A New Synthetic Method of Preparing Iodohydrin and Bromohydrin Derivatives through *in Situ* Generation of Hypohalous Acids from H_5IO_6 and $NaBrO_3$ in the Presence of $NaHSO_3$

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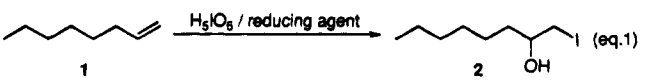
Hypohydrous acids such as hypoiodous acid (IOH) and hypobromous acid (BrOH) were found to be easily generated from H_5IO_6 and $NaBrO_3$ in the presence of an appropriate reducing agent such as $NaHSO_3$. Iodohydrin and bromohydrin derivatives were synthesized in good yields from the reaction of a wide variety of organic compounds bearing carbon–carbon double bonds, with H_5IO_6 or $NaBrO_3$ and $NaHSO_3$. The iodohydroxylation of internal alkenes was achieved with high stereoselectivity to give anti products, although no stereoselectivity was observed in the bromohydroxylation of these alkenes. It was found that allylic alcohols undergo iodohydroxylation in anti-Markovnikov fashion to form iodo diols in good yields. Treatment of alkynes with H_5IO_6 combined with $NaHSO_3$ afforded the corresponding ketones in fair yields, but the same treatment with $NaBrO_3$ rather than H_5IO_6 produced the corresponding α,α-dibromo ketones along with small amounts of the dibromoalkenes.

The transformation of olefins into the corresponding halohydrins is frequently practiced in organic synthesis.[1] The formation of chlorohydrins and bromohydrins from alkenes is a well-established preparative procedure.[2] However, the direct synthesis of iodohydrins from olefins is usually difficult to achieve by the same procedure because of the ready reversibility of the addition of IOH to olefins in a dilute aqueous solution of iodine.[3] Therefore, iodohydrins are usually derived from the reaction of epoxides with hydroiodic acid[4] or metal iodide,[5] the halogen exchange reaction of chlorohydrins or bromohydrins with sodium iodides,[3b] or the iodomethylation of carbonyl compounds with CH_2I_2 in the presence of SmI_2,[6] etc.

Recently we have found that the apparent formation of hypoiodous acid, IOH, is easily achieved by treating periodic acid, $HIO_4{\cdot}2H_2O$ (abbreviated H_5IO_6), or sodium periodate, $NaIO_4$, with an appropriate reducing agent such as sodium bisulfate, $NaHSO_3$.[7] The combination reagent $H_5IO_6/NaHSO_3$ is an excellent vehicle for introducing both I and OH functions into carbon–carbon double bonds under mild conditions.[7] A part of our study of the iodohydrin synthesis by the *in situ* generation of IOH from H_5IO_6 and $NaHSO_3$ was already published as a letter.[7a] In the course of this study, we found that hypobromous acid, BrOH, can be generated from sodium bromate, $NaBrO_3$, and $NaHSO_3$ in a similar manner as IOH. In this paper, we wish to report in full detail on this new synthetic method for preparing iodohydrin and bromohydrin derivatives from a variety of olefinic compounds. In addition, we demonstrate the transformation of alkynes into ketones or α-halo ketones by reaction with these reagents.

Results and Discussion

To develop an appropriate reducing agent for the generation of hypoiodous acid (IOH) from H_5IO_6, 1-octene (**1**) was allowed to react with H_5IO_6 in the presence of a wide variety of reducing agents (eq 1 and Table 1).



The nature of the reducing agents markedly influenced the formation of iodohydrin **2**. Among the reducing agents examined, $NaHSO_3$ was found to be the most effective agent for the generation of apparent IOH, whereas Na_2SO_3 and $Na_2S_2O_3$ were less effective than $NaHSO_3$ (entries 2, 5, and 6). Na_2HPO_3, $FeSO_4$, and oxalic acid were inert in this capacity (entries 7–9). Several solvents were also tested in the present reaction. A mixed solvent of acetonitrile (CH_3CN) and water was found to be the best medium.

The amount of reducing agent $NaHSO_3$ added to H_5IO_6 considerably affected the yield of **2**. Of course, no

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Table 1. Conversion of 1-Octene (1) to 1-Iodo-2-octanol (12) with H_5IO_6 under Various Reaction Conditions[a]

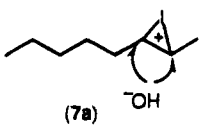
entry	reagent (equiv)		conv. %[b]	selectvty, %[b]
1	$H_5IO_6/NaHSO_3$	(1.2/1.2)	74	45
2	$H_5IO_6/NaHSO_3$	(1.2/2.4)	95	90
3[c]	$H_5IO_6/NaHSO_3$	(1.2/2.4)	95	40
4	$H_5IO_6/NaHSO_3$	(1.2/3.6)	>98	61
5	H_5IO_6/Na_2SO_3	(1.2/2.4)	62	45
6	$H_5IO_6/Na_2S_2O_3$	(1.2/2.4)	50	90
7	H_5IO_6/Na_2HPO_3	(1.2/2.4)	0	
8	$H_5IO_6/FeSO_4$	(1.2/2.4)	0	
9	$H_5IO_6/H_2C_2O_4$	(1.2/2.4)	0	
10	$NaIO_4/NaHSO_3$	(1.2/2.4)	39	80
11[d]	$NaIO_4/NaHSO_3$	(1.2/2.4)	95	90
12[e]	$NaIO_4/NaHSO_3$	(1.2/2.4)	>98	83
13[e]	$KIO_4/NaHSO_3$	(1.2/2.4)	0	

[a] Substrate (10 mmol) was allowed to react with reagent in CH_3CN (20 mL)/H_2O (44 mL) at 25 °C for 2 h. [b] Determined by GLC. [c] Aqueous $NaHSO_3$ was added in one portion to the reaction system. [d] Medium was acidified at pH 1 by 2 M H_2SO_4. [e] Solvent ^{t}BuOH, reaction time 4 h.

product was obtained by the reaction of **1** and H_5IO_6 alone. Using 2 equiv of $NaHSO_3$ per equiv of H_5IO_6, iodohydrin **2** was obtained in satisfactory yield (entry 2). However, when aqueous $NaHSO_3$ was added in one portion to the solution of **1** and H_5IO_6, the yield of **2** decreased to 40% (entry 3). Sodium periodate, $NaIO_4$, could be used instead of H_5IO_6 when an acidic medium (pH 1) was employed (entry 11). Under neutral conditions, $NaIO_4$ was difficult to dissolve in the medium, and about 60% of **1** was recovered unchanged (entry 10). No reaction took place when KIO_4 was used in place of $NaIO_4$, probably because of its low solubility in the mixed solvent.

On the basis of these results, a variety of olefinic compounds was allowed to react with IOH generated from H_5IO_6 and $NaHSO_3$ (Table 2).

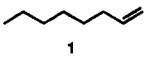
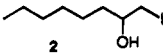
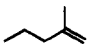
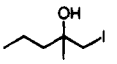
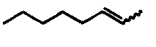
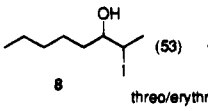
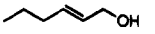
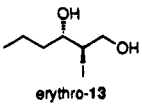
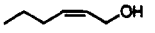
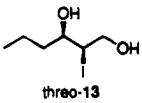
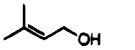
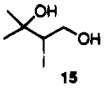
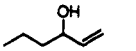
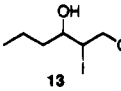
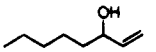
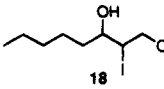
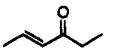
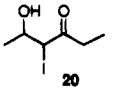
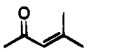
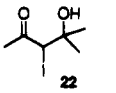
As can be seen in Table 2, this method appears to be quite general for the synthesis of iodohydrin derivatives. The addition of hypoiodous acid to terminal alkenes such as **1** and 2-methyl-1-pentene (**3**) occurred regioselectively in Markovnikov fashion, giving **2** and **4**, respectively, in good yields (entries 1 and 2). The iodohydroxylation of *cis*-2-butene (**5**) and cyclohexene (**10**) proceeded with high stereoselectivity as exemplified by clean conversion to anti iodohydrins **6** and **11**, respectively. In the case of 2-octene (*cis*/*trans* = 3/1) (**7**), a regioisomeric mixture of **8** and **9** was formed (entry 4). The preferential formation of **8** may reflect an electronic preference for nucleophilic attack (OH^- or H_2O) on the inner carbon (C-3) rather than on the C-2 carbon of the iodonium ion intermediate (**7a**). An approximate 2:1 ratio of **8** to **9** appears to be reasonable on the basis of the Sayzeff rule.



(7a)

It is interesting to note that the addition of IOH to primary allylic alcohols took place in anti-Markovnikov fashion to give the corresponding iodohydrin derivatives. For instance, the treatment of *trans*- or *cis*-2-hexen-1-ol (**12**) with hypoiodous acid derived from H_5IO_6 and $NaHSO_3$ led to *erythro*- or *threo*-2-iodo-1,3-hexanediol (**13**), respectively, in 80% and 76% yield. However, the reaction of a secondary allylic alcohol, 1-hexen-3-ol (**16**), with IOH proceeded in Markovnikov fashion to give a

Table 2. Iodohydroxylation of Unsaturated Carbon–Carbon Bond of Various Organic Compounds[a]

entry	substrate	conv. / %[b]	products (yield. / %) [isolated yield / %]
1	 1	95	 2 (90)
2	 3		 4 (78)
3	 5		 6 [68]
4	 7	98	 8 (53) 9 (26) threo/erythro= 3/1
5	 10	87	 11 (80)
6	 trans-12	80	 erythro-13 (80)
7	 cis-12	92	 threo-13 (76)
8	 14		 15 [60]
9	 16		 13 [51]
10	 17	80	 18 (80)
11	 19		 20 (66)
12	 21	85	 22 (81)

[a] Substrates were allowed to react under the same conditions as entry 2 in Table 1. [b] Determined by ^{1}H NMR and GLC.

diastereoisomeric mixture of *erythro*- and *threo*-**13**. Similarly, 1-octen-3-ol (**17**) produced a diastereoisomeric mixture of *erythro*- and *threo*-2-iodo-1,3-octanediol (**18**) in good yield.

The addition of IOH to **12** and **17** may be explained by considering the preferential attack of OH^- or H_2O from the less hindered side of the iodonium ion intermediate (Scheme 1). The regioselective formation of 2-halo 1,3-diols is noteworthy, since the ring opening of allylic epoxy alcohols results in 3-halo 1,2-diols as the principal products.[8]

The orientation of the addition of IOH to α,β-unsaturated ketones, such as 4-hexen-3-one (**19**) and 4-methyl-3-penten-2-one (**21**), was similar to that for allylic alcohols to afford the corresponding iodohydrin derivatives

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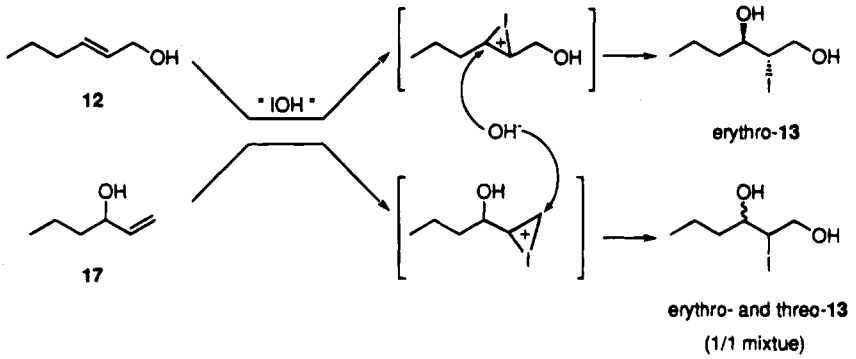
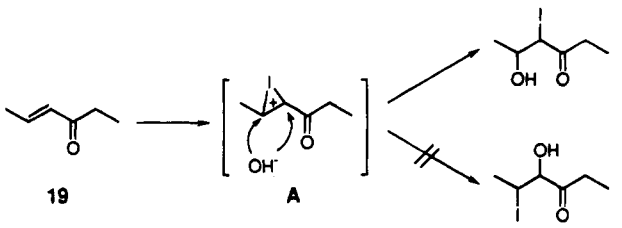
Scheme 1

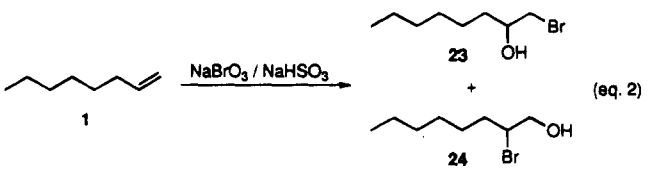


Scheme 2



in relatively good yields. From the electronic point of view, the regioselectivity in this reaction can be rationalized, *i.e.*, owing to the electron-withdrawing carbonyl function adjacent to the iodonium ion of the intermediate (**A**), the attack of a nucleophile OH^- on the iodonium ion **A** may be induced at the β-carbon rather than the α-carbon (Scheme 2).

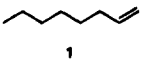
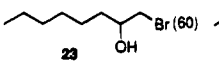
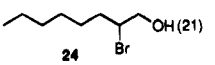
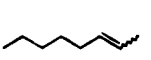
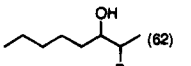
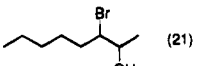
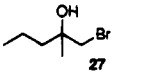
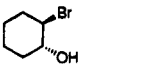
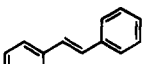
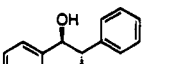
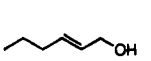
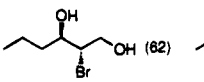
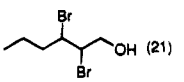
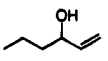
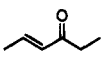
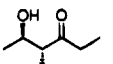
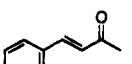
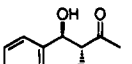
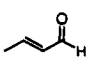
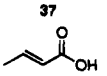
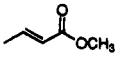
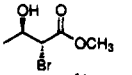
In order to extend the present strategy to bromohydrin synthesis, we examined the *in situ* generation of hypobromous acid from $NaBrO_3$ and $NaHSO_3$ under these conditions. Treatment of 1-octene (**1**) with $NaBrO_3$ in the presence of $NaHSO_3$ (2 equiv) gave rise to 1-bromo-2-octanol (**23**) in 60% yield along with 2-bromo-1-octanol (**24**) (21%) (eq 2). This result showed that BrOH can be generated *in situ* from $NaBrO_3$ and $NaHSO_3$ and trapped with **1** to form **23** and **24**.



The scope of the present method for bromohydrin preparation was examined. Table 3 indicates the selected examples for bromohydroxylation of various organic compounds bearing carbon–carbon double bonds using $NaBrO_3/NaHSO_3$ reagent.

In contrast to the iodohydroxylation of 1-octene **1**, where the addition was highly regioselective, to give the Markovnikov product 1-iodo-2-octanol (**2**), the bromohydroxylation afforded about a 3:1 regioisomeric mixture of 1-bromo-2-octanol (**23**) and 2-bromo-1-octanol (**24**). Similarly, 2-octene (**7**) gave a pair of regioisomers of 2-bromo-3-octanol (**25**) and 3-bromo-2-octanol (**26**) in 62% and 21% yields, respectively. However, 2-methyl-1-pentene (**3**) produced exclusively the Markovnikov product 1-bromo-2-methyl-2-pentanol (**27**). The bromohydroxylation of cyclohexene (**10**) and *trans*-stilbene (**29**) proceeded stereoselectively to form *trans*-2-bromocyclohexanol (**28**) and *erythro*-2-bromo-1,2-diphenylethanol (**30**) in 75% and 50% yields, respectively.

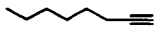
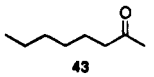
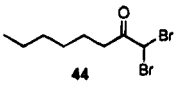
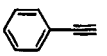
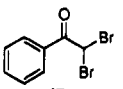
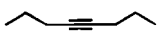
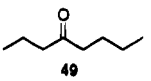
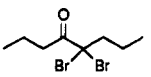
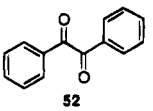
Table 3. Bromohydroxylation of Unsaturated Carbon–Carbon Bond of Various Organic Compounds[a]

entry	substrate	products (yield, %)[b]		
1	 1	 23 Br (60) OH	 24 OH (21) Br	
2	 7	 25 OH (62) Br	 26 Br (21) OH	
3	 3	 27 OH Br	(60)	
4	 10	 28 Br OH	(75)	
5[c]	 29	 30 OH Br	(50)	
6	 12	 erythro-31 OH OH (62) Br	 32 Br OH (21) Br	
7	 16	erythro and threo-31	(33)	
8	 19	 33 OH O Br	(70)	
9	 21	 34 O OH Br	(99)	
10	 35	 36 OH O Br	(60)	
11	 37	 38 OH O OH Br	(56)	
12	 39	38	(65)	
13	 40	 41 OH O OCH3 Br	(75)	

[a] Substrate (10 mmol) was allowed to react with $NaBrO_3$/$NaHSO_3$ (12/24 mmol) in CH_3CN (20 mL)/H_2O (44 mL) at 25 °C for 2 h. [b] Determined by GLC. [c] Isolated yield.

Although the addition of IOH to allylic alcohol **12** was highly regio- and stereoselective, in the bromohydroxy-

Table 4. Reaction of Alkynes with $H_5IO_6/NaHSO_3$ and $NaBrO_3/NaHSO_3$

entry	alkyne	reagent	products (yield, %)[a]	
1	 42	$H_5IO_6/NaHSO_3$	 43	(42)
2	42	$NaBrO_3/NaHSO_3$	 44	(64)
3	 45	$H_5IO_6/NaHSO_3$	 46	(45)
4	45	$NaBrO_3/NaHSO_3$	 47	(87)
5	 48	$H_5IO_6/NaHSO_3$	 49	(35)
6	48	$NaBrO_3/NaHSO_3$	 50	(50)
7	 51	$H_5IO_6/NaHSO_3$	 52	(58)
8[b]	51	$NaBrO_3/NaHSO_3$	52	(27)

[a] Determined by GLC. [b] 1,2-Diphenyl-1,2-dibromoethylene was formed in 29% yield.

lation of *trans*-**12** with the $NaBrO_3/NaHSO_3$ reagent, a mixture of *erythro*-2-bromo-1,3-hexanediol (**31**) and 2,3-dibromo-1-hexanol (**32**) was formed. The reaction of 1-hexen-3-ol (**16**) took place regioselectively, but not stereoselectively, to afford a mixture of *threo*- and *erythro*-**31**.

However, BrOH, derived from the $NaBrO_3/NaHSO_3$ system, added to α,β-unsaturated carbonyl compounds in regio- and stereoselective fashion to form bromohydrin derivatives in fair to good yields. For example, the reaction of 4-hexen-3-one (**19**) gave rise to *erythro*-4-bromo-5-hydroxy-3-hexanone in 70% yield. 4-Methyl-3-hexen-2-one (**21**) gave bromohydrin **34** in almost quantitative yield. When crotonaldehyde (**37**) was treated with the $NaBrO_3/NaHSO_3$ reagent, the addition of BrOH and the oxidation of the aldehyde function to a carboxylic acid occurred simultaneously, forming 2-bromo-3-hydroxybutanoic acid (**38**). Thus, in the reaction of crotonic acid (**39**) with BrOH, the yield of **38** was improved to 65%. Methyl crotonate (**40**) gave bromohydrin **41** in good yield (75%).

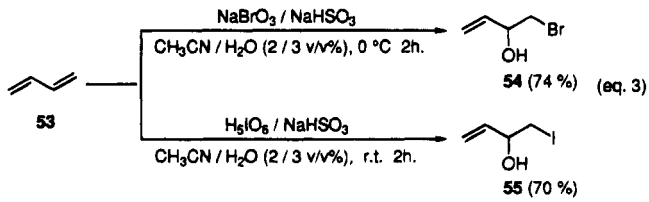
Significant differences were observed in the reaction of alkynes with the *in situ* generated hypoiodous and hypobromous acids. These results are summarized in Table 4.

The reaction of 1-octyne (**42**) with IOH derived from H_5IO_6 and $NaHSO_3$ in a mixed solvent of CH_3CN and H_2O (1/1 v/v) at room temperature gave 2-octanone (**43**) as the principal product. However, the same reaction using $NaBrO_3$ and $NaHSO_3$ produced 1,1-dibromo-2-octanone in 64% yield. Dibromo ketones are usually prepared from the reaction of alkynes with NBS.[9] Treatment of phenylacetylene (**45**) with $NaBrO_3/NaHSO_3$ gave 1,1-dibromoacetophenone in good yield (87%). Internal alkynes such as 4-octyne (**48**) reacted similarly with $NaBrO_3/NaHSO_3$ to give α,α-dibromo ketone **50**. However, treatment of diphenylacetylene (**51**) with $H_5IO_6/NaHSO_3$ or $NaBrO_3/NaHSO_3$ afforded benzil (**52**) in 58% or 27% yield, respectively.

Although the difference in the selectivity of these reactions is difficult to explain clearly at the present time, a plausible reaction path is shown in Scheme 3. It is probable that the reaction is initiated by the addition of XOH (X = I or Br) to the alkyne, in a manner similar to that of olefins, to form an α-halo enol (**B**) that lies in equilibrium with an α-halo ketone (**C**).

Subsequently, to the resulting enol **B** another BrOH is added, forming the α,α-dibromo ketone *via* dehydration. In the case of the reaction with IOH, the deiodination from the α-iodo ketone **C**, which lies in equilibrium with the enol **B**, with some base existing in the reaction system, such as I^-, seems to occur in preference to the addition of the IOH to the enol **B**, to form the ketone.

When butadiene (**53**) was allowed to react with BrOH and IOH under similar conditions, the addition took place primarily in 1,2-fashion to form the corresponding halohydrins 1-bromo-3-buten-2-ol (**54**) and 1-iodo-3-buten-2-ol (**55**).



In summary, it is apparent that the present method is a simple one for the preparation of iodohydrin and bromohydrin derivatives. The reaction conditions are mild, the workup is very simple, and the yields are routinely high. In addition, alkynes were converted into ketones or α,α-dibromo ketones in moderate to good yields.

Experimental Section

General Instruments and Materials. The instruments used were as follows: GLC, Shimadzu GC-12A and GC-14A; ^1H NMR, JEOL JNM-GSX-400 and JNM-EX-270; ^{13}C NMR HITACHI R-90H and JEOL JNM-GSX-400 and JNM-EX-270; IR, Perkin-Elmer 1600 series. All materials were all purchased from commercial sources, unless otherwise specified.

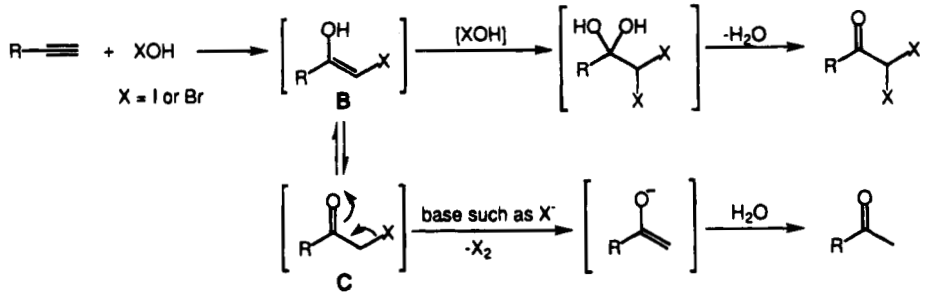
Typical Procedure for the Synthesis of Iodohydrin Derivatives. To a solution of the substrate (10 mmol) and $HIO_4 \cdot 2H_2O$ (12 mmol) in CH_3CN (20 mL) and H_2O (6 mL) was added 1 M $NaHSO_3$ (24 mL) dropwise over a period of about 1 h, and the mixture was stirred at 25 °C for 2 h. After the reaction, the resulting solution was extracted with diethyl ether (100 mL × 3). Then the combined organic layer was washed with aqueous Na_2SO_3 and dried over $MgSO_4$. After filtration, the solvent was evaporated in vacuo to leave crude materials, which were purified by column chromatography on silica gel (Merck silica gel 60) to give the corresponding iodohydrin derivatives.

1-Iodo-2-octanol (2): ^1H NMR ($CDCl_3$/TMS) δ 0.89 (t, J = 7.0 Hz, 3H), 1.26–1.37 (m, 9H), 1.42–1.57 (m, 1H), 2.04 (d, J = 5.1 Hz, 1H), 3.24 (dd, J = 10.0 and 6.0 Hz, 1H), 3.40 (dd, J = 10.0 and 3.4 Hz, 1H), 3.50–3.53 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.1, 16.4, 22.6, 25.6, 29.1, 31.7, 36.6, 70.9; IR (NaCl) 3370 (br), 2970, 2940, 2860, 1470, 1420, 1380, 1180, 1120, 1020 cm^{-1}.

1-Iodo-2-methyl-2-pentanol (4): ^1H NMR ($CDCl_3$/TMS) δ 0.95 (t, J = 7.3 Hz, 3H), 1.34 (s, 3H), 1.34–1.42 (m, 2H),

(9) Reed, S. F., Jr. *J. Org. Chem.* **1965**, *30*, 2195.

Scheme 3



1.59–1.64 (m, 2H), 3.35 (d, J = 2.4 Hz, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.7, 17.9, 23.5, 26.1, 43.3, 70.9; IR (NaCl) 3413 (br), 2960, 2933, 2872, 1465, 1376, 1178, 1137 cm^{-1}.

***threo*-3-Iodo-2-butanol (6)**: ^{1}H NMR ($CDCl_3$/TMS) δ 1.25 (d, J = 6.2 Hz, 3H), 1.95 (d, J = 7.3 Hz, 3H), 3.21–3.27 (m, 2H), 4.19–4.26 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 22.4, 25.3, 41.4, 72.6; IR (NaCl) 3370 (br), 2975, 2923, 2866, 1446, 1376, 1176, 1150, 1105, 1083, 1022, 966, cm^{-1}.

2-Iodo-3-octanol (8): ^{1}H NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 0.89 (t, J = 7.6 Hz, 3H), 1.27–1.39 (m, 4H), 1.49–1.54 (m, 4H), 1.84 (d, J = 7.6 Hz, 0.6H), 1.97 (d, J = 7.6 Hz, 2.4H), 2.77–2.83 (m, 0.8H), 3.40–3.44 (m, 0.2H), 4.30 and 4.42 (qt, J = 3.7 and 7.1 Hz for δ 4.30, qd, J = 3.2 and 7.1 Hz for δ 4.42, 1H) 5.30 (s, 1H); ^{13}C NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 14.0, 22.2, 22.5, 25.1, 25.3, 25.6, 31.6, 34.0, 37.0, 38.3, 40.1, 75.6, 76.1; IR (NaCl) 3380 (br), 2950, 2910, 2850, 1460, 1440, 1370, 1160, 1130, 1110, 1050, 1000, 930 cm^{-1}.

3-Iodo-2-octanol (9): ^{1}H NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 0.90 (t, J = 7.6 Hz, 3H), 1.25 (d, J = 7.8 Hz, 0.75H), 1.31 (d, J = 7.8 Hz, 2.25H), 1.30–1.38 (m, 2H), 1.73–2.01 (m, 2H), 3.27 and 3.28 (dq, J = 4.2 and 7.8 Hz for δ 3.27, dq, J = 3.5 and 7.8 Hz for δ 3.28, 1H), 3.48 (brs, 1H) 4.13 (td, J = 9.5 and 4.2 Hz, 0.75 H), 4.33 (td, J = 9.5 and 4.2 Hz, 0.25H); ^{13}C NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 14.0, 21.1, 22.4, 22.9, 29.4, 30.9, 35.6, 36.9, 50.9, 70.5; IR (NaCl) 3300 (br), 2960, 2940, 2860, 1470, 1380, 1140, 1120, 1050, 1020, 940, 840, 720 cm^{-1}.

***trans*-2-Iodocyclohexanol (11)**: ^{1}H NMR ($CDCl_3$/TMS) δ 1.25–1.42 (m, 3H), 1.53 (ddd, J = 4.2, 4.2, and 10.0 Hz, 1H), 1.84 (ddd, J = 4.4, 4.4, and 9.8 Hz, 1H), 2.02–2.15 (m, 2H), 2.44–2.51 (m, 2H), 3.67 (ddd, J = 10.0, 10.0 and 4.4 Hz, 1H), 4.04 (ddd, J = 12.3, 9.8, and 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 24.3, 27.9, 33.7, 38.5, 43.1, 75.9; IR (NaCl) 3300 (br), 2940, 2850, 1720, 1680, 1630, 1450, 1360, 1270, 1250, 1220, 1190, 1160, 1110, 1060, 1030, 1000, 950, 890, 860, 850, 790 cm^{-1}.

***erythro*-2-Iodo-1,3-hexanediol (*erythro*-13)**: ^{1}H NMR ($CDCl_3$/TMS) δ 0.96 (t, J = 7.3 Hz, 3H), 1.35–1.80 (m, 4H), 2.93 (brd, 1H), 3.04 (brt, 1H), 3.78–4.28 (m, 4H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.2, 19.2, 38.2, 43.2, 66.5, 75.4; IR (NaCl) 3354 (br), 2958, 2872, 1463, 1379, 1266, 1124, 1065, 1001, 963, 845 cm^{-1}.

***threo*-2-Iodo-1,3-hexanediol (*threo*-13)**: ^{1}H NMR ($CDCl_3$/TMS) δ 0.96 (t, J = 7.1 Hz, 3H), 1.36–1.65 (m, 4H), 2.20 (s, 1H), 2.62 (brs, 1H), 3.07–3.11 (m, 1H), 3.98 (t, J = 5.6 Hz, 2H), 4.29 (dt, J = 2.3 and 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.2, 18.9, 40.6, 47.6, 67.6, 72.1; IR (NaCl) 3362 (br), 2957, 2931, 2871, 1464, 1456, 1379, 1318, 1129, 1078, 1047, 1022, 963, 842 cm^{-1}.

2-Iodo-3-methyl-1,3-butanediol (15): ^{1}H NMR ($CDCl_3$/TMS) δ 1.44 (s, 3H), 1.48 (s, 3H), 3.06 (brs, 1H), 3.22 (brs, 1H), 3.95 (m, 1H), 4.04 (m, 1H), 4.30 (t, J = 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 28.3, 28.8, 50.2, 67.0, 73.6; IR (NaCl) 3346 (br), 2976, 2933, 2879, 1462, 1436, 1380, 1366, 1165, 1106, 1070, 1027, 1008, 975, 948, 858, 782, 748, 691 cm^{-1}.

2-Iodo-1,3-octanediol (18): ^{1}H NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 0.90 and 0.91 (t, J = 7.8 Hz for δ 0.90 and t, J = 7.8 for δ 0.91, 3H), 1.24–1.42 (m, 6H), 1.49–1.63 (m, 2H), 1.75–1.81 (m, 1H), 1.90–2.01 (m, 2H), 2.77 and 2.88 (brs for δ 2.77 and brs for δ 2.88, 1H), 3.82–3.85 and 3.86 (m for δ 3.82–3.85, dd, J = 7.8 and 11.6 Hz for δ 3.86, 1H), 3.98 (d, J = 6.8 Hz, 1H), 4.04 (dd, J = 7.8 and 11.6 Hz, 1H), 4.25 and 4.28 (t, J = 7.8 Hz for δ 4.25, dt, J = 3.4 and 6.8 Hz for δ 4.28, 1H); ^{13}C NMR (mixture for *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 13.8, 22.4, 24.9, 25.1, 31.4, 35.6, 37.9, 42.2, 45.7, 66.0, 66.2, 70.7, 74.5; IR (NaCl) 3370 (br), 2970, 2940, 2870, 1470, 1380, 1130, 1060, 1010 cm^{-1}.

5-Hydroxy-4-iodo-3-hexanone (20): ^{1}H NMR (mixture of *threo* and *erythro* isomers) ($CDCl_3$/TMS) δ 1.14 (tt, J = 7.3 and 7.3 Hz, 8.4H), 1.19 (d, J = 6.3 Hz, 3H), 1.46 (d, J = 6.3 Hz, 5.7H), 2.53–2.68 (m, 3H), 2.90–3.07 (m, 2.7H), 3.22 (brs, 1.8H), 3.35–3.40 (m, 1H), 3.55 (brs, 1H), 4.23 (m, 1.8H), 4.39 (d, J = 8.3 Hz, 1.8H), 4.57 (d, J = 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.3, 8.4, 21.1, 22.0, 33.4, 33.5, 35.6, 35.8, 65.7, 69.0, 207.2, 208.0; IR (NaCl) 3448 (br), 2977, 2938, 1706, 1458, 1407, 1376, 1072, 925 cm^{-1}.

4-Hydroxy-3-iodo-4-methyl-2-pentanone (22): ^{1}H NMR ($CDCl_3$/TMS) δ 1.41 (s, 3H), 1.48 (s, 3H), 2.46 (s, 3H), 3.62 (s, 1H), 4.60 (s, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 25.3, 28.2, 29.9, 44.5, 70.6, 205.1; IR (NaCl) 3478 (br), 2978, 2934, 1695, 1359, 1313, 1211, 1145, 958 cm^{-1}.

Typical Procedure for the Synthesis of Bromohydrin Derivatives. $NaBrO_3$ (12 mmol) was dissolved in water (6 mL) and the solution was adjusted to pH 1 with 2 M H_2SO_4. To the resulting solution was added substrate (10 mmol) in CH_3CN (20 mL); 1 M $NaHSO_3$ (24 mL) was added dropwise over a period of about 1 h and the reaction mixture was stirred at 25 °C for 2 h. By a similar workup and purification as described in the synthesis of iodohydrin derivatives, bromohydrin derivatives were obtained.

1-Bromo-2-octanol (23): ^{1}H NMR ($CDCl_3$/TMS) δ 0.89 (t, J = 6.6 Hz, 3H), 1.29–1.51 (m, 8H), 1.54 (t, J = 6.6 Hz, 2H), 2.22 (d, 1H), 3.39 (td, J = 7.3 and 10.3 Hz, 1H), 3.54 (td, J = 7.3 and 10.3 Hz, 1H), 3.75–3.81 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.0, 22.5, 25.6, 29.1, 31.7, 35.1, 40.7, 71.0; IR (NaCl) 3375 (br), 2928, 2857, 1466, 1422, 1378, 1221, 1127, 1036, 665 cm^{-1}.

2-Bromo-1-octanol (24): ^{1}H NMR ($CDCl_3$/TMS) δ 0.89 (t, J = 6.7 Hz, 3H), 1.26–1.61 (m, 8H), 1.82–1.87 (q, J = 7.3 Hz, 2H), 2.05 (brt, 1H), 3.73–3.85 (m, 2H), 4.12–4.18 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.0, 22.6, 27.4, 28.7, 31.6, 34.9, 60.3, 67.3; IR (NaCl) 3379 (br), 2956, 2928, 2857, 1466, 1422, 1378, 1222, 1127, 1036, 666 cm^{-1}.

2-Bromo-3-octanol (25): ^{1}H NMR ($CDCl_3$/TMS) δ 0.90 (t, J = 6.8 Hz, 3H), 1.25–1.60 (m, 9H), 1.85–1.91 (m, 2H), 2.06 (brs, 1H), 3.76 (m, 1H), 4.00 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.0, 21.2, 22.4, 27.4, 31.2, 35.4, 66.8, 70.2; IR (NaCl) 3383 (br), 2957, 2931, 2860, 1462, 1458, 1378, 1260, 1142, 1102, 1061, 639 cm^{-1}.

3-Bromo-2-octanol (26): ^{1}H NMR ($CDCl_3$/TMS) δ 0.90 (t, J = 6.8 Hz, 3H), 1.25–1.32 (m, 8H), 1.60–1.81 (m, 3H), 2.03 (d, J = 7.3 Hz, 1H), 3.80–3.84 (m, 1H), 4.17–4.21 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.0, 19.0, 22.4, 27.6, 31.1, 33.9, 66.3, 70.3; IR (NaCl) 3387 (br), 2957, 2933, 2860, 1459, 1378, 1227, 1120, 1102, 1073, 638 cm^{-1}.

1-Bromo-2-methyl-2-pentanol (27): ^{1}H NMR ($CDCl_3$/TMS) δ 0.95 (t, J = 7.1 Hz, 3H), 1.30 (s, 3H), 1.34–1.41 (m, 2H), 1.57–1.61 (m, 2H), 1.90 (brs, 1H), 3.43–3.49 (dd, J = 10.3 and 15.0 Hz, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.4, 17.3, 24.9, 42.2, 45.3, 71.2; IR (NaCl) 3418 (br), 2960, 2873, 1709, 1456, 1378, 1028, 668 cm^{-1}.

2-Bromocyclohexanol (28): ^{1}H NMR ($CDCl_3$/TMS) δ 1.24–1.42 (m, 3H), 1.66–1.89 (m, 1H), 2.09–2.21 (m, 1H),

2.27–2.39 (m, 1H), 2.63 (s, 1H), 3.55–3.68 (m, 1H), 3.86–3.96 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 24.3, 26.8, 33.8, 36.4, 61.9, 75.6; IR (NaCl) 3411 (br), 2939, 2862, 1718, 1449, 1188, 1074, 690 cm^{-1}.

2-Bromo-1,2-diphenylethanol (30): ^{1}H NMR ($CDCl_3$/TMS) δ 5.07 (d, J = 6.6 Hz, 1H), 5.16 (d, J = 6.6 Hz, 1H), 7.16–7.37 (m, 10H); ^{13}C NMR ($CDCl_3$/TMS) δ 58.9, 78.0, 127.0, 128.1, 128.3, 128.4, 128.7, 128.9, 137.6, 139.7; IR (NaCl) 3438 (br), 2923, 2854, 1454, 1377, 1215, 1061, 1030, 761, 699 cm^{-1}.

2-Bromo-1,3-hexanediol (31): ^{1}H NMR ($CDCl_3$/TMS) δ 0.96 (t, J = 6.3 Hz, 3H), 1.36–1.73 (m, 4H), 2.55 (s, 2H), 3.76–4.15 (m, 4H); ^{13}C NMR ($CDCl_3$/TMS) δ 13.8, 18.8, 36.5, 60.1, 64.3, 73.5; IR (NaCl) 3358 (br), 2960, 2874, 1458, 1381, 1070, 968, 847 cm^{-1}.

2,3-Dibromo-1-hexanol (32): ^{1}H NMR ($CDCl_3$/TMS) δ 0.97 (t, J = 7.4 Hz, 3H), 1.42–1.73 (m, 2H), 1.84–2.21 (m, 3H), 4.06–4.17 (brs, 2H), 4.26–4.36 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 13.3, 19.9, 39.0, 54.6, 60.6, 66.0; IR (NaCl) 3386 (br), 2960, 2874, 1458, 1381, 1152, 1056 cm^{-1}.

4-Bromo-5-hydroxy-3-hexanone (33): ^{1}H NMR ($CDCl_3$/TMS) δ 1.12 (t, J = 7.2 Hz, 3H), 1.40 (d, J = 6.2 Hz, 3H), 2.56–2.66 (m, 1H), 2.86–2.98 (m, 1H), 4.12 (d, J = 8.1 Hz, 1H), 4.24 (m, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 7.8, 20.1, 33.6, 55.5, 68.1, 205.5; IR (NaCl) 3425 (br), 2981, 2938, 1715, 1454, 1374, 1270, 695 cm^{-1}.

3-Bromo-4-hydroxy-4-methyl-2-pentanone (34): ^{1}H NMR ($CDCl_3$/TMS) δ 1.40 (s, 3H), 1.41 (s, 3H), 2.42 (s, 3H), 3.08 (s, 1H), 4.26 (s, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 27.0, 27.9, 29.0, 62.1, 71.3, 204.0; IR (NaCl) 3482 (br), 2982, 1702, 1360, 1230, 1149, 958 cm^{-1}.

3-Bromo-4-hydroxy-4-phenyl-2-butanone (36): ^{1}H NMR ($CDCl_3$/TMS) δ 2.39 (s, 3H), 3.34 (d, J = 4.4 Hz, 1H), 4.38 (d, J = 8.8 Hz, 1H), 5.04 (dd, J = 4.4 and 8.8 Hz, 1H), 7.36 (m, 5H); ^{13}C NMR ($CDCl_3$/TMS) δ 27.7, 54.3, 74.7, 127.0, 128.5, 128.7, 139.1, 202.7; IR (KBr) 3418 (br), 3058, 2993, 1722, 1455, 1359, 1207, 765, 692, 604 cm^{-1}.

2-Bromo-3-hydroxybutanoic acid (38): ^{1}H NMR ($CDCl_3$/TMS) δ 1.45 (d, J = 6.8 Hz, 3H), 4.12 (d, J = 8 Hz, 1H), 4.28 (dq, J = 6.8 and 8.0 Hz, 1H), 6.78 (brs, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 20.1, 49.0, 69.3, 173.4; IR (KBr) 3289 (br), 2992 (br), 2843 (br), 2648 (br), 2514, 1718, 1705, 1688, 1459, 1438, 1384, 1278, 1259, 1178, 1132, 1090, 1067, 962, 941, 898, 870, 796, 676, 661 cm^{-1}.

Methyl 2-bromo-3-hydroxybutanonate (41): ^{1}H NMR ($CDCl_3$/TMS) δ 1.40 (d, J = 6.6 Hz, 3H), 2.98 (brs, 1H), 3.81 (s, 3H), 4.13 (dq, J = 6.0 and 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 20.0, 49.3, 52.9, 68.8, 169.5; IR (NaCl) 3442 (br), 2983, 2958, 1744, 1439, 1378, 1282, 1154, 1088, 1007, 937, 874, 645 cm^{-1}.

Typical Procedure for the Reaction of Alkynes. $NaBrO_3$ (24 mmol) was dissolved in water (6 mL) and the solution was adjusted to pH 1 with 2 M H_2SO_4. To the resulting solution was added substrate (10 mmol) in CH_3CN (20 mL). Then 2 M $NaHSO_3$ (24 mL) was added dropwise over a period of about 1 h, and the reaction mixture was stirred at 25 °C for 2 h. By a similar workup and purification as described in the synthesis of iodohydrin derivatives, ketones or α,α-dibromo ketones were obtained.

1,1-Dibromo-2-octanone (44): ^{1}H NMR ($CDCl_3$/TMS) δ 0.89 (t, J = 3.4 Hz, 3H), 1.20–1.71 (m, 8H), 2.90 (t, J = 7.2 Hz, 2H), 5.79 (s, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.2, 22.7, 24.6, 28.8, 31.7, 35.2, 43.2, 197.3; IR (NaCl) 2956, 2930, 2858, 1723, 1604, 1466, 1150, 707, 659 cm^{-1}.

2,2-Dibromo-1-phenylethanone (47): ^{1}H NMR ($CDCl_3$/TMS) δ 6.72 (s, 1H), 7.51 (dd, J = 7.3 and 8.4 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 8.08 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 39.7, 128.9, 129.7, 130.9, 134.4, 186.0; IR (NaCl) 3062, 3014, 1698, 1594, 1448, 1271, 1193, 981, 801, 704, 684, 628 cm^{-1}.

5,5-Dibromo-4-octanone (50): ^{1}H NMR ($CDCl_3$/TMS) δ 0.99 (m, 6H), 1.71 (m, 4H), 2.44 (m, 2H), 3.07 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$/TMS) δ 13.2, 13.4, 18.6, 20.9, 38.0, 46.8, 71.6, 198.0; IR (NaCl) 2960, 2936, 2874, 1720, 1460, 1380, 1240, 1149, 1102, 628 cm^{-1}.

Procedure for the Reaction of 1,3-Butadiene. $NaBrO_3$ or H_5IO_6 (6 mmol) was dissolved in water (6 mL). To the resulting solution was added substrate (5 mmol) in CH_3CN (20 mL). Then 0.5 M $NaHSO_3$ (24 mL) was added dropwise over a period of about 1 h, and the reaction mixture was stirred at 25 or 0 °C for 2 h. By a similar workup and purification as described in the synthesis of iodohydrin derivatives, bromohydrin derivatives were obtained.

1-Bromo-3-buten-2-ol (54): ^{1}H NMR ($CDCl_3$/TMS) δ 2.21 (brs, 1H), 3.41 (dd, J = 7.3 and 10.3 Hz, 1H), 3.54 (dd, J = 4.0 and 10.3 Hz, 1H0, 4.34–4.39 (m, 1H), 5.27 (d, J = 10.3 Hz, 1H), 5.40 (d, J = 17.2 Hz, 1H), 5.87 (ddd, J = 5.5, 10.3 and 17.2 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 39.3, 72.2, 117.8, 137.1; IR (NaCl) 3384 (br), 1688, 1641, 1421, 1221, 1100, 1067, 992, 933, 700 cm^{-1}.

1-Iodo-3-buten-2-ol (55): ^{1}H NMR ($CDCl_3$/TMS) δ 2.24 (brs, 1H), 3.25 (dd, J = 7.0 and 10.3 Hz, 1H), 3.37 (dd, J = 4.0 and 10.3 Hz, 1H), 4.17 (q, J = 5.5 Hz, 1H), 5.26 (d, J = 10.6 Hz, 1H), 5.37 (d, J = 17.2 Hz, 1H), 5.85 (ddd, J = 5.5, 10.6 and 17.2 Hz, 1H); ^{13}C NMR ($CDCl_3$/TMS) δ 14.4, 71.8, 117.1, 137.9; IR (NaCl) 3376 (br), 1413, 1184, 1089, 1059, 986, 931 cm^{-1}.

Supplementary Material Available: Copies of ^{1}H and ^{13}C NMR spectra of **2**, **4**, **6**, **8**, **9**, **11**, **13**, **15**, **18**, **20**, **22–28**, **30**, **31**, **32** (^{1}H only), **33**, **34**, **36**, **38**, **41**, **44**, **47**, **50**, **54**, **55**, *cis*- and *trans*-2-hexanol–IOH, and 2,3-dibromo-1-hexanol (^{1}H only) (74 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.