Halocyclization of Unsaturated Alcohols and Carboxylic Acids Using Bis(*sym*-collidine)iodine(I) Perchlorate[1,2]

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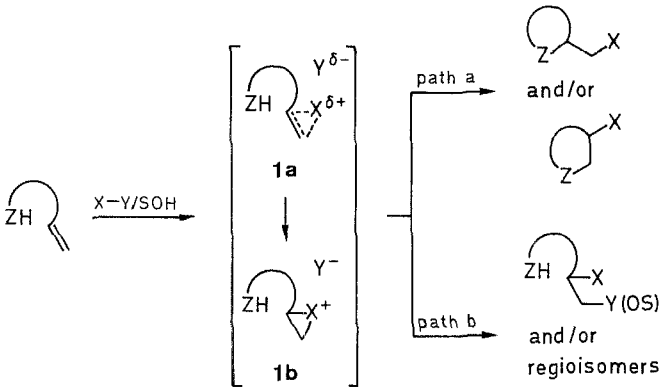
Reaction of $I(collidine)_2^+ ClO_4^-$ with unsaturated alcohols and carboxylic acids in dichloromethane at ambient temperature has afforded three- to seven-membered-ring iodoethers and four- to seven-membered-ring iodolactones, respectively, in moderate yields and generally with high regioselectivity. The reaction is of particular utility for synthesis of 2-(1-iodoalkyl)oxiranes and -oxetanes.

Halocyclization of unsaturated carboxylic acids (halolactonization) and alcohols (halocycloetherification) can be effected by a variety of electrophilic halogenating agents,[3,4] such as iodine,[5,6] *tert*-butyl hypobromite,[7] *N*-halosuccinimides,[8] and bis(*sym*-collidine)iodine(I) salts.[9-11] Such reactions have generally been utilized for the synthesis of five- and six-membered rings,[12] with few reports on the synthesis of small-ring heterocycles.[13-19] Although mechanistic information is sparse, there is evidence that many cyclizations of these types proceed via initially formed π-complexes,[20] such as **1a**, rather than ensuing halonium ion intermediates **1b** (Scheme **A**, path a). In cases where cyclization is energetically disfavored, reactions of such intermediates with nucleophiles (either present, or generated in the reaction media) often compete yielding acyclic 1,2-adducts (path b).



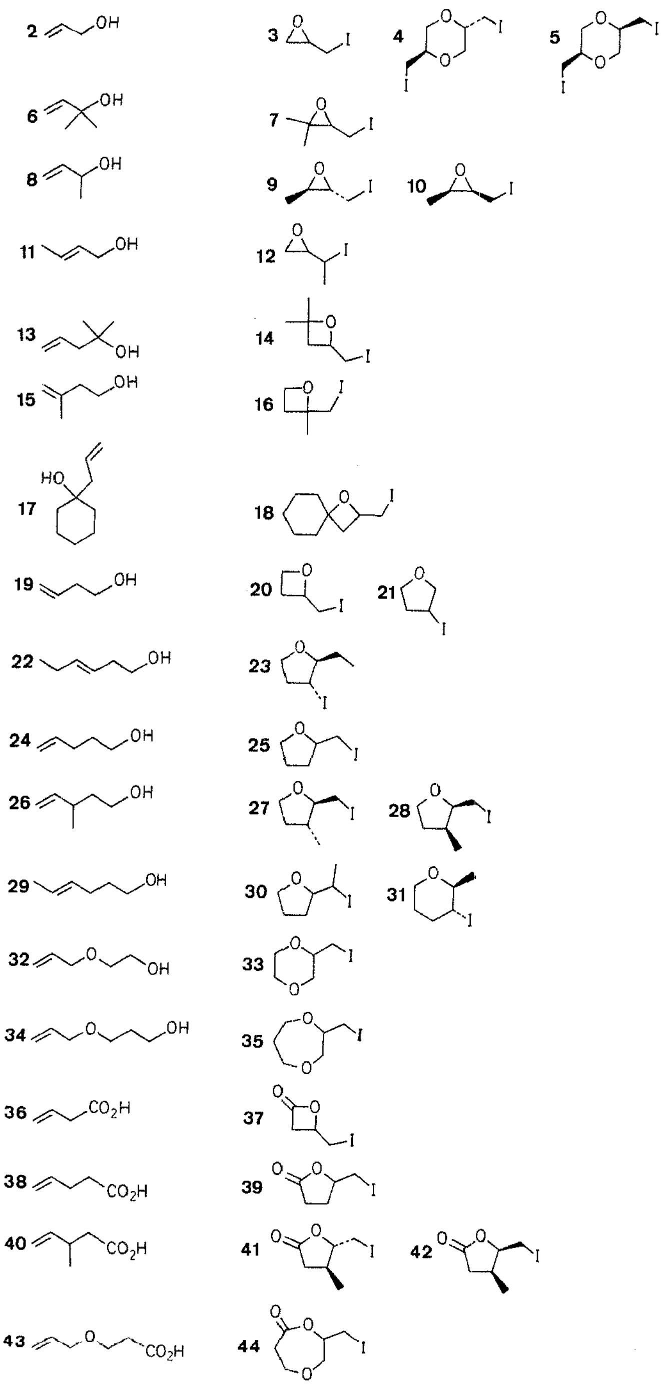
X–Y = halonium ion (X^+) donor
Y^- = nucleophile
ZH = OH or CO_2H
SOH = hydroxylic solvent

Scheme **A**

Herein we report initial results on the unique behavior of bis(*sym*-collidine)iodine(I) perchlorate, $I(collidine)_2^+ ClO_4^-$. This I^+ transfer reagent[21,22] is easily prepared in dichloromethane and reacted *in situ* with a variety of unsaturated alcohols and carboxylic acids at ambient temperature to afford three- to seven-membered-ring ethers and four- to seven-membered-ring lactones, respectively, isolated in reasonable yields (Table 1).

Table 1. Iodocyclization of Unsaturated Alcohols and Carboxylic Acids With I $(collidine)_2^+ ClO_4^-$

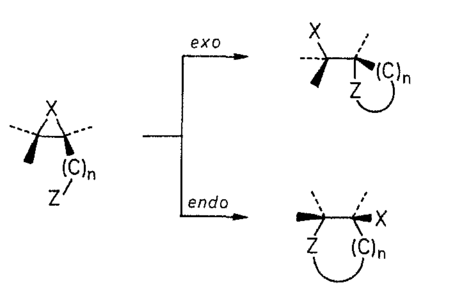
Unsaturated Alcohol or Acid	Cyclic Iodoether or Iodolactone



It should be noted that while four- to six-membered-ring lactones and five and six-membered-ring ethers are commonly obtained by iodocyclization of the respective unsaturated acids[17] or alcohols[6] with iodine–ether/aqueous sodium hydrogen carbonate (or similar system), preliminary work in our laboratory indicates that small-ring ethers as well as seven-membered-ring ethers and lactones will not be generally accessible in this manner. Thus, 2-methyl-3-buten-2-ol (**6**) (known to be particularly prone to intramolecular hydroxyl participation[15]) affords the iodohydrin (1-iodo-2,3-dihydroxy-3-methylbutane) in addition to a lesser amount of oxirane **7**. Under such conditions, 3-methyl-3-buten-1-ol (**15**) and the 3-allyloxypropanoic acid (**43**) also fail to give the respective oxetane **16** or seven-membered-ring lactone **44**. Reaction of alcohols **6** and **15** with iodine in dichloromethane also fails to provide the respective oxirane **7** or oxetane **16** in detectable amounts.

Three- to six-membered-ring ethers have previously been obtained by reaction of unsaturated alcohols with bis(pyridine)iodine(I) nitrate (or the *sym*-collidine analogue); with the exception of oxolanes, such products were generally isolated in low yields as side-products to acyclic *β*-iodopyridinium salts and/or *β*-iodo nitrates.[9,10] The facile formation of cyclic products, especially oxiranes and oxetanes with $I(collidine)_2^+ ClO_4^-$ apparently derives from the low nucleophilicity of perchlorate ion, thus favoring ring closure via intramolecular hydroxyl attack, relative to formation of acyclic iodo perchlorates.[23]

The regioselectivities observed for iodocyclization of the unsaturated alcohols (Table 1) are similar to those for other intramolecular nucleophilic displacement reactions in which leaving groups are part of three-membered (e.g. halonium,[17] cyclopropane,[24] or oxirane[25–27]) rings. Owing at least in part to the geometric requirements of three-membered rings, coupled with those for cyclization (rearside attack with approximate coplanarity of the nucleophilic with the three-membered ring), reactions of this type, under kinetic control, often show a stereoelectronic preference for *exo*-mode closure, thus favoring formation of products having the smaller of the two possible ring sizes (Scheme **B**, Entries 1–4).[28,29] Such selectivity is, however, subject to steric and electronic effects of substituents.[17,26,27]



Entry	X	–Z (or ZH)	n	Ref.
1	O	$-\bar{C}HCN$	1–4	25, 26
2	O	$-O^-$	2,3	27
3	$C(CO_2Et)_2$	$-\bar{C}(CO_2Et)_2$	1–4	24
4	Br^+	$-CO_2^-$	2,3	17
5	I^+ or I(collidine)$^+$	–OH	1,2	–

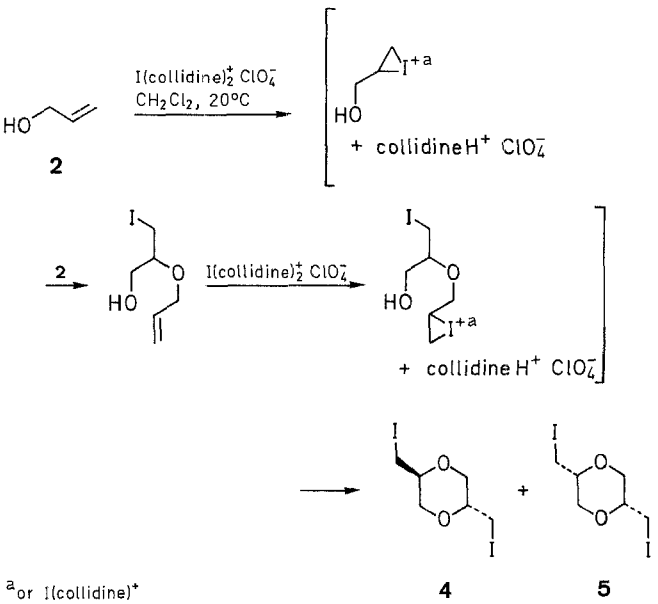
Scheme **B**

Although actual structures for intermediates involved in iodocyclization with $I(collidine)_2^+ ClO_4^-$ are not known, it is considered likely that formation of such species would involve only

minor alteration of carbon–carbon double bond planarity.[30] A Dreiding-type model for such an iodonium (or extended iodonium) intermediate from allyl alcohol (Scheme **B**, Entry 5, n = 1) reveals no apparent restriction for hydroxyl attack at C-2, other than ring strain of the incipient oxirane ring,[31] but indicates that attack at C-3 (oxetane formation) should be precluded by large bond-angle deformations required to bring the hydroxyl within bonding distance of C-3 and anywhere near to coplanarity with the iodonium ring. Likewise, a model for the intermediate from the homoallylic alcohol, 3-buten-1-ol **(19)**, suggests a preference for *exo*-mode closure to the smaller four-membered ring over *endo* closure to the five-membered one. However, here the hydroxyl proximity and alignment for oxolane formation are considerably better than for analogous oxetane formation from the iodonium ion of allyl alcohol, and the possibility of oxolane formation cannot be excluded. For extended-chain alcohols, e.g. **24**, **26**, and **32**, although *endo* closure would be even more accessible stereoelectronically, *exo* closure should also be more favorable due to decreased ring strain (lower $\Delta H^{\neq}$), relative to that for oxetane formation from **19**.

In line with these considerations, reaction of the allylic alcohols **6**, **8**, and **11** with $I(collidine)_2^+ ClO_4^-$ gave only iodomethyloxiranes. Likewise, allyl alcohol gave the expected oxirane **3**, accompanied, however, by the 2,6-bis(iodomethyl)-1,4-dioxanes **4** and **5**. The latter apparently result from trapping of the iodonium intermediate from allyl alcohol by additional allyl alcohol, followed by iodocyclization (Scheme **C**).

Reaction of $I(collidine)_2^+ ClO_4^-$ with 3-buten-1-ol **(19)** afforded a 1:1 mixture of 2-iodomethyloxetane **(20)** and 3-iodooxolane **(21)**, whereas the substituted homoallylic alcohols **13**, **15**, and **17** yielded only iodomethyloxetanes. Sole formation of oxetanes from alcohols **13** and **17** is presumably due to potentiation of *exo* closure by *gem* dialkylation at carbons α to the hydroxyl group. It is known that alkyl and *gem*-dialkyl substituents often accelerate rates and relative rates (3- > 4-membered ring) of closure of cyclic ethers.[32] Sole formation of oxetane **16** from iodocyclization of 3-methyl-3-buten-1-ol **(15)** is apparently due to the effect of the methyl group in altering charge distribution on the three-membered iodonium intermediate, rendering it more electrophilic at C-3. Not unexpectedly, switching the alkyl group to C-4 of 3-buten-1-ol, as in **22**, effects reversal of regiospecificity, providing only the oxolane **23**.[33,34] Similar Markovnikov orientation has been observed for bromo- and iodolactonization reactions,[17] in which the pattern of alkyl substitution of the carbon–carbon double bond alters the regioselectivity of β- vs γ-lactone formation.



[a] or I(collidine)$^+$

Scheme C

Table 2. Analytical and Spectral Data for Iodoethers and Lactones

Product	Yield[a] (%) (mole ratio)	mp (°C) or bp (°C)/Torr)[b]	Molecular Formula[c] or Lit. mp (°C) or bp (°C)/Torr)	IR (neat/KBr)[d] ν(cm^{-1})	^{1}H-NMR (CDCl$_3$/TMS)[e] δ, J(Hz)	^{13}C-NMR (CDCl$_3$/TMS) δ
3[f]	32	40/0.2	63/20[43]	1250, 980, 910, 860, 840	2.52–2.62 (m, 2H, H-3); 2.90–3.05 (m, 1H, CH$_a$H$_b$I); 3.10–3.30 (m, 3H, H-2, CH$_a$H$_b$I)	–
4[f]	12	157–158	158[44]	1240, 1090, 920	3.0–3.2 (m, 4H, 2 × CH$_2$I); 3.3–3.8 (m, 4H); 3.9–4.3 (br d, 2H, H-2, H-5)	–
5[f]	12	94–95	97[44] $C_6H_{10}I_2O_2$ (368.0)	1095, 925	3.2–3.4 (m, 4H, 2 × CH$_2$I); 3.3–3.9 (m's, 6H)	–
7	68	45/0.2	52/6[9]	1245, 850	1.30 (2s, 6H, 2 × CH$_3$); 2.8–3.5 (m's, 3H)	–
9, 10[g]	71 (76:24)	36–40/ 2.7	C_4H_7IO (198.0)	1240, 860	**9:** 1.32 (d, 3H, CH$_3$, J = 5.1)[h]	5.01 (CH$_2$I); 17.29 (CH$_3$); 58.54, 59.08 (C-2, C-3)
					10: 1.27 (d, 3H, CH$_3$, J = 5.4)	1.20 (CH$_2$I); 12.34 (CH$_3$); 55.32, 56.38 (C-2, C-3)
12	–[i]				1.80–2.05 (d, 3H, CH$_3$); 2.56 (dd, 1H, H$_a$-3); 2.90 (dd, 1H, H$_b$-3); 3.20 (m, 1H, 2-H); 3.65 (m, 1H, CHI)	–
14	62	40/0.2	$C_6H_{11}IO$ (226.1)	1250, 960	1.43 (s, 3H, CH$_3$); 1.46 (s, 3H, CH$_3$); 2.05 (m, 1H, H$_b$-3, J_{gem} = 11.0, J_{2,H_b} = 6.5); 2.45 (m, 1H, H$_a$-3, J_{2,H_a} = 7.1); 3.30 (m, 2H, CH$_c$H$_d$I, J_{H_c,H_d} = 7.2, J_{2,H_c} = 5.2, J_{2,H_d} = 8.3); 4.60 (m, 1H, H-2)	–

Table 2. (continued)

Product	Yield[a] (%) (mole ratio)	mp (°C) or bp (°C)/ Torr)[b]	Molecular Formula[c] or Lit. mp (°C) or bp (°C)/Torr)	IR (neat/KBr)[d] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS) δ
16	67	40/0.2	C_5H_9IO (212.0)	1240, 955	1.60 (s, 3H, CH_3); 2.41 (m, 1H, H_a-3, J_{gem} = 9.6); 2.51 (m, 1H, H_b-3); 3.35 (dd, 2H, CH_2I); 4.43 (m, 2H, H-4)	–
18	64	60/0.2	$C_9H_{15}IO$ (266.1)	965	1.20–1.80 (br s, 10H); 1.91 (m, 1H, H_b-3, J_{gem} = 11.1, J_{2,H_b} = 6.7); 2.40 (m, 1H, H_a-3, J_{2,H_a} = 7.3); 3.30 (m, 2H, CH_2I); 4.61 (m, 1H, H-2)	–
20, 21	–[j] (~50:50)	40/0.2		1220, 900	**20:** 2.70 (m, 2H, H-3); 3.39 (d, 2H, CH_2I); 4.50 (m, 2H, H-4); 4.81 (m, 1H, H-2)	–
					21: 2.10–2.50 (m, 2H, H-4); 3.80–4.80 (m, 5H, H-2, H-3, H-5)	–
23[33]	70	26–33/ 0.40			1.00 (t, 3H, CH_3); 1.40–1.60 (m, 1H, $-CH_aH_bCH_3$); 1.70–1.90 (m, 1H, $CH_aH_bCH_3$); 2.20–2.40 (m, 1H, H_a-4); 2.44–2.64 (m, 1H, H_b-4); 3.75–4.04 (m's, 4H, H-5, H-2, H-3)	10.12 (CH_3); 23.15, 25.70 (CH_2CH_3, C-3); 38.4 (C-4); 66.7 (C-5); 89.2 (C-2)
25[10,34]	82	45/0.2	68–70	1180, 1100, 1050	1.50–2.30 (m's, 4H, H-3, H-4); 3.1–3.3 (m, 2H, CH_aH_bI); 3.5–4.2 (m's, 3H, H-2, H-5)[f]	–
27, 28	80 (56:44)[k]	45/0.85	$C_6H_{11}IO$ (226.1)	1450, 1070, 1000	**27:** 1.11 (d, 3H, CH_3, J = 6.6)	9.88 (CH_2I); 17.66 (CH_3); 34.74 (C-4); 39.33 (C-3); 67.38 (C-5); 84.37 (C-2)
					28: 0.98 (d, 3H, CH_3, J = 7.0)	4.92 (CH_2I); 13.29 (CH_3); 33.80 (C-4); 33.55 (C-3); 66.87 (C-5); 81.53 (C-2)
30[33], **31**[1]	(85:12)[m]				**30:** 1.89 (d, 3H, CH_3, J = 6.9)	24.8, 26.1 (CH_3, CHI); 31.8, 33.2 (C-3, C-4); 69.0 (C-5); 83.6 (C-2)
					31: 1.42 (d, 3H, CH_3, J = 6.1)	22.2 (CH_3); 29.8 (C-5); 34.3 (C-4); 38.5 (C-3); 68.7 (C-6); 79.2 (C-2)
33[46]	69	55/0.2	90/15	1125, 910, 880	3.05 (dd, 2H, CH_2I); 3.2–4.4 (m's, 7H)	–
35	12	60/0.2	$C_6H_{11}IO_2$ (242.1)	1110	2.0 (m, 2H, H-6); 3.1 (d, 2H, CH_2I); 3.2–4.4 (m's, 7H)	–
37[47]	72	–[n]		1830	3.1–3.8 (m's, 4H, CH_2I, H-3); 4.4–4.9 (m, 1H, H-2)	–
39	83	–[n]		1760	1.7–2.7 (m's, 4H, H-3, H-4); 3.35 (m, 2H, CH_2I); 4.4–4.7 (m, 1H, H-2)	–
41, 42[36,1]	81 (55:45)[o]	80/0.07		1760	**41:** 1.22 (d, 3H, CH_3, J = 6.6)	5.93 (CH_2I); 18.35 (CH_3); 35.94 (C-3); 36.76 (C-4); 84.77 (C-2); 175.16 (C=O)
					42: 1.07 (d, 3H, CH_3, J = 7.4)	0.27 (CH_2I); 12.77 (CH_3); 32.72 (C-3); 37.86 (C-4); 81.92 (C-2); 175.75 (C=O)
44	25	94–95 (EtOH)	$C_6H_9IO_3$ (256.0)	1730	2.5–3.1 (m, 2H, H-6); 3.25 (m, 2H, CH_2I); 3.5–4.3 (m's, 4H, H-3, H-5); 4.55 (m, 1H, H-2)	1.2 (CH_2I); 39.0 (C-6); 64.7 (C-5); 74.2 (C-3); 78.9 (C-2); 171.7 (C-7)

[a] Yields of isolated products.
[b] With the exception of **9**, **10**; **27**, **28**; **41**, **42**, liquids were evaporatively distilled; bp's refer to bath temp.
[c] Satisfactory microanalyses obtained: C ±0.25, H ±0.20, I ±0.25; for **14**: C −0.30.
[d] IR bands for **3–35** are in line with those for ν_{COC} (also δ_{CH} for oxiranes) in other three- to seven-membered-ring ethers. Carbonyl bands for **36–43** are typical for four- to seven-membered-ring lactones.[41]
[e] Protons on carbon α to oxygen in unsubstituted three- to six-membered-ring ethers are typically at $\delta \approx 2.5$, 4.7, 3.8, and 3.5, respectively.[42]
[f] NMR data are similar to literature values or to those for samples prepared alternately.
[g] Inseparable by distillation or TLC (silica gel). Mole ratio determined from ^{1}H-NMR spectrum (methyl peak areas); ^{13}C- and ^{1}H-NMR assignments were confirmed by alternate synthesis of **9**.
[h] See experimental for complete ^{1}H-NMR data.
[i] Not isolated quantitatively. The ^{1}H-NMR spectrum of a distilled sample was similar to that of the Br analogue.[45]
[j] Inseparable by distillation; mole ratio determined by ^{1}H-NMR. NMR assignments were verified by alternate synthesis of **21**.
[k] Isomer ratio by GLC (125°C) and by ^{1}H-NMR (methyl peaks). Stereochemical assignment was afforded by ^{13}C-NMR, run under spin-relaxed conditions; ^{13}C shifts were assigned by polarization transfer (DEPT).
[l] Mole ratio by GLC (125°C).
[m] Product not isolated; ^{1}H-NMR indicates high yield, purity.
[n] Yields of crude products.
[o] Ratio determined by GLC (175°C) and ^{1}H-NMR (methyls). Stereochemical assignment was verified by alternate synthesis of a sample enriched in **41**.[36]

In contrast to the non-regiospecific iodocyclization of 3-buten-1-ol **(19)**, reaction of 3-butenoic acid **(36)** with $I(collidine)_2^+ ClO_4^-$ gave only the β-lactone **(37)**. The latter has also been obtained from reaction of the thallium(I) salt of **36** with iodine.[18]

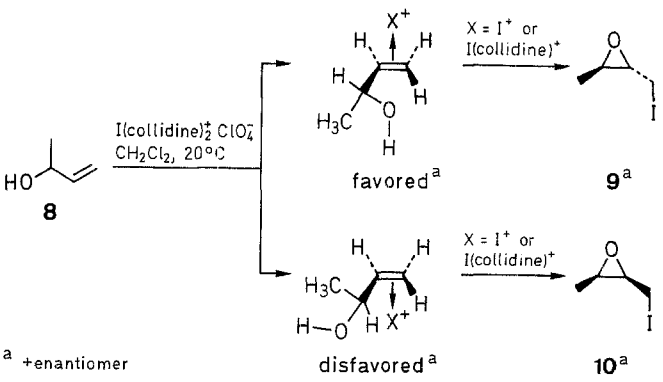
Iodocyclization of the homologous acids **38** and **40**, and the longer chain alcohols **24**, **26**, and **32** to the smaller five- or six-membered-ring lactones or ethers was anticipated, based on reports of related reactions. Such substrates with terminal double bonds are, of course, more amenable to *exo* closure, due to increased electrophilicity at the penultimate carbons of the iodonium intermediates.

Iodocyclization of (*E*)-4-hexen-1-ol **(29)** with sodium iodide, 3-chloroperoxybenzoic acid, and 18-crown-6 in chloroform is known to give the oxolane **30.**[33] Under similar conditions, or by reaction of **29** (97% *E*-isomer) with $I(collidine)_2^+ ClO_4^-$ we obtain two minor products (relative yields 12% and 3%) by GLC. Chemical ionization GC-MS indicates these to be isomeric with **30** (MH^+, $m/z = 227$). The EI fragmentations for both **30** and the least (3%) isomer show intense peaks at $m/z = 71$ ($M^+ - CH_3CHI$) suggesting similar (diastereomeric) structures. The latter product apparently forms via iodocyclization of (*Z*)-4-hexen-1-ol present in the starting material. EI fragmentation for the third isomer is similar to that for **30**; however, the $m/z = 71$ peak (oxolane ring) is absent. The presence of an additional methyl doublet at $\delta = 1.42$ in the ^{1}H-NMR spectrum of crude or distilled product suggests this isomer to be the oxane **31**. This is further supported by ^{13}C-NMR (Table 2).

It should be noted that, unlike the case of 3-buten-1-ol **(19)**, a methyl substituent on the terminus of 4-penten-1-ol **(24)** is insufficient to effect crossover from *exo* to *endo* specificity, revealing an increased bias for *exo* (five-membered ring) relative to *endo* (six-membered ring) closure. Such *endo* specificity has, however, been achieved with cases in which the double bond is terminally dialkylated.[3,7] The possibility that oxolane **21** or oxane **31** might form via isomerization of the respective oxetane **20** and oxolane **30** has not been excluded, but is considered unlikely since other cyclic ethers and lactones obtained (Table 1) are generally those expected from kinetic control.

Cyclization of 4-oxa-6-hepten-1-ol **(34)** and 3-oxa-6-heptenoic acid **(43)** with $I(collidine)_2^+ ClO_4^-$ gave the 1,4-dioxepanes **35** and **44**, respectively, albeit in low yields. *Exo* regiospecificity was again anticipated, owing especially to increased activation entropies for formation of larger (especially eight-membered) rings.[35]

Reaction of (*RS*)-3-buten-2-ol **(8)** with $I(collidine)_2^+ ClO_4^-$ gives *trans*-oxirane **9** in preference to the *cis*-isomer **10** (76:24). Recent *ab initio* calculations on interaction of Cl^+ with 3-buten-2-ol enantiomers reveals likely formation of the diastereomeric π-complexes shown in Scheme **D** (X = Cl).[20] Inasmuch as similar selectivity should obtain for I^+ or $I(collidine)^+$ transfer, it may be noted that the more stable π-complex has the correct stereochemistry to form *trans*-oxirane, while the less stable complex would give *cis*-oxirane (assuming oxirane formation *via* rearside hydroxyl attack). Similar, albeit greater, *trans* stereoselectivity has been found for bromocyclization of (*E*)- and (*Z*)-3-penten-2-ols to the 2-(1-bromoethyl)-3-methyloxiranes (bromine/sodium hydroxide).[14] The latter appear to be mechanistically related to the iodocyclization of 3-buten-2-ol, the increased stereoselectivity for bromocyclization being consistent with the greater degree of bonding (Br > I) expected in the transition state for π-complexation.



Scheme **D**

Iodocyclization of 3-methyl-4-penten-1-ol **(26)** and 3-methyl-4-pentenoic acid **(40)** with $I(collidine)_2^+ ClO_4^-$ are considerably less stereoselective, giving the respective *trans*- and *cis*-oxolanes **27/28** and γ-lactones **41/42** in $\approx$ 55:45 ratios. This apparently reflects decreased π-face differentiation for formation of the expected iodonium complexes due to increased separation of double bonds from the stereogenic sites. Reaction of **40** with *N*-iodosuccinimide in chloroform is reported to give predominantly the *cis*-lactone **42.**[36] The latter is, however, proposed to occur via the acyl hypoiodite intermediate.

IR spectra were recorded on a Perkin-Elmer 299 grating spectrometer. ^{1}H-NMR data were obtaining using a Perkin-Elmer R-32 (90 MHz) instrument, except for **8**, **9**, **26–28**, **30**, **31**, **40**, and **42**, which were run on a Varian Associates XL-200 instrument. ^{13}C-NMR spectra were run on a Varian XL-200, except for **44**, which was run on a Varian CFT-20 spectrometer. GC analyses were done on a Hewlett-Packard 5890 instrument using a 6 ft. × 1/8 in. (183 × 0.32 cm) stainless steel column; 10% OV-17 on Chromosorb W, 100/120 mesh. GC-MS was carried out on a VG-70SE spectrometer. Elemental analyses were obtained from Galbraith Laboratories, Knoxville, TN.

Alcohols **13**[37] and **17**[38] and carboxylic acids **40**[39] and **43**[40] were synthesized via published methods. Lithium aluminum hydride reduction of **40** provided alcohol **26**. Alcohol **34** was obtained by reaction of allyl alcohol with oxetane in ether – boron trifluoride (see below). Other alcohols and carboxylic acids were obtained from Aldrich Chemical Co., except alcohol **32** (K & K Labs Division of ICN Biomedicals, Plainview, NY). Alcohols were distilled from calcium hydride prior to use; carboxylic acids were used as purchased.

Iodocyclization Reactions; General Procedure:

Dry bis(*sym*-collidine)silver(I) perchlorate[21] (13.0 g, 28 mmol) is slurried in dry CH_2Cl_2 (150 mL) with vigorous magnetic stirring under nitrogen. Iodine (7.1 g, 28 mmol) is added in one portion, and the mixture stirred for 20 min, during which time AgI precipitates. To the resulting reagent (removal of AgI is unnecessary) is added the unsaturated alcohol or carboxylic acid (20 mmol) in one portion. The mixture is stirred for 1.5 h and filtered; the filtrate is washed successively with 10% aq. $Na_2S_2O_3$ (75 mL), 10% aq. HCl (2 × 100 mL), and dried (K_2CO_3). After filtering, the CH_2Cl_2 is carefully evaporated under reduced pressure ($\approx$ 150 Torr). The crude products are purified by microscale or evaporative distillation or recrystallization. Products thus obtained are homogenous on TLC (silica gel, CH_2Cl_2). Yields, analytical, and spectral data are reported in Table 2.

Pure $I(collidine)_2^+ ClO_4^-$[21] is isolable by successive evaporation and recrystallization of the crude reagent from CH_2Cl_2/hexanes (after removal of AgI). Although purified reagent was used for several reactions, it afforded no apparent advantage; thus iodocyclizations were generally carried out as described with reagent generated *in situ*. Owing to the hazards associated with organic perchlorates, isolation of crystalline reagent is deemed inadvisable.

***trans*-2-Iodomethyl-3-methyloxirane (9):**

trans-2-Hydroxymethyl-3-methyloxirane: was obtained by epoxidation of 2-buten-1-ol (> 95% E) with vanadyl acetylacetonate/*tert*-butyl

hydroperoxide/CH_2Cl_2,[48] distills at 49–50°C (3.0 Torr); Lit.[49] bp 59–60°C (10 Torr).

trans-2-(p-toluenesulfonyloxymethyl)-3-methyloxirane: To a vigorously stirred, cold (0°C) solution of the epoxy alcohol obtained above (1.00 g, 11.4 mmol) in dry pyridine (10 mL) under nitrogen, is added *p*-toluenesulfonyl chloride (1.91 g, 10 mmol) in several portions over 1 h. The solution is stored for 2 d at −10°C and then poured onto crushed ice (100 g).[50] The crystalline tosylate is filtered and dissolved in hot EtOH (18 mL); water (~9 mL) is then added dropwise until slight turbidity persists. After cooling slowly, the crystalline tosylate of *trans*-2-hydroxymethyl-3-methyloxirane is isolated by suction filtration and dried *in vacuo*; mp 53°C; yield: 1.41 g (58%).

$C_{11}H_{14}O_4S$	calc.	C 54.55	H 5.78	S 13.24
(242.3)	found	54.67	5.75	13.17

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 1.30 (d, 3H, CH_3); 2.41 (s, 3H, $ArCH_3$); 2.87 (dd, 1H, H-3); 2.92 (ddd, 1H, H-2); 3.90 (dd, 1H, CH_aH_bO); 4.18 (dd, 1H, CH_aH_bO); 7.35 (d, 2H$_{arom}$); 7.80 (d, 2H$_{arom}$); $J_{CH_{3,3}}$ = 5.1 Hz, $J_{2,3}$ = 2.2 Hz, J_{2,H_a} = 3.7 Hz, J_{2,H_b} = 5.7 Hz, J_{H_a,H_b} = −11.2 Hz, J_{arom} = 9 Hz.

NMR assignments for non-aromatic protons were verified by spectral simulation (Varian program).

trans-2-Iodomethyl-3-methyloxirane **(9)**: the tosylate obtained above (726 mg, 3 mmol) is added to a solution of NaI (495 mg, 3.3 mmol) in dry acetone (13 mL) and stirred at 25–30°C. When starting tosylate is no longer detectable (≈4d) by TLC (silica gel, CH_2Cl_2), the mixture is diluted with water (25 mL) and extracted with CH_2Cl_2 (25 mL). The extract is dried (K_2CO_3), the solvent is removed (≈150 Torr) and the crude product evaporatively distilled at 39–40°C (4.2 Torr) to give **(9)**; yield: 420 mg (70%).

^{1}H-NMR (200 MHz, $CDCl_3$): δ = 1.32 (d, 3H, CH_3); 2.90 (dd, 1H, H-3); 2.98 (ddd, 1H, H-2); 3.06 (dd, 1H, CH_aH_b); 3.23 (dd, 1H, CH_aH_b); $J_{CH_{3,3}}$ = 5.2 Hz, $J_{2,3}$ = 1.9 Hz, J_{2,H_a} = 5.9 Hz, J_{2,H_b} = 6.8 Hz; J_{H_a,H_b} = −9.9 Hz.

NMR assignments for **9** were determined by spectral simulation.

3-Iodooxolane (21):
A procedure paralleling that for preparation of 3-bromooxolane[51] is used. 3-Hydroxyoxolane is converted to the tosylate with *p*-toluenesulfonyl chloride in dry pyridine. The crude oily tosylate (2.58 g, 10.7 mmol) is refluxed with an excess of NaI (3.20 g, 21 mmol) in dry acetone (75 mL) for 2 d. The mixture is then diluted with water (50 mL), extracted with CH_2Cl_2 (75 mL), and the extract is dried (K_2CO_3). After filration, the solvent is removed under reduced pressure (≈150 Torr) to yield crude **21** (1.80 g, 85%), purified by evaporative distillation at 40°C (0.2 Torr).

C_4H_7IO	calc.	C 24.27	H 3.54	I 64.11
(198.0)	found	24.40	3.58	63.96

IR (KBr): ν = 2990, 2870, 1220, 1160, 1075, 1040, 900 cm^{-1}.

The ^{1}H-NMR spectrum of **21** is in accord with the resonances assigned to this compound from the spectrum for the mixture of **20**, **21** obtained from iodocyclization of **19** (Table 2).

3-Methyl-4-penten-1-ol (26):
A solution of 3-methyl-4-pentenoic acid (**40**; 5.70 g, 50 mmol) in anhydrous ether (50 mL) is added dropwise, with stirring under nitrogen, to a suspension of lithium aluminum hydride (1.43 g, 38 mmol) in anhydrous ether (50 mL). The mixture is stirred for 3 h under reflux before quenching by cautious addition of 10% aq. KOH (50 mL). After stirring for an additional 5 min, the mixture is filtered; the ether layer is separated and dried ($MgSO_4$). The solvent is evaporated, and the residue is distilled to yield **26**; 2.35 g (47%); bp 55–57°C (11 Torr). An alternate synthesis of **26** has been reported.[52]

^{1}H-NMR ($CDCl_3$): δ = 1.03 (d, 3H, CH_3); 1.50–1.70 (m, 2H, H-2); 1.76 (s, 1H, OH); 2.18–2.45 (m, 1H, H-3); 3.67 (t, 2H, H-1); 4.97 (dd, 1H, H-5 (*cis* to H-4); 5.02 (dd, 1H, H-5 (*trans* to 4-H)); 5.73 (ddd, 1H, H-4); $J_{1,2}$ = 6.6 Hz, J_{3,CH_3} = 6.8 Hz, $J_{3,4}$ = 8 Hz, $J_{4,5\,cis}$ = 10 Hz, $J_{4,5\,trans}$ = 17 Hz, $J_{5,5\,gem}$ = 1.0 Hz.

4-Oxa-6-hepten-1-ol (34):
In a 50 mL round-bottomed flask, outfitted with a 10 mL pressure-equalizing dropping funnel, a magnetic stirrer, and a nitrogen inlet, is placed allyl alcohol (11.6 g, 20 mmol) and ether–boron trifluoride complex (3 mL). Oxetane (5.8 g, 10 mmol) is added dropwise with stirring. The exothermic reaction observed after a brief induction period is maintained at 60°C by the rate at which oxetane is added and by cooling. The mixture is stirred for an additional 2 h at room temperature, then diluted with CH_2Cl_2 (100 mL). The resulting solution is washed with saturated aq. $NaHCO_3$ (100 mL) and dried (K_2CO_3). The CH_2Cl_2 is removed at reduced pressure (≈150 Torr). Distillation of the crude product gives **34**; yield: 4.20 g (36%); bp 79–82°C/21 Torr; This alcohol has been reported,[53] but was not fully characterized.

$C_6H_{12}O_2$	calc.	C 62.09,	H 10.34
(116.2)	found	61.78	10.22

^{1}H-NMR ($CDCl_3$): δ = 1.82 (m, 2H, H-2); 3.32 (br s, 1H, OH); 3.50–3.85 (m, 4H, 1-H, H-3); 3.90–4.10 (m, 2H, H-5); 5.05–5.45 (m's, 2H, H-7); 5.60–6.20 (m, 1H, H-6).

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