 (s, C-2′), 73.4 (d, C-5), 65.7 (t, C-4′), 65.0 (t, C-5′), 48.7 (d, C-4), 38.5 (d, C-6), 36.9 (t, C-2), 28.2 (t, C-1″), 13.7 (q, CH_3C-4), 8.3 (q, C-2″), 7.7 (q, C-1), 6.9 (q, C-7); HRMS m/z calcd for $C_{13}H_{24}O_4$ + H 245.1753, found 245.1750 (CI, NH_3).

(4*S*,5*R*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-methoxymethoxy-4-methylheptan-3-one (17b). According to the general procedure for preparation of MOM ethers, the crude product obtained after reaction of **17a** (750 mg, 3.06 mmol) for 17 h was fractionated by FCC (15% ethyl acetate in hexane) to afford the title compound (877 mg, 99%): pale yellow viscous oil, TLC R_f = 0.3 (15% ethyl acetate in hexane); spectroscopic data were consistent with those previously reported for (+)-(4*S*)-**17b** (NMR data was obtained in C_6D_6).[46] ^{1}H NMR ($CDCl_3$) δ 4.64 (1H, d, J = 6.5 Hz, HCO_2), 4.61 (1H, d, J = 6.5 Hz, HCO_2), 4.00 (1H, dd, J = 1.5, 7 Hz, HC-5), 3.95- 3.85 (4H, m, H_2C-4′, H_2C-5′), 3.33 (3H, s, H_3CO), 2.93 (1H, dq, J = 7, 7 Hz, HC-4), 2.61 (1H, dq, J = 18, 7 Hz, HC-2), 2.50 (1H, dq, J = 18, 7 Hz, HC-2), 1.90 (1H, dq, J = 1.5, 7 Hz, HC-6), 1.73- 1.60 (2H, m, H_2C-1″), 1.04 (3H, t, J = 7 Hz, H_3C-1), 1.01 (3H, d, J = 7 Hz, H_3CC-4), 0.96 (3H, d, J = 7 Hz, H_3C-7), 0.85 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 213.6 (s, C-3), 113.6 (s, C-2′), 97.3 (t, OCH_2O), 77.2 (d, C-5), 65.4 (t, C-4′), 65.1 (t, C-5′), 56.4 (q, CH_3O), 50.8 (d, C-4), 40.4 (d, C-6), 36.5 (t, C-2), 26.9 (t, C-1″), 12.5 (q, CH_3C-4), 10.0 (q, C-7), 7.8 (q, C-1 or C-2″), 7.6 (q, C-1 or C-2″); HRMS m/z calcd for $C_{15}H_{28}O_5$ + Na^+ 311.1828, found 311.1832 (ESI).

(4*S*,5*R*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-4-methyl-5-((triethylsilyl)oxy)-heptan-3-one (17c). According to the general procedure for preparation of Et_3Si ethers (Et_3N), the crude product obtained after reaction of **17a** (497 mg, 2.04 mmol) for 17 h was fractionated by FCC (15% ethyl acetate in hexane) to afford the title compound (719 mg, 98%): colorless oil, TLC R_f = 0.6 (40% Et_2O in hexane); spectroscopic data were consistent with those previously reported for (−)-(4*R*)-**17c**.[15m]

(4*S*,5*S*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-hydroxy-4-methylheptan-3-one (18a). BF_3·OEt_2 (1.7 mL, 1.9 g, 13 mmol) was added dropwise via syringe over 5 min to a stirred solution of crude **16** (2.08 g, ≤13.2 mmol) and **13** (4.16 g, 26.4 mmol) in CH_2Cl_2 (200 mL) at −78 °C under argon. After 1.5 h, the reaction was quenched by addition of saturated aq NH_4Cl (10 mL), and after warming to ambient temperature, the mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to obtain the crude product whose ^{1}H NMR indicated the presence of a 10:1 mixture of **18a** and **17a**, respectively. Fractionation of the crude product by FCC (30% ethyl acetate in hexane) gave a 2.5:1 mixture of **18a** and **17a**, respectively (343 mg, 11%), and the title compound (2.03 g, ≥63%): colorless oil, TLC R_f = 0.4 (35% ethyl acetate in hexane); IR ν_{max} 3529, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.09 (1H, d, J = 9 Hz, HC-5), 4.03−3.92 (4H, m, H_2C-4′, H_2C-5′), 3.10 (1H, br s, HO), 2.78 (1H, dq, J = 9, 7 Hz, HC-4), 2.54 (1H, dq, J = 18, 7 Hz, H_2C-2), 2.41 (1H, dq, J = 18, 7 Hz, H_2C-2), 1.81 (1H, dq, J = 1, 7 Hz, HC-6), 1.68 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.21 (3H, d, J = 7 Hz, H_3CC-4), 1.03 (3H, t, J = 7 Hz, H_3C-1), 0.93 (3H, d, J = 7 Hz, H_3C-7), 0.86 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 214.7 (s, C-3), 114.7 (s, C-2′), 71.6 (d, C-5), 65.7 (t, C-4′), 65.0 (t, C-5′), 50.2 (d, C-4), 39.9 (d, C-6), 35.6 (t, C-2), 28.1 (t, C-1″), 14.9 (q, CH_3C-4), 8.2 (q, C-2″), 7.8 (q, C-1), 7.4 (q, C-7); HRMS m/z calcd for $C_{13}H_{24}O_4$ + Na^+ 267.1566, found 267.1567 (ESI).

(4*S*,5*S*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-methoxymethoxy-4-methylheptan-3-one (18b). According to the general procedure for preparation of MOM ethers, the crude product obtained after reaction of **18a** (1.0 g, 4.1 mmol) for 3 days was fractionated by FCC (15% ethyl acetate in hexane) to afford the title compound (1.16 g, 98%): colorless oil, TLC R_f = 0.4 (40% ethyl acetate in hexane); IR ν_{max} 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.68 (1H, d, J = 6.5 Hz, HCO_2), 4.54 (1H, d, J = 6.5 Hz, HCO_2), 3.97 (1H, dd, J = 3, 5 Hz, HC-5), 3.95−3.90 (4H, m, H_2C-4′, H_2C-5′), 3.32 (3H, s, H_3CO), 2.81 (1H, dq, J = 5, 7 Hz, HC-4), 2.65 (1H, dq, J = 18, 7 Hz, H_2C-2), 2.44 (1H, dq, J = 18, 7 Hz, H_2C-2), 1.91 (1H, dq, J = 3, 7 Hz, HC-6), 1.69−1.57 (2H, m, H_2C-1″), 1.06 (3H, d, J = 7 Hz, H_3CC-4), 1.01 (3H, t, J = 7 Hz, H_3C-1), 0.87 (3H, d, J = 7 Hz, H_3C-7), 0.83 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 213.7 (s, C-3), 113.5 (s, C-2′), 97.4 (t, OCH_2O), 77.7 (d, C-5), 65.2 (t × 2, C-4′ and C-5′), 56.4 (t, CH_3O), 51.2 (d, C-4), 41.5 (d, C-6), 35.6 (t, C-2), 26.8 (t, C-1″), 12.0 (q, CH_3C-4), 10.5 (q, C-7), 7.9 (q, C-1), 7.6 (q, C-2″); HRMS m/z calcd for $C_{15}H_{28}O_5$ + Na^+ 311.1828, found 311.1827 (ESI).

(4*S*,5*S*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-4-methyl-5-((triethylsilyl)oxy)heptan-3-one (18c). According to the general procedure for preparation of Et_3Si ethers (imidazole), the crude product obtained after reaction of **18a** (1.0 g, 4.1 mmol) for 16 h was fractionated by FCC (5% ethyl acetate in hexane) to afford the title compound (1.43 g, 97%): colorless viscous oil, TLC R_f = 0.6 (20% ethyl acetate in hexane); spectroscopic data were consistent with those previously reported for (−)-(4*R*)-**18c**.[12k]

(4*S*,5*S*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-hydroxy-4-methylheptan-3-one (19a). Fractionation of an ca. 6:1 mixture of **19a** and **17a**, respectively (30 mg; obtained from the preparation of **20a**), by PTLC (1:1:2 Et_2O/benzene/hexane; developed thrice) afforded the title compound (24 mg, 80%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3481, 1712 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.28 (1H, br s, HO), 4.09 (1H, dd, J = 2.5, 9.5 Hz, HC-5), 4.01−3.93 (4H, m, H_2C-4′, H_2C-5′), 2.60−2.46 (3H, m, H_2C-2, HC-4), 1.83 (1H, dq, J = 9.5, 7 Hz, HC-6), 1.81−1.69 (2H, m, H_2C-1″), 1.08 (3H, d, J = 7 Hz, H_3CC-4), 1.05 (3H, t, J = 7 Hz, H_3C-1), 0.89 (3H, d, J = 7 Hz, H_3C-7), 0.88 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 213.6 (s, C-3), 114.9 (s, C-2′), 73.0 (d, C-5), 65.4 (t, C-4′), 65.0 (t, C-5′), 49.1 (d, C-4), 41.4 (d, C-6), 33.7 (d, C-2), 25.7 (t, C-1″), 12.8 (q, C-7), 8.04 (q, C-1 or CH_3C-4), 8.01 (q, C-1 or CH_3C-4), 7.0 (q, C-2″); HRMS m/z calcd for $C_{13}H_{24}O_4$ + Na^+ 267.1566, found 267.1560 (ESI).

(4*S*,5*S*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-methoxymethoxy-4-methylheptan-3-one (19b). According to the general procedure for preparation of MOM ethers, the crude product obtained after reaction of a 6:1 mixture of **19a** and **17a**, respectively (1.31 g, 5.36 mmol; obtained from the preparation of **20a**), for 10 h was fractionated by FCC (20−40% ethyl acetate in hexane) to give a 1:1 mixture of **19b** and **17b** (183 mg, 11%) and the title compound (1.088 g, 70%; 80% based on **19a**): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 1711 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.64 (1H, d, J = 6.5 Hz, HCO_2), 4.62 (1H, d, J = 6.5 Hz, HCO_2), 4.06 (1H, dd, J = 3.5, 6 Hz, HC-5), 3.92−3.78 (4H, m, H_2C-4′, H_2C-5′), 3.34 (3H, s, H_3CO), 3.03 (1H, dq, J = 6, 7 Hz, HC-4), 2.52 (2H, ap q, J = 7.5 Hz, H_2C-2), 2.22 (1H, dq, J = 3.5, 7 Hz, HC-6), 1.69−1.61 (2H, m, H_2C-1″), 1.14 (3H, d, J = 7 Hz, H_3CC-4), 1.03 (3H, t, J = 7.5 Hz, H_3C-1), 1.01 (3H, d, J = 7 Hz, H_3C-7), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 214.1 (s, C-3), 113.3 (s, C-2′), 97.8 (t, OCH_2O), 78.6 (d, C-5), 65.5 (t, C-4′), 64.8 (t, C-5′), 56.1 (q, CH_3O), 48.1 (d, C-4), 42.2 (d, C-6), 34.5 (t, C-2), 28.3 (t, C-1″), 14.1 (q, CH_3C-4), 10.9 (q, C-7), 8.0 (q, C-1 or C-2′), 7.9 (q, C-1 or C-2″); HRMS m/z calcd for $C_{15}H_{28}O_5$ + Na^+ 311.1828, found 311.1841 (ESI).

(4*S*,5*S*,6*S*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-4-methyl-5-((triethylsilyl)oxy)heptan-3-one (19c). From **25sa** (Pg = Et_3Si). A suspension of Raney nickel (W2; 1 mL settled volume) in EtOH (2 mL) was added to **25sa** (Pg = Et_3Si) (68 mg, 0.16 mmol), and the mixture was heated under reflux with vigorous stirring. After 3 h (reaction was complete by TLC analysis), the mixture was decanted, and the solid was suspended in EtOH (3 mL) and heated under reflux with vigorous stirring for several min. This washing procedure was repeated with ethyl acetate (×1), and acetone (×2). The combined organic layers were filtered through Celite, concentrated, and fractionated by PTLC (20% Et_2O in hexane) to give the title compound (48 mg, 82%); spectral data were consistent with those reported below. From **19a**. According to the general procedure for preparation of Et_3Si ethers (imidazole), the crude product obtained after reaction of a 6:1 mixture of **19a** and **17a**, respectively (900 mg, 3.69 mmol; obtained from the preparation of **20a**), for 10 h was fractionated by FCC (40% hexane in CH_2Cl_2) to afford a 2:1 mixture of **19c** and **17c**, respectively (150 mg, 11%), and the title compound (1.050 g, 79%; 90% based on **19a**): colorless viscous oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); IR ν_{max} 1712 cm^{-1}; ^{1}H NMR ($CDCl_3$)

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δ 4.32 (1H, dd, J = 3, 6 Hz, HC-5), 3.91−3.74 (4H, m, H_2C-4′, H_2C-5′), 2.97 (1H, dq, J = 6, 7 Hz, HC-4), 2.56−2.43 (1H, ddq, H_2C-2), 2.08 (1H, dq, J = 3, 7 Hz, HC-6), 1.69−1.58 (2H, m, H_2C-1″), 1.09 (3H, d, J = 7 Hz, H_3CC-4), 1.01 (3H, t, J = 7.5 Hz, H_3C-1), 0.98 (3H, d, J = 7 Hz, H_3C-7), 0.95 (9H, t, J = 8 Hz, $H_3CCSi \times 3$), 0.85 (3H, t, J = 7.5 Hz, H_3C-2″), 0.60 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 214.7 (s, C-3), 113.4 (s, C-2′), 71.7 (d, C-5), 65.4 (t, C-4′), 64.7 (t, C-5′), 48.6 (d, C-4), 44.6 (d, C-6), 34.6 (t, C-2), 28.3 (t, C-1″), 14.9 (q, CH_3C-4), 10.4 (q, C-7), 8.0 (q, C-2″), 7.9 (q, C-1), 7.2 (q × 3, CH_3CSi), 5.4 (t × 3, CH_2Si); HRMS m/z calcd for $C_{19}H_{38}O_4Si + Na^+$ 381.2431, found 381.2426 (ESI).

(4*S*,5*R*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-hydroxy-4-methylheptan-3-one (20a). From **25aa** (Pg = H). A suspension of Raney nickel (W2; 1 mL settled volume) in EtOH (2 mL) was added to **25aa** (Pg = H) (39 mg, 0.13 mmol), and the mixture was heated under reflux with vigorous stirring. After 2.5 h (reaction was complete by TLC analysis), the mixture was decanted, and the solid was suspended in EtOH (3 mL) and heated under reflux with vigorous stirring for several min. This washing procedure was repeated with ethyl acetate (×1) and acetone (×2). The combined organic layers were filtered through Celite, concentrated, and fractionated by PTLC (60% Et_2O in hexane) to give the title compound (25 mg, 80%); spectral data were consistent with those reported below. From **13** and **16**. $MgBr_2{\cdot}OEt_2$ (32.71 g, 126.7 mmol) was added to a stirred solution of crude **16** (9.83 g, ≤62.2 mmol) and **13** (11.1 g, 70.2 mmol) in CH_2Cl_2 (500 mL) at 0 °C under argon. After 2 h (reaction complete by TLC analysis), the reaction vessel was transferred to a −15 °C bath (ice/NaCl), and ice-cold phosphate buffer (pH 6.8, 250 mL) was added with vigorous stirring. After 15 min, the organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to give the crude product as a pale yellow oil whose ^{1}H NMR spectrum indicated the presence of a 10:10:1 mixture of **20a**, **19a**, and **17a**, respectively. Fractionation of the crude product by FCC (20% ethyl acetate in hexane) gave a 6:1 mixture of **19a** and **17a**, respectively (5.91 g, ≥39%), and the title compound (6.38 g, ≥42%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3476, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.39 (1H, d, J = 3 Hz, HO), 4.01−3.92 (4H, m, H_2C-4′, H_2C-5′), 3.72 (1H, ddd, J = 3, 3.5, 8.5 Hz, HC-5), 2.74 (1H, dq, J = 3.5, 7 Hz, HC-4), 2.58 (1H, dq, J = 18.5, 7.5 Hz, HC-2), 2.50 (1H, dq, J = 18.5, 7.5 Hz, HC-2), 1.91 (1H, dq, J = 8.5, 7 Hz, HC-6), 1.71 (2H, m, HC-1″), 1.24 (3H, d, J = 7 Hz, H_3CC-4), 1.01 (3H, t, J = 7.5 Hz, H_3C-1), 0.91 (3H, d, J = 7 Hz, H_3C-7), 0.88 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 215.4 (s, C-3), 114.8 (s, C-2′), 76.1 (d, C-5), 65.2 (t, C-4′), 65.0 (t, C-5′), 49.7 (d, C-4), 42.0 (d, C-6), 35.1 (t, C-2), 26.0 (t, C-1″), 14.5 (q, CH_3C-4), 13.1 (q, C-7), 7.8 (q, C-1), 7.1 (q, C-2″); HRMS m/z calcd for $C_{13}H_{24}O_4 + Na^+$ 267.1566, found 267.1556 (ESI).

(4*S*,5*R*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-5-methoxymethoxy-4-methylheptan-3-one (20b). According to the general procedure for preparation of MOM ethers, the crude product obtained after reaction of **20a** (1.717g, 7.04 mmol) for 10 h was fractionated by FCC (20−40% ethyl acetate in hexane) to give recovered **20a** (100 mg, 6%) and the title compound (1.713 g, 85%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); ^{1}H NMR ($CDCl_3$) δ:4.52 (2H, ap s, H_2CO_2), 3.98−3.91 (4H, m, H_2C-4′, H_2C-5′), 3.76 (1H, dd, J = 2.5, 8.5 Hz, HC-5), 3.30 (3H, s, H_3CO), 3.13 (1H, dq, J = 8.5, 7 Hz, HC-4), 2.60−2.48 (2H, m, H_2C-2), 2.15 (1H, dq, J = 2.5, 7 Hz, HC-6), 1.82−1.67 (2H, m, H_2C-1″), 1.05 (3H, d, J = 7 Hz, H_3C-7), 1.03 (3H, d, J = 7 Hz, H_3CC-4), 1.02 (3H, t, J = 7.5 Hz, H_3C-1), 0.89 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ:215.1 (s, C-3), 113.6 (s, C-2′), 98.1 (t, OCH_2O), 83.1 (d, C-5), 65.6 (t, C-4′), 65.3 (t, C-5′), 56.3 (q, CH_3O), 48.6 (d, C-4), 41.8 (d, C-6), 37.1 (t, C-2), 28.9 (t, C-1″), 14.8 (q, CH_3C-4), 12.2 (q, C-7), 7.8 (q × 2, C-1, C-2″); HRMS m/z calcd for $C_{15}H_{28}O_5 + Na^+$ 311.1828, found 311.1816 (ESI).

(4*S*,5*R*,6*R*)-*rel*-6-(2-Ethyl-1,3-dioxolan-2-yl)-4-methyl-5-((triethylsilyl)oxy)heptan-3-one (20c). According to the general procedure for preparation of Et_3Si ethers (imidazole), the crude product obtained after reaction of **20a** (286 mg, 1.17 mmol) for 40 h was fractionated by FCC (10% ethyl acetate in hexane) to afford the title compound (365 mg, 87%) colorless viscous oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); IR ν_{max} 1717 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ:4.02 (1H, dd, J = 2.5, 8 Hz, HC-5), 3.98−3.90 (4H, m, H_2C-4′, H_2C-5′), 3.06 (1H, dq, J = 8, 7 Hz, HC-4), 2.55 (1H, dq, J = 18.5, 7 Hz, HC-2), 2.48 (1H, dq, J = 18.5, 7 Hz, HC-2), 2.01 (1H, dq, J = 2.5, 7 Hz, HC-6), 1.77 (1H, dq, J = 14.5, 7.5 Hz, HC-1″), 1.69 (1H, dq, J = 14.5, 7.5 Hz, HC-1″), 1.02 (3H, d, J = 7 Hz, H_3C-7), 1.01 (3H, t, J = 7 Hz, H_3C-1), 1.00 (3H, d, J = 7 Hz, H_3CC-4), 0.93 (9H, t, J = 8 Hz, $H_3CCSi \times 3$), 0.85 (3H, t, J = 7.5 Hz, H_3C-2″), 0.58 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ:215.2 (s, C-3), 113.7 (s, C-2′), 76.6 (d, C-5), 65.4 (t, C-4′), 65.3 (t, C-5′), 49.6 (d, C-4), 44.1 (d, C-6), 37.1 (t, C-2), 28.9 (t, C-1″), 15.3 (q, CH_3C-4), 11.9 (q, C-7), 7.8 (q, C-1), 7.6 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd for $C_{19}H_{38}O_4Si + Na^+$ 381.2431, found 381.2419 (ESI).

(2*S*,3*R*,4*S*,6*S*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (21aa; Pg = MOM). See the preparation **21sa** (Pg = MOM): pale yellow oil, TLC R_f = 0.6 (30% Et_2O in CH_2Cl_2); IR ν_{max} 3512, 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.66 (1H, d, J = 6 Hz, HCO_2), 4.59 (1H, d, J = 6 Hz, HCO_2), 3.99 (1H, dd, J = 1.5, 8 Hz, HC-3), 3.98- 3.93 (4H, m, H_2C-4′, H_2C-5′), 3.49 (1H, ddd, J = 4.5, 5.5, 7.5 Hz, HC-7), 3.34 (3H, s, H_3CO), 3.07 (1H, dq, J = 8, 7 Hz, HC-4), 2.83 (1H, dq, J = 7.5, 7 Hz, HC-6), 2.60 (1H, d, J = 5.5 Hz, HO), 1.99 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.77 (1H, dqq, J = 4.5, 7, 7 Hz, HC-8), 1.72- 1.63 (2H, m, H_2C-1″), 1.12 (3H, d, J = 7 Hz, H_3CC-6), 1.04 (3H, d, J = 7 Hz, H_3CC-4), 0.99 (3H, d, J = 7 Hz, H_3C-1), 0.98 (3H, d, J = 7 Hz, H_3C-9), 0.91 (3H, d, J = 7 Hz, H_3C-9′), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 217.9 (s, C-5), 113.5 (s, C-2′), 97.4 (t, OCH_2O), 78.3 (d, C-7), 76.2 (d, C-3), 65.4 (t, C-4), 65.2 (t, C-5), 56.8 (q, CH_3O), 50.7 (d, C-4), 50.0 (d, C-6), 40.5 (d, C-2), 30.2 (d, C-8), 27.3 (t, C-1″), 20.4 (q, C-9), 15.6 (q, C-9′), 13.6 (q, CH_3C-4), 13.4 (q, CH_3C-6), 9.9 (q, C-1), 7.9 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2415 (ESI).

(2*S*,3*R*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (21as; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **17b** (55 mg, 0.19 mmol) with *i*-PrCHO gave a crude product containing a 3.5:1 mixture of **21ss** (Pg = MOM) and **21as** (Pg = MOM), respectively. Fractionation of the crude product by FCC (15% ethyl acetate in hexane) gave **21ss** (Pg = MOM) (48 mg, 70%) and the title compound (14 mg, 20%): dark yellow oil, TLC R_f = 0.35 (30% ethyl acetate in hexane); IR ν_{max} 3511, 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.64 (1H, d, J = 6 Hz, H_2CO), 4.58 (1H, d, J = 6 Hz, H_2CO), 3.99 (1H, dd, J = 1, 8 Hz, HC-3), 3.98- 3.90 (4H, m, H_2C-4′, H_2C-5′), 3.50 (1H, dd, J = 2, 9 Hz, HC-7), 3.33 (3H, s, H_3CO), 3.13 (1H, dq, J = 8, 7 Hz, HC-4), 2.85 (1H, dq, J = 2, 7 Hz, HC-6), 2.81 (1H, br s, HO), 1.97 (2H, dq, J = 1, 7 Hz, HC-2), 1.71- 1.62 (3H, m, H_2C-1″, HC-8), 1.12 (3H, d, J = 7 Hz, H_3CC-6), 1.04 (3H, d, J = 7 Hz, H_3C-9), 1.04 (3H, d, J = 7 Hz, H_3CC-4), 0.98 (3H, d, J = 7 Hz, H_3C-1), 0.87 (3H, d, J = 7 Hz, H_3C-9′), 0.86 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 218.0 (s, C-5), 113.5 (s, C-2′), 97.5 (t, OCH_2O), 76.90 (d, C-7), 76.87 (d, C-3), 65.4 (t, C-4′), 65.2 (t, C-5′), 56.7 (q, CH_3O), 49.1 (d, C-4), 48.7 (d, C-6), 40.4 (d, C-2), 31.0 (d, C-8), 27.3 (t, C-1″), 19.8 (q, C-9), 19.2 (q, C-9′), 13.8 (q, CH_3C-4), 9.9 (q, C-1), 7.9 (q, C-2″ or CH_3C-6), 7.8 (q, C-2″ or CH_3C-6); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2400 (ESI).

(2*S*,3*R*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (21as; Pg = Et_3Si). According to the general procedure, reaction of the lithium (*Z*)-enolate of **17c** (54 mg, 0.15 mmol) (quenching the enolate with Me_3SiCl indicated a dr of 3:1) with *i*-PrCHO gave a crude product containing a 15:1:6 mixture of **21as** (Pg = Et_3Si), **21ss** (Pg = Et_3Si), and **21sa** (Pg = Et_3Si) (presumably from the (*E*)-enolate), respectively. Fractionation of the crude product by PTLC (70% ether in hexane) gave **21sa** (Pg = Et_3Si) (15 mg, 23%), **21ss** (Pg = Et_3Si) (3 mg, 5%), and the title compound (36 mg, 55%): colorless oil, TLC R_f = 0.3 (40% Et_2O in hexane); IR ν_{max} 3499, 1708 cm^{-1}; ^{1}H

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NMR ($CDCl_3$) δ 4.25 (1H, dd, J = 1.5, 5 Hz, HC-3), 3.92−3.79 (4H, m, H_2C-4′, H_2C-5′), 3.45 (1H, ddd, J = 2, 3.5, 9 Hz, HC-7), 3.02 (1H, dq, J = 5, 7 Hz, HC-4), 2.94 (1H, dq, J = 2, 7 Hz, HC-6), 2.41 (1H, d, J = 3.5 Hz, HO), 1.89 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.72−1.56 (3H, m, HC-8, H_2C-1″), 1.06 (3H, d, J = 7 Hz, H_3CC-6), 1.05 (6H, ap d, J = 7.5 Hz, H_3C-9, H_3CC-4), 0.97 (9H, d, J = 8 Hz, $H_3CCSi \times 3$), 0.93 (3H, d, J = 7 Hz, H_3C-1), 0.89 (3H, d, J = 6.5 Hz, H_3C-9′), 0.83 (3H, t, J = 7.5 Hz, H_3C-2″), 0.63 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 216.6 (s, C-5), 114.0 (s, C-2′), 77.0 (d, C-7), 70.4 (d, C-3), 65.2 (t, C-4′), 65.0 (t, C-5′), 52.9 (d, C-4), 47.8 (d, C-6), 40.9 (d, C-2), 31.2 (d, C-8), 26.5 (t, C-1″), 19.8 (q, C-9), 19.2 (q, C-9′), 11.6 (q, CH_3C-4), 10.9 (q, C-1), 8.0 (q, CH_3C-6), 7.33 (q, C-2″), 7.26 (q × 3, CH_3CSi), 5.5 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.3006 (ESI).

(2*S*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (21sa; Pg = MOM). According to the general procedure, reaction of **17b** (31 mg, 0.11 mmol) with $(c\text{-Hex})_2BCl$ (1.8 equiv) and Et_3N (2.2 equiv) at −50 °C for 2 h followed by addition of *i*-PrCHO (5 equiv) at −78 °C and workup after 2 h gave a crude product containing a 2:1 mixture of **21sa** (Pg = MOM) and **21aa** (Pg = MOM), respectively. Fractionation of the crude product by FCC (15% Et_2O in CH_2Cl_2) gave **21aa** (Pg = MOM) (10 mg, 26%) and the title compound (24 mg, 62%): pale yellow oil, TLC R_f = 0.7 (30% Et_2O in CH_2Cl_2); IR ν_{max} 3482, 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.67 (1H, d, J = 6 Hz, HCO_2), 4.60 (1H, d, J = 6 Hz, HCO_2), 4.03 (1H, dd, J = 1.5, 8 Hz, HC-3), 3.97−3.91 (4H, m, H_2C-4′, H_2C-5′), 3.56 (1H, ddd, J = 3.5, 4, 8.5 Hz, HC-7), 3.35 (3H, s, H_3CO), 3.27 (1H, d, J = 4 Hz, HO), 3.18 (1H, dq, J = 8, 7 Hz, HC-4), 2.86 (1H, dq, J = 8.5, 7 Hz, HC-6), 1.99 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.80 (1H, dqq, J = 3.5, 7, 7 Hz, HC-8), 1.69- 1.62 (2H, m, H_2C-1″), 1.04 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 7 Hz, H_3CC-4), 1.01 (3H, d, J = 7 Hz, H_3C-9), 0.99 (1H, d, J = 7 Hz, H_3C-1), 0.89 (3H, d, J = 7 Hz, H_3C-9′), 0.86 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 218.3 (s, C-5), 113.6 (s, C-2′), 97.7 (t, OCH_2O), 77.3 (d, C-7), 77.0 (d, C-3), 65.3 (t, C-4′), 65.1 (t, C-5′), 56.7 (q, CH_3O), 51.1 (d, C-6), 50.7 (d, C-4), 40.0 (d, C-2), 29.4 (d, C-8), 27.3 (t, C-1″), 20.5 (q, C-9), 14.6 (q, C-9′), 13.9 (q, CH_3C-4), 13.5 (q, CH_3C-6), 9.9 (q, C-1), 7.9 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2405 (ESI).

(2*S*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (21sa; Pg = Et_3Si). According to the general procedure, reaction of **17c** (38 mg, 0.11 mmol) with $(c\text{-Hex})_2BCl$ (1.3 equiv) and Et_3N (1.6 equiv) at −50 °C for 1.5 h followed by addition of *i*-PrCHO (5 equiv) at −78 °C and workup after 1.5 h gave a crude product containing a single aldol adduct. Fractionation of the crude product by FCC (20% Et_2O in hexane) gave the title compound (37 mg, 80%): colorless oil, TLC R_f = 0.55 (40% Et_2O in hexane); IR ν_{max} 3502, 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.25 (1H, dd, J = 1.5, 4.5 Hz, HC-3), 3.92−3.85 (4H, m, H_2C-4′, H_2C-5′), 3.61 (1H, ddd, J = 3, 4.5, 8.5 Hz, HC-7), 3.07 (1H, dq, J = 4.5, 7 Hz, HC-4), 2.97 (1H, d, J = 4.5 Hz, HO), 2.83 (1H, dq, J = 8.5, 7 Hz, HC-6), 2.02 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.78 (1H, dqq, J = 3, 7, 7 Hz, HC-8), 1.66 (1H, dq, J = 7.5, 14.5 Hz, HC-1″), 1.59 (1H, dq, J = 7.5, 14.5 Hz, HC-1″), 1.06 (3H, d, J = 7 Hz, H_3CC-4), 1.03 (3H, d, J = 7 Hz, H_3CC-6), 1.02 (3H, d, J = 8 Hz, H_3C-9), 0.99 (9H, t, J = 7 Hz, $H_3CCSi \times 3$), 0.94 (3H, d, J = 7 Hz, H_3C-1), 0.89 (3H, d, J = 7.5 Hz, H_3C-9′), 0.84 (3H, t, H_3C-2″), 0.65 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 216.9 (s, C-5), 114.2 (s, C-2′), 76.4 (d, C-7), 69.3 (d, C-3), 65.1 (t, C-4′), 64.8 (t, C-5′), 53.7 (d, C-4), 50.9 (d, C-6), 40.0 (d, C-2), 29.3 (d, C-8), 26.3 (t, C1″), 20.6 (q, C-9), 14.6 (q, C-9′), 14.2 (q, CH_3C-6), 11.4 (q, CH_3C-4), 11.0 (q, C-1), 7.5 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.5 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.3021 (ESI).

(2*S*,3*R*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (21ss; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **17b** (36 mg, 0.13 mmol) with $TiCl(Oi\text{-}Pr)_3$ at −50 °C for 1 h followed by addition of *i*-PrCHO at −78 °C and workup after 1.5 h gave a crude product containing a 13:1 mixture of **21ss** (Pg = MOM) and **21as** (Pg = MOM), respectively. Fractionation of the crude product by FCC (70% ether in hexane) gave **21as** (Pg = MOM) (3 mg, 7%) and the title compound (39 mg, 87%): pale yellow oil, TLC R_f = 0.5 (30% ethyl acetate in hexane); IR ν_{max} 3481, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.59 (1H, d, J = 5.5 Hz, HCO_2), 4.57 (1H, d, J = 5.5 Hz, HCO_2), 3.97−3.80 (5H, m, HC-3, H_2C-4′, H_2C-5′), 3.64 (1H, ddd, J = 1.5, 3, 9.5 Hz, HC-7), 3.39 (1H, d, J = 3 Hz, HO), 3.31 (1H, s, H_3CO), 3.07 (1H, dq, J = 8, 7 Hz, HC-4), 2.79 (1H, dq, J = 1.5, 7 Hz, HC-6), 1.94 (1H, dq, J = 1, 7 Hz, HC-2), 1.71−1.59 (3H, m, H_2C-1″, HC-8), 1.06 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.98 (3H, d, J = 7 Hz, H_3CC-4), 0.97 (3H, d, J = 7 Hz, H_3C-1), 0.84 (3H, t, J = 7.5 Hz, H_3C-2″), 0.84 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 217.8 (s, C-5), 113.4 (s, C-2′), 97.8 (t, OCH_2O), 77.4 (d, C-3), 75.4 (d, C-7), 65.3 (t, C-4′), 65.1 (t, C-5′), 56.7 (q, CH_3O), 49.0 (d, C-6), 48.7 (d, C-4), 40.3 (d, C-2), 30.6 (d, C-8), 27.4 (q, C-1″), 20.3 (q, C-9), 19.1 (q, C-9′), 13.8 (q, CH_3C-4), 9.6 (q, C-1), 7.94 (q, C-2″ or CH_3C-6), 7.88 (q, C-2″ or CH_3C-6); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2407 (ESI).

(2*S*,3*R*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (21ss; Pg = Et_3Si). According to the general procedure, reaction of the lithium (*Z*)-enolate of **17c** (28 mg, 0.078 mmol) with $TiCl(Oi\text{-}Pr)_3$ at −50 °C for 1 h followed by addition of *i*-PrCHO at −78 °C and workup after 1.5 h gave a crude product containing a 10:1 mixture of **21ss** (Pg = Et_3Si) and **21as** (Pg = Et_3Si), respectively. Fractionation of the crude product by PTLC (30% ethyl acetate in hexane) gave **21as** (Pg = Et_3Si) (3 mg, 9%) and the title compound (26 mg, 84%): colorless oil, TLC R_f = 0.5 (40% Et_2O in hexane); IR ν_{max} 3525, 1696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.21 (1H, dd, J = 1.5, 4 Hz, HC-3), 3.92−3.78 (4H, m, H_2C-4′, H_2C-5′), 3.60 (1H, ddd, J = 1, 1.5, 9.5 Hz, HC-7), 3.45 (1H, d, J = 1.5 Hz, HO), 3.05 (1H, dq, J = 4, 7 Hz, HC-4), 2.85 (1H, dq, J = 1, 7.5 Hz, HC-6), 1.93 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.72−1.54 (3H, m, HC-8, H_2C-1″), 1.12 (3H, d, J = 7.5 Hz, H_3CC-6), 1.05 (3H, d, J = 6.5 Hz, H_3C-9), 1.03 (3H, d, J = 7 Hz, H_3CC-4), 0.98 (9H, t, J = 8 Hz, $H_3CCSi \times 3$), 0.93 (3H, d, J = 7 Hz, H_3C-1), 0.85 (3H, d, J = 6.5 Hz, H_3C-9′), 0.84 (3H, t, J = 7.5 Hz, H_3C-1″), 0.63 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 218.5 (s, C-5), 114.0 (s, C-2′), 75.7 (d, C-7), 70.5 (d, C-3), 65.2 (t, C-4′), 64.9 (t, C-5′), 52.8 (d, C-4), 47.3 (d, C-6), 40.6 (d, C-2), 30.5 (d, C-8), 26.3 (t, C-1″), 20.2 (q, C-9), 18.9 (q, C-9′), 11.0 (q × 2, C-1, CH_3C-4), 9.0 (q, CH_3C-6), 7.3 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.5 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.2991 (ESI).

(2*R*,3*S*,4*S*,6*S*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (22aa; Pg = MOM). According to the general procedure, reaction of the lithium (*E*)-enolate (dr 3.4:1) of **18b** (250 mg, 0.868 mmol) with *i*-PrCHO gave a crude product containing a 12:5:3:2 mixture of **22aa** (Pg = MOM), **22sa** (Pg = MOM), **22as** (Pg = MOM), and **22ss** (Pg = MOM), respectively. Fractionation of the crude product by FCC (20−40% ethyl acetate in hexane) gave **22sa** (Pg = MOM) (8 mg, 21%), **22as** (Pg = MOM) (3 mg, 8%), and 5:1 mixture of **22aa** (Pg = MOM) and **22ss** (Pg = MOM), respectively (16 mg, 43%) that was further fractionated by PTLC (10% acetone in hexanes) to afford a 1.2:1 mixture of **22aa** (Pg = MOM) and **22ss** (Pg = MOM), respectively (7 mg, 19%), and the title compound (8 mg, 21%): colorless oil, TLC R_f = 0.34 (20% acetone in hexane); IR ν_{max} 3502, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.70 (1H, d, J = 6.5 Hz, HCO_2), 4.58 (1H, d, J = 6.5 Hz, HCO_2), 4.05 (1H, dd, J = 3, 5.5 Hz, HC-3), 3.97−3.94 (4H, m, H_2C-4′, H_2C-5′), 3.43 (1H, ddd, J = 4.5, 6.5, 7 Hz, HC-7), 3.36 (3H, s, H_3CO), 3.01 (1H, dq, J = 5.5, 7 Hz, HC-4), 2.96 (1H, dq, J = 7, 7 Hz, HC-6), 2.40 (1H, d, J = 6.5 Hz, HO), 1.94 (1H, dq, J = 3, 7 Hz, HC-2), 1.76−1.63 (3H, m, HC-8, H_2C-1″), 1.13 (3H, d, J = 7 Hz, H_3CC-4), 1.09 (3H, d, J = 7 Hz, H_3CC-6), 0.96 (3H, d, J = 6.5 Hz, H_3C-9), 0.94 (3H, d, J = 7 Hz, H_3C-1), 0.90 (3H, d, J = 6.5 Hz, H_3C-9′), 0.86 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 218.6 (s, C-5), 113.6 (s, C-2′), 97.5 (t, OCH_2O), 78.9 (d, C-7), 76.5 (d, C-3), 65.3 (t, C-4′), 65.2 (t, C-5′), 56.5 (q, CH_3O), 52.0 (d, C-4), 48.1 (d, C-6), 42.3 (d, C-2), 30.4 (d, C-8), 27.0 (t, C-1″), 20.3 (q, C-9), 15.8 (q, C-9′), 14.2 (q, CH_3C-6), 12.4 (q, CH_3C-4), 10.4 (q, C-1), 7.7 (q, C-2″);

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HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2396 (ESI).

(2*R*,3*S*,4*S*,6*S*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (22aa; Pg = Et$_3$Si). According to the general procedure, reaction of the lithium (*E*)-enolate (dr 2.8:1) of **18c** (30 mg, 0.084 mmol) with *i*-PrCHO gave a crude product containing a 5:4:2:1 mixture of **22aa** (Pg = Et_3Si), **22sa** (Pg = Et_3Si), **22as** (Pg = Et_3Si), and **22ss** (Pg = Et_3Si), respectively. Fractionation of the crude product by FCC (20−40% ether in hexanes) gave **22as** (Pg = Et_3Si) (6 mg, 17%), **22sa** (Pg = Et_3Si) (6 mg, 17%), a 3:2:1 mixture of **22sa** (Pg = Et_3Si), **22aa** (Pg = Et_3Si), and **22ss** (Pg = Et_3Si), respectively (7 mg, 19%), and a 10:1:0.3 mixture of **22aa** (Pg = Et_3Si), **22ss** (Pg = Et_3Si), and **22sa** (Pg = Et_3Si), respectively (8 mg, 22%). The latter fraction was fractionated by PTLC (30% Et_2O in hexane) to obtain the title compound (5 mg, 14%; dr >15:1): colorless liquid, TLC R_f = 0.45 (20% ethyl acetate in hexane); IR ν_{max} 3518, 1704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.18 (1H, dd, J = 3, 5.5 Hz, HC-3), 3.97−3.86 (4H, m, H_2C-4′, H_2C-5′), 3.41 (1H, ddd, J = 5, 6.5, 7 Hz, HC-7), 2.98 (1H, dq, J = 5.5, 7 Hz, HC-4), 2.91 (1H, dq, J = 7, 7 Hz, HC-6), 2.45 (1H, d, J = 6.5 Hz, HO), 1.87 (1H, dq, J = 3, 7 Hz, HC-2), 1.72 (1H, dqq, J = 5, 6.5, 6.5 Hz, HC-8), 1.72−1.56 (2H, m, H_2C-1″), 1.09 (3H, d, J = 7 Hz, H_3CC-6), 1.08 (3H, d, J = 7 Hz, H_3CC-4), 0.97 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.96 (3H, d, J = 6.5 Hz, H_3C-9), 0.91 (3H, d, J = 6.5 Hz, H_3C-9′), 0.88 (3H, d, J = 7 Hz, H_3C-1), 0.85 (3H, t, J = 7.5 Hz, H_3C-2″), 0.65 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.7 (s, C-5), 113.8 (s, C-2′), 78.9 (d, C-7), 71.9 (d, C-3), 65.2 (t, C-4′), 65.0 (t, C-5′), 52.9 (d, C-4), 48.4 (d, C-6), 42.4 (d, C-2), 30.6 (d, C-8), 27.3 (t, C-1″), 20.3 (q, C-9), 16.1 (q, C-9′), 14.3 (q, CH_3C-6), 13.3 (q, CH_3C-4), 10.3 (q, C-1), 7.6 (q, C-2″), 7.3 (q × 3, CH_3CSi), 5.6 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si$ + Na^+ 453.3006, found 453.2986 (ESI).

(2*R*,3*S*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (22as; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **18b** (33 mg, 0.11 mmol) with *i*-PrCHO gave a crude product containing a 20:14:2.5:1:2 mixture of **22as** (Pg = MOM), **22ss** (Pg = MOM), **22aa** (Pg = MOM), **22sa** (Pg = MOM), and **19b**, respectively. Fractionation of the crude product by FCC (20−30% ethyl acetate in hexane) gave a 2.2:1 mixture of **19b** and **22sa** (Pg = MOM), respectively (4 mg), a 1.2:1 mixture of **22ss** (Pg = MOM) and **22aa** (Pg = MOM), respectively (6 mg, 15%), **22ss** (Pg = MOM) (10 mg, 24%), and the title compound (18 mg, 44%): colorless liquid, TLC R_f = 0.4 (35% ethyl acetate in hexane); IR ν_{max} 3511, 1703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.69 (1H, d, J = 6.5 Hz, HCO_2), 4.58 (1H, d, J = 6.5 Hz, HCO_2), 4.04 (1H, dd, J = 3, 5 Hz, HC-3), 3.95 (4H, br s, H_2C-4′, H_2C-5′), 3.45 (1H, ddd, J = 2.5, 3, 8.5 Hz, HC-7), 3.35 (3H, s, H_3CO), 3.02−3.07 (2H, m, HC-4, HC-6), 2.57 (1H, d, J = 3 Hz, HO), 1.92 (1H, dq, J = 3, 7 Hz, HC-2), 1.73−1.62 (3H, m, H_2C-1″, HC-8), 1.13 (3H, d, J = 7 Hz, H_3CC-4), 1.07 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.94 (3H, d, J = 7 Hz, H_3C-1), 0.88 (3H, d, J = 6.5 Hz, H_3C-9′), 0.86 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 218.0 (s, C-5), 113.5 (s, C-2′), 97.6 (t, OCH_2O), 77.0 (d, C-3), 76.8 (d, C-7), 65.25 (t, C-4′), 65.23 (t, C-5′), 56.5 (q, CH_3O), 50.4 (d, C-4), 46.9 (d, C-6), 42.2 (d, C-2), 31.1 (d, C-8), 26.9 (t, C-1″), 19.6 (q, C-9), 19.2 (q, C-9′), 12.5 (q, CH_3C-4), 10.6 (q, C-1), 8.7 (q, CH_3C-6), 7.7 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2410 (ESI).

(2*R*,3*S*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (22as; Pg = Et$_3$Si). According to the general procedure, reaction of the lithium (*Z*)-enolate of **18c** (32 mg, 0.089 mmol) with *i*-PrCHO gave a crude product containing a 24:12:3:1 mixture of **22as** (Pg = Et_3Si), **22ss** (Pg = Et_3Si), **22aa** (Pg = Et_3Si), and **22sa** (Pg = Et_3Si), respectively. Fractionation of the crude product by FCC (10−20% ethyl acetate in hexane) gave recovered **18c** (2 mg, 7%), a 15:5:1 mixture of **22ss** (Pg = Et_3Si), **22aa** (Pg = Et_3Si), and **22sa** (Pg = Et_3Si), respectively (13 mg, 34%), a 3:1:1 mixture of **22as** (Pg = Et_3Si), **22sa** (Pg = Et_3Si), and **22aa** (Pg = Et_3Si), respectively (3 mg, 8%), and the title compound (16 mg, 42%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3514, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.19 (1H, dd, J = 3.5, 5 Hz, HC-3), 3.86−3.95 (4H, m, H_2C-4′, H_2C-5′), 3.43 (1H, br d, J = 9 Hz, HC-7), 3.00 (1H, dq, J = 5, 7 Hz, HC-4), 2.96 (1H, dq, J = 2, 7 Hz, HC-6), 2.74 (1H, br s, HO), 1.85 (1H, dq, J = 3.5, 7 Hz, HC-2), 1.73−1.58 (3H, m, H_2C-1″, HC-8), 1.09 (3H, d, J = 7 Hz, H_3CC-4), 1.06 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.96 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.88 (3H, d, J = 7 Hz, H_3C-1), 0.87 (3H, d, J = 6.5 Hz, H_3C-9′), 0.84 (3H, t, J = 7.5 Hz, H_3C-2″), 0.63 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.2 (s, C-5), 113.7 (s, C-2′), 76.5 (d, C-7), 71.9 (d, C-3), 65.2 (t, C-4′), 65.1 (t, C-5′), 51.6 (d, C-4), 46.8 (d, C-6), 42.6 (d, C-2), 31.0 (d, C-8), 27.2 (t, C-1″), 19.7 (q, C-9), 19.1 (q, C-9′), 13.2 (q, CH_3C-4), 10.7 (q, C-1), 8.8 (q, CH_3C-6), 7.6 (q, C-2″), 7.3 (q × 3, CH_3CSi), 5.6 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si$ + Na^+ 453.3006, found 453.3000 (ESI) .

(2*R*,3*S*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (22sa; Pg = MOM). According to the general procedure, reaction of **18b** (55 mg, 0.19 mmol) with (c-Hex)$_2$BCl (2 equiv) and Et_3N (2.3 equiv) at 0 °C for 2 h followed by addition of *i*-PrCHO (5 equiv) and workup after 2 h gave a crude product containing an inseparable 14:1 mixture of single aldol adduct and **18b**, respectively. The above mixture was taken up in DMF (0.5 mL), and Et_3Si-Cl (0.044 mL, 40 mg, 0.26 mmol) and imidazole (22 mg, 0.32 mmol) were added. After 12 h, the reaction mixture was diluted with ethyl acetate and sequentially washed with saturated aq NH_4Cl and brine. The organic layer was dried over Na_2SO_4, concentrated, and fractionated by FCC (10−20% ethyl acetate in hexane) to give **18b** (5 mg, 9%) and Et_3Si-protected derivative of **22sa** (Pg = MOM) (60 mg, 66% from **18b**). The latter was taken up in CH_3CN (4.0 mL), and pyridine (0.41 mL), H_2O (0.018 mL), and HF·pyridine (0.28 mL) were added with stirring. After 4 h, the reaction mixture was diluted with ethyl acetate and sequentially washed with saturated aq $NaHCO_3$, saturated aq $CuSO_4$, and brine. The organic layer was dried over Na_2SO_4, concentrated, and fractionated by FCC (20% ethyl acetate in hexane) to afford title compound (44 mg, 97%; 64% from **18b**): colorless oil, TLC R_f = 0.38 (30% ethyl acetate in hexane); IR ν_{max} 3474, 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.67 (1H, d, J = 7 Hz, HCO_2), 4.51 (1H, d, J = 7 Hz, HCO_2), 4.07 (1H, dd, J = 3.5, 4.5 Hz, HC-3), 4.04−3.93 (4H, m, H_2C-4′, H_2C-5′), 3.69 (1H, ddd, J = 3, 4.5, 8.5 Hz, HC-7), 3.33 (3H, s, H_3CO), 3.28 (1H, d, J = 4.5 Hz, HO), 2.97 (1H, dq, J = 3.5, 7 Hz, HC-4), 2.90 (1H, dq, J = 8.5, 7 Hz, HC-6), 2.06 (1H, dq, J = 4.5, 7.5 Hz, HC-2), 1.77 (1H, dqq, J = 3, 7, 7 Hz, HC-8), 1.72−1.61 (2H, m, H_2C-1″), 1.10 (3H, d, J = 7 Hz, H_3CC-4), 1.01 (3H, d, J = 7 Hz, H_3C-9), 0.98 (3H, d, J = 7 Hz, H_3CC-6), 0.96 (3H, d, J = 7.5 Hz, H_3C-1), 0.88 (3H, t, J = 7.5 Hz, H_3C-2″), 0.87 (3H, d, J = 7 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 216.6 (s, C-5), 113.8 (s, C-2′), 97.6 (t, OCH_2O), 76.4 (d, C-3), 76.2 (d, C-7), 65.3 (t, C-4′), 65.0 (t, C-5′), 56.3 (q, CH_3O), 51.8 (d, C-4), 50.1 (d, C-6), 42.9 (d, C-2), 29.3 (d, C-8), 27.0 (t, C-1″), 20.5 (q, C-9), 14.65 (q, CH_3C-6 or C-9′), 14.63 (q, CH_3C-6 or C-9′), 11.6 (q, C-1), 10.5 (q, CH_3C-4), 8.0 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2426 (ESI).

(2*R*,3*S*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (22sa; Pg = Et$_3$Si). According to the general procedure, reaction of **18c** (32 mg, 0.089 mmol) with (c-Hex)$_2$BCl (2 equiv) and Et_3N (2.2 equiv) at 0 °C for 30 min followed by addition of *i*-PrCHO (5 equiv) at −78 °C and workup after 2 h gave a crude product containing a 3.5:1 mixture of **22sa** (Pg = Et_3Si) and **22aa** (Pg = Et_3Si), respectively. Fractionation of the crude product by FCC (20−30% Et_2O in hexane) gave a 2:1 mixture of **22aa** (Pg = Et_3Si) and **22sa** (Pg = Et_3Si), respectively (12 mg, 31%), and the title compound (23 mg, 60%): colorless oil, TLC R_f = 0.42 (20% ethyl acetate in hexane); IR ν_{max} 3508, 1706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.17 (1H, dd, J = 5, 5.5 Hz, HC-3), 3.95−3.88 (4H, m, H_2C-4′, H_2C-5′), 3.46 (1H, ddd, J = 4.5, 6.5, 7 Hz, HC-7), 2.99 (1H, dq, J = 5, 7 Hz, HC-4), 2.90 (1H, dq, J = 7, 7 Hz, HC-6), 2.61 (1H, d, J = 6.5 Hz, HO), 1.94 (1H, dq, J = 5.5, 7 Hz, HC-2), 1.73 (1H, dqq, J = 4.5, 6.5 Hz, HC-8), 1.68 (1H, dq, J = 14, 7.5 Hz, HC-1″), 1.58 (1H, dq, J = 14, 7.5 Hz, HC-1″), 1.10 (3H, d, J = 7 Hz, H_3CC-6), 1.09 (3H, d, J = 7 Hz, H_3CC-4), 0.97 (3H, d, J = 6.5 Hz, H_3C-9), 0.97 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.91 (3H, d, J = 6.5 Hz, H_3C-9′), 0.90 (3H,

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d, J = 7 Hz, H_3C-1), 0.85 (3H, t, J = 7,5 Hz, H_3C-2″), 0.64 (6H, ap q, J = 8 Hz, $CH_2Si \times 3$); ^{13}C NMR ($CDCl_3$) δ 219.3 (s, C-5), 113.8 (s, C-2′), 78.4 (d, C-7), 72.0 (d, C-3), 65.14 (t, C-4′), 65.11 (t, C-5′), 52.5 (d, C-4), 48.9 (d, C-6), 42.2 (d, C-2), 30.3 (d, C-8), 27.2 (t, C-1″), 20.3 (q, C-9), 16.0 (q, C-9′), 14.6 (q, CH_3C-6), 13.0 (q, CH_3C-4), 10.9 (q, C-1), 7.6 (q, C-2″), 7.3 (q × 3, CH_3CSi), 5.6 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.2998 (ESI).

(2*R*,3*S*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (22ss; Pg = MOM). According to the general procedure, reaction of **18b** (30 mg, 0.10 mmol) with 9-BBN-OTf (1.6 equiv) and Et_3N (1.9 equiv) at −78 °C for 2 h followed by addition of *i*-PrCHO (5 equiv) and workup after 2 h gave a crude product containing a single aldol adduct by ^1H NMR. Fractionation of the crude product by FCC (50% ether in hexane) gave **18b** (2 mg, 7%) and the title compound (29 mg, 77%): colorless viscous oil, TLC R_f = 0.36 (60% ethyl acetate in hexane); IR ν_{max} 3500, 1697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.70 (1H, d, J = 6.5 Hz, HCO_2), 4.56 (1H, d, J = 6.5 Hz, HCO_2), 3.90−3.99 (5H, m, HC-3, H_2C-4′, H_2C-5′), 3.55 (1H, ddd, J = 1.5, 2, 9.5 Hz, HC-7), 3.39 (1H, d, J = 2 Hz, HO), 3.34 (3H, s, H_3CO), 3.07 (1H, dq, J = 4.5, 7 Hz, HC-4), 3.02 (1H, dq, J = 1.5, 7.5 Hz, HC-6), 2.03 (1H, dq, J = 3, 7 Hz, HC-2), 1.59−1.71 (3H, m, H_2C-1″, HC-8), 1.11 (3H, d, J = 7.5 Hz, H_3CC-6), 1.08 (3H, d, J = 7 Hz, H_3CC-4), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.90 (3H, d, J = 7 Hz, H_3C-1), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″), 0.83 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 219.7 (s, C-5), 113.6 (s, C-2′), 97.4 (t, OCH_2O), 77.4 (d, C-3), 76.1 (d, C-7), 65.2 (d, C-4′), 65.1 (d, C-5′), 56.5 (q, CH_3O), 49.8 (d, C-4), 46.5 (d, C-6), 41.3 (d, C-2), 30.5 (d, C-8), 26.8 (t, C-1″), 19.9 (q, C-9), 18.9 (q, C-9′), 12.0 (q, CH_3C-4), 10.8 (q, C-1), 9.3 (q, CH_3C-6), 7.8 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2395 (ESI).

(2*R*,3*S*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (22ss; Pg = Et_3Si). According to the general procedure, reaction of **18c** (33 mg, 0.092 mmol) with 9-BBN-OTf (1.6 equiv) and Et_3N (1.9 equiv) at −78 °C for 4 h followed by addition of *i*-PrCHO (5 equiv) and workup after 2 h gave a crude product containing a single aldol adduct by ^1H NMR. Fractionation of the crude product by FCC (15% ethyl acetate in hexane) gave recovered **18c** (6 mg, 18%) and the title compound (26 mg, 67%): colorless oil, TLC R_f = 0.41 (20% ethyl acetate in hexane); IR ν_{max} 3522, 1691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.09 (1H, dd, J = 3, 4 Hz, HC-3), 3.95−3.88 (4H, m, H_2C-4′, H_2C-5′), 3.51 (1H, ddd, J = 1.5, 2, 9.5 Hz, HC-7), 3.43 (1H, d, J = 2 Hz, HO), 3.00 (1H, dq, J = 4, 7 Hz, HC-4), 2.99 (1H, dq, J = 1.5, 7.5 Hz, HC-6), 1.91 (1H, dq, J = 3, 7 Hz, HC-2), 1.70−1.53 (3H, m, HC-8, H_2C-1″), 1.10 (3H, d, J = 7.5 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 1.01 (3H, d, J = 7 Hz, H_3CC-4), 0.97 (9H, t, J = 8 Hz, $H_3CCSi \times 3$), 0.85 (3H, t, J = 7.5 Hz, H_3C-2″), 0.820 (3H, d, J = 6.5 Hz, H_3C-9′), 0.815 (3H, d, J = 7 Hz, H_3C-1), 0.63 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 220.4 (s, C-5), 113.7 (s, C-2′), 76.3 (d, C-7), 73.0 (d, C-3), 65.1 (t, C-4′), 65.0 (t, C-5′), 51.3 (d, C-4), 47.3 (d, C-6), 41.0 (d, C-2), 30.4 (d, C-8), 26.8 (t, C-1″), 19.9 (q, C-9), 18.9 (q, C-9′), 13.1 (q, CH_3C-4), 10.5 (q, C-1), 9.3 (q, CH_3C-6), 7.5 (q, C-2″), 7.3 (q × 3, CH_3CSi), 5.5 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.3013 (ESI).

(2*S*,3*S*,4*S*,6*S*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (23aa; Pg = MOM). According to the general procedure, reaction of the lithium (*E*)-enolate (dr 7:1) of **19b** (250 mg, 0.868 mmol) with *i*-PrCHO gave a crude product containing a 8:4:1:1 mixture of **23aa** (Pg = MOM), **23sa** (Pg = MOM), **23as** (Pg = MOM), and **23ss** (Pg = MOM), respectively. Fractionation of the crude product by FCC (20−30% ethyl acetate in hexane) gave **23sa** (Pg = MOM) (79 mg, 25%) and an inseparable 10:1 mixture of **23aa** (Pg = MOM) and **23ss** (Pg = MOM), respectively (128 mg, 41%): colorless viscous oil, TLC R_f = 0.3 (40% ethyl acetate in hexane); IR ν_{max} 3502, 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ (major isomer) 4.69 (1H, d, J = 6.5 Hz, HCO_2), 4.62 (1H, d, J = 6.5 Hz, HCO_2), 4.23 (1H, dd, J = 2.5, 3 Hz, HC-3), 3.96−3.89 (4H, m, H_2C-4′, H_2C-5′), 3.45 (1H, br q, J = 5, 6.5, 7 Hz, HC-7), 3.34 (3H, s, H_3CO), 3.26 (1H, dq, J = 2.5, 7.5 Hz, HC-4), 2.98 (1H, dq, J = 6.5, 7 Hz, HC-6), 2.53 (1H, d, J = 7 Hz, HO), 2.26 (1H, dq, J = 3, 7 Hz, HC-2), 1.73 (1H, dqq, J = 5, 6.5, 7 Hz, HC-8), 1.67−1.57 (2H, m, H_2C-1″), 1.18 (3H, d, J = 7.5 Hz, H_3CC-4), 1.11 (3H, d, J = 7 Hz, H_3CC-6), 1.02 (3H, d, J = 7 Hz, H_3C-1), 0.96 (3H, d, J = 7 Hz, H_3C-9), 0.909 (3H, d, J = 6.5 Hz, H_3C-9′), 0.906 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ (major isomer) 219.1 (s, C-5), 113.1 (s, C-2′), 96.9 (t, OCH_2O), 78.8 (d, C-7), 74.8 (d, C-3), 65.7 (t, C-4′), 64.8 (t, C-5′), 56.0 (q, CH_3O), 47.7 (d, C-4), 46.4 (d, C-6), 43.2 (d, C-2), 30.5 (d, C-8), 28.9 (t, C-1″), 20.3 (q, C-9), 16.0 (q, C-9′), 14.9 (q, CH_3C-6), 12.4 (q, CH_3C-4), 10.0 (q, C-1), 8.2 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2411 (ESI).

(2*S*,3*S*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (23as; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **19b** (48 mg, 0.17 mmol) with *i*-PrCHO gave a crude product containing a 1.5:1 mixture of **23as** (Pg = MOM) and **23ss** (Pg = MOM), respectively. Fractionation of the crude product by FCC (60% ether in hexane) gave **23ss** (Pg = MOM) (20 mg, 33%) and the title compound (32 mg, 53%): colorless viscous oil, TLC R_f = 0.3 (40% ethyl acetate in hexane); IR ν_{max} 3505, 1701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.68 (1H, d, J = 7 Hz, HCO_2), 4.63 (1H, d, J = 7 Hz, HCO_2), 4.19 (1H, dd, J = 3, 3.5 Hz, HC-3), 3.97−3.85 (4H, m, H_2C-4′ and 5′), 3.44 (1H, ddd, J = 2, 2.5, 9 Hz, HC-7), 3.35 (3H, s, H_3CO), 3.29 (1H, dq, J = 3.5, 7.5 Hz, HC-4), 3.05 (1H, d, J = 2.5 Hz, HO), 3.01 (1H, dq, J = 2, 7 Hz, HC-6), 2.25 (1H, dq, J = 3, 7 Hz, HC-2), 1.71−1.54 (3H, m, HC-8, H_2C-1″), 1.18 (3H, d, J = 7.5 Hz, H_3CC-4), 1.09 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 1.02 (3H, d, J = 7 Hz, H_3C-1), 0.90 (3H, t, J = 7.5 Hz, H_3C-2″), 0.86 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 219.4 (s, C-5), 113.1 (s, C-2′), 97.1 (t, OCH_2O), 76.7 (d, C-7), 75.6 (d, C-3), 65.8 (t, C-4′), 64.8 (t, C-5′), 56.0 (q, CH_3O), 46.9 (d, C-4), 45.0 (d, C-6), 43.1 (d, C-2), 30.8 (d, C-8), 28.9 (t, C-1″), 19.7 (q, C-9), 19.2 (q, C-9′), 13.2 (q, CH_3C-4), 10.0 (q, C-1), 9.3 (q, CH_3C-6), 8.1 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$+NH_4 378.2856, found 378.2846 (CI, NH_3).

(2*S*,3*S*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (23as; Pg = Et_3Si). According to the general procedure, reaction of the lithium (*Z*)-enolate of **19c** (53 mg, 0.15 mmol) with *i*-PrCHO gave a crude product containing a 8:5:1 mixture of **23as** (Pg = Et_3Si), **23ss** (Pg = Et_3Si), and **23sa** (Pg = Et_3Si) (presumably from the (*E*)-enolate), respectively. Fractionation of the crude product by PTLC (70% ether in hexane) gave **23sa** (Pg = Et_3Si) (3 mg, 5%), **23ss** (Pg = Et_3Si) (18 mg, 28%), and the title compound (31 mg, 49%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3510, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.44 (1H, dd, J = 3, 4 Hz, HC-3), 3.95−3.82 (4H, m, H_2C-4′, H_2C-5′), 3.44 (1H, ddd, J = 2, 2, 9 Hz, HC-7), 3.23 (1H, dq, J = 4, 7.5 Hz, HC-4), 3.12 (1H, d, J = 2 Hz, HO), 2.97 (1H, dq, J = 2, 7 Hz, HC-6), 2.06 (1H, dq, J = 3, 7 Hz, HC-2), 1.67 (1H, dqq, J = 9, 6.5, 6.5 Hz, HC-8), 1.64−1.53 (2H, m, H_2C-1″), 1.14 (3H, d, J = 7 Hz, H_3CC-6), 1.07 (3H, d, J = 7.5 Hz, H_3CC-4), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.99 (3H, d, J = 7 Hz, H_3C-1), 0.94 (9H, t, J = 8 Hz, $H_3CCSi \times 3$), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″), 0.85 (3H, d, J = 6.5 Hz, H_3C-9′), 0.61 (6H, ap q, J = 8 Hz, $H_2CSi \times 3$); ^{13}C NMR ($CDCl_3$) δ 219.6 (s, CO), 113.2 (s, C-2′), 76.7 (d, C-7), 69.2 (d, C-3), 65.8 (t, C-4′), 64.8 (t, C-5′), 47.2 (d, C-4), 45.9 (d, C-2), 44.9 (d, C-6), 30.8 (d, C-8), 29.0 (t, C-1″), 19.8 (q, C-9), 19.1 (q, C-9′), 13.9 (q, CH_3C-4), 9.5 (q, C-1), 9.3 (q, CH_3C-6), 8.2 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.3006 (ESI).

(2*S*,3*S*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (23sa; Pg = MOM). According to the general procedure, reaction of **19b** (40 mg, 0.14 mmol) with $(c\text{-Hex})_2BCl$ (2.5 equiv) and Et_3N (2.8 equiv) at −78 °C for 1 h followed by addition of *i*-PrCHO (3.5 equiv) and workup after 2 h gave a crude product containing a single aldol adduct. Fractionation of the crude PTLC (30% ethyl acetate in hexane) afforded the title compound (43 mg, 87%): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); IR ν_{max} 3486, 1710 cm^{-1}; ^1H

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NMR ($CDCl_3$) δ 4.64 (1H, d, J = 7 Hz, HCO_2), 4.58 (1H, d, J = 7 Hz, HCO_2), 4.20 (1H, dd, J = 2.5, 4 Hz, HC-3), 3.99−3.89 (4H, m, H_2C-4′, H_2C-5′), 3.62 (1H, ddd, J = 3.5, 5, 8.5 Hz, HC-7), 3.33 (3H, s, H_3CO), 3.14 (1H, dq, J = 2.5, 7 Hz, HC-4), 3.07 (1H, d, J = 5 Hz, HO), 2.93 (1H, dq, J = 8.5, 7 Hz, HC-6), 2.25 (1H, dq, J = 4, 7 Hz, HC-2), 1.74 (1H, dqq, J = 3.5, 7, 7 Hz, HC-8), 1.68 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.16 (3H, d, J = 7 Hz, H_3CC-4), 1.02 (3H, d, J = 7 Hz, H_3C-1), 1.009 (3H, d, J = 7 Hz, H_3CC-6), 1.005 (3H, d, J = 7 Hz, H_3C-9′), 0.90 (3H, t, J = 7.5 Hz, H_3C-2″), 0.88 (3H, d, J = 7 Hz, H_3C-9); ^{13}C NMR ($CDCl_3$) δ 217.4 (s, C-5), 113.2 (s, C-2′), 97.3 (t, OCH_2O), 77.0 (d, C-7), 75.9 (d, C-3), 65.6 (t, C-4′), 64.8 (t, C-5′), 56.1 (q, CH_3O), 48.5 (d, C-6), 48.1 (d, C-4), 43.4 (d, C-2), 29.6 (d, C-8), 28.5 (t, C-1″), 20.5 (q, C-9), 14.9 (q, C-9′), 14.8 (q, CH_3C-6), 11.6 (q, CH_3C-4), 10.6 (q, C-1), 8.1 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2411 (ESI).

(2*S*,3*S*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (23sa; Pg = Et$_3$Si). According to the general procedure, reaction of **19c** (23 mg, 0.064 mmol) with $(c\text{-Hex})_2BCl$ (1.3 equiv) and Et_3N (1.6 equiv) at −50 °C for 2.5 h followed by addition of *i*-PrCHO (5 equiv) at −78 °C and workup after 2 h gave a crude product containing a 17:1 mixture of aldol adducts. Fractionation of the crude product by PTLC (70% Et_2O in hexane) gave recovered **19c** (2 mg, 8%) and the title compound (23 mg, 83%): colorless oil, TLC R_f = 0.3 (40% Et_2O in hexane); IR ν_{max} 3500, 1706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.49 (1H, dd, J = 3, 3.5 Hz, HC-3), 3.96−3.85 (4H, m, H_2C-4′, H_2C-5′), 3.45 (1H, ddd, J = 4.5, 5.5, 7 Hz, HC-7), 3.15 (1H, dq, J = 3.5, 7.5 Hz, HC-4), 2.93 (1H, dq, J = 7, 7 Hz, HC-6), 2.81 (1H, d, J = 5.5 Hz, HO), 2.08 (1H, dq, J = 3, 7 Hz, HC-2), 1.71 (1H, dqq, J = 4.5, 6.5, 7 Hz, HC-8), 1.62 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.16 (3H, d, J = 7.5 Hz, H_3CC-4), 1.06 (3H, d, J = 7 Hz, H_3CC-6), 0.99 (3H, d, J = 7 Hz, H_3C-1), 0.97 (3H, d, J = 7 Hz, H_3C-9), 0.94 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.90 (3H, d, J = 6.5 Hz, H_3C-9′), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″), 0.61 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.0 (s, C-5), 113.3 (s, C-2′), 78.5 (d, C-7), 68.8 (d, C-3), 65.7 (t, C-4″), 64.8 (t, C-5′), 49.2 (d, C-4), 47.5 (d, C-6), 45.9 (d, C-2), 30.3 (d, C-8), 28.8 (t, C-1″), 20.4 (q, C-9), 15.7 (q, C-9′), 14.8 (q, CH_3C-6), 13.2 (q, CH_3C-4), 9.6 (q, C-1), 8.2 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si$ + Na^+ 453.3006, found 453.3018 (ESI).

(2*S*,3*S*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (23ss; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **19b** (72 mg, 0.25 mmol) with $TiCl(Oi\text{-}Pr)_3$ at −50 °C for 75 min followed by addition of *i*-PrCHO at −78 °C and workup after 3 h gave a crude product containing a 17:1 mixture of **23ss** (Pg = MOM) and **23as** (Pg = MOM), respectively. Fractionation of the crude product by FCC (60% Et_2O in hexane) gave **23as** (Pg = MOM) (4 mg, 4%) and the title compound (75 mg, 83%): colorless viscous oil, TLC R_f = 0.3 (40% ethyl acetate in hexane); IR ν_{max} 3512, 1698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.64 (2H, br s, H_2CO_2), 4.23 (1H, dd, J = 3, 4 Hz, HC-3), 3.96−3.88 (4H, m, H_2C-4′, H_2C-5′), 3.52 (1H, br d, J = 9 Hz, HC-7), 3.34 (3H, s, H_3CO), 3.25 (1H, dq, J = 4, 7 Hz, HC-4), 3.19 (1H, br s, HO), 2.98 (1H, dq, J = 1.5, 7 Hz, HC-6), 2.26 (1H, dq, J = 3, 7 Hz, HC-2), 1.71−1.60 (3H, m, H_2C-1″, HC-8), 1.15 (3H, d, J = 7 Hz, H_3CC-4), 1.09 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 1.01 (3H, d, J = 7 Hz, H_3C-1), 0.89 (3H, t, J = 7.5 Hz, H_3C-2″), 0.85 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 218.9 (s, C-5), 113.2 (s, C-2′), 97.1 (t, OCH_2O), 76.3 (d, C-3 or C-7), 76.2 (d, C-3 or C-7), 65.7 (t, C-4′), 64.7 (t, C-5′), 56.1 (q, CH_3O), 46.6 (d, C-4), 45.7 (d, C-6), 42.9 (d, C-2), 30.6 (d, C-8), 28.7 (t, C-1″), 20.0 (q, C-9), 19.1 (q, C-9′), 13.3 (q, CH_3C-4), 9.9 (q, C-1), 9.3 (q, CH_3C-6), 8.1 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2416 (ESI).

(2*S*,3*S*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (23ss; Pg = Et$_3$Si). According to the general procedure, reaction of the lithium (*Z*)-enolate of **19c** (36 mg, 0.10 mmol) with $TiCl(Oi\text{-}Pr)_3$ at −50 °C for 90 min followed by addition of *i*-PrCHO at −78 °C and workup after 4 h gave a crude product containing a 13:1 mixture of **23ss** (Pg = Et_3Si) and **23as** (Pg = Et_3Si), respectively. Fractionation of the crude product by FCC (70% ether in hexane) gave **23as** (Pg = Et_3Si) (2 mg, 5%) and the title compound (35 mg, 81%): colorless viscous oil, TLC R_f = 0.3 (10% ethyl acetate in hexane); IR ν_{max} 3510, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.40 (1H, d, J = 3, 4.5 Hz, HC-3), 3.95−3.84 (4H, m, H_2C-4′, H_2C-5′), 3.49 (1H, ddd, J = 2, 2.5, 9 Hz, HC-7), 3.25 (1H, d, J = 2.5 Hz, HO), 3.20 (1H, dq, J = 4.5, 7 Hz, HC-4), 2.94 (1H, dq, J = 2, 7 Hz, HC-6), 2.08 (1H, dq, J = 3, 7 Hz, HC-2), 1.67 (1H, dqq, J = 9, 7, 7 Hz, HC-8), 1.64−1.55 (2H, m, H_2C-1″), 1.11 (3H, d, J = 7 Hz, H_3CC-4), 1.08 (3H, d, J = 7 Hz, H_3CC-6), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.99 (3H, d, J = 7 Hz, H_3C-1), 0.95 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.87 (3H, t, J = 7.5 Hz, H_3C-2″), 0.85 (3H, d, J = 6.5 Hz, H_3C-9′), 0.60 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.1 (s, CO), 113.2 (s, C-2′), 76.3 (d, C-7), 69.8 (d, C-3), 65.7 (t, C-4′), 64.7 (t, C-5′), 47.1 (d, C-4), 45.90 (d, C-2 or C-6), 45.86 (d, C-2 or C-6), 30.6 (d, C-8), 28.8 (t, C-1″), 20.0 (q, C-9), 19.1 (q, C-9′), 14.1 (q, CH_3C-4), 9.4 (q, C-1), 9.2 (q, CH_3C-6), 8.2 (q, C-2″), 7.1 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si$ + Na^+ 453.3006, found 453.3008 (ESI).

(2*R*,3*R*,4*S*,6*S*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (24aa; Pg = MOM). See the preparation of **24sa** (Pg = MOM): colorless viscous oil, TLC R_f = 0.3 (30% ethyl acetate in hexane); IR ν_{max} 3514, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.54 (1H, d, J = 6.5 Hz, HCO_2), 4.51 (1H, d, J = 6.5 Hz, HCO_2), 3.99−3.92 (4H, m, H_2C-4′, H_2C-5′), 3.80 (1H, dd, J = 2, 9.5 Hz, HC-3), 3.49 (1H, br d, J = 6 Hz, HC-7), 3.34 (1H, dq, J = 9.5, 7 Hz, HC-4), 3.32 (3H, s, H_3CO), 2.81 (1H, dq, J = 6, 7 Hz, HC-6), 2.68 (1H, br s, HO), 2.15 (1H, dq, J = 2, 7 Hz, HC-2), 1.84−1.70 (3H, m, HC-8, H_2C-1″), 1.11 (3H, d, J = 7 Hz, H_3CC-6), 1.10 (3H, d, J = 7 Hz, H_3C-1), 1.05 (3H, d, J = 7 Hz, H_3CC-4), 0.98 (3H, d, J = 7 Hz, H_3C-9), 0.91 (3H, d, J = 7 Hz, H_3C-9′), 0.90 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 219.0 (s, C-5), 113.8 (s, C-2′), 98.7 (t, OCH_2O), 82.9 (d, C-3), 77.9 (d, C-7), 65.5 (t, C-4′), 65.3 (t, C-5′), 56.6 (q, CH_3O), 49.9 (d, C-6), 48.9 (d, C-4), 41.3 (d, C-2), 30.2 (t, C-8), 28.9 (d, C-1″), 20.5 (q, C-9), 15.8 (q, C-9′), 14.6 (q, CH_3C-4), 13.5 (q, CH_3C-6), 12.9 (q, C-1), 7.7 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2399 (ESI).

(2*R*,3*R*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (24as; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **20b** (51 mg, 0.18 mmol) with *i*-PrCHO gave a crude product containing a 8:1 mixture of **24as** (Pg = MOM) and **24ss** (Pg = MOM), respectively. Fractionation of the crude product by FCC (40% ether in hexane) gave **24ss** (Pg = MOM) (4 mg, 6%) and the title compound (49 mg, 77%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); ^1H NMR ($CDCl_3$) δ 4.52 (1H, d, J = 6.5 Hz, HCO_2), 4.50 (1H, d, J = 6.5 Hz, HCO_2), 3.98−3.92 (4H, m, H_2C-4′, H_2C-5′), 3.79 (1H, dd, J = 2, 9 Hz, HC-3), 3.48 (1H, ddd, J = 2, 3, 9 Hz, HC-7), 3.36 (1H, dq, J = 9, 7 Hz, HC-4), 3.30 (3H, s, H_3CO), 2.98 (1H, br d, J = 3 Hz, HO), 2.84 (1H, dq, J = 2, 7 Hz, HC-6), 2.15 (1H, dq, J = 2, 7.5 Hz, HC-2), 1.81−1.62 (3H, m, HC-8, H_2C-1″), 1.11 (3H, d, J = 7 Hz, H_3CC-6), 1.07 (3H, d, J = 7.5 Hz, H_3C-1), 1.05 (3H, d, J = 7 Hz, H_3CC-4), 1.03 (3H, d, J = 6.5 Hz, H_3C-9), 0.89 (3H, t, J = 7.5 Hz, H_3C-2″), 0.86 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 219.6 (s, C-5), 113.7 (s, C-2′), 98.4 (t, OCH_2O), 83.2 (d, C-3), 76.7 (d, C-7), 65.6 (t, C-4′), 65.3 (t, C-5′), 56.5 (q, CH_3O), 48.3 (d, C-6), 47.8 (d, C-4), 41.5 (d, C-2), 30.9 (d, C-8), 29.0 (t, C-1″), 19.7 (q, C-9), 19.1 (q, C-9′), 15.1 (q, CH_3C-4), 12.5 (q, C-1), 8.1 (q, CH_3C-6), 7.8 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6$ + Na^+ 383.2404, found 383.2414 (ESI).

(2*R*,3*R*,4*S*,6*S*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (24as; Pg = Et$_3$Si). According to the general procedure (but with 1.4 equiv of LiHMDS and enolization at −78 °C for 2 h), reaction of the lithium (*Z*)-enolate of **20c** (33 mg, 0.092 mmol) with *i*-PrCHO gave a crude product containing a 2.7:1 mixture of **24as** (Pg = Et_3Si) and **24ss** (Pg = Et_3Si), respectively. Fractionation of the crude product by PTLC (40% Et_2O in hexane, developed thrice) gave **24ss** (Pg = Et_3Si) (7 mg, 18%) and the title compound (24 mg, 61%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3515, 1704 cm^{-1};

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^{1}H NMR ($CDCl_3$) δ 4.08 (1H, dd, J = 1.5, 8.5 Hz, HC-3), 3.99−3.91 (4H, m, H_2C-4′, H_2C-5′), 3.47 (1H, br d, J = 9 Hz, HC-7), 3.23 (1H, dq, J = 8.5, 7 Hz, HC-4), 3.06 (1H, br s, HO), 2.86 (1H, dq, J = 1.5, 7 Hz, HC-6), 2.05 (1H, dq, J = 1.5, 7 Hz, HC-2), 1.78−1.64 (3H, m, H_2C-1″, HC-8), 1.08 (3H, d, J = 7 Hz, H_3CC-6), 1.05 (3H, d, J = 7 Hz, H_3C-1), 1.04 (6H, ap d, J = 7 Hz, H_3C-9, H_3CC-4), 0.93 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.88 (3H, t, J = 7.5 Hz, H_3C-2″), 0.85 (3H, d, J = 7 Hz, H_3C-9′), 0.59 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.1 (s, C-5), 113.6 (s, C-2′), 76.7 (d, C-7), 75.9 (d, C-3), 65.5 (t, C-4′), 65.2 (t, C-5′), 48.3 (d, C-4), 47.7 (d, C-6), 44.4 (d, C-2), 30.9 (d, C-8), 29.1 (t, C-1″), 19.9 (q, C-9), 19.5 (q, C-9′), 15.4 (q, CH_3C-4), 11.6 (q, C-1), 8.0 (q × 2, C-2″, CH_3C-6), 7.2 (q × 3, CH_3CSi), 5.3 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.2991 (ESI).

(2*R*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (24sa; Pg = MOM). According to the general procedure, reaction of **20b** (50 mg, 0.17 mmol) with (*c*-Hex)$_2$BCl (2 equiv) and Et_3N (2.2 equiv) at −78 °C for 2.5 h followed by addition of *i*-PrCHO (3 equiv) and workup after 3 h gave a crude product containing a 6:1 mixture of **24sa** (Pg = MOM) and **24aa** (Pg = MOM), respectively. Fractionation of the crude product by PTLC (30% ethyl acetate in hexane) afforded **24aa** (Pg = MOM) (4 mg, 6%) and the title compound (44 mg, 70%): colorless viscous oil, TLC R_f = 0.3 (30% ethyl acetate in hexane); IR ν_{max} 3488, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.55 (1H, d, J = 7 Hz, HCO_2), 4.54 (1H, d, J = 7 Hz, HCO_2), 3.98−3.91 (4H, m, H_2C-4′, H_2C-5′), 3.87 (1H, dd, J = 2.5, 9 Hz, HC-3), 3.45 (1H, ddd, J = 4, 5, 8 Hz, HC-7), 3.37 (1H, dq, J = 9, 7 Hz, HC-4), 3.31 (3H, s, H_3CO), 3.11 (1H, d, J = 5 Hz, HO), 2.89 (1H, dq, J = 8, 7 Hz, HC-6), 2.20 (1H, dq, J = 2.5, 7 Hz, HC-2), 1.79 (1H, dqq, J = 4, 7, 7 Hz, HC-8), 1.79−1.64 (2H, m, H_2C-1″), 1.07 (3H, d, J = 7 Hz, H_3C-1), 1.061 (3H, d, J = 7 Hz, H_3CC-6), 1.057 (3H, d, J = 7 Hz, H_3CC-4), 0.98 (3H, d, J = 7 Hz, H_3C-9), 0.91 (3H, d, J = 7 Hz, H_3C-9′), 0.90 (3H, t, J = 7.5 Hz, H_3C-2″); ^{13}C NMR ($CDCl_3$) δ 219.9 (s, C-5), 113.4 (s, C-2′), 98.3 (t, OCH_2O), 83.7 (d, C-3), 78.4 (d, C-7), 65.6 (t, C-4′), 65.1 (t, C-5′), 56.5 (q, CH_3O), 50.9 (d, C-6), 48.7 (d, C-4), 41.7 (d, C-2), 29.8 (d, C-8), 29.0 (t, C-1″), 20.4 (q, C-9), 15.3 (q, C-9′), 14.9 (q, CH_3C-4), 14.0 (q, CH_3C-6), 11.8 (q, C-1), 7.9 (q, C-2″); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2413 (ESI).

(2*R*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (24sa; Pg = Et_3Si). According to the general procedure, reaction of **20c** (43 mg, 0.12 mmol) with (*c*-Hex)$_2$BCl (2 equiv) and Et_3N (2.5 equiv) at 0 °C for 20 min followed by addition of *i*-PrCHO (5 equiv) at −78 °C and workup after 2 h gave a crude product containing a single aldol adduct. Fractionation of the crude product by PTLC (60% Et_2O in hexane) gave the title compound (32 mg, 62%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3438, 1711 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.23 (1H, dd, J = 2, 8.5 Hz, HC-3), 4.01−3.90 (4H, m, H_2C-4′, H_2C-5′), 3.44 (1H, ddd, J = 3, 3.5, 9 Hz, HC-7), 3.39 (1H, br d, J = 3 Hz, HO), 3.29 (1H, dq, J = 8.5, 7 Hz, HC-4), 2.83 (1H, dq, J = 9, 7 Hz, HC-6), 2.11 (1H, dq, J = 2, 7.5 Hz, HC-2), 1.80 (1H, dqq, J = 3.5, 6.5, 7 Hz, HC-8), 1.66 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.06 (3H, d, J = 7.5 Hz, H_3C-1), 1.02 (3H, d, J = 7 Hz, H_3CC-4), 1.00 (3H, d, J = 6.5 Hz, H_3C-9), 0.99 (3H, d, J = 7 Hz, H_3CC-6), 0.94 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.893 (3H, t, J = 7.5 Hz, H_3C-2″), 0.891 (3H, d, J = 7 Hz, H_3C-9′), 0.68−0.56 (6H, m, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 219.6 (s, C-5), 113.2 (s, C-2′), 78.1 (d, C-7), 75.7 (d, C-5), 65.6 (t, C-4′), 64.9 (t, C-5′), 50.6 (d, C-6), 49.6 (d, C-4), 45.4 (d, C-2), 29.4 (d, C-8), 29.1 (t, C-1″), 20.5 (q, C-9), 14.7 (q, CH_3C-4), 14.3 (q, C-9′), 13.6 (q, CH_3C-6), 10.2 (q, C-1), 8.3 (q, C-2″), 7.1 (q × 3, CH_3CSi), 5.1 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.2986 (ESI).

(2*R*,3*R*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(methoxymethoxy)-4,6,8-trimethylnonan-5-one (24ss; Pg = MOM). According to the general procedure, reaction of the lithium (*Z*)-enolate of **20b** (61 mg, 0.21 mmol) with TiCl(O*i*-Pr)$_3$ at −50 °C for 90 min followed by addition of *i*-PrCHO at −78 °C and workup after 4 h gave a crude product containing a 13:1 mixture of **24ss** (Pg = MOM) and **24as** (Pg = MOM), respectively. Fractionation of the crude product by FCC (70% ether in hexane) gave **24as** (Pg = MOM) (4 mg, 5%) and the title compound (58 mg, 76%): colorless viscous oil, TLC R_f = 0.3 (40% ethyl acetate in hexane); IR ν_{max} 3511, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.55 (1H, d, J = 6 Hz, HCO_2), 4.53 (1H, d, J = 6 Hz, HCO_2), 4.00−3.90 (4H, m, H_2C-4′, H_2C-5′), 3.78 (1H, dd, J = 2, 9 Hz, HC-3), 3.63 (1H, br d, J = 9.5 Hz, HC-7), 3.39 (1H, dq, J = 9, 7 Hz, HC-4), 3.32 (4H, br s, H_3CO, HO), 2.85 (1H, br q, J = 7 Hz, HC-6), 2.19 (1H, dq, J = 2, 7 Hz, HC-2), 1.79−1.65 (3H, m, H_2C-1″, HC-8), 1.07 (6H, br d, J = 7 Hz, H_3C-1, H_3CC-6), 1.05 (6H, br d, J = 7 Hz, H_3C-9, H_3CC-4), 0.90 (3H, t, J = 7.5 Hz, H_3C-2″), 0.86 (3H, d, J = 6.5 Hz, H_3C-9′); ^{13}C NMR ($CDCl_3$) δ 219.2 (s, C-5), 113.5 (s, C-2′), 98.2 (t, OCH_2O), 83.4 (d, C-3), 75.7 (d, C-7), 65.6 (t, C-4′), 65.1 (t, C-5′), 56.7 (q, CH_3O), 49.1 (d, C-6), 46.7 (d, C-4), 41.4 (d, C-2), 30.5 (d, C-8), 29.0 (t, C-1″), 20.2 (q, C-9), 19.2 (q, C-9′), 15.4 (q, CH_3C-4), 12.3 (q, C-1), 7.9 (q × 2, C-2″, CH_3C-6); HRMS m/z calcd for $C_{19}H_{36}O_6 + Na^+$ 383.2404, found 383.2405 (ESI).

(2*R*,3*R*,4*S*,6*R*,7*S*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-7-hydroxy-3-(triethylsilyloxy)-4,6,8-trimethylnonan-5-one (24ss; Pg = Et_3Si). Freshly prepared LiHMDS (0.75 M in THF/hexane; 0.29 mL, 0.22 mmol) was added dropwise via syringe to a stirred solution of **20c** (53 mg, 0.15 mmol) and $(Me_3Si)_2NH$ (0.031 mL, 24 mg, 0.15 mmol) in THF (0.20 mL) at −50 °C under Ar. After 2 h, reaction of the resulting lithium (*Z*)-enolate with TiCl$_2$(O*i*-Pr)$_2$ at −78 °C for 2 h followed by addition of *i*-PrCHO and workup after 3 h according to the general procedure gave a crude product containing a 9.2:1 mixture of **24ss** (Pg = Et_3Si) and **24as** (Pg = Et_3Si), respectively. Fractionation of the crude product by PTLC (40% ether in hexane) gave **24as** (Pg = Et_3Si) (3 mg, 5%) and the title compound (35 mg, 55%): colorless viscous oil, TLC R_f = 0.3 (20% ethyl acetate in hexane); IR ν_{max} 3519, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.04 (1H, dd, J = 2.5, 7 Hz, HC-3), 4.01−3.90 (4H, m, H_2C-4′, H_2C-5′), 3.57 (1H, br d, J = 9.5 Hz, HC-7), 3.55 (1H, br s, HO), 3.23 (1H, dq, J = 7, 7 Hz, HC-4), 2.85 (1H, dq, J = 1, 7.5 Hz, HC-6), 2.09 (1H, dq, J = 2.5, 7 Hz, HC-2), 1.68 (2H, ap q, J = 7.5 Hz, H_2C-1″), 1.68−1.60 (1H, m, HC-8), 1.10 (3H, d, J = 7.5 Hz, H_3CC-6), 1.05 (3H, d, J = 7 Hz, H_3C-1), 1.05 (6H, d, J = 7 Hz, H_3C-9 and H_3CC-4), 0.93 (9H, t, J = 8 Hz, H_3CCSi × 3), 0.89 (3H, t, J = 7.5 Hz, H_3C-2″), 0.81 (3H, d, J = 7 Hz, H_3C-9′), 0.58 (6H, ap q, J = 8 Hz, H_2CSi × 3); ^{13}C NMR ($CDCl_3$) δ 220.4 (s, C-5), 113.1 (s, C-2′), 76.6 (d, C-3), 75.8 (d, C-7), 65.6 (t, C-4′), 65.0 (t, C-5′), 48.1 (d, C-6), 46.7 (d, C-4), 45.3 (d, C-2), 30.4 (d, C-8), 28.9 (t, C-1″), 20.3 (q, C-9), 18.8 (q, C-9′), 15.8 (q, CH_3C-4), 10.2 (q, C-1), 8.3 (q, CH_3C-6), 8.1 (q, C-2″), 7.2 (q × 3, CH_3CSi), 5.2 (t × 3, CH_2Si); HRMS m/z calcd for $C_{23}H_{46}O_5Si + Na^+$ 453.3006, found 453.3006 (ESI).

(4*S*,5*S*,6*R*)-*rel*-4-((2*S*,3*R*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (27a). Et_2BOMe (15 μL, 12 mg, 0.11 mmol) was added to a stirred solution of **21as** (Pg = MOM) (27 mg, 0.075 mmol) in THF (0.60 mL) at −78 °C under argon. The mixture was removed from the cooling bath, and the Et_2BOMe slowly dissolved. After 20 min, the mixture was cooled to −78 °C, and MeOH (0.15 mL) and $NaBH_4$ (11 mg, 0.28 mmol) were added. After 1 h, the mixture was allowed to slowly warm to ambient temperature. After 6 h, the mixture was diluted with CH_2Cl_2, and the reaction was quenched by addition of 30% aqueous H_2O_2 (0.30 mL) followed by aq NaOH (0.1 M; 1.4 mL) at 0 °C. After 30 min, the organic layer was washed with water, dried over Na_2SO_4, concentrated, and fractionated by FCC (40% ethyl acetate in hexane) to afford the *syn* diol (27 mg, 99%) as a single diastereomer by ^{1}H NMR. 2,2-Dimethoxypropane (0.2 mL, excess) and *p*-TsOH·H_2O (2 mg, 0.01 mmol) were added to a solution of *syn* diol (27 mg, 0.075 mmol) in CH_2Cl_2 (0.80 mL) at 0 °C under Ar. The reaction was monitored by TLC, and when complete (10−30 min) the mixture was diluted with CH_2Cl_2, washed with saturated aq $NaHCO_3$, dried over Na_2SO_4, concentrated, and fractionated by PTLC (30% ethyl acetate in hexane) to give the title compound (27 mg, 90%): colorless oil, TLC R_f = 0.65 (30% ethyl acetate in hexane); ^{1}H NMR (C_6D_6) δ 4.82 (1H, d, J = 6.5 Hz, HCO_2), 4.68 (1H, d, J = 6.5 Hz, HCO_2), 4.23 (1H, br s, HC-3′), 3.70−3.55 (4H, m, H_2C-4″, H_2C-5″), 3.64 (1H, dd, J = 1.5, 10 Hz, HC-4), 3.29 (3H, s, H_3CO), 3.25 (1H, dd, J = 1.5, 9.5 Hz, HC-6), 2.28 (1H, ddq, J = 3, 10, 7 Hz, HC-2′),

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1.22 (1H, dq, J = 2, 7 Hz, HC-4′), 1.88−1.70 (3H, m, H_3CC-2″, HCC-6), 1.51 (3H, s, H_3CC-2), 1.47 (1H, ddq, J = 1.5, 1.5, 6.5 Hz, HC-5), 1.43 (3H, s, H_3CC-2), 1.28 (3H, d, J = 7 Hz, H_3C-5′), 1.09 (3H, d, J = 6.5 Hz, H_3CCC-6), 1.00 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.98 (3H, d, J = 6.5 Hz, H_3CC-5), 0.95 (3H, d, J = 7 Hz, H_3C-1′), 0.71 (3H, d, J = 7 Hz, H_3CCC-6); ^{13}C NMR (C_6D_6) δ 114.8 (s, C-2″), 99.2 (s, C-2), 97.3 (t, OCH_2O), 80.3 (d, C-6), 76.6 (d, C-3′), 74.6 (d, C-4), 65.7 (t, C-4″), 65.6 (t, C-5″), 56.0 (q, CH_3O), 41.1 (d, C-4′), 41.0 (d, C-2′), 31.5 (d, C-5), 30.8 (q, CH_3C-2), 30.1 (d, CHC-6), 28.0 (t, CH_2C-2″), 20.5 (q, CH_3CC-6), 20.0 (q, CH_3C-2), 17.9 (q, CH_3CC-6), 12.1 (q, C-5′), 11.6 (q, C-1′), 8.5 (q, CH_3CC-2″), 5.3 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2861 (ESI).

(4*S*,5*S*,6*R*)-*rel*-4-((2*S*,3*S*,4*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (27b). DIBAL-H (1 M in cyclohexane; 0.060 mL, 0.06 mmol) was added dropwise via syringe to a stirred solution of **22as** (Pg = MOM) (11 mg, 0.030 mmol) in CH_2Cl_2 (1 mL) at −78 °C. After 3 h, the reaction was quenched by addition of MeOH (1 mL), and the mixture was allowed to warm to ambient temperature. Aqueous Rochelle's salt (1 M) was added, and after vigorous stirring for 30 min, the mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to get the crude product whose ^{1}H NMR spectrum indicated the presence of a >10:1 mixture of diols. Reaction of the crude diol with 2,2-dimethoxypropane as described for **27a** [fractionation by PTLC (15% ethyl acetate in hexane)] gave the title compound (8 mg, 65%): colorless viscous oil, TLC R_f = 0.63 (20% ethyl acetate in hexane); ^{1}H NMR (C_6D_6) δ 4.81 (1H, d, J = 6 Hz, HCO_2), 4.68 (1H, d, J = 6 Hz, HCO_2), 4.20 (1H, br d, J = 6 Hz, HC-3′), 3.86 (1H, dd, J = 2, 10 Hz, HC-4), 3.51−3.73 (4H, m, H_2C-4′, H_2C-5′), 3.30 (1H, dd, J = 2, 9.5 Hz, HC-6), 3.29 (3H, s, H_3CO), 2.19 (1H, dq, J = 6, 7.5 Hz, HC-4′), 2.07 (1H, br dq, J = 9, 7 Hz, HC-2′), 1.73−1.81 (3H, m, H_2CC-2″, HCC-6), 1.57 (1H, ddq, J = 2, 2, 7 Hz, HC-5), 1.49 (3H, s, H_3CC-2), 1.47 (3H, s, H_3CC-2), 1.23 (3H, d, J = 7.5 Hz, H_3C-5′), 1.08 (3H, d, J = 6.5 Hz, H_3CCC-6), 0.98 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.966 (3H, d, J = 6.5 Hz, H_3CC-5), 0.963 (3H, d, J = 7 Hz, H_3C-1′), 0.69 (3H, d, J = 7 Hz, H_3CCC-6); ^{13}C NMR (C_6D_6) δ 114.4 (s, C-2″), 99.29 (s, C-2), 99.21 (t, OCH_2O), 80.2 (d, C-6), 77.6 (d, C-3′), 75.0 (d, C-4), 65.9 (t, C-4″), 65.4 (t, C-5″), 56.1 (q, CH_3O), 44.2 (d, C-4′), 41.7 (d, C-2′), 31.3 (d, C-5), 30.8 (q, CH_3C-2), 30.1 (d, CHC-6), 28.4 (t, CH_2C-2″), 20.5 (q, CH_3CC-6), 20.4 (q, CH_3C-2), 17.8 (q, CH_3CC-6), 12.8 (q, C-5′), 8.8 (q, C-1′), 8.4 (q, CH_3CC-2″), 5.2 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2887 (ESI).

(4*S*,5*S*,6*R*)-*rel*-4-((2*S*,3*S*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (27c). Reduction of **23as** (Pg = MOM) (22 mg, 0.061 mmol) with DIBAL-H as described for **27b** gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 5:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane) gave the *syn* diol (12 mg, 54%) along with a mixture of diols. Reaction of the *syn* diol (12 mg, 0.033 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (8 mg, 62%; 34% from **23as**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^{1}H NMR (C_6D_6) δ 4.73 (1H, d, J = 6.5 Hz, HCO_2), 4.67 (1H, d, J = 6.5 Hz, HCO_2), 4.40 (1H, br d, J = 4.5 Hz, HC-3′), 3.74 (1H, br d, J = 10 Hz, HC-4), 3.66−3.49 (4H, m, H_2C-4″, H_2C-5″), 3.23 (3H, s, H_3CO), 3.22 (1H, br d, J = 6.5 Hz, HC-6), 2.59 (1H, dq, J = 4.5, 7 Hz, HC-4′), 2.38 (1H, dq, J = 10, 7 Hz, HC-2′), 2.02 (1H, dq, J = 14.5, 7.5 Hz, HCC-2″), 1.79−1.71 (2H, m, HCC-2″, HCC-6), 1.60 (1H, br q, J = 6.5 Hz, HC-5), 1.48 (3H, s, H_3CCC-6), 1.39 (3H, s, H_3CCC-6), 1.31 (3H, d, J = 7 Hz, H_3C-5′), 1.11 (3H, t, J = 7.5 Hz, H_3CCC-2″), 1.09 (3H, d, J = 7 Hz, H_3C-1′), 1.07 (3H, d, J = 7 Hz, H_3CCC-6), 0.98 (3H, d, J = 6.5 Hz, H_3CC-5), 0.68 (3H, d, J = 7 Hz, H_3CCC-6); ^{13}C NMR (C_6D_6) δ 113.8 (s, C-2″), 99.3 (s, C-2), 98.0 (t, OCH_2O), 80.3 (d, C-6), 76.7 (d, C-3′), 75.4 (d, C-4), 66.2 (t, C-4″), 64.8 (t, C-5″), 55.7 (q, CH_3O), 43.7 (d, C-4′), 36.5 (d, C-2′), 31.0 (d, C-5), 30.6 (q, CH_3C-2), 30.1 (d, CHC-6), 28.9 (t, CH_2C-2″), 20.5 (q, CH_3CC-6), 20.2 (q, CH_3C-2), 17.8 (q, CH_3CC-6), 10.55 (q, C-1′ or C-5′), 10.51 (q, C-1′ or C-5′), 8.7 (q, CH_3CC-2″), 5.1 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2878 (ESI).

(4*S*,5*S*,6*R*)-*rel*-4-((2*S*,3*R*,4*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (27d). A solution of **24as** (Pg = MOM) (52 mg, 0.14 mmol) in THF (0.5 mL) was added to a stirred solution of $LiAlH_4$ (6 mg, 0.2 mmol) in THF (2.0 mL) at 0 °C under Ar. The mixture was allowed to warm to ambient temperature, and after 1.5 h, the reaction was quenched by addition of aq NaOH (1 M). The mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to give the crude product whose ^{1}H NMR spectrum indicated the presence of a 2:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane) gave the *syn* diol (30 mg, 60%; less polar) and the *anti* diol (15 mg, 30%). Reaction of the *syn* diol (30 mg, 0.083 mmol) with 2,2-dimethoxypropane as described for **27a** gave a crude produce whose ^{1}H NMR spectrum indicated the presence of a 3:1 mixture of **27d** and its corresponding MOM-deprotected derivative (tentatively identified), respectively. Fractionation of the crude product by PTLC (5% ethyl acetate in hexane) gave the title compound (15 mg, 50%; 30% from **24as**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^{1}H NMR (C_6D_6) δ 4.81 (1H, d, J = 6.5 Hz, HCO_2), 4.74 (1H, d, J = 6.5 Hz, HCO_2), 4.07 (1H, br d, J = 10 Hz, HC-4), 3.68 (1H, br d, J = 8 Hz, HC-3′), 3.64−3.53 (4H, m, H_2C-4″, H_2C-5″), 3.30 (1H, br d, J = 9.5 Hz, HC-6), 3.28 (3H, s, H_3CO), 2.64 (1H, dq, J = 8, 7 Hz, HC-4′), 2.23 (1H, br dq, J = 10, 7 Hz, HC-2′), 2.01−1.87 (2H, m, H_2CC-2″), 1.78 (1H, dqq, J = 9.5, 6.5, 6.5 Hz, HCC-6), 1.53 (1H, br q, J = 7 Hz, HC-5), 1.49 (3H, s, H_3CC-2), 1.44 (3H, s, H_3CC-2), 1.15 (3H, d, J = 7 Hz, H_3C-5′), 1.09 (3H, t, J = 7.5 Hz, H_3CC-2″), 1.08 (3H, d, J = 6.5 Hz, H_3CCC-6), 1.05 (3H, d, J = 7 Hz, H_3C-1′), 0.99 (3H, d, J = 6.5 Hz, H_3CC-5), 0.70 (3H, d, J = 6.5 Hz, H_3CCC-6); ^{13}C NMR (C_6D_6) δ 114.3 (s, C-2″), 99.5 (t, OCH_2O), 98.9 (s, C-2), 86.2 (d, C-3′), 80.6 (d, C-6), 74.9 (d, C-4), 65.5 (t, C-4″), 65.3 (t, C-5″), 56.0 (q, CH_3O), 43.0 (d, C-4′), 37.3 (d, C-2′), 31.7 (d, C-5), 30.7 (q, CH_3C-2), 30.1 (d, CHC-6), 29.3 (t, CH_2C-2″), 20.5 (q, CH_3CC-6), 20.0 (q, CH_3C-2), 17.8 (q, CH_3CC-6), 14.4 (q, C-1′), 14.0 (q, C-5′), 8.5 (q, CH_3CC-2″), 5.3 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2887 (ESI).

(4*R*,5*R*,6*S*)-*rel*-4-((2*S*,3*S*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (28c). Reduction of **23ss** (Pg = MOM) (28 mg, 0.078 mmol) with DIBAL-H as described for **27b** gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 15:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane) gave the *syn* diol (20 mg, 72%). Reaction of the *syn* diol (20 mg, 0.055 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (20 mg, 88%; 63% from **23ss**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^{1}H NMR (C_6D_6) δ 4.84 (1H, d, J = 7 Hz, HCO_2), 4.56 (1H, d, J = 7 Hz, HCO_2), 3.99 (1H, br d, J = 9.5 Hz, HC-4), 3.83 (1H, br d, J = 7 Hz, HC-3′), 3.51−3.43 (4H, m, H_2C-4″, H_2C-5″), 3.45 (1H, br d, J = 9.5 Hz, HC-6), 3.21 (3H, s, H_3CO), 2.37 (1H, dq, J = 7, 7 Hz, HC-4′), 2.16 (1H, br dq, J = 9.5, 7 Hz, HC-2′), 2.12 (1H, br q, J = 7 Hz, HC-5), 1.86 (1H, dqq, J = 9.5, 6.5, 6.5 Hz, HCC-6), 1.72 (2H, ap q, J = 7.5 Hz, HC-2), 1.59 (3H, s, H_3CC-2), 1.46 (3H, s, H_3CC-2), 1.36 (3H, d, J = 7 Hz, H_3C-1′), 1.14 (3H, d, J = 6.5 Hz, H_3CCC-6), 1.10 (3H, d, J = 7 Hz, H_3CC-5), 1.06 (3H, d, J = 7 Hz, H_3C-5′), 0.95 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.82 (3H, d, J = 6.5 Hz, H_3CCC-6); ^{13}C NMR (C_6D_6) δ 113.7 (s, C-2″), 99.4 (s, C-2), 99.5 (t, OCH_2O), 80.5 (d, CH-6), 79.3 (d, CH-3′), 76.6 (d, CH-4), 65.4 (t, C-4″), 65.0 (t, C-5″), 56.1 (q, CH_3O), 42.3 (d, CH-4′), 37.4 (d, CH-2′), 30.9 (d, C-5), 30.9 (q, CH_3C-2), 30.1 (d, CHC-6), 28.9 (t, CH_2C-2″), 20.6 (q, CH_3CC-6), 20.2 (q, CH_3C-2), 18.0 (q, CH_3CC-6), 12.6 (q, C-5′), 11.4 (q, C-1′), 8.4 (q, CH_3CC-2″), 5.7 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2862 (ESI).

(4*R*,5*R*,6*S*)-*rel*-4-((2*S*,3*R*,4*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (28d). Reduction of **24ss** (Pg = MOM) (61 mg, 0.17

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mmol) with $LiAlH_4$ as described for **27d** gave a crude product whose ^1H NMR spectrum indicated the presence of a 4:1 mixture of diols. Fractionation of the crude product by PTLC (30% ethyl acetate in hexane, developed twice) gave the *syn* diol (10 mg, 17%; more polar) and the *anti* diol (42 mg, 69%). Reaction of the *syn* diol (10 mg, 0.028 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (10 mg, 90%; 15% from **24ss**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^1H NMR ($CDCl_3$) δ 4.662 (1H, d, J = 7 Hz, HCO_2), 4.659 (1H, d, J = 7 Hz, HCO_2), 3.97 (1H, dd, J = 2, 5.5 Hz, HC-4), 3.97−3.90 (4H, m, H_2C-4″, H_2C-5″), 3.51 (1H, dd, J = 3.5, 5.5 Hz, HC-3′), 3.40 (3H, s, H_3CO), 3.27 (1H, dd, J = 2, 9.5 Hz, HC-6), 2.12 (1H, dq, J = 5.5, 7 Hz, HC-4′), 2.07 (1H, ddq, J = 3.5, 5.5, 7 Hz, HC-2′), 1.77−1.69 (2H, m, H_2CC-2″), 1.65 (1H, dqq, J = 9.5, 6.5, 6.5 Hz, HCC-6), 1.59 (1H, ddq, J = 2, 2, 7 Hz, HC-5), 1.38 (3H, s, H_3CC-2), 1.37 (3H, s, H_3CC-2), 1.02 (3H, d, J = 7 Hz, H_3C-1′), 0.97 (3H, d, J = 7 Hz, H_3C-5′), 0.93 (3H, d, J = 6.5 Hz, H_3CC-6), 0.89 (3H, d, J = 7 Hz, H_3CC-5), 0.89 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.79 (3H, d, J = 6.5 Hz, H_3CC-6); ^{13}C NMR ($CDCl_3$) δ 113.7 (s, C-2″), 98.9 (s, C-2), 97.5 (t, OCH_2O), 82.6 (d, C-3′), 80.2 (d, C-6), 73.2 (d, C-4), 65.5 (t, C-4″), 65.2 (t, C-5″), 56.0 (q, CH_3O), 42.4 (d, C-4′), 38.5 (d, C-2′), 33.6 (d, C-5), 30.3 (q, CH_3C-2), 29.4 (d, CHC-6), 28.8 (t, CH_2C-2″), 20.1 (q, CH_3CC-6), 19.8 (q, CH_3C-2), 17.6 (q, CH_3CC-6), 14.3 (q, C-1′), 12.5 (q, C-5′), 8.0 (q, CH_3CC-2″), 5.8 (q, CH_3C-5); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2865 (ESI).

(4*S*,5*R*,6*R*)-*rel*-4-((2*S*,3*R*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (29a). Reduction of **21sa** (Pg = MOM) (30 mg, 0.084 mmol) with $Et_2BOMe/NaBH_4$ as described for **27a** gave the *syn* diol (29 mg, 96% yield) as a single diastereomer by ^1H NMR. Reaction of the *syn* diol (20 mg, 0.055 mmol) with 2,2-dimethoxypropane as described for **27a** [fractionation by PTLC (30% ethyl acetate in hexane)] gave the title compound (30 mg, 93%; 90% from **21sa**): colorless oil, TLC R_f = 0.6 (30% ethyl acetate in hexane); ^1H NMR ($CDCl_3$) δ 4.70 (1H, d, J = 6.5 Hz, HCO_2), 4.65 (1H, d, J = 6.5 Hz, HCO_2), 4.12 (1H, ap q, J = 7 Hz, HC-4″), 3.95−3.86 (4H, m, HC-3′, HC-4″, H_2C-5″), 3.43 (1H, dd, J = 3.5, 10.5 Hz, HC-4), 3.36 (3H, s, H_3CO), 3.26 (1H, dd, J = 2, 10 Hz, HC-6), 2.48 (1H, br q, J = 7 Hz, HC-4′), 2.28 (1H, ddq, J = 3.5, 3.5, 7 Hz, HC-2′), 1.96−1.86 (2H, m, HCC-6, HC-5), 1.74 (1H, dq, J = 14.5, 7.5 Hz, HCC-2″), 1.59 (1H, dq, J = 14.5, 7.5 Hz, HCC-2″), 1.33 (3H, s, H_3CC-2), 1.29 (3H, s, H_3CC-2), 1.04 (3H, d, J = 7 Hz, H_3C-1′), 0.97 (3H, d, J = 7 Hz, H_3C-5′), 0.93 (3H, d, J = 7 Hz, H_3CCC-6), 0.88 (3H, d, J = 7 Hz, H_3CCC-6), 0.85 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.78 (3H, d, J = 6.5 Hz, H_3C-5); ^{13}C NMR ($CDCl_3$) δ 114.6 (s, C-2″), 98.2 (s, C-2), 97.8 (t, OCH_2O), 78.8 (d, C-6), 78.2 (d, C-4), 77.1 (t, C-3′), 65.1 (d, C-4″ or C-5″), 65.0 (t, C-4″ or C-5″), 55.9 (q, CH_3O), 40.7 (d, C-4′), 38.3 (d, C-2′), 32.8 (d, C-5), 30.4 (q, CH_3C-2), 28.2 (d, CHC-6), 25.7 (t, CH_2C-2″), 20.4 (q, CH_3CC-6), 19.1 (q, CH_3C-2), 14.7 (q, CH_3CC-6), 13.0 (q, C-1′), 11.4 (q, CH_3C-5), 10.7 (q, C-5′), 7.1 (q, CH_3CC-2″); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2865 (ESI).

(4*S*,5*R*,6*R*)-*rel*-4-((2*S*,3*S*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (29c). Reduction of **23sa** (Pg = MOM) (34 mg, 0.094 mmol) with DIBAL-H as described for **27b** gave a crude product whose ^1H NMR spectrum indicated the presence of a 5:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane) gave the *syn* diol (20 mg, 59%) and the *anti* diol (4 mg, 12%). Reaction of the *syn* diol (8 mg, 0.022 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (6 mg, 66%; 39% from **23sa**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^1H NMR (C_6D_6) δ 5.16 (1H, d, J = 6.5 Hz, HCO_2), 4.68 (1H, d, J = 6.5 Hz, HCO_2), 4.22 (1H, br d, J = 3 Hz, HC-3′), 3.59−3.47 (4H, m, H_2C-4″, H_2C-5″), 3.35 (1H, dd, J = 1.5, 10.5 Hz, HC-4), 3.27 (1H, br d, J = 10 Hz, HC-6), 3.26 (3H, s, H_3CO), 2.56 (1H, dq, J = 3, 7 Hz, HC-4′), 2.52 (1H, br q, J = 7 Hz, HC-2′), 1.91 (1H, dq, J = 15, 7 Hz, HCC-2″), 1.83 (1H, dqq, J = 1.5, 7, 7 Hz, HCC-6), 1.75 (1H, dq, J = 15, 7 Hz, HCC-2″), 1.70 (1H, ddq, J = 10, 10.5, 6.5 Hz, HC-5), 1.46 (3H, s, H_3CC-2), 1.35 (3H, d, J = 7 Hz, H_3C-1′), 1.312 (3H, s, H_3CC-2), 1.311 (3H, d, J = 7 Hz, H_3C-5′), 1.13 (3H, t, J = 7.5 Hz, H_3CCC-2″), 1.08 (3H, d, J = 7 Hz, H_3CCC-6), 1.01 (3H, d, J = 7 Hz, H_3CCC-6), 0.76 (3H, d, J = 6.5 Hz, H_3CC-5); ^{13}C NMR (C_6D_6) δ 113.7 (s, C-2″), 98.5 (t, OCH_2O), 98.2 (s, C-2), 80.5 (d, C-4), 78.5 (d, C-6), 77.3 (d, C-3′), 66.1 (t, C-4″), 64.9 (t, C-5″), 55.7 (q, CH_3O), 46.0 (d, C-4′), 36.3 (d, C-2′), 33.5 (d, C-5), 30.6 (q, CH_3C-2), 29.4 (t, CH_2C-2″), 29.0 (d, CHC-6), 20.9 (q, CH_3CC-6), 19.7 (q, CH_3C-2), 16.1 (q, C-1′), 15.0 (q, CH_3CC-6), 12.8 (q, H_3CC-5), 10.5 (q, C-5′), 8.5 (q, H_3CCC-2″); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2870 (ESI).

(4*S*,5*R*,6*R*)-*rel*-4-((2*S*,3*R*,4*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (29d). Reduction of **24sa** (Pg = MOM) (32 mg, 0.11 mmol) with $LiAlH_4$ as described for **27d** gave a crude product whose ^1H NMR spectrum indicated the presence of a 5:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane) gave the *syn* diol (17 mg, 45%) along with a mixture of diols. Reaction of the *syn* diol (17 mg, 0.047 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (15 mg, 85%; 38% from **24sa**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^1H NMR (C_6D_6) δ 5.00 (1H, d, J = 6.5 Hz, HCO_2), 4.95 (1H, d, J = 6.5 Hz, HCO_2), 3.71 (1H, dd, J = 2, 9.5 Hz, HC-3′), 3.59−3.53 (4H, m, H_2C-4″, H_2C-5″), 3.47 (1H, br d, J = 10.5 Hz, HC-4), 3.31 (3H, s, CH_3O), 3.20 (1H, br d, J = 1.5, 9.5 Hz, HC-6), 2.76 (1H, dq, J = 9.5, 7 Hz, HC-2′), 2.31 (1H, ddq, J = 9.5, 10.5, 6.5 Hz, HC-5), 2.21 (1H, dq, J = 2, 7 Hz, HC-4′), 2.10 (1H, dq, J = 14.5, 7.5 Hz, HCC-2″), 1.97 (1H, dq, J = 14.5, 7.5 Hz, HCC-2″), 1.82 (1H, dqq, J = 1.5, 7, 7 Hz, HCC-6), 1.46 (3H, s, H_3CC-2), 1.33 (3H, d, J = 7 Hz, H_3C-5′), 1.32 (3H, s, H_3CC-2), 1.15 (3H, d, J = 7 Hz, H_3C-1′), 1.07 (3H, d, J = 7 Hz, H_3CCC-6), 1.06 (3H, t, J = 7.5 Hz, H_3CCC-2″), 1.02 (3H, d, J = 7 Hz, H_3CCC-6), 0.79 (3H, d, J = 6.5 Hz, H_3CC-5); ^{13}C NMR (C_6D_6) δ 114.9 (s, C-2″), 100.5 (t, OCH_2O), 98.4 (s, C-2), 86.1 (d, C-3′), 80.8 (d, C-4), 79.4 (d, C-6), 65.6 (t, C-4″), 65.5 (t, C-5″), 56.4 (q, CH_3O), 42.4 (d, C-4′), 37.0 (d, C-2′), 34.0 (d, C-5), 30.7 (q, CH_3C-2), 29.5 (t, CH_2C-2″), 28.9 (d, CHC-6), 21.0 (q, CH_3CC-6), 19.6 (q, CH_3C-2), 18.6 (q, C-1′), 15.1 (q, CH_3CC-6), 15.0 (q, C-5′), 12.6 (q, CH_3C-5), 8.0 (q, CH_3CC-2″); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2886 (ESI).

(4*R*,5*S*,6*S*)-*rel*-6-((4*S*,5*R*,6*R*)-6-Isopropyl-2,2,5-trimethyl-1,3-dioxan-4-yl)-5-(methoxymethoxy)-4-methylheptan-3-one (29e). Reduction of **22sa** (Pg = MOM) (30 mg, 0.083 mmol) with DIBAL-H as described for **27b** gave a crude product whose ^1H NMR spectrum indicated the presence of a 17:1 mixture of diols. Fractionation of the crude product by FCC (50% ethyl acetate in hexane) provided the *syn* diol (23 mg, 76%). Reaction of the *syn* diol (23 mg, 0.064 mmol) with 2,2-dimethoxypropane as described for **27a** [2 h reaction time; fractionation by PTLC (15% ethyl acetate in hexane)] gave an inseparable mixture of the expected **29c** and **29e** (24 mg). The mixture (8.5 mg) was taken up in acetone (2 mL), and *p*-TsOH·H_2O (a small crystal; ca. 0.3 mg, 0.002 mmol) was added. After 4 h, the reaction was quenched and processed as above to give title compound (7 mg, 66%; 50% from **22sa**): colorless liquid, TLC R_f = 0.46 (15% ethyl acetate in hexane); IR ν_{max} 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.83 (1H, d, J = 6.5 Hz, HCO_2), 4.52 (1H, d, J = 6.5 Hz, HCO_2), 4.01 (1H, dd, J = 2.5, 5.5 Hz, HC-5), 3.35 (3H, s, H_3CO), 3.32 (1H, dd, J = 2, 10.5 Hz, HC-4′), 3.27 (1H, dd, J = 2, 10 Hz, HC-6′), 2.81 (1H, dq, J = 5.5, 7 Hz, HC-4), 2.67 (1H, dq, J = 18, 7 Hz, HC-2), 2.49 (1H, dq, J = 18, 7.5 Hz, HC-2), 1.87 (1H, dqq, J = 2, 7, 7 Hz, HCC-6′), 1.81 (1H, ddq, J = 2, 2.5, 7 Hz, HC-6), 1.58 (1H, ddq, J = 10, 10.5, 6.5 Hz, HC-5′), 1.34 (3H, s, H_3CC-2′), 1.33 (3H, s, H_3CC-2′), 1.12 (3H, d, J = 7 Hz, H_3CC-4), 1.04 (3H, t, J = 7 Hz, H_3C-1), 0.94 (3H, d, J = 7 Hz, H_3C-7), 0.93 (3H, d, J = 7 Hz, H_3CC-6′), 0.85 (3H, d, J = 7 Hz, H_3CC-6′), 0.69 (3H, d, J = 6.5 Hz, H_3CC-5′); ^{13}C NMR ($CDCl_3$) δ 213.9 (s, C-3), 97.9 (s, C-2′), 97.9 (t, OCH_2O), 78.6 (d, C-4′), 78.0 (d, C-5), 78.0 (d, C-6′), 56.4 (q, CH_3O), 51.3 (d, C-4), 36.9 (d, C-6), 35.8 (t, C-2), 32.9 (d, C-5′), 30.1 (q, CH_3C-2′), 28.4 (d, CHC-6′), 20.4 (q, CH_3CC-6′), 19.3 (q, CH_3C-2′), 14.6 (q, CH_3CC-6′), 14.3 (q, C-7), 12.6 (q, CH_3C-4), 12.2 (q, CH_3C-5′), 7.9 (q, C-1);

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HRMS m/z calcd for $C_{20}H_{38}O_5$ + Na^+ 381.2617, found 381.2620 (ESI).

(4*R*,5*S*,6*S*)-*rel*-4-((2*R*,3*R*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (29f). Reduction of **22sa** (Pg = Et_3Si) (50 mg, 0.12 mmol) with DIBAL-H as described for **27b** gave a crude product whose ^{1}H NMR spectrum indicated the presence of a >10:1 mixture of diols along with **22sa** (Pg = Et_3Si). Fractionation of the crude product by FCC (15% ethyl acetate in hexane) provided the *syn* diol (32 mg, 63%). Reaction of the *syn* diol (25 mg, 0.058 mmol) with 2,2-dimethoxypropane as described for **27a** [1 h reaction time at −50 °C; fractionation by PTLC (10% ethyl acetate in hexane)] gave the title compound (11 mg, 53%; 33% from **22sa**): colorless solid, TLC R_f = 0.3 (10% ethyl acetate in hexane); IR ν_{max} 3516 cm^{-1}; ^{1}H NMR (C_6D_6) δ 4.34 (1H, br d, J = 6 Hz, HC-3′), 3.56 (1H, br s, HO), 3.54−3.48 (4H, m, H_2C-4′, H_2C-5′), 3.43 (1H, br d, J = 10.5 Hz, HC-4), 3.18 (1H, br d, J = 10 Hz, HC-6), 2.29 (1H, br q, J = 7 Hz, HC-2′), 2.10 (1H, dq, J = 6, 7 Hz, HC-4′), 1.96 (1H, ddq, J = 10, 10.5, 6.5 Hz, HC-5), 1.88 (1H, m, J = 15, 7.5 Hz, HCC-2″), 1.73−1.80 (2H, m, HCC-2″, HCC-6), 1.45 (3H, d, J = 7 Hz, H_3C-5′), 1.34 (3H, s, H_3CC-2), 1.29 (3H, d, J = 7 Hz, H_3C-1′), 1.19 (3H, s, H_3C-2), 1.01 (3H, d, J = 7 Hz, H_3CCC-6), 0.98 (3H, t, J = 7 Hz, H_3CCC-2″), 0.93 (3H, d, J = 7 Hz, H_3CCC-6), 0.66 (3H, d, J = 6.5 Hz, H_3CC-5); ^{13}C NMR (C_6D_6) δ 114.5 (s, C-2′), 98.8 (s, C-2), 81.8 (d, C-4), 78.6 (d, C-6), 70.0 (d, C-3′), 65.5 (t, C-4′), 65.2 (t, C-5′), 43.9 (d, C-4′), 37.7 (d, C-2′), 33.6 (d, C-5), 30.6 (d, CH_3C-2), 28.8 (d, CHC-6), 26.7 (t, CH_2C-2″), 20.8 (q, CH_3CC-6), 19.3 (q, CH_3C-2), 14.8 (q, CH_3CC-6), 13.1 (q, C-1′), 12.5 (q, C-5′), 11.9 (q, CH_3C-5), 7.7 (q, CH_3CC-2″); HRMS m/z calcd for $C_{20}H_{38}O_5$ + Na^+ 381.2611, found 381.2618 (ESI).

(4*S*,5*R*,6*R*)-*rel*-4-((2*S*,3*R*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (30a). Reduction of **21aa** (Pg = MOM) (24 mg, 0.067 mmol) with $Et_2BOMe/NaBH_4$ as described for **27a** gave the *syn* diol (21 mg, 90%; dr 10:1 by ^{1}H NMR). Reaction of the *syn* diol (21 mg, 0.058 mmol) with 2,2-dimethoxypropane as described for **27a** [fractionation by PTLC (25% ethyl acetate in hexane)] gave the title compound (21 mg, 91%; 78% from **21aa**): colorless oil, TLC R_f = 0.60 (20% ethyl acetate in hexane); ^{1}H NMR ($CDCl_3$) δ 4.68−4.66 (2H, m, H_2CO_2), 3.98−3.93 (4H, m, H_2C-4″, H_2C-5″), 3.70 (1H, br d, J = 10 Hz, HC-4), 3.65 (1H, br d, J = 8 Hz, HC-3′), 3.40 (3H, s, H_3CO), 3.33 (1H, dd, J = 2, 10 Hz, HC-6), 2.08 (1H, br q, J = 7 Hz, HC-4′), 1.90−1.82 (2H, m, HC-2′, HCC-6,), 1.79−1.67 (2H, m, H_2CC-2″), 1.54 (1H, ddq, J = 10, 10, 6.5 Hz, HC-5), 1.38 (3H, s, H_3CC-2), 1.29 (3H, s, H_3CC-2), 0.96 (3H, d, J = 7 Hz, H_3C-5′), 0.93 (3H, d, J = 7 Hz, H_3CCC-6), 0.87 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.85 (3H, d, J = 7 Hz, H_3C-1′), 0.84 (3H, d, J = 7 Hz, H_3CCC-6), 0.71 (3H, d, J = 6.5 Hz, H_3CC-5); ^{13}C NMR ($CDCl_3$) δ 114.2 (s, C-2″), 98.2 (t, OCH_2O), 97.5 (s, C-2), 79.1 (d, C-3′), 77.9 (d, C-6), 73.5 (d, C-4), 65.3 (t, C-4″), 65.2 (t, C-5″), 56.2 (q, CH_3O), 40.8 (d, C-4′), 38.5 (d, C-2′), 32.4 (d, C-5), 30.3 (q, CH_3C-2), 28.5 (d, CHC-6), 27.2 (t, CH_2C-2″), 20.4 (q, CH_3CC-6), 19.9 (q, CH_3C-2), 14.5 (q, CH_3CC-6), 12.0 (q, CH_3C-5), 9.6 (q, C-1′), 9.4 (q, C-5′), 7.9 (q, CH_3CC-2″); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2884 (ESI).

(4*R*,5*S*,6*S*)-*rel*-4-((2*S*,3*S*,4*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-(methoxymethoxy)pentan-2-yl)-6-isopropyl-2,2,5-trimethyl-1,3-dioxane (30c). Reduction of **23aa** (Pg = MOM) (31 mg, 0.086 mmol) with $LiAlH_4$ as described for **27d** gave a crude product whose ^{1}H NMR spectrum indicated the presence of a 1:1 mixture of diols. Fractionation of the crude product by PTLC (40% ethyl acetate in hexane, developed twice) gave the *syn* diol (13 mg, 42%; less polar) and the *anti* diol (14 mg, 45%). Reaction of the *syn* diol (13 mg, 0.036 mmol) with 2,2-dimethoxypropane as described for **27a** gave the title compound (11 mg, 78%; 33% from **23aa**): colorless viscous oil, TLC R_f = 0.3 (5% ethyl acetate in hexane); ^{1}H NMR ($CDCl_3$) δ 4.77 (1H, d, J = 6.5 Hz, HCO_2), 4.57 (1H, d, J = 6.5 Hz, HCO_2), 3.98−3.89 (4H, m, H_2C-4″, H_2C-5″), 3.64 (1H, dd, J = 2.5, 4 Hz, HC-3′), 3.41 (1H, dd, J = 2.5, 10 Hz, HC-4), 3.37 (3H, s, H_3CO), 3.28 (1H, dd, J = 2, 10 Hz, HC-6), 2.35 (1H, ddq, J = 2.5, 4, 7 Hz, HC-2′), 2.18 (1H, dq, J = 2.5, 7 Hz, HC-4′), 1.86 (1H, dqq, J = 2, 7, 7 Hz, HCC-6), 1.75−1.65 (2H, m, H_2CC-2″), 1.56 (1H, ddq, J = 10, 10, 6.5 Hz, HC-5), 1.35 (3H, s, H_3CC-2), 1.30 (3H, s, H_3CC-2), 1.02 (3H, d, J = 7 Hz, H_3C-5′), 0.92 (3H, d, J = 7 Hz, H_3CCC-6), 0.91 (3H, t, J = 7.5 Hz, H_3CCC-2″), 0.87 (3H, d, J = 7 Hz, H_3C-1′), 0.83 (3H, d, J = 7 Hz, H_3CCC-6), 0.70 (3H, d, J = 6.5 Hz, H_3CC-5); ^{13}C NMR ($CDCl_3$) δ 113.6 (s, C-2″), 97.6 (s and t, C-2 and OCH_2O), 81.0 (d, C-3′), 78.2 (d, C-4), 77.4 (d, C-6), 65.6 (t, C-4″), 65.0 (t, C-5″), 55.9 (q, CH_3O), 43.5 (d, C-4′), 34.9 (d, C-2′), 32.8 (d, C-5), 30.3 (q, CH_3C-2), 29.0 (t, CH_2C-2″), 28.3 (d, CHC-6), 20.4 (q, CH_3CC-6), 19.7 (q, CH_3C-2), 14.5 (q, CH_3CC-6), 11.3 (q, CH_3C-5), 10.5 (q, C-5′), 9.2 (q, C-1′), 8.0 (q, CH_3CC-2″); HRMS m/z calcd for $C_{22}H_{42}O_6$ + Na^+ 425.2873, found 425.2890 (ESI).

(2*S*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-3,7-bis(methoxymethoxy)-4,6,8-trimethylnonan-5-one (31a). From **21sa** (Pg = Et_3Si). Tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) (34 mg, 0.12 mmol) and H_2O (5 μL, 5 mg, 0.3 mmol) were sequentially added to a stirred solution of **21sa** (Pg = Et_3Si) (27 mg, 0.063 mmol) in DMF (0.2 mL). After 16 h, (reaction complete by TLC), the mixture was diluted with ethyl acetate and washed sequentially with saturated aq NH_4Cl and H_2O. The organic layer was dried over Na_2SO_4, concentrated to give the crude diol **21as** (Pg = H) (21 mg). According to the general procedure for preparation of MOM ethers, the crude product obtained after reaction of the above diol (21 mg) for 2 days was fractionated by PTLC (30% Et_2O in CH_2Cl_2) to afford the title compound (22 mg, 87%). From **21sa** (Pg = MOM). Using the general procedure for preparation of MOM ethers, reaction of **21sa** (Pg = MOM) (25 mg, 0.069 mmol) for 2 days followed by fractionation as above afforded the title compound (26 mg, 93%): colorless oil, TLC R_f = 0.6 (30% Et_2O in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 4.67 (1H, d, J = 6 Hz), 4.65 (1H, d, J = 6.5 Hz), 4.62 (1H, d, J = 6 Hz), 4.59 (1H, d, J = 6.5 Hz), 3.96−3.90 (5H, m), 3.59 (1H, dd, J = 5, 6 Hz), 3.37 (6H, ap s), 3.15 (1H, dq, J = 6, 7 Hz), 2.96 (1H, dq, J = 6.5 7 Hz), 2.04 (1H, dq, J = 1.5, 7 Hz), 1.86−1.76 (1H, m), 1.74−1.63 (2H, m), 1.15 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 0.98 (3H, d, J = 7 Hz), 0.94 (3H, d, J = 7 Hz), 0.92 (3H, d, J = 7 Hz), 0.86 (3H, t, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 215.3, 113.7, 98.3, 97.5, 85.5, 76.8, 65.3, 65.2, 56.4, 56.1, 49.8, 49.3, 40.7, 30.1, 26.9, 20.5, 17.7, 13.1, 13.0, 10.4, 7.7; HRMS m/z calcd for $C_{21}H_{40}O_7$ + Na^+ 427.2666, found 427.2651 (ESI).

(2*S*,3*S*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-3,7-bis(methoxymethoxy)-4,6,8-trimethylnonan-5-one (31c). From **23sa** (Pg = Et_3Si). Using the same procedure as described for **31a**, **23sa** (Pg = Et_3Si) (50 mg, 0.12 mmol) was treated TASF and then MOM-Cl/*i*-Pr_2EtN) followed by fractionation of the crude product by PTLC (40% ethyl acetate in hexane) to afford the title compound (32 mg, 79%). From **23sa** (Pg = MOM). Using the general procedure for preparation of MOM ethers, reaction of **23sa** (Pg = MOM) (18 mg, 0.050 mmol) for 2 days followed by fractionation as above afforded the title compound (20 mg, 99%): colorless oil, TLC R_f = 0.35 (30% ethyl acetate in hexane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.72 (1H, d, J = 6.5 Hz), 4.60 (1H, d, J = 6.5 Hz), 4.55 (1H, d, J = 6.5 Hz), 4.50 (1H, d, J = 6.5 Hz), 4.21 (1H, dd, J = 2, 3 Hz), 3.99−3.89 (4H, m), 3.59 (1H, dd, J = 2.5, 8.5 Hz), 3.35 (3H, s), 3.32 (3H, s), 3.16 (1H, dq, J = 2, 7 Hz), 3.11 (1H, dq, J = 7, 8.5 Hz), 2.28 (1H, dq, J = 3, 7 Hz), 1.83 (1H, dqq, J = 3, 7, 7 Hz), 1.74−1.61 (2H, m), 1.19 (3H, d, J = 7 Hz), 1.02 (3H, d, J = 7 Hz), 0.99 (6H, ap d, J = 7 Hz), 0.905 (3H, d, J = 7 Hz), 0.903 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.2, 113.2, 98.7, 97.5, 85.7, 75.6, 65.8, 64.9, 56.1, 55.9, 48.2, 47.4, 43.6, 29.6, 28.7, 20.2, 16.5, 14.3, 12.3, 10.3, 8.1; HRMS m/z calcd for $C_{21}H_{40}O_7$ + Na^+ 427.2666, found 427.2659 (ESI).

(2*R*,3*R*,4*S*,6*R*,7*R*)-*rel*-2-(2-Ethyl-1,3-dioxolan-2-yl)-3,7-bis(methoxymethoxy)-4,6,8-trimethylnonan-5-one (31d). From **24sa** (Pg = Et_3Si). Using the same procedure as described for **31a**, **24sa** (Pg = Et_3Si) (23 mg, 0.053 mmol) was treated TASF and then MOM-Cl/*i*-Pr_2EtN) followed by fractionation of the crude product by PTLC (25% Et_2O in CH_2Cl_2) to afford the title compound (19 mg, 88%). From **24sa** (Pg = MOM). Using the general procedure for preparation of MOM ethers, reaction of **24sa** (Pg = MOM) (28 mg, 0.077 mmol) for 2 days followed by fractionation as above afforded the

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title compound (29 mg, 92%): colorless oil, TLC R_f = 0.55 (30% Et_2O in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 4.65 (1H, d, J = 6.5 Hz), 4.58 (1H, d, J = 6.5 Hz), 4.57 (1H, d, J = 6.5 Hz), 4.56 (1H, d, J = 6.5 Hz), 3.98−3.92 (4H, m), 3.78 (1H, dd, J = 3, 8 Hz), 3.55 (1H, dd, J = 4, 6.5 Hz), 3.36 (3H, s), 3.34 (3H, s), 3.32 (1H, dq, J = 7.5, 7 Hz), 3.02 (1H, dq, J = 7 Hz), 2.18 (1H, dq, J = 3, 7 Hz), 1.85−1.69 (3H, m), 1.10 (3H, d, J = 7 Hz), 1.09 (3H, d, J = 7 Hz), 1.05 (3H, d, J = 7 Hz), 0.96 (3H, d, J = 7 Hz), 0.93 (3H, d, J = 7 Hz), 0.90 (3H, d, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 216.5, 113.7, 98.8, 98.6, 85.4, 83.6, 65.6, 65.2, 56.3, 56.1, 49.7, 48.5, 41.8, 29.9, 29.0, 20.6, 17.2, 14.8, 13.4, 12.4, 7.8; HRMS m/z calcd for $C_{21}H_{40}O_7$ + Na^+ 427.2666, found 427.2656 (ESI).

■ ASSOCIATED CONTENT

Supporting Information

Tables of NMR data for aldol adducts **11b** and copies of ^1H and ^{13}C NMR spectra for all reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: dale.ward@usask.ca.

Notes

The authors declare no competing financial interest.

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(26) Labels for the aldol adducts **11b** are assigned systematically. The bold numerals (i.e., **21**−**24**) refer to the C2, C3, C4 relative configuration that originates from the starting ketone (i.e., **17**−**20**). For example all adducts **21** have 2,3-*syn*-3,4-*anti* relative configuration and arise from reactions of **17**. The lower case letters associated with the numeric labels **21**−**24** refer to the C-4, C-6 relative configuration (first letter) and the C-6, C-7 relative configuration (second letter) with "**a**" designating an *anti* relationship and "**s**" designating a *syn* relationship; thus, **21sa** refers to 4,6-*syn*-6,7-*anti*-**21**. In the general case of an aldol reaction of **4** with **10** under kinetic control, the relative configuration in adducts **11** indicates the enolate face that has reacted [i.e., 1,3-*syn*-**11** (= 4,6-*syn*-**21**−**24**) results from a *lk*-1,3-addition (e.g., addition to the *si* face of the enolate from a (3*S*)-**4** ketone)] and the relative topicity of the process [i.e., 1,1′-*anti*-**11** (= 6,7-*anti*-**21**−**24**) results from a *lk*-approach (e.g., addition of the *si* face of **10** to the *si* face of the enolate]. For definitions and applications of the *lk* (like) and *ul* (unlike) descriptors, see: Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654−660.

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