Chemistry of Aldolate Dianions. Effects of β-Heteroatom Substituents on Ketone Enolization

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Abstract: β-Hydroxy ketones can be doubly deprotonated with >2 equiv of an amide base at low temperature providing both proximal or distal aldolate dianions in good to excellent yield. A variety of substitutionally biased β-hydroxy ketones give exclusively distal dianions. If the distal site is blocked, proximal dianions are formed in good yield; however, chromatographic separation of the silylated products leads to decreased yields. Comparative enolization studies of 4-hydroxy-2-butanone, 1-hydroxy-3-pentanone, and hydroxyl-substituted derivatives reveal a kinetic factor favoring proximal deprotonation of β-OTMS and β-alkoxy ketones. However, there is a thermodynamic factor favoring distal dianions that becomes significant as solutions of the dianions are warmed. Thermal stability studies indicate good room temperature stability of the dianions toward elimination and retroaldolization processes; control studies in this area also support the presence of a dianionic species. Precedent suggests that the dianions exist as internally chelated species, and we speculate that ion triplets containing bridging lithiums are good candidates for the structure of both proximal and distal dianion species. The distal dianions undergo clean reaction with aldehydes and acyl cyanides leading to β,β′-dihydroxy ketones and β-hydroxy-β′-oxo ketones, respectively.

Introduction

Enolate formation is a ubiquitous process in organic chemistry because of the key position enolates hold in organic synthesis as important intermediates for carbon–carbon bond-forming processes.[1] Recent developments in the area of stereoregulated alkylation and condensation reactions have increased their utility, allowing stereocontrol in the formation of both carbon–carbon and carbon–oxygen bonds. Much effort has gone into the development of methods that will allow both regio-[2] and stereocontrol[3] in the preparation of enolates. Although there have been isolated studies on the effects of α-heteroatom substitution on enolate formation, many are anecdotal in nature. There have been only a few systematic studies in this area.[4] Some of these data for the enolization of α-heteroatom-substituted ketones are shown in Table I. From these data it is difficult to draw valid conclusions regarding the effect of an α-heteroatom on enolization processes. In the cases of exocyclic α-heteroatom substitution (entries 1–10) any kinetic electronic effect of the heteroatom is superimposed on the steric effect of α-substitution. Entries 11–16 eliminate this complication, but now the possible intervention of stereoelectronic effects of the (presumably) axial heteroatom lone pair electrons complicates the picture. Therefore, conclusions based upon these results must be viewed carefully, due to the incompleteness of the database. There are insufficient examples in the literature to allow a complete analysis that accounts for the delicate balance of steric and electronic effects involved in the transition states for kinetic deprotonations. Several factors must be taken into account when designing a study of this nature. It is important that the degree of α-substitution about the ketone be similar to eliminate steric factors. Under *kinetic* conditions, the added steric effects found in an unsymmetrically substituted ketone may be more than large enough to overshadow the various electronic effects at the transition state. Further, in conformationally constrained ketones the stereoelectronic effects of the heteroatom lone pairs must also be considered. Finally, in *thermodynamic* ketone enolizations only those steric and electronic effects that influence *enolate* ground-state stabilities should be considered. One must be careful in inferring relative enolate ground-state stabilities from studies of enol ether or enol acetate equilibria.

The effects of β-heteroatom-containing groups on enolate formation are less well-known. With the exception of β-heteroatom-substituted ester enolates, little work has been done in this area.[5] The double deprotonation of a variety of α- and β-hydroxy-substituted esters with two equivalents of a strong base has been shown to afford ester enolate dianions. Examples of this process can be seen in the facile formation of the enolate dianions of the β-hydroxy esters **1**,[6,7] and lactones **2**,[8] as well as of α-hydroxy esters **3**[9] and lactones **4**. The double deprotonation of α-hydroxy ketones is also precedented.[10] Similarly, β-amido esters can be doubly deprotonated[11] to afford enolate dianions **5**. In light of the variety of studies and synthetic applications of β-hydroxy ester enolate dianions, it seems curious that the double deprotonation of readily available β-hydroxy ketones to afford enolate dianions has not been studied in a systematic manner.[12] This gap in the study of enolates may be due in part to concerns about retroaldolization, dehydration, enolate scrambling and other possible side reactions.

On the basis of our interest in the development of new methods for the preparation of oxygen heterocycles,[13] dianions such as **6**

(1) (a) Heathcock, C. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 3, Chapter 2. (b) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 3, Chapter 1. (c) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1.

(2) d'Angelo, J. *Tetrahedron* **1976**, *32*, 2979.

(3) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (b) Fataftah, Z. A.; Kopka, I. E.; Rathke, M. W. *J. Am. Chem. Soc.* **1980**, *102*, 3959.

(4) (a) Kowalski, C.; Creary, X.; Rollin, A. J.; Burke, M. C. *J. Org. Chem.* **1978**, *43*, 2601. (b) Wilson, S. R.; Walters, M. E.; Orbaugh, B. *J. Org. Chem.* **1976**, *41*, 378. (c) Coates, R. M.; Pigott, H. D.; Ollinger, J. *Tetrahedron Lett.* **1974**, 3955. (d) Garst, M. E.; Bonfiglio, J. N.; Grudoski, D. A.; Marks, J. *J. Org. Chem.* **1980**, *45*, 2307. (e) Goldsmith, D. J.; Dickinson, C. M.; Lewis, A. J. *Heterocycles* **1987**, 25, 291. (f) Hirsch, J. A.; Wang, X. L. *Synth. Commun.* **1982**, *12*, 333.

(5) For studies on the enolization tendencies of β-amino ketones, see: Pratt, N.; Albizati, K. F. *J. Org. Chem.* **1990**, *55*, 770.

(6) (a) Seebach, D.; Wasmuth, D. *Helv. Chim. Acta* **1980**, *63*, 197. (b) Zuger, M.; Weller, T.; Seebach, D. *Helv. Chim. Acta* **1980**, *63*, 2005. (c) Wasmuth, D.; Arigoni, D.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 344.

(7) (a) Kraus, G. A.; Taschner, M. J. *Tetrahedron Lett.* **1977**, 4575. (b) Frater, G. *Helv. Chim. Acta* **1979**, *62*, 2825. (c) Frater, G. *Helv. Chim. Acta* **1979**, *62*, 2829. (d) Frater, G. *Helv. Chim. Acta* **1980**, *63*, 1383. (e) Frater, G. *Tetrahedron Lett.* **1981**, *22*, 425.

(8) (a) Shieh, H.-M.; Prestwich, G. D. *J. Org. Chem.* **1981**, *46*, 4319. (b) Chamberlin, A.; Dezube, M. *Tetrahedron Lett.* **1982**, *23*, 3055.

(9) Kaneko, T.; Turner, D. L.; Newcomb, M.; Bergbrieter, D. E. *Tetrahedron Lett.* **1979**, 103.

(10) Wilson, S. R.; Walters, M. E.; Orbaugh, B. *J. Org. Chem.* **1976**, *41*, 378.

(11) (a) Seebach, D.; Estermann, H. *Tetrahedron Lett.* **1987**, *28*, 3103–3106. (b) Estermann, H.; Seebach, D. *Helv. Chim. Acta* **1988**, *71*, 1824–1839.

(12) A few anecdotal occurrences of this phenomenon have been reported: (a) McCarthy, P. A.; Kageyama, M. *J. Org. Chem.* **1987**, *52*, 4681–4686 (a single example). (b) Kowalski, C. J.; Fields, K. W. *J. Am. Chem. Soc.* **1982**, *104*, 1777–1779 (showed that aldolate dianions can be generated by the addition of α-keto dianions to sterically congested carbonyls). (c) Szajewski, R.; P. PhD. dissertation, Columbia University, 1975 (a brief study in conjunction with prostaglandin synthesis).

(13) For a compilation of references to important substances and work in this area, see: Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617.

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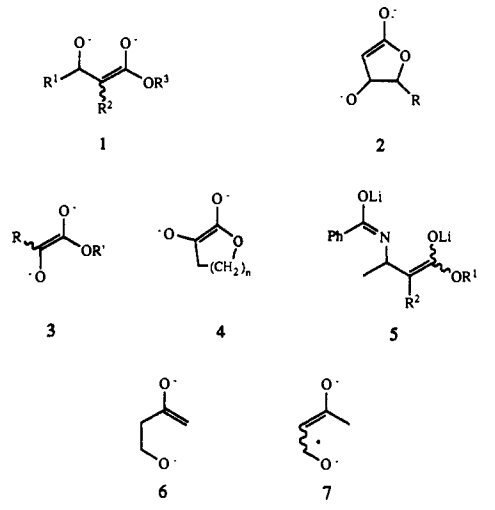
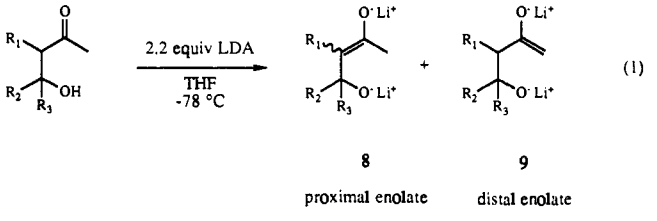


and **7** formed by the double deprotonation of β-hydroxy ketones seemed to be logical intermediates for oxygen heterocycle synthesis. We felt that the bis-nucleophilicity of such species could serve as the basis for the construction of a variety of highly functionalized oxygen heterocycles. We have found that the addition of β-hydroxy ketones to solutions of amide bases at −78 °C in THF results in smooth double deprotonation to cleanly provide dianions in good to excellent yields (eq 1). Removal of an enolizable proton



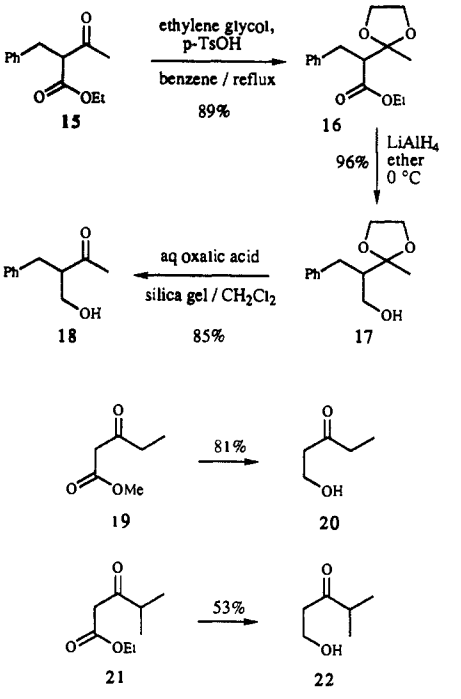
(1)

vicinal to the β-heteroatom substituent results in a *proximal* enolate (**8**) while removal of an enolizable proton furthest from the β-heteroatom substituent results in a *distal* enolate (**9**). Further, we have found that a β-hydroxyl group has profound effects on the formation of ketone enolates. We wish to describe in detail our initial fundamental studies on the generation, chemical stability, and reactivity of β-hydroxy ketone enolate (aldolate) dianions[14] and related β-heteroatomic species.

Results and Discussion

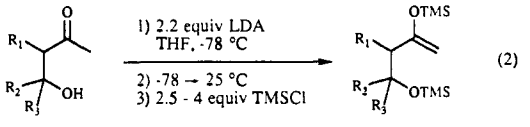
Preparation of β-Hydroxy Ketone Substrates. To study this phenomenon in depth a large number of β-hydroxy ketone substrates representing a variety of α-substitution patterns was required. We naturally turned to the aldol condensation to prepare many of these substrates. β-Hydroxy ketones **10** and **11** were prepared by addition of cyclohexanone enolate to benzaldehyde following the procedure of Heathcock and were separated by preparative HPLC on silica.[15] Compounds **12–14a–e** were prepared by addition of the appropriate aldehyde to a ketone enolate generated by deprotonation with LDA in THF at −78 °C in what has by now become standard procedure. Compound **13** was prepared by addition of formaldehyde to the enolate of 3-pentanone as described by Smith.[16] Despite these simple preparations, early in the course of these studies it became apparent that a general method was needed for the preparation of β-hydroxy ketones not easily available via directed aldol condensation. Accordingly, a general method was developed which is illustrated in Scheme I for the preparation of the benzyl-substituted β-hydroxy ketone **18**. This approach takes advantage of the easy availability of β-ketoesters with varying substitution patterns. The

Scheme I. General Preparation of α-(Hydroxymethyl)-ketones



procedure consists of ketalization of **15** → **16**, followed by reduction with lithium aluminum hydride to afford the alcohol **17**. The β-hydroxy ketal is then deketalized with wet silica gel following the method of Conia.[17] Under the mild deprotection conditions employed there is no sign of dehydration of the often sensitive β-hydroxy ketone functionality. This method was also used for the preparation of β-hydroxy ketones **20** (from **19**) and **22** (from **21**) in 81% and 53% overall yields, respectively.[18]

Generation and Silylation of Distal Aldolate Dianions. A wide range of β-hydroxy ketones with varying substitution patterns were found to give regioisomerically pure solutions of distal aldolate dianions by use of standard kinetic enolate formation conditions. Addition of the β-hydroxy ketone to a solution of 2.2 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran at −78 °C followed by warming to 25 °C for a short period resulted in smooth double deprotonation to provide exclusively (>97% regioselectivity) the distal aldolate dianions, in which enolization had taken place away from the β-oxido group (eq 2). The regioselectivity of



(2)

enolate formation was examined via standard silylation techniques using 2.5–4 equiv of chlorotrimethylsilane (TMSCl) to provide the distal β-((trimethylsilyl)oxy) trimethylsilyl enol ethers (**26–33**) in good to excellent yields (Table II). The distal silyl ethers, with the exception of entry 5, are obtained spectroscopically pure and required little or no further purification. No traces of elimination or retroaldol products were observed. In the case of entries 7 and 8, double deprotonation of diastereomerically pure β-hydroxy ketones results in the formation of the diastereomerically pure distal β-silyloxy silyl enol ethers **32** and **33**, with no traces of epimerization products. The distal silyl enol ethers are stable at room temperature for weeks and can be stored at −25 °C for months with no signs of decomposition. All of the substrates in Table II are substitutionally biased. The dianion obtained is the one expected on the basis of a kinetic deprotonation, i.e., deprotonation of the least substituted carbon. However, it is noteworthy

(14) Some of this work has already appeared in communication form: Martin V. A.; Albizati, K. F. *J. Org. Chem.* **1988**, *53*, 5986.
(15) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.
(16) Smith, A. B., III; Levenberg, P. A. *Synthesis* **1981**, 567.
(17) Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 1963.
(18) For more examples and full experimental details see: Hitchcock, S. R.; Perron, F.; Martin V. A.; Albizati, K. F. *Synthesis*. In press.

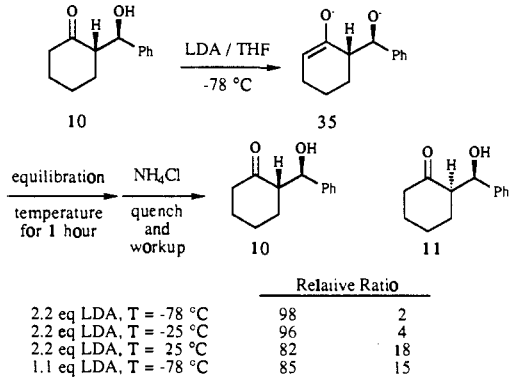
Table I. Product Distributions in the Enolization of α-Heteroatom-Substituted Ketones

entry	substrate	conditions	base	distal:proximal	ref
	α-substituted ketone → distal product + proximal product				
1	X = Cl, R = Ac	kinetic	LHMDS	6:94	4a
2	X = Br, R = Ac	kinetic	LHMDS	18:82	4a
3	X = OMe, R = TMS	kinetic	LDA	85:15	4a
4	X = OH (O^-), R = TMS	kinetic	LDA	84:16	4b
5	X = OH (O^-), R = TMS	thermodynamic	Et_3N	33:67	4b
6	X = SPh	thermodynamic	NaH	proximal only	4c
7	X = NMe_2, R = TMS	kinetic	LDA	98:2	4d
8	X = NMe_2, R = TMS	thermodyanmic	LHMDS	98:2	4d
9	X = N(Ph)CO_2Me, R = TMS	kinetic	LDA	33:67	4d
10	X = N(Ph)CO_2Me, R = TMS	thermodynamic	LHMDS	2:98	4d
	α-substituted ketone → distal product + proximal product				
11	X = NEt, R = TMS	kinetic	LDA	83:17	4d
12	X = NEt, R = TMS	thermodynamic	LHMDS	98:2	4d
13	X = NCO_2Et, R = TMS	kinetic	LDA	22:88	4d
14	X = NCO_2Et, R = TMS	thermodynamic	LHMDS	33:67	4d
15	X = O, R = Ac	kinetic	LDA	77:23	4e
16	X = O, R = TMS	thermodynamic	Et_3N	distal only	4f

that the enolizations are regiospecific within the limits of ^1H NMR spectroscopic detection, which we have determined to be ca. 1–2% on our spectrometers. Thus, the β-hydroxy ketone substrates examined here exhibit regioselectivity comparable to or greater than the corresponding all-carbon analogues.[19]

Distal Dianion Stability Studies. Early in our work, we deemed it useful to study the general thermal stability of the dianions to ascertain the synthetically useful temperature range over which the reagents could be used. The experience we had accumulated up to that time indicated that we were dealing with a species with appreciable thermal stability. For example, when we allowed the enolate mixtures obtained from **23a** and **34a** to equilibrate at room temperature, we obtained the same chemical yields (ca. 70–80%) as when the dianions were kept at −78 °C for various periods of time. We undertook a systematic study of a pair of diastereomeric β-hydroxy ketones to ascertain if elimination, retroaldolization, or epimerization was a function of temperature. The diastereomeric aldols **10** or **11** were treated with 2.2 equiv of LDA at low temperature and allowed to stand at −78, −25, and 25 °C for 1 h and quenched. These results are shown in Scheme II. The ratio of **10**:**11** in the product mixtures was determined by ^1H NMR integration of the carbinol resonances. When **10** was treated with 2.2 equiv of base and held at −78 °C for 1 h only traces of the epimerization product were observed. When kept at −25 °C, slightly more epimerization was observed and at room temperature the epimerization was significant. However, when the monoanion was generated with 1 equiv of LDA, considerable epimerization was observed at −78 °C after 1 h. More importantly, only under monoanion conditions were significant (10–15%) quantities of retroaldol products (cyclohexanone, benzaldehyde, and further condensation products) observed. From this study several conclusions can be drawn. Apparently, the species generated with 1 equiv of base is different from the species generated with 2 equiv of base. This suggests that the species formed with 2 equiv of base is not an equilibrium mixture of monoanions but is consistent

Scheme II. Thermal Stability Study of Distal Dianion **35**

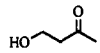
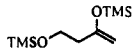
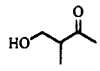
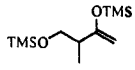
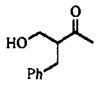
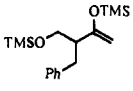
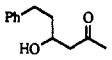
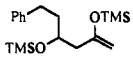
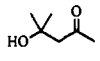
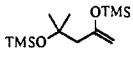
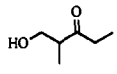
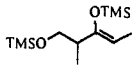
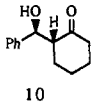
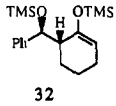
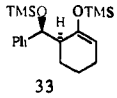


with the formation of a new species, most simply formulated as a dianion (**35**). Further, since we do not observe retro-aldol products under dianion conditions, we conclude that epimerization is occurring via an enolate equilibration process rather than a retroaldol–aldol process. This is in agreement with what we observed in the comparative enolization studies as well as our general observations of several of the distal dianion species over the past 2 years. Finally, distal aldolate dianions are more stable to elimination and retro-aldol processes than the corresponding β-oxido ketone (monoanion) species, as one might predict.

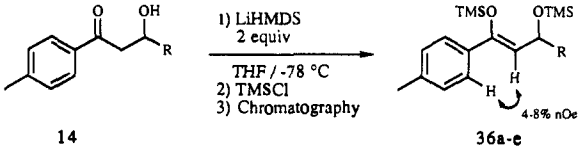
Generation, Silylation, and Thermal Stability of Proximal Aldolate Dianions. We wished to study various aspects of proximal aldolate dianion formation and stability unfettered by the potential formation of regioisomers. This was easily accomplished by blocking the distal side of the ketone with non-enolizable substituents. After much experimentation, it was determined that the best conditions for generating solutions of proximal dianions consisted of adding the β-hydroxy ketone to 2.2 equiv of lithium hexamethyldisilazide in THF at −78 °C for 15 min (Scheme III). Even under these optimized conditions, some substrates exhibited significant amounts (10–30%) of elimination and retroaldolization products. Trapping with excess TMSCl as before provided the proximal β-((trimethylsilyl)oxy) trimethylsilyl enol ethers **36a–e**. Unlike the distal dianion cases, the silyl ethers were not obtained cleanly. Purification of these substances by preparative HPLC on silica led to decreased yields in many instances. In all cases,

(19) We ran the classical benchmark (2-octanone) for the determination of the regioselectivity of hindered bases in ketone deprotonation. For this substrate under conditions B, Heathcock reported exclusive formation of the least substituted enolate in 54% yield. This work was repeated later (ref 20) and a 50% yield of a 94:6 ratio of silyl enol ethers was reported. In our hands, the results with the classical deprotonation procedure were different from either of these (Table IV, last three entries).

Table II. Generation and Trapping of Distal Aldolate Dianions with TMSCl

entry	β-hydroxy ketone	silylation product	% yield
1	 23a	 26	81
2	 24	 27	80
3	 18	 28	85
4	 12	 29	88
5	 25	 30	70
6	 13	 31	93
7	 10	 32	74
8	 11	 33	81

Scheme III. Formation and Trapping of Enforced Proximal Aldolate Dianions



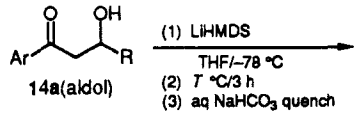
14 36a-e

	R	% yield
a	Me	20
b	Et	93
c	i-Pr	54
d	t-Bu	28
e	2-furyl	42

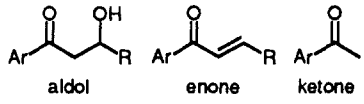
a single geometric isomer could be obtained at low temperature, which was assigned the *Z* configuration based on the observation of a 4–8% nuclear Overhauser enhancement of the vinyl hydrogen when the ortho protons on the aryl ring were irradiated.

As with the distal dianions, information concerning the general thermal stability of the proximal dianions was desirable to facilitate studies on synthetic utility. A set of experiments similar to those described above was carried out. In this study, percent recovery of starting material and production of enone by elimination processes or products from retroaldol reactions were the parameters examined. We additionally looked at the effects of countercations on proximal dianion stability by simply varying the metal hexamethyldisilazide base used to generate the lithium, sodium, and potassium proximal dianions. One aldol adduct (**14a**), chosen for

Table III. Stability Study of Proximal Aldolate Dianions



14a(aldol)



aldol enone ketone

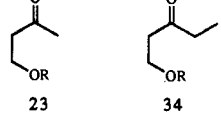
Ar = p-methylphenyl; R = methyl

entry	base	equiv	T, °C	% aldol recovery[a]	% enone	% ketone
1	LiHMDS	2.2	-78	94	0	0
2	LiHMDS	2.2	0	91	0	0
3	LiHMDS	1	-78	90	0	0
4	LiHMDS	1	0	91	0	0
5	NaHMDS	2.2	-78	68	0	10[b]
6	NaHMDS	2.2	0	0	57[b]	0
7	NaHMDS	1	-78	96	0	0
8	NaHMDS	1	0	0	0	55[b]
9	KHMDS	2.2	-78	60	0	15[b]
10	KHMDS	2.2	0	0	76[b]	0
11	KHMDS	1	-78	98	0	0
12	KHMDS	1	0	0	0	73[b]

[a] Refers to isolated yields. [b] A number of uncharacterized minor products were obtained.

the spectral simplicity of the anticipated elimination and retroaldolization products, was studied systematically. From the results shown in Table III, it is readily apparent that the dilithio species exhibits appreciable stability, with little or no elimination or retroaldolization products observable after 3 h at room temperature (entries 1 and 2). However, the sodium and potassium counterparts exhibit significant decomposition at −78 °C (entries 5 and 9), and at 0 °C (entries 6 and 10) no β-hydroxy ketone was recovered. When **14a** was treated with 1 equiv of base, the lithium monoanion exhibited good stability up to 0 °C (entries 3 and 4). The sodium and potassium monoanions undergo complete retroaldolization when warmed to 0 °C (entries 8 and 12) but are recovered near-quantitatively after standing for 3 h at −78 °C (entries 7 and 11). This again contrasts with the species formed from 2.2 equiv of base, which does not exhibit retroaldolization or elimination products. It is interesting that the species formed with 2 equiv of base only gives elimination product (no retro product observed) while the species formed with 1 equiv of base only gives retroaldol product (no elimination product observed). While not as clear as in the distal.dianion stability study, these data suggest the existence of different species under conditions of 1 and 2 equiv of base, supporting the existence of a dianion. Additionally, these results can be explained by the greater oxygen-complexing ability of lithium over sodium and potassium and suggest that both the mono- and dianions may exist to a great extent in internally chelated forms. This is discussed in greater detail later on.

Comparative Enolization Studies. In order to gain a further understanding of the effects of a β-oxido group on ketone enolization, β-hydroxy ketones **23a** and **34a**, along with their monotrimethylsilyl (**23b**, **34b**) and THP ethers (**23c**, **34c**), were studied



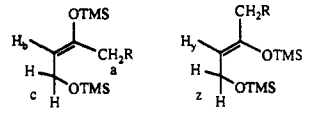
23 34

a R = H
b = TMS
c = THP

further. The prototypical β-hydroxy ketone **23a** was chosen, anticipating a clear kinetic difference between the two regioisomeric enolates. Yet, at the same time, it would still be possible to obtain significant amounts of both regioisomeric enolates under

kinetic conditions. Also, on the basis of a comparison with a typical methyl ketone such as 2-octanone, the thermodynamic enolate should not be the same as the kinetic enolate. The β-hydroxy ketone **34a** was chosen because its symmetrical substitution pattern would cancel out as nearly as possible the differences in enolate formation and stability due to steric effects and the electronic effects due to differing degrees of C substitution about the α position. Thus, **34** should behave similarly to a symmetrically α-substituted ketone. Ideally, the only remaining perturbing effects will be the nonsteric effects due to the β-hydroxyl group. Additionally, the corresponding β-((trimethylsilyl)oxy) and β-((tetrahydropyranyl)oxy) derivatives should provide benchmarks for measuring the effects of a β-oxido group on the enolization process since these groups are not ionizable.

All six substrates were examined under a standard set of reaction conditions. Method A is an internal quench procedure[20] consisting of addition of the β-hydroxy ketone to a preformed solution of TMSCl and LDA in THF at −78 °C, followed by an aqueous bicarbonate quench after 15 min. Method B is the classical method for the formation of kinetic enolates consisting of addition of the β-hydroxy ketone to a solution of LDA in THF at −78 °C, followed after 15 min by addition of TMSCl. After an additional 15 min the reaction is quenched by addition of aqueous bicarbonate. Method C consists of forming the aldolate dianion under classical conditions as in method B and allowing it to warm to room temperature for 15 min. This is followed by addition of TMSCl and an aqueous bicarbonate quench as in methods A and B. The ratios of the enol silane products were determined by 300-MHz ^{1}H NMR analysis and are accurate to within 1–2% when compared to ratios obtained with capillary gas chromatographic analysis. The assignment of the *E* and *Z* isomers was made by analysis of ^{1}H NMR chemical shifts and the relative magnitudes of the allylic and homoallylic coupling constants.[21] For example, in an *E*/*Z* isomer pair (**37*E*** and **37*Z***), the vinyl

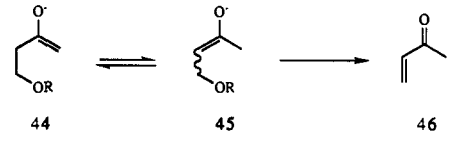


37*E* 37*Z*

proton of the *E* isomer was assigned to be farthest downfield of the two vinyl proton resonances. Further, it was found that the allylic coupling constant between the vinyl hydrogen and $-CH_2R$ was greater for the *Z* isomer ($J_{xy} > J_{ab}$) and the homoallylic coupling constant between the methylene and $-CH_2R$ was greater for the *E* isomer ($J_{xz} > J_{ac}$). These data are in accord with observed trends and reinforce the structural assignment made on the basis of the chemical shift criterion.

The results of subjecting **23a–c** to the standard set of enolization and trapping conditions are shown in Table IV. Several unexpected and interesting phenomena occurred. Under standard conditions for the formation of "kinetic" enolates (method B) the distal:proximal (D:P) ratios for the enolates formed from **23a** are close to that which would be expected classically. However, if this enolate mixture is formed under the classical conditions and allowed to warm to room temperature for a short time (method C) the D:P ratio increases to >96:4. This is highly significant since, under conditions of excess base and in the absence of other additivies, normal ketone enolates are configurationally and regioisomerically stable, i.e., they do not equilibrate. Upon warming to room temperature the aldolate dianion equilibrates to form almost exclusively the less substituted enolate. Equilibration is not generally observed *under these conditions*[22] with classical ketone enolates. In fact, when classical enolates are allowed to equilibrate under conditions of excess ketone, other factors being equal, the *more substituted* enolate is thermodynamically favored. Apparently, with β-oxido enolates, the less substituted enolate is favored by a large margin.

Comparison of the above results to those obtained for the monodeprotonation of the β-((trimethylsilyl)oxy) and β-((tetrahydropyranyl)oxy) ketones **23b** and **23c** reveals trends of synthetic significance. Similar results were observed in both cases. Monodeprotonation of **23b** with method A or B results in much less selective deprotonation (57:43 and 71:29 D:P, respectively) than in an all-carbon analogue (2-octanone, Table IV, bottom). Further, when the enolate is allowed to warm to room temperature, no bis(trimethylsilyl ether) product was observed. We suspect that elimination of $TMSO^-$ or $THPO^-$ in the proximal enolates (*45*) is significant at higher temperatures. The methyl vinyl ketone (**46**) thus formed can then facilitate equilibration of the enolates (**44** ⇌ **45**), eventually resulting in complete elimination to volatile



44 45 46

R = TMS or THP

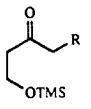
47

products, which were not observed. In a few runs, we did observe small amounts of the diene **47**, presumably arising via silylation of a dienolate produced by deprotonation of **46**. The synthetic significance of these results is that the greatest D:P selectivity occurs when the dianion is allowed to warm, which may not be feasible with traditionally hydroxyl-protected β-hydroxy ketones.

In order to obtain a better measure of the nature and the magnitude of the effect of a β-hydroxy (or β-oxido) group on ketone enolization, 1-hydroxy-3-pentanone (**34a**) and its β-*O*-trimethylsilyl (**34b**) and β-*O*-tetrahydropyranyl ethers (**34c**) were studied under the same deprotonation conditions (Table V). Subjecting **34a** to the classical enolate-forming conditions of method B results in a 70:30 D:P ratio. As with **23a**, formation of the dianion of **34a** under classical conditions followed by warming to room temperature results in equilibration to a synthetically significant 95:5 D:P ratio. This stands in dramatic contrast to monodeprotonation of the β-((trimethylsilyl)oxy) substrate **34b**. With method A, the D:P ratio reverses to 10:90 favoring the proximal isomer, while with method B the ratio is 27:73. As in the case of **23b** and **23c**, allowing the enolates formed from **34b** and **34c** to warm to room temperature results in complete decomposition of the enolates to uncharacterizable products. No β-((trimethylsilyl)oxy) silyl enol ethers are formed. Again, the synthetic significance is clear: *a β-hydroxyl group can direct enolate formation to provide a distal dianion in an otherwise symmetrically α-substituted ketone, whereas a β-alkoxy or β-silyloxy group exerts a weak directing effect favoring proximal enolates. Clearly, aldolate dianions possess greater chemical stability to elimination processes compared to the β-silyloxy or β-alkoxy enolates, as might be expected.*

The trends observed in the enolization and trapping of ketones having non-ionizable β-heterofunctional groups provide explanations for the skewed (or reversed) distal:proximal ratios in the enolization of **23a** and **34a** under the internal quench procedure (method A). As we have shown for several substrates, the presence of a non-ionizable β-heteroatomic group directs enolization toward the proximal position. Under the internal quench conditions the rate of silylation of the hydroxyl group may be comparable to or greater than the rate of enolate formation such that significant quantities of the monosilylated species **52** are produced. Thus, under the conditions of method A, enolate formation may be occurring not on the free β-hydroxy ketone but rather upon a mixture of β-hydroxy ketone and β-silyloxy ketone. The presence of the β-silyloxy ketone results in the formation of larger amounts

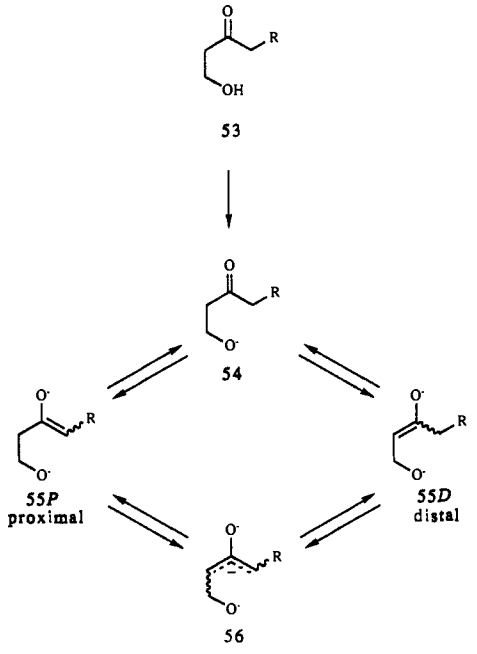
(20) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.
(21) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: New York, 1969; pp 316–328.
(22) However, configurational equilibrium apparently can occur in the presence of HMPA. See ref 3b.



52 R = H or CH_3

of the proximal product than would initially be expected.

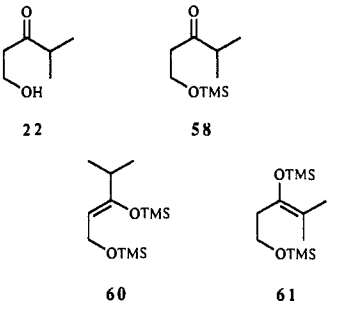
Similar reasoning can explain the deviation in the distal:proximal ratio found for the double deprotonation of **23a** under classical conditions for kinetic enolate formation (method B). Under conditions B, an 80:20 (D:P) ratio is obtained. The ratio we obtained in a control experiment with 2-octanone was 90:10. A literature value for the enolization of 2-octanone under the same conditions is 94:6.[20] At least two explanations can be proposed to explain the difference between enolization of 2-octanone (**41**) and **24a**. One plausible description of the process by which an aldolate dianion is formed would consist of initial deprotonation of the β-hydroxyl (**53**) to give the β-oxido ketone **54** followed by



enolization of the ketone to give the aldolate dianion **55**. This scenario is supported by the expected difference in pK_a's between a primary alcohol ($pK_a \approx 16$) and a methyl ketone ($pK_a \approx 21$) and by the well-known difference in kinetic acidities between carbon-bound hydrogens and hydrogens attached to heteroatoms. We have already shown how the presence of a β-oxido group results in a *thermodynamic* driving force favoring distal enolates. We have also shown that the presence of a non-ionizable β-heteroatom-containing group results in a *kinetic* preference for the formation of proximal enolates. This suggests a possible explanation consistent with the initial formation of a β-oxido monoanion. Although the β-oxido group provides a thermodynamic driving force for distal enolate formation, it may also provide the same kinetic preference (although of a slightly weaker magnitude) as other β-heteroatom-containing functional groups for the formation of proximal enolates. Even though the hydroxyl group has been converted to an anion it is still a heteroatom possessing lone pairs of electrons. It is reasonable to expect that the origin of the kinetic preference for proximal deprotonation of β-OR ketones will still be present in β-oxido ketones.

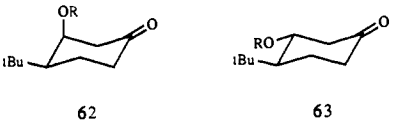
The aldolate dianion equilibration process, under classically nonequilibrating conditions in the absence of additives,[3b] is unique. The simplest explanation is that trace amounts of the β-oxido ketone **54** are present due to incomplete deprotonation, protonation of the dianion by a solvent, or other reasons. The presence of a non-enolized species could serve to equilibrate the enolates via the classically accepted mechanism. Equilibration is expected to be faster at higher temperatures, which is observed here. A more interesting possibility involves further deprotonation of the dianion to afford a trianion (*56*) as the species responsible for equilibration. At this time we have not observed such a species, although dianions of aliphatic ketones and related species are known.[23]

The β-hydroxy ketone **22** provides an interesting case because the classical thermodynamic enolate from this substance is predicted to be distal, which is predicted to be reinforced by the presence of the β-hydroxy group based on what we have observed in other cases. Our results using this substrate have been inconclusive. The major product (ca. 50%) obtained under all conditions is the monosilyl ether **58**. Using methods A, B, or C

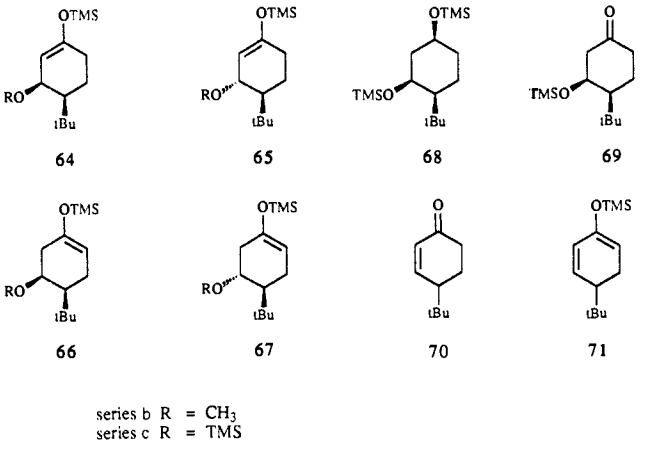


we observed mostly proximal product, tentatively identified as **60** (*Z*) along with smaller amounts of the distal isomer **61**. Attempts at obtaining cleaner mixtures (longer reaction times, more equiv base) not containing **58** or starting β-hydroxy ketone have not been successful. Because it is not clear that a dianion is being formed cleanly in this case, we are reluctant to draw conclusions from this information.

Enolization of Conformationally Defined β-Hydroxy Ketones. The orientation of the C–O bond of the β-hydroxy or alkoxy group with respect to the carbonyl oxygen may play an important role in the enolization process in addition to affecting dianion stability. It is not clear what role (if any) is played by metal ion chelation in either the deprotonation of β-hydroxy ketones or in thermodynamic stabilization of the resulting dianions. Two simple but useful probes of this question are the conformationally locked β-hydroxy ketones **62a** and **63a**, in which the hydroxyl groups are held in specific orientations with respect to the carbonyl. In addition, neither **62a** nor **63a** appears to be capable of chelating



series a R = H
series b R = CH_3

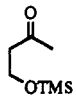
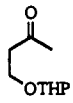
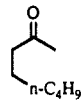


series b R = CH_3
series c R = TMS

a metal ion between the two oxygen atoms. These substrates[24] along with their corresponding methyl ethers (**62b** and **63b**) were

(23) Harris, T. M.; Hubbard, J. S. *J. Am. Chem. Soc.* **1980**, *102*, 2110.
(24) Evans, D. A.; Chapman, K. C.; Carriera, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.

Table IV. Product Ratios from the Silylation of **23a–c** and 2-Octanone (**41**)

Substrate	Conditions[b]	Product Ratios[a] 26	38*E*	38*Z*	Distal:Proximal Ratio	Total % yield all isomers
 **23a**	A	70	20	10	70 : 30	70
	B	80	<2	10	80 : 20	70
	C	96	<2	<2	96 : <4	70
 **23b**	A	57	33	10	57 : 43	77
	B	71	20	9	71 : 29	81
	C	--	--	--	--	--[c]
		39	**40*E***	**40*Z***		
 **23c**	A	52	38	10	52 : 48	87
	B	71	22	7	71 : 29	83
	C	--	--	---	--	--[c]
		42	**43**			
 **41**	A	94	6		94 : 6	78
	B	90	10		90 : 10	79
	C	90	10		90 : 10	94

[a] Ratios determined by 300-MHz ^{1}H NMR. [b] See text. [c] No starting material or bis(trimethylsilyl ether) products were observed.

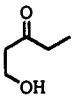
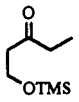
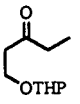
prepared and subjected to the same enolization conditions as in the earlier studies. The results are shown in Table VI. Under the three sets of deprotonation conditions applied, the equatorial hydroxy substrate **63a** enolized exclusively in the distal direction providing **67c**. The proximal isomer **65c** was never detected spectroscopically. The corresponding methyl ether (**62b**), however, exhibited decreased distal selectivity under conditions A and B. As expected, when the distal/proximal enolate mixture from **62b** was allowed to warm, elimination of the β-group became significant, leading to 35% of the diene **71**, presumably via enolization and silylation of the enone **70**.

The axial β-hydroxy and β-methoxy compounds **63a** and **63b** behaved quite differently. Under condition A, the axial ketoalcohol **63a** was not cleanly deprotonated. While the distal isomer **67c** was favored, a large amount of the mono-silylated product **69** and the carbonyl-reduced and silylated product **68** were formed. Repeated attempts to mitigate this problem were unsuccessful, and we were reluctant to vary the conditions dramatically because we wished to retain the internal consistency of the results. Under conditions B, however, double deprotonation was clean and proceeded to 79:21 D:P ratio. Under conditions C enolate decomposition was observed in the form of the reduced compound **68** (11%) and the crossover distal isomer **67c** (11%). This latter product can arise by a retroaldol ring opening and reclosure process followed by enolization prior to trapping with TMSCl.

The axial β-methoxy substrate **62b** gave approximately the same D/P ratio under both conditions A and B providing mostly proximal silyl ether **64b**. Under conditions C only the distal product **66b** and the elimination product **71** were produced. No proximal product was observed. This is consistent with a scenario in which the proximal enolate eliminates quantitatively to the enone **70** which is kinetically deprotonated and silylated to **71**.

From these results it is clear that prior chelation of the metal cation between the β-oxido group and the carbonyl is not necessary for double deprotonation to occur. Additionally, the results are somewhat different from those obtained in the acyclic cases. Again, the distal isomer is favored in the β-hydroxy cases and elimination is a problem when the β-alkoxy enolates are allowed to warm to room temperature. However, the orientation of the β-group is clearly an important factor. The presence of an equatorial hydroxyl gives clean distal deprotonation with no ketone reduction while the presence of an axial hydroxyl leads to D/P mixtures along with varying amounts of reduction product. In addition, an equatorial β-methoxy favors distal deprotonation while an axial β-methoxy favors proximal deprotonation. Side reactions that occur with substrate **62a** complicate interpretation of these data. We have not unambiguously observed an equilibration phenomenon as in the acyclic cases. Also of significance is the

Table V. Product Ratios from the Silylation of **34a–c**

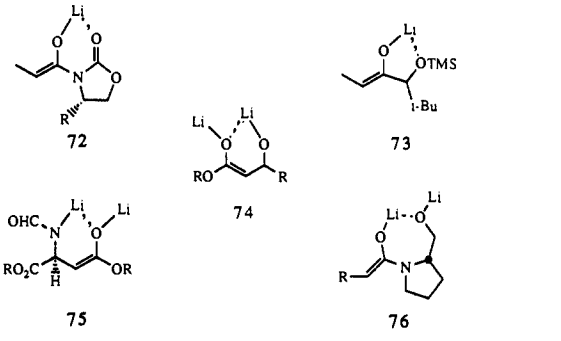
Substrate	Conditions[b]	Product Ratios[a] 48Z	48E	49E	49Z	Distal : Proximal Ratio	Total % yield all isomers
 **34a**	A	16	17	36	31	33 : 67	82
	B	47 (81	23 <2	28 <2	<2 16	70 : 30 83 : 17	77 65)[c]
	C	66	30	<2	4	95 : 5	73
 **34b**	A	3	7	66	24	10 : 90	86
	B	13	15	43	30	27 : 73	68
	C	--	--	--	--	-- : --	--[d]
		50Z	**50E**	**51E**	**51Z**		
 **34c**	A	--	--	--	--	6 : 94	83
	B	--	--	--	--	21 : 79	74
	C	--	--	--	--	-- : --	--[d]

[a] Ratios determined by 300-MHz. ^{1}H NMR. [b] See text. [c] 2.2 equiv of HMPA added to enolate solution before adding TMSCl. [d] No starting material or bis(trimethylsilyl ether) products were observed.

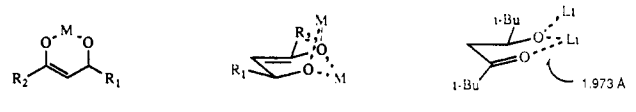
reversal of regioselectivity between **62a** and **62b** under conditions B. In these cases it is reasonable to expect the product ratios to reflect relative kinetic acidities of the α-hydrogens. The data indicate that an axial β-alkoxy group increases the kinetic acidity of the proximal hydrogens relative to an equatorial alkoxy group. Further experimentation is required to confidently account for this phenomenon. It is clear, however, that the cyclic substrates behave somewhat differently from the acyclic β-hydroxy ketones, and this suggests that metal atom chelation of the carbonyl and hydroxyl groups is important either in the transition state for enolization or in determining the ground-state stability of the distal and proximal dianions.

Aldolate Dianion Structure. There are many examples of mono- and polyanionic intermediates that are believed to be internally metal-chelated species, which imparts some degree of structural rigidity. Some examples of carbanions in this category (**72–76**) are shown in Chart I.[6a,b,7d,25] While important strides have been made in determining the solid-state structure of many simple enolates,[26] evidence for chelated enolate structures is usually derived from the diastereoselectivity and/or enantioselectivity in the reactions of such species with electrophiles. We speculate that aldolate dianions possess similar bidentate-chelated structures. It has been shown that the lithium aldolate *monoanion* derived

Chart I



from the reaction of lithium pinacolonate and trimethylacetaldehyde is tetrameric in the solid state, with the monomeric unit possessing a flattened chairlike structure with a lithium coordinated to the carbonyl oxygen as shown in **78**.[27] On the basis of these



77a M = divalent metal 77b M = monovalent metal 78

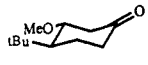
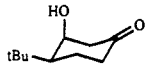
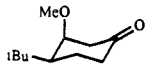
data, a simple six-membered cyclic structure such as **77a** for divalent metal aldolate dianions is reasonable. Similar structures have been invoked frequently with other polyanionic species.[28] In

(25) (a) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737. (b) Heathcock, C. H.; Pirrung, M. C.; Lampe, J.; Buse, C. T.; Young, S. D. *J. Org. Chem.* **1981**, *46*, 2290. (c) Frater, G. *Helv. Chim. Acta* **1979**, *62*, 2825, 2829. (d) Frater, G. *Tetrahedron Lett.* **1981**, *22*, 425. (e) Seebach, D.; Wasmuth, D. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 971. (f) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

(26) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624–1654.

(27) Williard, P.; Salvino, J. M. *Tetrahedron Lett.* **1985**, *26*, 3931.

Table VI. Enolization and Silylation of **62** and **63**

Substrate	Conditions [a]	distal : proximal [b]	OTMS tBu 71	yield [c]
 **63a**	A	100 : 0		82
	B	100 : 0		90
	C	100 : 0		85
 **63b**	A	66 : 35		88
	B	83 : 17		97
	C	36 : 29	35	97
 **62a**	A	57 : 23		89[d]
	B	79 : 21		82
	C	44 : 24		93[e]
 **62b**	A	27 : 73		88
	B	29 : 71		85
	C	53 : 0	47	97

[a] See text. [b] Ratios determined by ^{1}H NMR integration. [c] Yields represent reaction product mixtures containing no extraneous peaks by ^{1}H NMR. [d] Reaction also gave 7% of compound **68** and 13% of compound **69**. [e] Reaction also gave **67c** (12%), **68** (11%), and 9% of a non-isolable substance.

cases of monovalent metals, we speculate that aldolate dianion structure may resemble an ion triplet (**77b**) with bridging by both metal atoms. Analogous structures can be drawn for the distal dianions. This phenomenon has been observed crystallographically with several dilithiocarbanions[29] and has been the subject of a review by Streitwieser.[30]

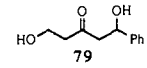
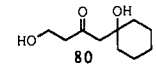
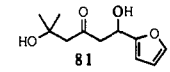
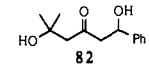
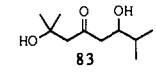
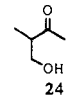
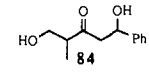
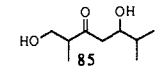
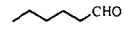
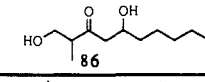
Reaction of Aldolate Dianions with Other Electrophiles. Distal aldolate dianions react readily with a variety of aldehydes at −78 °C to provide β,β′-dihydroxy ketones (**79–86**) in good yield. The results are shown in Table VII. The aldol adducts were obtained in high purity with only simple flash chromatography required in a few cases. The reaction with ketones is generally poor as exemplified by entry 2. Presumably, enolate equilibration of the dianion with the added ketone leads to complex product mixtures and recovered starting material. Reaction of the chiral lithio dianion of **24** with aldehydes exhibits essentially no 1,4-asymmetric induction, providing approximately 1:1 mixtures of diastereomers.

When treated with acyl chlorides, low yields of acylation products were observed, accompanied by acylated *N,N*-diisopropylamine. However, when the dianions were treated with acyl cyanides, the process improved markedly, providing C-acylation products (**87a–d**) in 40–60% yield (Scheme IV).[31]

Summary

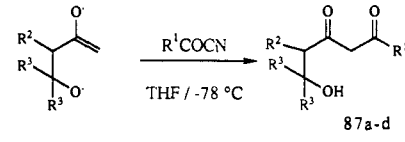
We have shown that β-hydroxy ketones can be doubly deprotonated with >2 equiv of an amide base at low temperature to provide both proximal and distal aldolate dianions in good to excellent yield as judged by trapping with TMSCl. Comparative enolization studies of 4-hydroxy-2-butanone, 1-hydroxy-3-pentanone, and their hydroxyl derivatives reveal a moderate *kinetic* factor favoring proximal deprotonation of β-OH, β-OTMS, and β-alkoxy ketones. However, there is a strong *thermodynamic* factor favoring distal dianions that becomes significant as solutions of the dianions are warmed. A β-hydroxy group can therefore serve as a regiocontrol element in the enolization of symmetrically

Table VII. Reactions of Aldolate Dianions with Aldehydes and Ketones

Entry	β-Hydroxy ketone	Carbonyl Component	Product	% Yield
1	 **23a**		 **79**	66[a]
2			 **80**	21
3	 **25**		 **81**	91
4			 **82**	80[a]
5			 **83**	56[a]
6	 **24**		 **84**	93[b]
7			 **85**	76[a,b]
8			 **86**	67[a,b]

[a] Isolated by chromatography on silica. [b] An approximately 1:1 mixture of diastereomers was obtained.

Scheme IV



	R_1	R_2	R_3	%Yield
87a	Ph	H	H	48
87b	Ph	H	CH_3	50
87c	Ph	CH_3	H	54
87d	OEt	H	CH_3	66

α-substituted ketones. Thermal stability studies indicate excellent room temperature stability of the dianions toward elimination and retroaldolization processes. Precedent suggests that the dianions exist as internally chelated species, and we speculate that ion-triplets containing bridging lithiums are good candidates for the structure of both proximal and distal dianion species. The distal dianions undergo clean reaction with aldehydes and acyl cyanides leading to β,β′-dihydroxy ketones and β-hydroxy-β′-oxo ketones, respectively. Further studies in this area are continuing.

Experimental Section

General. ^{1}H NMR data were measured at 300 MHz and ^{13}C data at 75 MHz. NMR spectral data taken in $CDCl_3$ used the residual $CHCl_3$ singlet at δ 7.26 as the standard for ^{1}H data and the triplet centered at δ 77.0 as the standard for ^{13}C spectra. Data taken in C_6D_6 used the singlet for residual C_6D_5H at δ 7.16 as the ^{1}H standard and the triplet at δ 128.0 for the ^{13}C standard. Infrared spectroscopic samples were prepared as neat oils (liquids) or as KBr pellets (solids). All electron impact high resolution mass spectral (HRMS) data were measured at 70 eV. All of the experiments were carried out under an atmosphere of dry nitrogen in flame-dried flasks. THF and diethyl ether were freshly distilled from sodium/benzophenone ketyl and were transferred via syringes. Diisopropylamine and hexamethyldisilazane were distilled from CaH_2 under nitrogen. Alkyllithium reagents were obtained from the Aldrich Chemical Co. as standardized solutions. High performance liquid chromatography (HPLC) was performed on either a Varian 5000 liquid chromatograph or a semipreparative component system obtained from the Rainin Instrument Corp. HPLC separations were performed on 250 × 20 mm 8 μm silica Magnum semipreparative columns obtained from Rainin. In vacuo removal of solvent refers to the use of a rotary evaporator operating at aspirator pressure.

(28) For a review see: Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737.
(29) (a) Walczak, M.; Stucky, G. *J. Am. Chem. Soc.* **1976**, *98*, 5531. (b) Schubert, U.; Neugebauer, W.; Schleyer, P.v.R. *J. Chem. Soc., Chem. Commun.* **1982**, 1184. (c) Schleyer, P.v.R. *Pure Appl. Chem.* **1983**, *55*, 355.
(30) Streitwieser, A., Jr. *Acc. Chem. Res.* **1984**, *17*, 353.
(31) Mander, L. E.; Sethi, S. P. *Tetrahedron Lett.* **1983**, *24*, 5425.

General Procedure for Aldol Reaction Synthesis of 10–14e. Lithium diisopropylamide (1.05 equiv) was generated at −78 °C by addition of 1.05 equiv of a 2.5 M solution of *n*-BuLi in hexane to a THF solution of 1.1 equiv of diisopropylamine. After the solution was stirred for 10 min, 1.0 equiv of a 1.0 M solution of the methyl ketone in THF was added dropwise. After 30 min, 1.02 equiv of the appropriate aldehyde was added at −78 °C and the reaction mixture was stirred for 15 min. The reaction was quenched by addition of ice cold aqueous saturated $NaHCO_3$ and the mixture was extracted three times with CH_2Cl_2. The combined extracts were dried over Na_2SO_4 and filtered, and the solvent was removed in vacuo. Purification was effected by chromatography on silica where appropriate.

2-(Hydroxyphenylmethyl)cyclohexanone (*S*,R isomer, 10):** ^1H NMR ($CDCl_3$) δ 7.36–7.25 (m, 5 H), 4.78 (d, *J* = 9 Hz, 1 H), 4.05 (br s, 1 H), 2.65–2.56 (m, 1 H), 2.49–2.41 (m, 1 H), 2.38–2.27 (m, 1 H), 2.09–1.99 (m, 1 H), 1.78–1.68 (m, 1 H), 1.67–1.43 (m, 3 H), 1.34–1.19 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 215.1, 140.9, 128.1, 127.5, 126.8, 74.3, 57.2, 42.3, 30.5, 27.5, 24.3; LRMS *m/z* (peak intensity) 204 (M^+, 3), 186 (17), 107 (25), 106 (58), 105 (62), 98 (100), 91 (6), 83 (21), 79 (25), 78 (15), 77 (76), 70 (52), 69 (19), 55 (57), 51 (34), 50 (17).

2-(Hydroxyphenylmethyl)cyclohexanone (*S*,S isomer, 11):** ^1H NMR ($CDCl_3$) δ 7.41–7.23 (m, 5 H), 5.41 (br s, 1 H), 3.11 (*J* = 3 Hz, 1 H), 2.67–2.57 (m, 1 H), 2.51–2.33 (m, 2 H), 2.14–2.06 (m, 1 H), 1.90–1.48 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 214.6, 141.6, 128.1, 126.9, 125.7, 70.6, 57.1, 42.6, 27.8, 26.0, 24.8; HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1147; LRMS *m/z* (peak intensity) 204 (M^+, 3), 186 (17), 107 (25), 106 (58), 105 (62), 98 (100), 91 (6), 83 (21), 79 (25), 78 (15), 77 (76), 70 (52), 69 (19), 55 (57), 51 (34), 50 (17).

4-Hydroxy-6-phenyl-2-hexanone (12): 31% yield; ^1H NMR ($CDCl_3$) δ 7.32–7.16 (m, 5 H), 4.06 (m, 1 H), 3.24 (d, *J* = 4 Hz, 1 H), 2.87–2.78 (m, 1 H), 2.75–2.64 (m, 1 H), 2.59 (m, 2 H), 2.16 (s, 3 H), 1.89–1.64 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 209.8, 141.7, 128.4, 128.3, 125.8, 66.7, 49.9, 37.9, 31.6, 30.6; IR (neat liq) 3436 (br), 3086, 3063, 3027, 3003, 2929, 2862, 1708, 1603, 1496, 1454, 1362, 1166, 1093, 1067, 749, 701; HRMS calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1153.

3-Hydroxy-1-(4-methylphenyl)-1-butanone (14a): 59% yield; ^1H NMR (C_6D_6) δ 7.69 (d, *J* = 8 Hz, 2 H), 6.89 (d, *J* = 8 Hz, 2 H), 4.34 (m, 1 H), 4.02 (s, 1 H), 2.86 (dd, *J* = 17, 8 Hz, 1 H), 2.66 (dd, *J* = 17, 4 Hz, 1 H), 2.01 (s, 3 H), 1.16 (d, *J* = 6 Hz, 3 H); ^{13}C NMR (C_6D_6) δ 199.4, 143.7, 134.8, 129.1, 128.4, 64.1, 46.9, 22.8, 21.1; IR (thin film) 3434, 2971, 1676, 1409, 1181, 1007, 810 cm^{-1}; HRMS calcd for $C_{11}H_{14}O_2$ (M^+) 178.0993, found 178.0999.

3-Hydroxy-1-(4-methylphenyl)-1-pentanone (14b): 83% yield; ^1H NMR (C_6D_6) δ 7.69 (d, *J* = 8 Hz, 2 H), 6.89 (d, *J* = 8 Hz, 2 H), 4.07 (m, 1 H), 3.83 (s, 1 H), 2.82 (dd, *J* = 17, 9 Hz, 1 H), 2.67 (dd, *J* = 17, 4 Hz, 1 H), 2.01 (s, 3 H), 1.45 (m, 2 H), 0.91 (t, *J* = 8 Hz, 3 H); ^{13}C NMR (C_6D_6) δ 199.7, 143.6, 134.9, 129.1, 128.4, 69.0, 44.9, 29.8, 21.1, 10.0; IR (thin film) 3444, 2964, 1673, 1607, 1409, 1181, 810 cm^{-1}; HRMS calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1146.

3-Hydroxy-4-methyl-1-(4-methylphenyl)-1-pentanone (14c): 90% yield; ^1H NMR (C_6D_6) δ 7.74 (d, *J* = 8 Hz, 2 H), 6.91 (d, *J* = 8 Hz, 2 H), 3.95 (m, 1 H), 3.46 (s, 1 H), 2.82 (dd, *J* = 17, 9 Hz, 1 H), 2.73 (dd, *J* = 17, 3 Hz, 1 H), 2.03 (s, 3 H), 1.67 (m, 2 H), 0.97 (d, *J* = 7 Hz, 3 H), 0.90 (d, *J* = 7 Hz, 3 H); ^{13}C NMR (C_6D_6) δ 200.4, 143.8, 135.2, 129.3, 128.6, 72.4, 42.5, 33.6, 21.4, 19.0, 17.7; IR (thin film) 3514, 2959, 1669, 1607, 1002, 811 cm^{-1}; HRMS calcd for $C_{13}H_{18}O_2$ ($M^+ - H_2O$) 188.1201, found 188.1205.

3-Hydroxy-4,4-dimethyl-1-(4-methylphenyl)-1-pentanone (14d): 97% yield; ^1H NMR (C_6D_6) δ 7.76 (d, *J* = 8 Hz, 2 H), 6.92 (d, *J* = 8 Hz, 2 H), 3.86 (m, 1 H), 3.59 (d, *J* = 3 Hz, 1 H), 2.88 (dd, *J* = 17, 3 Hz, 1 H), 2.80 (dd, *J* = 17, 9 Hz, 1 H), 2.04 (s, 3 H), 0.94 (s, 9 H); ^{13}C NMR (C_6D_6) δ 200.7, 143.8, 135.3, 129.4, 128.6, 75.1, 40.2, 34.6, 26.0, 21.4; IR (thin film) 3527, 2925, 1675, 1607, 1181, 809 cm^{-1}; HRMS calcd for $C_{14}H_{20}O_2$ (M^+ − *t*-Bu) 163.0759, found 163.0762.

3-(2-Furyl)-3-hydroxy-1-(4-methylphenyl)-1-propanone (14e): 85% yield; ^1H NMR (C_6D_6) δ 7.62 (d, *J* = 8 Hz, 2 H), 7.06 (dd, *J* = 2, 1 Hz, 1 H), 6.80 (d, *J* = 8 Hz, 2 H), 6.21 (d, *J* = 3 Hz, 1 H), 6.05 (dd, *J* = 3, 2 Hz, 1 H), 5.32 (m, 1 H), 3.74 (d, *J* = 5 Hz, 1 H), 3.25 (dd, *J* = 17, 9 Hz, 1 H), 3.01 (dd, *J* = 17, 3 Hz, 1 H), 1.94 (s, 3 H); ^{13}C NMR (C_6D_6) δ 198.4, 156.5, 143.7, 141.5, 134.5, 129.1, 128.4, 110.3, 106.1, 64.3, 43.7, 21.1; IR (thin film) 3500, 3104, 1664, 1608, 1225, 1025, 812, 735, cm^{-1}; HRMS calcd for $C_{14}H_{14}O_3$ (M^+) 230.0942, found 230.0947.

Ethyl α-Benzylacetoacetate (15). In a 500-mL three-necked flask equipped with a reflux condenser, drying tube, pressure equalizing dropping funnel, and magnetic stirring bar, a solution of sodium ethoxide was prepared by dissolving sodium metal (4.73 g, 0.206 mol) in 130 mL of absolute ethanol. After reaction of the sodium was complete, ethyl acetoacetate (26.30 g, 0.200 mol) was added and the solution refluxed for 30 min. Benzyl chloride (27.85 g, 0.22 mol) was added dropwise over a 10-min period. The reaction mixture was allowed to reflux for 6 h. After cooling to room temperature, the reaction mixture was filtered to remove sodium chloride. The sodium chloride was washed with 50 mL of absolute ethanol. The ethanol was evaporated in vacuo from the combined filtrates and the crude product purified by vacuum distillation. The fraction boiling in the range of 80–110 °C (0.01 Torr) was collected (lit.[32] bp 110.5–112 °C, 2 Torr). The reaction yielded 30.1 g (0.136 mol, 68%) of ethyl α-benzylacetoacetate: ^1H NMR ($CDCl_3$) δ 7.28–7.16 (m, 5 H), 4.13 (q, *J* = 7.1, 2 H), 3.78 (t, *J* = 7.6, 1 H), 3.15 (d, *J* = 7.7, 2 H), 2.17 (s, 1 H), 1.18 (t, *J* = 7.2, 3 H); ^{13}C NMR ($CDCl_3$) δ 202.1, 168.9, 138.0, 128.6, 128.4, 126.5, 61.2, 61.1, 33.8, 29.3, 13.8; IR (cm^{-1}) (neat) 3031, 2985, 2938, 1742, 1716, 1645 (w), 1606, 1498, 1455, 1360, 1216, 1149, 1031, 857, 751, 701.

Ethyl 2-(2-Methyl-1,3-dioxolan-2-yl)-3-phenylpropanoate (16). In a 500-mL flask equipped with a magnetic stirring bar, a Dean-Stark apparatus, and a condenser were placed ethyl α-benzylacetoacetate (18.3 g, 0.0831 mol), ethylene glycol (13.8 g, 0.227 mol), camphor sulfonic acid (0.300 g, 0.00136 mol), and 300 mL of benzene. The mixture was refluxed for 23 h. After dilution with 200 mL of diethyl ether, the reaction mixture was washed twice with 200-mL portions of saturated aqueous sodium bicarbonate and twice with 200-mL portions of saturated aqueous sodium chloride and dried over anhydrous sodium sulfate. Removal of solvent in vacuo yielded 20.4 g (0.0772 mol, 93%) of pure ketal: ^1H NMR ($CDCl_3$) δ 7.30–7.17 (m, 5 H), 4.09–3.99 (overlapping m, 6 H), 3.06–2.96 (overlapping m, 3 H), 1.51 (s, 3 H), 1.09 (t, *J* = 7.1, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.8, 139.2, 128.6, 128.2, 126.1, 109.3, 64.8, 64.7, 60.2, 56.2, 34.1, 21.6, 13.9; IR (cm^{-1}) (neat) 3064 (w), 3031 (w), 2984, 2891, 1736, 1377, 1218, 1172, 1149, 1136, 1038, 951, 881, 749, 701; EIMS, *m/z* (rel intensity) 249 (2), 191 (5), 178 (4), 159 (3), 147 (8), 131 (11), 105 (10), 104 (24), 103 (11), 91 (40), 88 (19), 87 (100), 78 (8), 77 (11), 65 (7); HRMS calcd for $C_{15}H_{21}O_3$ ($M + H^+$) 265.1440, found 265.1443.

2-(2-Methyl-1,3-dioxolan-2-yl)-3-phenyl-1-propanol (17). In a flame-dried 500-mL three-necked flask equipped with a dropping funnel, magnetic stirring bar, rubber septum, and a nitrogen inlet was placed lithium aluminum hydride (1.56 g, 0.0411 mol) and 200 mL of diethyl ether. After the lithium aluminum hydride slurry was cooled to 0 °C, a solution of ketal–ester (8.64 g, 0.0327 mol) in 100 mL of diethyl ether was added dropwise with stirring. After addition of the ester had commenced, the ice bath was removed and the reaction mixture was allowed to warm to room temperature. After 17 h the reaction mixture was worked up with a slight modification of the procedure of Steinhardt.[33] To the stirring reaction mixture was slowly added 1.56 mL of water, 4.68 mL of 15% aqueous sodium hydroxide, 4.68 mL of water, and 20 g of anhydrous sodium sulfate. After 10 min the mixture was filtered and washed with 50 mL of diethyl ether, and the solvent was removed in vacuo, yielding 6.96 g (0.0313 mol, 96%) of the hydroxy ketal: ^1H NMR ($CDCl_3$) δ 7.37–7.18 (m, 5 H), 4.04 (4 H), 3.66–3.55 (m, 2 H), 3.05 (br s, 1 H), 2.97 (dd, *J* = 13.7, 3.2, 1 H), 2.45 (dd, *J* = 13.6, 11.3, 1 H), 2.12 (octet, 1 H), 1.43 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 140.3, 128.9, 128.3, 125.9, 112.3, 64.5, 64.4, 61.4, 49.9, 32.7, 21.0; IR (cm^{-1}) (neat) 3488 (br), 3031, 2984, 2944, 2891, 1497, 1457, 1384, 1211, 1151, 1085, 1050, 1038, 949, 869, 747, 702; EIMS, *m/z* (rel intensity) 147 (3), 136 (5), 118 (11), 117 (17), 105 (6), 92 (11), 91 (37), 87 (100), 77 (8), 65 (8), 51 (7); $C_{13}H_{18}O_3$ M^+ not observed, exact mass calcd for $C_{12}H_{15}O_3$ ($M^+ - CH_3$) 207.1021, found 207.1026.

2-Benzyl-1-hydroxy-3-butanone (18). The procedure of Conia[17] was modified slightly. Aqueous oxalic acid (7.5 mL, 10%) was added to a stirring slurry of 38 g of 230–400 mesh silica gel in 300 mL of CH_2Cl_2 in an Erlenmeyer flask. After about 15 min the aqueous "phase" disappeared and 6.79 g (30.6 mmol) of ketal was added as a solution in ca. 50 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature. Small aliquots (ca. 1 mL) were withdrawn at appropriate intervals, filtered, and evaporated. ^1H NMR analysis was used to ascertain the course of the reaction. After the reaction was judged to be complete, 3 g of solid $NaHCO_3$ was added and the reaction mixture was allowed to stir for a few minutes and filtered. The solid residue was washed with CH_2Cl_2 and the filtrate was evaporated in vacuo to leave the spectroscopically pure β-hydroxy ketone **17** (4.64 g, 85%): ^1H NMR ($CDCl_3$) δ 7.34–7.29 (m, 2 H), 7.27–7.19 (m, 3 H), 3.75 (t, *J* = 5.5, 3 H), 3.04–2.91 (overlapping m, 2 H), 2.79 (dd, *J* = 13.3, 7.4, 1 H), 2.55 (br s, 1 H), 2.13 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.3, 138.7, 128.8, 128.5, 126.4, 62.3, 56.0, 34.1, 30.5; IR (cm^{-1}) (neat) 3436 (br), 3086 (w), 3064 (w), 3028, 3003 (w), 2933, 2884, 1710, 1603, 1497, 1455, 1358, 1165, 1081, 1038, 788, 740, 701; EIMS, *m/z* (rel intensity) 178 (2, M^+), 160 (31), 148 (12), 147 (75), 129 (8), 118 (24), 117 (100), 115 (9), 105 (15),

(32) Kabachnik, M. I.; Ioffe, S. T.; Popov, E. M.; Vatsuro, K. V. *Tetrahedron* **1961**, *12*, 76–94.

(33) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; p 584.

92 (13), 91 (84), 78 (9), 77 (13), 65 (15), 51 (11); exact mass calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.0997.

β-Hydroxy Ketones 20 and 22. These substances were prepared by using 3-step procedures similar to that above for **18**. Full spectral data on **20** and **22** can be found in an allied manuscript.[18]

General Method for the Preparation of Distal β-Silyloxy Silyl Enol Ethers. A solution of LDA (2.2 equiv) was prepared by addition of 2.0 mL of a 2.5 M solution of *n*-BuLi in hexane (5.0 mmol, 2.2 equiv) to a solution of 0.75 mL of diisopropylamine (5.35 mmol, 2.36 equiv) in 5 mL of THF at −78 °C. After 15 min the β-hydroxy ketone (2.27 mmol, 1.0 equiv) was added dropwise (≈2 drops/s). After 15 min the reaction mixture was warmed to 25 °C and stirred for an additional 15 min. The solution of the aldolate dianion was then cooled to 0 °C and silylated by the rapid addition of chlorotrimethylsilane (0.72 mL, 5.69 mmol, 2.5 equiv). The reaction mixture was then warmed to room temperature, quenched after 15 min by addition of 75 mL of a solution of saturated aqueous sodium bicarbonate, and extracted twice with 25-mL portions of CH_2Cl_2. The organic phase was washed twice with 50-mL portions of saturated aqueous sodium bicarbonate, filtered, and dried over sodium sulfate. Removal of solvent in vacuo afforded the β-silyloxy silyl enol ethers ≥95% spectroscopically pure.

2,4-Bis((trimethylsilyl)oxy)-1-butene (26) (Table II, entry 1): ^{1}H NMR (C_6D_6) δ 4.12 (s, 1 H), 4.11 (s, 1 H), 3.72 (t, *J* = 6.8, 2 H), 2.30 (t, *J* = 6.7, 2 H), 0.12 (s, 9 H), 0.05 (s, 9 H); ^{13}C NMR (C_6D_6) δ 156.8, 91.4, 60.4, 40.6, 0.1, −0.4; IR (cm^{-1}) (neat) 2960, 2904, 2873, 1659, 1636, 1253, 1100, 1068, 1010, 926, 847, 755; HRMS calcd for $C_{10}H_{24}O_2Si_2$ 232.1318, found 232.1314.

3-Methyl-2,4-bis((trimethylsilyl)oxy)-1-butene (27) (Table II, entry 2): ^{1}H NMR (C_6D_6) δ 4.11 (s, 1 H), 4.09 (d, *J* = 1, 1 H), 3.74 (dd, *J* = 9.5, 6, 1 H), 3.45 (dd, 9.5, 7, 1 H), 2.35 (sextet, *J* = 7, 1 H), 1.07 (d, *J* = 7, 3 H), 0.13 (s, 9 H), 0.06 (s, 9 H); ^{13}C NMR (C_6D_6) δ 161.1, 89.7, 65.8, 43.6, 15.3, 0.1, −0.4; IR (cm^{-1}) (neat) 3113 (w), 2961, 2902, 2867, 1658, 1627, 1459, 1388, 1327, 1283, 1253, 1226, 1086, 1052, 1011, 916, 879, 847 (br), 753, 689; HRMS calcd for $C_{11}H_{26}O_2Si_2$ 246.1471, found 246.1475.

3-Benzyl-2,4-bis((trimethylsilyl)oxy)-1-butene (28) (Table II, entry 3): ^{1}H NMR (C_6D_6) δ 7.16–6.99 (m, 5 H), 4.04 (d, *J* = 1.1, 1 H), 4.02 (d, *J* = 1.2, 1 H), 3.72 (dd, *J* = 9.8, 6.6, 1 H), 3.58 (dd, *J* = 9.8, 6.2, 1 H), 2.87 (dd, *J* = 13.5, 6.3, 1 H), 2.75 (dd, *J* = 13.5, 8.2, 1 H), 2.62–2.53 (m, 1 H), 0.11 (s, 9 H), 0.06 (s, 9 H); ^{13}C NMR (acetone D_6) δ 159.0, 141.3, 129.8, 128.7, 126.4, 91.2, 64.2, 51.5, 35.8, 0.2, −0.3; IR (cm^{-1}) (neat) 3111 (w), 3088 (w), 3065 (w), 3029, 2959, 2902, 2866, 1658, 1625, 1497, 1455, 1281, 1253 (s), 1107, 1020, 878, 845 (s), 747, 699; EIMS, *m/z* (rel intensity) 322 (3, M$^+$), 307 (3), 232 (28), 231 (55), 219 (43), 147 (22), 103 (22), 91 (21), 75 (23), 73 (100), 45 (12); HRMS calcd for $C_{17}H_{30}O_2Si_2$ 322.1784, found 322.1789.

6-Phenyl-2,4-bis((trimethylsilyl)oxy)-1-hexene (29) (Table II, entry 4): ^{1}H NMR (C_6D_6) δ 7.17–6.97 (m, 5 H), 4.07 (s, 1 H), 4.06 (s, 1 H), 4.04–3.97 (m, 1 H), 2.76 (ddd, *J* = 16.2, 10.4, 5.6, 1 H), 2.57 (ddd, *J* = 16.3, 10.3, 6.0, 1 H), 2.54 (dd, *J* = 13.5, 5.8, 1 H), 2.16 (dd, *J* = 13.6, 6.9, 1 H), 1.92–1.69 (m, 2 H), 0.12 (s, 9 H), 0.09 (s, 9 H); ^{13}C NMR (C_6D_6) δ 156.8, 142.8, 128.7, 128.6, 126.0, 92.1, 69.9, 46.0, 39.3, 32.3, 0.6, 0.1; IR (cm^{-1}) (neat) 3112, 3087, 3064, 3028, 2958, 1632, 1305, 1252, 1089, 1014, 844, 750, 698; CIMS, *m/z* (rel intensity) 337 (M + 1, 1), 321 (4), 231 (15), 208 (17), 207 (84), 206 (16), 117 (13); EIMS, *m/z* (rel intensity) 336 (M$^+$, 0.2), 231 (38), 208 (15), 207 (77), 206 (48), 147 (21), 117 (71), 103 (11), 91 (100), 75 (25), 73 (94); HRMS calcd for $C_{17}H_{29}O_2Si_2$ (M$^+$ − CH_3) 321.1706, found 321.1711.

4-Methyl-2,4-bis((trimethylsilyl)oxy)-1-pentene (30) (Table II, entry 5): ^{1}H NMR (C_6D_6) δ 4.15 (s, 1 H), 4.13 (s, 1 H), 2.33 (s, 2 H), 1.35 (s, 6 H), 0.17 (s, 9 H), 0.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 157.3, 92.9, 74.0, 52.3, 30.3, 2.8, 0.3; IR (cm^{-1}) (neat) 3114 (w), 2963, 2902, 1655, 1636, 1618, 1381, 1366, 1321, 1253, 1156, 1048, 1027, 842 (br), 753, 687; CIMS, *m/z* (rel intensity) 261 (1), 260 (1), 245 (12), 205 (3), 171 (8), 132 (12), 131 (100).

(*Z*)-4-Methyl-3,5-bis((trimethylsilyl)oxy)-2-pentene (31) (Table II, entry 6) was made according to the standard procedure except that the solvent used was a 25% HMPA in THF mixture: ^{1}H NMR (C_6D_6) δ 4.53 (q, *J* = 7 Hz, 1 H), 3.76 (q, *J* = 10, 5 Hz, 1 H), 3.38 (dd, *J* = 10, 8 Hz, 1 H), 2.28 (m, 1 H), 1.53 (dd, *J* = 7, 1 Hz, 1 H), 0.10 (s, 9 H), 0.08 (s, 9 H); ^{13}C NMR (C_6D_6) δ 153.4, 101.6, 66.1, 43.5, 15.6, 11.2, 0.8, −0.4; IR (neat) 2960, 1675, 1252, 1191, 1081, 874, 842, 753 cm^{-1}; HRMS calcd for $C_{12}H_{28}O_2Si_2$ (M$^+$) 260.1627, found 260.1631.

32 (Table II, entry 7): ^{1}H NMR (C_6D_6) δ 7.54 (d, *J* = 7.7, 2 H), 7.27–7.02 (m, 3 H), 5.54 (d, *J* = 2.7, 1 H), 4.88 (sharp m, 1 H), 2.67 (s, 1 H), 1.82–1.50 (m, 4 H), 1.19–1.06 (m, 1 H), 0.96–0.82 (m, 1 H), 0.19 (s, 9 H), 0.09 (s, 9 H); ^{13}C NMR (C_6D_6) δ 150.2, 142.7, 127.7, 127.1, 126.9, 107.0, 73.6, 48.2, 24.2, 22.9, 20.8, 0.4, 0.1; IR (cm^{-1}) (neat) 3088, 3064, 3033, 2957, 2860, 2843, 1665, 1495, 1454, 1253, 1210, 1173, 1093, 1063, 922, 888, 847, 750, 704; EIMS, *m/z* (rel intensity) 333 (1), 180 (16), 179 (100), 163 (2), 147 (4), 105 (3), 91 (3), 73 (49), 57 (4); HRMS calcd for $C_{18}H_{29}O_2Si_2$ (M$^+$ − CH_3) 333.1706, found 333.1710.

33 (Table II, entry 8): ^{1}H NMR (C_6D_6) δ 7.32–7.00 (m, 5 H), 5.38 (s, 1 H), 4.95 (d, *J* = 3.1, 1 H), 2.22–2.29 (m, 1 H), 1.98–0.79 (m, 6 H), 0.13 (s, 9 H), 0.07 (s, 9 H); ^{13}C NMR (C_6D_6) δ 150.7, 145.2, 128.1, 126.7, 126.3, 106.4, 73.4, 48.3, 24.6, 22.3, 21.8, 0.4, 0.3; IR (cm^{-1}) (neat) 3087, 3063, 3045, 3028, 2957, 2937, 2860, 1667, 1450, 1251, 1199, 1176, 1106, 1069, 1011, 924, 917, 909, 844, 752, 700; EIMS, *m/z* (rel intensity) 348 (M$^+$, 1), 333 (1), 271 (1), 258 (2), 219 (7), 181 (5), 180 (17), 179 (100), 148 (6), 147 (41), 75 (19), 73 (69); HRMS calcd for $C_{19}H_{32}O_2Si_2$ 348.1940, found 348.1961.

General Procedure for Thermal Stability Studies of Distal Dianions (Scheme II). A solution of LDA (2.2 equiv) was prepared by the addition of 0.50 mL of a 2.5 M solution of *n*-BuLi in hexane (1.25 mmol, 2.2 equiv) to a solution of 0.19 mL of diisopropylamine (1.36 mmol, 2.39 equiv) in 4.0 mL of THF at −78 °C. After 15 min the β-hydroxy ketone **10** (0.116 g, 0.567 mmol) was added dropwise as a solution in 3.0 mL of THF. After 15 min at −78 °C, the solution was warmed to the equilibration temperature by replacing the dry ice–isopropyl alcohol bath with a bath of the appropriate temperature. The reaction was quenched after 1 h by rapid addition of 30 mL of a 10% aqueous ammonium chloride solution and extracted twice with 25-mL portions of diethyl ether. The combined organic phases were washed with 30 mL of a saturated aqueous sodium chloride solution, filtered, and dried over sodium sulfate. The solvent was removed in vacuo to afford the recovered β-hydroxy ketone **10** and other reaction products in 74–87% yield.

General Procedure for Generation and Silylation of Enforced Proximal Aldolate Dianions 36a–e (Scheme III). Lithium hexamethyldisilazide (2.2 equiv) was generated at −78 °C by addition of 2.2 equiv of *n*-BuLi to a THF solution of 2.4 equiv of hexamethyldisilazane. After the solution was stirred for 10 min 1.0 equiv of the β-hydroxy ketone (as a 1.0M solution in THF) was added dropwise. After 15 min 2–5 equiv of TMSCl was added rapidly. After 15 min the reaction was quenched by the addition of the ice cold aqueous saturated $NaHCO_3$. The mixture was extracted three times with CH_2Cl_2 and the combined extracts were dried over Na_2SO_4. The solvent was removed in vacuo. Purification was accomplished by chromatography on silica (HPLC or flash column) with hexane/EtOAc (95:5) as eluant.

(*Z*)-1-(4-Methylphenyl)-1,3-bis((trimethylsilyl)oxy)-1-butene (36a): ^{1}H NMR (C_6D_6) δ 7.37 (d, *J* = 8 Hz, 2 H), 6.90 (d, *J* = 8 Hz, 2 H), 5.40 (d, *J* = 9 Hz, 1 H), 5.04 (m, 1 H), 2.06 (s, 3 H), 1.45 (d, *J* = 6 Hz, 1 H), 0.23 (s, 9 H), 0.09 (s, 9 H); ^{13}C NMR (C_6D_6) δ 148.8, 137.8, 136.6, 129.1, 126.1, 116.3, 64.5, 25.1, 21.1, 0.6; IR (cm^{-1}) (neat liq) 2962, 1649, 1511, 1251, 1071, 842; HRMS calcd for $C_{17}H_{30}O_2Si_2$ (M$^+$) 322.1784, found 322.1789.

(*Z*)-1-(4-Methylphenyl)-1,3-bis((trimethylsilyl)oxy)-1-pentene (36b): ^{1}H NMR (C_6D_6) δ 7.35 (d, *J* = 8 Hz, 2 H), 6.91 (d, *J* = 8 Hz, 2 H), 5.32 (d, *J* = 9 Hz, 1 H), 4.72 (m, 1 H), 2.08 (s, 3 H), 1.72 (m, 2 H), 1.07 (t, *J* = 7 Hz, 3 H), 0.22 (s, 9 H), 0.09 (s, 9 H); ^{13}C NMR (C_6D_6) δ 149.1, 137.4, 136.5, 128.8, 125.8, 114.7, 69.2, 31.5, 20.8, 10.2, 0.4, 0.3; IR (cm^{-1}) (neat liq) 2959, 1648, 1511, 1251, 1063, 842; HRMS calcd for $C_{17}H_{32}O_2Si_2$ (M$^+$) 336.1940, found 336.1944.

(*Z*)-4-Methyl-1-(4-methylphenyl)-1,3-bis((trimethylsilyl)oxy)-1-pentene (36c): ^{1}H NMR (C_6D_6) δ 7.27 (d, *J* = 8 Hz, 2 H), 6.87 (d, *J* = 8 Hz, 2 H), 5.20 (d, *J* = 9 Hz, 1 H), 4.48 (m, 1 H), 2.05 (s, 3 H), 1.82 (m, 1 H), 1.00 (dd, *J* = 7.0, 16.0 Hz, 6 H), 0.15 (s, 9 H), 0.03 (s, 9 H); ^{13}C NMR (C_6D_6) δ 150.1, 137.8, 137.1, 129.1, 126.3, 113.7, 72.8, 35.6, 21.2, 19.3, 18.2, 0.8, 0.5; IR (cm^{-1}) (neat liq) 2958, 1648, 1511, 1251, 1050, 844; HRMS calcd for $C_{19}H_{34}O_2Si_2$ (M$^+$ − CH_3) 335.1862, found 335.1857.

(*Z*)-4,4-Dimethyl-1-(4-methylphenyl)-1,3-bis((trimethylsilyl)oxy)-1-pentene (36d): ^{1}H NMR (C_6D_6) δ 7.31 (d, *J* = 8 Hz, 2 H), 6.89 (d, *J* = 8 Hz, 2 H), 5.21 (d, *J* = 9.5 Hz, 1 H), 4.45 (d, *J* = 9.5 Hz, 1 H), 2.05 (s, 3 H), 1.06 (s, 9 H), 0.22 (s, 9 H), 0.07 (s, 9 H); ^{13}C NMR (C_6D_6) δ 150.9, 137.8, 137.5, 129.1, 126.5, 112.2, 75.2, 36.5, 26.3, 21.1, 1.2, 0.6; IR (cm^{-1}) (neat liq) 2957, 1648, 1511, 1251, 1059, 841; HRMS calcd for $C_{16}H_{27}O_2Si_2$ (M$^+$ − *t*-Bu) 307.1549, found 307.1555.

(*Z*)-3-(2-Furyl)-1-(4-methylphenyl)-1,3-bis((trimethylsilyl)oxy)-1-propene (36e): ^{1}H NMR (C_6D_6) δ 7.34 (d, *J* = 8 Hz, 2 H), 7.10 (m, 1 H), 6.86 (d, *J* = 8 Hz, 2 H), 6.22 (d, *J* = 3 Hz, 1 H), 6.07 (dd, *J* = 2, 2 Hz, 1 H), 5.99 (d, *J* = 9 Hz, 1 H), 5.77 (d, *J* = 9 Hz, 1 H), 2.02 (s, 3 H), 0.19 (s, 9 H), 0.06 (s, 9 H); ^{13}C NMR (C_6D_6) δ 157.4, 150.9, 141.8, 138.2, 136.2, 129.1, 126.2, 111.3, 110.4, 106.2, 64.1, 21.1, 0.5, 0.4; IR (cm^{-1}) (neat liq) 2958, 1648, 1510, 1252, 1047, 845; HRMS calcd for $C_{20}H_{30}O_3Si_2$ 374.1733 (M$^+$), found 374.1735.

Proximal Aldolate Dianion Stability Studies (Table III). The β-hydroxy ketone **14a** was treated with either 2.1 or 1.05 equiv of the alkali metal hexamethyldisilazide (generated as above with *n*-BuLi, or purchased as NaHMDS or KHMDS) in THF at −78 °C. After the solution was stirred for 3 h at the appropriate temperature the reaction was

quenched and worked up as in the general silylation procedure above.

Preparation of Substrates for Comparative Enolization Studies. 4-((Trimethylsilyl)oxy)-2-butanone (23b)[34] was prepared in the same manner as for **34b** in 80% yield.

4-[(Tetrahydropyran-2-yl)oxy]-2-butanone (23c)[35] was prepared in the same manner as **34c** in 81% yield.

1-((Trimethylsilyl)oxy)-3-pentanone (34b). Chlorotrimethylsilane (0.88 mL, 6.97 mmol, 1.02 equiv) was added to a solution of 1-hydroxy-3-pentanone (0.698 g, 6.83 mmol, 1.0 equiv) in 20 mL of methylene chloride at 5 °C. This was followed by the addition of 1.0 mL of triethylamine (7.17 mol, 1.05 equiv). After 10 min the reaction mixture was warmed to 25 °C. After 2 h the reaction was quenched by addition to 100 mL of a solution of saturated aqueous $NaHCO_3$ and extracted with 75 mL of CH_2Cl_2. The organic phase was washed two times with 100-mL portions of saturated aqueous $NaHCO_3$, filtered, and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo to afford 0.96 g (80%) of >97% pure 1-((trimethylsilyl)oxy)-3-pentanone (**25b**): ^1H NMR ($CDCl_3$) δ 3.70 (t, J = 6 Hz, 2 H), 2.19 (t, J = 6 Hz, 2 H), 1.93 (q, J = 7 Hz, 2 H), 0.85 (t, J = 6 Hz, 3 H), 0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 207.9, 58.2, 45.0, 36.5, 7.6, -0.6; IR (cm^{-1}) (neat) 2959, 2903, 2881, 1716, 1461, 1413, 1390, 1380, 1358, 1252, 1104, 1090, 909, 883, 843, 750; LRMS chemical ionization m/z (relative intensity) 175 (100, M^+), 159 (80), 145 (15), 129 (20), 103 (50), 85 (17).

1-[(Tetrahydropyran-2-yl)oxy]-3-pentanone (34c). One equivalent of 1-hydroxy-3-pentanone (0.75 g, 7.34 mol) was added to a stirred solution of 0.82 g of 3,4-dihydro-2*H*-pyran (9.75 mmol, 1.3 equiv) in 10 mL of CH_2Cl_2 at 0 °C. A catalytic amount (0.051 g) of camphorsulfonic acid was added. After 2.3 h 0.5 g of solid $NaHCO_3$ was added. After a further 30 min the reaction mixture was warmed to 25 °C over a 30-min period and filtered through florisil, and the solvent and excess 3,4-dihydro-2*H*-pyran were removed in vacuo. The crude product was purified by HPLC on silica and eluted with 80:20 hexane/ethyl acetate to afford 1.02 g of pure 1-[(tetrahydropyran-2-yl)oxy]-3-pentanone (**34c**) (75%): ^1H NMR (C_6D_6) δ 4.46 (t, J = 3 Hz, 1 H), 3.96-3.90 (m, 1 H), 3.75-3.67 (m, 1 H), 3.55-3.44 (m, 1 H), 3.33-3.26 (m, 1 H), 2.22 (t, J = 6 Hz, 2 H), 1.93 (q, J = 7 Hz, 2 H), 1.63-1.55 (m, 1 H), 1.50-1.42 (m, 2 H), 1.31-1.13 (m, 3 H), 0.83 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 207.6, 98.8, 62.8, 61.7, 42.4, 36.2, 30.8, 25.8, 19.6, 7.6; IR (cm^{-1}) (neat) 2942, 2877, 1716, 1456, 1354, 1201, 1138, 1121, 1077, 1036, 977, 971; HRMS exact mass calcd for $C_{10}H_{19}O_3$ (M^+ + H) 187.1334, found 187.1330.

General Procedure for Comparative Enolization Studies. Standard solutions of LDA were prepared by the addition of 1.0 mL of a 2.5 M solution of *n*-BuLi in hexane (2.5 mmol, 2.2 equiv) to a solution of 0.375 mL of diisopropylamine (2.68 mmol; 2.36 equiv) in 2.5 mL of THF at -78 °C. After 15 min the standard solutions were used for the three enolization procedures (methods A, B, and C).

Method A. Chlorotrimethylsilane (0.36 mL, 2.84 mmol, 2.5 equiv) was added to the preformed solution of LDA at -78 °C. After 15 s the ketone (1.14 mmol) was added dropwise (≈2 drops/s) to the stirred solution of LDA and chlorotrimethylsilane. After 15 min the reaction was quenched at -78 °C and worked up with use of the standard procedure.

Method B. The ketone (1.14 mmol) was added dropwise (≈2 drops/s), with stirring, to a solution of LDA at -78 °C. After 15 min chlorotrimethylsilane (0.36 mL, 2.84 mmol, 2.5 equiv) was quickly added. After 15 min the reaction was quenched at -78 °C and worked up with use of the standard procedure.

Method C. The ketone (1.14 mmol, 1.0 equiv) was added dropwise (≈2 drops/s), with stirring, to a solution of LDA at -78 °C. After 15 min at -78 °C the reaction was warmed to 25 °C over a 5-min period. After 15 min chlorotrimethylsilane (0.36 mL, 2.84 mmol, 2.5 equiv) was quickly added. After 15 min the reaction was quenched at 25 °C and worked up with use of the standard procedure.

Standard Quench and Workup Procedure. The reactions were quenched by the rapid addition of 75 mL of a solution of saturated aqueous sodium bicarbonate. The aqueous mixture was worked up by extraction with two 25-mL portions of CH_2Cl_2. The combined organic phases were washed with two 50-mL portions of saturated aqueous sodium bicarbonate, filtered, and dried over sodium sulfate. Solvents were removed in vacuo to afford the trimethylsilyl enol ethers.

1,3-Bis((trimethylsilyl)oxy)pentene Isomers Derived from 1-Hydroxy-3-pentanone (34a). The four isomeric substances obtained from the dianion of β-hydroxy ketone **34a** were characterized as mixtures. The mixture prepared by dianion formation and trapping under conditions A was enriched in the two proximal isomers (**49*E*** and **49*Z***) while the mixture generated under conditions C was enriched in the two distal isomers (**48*Z*** and **48*E***). The ^1H NMR data for all four isomers and ^{13}C NMR data for the two distal isomers were obtained from these mixtures and are listed here.

(*Z*)-1,3-Bis((trimethylsilyl)oxy)-3-pentene (48*Z*): ^1H NMR ($CDCl_3$) δ 4.53 (bq, J = 7 Hz, R(TMSO)C=C*H*Me), 3.74 (m, CH_2OTMS), 2.27 (bt, J = 7 Hz, CH_2CH$_2$OTMS), 1.5 (d, J = 6.6 Hz, CH_3CHR), 0.1 (s, OSi(CH_3)$_3$), 0.0 (s, OSi(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 148.6, 103.9, 60.8, 40.8, 11.0, 0.6, -0.4.

(*E*)-1,3-Bis((trimethylsilyl)oxy)-3-pentene (48*E*): ^1H NMR ($CDCl_3$) δ 4.75 (q, J = 6.9 Hz, R(TMSO)C=C*H*Me), 3.74 (m, CH_2OTMS), 2.36 (t, J = 7.0 Hz, CH_2CH$_2$OTMS), 1.49 (d, J = 6.9 Hz, CH_3CHR), 0.2 (s, OSi(CH_3)$_3$), 0.0 (s, OSi(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 149.5, 102.4, 60.3, 35.4, 12.0, 0.38, -0.8.

(*E*)-1,3-Bis((trimethylsilyl)oxy)-2-pentene (49*E*): ^1H NMR (C_6D_6) δ 4.92 (t, J = 8 Hz, 1 H), 4.01 (d, J = 8 Hz, 2 H), 2.08 (q, J = 8 Hz, 2 H), 1.02 (t, J = 8 Hz, 3 H), 0.16 (s, 9 H), 0.10 (s, 9 H).

(*Z*)-1,3-Bis((trimethylsilyl)oxy)-2-pentene (49*Z*): ^1H NMR (C_6D_6) δ 4.80 (t, J = 7 Hz, 1 H), 4.19 (d, J = 7 Hz, 2 H), 1.92 (q, J = 7 Hz, 2 H), 0.95 (t, J = 8 Hz, 3 H), 0.13 (s, 9 H), 0.12 (s, 9 H).

Trimethylsilyl Enol Ether Mixtures from 23c and 34c. The mixture from **23c** was separated by HPLC on silica and eluted with 95:5 hexane/ethyl acetate to give pure **39**, **40*E***, and **40*Z***. The mixture from **34c** could only be partially separated to give **51*E*** as a single compound.

4-[(Tetrahydropyran-2-yl)oxy]-2-((trimethylsilyl)oxy)-1-butene (39): ^1H NMR (C_6D_6) δ 4.54 (t, J = 3.2, 1 H), 4.11 (s, 2 H), 3.95 (ol ddd, J = 9.6, 7.0, 6.9, 1 H), 3.74 (m, 1 H), 3.53 (ol ddd, J = 9.6, 6.9, 6.9, 1 H), 3.35-3.28 (m, 1 H), 2.36 (t, J = 6.9, 2 H), 1.74-1.61 (m, 1 H), 1.53-1.47 (m, 2 H), 1.35-1.15 (m, 3 H), 0.09 (s, 9 H); ^{13}C NMR (C_6D_6) δ 157.0, 98.5, 91.1, 64.9, 61.4, 37.6, 30.9, 25.9, 19.5, 0.04; IR (cm^{-1}) (neat) 3114, 2958, 2941, 2873, 1655, 1636, 1442, 1353, 1308, 1276, 1253, 1200, 1138, 1122, 1076, 1061, 1035, 1008, 868, 846; EIMS, m/z (rel intensity) 244 (M^+, 0.1), 174 (7), 173 (52), 171 (7), 145 (13), 144 (81), 143 (15), 130 (7), 129 (55), 127 (12), 86 (6), 85 (100); CIMS, m/z (rel intensity) 245 (M^+ + 1, 3), 227 (8), 173 (11), 144 (14), 143 (25), 85 (24), 58 (7), 57 (93), 43 (100).

(*E*)-4-[(Tetrahydropyran-2-yl)oxy] 2-((trimethylsilyl)oxy)-2-butene (40*E*): ^1H NMR (C_6D_6) δ 4.97 (t, J = 7.7, 1 H), 4.65 (t, J = 3.7, 1 H), 4.21 (dd, J = 11.8, 7.2, 1 H), 3.99 (dd, J = 11.8, 8.4, 1 H), 3.77 (m, 1 H), 3.37-3.30 (m, 1 H), 1.79-1.67 (m, 1 H), 1.72 (s, 3 H), 1.56-1.51 (m, 2 H), 1.37-1.19 (m, 3 H), 0.07 (s, 9 H); ^{13}C NMR (C_6D_6) δ 153.4, 104.2, 96.7, 63.2, 61.6, 31.0, 26.0, 19.7, 18.1, 0.2; IR (cm^{-1}) (neat) 2953, 2873, 1666, 1441, 1384, 1353, 1253, 1215, 1200, 1133, 1115, 1077, 1038, 1023, 1006, 894, 845, 756; CIMS, m/z (rel intensity) 245 (M^+ + 1, 0.1), 175 (4), 174 (6), 173 (40), 159 (11), 145 (9), 144 (47), 143 (60), 129 (22), 85 (18), 75 (8), 73 (17); EIMS, m/z (rel intensity) 174 (7), 173 (51), 159 (19), 145 (14), 144 (69), 143 (80), 129 (47), 127 (11), 85 (41), 75 (39), 73 (100).

(*Z*)-4-[(Tetrahydropyran-2-yl)oxy]-2-((trimethylsilyl)oxy)-2-butene (40*Z*): ^1H NMR (C_6D_6) δ 4.82 (t, J = 6.8, 1 H), 4.70 (t, J = 3.3, 1 H), 4.44 (ddd, J = 11.7, 6.6, 0.8, 1 H), 4.21 (ddd, J = 11.6, 7.0, 0.7, 1 H), 3.84 (m, 1 H), 3.41-3.34 (m, 1 H), 1.78-1.67 (m, 1 H), 1.62-1.54 (m, 2 H), 1.58 (s, 3 H), 1.38-1.16 (m, 3 H), 0.07 (s, 9 H); ^{13}C NMR (C_6D_6) δ 150.2, 106.5, 97.6, 61.9, 61.4, 31.1, 26.0, 22.8, 19.6, 0.5; IR (cm^{-1}) (neat) 2952, 2946, 2874, 1679, 1442, 1380, 1312, 1254, 1196, 1117, 1035, 1022, 996, 846; CIMS, m/z (rel intensity) 245 (M^+ + 1, 0.3), 173 (7), 144 (9), 143 (37), 85 (25), 71 (8), 59 (9), 58 (7), 57 (86), 43 (100); EIMS, m/z (rel intensity) 174 (2), 173 (17), 159 (11), 144 (19), 143 (41), 129 (22), 117 (10), 85 (92), 77 (10), 75 (62), 73 (100).

(*E*)-1-[(Tetrahydropyran-2-yl)oxy]-3-((trimethylsilyl)oxy)-2-pentene (51*E*): ^1H NMR (C_6D_6) δ 4.84 (t, J = 7.8, 1 H), 4.64 (t, J = 3.4, 1 H), 4.19 (dd, J = 11.8, 7.2, 1 H), 3.98 (dd, J = 11.8, 8.4, 1 H), 3.76 (m, 1 H), 3.36-3.29 (m, 1 H), 2.09 (q, J = 7.4, 2 H), 1.76-1.62 (m, 1 H), 1.54-1.49 (m, 2 H), 1.36-1.14 (m, 3 H), 0.97 (t, J = 7.4, 3 H), 0.06 (s, 9 H); ^{13}C NMR (C_6D_6) δ 157.9, 102.3, 96.1, 62.3, 61.1, 30.6, 25.6, 24.6, 19.2, 11.9, -0.2; IR (cm^{-1}) (neat) 3048, 2956, 2943, 2875, 2854, 1659, 1465, 1454, 1442, 1355, 1253, 1200, 1133, 1115, 1078, 1021, 1001, 884, 845; EIMS, m/z (rel intensity) 173 (28), 159 (15), 158 (36), 157 (34), 147 (31), 143 (23), 131 (13), 101 (27), 85 (100), 75 (89), 73 (91); HRMS calcd for $C_8H_{17}O_2Si$ (M^+ - C_5H_9O) 173.0998, found 173.1001.

Preparation of Conformationally Defined β-Hydroxy Ketones. *cis*-4-*tert*-Butyl-3-hydroxycyclohexanonone (**62**) and *trans*-4-*tert*-butyl-3-hydroxycyclohexanone (**63**) were prepared according to the procedure of Evans.[24] The methoxy-substituted derivatives **62b** and **63b** were prepared as described below.

***trans*-4-*tert*-Butyl-3-methoxycyclohexanone Ethylene Ketal.** In a dry 100-mL flask was placed 50 mL of dry THF and NaH (1.0 g, 0.042 mol) and the solution was cooled to 0 °C. To this suspension was added 4.0 g (0.024 mol) of *trans*-4-*tert*-butyl-3-hydroxycyclohexanone ethylene ketal[24] and the reaction mixture was allowed to warm to room temper-

(34) Banerji, A.; Kalena, G. P. *Synth. Commun.* **1982**, *12*, 225-230.
(35) White, J. D.; Carter, J. P.; Kezar, H. S., III, *J. Org. Chem.* **1982**, *47*, 929-932.

ature and stirred an additional 2 h. An excess of methyl iodide (0.2 mol) was added and the reaction was stirred for 3 h, after which time the reaction was quenched with saturated aqueous $NaHCO_3$. The resulting organic layer (mostly THF) was separated and the aqueous layer was back-extracted 2× with ether. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and with brine and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by chromatography on silica with hexanes/EtOAc as eluant to provide 4.07 g (90%) of the title compound: ^1H NMR ($CDCl_3$) δ 3.91 (overlapping m, 4 H), 3.28 (s, 3 H), 3.20 (m, 1 H), 2.19 (dt, J = 14, 3, 3 Hz, 1 H), 1.70 (overlapping m, 2 H), 1.41 (overlapping m, 2 H), 1.20 (overlapping m, 2 H), 0.95 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 109.1, 80.0, 64.3, 64.1, 55.1, 50.6, 39.6, 34.4, 32.7, 29.1, 22.7; IR (cm^{-1}) (neat) 2957, 2878, 2825, 1483, 1184, 1091, 1038, 945, 912, 812; HRMS calcd for $C_{13}H_{24}O_3$ (M^+) 228.1725, found 228.1724.

***cis*-4-*tert*-Butyl-3-methoxycyclohexanone Ethylene Ketal.** With use of a procedure analogous to that directly above, *cis*-4-*tert*-butyl-3-hydroxycyclohexanone ethylene ketal[24] was converted to the methyl ether in 86% yield: ^1H NMR ($CDCl_3$) δ 3.99 (overlapping, m, 2 H), 3.90 (overlapping m, 2 H), 3.71 (bs, 1 H), 3.30 (s, 3 H), 2.22 (dt, J = 14, 3, 3 Hz, 1 H), 1.91–1.40 (m, 5 H), 2.05 (m, 1 H), 0.93 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 108.6, 77.6, 65.0, 63.4, 50.2, 36.0, 35.3, 32.5, 28.7, 20.0; IR (cm^{-1}) (neat) 2951, 2871, 1483, 1443, 1364, 1184, 1164, 1118, 1091, 1038, 972; HRMS calcd for $C_{13}H_{24}O_3$ (M^+) 228.1725, found 228.1724.

***trans*-4-*tert*-Butyl-3-methoxycyclohexanone (63b).** To 4.0 g of *trans*-4-*tert*-butyl-3-methoxycyclohexanone ethylene ketal was added 200 mL of 50% aqueous HOAc. The solution was stirred for 5 h and 100 mL of water was added. Solid $NaHCO_3$ was added until the solution was basic and the mixture was extracted 4× with ether. The combined ether extracts were washed with brine and dried over Na_2SO_4. Removal of the solvent in vacuo provides 3.1 g of pure **63b**: ^1H NMR ($CDCl_3$) δ 3.60 (m, 1 H), 3.25 (s, 3 H), 2.62 (dd, J = 4, 16 Hz, 1 H), 2.40–2.20 (overlapping m, 3 H), 1.83 (m, 1 H), 1.51 (overlapping m, 2 H), 0.96 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 211.8, 76.3, 55.6, 50.1, 42.6, 38.2, 32.8, 27.6, 21.3; IR (cm^{-1}) (neat) 2957, 2904, 2825, 1727, 1463, 1397, 1370, 1330, 1217, 1191, 1084; HRMS calcd for $C_{11}H_{20}O_2$ (M^+) 184.1463, found 184.1461.

***cis*-4-*tert*-Butyl-3-methoxycyclohexanone (62b).** In a manner analogous to that directly above, *cis*-4-*tert*-butyl-3-methoxycyclohexanone ethylene ketal was converted to **62b** in 49% yield: ^1H NMR ($CDCl_3$) δ 3.94 (br s, 1 H), 3.26 (s, 3 H), 2.75 (dt, J = 15, 3, 3 Hz, 1 H), 2.5–2.2 (overlapping m, 3 H), 2.00 (m, 1 H), 1.89 (m, 1 H), 1.47 (br d, J = 15 Hz, 1 H), 0.97 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 211.0, 79.2, 55.8, 50.3, 44.9, 41.5, 32.7, 28.9, 22.1; IR (cm^{-1}) (neat) 2950, 2919, 2871, 2835, 1722, 1470, 1374, 1337, 1251, 1184, 1085, 1032; HRMS calcd for $C_{11}H_{20}O_2$ (M^+) 184.1463, found 184.1465.

***cis*-4-*tert*-Butyl-3-methoxy-1-((trimethylsilyl)oxy)-1-cyclohexene (64b):** ^1H NMR (C_6D_6) δ 5.22 (d, J = 6 Hz, 1 H), 3.71 (m, 1 H), 3.10 (s, 3 H), 2.20–1.80 (overlapping m, 3 H), 1.43 (m, 1 H), 1.10 (m, 1 H), 1.01 (s, 9 H), 0.16 (s, 9 H); ^{13}C NMR (C_6D_6) δ 155.9, 103.7, 74.8, 54.5, 48.4, 32.5, 32.1, 28.7, 19.7, 0.3; IR (cm^{-1}) (neat) 2970, 2904, 2878, 2811, 1663, 1384, 1304, 1251, 1191, 1083, 979, 885, 845; HRMS calcd for $C_{10}H_{18}O_2Si$ (M^+ – *t*-C_4H_{10}) 198.1076, found 198.1078.

***cis*-4-*tert*-Butyl-1,3-bis((trimethylsilyl)oxy)-1-cyclohexene (64c):** ^1H NMR (C_6D_6) δ 5.16 (d, J = 6 Hz, 1 H), 4.51 (br s, 1 H), 2.15–1.75 (overlapping m), 1.48 (m, 1 H), 1.05 (s, 9 H), 0.21 (s, 9 H), 0.19 (s, 9 H); ^{13}C NMR (C_6D_6) δ 155.0, 107.4, 67.7, 49.1, 32.4, 32.2, 28.5, 19.0, 1.21, 0.49; IR (cm^{-1}) (neat) 2957, 2898, 1662, 1250, 1204, 1191, 1078, 1018, 885, 848, 739; HRMS calcd for $C_{16}H_{34}O_2Si_2$ (M^+) 314.2097, found 314.2095.

***trans*-4-*tert*-Butyl-3-methoxy-1-((trimethylsilyl)oxy)-1-cyclohexene (65b):** ^1H NMR (C_6D_6) δ 5.16 (br s, 1 H), 3.80 (br s, 1 H), 3.14 (s, 3 H), 2.00 (overlapping m, 2 H), 1.65 (m, 1 H), 1.40 (m, 1 H), 1.26 (m, 1 H), 0.96 (s, 9 H), 0.19 (s, 9 H); ^{13}C NMR (C_6D_6) δ 154.8, 104.3, 76.9, 53.4, 47.0, 32.7, 30.2, 28.9, 23.4, 0.36; IR (cm^{-1}) (neat) 2957, 2897, 2871, 2811, 1670, 1470, 1364, 1231, 1198, 1091, 912, 885, 845, 752; HRMS calcd for $C_{14}H_{28}O_2Si$ (M^+) 256.1858, found 256.1860.

***cis*-5-*tert*-Butyl-4-methoxy-2-((trimethylsilyl)oxy)-1-cyclohexene (66b):** ^1H NMR (C_6D_6) δ 5.30 (m, 1 H), 3.87 (m, 1 H), 3.13 (s, 3 H), 2.06 (m, 2 H), 1.68 (m, 1 H), 1.47 (m, 1 H), 1.30 (m, 1 H), 0.97 (s, 9 H), 0.20 (s, 9 H); ^{13}C NMR (C_6D_6) δ 154.8, 104.2, 79.6, 53.3, 47.0, 32.6, 30.3, 28.8, 23.4, 0.33; IR (cm^{-1}) (neat) 2957, 2878, 2811, 1669, 1477, 1369, 1244, 1198, 1091, 912, 885, 846; HRMS calcd for $C_{10}H_{18}O_2Si$ (M^+ – *t*-C_4H_{10}) 198.1076, found 198.1077.

***cis*-5-*tert*-Butyl-2,4-bis((trimethylsilyl)oxy)-1-cyclohexene (66c):** ^1H NMR (C_6D_6) δ 5.02 (m, 1 H), 4.32 (br s, 1 H), 2.49–2.49 (overlapping m, 2 H), 2.13 (br d, J = 18 Hz, 1 H), 1.90 (m, 1 H), 1.05 (dd, J = 4, 11 Hz, 1 H), 0.99 (s, 9 H), 0.24 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR (C_6D_6) δ 147.0, 103.4, 67.5, 48.5, 41.2, 32.2, 28.8, 20.6, 0.88, 0.54; IR (cm^{-1}) (neat) 2910, 2871, 1676, 1363, 1244, 1229, 1191, 1184, 1111, 1084, 1031, 1018, 965, 995, 839, 752; HRMS calcd for $C_{16}H_{34}O_2Si_2$ (M^+) 314.2097, found 314.2093.

***trans*-5-*tert*-Butyl-4-methoxy-2-((trimethylsilyl)oxy)-1-cyclohexene (67b):** ^1H NMR (C_6D_6) δ 4.81 (m, 1 H), 3.17 (m, 1 H), 3.05 (s, 3 H), 2.49 (dd, J = 5, 16 Hz, 1 H), 2.10 (m, 1 H), 2.00 (m, 1 H), 1.67, (m, 1 H), 1.49 (m, 1 H), 1.01 (s, 9 H), 0.20 (s, 9 H); ^{13}C NMR (C_6D_6) δ 147.7, 102.6, 79.6, 55.3, 47.4, 36.2, 32.6, 28.9, 25.0, 0.11; IR (cm^{-1}) (neat) 2957, 2871, 2811, 1669, 1476, 1377, 1364, 1251, 1204, 1091, 912, 885, 845, 752; HRMS calcd for $C_{14}H_{28}O_2Si$ (M^+) 256.1858, found 256.1860.

***trans*-5-*tert*-Butyl-2,4-bis((trimethylsilyl)oxy)-1-cyclohexene (67c):** ^1H NMR (C_6D_6) δ 4.80 (m, 1 H), 3.90 (m, 1 H), 2.39 (overlapping m, 2 H), 2.02 (m, 1 H), 1.72 (m, 1 H), 1.43 (m, 1 H), 0.98 (s, 9 H), 0.16 (s, 9 H), 0.03 (s, 9 H); ^{13}C NMR (C_6D_6) δ 147.5, 102.8, 71.5, 49.0, 41.6, 32.6, 28.8, 24.7, 0.7, 0.4; IR (cm^{-1}) (neat) 2957, 2904, 2871, 1689, 1384, 1364, 1251, 1198, 1091, 932, 912, 892, 846, 753; HRMS calcd for $C_{16}H_{34}O_2Si_2$ (M^+) 314.2097, found 314.2093.

(1*S,3*S**,4*S**)-4-*tert*-Butyl-1,3-bis((trimethylsilyl)oxy)cyclohexane (68):** ^1H NMR (C_6D_6) δ 4.02 (m, 1 H), 3.88 (m, 1 H), 2.29 (m, 1 H), 1.86 (m, 2 H) 1.30–0.75 (overlapping *m*, 4 H), 1.06 (s, 9 H), 0.25 (s, 9 H), 0.17 (s, 9 H); ^{13}C NMR (C_6D_6) δ 68.3, 66.1, 51.7, 40.8, 35.0, 28.2, 16.0, 0.77, –0.13 (quaternary of *tert*-butyl not observed); IR (cm^{-1}) (neat) 2950, 2900, 2871, 1250, 1177, 1118, 1065, 1031, 898, 878, 839, 759; HRMS calcd for $C_{13}H_{26}OSi$ (M^+ – TMSOH) 226.1752, found 226.1749.

5-*tert*-Butyl-2-((trimethylsilyl)oxy)-1,3-cyclohexadiene (71): ^1H NMR (C_6D_6) δ 5.86 (m, 1 H), 5.64 (br d, 1 H), 4.83 (m, 1 H), 2.01 (overlapping m, 3 H), 0.77 (s, 9 H), 0.15 (s, 9 H); ^{13}C NMR (C_6D_6) δ 131.0, 127.2, 105.3, 101.8, 44.3, 27.4, 23.1, 0.24; IR (cm^{-1}) (neat) 3050, 2964, 2904, 2871, 2825, 1656, 1596, 1477, 1404, 1397, 1364, 1251, 1231, 1221, 1184, 1178, 899, 846; HRMS calcd for $C_{13}H_{24}OSi$ (M^+) 224.1596, found 224.1600.

General Procedure for the Preparation of β,β'-Dihydroxy Ketones (Table VII). A solution of a distal aldolate dianion was generated as described above. While the solution was stirred at –78 °C 1.0–1.05 equiv of the appropriate aldehyde was added dropwise via syringe. The reaction mixture was stirred for 30–40 min and quenched with aqueous saturated $NaHCO_3$. The mixture was extracted three times with ether. The combined extracts were washed with aqueous saturated NaCl solution and dried with Na_2SO_4 and the solvent removed in vacuo. The crude reaction products could be purified by chromatography on silica, if necessary. Diastereomeric mixtures were separated by HPLC on silica and eluted with hexane–ethyl acetate.

1,5-Dihydroxy-1-phenyl-3-pentanone (79) (Table VII, entry 1): ^1H NMR ($CDCl_3$) δ 7.30 (m, 5 H), 5.13 (dd, J = 3, 9 Hz, 1 H), 3.88 (br, 1 H), 3.78 (t, J = 6 Hz, 2 H), 3.64 (br, 1 H), 2.89 (dd, J = 10, 16 Hz, 1 H), 2.69 (dd, J = 3, 16 Hz, 1 H), 2.61 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 211.0, 142.8, 128.5, 127.7, 125.6, 69.9, 57.5, 51.8, 45.5; IR (cm^{-1}) (neat) 3391, 3088, 3063, 3032, 2940, 2895, 1709, 1495, 1454, 1389, 1201, 1054, 891, 757, 702; HRMS exact mass calcd for $C_{11}H_{14}O_3$ (M^+) 194.0943, found 194.0939.

4-Hydroxy-1-(1-hydroxycyclohexyl)-2-butanone (80) (Table VII, entry 2): ^1H NMR ($CDCl_3$) δ 3.85 (t, J = 5.4, 2 H), 2.79 (bs, 2 H), 2.70 (t, J = 5.4, 2 H), 2.61 (s, 2 H), 1.71–1.24 (ol m, 10 H); ^{13}C NMR ($CDCl_3$) δ 213.3, 71.0, 57.6, 52.9, 46.6, 37.6, 25.6, 21.9; IR (cm^{-1}) (neat) 3400, 2933, 2860, 1699, 1447, 1404, 1359, 1052, 970; EIMS, *m/z* (rel intensity) 186 (M^+, 8), 169 (47), 168 (41), 130 (27), 125 (26), 123 (14), 112 (19), 99 (57), 98 (26), 97 (20), 95 (13), 88 (34), 83 (12), 81 (63), 73 (100), 71 (18), 70 (41), 69 (28), 43 (57); exact mass calcd for $C_{10}H_{18}O_3$ (M^+) 186.1256, found 186.1260.

1-(2-Furyl)-1,5-dihydroxy-5-methyl-3-hexanone (81) (Table VII, entry 3): mp 69–71 °C; ^1H NMR (C_3D_6O) δ 7.44 (d, J = 1.7, 1 H), 6.31 (dd, J = 3.2, 1.8, 1 H), 6.26 (d, J = 2.8, 1 H), 5.19–5.13 (m, 1 H), 4.64 (d, J = 5.1, 1 H), 4.02 (s, 1 H), 3.06 (dd, J = 16.4, 8.5, 1 H), 2.93 (dd, J = 16.4, 4.7, 1 H), 2.68 (s, 2 H), 1.22 (s, 3 H), 1.21 (s, 3 H); ^{13}C NMR (C_3D_6O) δ 210.0, 157.5, 142.4, 110.8, 106.2, 70.0, 63.8, 55.4, 50.5, 29.7; IR (cm^{-1}) (neat) 3307, 3243, 2976, 2940, 2878, 1707, 1502, 1368, 1306, 1091, 1066, 1014, 868, 740; EIMS, *m/z* (rel intensity) 212 (M^+, 1), 194 (22), 121 (20), 111 (14), 110 (100), 97 (81), 96 (11), 95 (25), 94 (21), 69 (10), 59 (49); exact mass calcd for $C_{11}H_{16}O_4$ (M^+) 212.1049, found 212.1053.

1,5-Dihydroxy-5-methyl-1-phenyl-3-hexanone (82) (Table VII, entry 4): mp 77–78.5 °C; ^1H NMR ($CDCl_3$) δ 7.39–7.24 (m, 5 H), 5.17–5.11 (m, 1 H), 3.75 (s, 1 H), 3.69 (s, 1 H), 2.90 (dd, J = 16.8, 9.3, 1 H), 2.71 (dd, J = 16.8, 3.4, 1 H), 2.59 (d, J = 9.9, 1 H), 1.24 (s, 3 H), 1.23 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.0, 149.2, 128.4, 127.5, 125.5, 69.7, 54.3, 52.8, 29.2, 29.1; IR (cm^{-1}) (diffuse reflectance) 3323, 3260, 3081, 3029, 2982, 2934, 1701, 1451, 1424, 1382, 1305, 1211, 1184, 1059, 1003, 912, 760, 696; HRMS exact mass calcd for $C_{13}H_{12}O_2$ (M^+ – H_2O) 204.1150, found 204.1145.

2,6-Dihydroxy-2,7-dimethyl-4-octanone (83) (Table VII, entry 5): ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 1 H), 3.76 (br d, J = 3, 1 H), 3.29 (br d, J = 1, 1 H), 2.58 (m, 2 H), 2.47 (m, 2 H), 1.59 (octet, J = 6.5, 1 H), 1.18 (s, 6 H), 0.84 (d, J = 6.5, 3 H), 0.82 (d, J = 6, 3 H); ^{13}C NMR ($CDCl_3$) δ 213.4, 72.1, 69.6, 54.3, 47.9, 33.1, 29.2, 29.1, 18.1, 17.5; IR (cm^{-1}) (neat) 3423, 2969, 2935, 2878, 1699, 1468, 1382, 1368, 1148, 1077, 1043, 1001, 913; CIMS (CI^+), m/z (rel intensity) 189 (M + 1, 15), 171 (33), 131 (14), 115 (25), 113 (25), 99 (7), 73 (10); EIMS, m/z (rel intensity) 155 (5), 145 (4), 127 (13), 113 (8), 112 (13), 109 (8), 101 (11), 97 (32), 87 (30), 83 (34), 73 (27), 72 (29), 71 (18), 70 (13), 69 (21), 59 (100), 58 (68), 57 (14), 56 (11), 55 (32); M^+ not observed; exact mass calcd for $C_{10}H_{19}O_2$ (M^+ - OH) 171.1385, found 171.1389.

1,5-Dihydroxy-4-methyl-1-phenyl-3-pentanone (84) (Table VII, entry 6, high R_f isomer): mp 74–76 °C; ^{1}H NMR ($CDCl_3$) δ 7.39–7.27 (m, 5 H), 5.21 (d, J = 17, 1 H), 3.74 (t, J = 9, 1 H), 3.68–3.63 (ol m, 2 H), 3.01 (dd, J = 17, 9.5, 1 H), 2.83–2.73 (m, 3 H), 1.10 (d, J = 7, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.5, 142.8, 128.5, 127.6, 125.6, 69.8, 64.1, 50.0, 48.8, 12.7; IR (cm^{-1}) (Nujol) 3325, 1710, 1211, 1091, 1081, 1067, 1037, 1023, 997; EIMS, m/z (rel intensity) 208 (M^+, 3), 149 (23), 131 (24), 107 (43), 106 (95), 105 (96), 103 (14), 102 (11), 84 (13), 79 (19), 78 (21), 77 (100); exact mass calcd for $C_{12}H_{16}O_3$ (M^+) 208.1099, found 208.1101.

1,5-Dihydroxy-4-methyl-1-phenyl-3-pentanone (84) (Table VII, entry 6, low R_f isomer): ^{1}H NMR ($CDCl_3$) δ 7.38–7.25 (m, 5 H), 5.20 (dd, J = 9.5, 2.5, 1 H), 3.90 (bs, 1 H), 3.77–3.67 (ol m, 2 H), 3.23 (bs, 1 H), 3.05 (dd, J = 17, 10, 1 H), 2.82–2.72 (ol m, 2 H), 1.06 (d, J = 7, 3 H); ^{13}C NMR ($CDCl_3$) δ 214.2, 143.0, 128.5, 127.6, 125.6, 70.2, 64.2, 50.5, 49.2, 12.5; IR (cm^{-1}) (neat) 3403, 3088, 3064, 3032, 2972, 2937, 2881, 1707, 1495, 1455, 1384, 1206, 1062, 1029, 759, 702; EIMS, m/z (rel intensity) 208 (M^+, 1), 149 (10), 131 (25), 107 (24), 106 (99), 105 (97), 103 (13), 84 (12), 78 (18), 77 (100), 72 (12), 69 (20), 61 (22), 57 (13), 51 (40), 50 (21); exact mass calcd for $C_{12}H_{16}O_3$ (M^+) 208.1099, found 208.1095.

1,5-Dihydroxy-2,6-dimethyl-3-heptanone (85) (Table VII, entry 7, low R_f isomer): ^{1}H NMR ($CDCl_3$) δ 3.82 (8-line pattern, J = 2, 5, 12 Hz, 1 H), 3.66 (m, 2 H), 3.48 (br, 1 H), 2.78 (m, 1 H), 2.65 (dd, J = 10, 17 Hz, 1 H), 2.51 (dd, J = 3, 17 Hz, 1 H), 1.62 (m, 1 H), 1.02 (d, J = 7 Hz, 3 H), 0.88 (d, J = 5 Hz, 3 H), 0.86 (d, J = 5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.7, 72.6, 64.3, 49.2, 45.5, 33.2, 18.2, 17.6, 12.7; IR (cm^{-1}) (neat) 3401, 2965, 2938, 2879, 1706, 1465, 1385, 1370, 1264, 1136, 1066, 1029, 1001, 978; EIMS, m/z (rel intensity); exact mass calcd for $C_9H_{19}O_3$ (M + H) 175.1334, found 175.1340.

1,5-Dihydroxy-2,6-dimethyl-3-heptanone (85) (Table VII, entry 7, high R_f isomer): ^{1}H NMR ($CDCl_3$) δ 3.79 (m, 1 H), 3.56 (m, 1 H), 3.56 (m, 1 H), 3.50 (br, 1 H), 2.74 (m, 1 H), 2.52 (m, 2 H), 1.61 (m, 1 H), 1.00 (d, J = 7 Hz, 3 H), 0.86 (d, J = 6 Hz, 3 H), 0.84 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.6, 72.1, 64.0, 48.7, 45.1, 33.1, 18.2, 17.6, 12.7; IR (cm^{-1}) (neat) 3408, 2965, 2937, 2879, 1705, 1465, 1385, 1370, 1032, 1001; HRMS exact mass calcd for $C_9H_{19}O_3$ (M^+ + H) 175.1334, found 175.1330.

1,5-Dihydroxy-2-methyl-3-decanone (86) (Table VII, entry 8, high R_f isomer): ^{1}H NMR ($CDCl_3$) δ 4.05 (bs, 1 H), 3.72–3.59 (ol bm, 3 H), 3.44 (bs, 1 H), 2.83–2.72 (m, 1 H), 2.66 (dd, J = 17, 9, 1 H), 2.57 (dd, J = 17, 3.1, 1 H), 1.49–1.01 (ol m, 8 H), 1.03 (d, J = 6.8, 3 H), 0.87 (t, J = 6.6, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.4, 68.0, 64.3, 49.1, 48.5, 36.6, 31.6, 25.0, 22.5, 13.9, 12.7; IR (cm^{-1}) (neat) 3395, 2957, 2931, 2874, 2861, 1707, 1460, 1379, 1128, 1070, 1028, 978; EIMS, m/z (rel intensity) 203 (M + 1, 14), 185 (41), 143 (25), 131 (19), 125 (39), 103 (49), 102 (11), 101 (18), 97 (24), 87 (100), 85 (19), 84 (14), 83 (68), 73 (11), 72 (20), 71 (21), 55 (91); exact mass calcd for $C_{11}H_{23}O_3$ (M + H) 203.1647, found 203.1645.

1,5-Dihydroxy-2-methyl-3-decanone (86) (Table VII, entry 8, low R_f isomer): ^{1}H NMR ($CDCl_3$) δ 4.25 (bs, 1 H), 3.72–3.65 (bm, 1 H), 3.64–3.59 (bm, 1 H), 3.40 (bs, 1 H), 3.15 (bs, 1 H), 2.83–2.72 (m, 1 H), 2.61 (d, J = 6.0, 2 H), 1.50–1.28 (ol m, 8 H), 1.07 (d, J = 7.2, 3 H), 0.87 (t, J = 6.6, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.5, 67.6, 64.1, 48.7, 48.2, 36.5, 31.6, 25.1, 22.5, 13.9, 12.8; IR (cm^{-1}) (neat) 3389, 2957, 2932, 2873, 2860, 1705, 1460, 1379, 1128, 1070, 1026, 979; EIMS, m/z (rel intensity) 203 (M + H, 3), 185 (16), 143 (23), 131 (18), 125 (36), 103 (29), 101 (16), 97 (24), 87 (95), 85 (15), 84 (13), 83 (65), 72 (20), 71 (21), 69 (21), 61 (18), 59 (67), 57 (51), 56 (42), 55 (100); exact mass calcd for $C_{11}H_{23}O_3$ (M + H) 203.1647, found 203.1648.

General Procedure for Reaction of Aldolate Dianions with Acyl Cyanides. Solutions of distal aldolate dianions (2.27 mmol in 5 mL of THF) were generated as described above. To these solutions at -78 °C was added a solution of the acyl cyanide (2.27 mmol in 5 mL of THF). The reaction mixtures were allowed to stir for 15 min before quenching with 3 N HCl to pH <1. The reaction mixtures were extracted with ether (3×), washed with water, and dried over Na_2SO_4 and the solvent was removed in vacuo. Purification was achieved by chromatography on silica with EtOAc/hexane mixtures as eluants. All of the diketones exist primarily in an enolized form in NMR solvents.

5-Hydroxy-1-phenyl-1,3-pentanedione (87a): ^{1}H NMR ($CDCl_3$) δ 7.85 (m, 2 H), 7.44 (m, 3 H), 6.20 (s, 1 H), 3.96 (t, J = 6 Hz, 2 H), 2.71 (t, J = 6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 196.9, 181.7, 134.2, 132.3, 128.6, 126.9, 96.8, 58.9, 41.9; IR (cm^{-1}) (neat) 3408, 2958, 2888, 1717 (w), 1600, 1460, 1422, 1271, 1052, 767, 694; HRMS calcd for $C_{11}H_{12}O_3$ (M^+) 192.0786, found 192.0790.

5-Hydroxy-5-methyl-1-phenyl-1,3-hexanedione (87b): ^{1}H NMR (C_6D_6) δ 7.72 (m, 2 H), 7.06 (m, 2 H), 5.94 (s, 1 H), 2.30 (s, 2 H), 1.18 (s, 6 H); ^{13}C NMR (C_6D_6) δ 196.7, 182.7, 134.6, 132.3, 128.5, 127.8, 98.1, 70.0, 51.6, 29.5; IR (cm^{-1}) (neat) 3439, 3066, 2975, 2937, 1603, 1573, 1493, 1462, 1379, 1271, 1187, 1158, 909, 765, 698; HRMS calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1103.

5-Hydroxy-4-methyl-1-phenyl-1,3-pentanedione (87c): ^{1}H NMR ($CDCl_3$) δ 7.86 (m, 2 H), 7.49 (m, 3 H), 6.23 (s, 1 H), 3.83 (dd, J = 11, 7 Hz, 1 H), 3.73 (dd, J = 11, 4 Hz, 1 H), 2.72 (m, 1 H), 1.21 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 199.9, 183.0, 134.5, 132.3, 128.6, 126.9, 95.8, 64.9, 45.4, 14.1; IR (cm^{-1}) (neat) 3403, 3066, 2974, 2936, 2882, 1603, 1575, 1457, 1300, 1267, 1184, 1158, 1029, 771, 733, 694; EIMS, m/z (rel intensity) 333 (1), 180 (16), 179 (100), 163 (2), 147 (4), 105 (3), 91 (3), 73 (49), 57 (4); HRMS calcd for $C_{12}H_{14}O_3$ 206.0942, found 209.0937.

Ethyl 5-Hydroxy-5-methyl-3-oxohexanoate (87d): ^{1}H NMR (C_6D_6) δ 4.13 (q, 2 H), 3.42 (s, 2 H), 2.68 (s, 2 H), 1.22 (t, 3 H); ^{13}C NMR (C_6D_6) δ 204.5, 167.0, 69.7, 61.5, 53.8, 50.7, 29.3, 14.1; IR (cm^{-1}) (neat) 3440, 2979, 2938, 1742, 1708, 1650, 1467, 1410, 1369, 1319, 1254, 1239, 1179, 1158, 1097, 1075, 1031, 939, 910; HRMS calcd for $C_8H_{13}O_4$ (M^+ - CH_3) 173.0813, found 173.0817. This substance exists primarily in the ketoester form; however, a small amount of the enol form is present in dilute solutions of NMR solvents, as judged by the ^{1}H and ^{13}C shifts of minor peaks. The substance was chromatographically homogeneous by TLC and HPLC.

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Supplementary Material Available: Spectra representing a chromatographic fraction that is enriched in compounds **40*E***, **40*Z***, and **41*Z*** (8 pages). Ordering information is given on any current masthead page.