Directed Reduction of β-Hydroxy Ketones Employing Tetramethylammonium Triacetoxyborohydride

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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 diastereomically 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 polyene3 families. Our recent focus on the development of hydroxy-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

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.
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 (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 an array of polyols such as that illustrated in Scheme II. In these hydroxyl-directed reactions, the reduction process itself creates stereoregular polyols. In order to pursue these objectives, we required a reagent that would stereoselectively reduce $\beta$-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.2

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 immediate species in this reaction has been suggested to be sodium triacetoxyborohydride on the basis of its infrared spectrum and hydrolysis products.3 Several workers, beginning with Saksena, have implicated this species in apparent intramolecular, hydroxyl-directed ketone reductions (eq 1–4).4 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.5,6 Gribble has exploited this fact, employing triacetoxyborohydrides in the selective reduction of aldehydes in the presence of ketones.7,8 Furthermore, it has been shown that the reducing power of the sodium borohydride/acetic acid system is substantially increased in the presence of alcohols.9 Thus, as suggested by Saksena, a hypothetical alkoxycarboxyborohydride 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 $\beta$-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 $\beta$-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.10 The synthesis of 2 proceeded according to the plan outlined in Scheme III. Diketene was treated with 3-phenylpropanol11 in the presence of NaH. Furthermore, it has been shown that the reducing power of the sodium borohydride/acetic acid system is substantially increased in the presence of alcohols.12 Thus, as suggested by Saksena, a hypothetical alkoxycarboxyborohydride 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 $\beta$-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.

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of triethylamine to afford \(\beta\)-keto ester 1. Generation of the derived acetooacetate dienolate with excess lithium disopropylamide (LDA) and subsequent aldol addition with isobutyrilaldehyde provided the desired \(\beta\)-hydroxy keto ester 2. The results of our initial reaction studies are shown in Table I.

Application of the conventional reduction conditions (solid \(\mathrm{NaBH_4}\) 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 tetramethylammonium, \(\mathrm{H_2}\) hydroxy ester 2 was reduced with tetramethylammonium borohydride\(^\text{10}\) 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.

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 \(\beta\)-hydroxy ketone 2 with excellent diastereoselectivity (entry K). These conditions subsequently proved to be nearly optimal for a range of hydroxy ketone substrates.

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 \(\beta\)-hydroxy ketone boron aldolates to reduce with the opposite sense of asymmetric induction (eq 6)\(^\text{10}\) strongly supports the intramolecular hydride delivery postulate.

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\text{Reduction of } \beta\text{-hydroxy ketones, unsubstituted at the } \alpha\text{-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 acetylcacetate 1 under the same conditions.


(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 triethylammonium salts. We prepared \(\mathrm{Me_4NBr}\) from \(\mathrm{NaBr}\) and \(\mathrm{Me}_2\)NOH by a slight modification of the procedure of Gibb (see Experimental Section). Banus, M.-D.; Bradson, R. W.; Gibb, T. R. P. J. Am. Chem. Soc. 1952, 74, 2346–2348.

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**Table II. Diastereoselective β-hydroxy ketone reductions with Me₃NHB(OAc)₃.**

| Entry | Reactant | Product | Time (Temp) | Ratio | Yield, %
<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Me Me OH</td>
<td>Me Me OH</td>
<td>5 h (-40 °C)</td>
<td>95 : 5</td>
<td>92</td>
</tr>
<tr>
<td>B</td>
<td>Me Me OH</td>
<td>Me Me OH</td>
<td>18 h (-40 °C)</td>
<td>95 : 5</td>
<td>90</td>
</tr>
<tr>
<td>C</td>
<td>Me Me OH</td>
<td>Me Me OH</td>
<td>6 h (-40 °C)</td>
<td>92 : 8</td>
<td>69</td>
</tr>
<tr>
<td>D</td>
<td>Me Me OH</td>
<td>Me Me OH</td>
<td>5 h (-40 °C)</td>
<td>98 : 4</td>
<td>86</td>
</tr>
<tr>
<td>E</td>
<td>Me Me OH</td>
<td>Me Me OH</td>
<td>16 h (-30 °C)</td>
<td>94 : 6</td>
<td>82</td>
</tr>
</tbody>
</table>

*Ratios determined either by HPLC or VPC. \(^*\)Values refer to isolated yields of major diastereomer of >99% diastereomeric purity. \(^*\)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).14

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 supports this statement that is 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 T₄ and T₆, each of which involves intramolecular hydride delivery as well as activation by acid catalysis. The 1,3-diaxial interaction, R₂ ↔ OAC, should destabilize T₆ to a greater extent than the analogous 1,3-diaxial interaction, HO⁺ ↔ OAc, destabilizes the favored transition state T₄. Further modification of these transition-state geometries to include the Burgi-Dunitz nucleophilic attack angle15 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-hydroxyketones.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.16 Parenthetically, we have found that some highly substituted aldehyde adducts do not require the tetramethylammonium salt for diastereoselective reduction. For example, the β-ketimide 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, 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

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Table III. α-Substituted β-Hydroxy Ketone Reductions with Me₃NB(OAc)₃

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reactant</th>
<th>Product</th>
<th>Time (Temp)</th>
<th>Ratio*</th>
<th>Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Me</td>
<td>Me</td>
<td>18 h (-20 °C)</td>
<td>98 : 2</td>
<td>22</td>
</tr>
<tr>
<td>B</td>
<td>Me</td>
<td>Me</td>
<td>18 h (-20 °C)</td>
<td>98 : 2</td>
<td>84</td>
</tr>
<tr>
<td>C</td>
<td>El</td>
<td>El</td>
<td>30 min (25 °C)</td>
<td>&gt;98 : 2</td>
<td>99</td>
</tr>
<tr>
<td>D</td>
<td>Me</td>
<td>Me</td>
<td>18 h (-40 °C)</td>
<td>93 : 7</td>
<td>88</td>
</tr>
<tr>
<td>E</td>
<td>Me</td>
<td>Me</td>
<td>18 h (-40 °C)</td>
<td>79 : 21</td>
<td>73</td>
</tr>
</tbody>
</table>

*Ratios determined either by HPLC or VPC. *Values refer to isolated yields of major diastereomer of >99% diastereomeric purity. *Na₂B(OAc)₃ used as reductant. *This experiment carried out by Dr. V. Novack.

Scheme V

![Chemical structure](image)

Figure 1. Representative ¹¹B chemical shifts.

Steroelectronic considerations, the Ahn-Eisenstein model[20] for carbonyl addition predicts that the α substituent (Me or OMe) should be preferentially oriented antiperiplanar to the forming C-H bond for optimal transition-state stabilization as illustrated in T₁ (Scheme V). The stereochemical course of the reduction of hydroxy ketone 7a, via the presumed transition state T₁, 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 α 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 stereoelectronic 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 ¹¹B 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 ¹¹B-¹H coupling. As is illustrated in Figure 1, the ¹¹B chemical shifts of relevant tricoordinate boron derivatives fall in the range +15 to +30 ppm (BF₃ etherate standard). In contrast, the ¹¹B chemical shifts of relevant four-coordinate species appear at substantially lower field (typically -5 to +5 ppm). On the basis of these data, we felt that the chemical shift of an alkoxycarboxyborohydride should be sufficiently distinct from that of triacetoxyborohydride for its detection by ¹¹B 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 ¹¹B chemical shifts are consistent with the structures drawn below. The reduction of hydroxy ketone 2 with tetrachloroethylborohydride was analogously followed by ¹¹B 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...

(19) The stereochemical relationships of diols 8 and 9 were determined from ¹H-¹H coupling constants of the corresponding acetones (see Experimental Section).
(22) Reference 21, p. 137.
Directed Reduction of β-Hydroxy Ketones

Scheme VI

![Chemical structures](image)

Directed Reduction, exclusively the trans diol hydride/acetic acid reduction. Interestingly, the equatorial hydroxy ketone for intramolecular hydride delivery in these reductions, a mechanistic hypothesis first proposed by Saksena for sodium borohydride in acetone solvent provides compelling evidence for unusually reactive ketones such as cyclohexanones not geometrically disposed for facile intramolecular delivery. 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,β-unsaturated ethylene ketal 12, derived from 4-tert-butylnisole by dissolving metal reduction and subsequent ketonization, was converted stereaspecifically 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 15 by the illustrated series of three reactions.

Hydroxy ketones 14 and 17 were treated with tetramethylammonium triacetoxycarbonylarbodiode in both acetonitrile/acetate acid and acetone/acetate 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. Interestingly, the equatorial hydroxy ketone 14 underwent an equally diastereoselective, albeit much slower, reduction in acetone/acetate 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/acetate 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.

Internally Propagated Reductions

The preceding studies afford good precedent for the intramolecular reduction of β-hydroxy ketones with triacetoxycarbonylarbodiode and provide some insight into both the rate-determining step (ligand exchange) and mode of catalysis with Bronsted 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 (R₁ = CHMe₂; R₂ = (CH₃)₂Ph) is stereoselectively reduced with tetrabutylationmonium triacetoxycarbonylarbodiode to the illustrated anti diol (Table II, entry C). Since neither acetylacetone nor acetylacetate is 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.
borates from the partially reduced substrate. In this regard, alkoxyl borates generally have exceptionally high oxygen-ligand metathesis rates. On the other hand, 1,3-dioles and related bidentate ligands such as triol esters and derived lactones (Schemes 27, 28 and 29) were synthesized and unambiguously characterized both as their boron-free, partially reduced substrate. In this regard, alkoxy boron chemistry; ref 26, Chapters 5 and 6. (28) Oster, T. A.; Harris, T. M. Tetrahedron Lett. 1983, 24, 1851-1854.

ester 3 was silylated with tert-butylimethylsilyl 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 C₃ diastereomers. This mixture was separated chromatographically and the silyl groups removed with HF/pyridine to afford the Anti-MAnt 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 triacetoxaborohydride (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 procedure for 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-

![Scheme VIII](image_url)

![Scheme IX](image_url)

Anti and syn diol esters 3 and 4, prepared by zinc borohydride reduction of 2, were separated chromatographically. The anti diol...
**Directed Reduction of β-Hydroxy Ketones**

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). Substitution 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 Selladie using either ZnCl2/DIBAL-H (syn diastereoversity) (eq 19) or DIBAL-H (anti diastereoversity) (eq 20) closely parallel these trends, and one may now speculate, with somewhat more confidence, that these reductions might proceed via the illustrated intermediates.20

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**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.
Suspended in 500 mL of 95% ethanol and filtered. The filter cake was washed (200 mL) with 100 mL of 95% ethanol and filtered; this process was repeated a total of ten times. The mixture was dried overnight in vacuo. The product was prismatic needles: mp 96.5–98.0 °C.

This analytically pure Me₃NB(OAc)₃ powder proved to be satisfactory for all applications but could be recrystallized from ethyl acetate or 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. This mixture was puriﬁed by flash chromatography on silica gel (60 × 180 mm column, 40% ethyl acetate in hexane, 100-mL fractions).

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 diluted with water and extracted with 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 for 20 min the mixture was poured into a separatory funnel containing excess 1 N sodium hydrogen sulfate. The layers were shaken vigorously and separated. The aqueous layer was extracted with 70% ether in hexanes, and concentrated in vacuo to give 6.10 g of an orange oil. The mixture was diluted with water and extracted with dichloromethane (30% ethyl acetate in hexane); IR (neat) 3490 (br), 3095, 3072, 3035, 2975, 1750, 1503, 1340, 752, 707 cm⁻¹; 'H NMR (300 MHz, CDCl₃) 7.24 (m, 5 H, aromatic), 4.35 (m, 1 H, CH(OH)-CH₂CO₂R), 2.69 (t, 2 H, CH₂Ph, J = 5.90, 17.11 Hz), 2.45 (s, 2 H, CH₂CH(OH), J = 8.17, 17.11 Hz), 2.21 (dddd, 1 H, CH-). Anal. Calcd for C₁₇H₂₆O₄: C, 69.36; H, 8.90. Found: C, 69.71; H, 8.92.
methylheptanoic acid 3-lactone (3a) in 1.0 mL of anhydrous dichloro-
 methane was added 57 mg (0.72 mmol) of pyridine in 1.0 mL of benzene.
The mixture was stirred at ambient temperature for 3 h and diluted with dichloromethane. The mixture was warmed with aqueous 1 N sodium hydroxide solution and then washed with saturated aqueous sodium bicarbonate. The organic layer was 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 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 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 1.55 g (81%) of a colorless oil which was used without purification. To a solution of 4.5 g (15.0 mmol) of tetramethylammonium triacetoxyborohydride in 35 mL of anhydrous tetrahydrofuran at −78 °C was added 206 mg (7.6 mL of a 1 M solution in ether) of lithium aluminium 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 mL of water was added followed by 900 mL of 15% aqueous sodium bicarbonate. The mixture was stirred for 2 h at 0 °C. A solution of 2.16 g (16.3 mmol) of N-methoxy-N,2-dimethyl-
proponiamide 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 30 mL of 5.0 N aqueous hydrochloric acid, and extracted with ether (3X). The combined organic layers were washed with 1 N aqueous sodium hydroxide solution and finally 300 mL of water. The mixture was stirred for 2 h at 0 °C and a solution of 3.0 g of diisopropylamine in 25 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrahydrofuran was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC). The mixture was stirred at −40 °C, and a solution of 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of n-butyllithium was added. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC). The mixture was stirred at −40 °C, and a solution of 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of n-butyllithium was added. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC). The mixture was stirred at −40 °C, and a solution of 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of n-butyllithium was added. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC). The mixture was stirred at −40 °C, and a solution of 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of n-butyllithium was added. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC). The mixture was stirred at −40 °C, and a solution of 1.11 g (6.68 mL of a 2.60 M solution in hexane, 17.4 mmol) of n-butyllithium was added. The mixture was warmed to 0 °C, stirred for 30 min, and recooled to −78 °C. A solution of 2.8-phenyl-3-propynyl amide (4.0 mmol) in 10 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 2.3 g (14.4 mmol) of the above aldehyde in 5.0 mL of anhydrous tetrachloroethane was added. The mixture was poured into excess aqueous 1 N sodium hydroxide solution and diluted with ether. The mixture was washed twice with 1 N sodium hydroxide solution, dried with anhydrous magnesium sulfate, and concentrated in vacuo to give 0.54 (50% ethyl acetate in hexane, 100-mL fractions) to give 3.01 g (62.3%) of the hydroxy ketal of anhydro diol as a colorless oil (>99% HPLC).
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 pure anti diol (>99% by HPLC) as colorless needles: Rf 0.23 (30% ethyl acetate in hexanes); mp 79–80 °C; IR (CHCl₃) 3620, 3460 (br), 2961, 2837, 1467, 1387, 1368, 1050 cm⁻¹; 1H NMR (300 MHz, CDCl₃) 6.53 (d, 1H, CH₃, J = 8.1 Hz, 2.20 (d, 1H, CH₂OH, J = 4.8 Hz, 2.00 (d, 1H, CH₂OCH₃)); 13C NMR (75.5 MHz, CDCl₃) 74.39, 51.20, 41.66, 41.53, 41.48, 36.15, 33.12, 29.94, 19.10, 17.58.

Analyzed for C₆H₁₀O₂: C, 71.01; H, 7.24; Found: C, 71.00; H, 7.22.

(4R,5S,5S)-5-Hydroxy-2,4,6-trimethyl-3-heptanone (Table III, Entry B 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 (1.0 equiv) of n-butyllithium. The mixture was recooled to −78 °C, and a solution of dibutylborane tri triflate followed by 6.13 mL (43.7 mmol, 1.2 equiv) of triethylamine in pentane, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 4.5 g of yellow oil. The mixture was purified by MPLC (two Merck Lobar columns, 10% tert-butyl methyl ether/hexane, 125-mL fractions) to give 2.2 g of pure erythro aldol adduct as a colorless oil and a 1.5 g of a mixture of erythro and threo isomers. The erythro isomer was purified by MPLC (Merck Lobar column, 10% tert-butyl methyl ether/hexane, 125-mL fractions) to give 322 mg of the pure erythro aldol adduct as a colorless oil.

Antialdol adduct: Rf 0.53 (30% tert-butyl methyl ether/hexane); IR (film) 3500 (br), 2974, 2952, 2882, 1710, 1470, 1387, 1097 cm⁻¹; 1H NMR (300 MHz, CDCl₃) 3.44 (dt, 1H, J = 5.0, 6.9 Hz, CHO), 2.93 (quintet, 1H, J = 7.0 Hz, CHOCH₂OH), 2.57 (septet, 1H, J = 7.0 Hz, OCH₃), 1.73 (triplet, 1H, J = 7.0 Hz, CH₂OH), 1.17 (d, 3H, J = 6.9 Hz, CH₃), 0.93 (d, 3H, J = 6.9 Hz, CH₃); 13C NMR (75.5 MHz, CDCl₃) 204.08, 78.17, 66.20, 47.07, 30.16, 17.49, 17.69, 15.46, 14.32.

Analyzed for C₆H₁₀O₂: C, 69.72; H, 11.70. Found: C, 69.52; H, 11.61.

Anal. Calcd for C₆H₁₀O₂: C, 70.91; H, 7.00; Found: C, 70.90; H, 6.98.

Syn aldol adduct: Rf 0.44 (30% tert-butyl methyl ether/hexane); IR (film) 3500 (br), 2970, 2938, 2880, 1702, 1463, 1390, 1090, 1000 cm⁻¹; 1H NMR (300 MHz, CDCl₃) 3.45 (dt, 1H, J = 2.2, 8.2 Hz, CHO), 3.02 (d, 1H, J = 2.2 Hz, CHO), 2.93 (dq, 1H, J = 2.7, 7.2 Hz, CH₂OCH₃(OH)), 2.78 (q, 2H, J = 7.0 Hz, CH₂CH₂OCH₃), 1.70 (d, 3H, J = 6.9 Hz, CH₃), 0.92 (d, 3H, J = 6.9 Hz, CH₃), 0.91 (d, 3H, J = 6.9 Hz, CH₃); 13C NMR (75.5 MHz, CDCl₃) 216.70, 76.22, 45.29, 39.72, 30.47, 18.92, 18.54, 18.22, 17.88, 9.70.

Analyzed for C₆H₁₀O₂: C, 69.72; H, 11.70. Found: C, 69.71; H, 11.78.

Reduction of (4S*,5S*,5S*)-5-Hydroxy-2,4,6-trimethyl-3-heptanone with Tetramethylammonium Triacetoxyborohydride (Table III, Entry A). To a solution of 1.23 g (4.66 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 (3R,5S)-5-hydroxy-2,4,6-trimethyl-3-heptanone in 1.0 mL of anhydrous acetonitrile via canula. The flask 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 9 h. The reaction was quenched with 500 mL of 4-hydroxy-2-butanone and stirred for 30 min. The mixture was diluted with 10 mL of acetonitrile and 10 mL of water and cooled to 0 °C. The solution was treated with 20% aqueous sodium hydroxide, and extracted six times with ether. The combined organic layers were washed with aqueous sodium chloride, 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. The mixture was dissolved in 6 mL of CH₂Cl₂, 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
Precise mass m/z for C_{16}H_{27}O_{3}: calcd 268.1036, found 268.1032.

Syn aldol adduct: R=0.53 (30% ethyl acetate/hexane); IR (film) 3500 (br), 2977, 2939, 2878, 1729, 1712, 1500, 1472, 1459, 1386, 1396, 1104, 1044, 1030, 738, 700 cm⁻¹; 1H NMR (300 MHz, CDCl₃) δ 7.35 (m, 5 H, aromatic H's), 4.73 (d, 1 H, J = 11.4 Hz, CH(PhH)), 4.38 (d, 1 H, J = 4.1 Hz, CH(PhH)), 2.83 (t, 2 H, J = 7.0 Hz, CH₂OH), 1.12 (s, 6 H, (CH₃)₂), 0.89 (s, 3 H, CH₃), 1.10 (d, 3 H, J = 6.8 Hz, CHO); 13C NMR (75.5 MHz, CDCl₃) δ 214.75, 137.12, 136.47, 128.18, 128.17, 83.31, 77.26, 72.84, 36.08, 31.16, 19.29, 18.00, 15.81 17.96.

Precise mass m/z for C_{16}H_{26}O_{3}: calcd 265.1036; found 265.1032.

(3R,4S,5S), 2.6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone (Diol Anisol): 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 (3.42 mmol, 10.4 equiv) of sodium borohydride. The mixture was stirred for 1 h at ambient temperature and quenched by 1 N aqueous hydrochloric acid. 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 to give 100g of colorless oil.

Syn aldol: R=0.32 (15% ethyl acetate/hexane); mp 76.5–77.8 °C; IR (CCl₄) 3500 (br), 2968, 2938, 2878, 1515, 1443, 1470, 1455, 1210, 1005 cm⁻¹; 1H NMR (300 MHz, CDCl₃) δ 7.33 (m, 5 H, aromatic H's), 4.57 (2 H, J = 5.3 Hz, CH₂), 3.65 (2 H, J = 2.8 Hz, OCH₂), 3.45 (1 H, J = 6.2 Hz, CHO); 1H NMR (75.5 MHz, CDCl₃) δ 137.92, 128.47, 128.7, 72.76, 75.99, 77.84, 72.67, 29.45, 20.08, 18.6 (2H). Anal. Caled for C_{16}H_{27}O₃: C, 72.14; H, 8.94. Found: C, 72.00; H, 9.94.

A small portion was converted to the corresponding acetone (dimethoxypropane/p-toluenesulfonic acid, 3:1): VPC (30 min DB-1710, 150 °C, 1 psi, t, 5.59 min); 1H NMR (300 MHz, CDCl₃) δ 7.33 (m, 5 H, aromatic H's), 4.58 (2 H, J = 5.3 Hz, CH₂), 3.64 (2 H, J = 2.8 Hz, OCH₂), 3.45 (1 H, J = 6.2 Hz, CHO). The mixture was stirred vigorously for 4 h and filtered. The resulting solution was evaporated to dryness.

Syn aldol: R=0.23 (15% ethyl acetate/hexane); mp 87–88.5 °C; IR (CCl₄) 3420 (br), 3019, 2962, 2936, 2877, 1499, 1471, 1456, 1386, 1358, 1060 (br) cm⁻¹; 1H NMR (300 MHz, CDCl₃) δ 7.35 (m, 5 H, aromatic H's), 4.73 (d, 1 H, J = 11.4 Hz, CH(PhH)), 4.38 (d, 1 H, J = 4.1 Hz, CH(PhH)), 2.83 (t, 2 H, J = 7.0 Hz, CH₂OH), 1.12 (s, 6 H, (CH₃)₂), 0.89 (s, 3 H, CH₃), 1.10 (d, 3 H, J = 6.8 Hz, CHO); 13C NMR (75.5 MHz, CDCl₃) δ 214.75, 137.12, 136.47, 128.18, 128.07, 83.44, 76.64, 72.79, 37.08, 29.70, 19.61, 18.57, 18.22, 16.23.
ether/dichloromethane, 20% separated by flash chromatography on silica gel (10% tert-butyl methyl ether/dichloromethane, 20 x 180 mm column, 8-mL fractions) to give title compound, syn diol as a colorless oil: Rf = 0.32 (15% tert-butyl methyl ether/dichloromethane, 20 x 180 mm column, 8-mL fractions) to give title compound, syn diol as a colorless oil: Rf = 0.32 (15% tert-butyl methyl ether/dichloromethane, 20 x 180 mm column, 8-mL fractions). The mixture was purified by flash chromatography on silica gel (40% ethyl acetate/hexane, 60 x 180 mm column, 50-mL fractions) to give 5.46 mg of 8a as colorless prisms: Rf = 0.21 (10% IPA/dichloromethane); mp 53.0-54.5 °C; IR (film) 3460 (br), 2970, 2880, 1475, 1390, 1070, 1032, 980 cm-1; 'H NMR (300 MHz, CDCl3) δ 3.73 (m, 2 H, CH,OH), 3.42 (ddd, 1 H, J = 12.3, 10.7, 6.7 Hz, CHOH), 1.60 (m, 1 H, CH(CH3),), 1.41 (s, 3 H, CH2CH2CH2), 0.96 (d, 6 H, J = 6.6 Hz, CH2).

Reduction of (4R,5S*)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone with Tetrabutylammonium Triacetoxoborohydride (Table III, Entry D). To a solution of 1.40 g (5.32 mmol) of tetramethylammonium triacetoxoborohydride in 2.0 mL of anhydrous acetic acid at -40 °C was added a solution of 60% methanol (0.188 mmol, 10% IPA) and 1.52 g (5.78 mmol) of (4R,5S*)-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 cooled to 0 °C, the mixture was cooled to 0 °C, and treated with 115 mL of anhydrous methanol followed by 46 mL of 30% hydrogen peroxide (dropwise). The mixture was stirred at ambient temperature for 30 min at 50 °C, 15 psi, and concentrated in vacuo two times to give 56.4 mg of a colorless, crystalline solid. 'H NMR analysis indicated the presence of some residual boron. The mixture was diluted with 2 N aqueous sodium hydroxide and extracted with dichloromethane (5 x 10 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate (2x). The aqueous layers were back extracted with dichloromethane (2 x 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 x 180 mm column, 50-mL fractions) to give 5.46 mg of 8a as colorless prisms: Rf = 0.21 (10% IPA/dichloromethane); mp 53.0-54.5 °C; IR (film) 3460 (br), 2970, 2880, 1475, 1390, 1070, 1032, 980 cm-1; 'H NMR (300 MHz, CDCl3) δ 3.73 (m, 2 H, CH,OH), 3.42 (ddd, 1 H, J = 12.3, 10.7, 6.7 Hz, CHOH), 1.60 (m, 1 H, CH(CH3),), 1.41 (s, 3 H, CH2CH2CH2), 0.96 (d, 6 H, J = 6.6 Hz, CH2).

Reduction of (4R,5S*)-2,6-Dimethyl-5-hydroxy-4-(phenylmethoxy)-3-heptanone with Tetrabutylammonium Triacetoxoborohydride (Table III, Entry D). To a solution of 1.40 g (5.32 mmol) of tetramethylammonium triacetoxoborohydride in 2.0 mL of anhydrous acetic acid at -40 °C was added a solution of 60% methanol (0.188 mmol, 10% IPA) and 1.52 g (5.78 mmol) of (4R,5S*)-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 cooled to 0 °C, the mixture was cooled to 0 °C, and treated with 115 mL of anhydrous methanol followed by 46 mL of 30% hydrogen peroxide (dropwise). The mixture was stirred at ambient temperature for 30 min at 50 °C, 15 psi, and concentrated in vacuo two times to give 56.4 mg of a colorless, crystalline solid. 'H NMR analysis indicated the presence of some residual boron. The mixture was diluted with 2 N aqueous sodium hydroxide and extracted with dichloromethane (5 x 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. 'H NMR analysis indicated the presence of a >10:1 mixture of anti and syn diols. The mixture was purified by flash chromatography on silica gel (40% ethyl acetate/hexane, 60 x 180 mm column, 50-mL fractions) to give 5.46 mg of 8a as colorless prisms: Rf = 0.21 (10% IPA/dichloromethane); mp 53.0-54.5 °C; IR (film) 3460 (br), 2970, 2880, 1475, 1390, 1070, 1032, 980 cm-1; 'H NMR (300 MHz, CDCl3) δ 3.73 (m, 2 H, CH,OH), 3.42 (ddd, 1 H, J = 12.3, 10.7, 6.7 Hz, CHOH), 1.60 (m, 1 H, CH(CH3),), 1.41 (s, 3 H, CH2CH2CH2), 0.96 (d, 6 H, J = 6.6 Hz, CH2).
Directed Reduction of $\beta$-Hydroxy Ketones

was stirred for 30 min and a solution of 4.76 g (25.9 mmol) of methyl benzylxocetate in 20 mL of anhydrous THF was added dropwise via cannula. The reaction was stirred at room temperature for 1 h, and recooled to -78°C. Isobutylaldehyde (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 x 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 x 180 mm column, 50-mL fractions) to afford 2.46 g of a mixture of diastereomers. R: 0.42 (30% ethyl acetate/hexane).

To a solution of 2.46 g (9.76 mmol) of the above mixture of diastereomers in 100 mL of anhydrous THF at -78°C was added 40.0 mL of 1.0 M ether, 41.0 mL of 4.0 mol/L 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 x 180 mm column, 50-mL fractions) to afford 444 mg of the erythro diol 8b as a colorless, crystalline solid and 760 mg of the three diol 9b as a colorless oil.

Erythro diol 8b: R$\_3$ 0.34 (75% ethyl acetate/hexane); mp 72.7-73.4°C; (CDCl$_3$, 500 MHz, δ 3.59 (d, J = 4.70 Hz, CH$_2$CON)), 3.57 (d, J = 6.20 Hz, CH$_2$CON)).

To a solution of 1.71 g (7.73 mmol, 3513. mg (100% mass balance) of 411.8 mg of the tert-butyldimethylsiloxy ketone as a pale-yellow oil. The mixture was purified by flash chromatography on silica gel (75% ethyl acetate/hexane, 60 x 180 mm column, 50-mL fractions) to afford 444 mg of the erythro diol 8b as a colorless, crystalline solid and 760 mg of the three diol 9b as a colorless oil.

Reduction of 1-Hydroxy-4-methyl-2-(phenylmethoxy)-3-pentanone (7b) with Me$_2$NH(OAc)$_2$. To a solution of 1.36 g (5.17 mmol, 21.6 equiv) of Me$_2$NH(OAc)$_2$ in 4.0 mL of anhydrous acetone and 40°C was added a solution of 53.2 mg (0.239 mmol) of (2P)-1-hydroxy-4-methyl-2-(phenylmethoxy)-3-pentanone (7b) in 2.0 mL of 87% (500 MHz, δ 7.36 (5.1 H, CH$_3$), 4.70 (d, J = 11.5 Hz, C($\equiv$O)H)), 4.56 (d, J = 11.5 Hz, C($\equiv$O)H)), 4.10 (d, J = 4.4 Hz, 5.2 Hz, CH$_3$C($\equiv$O)), 3.86 (m, 2 H, 2 OH, CH$_2$OH)), 3.00 (heptet, J = 6.9 Hz, CH$_2$C($\equiv$O)), 2.71 (t, J = 6.8 Hz, CH$_3$), 1.28 (m, 3 H), 0.86 (d, J = 6.8 Hz, CH$_3$).

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80.0 mg of p-toluene-sulfonyl 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 chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The aqueous layer was extracted with ether (3 × 50 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 reaction was allowed to warm to ambient temperature and stirred at room temperature before it was quenched with 30 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, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified sample indicated the presence of trans diol 20 (8.87 min) and syn diol 21 (9.40 min) in a ratio of 88:12. Purification of the residue by flash chromatography on silica gel (20 cm × 0.4 cm) using a gradient of hexane/ethyl acetate afforded 1.3 g of hydroxy ketone 22 (75% yield). The hydroxy ketone 22 was purified by flash chromatography on silica gel (20 cm × 0.5 cm) using a gradient of hexane/ethyl acetate; IR (film) cm⁻¹; IH NMR (CDCl₃, 2.12–1.90 ppm); 1H NMR (CDCl₃, 2.15–1.90 ppm). 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 10.0 mL of acetic acid was stirred for 3 h at ambient temperature. The aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layers were washed with 5.0 mL of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The aqueous layer was extracted with ether (3 × 20 mL), and the combined organic layers were washed with 5.0 mL of saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The reaction was allowed to warm to ambient temperature and stirred 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 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated in vacuo. Capillary GC analysis (DB 1701, 130 °C, 8 psi) of the unpurified sample indicated the presence of trans diol 20 (8.87 min) and syn diol 21 (9.40 min) in a ratio of 88:12. Purification of the residue by flash chromatography on silica gel (20 cm × 0.4 cm) using a gradient of hexane/ethyl acetate afforded 1.3 g of hydroxy ketone 22 (75% yield).
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Directed Reduction of β-Hydroxy Ketones


288, 19.9. An analytical sample was prepared by recrystallization from hexane to afford colorless needles: mp 113-114°C.


Reduction of (3R*,4R*)-4-(1,1-Dimethyl-1-oxo-3-phenylpropyl)-3-hydroxyhexane-17-one with MeCNH₂OAc in Acetic Acid Solution. To a solution of 467 mg (2.21 mmol, 5.0 equiv) of (3R*,4R*)-4-(1,1-dimethyl-1-oxo-3-phenylpropyl)-3-hydroxyhexane-17-one (0.441 mmol) in 10.0 mL of acetonitrile was added 75.0 mL (0.441 mmol) of hydroxy ketone 17 in 1.0 mL of acetonitrile. The reaction mixture was stirred at room temperature for 7 h before it was quenched with 3.0 mL of a saturated aqueous sodium chloride solution. After it had cooled, the solution was treated with 3.0 mL of 1.0 M aqueous potassium tartrate solution and stirred for 20 min. The aqueous solution was extracted with ethyl acetate (10 x 2 mL). The combined organic extract was washed with 2.0 mL of saturated aqueous potassium carbonate solution, dried over anhydrous sodium sulfate, and concentrated in vacuo to give 2.09 g (89%) of 18 as a crystalline solid.

3-Phenylpropyl 3,5-Dioxoheptanoate (27). To a solution of 1.0 g (10.7 mmol) of diisopropylamine in 100 mL of anhydrous tetrahydrofuran at -78°C was added 6.53 g (64.0 mL of a 1.60 M solution in hexanes, 102 mmol) of n-butyllithium. The solution was warmed to 0°C and stirred for 2.0 min. A solution of 3-phenylpropyl chloroformate (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. Next methoxy-N-N-methylamidite (1g) (16.8 mmol) was added neat, and the mixture was stirred at ambient temperature overnight. The mixture was concentrated in vacuo, diluted with cold aqueous 1 N sodium hydroxide solution, and extracted three times with ether. The organic layers were diluted with 1:1 with pentane, dried with anhydrous sodium sulfate, and concentrated in vacuo to give 12.2 g (85%) of pale yellow oil. The mixture was purified by flash chromatography on silica gel (20×200 mm column 1:1 hexane:ethyl acetate) to give 68 mg (89%) of diol 18 as a crystalline solid.

3-Phenylpropyl 3,5-Dioxoheptanoate (27). To a solution of 0.81 g (6.63 mmol) of diisopropylamine in 40 mL of anhydrous tetrahydrofuran at -78°C was added 3.27 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 phenylpropyl (3S*,5R*,7S*)-5,7-bis(tert-butyldimethylsiloxy)-6-methylheptanoate (31) in 10.0 mL of anhydrous tetrahydrofuran was added dropwise via cannula over 15 min. The mixture was allowed to stir at 0°C for 2 h and cooled to -78°C. Isobutylaldehyde (1.33 g, 18.5 mmol) was added, and the mixture was stirred for 1 min and poured into excess 1 N aqueous sodium hydroxide solution. The mixture was diluted with ether and the layers shaken vigorously. The organic layer was washed with saturated aqueous sodium bicarbonate and concentrated in vacuo to give 0.11 g (75%) of 29.

3-Phenylpropyl 3,5-Dioxoheptanoate (27). To a solution of 50.0 mg (0.08 mmol) of 3-phenylpropyl chloroformate (1) in 1.5 mL of anhydrous tetrahydrofuran at -78°C was added 0.5 mL of a 1.56 M solution of tert-butylmethyl ether/dichloromethane. After 1 min the mixture was poured into 25 mL of 1 N aqueous sodium hydroxide solution, and the mixture was stirred at 0°C for 30 min, and recooled to -78°C. A solution of 381 mg (1.51 mL of a 1.56 M solution in dichloromethane, 3.33 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 mL, 10 mmol) was added and the mixture was stirred vigorously for 1 h before it was recooled to 0°C. The mixture was washed with saturated aqueous sodium bicarbonate and concentrated in vacuo to give 1.00 g (100%) of 30. The mixture was purified by flash chromatography on silica gel (60×180 mm column, 2.5% ethyl acetate in hexanes, 50 mL fractions) to afford 0.62 g (92%) of the title adduct as a colorless oil. The mixture was purified by flash chromatography on silica gel (300×760 mm column, 2.5% ethyl acetate in hexanes, 50 mL fractions) to afford 0.48 g (90%) of the title adduct as a colorless oil.
anti-5,7-bis(tert-butylimidemethylsiloxy)-3-hydroxy-8-methylnonanoate (36), \( R_1 0.38 \) (dichloromethane) in 10.0 mL of freshly distilled acetone at 0 °C was added 1.0 mL of pyridinium fluoroide (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 carbonate 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 x 180 mm column, 25% acetone in ethyl acetate, 8-mL fractions) to give 4.7 mg (42%) of the title compound. 3,5,7-Trimethylheptanoic acid &lactone (39a). To a solution of 18.6 mg (55.0 μmol) of 3-phenylpropyl anti-3,5-dihydroxy-6-methylheptanoate was added 183 mg (2.32 mmol) of pyridine and 1.16 mL (11.6 mmol) of benzoyl chloride. After 10 min the mixture was warmed to ambient temperature, the precipitated solids, washed with dichloromethane, and the mother liquor was concentrated in vacuo to give 128 mg of a colorless oil. The mixture was purified by flash chromatography on silica gel (15 x 180 mm column, 40% ethyl acetate in hexanes, 8-mL fractions) to give 6.6 mg (69%) of the title compound: \( R_f 0.29 \) (75% ethyl acetate in hexanes). 3,5,7-Tris(tert-butyldimethylsiloxy)-3-hydroxy-8-methylnonanoic acid &lactone (39b). To a solution of 4.7 mg (23.2 μmol) of anti-3,5,7-trihydroxy-8-methylheptanoic acid &lactone (39a) in 3.0 mL of anhydrous dichloromethane at 0 °C was added 183 mg (2.32 mmol) of pyridine and 1.16 mL (11.6 mmol) of benzoyl chloride. After 10 min the mixture was warmed to ambient temperature, the precipitated solids were filtered off, and the mother liquor was concentrated in vacuo to give 67.1 mg of a colorless solid. The mixture was purified by flash chromatography on silica gel (15 x 180 mm column, 40% ethyl acetate in hexanes, 8-mL fractions) to afford 4.7 mg (42%) of the title compound: \( R_f 0.25 \) (30% ethyl acetate in hexanes); \( \nu \text{ cm}^{-1} 3010, 2965, 1725, 1183 \); \( \delta \text{ (H, H, CH)} \), \( \delta \text{ (H, aromatic C)} \), \( 4.27 \text{ (m, 1 H, CH), 4.15} \text{ (m, 2 H, CH}, \), \( \delta \text{ (1, 2 H, CH}_{2} \text{CH}_{2}, \), \( 1.67 \text{ (m, 5 H, CH}_{2}, \), and \( \delta \text{ (OH, CH}_{2} \text{CH}_{2} \text{CH}_{2} \text{}) \).
with 389 mg (1.15 mmol) of syn-3,5,7-trihydroxy-8-methylnonanoic acid and 10% ethyl acetate in hexane, 50-mL fractions) to afford 621 mg (95%) of the title compound of epimeric aidoles adds 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* 0.39 (10% ethyl acetate/hexanes); 1H NMR (300 MHz, CDCl3) 7.74 (m, 5 H, aromatic CH), 5.45 (s, 1 H, CH2OH), 4.27 (t, 2 H, CH2Ph), 2.66 (t, 2 H, CH2C02R), 1.98 (m, 2 H, CH2CH2Ph), 1.50-1.83 (m, 3 H, (CH3)2CHCH(OTBS)CH2), 0.90 (2d, 6 H, CH(CH3)2), 0.85 (2d, 6 H, CH2Si(CH3)2).

3-Phenylpropyl 

3(3S*,5S*,7S*)-3,5,7-Trimethyl-8-methylnonanoic Acid 1-Lactone (45a). The procedure used was identical with that used for the production of 3(3S*,5R*,7S*)-3,5,7-trimethyl-8-methylnonanoic acid 1-lactone (39a). Thus, 15.2 mg (45.0 mmol) of 3-phenylpropyl syn, syn-3,5,7-trihydroxy-8-methylnonanoic acid (44) was treated with trifluoroacetic acid and 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% ethyl acetate in ethyl acetate, 8-mL fractions) to give 5.6 mg (62%) of the title compound: Rf 0.17 (75% ethyl acetate in hexane); 1H NMR (300 MHz, CDCl3) 7.24 (m, 5 H, aromatic CH), 4.93 (ddt, 1 H, CHOCOR, J = 2.9, 6.6, 11.4 Hz), 4.39 (br m, 1 H, CHOH), 3.60 (br m, 1 H, CHOH), 2.93 (br s, 1 H, OH), 2.73 (dd, 1 H, CHHCOR, J = 4.65, 17.71 Hz), 2.65 (dd, 1 H, CHHCH2OH, J = 4.32, 17.66 Hz), 2.64 (br, 1 H, CHOH), 0.28 (d, 1 H, CH2), 0.95 (2d, 6 H, CH2), 0.80 (m, 4 H, 2 CH2CH2OH, 2 CH2CH(CH2)CO2R, equatorial, J = 1.52, 14.66 Hz), 1.67-1.95 (m, 4 H, 2 CH2CH2OH, 2 CH2CH2CH(OH)CH2CO2R), 0.94 (2d, 6 H, CH2).

3(3R*,5S*,7S*)-3-Bis(benzyloxy)-8-methylnonanoic Acid 1-Lactone (45b). The procedure used was identical with that used for the production of 3(3S*,5R*,7S*)-3,5,7-trihydroxy-8-methylnonanoic acid 1-lactone (39b). Thus, 5.6 mg (27.7 mmol) of syn, syn-3,5,7-trihydroxy-8-methylnonanoic acid 1-lactone (45a) was treated with 194 mg (1.38 mmol) of benzyl 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, 10% ethyl acetate in hexanes, 8-mL fractions) to give 9.8 mg (86%) of the title compound as a colorless oil: 1H NMR (300 MHz, CDCl3) 7.88 (d, 4 H, aromatic CH), 7.25-7.60 (m, 6 H, aromatic CH), 5.50 (m, 1 H, CHOBz), 5.13 (d, 1 H, CHO), 4.27 (br, 2 H, CH2OH), 3.97 (2d, 1 H, CH2OH, J = 5.04, 18.40 Hz), 2.85 (dd, 1 H, CH2OH, J = 1.17, 3.36, 18.54 Hz), 2.63 (m, 1 H, CH2CH(OH)(OBz)-CH2CO2R), 2.36 (dd, 1 H, CH2CH(OH)(OBz)-CH2CO2R, J = 4.32, 10.57, 14.56 Hz), 1.80-2.08 (m, 3 H, (CH3)2CHCH(OBz)CH2), 1.01 (2d, 6 H, CH2).
Synthesis and Molecular Structure of [7]Circulene

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Abstract: The polycyclic aromatic compound with a circular arrangement of seven benzene rings, [7]circulene (3), was prepared by treatment of 1,6-dehydro-2,15-diformylhexahelicene (30) with low-valent titanium, and its unusual saddle-shaped structure was confirmed by 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,1 a there have been prepared [5]circulene (coronene) (2)1 2 and [6]-circulene (coronene) (2).2 Conspicuous features in this class of compounds are the existence of three types of geometry, bowl-