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STEREO- AND REGIOSELECTIVITY IN IODO DIOL FORMATION FROM ACYCLIC ALLYLIC ALCOHOLS

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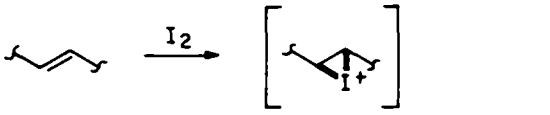
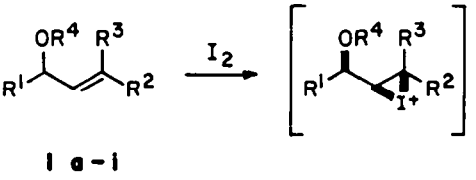
Abstract—Reaction of electrophiles with a variety of acyclic allylic alcohols was investigated. Both aqueous iodine and acetylhypoiodite convert certain alkenols into iodo diols and acetoxy iodo alcohols, respectively, with regio- and stereoselectivities as high as 99%. Protection of the alcohol group lowers the selectivity only slightly. Structural factors that control the regioselectivity of iodohydrin formation in these substrates have been delineated. Some of the iodo diols have been deiodinated, illustrating a simple two step procedure for converting allylic alcohols into threo-1,3-diols.

THE conversion of alkenes into 1,2-halohydrins and related derivatives has been studied extensively.[1] It has been established that the relative stereochemistry of the two substituents introduced in this reaction generally results from antarafacial attack of the nucleophile on an initially-formed halonium ion.

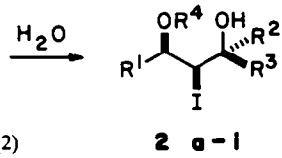


(1)

In the absence of overwhelming steric, electronic, or stereoelectronic effects, the nucleophile attacks the more highly substituted position in unsymmetrical substrates, although this preference often is not a strong one. The effects of pre-existing chiral centers in the alkene upon the regio- and stereochemical outcome of the reaction have been well-delineated in cyclic systems, but not in substituted acyclic alkenes.[2] We therefore have conducted a systematic study of iodohydrin formation from acyclic allylic alcohols, with the intention of developing a simple and selective route to diols. In some cases the reaction has been found to proceed with very high (90–99%) regio- and stereoselectivity, and in others the results have been found to be less satisfactory.

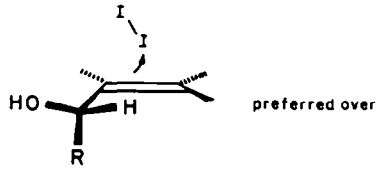


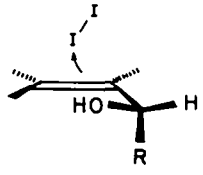
1 a–i



(2) **2 a–i**

The most useful type of substrate studied was 1,2-disubstituted allylic alcohols (Table 1), which react with iodine in a two phase mixture of tetrahydrofuran and pH 5 aqueous phosphate buffer at 0° to give 2-iodo-1,3-diols with regio- and stereoselectivities as high as 99%.[3] The reaction is not greatly affected by increased steric bulk on either substituent of the double bond, but protection of the alcohol group lowers the stereoselectivity somewhat. The example which exhibited the poorest stereoselectivity (77%) was the *Z*-allylic alcohol, **1e**, which was surprising (and as yet unexplained), since the other *Z*-allylic alcohol (**1f**) reacted with good selectivity (97%). The major product in all cases arises from attack by I_2 on the β-face of the double bond, as shown, followed by opening of the resulting iodonium ion at the position farther from the OR group. This type of regioselective opening, which is precedented in the bromination of allylic alcohols,[4] in the opening of protonated epoxy alcohols by nucleophiles,[5] and in the mercuriamination[6] of crotyl alcohol, is discussed in more detail below. The stereoselectivity may be rationalized according to Houk's conformational and orbital overlap arguments.[7]





(3)

The combination of high regio- and stereoselectivity in the formation of iodo diols results in efficient relative asymmetric induction from the original alcohol chiral center to the newly-formed one in

Table 1. Conversion of allylic alcohols and ethers (1a-i) into iodo diol derivatives (2a-i)[a]

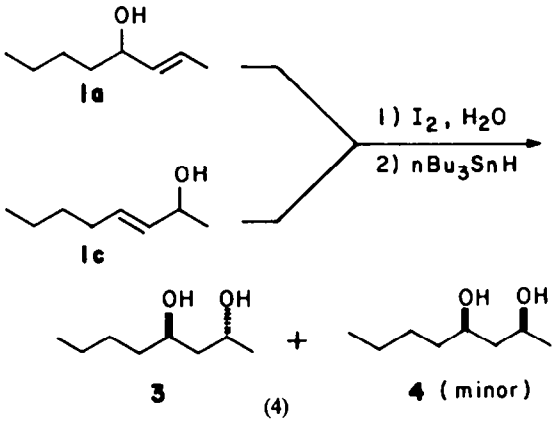
Compound Numbers							
Starting Alkene	Iodo diol	Substituents R^1	R^2	R^3	R^4	Yield[b]	Selectivity[c]
1a	2a	n-Bu	Me	H	H	93%	99%
1b	2b	t-Bu	Me	H	H	72%	97%
1c	2c	Me	n-Bu	H	H	93%	93%
1d	2d	Me	i-Pro	H	H	66%	88%
1e	2e	n-Bu	H	Me	H	77%	77%
1f	2f	Me	H	n-Bu	H	72%	97%
1g	2g	n-Bu	Me	H	CH_2Ph	91%	90%
1h	2h	n-Bu	Me	H	$SiBuMe_2$	99%	88%
1i	2i	n-Bu	Me	H	Me	85%	88%

[a] See text for structures of 1 and 2.

[b] Crude yields. Iododiol mixtures are generally otherwise homogeneous by TLC and ^1H NMR, and silica chromatography does not significantly increase the purity.

[c] See footnote 3 for definition.

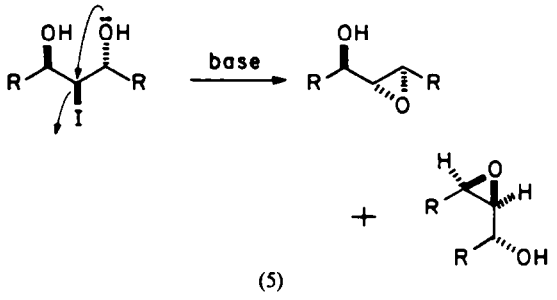
the 3-position, particularly in the case of *E*-allylic alcohols. Several of these products were therefore reduced with tri-n-butyltin hydride to illustrate the use of this reaction in the synthesis of *threo*-1,3-diols. This simple procedure thus complements existing methods[8] for the preparation of 1,3-diol diastereomers.



(4)

ther,[9] the iodohydrins shown in Table 1 are formed routinely in the THF-pH 5 phosphate buffer mixture at 0°.

The structures of the iodo diols and their derivatives were determined spectroscopically and by conversion to epoxy alcohols of known stereochemistry. Specifically, treatment of crude reaction mixtures with one equivalent of sodium methoxide in methanol[10] produced a mixture of two major epoxy alcohols in varying proportions, one of which corresponds (by capillary GC) to one of the epoxy alcohols obtained by Sharpless epoxidation[11] of the starting



(5)

A number of different reaction conditions for iodohydrin formation were investigated in the early stages of this work. Although changes in organic solvent, aqueous phase, and base had little effect on product distributions, the rate of the reaction was highly dependent upon pH. Because HI is a by-product of iodohydrin formation, it is desirable to conduct the reaction in the presence of a buffer; however, in a two-phase system of tetrahydrofuran-aqueous bicarbonate (pH ~ 8.5) reaction of the allylic alcohol **1a** is very slow at 0° ($\leq$ 10% reaction after 24 hr). Conversely, by replacing the bicarbonate buffer with pH 5 or pH 2 phosphate, the same reaction is complete within 2 hr. The rate at pH 7 (phosphate buffer) is intermediate. Although we did not investigate this interesting pH dependence further, the iodohydrins shown in Table 1 are formed routinely in the THF-pH 5 phosphate buffer mixture at 0°.

The structures of the iodo diols and their derivatives were determined spectroscopically and by conversion to epoxy alcohols of known stereochemistry. Specifically, treatment of crude reaction mixtures with one equivalent of sodium methoxide in methanol[10] produced a mixture of two major epoxy alcohols in varying proportions, one of which corresponds (by capillary GC) to one of the epoxy alcohols obtained by Sharpless epoxidation[11] of the starting allylic alcohol, and the other of which does *not* correspond to the other Sharpless diastereomer. This is the behavior expected of the nearly symmetrical 2-iodo-1,3-diols but not of their 3-iodo-1,2-diol regioisomers, confirming both the stereo- and regiochemical assignments. The decoupled 250 MHz ^1H NMR spectra were also consistent with the assigned regiochemistries. The derivatives **2g** and **2h** were deprotected and correlated chromatographically with the corresponding iodo diols. It is interesting that the benzyl ether group of **2g** could be selectively removed without disturbing the secondary iodide using catalytic hydrogenation over Pt (Adam's catalyst). The methyl ether **2i** was identical to the major diastereomer obtained by Sharpless epoxidation of **1a** followed by O-methylation.

Allylic alcohols with different double bond substitution patterns gave disappointing but instructive results. The substrates **5** and **6** produced several major products, showing little regiochemical preference in attack on the iodonium ion by water. The 1,1-disubstituted alkene **7** exhibited completely reversed regioselectivity but relatively low diastereofacial selectivity of iodonium ion formation, giving a 4:1 mixture of iodo-1,2-diols. Based on these results, and those in Table 1, it is possible to make a simple generalization about the regioselectivity of these reactions: a RCH(OH) group is the equivalent of hydrogen in directing the attack of a nucleophile on the iodonium ion. In other words, the electro-

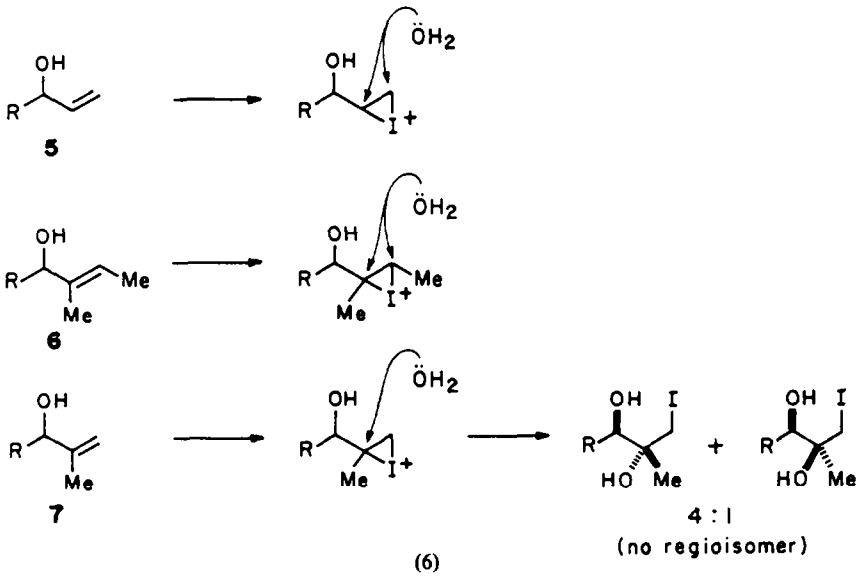
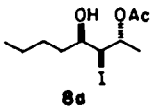
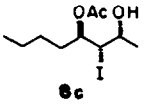
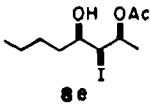
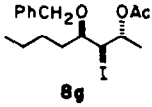
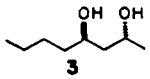


Table 2. Reactions of 1 with other electrophiles

Electrophile/ Nucleophile	Starting Material	Major Product	Selectivity[a]	Yield[b]
IOAc	1a	 **8a**	98%	78%
IOAc	1c	 **8c**	95%	90%
IOAc	1e	 **8e**	94%	85%
IOAc	1g	 **8g**	85%	82%
$Hg(OAc)_2$[c]	1a	 **3**	80%	75%
$H-BH_2$[d]	1a	e	low	—

a. See footnote 3 for definition. Determined by HPLC.
b. Crude yield.
c. Followed by *in situ* reduction with $NaBH_4$.
d. Followed by *in situ* oxidation with alkaline peroxide.
e. At least 3 major products were detected by TLC and ^1H NMR.

negative oxygen substituent negates the electron donating effect of the carbon to which it is attached. Whether this effect is purely inductive or has a more subtle origin is unclear, but in a practical sense it limits the useful types of allylic alcohol substrates to those shown in Table 1.

Because the 1,2-disubstituted alkenols exhibited such high stereo- and regioselectivities in iodohydrin formation, we also subjected them to other electrophilic reagents. While reaction of **1a** with bromine in the presence of water gave a number of products, treatment of several substrates (Table 2) with acetylhypoiodite under Prevost conditions[12] resulted in a very clean reaction to give protected iodo diols.[13] This reagent thus provides an alternative route to selectively protected 1,3-diols. It should be noted that this electrophile reacts with the *Z*-allylic alcohol **1e** with considerably higher stereoselectivity than does I_2/H_2O (94 vs 77%). Oxymercuration–demurcuration[14] of the allylic alcohol **1a** gave a 4:1 mixture of 1,3-diols, favoring the *threo*-diastereomer. This reaction shows that mercury(II) preferentially attacks the same face of the double bond but with reduced selectivity. Finally, hydroboration–oxidation of **1a** under the conditions used very effectively by Still[8c] to generate 2-methyl-1,3-diols gave mixtures of diols and other products in this case.[15,16]

In conclusion, certain acyclic allylic alcohols have been found to undergo very regio- and stereoselective iodohydrin formation. The reaction is insensitive to steric factors removed from the double bond, but substituents on the double bond affect the regioselectivity of the reaction in the predictable way, the most useful substrates being 1,2-disubstituted allylic alcohols or their O-protected counterparts. Reduction of the products produces 1,3-diols, constituting a convenient and selective method of preparing especially the *threo*-diastereomers. Acyl hypoiodites react with allyl alcohols in a similarly selective manner, but several other electrophiles tested attack the same substrate with lower diastereofacial selectivities.

EXPERIMENTAL

General. THF was distilled from K metal. EtOAc and CH_2Cl_2 were distilled from calcium hydride. All other solvents were commercial reagent grade and dried over 3A molecular sieves. IR spectra were recorded on a Perkin–Elmer 283 spectrophotometer. ^1H NMR spectra were obtained on a Bruker WM 250 (250 MHz) spectrometer. Mass spectra were recorded on a Finnigan 9610 spectrometer at 70 eV. High pressure liquid chromatography (HPLC) was performed on a Waters Analytical instrument using a 30 cm μ-Porasil column and a 254 nm uv detector. Gas chromatography was conducted on a Hewlett–Packard Model 5830 A chromatograph equipped with a flame ionization detector. Thin layer chromatography (TLC) was performed on 0.25 mm E. Merck precoated silica gel plates (60 F-254). Flash chromatography was carried out on silica gel, 230–400 mesh (Merck). Elemental Analysis was performed by Robertson Laboratory, Inc.

Preparation of allylic alcohols. Starting allylic alcohols were prepared using standard methods and were purified by distillation prior to use: addition of n-BuLi or t-BuLi to crotonaldehyde afforded **1a** or **1b**, respectively. Addition of MeLi to *trans*-2-hepten-1-ol yielded **1c**. Reduction of 5-methyl-3-hexene-2-one with $NaBH_4$ gave **1d**. Addition of 1-lithiopropyne to pentanal followed by hydrogenation using Lindlar's catalyst produced **1e**. Deprotonation of 1-hexyne with n-BuLi followed by addition of acetaldehyde and subsequent reduction using Lindlar's catalyst produced **1f**. Reaction of **1a** with NaH and then with benzyl bromide, t-butyl-dimethylchlorosilane, or MeI lead to **1g**, **1h** and **1i**, respectively. All alkenes were $\geq 97\%$ isomerically pure by capillary GC.

General preparation of iodo diols. One millimole of the protected or unprotected allylic alcohol was dissolved in 1 mL of THF and 5 mL of 0.50 M pH 5 phosphate buffer at 0°. A soln of I_2 (3 mmol) in 4.0 mL of THF was then added slowly to the rapidly stirred mixture. After 3 hr the mixture was quenched with Na_2SO_3aq and extracted twice with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. ^1H NMR and HPLC ratios were then determined on the crude products (**2a–i**), which were otherwise homogeneous by TLC. All of the aforementioned iodo diols gave IR spectra having an OH stretch from 3500–3300 cm^{-1}. The chemical ionization mass spectra of the iodo diols showed parent ions (M^+), M^+-H_2O, M^+-HI, M^+-HI-H_2O, and corresponding alkyl degradation patterns. Most of the iodo diols (except **2a**) were unstable liquids which decomposed upon standing and could not be analyzed for C, H and I satisfactorily. Yields are tabulated in Tables 1 and 2.

rel-[2R,3R,4R,]-3-*Iodo*-2,4-*octanediol* (**2a**). White solid; recrystalized from distilled hexane: m.p. 50°; ^1H NMR (250 MHz, $CDCl_3$), 4.20 (dd, J = 5.2, 2.2 Hz, H-3), 4.13 (app. quintet, J = 6.0 Hz, H-2), 3.20 (m, H-4), 2.60 (bd, OH, C-2, 2.45 (bd, OH, C-4), 1.46 (d, J = 6.3 Hz, 3H, H-1), 1.40–1.30 (m, 6H), 0.93 (t, J = 6.6 Hz, 3H, H-8); minor isomer: δ 4.29, 4.03, 3.75; TLC (1:1, hexane–ether, R_f 0.25); HPLC (3:1, hexane–ether, 9.8 min, 1%, 10.2 min, 99%). (Found: C, 35.22; H, 6.6; I, 46.90. Calc for $C_8H_{17}IO_2$: C, 35.31, H, 6.30, I, 46.63%).

rel-[2R, 3R, 4R]-3-*Iodo*-5,5-*dimethyl*-2,4-*hexanediol* (**2b**). Clear oil: ^1H NMR (250 MHz, $CDCl_3$) 4.51 (dd, J = 7.8, 3.5 HZ, H − 3), 3.86 (m, H-2), 2.82 (d, J = 7.8 Hz, H-4), 2.31 (d, J = 6.1 Hz, OH, C-2), 2.21 (d, J = 7.8 Hz, OH, C-4), 1.37 (d, J = 6.4 Hz, 3H, H-1), 1.00 (s, 9H, CMe_3); minor isomer not observed by NMR; TLC (2:1, hexane–ether, R_f 0.15); HPLC (2:1 hexane–ether, 3.7 min., 97%, 5.1 min, 3%).

rel-[2R,3S,4R]-3-*Iodo*-2,4-*octanediol* (**2c**). Clear oil: ^1H NMR (250 MHz, $CDCl_3$) 4.23 (dd, J = 4.4, 2.0 Hz, H-3), 3.99 (app. quintet, J = 4.4 Hz, H-4), 3.44 (dq, J = 6.2, 2.0 Hz, H-2), 1.75 (bs, OH), 1.60 (bs, OH), 1.35 (m, 6H), 0.93 (bt, 3H, H-8); minor isomer: 4.29, 4.03, 3.74; TLC (2:1, hexane–ether, R_f 0.10); HPLC (1:1, isooctane–ether, 4.4 min, 93%, 7.1 min, 7%).

rel-[2R,3S,4R]-3-*Iodo*-5-*methyl*-2,4-*hexanediol* (**2d**). Clear oil: ^1H NMR (250 MHz, $CDCl_3$) 4.37 (dd, J = 5.2, 1.6 Hz, H-3), 3.80 (dd, J = 6.2, 5.2 Hz, H-4), 3.42 (app. quintet, J = 6.0 Hz, H-2), 2.86 (d, J = 6.5 Hz, OH, C-2), 2.75 (d, J = 5.2 Hz, OH, C-4), 2.19 (m, H-5), 1.25 (d, J = 6.1 Hz, 3H, H-1), 1.00 (d, J = 6.6 Hz, 3H, H-6), 0.96 (d, J = 6.6 Hz, 3H, H-6); minor isomer: 4.50, 3.98, 3.94; TLC (1:1, hexane–ether, R_f 0.25); HPLC (3:1 isooctane–ether, 1% 2-propanol, 7.3 min, 88%, 8.9 min, 12%).

rel-[2S,3R,4R]-3-*Iodo*-2,4-*octanediol* (**2e**). Clear oil; ^1H NMR (250 MHz, $CDCl_3$) 4.18 (app t, J = 2.0 Hz, H-3), 3.36 (dq, J = 6.1, 2.0 Hz, H-2), 3.06 (dt, J = 7.4, 2.0 Hz, H-4), 2.85 (bs, OH), 2.62 (bs, OH), 1.45–1.30 (m, 6H), 1.27 (d, J = 6.1 Hz, 3H, H-1), 0.92 (t, J = 6.8 Hz, 3H, H-8); minor isomer: 4.23, 3.99, 3.44 (same as **2c**); TLC (1:1, hexane–ether, R_f 0.25); HPLC (3:1, isooctane–ether, 1% 2-propanol, 6.6 min, 76%, 7.8 min, 24%).

rel-[2R,3S,4S]-3-*Iodo*-2,4-*octanediol* (**2f**). Clear oil; ^1H NMR (250 MHz, $CDCl_3$) 4.18 (app t, J = 2.0 Hz, H-3), 3.36 (dq, J = 6.0, 2.2 Hz, H-2), 3.06 (app. septet, J = 5.5, 2.0 Hz, H-4), 1.82 (bd, OH), 1.58 (bd, OH), 1.29 (d, J = 6.0 Hz, 3H, H-1), 1.35 (m, 6H), 0.92 (bt, 3H, H-8); minor isomer: 4.20, 4.13, 3.20 (same as **2a**); TLC (1:1 hexane–ether, R_f 0.25); HPLC (3:1, isooctane–ether, 1% 2-propanol, 6.6 min, 97%, 7.8 min, 3%).

rel-[2R,3R,4R]-4-*Benzyloxy*-3-*iodo*-2-*octanol* (**2g**). Clear

oil; ^{1}H NMR (250 MHz, $CDCl_3$) 7.37 (m, 5H), 4.65 (ABq, J_{AB} = 11.5 Hz, $\Delta\nu_{AB}$ = 10.3 Hz, 2H), 4.21 (dd, J = 8.1, 3.0 Hz, H-3), 3.98 (ddq, J = 8.1, 5.7, 4.0 Hz, H-2), 3.44 (dt, J = 5.3, 3.0 Hz, H-4), 3.04 (d, J = 4.0 hz, OH), 1.41 (d, J = 5.7 Hz, 3H, H-1), 1.34 (m, 6H), 0.92 (bt, 3H, H-8); minor isomer: 4.37, 4.32, 3.75; TLC (8:1, hexane–ether, R_f 0.10); HPLC (10:1, hexane–ether, 6.3 min, 90%, 8.1 min, 10%). A sample was reduced using Adam's catalyst and was found to be identical to **2a** by ^{1}H 250 NMR and TLC.

rel-[2R,3R,4R]-4-*t*-*Butyldimethylsiloxy*-3-*iodo*-2-*octanol* (**2h**). Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 4.05 (app. q, J = 5.6 Hz, H-2), 4.02 (app. d, J = 2.4 Hz, H-3), 3.80 (ddd, J = 8.0, 4.4, 2.4 Hz, H-4), 3.50 (bs, OH), 1.44 (d, J = 5.6 Hz, 3H, H-1), 1.36 (m, 6H), 0.93 (bt, 3H, H-8), 0.92 (s, 9H, CMe_3), 0.15 (s, 3H, Si-Me), 0.12 (s, 3H, Si–Me); minor isomer: 4.23, 3.99, 3.44; TLC (10:1, hexane–ether, R_f 0.28); HPLC (50:1, isooctane–ether, 8.5 min, 88%, 12.2 min, 12%). A sample was deprotected using one equivalent of HF in CH_3CN and was found to be identical to **2a** by TLC and ^{1}H 250 NMR.

rel-[2R,3R,4R]-3-*Iodo*-4-*methoxy*-2-*octanediol* (**2i**). Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 4.22 (dd, J = 7.5, 3.0 Hz, H-3), 3.98 (app. quintet, J = 6.2 Hz, H-2), 3.47 (s, 3H, OMe), 3.21 (ddd, J = 7.5, 3.0, 3.0 Hz, H-4), 1.44 (d, J = 6.2 Hz, 3H, H-1), 1.73 (bs, OH), 1.36 (m, 6H), 0.94 (bt, 3H, H-8); minor isomer: 4.29, 3.74, 3.35; TLC (10:1, hexane–ether, R_f 0.10); HPLC (10:1, hexane–ether, 9.4 min, 87%, 11.2 min, 13%).

rel-[2R,4R]-2,4-*Octanediol* (**3**). The general procedure for forming iodo diols was followed starting with **1a** (224 mg, 1.75 mmol) and I_2 (1.33 g, 5.24 mmol), which yielded **2a** (432 mg, 93%). The crude product **2a** (124 mg, 0.456 mmol) was combined with 2.0 mL of dry toluene and a catalytic amount of AIBN (2,2'-Azobisisobutyronitrile, ~ 10 mg) and then tri-butyltin hydride (0.633 g, 2.28 mmol) was added to the mixture. After 24 hr, the soln was concentrated *in vacuo*, diluted with CH_3CN, washed twice with hexanes to remove excess tin hydride and tin iodide, dryed ($MgSO_4$), and concentrated *in vacuo* to give **3** (55.7 g, 84%) as the major isomer: Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 4.18 (app. quintet, J = 4.5 Hz, H-2), 3.94 (m, H-4), 2.41 (d, J = 4.4 Hz, OH), 2.34 (d, J = 4.5 Hz, OH), 1.61 (dd, J = 6.0, 5.2 Hz, 2H, H-3), 1.55–1.28 (m, 4H), 1.24 (d, J = 6.3 Hz, 3H, H-1), 0.92 (t, J = 5.5 Hz, 3H, H-8); TLC (2:1, hexane–ether, R_f 0.10); Homogeneous by TLC and 250 MHz NMR. The product from reaction of **2c** with tri-n-butyltin hydride afforded a diol that was identical with **3** by 250 MHz NMR and by TLC.

Preparation of iodohydroxy acetates. One millimole of the allylic alcohol was placed in a round bottom flask with 1.0 mL of dry THF at −78°. The liquid layer which resulted from mixing a soln of I_2 (2.0 mmol) and AgOAc (2.0 mmol) in 2.0 mL of dry THF was added slowly to the stirred soln. The precipitated AgI was washed with 2.0 mL more of THF and the washings added slowly to the mixture. The reaction was allowed to warm to 0° and quenched in the same manner as were the iodo diols. ^{1}H NMR ratios and HPLC ratios were then determined on the crude products (**8a, 8c, 8e,** and **8g**). The iodohydroxyacetates all gave similar IR spectra: 3500–3300 (OH), 1730 (C = O), 1375 and 1240 cm^{-1}. The chemical ionization mass spectra of the compounds showed parent ions (M^+) and M^+-H_2O, $M^+-CH_3CO_2H$, M^+-HI, and the appropriate alkyl degradation patterns.

rel-[2R,3R,4R]-2-*Acetoxy*-3-*iodo*-4-*octanol* (**8a**). Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 4.98 (app. quintet, J = 6.3 Hz, H-2), 4.18 (dd, J = 7.4, 2.4 Hz, H-3), 2.88 (m, H-4), 2.19 (bd, J = 6.6 Hz, OH), 2.11 (s, 3H, $-O_2CCH_3$), 1.50 (d, J = 6.3 Hz, 3H, H-1) 1.55–1.25 (m, 6H), 0.92 (t, J = 6.7 Hz, 3H, H-8); minor isomer: 4.21, 4.12, 3.20; TLC (1:1, hexane–ether, R_f 0.45); HPLC (8:1, hexane–ether, 8.7 min, 98%, 13.0 min 2%).

rel-[2R,3S,4R,]-4-*Acetoxy*-3-*iodo*-2-*octanol* (**8c**). Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 4.95 (dt, J = 7.8, 3.0 Hz, H-4), 4.12 (dd, J = 7.8, 2.6 Hz, H-3), 3.11 (app. dt, J = 5.9, 2.6 Hz, H-2), 2.53 (d, J = 5.5 Hz, OH), 2.14 (s, 3H, $-O_2CCH_3$), 1.40–1.30 (m, 6H), 1.25 (d, J = 5.9 Hz, 3H, H-1), 0.91 (bt, 3H, H-8); minor isomer not observed by NMR; TLC (1:1, hexane–ether, R_f 0.40); HPLC (5:1, hexane–ether, 8.1 min, 95%, 9.4 min, 5%).

rel-[2S,3R,4R]-2-Acetoxy-3-iodo-4-octanol (**8e**). Clear oil; ^{1}H NMR (250 MHz $CDCl_3$) 4.99 (app. quintet, J = 6.0 Hz, H-2)), 4.18 (dd, J = 6.0, 3.0 Hz, H-3), 3.99 (m, H-4), 2.09 (s, 3H, $-O_2CCH_3$), 1.62 (bs, OH), 1.38 (d, J = 6.0 Hz, 3H, H-1), 1.45–1.25 (m, 6H), 0.92 (t, J = 6.8 Hz, 3H, H-8); minor isomer: 4.80, 3.96, 3.63; TLC (1:1, hexane–ether, R_f 0.47); HPLC (3:1 isooctane–ether, 1% 2-propanol, 2.9 min, 94%, 3.6 min 6%).

rel - [2R,3R,4R] - 2 - *Acetoxy* - 4 - *benzyloxy* - 3 - *iodo-octane* (**8g**). Clear oil; ^{1}H NMR (250 MHz, $CDCl_3$) 7.33 (m, 5H), 4.58 (ABq, J_{AB} = 11.4 Hz, $\Delta\nu_{AB}$ = 13.3 Hz, 2H), 4.84 (app. quintet, J = 6.5 Hz, H-2), 4.30 (dd, J = 6.5, 3.6 Hz, H-3), 3.06 (dt, J = 6.3, 3.6 Hz, H-4), 2.00 (s, 3H, $-O_2CCH_3$), 1.45 (d, J = 6.5 Hz, 3H, H-1), 1.50–1.20 (m, 6H), 0.92 (t, J = 7.1 Hz, 3H, H-8); minor isomer: 4.52, 4.14, 3.33; TLC (8:1, hexane–ether, R_f 0.35); HPLC (8:1, hexane–ether, 4.2 min, 85%, 5.2 min, 15%).

General preparation of epoxy alcohols from iodo diols. The iodo diol (0.50 mmol) was dissolved in MeOH (1.0 mL) at −20° and 0.20 M KOH in MeOH (2.5 mL, 0.50 mmol) was

Table 3. Capillary gas chromatographic correlation of epoxy alcohols from **2a**, **2b** and **2d** with sharpless epoxy alcohols[a]

Epoxy alcohol Mixtures from Iodo Diols			Epoxy alcohol Mixtures from Sharpless Oxidation		
Starting Material	GC Ratio	Retention times (min)	Starting Alkene	GC Ratio	Retention times (min)
2a	45/55	11.2/11.5	1a	70/30	11.2/11.3
2b	70/30	9.1/13.7	1b	92/8	9.1/9.2
2d	30/70	8.0/8.9	1d	61/39	8.0/8.2
2i	---	10.90	1a[b]	40/60	10.81/10.90

a Epoxy alcohols were also correlated with Sharpless products by 250 MHz NMR. Minor Sharpless products did not correspond to either epoxy alcohol formed from the iodo diols.

b Sharpless epoxy alcohol was treated with methyl iodide and KOH in pentane to achieve methylation without competing Payne rearrangement (see reference in footnote 10).

added. The reaction was quenched with 1.0 N HCl soln when no iodo diol remained by TLC, extracted twice with ether, dried ($MgSO_4$), and concentrated *in vacuo* to yield the epoxy alcohols (Table 3) in quantitative yields.

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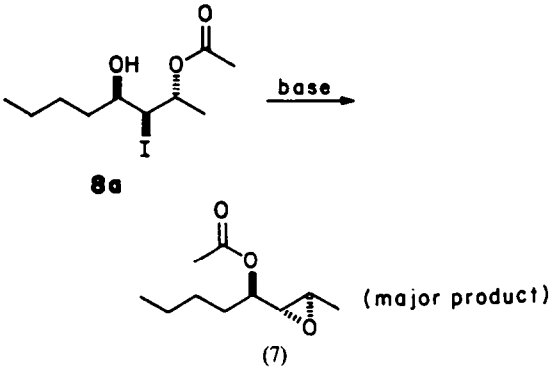

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