Origin of the "β-Oxygen Effect" in the Barton Deoxygenation Reaction

David Crich,*,† Athelstan L. J. Beckwith,*,‡ Chen Chen,† Qingwei Yao,† Ian G. E. Davison,‡ Robert W. Longmore,‡ Cecilia Anaya de Parrodi,§ Leticia Quintero-Cortes,§ and Jesús Sandoval-Ramirez§

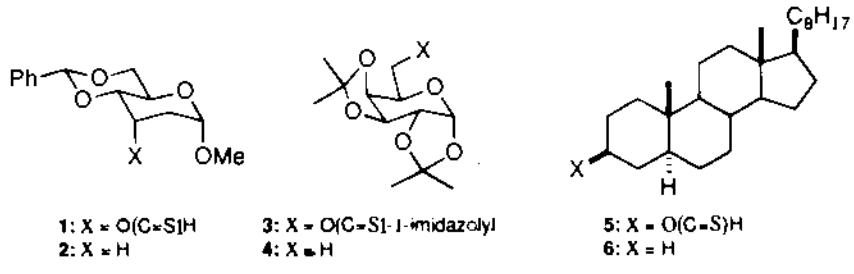
Contribution from the Department of Chemistry (M/C 111), University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061, Research School of Chemistry, The Australian National University, Canberra, ACT 0200, Australia, and Unidad de Investigación en Síntesis Orgánica, Facultad de Ciencias Químicas, Universidad Autónoma de Puebla, Puebla, México

Received March 9, 1995[⊗]

Abstract: Phololysis of *O*-neopenlyl *S*-lribulylslannyl dilhiocarbonate wilh hexaphenyl dislannane, and 4-melhoxyacetophenone as sensitizer, resulls in crossover of lhe slannyl groups. The reaclion of *O*-oclyl *O'*-(2-buloxyelhyl) lhiocarbonale wilh lribulyllin deuleride or lris(lrimelhylsilyl)silane and a radical initialor shows no significant preference for the cleavage of either C−O bond. Intermolecular compelilions belween *O*-oclyl *O'*-phenyl lhiocarbonale and *O*-(2-buloxyelhyl) *O'*-phenyl lhiocarbonale for a deficiency of slannane or silane also indicated no significanl preference for reaction of the β-oxygen-substituted substrate, leading lo lhe conclusion lhal in conformalionally unreslricled syslems lhere is no significanl β-oxygen effecl in lhe Barton deoxygenalion reaclion. Compelilion experiments between the *cis*- and *trans*-*O*-(4-phenylcyclohexyl) *S*-melhyl dithiocarbonates and lhe *cis*- and *trans*-O-(2-phenyl-1,3-dioxan-5-yl) *S*-methyl dilhiocarbonates for reaclion wilh lribulylslannane reveal lhal in every case lhe helerocyclic syslem is more reaclive. The *cis*-isomers of 4-phenylcyclohexyl *S*-methyl dithiocarbonate and *O*-(2-phenyl-1,3-dioxan-5-yl) *S*-methyl dithiocarbonate, with lheir axial xanthales, are more reaclive lhan the corresponding *trans*-isomers. Molecular mechanics calculalions suggesl lhal lhe grealer reaclivily of lhe *cis*-series wilh respecl lo lhe *trans* is due to lhe greater relief of slrain on fragmentation.

Introduction

In 1982 lhe Barton group published a series of observalions on the effect of β-oxygen substituents in radical deoxygenalion and deamination reaclions.[1,2] Their principal findings were lhal various thionocarbonyl esters and isonitriles bearing alkoxy and/or acyloxy groups in lhe β-position underwenl deoxygenalion and deamination, respeclively, on lrealmenl wilh lri-*n*-bulyllin hydride at lower temperatures than the corresponding unsubstituted species. For example, lhe lhionocarbonyl eslers **1** and **3** gave 29% and 31%, respectively, of the corresponding deoxy compounds **2** and **4** in loluene al reflux, whereas choleslanyl lhioformate (**5**) gave only 9% of cholestane (**6**) under the same condilions and only 24% in xylene al reflux.



1: X = O(C=S)H
2: X = H
3: X = O(C=S)-1-imidazolyl
4: X = H
5: X = O(C=S)H
6: X = H

The conclusion drawn from lhese sludies was lhat "β-bonded oxygen has a marked effecl in slabilising carbon radicals lhus permitling homolylic fission not seen olherwise". However,

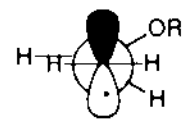


Figure 1. Prcferred conformation of β-alkoxyethyl radical.

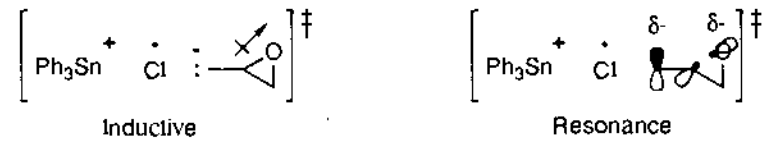


Figure 2. Inductive and resonance-stabilized polar transition states proposed by Gleicher.

as noted by Barton, ESR spectroscopic studies on β-alkoxyethyl radicals do not indicate stabilization by bridging and even suggest a preferred conformation in which the singly occupied p orbital is synclinal rather than periplanar to the β-oxygen bond (Figure 1).[3,4] More recently, Gleicher has published a related observation in which epichlorohydrin was reduced by triphenyltin hydride some 2.00 times faster than cyclohexyl chloride at 70 °C.[5] To rationalize this observation, Gleicher suggested both that a polar transition state for chlorine abstraction would be stabilized inductively by the β-oxygen bond (Figure 2) and also that the transition state might be stabilized by resonance delocalization of the developing negative charge into the β-C−O bond (Figure 2). The more rapid reduction of epichlorohydrin with respect to cyclohexyl chloride would therefore be due to

† University of Illinois at Chicago.
‡ Australian National University.
§ Universidad Autónoma de Puebla.
⊗ Abstract published in *Advance ACS Abstracts,* August 1, 1995.

(1) Barton, D. H. R.; Hartwig, W.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1982**, 447.
(2) In radical nomenclature the α-center is that bearing the singly occupied orbital and the β-center the adjacent one.
(3) Chen, K. S.; Kochi, J. K. *J. Am. Chem. Soc.* **1974**, *96*, 1383.
(4) (a) Beckwith, A. L. J.; Brumby, S.; Davison, I. G. E.; Duggan, P.; Longmore, R. N. *Book of Abstracts of the 6th Int. Symposium on Organic Free Radicals, Netherlands, Aug. 23−28*; Leiden University: Leiden, The Netherlands, 1992; p 344. (b) Beckwith, A. L. J. *Chem. Soc. Rev.* **1993**, *22*, 143.
(5) Krosley, K. W.; Gleicher, G. J.; Clapp, G. E. *J. Org. Chem.* **1992**, *57*, 840.

0002-7863/95/1517-8757$09.00/0

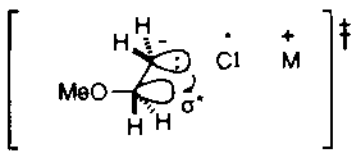


Figure 3. Polar transition state proposed by Roberts.

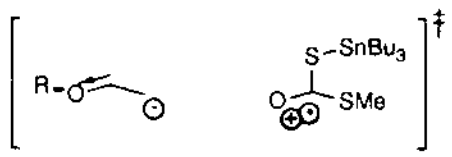
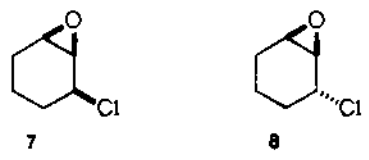


Figure 4. Polar transition state for the Barton–McCombie reaction proposed by Jenkins.

a lowering of the activation energy for the rate-determining abstraction step rather than to any stabilization of the eventual radical.

Roberts and Steel measured the relative rates of chlorine abstraction by both silyl and amineborinyl radicals from various alkyl chlorides, by the ESR method.[6] Like Gleicher, these authors found that chlorine atom abstraction was faster in the presence of β-oxygen bonds. They also noted that the rate acceleration was significantly more important when the abstracting radical was the more nucleophilic $Me_3N{\rightarrow}B(H)(Bu)^{\bullet}$ radical rather than the $Et_3Si^{\bullet}$ radical. Stabilization of a polar transition state for chlorine atom abstraction was again proposed to explain these observations. It was suggested that this stabilization might be attributed either to delocalization of the developing negative charge at the α-carbon into the σ^* orbital of the β-C–O bond (Figure 3) or simply to the inductive effect of the β-C–O bond. Evidently, the former possibility would tend to suggest that the β-oxygen effect should be at a maximum in chlorides in which the C–Cl and C–O bonds are locked in an antiperiplanar conformation, while the latter implies no such stereoelectronic component. In this respect it is noteworthy that Gleicher also reported[5] that *cis*-2-chloro-7-oxabicyclo[4.1.0]heptane (**7**) was approximately 2 times as reactive as its *trans*-isomer **8** toward triphenyltin hydride under the same conditions, thus pointing to a possible stereoelectronic component to the β-oxygen effect but one that is not in agreement with both his and Roberts' notion of delocalization of developing negative charge at the transition state into the σ^* orbital of the β-C–O bond.



While the work reported in this paper was in progress, Jenkins advanced a polar transition state for the Barton–McCombie reaction, similar to that put forward by Roberts for the reaction of alkyl chlorides with metalloid radicals, in order to explain the Barton β-oxygen effect (Figure 4).[7]

A somewhat different situation pertains for α,β-dialkoxy-substituted alkyl radicals. The α,β-dimethoxyethyl radical has been studied by ESR spectroscopy and found to exist in an eclipsed conformation in which the stabilizing interaction between the unpaired electron and the β-C–O bond is maximized (Figure 5).[8] This extended anomeric effect (Figure 6)[8,9] is responsible for the tetraacetylglucopyranos-1-yl radical adopting the $B_{2,5}$ conformation (Figure 7), while the corresponding mannopyranosyl radical retains the $^4C_1$ chair conformation.[9] This stabilization is reflected in the differing rates of chlorine atom abstraction by the tributylstannyl radical from tetraaceloxy-α-mannopyranosyl chloride and tetraaceloxy-α-glucopyranosyl chloride with the mannosyl chloride, in which the C–Cl and β-C–O bonds are already antiperiplanar, being more reactive by a factor of 7.8 in benzene at 80 °C.[9a] Interestingly, the existence of a reverse Perlin effect in ^{13}C-NMR spectroscopy of 1,3-dioxanes, attributed to the lengthening of C–H antiperiplanar to β-C–O bonds, has recently been demonstrated.[10]

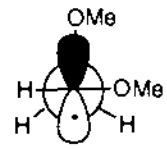


Figure 5. Preferred conformation of the α,β-dimethoxyethyl radical.

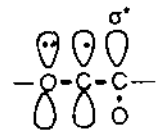


Figure 6. Extended anomeric effect in α,β-dialkoxy radicals.

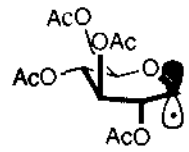


Figure 7. Conformation of the tetraacetylglucopyranosyl radical.

We present here the results of a study designed to probe the origin of the Barton β-oxygen effect by means of a series of competition experiments conducted with a number of both conformationally rigid and flexible thiocarbonyl esters.[11] Molecular mechanics calculations, which greatly facilitated interpretation of the experimental data, are also presented.

Results and Discussion

Thiocarbonyl esters were chosen as substrates for this study because (i) of their efficient reaction with tin hydrides,[12-14] (ii) their use would allow maximum approach to the original work of Barton,[1] and, importantly, (iii) the mechanism of their reaction, as opposed to that of isonitriles, with stannyl radicals is relatively well understood.[15] The accepted mechanism involves rapid, reversible addition of the stannyl radical to the thiocarbonyl group followed by slower fragmentation of the adduct radical with cleavage of the carbon oxygen bond (Scheme 1). Thus, the apparent rate constant for the formation of the

(6) (a) Roberts, B. P.; Steel, A. J. *Tetrahedron Lett.* **1993**, *34*, 5167. (b) Roberts, B. P.; Steel, A. J. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2411.

(7) Jenkins, I. D. *J. Chem. Soc., Chem. Commun.* **1994**, 1227.

(8) (a) Beckwith, A. L. J.; Brumby, S. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1801. (b) Dobbs, A. J.; Gilbert, B. C.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1972**, 786. (c) Gilbert, B. C.; Trenwith, M.; Dobbs, A. J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1772.

(9) (a) Dupuis, J.; Giese, B.; Rüegge, D.; Fischer, H.; Korth, H.-G.; Sustmann, R. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 896. (b) Korth, H. G.; Sustmann, R.; Dupuis, J.; Giese, B. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1453.

(10) Anderson, J. E.; Bloodworth, A. J.; Cai, J.; Davies, A. G.; Schiesser, C. H. *J. Chem. Soc., Perkin Trans. 2* **1993**, 601.

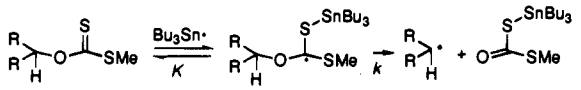
(11) Some of these results have been presented in preliminary form; see ref 4.

(12) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

(13) Crich, D.; Quintero, L. *Chem. Rev.* **1989**, *89*, 1413 and references therein.

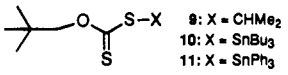
(14) There is an extensive literature[13] on the reactions of carbohydrate-based thiocarbonyl esters with tributyltin hydride under free radical conditions from which, in principle, it is possible to extract valuable information on any stereoelectronic effect due to β-oxygen bonds. The very thorough and comprehensive work of Stick and co-workers is particularly attractive in this light; see: (a) Copeland, C.; Stick, R. V. *Aust. J. Chem.* **1978**, *31*, 449. (b) Patroni, J. J.; Stick, R. V. *Aust. J. Chem.* **1979**, *32*, 411. (c) Conway, R. J.; Nagel, J. P.; Stick, R. V.; Tilbrook, D. M. G. *Aust. J. Chem.* **1985**, *38*, 939. (d) Fuller, T. S.; Stick, R. V. *Aust. J. Chem.* **1980**, *33*, 2509. Unfortunately, the widely differing steric environments encountered in the various carbohydrate series introduce considerable ambiguity into the interpretation of this body of data.

Scheme 1. Barton–McCombie Reaction

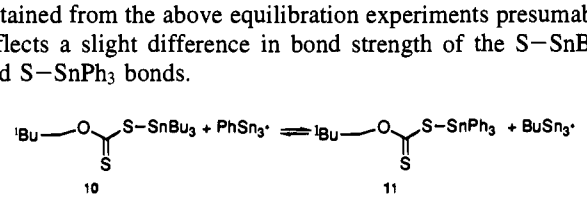


deoxygenated radical should be Kk, where K is the equilibrium constant and k is the rate constant for the carbon–oxygen bond scission. However, the close concordance of the results (*vide infra*) of experiments involving the use of Bu_3SnH or tms_3SiH as reagent and the concordance of the results of intermolecular competitions, in which the value of K may be important, with those of intramolecular competitions, in which the value of K is irrelevant, suggest that there is little variation in the value of K. Hence we conclude that any β-oxygen effect observed in the competition experiments can be taken to be mainly the result of perturbation of the transition state for cleavage of the scissile C–O bond in the adduct radical rather than of the reactivity of the thiocarbonyl bond.

The reversible addition of stannyl radicals to thiocarbonyl esters was a key factor in the choice of this system. Therefore, before proceeding with the proposed competition reactions, we resolved to establish this central point better. *O*-Neopentyl *S*-isopropyl xanthate (**9**), prepared in the standard manner, was allowed to react, with AIBN initiation, with a slight deficiency of both Bu_3SnH and Ph_3SnH to give the *S*-stannyl xanthates **10** and **11**, respectively.[16,17] By design, **10** and **11** prepared in this manner were contaminated with 5–10% of **9** but, importantly, not by unreacted stannane. Kugelrohr distillation removed the excess of **9** and provided essentially pure samples of the pungent, yellow oils **10** and **11** which were characterized by ^1H- and ^{13}C-NMR and UV–spectroscopy.

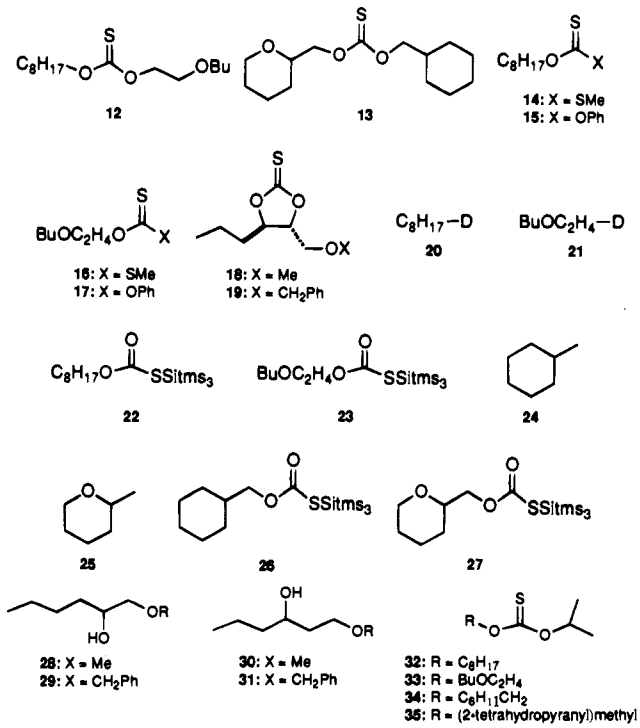


Photolysis of **10** with 0.5 equiv of hexaphenyldistannane and 4-methoxyacetophenone in benzene under conditions recommended by Neumann[18] for the generation of stannyl radicals resulted, after 50 h, in the formation of an 82:18 mixture of **10** and **11** as demonstrated by ^1H-NMR. Similarly, photolysis of **11** with 0.5 equiv of hexabutyldistannane under the same conditions gave a comparable 75:25 mixture of **10** and **11**. Comparable results were obtained when the equilibrations were conducted in benzene at reflux using Ph_3SnH and Bu_3SnH together with AIBN initiation as sources of stannyl radicals; however, the reaction mixtures were complicated by the formation of reduction products, and hence the photolytic procedure was preferred. The equilibrium of eq 1, and with it the reversibility of stannyl radical addition to thiocarbonyl esters, is therefore firmly established. The uneven ratio of **10** and **11** obtained from the above equilibration experiments presumably reflects a slight difference in bond strength of the S–$SnBu_3$ and S–$SnPh_3$ bonds.



A number of thionocarbonyl esters (**12**–**17**) of simple aliphatic alcohols and β-alkoxy alcohols, as well as two cyclic carbonates (**18**, **19**), were prepared by standard means to enable us to conduct a series of inter- and intramolecular competition reactions. With the exception of **18** and **19**, each of these substrates is derived from primary alcohols and, as reported by Barton for such substrates,[19] reacted only very sluggishly under typical Barton–McCombie conditions (benzene or toluene at reflux with Bu_3SnH and AIBN initiation). This problem was addressed in several different manners. Thus, some reactions were conducted at higher temperatures, either in *tert*-butylbenzene at reflux or in a sealed tube at 180 °C, in order to promote the fragmentation of the initial adduct radical. More efficient initiation using di-*tert*-butyl peroxide, with its longer half-life, was also successful. Finally, we reasoned that the poor reactivity of primary alkyl thiocarbonyl esters with stannanes is due to the ease of reversibility of stannyl radical addition to the thiocarbonyl group as compared to cleavage of the primary alkyl–oxygen bond in the adduct radical. This led to the conclusion that use of tris(trimethylsilyl)silane[20] in place of the stannane would be beneficial owing to the stronger S–Si bond. Gratifyingly, use of tms_3SiH did indeed lead to much cleaner reactions with good conversion even in benzene at reflux. The results of the various experiments with this series of compounds are presented in Table 1.

A variety of different analytical protocols were adopted. The high-temperature reduction of **12**, and that of **14** and **16**, was conducted with tributyltin deuteride,[21] as opposed to the hydride, which enabled direct measurement of the product ratio by ^2H-NMR. These reactions were also analyzed by GC. For the reactions conducted with tms_3SiH in benzene at reflux, results were determined by ^1H-NMR of the crude reaction mixtures either from the ratio of unreacted substrates or from that of the byproducts **22**, **23**, **26**, and **27**. Authentic samples of **22**, **23**, **26**, and **27** were prepared by reaction of an excess of tms_3SiH with **32**–**35**, respectively, to assist in the spectral analysis.



Inspection of Table 1, entries 1–6, reveals the abnormally high ratios for cleavage of the alkyl–O rather than β-alkoxyalkyl–O bond observed when the reaction mixture is analyzed by GC, as compared to analysis by a ^1H- or ^2H-NMR method. This prompts us to suggest that, although the instrument was

(15) (a) Barton, D. H. R.; Crich, D.; Löbberding, A.; Zard, S. Z. *Tetrahedron* **1986**, *42*, 2329. (b) Crich, D. *Tetrahedron Lett.* **1988**, *29*, 5805. (c) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1990**, *31*, 3991. (d) Barker, P. J.; Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1988**, 683. (e) Bachi, M. D.; Bosch, E. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1517. (f) Bachi, M. D.; Bosch, E.; Denenmark, D.; Girsh, D. *J. Org. Chem.* **1992**, *57*, 6803.

Table 1. Competition Reactions of Conformationally Flexible Thiocarbonyl Esters with $Bu_3SnD(H)$ and tms_3SiH

entry	substrates	initial ratio	T (°C)	reagent (equiv)[a]	Anal. method[b]	result	preferred cleavage
1a[c]	**12**		180[d]	Bu_3SnD (1)	A	**20:21** = 1.9:1	alkyl
1b[c]	**12**		180[d]	Bu_3SnD (1)	B	**20:21** = 1.1:1.0	none
2a[c]	**12**		120[e]	Bu_3SnD (1)	A	**20:21** = 1.3:1	alkyl
2b[c]	**12**		120[e]	Bu_3SnD (1)	B	**20:21** = 0.96:1	none
3	**12**		80[f]	tms_3SiH (1)	C	**22:23** = 1:1.1	alkyl
4	**13**		169[g]	Bu_3SnH (1)	A	**24:25** = 1.76:1	alkyl
5	**13**		80[f]	tms_3SiH (1)	C	**26:27** = 1:1	none
6a[c]	**14:16**	1:1.15	180[d]	Bu_3SnD (0.38)	A	**20:21** = 1.4:1	alkyl
6b[c]	**14:16**	1:1.15	180[d]	Bu_3SnD (0.38)	B	**20:21** = 0.8:1.0	β-alkoxyalkyl
7	**14:16**	1:1	80[f]	tms_3SiH (1)	D	**14:16** = 1.6:1	β-alkoxyalkyl
8	**15:17**	1:1	80[f]	tms_3SiH (1)	D	**15:17** = 1:1.2	alkyl
9	**18**		110[h]	Bu_3SnH (2)	E	**28:30** = 1.5:1	alkyl
10	**19**		80[f]	tms_3SiH (1)	F	**29:31** = 1:1.6	β-alkoxyalkyl

[a] For the intermolecular competitions, the number of equivalents refers to the sum of the two thiocarbonyl esters. [b] A, GC of products; B, ^{2}H-NMR of products; C, ^{1}H-NMR of Si-silyl thiocarbonates; D, ^{1}H-NMR of residual substrates; E, saponification and analysis of products by GC; F, mild acid hydrolysis and analysis by ^{1}H-NMR. [c] Same experimental run, analyzed by two methods. [d] Toluene in sealed tube with AIBN initiation at 180 °C. [e] Decane in sealed tube with di-*tert*-butyl peroxide initiation at 120 °C. [f] Benzene at reflux. [g] *tert*-Butylbenzene at reflux. [h] Toluene at reflux.

correctly calibrated, the GC data (entries 1a, 4, and 6a) should be treated with caution and the abnormally high ratios tentatively attributed to an artifact of the method, possibly decomposition in the injector port. The relatively good agreement between the data obtained by ^{2}H-NMR for experiments run at high temperature (entries 1b, 2b, and 6b) and those run at 80 °C with tms_3SiH and analyzed by ^{1}H-NMR (entries 3, 5, and 8), each of which shows only a very minor preference, if any, for cleavage of either bond, serves to dispel the notion of any β-oxygen effect in these simple, conformationally labile systems. For the same reason, the possibility that a competing Chugaev reaction[22] is skewing[23] the results obtained at high temperature can be set aside. Entry 7 of Table 1 indicates an apparent preference for cleavage of the β-alkoxyalkyl−O bond; however, inspection of the reaction mixture revealed the presence of substantial quantities of other, unidentified products. There exists therefore a significant possibility that this result is biased by the preferential loss of one of the substrates in an unanticipated side reaction. Recalling the clean reactions of **12** and **13** with tms_3SiH, we therefore prepared **15** and **17** and allowed them to compete for reaction with a deficiency of tms_3SiH. As is seen from Table 1, entry 8, this restored the pattern with a slight preference for consumption of the substrate lacking the β-oxygen bond. For the cyclic carbonate **18**, it was possible to employ conditions similar to those described originally by Barton and Subramanian for this type of substrate.[24] Again, direct GC analysis of the products revealed a significant preference for cleavage to give the alkyl radical (Table 1, entry 9). However, treatment of **19**, which differed from **18** only in the replacement of the methyl ether by a benzyl ether, with tms_3SiH in benzene at reflux gave the opposite result (Table 1, entry 10). The situation with the cyclic thionocarbonates is therefore not clear. In entry 10, an acidic workup was employed to destroy the intermediate *S*-silyl thiocarbonates, rather than the basic workup prescribed by Barton and Subramanian and used in entry 9. This difference in protocol was implemented when it was realized that the basic hydrolysis, applied to a reaction of **19** with Bu_3SnH, was incomplete even after stirring overnight at room temperature, whereas the acidic hydrolysis was much more efficient. Nevertheless, even incomplete base hydrolysis gave similar ratios to those reported in entry 10 (Table 1), and hence the difference between entries 9 and 10 is not a factor of the differing workup protocols.[25]

Next we turned to a series of more conformationally rigid probes (**36**−**39**). The 1,3-dioxan-5-ol system was selected for this study because it presented two identical β-oxygen bonds and so the possibility of amplification of any small effect on the limit of detection. Preparation of **36** and **37** from the precursor 4-phenylcyclohexanols was routine. The xanthates **38** and **39**, each having two β-oxygen bonds, were prepared from the corresponding alcohols **40** and **41**. Synthesis of the *cis*-alcohol **40** was straightforward, simply requiring heating of glycerol and benzaldehyde in toluene in a Dean−Stark apparatus with catalysis by *p*-toluenesulfonic acid followed by removal of solvent and recrystallization. For the obtention of diastereoisomerically pure **40**, this Dean−Stark procedure is superior to literature processes which give mixtures with **41** and the two isomeric dioxolanes.[26] The isolation of a pure sample of the less stable *trans*-isomer **41** was more problematic. In principle,[26] **41** was available by chromatography of the mother liquers from the crystallization of **41**, but in practice, we were never able to achieve a satisfactory separation owing to apparent epimerization on the column. Ultimately, **41** was oxidized to the known ketone **42**[27] by the Swern protocol then reduced with sodium borohydride. In accordance with the calculations of Houk,[28] an excellent ratio of 1:10 of **40**:**41** was obtained in this reduction.

(16) The cleavage of the C−S bond in **9**, on AIBN-initiated reaction with stannanes, was predictable on the basis of the earlier observation of the preferential stannane-mediated C−S bond cleavage in *O*-3β-cholestanyl *S*-isopropyl xanthate reported by Barton.[15a]

(17) For an alternative preparation, and radical reactions, of **11**, see: Boivin, J.; Camara, J.; Zard, S. Z. *J. Am. Chem. Soc.* **1992**, *114*, 7909.

(18) Harenda, M.; Junggebauer, J.; Lessmann, K.; Neumann, W. P.; Tews, H. *SynLett.* **1993**, 286.

(19) Barton, D. H. R.; Motherwell, W. B.; Stange, A. *Synthesis* **1981**, 743.

(20) (a) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1990**, *31*, 4681. (b) Ballestri, M.; Chatgilialoglu, C.; Clark, K. B.; Griller, D.; Giese, B.; Kopping, B. *J. Org. Chem.* **1991**, *56*, 678.

(21) Interestingly, in the reduction of **12**, and of **14** and **16**, in toluene at 180 °C by Bu_3SnD, benzylic deuteration of the solvent was evident in the ^{2}H-NMR, as observed from a change in the ratio of aromatic to methyl deuteriums from 5:3 to ca. 1:1.

(22) Nace, H. R. *Org. React.* **1962**, *12*, 57.

(23) It is reasonably well appreciated, at least for selenoxides, that pericyclic syn elimination toward an electronegative group such as an alkoxy group is substantially retarded; see: Reich, H. J.; Shah, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 3250.

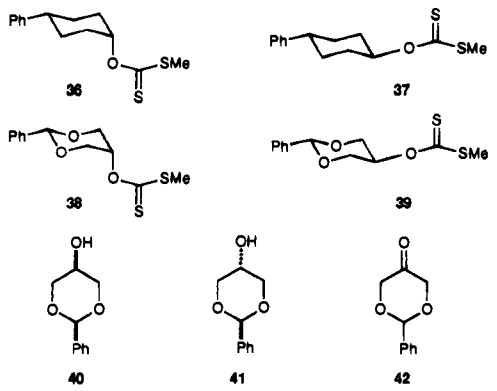
(24) Barton, D. H. R.; Subramanian, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1718.

(25) Unanticipated, seemingly contra-thermodynamic fragmentations of cyclic thionocarbonates have been observed previously and attributed, in one case, to greater relief of strain. (a) Redlich, H.; Sudau, W.; Paulsen, H. *Tetrahedron* **1985**, *41*, 4253. (b) Ziegler, F. E.; Zheng, Z. *J. Org. Chem.* **1990**, *55*, 1416.

(26) (a) Baggett, N.; Brimacombe, J. S.; Foster, A. B.; Stacey, M.; Whitten, D. H. *J. Chem. Soc.* **1960**, 2574. (b) Juaristi, E.; Antúnez, S. *Tetrahedron* **1992**, *48*, 5941.

(27) Chang, M. O.; Crawford, R. J. *Can. J. Chem.* **1981**, *59*, 2556.

(28) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908.



A complete series of six reductions were conducted in which equimolar amounts of two of the xanthates **36**–**39** were treated with a 50% deficiency of tributyltin hydride in the presence of AIBN in toluene at reflux. The initial and final ratios of the substrates in each experiment were determined by integration of the ^{1}H-NMR spectrum and are grouped in Table 2.

The relative rate constants for the various competitions at ca. 50% conversion, given in Table 2, were derived by substitution of the experimental data into the following version of the Ingold–Shaw equation[29] (eq 2), where $[A]_0$ and $[B]_0$ are the initial concentrations of reactants and $[A]_t$ and $[B]_t$ are the concentrations at time t.[30]

$$k_A/k_B = \ln([A]_0/[A]_t)/\ln([B]_0/[B]_t) \qquad (2)$$

It follows that the order of rate constants is $k_{38} > k_{39} > k_{36} > k_{37}$ and thus that the dioxanyl xanthates **38** and **39**, with their β-oxygen bonds, are always consumed more rapidly than the cyclohexyl xanthates **36** and **37**. It is also evident that the difference in rate is to some extent dependent on the relative stereochemistries of the two competition partners: in both the cyclohexyl and the dioxanyl series, the axial xanthate is more reactive than the equatorial one. The most significant difference in reaction rate of two substrates is observed in the competition between the equatorial cyclohexyl xanthate **37** and the axial dioxanyl xanthate **38** (Table 1, entry 4) and the least in that between the axial cyclohexyl xanthate **36** and the equatorial dioxanyl xanthate **39** (Table 1, entry 3). This pattern of reactivity closely matches the recent report of Roberts[6b] on the reaction of alkyl chlorides with amineborinyl radicals. In this study, competition experiments with *cis*- and *trans*-2-chloro-4-*tert*-butyl-1,3-dioxane and *cis*- and *trans*-4-*tert*-butylcyclohexyl chloride revealed the dioxanyl chlorides to be more reactive than the cyclohexyl chlorides and also, in both series, the *cis*-isomers to be more reactive than the *trans*.

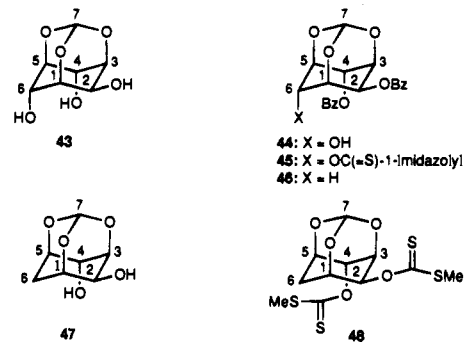
An intramolecular competition reaction with a rigid framework containing precisely defined synclinal and antiperiplanar β-oxygen bonds was also desirable. In designing such a system, we were attracted to the use of an adamantane-like skeleton along the lines of the 5-phenyladamantyl derivatives pioneered by Whiting,[31] and exploited by le Noble in his work on stereoelectronic effects in radical reactions,[32] but containing β-oxygen bonds. *myo*-Inositol 1,3,5-orthoformate (**43**)[33–35] was a convenient starting point for the preparation of such a probe

Table 2. Competition Reactions of Conformationally Rigid Thiocarbonyl Esters with Tributyltin Hydride[a]

entry	substrates	initial ratio	ratio at ~50% overall conversion	rate constant ratio
1	**36:38**	1:0.84	1:0.33	$k_{36}/k_{38} = 0.28$
2	**37:39**	1:0.87	1:0.48	$k_{37}/k_{39} = 0.44$
3	**36:39**	1:0.88	1:0.65	$k_{36}/k_{39} = 0.65$
4	**37:38**	1:1	1:0.20	$k_{37}/k_{38} = 0.105$
5	**36:37**	1:1.34	1:2.70	$k_{36}/k_{37} = 2.56$
6	**38:39**	1:1.18	1:2.31	$k_{38}/k_{39} = 2.53$

[a] Reactions were conducted in toluene at reflux with 0.5 mol equiv of Bu_3SnH with respect to the total moles of xanthate.

(**48**).[36] Reaction of **43** with benzoyl chloride in pyridine gave the dibenzoate **44** in 92% yield. Barton–McCombie deoxygenation of the derived xanthate **45** gave the 6-deoxy-*myo*-inositol derivative **46** in 56% overall yield. Saponification then gave **47**, and finally reaction with sodium hydride and then with carbon disulfide and methyl iodide provided the bisxanthate **48**. In the bisxanthate **48**, one xanthate group has two synclinal β-oxygen bonds and the other two antiperiplanar β-oxygen bonds; neither xanthate group is subject to severe 1,3-diaxial type steric interactions.



Treatment of **48** with 0.5 equiv of tributyltin hydride under the standard conditions followed by inspection of the crude reaction mixture by ^{1}H-NMR spectroscopy immediately revealed that, as in the cases of **38** and **39**, the xanthate with the synclinal β-oxygen bonds was cleaved most rapidly. Chromatography on silica gel led to the isolation of two very major products (**49** and **50**)[37] in 47% and 32% yields, respectively. The ratio of **49**:**50** in the crude reaction mixture was 1.5:1.0, as determined by ^{1}H-NMR spectroscopy. The less important product is readily explained by the simple reductive deoxygenation of the xanthate antiperiplanar to two β-oxygen bonds (Scheme 2, path a). The major product is explained by the mechanism outlined in path b of Scheme 2 in which the xanthate with the synclinal β-oxygen bonds is cleaved first followed by migration of the remaining xanthate group and eventual trapping by the tin hydride. Related migrations have been previously implied in the chemistry of bisxanthate esters.[13,38] Evidently **48** conforms with the pair **38** and **39** in which the bond synclinal to the β-oxygen is more

(29) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2918.

(30) The data obtained in this manner are reasonably self-consistent as is seen from the simple calculations:
$k_{36}/k_{38} \times k_{38}/k_{39} = k_{36}/k_{39} = 0.7$ (compare Table 2, entry 3)
$k_{37}/k_{39} \times k_{38}/k_{39} = k_{37}/k_{38} = 0.17$ (compare Table 2, entry 4)

(31) Sinnott, M. L.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1446.

(32) Bodepudi, V. R.; le Noble, W. J. *J. Org. Chem.* **1991**, *56*, 2001.

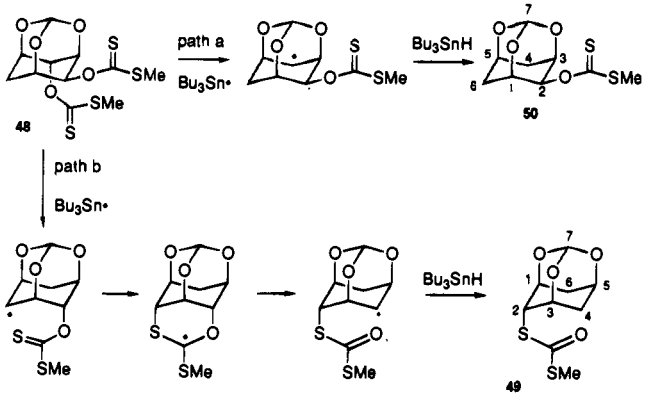
(33) (a) Lee, H. W.; Kishi, Y. *J. Org. Chem.* **1985**, *50*, 4402. (b) Baudin, G.; Glänzer, B. I.; Swaminathan, K. S.; Vasella, A. *Helv. Chim. Acta* **1988**, *71*, 1367. (c) Billington, D. C.; Baker, R.; Kulagowski, J. J.; Mawer, I. M.; Vacca, J. P.; deSolms, S. J.; Huff, J. R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1423.

(34) For the trivial nomenclature of cyclitols, see: Posternak, Th. *The Cyclitols*; Holden-Day, San Francisco, CA, 1965.

(35) For the use of inositol orthoformates as molecular probes, see: Tse, B.; Kishi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 7892.

(36) For the purpose of convenience, in the series of compounds **43**–**50**, we will consider the base (as drawn) of the trioxaadamantane framework, formed from the original six inositol carbons, as a chair and the bonds extending from it as either axial or equatorial. Thus, for example, compound **45** has an axial and an equatorial benzoate group and an axial thiocarbonyl imidazolide moiety.

Scheme 2. Pathways for the Formation of **49** and **50** from **48**



readily cleaved than the antiperiplanar one. In a final experiment **48** was partially reduced with tris(trimethylsilyl)silane with virtually identical results with the stannane reduction indicating that the observed difference in reaction rates is not the result of precoordination of the stannane to the synclinal β-oxygen bond.[39]

Comparison of the results outlined in Tables 1 and 2 reveals a dramatic difference in behavior for the conformationally flexible and rigid systems with the former, with the exception of the cyclic thionocarbonate **19**, not exhibiting the Barton β-oxygen effect and the latter clearly showing an effect that at first sight might be interpreted in this way. Furthermore, as is clear from Table 2, in conformationally locked species, stereochemistry is important with acceleration being most pronounced in the axial series, corresponding to synclinal β-oxygen bonds for the dioxane derivative. In the light of these observations, it is important to note that all of the examples described by Barton either involve conformationally rigid systems such as **1** in which the thiocarbonyl ester is synclinal to a β-oxygen bond or, for primary cases such as **3**, have at least one β-oxygen bond synclinal to the thiocarbonyl ester in all possible staggered conformations.

The polar transition state put forward by Jenkins (Figure 4) should have no stereochemical or conformational bias and therefore, in view of the the results of Table 1, can only be of minor importance. It should be noted though that the energy of the transition state proposed in Figure 4 will be affected by the nature of the group X. Thus, those thiocarbonyl derivatives in which X is better able to stabilize a radical cation-like species might be expected to be more susceptible to polar effects and so more likely to exhibit the β-oxygen effect. The above experiments suggest that the original β-oxygen effect is at least in part stereoelectronic[40,41] in nature and is maximized when the scissile C−O bond is synclinal to a β-oxygen bond.

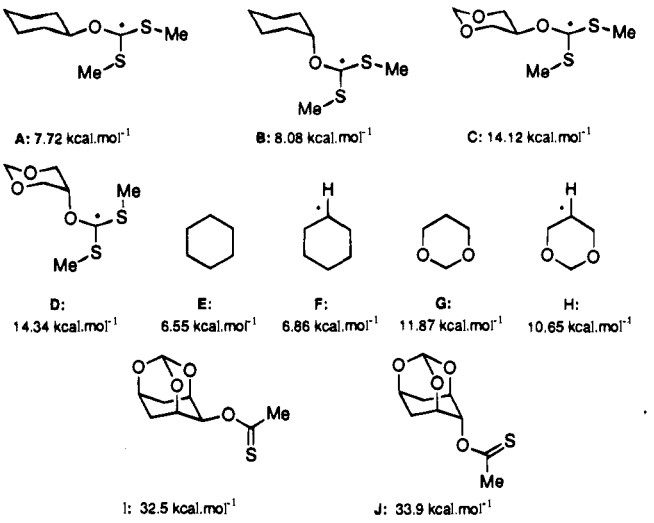


Figure 8. Calculated strain energies.

In an attempt to shed some light on the above observations with conformationally rigid systems, molecular mechanics calculations (Chem 3D)[42] were performed on a series of model adduct radicals (**A**−**D**), the corresponding radicals obtained in the course of the deoxygenation reaction (**F** and **H**), and the hydrocarbons (**E** and **G**) with the results outlined in Figure 8.

The differing strain energies of **A** and **B** clearly indicate that **B** should undergo fragmentation to **F** more rapidly than **A**. This is readily understood in terms of the greater torsional strain present in **B** and is in agreement with the experimental observation that **36** is reduced more quickly than **37** (Table 2, entry 5). Similarly, cleavage of **D** is predicted to occur with greater relief of strain than that of **C**, in accord with experiment (Table 2, entry 6). More important is the observation that cleavage of **C** or **D** to **H** is predicted to be more exothermic than cleavage of either **A** or **B** to **F**, in agreement with the experimental findings (Table 2, entries 1−4). The reason for this appears to lie in the relief of ring strain found in the conversion of C-5 in 1,3-dioxane from sp^3 (**G**) to sp^2 (**H**) hybridization as contrasted with the increase in strain observed for a parallel change in cyclohexane (**E** to **F**). Further analysis

(37) The correct structural elucidation of compounds **49** and especially **50** is crucial to the argument and deserves comment. In the series **43**−**50**, the three-bond coupling constants within the axial and equatorial hydrogen atoms are all reduced below the normal for 60° torsion angles owing to the electronegativity of the multiple oxygen substituents. Thus, most of the hydrogen atoms attached to the various trioxaadamantanes described appear, in the 300 MHz ^{1}H-NMR spectra, as poorly resolved multiplets. Fortuitously, each equatorial hydrogen also has the ideal W spatial relationship to enable four-bond coupling to at least one other equatorial hydrogen, whereas the axial hydrogens have no such possibility. In practice, two types of multiplets are observed, those involved only in simple three-bond coupling and those involved in both three- and four-bond couplings, with the latter being correspondingly broader. It is this additional breadth of the equatorial multiplets, with respect to the axial ones, that enables them to be distinguished by simple comparison of the widths at half-height ($w_{1/2}$). For example, the H-2 signal of **46** is a narrow multiplet representative of an axial hydrogen, while the corresponding signal in **49** is much broader indicating an equatorial hydrogen atom. The existence of ^4J coupling between H-2 and H-4/6eq in **49**, and its absence in **50**, was further confirmed by spin-decoupling experiments. Of course it is also possible to deduce the stereochemistry at C-2 in **50** simply from chemical shift values, but this is not the case for **49** owing to the lack of related compounds for comparison.

(38) (a) Sano, H.; Takeda, T.; Migita, T. *Chem. Lett.* **1988**, 119. (b) Rao, A. V. R.; Reddy, K. A.; Gurjar, M. K.; Kunwar, A. C. *J. Chem. Soc., Chem. Commun.* **1988**, 1273. (c) France, C. J.; McFarlane, I. M.; Newton, C. G.; Pritchen P.; Barton, D. H. R. *Tetrahedron* **1991**, *48*, 6381. (d) Boquel, P.; Cazalet, C. L.; Chapleur, Y.; Samreth, S.; Bellamy, F. *Tetrahedron Lett.* **1992**, *33*, 1997.

(39) Prof. W. B. Motherwell, University College London, is thanked for originally pointing out this possibility. Also see: Barrett, A. G. M.; Melcher, L. M. *J. Am. Chem. Soc.* **1991**, *113*, 8177.

(40) (a) For a previous discussion of stereoelectronic effects in free radical chemistry rationalized in terms of the Cieplek effect,[41] see le Noble in ref 32. (b) For an explanation of the le Noble results in terms of the electrostatic field effect, see: Adock, W.; Clark, C. I.; Trout, N. A. *Tetrahedron Lett.* **1994**, *35*, 297.

(41) For extension of the Cieplak effect to radical reactions, see: Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1987**, *109*, 5875.

(42) Similar calculations have been conducted with Macromodel and PC Model and with the ChemX and MM2 (82) force fields, each of which was modified by addition of the parameters for a carbon-centered radical reported by Beckhaus (Peyman, A.; Hickl, E.; Beckhaus, H.-D. *Chem. Ber.*, **1987**, *120*, 713). Considerable variation was found in the absolute values of strain energies and, to a lesser extent, in the differences between them. However, all of the methods of calculation are in general agreement with the trends outlined in Figure 8. Significantly, they all support the general conclusion that the change in strain energy between cyclohexane **E** and cyclohexyl radical **F** is more unfavorable than that between dioxane **G** and its radical **H**.

will be required to identify the reason for this difference between the cyclohexyl and dioxanyl systems. However, it may be relevant that previous workers have suggested[43] that the introduction of an sp^2 center into a cylohexane ring brings togeher the β-axial protons thus increasing the torsional strain. Since there are no axial protons in the equivalent positions of the dioxane ring, there is no commensurate increase in strain energy.[44] Thus, in each of the above cases (Table 2), the results can be satisfactorily explained in terms of differing strain energies (torsional and ring) present in the various adduct and fragmented radicals. In contrast calculated energies for the model orthoformates **I** and **J** predict that the axial xanthate bond should be cleaved most rapidly. This is clearly not in agreement with the experimental facts (Scheme 2) and suggests that differential strain in cyclohexanes and dioxanes cannot be the whole answer. Similarly, the observation of the β-oxygen effect in certain acyclic systems by Barton (e.g., **3**) cannot be explained in this manner. We suggest that relief of unfavorable dipolar interactions between synclinal carbon−oxygen bonds[45] also has a role to play and can be dominant in certain cases. Thus, the faster reaction of **38** than **39** may be due not only to the greater relief of ring strain but also to the relief of dipolar interactions with the synclinal β-oxygen bonds. Likewise, the more rapid cleavage of the equatorial xanthate ester in **48** is seen to be the result of the relief of dipolar interactions. The same must be true for the accelerated fragmentation of **3** in which the sissile C−O bond is synclinal to at least one β-oxygen bond in all staggered conformations.

In summary, competition reactions with a series of simple, conformationally labile, thiocarbonyl esters reveal no evidence for accelerated cleavage to give a carbon radical substituted with a β-oxygen bond. On the other hand, competition reactions between a series of axial and equatorial cyclohexyl and 1,3-dioxan-5-yl xanthates clearly demonstrate the dioxanyl series to be more reactive. Molecular mechanics calculations indicate that these results are best understood mainly in terms of the greater relief of strain on fragmentation of the dioxanyl series as compared to that of the cyclohexyl series. The calculations also satisfactorily account for the greater reactivity of the axial isomer in both series. An intramolecular competition based on a rigid inositol orthoformate skeleton however suggests that the relief of unfavorable dipolar interactions may contribute to the acceleration of cleavage when the thiocarbonyl ester is forced into a synclinal relationship with a β-oxygen bond. This relief of dipolar interactions would appear to be the underlying reason for the rate differences originally noted by Barton for acyclic, but highly functionalized, systems. It is clear that polar effects do not contribute significantly to the stabilization of the transition state for fragmentation in the Barton−McCombie reaction and that, in agreement with previous ESR work, it is not necessary to postulate stabilization of carbon radicals by a β-oxygen bond. Finally, we stress that the effects observed in the cyclohexyl/dioxanyl competitions, though real, are small with the biggest rate difference between a substrate containing β-oxygens and its carbon analogue being 3.6 (k_{38}/k_{36}), corresponding to a difference of only 1 kcal mol^{-1} in activation energy at 110 °C.

Experimental Section

General. Melting points are uncorrected and were determined with a Kofler hot stage microscope. IR spectra were recorded with a Perkin Elmer 1605 spectrophotometer. ^{1}H-NMR spectra were recorded at 300 MHz with a Bruker AC 300 instrument. ^{13}C-NMR spectra were recorded at 75 MHz with the same instrument operating in the ^{13}C mode. Chemical shifts (δ) are in ppm downfield from tetramethylsilane as internal standard; *J*-values are given in hertz (Hz). EI MS mass spectra (70 eV) were recorded with an AEI MS-30 mass spectrometer. Microanalyses were performed by Midwest Microanalytical, Indianapolis, IN. All solvents were dried and distilled by standard techniques. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl before use. Ether refers to diethyl ether and light petroleum to the fraction boiling in the range 40−60 °C.

***O*-Neopentyl *S*-Isopropyl Dithiocarbonate (9).** Neopentyl alcohol (2.00 g, 22.7 mmol) was dissolved in THF (20 mL) and treated at room temperature with sodium hydride (60% suspension in mineral oil, 2.00 g, 50 mmol) and, after stirring for 30 min, dropwise with ice cooling with CS_2 (3.0 mL, 50 mmol). After stirring for a further 30 min at 0 °C, isopropyl iodide (5.00 mL, 50 mmol) was added dropwise and the reaction mixture allowed to come to room temperature with stirring overnight before it was poured into dilute acetic acid (50 mL) and extracted with ether (3 × 50 mL). The extracts were washed with water (3 × 50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated to give a viscous oil which yielded the title compound, as a viscous yellow oil (3.684 g, 73%), after bulb to bulb distillation (bath temperature 70 °C, 0.1 mmHg): ^{1}H-NMR δ 1.02 (s, 9 H), 1.39 (d, J 6.9 Hz, 6 H), 3.83 (septet, J 6.9 Hz, 1 H), 4.24 (s, 2 H); ^{13}C-NMR δ 22.38, 26.59, 31.73, 40.36, 82.89, 214.56. Anal. Calcd for $C_9H_{18}OS_2$: C, 52.38; H, 8.78. Found: C, 52.37; H, 8.88.

***O*-Neopentyl *S*-Tributylstannyl Dithiocarbonate (10).** A solution of **9** (103 mg, 0.50 mmol), *n*-Bu_3SnH (145 mg, 0.50 mmol), and AIBN (8 mg, 0.050 mmol) in PhH (10 mL) was heated to reflux under Ar for 2 h. After removal of the volatiles *in vacuo*, ^{1}H-NMR revealed clean formation of **10**, contaminated only with 5−10% of the unreacted **9**, which was readily removed by careful Kugelrohr distillation. The title compound was characterized by its ^{1}H-NMR methylene singlet at δ 4.13 and its ^{13}C-NMR thiocarbonyl signal at δ 219.04. UV: λ_{max}(dioxane) = 290 nm with ϵ = 4200.

***O*-Neopentyl *S*-Triphenylstannyl Dithiocarbonate (11).**[17] This compound was prepared in exactly the same way as described for the preparation of **10.** Compound **11** had its ^{1}H-NMR methylene singlet at δ 4.02 and its ^{13}C-NMR thiocarbonyl signal at δ 216.17. UV: λ_{max}(dioxane) = 286 nm with ϵ = 7400.

Photolysis of 10 in the Presence of Hexaphenyldistannane and 4-Methoxyacetophenone. A solution of **10** (prepared from 0.50 mmol of **9** and 0.50 mmol of *n*-Bu_3SnH), $Ph_3SnSnPh_3$ (175 mg, 0.25 mmol), and 4-methoxyacetophenone (75 mg, 0.50 mmol) in benzene (10 mL) was irradiated under Ar with a 250 W sunlamp at room temperature. After 24 h, the ratio **10/11** was determined by ^{1}H-NMR of the crude reaction mixture to be 84/16. Continued irradiation for a total of 50 h resulted in the formation of an 82/18 mixture of **10/11**.

Photolysis of 11 in the Presence of Hexabutyldistannane and 4-Methoxyacetophenone. A solution of **11** (prepared form 0.50 mmol of **9** and 0.50 mmol of Ph_3SnH), $Bu_3SnSnBu_3$ (82 mg, 0.25 mmol), and 4-methoxyacetophenone (75 mg, 0.50 mmol) in benzene (10 mL) was photolyzed under the same conditions as for **10**. After 40 h, the ratio of **10/11** was determined by ^{1}H-NMR to be 75/25.

***(E)*-1-Methoxy-2-hexene.** A solution of (2*E*)-hexen-1-ol (5.0 g, 50 mmol) in THF (10 mL) was added dropwise with stirring over 30 min to a suspension of NaH (2.4 g of 60% dispersion in mineral oil, 60 mmol) and iodomethane (9.9 g, 70 mmol) in THF (40 mL) at room temperature. The mixture was then heated at reflux for 30 min, cooled, and washed with brine (50 mL). The aqueous washings were extracted with ether (3 × 30 mL), and the combined organic layers were dried ($MgSO_4$). The solvent was removed and the residue distilled (126−128 °C, 721 mmHg) to give the title compound (5.0 g, 88%) as a

(43) Anteunis, M.; Camerlynck, R. *Tetrahedron* **1975**, *31*, 1841.

(44) A greater flattening is found for the transformation of dioxane to the dioxanyl radical than for that of cyclohexane to the cyclohexanyl radical. Thus, the C1−C2−C3−C4 torsion angle in **E** is 57.7° and that in **F** is 51.9°, a change of −5.8°. For **G** and **H**, the corresponding angles are 58.8°, 52.1°, and −6.7°. A similar difference in flattening was inferred by Roberts from his ESR study of *tert*-butyl-substituted cyclohexyl and dioxanyl radicals.[6b]

(45) Although evidence for the existence of an attractive gauche interaction in derivatives of *cis*-2-phenyl- and *cis*-2-isopropyl-1,3-dioxan-5-ol has been presented, it should be remembered that, in nonpolar solvents, the *trans*-isomer is favored due to minimization of unfavorable dipolar interactions; see: (a) Abraham, R. J.; Banks, H. D.; Eliel, E. L.; Hofer, O.; Kaloustian, M. K. *J. Am. Chem. Soc.* **1972**, *94*, 1913. (b) Also see ref 26b.

colorless liquid: ^{1}H-NMR δ 0.88 (t, J = 7.3 Hz, 3 H), 1.39 (sextet, J = 7.4 Hz, 2 H), 1.96−2.06 (m, 2 H), 3.30 (s, 3 H), 3.84 (d, J = 7.1 Hz, 2 H), 5,46−5.58 (m, 1 H), 5.62 −5.74 (m, 1 H); ^{13}C-NMR δ 13.67, 22.20, 34.37, 57.65, 73.29, 126.17, 134.85.

***threo*-1-Methoxyhexane-2,3-diol.** A solution of *N*-methylmorpholine *N*-oxide (4.5 g, 38.5 mmol) in water (7 mL) was aded to a stirred solution of the (*E*)-1-methoxy-2-hexene (4.0 g, 35 mmol) in a mixture of acetone (300 mL) and water followed by a solution of OsO_4 (91 mg, 0.35 mmol) in *tert*-butyl alcohol (3.5 mL). The mixture was stirred at room temperature for 24 h, treated with saturated aqueous $NaHSO_3$ (20 mL), and stirred at room temperature for a further 10 min. Brine (250 mL) was then added and the resulting mixture extracted with ethyl acetate (3 × 200 mL). The combined extracts were washed with brine (100 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residue distilled (90 °C, 2 mmHg) to give the title diol (3.9 g, 75%) as a clear liquid: ^{1}H-NMR δ 0.91 (t, J = 7.0 Hz, 3 H), 1.30−1.57 (m, 4 H), 2.67 (bs, 1 H), 2.85 (bs, 1 H), 3.37 (s, 3 H), 3.46 (dd, J = 9.7, 5.9 Hz, 1 H), 3.51 (dd, J = 9.5, 3.2 Hz, 1 H), 3.58 (bs, 2 H); ^{13}C-NMR δ 1.01, 18.80, 35.59, 59.26, 71.92, 72.22, 75.26; MS 149 ($M^{\bullet+}$), 131, 116, 105, 87, 73, 60, 55. Anal. Calcd for $C_7H_{16}O_3$: C, 56.73; H, 10.88. Found: C, 56.69; H, 10.73.

***threo*-4-(Methoxymethyl)-5-propyl-1,3-dioxolane-2-thione (18).** Thiophosgene (0.25 g, 2.2 mmol) was added to a stirred solution of 1-(trimethylsilyl)imidazole (0.62 g, 4.4 mmol) in benzene (5 mL) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C and then allowed to warm to room temperature and stirred for a further 30 min before the solvent was removed *in vacuo* and the residue taken up in THF (4 mL) and added dropwise to a stirred solution of *threo*-1-methoxyhexane-2,3-diol (300 mg, 2.0 mmol) in THF (3 mL) at room temperature. The reaction mixture was heated to reflux overnight and cooled and the solvent removed *in vacuo*. The residue was dissolved in CH_2Cl_2 (20 mL), washed with cold 2 M HCl (10 mL), water (10 mL), and brine (10 mL), and dried ($MgSO_4$). After concentration the crude product was chromatographed (SiO_2, CH_2Cl_2) to give **18** (0.27 g, 71%) as a clear liquid: ^{1}H-NMR δ 0.96 (t, J = 7.3 Hz, 3 H), 1.35−1.59 (m, 2 H), 1.61−1.87 (m, 2 H), 3.39 (s, 3 H), 3.57 (dd, J = 11.1, 3.8 Hz, 1 H), 3.64 (dd, J = 11.1, 3.9 Hz, 1 H), 4.53 (dt, J = 6.7, 3.4 Hz, 1 H), 4.74−4.80 (m, 1 H); ^{13}C-NMR δ 13.55, 17.82, 35.46, 59.68, 70.64, 83.66, 84.57; MS 190 ($M^{\bullet+}$), 145, 113, 81, 71, 55. HRMS (70 eV) calcd for $C_8H_{14}O_3S$: 190.0664. Found: 190.0663.

1-Methoxyhexan-2-ol (28): Preparation of an Authentic Sample. A crude sample of 1,2-epoxyhexane was obtained by *m*-CPBA oxidation of 1-hexene (0.84 g, 10 mmol). Subsequent heating under reflux in methanolic NaOMe as described by Kas'yan and co-workers[46] gave the alcohol **28** (0.57 g, 43%): bp 55−56 °C, 12 mmHg (lit.[46] bp 55−57 °C, 12 mmHg); ^{1}H-NMR δ 0.85−0.91 (m, 3 H), 1.22−1.49 (m, 6 H), 2.35 (bs, 1 H), 3.21 (dd, J = 9.5, 8.1 Hz, 1 H), 3.36 (s, 3 H), 3.38 (dd, J = 9.3, 2.8 Hz, 1 H), 3.70−3.80 (m, 1 H); ^{13}C-NMR δ 14.00, 22.74, 27.69, 32.81, 59.01, 70.25, 77.11.

1-Methoxyhexan-3-ol (30): Preparation of an Authentic Sample. A solution of 1-bromopropane (1.29 g, 10.5 mmol) in ether (2 mL) was added to magnesium (255 mg, 10.5 mmol) in ether (3 mL) at a rate sufficient to promote gentle reflux of the reaction mixture. After the addition was complete, refluxing was continued for a further 1 h. The mixture was then cooled to 0 °C, and a solution of 3-methoxypropanal (880 mg, 10.0 mmol) in ether (2 mL) was added over 30 min. The reaction mixture was then heated at reflux for 30 min, cooled to room temperature, and added to water (10 mL). Ammonium chloride solution (5 M) was added until the solid precipitate had redissolved, the organic layer was separated, and the remaining aqueous layer was extracted with further portions of ether (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent was removed *in vacuo*. Distillation of the residue (80−82 °C, 9 mmHg) gave **30** as a colorless liquid (650 mg, 49%): ^{1}H-NMR δ 0.85−0.92 (m, 3 H), 1.26−1.50 (m, 4 H), 1.61−1.70 (m, 2 H), 2.87 (bs, 1 H), 3.32 (s, 3 H), 3.46−3.64 (m, 2 H), 3.70−3.80 (m, 1 H); ^{13}C-NMR δ 14.06, 18.72, 36.23, 39.58, 58.82, 71.09, 71.69; MS 133 ($M^{\bullet+}$), 115, 100, 89, 83, 71, 67, 60, 55. Anal. Calcd for $C_7H_{16}O_2$: C, 63.60; H, 12.20. Found: C, 63.56; H, 12.48.

(46) Kas'yan, L. I.; Stepanova, N. V.; Belyakova, T. A.; Kunanets, V. K.; Lutsenko, A. I.; Zefirov, N. S. *J. Org. Chem., USSR (Engl. Transl.)* **1984**, *20*, 2090.

***threo*-1-(Benzyloxy)hexane-2,3-diol.** A solution of 2-(*E*)-hexen-1-ol (1.0 g, 10 mmol) in THF (5 mL) was added dropwise under Ar to a stirred suspension of NaH (600 mg, 60% dispersion in mineral oil, 15 mmol, prewashed with Et_2O) in THF (20 mL). After stirring at room temperature for 15 min, $PhCH_2Br$ (2.05 g, 12 mmol) was slowly introduced. After stirring at room temperature overnight, water (50 mL) was added and the reaction mixture extracted with EtOAc (4 × 30 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. Kugelrohr distillation gave 1.90 g (100%) of (*E*)-1-(benzyloxy)-2-hexene as a colorless oil: ^{1}H-NMR δ 0.91 (t, J = 7.3 Hz, 3 H), 1.41 (m, J = 7.4 Hz, 2 H), 2.04 (q, J = 7.25 Hz, 2 H), 3.98 (dd, J = 0.7, 6.7 Hz, 2 H), 4.51 (s, 2 H), 5.56−5.77 (m, 2 H), 7.26−7.43 (m, 5 H); ^{13}C-NMR δ 13.64, 22.16, 34.33, 70.88, 71.74, 126.24, 127.44, 127.72, 128.27, 134.77, 138.38.

A solution of the above alkene (1.90 g, 10 mmol) in a mixture of acetone (50 mL) and water (10 mL) was treated in portions, with stirring, with *N*-methylmorpholine *N*-oxide (1.30 g, 11 mmol) followed by OsO_4 (5 mg) in *tert*-butyl alcohol (2 mL). The reaction mixture was stirred at room temperature overnight before quenching the reaction with dilute aqueous $NaHSO_3$ and repeated extraction with EtOAc. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. Removal of the solvent and column chromatography (SiO_2, hexane/EtOAc, 1/1) gave 2.04 g (91%) of the title compound as a colorless oil: ^{1}H-NMR (400 MHz) δ 0.92 (t, J = 7.0 Hz, 3 H), 1.33−1.54 (m, 4 H), 3.55−3.65 (m, 4 H), 4.53 (d, J = 11.8 Hz, 1 H), 4.58 (d, J = 11.8 Hz, 1 H), 7.29−7.38 (m, 5 H); ^{13}C-NMR δ 13.95, 18.73, 35.52, 71.88, 72.27, 72.71, 73.56, 127.71, 127.85, 128.44, 137.53. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.64; H, 8.89.

***threo*-4-[(Benzyloxy)methyl]-5-propyl-1,3-dioxolane-2-thione (19).** A mixture of *threo*-1-(benzyloxy)hexane-2,3-diol (673 mg, 3.0 mmol), 1,1′-thiocarbonyl diimidazole (561 mg, 3.15 mmol), and DMAP (38 mg, 10 mol %) in THF (25 mL) was heated to reflux under Ar overnight. After cooling to room temperature, saturated $NaHCO_3$ (20 mL) was added and the reaction mixture extracted with EtOAc (3 × 25 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography (SiO_2, CH_2Cl_2) gave **19** (730 mg, 91%) as a slightly yellow oil: ^{1}H-NMR δ 0.97 (t, J = 7.3 Hz, 3 H), 1.39−1.84 (m, 4 H), 3.65 (dd, J = 3.7, 11.2 Hz, 1 H), 3.73 (dd, J = 4.2, 11.1 Hz, 1 H), 4.54- 4.65 (m, 3 H), 4.79 (m, 1 H), 7.30−7.39 (m, 5 H); ^{13}C-NMR δ 13.49, 17.72, 35.41, 67.94, 73.70, 83.71, 84.52, 127.72, 128.06, 128.52, 191.40. Anal. Calcd for $C_{14}H_{18}O_3S$: C, 63.13; H, 6.81. Found: C, 92.92; H, 6.84.

2-[[(1-Imidazolyl)thiocarbonyl]oxy]propane. A solution of 2-propanol (150 mg, 2.5 mmol) and 1,1′-thiocarbonyldiimidazole (490 mg, 2.75mmol) in THF (15 mL) was heated to reflux under Ar for 3 h. After cooling to room temperature, the reaction mixture was poured into water (20 mL) and extracted with Et_2O (3 × 15 mL). The combined organic extracts were washed with brine and dried (Na_2SO_4). Removal of the solvent and column chromatography (SiO_2, EtOAc/hexane, 1/1) gave 2-[[(1-imidazolyl)thiocarbonyl]oxy]propane (372 mg, 82%) as a colorless oil: ^{1}H-NMR δ 1.48 (d, J = 6.1 Hz, 6 H), 5.71 (heptet, J = 6.2 Hz, 1 H), 7.02 (bs, 1 H), 7.63 (t, J = 1.4 Hz, 1 H), 8.33 (bs, 1 H); ^{13}C-NMR δ 21.14, 78.18, 117.82, 130.60, 136.72, 183.49. Anal. Calcd for $C_7H_{10}N_2OS$: C, 49.39; H, 5.92. Found: C, 49.33; H, 5.90.

***O*-Octyl *O′*-Isopropyl Thionocarbonate (32).** A solution of *n*-octanol (78 mg, 0.60 mmol), 2-[[(1-imidazolyl)thiocarbonyl]oxy]-propane (85 mg, 0.50 mmol) and DMAP (6 mg, 0.050 mmol) in $PhCH_3$ (10 mL) was heated to reflux under Ar overnight. After cooling to room temperature, water (15 mL) was added and the reaction mixture extracted with EtOAc (2 × 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography (SiO_2, hexane/CH_2Cl_2, 3/2) gave the title thiocarbonate (101 mg, 87%) as a colorless oil: ^{1}H-NMR δ 0.88 (t, J = 6.6 Hz, 3 H), 1.28−1.33 (m, 10 H), 1.37 (d, J = 6.2 Hz, 6 H), 1.74 (quintet, J = 7.0 Hz, 2 H), 4.40 (t, J = 6.7 Hz, 2 H), 5.43 (heptet, J = 6.2 Hz, 1 H); ^{13}C-NMR δ 13.99, 21.21, 22.53, 25.72, 28.18, 29.05, 29.10, 31.66, 73.05, 77.07, 194.81. Anal. Calcd for $C_{12}H_{24}O_2S$: C, 62.02; H, 10.41. Found: C, 62.20; H, 10.21.

***O*-(2-Butoxyethyl) *O′*-Isopropyl Thionocarbonate (33).** This compound was prepared from butoxyethanol analogously to the

preparation of *O*-isopropyl *O'*-octyl thionocarbonate in 73% yield: ^{1}H-NMR δ 0.91 (t, J = 7.3 Hz, 3 H), 1.36 (d, J = 6.3 Hz, 6 H), 1.32−1.40 (m, 2 H), 1.57 (quintet, J = 6.7 Hz, 2 H), 3.47 (t, J = 6.6 Hz, 2 H), 3.72 (t, J = 4.80 Hz, 2 H), 4.55 (t, J = 4.8 Hz, 2 H), 5.42 (heptet, J = 6.2 Hz, 1 H); ^{13}C-NMR δ 13.8, 19.12, 21.17, 31.52, 67.83, 71.17, 71.67, 77.44, 194.70. Anal. Calcd for $C_{10}H_{20}O_3S$: C, 54.51; H, 9.15. Found: C, 54.39; H, 9.16.

***O*-Octyl *S*-Tris(trimethylsilyl)silyl Thiocarbonate (22): Preparation of an Authentic Sample.** A solution of **32** (46 mg, 0.20 mmol), tms_3SiH (65 mg, 0.26 mmol), and AIBN (6.6 mg, 20 mol %) in PhH (5 mL) was heated to reflux for 4 h. After removal of the volatiles *in vacuo*, ^{1}H-NMR revealed essentially quantitative formation of **22**: partial ^{1}H-NMR δ 0.88 (t, J = 6.6 Hz, 3 H), 1.26−1.36 (m, 10 H), 1.64 (quintet, J = 7.0 Hz, 2 H), 4.12 (t, J = 6.8 Hz, 2 H); partial ^{13}C-NMR δ 13.99, 22.53, 25.67, 28.67, 29.07, 31.67, 67.73, 170.80.

***O*-(2-Butoxyethyl) *S*-Tris(trimethylsilyl)silyl Thiocarbonate (23): Preparation of an Authentic Sample.** Reaction of **33** with tms_3SiH under the same conditions as for the formation of **22** resulted in clean formation of **23**: partial ^{1}H-NMR δ 0.91 (t, J = 7.3 Hz, 3 H), 1.36 (sexet, J = 7.4 Hz, 2 H), 1.55 (m, 2 H), 3.45 (t, J = 6.6 Hz, 2 H), 3.62 (t, J = 4.9 Hz, 2 H), 4.29 (t, J = 4.9 Hz, 2 H); partial ^{13}C-NMR δ 13.81, 19.14, 31.58, 66.48, 68.35, 71.10, 170.94.

***O*-Cyclohexylmethyl *O'*-Isopropyl Thionocarbonate (34).** A solution of 2-[[(1-imidazolyl)thiocarbonyl]oxy]propane (170 mg, 1.0 mmol), cyclohexylmethanol (137 mg, 1.20 mmol), and DMAP (12 mg, 0.10 mmol) in $PhCH_3$ (10 mL) was heated to reflux under Ar for 12 h. After cooling to room temperature, water (15 mL) was added and the reaction mixture extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography (SiO_2, EtOAc/hexane, 1/3) gave the title compound (184 mg, 85%) as a colorless oil: ^{1}H-NMR δ 0.95−1.80 (m, 11 H), 1.36 (d, J = 6.2 Hz, 6 H), 4.2 (d, J = 6.2 Hz, 2 H), 5.43 (heptet, J = 6.2 Hz, 1 H); ^{13}C-NMR δ 21.28, 25.56, 26.24, 29.58, 36.86, 77.10, 78.12, 195.0. Anal. Calcd for $C_{11}H_{20}O_2S$: C, 61.07; H, 9.32. Found: C, 61.20; H, 9.40.

***O*-(Tetrahydropyran-2-ylmethyl) *O'*-Isopropyl Thionocarbonate (35).** This compound was prepared from 2-tetrahydropyranmethanol in the same way as described for the preparation of **34** in 81% yield: ^{1}H-NMR δ 1.36 (d, J = 6.3 Hz, 6 H), 1.43−1.62 (m, 5 H), 1.89 (m, 1 H), 3.43 (dt, J = 2.7, 11.3 Hz, 1 H), 3.68 (m, 1 H), 4.01 (dt, J = 11.4, 2.2 Hz, 1 H), 4.32 (dd, J = 6.9, 11.4 Hz, 1 H), 4.39 (dd, J = 3.6, 11.4 Hz, 1 H), 5.42 (heptet, J = 6.2 Hz, 1 H); ^{13}C-NMR δ 21.23, 22.91, 25.64, 27.70, 68.34, 74.85, 75.40, 77.55, 194.81. Anal. Calcd for $C_{10}H_{18}O_3S$: C, 55.02; H, 8.31. Found: C, 55.24; H, 8.47.

***O*-Cyclohexylmethyl *S*-Tris(trimethylsilyl)silyl Thiocarbonate (26): Preparation of an Authentic Sample.** A solution of the thiocarbonate **34** (43 mg, 0.20 mmol), tms_3SiH (65 mg, 0.26 mmol), and AIBN (6.6 mg, 0.02 mmol) in PhH (5 mL) was heated to reflux under Ar for 4 h. After removal of the volatiles *in vacuo*, ^{1}H-NMR of the reaction crude revealed the formation of **26** in a clean reaction: partial ^{1}H-NMR δ 0.93−1.75 (m, 11 H), 3.95 (d, J = 6.6 Hz, 2 H); partial ^{13}C-NMR δ 25.55, 26.29, 29.46, 37.16, 72.70, 170.95.

***O*-(Tetrahydropyran-2-ylmethyl) *S*-Tris(trimethylsilyl)silyl Thiocarbonate (27): Preparation of An Authentic Sample.** Reaction of the thiocarbonate **35** with tms_3SiH under the same conditions as for the formation of **26** resulted in clean formation of **27**: partial ^{1}H-NMR δ 1.26−1.67 (m, 6 H), 3.42 (dt, J = 2.5, 11.2 Hz, 1 H), 3.55 (m, 1 H), 3.99 (bd, J = 11.3 Hz, 1 H), 4.08 (d, J = 5.2 Hz, 2 H); ^{13}C-NMR δ 0.44, 22.92, 25.67, 27.78, 68.25, 70.19, 75.26, 171.04.

***O*-(2-Butoxyethyl) *O'*-Octyl Thionocarbonate (12).** *n*-Octanol (130 mg, 1.00 mmol) was added to a solution of 1,1'-thiocarbonyldi-2,2'-pyridone (232 mg, 1.00 mmol) and DMAP (6 mg, 0.05 mmol) in CH_2Cl_2 (4 mL) and the mixture stirred at room temperature for 3 days. 2-Butoxyethanol (118 mg, 1.00 mmol) was then added and the reaction heated to 80 °C overnight in a sealed tube. Removal of the solvent and chromatography (SiO_2, CH_2Cl_2/hexanes, 1/1) gave **12** as a colorless oil (110 mg, 38%): ^{1}H-NMR δ 0.88 (t, J = 6.8 Hz, 3 H), 0.91 (t, J = 7.3 Hz, 3 H), 1.20−1.45 (m, 12 H), 1.51−1.80 (m, 4 H), 3.48 (t, J = 6.7 Hz, 2 H), 3.71−3.74 (m, 2 H), 4.42 (t, J = 6.7 Hz, 2 H), 4.55−4.58 (m, 2 H); ^{13}C-NMR δ 13.87, 14.05, 19.20, 22.60, 25.75, 28.20, 29.12, 31.59, 31.73, 67.88, 71.24, 71.99, 73.60, 195.71; MS 291 (M + 1$^+$), 179, 135, 123, 100, 85, 71, 56. Anal. Calcd for $C_{15}H_{30}O_3S$: C, 62.03; H, 10.41. Found: C, 62.37; H, 10.75.

***O*-Octyl *S*-Methyl Dithiocarbonate (14).** 1-Octanol (1.30 g, 10.0 mmol), sodium hydride (0.60 g of 60% dispersion in mineral oil, 15 mmol, washed with pentane), and imidazole (20 mg) in THF (30 mL) were heated to reflux for 3 h. CS_2 (2.3 g, 30 mmol) was added, the mixture was refluxed for 1 h, and then MeI (4.30 g, 30 mmol) was added and refluxing continued for 1 h. Acetic acid (6 mL) was then added and the mixture diluted with water (100 mL) and extracted with CH_2Cl_2 (100 mL). The organic layer was washed with 10% HCl (100 mL), 10% $NaHCO_3$ (100 mL), and water (100 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give the title compound **14** as a colorless oil (1.88 g, 100%): ^{1}H-NMR δ 0.89 (t, J = 6.8 Hz, 3 H), 1.24−1.47 (m, 12 H), 1.80 (quintet, J = 7.4 Hz, 2 H), 2.56 (s, 3 H), 4.59 (t, J = 6.8 Hz, 2 H); ^{13}C-NMR δ 14.01, 18.81, 22.56, 25.81, 28.16, 29.08 (2 C), 31.68, 74.18, 215.85. Anal. Calcd for $C_{10}H_{20}OS_2$: C, 54.50; H, 9.15. Found: C, 54.70; H, 9.13.

***O*-(2-Butoxyethyl) *S*-Methyl Dithiocarbonate (16).** Treatment of 2-butoxyethanol (1.18 g, 10.0 mmol) with NaH, CS_2, and MeI as described for the formation of **14** gave the title compound **16** (2.00 g, 96%) as a light yellow oil: ^{1}H-NMR δ 0.92 (t, J = 7.3 Hz, 3 H), 1.38 (m, 2 H), 1.67 (m, 2 H), 2.56 (s, 3 H), 3.49 (t, J = 6.6 Hz, 2 H), 3.77 (m, 2 H), 4.73 (m, 2 H); ^{13}C-NMR δ 13.79, 18.94, 19.13, 31.56, 67.54, 71.16, 72.76, 215.93. Anal. Calcd for $C_8H_{16}O_2S_2$: C, 46.12; H, 7.74. Found: C, 45.91; H, 7.67.

***O*-Cyclohexylmethyl *O'*-(Tetrahydropyran-2-ylmethyl) Thionocarbonate (13).** A solution of 2-tetrahydropyranmethanol (290 mg, 2.5 mmol) and 1,1'-thiocarbonyldiimidazole (500 mg, 2.8 mmol) in THF (10 mL) was heated to reflux under Ar for 1.5 h. After cooling to room temperature, water (20 mL) was added and the reaction mixture extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine and dried (Na_2SO_4). Removal of the solvent and column chromatography (SiO_2, hexane/ EtOAc, 3/2) gave 2-[[[(1-imidazolyl)thiocarbonyl]oxy]methyl]tetrahydropyran (527 mg, 93%) as a colorless oil: ^{1}H-NMR δ 1.36−1.68 (m, 5 H), 1.93 (m, 1 H), 3.47 (dt, J = 3.4, 10.9 Hz, 1 H), 3.77 (md, J = 11.4 Hz, 1 H), 4.02 (m, 1 H), 4.56 (dd, J = 6.7, 11.5 Hz, 1 H), 4.65 (dd, J = 3.3, 11.5 Hz, 1 H), 7.03 (s, 1 H), 7.65 (s, 1 H), 8.36 (s, 1 H).

A solution of this thiocarbonyl imidazolide (520 mg, 2.3 mmol), cyclohexylmethanol (286 mg, 2.5 mmol), and DMAP (28 mg, 10 mol %) in $PhCH_3$ (15 mL) was heated to reflux under Ar for 16 h. After cooling to room temperature, water (20 mL) was added and the mixture extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to dryness. Column chromatography (SiO_2, hexane/EtOAc, 3/1) gave the thionocarbonate **13** (437 mg, 88%) as a colorless oil: ^{1}H-NMR δ 0.94−1.89 (m, 17 H), 3.45 (dt, J = 2.8, 11.3 Hz, 1 H), 3.67 (m, 1 H), 4.01 (dt, J = 11.3, 2.0 Hz, 1 H), 4.22 (d, J = 6.3 Hz, 2 H), 4.35 (dd, J = 6.8, 11.5 Hz, 1 H), 4.40 (dd, J = 3.9, 11.5 Hz, 1 H); ^{13}C-NMR δ 22.90, 25.54, 25.63, 26.24, 27.69, 29.53, 36.79, 68.33, 74.84, 75.62, 78.66, 195.89. Anal. Calcd for $C_{14}H_{24}O_3S$: C, 61.73; H, 8.88. Found: C, 61.65; H, 8.84.

Reaction of the Thionocarbonate 12 with Tributyltin Deuteride. (a) At 180 °C. A solution of **12** (29 mg, 0.10 mmol), tributyltin deuteride (29 mg, 0.10 mmol), and AIBN (3 mg, 20 μmol) in toluene (1 mL) was heated at 180 °C in a sealed tube overnight. Analysis of the mixture with GC with *p*-xylene (3.5 mg) as an internal standard gave 1-deuteriooctane (**20**) (3.1 mg, 27%) and butyl 2-deuterioethyl ether (**21**) (1.4 mg, 14%), i.e., **20**:**21** = 1.9:1.0. The reaction mixture was then analyzed by ^{2}H-NMR spectroscopy at 77 MHz. Integration of the peaks at 0.85 and 1.07 ppm, due to 1-deuteriooctane (**20**) and butyl 2-deuterioethyl ether (**21**), respectively, gave the **20**:**21** ratio as 1.1:1.0.

(b) At 120 °C. A solution of **12** (29 mg, 0.10 mmol), tributyltin deuteride (29 mg, 0.10 mmol), and di-*tert*-butyl peroxide (73 mg, 0.50 mg) in decane (1 mL) was heated in a sealed tube at 120 °C overnight. After cooling to room temperature, toluene (5.8 mg) was added as an internal standard. Analysis by GC gave 1-deuteriooctane (**20**) (6.0 mg, 53%) and butyl 2-deuterioethyl ether (**21**) (4.3 mg, 42%), i.e., **20**:**21** = 1.3:1.0. Analysis of the same reaction mixture by ^{2}H-NMR gave the **20**:**21** ratio as 0.96:1.0.

Reaction of the *Thiono*carbonate 12 with Tris(trimethylsilyl)-silane. A solution of **12** (58 mg, 0.20 mmol), tms_3SiH (60 mg, 0.24 mmol), and AIBN (6.6 mg, 20 mol %) in PhH (5 mL) was heated to reflux under Ar for 5 h. After removal of the volatiles *in vacuo*, examination by ^{1}H-NMR of the crude reaction mixture revealed the formation of two products (**22** and **23**) in the ratio 1.0:1.1, along with 13−16% of the unreacted starting material **12**.

Reaction of the Thionocarbonate 13 with Tributyltin Hydride. A solution of the thionocarbonate **13** (27.2 mg, 0.1 mmol), tributyltin hydride (87.3 mg, 0.3 mmol), and AIBN (1.6 mg, 10 μmol) in *tert*-butylbenzene (1 mL) was added dropwise over 45 min to refluxing *tert*-butylbenzene (2 mL). After being refluxed for 1.5 h, the mixture was shown by TLC to still contain unreacted **13**. A further portion of tributyltin hydride (29.1 mg, 0.1 mmol) and AIBN (1.6 mg, 10 μmol) in *tert*-butylbenzene (1 mL) was then added over 30 min and refluxing continued for 1.5 h. The mixture was cooled to room temperature, 2.5 M NaOH (1 mL) was added, and stirring was continued overnight. The aqueous layer was then extracted with Et_2O (2 × 1 mL), and the organic layers were combined. Analysis of this mixture by GC revealed the ratio of methylcyclohexane (**24**) to 2-methyltetrahydropyran (**25**) to be 1.76:1.0.

Reaction of the Thionocarbonate 18 with Tributyltin Hydride. A solution of the thionocarbonate **18** (95 mg, 0.50 mmol), tributyltin hydride (290 mg, 1.0 mmol), AIBN (8 mg, 50 μmol), and decane (15 mg, as an internal reference) in toluene (5 mL) was added dropwise over 45 min to refluxing toluene (10 mL). Refluxing was continued for 4 h, the mixture was then cooled to room temperature, and 2.5 M NaOH (5 mL) was added. The resulting mixture was stirred overnight at room temperature. Analysis of the organic layer by GC showed 1-methoxyhexan-2-ol (**28**) (15 mg, 23%) and 1-methoxyhexan-3-ol (**30**), i.e., **28**:**30** = 1.5:1.0.

Reaction of the Thionocarbonate 19 with Tris(trimethylsilyl)-silane: Isolation of 29 and 31. A solution of **19** (266 mg, 1.0 mmol), tms_3SiH (374 mg, 1.5 mmol), and AIBN (33 mg, 20 mol %) in benzene (5 mL) was heated to reflux for 5 h. After the solvent was removed under reduced pressure, the residue was taken up with Et_2O (10 mL) and treated with 1 M HCl (10 mL). The reaction mixture was then stirred at room temperature overnight. The aqueous layer was separated and extracted with Et_2O (2 × 10 mL). The organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. Column chromatography (SiO_2, hexane/Et_2O, 3/2) gave **29**[47] (46 mg, 22%): ^{1}H-NMR δ 0.90 (t, J = 7.0 Hz, 3 H), 1.23−1.43 (m, 6 H), 3.32 (dd, J = 8.0, 9.3 Hz, 1 H), 3.51 (dd, J = 3.0, 9.3 Hz, 1 H), 3.81 (m, 1 H), 4.56 (s, 2 H) 7.34 (m, 5 H); ^{13}C-NMR δ 13.92, 22.64, 27.59, 32.72, 70.35, 73.24, 74.57, 127.66, 128.37, 137.91.

Further elution gave **31** (76 mg, 36.5%) as a colorles oil: ^{1}H-NMR δ 0.92 (t, J = 6.9 Hz, 3 H), 1.37−1.47 (m, 4 H), 1.74 (quartet, J = 5.5 Hz, 2 H), 3.62−3.76 (m, 2 H), 3.82 (m, 1 H), 4.53 (s, 2 H), 7.33 (m, 5 H); ^{13}C-NMR δ 14.04, 18.89, 36.31, 39.54, 69.23, 71.10, 73.23, 127.57, 127.64, 128.36, 137.86.

Competitive Reaction of the Dithiocarbonates 14 and 16 with Tributyltin Deuteride. A solution of **14** (34 mg, 0.16 mmol) and **16** (37 mg, 0.18 mmol), tributyltin deuteride (44 mg, 0.15 mmol), and AIBN (5 mg, 30 μmol) in toluene (2 mL) was heated in a sealed tube at 180 °C overnight. Analysis of the mixture by GC, with *p*-xylene (6.1 mg) as an internal standard, gave 1-deuteriooctane (**20**) (4.0 mg, 23%) and butyl 2-deuterioethyl ether (**21**) (2.4 mg, 16%), i.e., **20**:**21** = 1.4:1.0. However, analysis by ^{2}H-NMR spectroscopy at 77 MHz, as described above for the reaction of **12** with Bu_3SnD, gave the **20**:**21** ratio as 0.80:1.0

Competitive Reaction of the Dithiocarbonates 14 and 16 with Tris(trimethylsilyl)silane. A solution of **14** (44 mg, 0.20 mmol), **16** (42 mg, 0.20 mmol), tms_3SiH (60 mg, 0.24 mmol), and AIBN (6.6 mg, 0.040 mmol) in PhH (5 mL) was heated to reflux under Ar for 5 h. After removal of the volatiles *in vacuo*, *n*-octanol (260 mg, 0.20 mmol) was added as the internal standard. ^{1}H-NMR measurement of the crude reaction mixture indicated that the amounts of the unreacted **14** and **16** were 0.070 and 0.043 mmol, respectively, corresponding to the ratio **14**:**16** =1.6:1.0, with 72% total conversion of the xanthates.

(47) Bonini, C.; Righi, G.; Sotgiu, G. *J. Org. Chem.* **1991**, *56*, 6206.

Competitive Reaction of the Thionocarbonates 15 and 17 with Tris(trimethylsilyl)silane. A mixture of **15** (0.20 mmol) and **17** (0.20 mmol) in PhH was allowed to react with tms_3SiH under exactly the same conditions as for the competition reaction of **14** and **16** with tms_3SiH. ^{1}H-NMR measurement of the crude reaction mixture using *n*-octanol as internal standard indicated that the amounts of the unreacted **15** and **17** were 0.076 and 0.091 mmol, respectively, corresponding to the ratio **15**:**17** =1.3:1.0, with 58% total conversion of the xanthates.

***O*-(*cis*-4-Phenylcyclohexyl) *S*-Methyl Dithiocarbonate (36).** *cis*-4-Phenylcyclohexanol (57 mg, 0.32 mmol) was dissolved in THF (0.6 mL) under an argon atmosphere and treated with sodium hydride (80%, 14 mg, 0.48 mmol). When the evolution of gas was complete, carbon disulfide (0.1 mL, 1.6 mmol) was added and the reaction mixture stirred at room temperature for 30 min. Methyl iodide (0.2 mL, 3.2 mmol) was then added and the reaction mixture heated to reflux for 40 min before cooling to room temperature and addition of water (5 mL). The reaction mixture was extracted with ether (3 × 15 mL), and the extracts were dried ($MgSO_4$), concentrated, and purified by thin layer preparative chromatography (SiO_2, petroleum/ether, 50/1) to give the xanthate **36** (60 mg, 92%) as a colorless solid: mp 44−46 °C (Me_2CHOH); ^{1}H-NMR, δ: 1.7−1.9 (m, 6 H), 2.5 (m, 2 H), 2.59 (s, 3 H), 2.61 (m, 1 H), 5.90 (m, 1 H), 7.1−7.35 (m, 5 H); ^{13}C-NMR δ 18.74, 28.67, 29.84, 43.22, 78.99, 126.15, 126.75, 128.43, 146.75, 214.79; IR (film) υ_{max} 3132, 2970, 1724, 1424, 1238, 1215, 1094, 1042 cm^{-1}. Anal. Calcd for $C_{14}H_{18}OS_2$: C, 63.12; H, 6.81. Found: C, 62.87; H, 7.00.

***O*-(*trans*-4-Phenylcyclohexyl) *S*-Methyl Dithiocarbonate (37).** *trans*-4-Phenylcyclohexanol was converted to the xanthate **37** as described for the *cis*-isomer in 99% isolated yield. The xanthate **37** was a colorless solid: mp 108−109 °C (Et_2O); ^{1}H-NMR δ 1.6−1.75 (m, 4 H), 2.00 (m, 2 H), 2.32 (m, 2 H), 2.56 (m, 4 H, H-4), 5.60 (m, 1 H), 7.1−7.35 (m, 5 H); ^{13}C-NMR δ 18.87, 31.37, 32.09, 43.28, 82.70, 126.28, 128.47, 145.94; IR (film) υ_{max} 3130, 1645, 1226, 1042, 997 cm^{-1}. Anal. Calcd for $C_{14}H_{18}OS_2$: C, 63.12; H, 6.81. Found: C, 62.87; H, 7.00.

***cis*-5-Hydroxy-2-phenyl-1,3-dioxane (40).** To a mixture of glycerol (55.07 g, 0.60 mmol) and benzaldehyde (50.0 g, 0.47 mmol) in toluene (69 mL) was added concentrated sulfuric acid (3 drops), and the resulting mixture was heated to reflux in a Dean−Stark water separator under nitrogen. When the separation of water was complete (7.3 mL, 86%), the reaction mixture was allowed to cool to room temperature and the solvent removed under reduced pressure to give a white solid which was recrystallized from ether/petroleum ether. Repeated recrystallization from the same solvent gave the pure *cis*-alcohol (47.7 g, 56%): mp 62−63.5 °C (lit.[26] mp 62.5−63 °C); ^{1}H-NMR δ 3.20 (br s, 1 H), 3.60 (m, 1 H), 4.15 (m, 4 H), 5.55 (s, 1 H), 7.37 (m, 3 H), 7.48 (m, 2 H).

2-Phenyl-1,3-dioxan-5-one (42). To a solution of oxalyl chloride (0.20 mL, 2.3 mmol) in CH_2Cl_2 (10 mL) under an argon atmosphere at −78 °C was added DMSO (0.35 mL, 4.9 mmol) slowly. After 5 min a solution of the alcohol **40** (0.37 g, 2.1 mmol) in CH_2Cl_2 (5.0 mL) was added. After consumption of **40** (TLC control), triethylamine (1.0 mL, 7.1 mmol) was added. The yellow reaction mixture was then allowed to warm to room temperature before the reaction was quenched with water (5 mL) and diluted with ether (30 mL). The organic layer was repeatedly washed with water, dried ($MgSO_4$), filtered, and concentrated to give the ketone **42** (0.355 g, 97%) as an oil that solidified to a white solid on standing at −18 °C under argon: mp 67−68 °C (lit.[27] mp 68−69 °C); ^{1}H-NMR δ 4.50 (m, 4 H), 5.90 (s, 1 H), 7.40 (m, 3 H), 7.50 (m, 2 H).

***trans*-5-Hydroxy-2-phenyl-1,3-dioxane (41).** To a solution of the ketone **42** (0.91 g, 5.1 mmol) in methanol (30 mL) at 0 °C was added sodium borohydride (0.965 g, 26 mmol) portionwise, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with ether (70 mL) and the organic phase washed with water (3 × 25 mL), dried ($MgSO_4$), filtered, and evaporated to yield the alcohol **41** (0.352 g, 38%) as a 1:10 *cis*:*trans* mixture with **40**: mp 64−65 °C (lit.[26] mp 63−64 °C); ^{1}H-NMR δ 3.55 (m, 2 H), 3.85 (m, 1 H), 4.25 (m, 2 H), 5.40 (s, 1 H), 7.35 (m, 3 H), 7.45 (m, 2 H).

***O*-(*cis*-2-Phenyl-1,3-dioxan-5-yl) *S*-Methyl Dithiocarbonate (38).** The xanthate **38** was prepared from the alcohol **40** in 91% yield as

described for the preparation of **36** above. It was a pale yellow solid: mp 94 °C; ^{1}H-NMR δ 2.61 (s, 3 H), 4.24 (m, 2 H), 4.48(m, 2 H), 5.54 (m, 1 H), 5.59 (s, 1 H), 7.38 (m, 3 H), 7.50 (m, 2 H); ^{13}C-NMR δ 18.71, 68.65, 74.00, 101.40, 126.15, 128.38, 129.19, 138.00, 215.10; IR (film) υ_{max} 3136, 2250, 1645, 1451, 1388, 1240, 1219, 1135, 1103, 1050, 1008 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_3S_2$: C, 53.31; H, 5.22; S, 23.72. Found: C, 53.52; H, 5.29; S, 23.89.

***O*-(*trans*-2-Phenyl-1,3-dioxan-5-yl) *S*-Methyl Dithiocarbonate (39).** The xanthate **39** was prepared from the alcohol **41** as described for the preparation of **36** above. It was a pale yellow solid: mp 74 °C; ^{1}H-NMR δ 2.58 (s, 3 H), 3.84 (m, 3 H), 4.55 (m, 2 H), 5.51 (s, 1 H), 5.80 (m, 1 H), 7.38 (m, 3 H), 7.50(m, 2 H); ^{13}C-NMR δ 19.48, 67.70, 70.29, 101.44, 126.15, 128.38, 129.19, 137.10, 215.10; IR (film) υ_{max} 3125, 2450, 1645, 1456, 1377, 1271, 1192, 1150, 1066 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_3S_2$: C, 53.31; H, 5.22. Found: C, 53.41; H, 5.27.

Competitive Reduction Experiments for 36−39: General Protocol. Each of two dithiocarbonate esters was weighed into a sample tube (~0.05 mmol each) together with DMAP (~5 mg) and the true ratio determined by ^{1}H-NMR spectroscopy at 300 MHz in $CDCl_3$. The solvent was then removed under vacuum and the residue dried at 0.1 mmHg for 5 min before it was taken up in toluene (1 mL) and brought to gentle reflux under N_2. AIBN (~1 mg) was added, immediately followed by Bu_3SnH (13 μL, 0.05 mmol) causing immediate evolution of gas (presumed to be COS). After 2 h at reflux, the reaction mixture was allowed to cool to room temperature and then evaporated to dryness. The final ratio of the two xanthate esters was determined by ^{1}H-NMR in $CDCl_3$ solution. Each reduction proceeded cleanly and gave (methylthio)tributylstannane, as evidenced by a sharp singlet at δ_H 2.10 and the appropriate reduction product 2-phenyl-1,3-dioxane[48] and/or phenylcyclohexane[49] identified in the reaction mixtures through comparison with authentic samples. 2-Phenyl-1,3-dioxane: ^{1}H-NMR δ_H 1.45 (m, 1 H), 2.25 (m, 1 H), 3.98 (dt, 2 H), 4.28 (ddd, 2 H), 5.51 (s, 1 H), 7.28−7.52 (m, 5 H).

Phenylcyclohexane: δ_H 1.30 (m, 1 H), 1.40 (m, 4 H), 1.75 (m, 1 H), 1.85 (m, 4 H), 2.50 (m, 1 H).

(±)-2,4-Di-*O*-benzoyl-*myo*-inositol 1,3,5-Orthoformate (44). *myo*-Inositol 1,3,5-orthoformate (**43**) (190 mg, 1.0 mmol) was dissolved in pyridine (1.0 mL) and treated dropwise at room temperature with benzoyl chloride (308 mg, 2.2 mmol). After stirring at room temperature for 1 h, the reaction mixture was diluted with ether (10 mL) and then with water (4 mL). The aqueous layer was further extracted with ether (2 × 10 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. Column chromatography (SiO_2, EtOAc/hexanes, 1/9) gave a colorless oil (358 mg, 90%) which solidified on standing: white crystals, obtained from hexane/ether; mp 173−174 °C; ^{1}H-NMR δ 2.70 (m, 1 H, OH), 4.50 (m, 1 H, H-3), 4.62 (m, 2 H, H-1, H-5), 4.74 (m, 1 H, H-6), 5.66 (m, 2 H, H-2, H-7), 5.84 (dt, 1 H, ^4J = 1.7 Hz, ^3J = 3.9 Hz, H-4), 7.44−7.50 (m, 4 H), 7.57−7.63 (m, 2 H), 8.07 (m, 2 H), 8.16 (m, 2 H); ^{13}C-NMR δ 63.74, 67.46, 68.51, 68.58, 69.67, 71.83, 102.98, 128.53 (2 C), 128.71 (2 C), 128.89, 129.43, 129.91, 129.98, 133.56 (2 C), 133.78 (2 C), 166.21; IR (film) υ_{max} 3496, 3072, 2968, 2902, 1724, 1602 cm^{-1}. Anal. Calcd for $C_{21}H_{18}O_8$: C, 63.26; H, 4.55. Found: C, 63.30; H 4.53.

(±)-2,4-Di-*O*-benzoyl-6-*O*-(1-imidazolylthiocarbonyl)-*myo*-inositol 1,3,5-Orthoformate (45). The alcohol **44** (3.98 g, 10 mmol) in 1,2-dichloromethane (80 mL) under an argon atmosphere was treated with 1,1′-thiocarbonyldiimidazole (2.97 g of 90%, 15 mmol) and the reaction mixture heated to reflux for 10 h before cooling to room temperature and quenching the reaction with water (50 mL). The aqueous phase was extracted with dichloromethane (2 × 50 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. Column chromatography (SiO_2, EtOAc/hexanes, 1/1) gave **45** (4.06 g, 80%) as a white crystalline solid: mp 156−157 °C; ^{1}H-NMR δ 4.69−4.75 (m, 2 H, H-1, H-5), 5.20 (m, 1 H, H-3), 5.61 (q, 1 H, ^4J = 1.6 Hz, H-7), 5.77 (m, 1 H, H-2), 5.89 (dt, 1 H, ^4J = 1.6 Hz, ^3J = 3.9 Hz, H-4), 6.17 (dt, 1 H, ^4J = 1.6 Hz, ^3J = 3.9 Hz, H-6), 6.87 (dd, 1 H, J = 0.8, 1.7 Hz), 7.28 (tt, 2 H, J = 1.7, 7.8 Hz), 7.44 (dd, 1 H, J = 0.8 Hz), 7.49 (tt, 2 H, J = 1.7, 7.8 Hz), 7.51 (tt, 2 H, J = 1.4, 7.4 Hz), 7.62 (tt, 1 H, J = 1.4, 7.4 Hz), 7.75 (dt, 2 H, J = 1.3, 7.9 Hz), 8.17 (dt, 2 H, J = 1.4, 7.7 Hz), 8.22 (t, 1 H, J = 0.8 Hz); ^{13}C-NMR δ 63.50, 65.76, 67.89, 68.62, 69.15, 74.51, 103.24, 117.47, 128.03, 128.60, 128.65, 128.98, 129.32, 129.97, 131.26, 133.79, 134.02, 137.25, 164.95, 166.14, 181.58; IR (film) υ_{max} 3132, 2966, 1723, 1602, 1452, 1396, 1287, 1263, 1164 cm^{-1}. Anal. Calcd for $C_{25}H_{20}N_2O_8S$: C, 59.05; H, 3.96; N, 5.51. Found: C, 58.95; H, 3.89; N, 5.49.

(±)-6-Deoxy-2,4-di-*O*-benzoyl-*myo*-inositol 1,3,5-Orthoformate (46). Tri-*n*-butyltin hydride (2.14 g, 7.4 mmol) and AIBN (52 mg) in toluene (40 mL) were added dropwise over 40 min to a solution of **45** (3.40 g, 6.69 mmol) in toluene (100 mL) at reflux under argon. After a further 1 h at reflux, the reaction mixture was allowed to cool to room temperature, the solvent removed under vacuum, and the deoxyinositol derivative **46** isolated (2.00 g, 78%) by chromatography on silica gel (EtOAc/hexanes, 1/4). It was a white crystalline solid: mp 190−191 °C; ^{1}H-NMR δ 2.15 (d, 1 H, ^2J = 13.9 Hz, H-6$_{ax}$), 2.82 (d, 1 H, ^2J = 13.9 Hz, H-6$_{eq}$), 4.47−4.52 (m, 2 H, H-1, H-5), 4.63 (dt, 1 H, ^4J = 1.8 Hz, ^3J = 3.7 Hz, H-3), 5.30 (t, 1 H, J = 1.3 Hz, H-2), 5.70 (bs, 1 H, H-7), 5.83 (dt, 1 H, ^4J = 1.6 Hz, ^3J = 4.2 Hz, H-4), 7.46 (tt, 2 H, J = 1.4, 7.8 Hz), 7.58 (tt, 2 H, J = 1.2, 7.4 Hz), 7.62 (tt, 2 H, J = 1.2, 7.4 Hz), 8.04 (dt, 2 H, J = 0.7 Hz), 8.15 (dt, 2 H, J = 0.7, 7.9 Hz); ^{13}C-NMR δ 27.92, 66.78, 67.05, 67.69, 67.96, 69.86, 104.09, 128.50 (2 C), 128.65, 128.73 (2 C), 129.40, 129.79 (2 C), 129.97 (2 C), 133.52, 133.08, 164.95, 166.23; IR (film) υ_{max} 3061, 2974, 1727, 1601, 1584, 1492, 1452, 1370, 1346 cm^{-1} HRMS (EI, 70 eV) calcd for $C_{21}H_{18}O_7$: 382.1053. Found: 382.1047 (M^+). Anal. Calcd for $C_{21}H_{18}O_7$: C, 65.97; H, 4.74. Found: C, 65.59; H, 5.03.

(±)-6-Deoxy-*myo*-inositol 1,3,5-Orthoformate (47). The dibenzoate **46** (200 mg, 0.52 mmol) was dissolved in THF (5 mL) and ethanol (1 mL), treated with 10% aqueous sodium hydroxide (2 mL), and vigorously stirred at room temperature for 1 h. The solvents were then removed under vacuum, and the residue was dissolved in methanol, filtered, evaporated, and purified by column chromatography (SiO_2, EtOAc) to give the ortho ester **47** (78 mg, 86%) as a white crystalline solid: mp 250−251 °C; ^{1}H-NMR (CD_3COCD_3) δ: 2.01 (bd, 1 H, ^2J = 13.5 Hz, H-6$_{ax}$), 2.45 (dm, 1 H, ^2J = 13.5 Hz, H-6$_{eq}$), 3.61 (m, 1 H, H-2), 4.01 (m, 3 H, H-1, H-3, H-5), 4.41 (m, 1 H, H-4), 5.36 (bs, 1 H, H-7); ^{13}C-NMR (CD_3OD) δ 27.15, 64.08, 65.97, 69.60, 71.53, 75.17, 104.29; IR (film) υ_{max} 3504, 2950, 2930, 2856, 1469, 1256 1162 cm^{-1}. Anal. Calcd for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.27; H, 5.71.

(±)-6-Deoxy-2,4-di-*O*-(*S*-methyldithiocarbonyl)-*myo*-inositol 1,3,5-Orthoformate (48). The diol **47** (52 mg, 0.3 mmol) was dissolved in THF (5 mL) and treated under argon at room temperature with sodium hydride (36 mg of 80%, 1.2 mmol). After stirring for 5 min, carbon disulfide (0.12 mL, 2 mmol) was added and stirring continued for a further 30 min before methyl iodide (0.125 mL, 2 mmol) was added. After stirring for 30 min more at room temperature, water (5 mL) was added and the reaction mixture extracted with benzene (2 × 30 mL). The extracts were dried (Na_2SO_4), concentrated, and purified by column chromatography (SiO_2, EtOAc/hexanes, 1/9) to give the dixanthate ester **48** (80 mg, 75%) as a colorless oil which could be crystallized from ether: mp 114−116 °C; ^{1}H-NMR δ 2.04 (d, 1 H, ^2J = 14.1 Hz, H-6$_{ax}$), 2.60 (s, 3 H), 2.62 (s, 3 H), 2.79 (dm, 1 H, ^2J = 14.1 Hz, H-6$_{eq}$), 4.51 (m, 2 H, H-1, H-5), 4.73 (m, 1 H, H-3), 5.64 (bs, 1 H, H-7), 5.74 (m, 1 H, H-2), 6.28 (m, 1 H, H-4); ^{13}C-NMR δ 19.19, 19.58, 27.94, 66.12, 67.37, 68.62, 74.10, 74.25, 103.68, 214.02, 215.47; IR (film) υ_{max} 2963, 2923, 2856, 1424, 1283, 1199, 1161, 1082 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_5S_4$: C, 37.27; H, 3.98. Found: C, 37.46; H, 4.09.

Partial Reduction of 48 with Tributyltin Hydride: Isolation of 49 and 50. To a stirred solution of the bisxanthate **48** (100 mg, 0.28 mmol) in toluene at reflux under argon was added a solution of tri-*n*-butyltin hydride (81 mg, 0.28 mmol) and AIBN (2.5 mg) in toluene (0.5 mL). The reaction mixture was heated to reflux for a further 1 h before cooling to room temperature, removal of the solvent under vacuum, and chromatography on silica gel. Elution with EtOAc/hexanes (1/3) gave first the 2,4,6-trideoxy-2-thio-2-(*S*-methylthiocarbonyl)-*scyllo*-inositol 1,3,5-orthoformate (**49**) (32 mg, 47%): mp 125−128 °C (ether/hexanes); ^{1}H-NMR δ 1.84 (d, 2 H, ^2J = 13.9 Hz, H-4$_{ax}$, H-6$_{ax}$), 2.46 (s, 3 H), 2.61 (dm, 2 H, ^2J = 13.9 Hz, H-4$_{eq}$, H-6$_{eq}$), 4.25 (m, 1 H, H-5), 4.29 (m, 2 H, H-1, H-3), 4.70 (m, 1 H, H-2), 5.65 (bs,

(48) Fischer, E. *Ber. Deutsh. Chem. Ges.* **1894**, *27*, 1524.
(49) Commercial from Aldrich.

1 H, H-7); ^{13}C-NMR δ 17.52, 29.65 (2 C), 43.94, 66.08, 69.43 (2 C), 104.83, 186.85; IR (film) υ_{max} 2959, 2929, 2855, 1718, 1648, 1443, 1379, 1306, 1207, 1163, 1113 cm^{-1}. HRMS (EI, 70 eV). Calcd for $C_9H_{12}O_4S_2$: 248.0177. Found: 248.0172 (M^+, 2.6). Anal. Calcd for $C_9H_{12}O_4S_2$: C, 43.53; H, 4.87. Found: C, 43.35; H, 4.90.

Further elution with the same solvent gave the 4,6-dideoxy-2-(*S*-methyldithiocarbonyl)-*myo*-inositol 1,3,5-orthoformate (**50**) (22 mg, 32%): mp 116−118 °C (ether/hexanes); ^{1}H-NMR δ 1.82 (bd, 2 H, ^2J = 13.5 Hz, H-4$_{ax}$, H-6$_{ax}$), 2.62 (s, 3 H), 2.86 (dm, ^2J = 13.5 Hz, 2 H, H-4$_{eq}$, H-6$_{eq}$), 4.37 (m, 1 H, H-5), 4.53 (m, 2 H, H-1, H-3), 5.60 (dt, 1 H, ^4J = 1.1, 1.3 Hz, H-7), 5.66 (bs, 1 H, H-2); ^{13}C-NMR δ 19.11, 32.53 (2 C), 65.70, 68.62 (2 C), 77.67, 105.02, 215.80; IR (film) υ_{max} 2962, 2927, 1221, 1165, 1070, 981, 912, 817 cm^{-1}. Anal. Calcd for $C_9H_{12}O_4S_2$: C, 43.53; H, 4.87; S, 25.83. Found: C, 43.73; H, 4.74; S, 25.94.

Partial Reduction of 48 with Tris(trimethylsilyl)silane. The bisxanthate **48** (18 mg, 0,05 mmol) was heated to reflux under argon in toluene (2 mL) and treated dropwise with a solution of tris-(trimethylsilyl)silane (13.5 mg, 0.055 mmol) over 10 min. After a further 2 h at reflux, the solvent was removed under reduced pressure and the ratio of **49**:**50** determined by ^{1}H-NMR spectroscopy of the crude reaction mixture in $CDCl_3$ (1.4:1.0).

Acknowledgment. We thank the NSF (CHE 9222697) and CONACYT (Research Grant No. 3079-E9306) for partial support of this work and the Australian Research Council for the award of a Postdoctoral Fellowship to I.G.E.D. D.C. is a Fellow of the A.P. Sloan Foundation. Q.Y. is a Dean's Scholar of the University of Illinois at Chicago. We are grateful to Professor D. H. R. Barton (Texas A & M University) and members of his Radicaux Libres group (1981 vintage) for stimulation and encouragement. The assistance of Ms. R. Gajee with the initial preparation of some starting materials is appreciated.

Supporting Information Available: ^{1}H-NMR spectra (300 MHz) of **10**, **11**, **22**, **23**, **26**, and **27** (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA950789R