Comparative Diastereoselectivity Analysis of Crotylindium and 3-Bromoallylindium Additions to \( \alpha \)-Oxy Aldehydes in Aqueous and Nonaqueous Solvent Systems

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Received July 16, 1996

The couplings of crotyl bromide (1) and 1,3-dibromopropene (2) to a triad of conformationally unrestricted \( \alpha \)-oxy aldehydes in water, aqueous THF (1:1), and anhydrous THF are described. In no example involving 1 was the formation of anti, syn product detected. The proportion of syn isomers reached a maximum (syn/anti = 5:6:1) when the neighboring hydroxyl group was unprotected and water was the reaction medium. Although internal chelation also operates to some degree with 2, considerable erosion of this mechanistic pathway (maximum now only 2:1) in favor of Felkin and “anti-Felkin” transition states is reflected in the product distributions. This trend can be synthetically advantageous, and a utilitarian example is demonstrated. The indium reagents studied here are notably efficient nucleophilic reaction partners in water.

The desirability of producing functionalized acyclic molecules in a highly diastereoselective manner has prompted extensive examination of the condensation of prochiral allylic bromides. Many types of organometallic reagents, most notably those where \( M = B, A l, C r, S i, S n, T i, \) and \( Z r \), are now recognized to be capable of delivering a specific stereochemical outcome. The remarkable and highly utilitarian interdependence of metal, allylic double-bond geometry and syn or anti configuration of the resultant homoallylic alcohol has been conveniently classified into three categories. To rationalize the different carbon-carbon bond-forming stereoselectivities, each type is characterized by a transition state structure featuring a unique arrangement of the reacting double bonds.

All of the above transformations are effected in organic solvent, most often under anhydrous conditions. In light of the ability of indium to be capable of promoting allylations in water and our specific interest in the levels of diastereoselectivity attainable in aqueous media, we have recently undertaken an analysis of the diastereoselectivity attending the coupling of the two electronically distinct 3-substituted allylic bromides 1 and 2 to \( \alpha \)-oxy aldehydes 3–5 in solvents ranging from anhydrous tetrahydrofuran to pure water. Very recently, Isaac and Chan have proposed that the allylindium intermediates formed under these conditions are amenable to regioisomeric equilibration. The pre-equilibrium allows for E to Z conversion where relevant and makes provision for steric control of the coupling process when the allyl R′ or R′′ substituent is sterically bulky. Otherwise, the reaction is \( \gamma \)-regioselective.

In the present investigation, only allyl inversion has been seen. Chelation control again operates to an appreciable level when the aldehyde carries a free hydroxyl substituent as in 4. A noteworthy feature associated with the use of 2 is the option this dibromide offers for reversing to a significant degree the high syn selectivity associated with the direct condensation of 4 with allyl bromide.

Finally, our findings are rationalized in terms of cyclic transition states in which the aldehyde carbonyl is coordinated via the oxygen atom to the indium of the organometallic. The diastereoselectivity data show that the chiral reagent/chiral substrate pairs are not particularly conducive to high levels of reaction stereoselectivity in most cases.

Results

When 2-(benzyloxy)propanal (3) was stirred with crotyl bromide and indium powder in water at rt for 4 h, a mixture of products resulted. Flash chromatography on silica gel resulted in separation of a 1:1 mixture of

\[ \text{OH} \quad \text{Br} \quad \text{H} \]

(7:5:1)

1. \( R = \text{CH}_3 \)
2. \( R = \text{Br} \)
3. \( R = \text{CH}_2\text{Ph} \)
4. \( R = \text{H} \)
5. \( R = \text{TBS} \)

\[ \text{OH} \quad \text{Br} \quad \text{OH} \quad \text{OH} \]

\( \text{CH}_3 \quad \text{Br} \quad \text{CH}_3 \)

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the syn,syn (6) and syn,anti (7) alcohols from the anti,anti diastereomer 8. None of the anti,syn product could be detected by either high-field $^1$H or $^{13}$C NMR (Table 1, entry 1). The stereochemical assignments are based on direct comparison of the $^{13}$C NMR signals with those assigned earlier by Martin and Li (see Experimental Section). The 0.5:0.5:1 diastereoselectivity of this reaction was observed as well in 1:1 H$_2$O-THF and in THF, although the reaction rate in pure organic solvent was notably slower (entry 3).

The next series of experiments was performed with the unprotected 2-hydroxypropanal (4). Admixing of this aldehyde with crotyl bromide and indium in the same three solvent systems led again to only three diastereomeric products (entries 4–6). The polarity differences of these diols on silica gel allowed for their partial chromatographic separation. Once these fractions had been individually subjected to catalytic hydrogenation, it proved conveniently possible to isolate pure 11 and a 1:1 mixture of 9 and 10. The product ratios given in Table 1 were derived from $^1$H NMR integrations and from sample weights determined at this stage. Structural assignments were made possible by direct $^{13}$C NMR comparisons with authentic samples.

For convenience, the product mixtures derived from adding the crotylindium reagent to 5 were directly hydrolyzed with p-toluenesulfonic acid in methanol and hydrogenated to 9–11 for characterization purposes (entries 7–9). We have previously reported that indium-promoted allylations performed in water become increasingly acidic (to a pH level of approximately 2.9) as they proceed to completion. The same phenomenon was, of course, observed here. Where entries 7 and 8 are concerned, deprotection of the silyl ether can materialize, particularly if stirring is allowed to proceed for an extended period of time. The predescribed workup protocol obviates any complications in determining product ratios stemming potentially from this source.

In addition to the persistent absence of the anti,syn diastereomer in entries 1–9, attention is called to the trend reflected in the product compositions. In the absence of a hydroxyl protecting group $\alpha$ to the aldehyde carbonyl as in 4, the syn diols are favored by as much as 5:6:1 in H$_2$O over the anti isomer. The loss of this acidic proton as in 3 and 5 results in a decrease in the relative proportion of the syn diols. In the most extreme case, the presence of a tert-butyldimethylsilyl residue favors anti diol formation by a factor of 3:1.

### Table 1. Indium-Promoted Addition of Crotyl Bromide (1) to $\alpha$-Oxy Aldehydes at 25 °C

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehyde</th>
<th>solvent</th>
<th>reaction yield, time, h</th>
<th>product ratios</th>
<th>syn, syn</th>
<th>syn,anti</th>
<th>anti,anti</th>
<th>anti,syn</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O</td>
<td>4 89</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O-THF (1:1)</td>
<td>4 87</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>THF</td>
<td>12 74</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O</td>
<td>3.5 79</td>
<td>2.8</td>
<td>2.8</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O-THF (1:1)</td>
<td>3.5 78</td>
<td>1.5</td>
<td>1.5</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>PhCHO$\tilde{\text{H}}$</td>
<td>THF</td>
<td>7.5 64</td>
<td>2.3</td>
<td>2.3</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>TBSO PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O</td>
<td>4.5 91</td>
<td>0.5</td>
<td>0.5</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>TBSO PhCHO$\tilde{\text{H}}$</td>
<td>H$_2$O-THF (1:1)</td>
<td>4 88</td>
<td>0.5</td>
<td>0.5</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>TBSO PhCHO$\tilde{\text{H}}$</td>
<td>THF</td>
<td>11 71</td>
<td>0.5</td>
<td>0.5</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

* All of the reactions were conducted minimally in duplicate at a concentration of 0.1 M with vigorous stirring for the indicated time span. The product distributions in all cases were determined by $^1$H NMR integration at 300 MHz. a Yields determined after hydrogenation; all other yields refer to post-chromatographic purification.

(7) Martin, S. F; Li, W. J. Org. Chem. 1989, 54, 6129. The compilations of $^{13}$C NMR shifts provided for 6 and 8 in this paper are incomplete. As shown herein, the syn,syn isomer exhibits a necessary 12th carbon peak at 126.5 ppm. For the anti,anti isomer, the unlisted carbon signal is seen at 127.0 ppm.

A quick scan of Table 2 will reveal that the reactions of dibromide 2 with 3 and 5 are more anti-selective than those involving crotyl bromide. In each of the alkylation represented by entries 10–18, it was necessary to monitor reaction progress carefully, especially when complete consumption of the aldehyde was being approached, in order to minimize reductive debromination of the halohydrin products.9 With this precaution in place, each of the processes was found to deliver all four possible diastereomers. In order to secure proper stereochemical assignments, attention was initially directed to chemical correlation with epoxides on the one hand and acetonides on the other. Through analysis of the oxirane proton coupling constants in 12, the syn/anti relationship of the neighboring bromine- and hydroxyl-substituted carbons would be made apparent. With subsequent scrutiny of the spectral details of 13, full analysis of the interrelationship of all three stereogenic centers would be realized. Unfortunately, overlapping absorptions in the 1H NMR spectra of 13 and its diastereomers precluded the use of these derivatives for characterization purposes.

An alternative workable solution consisted of removal of the allylic bromine via reduction with indium in water. This protocol operates without migration of the double bond to deliver known diols,10 thereby permitting direct comparison of 1H and 13C NMR features.

From the results compiled in Table 2, the apparent role played by the vinylic bromine in 2 would appear to be significant erosion of the chelation capability of the neighboring α-hydroxyl substituent in 4. Not surprisingly, the presence of an O-benzyl group as in 3 does not give rise to any improved stereochemical bias. In contrast, the bulky tert-butyldimethylsilyl residue in 5 increases the anti selectivity rather steeply to a level approaching 1:10. This finding is significant in that a route complementary to the syn-selective direct alkylation of the α-hydroxy aldehyde is now opened.

Discussion

We have previously demonstrated that the stereochemical course of allylindium reactions to α- and β-oxy aldehydes in water as the reaction medium is strongly influenced by the protecting group resident on the neighboring oxygen.1a,c Significantly, free hydroxyl derivatives react with excellent diastereofacial control at accelerated rates to provide heightened percentages of syn-1,2-diol and anti-1,3-diol products. These observations have given rise to the conclusion that the chelated transition states A and B are adopted in these reactions.

Table 2. Indium-Promoted Addition of 1,3-Dibromopropene (2) to α-Oxy Aldehydes at 25 °Ca

<table>
<thead>
<tr>
<th>entry</th>
<th>aldehyde</th>
<th>solvent</th>
<th>reaction yield, %</th>
<th>product ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>PhCH2O</td>
<td>H2O</td>
<td>2.5 88</td>
<td>0.5 0.5 1 1</td>
</tr>
<tr>
<td>11</td>
<td>CH3</td>
<td>H2O-THF (1:1)</td>
<td>2.5 88</td>
<td>0.5 0.5 1 1</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>THF</td>
<td>7.0 75</td>
<td>0.5 0.5 1 1</td>
</tr>
<tr>
<td>13</td>
<td>HO</td>
<td>H2O</td>
<td>4.0 80b</td>
<td>1 1 0.5 0.5</td>
</tr>
<tr>
<td>14</td>
<td>4</td>
<td>H2O-THF (1:1)</td>
<td>4.5 80b</td>
<td>1 1 0.5 0.5</td>
</tr>
<tr>
<td>15</td>
<td>5</td>
<td>THF</td>
<td>9.0 68b</td>
<td>0.8 0.8 0.5 0.5</td>
</tr>
<tr>
<td>16</td>
<td>TBSO</td>
<td>H2O</td>
<td>2.5 88</td>
<td>0.5 0.5 4.5 4.5</td>
</tr>
<tr>
<td>17</td>
<td>4</td>
<td>H2O-THF (1:1)</td>
<td>2.0 90</td>
<td>0.5 0.5 5 5</td>
</tr>
<tr>
<td>18</td>
<td>5</td>
<td>THF</td>
<td>10 79</td>
<td>0.5 0.5 5 5</td>
</tr>
</tbody>
</table>

a Consult footnote a of Table I. b Yields based on unpurified products; all other yields refer to post-chromatographic purification.
Substitution of the hydroxyl proton by CH₃, C₂H₅CH₂, or CH₂OCH₂⁻ is predictably ameliorative of the chelation control pathway as reflected in a modest erosion of the allylylation diastereoselectivity. Larger groups such as tert-butyl(dimethyl)silyl effectively deter transient binding of the attached oxygen to the indium, at least in water, and promote alternative conversion to product via Felkin–Ahn transition states. Thus, steric effects appear to exert a significant influence on the outcome of these single asymmetric induction processes.

The focus of the present investigation was to determine to what extent and in which direction the stereochemistry inherent in the olefin geometry of 1 and 2 would be transmitted to the newly formed C–C bond in the product. Although crotyl bromide added to 4 with a preference for adoption of the cyclic chelated transition states C and D (syn selectivity as high as 5:6:1), the replacement of methyl by a γ-bromine is accompanied by an unexpected dropoff in the level of syn product (now γ states preference for adoption of the cyclic chelated transition product. Although crotyl bromide added to 4 allylation diastereoselectivity. Larger groups such as control pathway as reflected in a modest erosion of the stericsize of this atom, to the longer C–Br bond, or to a combination of these influences. The indication exists that E/Z equilibration is also facile in this instance. The notable preference exhibited by 2 for reaction via the transition states E and F or G is sufficiently elevated when R⁰ is TBS to favor formation of the anti isomer to the extent of 10:1! This appreciable kinetic selectivity holds synthetic utility. Following reductive debromination and desilylation, anti diol 15 is obtained predominantly. This diastereoselection is opposite to that realized upon direct condensation of 4 with allylindium in water, a process which is highly syn-selective.

Lastly, we point out the greater efficiency of indium-promoted crotylation and bromoallylation in water and aqueous THF. A 10–20% enhancement in combined product yield was universally observed. Although these C–C bond-forming reactions happen not to be particularly diastereoselective when conducted in aqueous environments, each transformation occurs with remarkably few, if any, side reactions. The higher reaction rate in water than in aqueous THF may be a result of the

\[
\begin{align*}
\text{E} & \quad \text{anti,anti} \\
\text{F} & \quad \text{anti,syn} \\
\text{G} & \quad \text{anti,anti} \\
\text{H} & \quad \text{anti,syn}
\end{align*}
\]

\[
\begin{align*}
\text{C} & \quad \text{syn,syn} \\
\text{D} & \quad \text{syn,anti}
\end{align*}
\]
hydrostatic pressure that materializes around the small globules that make their appearance in purely aqueous environments. This phase separation is not seen in 1:1 aqueous THF.

**Experimental Section**

**Additions Involving Crotyl Bromide and Aldehyde 3.**

A. In H$_2$O. To a 100 mg (0.617 mmol) mixture (79% combined yield) and 3 (77 mg, 0.670 mmol). After 4 h, ethyl acetate (10 mL) was introduced and the layers were separated 45 min later. The aqueous phase was extracted with ethyl acetate (3 × 10 mL), and the combined organic phases were dried and evaporated. Chromatography of the residue on silica gel (elution with 20:1 hexanes/ethyl acetate) gave a mixture of two syn diastereomers together with 58 mmol of the anti,anti diol (67% combined). The products were identified on the basis of their 13C NMR chemical shifts in CDCl$_3$. From 300 mg (1.59 mmol) of crotyl bromide (321 mg, 2.39 mmol), and indium powder (201 mg, 1.75 mmol) was stirred in THF (17.5 mL) for 11 h before being processed in the usual way to give two fractions in a 1:3 ratio (combined weight of 272 mg or 71%). Independent hydrogenation of each fraction gave a 1:1 mixture of 9 and 10 (15 mg) and pure 11 (46 mg). These diols were identified by means of their 13C NMR spectra as described above.

B. In H$_2$O–THF (1:1). A mixture of 3 (100 mg, 0.617 mmol), crotyl bromide (123 mg, 0.914 mmol), and indium powder (77 mg, 0.670 mmol) in 1:1 H$_2$O–THF (6.6 mL) was stirred for 4 h. Following product isolation in the predescribed manner, there was isolated 60 mg of a 1:1 mixture of the syn diastereomers together with 58 mmol of the anti,anti diol (67% combined). The products were identified on the basis of their 13C NMR chemical shifts.

C. In THF. A mixture of 3 (100 mg, 0.617 mmol), crotyl bromide (127 mg, 0.914 mmol), and indium powder (77 mg, 0.670 mmol) in THF (6.7 mL) was stirred at rt for 12 h before being processed in the usual way. The first chromatographic fraction (50 mg) consisted of equal amounts of the syn,syn and syn,anti diols. To elute subsequently was a pure fraction of the anti,anti product (51 mg, 74% combined).

**Additions Involving Dibromide 2 and Aldehyde 3.**

A. In H$_2$O. A mixture of 4 (80 mg, 1.08 mmol), crotyl bromide (218 mg, 1.62 mmol), and indium powder (136 mg, 1.18 mmol) in water (11.8 mL) was stirred at rt for 3.5 h and worked up in the predescribed manner. The mixture was subjected to flash chromatography (silica gel, elution with 21:1 hexanes/ethyl acetate) to give two fractions in a 5:5:1 ratio. Each fraction was separately hydrogenated and purified viaflash chromatography (silica gel, elution with 21:1 hexanes/ethyl acetate) to give a 1:1 mixture of the syn diastereomers (61 mg) and a second pure anti fraction (60 mg, 89% combined yield). The components were identified on the basis of their 1H NMR spectra.

B. In H$_2$O–THF (1:1). A mixture of 3 (100 mg, 0.617 mmol), crotyl bromide (127 mg, 0.914 mmol), and indium powder (77 mg, 0.670 mmol) in 1:1 H$_2$O–THF (6.6 mL) was stirred for 4 h. Following product isolation in the predescribed manner, there was isolated 60 mg of a 1:1 mixture of two syn diastereomers (61 mg) and a second pure anti fraction (60 mg, 89% combined yield). The components were identified on the basis of their 1H NMR spectra. The mixture was subjected to flash chromatography (silica gel, elution with 21:1 hexanes/ethyl acetate) to give two fractions in a 1:3 ratio (61 mg, 97%). Independent hydrogenation of each fraction gave a 1:1 mixture of 9 and 10 in addition to 13 mg of 11.

C. In THF. A mixture of 5 (300 mg, 1.59 mmol), crotyl bromide (321 mg, 2.39 mmol), and indium powder (201 mg, 1.75 mmol) was stirred in THF (17.5 mL) for 11 h before being processed in the usual way to give two fractions in a 1:3 ratio (combined weight of 272 mg or 71%). Independent hydrogenation of each fraction gave 35 mg of the 46:100 mixture and pure 11 (106 mg). These diols were identified by the 13C NMR spectra.

**Additions Involving Dibromide 2 and Aldehyde 3.**

A. In H$_2$O. A mixture of 3 (135 mg, 0.834 mmol) and water (8.7 mL) was treated with 1,3-dibromopropene (334 mg, 1.668 mmol) and indium powder (101 mg, 0.876 mmol) and stirred at rt for 2.5 h. Following the addition of ethyl acetate (15 mL) and additional stirring (30 min), the separated aqueous layer was extracted with ethyl acetate (3 × 15 mL), the combined organic phases were dried and evaporated. The residue was subjected to flash chromatography on silica gel (elution with 20:1 hexanes/ethyl acetate) to give a colorless oil (209 mg, 88%).

An 80 mg (0.280 mmol) sample of this bromohydrin was dissolved in dry THF (20 mL), treated with sodium hydride (13 mg, 0.54 mmol), and stirred at rt for 7.5 h. After the addition of CH$_3$Cl$_2$ (15 mL) and water (10 mL), the aqueous phase was separated and extracted with CH$_3$Cl$_2$ (3 × 15 mL). The combined organic phases were dried and concentrated. The residue was purified by flash chromatography on silica gel (elution with 20:1 hexanes/ethyl acetate) to yield the stereoisomer epoxides as a colorless oil (76 mg, 95%).

The presence of all four possible diastereomers was readily discerned by 1H NMR spectroscopy at 300 MHz (in CDCl$_3$). The two trans epoxides exhibited key signals at $\delta$ 3.16–3.12 (m, 0.11 H) and $\delta$ 3.04 (dd, $J_1 = 4.0, 0.2$ Hz, 0.2 H), while the corresponding absorptions of the cis epoxides appeared at $\delta$ 2.97 (dd, $J_2 = 2.2, 0.6$ Hz, 0.1 H) and 2.66 (dd, $J_1 = 2.1, 5.3$ Hz, 0.2 H). On the basis of the ensuing experiment, these epoxides are recognized to be a–d, respectively. The 13C NMR spectrum (75 MHz, CDCl$_3$) of this mixture exhibited nonoverlapping sets of signals at $\delta$ 3.0–3.15 (21.9, 18.7, 17.4) ppm.) On the basis of the ensuing experiment, these epoxides are recognized to be a–d, respectively. The 13C NMR spectrum (75 MHz, CDCl$_3$) of this mixture exhibited nonoverlapping sets of signals at $\delta$ 3.0–3.15 (21.9, 18.7, 17.4) ppm.)

In a separate experiment, a sample of the bromohydrin mixture (256 mg, 0.900 mmol) and indium powder (103 mg, 0.900 mmol) was stirred in H$_2$O (9 mL) at rt for 8 h, at which time 1 N HCl (10 mL) was added with stirring. Ethyl acetate (15 mL) was next introduced, and the separated aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic phases were dried and evaporated, and the residual oil was purified via flash chromatography (silica gel, elution with 20:1 hexanes/ethyl acetate) to give a mixture of the stereoisomer epoxides (174 mg, 95%). The syn and anti configurations were elucidated by comparison of 1H NMR spectra with those of known compounds. Integration of the distinct methyl doublets ($\delta$ 15.3 for syn, $\delta$ 13.7 for anti) showed the syn/anti ratios to be 1:2.
B. In $\text{H}_2\text{O}$–THF (1:1). Reaction of 3 (200 mg, 1.21 mmol) with 1,3-dibromopropene (484 mg, 2.42 mmol) and indium powder (153 mg, 1.33 mmol) in 1:1 H$_2$O–THF (13.2 mL) for 2.5 h gave 291 mg (88%) of the bromohydrin diastereomers. Following cyclization to epoxides a–d and independent indium-promoted reduction, the product ratio was determined to be closely comparable to that observed in part A.

C. In THF. Reaction of 3 (200 mg, 1.21 mmol) with 1,3-dibromopropene (148 mg, 2.42 mmol) and indium powder (153 mg, 1.33 mmol) in THF (13.2 mL) for 7 h afforded 268 mg (75%) of bromohydrin isomers. Subsequent to chemical correlation in the predescribed manner, the product distribution was found to be identical to that established in experiments A and B.

Additions Involving Dibromide 2 and Aldehyde 4. A. In H$_2$O. A mixture of 4 (80 mg, 1.08 mmol), 1,3-dibromopropene (432 mg, 2.16 mmol), and indium powder (130 mg, 1.13 mmol) in water (11 mL) was stirred at rt for 4 h and processed as described above to give 168 mg (80%) of the bromohydrin as a colorless oil.

To a solution of this material (249 mg, 1.28 mmol) in anhydrous methanol (25 mL) was added potassium carbonate (270 mg, 1.92 mmol), and stirring was maintained for 12 h prior to solvent evaporation. The solid was separated by filtration, and the filtrate was concentrated to give the epoxy powder (153 mg, 1.33 mmol) in THF (13.2 mL) for 7 h afforded 268 mg (75%) of bromohydrin isomers. Subsequent to chemical correlation in the predescribed manner, the product distribution was found to be identical to that established in experiments A and B.

Additions Involving Dibromide 2 from Aldehyde 5. In H$_2$O. A mixture of 5 (190 mg, 1.0 mmol), 1,3-dibromopropene (400 mg, 2.0 mmol), and indium powder (126 mg, 1.1 mmol) in water (11 mL) was stirred at rt for 2.5 h and worked up in the predescribed manner to give 272 mg (88%) of bromohydrin mixture as a colorless oil. To a solution of this material (270 mg, 0.870 mmol) in THF (10 mL) was added sodium hydride (24 mg, 0.979 mmol). After 10 h of stirring, water was added, and the separated aqueous layer was extracted with CH$_2$Cl$_2$ (24 mg, 0.979 mmol). After 10 h of stirring, water was added, and the separated aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 15 mL). The combined organic layers were washed with water, dried, and evaporated. The residue was purified via flash chromatography on silica gel (elution with 20:1 hexanes/ethyl acetate) to give epoxides e–h as a colorless oil (182 mg, 92%). The relative percentages of the four epoxides were ascertained by integration of the characteristic peaks denoted earlier.

In a separate experiment, 300 mg (0.971 mmol) of the bromohydrin mixture in water (10 mL) was treated with indium powder (115 mg, 0.971 mmol) and stirred for 8 h. A white precipitate was formed during this time. Hydrochloric acid (10 mL of 1 N) was added, and after 10 min of stirring the reaction mixture was extracted with ethyl acetate (3 × 15 mL), the combined organic phases were dried and concentrated, and the residue was purified by flash column chromatography (silica gel, elution with 50:1 hexanes/ethyl acetate). The colorless oil so obtained (198 mg, 89%) was dissolved in anhydrous methanol (10 mL), treated with a crystal of p-toluenesulfonic acid, and stirred at rt for 5 h prior to solvent evaporation. Purification of the residue by flash chromatography on silica gel (elution with 2:1 hexanes/ethyl acetate) gave a 1:9 mixture of the syn and anti diols (85 mg, 85%), as determined by $^1$H NMR analysis (see above).

B. In H$_2$O–THF (1:1). From a mixture of 5 (190 mg, 1.0 mmol), 1,3-dibromopropene (400 mg, 2.0 mmol), and indium powder (126 mg, 1.1 mmol) in 1:1 H$_2$O–THF (11.0 mL), there was isolated after 2 h 278 mg (90%) of the bromohydrin mixture as a colorless oil. This unpurified material was transformed into the epoxides as described above and comparably analyzed.

C. In THF. Stirring 5 (190, 1.0 mmol) and 1,3-dibromopropene (400 mg, 2.0 mmol) with indium powder (126 mg, 1.1 mmol) in THF (11 mL) for 10 h gave 244 mg (79%) of the bromohydrin mixture. Conversion to the epoxides in the predescribed manner allowed for analysis of the product ratios reported in Table 2.

Acknowledgment. Financial support from the Environmental Protection Agency and the Emissions Reduction Research Center at the New Jersey Institute of Technology is gratefully acknowledged. The authors thank Prof. S. F. Martin for an authentic sample of the anti,syn diol analogue of 9–11 which permitted verification of its absence from the crotyl bromide additions to 3–5, and Dr. Methvin Isaacs for relevant discussions.