A Selectivity Study of Activated Ketal Reduction with Borane Dimethyl Sulfide

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A chemo- and regioselectivity study of the reagent combination BH_3·SMe_2/TMSOTf for ketal reduction has been undertaken. It has revealed that simple 1,3-dioxanes reduce cleanly at low temperature in CH_2Cl_2 while simple 1,3-dioxolanes may give complete ring cleavage and dimerization products. A study of reduction of 4-substituted 1,3-dioxolanes has revealed a solvent-directed regioselectivity which in THF favors the secondary protected derivative. A mechanism is postulated to account for the selectivities based on recent thinking on acetal substitution reactions.

Introduction

The dissociative nucleophilic substitution[1] of Lewis acid activated acetals and ketals has grown to become an outstanding class of reaction in organic synthesis, and in recent times much interest has been shown in the mechanism and origin of stereoselectivity[2] of substitution of chiral acetals, a concept initiated by Johnson *et al.*[3] in the 1960s. Similarly, ketal reduction, although put into perspective only relatively recently,[4] also enjoys a much longer history as an alternative reaction to direct carbonyl group reduction. The first reduction of a ketal was reported in 1951 when Doukas and Fontaine[5] showed that the spiroketal diosgenine could be reduced by $LiAlH_4$ in anhydrous ether saturated with hydrogen chloride gas. Subsequently, Eliel *et al.*[6] established that the reducing properties of $LiAlH_4$ may be considerably altered by the addition of Lewis acids, notably $AlCl_3$, and the active species was established by Brown *et al.*[7] as being AlH_3, AlH_2Cl, or $AlHCl_2$ depending on the molar proportions of $LiAlH_4$ to $AlCl_3$. In the three decades following these pioneering studies many reagents for ketal reduction comprising a hydride source in conjunction with an activator have been developed. Notably, the hydride sources have been based on aluminum[8] (ambiphilic type), silicon,[9] and boron.[10] Of particular interest are the studies by Yamamoto on the stereoselectivity of chiral acetal reduction which have established that AlH_3 and Et_3SiH/$TiCl_4$ reduce via syn and anti delivery of hydride, respectively. We have recently reported[11] that borane dimethyl sulfide in conjunction with trimethylsilyl trifluoromethanesulfonate (TMSOTf) is a potent reagent combination for ketal reduction, and in this paper we report on its chemo- and regioselectivity toward a range of substrates with emphasis on the mechanistic aspects of the reaction in the light of recent thinking in the field of acetal substitution reactions.

• Abstract published in *Advance ACS Abstracts,* October 15, 1993.

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Table I. Reduction of Ketals with BH_3·SMe_2/TMSOTf (2 Equiv Each)

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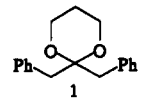
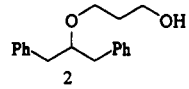
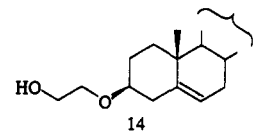
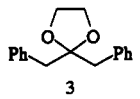
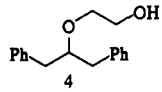
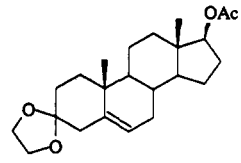
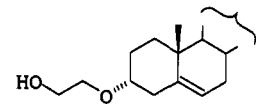
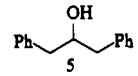
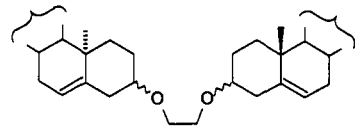
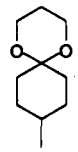
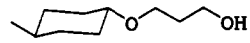
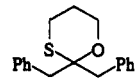
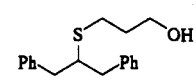
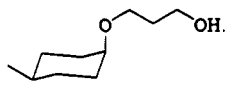
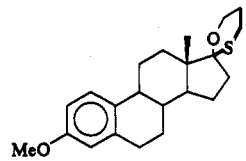
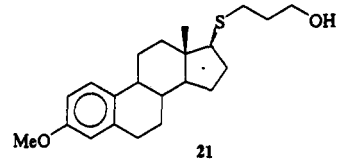
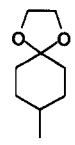
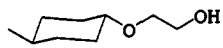
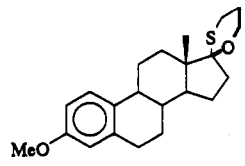
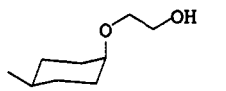
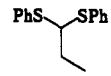
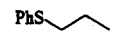
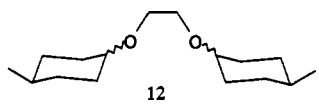
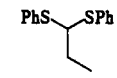
 1	 2	95		 14	82.7
 3	 4	51	 13	 15	0.9
	 5	20		 16	16.2
 6	 7	83	 17	 18	72
	 8	14	 19	 21	84 from 19
 9	 10	13	 20		97 from 20
	 11	7	 22	 23	37
	 12	71		 22	42

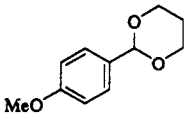
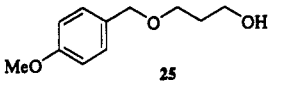
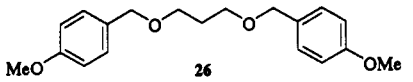
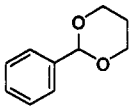
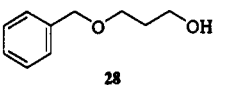
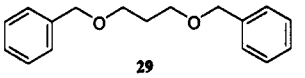
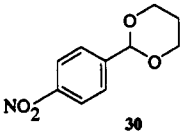
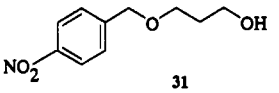
Results and Discussion

1. Chemoselectivity Studies. The initial screening studies regarding the choice of Lewis acid revealed that TMSOTf is superior to other Lewis acids ($TiCl_4$, $SnCl_4$, BF_3·OEt_2) as evidenced by a much lower temperature and reaction time. Typically, a simple ketal such as 2,2-dibenzyl-1,3-dioxane (1) is reduced at −78 °C in 1 h in CH_2Cl_2 (95%) compared to −78 to 0 °C for $TiCl_4$ and $SnCl_4$ (70% and 88%, respectively) for the same substrate, Table I. The greater reactivity with TMSOTf presumably reflects the greater ease of activation of borane to the "ate" complex ($^-BH_3OTf$ vs $^-BH_3Cl$) preceeding the hydride delivery step and was considered to be a crucial aspect regarding selectivity aspects.

Various substrates for reduction were selected in order to probe various facets of chemoselectivity. Initially, the influence of ketal ring size and type was investigated, and the results are shown in Table I. Of the solvents screened, CH_2Cl_2 was found to be the most efficient while reactions proceeded very sluggishly in THF and with the complication of solvent polymerization. One mol equiv of both BH_3·SMe_2 and TMSOTf were required for complete reaction. In this section of the study, however, 2 mol equiv of each reagent was used without adverse side reactions occurring.

Several features emerge from the results of Table I. 1,3-Dioxanes and 1,3-oxathianes reduced in high yield and without byproduct formation. As expected, the latter

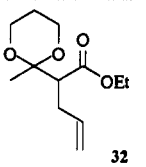
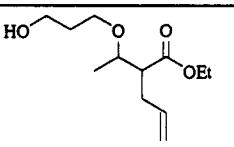
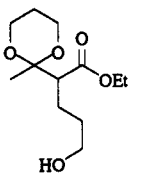
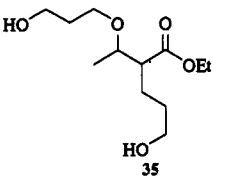
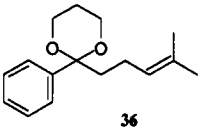
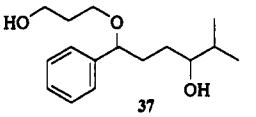
Table II. Reduction of Substituted Benzylidene Ketals with BH_3·SMe_2/TMSOTf

substrate	product(s)	yield (%)
 24	 25	33
	 26	35
 27	 28	75
	 29	25
 30	 31	77

opened regioselectively to the sulfide. By comparison, the 1,3-dioxolanes give varying amounts of unprotected alcohol or dimeric condensation products from the spiro systems. While the former implies a complete ring cleavage pathway, the latter presumably arise via competitive nucleophilic substitution of an activated ketal species by a molecule of reduced ketal as its silyl ether. This pathway is disfavored in sterically demanding cases such as the androstane derivative (substrate **13**). Regarding simple diastereoselectivity, the spiro systems (substrates **6**, **9**, **13**) all gave as major product that from pseudoaxial hydride attack similar to borohydride reduction[12] of conformationally rigid cyclohexanones. Stereoselectivity was particularly good for the androstane derivative **13**. The two diastereomers **19** and **20**, derived from ketalization of estrone methyl ether with 3-mercaptopropan-1-ol, both reduced to the same β-sulfide indicating α-hydride delivery to the same open thionium ion in each case.

It was important at this stage to acknowledge the different reactivities of simple 1,3-dioxane and dioxolane ketals and attempt to rationalize them in the light of recent mechanistic thinking in the field, notably by Denmark.[2] A competition experiment using 1 mol equiv each of dibenzyl dioxane and dioxolane **1** and **3** with 1 mol equiv each of BH_3·SMe_2/TMSOTf in CH_2Cl_2 at −78 °C resulted in chemoselective opening of the dioxane ring **1** to afford **2** in 67% yield with recovery of unreacted dioxolane **3** in 95% yield. This reflects the greater ease of C–O bond perturbation in the dioxane case in order to relieve 1,3-diaxial strain between the C-2 axial substituent and the axial hydrogens at C-4 and C-6. Furthermore, reduction of a series of substituted benzylidene acetals as a 1,3-dioxane series revealed that stabilization of oxocarbenium ion character in the transition state encourages dimer formation, Table II. Hence, it may be concluded that C–O bond perturbation in simple 1,3-dioxolanes requires a higher temperature and occurs to a more advanced oxocarbenium ion character in reduction with the reagent resulting in side reactions. By comparison, C–O bond perturbation occurs more readily in 1,3-dioxanes, and reduction may proceed nearer to the intimate ion pair end of the Denmark mechanistic spectrum.[2]

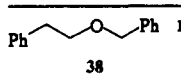
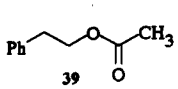
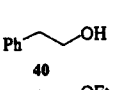
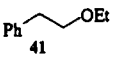
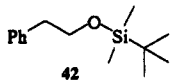
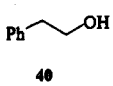
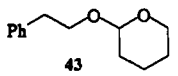
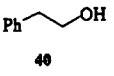
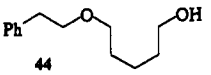
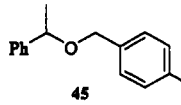
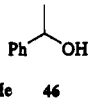
Table III. Chemoselectivity Study of Reduction and/or Hydroboration Using BH_3·SMe_2/TMSOTf

substrate	product	yield (%)
 32	 33	77
32	 34	80
32	 35	36
 36	 37	72

A separate study was then carried out to address the question of hydroboration activity of the reagent versus ketal reduction, an aspect unique to this reagent, Table III. The 1,3-dioxane derivative (**32**) of ethyl allylacetoacetate was prepared and reacted with BH_3·SMe_2 and TMSOTf at −78 °C. Chemoselective reduction of the ketal occurred at −20 °C with no hydroboration of the double bond. Conversely, the latter option could be accomplished without ketal reduction by omitting the Lewis acid and hydroborating at 0 °C in the normal way. Finally,

(12) Pelter, A.; Smith, K. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, 1979; Vol. 3, pp 689–940.

Table IV. Reactivity of Various Hydroxyl Protecting Groups toward BH_3·SMe_2/TMSOTf

substrate	product(s)	condns	yield (%)
 38	no reaction	−78 °C to rt	*a*
 39	 40	−78 to 0 °C	57
	 41		40
 42	 40	−78 °C	70
 43	 40	−78 to −20 °C	83
	 44		10
 45	 46	−78 to −50 °C	60

[a] Starting material recovered.

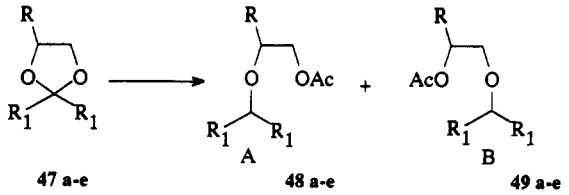
intramolecular reduction was accomplished on the substrates **32** and **36** by hydroboration at 0 °C followed by TMSOTf addition at −78 °C. Reduction occurred at around −20 °C, and the diols **35** and **37** were isolated as a 3:2 and a 1:1 mixture of diastereomers, respectively, after chromatography.

In the context of using this potent reagent combination for ketal reduction of a multifunctionalized substrate, the reactivity of various hydroxyl protecting groups were examined, and the results are displayed in Table IV.

The benzyl, *p*-methoxybenzyl, THP, and TBDMS ethers as well as the acetate of 2-phenylethanol were all subjected to the reduction conditions. Only the benzyl ether proved to be resistant to the reagent, while the THP ether reduced predominantly via exocyclic bond cleavage.[13] The *p*-methoxybenzyl group was also removed under these conditions, a feature of importance to carbohydrate protection methodology.[14]

2. Regioselectivity Studies. Although reductive ring opening of cyclic ketals has been used primarly as an alternative to direct carbonyl reduction, it may also be used as a means of monoprotecting[15] one hydroxyl group of a diol. Considerable research effort has been directed at achieving chemoselective protection of unsymmetrical, vicinal primary, secondary diols to afford the thermodynamically and kinetically less favored secondary protected derivatives, and the most common methodological approach is via cyclic intermediates.[16] A seminal study on the reduction of unsymmetrical vicinal diols using the

Scheme I



47 a-e 48 a-e 49 a-e

a: R=Ph, R_1=Me
b: R=Ph, R_1=Et
c: R=Ph, R_1=CH_2Ph
d: R=Bu, R_1=Et
e: R=Bu, R_1=CH_2Ph

reagent combination $LiAlH_4/AlCl_3$ was carried out in the early 1960s by Brown and Leggetter. In a series of papers[17] the authors delineated the structural features affecting ring opening of a series of substituted dioxolanes and rationalized the regioselectivities as proceeding via the thermodynamically more stable oxocarbenium ion. We rationalized, in view of the much lower temperature of reaction as well as the question of mechanistic differences between the dioxanes and dioxolanes mentioned previously, that the reagent BH_3·SMe_2/TMSOTf might offer a different selectivity profile and that an independent study was justified. The initial investigation was carried out on the 2-substituted 1,3-dioxolanes (**47a–e**) of 1,2-hexanediol and 1-phenyl-1,2-ethanediol. The 2-substituents were varied as methyl, ethyl, and benzyl for the phenyl derivative and ethyl and benzyl for the dioxolane of 1,2-hexanediol, Scheme I. The product mixtures were acetylated in each case, and isomer ratios (secondary protected **48a–e**/primary protected **49a–e**) were ascertained by integration of the 200-MHz ^1H NMR spectra of isomer combinations after chromatography. Emphasis was placed on the contrasting results obtained by varying the solvent from CH_2Cl_2 to THF. Reaction progress was monitored by TLC and was always found to be slower in THF. Other etheral solvents such as diethyl ether, diisopropyl ether, dioxane, and tetrahydropyran generally gave results similar to CH_2Cl_2, and with the latter two, reaction could not be commenced at −78 °C since this temperature was below the solvent melting point. Table V summarizes the results.

Several points emerge from Table V. Firstly, for a particular solvent and R group the isomer ratio **48:49** increases in favor of the desired isomer **48** with increasing steric bulk of R_1, and this trend is pronounced in THF. However, for bulky R_1 higher reaction temperatures were required and this led to complications with polymerization of the THF. Secondly, for the same R_1 and solvent, the isomer ratio favored **48** more for R = Ph than for R = Bu. The isomer ratio **48:49** was much higher in THF than in CH_2Cl_2 for the same R and R_1 groups and in some cases inverted, e.g., entries **9**, **10**, or preparatively useful, entries **4**, **8**, **14**. The use of the bulkier silylating agent TBDMSOTf or hydride source thexylborane in CH_2Cl_2 favored isomer **49** (results not in Table V).

(13) (a) Guindon, Y.; Bernstein, M. A.; Anderson, P. C. *Tetrahedron Lett.* **1987**, *28*, 2225. (b) Guindon, Y.; Anderson, P. C. *Tetrahedron Lett.* **1987**, *28*, 2485. (c) Deslongschamps, P. In *Stereoelectronic Effects on Organic Chemistry*; Pergamon Press: Oxford, 1983.

(14) (a) Hébert, N.; Beck, A.; Lennox, R. B.; Just, G. *J. Org. Chem.* **1992**, *57*, 1777. (b) Green, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991.

(15) Bartels, B.; Hunter, R. *J. Chem. Soc., Perkin Trans 1* **1991**, 2887.

(16) (a) Reginato, G.; Ricci, A.; Roelens, S.; Scapecchi, S. *J. Org. Chem.* **1990**, *55*, 5132–5139. (b) Ricci, A.; Roelens, S.; Vannuchi, A. *J. Chem. Soc., Chem. Commun.* **1985**, 1457. (c) David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643. (d) Pautard, A. M.; Evans, S. A., Jr. *J. Org. Chem.* **1988**, *53*, 2300. (e) Barton, D. H. R.; Zhu, J. *Tetrahedron* **1992**, *48*, 8337.

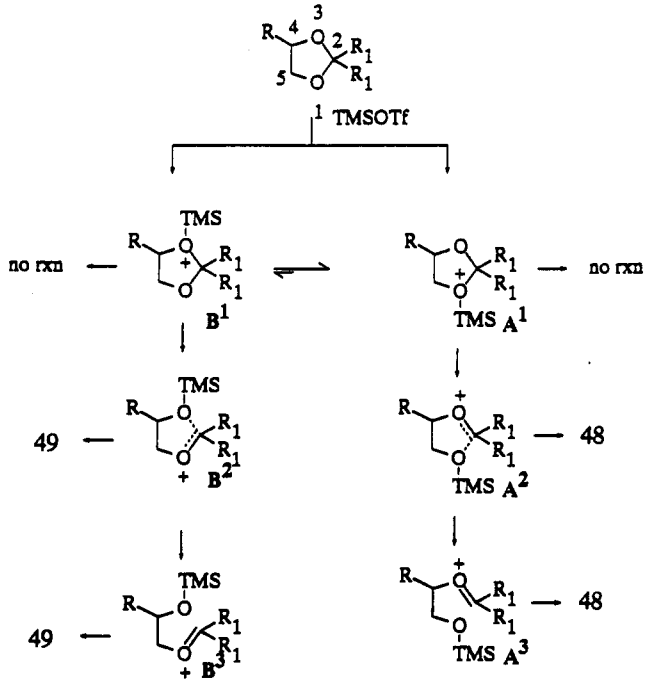
(17) (a) Diner, U. E.; Brown, R. K. *Can. J. Chem.* **1967**, *45*, 2547. (b) Diner, U. E.; Brown, R. K. *Can. J. Chem.* **1967**, *45*, 1297. (c) Leggetter, B. E.; Brown, R. K. *Can. J. Chem.* **1964**, *42*, 990. (d) Leggetter, B. E.; Brown, R. K. *Can. J. Chem.* **1964**, *42*, 1005. (e) Davis, H. A.; Brown, R. K. *Can. J. Chem.* **1971**, *49*, 2166. (f) Davis, H. A.; Brown, R. K. *Can. J. Chem.* **1971**, *49*, 2563. (g) Leggetter, B. E.; Brown, R. K. *Can. J. Chem.* **1966**, *43*, 1030. (h) Leggetter, B. E.; Diner, U. E.; Brown, R. K. *Can. J. Chem.* **1964**, *42*, 2113. (i) Leggetter, B. E.; Brown, R. K. *Can. J. Chem.* **1963**, *41*, 2671.

Table V. Product Yields and Isomer Ratios from Reductive Cleavage of Ketals 47a–e Using Borane Dimethyl Sulfide and TMSOTf (2 Equiv) Followed by Acetylation

entry	R	R_1	solvent	temp (°C)	ratio 48:49	yield (%)
1	Ph	Me	CH_2Cl_2	−78	63:37	60
2	Ph	Me	THF	−78 to +10	81:19	67
3	Ph	Et	CH_2Cl_2	−78 to −30	63:37	84
4	Ph	Et	THF	−78 to +10	98:2	88
5	Ph	Et	diethyl ether	−78 to 0	63:37	76
6	Ph	Et	diisopropyl ether	−78 to 0	62:38	84
7	Ph	CH_2Ph	CH_2Cl_2	−78 to −20	48:52	69
8	Ph	CH_2Ph	THF	−78 to rt	99:1	56[a]
9	Bu	Et	CH_2Cl_2	−78 to −20	29:71	73
10	Bu	Et	THF	−78 to +4	83:17	72
11	Bu	Et	dioxane	rt	67:33	70
12	Bu	Et	THP[b]	−50 to −30	51:49	80
13	Bu	CH_2Ph	CH_2Cl_2	−78 to −20	31:69	91
14	Bu	CH_2Ph	THF	−78 to rt	90:10	87
15	Bu	CH_2Ph	diethyl ether	−78 to rt	38:62	83

[a] THF polymerized; yield is unacetylated product. [b] THP = tetrahydropyran.

Scheme II



In the light of recent thinking on dissociative ketal substitution reactions the following mechanism is postulated to account for these trends, in particular the solvent-dependent regioselectivities, Scheme II.

The mechanism depicts two pathways, depending on the regioselectivity of initial silylation, and which pass via intermediates A^1, A^2, A^3 or B^1, B^2, B^3 and give rise to isomer 48 or 49, respectively. A^1/B^1 represent closed silyloxonium ions, while A^2/B^2 correspond to intimate ion pairs and A^3/B^3 external ion pairs in the mechanistic spectrum. A^1 may be considered as the product of silylation of the sterically less hindered oxygen and thus kinetically favored. Hence, silylation initially gives rise to a higher population of A^1 than B^1. Furthermore, since the possibility of the relative reduction rates of the closed silyloxonium ions A^1 and B^1 being solvent controlled appears to be unlikely, the mechanism proposes that no significant reduction occurs at the A^1/B^1 complex level. For pathway A to occur, reaction has to proceed via bond lengthening of C-2–O-1 to form A^2. This step is energetically less favorable than the same step in pathway B, since for the latter ($B^1 \rightarrow B^2$) there is 1,3-steric strain relief between groups R^1 and R. Conversely, further opening to the external ion pairs A^3 or B^3 leads to a thermodynamically more stable species in the A pathway by inductive effects (apparently greater for R = Ph than Bu). THF may play an important role in this regard. To account for the solvent effect on the isomer ratios, since the reactions in THF always required higher temperatures than in CH_2Cl_2 we propose that THF plays a mediating role as silylated THF, Figure 1, which being sterically more discriminating than TMSOTf favorably influences the initial ratio of A^1 to B^1.

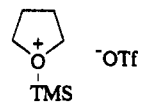
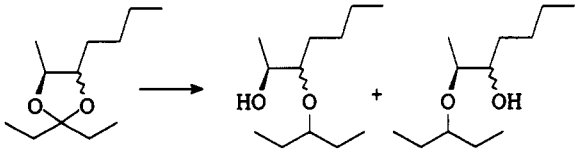


Figure 1.

The regioselectivity results in THF indicate that ring opening of A^1 to a suitably electrophilic point in the Denmark-type mechanistic spectrum followed by hydride delivery occurs faster than the interconversion to B^1 and the subsequent reduction via pathway B. This is presumably due to A^1 being sufficiently energetic to pass to A^2 and beyond on account of the higher temperature at which the silylation occurs. The regioselectivities are particularly good for R = Ph in which inductive stabilization of the developing positive charge at the C-2 carbon helps to counteract unfavorable 1,3-steric strain due to C-2–O-3) bond compression on passing from A^1 to A^3 via A^2. In CH_2Cl_2, the regioselectivity ratios indicate that for the same substrate more reduction occurs via the B pathway than in THF. Furthermore, the variation compared to THF in the ratio of 48:49 is more pronounced for R = Bu. In CH_2Cl_2, since silylation may proceed unimpeded at −78 °C, as evidenced by reduction at this temperature, the results indicate that equilibration of A^1 to B^1 followed by opening of B^1 to B^2, in which there is 1,3-steric strain relief, competes favorably with the conversion of A^1 to A^2. In CH_2Cl_2, 49 is favored to 48 more in the case of R = Bu compared with R = Ph for the same R^1 group (e.g., entry 9 vs 3), indicating the greater steric strain relief and reduced inductive stabilization for the former. The effect of the other solvents, diethyl ether and diisopropyl ether, can be explained along the same lines as CH_2Cl_2, and it is evident that they do not influence the reagents in the same way as the more Lewis basic THF. Furthermore, the higher ratios of 48:49 (entries 11 and 12) for the solvents dioxane and THP on account of the higher reaction temperature also lend credibility to the aforementioned proposals. Another mechanistic aspect which should be commented on is the nature of the reducing species and the influence of solvent on it. In CH_2Cl_2, $BH_3{\cdot}SMe_2$ will exist as such whereas in THF it is most likely resolvated to $BH_3{\cdot}THF$. However, the question remains as to whether $BH_3{\cdot}SMe_2$ and $BH_3{\cdot}THF$ are the reductants in CH_2Cl_2 and THF, respectively, or whether they are not activated to the "ate" complex $^-BH_3OTf$ which is the true reductant. As mentioned previously, this possibility is suggested by the vast difference in reduction rates using $BH_3{\cdot}SMe_2$ with $TiCl_4$ and TMSOTf in CH_2Cl_2. If $^-BH_3OTf$ is the true reductant, displacement of donor THF from $BH_3{\cdot}THF$ would require a higher temperature than the analogous displacement of

Scheme III



50a: trans
50b: cis

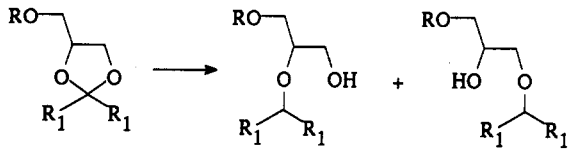
51 52

Table VI. Reduction of Ketals (50a (Trans) and 50b (Cis) with BH_3·SMe_2/TMSOTf (2 Equiv Each)

entry	ketal	solvent	temp (°C)	ratio 51:52[a]	yield[b] (%)
1	trans	CH_2Cl_2	−78 to −50	25:75	31[c]
2	trans	THF	−78 to +4	74:26	50[c]
3	cis	CH_2Cl_2	−78 to −50	25:75 (27:73)	92
4	cis	THF	−78 to rt	70:30 (68:32)	83[d]

[a] Ratio determined by ^1H NMR, ratio in (parentheses) from GC–MS (Cape Technicon). [b] Isolated yield after chromatography. [c] Acetylated products (acetic anhydride, pyridine, DMAP). [d] 14% of starting material recovered.

Scheme IV



53a-d 54a-d 55a-d

a: R=CH_2Ph, R_1=Me
b: R=CH_2Ph, R_1=CH_2Ph
c: R=H, R_1=CH_2Ph
d: R=Si ^{t}BuMe$_2$, R_1=CH_2Ph

SMe_2 and this would also have ramifications for the reduction regioselectivity profile in THF.

To further investigate this solvent-dependent regioselectivity, the more subtle case of the secondary, secondary vicinal diol 2,3-heptanediol was studied, (Scheme III). The cis and trans ketals **50a** and **50b**, prepared from the diol with pentan-3-one, were individually reduced with the reagent combination in THF and then in CH_2Cl_2, and the isomer ratios are reported in Table VI.

In this case product isomer ratios were determined by integration of the ^1H NMR signals for H-2 and H-3 of the secondary alcohols for the cis and the acetates for the trans. In the former, the ratios were corroborated satisfactorily by GC–MS data. The results indicate that in CH_2Cl_2 the pathway followed is predominantly via the intimate ion pair involving silylation at the C-3 oxygen in whch C–O bond perturbation is steric-strain relief driven. Conversely, in THF, the preferred reaction pathway involves silylation at the sterically more accessible C-2 oxygen which is sufficiently energetic to open to the intimate ion pair and beyond, faster than equilibrate to the silyloxonium ion involving the C-3 oxygen. Thus, the same solvent-dependent regioselectivity trends are observed as before.

Finally, to complete the dioxolane regioselectivity study, the glycerol derivative 2,2-dimethyl-4-[(benzyloxy)methyl]-1,3-dioxolane was reduced in both THF and in CH_2Cl_2, Scheme IV. The substrate was prepared by benzylation of 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane (solketal). Recently, Corcoran[18] has shown that high levels of regioselectivity may be obtained in the cleavage of chiral 2-substituted 3-(methoxymethyl)-1,3-dioxanes by appropriate choice of Lewis acid. The regioselectivity was rationalized on the basis that the oxygen proximal to the substituent is activated by the divalent Lewis acid $TiCl_4$ via chelation control whereas the distal oxygen is preferred for monovalent Lewis acids, e.g., BF_3·Et_2O, on steric grounds. In the present case the primary protected derivative **55** was anticipated as being the major product on the basis of the influence of the C-4 (benzyloxy)methyl substituent in destabilizing oxocarbenium ion character development between C-2 and O-3. Indeed, a 5:95 ratio of isomers **54:55** was obtained in CH_2Cl_2. In THF the ratio changed to 27:73 indicating the same trend as before, i.e., toward the secondary derivative compared to CH_2Cl_2. Varying the R_1 group to benzyl and the R group as H, benzyl, and TBDMS also resulted in predominant formation of the primary protected derivated **55** *via* influence of the oxygen in the C-4 substituent. As anticipated from the protecting group study (Table IV), the reduction of the TBDMS derivative resulted in loss of the silicon protecting group, Table VII.

Table VII. Reduction of Ketals 53a–d with BH_3·SMe_2/TMSOTf (2 Equiv Each)

entry	R	R_1	solvent	temp (°C)	ratio 54:55[a]	yield (%)
1	CH_2Ph	Me	CH_2Cl_2	−78 to −70	5:95	86
2	CH_2Ph	Me	THF	−78 to −30	27:73	69
3	CH_2Ph	CH_2Ph	CH_2Cl_2	−78 to −70	5:95	72
4	H	CH_2Ph	CH_2Cl_2	−78 to −15	only 55[c]	74
5	SitBuMe$_2$	CH_2Ph	CH_2Cl_2	−78	only 55[c] (R = H)[d]	88

[a] Ratio obtained from ^1H NMR. [b] Isolated yield after chromatography. [c] No evidence of isomer 54 from NMR spectrum. [d] Silyl protecting group was hydrolyzed under reaction conditions.

Conclusion

BH_3·SMe_2/TMSOTf is a potent reagent combination for ketal reduction displaying the first reported solvent-directed regioselectivity profile with unsymmetrical 1,3-dioxolanes. Yamamoto[2i] has recently shown that solvent has a marked effect on the stereoselectivity of reduction of a bicyclic ketal using DIBAH, but in his case the two oxygen atoms were equivalent and oxygen site selectivity was not an issue. The observed trends may be accommodated using the Denmark mechanistic spectrum for ketal ring opening in which the reaction course is governed by the relative kinetics of ketal C–O bond perturbation rather than the thermodynamics of the individual open oxocarbenium ions. Furthermore, the study points toward the development of more selective silylating agents for regioselective substitution reactions of unsymmetrical 1,3-dioxolanes. Further results on the application of the reagent to more complex systems will be reported in due course.

Experimental Section

General. Characterization of Compounds. All melting points (mp) were determined on a Reichert Jung hot stage microscope and are uncorrected. Infrared spectra were recorded in chloroform using a Perkin-Elmer 983 spectrophotometer. Routine proton nuclear magnetic resonance (^1H NMR) were

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recorded on a Varian EM 360 (60-MHz spectrometer) or a Bruker90 (90-MHz spectrometer). High-resolution proton (^{1}H NMR) and carbon (^{13}C NMR) spectra were recorded on a Varian VXR-200 (200.057 MHz and 50.31 MHz, respectively) in deuteriochloroform. The chemical shifts are given in ppm relative to the signal of tetramethylsilane. Mass spectra were recorded on a VG micromass 16F mass spectrometer (UCT) or at the mass spectrometry unit (Cape Technicon). Optical rotations were determined in chloroform solution at 20 °C with a Perkin-Elmer 141 polarimeter. The concentration c refers to g/100 mL. Microanalyses for C, H, and N were carried out using a Heraeus CHN-rapid combustion analyzer (UCT) or submitted to MATECH (CSIR, Pretoria). All reactions were monitored by thin-layer chromatography (TLC) using Merck TLC aluminum sheets, silica gel 60 F_{254}, layer thickness 0.2 mm. Ceric ammonium sulfate or anisaldehyde spray reagents were used for product relevation. Column chromatography was carried out on silica gel (Merck, silica gel 60, particle size 0.063–0.200 mm (70–230 mesh ASTM). The yields of products are given in the Tables. All nonaqueous reactions were carried out under a nitrogen atmosphere, and reagents were introduced using syringe techniques. The following compounds were prepared by known methods: 3,3-(ethylenedioxy)androst-5-en-17β-yl acetate (**13**),[19] 1,1-bis(phenylthio)-propane (**22**), the derivatives of 2-phenylethanol **38–46**, 2,2-dimethyl-4-phenyl-1,3-dioxolane (**47a**),[20] and 4-[(benzyloxy)-methyl]-2,2-dimethyl-1,3-dioxolane (**53**).[21]

Synthesis of Acetals/Ketals. Acetals and ketals were synthesized by one of the following methods. **Method A.** To a stirred solution of aldehyde/ketone in dry benzene were added diol (1.1–2 equiv) and p-TsOH (catalytic amount). The mixture was refluxed in a Dean-Stark apparatus for the azeotropic removal of water. The reaction was normally followed by TLC unless the R_f of the starting material coincided with the product. In this case the reaction was followed by NMR spectroscopy (60 MHz). Upon completion, the reaction was cooled to room temperature and poured into a saturated aqueous $NaHCO_3$ solution and the product extracted with a suitable solvent (CH_2Cl_2 or diethyl ether). The organic fractions were combined, dried over $MgSO_4$, and filtered, and the solvent was evaporated *in vacuo*. The products were purified by vacuum distillation, recrystallization, or column chromatography. **Method B.** The same as method A except no aqueous workup was used. The acid was destroyed by the addition of solid Na_2CO_3 and the product obtained by filtration and removal of the benzene *in vacuo*. The following acetals and ketals were synthesized using one of the aforementioned procedures.

2,2-Dibenzyl-1,3-dioxane (1): mp 63–65 °C (from methanol); ν_{max} ($CHCl_3$) 3005, 2960, 2870, 1605, 1100, and 740 cm^{-1}; ^{1}H NMR 1.69 (2H, quin, J = 5.7 Hz), 2.97 (4H, s), 4.05 (4H, t, J = 5.7 Hz), and 7.23 (10H, m); ^{13}C NMR 25.1, 40.3, 59.7, 100.4, 126.1, 127.8, 130.6, and 136.8; m/z 268 (M$^+$, 3), 210 (4), 177 (95), 119 (13), and 91 (100). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.6; H, 7.5. Found: C, 80.5; H, 7.3.

2,2-Dibenzyl-1,3-dioxolane (3):[10a] mp 62–64 °C, ν_{max} ($CHCl_3$) 3060, 2950, 1490, 1120, 1045, and 740 cm^{-1}; ^{1}H NMR 2.93 (4H, s), 3.43 (4H, s), and 7.26 (10H, m); ^{13}C NMR 44.7, 65.4, 110.8, 126.2, 127.7, 130.7, and 136.5; m/z 163 (M$^+$ – 91, 87), 91 (100), 83 (30), and 55 (32).

9-Methyl-1,5-dioxaspiro[5.5]undecane (6):[22] bp 61–64 °C (1 mmHg); ν_{max} ($CHCl_3$) 2950, 2870, 1445, 1370, and 1105 cm^{-1}; ^{1}H NMR 0.74 (3H, d, J = 6.2 Hz), 0.94–1.46 (7H, m), 1.53 (2H, m) 2.05 (2H, m), and 3.73 (4H, quin, J = 5.6 Hz); ^{13}C NMR 21.5, 25.6, 30.6, 31.8, 32.2, 58.8, 59.1, and 97.6; m/z 113 (M$^+$ – 57, 100), 103 (25), 97 (10), 83 (15), 69 (18), and 55 (38). Anal. Calcd for $C_{10}H_{18}O_2$: 70.05; 10.6. Found: C, 70.1; H, 10.3.

8-Methyl-1,4-dioxaspiro[4.5]decane (9):[22] bp 41–44 °C (1.0 mmHg) ν_{max} ($CHCl_3$) 2950, 2870, 1450, 1365, 1270, 1105, 935, and 660 cm^{-1}; ^{1}H NMR 0.91 (3H, d, J = 6.2 Hz), 1.12–1.77 (9H, m), and 3.92 (4H, s); ^{13}C NMR 21.5, 31.3, 32.1, 34.4, 63.9, 64.0, and 108.7; m/z 156 (M$^+$, 5), 113 (8), 105 (50), 99 (100), and 87 (20).

2,2-Dibenzyl-1,3-thioxane (17): mp 68–69 °C (methanol); ν_{max} ($CHCl_3$) 3065, 1605, 1450, 1205, 1080, and 700 cm^{-1}; ^{1}H NMR 1.79 (2H, m), 2.84 (2H, dd, J = 5.9 and 7.6 Hz), 3.10 (2H, d, J = 14.5 Hz), 3.29 (2H, d, J = 14.4 Hz), 4.08 (2H, t, J = 5.6 Hz), and 7.29 (10H, s); ^{13}C NMR 24.1, 24.7, 43.8, 61.8, 84.9, 126.5, 127.6, 130.8, and 136.6; m/z 193 (M$^+$ – 91, 95), 91 (100). Anal. Calcd for $C_{18}H_{20}Os$: C, 76.1; H, 7.0. Found: C, 75.6; H, 7.2.

(*S*)-3-Methoxy-17,17-(3-oxathian-2-yl)estra-1,3,5(10)-triene (19): mp 139–143 °C; $[\alpha]_D$ ($CHCl_3$) +54.7° (c = 1.00); ν_{max} ($CHCl_3$) 3015, 2945, 1605, 1495, 1215, 735, and 665 cm^{-1}; ^{1}H NMR 0.86 (3H, s), 1.26–2.42 (12H, m), 2.58–3.08 (5H, m), 3.77 (3H, s), 3.87–3.97 (2H, m), 6.62 (1H, d, J = 2.7 Hz), 6.70 (1H, dd, J = 2.7 and 8.6 Hz), and 7.22 (1H, d, J = 8.5 Hz); ^{13}C NMR 15.4, 24.3, 24.8, 26.3, 26.3, 27.9, 29.8, 30.0, 33.6, 39.1, 43.6, 47.8, 49.7, 55.2, 62.1, 93.0, 111.3, 126.3, 132.7, 137.9, and 157.2; m/z 358 (M$^+$, 43), 284 (18), 266 (46), and 129 (100). Anal. Calcd. for $C_{22}H_{30}O_2S$: C, 73.7; H, 8.4. Found: C, 73.6; H, 8.6.

(*R*)-3-Methoxy-17,17-(3-oxathian-2-yl)estra-1,3,5(10)-triene (20): mp 124–125 °C; $[\alpha]_D$($CHCl_3$) +1.3° (c = 1.00); ν_{max} ($CHCl_3$) 3015, 2940, 1605, 1495, 1215, 782, 734, and 665 cm^{-1}; ^{1}H NMR 0.91 (3H, s), 1.21–2.55 (13H, m), 2.78–3.05 (4H, m), 3.76 (3H, s), 3.79–4.2 (2H, m), 6.61 (1H, d, J = 2.7 Hz), 6.70 (1H, dd, J = 2.8 Hz, J = 8.5 Hz), and 7.19 (1H, d, J = 8.6 Hz); ^{13}C NMR 13.9, 23.2, 25.3, 25.9, 26.7, 27.4, 29.9, 34.2, 36.0, 39.3, 43.5, 48.5, 49.4, 55.2, 65.0, 95.5, 111.4, 113.7, 126.2, 132.5, 137.8, and 157.2; m/z 358 (M$^+$, 43), 284 (18), 266 (46), and 129 (100). Anal. Calcd for $C_{22}H_{30}O_2S$: C, 73.7; H, 8.4. Found: C, 73.4; H, 8.6.

2-(p-Methoxyphenyl)-1,3-dioxane (24): mp 39–42 °C; ν_{max} ($CHCl_3$) 2955, 1615, 1170, 1105, 1040, 790, and 755 cm^{-1}; ^{1}H NMR 1.44 (1H, d, J = 13.5 Hz), 2.23 (1H, m), 3.81 (3H, s), 3.99 (2H, t), 4.27 (2H, d), 5.48 (1H, s), 6.91 (2H, d, J = 8.8 Hz), and 7.43 (2H, d, J = 8.8 Hz); ^{13}C NMR 26.4, 55.9, 70.0, 102.1, 114.1, 127.8, 131.9, and 160.4; m/z 194 (M$^+$, 45), 193 (70), 163 (12), 135 (100), 108 (16), and 77 (25). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.0; H, 7.2. Found: C, 68.25; H, 7.1.

2-Phenyl-1,3-dioxane (27):[8b] mp 39–42 °C; ν_{max} ($CHCl_3$) 3005, 2975, 1600, 1450, 1145, 1105, 1025, 735, and 695 cm^{-1}; ^{1}H NMR 1.3 (1H, d, J = 11 Hz), 2.0 (1H, m), 3.6 (2H, m), 4.1 (2H, m), 5.3 (1H, s), and 7.1 (5H, m); m/z 164 (M$^+$, 60), 163 (92), 105 (100), 87 (28), and 77 (44).

2-(p-Nitrophenyl)-1,3-dioxane (30): mp 108–110 °C as yellow crystals from petroleum ether; ν_{max} ($CHCl_3$) 3005, 2975, 1600, 1490, 1275, 1145, 1105, 735, and 695 cm^{-1}; ^{1}H NMR 1.51 (1H, d, J = 13.6 Hz), 22.5 (1H, m), 4.03 (2H, t), 4.32 (2H, d), 5.59 (1H, s), 7.68 (2H, d), and 8.26 (2H, d); ^{13}C NMR 26.3, 68.0, 100.4, 123.9, 127.7, and 145.7; m/z 209 (M$^+$, 32), 208 (62), 150 (100), 107 (91), 105 (28), 104 (24), 87 (57), and 77 (65). Anal. Calcd for $C_{10}H_{11}NO_4$: C, 57.4; N, 6.7; H, 5.3. Found: C, 57.6; N, 6.6; H, 5.5.

Ethyl 2-allyl-3,3(1,3-propanedioxy)butanoate (32): bp 93–95 °C, 2.0 mmHg; ν_{max} ($CHCl_3$) 2980, 2875, 1725, 1640, and 1185 cm^{-1}; ^{1}H NMR 1.10 (3H, t, J = 7.2 Hz), 1.30 (3H, s), 1.53 (2H, quin, J = 5.6 Hz), 2.25 (2H, m), 3.05 (1H, dd, J = 3.7 and 11.2 Hz), 3.75 (4H, m), 4.00 (2H, q, J = 7.2 Hz), 4.82 (1H, m, J = 12.1 Hz), 4.87 (1H, m J = 18.8 Hz), and 5.60 (1H, m); ^{13}C NMR 13.8, 18.9, 24.8, 31.4, 50.5, 59.2, 59.3, 59.9, 98.9, 116.0, 135.3, and 171.7; m/z 213 (M$^+$ – 15, 12), 101 (100), 73 (12), and 43 (58). Anal. Calcd for $C_{12}H_{20}O_4$: 63.1; H, 8.8. Found: C, 63.0; H, 8.5.

2-Phenyl-2-(4-methyl-3-pentenyl)-1,3-dioxane (36): bp 117–124 °C, 1.0 mmHg; ν_{max} ($CHCl_3$) 2965, 2870, 1460, 1185, 1140, 1085, 970, and 705 cm^{-1}; ^{1}H NMR 1.14 (2H, m), 1.47 and 1.57 (6H, 2 × s), 1.70 (2H, m), 2.02 (2H, m), 3.81 (4H, m), 4.96 (1H, t, J = 7.1 Hz), and 7.37 (5H, m); ^{13}C NMR 17.4, 21.6, 25.4, 25.6, 44.5, 60.8, 101.5, 123.9, 127.1, 127.4, 128.2, 131.0, and 139.9 (C-4′); m/z 246 (M$^+$, 10), 187 (6), 169 (6), 163 (100), 105 (96), and 77 (34%); HRMS m/z calcd for $C_{16}H_{22}O_2$ (M$^+$) 246.1620, found 246.1604.

2,2-Diethyl-4-phenyl-1,3-dioxolane (47b): ν_{max} ($CHCl_3$) 2975, 2880, 1460, 1170, 1075, and 775 cm^{-1}; ^{1}H NMR 1.03 (6H, m), 1.77 (4H, m), 3.66 (1H, dd, J = 8.0 and 8.8 Hz), 4.30 (1H, dd, J = 6.1 and 8.0 Hz), 5.08 (1H, dd, J = 6.0 and 8.9 Hz), and 7.39 (5H, m); ^{13}C NMR 8.0, 29.5, 29.8, 71.9, 78.1, 113.4, 126.1, 127.9, 128.4, and 138.7; m/z 206 (M$^+$, 2), 205 (11), 177 (36), 105 (35), 91 (16), 77 (19) and 57 (100).

2,2-Dibenzyl-4-phenyl-1,3-dioxolane (47c): mp 75–78 °C; ν_{max} ($CHCl_3$) 3085, 2880, 1450, 1250, 1180, 765, and 695 cm^{-1}; ^{1}H NMR 3.06 (2H, s), 3.13 (2H, s), 3.25 (1H, dd, J = 7.7 and 9.3 Hz),

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4.01 (1H, dd, J = 6.0 and 7.6 Hz), 4.38 (1H, dd, J = 6.1 and 9.3 Hz), 6.94–7.00 (2H, m), and 7.20–7.42 (13H, m); ^{13}C NMR 15.6, 28.9, 78.6, 111.8, 126.5, 126.8, 127.9, 128.0, 128.2, 128.4, 130.9, 131.2, 136.5, 136.6, and 137.6; m/z 239 (M^+ – 91, 55), 119 (17), 91 (100), and 77 (5). Anal. Calcd for $C_{23}H_{22}O_2$: C, 83.6; H, 6.7. Found: C, 83.6; H, 6.7.

4-Butyl-2,2-Diethyl-1,3-dioxolane (47d): bp 44 °C, 0.5 mmHg, ν_{max} ($CHCl_3$) 2935, 2870, 1460, 1170, 1120, 1055, 925, and 770 cm^{-1}; ^{1}H NMR 0.84 and 0.85 (9H, 2 × t, J = 7.4 and 7.5 Hz), 1.16–1.70 (10H, m), 3.40 (1H, m), 4.00 (2H, m); ^{13}C NMR 7.9, 8.2, 13.9, 22.7, 28.0, 29.8, 30.0, 33.2, 70.2, 76.3, 112.3; m/z 157 (M^+ – 29, 30), 143 (38), 103 (10), 87 (82), 83 (51), 69 (49), 55 (46), and 43 (100); HRMS m/z calcd for $C_9H_{17}O_2$ (M^+ – C_2H_5) 157.1228, found 157.1216.

2,2-Dibenzyl-4-butyl-1,3-dioxolane (47e): mp 43–46 °C; ν_{max} ($CHCl_3$) 3060, 2930, 1490, 1125, 765, and 695 cm^{-1}; ^{1}H NMR 0.84 (3H, t, J = 6.8 Hz), 1.00–1.34 (6H, m), 2.77 (1H, t, J = 7.9 Hz), 2.93 (4H, s), 3.42 (1H, m), 3.65 (1H, dd, J = 5.9 and 7.2 Hz), and 7.3 (10H, m); ^{13}C NMR 14.0, 22.6, 27.9, 32.3, 45.1, 45.2, 70.5, 76.7, 110.8, 126.2, 127.5, 127.7, 130.7, 131.0, 136.5, and 136.6; m/z 219 (M^+ – 91, 100), 137 (12), 91 (90), 83 (50), 55 (40). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.3; H, 8.4. Found: C, 80.3; H, 8.4.

***trans*-4-Butyl-2,2-diethyl-5-methyl-1,3-dioxolane (50a)**: ν_{max} ($CHCl_3$) 2970, 2930, 2870, 1460, 1380, 1170, 1090, 940, and 735 cm^{-1}; ^{1}H NMR 0.86 (9H, m), 1.20 (3H, d, J = 5.9 Hz), (1.24–1.51, 6H, m), 1.58 (2H, q, J = 7.4 Hz), 1.59 (2H, q, J = 7.4 Hz), 3.45 (1H, m, J = 5.9 and 8.5 Hz), and 3.65 (1H, qd, J = 5.9 and 8.9 Hz); ^{13}C NMR 7.9, 8.0, 13.8, 17.5, 22.8, 28.2, 30.7, 30.8, 32.0, 77.1, 82.8, and 111.2; m/z 171 (M^+ – 29, 27), 97 (30), and 57 (100); HRMS m/z calcd for $C_{10}H_{19}O_2$ (M^+ – C_2H_5) 171.1380, found 171.1380.

***cis*-4-Butyl-2,2-diethyl-5-methyl-1,3-dioxolane (50b)**: ν_{max} ($CHCl_3$) 2965, 2935, 2875, 1460, 1375, 1175, 1080, 945, and 755 cm^{-1}; ^{1}H NMR 0.83 (9H, m), 1.04 (3H, d, J = 6.4 Hz), 1.18–1.44 (6H, m), 1.54 (4H, quin, J = 7.4 Hz), 3.95 (1H, m), and 4.16 (1H, quin, J = 6.4 Hz); ^{13}C NMR 8.0, 8.6, 13.9, 15.7, 22.7, 28.6, 29.1, 29.7, 30.1, 73.4, 77.7, and 110.8; m/z 171 (M^+ – 29, 5), 171 (45), 143 (2), 115 (8), 114 (9), 97 (35), 86 (13), 57 (100), and 55 (45); HRMS m/z calcd for $C_{10}H_{19}O_2$ (M^+ – C_2H_5) 171.1380, found 171.1373.

4-[(Benzyloxy)methyl]-2,2-dibenzyl-1,3-dioxolane (53b) was obtained by standard benzylation (BnBr, NaH, THF, $Bu_4N^+I^-$ cat.) of **53c** in 73% yield after chromatography: ^{1}H NMR 2.86 (1H, dd, J = 9.7 and 5.7 Hz), 2.95 (4H, s), 3.07 (2H, m), 3.61 (1H, dd, J = 7.5 and 6.3 Hz), 3.77 (1H, quintet, J = 6.2 Hz), 4.32 (1H, d, J = 12.2 Hz), 4.43 (1H, d, J = 12.3 Hz), and 7.25 (15H, m); ^{13}C NMR 44.9, 45.0, 68.0, 70.7, 73.2, 75.4, 111.9, 126.2, 126.2, 126.3, 127.6, 127.6, 128.3, 130.7, 131.0, 136.2, 136.5, and 137.8.

2,2-Dibenzyl-4-(hydroxymethyl)-1,3-dioxolane (53c) was obtained by transketalization of 4-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (solketal) by the following procedure: To a solution of solketal (10 g, 76 mmol) in CH_2Cl_2 (50 mL) at 0 °C were added pyridine (10 mL, 124 mmol) and acetic anhydride (10 mL, 106 mmol). After 15 h the reaction was quenched with a saturated solution of $NaHCO_3$ and a crude product obtained by standard workup using ethyl acetate and an acid wash to remove pyridine. After evaporation of solvent, dibenzyl ketone (15.9 g, 79 mmol) and *p*-TsOH (50 mg, cat.) were added, and the mixture was stirred at 40 °C under reduced pressure (20 mmHg) to remove acetone. A solution of KOH (5 g, 88 mmol) in methanol (50 mL) was then added to saponify the ester. After 3 h the mixture was poured into water and extracted with ethyl acetate to afford **53c** (8.2 g, 38%) after column chromatography: mp 52–57 °C; ^{1}H NMR 1.85 (1H, br s), 3.05 and 3.08 (4H, 2s), 3.20–3.83 (5H, m), and 7.25 (10H, m); ^{13}C NMR 44.5, 63.2, 68.0, 76.5, 111.6, 126.4, 127.7, 127.9, 128.1, 130.7, 131.1, 136.5, and 136.6. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.1; H, 7.0. Found: C, 76.1; H, 7.2.

4-[(*tert*-Butyldimethylsilyl)oxy]methyl]-2,2-dibenzyl-1,3-dioxolane (53d) was obtained by standard silylation (TBDMSCl, imidazole, DMF) of **53c** in 80% after chromatography: mp 31–32 °C; ^{1}H NMR –0.04 (3H, s), –0.03 (3H, s), 0.83 (9H, s), 2.90 (1H, m), 2.94 (2H, s), 2.97 (2H, s), 3.22–3.45 (2H, m), 3.68 (2H, m), and 7.27 (10H, m); ^{13}C NMR –5.5, 18.2, 25.8, 44.8, 63.6, 68.1, 76.9, 111.6, 126.3, 127.7, 127.9, 130.7, 131.1, 136.4, and 136.6. Anal. Calcd for $C_{24}H_{34}O_3Si$: C, 72.4; H, 8.5. Found: C, 72.5; H, 8.9.

General Procedure for Ketal Reduction with BH_3·SMe_2/TMSOTf. To a stirred solution of the substituted ketal/acetal (1 mmol) in a solvent (CH_2Cl_2 or THF) at –78 °C were added BH_3·SMe_2 (2 equiv) followed by TMSOTf (0.40 mL, 2 equiv). The reaction was left to warm until it had gone to completion (followed by TLC) before being quenched with a saturated solution of $NaHCO_3$ (5 mL). The reaction mixture was left to warm to room temperature before being poured into a saturated solution of $NaHCO_3$ (10 mL), and the products were extracted with CH_2Cl_2. The organic extracts were dried with $MgSO_4$, filtered, and evaporated to yield the product(s). In cases where acetylation was used for characterization purposes, the crude product was dissolved in CH_2Cl_2 (5 mL), and pyridine (1.0 mL, 12.4 mmol), acetic anhydride (1.0 mL, 10.6 mmol), and (dimethylamino)pyridine (20 mg) were added. After 15 h the acetylated product was isolated by addition of a saturated solution of $NaHCO_3$, and the products were extracted with CH_2Cl_2. The organic extracts were washed with 0.1 M HCl before being dried with $MgSO_4$, filtered, and evaporated to yield the product(s). The products were purified by column chromatography on silica gel.

The following products were obtained by this procedure:

3-(Dibenzylmethoxy)propan-1-ol (2): ν_{max} ($CHCl_3$) 3515, 3000, 2940, 2870, 1600, 1090, 780, and 700 cm^{-1}; ^{1}H NMR 1.64 (2H, quin, J = 5.7 Hz), 2.22 (1H, br s), 2.82 (4H, d, J = 6.4 Hz), 3.41 (2H, t, J = 5.7 Hz), 3.54 (2H, t, J = 5.6 Hz), 3.72 (1H, quin, J = 6.4), 7.25 (10H, m); ^{13}C NMR 32.1, 40.8, 61.1, 68.6, 82.6, 126.1, 128.2, 129.2, and 138.7; m/z 179 (M^+ – 91, 100), 121 (92), 105 (77), 103 (32), 91 (80), and 59 (51); HRMS m/z calcd for $C_{18}H_{22}O_2$ (M^+) 270.1620, found 270.1590.

2-(Dibenzylmethoxy)ethan-1-ol (4): ν_{max} ($CHCl_3$) 3555, 3000, 2920, 2870, 1600, 1495, 1450, 1370, 1245, 1100, 1045, 745, 700, and 665 cm^{-1}; ^{1}H NMR 1.59 (1H, br s), 2.79 (4H, d, J = 6.3 Hz), 3.36 (4H, m), 3.70 (1H, quin, J = 6.3 Hz), and 7.20 (10H, m); ^{13}C NMR 41.1, 61.7, 71.1, 82.8, 126.2, 128.3, 129.2, and 138.7; m/z 165 (M^+ – 91, 100), 121 (75), and 91 (42).

Dibenzylmethanol (5):[23] ^{1}H NMR 1.58 (1H, br s), 2.67 (2H, dd, J = 7.9 and 13.7 Hz), 2.80 (2H, dd, J = 4.9 and 13.6 Hz), 3.99 (1H, tt, J = 4.8 and 7.9 Hz), and 7.20 (10H, m); ^{13}C NMR 43.3, 73.6, 126.5, 128.5, 129.4, and 138.4.

3-[(*trans*-4-methylcyclohexyl]oxy]propan-1-ol (7): ν_{max} ($CHCl_3$) 3450, 2925, 1450, 1095, and 745 cm^{-1}; ^{1}H NMR 0.74 (3H, d, J = 5.8 Hz), 0.87 (2H, m), 1.00–1.38 (3H, m), 1.63 (2H, m), 1.72 (2H, quin, J = 5.7 Hz), 1.93 (2H, m), 2.79 (1H, br s), 3.10 (1H, tt, J = 10.7 and 4.2 Hz), 3.57 (2H, t, J = 5.7 Hz), 3.67 (2H, t, J = 5.7 Hz); ^{13}C NMR 21.8, 31.9, 32.1, 32.2, 33.2, 61.9, 67.1, 78.5; m/z 172 (M^+, 2), 115 (100), 113 (38), 97 (37), 59 (47), and 57 (67); HRMS m/z calcd $C_{10}H_{20}O_2$ (M^+) 172.1463, found 172.1442.

3-[(*cis*-4-Methylcyclohexyl)oxy]propan-1-ol (8): ν_{max} ($CHCl_3$) 3470, 2930, 1450, 1075, and 745 cm^{-1}; ^{1}H NMR 0.84 (3H, d, J = 5.9 Hz), 1.12–1.48 (7H, m), 1.76 (2H, m), 1.79 (2H, quin, J = 5.5 Hz), 2.90 (1H, br s), 3.45 (1H, m), 3.57 (2H, t, J = 5.5 Hz), 3.75 (2H, t, J = 5.5 Hz); ^{13}C NMR 21.9, 29.3, 30.9, 31.5, 32.0, 63.0, 67.9, 74.5.

2-[(*trans*-4-Methylcyclohexyl)oxy]ethan-1-ol (10): ν_{max} ($CHCl_3$) 3580, 2925, 2860, 1455, 1205, 1110, 890, and 725 cm^{-1}; ^{1}H NMR 0.85 (3H, t, J = 6.4 Hz), 0.88–2.06 (9H, m), 2.24 (1H, br.s.), 3.19 (1H, tt, J = 4.2 and 10.8 Hz), 3.54 (2H, m), and 3.68 (2H, m); ^{13}C NMR 22.0, 32.1, 32.3, 33.3, 62.1, 69.0, and 78.7; HRMS m/z calcd for $C_9H_{18}O_2$ (M^+) 158.1307, found 158.1336.

2-[(*cis*-4-Methylcyclohexyl)oxy]ethan-1-ol (11): ν_{max} ($CHCl_3$) 3445, 2930, 1450, 1110, 890, and 725 cm^{-1}; ^{1}H NMR 0.88 (3H, t, J = 5.9 Hz), 1.20–1.90 (10H, m), 3.52 (3H, m), and 3.71 (3H, m); ^{13}C NMR 21.9, 29.4, 31.4, 62.2, 68.7, and 74.5; m/z 158 (M^+, 2), 101 (36), 97 (65), 96 (25), 81 (11), 57 (65), 55 (100), and 45 (40); HRMS m/z calcd for $C_9H_{18}O_2$ (M^+) 158.1307, found 158.1300.

1,2-Bis[(*trans*-4-methylcyclohexyl)oxy]ethane (12): ν_{max} ($CHCl_3$) 2995, 2930, 2865, 1455, 1350, 1205, 1095, 730 and 665 cm^{-1}; ^{1}H NMR 0.87 (6H, d, J = 6.4 Hz), 0.94–2.01 (16H, m), 3.20 (2H, tt, J = 4.2 and 10.7 Hz), and 3.59 (4H, s); ^{13}C NMR 22.8, 32.8, 33.0, 34.2, 68.3, and 79.4. Anal. Calcd for $C_{16}H_{30}O_2$: C, 75.6; H, 11.8. Found: C, 75.0; H, 11.5.

(23) Ivanov, K.; Vasilev, G. *C. R. Acad. Bulg, Sci.* **1956**, *9*(4), 61–4.

3-β-(2-Hydroxyethoxy)androst-5(6)-en-17β-yl acetate (14): $[\alpha]_D = -55.3°$ ($c = 0.988$); ν_{max} ($CHCl_3$) 3585, 2940, 1725, 1665, 1625, 1255, 1110, 1045, and 1035 cm^{-1}; ^1H NMR 0.68 (3H, s), 0.89 (3H, s), 0.78–2.32 (19H, m), 1.91 (3H, s), 2.68 (1H, br s); 3.08 (1H, tt, $J = 11.1$ and $J = 4.1$ Hz), 3.45 (2H, m), 3.58 (2H, m), 4.47 (1H, dd, $J = 9.0$ and 7.6 Hz), and 5.22 (1H, m); ^{13}C NMR 11.6, 19.1, 20.3, 20.8, 23.3, 27.2, 28.1, 31.2, 31.4, 36.5, 36.6, 36.9, 38.8, 42.1, 49.9, 50.8, 61.7, 68.9, 79.0, 82.5, 121.0, 140.5, and 170.9; m/z 315 ($M^+ - 62$, 22) and 314 (100). Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.4; H, 9.6. Found: C, 73.1; H, 9.65.

3-α-(2-Hydroxyethoxy)androst-5(6)-en-17β-yl acetate (15): ^1H NMR 0.74 (3H, s), 0.91 (3H, s), 1.00–2.32 (19H, m), 2.00 (3H, s), 3.45 (2H, m), 3.50–3.73 (4H, m), 4.55 (1H, m), and 5.31 (1H, m).

1,2-Bis[(17β-acetoxyandrost-5-en-3β-yl)oxy]ethane (16) (major diastereomer): mp 142–147 °C, ν_{max} ($CHCl_3$) 2935, 2855, 1720, 1370, 1255, 1205, 1030, 780, and 730 cm^{-1}; ^1H NMR, 0.76 (6H, s), 0.96 (6H, s), 1.00–2.40 (38H, m), 1.99 (6H, s), 2.00 (3H, s), 3.15 (2H, m), 3.57 (4H, s), 4.56 (2H, m), and 5.30 (2H, dd); m/z 690 (M^+, 1), 346 (28), 316 (81), 277 (100), 256 (83), 99 (95), and 43 (80); HRMS m/z calcd for $C_{44}H_{66}O_6$ (M^+) 690.4849, found 690.4862.

3-[(Dibenzylmethyl)thio]propan-1-ol (18): ν_{max} ($CHCl_3$) 3620, 3450, 3000, 2935, 1600, 1235, 1030, 730, and 700 cm^{-1}; ^1H NMR 1.46 (1H, br s), 1.64 (2H, quin, $J = 6.5$ Hz), 2.40 (2H, t, $J = 7.0$ Hz), 2.95 (5H, m), 3.54 (2H, t, $J = 6.0$ Hz), and 7.25 (10H, m); ^{13}C NMR 28.1, 31.9, 41.9, 49.4, 61.6, 126.3, 128.2, 129.2, and 139.4; m/z 286 (M^+, 16), 195 (64), 151 (26), 137 (43), 135 (26), 121 (48), 105 (82), and 91 (100).

3-Methoxyestra-1,3,5(10)-triene-17β-thiol S-(hydroxypropyl) ether (21): ν_{max} ($CHCl_3$) 3410, 2995, 1605, 1570, 1235, 1035, 900, and 740 cm^{-1}; ^1H NMR 0.77 (3H, s), 1.21–2.38 (17H, m), 2.66 (1H, t, $J = 9.3$ Hz), 2.68 (2H, t, $J = 7.0$ Hz), 2.83 (1H, m), 3.76 (2H, t, $J = 6.0$ Hz), 3.77 (3H, s), 6.63 (1H, d, $J = 2.7$ Hz), 6.70 (1H, dd, $J = 2.9$ and 8.5 Hz), and 7.20 (1H, d, $J = 8.3$ Hz); ^{13}C NMR 13.4, 24.3, 26.5, 27.7, 29.3, 29.9, 31.1, 32.6, 37.7, 39.3, 43.9, 44.5, 53.7, 56.6, 55.2, 62.0, 111.3, 113.7, 126.2, 132.4, 137.7, and 157.2; m/z 360 (M^+, 80), 301 (32), 227 (67), 137 (87), 121 (100), 57 (43); HRMS m/z calcd for $C_{22}H_{32}O_2S$ (M^+) 360.2123, found 360.2151.

1-(Phenylthio)propane (23):[24] ^1H NMR 1.02 (3H, t, $J = 7.3$ Hz), 1.67 (2H, sextet, $J = 7.3$ Hz), 2.89 (2H, t, $J = 7.3$ Hz), and 7.10–7.37 (5H, m); ^{13}C NMR 13.5, 22.6, 35.7, 125.6, 128.7, 128.9, and 136.9; m/z 218 (42, PhSSPh), 152 (M^+, 68), 123 (46), 110 (100), 109 (42), and 43 (30).

1-[(p-Methoxybenzyl)oxy]-3-propanol (25): ν_{max} ($CHCl_3$) 3485, 3000, 2935, 1610, 1245, 1170, 765, and 745 cm^{-1}; ^1H NMR 1.82 (2H, quin, $J = 5.8$ Hz), 2.47 (1H, s), 3.60 (2H, t, $J = 5.9$ Hz), 3.73 (2H, t, $J = 5.8$ Hz), 3.78 (3H, s), 4.43 (2H, s) 6.86 (2H, d, $J = 8.8$ Hz), and 7.24 (2H, d, $J = 8.8$, Hz); ^{13}C NMR 32.1, 55.2, 61.5, 68.8, 72.8, 113.8, 129.1, 130.1, and 159.1; m/z 197 (2), 196 (M^+, 19), 137 (75), and 121 (100).

1,3-Bis[(p-methoxybenzyl)oxy]propane (26): ν_{max} ($CHCl_3$) 3010, 2950, 2860, 1610, 1585, 1245, 1085, 845, and 730 cm^{-1}; ^1H NMR 1.84 (2H, quin, $J = 6.3$ Hz), 3.49 (4H, t, $J = 6.3$ Hz), 3.73 (6H, s), 4.36 (4H, s), 6.81 (4H, d, $J = 8.6$ Hz), 7.18 (4H, d, $J = 8.6$ Hz); ^{13}C NMR 30.2, 55.2, 67.1, 72.6, 113.7, 129.1, 130.6, and 159.0; m/z 316 (M^+, 5), 196 (18), 195 (100), 137 (70), and 121 (90).

1-(Benzyloxy)propan-3-ol (28): ν_{max} ($CHCl_3$) 3485, 3000, 2945, 1600, 1450, 1235, 741, and 695 cm^{-1}; ^1H NMR 1.83 (2H, quin, $J = 6.0$ Hz), 2.97 (1H, br s), 3.61 (2H, t, $J = 6.0$ Hz), 3.71 (2H, t, $J = 6.0$ Hz), 4.49 (2H, s), and 7.32 (5H, m); ^{13}C NMR 32.1, 60.8, 68.5, 73.0, 127.4, 128.1, and 137.9; m/z 166 (M^+, 8), 167 ($M^+ + 1$, 12), 107 (78), and 91 (100).

1,3-Bis(benzyloxy)propane 29:[25] ν_{max} ($CHCl_3$) 3065, 2950, 1600, 1450, 1205, 725, and 695 cm^{-1}; ^1H NMR 1.96 (2H, quin, $J = 6.3$ Hz), 3.62 (4H, t, $J = 6.3$ Hz), 4.53 (4H, s), and 7.35 (10H, m); ^{13}C NMR 30.3, 67.3, 73.0, 127.4, 127.6, and 138.5; m/z 165 ($M^+ - 91$, 70), 107 (72), and 91 (100).

1-[(p-Nitrobenzyl)oxy]propan-3-ol (31): ^1H NMR 1.95 (2H, quin, $J = 6.0$ Hz), 2.61 (1H, br s), 3.74 (2H, t, $J = 6.0$ Hz), 3.83 (2H, $J = 6.0$ Hz), 4.67 (2H, s), 7.54 (2H, d, $J = 8.9$ Hz), and 8.23 (2H, d, $J = 8.9$ Hz); ^{13}C NMR 32.9, 61.3, 69.7, 72.4, 124.1, 128.2, 146.5, and 147.8; m/z 212 ($M^+ + 1$, 8), 211 (M^+, 10), 152 (100), 136 (65), 107 (45), 106 (30), 89 (50), and 78 (60).

Ethyl 2-allyl-3-(3-hydroxypropoxy)butanoate (33) as a 3:2 mixture of diastereomers: ν_{max} ($CHCl_3$) 3510, 2980, 2870, 1720, 1640, and 1185 cm^{-1}; ^1H NMR 1.03 (3H, d, $J = 6.3$ Hz, H-4 minor), 1.04 (3H, d, $J = 6.2$ Hz, H-4 major), 1.11 (3H, t, $J = 7.2$ Hz, Eth-CH_3 both isomers), 1.62 (2H, m, H-2″ both isomers), 2.14 (2H, m, H-1′ major), 2.24 (2H, m, H-1′ minor), 2.40 (1H, m, H-2 both isomers), 2.57 (1H, br s, O-H minor), 2.90 (1H, br s, O-H major), 3.37 (2H, m, H-1″ both isomers), 3.54 (3H, m, H-3 and H-3″, both isomers), 3.99 (2H, q, $J = 7.2$ Hz, Eth-CH_2 minor), 4.00 (2H, q, $J = 7.2$ Hz, Eth-CH_2 major), 4.86 (1H, m, $J = 8.5$ Hz, H-3′ trans both isomers), 4.92 (1 H, m, $J = 17.1$ Hz, H-3′ cis both isomers), 5.60 (1H, m, H-2′ both isomers); ^{13}C NMR major isomer 14.0, 16.6, 32.2, 32.4, 51.7, 60.1, 60.6, 67.2, 76.3, 116.6, 134.7, and 173.7; minor isomer 14.0, 16.8, 32.1, 32.5, 50.9, 60.1, 60.7, 67.2, 75.8, 116.3, 135.2, and 173.2; m/z 215 ($M^+ - 15$, 0.2), 189 (2), 156 (7), 143 (5), 128 (25), 115 (29), 103 (74), 87 (18) and 59 (100); HRMS m/z calcd for $C_{12}H_{22}O_4$(M^+) 230.1518, found 230.1487.

Ethyl 2-(3-hydroxypropyl)-3,3-(1,3-propanedioxy)butanoate (34): ν_{max} ($CHCl_3$) 3616, 2960, 2875, 1720, 1245, 1145, and 1055 cm^{-1}; ^1H NMR 1.16 (3H, t, $J = 7.1$ Hz), 1.34 (3H, s), 1.38–1.70 (6H, m), 2.38 (1H, br s), 3.01 (1H, dd, $J = 3.8$ and 10.7 Hz), 3.51 (2H, t, $J = 6.4$ Hz), 3.78 (3H, m), 3.93 (1H, m), and 4.07 (2H, q, $J = 7.1$ Hz); ^{13}C NMR 14.1, 18.8, 23.6, 24.9, 30.8, 51.1, 59.4, 59.5, 60.3, 62.1, 99.3, and 172.8; m/z 245 ($M^+ - 1$, 0.5), 231 (4), 173 (5), 127 (6), 101 (100), and 73 (10). Anal. Calcd for $C_{12}H_{22}O_5$: C, 58.5; H, 9.0. Found: C, 58.3; H, 8.6.

Ethyl 2-(3-hydroxypropyl)-3-(3-hydroxypropoxy)butanoate (35) as a mixture of diastereomers: ν_{max} ($CHCl_3$) 3530, 2935, 1730, 1180, and 740 cm^{-1}; ^1H NMR 1.13 (3H, d, $J = 6.2$ Hz), 1.23 (3H, t, $J = 7.1$ Hz), 1.41–1.83 (5H, m), 2.46 (3H, m), 3.33–3.77 (8H, m), and 4.12 (2H, q, $J = 7.0$ Hz); ^{13}C NMR of major diastereomer 14.3, 16.9, 24.3, 30.4, 32.2, 51.8, 60.5, 61.2, 62.1, 67.6 77.0, and 174.7; m/z 248 (M^+, 1), 145 ($M^+ - 105$, 30), 103 (75), 59 (100); HRMS m/z calcd for $C_{12}H_{24}O_5$ (M^+) 248.1624, found 248.1660.

1-(3-Hydroxypropoxy)-5-methyl-1-phenylhexan-4-ol (37): 1:1 mixture of diastereomers; ν_{max} ($CHCl_3$) 3435, 3065, 3000, 2870, 1725, 1245, 730, and 660 cm^{-1}; ^1H NMR 0.83 (3H, d, $J = 6.7$ Hz, H-6 or 5-Me), 0.84 (3H, d, $J = 6.9$ Hz, H-6 or 5-Me), 1.20–1.98 (7H, m, H-5, H-2, H-3, H-2′), 2.05 (2H, br s, –OH), 3.30 (1H, m, H-4), 3.42 (2H, m, H-1′), 3.68 (2H, m, H-3′), 4.20 (1H, m, H-1), 7.24 (5H, m, Ph-H); ^{13}C mixture of diastereomers 17.2, 17.3, 18.7, 30.2, 30.5, 32.1, 33.4, 33.5, 34.6, 34.9, 61.2, 67.3, 76.4, 76.5, 82.8, 82.9, 126.4, 127.5, 128.4, and 142.3; m/z 207 ($M^+ - 59$, 11), 189 (3), 165 (100), and 107 (76); HRMS m/z calcd for $C_{10}H_{13}O_2$ ($M^+ - C_6H_{13}O$) 165.0915, found 165.0899.

2-Acetoxy-1-isopropoxy-1-phenylethane (48a): ^1H NMR 1.12 (3H, d, $J = 6.3$ Hz), 1.17 (3H, d, $J = 6.0$ Hz), 2.06 (3H, s), 3.56 (1H, septet, $J = 6.1$ Hz), 4.15 (2H, m), 4.63 (1H, dd, $J = 4.5$ and 7.5 Hz), and 7.34 (5H, m); ^{13}C NMR 21.0, 21.3, 23.3, 68.3, 69.9, 77.0, 126.8, 127.9, 128.4, 137.9, and 170.1: HRMS m/z calcd for $C_{10}H_{13}O$ ($M^+ - C_3H_5O_2$) 149.0966, found 149.0973.

1-Acetoxy-2-isopropoxy-1-phenylethane (49a): ^1H NMR 1.13 (3H, d, $J = 6.1$ Hz), 1.14 (3H, d, $J = 6.1$ Hz), 2.09 (3H, s), 3.51–3.75 (3H, m), 5.91 (1H, dd, $J = 4.3$ and 7.8 Hz), and 7.34 (5H, m); ^{13}C NMR 21.3, 22.0, 22.1, 71.0, 72.2, 75.0, 126.7, 128.1, 128.4, 137.9, and 170.1; HRMS m/z calcd for $C_{11}H_{14}O$ ($M^+ - CH_3COOH$) 162.1045, found 162.1025.

2-Acetoxy-1-(3-pentoxy)-1-phenylethane (48b): ^1H NMR 0.77 (3H, t, $J = 7.5$ Hz), 0.93 (3H, t, $J = 7.4$ Hz), 1.33–1.74 (4H, m), 2.04 (3H, s), 3.19 (1H, quin), 4.18 (2H, m), 4.61 (1H, dd, $J = 5.5$ and 6.8 Hz), and 7.34 (5H, m); ^{13}C NMR 8.7, 10.0, 20.9, 24.9, 26.5, 68.2, 77.4, 79.8, 127.1, 128.0, 128.3, 139.4, 170.7; m/z 177 ($M^+ - 73$, 29), 43 (100); HRMS m/z calcd for $C_{12}H_{17}O$ ($M^+ - C_3H_5O_2$) 177.1279, found 177.1261.

1-Acetoxy-2-(3-pentoxy)-1-phenylethane (49b): ^1H NMR 0.77 (3H, t, $J = 7.5$ Hz), 0.93 (3H, t, $J = 7.4$ Hz), 1.35–1.72 (4H, m), 2.08 (3H, s), 3.17 (1H, quintet, $J = 5.8$ Hz), 3.64 (1H, dd, $J = 4.4$ and 10.8 Hz), 3.72 (1H, dd, $J = 7.7$ and 10.8 Hz), 5.93 (1H, dd, $J = 4.4$ and 7.7 Hz), and 7.34 (5H, m); m/z 190 ($M^+ - 60$, 4), 43 (100).

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2-Acetoxy-1-(dibenzylmethoxy)-1-phenylethane (48c): ^{1}H NMR 2.07 (3H, s), 2.70–2.95 (4H, m), 3.80 (1H, quin, J = 5.9 Hz), 4.12 (1H, d, J = 4.9 Hz), 4.14 (1H, d, J = 6.9 Hz), 4.60 (1H, dd, J = 4.9 and 6.7 Hz) and 7–7.4 (15H, m); ^{13}C NMR 21.2, 40.0, 40.7, 67.9, 74.9, 82.9, 126.2, 126.3, 126.8, 128.4, 129.7, 138.9, and 170.1.

1-Acetoxy-2-(dibenzylmethoxy)-1-phenylethane (49c): ^{1}H NMR 2.06 (3H, s), 2.70–2.95 (4H, m), 3.55 (1H, dd, J = 4.2 and 10.5 Hz), 3.68 (1H, dd, J = 7.6 and 10.5 Hz), 3.80 (1H, quin, J = 5.9 Hz), 5.85 (1H, dd, J = 4.1 and 7.4 Hz), and 7.00–7.33 (15H, m); ^{13}C NMR 21.0, 40.6, 41.4, 72.6, 78.0, 79.7, 126.2, 126.3, 126.8, 128.4, 129.7, 138.9, and 170.8.

2-Acetoxy-1-(3-pentoxy)hexane (48d): ^{1}H NMR 0.82 (9H, t, J = 7.3 Hz), 1.15–1.60 (10H, m), 1.98 (3H, s), 3.05 (1H, quin, J = 5.9 Hz), 3.44 (2H, m), 4.90 (1H, m).

1-Acetoxy-2-(3′-pentoxy)hexane (49d): ^{1}H NMR 0.84 (9H, t, J = 7.4 Hz), 1.18–1.53 (10H, m), 2.00 (3H, s), 3.18 (1H, quin, J = 5.7 Hz), 3.45 (1H, quin, J = 5.5 Hz), 3.98 (1H, d, J = 2.1 Hz), and 4.00 (1H, d, J = 1.4 Hz): ^{13}C NMR 9.4, 9.5, 13.8, 20.7, 22.7, 26.1, 26.2, 27.4, 32.0, 66.4, 74.9, 80.6, and 170.8; both regioisomers **48d** and **49d** ν_{max} ($CHCl_3$) 2935, 1740, 1240, 1095, and 745 cm^{-1}; m/z 201 (M^+ – 29, 1), 157 (26), 143 (37), 87 (70), 83 (35), 69 (29), 55 (29), and 43 (100); HRMS m/z calcd for $C_{11}H_{21}O_3$ ($M^+ - C_2H_5$) 201.1490, found 201.1515.

2-Acetoxy-1-(dibenzylmethoxy)hexane (48e): ^{1}H NMR 0.89 (3H, t, J = 7.3 Hz), 1.0–1.52 (6H, m), 2.00 (3H, s), 2.79 (4H, m), 3.36 (2H, d, J = 4.9 Hz), 3.72 (1H, quin), 4.81 (1H, quin, J = 6.0 Hz), and 7.26 (10H, m); ^{13}C NMR 13.9, 21.1, 22.5, 27.3, 30.4, 40.6, 70.5, 73.0, 82.6, 125.9, 128.1, 129.3, 138.8, and 170.3; m/z 263 (M^+ – 91, 6), 143 (73), 83 (39), 55 (32), 43 (100).

1-Acetoxy-2-(dibenzylmethoxy)hexane (49e): ^{1}H NMR 0.89 (3H, t, J = 7.3 Hz), 1.05–1.52 (6H, m), 2.00 (3H, s), 2.79 (4H, m), 3.42 (1H, m), 3.85 (1H, quin), 3.85 (2H, d, J = 5.0 Hz), and 7.26 (10H, m); ^{13}C NMR 13.9, 20.8, 22.7, 27.1, 31.7, 41.2, 66.1, 75.9, 81.5, 125.9, 128.1, 129.3, 138.7, and 170.3.

(±)-2(*R*)-Acetoxy-3(*R*)-(3-pentoxy)heptane (51a): ν_{max} ($CHCl_3$) 2955, 2860, 1740, 1455, 1070, and 960 cm^{-1}; ^{1}H NMR 0.87 (9H, m), 1.18 (3H, d, J = 6.5 Hz), 1.21–1.67 (10H, m), 2.02 (3H, s), 3.20 (1H, quin, J = 5.8 Hz), 3.26 (1H, m), and 4.97 (1H, dq, J = 2.9, 6.5 Hz); ^{13}C NMR 9.4, 10.0, 14.0, 14.7, 21.4, 23.0, 26.1, 26.2, 27.9, 29.6, 70.9, 77.7, 80.8, and 170.5.

(±)-3(*R*)-Acetoxy-2(*R*)-(3-pentoxy)heptane (52a): ^{1}H NMR 0.87 (9H, m), 1.06 (3H, d, J = 6.4 Hz), 1.21–1.67 (10H, m), 2.05 (3H, s), 3.20 (1H, quin, J 5.8), 3.50 (1H, m), and 4.85 (1H, m); ^{13}C NMR 9.7, 9.8, 14.0, 16.1, 21.3, 22.7, 26.4, 26.4, 27.9, 28.8, 73.4, 76.0, 80.6, and 170.8.

Unacetylated 51a and 52a: m/z 173 (M^+ – 29, 4), 157 (42), 87 (100), 71 (76), 55 (31), and 43 (72); HRMS m/z calcd for $C_{10}H_{21}O_2$ ($M^+ - C_2H_5$) 173.1541, found 173.1536.

(±)-3(*R*)-(3-pentoxy)heptan-2(*S*)-ol (51b): ν_{max}, 3550, 2960, 1455, 1105, and 980 cm^{-1}; ^{1}H NMR 0.82–0.94 (9H, m), 1.10 (3H, d, J = 6.5 Hz), 1.23–1.55 (10H, m), 2.17 (1H, br s), 3.21 (2H, m), and 3.88 (1H, dq, J = 3.0 and 6.5 Hz); ^{13}C NMR 9.4, 9.8, 14.0, 17.4, 23.0, 26.1, 26.1, 28.0, 28.6, 68.0, 79.9, and 80.2; m/z 173 (M^+ – 29, 1), 157 (21), 87 (100), 71 (25), and 55 (24).

(±)-2(*S*)-(3-Pentoxy)heptan-3(*R*)-ol (52b): ^{1}H NMR 0.82–0.94 (9H, m), 1.05 (3H, d, J = 6.4 Hz), 1.23–1.55 (10H, m), 2.10 (1H, br s), 3.21 (1H, quin, J = 5.8 Hz), 3.41 (1H, dq, J = 3.0 and 6.5 Hz), and 3.64 (1H, ddd, J = 3.1, 4.7 and 7.7 Hz); ^{13}C NMR 9.6, 9.7, 13.7, 14.0, 22.8, 26.4, 26.5, 28.3, 31.8, 73.3, 75.6, and 79.8; m/z 173 (M^+ – 29, 3), 115 (65), 97 (31), 87 (10), 71 (100), 69 (34), 55 (25); HRMS m/z calcd for $C_{10}H_{21}O_2$ ($M^+ - C_2H_5$) 173.1541, found 173.1527.

Both regioisomers **51b** and **52b**: ν_{max} ($CHCl_3$) 3550, 2960, 1455, 1105, and 980 cm^{-1}.

1-Acetoxy-3-(benzyloxy)-2-isopropoxypropane (54a): ^{1}H NMR 1.12 (6H, d, J = 6.3 Hz), 2.01 (3H, s), 3.45–3.64 (3H, m), 3.72 (1H, m), 4.08 (1H, dd, J = 5.9 and 11.5 Hz), 4.19 (1H, dd, J = 4.5 and 11.4 Hz), 4.53 (2H, dd), and 7.31 (5H, m); ^{13}C NMR 20.7, 22.4, 22.5, 64.3, 70.0, 71.4, 73.2, 73.8, 127.4, 127.5, 128.1, 137.9, and 170.2.

2-Acetoxy-3-(benzyloxy)-1-isopropoxypropane (55a): ^{1}H NMR 1.12 (6H, d, J = 6.1 Hz), 2.07 (3H, s), 3.49–3.68 (5H, m), 4.54 (2H, dd), 5.12 (1H, quin, J = 2.6 Hz), and 7.32 (5H, m); ^{13}C NMR 21.1, 21.9, 21.9, 22.0, 66.3, 68.6, 71.8, 72.0, 73.1, 127.4, 128.1, 137.9, and 170.2; m/z 266 (M^+, 0.2), 159 (3), 91 (84), 58 (40), and 43 (100); HRMS m/z calcd for $C_{15}H_{22}O_4$ (M^+) 266.1581, found 266.1492.

3-(Benzyloxy)-1-(dibenzylmethoxy)-2-propanol (55b) together with traces of **3-(benzyloxy)-2-(dibenzylmethoxy)-1-propanol (54b)** (~95:5 ratio): ν_{max} ($CHCl_3$) 3550, 3065, 3000, 2920, 1600, 1360, 1095, 725, 700, and 660 cm^{-1}; ^{1}H NMR 2.12 (1H, br s), 2.76 (4H, d, J = 6.2 Hz), 3.21 (2H, d, J = 5.5 Hz), 3.30 (1H, dd, J = 6.0 and 9.7 Hz), 3.39 (1H, dd, J = 4.6 and 9.8 Hz), 3.69 (2H, m), 4.39 (2H, s), and 7.24 (15H, m); ^{13}C NMR 40.8, 69.4, 70.9, 71.0, 73.2, 83.0, 126.1, 127.4, 128.1, 128.2, 129.2, 137.9, and 138.5; HRMS m/z of the acetate, calcd for 327.1596 ($M^+ - C_6H_5CH_2$), found 327.1594.

1-(Dibenzylmethoxy)propane-2,3-diol (55c): ν_{max} 3680, 3560, 3015, 2920, 1600, 1215, 1055, 740, and 665 cm^{-1}; ^{1}H NMR 2.68 (2H, br s), 2.77 (4H, dd, J = 2.2 and 6.4 Hz), 3.34 (4H, m), 3.56 (1H, m), 3.72 (1H, quintet, J = 6.3 Hz), and 7.26 (10H, m); ^{13}C NMR 40.8, 63.5, 70.5, 71.3, 83.1, 126.1, 128.2, 129.1, 138.3, and 138.4; m/z 286 (M^+, 0.75), 287 (M^+ + 1, 0.55), 195 (100), 121 (78), and 75 (92); HRMS m/z calcd for $C_{11}H_{15}O_3$ ($M^+ - C_6H_5CH_2$) 195.1021, found 195.1021.

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Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra for all new compounds lacking combustion analysis (42 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.