30.49, 39.59, 112.30. Anal. Calcd for $C_{23}H_{40}N_2$: C, 80.23; H, 11.63; N, 8.14. Found: C, 80.08; H, 11.72; N, 8.07.

**Acknowledgment.** Support for this research from the NIH (HL-17921) and NSF (CHE 8319726) is gratefully acknowledged.

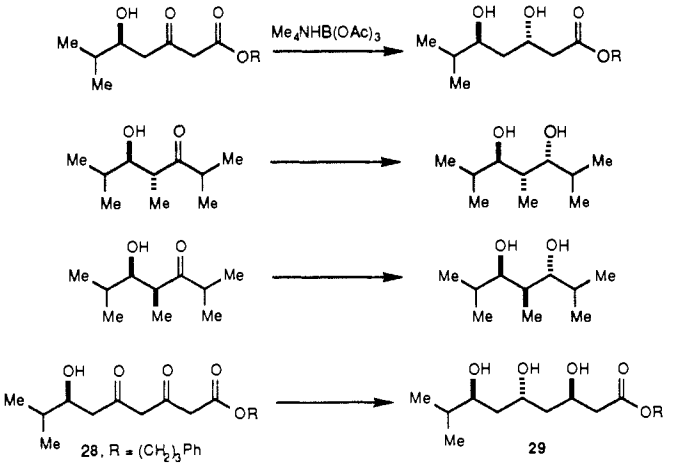
**Supplementary Material Available:** Details of the synthesis of intermediates not described in the Experimental Section (6 pages). Ordering information is given on any current masthead page.

# Directed Reduction of β-Hydroxy Ketones Employing Tetramethylammonium Triacetoxyborohydride

**D. A. Evans,* K. T. Chapman, and E. M. Carreira**

*Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138.* *Received July 10, 1987*

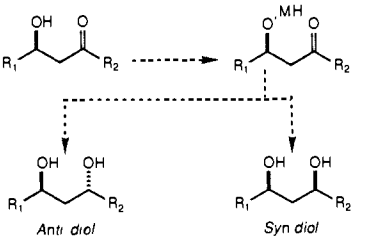
**Abstract:** The mild reducing agent tetramethylammonium triacetoxyborohydride reduces acyclic β-hydroxy ketones to their corresponding anti diols with high diastereoselectivity. α-Alkyl substitution does not significantly affect the stereoselectivity of these reductions. In all cases examined, good to excellent yields of diastereomerically homogeneous diols were obtained. The mechanism of these reductions involves an acid-promoted ligand exchange of acetate for substrate alcohol by the triacetoxyborohydride anion. The resultant hydride intermediate, presumably an alkoxydiacetoxyborohydride, reduces proximal



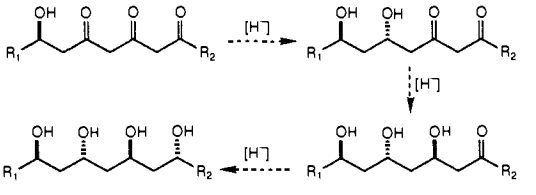

ketones by intramolecular hydride delivery. Ketones, β-ketoesters, and β-diketones are not reduced by tetramethylammonium triacetoxyborohydride in the absence of a suitably disposed hydroxyl group. Indeed both cyclic and acyclic β-hydroxy ketones may be conveniently reduced in a solvent of 1:1 acetone–acetic acid. Hydroxy diketo ester **28** undergoes sequential diastereoselective reductions with tetramethylammonium triacetoxyborohydride to afford a 50% isolated yield of anti–anti triol ester **29** in a unique stereopropagating reaction.

Over the last several years we have been concerned with the development of new stereoselective reactions relevant to the synthesis of polyketide-derived natural products in the polyether,[1] macrolide,[2] and polyene[3] families. Our recent focus on the development of hydroxyl-directed hydrogenation reactions, utilizing cationic rhodium catalysts, is an example of such a method that is genuinely useful in the predictable, stereoselective hydrogenation of hydroxy olefins in acyclic systems.[4,5] As a natural extension of this study we have initiated a complementary investigation aimed at the development of a family of hydride reagents which might participate in a strictly controlled, hydroxyl-directed reduction of hydroxy ketones and related substrates.[6] The sequence

Scheme I




Scheme II




(1) Westley, J. W. *Polyether Antibiotics*; Marcell Dekker: New York, 1982.
(2) Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585–607.
(3) (a) Hamilton-Miller, J. M. T. *Bacteriol. Rev.* **1973**, *37*, 166. (b) Thomas, A. H. *Analyst* **1976**, *101*, 321.
(4) (a) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3866. (b) Evans, D. A.; Morrissey, M. M. *Tetrahedron Lett.* **1984**, *25*, 4637. (c) Evans, D. A.; Morrissey, M. M.; Dow, R. L. *Tetrahedron Lett.* **1985**, *26*, 6005–6008.
(5) For an excellent review on this topic see: Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190–203.

0002-7863/88/1510-3560$01.50/0 

**Table I.** Reduction of β-Hydroxy Ketone **2**, Optimization Study

| entry | hydride | solvent | time | temp, °C | ratio 3:4[a] |
|---|---|---|---|---|---|
| A | $NaBH_4$ | $CH_3CO_2H$ | 30 min | 25 | 80:20 |
| B | $Me_4NBH_4$ | $CH_3CO_2H$ | 30 min | 25 | 92:8 |
| C | $Me_4NBH_4$ | $CH_3CN/CH_3CO_2H$ | 30 min | 25 | 83:17 |
| D | $NaHB(OAc)_3$ | $CH_3CO_2H$ | 15 min | 25 | 84:16 |
| E | $Me_4NHB(OAc)_3$ | $CH_3CO_2H$ | 15 min | 25 | 92:8 |
| F | $NaHB(OAc)_3$ | THF | 15 h | 25 | 77:23 |
| G | $Me_4NHB(OAc)_3$ | THF | 15 h | 25 | 69:31 |
| H | $NaHB(OAc)_3$ | THF/$CH_3CO_2H$ (cat.) | 30 min | 25 | 82:18 |
| I | $Me_4NHB(OAc)_3$ | THF/$CH_3CO_2H$ (cat.) | 30 min | 25 | 79:21 |
| J | $Me_4NHB(OAc)_3$ | $CH_3CN/CH_3CO_2H$ | 30 min | 25 | 92:8 |
| K | $Me_4NHB(OAc)_3$ | $CH_3CN/CH_3CO_2H$ | 5 h | −40 | 95:5 |
| L | $Me_4NHB(OAc)_3$ | $(CH_3)_2CO/CH_3CO_2H$ | 30 min | 25 | 92:8 |

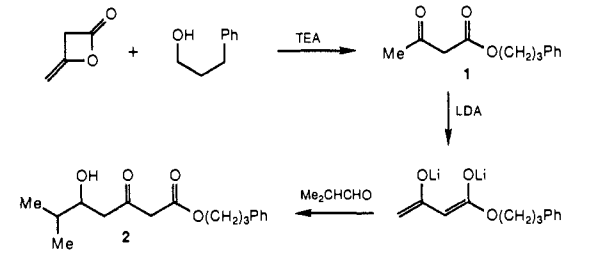
[a] Ratios determined by HPLC.

of events that were established for this reduction protocol is illustrated in Scheme I.

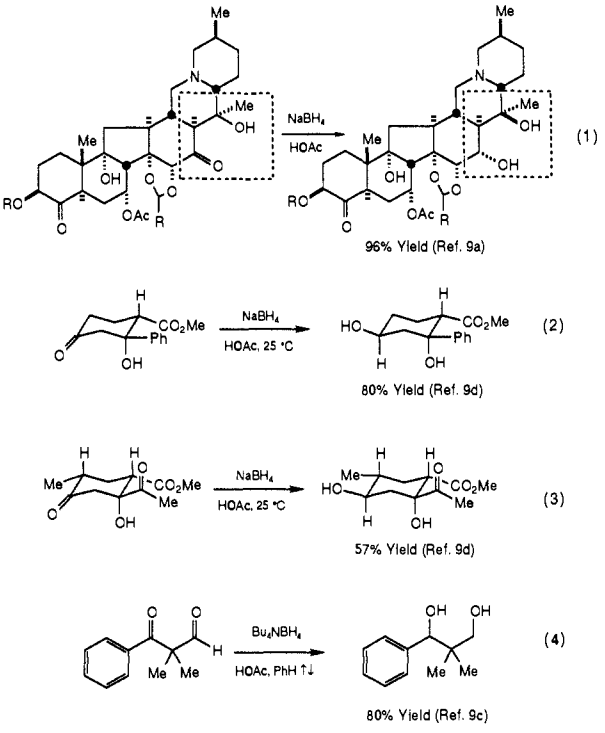
The requirements imposed on the hydride reagent (X–M–H) for the above process are twofold: the species must possess a readily exchangeable ligand, X, and a hydride reduction potential sufficiently low that competing bimolecular reductions of "unbound" metal hydride do not interfere with the desired reaction. At the outset, we were less concerned with the stereochemical course of the study (syn or anti reduction) than we were with trying to find a reagent that would meet the requirements outlined above. In a somewhat broader context, if such reactions could be developed one might envision being able to assemble a stereoregular array of polyols such as that illustrated in Scheme II. In these hydroxyl-directed reactions, the reduction process itself creates a new directing group which is now set up for iteration. As one might readily perceive, competing "nondirected" reductions would thwart such an iterative process. Although the propagated reduction sequence is illustrated in Scheme II for the anti stereochemical option, either stereochemical variant could, in principle, be developed. Such a strategy provides an exceedingly efficient entry into stereoregular polyols. In order to pursue these objectives, we required a reagent that would stereoselectively reduce β-hydroxy ketones through a transition state which is demonstrably intramolecular. Examination of the literature suggested that sodium borohydride in carboxylic acid media might be just such a reagent.[7]

When sodium borohydride is added to excess acetic acid with cooling, 3 equiv of hydrogen are liberated rapidly followed much more slowly by a fourth. The intermediate species in this reaction has been suggested to be sodium triacetoxyborohydride on the basis of its infrared spectrum and hydrolysis products.[8] Several workers, beginning with Saksena, have implicated this species in apparent intramolecular, hydroxyl-directed ketone reductions (eq 1–4).[9] In the last case (eq 4), Gribble has postulated that directed ketone reduction follows slow reduction of the aldehyde. In support of these claims, it has been demonstrated that the intermolecular reduction of ketones with this reagent is extremely sluggish.[9c,10] Gribble has exploited this fact, employing triacetoxyborohydrides

**Scheme III**




in the selective reduction of aldehydes in the presence of ketones.[9c,10a] Furthermore, it has been shown that the reducing




power of the sodium borohydride/acetic acid system is substantially increased in the presence of alcohols.[11] Thus, as suggested by Saksena, a hypothetical alkoxydiacetoxyborohydride intermediate might reduce proximal ketones not simply because it can do so intramolecularly but because it is actually a more potent reducing agent than is the triacetoxyborohydride parent. On the basis of these results, we chose to investigate the sodium borohydride/acetic acid system in the reduction of acyclic β-hydroxy ketones. Specifically, we sought to assess the reagent's potential for carrying out the propagating reduction concept suggested above and to clarify the mechanism of the apparent intramolecular hydroxyl-directed ketone reduction.

## Results and Discussion

Our initial experiments were designed to assay the stereoselectivity of acyclic β-hydroxy ketone reductions employing borohydrides in carboxylic acid media. Hydroxy keto ester **2** was chosen for these studies because of its obvious similarity to the ultimately desired hydroxy polyketone reduction substrates, as well as for the practical reason that its reduction products can be readily analyzed by HPLC without prior derivatization.[12] The synthesis of **2** proceeded according to the plan outlined in Scheme III. Diketene was treated with 3-phenylpropanol[13] in the presence

(6) For preliminary communication of this work see: Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939–5942.

(7) For a comprehensive review of uses of borohydrides in carboxylic acid media see: Gribble, G. W.; Nutaitis, C. F. *Org. Proc. Prep. Int.* **1985**, *17*(4–5), 317–384.

(8) (a) Marchini, P.; Liso, G.; Reho, A.; Libertore, F.; Moracci, F. M. *J. Org. Chem.* **1975**, *40*, 3453–3456. (b) Oklobdzija, M.; Fajdiga, T.; Kovak, T.; Zonno, F.; Sega, A.; Sunjic, V. *Acta Pharm. Jugosl.* **1980**, *30*, 121; *Chem. Abstr.* **1981**, *94*, 121481g.

(9) (a) Saksena, A. K.; Mangiaracina, P. *Tetrahedron Lett.* **1983**, *24*, 273. (b) Saksena, A. K.; Wong, J. K. *Ventron Alembic* **1983**, *31* (Sept.). (c) Gribble, G. W.; Nutaitis, C. F. *Tetrahedron Lett.* **1983**, *24*, 4287. (d) Turnbull, M. D.; Hatter, G.; Ledgerwood, D. E. *Tetrahedron Lett.* **1984**, *25*, 5449.

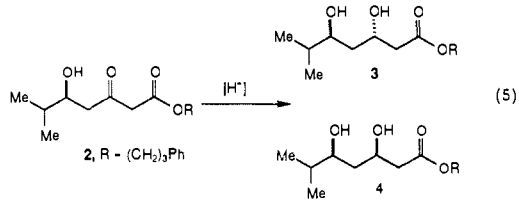
(10) (a) Gribble, G. W.; Ferguson, D. C. *J. Chem. Soc., Chem. Commun.* **1975**, 535. (b) Tolstikov, G. A.; Odinokov, V. N.; Galeeva, R. I.; Bakeeva, R. S.; Akhunova, V. R. *Tetrahedron Lett.* **1979**, 4851.

(11) (a) Hirao, A.; Itsuno, S.; Owa, M.; Nagami, S.; Mochizuki, H.; Zoorov, H. H.; Niakahama, S.; Yamazaki, N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 900. (b) Nasipuri, D.; Sakar, A.; Konar, S. K.; Ghosh, A. *Indian J. Chem.* **1982**, *21B*, 212–215.

(12) We have experienced difficulties in *quantitatively* acylating or silylating mixtures of syn and anti diol esters of this type; HPLC, VPC, or NMR analysis of the derivatized mixture frequently does not accurately reproduce the ratio present in the starting diol mixture.

of triethylamine to afford β-keto ester **1**. Generation of the derived acetoacetate dienolate with excess lithium diisopropylamide (LDA) and subsequent aldol addition with isobutyraldehyde provided the desired β-hydroxy keto ester **2**.[14] The results of our initial reduction studies are shown in Table I.

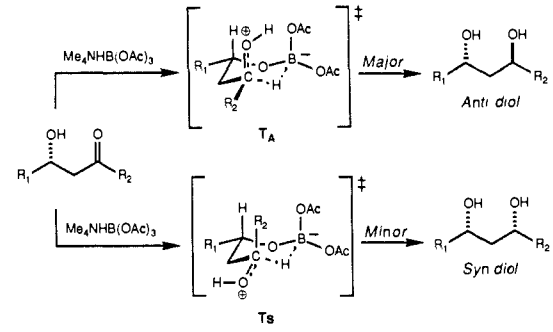
Application of the conventional reduction conditions[9a,b] (solid $NaBH_4$ added to neat acetic acid) to hydroxy ketone **2** afforded an 80:20 mixture of the desired diol esters **3** and **4** with the anti diastereomer **3** predominating (Table I, entry A). The modest level of diastereoselection observed under these conditions served as the starting point for a systematic evaluation of relevant reaction parameters (Table I). On the basis of the observation that the chemoselectivity of aldehyde reduction with borohydride/acetic acid mixtures is increased when the sodium counterion is replaced with tetrabutylammonium,[9c] hydroxy ester **2** was reduced with tetramethylammonium borohydride[15] in acetic acid. This variable change resulted in an increase in reaction diastereoselectivity to 92:8 (entry B). On the other hand, a similar reduction run in 1:1 acetonitrile/acetic acid solvent was less selective (entry C). Partial reduction of acetonitrile occurs in this reaction and the product amineboranes are probably responsible for the observed drop in stereoselectivity.



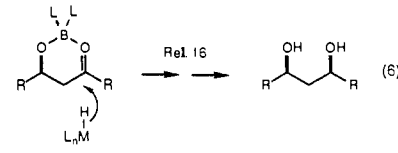

(5)

We were somewhat concerned a priori that the reducing agents prepared by the addition of borohydride to neat acetic acid might not be homogeneous and that impurities might lead to lower diastereoselectivities. We therefore synthesized and fully characterized both sodium triacetoxyborohydride and tetramethylammonium triacetoxyborohydride. These reagents are both white powders that can be stored for months at ambient temperature with little or no decomposition. Tetramethylammonium triacetoxyborohydride, which can be recrystallized from dichloromethane/ethyl acetate, is quite hygroscopic and is freely soluble in a range of organic solvents including dichloromethane, chloroform, and acetonitrile. When hydroxy ketone **2** was reduced with these isolated reagents under conditions otherwise identical with those above, diol products were produced with a modest increase in diastereoselectivity for the sodium counterion (entry D) and with no change for the tetramethylammonium counterion (entry E). These data, which proved to be reproducible, imply that sodium borohydride added directly to acetic acid does not *quantitatively* afford sodium triacetoxyborohydride; nevertheless, any impurities present during the in situ preparation do not significantly perturb the stereochemical course of the reduction. We next examined these diastereoselective reductions in the *absence* of added acetic acid (entries F and G). Treatment of **2** with either sodium triacetoxyborohydride or tetramethylammonium triacetoxyborohydride in anhydrous THF led to an exceedingly sluggish, poorly diastereoselective reduction with greater than 80% recovered starting material after 15 h at ambient temperature. The addition of catalytic quantities of acetic acid greatly enhanced the rates of these reactions and modestly increased the selectivities (entries H and I). We have found that an increase in the concentration of acetic acid in the reduction medium also results in an increase in the reaction diastereoselectivity. This effect appears to level off at about 50% acetic acid. Reduction of **2** with tetramethylammonium triacetoxyborohydride in 1:1 acetonitrile/acetic acid at ambient temperatures (entry J) displayed the same diastereoselectivity as that observed in neat acetic acid (entry E). Solutions of tetramethylammonium triacetoxyborohydride in 1:1 acetonitrile/acetic acid cooled to temperatures well below the freezing point of acetic acid reduced β-hydroxy ketone **2** with excellent diastereoselectivity (entry K). These conditions subsequently proved to be nearly optimal for a range of hydroxy ketone substrates.

Scheme IV

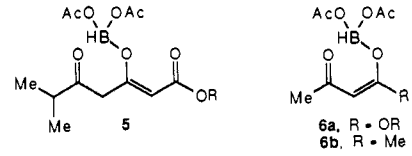



Finally, these reductions are quite tolerant of a wide range of reaction conditions. In an experiment designed to provide permissive evidence for the intramolecular hydride delivery postulate, the reduction of **2** was carried out in a solution of 1:1 acetone–acetic acid (Table I, entry L). This experiment afforded a stereochemical result identical with that obtained in acetonitrile–acetic acid (entry J). It should be pointed out that this experiment does not, in itself, constitute conclusive evidence for intramolecular hydride delivery. For example, on the basis of this experiment alone, intramolecular activation of the carbonyl by tricoordinate boron followed by external hydride delivery cannot be ruled out. Nonetheless, the known propensity of such β-hydroxy ketone boron aldolates to reduce with the *opposite* sense of asymmetric induction (eq 6)[16] strongly supports the intramolecular hydride delivery postulate.




(6)

Reduction of β-hydroxy ketones, unsubstituted at the α-position, with tetramethylammonium triacetoxyborohydride in acetonitrile/acetic acid consistently affords anti diols with high diastereoselectivity (Table II). In all cases, good to excellent yields of diastereomerically homogeneous diols may thus be obtained.

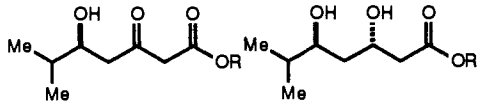
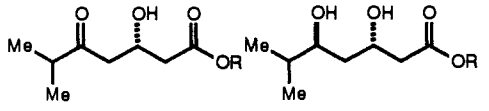
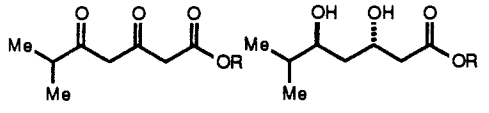
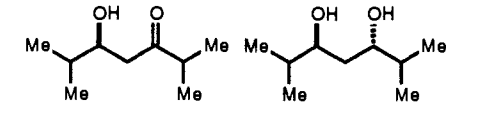
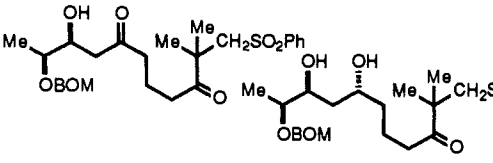



The examples shown in entries A and B provide complementary cases which proceed with equal stereoselectivity. The example in entry C illustrates that the related diketo ester may also be reduced, albeit somewhat more slowly. We speculate this reduction to proceed via the enol borohydride **5** illustrated below. In contrast, tetramethylammonium triacetoxyborohydride will not reduce either acetylacetone or acetylacetate **1** under the same

(13) Kimmel, W.; Cope, A. C. *J. Am. Chem. Soc.* **1943**, *65*, 1992.
(14) Unless otherwise stated, all chiral compounds reported herein were employed as racemic mixtures.
(15) The tetramethylammonium salts consistently proved easier to handle than the corresponding tetrabutylammonium salts. We prepared $Me_4NBH_4$ from $NaBH_4$ and $Me_4NOH$ by a slight modification of the procedure of Gibb (see Experimental Section): Banus, M. D.; Bragdon, R. W.; Gibb, T. R. P. *J. Am. Chem. Soc.* **1952**, *74*, 2346–2348.

(16) (a) Narasaka, K.; Pai, F.-C. *Tetrahedron* **1984**, *40*, 2233–2238 and references cited therein. (b) Sletzinger, M.; Verhoeven, T. R.; Volante, R. P.; McNamara, J. M. *Tetrahedron Lett.* **1985**, *26*, 2951–2954. (c) Chen, K.-M.; Hardtmann, G. E.; Prasad, K.; Repic, O.; Shapiro, M. J. *Tetrahedron Lett.* **1987**, *28*, 155–158. (d) Kathawala, F. G.; Prager, B.; Prasad, K.; Repic, O.; Shapiro, M. J.; Stabler, R. S.; Widler, L. *Helv. Chim. Acta* **1986**, *69*, 803–805. (e) Kiyooka, S.-i.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett.* **1986**, *27*, 3009–3012. (f) Suzuki, K.; Shimazaki, M.; Tschihashi, G. *Tetrahedron Lett.* **1986**, *27*, 6233–6236. (g) Bonadies, F.; Fabio, R. D.; Gubbiotti, A.; Mecozzi, S.; Bonini, C. *Tetrahedron Lett.* **1987**, *28*, 703–706.

Table II. Diastereoselective β-hydroxy ketone reductions with $Me_4NHB(OAc)_3$.

| Entry | Reactant | Product | Time (Temp) | Ratio[a] | Yield, %[b] |
|---|---|---|---|---|---|
| A |  | | 5 h (-40 °C)[c] | 95 : 5 | 92 |
| B |  | | 18 h (-40 °C)[c] | 95 : 5 | 90 |
| C |  | | 6 h (-40 °C)[c] | 92 : 8 | 69 |
| D |  | | 5 h (-40 °C) | 96 : 4 | 86 |
| E |  | | 16 h (-30 °C)[d] | 94 : 6 | 82 |

[a]Ratios determined either by HPLC or VPC. [b]Values refer to isolated yields of major diastereomer of > 99% diastereomeric purity. [c]R = $(CH_2)_3Ph$. [d]This experiment carried out by Dr. M. Lautens.

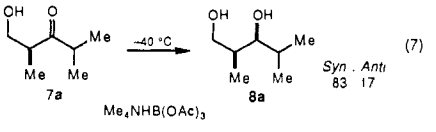
reaction conditions. Presumably, the conjugated ketone in enol borohydrides **6a** and **6b** is sufficiently deactivated so that reduction does not take place in these systems.

Table II, entry E provides an example where a regioselective ketone reduction may be achieved. In this case, the expected ketone proximal to the hydroxyl function is reduced with good selectivity. It is clear, however, that one cannot conclude that the carbonyl proximal to the hydroxyl directing group will *always* be preferentially reduced. Turnbull has provided a complementary case where there is an apparent predisposition for the reduction of a β-hydroxy over an α-hydroxy ketone (eq 3).[9d]

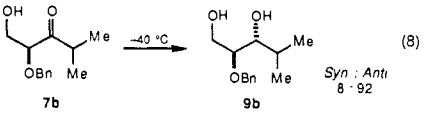
The stereochemical course of these reductions may be rationalized via the diastereomeric transition states illustrated in Scheme IV. It is presumed that the putative ligand exchange of the acetoxyl ligand in the reducing agent with the substrate hydroxyl function precedes the actual reduction step. Circumstantial evidence that supports this statement is that the presence of a substrate hydroxyl group is a requirement for carbonyl reduction. It is presumed that the diastereoselectivity of this reaction reflects a competition between chair-like transition states $T_A$ and $T_S$, each of which involves intramolecular hydride delivery as well as activation by acid catalysis. The 1,3-diaxial interaction, $R_2 \leftrightarrow OAc$, should destabilize $T_S$ to a greater extent than the analogous 1,3-diaxial interaction, $HO^+ \leftrightarrow OAc$, destabilizes the favored transition state $T_A$. Further modification of these transition-state geometries to include the Burgi–Dunitz nucleophilic attack angle[17] might be expected to increase their relative energy difference considerably. Similar arguments have recently been extended to explain the high anti diastereoselectivity observed in the reduction of β-hydrosilyloxy ketones.[18]

The rationalization for the stereochemical course of the reductions presented above becomes more tentative when applied to α-substituted β-hydroxy ketone substrates. A priori, one might reasonably expect syn α-substitution to enhance, and anti α-substitution to diminish, the diastereoselectivity of β-hydroxy ketone reduction. The somewhat surprising results for this family of substrates are summarized in Table III. Both anti and syn β-hydroxy ketones reduce with remarkably high levels of diastereoselectivity in all cases favoring the anti diol diastereomers. These examples substantiate the observation that *asymmetric induction from the distal hydroxyl-bearing stereogenic center overrides the intrinsic bias provided by the proximal methyl-bearing center irrespective of its relative configuration.* This stands in contrast to the majority of other stereoselective β-hydroxy ketone reductions wherein the proximal center dominates the stereochemical course of the reaction.[16a] Parenthetically, we have found that some highly substituted aldol adducts do not require the tetramethylammonium salt for diastereoselective reduction. For example, the β-ketoimide aldol adduct illustrated in entry C undergoes a remarkably stereoselective reduction with sodium triacetoxyborohydride in neat acetic acid to give a single product by HPLC and 300-MHz $^1H$ NMR analysis.

The set of reductions provided above prompted the examination of several β-hydroxy ketones bearing only α-substitution to ascertain the level and sense of asymmetric induction from substituents in this position. On the basis of the subordinate role that this stereocenter plays in the reductions reported in Table III, it is not surprising that ketones **7a** and **7b** are reduced with modest levels of asymmetric induction (eq 7 and 8). We were, however,




(7)

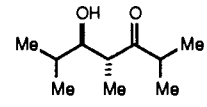
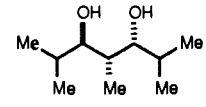
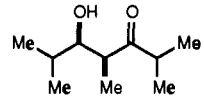
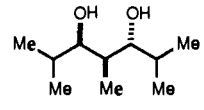
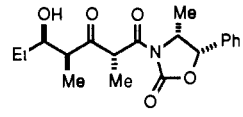
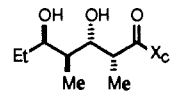
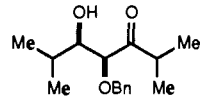
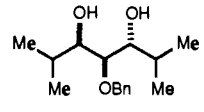
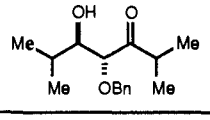
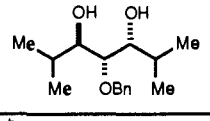



(8)

surprised to discover that α-benzyloxy ketone **7b** is reduced selectively to afford the anti diastereomer **9b** as the major product, while the α-methyl-substituted ketone congener **7a** afforded principally the syn product diastereomer **8a**.[19] On the basis of

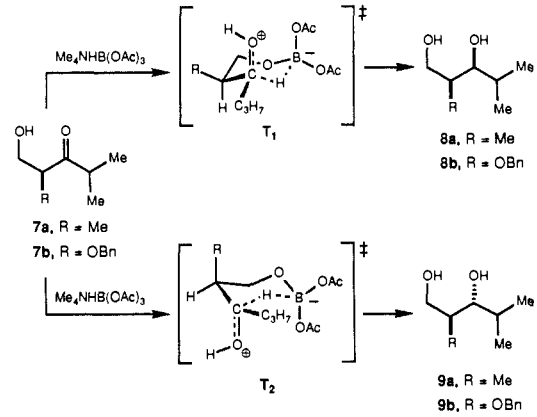
(17) Burgi, H. B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153.
(18) Anwar, S.; Davis, A. P. *J. Chem. Soc., Chem. Commun.* **1986**, 831.

**Table III.** α-Substituted β-Hydroxy Ketone Reductions with $Me_4NHB(OAc)_3$

| Entry | Reactant | Product | Time (Temp) | Ratio[a] | Yield, %[b] |
|---|---|---|---|---|---|
| A |  |  | 18h (-20 °C) | 98 : 2 | 92 |
| B |  |  | 18 h (-20 °C) | 98 : 2 | 84 |
| C |  |  | 30 min (25 °C)[c,d] | >98 : 2 | 99 |
| D |  |  | 18 h (-40 °C) | 93 : 7 | 88 |
| E |  |  | 18 h (-40 °C) | 79 : 21 | 73 |

[a]Ratios determined either by HPLC or VPC. [b]Values refer to isolated yields of major diastereomer of >99% diastereomeric purity. [c]$NaHB(OAc)_3$ used as reductant. [d]This experiment carried out by Dr. V. Novack.

**Scheme V**



stereoelectronic considerations, the Ahn–Eisenstein model[20] for carbonyl addition predicts that the α substituent (Me or OBn) should be preferentially oriented antiperiplanar to the forming C–H bond for optimal transition-state stabilization as illustrated in $T_1$ (Scheme V). The stereochemical course of the reduction of hydroxy ketone **7a**, via the presumed transition state $T_1$, is in full accord with this logic. Nonetheless, the fact that the closely related α-benzyloxy ketone **7b** does not follow this stereochemical prediction and is reduced preferentially to give the anti diastereomer **9b** (anti:syn = 92:8) underscores the tentative nature of the transition-state models presented in this discussion. Irrespective of the explanation, the tendency for α-benzyloxy groups to induce anti reduction (eq 8) also manifests itself in the reduction of the corresponding syn and anti aldol adducts (Table III, entries D and E). While both of these reductions afford products possessing the anti 1,3-diol relationship, the confluence of stereodirecting effects of the α-benzyloxy and β-hydroxyl bearing centers can be clearly seen in the lower diastereoselectivity observed in entry E.

The above discussion provides a model by which the stereochemical outcome of these reductions can be predicted. We hoped to provide additional evidence for the implied mechanistic scheme using $^{11}B$ NMR spectroscopy. This spectroscopic probe is particularly sensitive to the detection of three- versus four-coordinate boron hydrides due to the large differences in observed chemical shifts and the signal multiplicities arising from $^{11}B$–$^{1}H$ coupling. As is illustrated in Figure 1, the $^{11}B$ chemical shifts of relevant tricoordinate boron derivatives fall in the range +15 → +30 ppm ($BF_3$ etherate standard). In contrast, the $^{11}B$ chemical shifts of relevant four-coordinate species appear at substantially lower field (typically −5 → +5 ppm). On the basis of these data, we felt that the chemical shift of an alkoxydiacetoxyborohydride should be sufficiently distinct from that of triacetoxyborohydride for its detection by $^{11}B$ NMR spectroscopy. In two simple ligand exchange experiments which we have monitored by this spectroscopic probe, both malic and malonic acids underwent facile ligand metathesis with triacetoxyborohydride at ambient temperature to cleanly afford the tetracoordinate boronhydrides **10** and **11**, whose illustrated $^{11}B$ chemical shifts are consistent with the structures drawn below. The reduction of hydroxy ketone **2** with tetramethylammonium triacetoxyborohydride was analogously followed by $^{11}B$ NMR spectroscopy. During the course of this reduction, we observed no evidence for the production of any intermediate three- or four-coordinate boronhydride. *Thus, if it is assumed that the reduction of β-hydroxy ketones with tetramethylammonium triacetoxyborohydride involves intramolecular*

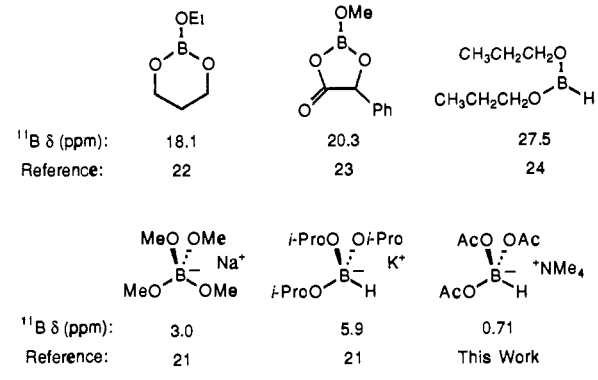



**Figure 1.** Representative $^{11}B$ chemical shifts.

(19) The stereochemical relationships of diols **8** and **9** were determined from $^{1}H$–$^{1}H$ coupling constants of the corresponding acetonides (see Experimental Section).

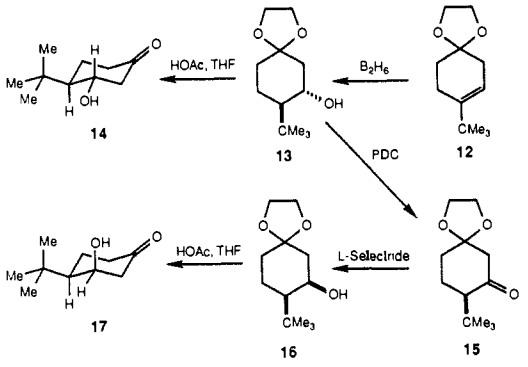
(20) Ahn, N. T.; Eisenstein, O. *Nouv. J. Chem.* **1977**, *1*, 61–70.

(21) Mooney, E. F.; Anderson, M. G. *Annu. Rev. NMR. Spectrosc.* **1969**, *2*, 219.

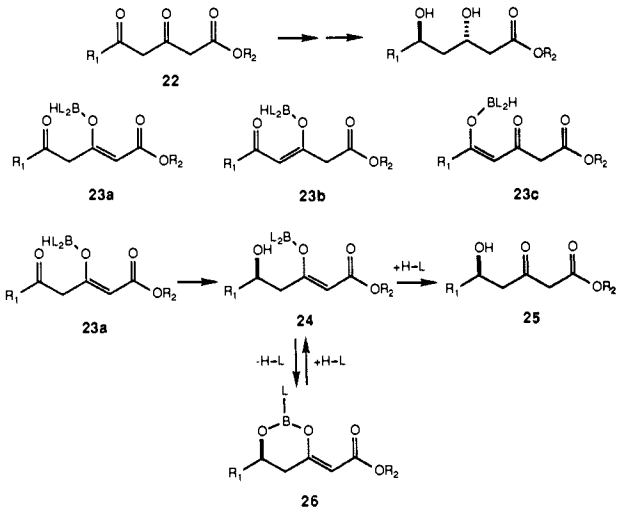
(22) Reference 21, p 137.

(23) Pasto, D. J.; Balasubramaniyan, V.; Wojtkowski, P. W. *Inorg. Chem.* **1969**, *8*, 594.

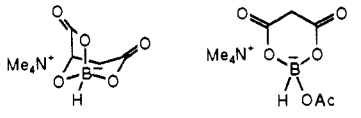
**Scheme VI**




**Scheme VII**

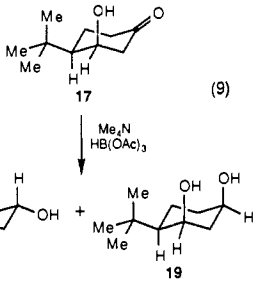



*hydride delivery, we conclude that the rate-determining step in the reduction of this family of substrates is ligand exchange rather than intramolecular hydride transfer.*

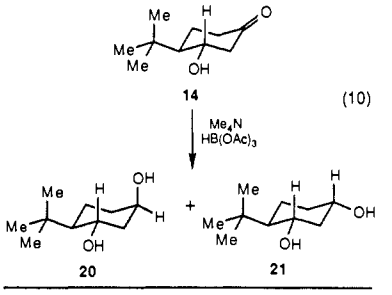



The preceding mechanistic discussion involving acyclic substrates fails to exclude the possibility of internal boron-mediated carbonyl activation followed by intermolecular reduction (eq 6) as a mechanistic alternative to intramolecular hydride delivery. The involvement of boron in this capacity can be ruled out, however, with cyclic β-hydroxy ketones such as **14** and **17** which are incapable of internal carbonyl activation. These substrates were synthesized according to the plan outlined in Scheme VI. The β,δ-unsaturated ethylene ketal **12**, derived from 4-*tert*-butylanisole by dissolving metal reduction and subsequent ketalization, was converted stereospecifically to the equatorial hydroxy ketone **14** via hydroboration and subsequent hydrolysis of the derived ketal **13**. The diastereomeric axial alcohol **17** was also efficiently prepared from **13** by the illustrated series of three reactions.

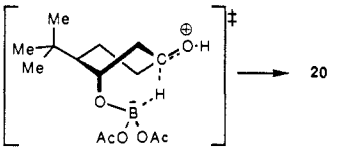
Hydroxy ketones **14** and **17** were treated with tetramethylammonium triacetoxyborohydride in both acetonitrile/acetic acid and acetone/acetic acid solvents. In both solvents, axial hydroxy ketone **17** reduced to give, within the limits of capillary VPC detection, exclusively the trans diol **18** (eq 9). Such a stereochemical outcome in acetone solvent provides compelling evidence for intramolecular hydride delivery in these reductions, a mechanistic hypothesis first proposed by Saksena for sodium borohydride/acetic acid reductions.[9a,b] Interestingly, the equatorial hydroxy ketone **14** underwent an equally diastereoselective, *albeit much slower*,[24] reduction in acetone/acetic acid to provide diol **20** (eq 10). For this reaction to proceed via intramolecular hydride delivery, it must do so through the twist-boat conformation shown below. The analogous reaction carried out in acetonitrile/acetic acid was less diastereoselective, presumably due to a considerable amount of intermolecular ketone reduction which was suppressed in the acetone medium. We have found this to be generally true for unusually reactive ketones such as cyclohexanones not geometrically disposed for facile intramolecular delivery.[25]




| Solvent | Ratio 18:19 | Yield, % |
|---|---|---|
| MeCN-HOAc | > 300:1 | 86 |
| MeCOMe-HOAc | > 300:1 | 86 |




| Solvent | Ratio 20:21 | Yield, % |
|---|---|---|
| MeCN-HOAc | 88:12 | 73 |
| MeCOMe-HOAc | > 300:1 | 54 |

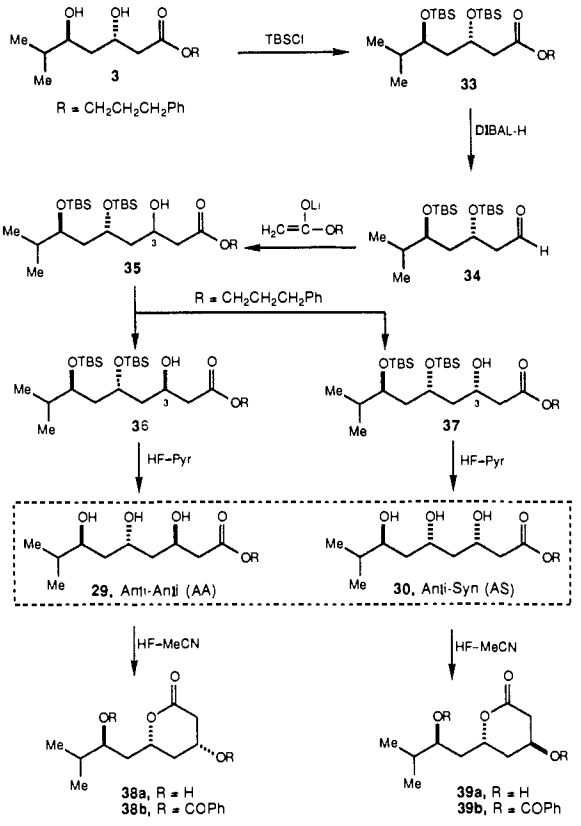



**Internally Propagated Reductions**

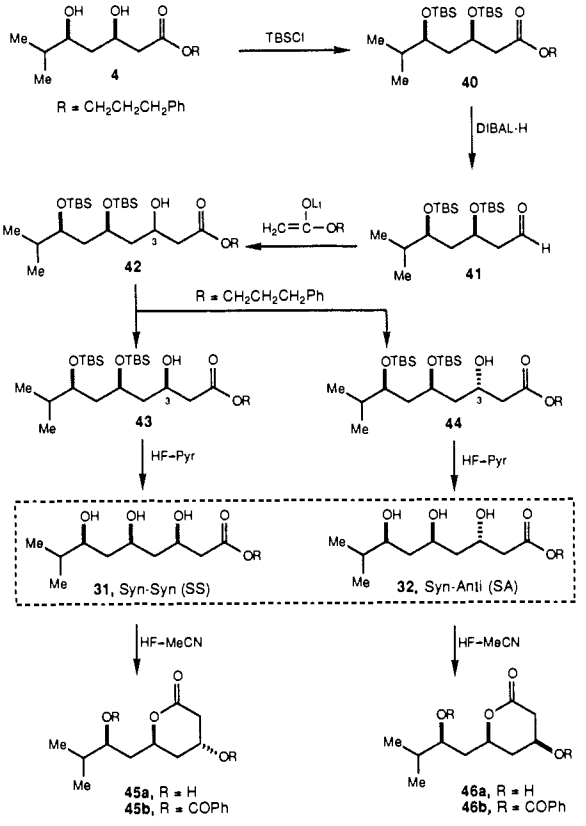
The preceding studies afford good precedent for the intramolecular reduction of β-hydroxy ketones with triacetoxyborohydride and provide some insight into both the rate-determining step (ligand exchange) and mode of catalysis with Brønsted acids. With this background information in hand, studies were initiated to probe the feasibility of "propagating reductions" of polycarbonyl substrates such as those illustrated in Scheme II. The first multistep reduction related to these projected processes that we have studied is shown in Scheme VII. We have previously described that the diketo ester **22** ($R_1$ = $CHMe_2$; $R_2$ = $(CH_2)_3Ph$) is stereoselectively reduced with tetramethylammonium triacetoxyborohydride to the illustrated anti diol (Table II, entry C). Since neither acetylacetone nor acetylacetate **1** is reduced under these conditions, we have concluded that **22** is reduced via a series of *intramolecular* reductions, the first of which is initiated by the conversion of **23** to **24**. In order for a second reduction to take place, it is imperative that boron ligand metathesis operate to purge

(24) More than 24 h were required for ca. 50% reduction in this case.
(25) Sodium borohydride in acetic acid is known to reduce cyclohexanones: Hutchins, R. O.; Su, W.; Sivakumar, R.; Cistone, F.; Stercho, Y. P. *J. Org. Chem.* **1983**, *48*, 3412.

Scheme VIII

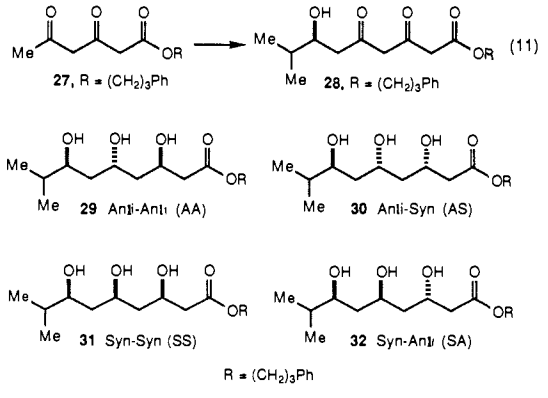



Scheme IX




boron from the partially reduced substrate. In this regard, alkoxy borates generally have exceptionally high oxygen–ligand metathesis rates.[26] On the other hand, 1,3-diols and related bidentate ligands such as **26** form quite stable borate complexes.[27] The fact that diketo esters such as **22** may be reduced with this reagent suggests that borate-free, partially reduced substrate **25** is kinetically accessible to additional boron hydride.

Hydroxy diketo ester **28** (R = $(CH_2)_3Ph$) was selected for our initial stereopropagation studies. The precursor to this substrate, **27**, was synthesized from β-keto ester **1** according to the acylation protocol recently described by Harris.[28] The resultant diketo ester **27** was enolized with 3.5 equiv of lithium diisopropylamide, and the trienolate was quenched with isobutyraldehyde to afford a 55% yield of **28** after chromatography on deactivated silica gel. Each of the four possible diastereomeric reduction products **29–32** was then synthesized and unambiguously characterized both as their triol esters and derived lactones (Schemes VIII and IX).

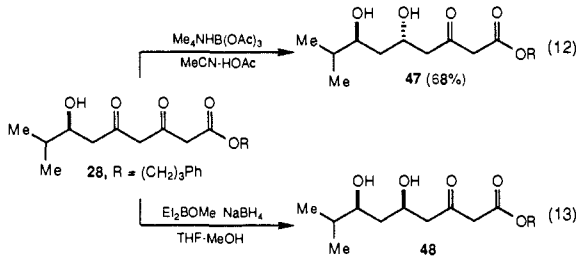



Anti and syn diol esters **3** and **4**, prepared by zinc borohydride reduction of **2**, were separated chromatographically. The anti diol ester **3** was silylated with *tert*-butyldimethylsilyl chloride in dimethylformamide, and the resultant disilyl ester was reduced with DIBAL-H in dichloromethane to give the corresponding aldehyde **34** (Scheme VIII). This aldehyde was then treated with the lithium enolate of 3-phenylpropyl acetate to provide the doubly protected triol ester **35** as a 1:1 mixture of $C_3$ diastereomers. This mixture was separated chromatographically and the silyl groups removed with HF/pyridine to afford the Anti–Anti triol ester **29** and the Anti–Syn triol ester **30**. Synthesis of the Syn–Syn and Syn–Anti triol esters **31** and **32** proceeded in an analogous fashion (Scheme IX). In order to unequivocally establish the stereochemical identity of the triol esters **29–32**, each diastereomer was lactonized with HF in acetonitrile. The stereochemical assignments in each case are based on the $^1H$ coupling constants of the resultant lactones (see the Experimental Section for Tables V and VI). Complementary nuclear Overhauser enhancement (NOE) experiments performed on the corresponding benzoate esters, **38b**, **39b**, **45b**, and **46b**, are fully consistent with each of these assignments. The four diastereomeric triol esters proved to be easily separable by HPLC and could be analyzed without derivatization.

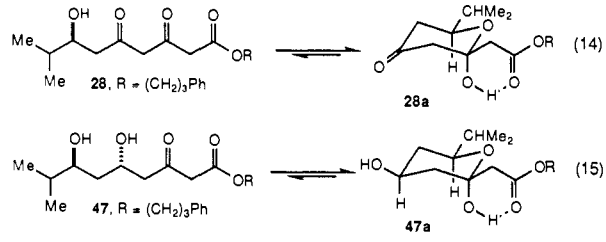
When hydroxy diketo ester **28** was treated with excess tetramethylammonium triacetoxyborohydride (ca. 0.1 M) in 1:1 acetonitrile/acetic acid at ambient temperature (30 min) a mixture of products was formed, of which the major product proved to be the mono-reduced anti dihydroxy keto ester **47** which was isolated in 68% yield (eq 12). The desired triol esters were obtained as a mixture of all four diastereomers collectively in 9% yield. The complete absence of syn dihydroxy keto ester **48**, prepared independently with the Merck[16b] procedure for syn-selective β-hydroxy ketone reduction (eq 13), seemed to indicate that the initial reduction was indeed proceeding with high anti diastereoselectivity. Nonetheless, it was clear that the mono-reduction product **47** was not participating in subsequent relay reduction. Resubmission of **47** to the above reaction conditions led simply to the isolation of starting material.

These results prompted us to examine ring–chain tautomerism in both the starting material **28** (eq 14) and the mono-reduction product **47** (eq 15). $^1H$ NMR spectroscopic analysis of **28** revealed that it exists as a mixture of four major tautomers in both chlo-

(26) See for example: Steinberg, H. *Organoboron Chemistry*; John Wiley and Sons: New York, 1964; Vol. 1, Chapter 4.
(27) See for example: ref 26, Chapters 5 and 6.
(28) Oster, T. A.; Harris, T. M. *Tetrahedron Lett.* **1983**, *24*, 1851–1854.

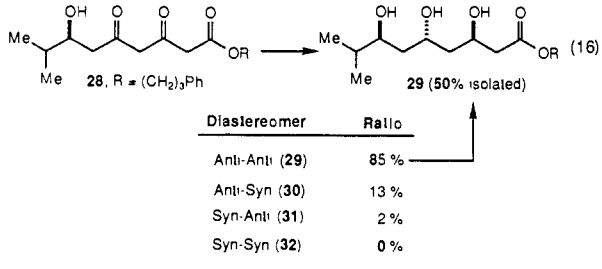



roform and acetic acid solution. The pale-yellow tautomeric




mixture can be crystallized from pentane containing a small amount of ether to give colorless needles, mp 43.0–43.3 °C. Dissolution of these crystals in freshly distilled deuteriochloroform followed by $^1$H NMR analysis revealed the presence of a single tautomer easily identifiable as cyclic tautomer **28a**. Upon standing in this solution, or much more rapidly in the presence of acetic acid, **28a** reaches equilibrium with the other ring–chain and proton tautomers and constitutes the major component (~70% in $CDCl_3$) of the tautomeric mixture. A similar study was carried out with the primary reduction product **47**. In $CDCl_3$ or acetic-$d_4$ acid solution, diol ester **47** exists *exclusively* in its cyclic tautomeric form **47a** (eq 15). This is hardly surprising since tautomer **47a** contains three equatorial substituents displayed about its cyclic hemiketal moiety and a strong intramolecular hydrogen bond. *These results, taken together, suggest that the initial directed reduction to give* **47** *(or* **47a***) could occur either from the acyclic tautomer* **28** *or its cyclic counterpart* **28a**.

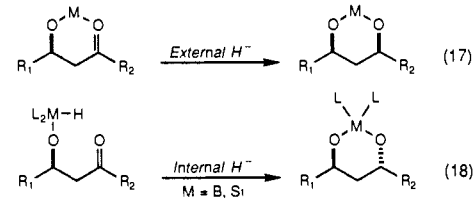
The initial series of reductions reported above employed dilute solutions (~0.1 M) of reagent. When hydroxy diketo ester **28** was treated with a 1.7 M solution of tetramethylammonium triacetoxyborohydride in neat acetic acid (30 min, ambient temperature) the desired triol esters were isolated in 63% yield together with 30% yield of monoreduced anti diol **47**. The triols were present in a ratio of 41:6.1:1:0 (eq 16), corresponding to an initial reduction diastereoselectivity of 47:1 and a second reduction selectivity from the anti diol of 7:1. Anti–anti triol **29** was isolated from this reaction in 50% yield after flash chromatography. These conditions, although not optimum with regard to conversion, are the best that have been found to date. We view the development of relay reactions, such as those illustrated below, to be a worthwhile objective, and the further development of these and related synthetic operations will be reported in due course.



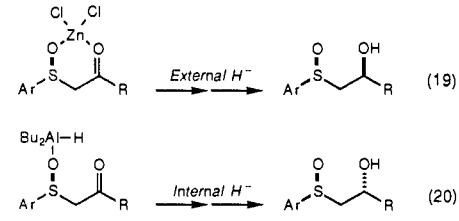

## Conclusions

Tetramethylammonium triacetoxyborohydride reduces acyclic β-hydroxy ketones with high anti diastereoselectivity. In every case that has been examined, good to excellent yields of diastereomerically homogeneous diols are easily obtained. These reductions proceed by an apparent rate-determining acid-promoted exchange of the substrate hydroxyl group for an acetate of the triacetoxyborohydride anion which precedes the reduction step. The reduction of ketones proceeds at convenient rates only if it can do so by intramolecular hydride delivery; acyclic β-hydroxy ketones are reduced rapidly and with unaltered diastereoselectivity even in 1:1 acetone/acetic acid solvent. We have established the suitability of these borohydride reagents for use in stereopropagating reductions. Such reactions provide unique and singularly efficient entries into the synthesis of stereoregular polyacetates.

With regard to stereoselectivity, a general pattern is emerging in the reduction of acyclic β-hydroxy ketones. Numerous examples of chelate-controlled addition of hydride reagents have firmly established a general preference for syn diastereoselectivity in the reduction of α-unsubstituted β-hydroxy ketones (eq 17). Sub-




stitution in the α-position either reinforces (syn-aldol adduct) or disrupts (anti-aldol adduct) this trend.[16] On the other hand, intramolecular delivery of hydride directed by the β-hydroxyl group leads to anti diastereoselective reduction (eq 18) as demonstrated both here (M = B) and elsewhere (M = Si).[17] Such intramolecular reactions appear to be characterized by diastereoselectivities essentially independent of α-substitution stereochemistry. The related reductions of β-arylsulfinyl ketones reported by Solladie using either $ZnCl_2$/DIBAL-H (syn diastereoselectivity) (eq 19) or DIBAL-H (anti diastereoselectivity) (eq 20) closely parallel these trends, and one may now speculate, with somewhat more confidence, that these reductions might proceed via the illustrated intermediates.[29]




## Experimental Section

Melting points are uncorrected. Tetrahydrofuran, diethyl ether, triethylamine, benzene, and toluene were distilled from sodium/benzophenone ketyl. Dichloromethane, diisopropylamine, and acetonitrile were distilled from calcium hydride. Acetic acid was dried by azeotropic distillation with benzene and subsequent fractional distillation from chromium trioxide. Methanol was distilled from magnesium methoxide. Dimethyl sulfoxide was distilled from calcium hydride and stored over 4 Å molecular sieves. Unless otherwise noted, all nonaqueous reactions were carried out under a dry nitrogen atmosphere with flame-dried glassware.

**Sodium Triacetoxyborohydride.** A 100-mL Schlenk flask equipped with a Schlenk filter was charged with 186 mg (4.93 mmol) of sodium borohydride and 50 mL of anhydrous benzene. The slurry was cooled to 10 °C and 860 μL (15.0 mmol, 3.04 equiv) of anhydrous acetic acid was added dropwise so as to maintain an internal temperature no higher than 20 °C. Hydrogen evolution was measured with a gas buret. After addition of acetic acid was complete the mixture was allowed to warm to ambient temperature and stirred at that temperature for 8 h. Hydrogen evolution had ceased at 330 mL (theoretical for 3.00 equiv is 331 mL) after 5 h. The colorless slurry was filtered and the resultant white powder washed with three 20-mL portions of freshly distilled, anhydrous ether. The combined ether filtrates did not liberate hydrogen when treated with 1 N aqueous hydrochloric acid. The powder was held under vacuum over night to afford 961 mg (92%) of analytically pure sodium triacetoxyborohydride as a white, hygroscopic solid: IR (Nujol) 2500, 1682, 1375, 1316, 1149, 1023, 962, 845 cm$^{-1}$; $^1$H NMR (250 MHz,

(29) (a) Solladie, G.; Demailly, G.; Greck, C. *J. Org. Chem.* **1985**, *50*, 1552–1554. (b) Solladie, G.; Frechou, C.; Demailly, G.; Greck, C. *J. Org. Chem.* **1986**, *51*, 1912–1914. (c) Solladie, G.; Frechou, C.; Demailly, G. *Tetrahedron Lett.* **1986**, *27*, 2867–2870. (d) Solladie, G.; Hutt, J.; Frechou, C. *Tetrahedron Lett.* **1987**, *28*, 61–64.

$CD_3CN$) $\delta$ 1.88 (s, 9 H, $CH_3CO_2B$); $^{13}C$ NMR (75.5 MHz, $CD_3CN$) $\delta$ 175.25, 23.36; $^{11}B$ NMR (96.3 MHz, $CD_3CN$) $\delta$ −1.47 (d, $J_{BH}$ = 122 Hz).

Anal. Calcd for $C_6H_{10}O_6BNa$: C, 34.00; H, 4.76. Found: C, 33.87; H, 4.79.

**Tetramethylammonium Borohydride.**[15] To 52.5 g (1.39 mol) of sodium borohydride was added 127 g (506 g of a 25% solution in water, 1.39 mol) of tetramethylammonium hydroxide. The mixture was diluted to 1 L with deionized water and concentrated in vacuo. The white solid was suspended in 500 mL of 95% ethanol and filtered. The filter cake was resuspended in 200 mL of 95% ethanol and filtered; this process was repeated a total of ten times. The mixture was dried overnight in vacuo (≤20 μm) at 80 °C to give 100.0 g (81%) of a colorless, microcrystalline solid. The solid can be recrystallized from hot acetonitrile or 2-propanol, but is generally not purified before use.

**Tetramethylammonium Triacetoxyborohydride.** A 500-mL Schlenk flask equipped with a Schlenk filter was charged with 10.8 g (121 mmol) of tetramethylammonium borohydride and 300 mL of freshly distilled benzene. The mixture was cooled to 10 °C, and 24.3 mL (425 mmol) of anhydrous acetic acid was added dropwise over 15 min. The mixture was warmed to ambient temperature, stirred for 3 h, and filtered. The white semisolid was washed with five 100-mL portions of freshly distilled ether and dried overnight in vacuo to give the title compound as a free-flowing, exceedingly hygroscopic white powder: IR ($CHCl_3$) 2473, 1695, 1490, 1378, 1308, 1118, 1025, 954, 850 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 4.4 (br, 1 H, B*H*), 3.34 (s, 12 H, $(CH_3)_4N$), 2.02 (s, 9 H, $CH_3CO_2B$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 172.60, 55.63, 23.24; $^{11}B$ NMR (96.3 MHz, $CD_3CN$) 0.71 ppm (d, 1 B, *B*H, $J_{BH}$ = 136 Hz).

Anal. Calcd for $C_{10}H_{22}NO_6B$: C, 45.65; H, 8.43. Found: C, 45.74; H, 8.36.

This analytically pure $Me_4NHB(OAc)_3$ powder proved to be satisfactory for all applications but could be recrystallized from ethyl acetate/dichomethane as follows. The powder was dissolved in a small portion of freshly distilled, anhydrous dichloromethane in a Schlenk flask equipped with a Schlenk filter (slightly cloudy solution). Freshly distilled, anhydrous ethyl acetate was added with gentle warming (≤35 °C) until the $Me_4NHB(OAc)_3$ began to come out of solution. The mixture was filtered rapidly and allowed to cool slowly to −20 °C to give colorless, prismatic needles: mp 96.5–98.0 °C.

Anal. Calcd for $C_{10}H_{22}NO_6B$: C, 45.65; H, 8.43. Found: C, 45.64; H, 8.39.

**3-Phenylpropyl 3-Oxobutanoate (1).** To a stirred solution of 33.0 g (242 mmol) of 3-phenylpropanol and 1 mL of triethylamine in 400 mL of anhydrous dichloromethane at 40 °C was added dropwise over 2 h a solution of 21.5 g (255 mmol) of freshly distilled diketene in 150 mL of anhydrous dichloromethane. After 3 h, an additional 8.58 g (102 mmol) of diketene in 12 mL of anhydrous dichloromethane was added. After 20 min the mixture was poured into a separatory funnel containing ice and 100 mL of aqueous 1 N sodium hydrogen sulfate. The layers were shaken vigorously and separated. The organic layer was dried with anhydrous magnesium sulfate and concentrated in vacuo to give an orange oil. The mixture was purified by vacuum distillation (bp 145–148 °C at 50 μm) to give 44.3 g (83%) of the title compound as a pale yellow oil: $R_f$ 0.32 (20% ethyl acetate in hexane); IR (neat) 3089, 3065, 3030, 2960, 2861, 1742, 1720, 1650, 1607, 1500, 1455, 1411, 1360, 1315, 1262, 1173, 1150, 1033, 748, 700 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 5.02 (s), 4.17 (t, 2 H, $CH_2O$), 3.46 (s, ca. 2 H, $COCH_2CO_2R$), 2.70 (t, 2 H, $CH_2Ph$), 2.28 (s, 3 H, $CH_3$), 1.98 (m, 2 H, $CH_2CH_2Ph$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 200.00, 166.81, 140.80, 128.17, 125.79, 64.33, 49.69, 31.78, 29.88, 29.71.

**3-Phenylpropyl 5-Hydroxy-6-methyl-3-oxoheptanoate (2).** To a stirred solution of 5.51 g (54.5 mmol) of diisopropylamine in 200 mL of anhydrous tetrahydrofuran at −78 °C was added 3.05 g (18.2 mL of a 1.60 M solution in hexane) of *n*-butyllithium. The mixture was allowed to warm to 0 °C and stir for 30 min at that temperature. A solution of 5.00 g (22.7 mmol) of 3-phenylpropyl 3-oxobutanoate in 50 mL of anhydrous tetrahydrofuran was added dropwise, and the mixture was stirred for 2 h at 0 °C. The mixture was cooled to −78 °C and 1.72 g (23.8 mmol) of 2-methylpropanal was added in one portion. The reaction was quenched after 5 min by addition of excess aqueous 1 N sodium hydrogen sulfate. The mixture was extracted twice with 70% ether in hexanes, and the combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo to give 6.10 g of an orange oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 30% ethyl acetate in hexane, 100-mL fractions). This afforded 2.91 g (44%) of the title compound as a pale yellow oil: $R_f$ 0.25 (30% ethyl acetate in hexane); IR (neat) 3490 (br), 3095, 3072, 3035, 2975, 1750, 1720, 1503, 1340, 752, 707 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.35–7.15 (m, 5 H, aromatic C*H*), 4.18 (t, 2 H, $CH_2O$), 3.86 (m, 1 H, $R_2CHOH$), 3.49 (s, 2 H, $ROCOCH_2CO$), 2.70 (m, 4 H, $CH_2CO$, $CH_2Ph$), 2.00 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.72 (m, 1 H, $(CH_3)_2CH$), 0.93 (t, 6 H, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 203.54, 166.92, 140.83, 128.30, 128.22, 125.91, 72.12, 64.60, 49.75, 46.78, 33.12, 31.89, 29.88, 18.20, 17.43.

Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.52; H, 8.18.

**3-Phenylpropyl (3*S**,5*S**)-3,5-Dihydroxy-6-methylheptanoate (3) and 3-Phenylpropyl (3*R**,5*S**)-3,5-Dihydroxy-6-methylheptanoate (4), Authentic Samples.** To a solution of 880 mg (3.01 mmol) of 3-phenylpropyl-5-hydroxy-6-methyl-3-oxoheptanoate in 10 mL of anhydrous dichloromethane at −78 °C was added 285 mg (21.5 mL of a 0.14 M solution in diethyl ether, 3.00 mmol) of zinc borohydride. The mixture was stirred at −78 °C for 3 h and warmed slowly to ambient temperature. After 1 h the mixture was poured into a separatory funnel containing excess aqueous 1 N sodium hydrogen sulfate. The layers were shaken vigorously and separated. The aqueous layer was extracted with dichloromethane and the combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo. Thin-layer chromatography (using 50% ethyl acetate in hexane as developer) showed two product spots, one at $R_f$ 0.39 and the other at $R_f$ 0.33 in approximately 2:1 ratio. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 40% ethyl acetate in hexane, 100-mL fractions). The syn and anti isomers were separated by medium-pressure liquid chromatography with use of 2 Merck Lobar B columns (40% ethyl acetate in hexane, 20-mL fractions). This afforded 193 mg of the syn isomer as a colorless oil and 77.9 mg of the anti isomer as a colorless oil.

**Syn diol 4:** $R_f$ 0.40 (50% ethyl acetate in hexane); IR (neat) 3420 (br), 3092, 3071, 3035, 2972, 1740, 1502, 1170, 740, 706 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.25 (m, 5 H, aromatic), 4.26 (m, 1 H, $CH(OH)CH_2CO_2R$), 4.14 (t, 2 H, $CH_2O$), 3.87 (s br, 1 H, O*H*), 3.66 (m, 1 H, $CHCH(OH)CH_2$), 3.25 (br s, 1 H, O*H*), 2.69 (t, 2 H, $CH_2Ph$), 2.50 (m, 2 H, $CHCH_2CO_2R$), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.60 (m, 3 H, $(CH_3)_2CH$ and $CH(OH)CH_2CH(OH)$), 0.92 (2d, 6 H, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 172.09, 140.91, 128.27, 128.20, 125.87, 76.68, 69.01, 63.89, 41.95, 38.97, 33.87, 32.00, 29.95, 18.08, 17.23.

Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.35; H, 8.90. Found: C, 68.92; H, 9.02.

**Anti diol 3:** $R_f$ 0.33 (50% ethyl acetate in hexane); IR (neat) 3420 (br), 3093, 3070, 3033, 2972, 1735, 1501, 1170, 750, 705 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic), 4.35 (m, 1 H, $CH(OH)CH_2CO_2R$), 4.13 (t, 2 H, $CH_2O$, $J$ = 6.6 Hz), 3.68 (q, 1 H, $CHOHCH(CH_3)_2$, $J$ = 5.7, 11.53 Hz), 3.41 (br s, 1 H, OH), 2.69 (t, 2 H, $CH_2Ph$, $J$ = 7.29 Hz), 2.57 (dd, 1 H, $CH_2CO_2R$, $J$ = 8.24, 16.46 Hz), 2.50 (dd, 1 H, $CH_2CO_2R$, $J$ = 4.34, 16.43 Hz), 2.35 (br s, 1 H, O*H*), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.68 (m, 1 H, $CH(CH_3)_2$), 1.62 (m, 2 H, $CH_2CH(OH)$), 0.95 (d, 3 H, $CH_3$, $J$ = 6.76), 0.91 (d, 3 H, $CH_3$, $J$ = 6.78 Hz); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 172.70, 141.04, 128.43, 128.32, 126.04, 73.42, 65.93, 64.07, 41.51, 39.42, 33.84, 32.16, 30.09, 18.50, 17.65.

Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.71; H, 8.87.

**(3*S**,5*S**)-3,5-Dihydroxy-6-methylheptanoic Acid δ-Lactone (3a).** To a stirred solution of 109 mg (0.37 mmol) of 3-phenylpropyl *anti*-3,5-dihydroxy-6-methylheptanoate (**3**) in 20 mL of methanol was added 3 drops of aqueous concentrated hydrochloric acid. After 30 min the mixture was neutralized with saturated aqueous sodium bicarbonate and concentrated in vacuo. The mixture was diluted with water and extracted with dichloromethane three times. The combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo. The mixture was dissolved in 20 mL of anhydrous dichloromethane and 10 mg of *p*-toluenesulfonic acid was added. After 30 min the mixture was neutralized with saturated aqueous sodium bicarbonate, and the layers were separated. The aqueous layer was extracted with dichloromethane three times and the combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo. The pale-yellow oil was purified by flash chromatography on silica gel (30 × 180 mm column, 50% ethyl acetate/hexane, 8-mL fractions) to afford 42.2 mg (72%) of the title compound as a colorless oil: IR (neat) 3430 (br), 2978, 2940, 1730, 1475, 1392, 1376, 1256 (s), 1050 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 4.24 (m, 1 H, C*H*OH), 3.99 (ddd, 1 H, C*H*OCO, $J$ = 2.95, 5.55, 12.0 Hz), 2.91 (ddd, 1 H, $CHHCO_2R$, $J$ = 1.46, 5.90, 17.11 Hz), 2.45 (dd, 1 H, $CHHCO_2R$, $J$ = 8.17, 17.11 Hz), 2.21 (dddd, 1 H, CH(OCOR)C*H*H, $J$ = 1.45, 2.91, 5.30, 13.52 Hz), 2.01 (d, 1 H, O*H*, $J$ = 4.15 Hz), 1.93 (m, 1 H, $CH(CH_3)_2$), 1.60 (ddd, 1 H, CH(OCOR)CH*H*, $J$ = 11.5, 12.0, 13.5), 1.01 (t, 6 H, $CH_3$, $J$ = 6.81 Hz); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 171.07, 81.87, 63.94, 39.61, 34.71, 32.39, 17.75, 17.51.

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.75; H, 9.08.

**(3*S**,5*S**)-3-Benzoyl-5-hydroxy-6-methylheptanoic Acid δ-Lactone (3b).** To a solution of 7.6 mg (0.05 mmol) of *anti*-3,5-dihydroxy-6-

methylheptanoic acid δ-lactone (**3a**) in 1.0 mL of anhydrous dichloromethane was added 57 mg (0.72 mmol) of pyridine followed by 81 mg (0.58 mmol) of benzoyl chloride. The mixture was stirred at ambient temperature for 3 h and diluted with dichloromethane. The mixture was washed with aqueous 1 N sodium hydrogen sulfate and then with saturated aqueous sodium bicarbonate. The organic layer was dried with anhydrous magnesium sulfate and concentrated in vacuo. The mixture was purified by flash chromatography on silica gel (10 × 180 mm column, 30% ethyl acetate/hexane, 6-mL fractions) to afford 10.5 mg (83%) of the title compound as a colorless oil: $R_f$ 0.54 (50% ethyl acetate/hexane); $^1$H NMR (300 MHz, $CDCl_3$) 8.02 (m, 2 H, aromatic C*H*), 7.52 (m, 3 H, aromatic C*H*), 5.47 (tt, 1 H, C*H*OBz, $J$ = 6.46, 8.53), 4.11 (ddd, 1 H, C*H*OCOR, $J$ = 2.90, 5.60, 12.00 Hz), 3.06 (ddd, 1 H, C*H*HCO$_2$R, $J$ = 0.89, 6.70, 17.2 Hz), 2.73 (dd, 1 H, CH*H*CO$_2$R, $J$ = 6.46, 17.20 Hz), 2.48 (dddd, 1 H, CH(OBz)C*H*H, $J$ = 0.89, 2.90, 6.23, 13.90 Hz), 1.97 (hp, 1 H, C*H*(CH$_3$)$_2$, $J$ = 6.87 Hz), 1.78 (ddd, 1 H, CH(OBz)CH*H*, $J$ = 8.53, 12.00, 13.90 Hz), 1.02 (2d, 6 H, C*H*$_3$, $J$ = 6.87 Hz).

**(3*R**,5*S**)-3,5-Dihydroxy-6-methylheptanoic Acid δ-Lactone (4a).** The procedure used was identical with that used for the lactonization of 3-phenylpropyl *anti*-3,5-dihydroxy-6-methylheptanoate (**3**). Thus, 109 mg (0.37 mmol) of 3-phenylpropyl *syn*-3,5-dihydroxy-6-methylheptanoate (**4**) was converted to 38.0 mg (65%) of title compound as a colorless oil: IR (neat) 3430 (br), 2978, 2942, 2890, 1728 (br), 1263, 1069, 1052, 1039 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) 4.48 (ddd, 1 H, C*H*OCO, $J$ = 3.1, 5.7, 11.6 Hz), 4.41 (br m, 1 H, C*H*OH), 2.72 (dd, 1 H, C*H*HCO$_2$, $J$ = 4.77, 17.62 Hz), 2.62 (ddd, 1 H, CH*H*CO$_2$, $J$ = 1.58, 3.65, 17.65 Hz), 2.10 (br d, 1 H, O*H*), 1.90 (m, 2 H, C*H*(CH$_3$)$_2$ and CH(OH)C*H*HCHOCO), 1.74 (ddd, 1 H, CH(OH)CH*H*CHOCO, $J$ = 3.38, 11.65, 14.84 Hz), 1.00 (t, 6 H, CH$_3$, $J$ = 6.92 Hz); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 171.14, 80.45, 62.51, 38.60, 32.64, 32.25, 17.76, 17.45.

Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.52; H, 8.83.

**(3*R**,5*S**)-3-Benzoyl-5-hydroxy-6-methylheptanoic Acid δ-Lactone (3b).** The procedure used was identical with that used for the benzoylation of *anti*-3,5-dihydroxy-6-methylheptanoic acid δ-lactone (**3a**). Thus, 9.5 mg (0.06 mmol) of *syn*-3,5-dihydroxy-6-methylheptanoic acid δ-lactone (**4a**) reacted with 101 mg (0.72 mmol) of benzoyl chloride in the presence of 71 mg (0.90 mmol) of pyridine to afford 10.5 mg (67%) of the title compound as a colorless oil: $R_f$ 0.54 (50% ethyl acetate/hexane); $^1$H NMR (300 MHz, $CDCl_3$) 8.03 (m, 2 H, aromatic C*H*), 7.51 (m, 3 H, aromatic C*H*), 5.55 (qn, 1 H, C*H*OBz, $J$ = 3.9 Hz), 4.46 (ddd, 1 H, C*H*OCOR, $J$ = 3.0, 5.6, 11.8 Hz), 2.89 (dd, 2 H, C*H*$_2$CO$_2$R, $J$ = 0.63, 4.68 Hz), 2.22 (m, 1 H, CH(OBz)C*H*H), 1.92 (m, 2 H, CH(OBz)CH*H* and C*H*(CH$_3$)$_2$), 1.02 (t, 6 H, C*H*$_3$).

**Reduction of 3-Phenylpropyl 5-Hydroxy-6-methyl-3-oxoheptanoate (2) with Tetramethylammonium Triacetoxyborohydride (Table II, Entry A).** To a solution of 716 mg (2.72 mmol) of tetramethylammonium triacetoxyborohydride in 1.5 mL of anhydrous acetonitrile was added 1.5 mL of anhydrous acetic acid and the mixture was stirred at ambient temperature for 30 min. The mixture was cooled to −40 °C, and a solution of 98.4 mg (0.34 mmol) of 3-phenylpropyl 5-hydroxy-6-methylheptanoate in 0.5 mL of anhydrous acetonitrile was added via cannula. The mixture was stirred at −40 °C for 18 h. The reaction was quenched with 4 mL of 0.5 N aqueous sodium potassium tartrate and the mixture was allowed to warm slowly to ambient temperature. The mixture was diluted with dichloromethane and washed with aqueous saturated sodium bicarbonate. The aqueous layer was back extracted with dichloromethane four times, and the combined organic layers were washed with saturated aqueous sodium bicarbonate. The aqueous layer was back extracted four times with dichloromethane, and the combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo. The mixture was passed rapidly through a 30 × 180 mm column of silica gel with 50% ethyl acetate in hexane as eluant to give 96.7 mg (99%) of a mixture of diols as a colorless oil. HPLC analysis (1% methanol in dichloromethane, λ = 258, 4 nm) indicated a 95:5 ratio of isomeric diols with the anti isomer as the major constituent. The mixture was separated by flash chromatography on silica gel (20 × 180 mm column, 30% ethyl acetate in hexane, 8-mL fractions) to afford 91.5 mg (93%) of the anti diol as a colorless oil (>99% HPLC).

**3-Phenylpropyl 3-Hydroxy-6-methyl-5-oxoheptanoate (Table II, Entry B Reactant).** To a solution of 1.5 g (9.48 mmol) of ethyl 4-methyl-3-oxopentanoate in 150 mL of freshly distilled toluene was added 100 mg of *p*-toluenesulfonic acid and 15 mL of ethylene glycol. The mixture was slowly distilled with periodic additions of anhydrous toluene so as to keep the volume at around 100 mL. When 200 mL of distillate had been collected (around 3 h) the mixture was cooled and washed twice with saturated aqueous sodium bicarbonate and once with water. The mixture was dried with anhydrous magnesium sulfate and concentrated in vacuo to give 1.55 g (81%) a colorless oil which was used without purification. To a solution of the above compound in 20 mL of anhydrous tetrahydrofuran at −78 °C was added 206 mg (7.6 mL of a 1 M solution in ether) of lithium aluminum hydride. After 30 min the mixture was allowed to warm to ambient temperature. After 30 min the mixture was recooled to −78 °C and 300 μL of water was added followed by 900 μL of 15% aqueous sodium hydroxide solution and finally 300 μL of water. The mixture was stirred for 15 min, diluted with 100 mL of dichloromethane, filtered, and concentrated in vacuo to give 1.16 g (95%) of a colorless oil ($R_f$ = 0.12, 30% ethyl acetate in hexane). To a solution of 2.47 g (31.6 mmol) of anhydrous dimethyl sulfoxide in 35 mL of anhydrous dichloromethane at −78 °C was added 2.00 g (15.8 mmol) of oxallyl chloride and the mixture was stirred for 15 min. A solution of 2.30 g (14.36 mmol) of the above alcohol in 5 mL of anhydrous dichloromethane was added and the mixture was stirred for 15 min. Triethylamine (5.81 g, 57.4 mmol) was added and the mixture was warmed to −23 °C ($CO_2$/$CCl_4$). After 30 min, thin-layer chromatography showed the oxidation to be complete. The mixture was poured into excess aqueous 1 N sodium hydrogen sulfate and extracted with pentane. The organic layer was washed twice with aqueous 1 N sodium hydrogen sulfate, dried with anhydrous magnesium sulfate, and concentrated in vacuo. To a solution of 1.92 g (19.0 mmol) of diisopropylamine in 25 mL of anhydrous tetrahydrofuran at −78 °C was added 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of *n*-butyllithium. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.82 g (15.8 mmol) of 3-phenylpropyl acetate in 5.0 mL of anhydrous tetrahydrofuran was added and the mixture was warmed to 0 °C. After 1 h the mixture was cooled to −78 °C and a solution of 2.30 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrahydrofuran was added via cannula. After 1 min the mixture was poured into excess aqueous 1 N sodium hydrogen sulfate and diluted with ether. The mixture was washed twice with 1 N sodium hydrogen sulfate, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 5.05 g of a pale yellow oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 30% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal ($R_f$ 0.45, 50% ethyl acetate in hexane). To a solution of 3.01 g (8.95 mmol) of the above hydroxy ketal in 250 mL of 20% water in acetone was added 250 mg of *p*-toluenesulfonic acid. The mixture was refluxed for 7 h and cooled. The mixture was poured into ice and neutralized with saturated aqueous sodium bicarbonate. The mixture was concentrated in vacuo and extracted three times with dichloromethane. The combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo to afford 2.61 g (100%) of a pale yellow oil: $R_f$ 0.33 (30% ethyl acetate in hexane); IR (neat) 3500 (br), 3091, 3070, 3037, 2980, 2943, 1740, 1720, 1502, 1472, 1460, 751, 707 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic), 4.47 (m, 1 H, CH$_2$C*H*(OH)CH$_2$), 4.13 (t, 2 H, C*H*$_2$O, $J$ = 6.6 Hz), 3.49 (d, 1 H, O*H*, $J$ = 3.7 Hz), 2.60 (m, 6 H, COC*H*$_2$CH(OH)C*H*$_2$ and C*H*$_2$Ph), 1.97 (hp, 1 H, C*H*(CH$_3$)$_2$, $J$ = 6.94 Hz), 1.11 (d, 6 H, C*H*$_3$, $J$ = 6.94 Hz); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 213.92, 171.56, 140.95, 128.28, 128.22, 125.88, 64.45, 63.88, 45.79, 41.30, 40.79, 32.01, 29.98, 17.75.

Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.71; H, 8.31.

**Reduction of 3-Phenylpropyl 3-Hydroxy-6-methyl-5-oxoheptanoate with Tetramethylammonium Triacetoxyborohydride (Table II, Entry B).** The procedure used was identical with that used for the reduction of 3-phenylpropyl 5-hydroxy-6-methyl-3-oxoheptanoate (Table II, entry A). Thus 100 mg (0.34 mmol) of 3-phenylpropyl 3-hydroxy-6-methyl-5-oxoheptanoate was caused to react with 750 mg (2.9 mmol) of tetramethylammonium triacetoxyborohydride to afford 98 mg (98%) of a mixture of diols as a colorless oil. HPLC analysis (1% methanol in dichloromethane, λ = 258, 4 nm) indicated a 95:5 ratio of isomeric diols with the anti isomer as the major constituent. The mixture was separated by flash chromatography on silica gel (20 × 180 mm column, 30% ethyl acetate in hexane, 8-mL fractions) to afford 90 mg (90%) of the anti diol as a colorless oil (>99% HPLC).

**3-Phenylpropyl 6-Methyl-3,5-dioxoheptanoate (Table II, Entry C Reactant).** To a solution of 3.65 g (36.1 mmol) of diisopropylamine in 35 mL of anhydrous tetrahydrofuran at −78 °C was added 1.97 g (19.2 mL of a 1.60 M solution in hexane, 30.8 mmol) of *n*-butyllithium. The mixture was warmed to 0 °C and stirred for 30 min. A solution of 3.31 g (15.0 mmol) of 3-phenylpropyl 3-oxobutanoate in 10.0 mL of anhydrous tetrahydrofuran was added dropwise over 15 min. After 2 h at 0 °C a solution of 2.16 g (16.5 mmol) of *N*-methoxy-*N*,2-dimethylpropionamide in 10 mL of anhydrous tetrahydrofuran was added and the mixture was stirred at ambient temperature for 5 h. The mixture was concentrated in vacuo and diluted with ether, acidified with 1 N aqueous hydrochloric acid, and extracted with ether (3×). The combined organic layers were washed three times with 1 N aqueous sodium hydrogen

sulfate, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 4.22 g of an orange oil. The mixture was purified by flash chromatography on silica gel (50 × 180 mm column, 15% ethyl acetate in hexane, 20-mL fractions) to afford 916 mg (21%) of the title compound as a pale yellow oil: $R_f$ 0.48 (30% ethyl acetate in hexane); IR (neat) 3097, 3073, 3038, 1981, 2943, 1748, 1610 (br), 1504, 1460, 1267, 750, 706 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic), 5.62 (s, enol C*H*), 4.17 (t, 2 H, $CH_2O$, $J$ = 6.5 Hz), 3.79 (s), 3.58 (s), 3.35 (s, $COCH_2CO$), 2.69 (t, 2 H, $CH_2Ph$, $J$ = 7.32 Hz), 2.49 (hp, 1 H, $CH(CH_3)_2$, $J$ = 6.91 Hz), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.16 (d, $CH_3$, $J$ = 6.94 Hz); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 197.35, 187.47, 167.34, 140.89, 128.24, 125.91, 97.61, 64.60, 64.48, 54.18, 49.14, 45.13, 41.68, 36.15, 31.92, 29.94, 19.10, 17.58.

Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.26; H, 7.51.

**Reduction of 3-Phenylpropyl 6-Methyl-3,5-dioxoheptanoate with Tetramethylammonium Triacetoxyborohydride (Table II, Entry C).** Tetramethylammonium triacetoxyborohydride (1.36 g, 5.17 mmol) was dissolved in 30 mL of anhydrous acetic acid, and the solution was stirred for 30 min. A solution of 316 mg (1.09 mmol) of 3-phenylpropyl 6-methyl-3,5-dioxoheptanoate in 4.0 mL of anhydrous acetic acid was added and the mixture was stirred at ambient temperature for 5 h. The reaction was quenched with 10 mL of a 0.5 M solution of aqueous sodium potassium tartrate. The mixture was poured onto ice, neutralized with saturated aqueous sodium bicarbonate, and extracted with dichloromethane (3×). The aqueous layer was saturated with sodium chloride and extracted with first dichloromethane and then ethyl acetate. The combined organic layers were dried with anhydrous magnesium sulfate and concentrated in vacuo to give 315 mg (98%) of a mixture of diols as a colorless oil. HPLC analysis (1% methanol in dichloromethane, λ = 258, 4 nm) indicated that the ratio of the anti to syn isomers was 92:8. The mixture was purified by flash chromatography on silica gel (30 × 180 mm column, 30% ethyl acetate in hexane, 15-mL fractions) to give 220 mg (69%) of the pure (>99% by HPLC) anti diol as a colorless oil.

**5-Hydroxy-2,6-dimethyl-3-heptanone (Table II, Entry D Reactant).** To a solution of 3.13 mL (22.4 mmol, 1.20 equiv) of diisopropylamine in 40.0 mL of anhydrous THF at −78 °C was added 13.2 mL (1.56 M in hexanes, 20.6 mmol, 1.10 equiv) of *n*-butyllithium. The mixture was stirred for 30 min at 0 °C and recooled to −78 °C. A solution of 2.00 mL (16.7 mmol) of methyl isopropyl ketone in 10 mL of anhydrous THF was added dropwise over 5 min and the mixture was stirred for 1 h at −78 °C. Isobutyraldehyde (1.87 mL, 20.6 mmol, 1.1 equiv) was added and the mixture was stirred for 5 min and poured into saturated aqueous ammonium chloride. The mixture was extracted with dichloromethane (4 × 100 mL) and the combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The mixture was purified by flash chromatography on silica gel (15% ethyl acetate/hexane, 60 × 180 mm column, 125-mL fractions) to give 2.60 g (88%) of the title compound as a colorless oil: $R_f$ 0.22 (15% ethyl acetate/hexane); IR (film) 3500 (br), 2970, 2940, 2880, 1708, 1470, 1387, 1370, 1060, 1037, 1001 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 3.79 (m, 1 H, C*H*OH), 3.10 (d, 1 H, $J$ = 3.2 Hz, O*H*), 2.46–2.69 (m, 3 H, $CH_2C$=OC*H*), 1.68 (m, 1 H, C*H*CHOH), 1.10 (d, 6 H, $J$ = 6.9 Hz, $CH_3$), 0.94 (d, 3 H, $J$ = 6.8 Hz, $CH_3$), 0.92 (d, 3 H, $J$ = 6.8 Hz, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 205.00, 71.99, 43.59, 41.17, 32.88, 18.12, 17.63, 17.33.

Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.22; H, 11.36.

**Reduction of 5-Hydroxy-2,6-dimethyl-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table II, Entry D).** To a solution of 1.31 g (4.98 mmol) of tetramethylammonium triacetoxyborohydride in 4.0 mL of anhydrous acetonitrile and 4.0 mL of anhydrous acetic acid at −40 °C was added a solution of 165 mg (1.04 mmol) of 5-hydroxy-2,6-dimethyl-3-heptanone in 1.0 mL of anhydrous acetonitrile via cannula. The flask formerly containing the ketone was rinsed with two additional 1.0-mL portions of anhydrous acetonitrile and these were added to the reaction mixture. The mixture was warmed to −20 °C and stirred for 5 h. The reaction was quenched with 500 μL of 4-hydroxy-2-butanone and the mixture was warmed to room temperature and stirred for 30 min. The mixture was diluted with 10 mL of acetonitrile and 10 mL of glycerol and stirred for 30 min. The mixture was concentrated in vacuo, basified with 2 N aqueous sodium hydroxide, and extracted six times with ether. After each extraction a small amount of sodium chloride was added to the aqueous layer. The combined organic layers were diluted 1:1 with pentane, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 249 mg of a colorless solid. The mixture was purified by flash chromatography on silica gel (20 × 180 mm column, 30% ethyl acetate in hexanes, 6-mL fractions) to give 156 mg (95%) of a mixture of diols as a colorless, crystalline solid. A small portion was benzoylated (PhCOCl/DMAP/$CH_2Cl_2$, 18 h, ambient temperature) and analyzed by HPLC (2% *tert*-butyl methyl ether/isooctane, λ = 226, 4 nm). Thus the mixture was shown to be 96:4 anti:syn. The mixture was recrystallized from hexanes to give 143 mg (86%) of the pure anti diol (>99% by HPLC) as colorless needles: $R_f$ 0.23 (30% ethyl acetate in hexanes); mp 79.0–80.0 °C; IR ($CHCl_3$) 3620, 3460 (br), 2961, 2873, 1467, 1387, 1368, 1050 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 3.65 (m, 2 H, C*H*OH), 2.20 (d, 2 H, O*H*, $J$ = 4.84 Hz), 1.71 (hp, 2 H, $J$ = 6.6, 6.66 Hz), 1.60 (dd, 2 H, $CH_2$, $J$ = 5.13, 6.35 Hz), 0.97 (d, 3 H, $CH_3$, $J$ = 6.68), 0.91 (d, 3 H, $CH_3$, $J$ = 6.75 Hz); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 73.99, 36.56, 33.66, 18.56, 17.97.

Anal. Calcd for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.34; H, 12.51.

**(4*R**,5*S**)-5-Hydroxy-2,4,6-trimethyl-3-heptanone (Table III, Entry B Reactant) and (4*S**,5*S**)-5-Hydroxy-2,4,6-trimethyl-3-heptanone (Table III, Entry A Reactant).** To a solution of 4.50 mL (36.4 mmol) of ethyl isopropyl ketone in 200 mL of anhydrous dichloromethane at −78 °C was added 40.1 mL (1 M in dichloromethane, 40.1 mmol, 1.10 equiv) of dibutylboryl triflate followed by 6.13 mL (43.7 mmol, 1.20 equiv) of triethylamine. The mixture was stirred for 1 h at 0 °C and recooled to −78 °C. Isobutyraldehyde (4.30 mL, 47.4 mmol, 1.3 equiv) was added and the mixture stirred at 0 °C for 1 h. The reaction was quenched with 160 mL of pH 7 buffer and concentrated in vacuo. The slurry was diluted with 200 mL of methanol and 200 mL of 30% hydrogen peroxide was added dropwise over 30 min. After 1.5 h at 0 °C, the mixture was concentrated in vacuo, diluted with water, and extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 4.5 g of yellow oil. The mixture was purified by MPLC (two Merck Lobar C columns, 10% *tert*-butyl methyl ether/hexane, 125-mL fractions) to give 2.5 g of pure threo aldol adduct as a colorless oil and 1.5 g of a mixture of erythro and threo adducts. The mixture was separated by MPLC (Merck Lobar C column, 10% *tert*-butyl methyl ether/hexane, 125-mL fractions) to give 322 mg of the pure erythro aldol adduct as a colorless oil.

**Anti aldol adduct**: $R_f$ 0.53 (30% *tert*-butyl methyl ether/hexane); IR (film) 3500 (br), 2974, 2942, 2882, 1710, 1470, 1387, 1017, 997 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 3.44 (dt, 1 H, $J$ = 5.0, 6.9 Hz, C*H*OH), 2.93 (quintet, 1 H, $J$ = 7.0 Hz, CHOHC*H*=O), 2.75 (heptet, 1 H, $J$ = 7.0 Hz, C=OC*H*$(CH_3)_2$), 2.54 (d, 1 H, $J$ = 7.0 Hz, O*H*), 1.72 (m, 1 H, CHOHC*H*$(CH_3)_2$), 1.12 (d, 3 H, $J$ = 7.1 Hz, $CH_3$), 1.11 (d, 3 H, $J$ = 6.9 Hz, $CH_3$), 1.10 (d, 3 H, $J$ = 6.9 Hz, $CH_3$), 0.96 (d, 3 H, $J$ = 6.8 Hz, $CH_3$), 0.92 (d, 3 H, $J$ = 6.7 Hz, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 201.04, 78.17, 46.60, 40.80, 30.16, 19.74, 17.69, 15.46, 14.32.

Anal. Calcd for $C_{10}H_2O_2$: C, 69.72; H, 11.70. Found: C, 69.52; H, 11.61.

**Syn aldol adduct**: $R_f$ 0.44 (30% *tert*-butyl methyl ether/hexane); IR (film) 3500 (br), 2970, 2938, 2878, 1702, 1469, 1385, 1369, 1010, 990 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 3.45 (dt, 1 H, $J$ = 2.2, 8.2 Hz, C*H*OH), 3.02 (d, 1 H, $J$ = 2.2 Hz, O*H*), 2.93 (dq, 1 H, $J$ = 2.7, 7.2 Hz, CHOHC*H*=O), 2.75 (heptet, 1 H, $J$ = 7.0 Hz, C=OC*H*$(CH_3)_2$), 1.66 (m, 1 H, CHOHC*H*$(CH_3)_2$), 1.11 (d, 3 H, $J$ = 7.0 Hz, $CH_3$), 1.10 (d, 6 H, $J$ = 7.1 Hz, $CH_3$), 1.02 (d, 3 H, $J$ = 6.6 Hz, $CH_3$), 0.87 (d, 3 H, $J$ = 6.7 Hz, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 216.70, 76.22, 45.29, 39.72, 30.47, 18.92, 18.54, 18.22, 17.88, 9.70.

Anal. Calcd for $C_{10}H_2O_2$: C, 69.72; H, 11.70. Found: C, 69.71; H, 11.78.

**Reduction of (4*S**,5*S**)-5-Hydroxy-2,4,6-trimethyl-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table III, Entry A).** To a solution of 1.23 g (4.68 mmol) of tetramethylammonium triacetoxyborohydride in 4.0 mL of anhydrous acetonitrile and 4.0 mL of anhydrous acetic acid at −40 °C was added a solution of 173 mg (1.01 mmol) of *threo*-5-hydroxy-2,4,6-trimethyl-3-heptanone in 1.0 mL of anhydrous acetonitrile via cannula. The flask formerly containing the ketone was rinsed with two additional 1.0-mL portions of anhydrous acetonitrile and these were added to the reaction mixture. The mixture was warmed to −20 °C and stirred for 18 h and then warmed to ambient temperature and stirred for 2 h. The reaction was quenched with 500 μL of 4-hydroxy-2-butanone and stirred for 30 min. The mixture was diluted with 10 mL of acetonitrile and 10 mL of glycerol and stirred for 30 min. The mixture was concentrated in vacuo, basified with 2 N aqueous sodium hydroxide, and extracted six times with ether. After each extraction a small amount of sodium chloride was added to the aqueous layer. The combined organic layers were diluted 1:1 with pentane, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 279 mg of a colorless solid. The mixture was purified by flash chromatography on silica gel (20 × 180 mm column, 30% ethyl acetate in hexanes, 6-mL fractions) to give 166 mg (96%) of a mixture of diols as a colorless crystalline solid. A small portion was benzoylated (PhCOCl/DMAP/$CH_2Cl_2$, 18 h, 50 °C) and analyzed by HPLC (2% *tert*-butyl methyl ether/isooctane, λ = 226, 4 nm). Thus the mixture was shown to be

97.5:2.5 anti:syn. The mixture was recrystallized from hexanes to give 161 mg (92%) of the pure anti diol (>99% by HPLC) as colorless needles.

**Reduction of (4*S**,5*R**)-5-Hydroxy-2,4,6-trimethyl-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table III, Entry B).** The procedure used was identical with that used for the reduction of (4*S**,5*S**)-5-hydroxy-2,4,6-trimethyl-3-heptanone (Table III, entry A). Thus, 151 mg (0.88 mmol) of *erythro*-5-hydroxy-2,4,6-trimethyl-3-heptanone was reduced with 1.32 g (5.02 mmol) of tetramethylammonium triacetoxyborohydride to afford 215 mg of a colorless solid. The mixture was purified by flash chromatography on silica gel (20 × 180 mm column, 30% ethyl acetate in hexanes, 6-mL fractions) to give 150 mg (100%) of a mixture of diols as a colorless crystalline solid. A small portion was benzoylated (PhCOCl/DMAP/$CH_2Cl_2$, 18 h, 50 °C) and analyzed by HPLC (2% *tert*-butyl methyl ether/isooctane, λ = 226, 4 nm). Thus the mixture was shown to be 97.5:2.5 anti:syn. The mixture was recrystallized from hexanes to give 126 mg (84%) of the pure anti diol (>99% by HPLC) as colorless needles.

**(4*R**,5*S**)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone (Table III, Entry D Reactant) and (4*R**,5*R**)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone (Table III, Entry E Reactant).** To a suspension of 5.85 g (60.0 mmol, 1.8 equiv) *N,O*-dimethylhydroxylamine hydrochloride in 100 mL of anhydrous THF at 0 °C was added 30.0 mL (2.0 M in toluene, 60.0 mmol, 1.8 equiv) of trimethylaluminum. The mixture was warmed to ambient temperature, stirred for 30 min, and recooled to 0 °C. A solution of 5.97 g (33.1 mmol) of methyl benzyloxyacetate in 20 mL of anhydrous THF was added dropwise over 5 min and the mixture was stirred at ambient temperature for 30 min, cooled to 0 °C, and carefully quenched with 1 N aqueous hydrochloric acid. The mixture was concentrated in vacuo and extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 6.91 g (100% mass balance) of a colorless oil. The amide was purified by molecular distillation (180 °C, 50 μm) to give 6.85 g (99%) as a colorless oil: $R_f$ 0.31 (75% ethyl acetate/hexane); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic H's), 4.68 (s, 2 H, $CH_2$Ph), 4.29 (s, 2 H, $CH_2$C=O), 3.63 (s, 3 H, $CH_3$O), 3.20 (s, 3 H, $CH_3$N). To a solution of 6.85 g (32.8 mmol) of the above amide in 60 mL of anhydrous THF at −78 °C was added 49.1 mL (2.0 M in THF, 98.3 mmol, 3.0 equiv) of isopropylmagnesium chloride. The mixture was allowed to warm to ambient temperature over 30 min and stirred at that temperature for 30 min. The mixture was poured into a slurry of ice and excess 1 N aqueous sodium bisulfate. The aqueous layer was extracted with dichloromethane (3 × 100 mL) and the combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give a colorless oil. The mixture was purified by flash chromatography on silica gel (20% ethyl acetate/hexane, 50 × 180 mm column, 50-mL fractions) to afford 5.35 g (85%) of the desired benzyloxy ketone: $R_f$ 0.54 (30% ethyl acetate/hexane); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 5 H, aromatic H's), 4.60 (s, 2 H, $CH_2$Ph), 4.16 (s, 2 H, $CH_2$C=O), 2.78 (heptet, 1 H, *J* = 6.9 Hz, C*H*$(CH_3)_2$), 1.10 (d, 3 H, CH$(CH_3)_2$). To a solution of 2.39 mL (17.1 mmol, 1.20 equiv) of diisopropylamine in 30 mL of anhydrous THF at −78 °C was added 9.34 mL (1.60 M in hexane, 14.9 mmol, 1.05 equiv) of *n*-butyllithium and the mixture was stirred for 30 min. A solution of 2.74 g (14.2 mmol) of the above benzyloxy ketone in 15 mL of anhydrous THF was added over 10 min and the mixture was stirred for 15 min. Isobutyraldehyde (1.42 mL, 15.7 mmol, 1.10 equiv) was added and the mixture was stirred for 5 min. The reaction was quenched with 10 mL of 5.0 M acetic acid in THF. The slurry was poured into excess 1 N aqueous sodium bisulfate and extracted with ether (3 × 100 mL). The combined organic layers were dried with anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give a pale-yellow oil. The mixture was purified by flash chromatography on silica gel (15% ethyl acetate/hexane, 50 × 180 mm column, 50-mL fractions) to afford a 1:1 mixture of aldol adducts as a colorless oil. The diastereomers were separated by flash chromatography on silica gel (5% ethyl acetate/dichloromethane, 50 × 180 mm column, 50 mL fractions) to give 763 mg of pure anti aldol adduct and 422 mg of pure syn aldol adduct as colorless oils.

**Anti aldol adduct**: $R_f$ 0.53 (30% ethyl acetate/hexane); IR (film) 3500 (br), 2977, 2940, 2880, 1718, 1500, 1470, 1459, 1385, 1104, 1028, 738, 699 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic H's), 4.62 (d, 1 H, *J* = 11.4 Hz, C*H*HPh), 4.44 (d, 1 H, *J* = 11.4 Hz, CH*H*Ph), 3.95 (d, 1 H, *J* = 6.6 Hz, C*H*OBn), 3.68 (q, 1 H, *J* = 5.1 Hz, C*H*OH, 3.09 (heptet, 1 H, *J* = 6.9 Hz, C=OC*H*$(CH_3)_2$), 2.04 (d, 1 H, *J* = 5.5 Hz, O*H*), 1.93 (m, 1 H, CHOHC*H*$(CH_3)_2$), 1.09 (2 overlapping d, 6 H, $CH_3$, $CH_3$), 0.97 (d, 3 H, *J* = 6.9 Hz, $CH_3$), 0.90 (d, 3 H, *J* = 6.7 Hz, $CH_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 216.53, 137.20, 128.47, 128.02, 127.86, 84.34, 76.64, 72.79, 37.08, 29.70, 19.61, 18.57, 18.22, 16.23.

Precise mass *m/z* for $C_{16}H_{27}O_3$ (M + 1): calcd 265.18036, found 265.18045.

**Syn aldol adduct**: $R_f$ 0.53 (30% ethyl acetate/hexane); IR (film) 3500 (br), 2977, 2939, 2878, 1729, 1712, 1500, 1472, 1459, 1386, 1369, 1104, 1044, 1030, 738, 700 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic H's), 4.73 (d, 1 H, *J* = 11.4 Hz, C*H*HPh), 4.38 (d, 1 H, *J* = 11.4 Hz, CH*H*Ph), 4.08 (d, 1 H, *J* = 2.8 Hz, C*H*Bn), 3.46 (ddd, 1 H, *J* = 2.9, 8.0, 9.1 Hz, C*H*OH), 2.95 (heptet, 1 H, *J* = 6.8 Hz, C=OC*H*$(CH_3)_2$), 2.11 (d, 1 H, *J* = 9.1 Hz, O*H*), 1.83 (octet, 1 H, *J* = 6.8 Hz, CHOHC*H*$(CH_3)_2$), 1.10 (2 overlapping d, 6 H, *J* = 6.7, 6.9 Hz, $CH_3$, $CH_3$), 1.01 (d, 3 H, *J* = 6.6 Hz, $CH_3$), 0.84 (d, 3 H, *J* = 6.7 Hz, $CH_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 214.75, 137.12, 128.47, 128.18, 128.17, 83.31, 77.26, 72.84, 36.08, 31.16, 19.29, 19.00, 18.51, 17.96.

Precise mass *m/z* for $C_{16}H_{27}O_3$ (M + 1): calcd 265.18036; found 265.17923.

**(3*R*,4*s*,5*S*)-2,6-Dimethyl-4-(phenylmethoxy)-3,5-heptanediol (Syn Diol) and (3*R**,5*R**)-2,6-Dimethyl-4-(phenylmethoxy)-3,5-heptanediol (Anti Diol), Authentic Sample.** To a solution of 109 mg (0.412 mmol) of *threo*-2,6-dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone in 20 mL of absolute ethanol was added 160 mg (4.32 mmol, 10.4 equiv) of sodium borohydride. The mixture was stirred for 1 h at ambient temperature and quenched with 1 N aqueous sodium bisulfate. The mixture was concentrated in vacuo and extracted with dichloromethane (3 × 15 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo. The mixture was diluted with methanol and concentrated in vacuo three times. The mixture was purified by flash chromatography on silica gel (3% IPA/dichloromethane, 20 × 180 mm column, 8-mL fractions) to afford a colorless oil which contained a lot of boron ($^1$H NMR). The mixture was dissolved in 5 mL of THF and diluted with 15 mL of 2 N aqueous sodium hydroxide and 4 mL of glycerol. The mixture was stirred vigorously for 4 h and extracted with ether (4 × 10 mL). The combined organic layers were diluted 1:1 with hexane, dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give the mixture of diols as a colorless oil containing no boron. The syn and anti diols were separated by flash chromatography on silica gel (15% ethyl acetate/hexane, 30 × 180 mm column, 8-mL fractions) to give title compounds as colorless needles.

**Syn diol**: $R_f$ 0.32 (15% ethyl acetate/hexane); mp 76.5–77.8 °C; IR ($CCl_4$) 3500 (br), 2968, 2938, 2878, 1551, 1543, 1470, 1455, 1251, 1070, 1005 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, aromatic H's), 4.57 (s, 2 H, $CH_2$Ph), 3.68 (br t, 2 H, *J* = 5.3 Hz, C*H*OH), 3.45 (t, 1 H, *J* = 6.2 Hz, C*H*OBn), 2.44 (br s, 2 H, O*H*), 2.09 (m, 2 H, C*H*$(CH_3)_2$), 1.00 (d, 6 H, *J* = 6.9 Hz, $CH_3$), 0.97 (d, 6 H, *J* = 6.7 Hz, $CH_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 137.92, 128.47, 127.82, 127.76, 79.59, 77.84, 72.67, 29.45, 20.08, 16.64.

Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.00; H, 9.94.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): VPC (30 m DB-1701, 150 °C, 15 psi, $t_r$ 5.59 min); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H, aromatic H's), 4.58 (s, 2 H, $CH_2$Ph), 3.54 (dd, 2 H, *J* = 2.1, 9.5 Hz, C*H*OCHOBnC*H*O), 3.19 (t, 1 H, *J* = 9.5 Hz, C*H*OBn), 2.07 (d of heptets, 2 H, *J* = 2.0, 6.9 Hz, C*H*$(CH_3)_2$), 1.39 (s, 3 H, $CH_3CCH_3$), 1.34 (s, 3 H, $CH_3CCH_3$), 0.99 (d, 6 H, *J* = 6.9 Hz, $CH_3$), 0.94 (d, 6 H, *J* = 6.9 Hz, $CH_3$).

**Anti diol**: $R_f$ 0.23 (15% ethyl acetate/hexane); mp 87.1–88.5 °C; IR ($CCl_4$) 3420 (br), 3019, 2962, 2936, 2877, 1499, 1471, 1456, 1386, 1358, 1060 (br) cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic H's), 4.73 (d, 1 H, *J* = 11.4 Hz, C*H*HPh), 4.53 (d, 1 H, *J* = 11.4 Hz, CH*H*Ph), 3.64 (qn, 1 H, *J* = 4.2 Hz, C*H*OH), 3.56 (dd, 1 H, *J* = 1.1, 3.7 Hz, C*H*OBn), 3.45 (br t, 1 H, *J* = 7.6 Hz, C*H*OH), 2.96 (d, 1 H, *J* = 5.0 Hz, O*H*), 2.79 (d, 1 H, *J* = 7.0 Hz, O*H*), 1.86 (m, 2 H, C*H*$(CH_3)_2$), 1.07 (d, 3 H, *J* = 6.6 Hz, $CH_3$), 1.01 (d, 3 H, *J* = 6.6 Hz, $CH_3$), 0.86 (d, 3 H, *J* = 6.7 Hz, $CH_3$), 0.78 (d, 3 H, *J* = 6.7 Hz, $CH_3$); $^{13}$C NMR (75.5 MHz, $CD_3CN$) δ 139.86, 129.19, 128.89, 128.45, 78.19, 77.32, 76.65, 72.57, 31.71, 31.13, 19.80, 19.67, 19.51, 18.67.

Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.04; H, 9.92.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): VPC (30 m DB-1701, 150 °C, 15 psi, $t_r$ 6.36 min); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 5 H, aromatic H's), 4.64 (d, 1 H, *J* = 11.6 Hz, C*H*HPh), 4.53 (d, 1 H, *J* = 11.6 Hz, CH*H*Ph), 3.60 (m, 2 H, C*H*OCHOBnC*H*O), 3.22 (dd, 1 H, *J* = 2.2, 9.9 Hz, C*H*OBn), 2.07 (d of heptets, 1 H, *J* = 6.6, 9.9 Hz, C*H*$(CH_3)_2$), 1.81 (d of heptets, *J* = 3.2, 6.8 Hz, C*H*$(CH_3)_2$), 1.38 (s, 3 H, $CH_3CCH_3$), 1.28 (s, 3 H, $CH_3CCH_3$), 0.98 (2 overlapping d, 6 H, *J* = 6.8, 6.6 Hz, $CH_3$, $CH_3$), 0.94 (d, 3 H, *J* = 6.8 Hz, $CH_3$), 0.88 (d, 3 H, *J* = 6.6 Hz, $CH_3$).

**(3*R*,4*s*,5*S*)-2,6-Dimethyl-4-(phenylmethoxy)-3,5-heptanediol, Authentic Sample.** The procedure used was identical with that used for the preparation of authentic samples of (3*R**,4*S**,5*S**)-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol and (3*R**,5*R**)-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol. Thus, 95.9 mg (0.363 mmol) of *erythro*-2,6-dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone was reduced with 160 mg (4.32 mmol, 11.9 equiv) of sodium borohydride to afford the desired mixture of diols as a colorless oil. The syn and anti diols were separated by flash chromatography on silica gel (10% *tert*-butyl methyl ether/dichloromethane, 20 × 180 mm column, 8-mL fractions) to give title compound, syn diol as a colorless oil: $R_f$ 0.32 (15% *tert*-butyl methyl ether/dichloromethane); IR (film) 3460 (br), 2965, 2938, 2878, 1499, 1470, 1454, 1390, 1367, 1050, 1029, 999, 729, 698 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 7.35 (m, 5 H, aromatic H's), 4.74 (s, 2 H, $CH_2Ph$), 3.60 (t, 1 H, $J$ = 4.0 Hz, $CHOBn$), 3.35 (dt, 2 H, $J$ = 4.0, 6.5 Hz, $CHOH$), 2.38 (d, 2 H, $J$ = 6.6 Hz, $OH$), 1.82 (octet, 2 H, $J$ = 6.7 Hz, $CH(CH_3)_2$), 0.99 (d, 6 H, $J$ = 6.7 Hz, $CH_3$), 0.96 (d, 6 H, $J$ = 6.7 Hz, $CH_3$); $^{13}C$ NMR (62.5 MHz, $CDCl_3$) $\delta$ 137.97, 128.47, 127.93, 127.82, 97.53, 77.51, 75.32, 30.91, 19.78, 17.64.

Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.05; H, 9.98.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): VPC (30 m DB-1701, 150 °C, 15 psi, $t_r$ 6.87 min); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.31 (m, 5 H, aromatic H's), 4.88 (s, 2 H, $CH_2Ph$), 3.53 (t, 1 H, $J$ = 1.6 Hz, $CHOBn$), 3.27 (dd, $J$ = 1.6, 9.7 Hz, $CHOCHOBnCHO$), 2.06 (d of heptets, 2 H, $J$ = 6.6, 9.6 Hz, $CH(CH_3)_2$), 1.45 (s, 3 H, $CH_3CCH_3$), 1.39 (s, 3 H, $CH_3CCH_3$), 0.98 (d, 6 H, $J$ = 6.6 Hz, $CH_3$), 0.94 (d, 6 H, $J$ = 6.6 Hz, $CH_3$).

**Reduction of (4*R**,5*S**)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table III, Entry D).** To a solution of 1.40 g (5.32 mmol) of tetramethylammonium triacetoxyborohydride in 2.0 mL of anhydrous acetonitrile and 2.0 mL of anhydrous acetic acid at −40 °C was added a solution of 49.8 mg (0.188 mmol) of (4*R**,5*S**)-2,6-dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone in 1.0 mL of dry acetonitrile via cannula. The mixture was stirred for 18 h at −40 °C, allowed to warm to ambient temperature, and stirred for 2 h. The mixture was added to a slurry of ice and saturated aqueous sodium bicarbonate and shaken. The solution was diluted with 2 N aqueous sodium hydroxide and extracted with dichloromethane (5 × 20 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was diluted with methanol and concentrated in vacuo three times to give 56.4 mg of a colorless, crystalline solid. $^1H$ NMR indicated the presence of some residual boron. The mixture was dissolved in 4 mL of THF and diluted with 2 N sodium hydroxide and 4 mL of glycerol. After 4 h of vigorous stirring, the mixture was diluted with water and extracted with dichloromethane (5 × 10 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 50.6 mg (100%) of a colorless, crystalline solid. $^1H$ NMR analysis indicated the presence of a >10:1 mixture of anti and syn diols. A small portion was converted to the corresponding mixture of acetonides (dimethoxypropane/*p*-toluenesulfonic acid, 3 h) and a 93:7 ratio confirmed by VPC (30 m DB-1701, 150 °C, 15 psi, $t_r$(major) 6.36 min, $t_r$ 6.87 min). The diols were separated by flash chromatography on silica gel (10% *tert*-butyl methyl ether/dichloromethane, 20 × 180 mm column, 8-mL fractions) to give 43.6 mg (88%) of the anti diol (3*R**,5*R**)-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol as a colorless, crystalline solid.

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.00; H, 9.15.

**Reduction of (4*R**,5*R**)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table III, Entry E).** The procedure used was identical with that used for the reduction of (4*R**,5*S**)-2,6-dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone (Table III, entry D). Thus, 50.4 mg (0.191 mmol) of (4*R**,5*R**)-2,6-dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone reacted with 1.52 g (5.78 mmol) of tetramethylammonium triacetoxyborohydride to afford 50.1 mg (99%) of a colorless, crystalline solid. $^1H$ NMR analysis indicated the presence of a 4:1 mixture of anti and syn diols. A small portion was converted to the corresponding mixture of acetonides (dimethoxypropane/*p*-toluenesulfonic acid, 3 h) and the 79:21 ratio confirmed by VPC (30 m DB-1701, 150 °C, 15 psi, $t_r$(major) 6.36 min, $t_r$(minor) 5.59 min). The diols were separated by flash chromatography on silica gel (15% ethyl acetate/hexane, 20 × 180 mm column, 8-mL fractions) to give 36.7 mg (73%) of the anti diol (3*R**,5*R**)-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol as a colorless, crystalline solid.

Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 71.87; H, 9.09.

**2,4-Dimethyl-1-hydroxy-3-pentanone (7a).** To a solution of 5.0 mL (40.5 mmol) of 2-methyl-3-pentanone in 200 mL of anhydrous dichloromethane at −78 °C was added 48.6 mL (1.0 M in dichloromethane, 48.6 mmol, 1.20 equiv) of dibutylboryl triflate and 9.17 mL (52.6 mmol, 1.30 equiv) of diisopropylethylamine. After 30 min at −78 °C and 30 min at 0 °C, the mixture was cooled to −78 °C and anhydrous formaldehyde (from 18 g of paraformaldehyde heated to 140 °C) was passed in with a stream of nitrogen. After 2 h (paraformaldehyde was nearly gone), the mixture was warmed to 0 °C and treated with 115 mL of methanol followed by 46 mL of 30% hydrogen peroxide (dropwise). The mixture was stirred at ambient temperature for 50 min and concentrated in vacuo. The colorless slurry was extracted with ethyl acetate (4 × 100 mL) and the combined organic layers were washed with saturated aqueous sodium bicarbonate (2×). The aqueous layers were back extracted with dichloromethane (2 × 50 mL) and the combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 11.5 g of a pale-yellow oil containing a white solid. The mixture was purified by flash chromatography on silica gel (40% ethyl acetate/hexane, 60 × 180 mm column, 50-mL fractions) to give 3.97 g (75%) of a clear, colorless oil: $R_f$ 0.36 (50% ethyl acetate/hexane); IR (film) 3460 (br), 2980, 2943, 2883, 1710, 1474, 1390, 1060, 1015 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.72 (m, 2 H, $CH_2OH$), 2.94 (dqn, 1 H, $J$ = 4.2, 7.3 Hz, $CHCHOH$), 2.79 (heptet, 1 H, $J$ = 6.9 Hz, $CH(CH_3)_2$), 2.21 (t, 1 H, $J$ = 6.2 Hz, $OH$), 1.11 (m, 9 H, $(CH_3)_2CH$, $CHCH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) $\delta$ 218.69, 64.38, 46.07, 39.70, 18.22, 17.76, 13.39.

Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.53; H, 10.73.

**(2*S**,3*S**)-2,4-Dimethyl-1,3-pentanediol (8a), Authentic Sample.** To a solution of 1.00 g (29.4 mmol) of sodium borohydride in 100 mL of absolute ethanol was added 470 mg (3.62 mmol) of 2,4-dimethyl-1-hydroxy-3-pentanone. After 30 min at ambient temperature, the reaction was quenched with excess 1 N aqueous sodium bisulfate. The mixture was saturated with ammonium sulfate and concentrated in vacuo. The colorless slurry was extracted with ethyl acetate (5 × 100 mL), and the combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 252 mg (53% mass balance) of a colorless oil. The diols were separated by flash chromatography on silica gel (5% IPA/dichloromethane on fully equilibrated silica gel, 40 × 180 mm column, 20-mL fractions) to give 54.6 mg of **8a** as colorless prisms: $R_f$ 0.21 (10% IPA/dichloromethane); mp 53.0–54.5 °C; IR (film) 3460 (br), 2970, 2880, 1475, 1390, 1070, 1032, 980 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.73 (m, 2 H, $CH_2OH$), 3.42 (ddd, 1 H, $J$ = 2.5, 4.5, 8.9 Hz, $CHOH$), 2.42 (br t, 1 H, $J$ = 4.5 Hz, $CH_2OH$), 1.85 (m, 1 H, $CHCH_3CHOH$), 1.70 (m, 1 H, $CH(CH_3)_2$), 1.01 (d, 3 H, $J$ = 6.5 Hz, $CH_3$), 0.95 (d, 3 H, $J$ = 7.1 Hz, $CH_3$), 0.86 (d, 3 H, $J$ = 6.7 Hz, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) $\delta$ 79.88, 67.91, 36.14, 31.39, 19.35, 19.01, 8.93.

Anal. Calcd for $C_7H_{16}O_2$: C, 63.60; H, 12.20. Found: C, 63.71; H, 12.36.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.07 (dd, 1 H, $J$ = 2.9, 11.5 Hz, equitorial $CHHO$), 3.59 (dd, 1 H, $J$ = 1.6, 11.4 Hz, axial $CHHO$), 3.37 (dd, 1 H, $J$ = 2.3, 9.8 Hz, $CHOCHCH_3$), 1.60 (m, 1 H, $CH(CH_3)_2$), 1.41 (s, 3 H, $CH_3CCH_3$), 1.40 (s, 3 H, $CH_3CCH_3$), 1.05 (d, 3 H, $J$ = 6.9 Hz, $CH_3$), 0.93 (d, 3 H, $J$ = 6.4 Hz, $CH_3$), 0.81 (d, 3 H, $J$ = 6.7 Hz, $CH_3$).

**Reduction of 2,4-Dimethyl-1-hydroxy-3-pentanone (7a) with $Me_4NHB(OAc)_3$.** To a solution of 2.58 g (9.81 mmol, 4.83 equiv) of $Me_4NHB(OAc)_3$ in 5.0 mL of anhydrous acetonitrile and 3.0 mL of anhydrous acetic acid at −40 °C was added a solution of 264 mg (2.03 mmol) of 2,4-dimethyl-1-hydroxy-3-pentanone (**7a**) in 2.0 mL of anhydrous acetonitrile. The mixture was stirred for 12 h at −40 °C, warmed to ambient temperature, and poured into 25 mL of water containing 100 mmol of sodium bicarbonate. The mixture was extracted continuously with dichloromethane for 12 h. The organic solution was concentrated in vacuo, diluted with 15 mL of methanol, and concentrated in vacuo three times to give 317 mg (120% mass balance) of a colorless oil. $^1H$ NMR analysis revealed the presence of a 5:1 ratio of erythro-to-threo diols. The mixture was purified by MPLC (5% IPA/dichloromethane, two Merck Lobar B columns, 10-mL fractions) to afford 209 mg (78%) of the erythro diol, (2*S**,3*S**)-4-methyl-2-(phenylmethoxy)-1,3-pentanediol (**8a**), as a colorless, crystalline solid.

**(2*S**,3*R**)-4-Methyl-2-(phenylmethoxy)-1,3-pentanediol (9b) and (2*S**,3*S**)-4-Methyl-2-(phenylmethoxy)-1,3-pentanediol (8b), Authentic Samples.** To a solution of 4.36 mL (31.1 mmol, 1.2 equiv) of diisopropylamine in 30 mL of anhydrous THF at −78 °C was added 2.85 mL (10 M in hexane, 28.5 mmol, 1.1 equiv) of *n*-butyllithium. The mixture

was stirred for 30 min and a solution of 4.76 g (25.9 mmol) of methyl benzyloxyacetate in 20 mL of anhydrous THF was added dropwise via cannula. The mixture was warmed to 0 °C, stirred at that temperature for 1 h, and recooled to −78 °C. Isobutyraldehyde (2.59 g, 28.51 mmol, 1.1 equiv) was added in one portion. The mixture was stirred for 5 min, poured into 100 mL of 1 N aqueous sodium bisulfate, and concentrated in vacuo. The slurry was extracted with ether (3 × 25 mL) and the combined organic layers were dried with anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give a yellow oil. The mixture was purified by flash chromatography on silica gel (20% ethyl acetate/hexane, 60 × 180 mm column, 50-mL fractions) to afford 2.46 g of a mixture of diastereomers as a colorless oil: $R_f$ 0.42, 0.47 (30% ethyl acetate/hexane). To a solution of 2.46 g (9.76 mmol) of the above mixture of aldol adducts in 100 mL of anhydrous THF at −78 °C was added 40.0 mL (1.0 M in ether, 40.0 mmol, 4.10 equiv) of lithium aluminum hydride. The mixture was allowed to warm to 0 °C over 30 min and recooled to −78 °C. The reaction was treated with 1.5 mL of water, 1.5 mL of 15% aqueous sodium hydroxide, and 4.5 mL of water. The resultant slurry was filtered and concentrated in vacuo to give 1.71 g (78% mass balance) of a yellow oil. The mixture was purified by flash chromatography on silica gel (75% ethyl acetate/hexane, 60 × 180 mm column, 50-mL fractions) to afford 744 mg of the erythro diol **8b** as a colorless, crystalline solid and 760 mg of the threo diol **9b** as a colorless oil.

**Erythro diol 8b**: $R_f$ 0.34 (75% ethyl acetate/hexane); mp 72.7–73.4 °C; IR ($CCl_4$) 3645, 3585, 3460 (br), 3100, 3078, 3041, 2972, 2940, 2882, 1501, 1477, 1459, 1359, 1373, 1240, 1212, 1142, 1100, 1058, 1032, 1000 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) δ 7.36 (m, 5 H, aromatic H's), 4.75 (d, 1 H, $J$ = 11.5 Hz, C*H*HPh), 4.61 (d, 1 H, $J$ = 11.4 Hz, CH*H*Ph), 3.91 (ddd, 1 H, $J$ = 4.2, 6.5, 11.8 Hz, CH*H*OH, 3.72 (ddd, 1 H, $J$ = 4.3, 5.4, 11.9 Hz, C*H*HOH), 3.55 (q, 1 H, $J$ = 4.1 Hz, C*H*OBn), 3.40 (dt, 1 H, $J$ = 3.9, 6.7 Hz, C*H*OH), 2.27 (d, 1 H, $J$ = 6.8 Hz, CHO*H*), 2.01 (dd, 1 H, $J$ = 5.5, 6.4 Hz, $CH_2O$*H*), 1.83 (octet, 1 H, $J$ = 6.7 Hz, C*H*$(CH_3)_2$), 0.97 (d, 3 H, $J$ = 6.7 Hz, C$H_3$), 0.91 (d, 3 H, $J$ = 6.7 Hz, C$H_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 137.95, 128.53, 127.92, 78.68, 76.58, 72.50, 62.41, 30.58, 19.51, 17.71.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.91; H, 8.99. Found: C, 69.69; H, 9.11.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): VPC (30 m DB-5, 125 °C, 15 psi, $t_r$ 13.31 min); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 5 H, aromatic H's), 4.74 (d, 1 H, $J$ = 12.1 Hz, C*H*HPh), 4.43 (d, 1 H, $J$ = 12.1 Hz, CH*H*Ph), 4.07 (dd, 1 H, $J$ = 2.1, 12.9 Hz, equatorial CH*H*O), 3.84 (dd, 1 H, $J$ = 2.1, 12.9 Hz, axial C*H*HO), 3.28 (dd, 1 H, $J$ = 1.9, 9.6 Hz, C*H*OCH$(CH_3)_2$), 3.26 (q, 1 H, $J$ = 2.0 Hz, C*H*OBn), 2.07 (m, 1 H, C*H*$(CH_3)_2$), 1.45 (s, 3 H, C$H_3$CCH$_3$), 1.42 (s, 3 H, CH$_3$CC$H_3$), 0.93 (d, 3 H, $J$ = 6.6 Hz, C$H_3$), 0.71 (d, 3 H, $J$ = 6.7 Hz, C$H_3$).

**Threo diol 9b**: $R_f$ 0.27 (75% ethyl acetate/hexane); IR (film) 3420 (br), 3098, 3072, 3040, 2970, 2940, 2882, 1500, 1471, 1458, 1100, 1050, 1030, 1000, 740, 700 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic H's), 4.62 (AB, 2 H, $J$ = 11.7 Hz, C*HH*Ph), 3.83 (br s, 2 H, $CH_2$OH), 3.59 (br t, 1 H, $J$ = 5.5 Hz, C*H*OH, 3.52 (q, 1 H, $J$ = 4.3 Hz, C*H*OBn), 2.38 (br s, 2 H, O*H*, O*H*), 1.83 (octet, 1 H, $J$ = 6.7 Hz, C*H*$(CH_3)_2$), 0.96 (d, 3 H, $J$ = 6.6 Hz, C$H_3$), 0.91 (d, 3 H, $J$ = 6.8 Hz, C$H_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 137.81, 128.56, 128.00, 127.93, 79.33, 76.42, 71.71, 60.90, 29.68, 19.09, 17.96.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.69; H, 9.02.

A small portion was converted to the corresponding acetonide (dimethoxypropane/*p*-toluenesulfonic acid, 3 h): VPC (30 m DB-5, 125 °C, 15 psi, $t_r$ 13.31 min); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.33 (m, 5 H, aromatic H's), 4.55 (d, 1 H, $J$ = 11.5 Hz, C*H*HPh), 4.45 (d, 1 H, $J$ = 11.5 Hz, CH*H*Ph), 3.88 (dd, 1 H, $J$ = 4.8, 11.6 Hz, equatorial CH*H*O), 3.66 (dd, 1 H, $J$ = 7.3, 11.6 Hz, axial C*H*HO), 3.50 (dd, 1 H, $J$ = 3.5, 8.9 Hz, C*H*OCHOBn), 3.42 (ddd, 1 H, $J$ = 4.8, 7.3, 8.9 Hz, C*H*OBn), 1.97 (d of heptets, 1 H, $J$ = 3.4, 6.9 Hz, C*H*$(CH_3)_2$), 1.42 (s, 3 H, C$H_3$CCH$_3$), 1.34 (s, 3 H, CH$_3$CC$H_3$), 0.96 (d, 3 H, $J$ = 7.0 Hz, C$H_3$), 0.86 (d, 3 H, $J$ = 6.8 Hz, C$H_3$).

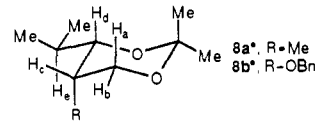
**1-Hydroxy-4-methyl-2-(phenylmethoxy)-3-pentanone (7b)**. To a solution of 454 mg (2.02 mmol) of 4-methyl-2-(phenylmethoxy)-1,3-pentanediol (mixture of isomers **8b** and **9b**) in 10.0 mL of anhydrous dichloromethane was added 367 μL (2.63 mmol, 1.3 equiv) of triethylamine, 366 mg (2.43 mmol, 1.20 equiv) of *tert*-butyldimethylsilyl chloride, and 12 mg of DMAP. The mixture was stirred for 12 h at ambient temperature and poured into 1 N aqueous sodium bisulfate. The mixture was extracted with ether (3 × 20 mL) and the combined organic layers were washed with saturated aqueous sodium bicarbonate, dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo. The mixture was purified by flash chromatography on silica gel (10% ethyl acetate/hexane, 30 × 180 mm column, 8-mL fractions) to afford 551 mg of the monosilylated diol as a colorless oil: $R_f$ 0.35 (10% ethyl acetate/hexane). To a solution of 523 mg (1.55 mmol) of the monosilyl diol in 7.75 mL of anhydrous dichloromethane at ambient temperature was added 872 mg (2.32 mmol, 1.50 equiv) of pyridinium dichromate, 1.5 g of freshly activated, freshly ground 3 Å molecular sieves, and finally 150 mL (2.62 mmol, 1.70 equiv) of anhydrous acetic acid. An exothermic reaction ensued. After 2 h at ambient temperature, 2 g of Celite was added and the mixture was diluted with 10 mL of dichloromethane, stirred for 20 min, and filtered. The mixture was concentrated in vacuo, dissolved in ether, and filtered through anhydrous magnesium sulfate. The pale-yellow solution was concentrated in vacuo to give 446 mg of a yellow oil. The mixture was purified by flash chromatography on silica gel (5% ethyl acetate/hexane, 30 × 180 mm column, 8 mL fractions) to afford 411 mg (79%) of the *tert*-butyldimethylsiloxy ketone as a pale-yellow oil: $R_f$ 0.38 (10% ethyl acetate/hexane); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aromatic H's), 4.62 (AB, 2 H, $J$ = 11.5 Hz, C*HH*Ph), 4.08 (t, 1 H, $J$ = 5 Hz, C*H*OBn), 3.89 (d, 2 H, $J$ = 5 Hz, $CH_2$OTBS), 3.04 (heptet, 1 H, $J$ = 6.7 Hz, C*H*$(CH_3)_2$), 1.06 (d, 6 H, $J$ = 6.7 Hz, $(CH_3)_2$CH), 0.88 (s, 9 H, $(CH_3)_3$Si), 0.05 (s, 6 H, $(CH_3)_2$Si). To a solution of 411 mg (1.22 mmol) of the above siloxy ketone in 10.0 mL of acetonitrile at 0 °C was added 1.0 mL of hydrogen fluoride–pyridine complex. After 2.5 h at 0 °C, the mixture was poured into saturated aqueous sodium bicarbonate and extracted with dichloromethane (4 × 20 mL). The combined organic layers were washed with first 1 N aqueous sodium bisulfate then saturated aqueous sodium bicarbonate. The aqueous layers were back extracted with dichloromethane (2 × 20 mL) and the combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 271 mg (100% mass balance) of a pale-yellow oil. The mixture was purified by flash chromatography on silica gel (40% ethyl acetate/hexane, 20 × 180 mm column, 8-mL fractions) to afford 255 mg (94%) of the title compound as a colorless oil: $R_f$ 0.10 (20% ethyl acetate/hexane); IR (film) 3480 (br), 3072, 3040, 2990, 2942, 2882, 1719, 1500, 1470, 1459, 1051, 742, 701 cm$^{-1}$; $^1$H NMR (250 MHz, $CDCl_3$) δ 7.36 (m, 5 H, aromatic H's), 4.70 (d, 1 H, $J$ = 11.5 Hz, C*H*HPh), 4.56 (d, 1 H, $J$ = 11.5 Hz, CH*H*Ph), 4.10 (dd, 1 H, $J$ = 4.4, 5.2 Hz, C*H*OBn), 3.86 (m, 2 H, $CH_2$OH), 3.00 (heptet, 1 H, $J$ = 6.9 Hz, C*H*$(CH_3)_2$), 2.17 (t, 1 H, $J$ = 6.8 Hz, O*H*), 1.08 (2 overlapping d, 6 H, $J$ = 6.9, 6.8 Hz, CH$(CH_3)_2$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) δ 214.29, 137.11, 128.48, 128.05, 127.89, 83.50, 72.60, 62.34, 36.63, 18.19, 17.70.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.98; H, 8.17.

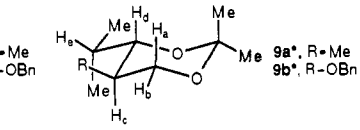
**Reduction of 1-Hydroxy-4-methyl-2-(phenylmethoxy)-3-pentanone (7b) with $Me_4NHB(OAc)_3$.** To a solution of 1.36 g (5.17 mmol, 21.6 equiv) of $Me_4NHB(OAc)_3$ in 4.0 mL of anhydrous acetonitrile and 4.0 mL of anhydrous acetic acid at −40 °C was added a solution of 53.2 mg (0.239 mmol) of (2*R**)-1-hydroxy-4-methyl-2-(phenylmethoxy)-3-pentanone (**7b**) in 2.0 mL of anhydrous acetonitrile. The mixture was stirred at 40 °C for 12 h and at ambient temperature for 1 h. The solution was poured into a slurry of ice and saturated aqueous sodium bicarbonate and extracted with dichloromethane (5 × 30 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated in vacuo to give 47.5 mg (90% mass balance) of a colorless oil. $^1$H NMR analysis revealed the presence of a ~10:1 mixture of threo and erythro diols. A small portion was converted to the corresponding mixture of acetonides (dimethoxypropane/*p*-toluenesulfonic acid, 3 h) and a 92:8 ratio confirmed by VPC (30 m DB-5, 125 °C, 15 psi, $t_r$(major) 11.73 min, $t_r$(minor) 13.18 min). The mixture was purified by flash chromatography on silica gel (60% ethyl acetate/hexane, 20 × 180 mm column, 8 mL fractions) to afford 40.7 mg (76%) of the threo diol, (2*R**,3*S**)-4-methyl-2-(phenylmethoxy)-1,3-pentanediol (**9b**), as a colorless oil.

**4-(1,1-Dimethylethyl)cyclohex-3-en-1-one Ethylene Ketal (12).** A solution of 7.00 g (42.1 mmol) of 2,5-dihydro-4-*tert*-butylanisole[30] and

**Table IV.** Coupling Constants from Acetonides Derived from Diols **8a,b** and **9a,b**




**8a***, R=Me
**8b***, R=OBn




**9a***, R=Me
**9b***, R=OBn

| **8a*** | *J*, Hz | **9a*** | *J*, Hz | **8b*** | *J*, Hz | **9b*** | *J*, Hz |
|---|---|---|---|---|---|---|---|
| $J_{ab}$ | 11.4 | $J_{ab}$ | 11.4 | $J_{ab}$ | 12.9 | $J_{ab}$ | 11.6 |
| $J_{ac}$ | 1.7 | $J_{ac}$ | 11.1 | $J_{ac}$ | 2.1 | $J_{ac}$ | 7.3 |
| $J_{bc}$ | 2.8 | $J_{bc}$ | 5.0 | $J_{bc}$ | 2.1 | $J_{bc}$ | 4.8 |
| $J_{cd}$ | 2.3 | $J_{cd}$ | 10.1 | $J_{cd}$ | 1.9 | $J_{cd}$ | 8.9 |
| $J_{dc}$ | 10.2 | $J_{de}$ | 2.4 | $J_{de}$ | 9.6 | $J_{dc}$ | 3.5 |

80.0 mg of *p*-toluenesulfonic acid in 200 mL of ethylene glycol was stirred for 8 h at ambient temperature. The solution was diluted with 200 mL of saturated sodium bicarbonate solution. The aqueous layer was extracted with ether (3 × 75 mL). The combined organic layers were washed with 20 mL of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The compound was purified by flash chromatography on silica gel (5.0 × 20.0 cm, 10:1 hexane/ethyl acetate) affording 6.75 g (82%) of the ethylene ketal: $R_f$ 0.43 (10:1 hexane/ethyl acetate); IR (film) 2960, 2880, 1460, 1465, 1450, 1430, 1380, 1365, 1310, 1250, 1220, 1145, 1125, 1065, 1050, 1000, 950, 870 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 5.36 (m, 1 H C=CC*H*), 3.97 (m, 4 H, OC$H_2$C$H_2$O), 2.26 (m, 4 H, C$H_2$CCHC$H_2$), 1.74 (t, 2 H, $J$ = 6.5 Hz, C$H_2$), 1.04 (s, 9 H, C(C$H_3$)$_3$).

**(3*S**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (14).** To a solution of 2.30 g (11.7 mmol) of ethylene ketal **12** at 0 °C in ether was cautiously added 1.38 mL (12.9 mmol, 1.10 equiv) of borane methyl sulfide. The reaction was allowed to warm to ambient temperature and stirred for 8 h. To the cold 0 °C was slowly added 10 mL of ethyl alcohol followed by 7.5 mL of 30% aqueous hydrogen peroxide solution and 7.5 mL of 3 N sodium hydroxide solution. The resulting mixture was stirred for 5 h at room temperature before it was diluted with 15 mL of water. The aqueous layer was extracted with ether (3 × 50 mL). The combined organic layers were washed with 10 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. A solution of the hydroboration product in 50% aqueous acetic acid was stirred for 36 h at ambient temperature. The reaction mixture was diluted with 15 mL of water and was cautiously neutralized by adding solid sodium bicarbonate. The resulting aqueous solution was extracted with ether (3 × 50 mL), and the combined organic layers were washed with 5.0 mL of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The hydroxy ketone **14** was purified by flash chromatography on silica gel (5.0 × 20 cm column, 1:1 hexane/ethyl acetate) to afford 1.09 g (57%) of a white crystalline solid: $R_f$ 0.27 (1:1 hexane/ethyl acetate); IR ($CH_2Cl_2$) 3605, 2965, 2875, 1710, 1480, 1365, 1215, 11675, 970 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.63 (br m, 1 H, CH$_2$C*H*CH), 2.56–2.27 (m, 4 H, C$H_2$C=OC$H_2$), 2.15–1.90 (m, 2 H, C$H_2$CHCH), 2.05 (d, 1 H, $J$ = 3.3 Hz, O*H*), 1.54 (dd, 1 H, $J$ = 12.9, 2.8 Hz), (CH$_3$)$_3$C*H*), 1.03 (s, 9 H, C(C$H_3$)$_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$ 210.9, 70.2, 50.9, 50.2, 41.4, 32.6, 28.7, 21.3.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.70; H, 10.78.

**4-(1,1-Dimethylethyl)-1,3-cyclohexanedione 1-(Ethylene Ketal) (15).** To a solution of 3.00 g (14.0 mmol) of alcohol **13** in 90 mL of dichloromethane was added in one portion 7.61 g (20.2 mmol, 1.44 equiv) of pyridinium dichromate followed by 1.04 g (5.40 mmol, 0.39 equiv) of pyridinium trifluoroacetate. The brown mixture was stirred at ambient temperature for 14 h and then filtered through a cake of silica. The filtrate was concentrated in vacuo. The concentrate was purified by flash chromatography on silica gel (5.0 × 20.0 cm, 4:1 hexane/ethyl acetate) to yield 2.41 g (81%) of a colorless liquid: $R_f$ 0.32 (4:1 hexane/ethyl acetate); IR (thin film) 2965, 2980, 1715, 1485, 1455, 1440, 1415, 1395, 1360, 1340, 1320, 1290, 1245, 1215, 1160, 1110, 1090, 1035, 1005, 945, 920 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.95 (m, 4 H, OC$H_2$C$H_2$O), 2.63 (d, 1 H, $J$ = 12.9 Hz, C*H*C=O), 2.49 (dd, 1 H, $J$ = 12.9, 2.6 Hz, C*H*C=O), 2.12–1.90 (m, 4 H, C$H_2$C$H_2$), 1.61–1.57 (m, 1 H, (CH$_3$)$_3$CC*H*), 1.01 (s, 9 H, C(C$H_3$)$_3$): $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$ 206.7, 110.5, 64.7, 64.5, 58.9, 53.3, 35.2, 31.8, 27.7, 22.6.

**(3*R**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (17).** To a solution of 2.13 g (10.0 mmol) of ethylene ketal **15** at 0 °C in 80.0 mL of tetrahydrofuran was cautiously added 25.1 mL (25.1 mmol, 2.51 equiv) of 1 M tetrahydrofuran solution of L-Selectride (Aldrich). The reaction was stirred for 4 h prior to quenching with 15 mL of ethanol. To the cold solution was slowly added 15 mL of ethyl alcohol followed by 40 mL of 30% aqueous hydrogen peroxide solution and 40 mL of 3 N sodium hydroxide solution. The resulting mixture was stirred for 1 h at ambient temperature. The aqueous layer was extracted with ether (3 × 75 mL). The combined organic layers were washed with 10 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. A solution of the reduction product in 50% aqueous acetic acid was stirred for 6 h at ambient temperature. The reaction mixture was diluted with 15 mL of water and was cautiously neutralized by adding solid sodium bicarbonate. The resulting aqueous solution was extracted with dichloromethane (4 × 10 mL) and the combined organic layers were washed with 5.0 mL of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The hydroxy ketone **17** was purified by flash chromatography on silica gel (3.0 × 22 cm, 2:1 hexane/ethyl acetate) to afford 605 mg (36%) of a white crystalline solid: $R_f$ 0.37 (2:1 hexane/ethyl acetate); IR ($CH_2Cl_2$) 3610, 2970, 2880, 1715, 1485, 1370, 1220, 1170, 975 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.63 (br m, 1 H, C$H_2$C*H*CH), 2.56–2.41 (m, 2 H, C$H_2$C=OC$H_2$), 2.39–2.27 (m, 2 H, C$H_2$C=OC$H_2$), 2.16–2.01 (m, 2 H, $J$ = CH$_2$C$H_2$CH), 1.57–1.52 (d, 1 H, OH), 0.99 (s, 9 H, C(C$H_3$)$_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) $\delta$ 210.9, 70.2, 50.9, 50.2, 41.4, 32.6, 28.7, 21.3.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.40; H, 10.82.

**Reduction of (3*S**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (14) with $Me_4NHB(OAc)_3$ in Acetonitrile–Acetic Acid Solution.** To a solution of 773 mg (2.94 mmol, 5.0 equiv) of tetramethylammonium triacetoxyborohydride and 336 μL (5.87 mmol, 10.0 equiv) of acetic acid in 10.0 mL of acetonitrile was added a solution of 100.0 mg (0.587 mmol) of the title compound in 1.0 mL of acetonitrile. The reaction mixture was stirred at ambient temperature for 10 h before it was quenched with 3.0 mL of saturated aqueous ammonium chloride solution. After effervescence had ceased, the solution was treated with 3.0 mL of 1.0 M aqueous sodium/potassium tartrate solution and stirred for 20 min. The aqueous solution was extracted with ethyl acetate (10 × 2 mL). The combined organic layers were washed with 2 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified sample indicated the presence of trans diol **20** ($t_r$ 8.76 min) and syn diol **21** ($t_r$ 9.40 min) in a ratio of 88:12. Purification of the residue by flash chromatography on silica gel (20 × 200 mm column, 1:1 hexane/ethyl acetate) yielded 74 mg (73%) of diol **20** as a crystalline solid: $R_f$ 0.53 (2:1 acetone–dichloromethane); IR ($CH_2Cl_2$) 3610, 2965, 2945, 2870, 1485, 1445, 1395, 1365, 1045, 1020, 995 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.18 (m, 1 H, CH$_2$CH$_2$C*H*), 3.96 (dt, 1 H, $J$ = 13.2, 4.1 Hz, CHC*H*OH), 2.05 (dm, 1 H, $J$ = 13.2, CHC$H_{eq}$H$_{ax}$CH), 1.76–1.08 (m, 8 H, CHC$H_{ax}$H$_{eq}$CH, CHC$H_2$C$H_2$CH, CH$_2$C*H*CHO*H*, O*H*), 1.02 (s, 9 H, C(C$H_3$)$_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 68.8, 67.4, 53.7, 43.9, 33.1, 32.9, 29.3, 20.6. An analytical sample was prepared by recrystallization from hexane to afford colorless needles: mp 148–150 °C.

Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.54; H, 11.75.

**Reduction of (3*S**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (14) with $Me_4NHB(OAc)_3$ in Acetone–Acetic Acid Solution.** To a solution of 580 mg (2.21 mmol, 5.0 equiv) of tetramethylammonium triacetoxyborohydride and 253 μL (4.41 mmol, 10.0 equiv) of acetic acid in 10.0 mL of acetone was added a solution of 75 mg (0.441 mmol) of the hydroxy ketone **17** in 1.0 mL of acetone. The reaction mixture was stirred for 24 h at room temperature before it was quenched with 3.0 mL of saturated aqueous ammonium chloride solution. After effervescence had ceased, the solution was treated with 3.0 mL of 1.0 M aqueous sodium/potassium tartrate solution and stirred for 20 min. The aqueous solution was extracted with ethyl acetate (10 × 2 mL). The combined organic layers were washed with 2.0 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified sample mixture indicated the presence of exclusively trans diol **20** ($t_r$ 8.87 min). Purification of the residue by flash chromatography on silica gel (20 × 200 mm column, 1:1 hexane/ethyl acetate) yielded 41 mg (54%) of diol **20** as a crystalline solid.

**Reduction of (3*R**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (17) with $Me_4NHB(OAc)_3$ in Acetonitrile–Acetic Acid Solvent.** To a solution of 467 mg (2.21 mmol, 5.0 equiv) of tetramethylammonium triacetoxyborohydride and 253 μL (4.41 mmol, 10.0 equiv) of acetic acid in 10.0 mL of acetonitrile was added a solution of 75.0 mg (0.441 mmol) of hydroxy ketone **17** in 1.0 mL of acetonitrile. The reaction mixture was stirred at room temperature for 2 h before it was quenched with 3.0 mL of saturated aqueous ammonium chloride solution. After effervescence had ceased, the solution was treated with 3.0 mL of 1.0 M aqueous sodium–potassium tartrate solution and stirred for 20 min. The aqueous solution was extracted with ethyl acetate (10 × 2 mL). The combined organic extracts were washed with 2 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified reaction mixture indicated the presence of exclusively trans diol **18** ($t_r$ 9.59 min). Purification of the residue by flash chromatography on silica gel (20 × 200 mm column, 1:1 hexane/ethyl acetate) gave 65 mg (86%) of diol **18** as a crystalline solid: $R_f$ 0.14 (1:1 acetone/dichloromethane); IR ($CH_2Cl_2$) 3615, 2955, 2870, 1365, 1325, 1060, 1020, 980 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.33 (br s, 1 H, CHC*H*OH), 3.98 (tt, 1 H, $J$ = 11.3, 4.5 Hz, CH$_2$C*H*CH$_2$), 2.07 (m, 2 H, CH$_2$C$H_{eq}$H$_{ax}$CH), 1.91 (br s, 1 H, O*H*), 1.60 (m, 1 H, CH$_2$C*H*CH), 1.48 (br s, 1 H, O*H*), 1.41–1.15 (m, 4 H, C$H_2$C$H_2$), 1.02 (s, 9 H, C(CH$_3$)$_3$); $^{13}$C NMR (75 MHz, $CDCl_3$) 69.2, 66.6, 50.6, 44.5, 36.3, 32.5,

(30) Bolon, D. A. *J. Org. Chem.* **1970**, *35*, 715.

28.8, 19.9. An analytical sample was prepared by recrystallization from hexane to afford colorless needles: mp 113–114 °C.

Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.70; H, 11.68.

**Reduction of (3*R**,4*R**)-4-(1,1-Dimethylethyl)-3-hydroxycyclohexanone (17) with $Me_4NHB(OAc)_3$ in Acetone–Acetic Acid Solvent.** To a solution of 467 mg (2.21 mmol, 5.0 equiv) of tetramethylammonium triacetoxyborohydride and 253 μL (4.41 mmol, 10.0 equiv) of acetic acid in 10.0 mL of acetonitrile was added a solution of 75.0 mg (0.441 mmol) of hydroxy ketone **17** in 1.0 mL of acetone. The reaction mixture was stirred at room temperature for 7 h before it was quenched with 3.0 mL of saturated aqueous ammonium chloride solution. After effervescence had ceased, the solution was treated with 3.0 mL of 1.0 M aqueous sodium/potassium tartrate solution and stirred for 20 min. The aqueous solution was extracted with ethyl acetate (10 × 2 mL). The combined organic extracts were washed with 2 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified reaction mixture indicated the presence of exclusively trans diol **18** ($t_r$ 9.59 min). Purification of the residue by flash chromatography on silica gel (20 × 200 mm column 1:1 hexane/ethyl acetate) gave 68 mg (89%) of diol **18** as a crystalline solid.

**3-Phenylpropyl 3,5-Dioxohexanoate (27).** To a solution of 10.9 g (107 mmol) of diisopropylamine in 100 mL of anhydrous tetrahydrofuran at −78 °C was added 6.55 g (64.0 mL of a 1.60 M sodium in hexanes, 102 mmol) of *n*-butyllithium. The mixture was warmed to 0 °C and stirred for 30 min. A solution of 10.7 g (48.8 mmol) of 3-phenylpropyl 3-oxobutanoate (**1**) in 30 mL of anhydrous tetrahydrofuran was added dropwise over 30 min, and the mixture was stirred at ambient temperature for 2 h. The solution was dark red. Neat *N*-methoxy-*N*-methylactamide (7.54 g, 73.14 mmol) was added, and the mixture was stirred at ambient temperature overnight. The mixture was concentrated in vacuo, diluted with cold aqueous 1 N sodium hydrogen sulfate, and extracted three times with ether. The organic layers were diluted 1:1 with pentane, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 12.2 g of an orange oil. The mixture was filtered through a short column of silica gel (60 × 60 mm column, 50% ethyl acetate/hexanes) and concentrated in vacuo to give 7.70 g of an orange oil. The mixture was purified by flash chromatography on deactivated silica gel (see general experimental section, 85 × 200 mm column, 30% ether in hexanes, 125-mL fractions). The pure (by TLC on deactivated plates) fractions were combined, washed twice with aqueous 1 N sodium hydrogen sulfate and once with saturated aqueous sodium bicarbonate, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 4.41 g (35%) of the title compound as a pale yellow oil: $R_f$ 0.33 (50% ethyl acetate/hexanes); $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 5.62 (s, enol C*H*), 4.27 (t, 2 H, $CH_2O$), 3.76 (s), 3.26 (s), 3.18 (s), 3.33 (s), 2.70 (t, 2 H, $CH_2Ph$), 2.37, (2s), 2.09 (s, 3 H, $CH_3$), 1.99 (m, 2 H, $CH_2CH_2Ph$).

**3-Phenylpropyl 7-Hydroxy-3,5-dioxo-8-methylnonanoate (28).** To a solution of 6.81 g (67.3 mmol) of diisopropylamine in 40 mL of anhydrous tetrahydrofuran at −78 °C was added 3.77 g (36.8 mL of a 1.60 M solution in hexanes, 58.9 mmol) of *n*-butyllithium. The mixture was warmed to 0 °C and stirred for 30 min. A solution of 4.41 g (16.8 mmol) of 3-phenylpropyl 3,5-dioxohexanoate (**27**) in 10.0 mL of anhydrous tetrahydrofuran was added dropwise via cannula over 15 min. The mixture was stirred at 0 °C for 2 h and cooled to −78 °C. Isobutyraldehyde (1.33 g, 18.5 mmol) was added neat, and the mixture was stirred for 1 min and poured into excess 1 N aqueous sodium hydrogen sulfate. The mixture was diluted with ether and the layers shaken vigorously and separated. The aqueous layer was extracted twice with ether. The combined organic layers were washed with pH 7 buffer, and the aqueous layer was back extracted twice with ether. The combined organic layers were diluted 1:1 with a 10% dichloromethane in pentane solution, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 5.51 g of a yellow oil. The mixture was purified by flash chromatography on deactivated silica gel (see general experimental section for deactivation procedure, 85 × 200 mm column, 3% *tert*-butyl methyl ether/dichloromethane, 125-mL fractions) to give 3.10 g (55%) of a pale-yellow oil which crystallized on standing. The solid was recrystallized from ether/pentane to give colorless needles: $R_f$ 0.42 (5% *tert*-butyl methyl ether/dichloromethane); mp 43.0–43.3 °C; IR (KBr) 3030, 2964, 1723 (br), 1500, 1470, 1457, 1410 (br), 1295, 1182, 1105, 1060, 1010, 947, 900 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 5.68 (s, enol C*H*), 5.62 (s, enol C*H*), 5.09 (d, enol C*H*), 4.18 (m, 2 H, $CH_2O$), 3.93 (m, 1 H, C*H*OH), 3.33 (s, O*H*), 2.09–2.85 (m), 2.00 (m, 2 H, $CH_2CH_2Ph$), 1.75 (heptet, 1 H, $CH(CH_3)_2$), 0.92 (2d, 6 H, $CH(CH_3)_2$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 205.02, 171.36, 140.83, 128.42, 128.27, 126.06, 97.16, 73.94, 64.39, 50.69, 44.39, 43.99, 32.72, 32.03, 29.97, 18.37, 18.02, 17.88.

Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.36; H, 7.94.

**3-Phenylpropyl (3*S**,5*S**)-3,5-Bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (33).** To a solution of 717 g (2.44 mmol) of 3-phenylpropyl *anti*-3,5-dihydroxy-6-methylheptanoate (**3**) in 10.0 mL of anhydrous dichloromethane at −10 °C was added 1.48 g (14.6 mmol) of triethylamine followed *immediately* by 1.93 g (7.31 mmol) of *tert*-butyldimethylsilyl triflate. The reaction mixture turned dark green. After 30 min the mixture was warmed to ambient temperature and stirred for 90 min. The mixture was poured into cold saturated aqueous sodium bicarbonate and extracted with pentane. The mixture was washed with aqueous 1 N sodium hydrogen sulfate and saturated aqueous sodium bicarbonate. The mixture was dried with anhydrous sodium sulfate and concentrated in vacuo to give 1.52 g of an orange oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 3% ethyl acetate/hexanes, 50-mL fractions) to afford 1.02 g (80%) of the title compound: $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.15 (m, 1 H, C*H*OTBS), 4.07 (t, 2 H, $CH_2O$), 3.60 (m, 1 H, C*H*OTBS), 2.69 (t, 1 H, $CH_2Ph$), 2.47 (ABX, 2 H $CH_2CO_2R$), 1.94 (m, 2 H, $CH_2CH_2Ph$), 1.45–1.78 (m, 3 H, $CH(CH_3)_2$ and $CH_2CHOTBS$), 0.89 (m, 24 H, $CH(CH_3)_2$ and $SiC(CH_3)_3$), 0.02–0.08 (4s, 12 H, $Si(CH_3)_2$).

**(3*S**,5*S**)-3,5-Bis(*tert*-butyldimethylsiloxy)-6-methylheptanal (34).** To a solution of 1.02 g (1.94 mmol) of 3-phenylpropyl *anti*-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (**33**) in 10.0 mL of anhydrous dichloromethane at −78 °C was added 332 mg (2.33 mL of a 1.0 M solution in dichloromethane, 2.33 mmol) of diisobutylaluminum hydride over 1 h via syringe pump. The mixture was stirred for 30 min at −78 °C and quenched with 0.5 mL of methanol. Sodium potassium tartrate (0.5 M, 10 mL) was added and the mixture was stirred vigorously at ambient temperature for 30 min. The mixture was extracted with pentane and the organic layer was dried with anhydrous sodium sulfate and concentrated in vacuo to give 1.00 g (100%). The mixture was purified by flash chromatography (60 × 180 mm column, 2.5% ethyl acetate in hexanes, 50-mL fractions) to give 693 mg (92%) of the title aldehyde as a colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) 9.80 (t, 1 H, RC*H*O), 4.25 (qn, 1 H, (C*H*OTBS), 3.64 (m, 1 H, C*H*OTBS), 2.56 (m, 2 H, $CH_2CHO$), 1.45–1.80 (m, 3 H, $CH(CH_3)_2$ and $CH_2CHOTBS$), 0.83–0.92 (2s and 2d, 24 H, $SiC(CH_3)_3$ and $CH(CH_3)_2$), 0.05–0.10 (s, 12 H, $Si(CH_3)_2$).

**3-Phenylpropyl (3*R**,5*R**,7*S**)-5,7-Bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (36) and (3*S**,5*R**,7*S**)-5,7-Bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (37).** To a solution of 260 mg (2.57 mmol) of diisopropylamine in 2.2 mL of anhydrous tetrahydrofuran at −78 °C was added 150 mg (1.51 mL of a 1.56 M solution in hexane, 2.35 mmol) of *n*-butyllithium. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 381 mg (2.14 mmol) of 3-phenylpropyl acetate in 1.0 mL of anhydrous tetrahydrofuran was added via cannula, and the solution was warmed to 0 °C. After 1 h at 0 °C the mixture was recooled to −78 °C and a solution of 690 mg (1.78 mmol) of *anti*-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanal (**34**) in 3.0 mL of anhydrous tetrahydrofuran was added via cannula. After 1 min the mixture was poured into 25 mL of aqueous 1 N sodium hydrogen sulfate and the mixture was extracted with pentane. The organic layer was washed with saturated aqueous sodium bicarbonate, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 1.13 g (105%) of pale yellow oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 7% ethyl acetate in hexane, 50-mL fractions) to give 860 mg (85%) of the title mixture of epimeric aldol adducts as a colorless oil. The two epimers were then separated by flash chromatography on silica gel (60 × 180 mm column, 80% dichloromethane in carbon tetrachloride, 50-mL fractions) to afford 351 mg (35%) of the anti, anti isomer and 327 mg (32%) of the anti, syn isomer. Anti, anti isomer, **36**: $R_f$ 0.38 (dichloromethane); $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.36 (m, 1 H, C*H*OH), 4.12 (t, 2 H, $CH_2O$), 4.00 (m, 1 H, C*H*OTBS), 3.51 (m, 2 H, O*H* and C*H*OTBS), 2.70 (t, 2 H, $CH_2Ph$), 2.51 (dd, 1 H, C*H*HCO$_2$R), 2.44 (dd, 1 H, CH*H*CO$_2$R), 1.98 (m, 2 H, $CH_2CH_2Ph$), 1.50–1.80 (m, 3 H, $(CH_3)_2CHCH(OTBS)CH_2$), 0.90 (2s, 18 H, $SiC(CH_3)_3$), 0.86 (2d, 6 H, $CH(CH_3)_2$), 0.10 (2s, 6 H, $Si(CH_3)_2$), 0.07 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$).

Anti, syn isomer, **37**: $R_f$ 0.33 (dichloromethane); $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.19 (m, 3 H, C*H*OH and $CH_2O$), 3.93 (qn, 1 H, C*H*OTBS), 3.60 (m, 1 H, C*H*OTBS), 3.33 (d, 1 H, O*H*), 2.70 (t, 2 H, $CH_2Ph$), 2.49 (ABX, 2 H, $CH_2CO_2R$), 1.97 (m, $CH_2CH_2Ph$), 1.48–1.80 (m, 3 H, $(CH_3)_2CHCH(OTBS)CH_2$), 0.90 (2s, 18 H, $SiC(CH_3)_3$), 0.86 (2d, 6 H, $CH(CH_3)_2$), 0.10 (s, 6 H, $Si(CH_3)_2$), 0.06 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$).

**3-Phenylpropyl (3*R**,5*R**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoate (29).** To a solution of 43.7 mg (0.08 mmol) of 3-phenylpropyl *anti*,-

*anti*-5,7-bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**36**, $R_f$ 0.38 (dichloromethane)) in 10.0 mL of freshly distilled acetonitrile at 0 °C was added 1.0 mL of pyridinium fluoride (Aldrich). After 30 min the mixture was poured into cold saturated aqueous sodium bicarbonate and extracted three times with dichloromethane. The combined organic layers were washed with aqueous 1 N sodium hydrogen sulfate and then with saturated aqueous sodium bicarbonate, each aqueous layer being back extracted twice with dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo to give 26.9 mg (103%) of a colorless solid. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 75% ethyl acetate in hexanes, 5-mL fractions) to give 20.5 mg (79%) of the title compound as a colorless solid: $R_f$ 0.29 (75% ethyl acetate in hexanes); mp 120.0–121.5 °C; IR ($CHCl_3$) 3460 (br), 3010, 2963, 1725, 1500, 1180, 1073 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H aromatic C*H*), 4.37 (m, 1 H, C*H*OH), 4.28 (m, 1 H, C*H*OH), 4.15 (t, 2 H, $CH_2O$), 3.67 (m, 1 H, C*H*OH), 3.57 (d, 1 H, O*H*), 3.32 (d, 1 H, O*H*), 2.69 (t, 2 H, $CH_2Ph$), 2.56 (m, 2 H, $CH_2CO_2R$), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.70 (m, 5 H, $CH(CH_3)_2$ and $CH_2CH(OH)CH_2CH(OH)$), 0.94 (d, 3 H, $CH_3$), 0.91 (d, 3 H, $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 172.64, 141.06, 128.44, 128.34, 126.04, 73.81, 66.28, 65.86, 64.13, 42.72, 41.59, 40.26, 33.89, 32.18, 30.10, 18.57, 17.71.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.47; H, 8.79.

**(3*R**,5*R**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoic Acid δ-Lactone (38a).** To a solution of 15.9 mg (47.0 μmol) of 3-phenylpropyl *anti*,-*anti*-3,5,7-trihydroxy-8-methylnonanoate (**29**) in 10.0 mL of anhydrous acetonitrile was added 3 drops of aqueous 50% hydrogen fluoride. After 10 min, 15 mL of aqueous saturated sodium bicarbonate was added, and the mixture was extracted five times with dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo to give 11.6 mg. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 25% acetone in ethyl acetate, 8-mL fractions) to give 5.0 mg (53%) of the title compound: $R_f$ 0.08 (75% ethyl acetate in hexane); $^1H$ NMR (300 MHz, $CDCl_3$) 4.49 (ddt, 1 H, C*H*OCOR, $J$ = 2.9, 2.9, 9.7, 11.7 Hz), 4.25 (m, 1 H, C*H*OH), 3.72 (m, 1 H, C*H*OH), 2.87 (ddd, 1 H, C*H*HCO$_2$R equatorial, $J$ = 1.15, 5.82, 17.02 Hz), 2.44 (dd, 1 H, CH*H*CO$_2$R axial, $J$ = 7.44, 17.09 Hz), 2.23 (dddd, 1 H, CH(OCO)C*H*HCH(OH)CH$_2$CO$_2$R equatorial, $J$ = 1.14, 2.97, 6.81, 13.57 Hz), 1.56–1.95 (m, 5 H, O*H* and C*H*(CH$_3$)$_2$, C*H*$_2$, CH(OCO)CH*H*CH(OH)CH$_2$CO$_2$R axial), 0.88 (d, 6 H, C*H*$_3$, $J$ = 6.82 Hz).

**(3*R**,5*R**,7*S**)-3,7-Bis(benzoyloxy)-5-hydroxy-8-methylnonanoic Acid δ-Lactone (38b).** To a solution of 5.0 mg (24.7 μmol) of *anti*,-*anti*-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**38a**) in 3.0 mL of anhydrous dichloromethane at 0 °C was added 195 mg (2.47 mmol) of pyridine and 174 mg (1.24 mmol) of benzoyl chloride. After 10 min the mixture was warmed to ambient temperature and stirred for 4.5 h. The reaction was quenched by addition of 10 mL of saturated aqueous sodium bicarbonate and the mixture was extracted twice with dichloromethane. The combined organic layers were washed with aqueous 1 N sodium hydrogen sulfate and saturated aqueous sodium bicarbonate. The organic layer was dried with anhydrous sodium sulfate and concentrated in vacuo to give 136 mg of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 40% ethyl acetate in hexanes, 8-mL fractions) to give 9.6 mg (95%) of the title compound as a colorless oil: $R_f$ 0.37 (30% ethyl acetate in hexanes); $^1H$ NMR (300 MHz, $CDCl_3$) 7.46–8.20 (m, 10 H, aromatic C*H*), 5.45 (m, 1 H, C*H*OBz), 5.36 (m, 1 H, C*H*OBz), 4.41 (m, 1 H, C*H*OCOR), 2.99 (dd, 1 H, C*H*HCO$_2$R, $J$ = 6.11, 17.02 Hz), 2.73 (dd, 1 H, CH*H*CO$_2$R, $J$ = 5.89, 17.09 Hz), 2.51 (ddd, 1 H, C*H*HCH(OBz)CH$_2$CO$_2$R, $J$ = 3.04, 6.55, 14.13 Hz), 1.92–2.11 (m, 3 H, C*H*$_2$CH(OBz)C*H*(CH$_3$)$_2$), 1.84 (ddd, 1 H, CH*H*CH(OBz)CH$_2$CO$_2$R, $J$ = 7.75, 11.74, 14.18 Hz), 1.00 (2d, 6 H, C*H*$_3$).

**3-Phenylpropyl (3S*,5R*,7S*)-3,5,7-Trihydroxy-8-methylnonanoate (30).** The procedure used was identical with that used for the production of 3-phenylpropyl (3*R**,5*R**,7*S**)-3,5,7-trihydroxy-8-methylnonanoate (**29**). Thus, 47.6 mg (0.08 mmol) of 3-phenylpropyl *anti*,*syn*-5,7-bis-(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**37**, $R_f$ 0.33 (dichloromethane)) was treated with pyridinium fluoride (Aldrich) to afford 30.6 mg (108%) of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 75% ethyl acetate in hexane, 5-mL fractions) to give 21.2 mg (71%) of the title compound as a colorless oil which crystallized upon standing: $R_f$ 0.33 (75% ethyl acetate in hexane); mp 51.0–52.8 °C; IR ($CHCl_3$) 3460 (br), 3010, 2965, 1725, 1183 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.27 (m, 2 H, C*H*OH, C*H*OH), 4.15 (t, 2 H, $CH_2O$), 4.05 (br s, 1 H, O*H*), 3.91 (br s, 1 H, O*H*), 3.70 (m, 1 H, C*H*OH), 2.71 (t, 2 H, $CH_2Ph$), 2.52 (m, 2 H, $CH_2CO_2R$), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.67 (m, 5 H, $CH(CH_3)_2$ and CH(OH)C*H*$_2$CH(OH)C*H*$_2$), 0.95 (d, 3 H, C*H*$_3$), 0.89 (d, 3 H, C*H*$_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$) 172.24, 140.97, 128.37, 128.27, 125.97, 73.31, 69.57, 68.72, 64.06, 42.42, 41.92, 39.99, 33.80, 32.08, 30.00, 19.45, 17.71.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.51; H, 8.83.

**(3S*,5R*,7S*)-3,5,7-Trihydroxy-8-methylnonanoic Acid δ-Lactone (39a).** To a solution of 18.6 mg (55.0 μmol) of 3-phenylpropyl *anti*,-*syn*-3,5,7-trihydroxy-8-methylnonanoate (**30**) in 10.0 mL of anhydrous acetonitrile was added 3 drops of aqueous 50% hydrogen fluoride. After 1 h, 15 mL of aqueous saturated sodium bicarbonate was added and the mixture was extracted five times with dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo to give 11.0 mg. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 25% acetone in ethyl acetate, 8-mL fractions) to give 4.7 mg (42%) of the title compound: $^1H$ NMR (300 MHz, $CDCl_3$) 5.00 (m, 1 H, C*H*OCOR, $J$ = 2.8, 5.6, 12.8, 14.2 Hz), 4.38 (br m, 1 H, C*H*OH), 3.78 (br m, 1 H, C*H*OH), 2.73 (dd, 1 H, C*H*HCO$_2$R axial, $J$ = 4.69, 17.71 Hz), 2.65 (ddd, 1 H, CH*H*CO$_2$R equatorial, $J$ = 1.32, 3.67, 17.69 Hz), 2.56 (br s, 1 H, O*H*), 2.00 (m, 1 H, CH*H*CH(OH)CH$_2$CO$_2$R), 1.53–1.84 (m, 4 H, C*H*(CH$_3$)$_2$ and C*H*$_2$, CH*H*CH(OH)CH$_2$CO$_2$R), 0.93 (d, 6 H, C*H*$_3$, $J$ = 6.80 Hz).

**(3S*,5R*,7S*)-3,7-Bis(benzoyloxy)-5-hydroxy-8-methylnonanoic Acid δ-Lactone (39b).** To a solution of 4.7 mg (23.2 μmol) of *anti*,*syn*-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**39a**) in 3.0 mL of anhydrous dichloromethane at 0 °C was added 183 mg (2.32 mmol) of pyridine and 163 mg (1.16 mmol) of benzoyl chloride. After 10 min the mixture was warmed to ambient temperature and stirred for 3.0 h. The reaction was quenched by addition of 10 mL of saturated aqueous sodium bicarbonate and the mixture was extracted twice with dichloromethane. The combined organic layers were washed with aqueous 1 N sodium hydrogen sulfate and saturated aqueous sodium bicarbonate. The organic layer was dried with anhydrous sodium sulfate and concentrated in vacuo to give 128 mg of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 40% ethyl acetate in hexanes, 8-mL fractions) to give 6.6 mg (69%) of the title compound as a colorless, crystalline solid: $R_f$ 0.25 (30% ethyl acetate in hexanes); $^1H$ NMR (300 MHz, $CDCl_3$) 7.28–8.00 (m, 10 H, aromatic C*H*), 5.49 (m, 1 H, C*H*OBz), 5.37 (m, 1 H, C*H*OBz), 4.81 (m, 1 H, C*H*OCOR), 2.92 (dd, 1 H, C*H*HCO$_2$R, $J$ = 5.20, 18.17 Hz), 2.83 (ddd, 1 H, C*H*HCO$_2$R, $J$ = 1.38, 3.76, 18.19 Hz), 2.22 (m, 1 H, C*H*HCH(OBz)CH$_2$CO$_2$R), 1.93–2.12 (m, 1 H, (CH$_3$)$_2$C*H*CH(OBz)C*H*$_2$CH(OCOR)C*H*H), 1.01 (2d, 6 H, CH(C*H*$_3$)$_2$).

**3-Phenylpropyl (3R*,5S*)-3,5-Bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (40).** The procedure used was identical with that for the preparation of 3-phenylpropyl (3*S**,5*S**)-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (**33**). Thus, 634 g (2.15 mmol) of 3-phenylpropyl *syn*-3,5-dihydroxy-6-methylheptanoate (**4**) was treated with 1.30 g (12.9 mmol) of triethylamine and 1.71 g (6.46 mmol) of *tert*-butyldimethylsilyl triflate to afford 1.45 g of an orange oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 3% ethyl acetate/hexanes, 50-mL fractions) to afford 671 mg (60%) of the title compound: $^1H$ NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.26 (m, 1 H, C*H*OTBS), 4.11 (m, 2 H, C*H*$_2$O), 3.59 (m, 1 H, C*H*OTBS), 2.71 (t, 1 H, C*H*$_2$Ph), 2.55 (dd, 1 H, C*H*HCO$_2$R), 2.42 (dd, 1 H, CH*H*CO$_2$R), 1.98 (m, 2 H, C*H*$_2$CH$_2$Ph), 1.55–1.85 (m, 3 H, C*H*(CH$_3$)$_2$ and C*H*$_2$CHOTBS), 0.94 (s, 9 H, SiC(C*H*$_3$)$_3$), 0.91 (d, 3 H, C*H*$_3$), 0.88 (s, 9 H, SiC(C*H*$_3$)$_3$), 0.84 (d, 3 H, C*H*$_3$), 0.09 (2s, 6 H, Si(C*H*$_3$)$_2$), 0.06 (s, 6 H, Si(C*H*$_3$)$_2$).

**(3R*,5S*)-3,5-Bis(*tert*-butyldimethylsiloxy)-6-methylheptanal (41).** The procedure used was identical with that used for the reduction of 3-phenylpropyl *anti*-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (**33**). Thus, 667 mg (1.28 mmol) of 3-phenylpropyl *syn*-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanoate (**40**) reacted with 218 mg (1.53 mL of a 1.0 M solution in dichloromethane, 1.53 mmol) of diisobutylaluminum hydride to give 683 mg (102%). The mixture was purified by flash chromatography (60 × 180 mm column, 3% ethyl acetate in hexanes, 50-mL fractions) to afford 452 mg (91%) of the title aldehyde as a colorless oil: $^1H$ NMR (300 MHz, $CDCl_3$) 9.80 (dd, 1 H, RC*H*O), 4.29 (m, 1 H, C*H*OTBS), 3.52 (qn, 1 H, C*H*OTBS), 2.57 (ddd, 1 H, C*H*HCHO), 2.44 (ddd, 1 H, CH*H*CHO), 1.45–1.82 (m, 3 H, C*H*(CH$_3$)$_2$ and C*H*$_2$CHOTBS), 0.87 (2s and 1d, 21 H, SiC(C*H*$_3$)$_3$ and CH(C*H*$_3$)(CH$_3$)), 0.80 (d, 3 H, C*H*$_3$), 0.03–0.08 (3s, 12 H, Si(C*H*$_3$)$_2$).

**3-Phenylpropyl (3R*,5S*,7S*)-5,7-Bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (43) and (3S*,5S*,7S*)-5,7-Bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (44).** The procedure used was identical with that used for the production of 3-phenylpropyl (3*R*,5*R**,7*S**)-5,7-bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**36**) and (3*S**,5*R**,7*S**)-5,7-bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**37**). Thus, 250 mg (1.40 mmol) of 3-phenylpropyl acetate was enolized with LDA and the enolate quenched

with 389 mg (1.15 mmol) of *syn*-3,5-bis(*tert*-butyldimethylsiloxy)-6-methylheptanal to afford 736 mg of a pale-yellow oil. The mixture was purified by flash chromatography on silica gel (60 × 180 mm column, 10% ethyl acetate in hexanes, 50-mL fractions) to give 621 mg (95%) of the title mixture of epimeric aldol adducts as a colorless oil. The two epimers were then separated by flash chromatography on silica (60 × 180 mm column, 6% ethyl acetate in hexanes, 50-mL fractions) to afford 269 mg (41%) of the syn, syn isomer and 279 mg (43%) of the syn, anti isomer.

**Syn, syn isomer, 43**: $R_f$ 0.39 (10% ethyl acetate/hexanes); $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.34 (m, 1 H, C*H*OH), 4.16 (m, 3 H, C*H*OTBS and $CH_2O$), 3.76 (d, 1 H, O*H*), 3.52 (m, 1 H, C*H*OTBS), 2.70 (t, 2 H, $CH_2Ph$), 2.54 (dd, 1 H, C*H*HCO$_2$R), 2.43 (dd, 1 H, CH*H*CO$_2$R), 1.97 (m, 2 H, $CH_2CH_2Ph$), 1.50–1.83 (m, 3 H, $(CH_3)_2CHCH(OTBS)CH_2$), 0.88 (2s, 18 H, $SiC(CH_3)_3$), 0.86 (2d, 6 H, $CH(CH_3)_2$), 0.10 (2s, 6 H, $Si(CH_3)_2$), 0.03 (s, 6 H, $Si(CH_3)_2$).

**Syn, anti isomer, 44**: $R_f$ 0.30 (10% ethyl acetate/hexanes); $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.00–4.24 (m, C*H*OH and C*H*OTBS and $CH_2O$), 3.60 (d, 1 H, O*H*), 3.55 (m, 1 H, C*H*OTBS), 2.70 (t, 2 H, $CH_2Ph$), 2.48 (d, 2 H, $CH_2CO_2R$), 1.97 (m, 2 H, $CH_2CH_2Ph$), 1.45–1.82 (m, $(CH_3)_2CHCH(OTBS)CH_2$), 0.90 (s, 18 H, $SiC(CH_3)_3$), 0.85 (2d, 6 H, $CH(CH_3)_2$), 0.11 (s, 6 H, $Si(CH_3)_2$), 0.03 (s, 6 H, $Si(CH_3)_2$).

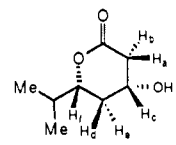
**3-Phenylpropyl (3*R**,5*S**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoate (31).** To a solution of 50.2 mg (0.09 mmol) of 3-phenylpropyl *syn,syn*-5,7-bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**43**, $R_f$ 0.30, 10% ethyl acetate in hexanes) in 10.0 mL of freshly distilled acetonitrile at 0 °C was added 1.0 mL of pyridinium fluoride (Aldrich). After 65 min the mixture was poured into cold saturated aqueous sodium bicarbonate and extracted three times with dichloromethane. The combined organic layers were washed with aqueous 1 N sodium hydrogen sulfate and then with saturated aqueous sodium bicarbonate, each aqueous layer being back-extracted twice with dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo to give 31.3 mg (105%) of a brown oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 75% ethyl acetate in hexanes, 5-mL fractions) to give 22.5 mg (75%) of the title compound as a colorless oil: $R_f$ 0.55 (75% ethyl acetate in hexanes); IR ($CHCl_3$) 3470 (br), 3015, 2967, 1725, 1607, 1185 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.40 (br s, 1 H, O*H*), 4.32 (m, 3 H, $CH_2O$ and C*H*OH), 3.95 (d, 1 H, O*H*), 3.67 (br q, 1 H, C*H*OH), 3.19 (br s, 1 H OH), 2.68 (t, 2 H, $CH_2Ph$), 2.49 (m, 2 H, $CH_2CO_2R$), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.50–1.75 (m, 5 H, C*H*(CH$_3$)$_2$ and CH(OH)C$H_2$CH(OH)C$H_2$(OH)), 0.92 (2d, 6 H, $CH_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 172.21, 140.98, 128.37, 128.27, 125.96, 77.25, 72.82, 68.52, 64.01, 43.15, 41.83, 39.93, 34.06, 32.08, 30.00, 18.11, 17.35.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.34; H, 8.96.

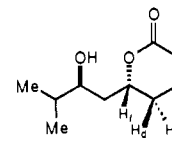
**(3*R**,5*S**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoic Acid δ-Lactone (45a).** The procedure used was identical with that used for the production of (3*S**,5*R**,7*S**)-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**39a**). Thus, 15.2 mg (45.0 μmol) of 3-phenylpropyl *syn,syn*-3,5,7-trihydroxy-8-methylnonanoate (**31**) was treated with aqueous 50% hydrogen fluoride to give 12.3 mg of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 18% acetone in ethyl acetate, 8-mL fractions) to give 5.6 mg (62%) of the title compound: $R_f$ 0.12 (75% ethyl acetate in hexane); $^1$H NMR (300 MHz, $CDCl_3$) 4.95 (ddt, 1 H, C*H*OCOR, $J$ = 2.9, 6.6, 11.4 Hz), 4.39 (br m, 1 H, C*H*OH), 3.60 (br m, 1 H, C*H*OH), 2.93 (br s, 1 H, O*H*), 2.73 (dd, 1 H, C*H*HCO$_2$R, $J$ = 4.65, 17.71 Hz), 2.65 (ddd, 1 H, CH*H*CO$_2$R, $J$ = 1.43, 3.62, 17.76 Hz), 2.64 (br d, 1 H, O*H*), 2.08 (dqn, 1 H, C*H*HCH(OH)CH$_2$CO$_2$R equatorial, $J$ = 1.52, 14.46 Hz), 1.67–1.95 (m, 4 H C*H*(CH$_3$)$_2$ and $CH_2$ and CH*H*CH(OH)CH$_2$CO$_2$R axial), 0.94 (2d, 6 H, $CH_3$).

**(3*R**,5*S**,7*S**)-3,7-Bis(benzoyloxy)-5-hydroxy-8-methylnonanoic Acid δ-Lactone (45b).** The procedure used was identical with that used for the production of (3*R**,5*R**,7*S**)-3,7-bis(benzoyloxy)-5-hydroxy-8-methylnonanoic acid δ-lactone (**38b**). Thus, 5.6 mg (27.7 μmol) of *syn,syn*-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**45a**) was treated with 194 mg (1.38 mmol) of benzoyl chloride in the presence of 219 mg (2.77 mmol) of pyridine and the product was purified by flash chromatography on silica gel (15 × 180 mm column, 30% ethyl acetate in hexanes, 8-mL fractions) to give 9.8 mg (86%) of the title compound as a colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) 7.88 (d, 4 H, aromatic C*H*), 7.25–7.60 (m, 6 H, aromatic C*H*), 5.50 (m, 1 H, C*H*OBz), 5.13 (ddd, 1 H, C*H*OBz, $J$ = 2.5, 5.2, 10.5 Hz), 4.76 (m, 1 H, C*H*OCOR), 2.92 (dd, 1 H, C*H*HCO$_2$R, $J$ = 5.04, 18.40 Hz), 2.85 (ddd, 1 H, CH*H*CO$_2$R, $J$ = 1.17, 3.36, 18.54 Hz), 2.63 (m, 1 H, C*H*HCH(OBz)CH$_2$CO$_2$R), 2.36 (ddd, 1 H, CH*H*CH(OBz)CH$_2$CO$_2$R, $J$ = 4.32, 10.57, 14.56 Hz), 1.80–2.08 (m, 3 H, (CH$_3$)C*H*CH(OBz)CH$_2$), 1.01 (2d, 6 H, CH(C$H_3$)$_2$).

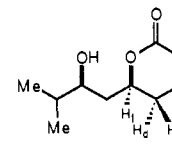
**Table V.** Anti-Diol Lactone Coupling Constants



3a



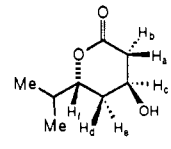
38a Anti-Anti (AA)



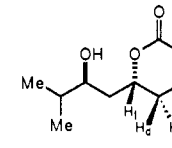
46a Syn-Anti (SA)

| 3a | $J$, Hz | 38a | $J$, Hz | 46a | $J$, Hz |
|---|---|---|---|---|---|
| $J_{ab}$ | 17.1 | $J_{ab}$ | 17.1 | $J_{ab}$ | 17.0 |
| $J_{ac}$ | 5.9 | $J_{ac}$ | 5.8 | $J_{ac}$ | 5.8 |
| $J_{ad}$ | 1.5 | $J_{ad}$ | 1.2 | $J_{ad}$ | 1.3 |
| $J_{bc}$ | 8.2 | $J_{bc}$ | 7.4 | $J_{bc}$ | 7.6 |
| $J_{cd}$ | 5.3 | $J_{cd}$ | 5.5 | $J_{cd}$ | 4.3 |
| $J_{ce}$ | 9.4 | $J_{ce}$ | 8.3 | $J_{ce}$ | 9.1 |
| $J_{de}$ | 13.5 | $J_{de}$ | 13.5 | $J_{dc}$ | 13.8 |
| $J_{df}$ | 2.5 | $J_{df}$ | 3.0 | $J_{df}$ | 3.1 |
| $J_{ef}$ | 11.6 | $J_{ef}$ | 11.5 | $J_{ef}$ | 11.7 |

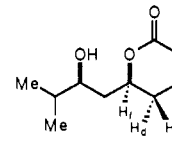
**Table VI.** Syn-Diol Lactone Coupling Constants



4a



39a Anti-Syn (AS)



45a Syn-Syn (SS)

| 4a | $J$, Hz | 39a | $J$, Hz | 45a | $J$, Hz |
|---|---|---|---|---|---|
| $J_{ab}$ | 17.6 | $J_{ab}$ | 17.7 | $J_{ab}$ | 17.7 |
| $J_{ac}$ | 4.9 | $J_{ac}$ | 3.8 | $J_{ac}$ | 3.6 |
| $J_{ad}$ | 1.4 | $J_{ad}$ | 1.4 | $J_{ad}$ | 1.4 |
| $J_{bc}$ | 3.6 | $J_{bc}$ | 4.7 | $J_{bc}$ | 4.7 |
| $J_{cd}$ | 3.4 | $J_{cd}$ | 3.6 | $J_{cd}$ | 3.6 |
| $J_{ce}$ | 3.4 | $J_{ce}$ | 1.9 | $J_{ce}$ | 3.1 |
| $J_{de}$ | 14.8 | $J_{de}$ | 14.5 | $J_{de}$ | 14.5 |
| $J_{df}$ | 3.1 | $J_{df}$ | 2.8 | $J_{df}$ | 2.4 |
| $J_{ef}$ | 11.6 | $J_{ef}$ | 11.5 | $J_{ef}$ | 11.6 |

**3-Phenylpropyl (3*S**,5*S**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoate (32).** The procedure used was identical with that used for the production of 3-phenylpropyl (3*R**,5*S**,7*S**)-3,5,7-trihydroxy-8-methylnonanoate (**31**). Thus, 56.5 mg (0.10 mmol) of 3-phenylpropyl *syn,anti*-5,7-bis(*tert*-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoate (**44**, $R_f$ 0.39, 10% ethyl acetate in hexanes) was treated with pyridinium fluoride (Aldrich) to afford 32.8 mg (97%) of a brown oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 75% ethyl acetate in hexanes, 5-mL fractions) to give 21.6 mg (64%) of the title compound as a colorless oil which crystallized on standing: $R_f$ 0.48 (75% ethyl acetate in hexanes); mp 50.7–52.0 °C; IR ($CHCl_3$) 3460 (br), 3010, 2963, 1725, 1180, 1086 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) 7.24 (m, 5 H, aromatic C*H*), 4.37 (m, 1 H, C*H*OH), 4.16 (m, 3 H, $CH_2O$ and C*H*OH), 3.77 (d, 1 H, O*H*), 3.68 (m, 1 H, C*H*OH), 3.13 (br s, 1 H, O*H*), 2.72 (t, 2 H, $CH_2Ph$), 2.55 (m, 2 H, $CH_2CO_2R$), 1.98 (m, 2 H, $CH_2CH_2CH_2Ph$), 1.65 (m, 5 H, C*H*(CH$_3$)$_2$ and CH(OH)C$H_2$CH(OH)C$H_2$(OH)), 0.92 (2d, 6 H, $CH_3$); $^{13}$C NMR (75.5 MHz, $CDCl_3$) 172.48, 141.01, 128.39, 128.29, 125.97, 77.54, 69.97, 65.43, 64.04, 42.96, 41.66, 39.53, 34.18, 32.10, 30.04, 18.18, 17.37.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93. Found: C, 67.52; H, 9.02.

**(3*S**,5*S**,7*S**)-3,5,7-Trihydroxy-8-methylnonanoic Acid δ-Lactone (46a).** The procedure used was identical with that used for the production of (3*S**,5*R**,7*S**)-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**39a**). Thus, 14.2 mg (42.0 μmol) of 3-phenylpropyl *syn,anti*-3,5,7-trihydroxy-8-methylnonanoate (**32**) was treated with aqueous 50% hydrogen fluoride to afford 11.2 mg of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 × 180 mm column, 18% acetone in ethyl acetate, 8-mL fractions) to give 5.5 mg (65%) of the title compound: $R_f$ 0.17 (75% ethyl acetate in hexane); $^1$H NMR (300 MHz, $CDCl_3$) 4.48 (ddt, 1 H, C*H*OCOR, $J$ = 3.1, 6.5, 11.6 Hz), 4.28 (br m, 1 H, C*H*OH), 3.59 (br m, 1 H, C*H*OH), 2.92 (ddd, 1 H, C*H*HCO$_2$R equatorial, $J$ = 1.2, 5.7, 17.0 Hz), 2.57 (br d, 1 H, O*H*), 2.50 (dd, 1 H, CH*H*CO$_2$R axial, $J$ = 7.6, 17.0 Hz), 2.38 (dddd, 1 H, C*H*HCH(OH)CH$_2$CO$_2$R equatorial, $J$ = 1.3, 3.2, 5.5, 13.8 Hz), 2.16 (br d, 1 H, O*H*, $J$ = 4.1 Hz), 1.93 (ddd, 1 H, C*H*H, $J$ = 6.5, 9.6, 14.4 Hz),

1.60–1.83 (m, 3 H, $CH(CH_3)_2$ and $CH_2$), 0.96 (2d, 6 H, $CH_3$).

**(3S*,5S*,7S*)-3,7-Bis(benzoyloxy)-5-hydroxy-8-methylnonanoic Acid δ-Lactone (46b).** The procedure used was identical with that used for the preparation of (3S*,5R*,7S*)-3,7-bis(benzoyloxy)-5-hydroxy-8-methylnonanoic acid δ-lactone (**39b**). Thus, 5.5 mg (27.2 μmol) of *syn,anti*-3,5,7-trihydroxy-8-methylnonanoic acid δ-lactone (**46a**) was treated with 191 mg (1.36 mmol) of benzoyl chloride in the presence of 215 mg (2.72 mmol) of pyridine and the product was purified by flash chromatography on silica gel (15 × 180 mm column, 30% ethyl acetate in hexanes, 8-mL fractions) to give 9.5 mg (85%) of the title compound as a colorless oil: $R_f$ 0.29 (30% ethyl acetate in hexanes); $^1H$ NMR (300 MHz, $CDCl_3$) 7.97–8.08 (m, 4 H, aromatic C*H*), 7.38–7.60 (m, 6 H, aromatic C*H*), 5.46 (m, 1 H, C*H*OBz), 5.13 (m, 1 H, C*H*OBz), 4.40 (m, 1 H, C*H*OCOR), 3.00 (dd, 1 H, C*H*$HCO_2R$, $J$ = 6.02, 17.04 Hz), 2.77 (ddd, 1 H, C*H*HCH(OBz)$CH_2CO_2R$, $J$ = 3.07, 6.51, 14.10 Hz), 2.71 (dd, 1 H, $CHHCO_2R$, $J$ = 6.03, 17.07 Hz), 2.35 (ddd, 1 H, 1CH*H*CHO(OBz)$CH_2CO_2R$, $J$ = 5.02, 9.80, 14.62 Hz), 1.92–2.10 (m, 3 H, $(CH_3)_2CHCH(OBz)CH_2$), 1.80 (ddd, 1 H, CH*H*CH(OBz)-$CH_2CO_2R$, $J$ = 7.80, 11.66, 14.13 Hz), 1.01 (2d, 6 H, $CH(CH_3)_2$).

**Reduction of 3-Phenylpropyl 7-Hydroxy-3,5-dioxo-8-methylnonanoate (28) with Tetramethylammonium Triacetoxyborohydride.** To a solution of 440 mg (1.67 mmol, 20.6 equiv) of tetramethylammonium triacetoxy borohydride in 700 μL of anhydrous acetic acid was added a solution of 27.1 mg (81.0 μmol) of 3-phenylpropyl 7-hydroxy-3,5-dioxo-8-methylnonanoate (**28**) in 300 μL of anhydrous acetic acid. The mixture was stirred at ambient temperature for 30 min. The solution was poured onto ice and the reaction vessel was rinsed onto the ice with 10 mL of dichloromethane. The biphasic mixture was washed with saturated aqueous sodium bicarbonate (2 × 100 mL), the aqueous layers being back extracted with dichloromethane (5 × 10 mL) after each wash. The combined organic layers were dried over anhydrous sodium sulfate and concentrated in vacuo to leave 30.7 mg (113% mass balance) of a colorless solid. The mixture was purified by flash chromatography on silica gel (ethyl acetate, 10 × 180 mm column, 4-mL fractions) to give 9.5 mg (35%) of a colorless oil which contained a 4:1 mixture of anti dihydroxy keto ester **47**. Also isolated was 15.5 mg (56%) of a mixture of triol esters **29–32** as a colorless, crystalline solid. The column was flushed with an additional 200 mL of ethyl acetate which was concentrated to give an additional 1.6 mg of the triol esters. The triols were combined (17.1 mg, 63%) and analyzed by HPLC (Zorbax 5 μm silica, 2% methanol in 70:30 isooctane/dichloromethane, 2 mL/min, λ = 258 nm). The triol esters were present in a ratio of 41:6.1:1:0 (Anti-Anti, **29**: Anti-Syn, **30**: Syn-Anti, **31**: Syn-Syn, **32**). The mixture was separated by flash chromatography on silica gel (3% methanol in 70:30 isooctane/dichloromethane, 15 × 180 mm column, 4-mL fractions) to give 13.6 mg (50%) of the Anti-Anti triol ester **29** as a colorless, crystalline solid.

**Acknowledgment.** Support was provided by the National Institutes of Health and the National Science Foundation. K.T.C. acknowledges a predoctoral fellowship from the Shell Company Foundation. E.M.C. acknowledges support from the National Science Foundation for a predoctoral fellowship. The NIH BRS Shared Instrumentation Grant Program 1 S10 RR01748-01A1 is acknowledged for providing NMR facilities.

**Registry No. 1**, 113778-34-0; (±)-**2**, 113778-35-1; (±)-**3**, 113778-36-2; (±)-**3a**, 113778-38-4; (±)-**3b**, 113778-39-5; (±)-**4**, 113778-37-3; (±)-**4a**, 113778-40-8; (±)-**4b**, 113778-64-6; (±)-**7a**, 113778-41-9; (±)-**7b**, 113778-44-2; (±)-**7b** (TBS ether), 113778-82-8; (±)-**8d**, 103729-84-6; (±)-**8a** (acetonide), 113778-76-0; DL-**8b**, 113778-42-0; DL-**8b** (acetonide), 113778-79-3; DL-**8b** (1-TBS ether), 113778-81-7; (±)-**9a**, 103729-88-0; DL-**9b**, 113778-43-1; DL-**9b** (acetonide), 113778-80-6; DL-**6b** (1-TBS ether), 113778-88-4; **12**, 55233-96-0; (±)-**13**, 113778-84-0; (±)-**14**, 113778-45-3; (±)-**15**, 113778-46-4; (±)-**17**, 113778-48-6; (±)-**18**, 113778-87-3; (±)-**20**, 113778-85-1; (±)-**21**, 113778-86-2; **22** ($R_1$ = $Me_2CH$; $R_2$ = $(CH_2)_3Ph$), 109704-49-6; (±)-**27**, 113778-56-6; (±)-**28**, 113778-57-7; (±)-**29**, 113778-58-8; (±)-**30**, 113830-18-5; (±)-**31**, 113830-19-6; (±)-**32**, 113830-20-9; (±)-**33**, 113778-59-9; (±)-**34**, 113778-60-2; (±)-**36**, 113830-25-4; (±)-**37**, 113778-61-3; (±)-**38a**, 113778-47-5; (±)-**38b**, 113778-49-7; (±)-**39a**, 113778-50-0; (±)-**39b**, 113778-51-1; (±)-**40**, 113778-62-4; (±)-**41**, 113778-63-5; (±)-**43**, 113830-21-0; (±)-**44**, 113830-22-1; (±)-**45a**, 113778-52-2; (±)-**45b**, 113778-53-3; (±)-**46a**, 113778-54-4; (±)-**46b**, 113778-55-5; (±)-**47**, 113778-83-9; TBSCl, 18162-48-6; $TBSOSO_2CF_3$, 69739-34-0; $NaBH_4$, 16940-66-2; $NaHB(OAc)_3$, 56553-60-7; $Me_4NBH_4$, 16883-45-7; $Me4NHB(OAc)_3$, 109704-53-2; $HO(CH_2)_3Ph$, 122-97-4; $Me_2CHCHO$, 78-84-2; $Zn(BH_4)_2$, 17611-70-0; $Me_2CHCOCH_2CO_2Et$, 7152-15-0; $AcO(CH_2)_3Ph$, 122-72-5; (±)-$Me_2CHCOCH_2CH(OH)CH_2CO_2(CH_2)_3Ph$, 113778-65-7; $Me_2CHCONMe(OMe)$, 113778-69-1; (±)-$Me_2CHCH(OH)CH_2COCHMe_2$, 113778-68-0; $MeCOCHMe_2$, 563-80-4; (±)-*anti*-$Me_2CHCH(OH)CH_2CH(OH)CHMe_2$, 103668-43-5; $EtCOCHMe_2$, 565-69-5; $Bu_2BOSO_2CF_3$, 60669-69-4; (±)-*anti*-$Me_2CHCH(OH)CH(Me)COCHMe_2$, 102285-80-3; (±)-*syn*-$Me_2CHCH(OH)CH(Me)COCHMe_2$, 102285-81-4; (±)-*anti-syn*-$Me_2CHCH(OH)CH(Me)CH(OH)CHMe_2$, 113889-53-5; MeONHMe·HCl, 6638-79-5; $BnOCH_2CO_2Me$, 31600-43-8; $BnOCH_2CONMe(OMe)$, 104863-68-5; $Me_2CHCl$, 75-29-6; $Me_2CHCOCH_2OBn$, 113778-75-9; (±)-*anti*-$Me_2CHCH(OH)CH(OBn)COCHMe_2$, 113778-70-4; (±)-*syn*-$Me_2CHCH(OH)CH(OBn)COCHMe_2$, 113778-71-5; (±)-*syn-anti*-$Me_2CHCH(OH)CH(OBn)CH(OH)CHMe_2$, 113778-73-7; *syn-syn*-$Me_2CHCH(OH)CH(OBn)CH(OH)CHMe_2$, 113830-24-3; *anti-anti*-$Me_2CHCH(OH)CH(OBn)CH(OH)CHMe_2$, 113830-23-2; DL-*threo*-$MeO_2CCH(OBn)CH(OH)CHMe_2$, 113778-77-1; DL-*erythro*-$MeO_2CCH(OBn)CH(OH)CHMe_2$, 113778-78-2; ACNMe(OMe), 78191-00-1; diketene, 674-82-8; ethyl 4-methyl-3,3-(ethylenedioxy)pentanoate, 27773-04-2; 3,3-(ethylenedioxy)-4-methyl-1-pentanol, 113778-66-8; 3,3-(ethylenedioxy)-4-methylpentanal, 95456-11-4; (±)-3-phenylpropyl 5,5-(ethylenedioxy)-3-hydroxy-6-methylheptanoate, 113778-67-9; *anti-anti*-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol acetonide, 113778-72-6; *syn-anti*-2,6-dimethyl-4-(phenylmethoxy)-3,5-heptanediol acetonide, 113778-74-8; 2,5-dihydro-4-*tert*-butylanisole, 22566-53-6.

# Synthesis and Molecular Structure of [7]Circulene[1]

**Koji Yamamoto,*† Tadashi Harada,† Yoshio Okamoto,† Hiroaki Chikamatsu,† Masao Nakazaki,† Yasushi Kai,*‡ Takuo Nakao,‡ Mitsuya Tanaka,‡ Shigeharu Harada,‡ and Nobutami Kasai*‡**

*Contribution from the Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan, and the Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan.* *Received September 21, 1987*

**Abstract:** The polycyclic aromatic compound with a circular arrangement of seven benzene rings, [7]circulene (**3**), was prepared by treatment of 1,16-dehydro-2,15-diformylhexahelicene (**30**) with low-valent titanium, and its unusual saddle-shaped structure with $C_2$ symmetry was supported by its X-ray analysis. Preparation, X-ray analysis, and optical stability of dehydro[7]circulene derivatives **17**, **29**, and **30** were also reported.

Within the family of polycyclic aromatic compounds with circular arrangement of benzene rings known as circulene,[2-4] there have been prepared [5]circulene (corannulene) (**1**)[5,6] and [6]-circulene (coronene) (**2**).[7] Conspicuous features in this class of compounds are the existence of three type's of geometry, bowl-

†Department of Chemistry.
‡Department of Applied Chemistry.

(1) Yamamoto, K.; Harada, T.; Nakazaki, M.; Nakao, T.; Kai, Y.; Harada, S.; Kasai, N. *J. Am. Chem. Soc.* **1983**, *105*, 7171–7172.

0002-7863/88/1510-3578$01.50/0 